6H,12H-6,12-Methanodibenzo[*b,f*][1,5]dioxocins from the Reactions of *o*-Coumaric Acids and Salicylaldehydes

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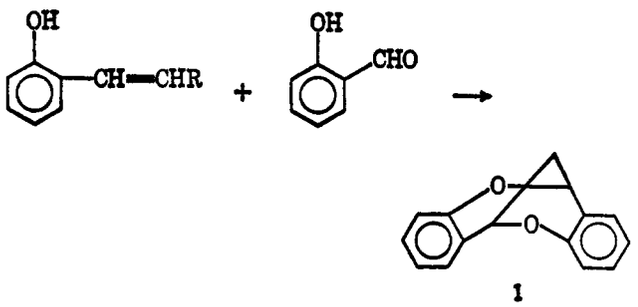
Received March 27, 1968

6H,12H-6,12-Methanodibenzo[*b,f*][1,5]dioxocin was prepared from the reaction of *o*-vinylphenol or *o*-coumaric acid and salicylaldehyde in 4.6% yield. 2-Methyl-, 2-bromo-, and 2-nitro-6H,12H-6,12-methanodibenzo[*b,f*]-[1,5]dioxocins were synthesized by the reactions of 2-hydroxy-5-methylcinnamic acid with salicylaldehyde and *o*-courmaric acid with 5-bromo- and 5-nitrosalicylaldehydes, respectively. The reactions of 2-hydroxy-1-naphthaldehyde gave heterocyclics containing a naphthalene ring. 6H,12H-6,12-Methanodibenzo[*b,f*][1,5]dioxocin was brominated to the 2,8-dibromo derivative. Both the 2-bromo and 2,8-dibromo derivatives were converted into the nitriles by the reaction with cuprous cyanide. Neither the mono nor dibromo compounds could be converted into Grignard reagents, but were readily metalated with *n*-butyllithium. The organometallics were carbonated to yield carboxylic acids. The heterocyclic ring system of the parent compound was cleaved by hydrogenolysis to 2,2′-trimethylenediphenol. (±)-2-Amino-6H,12H-6,12-methanodibenzo-[*b,f*]-[1,5]dioxocin, prepared by the catalytic hydrogenation of the corresponding nitro compound, was resolved *via* the tartrate salts to yield the optical isomers with specific rotations $[\alpha]^{25}D$ +389.0 and −393.3°. T he more abundant (+)-amino compound was reduced *via* diazotization to (+)-6H,12H-6,12-methanodibenzo'*b,f*][1,5]-dioxocin, $[\alpha]^{25}D$ +266.7°.

The reaction of either *o*-vinylphenol or *o*-coumaric acid and salicylaldehyde gave an unexpected neutral product. It was concluded on the basis of elemental and instrumental analyses and conversion of the product into a known compound that the product was the fused



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R=H or COOH

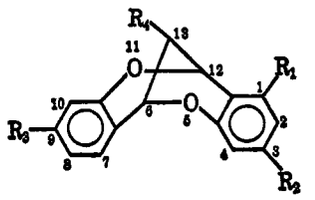
bicyclic heterocyclic structure, 6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (**1**). This article is concerned with the extension of the synthesis to substituted products, some chemistry of the parent compound, and the resolution of the 2-amino derivative.

The methanodioxocin ring structure was first recognized in 1,4,6,9-tetrahydro-3,4,8,9-tetramethyl-1,6-diphenyl-4,9-methano[1,5]dioxocino[2,3-*c*:6,7-*c*′]-dipyrazole, the product from the reaction of 2,4-pentanedione and 1-phenyl-3-methyl-2-pyrazolin-5-one.[1] The 6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin structure has recently received considerable attention since Nair, *et al.*,[2] concluded that cyanomaclurin, a compound isolated from the heartwood of *Artocarpus integrifolia* (jackwood),[3] was 1,3,9,13-tetrahydroxy-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (**2a**, Chart I). The same investigators synthesized compounds **2b** and **2c** for nmr spectral comparison. Their method consisted of cyclization of appropriate 2,2′-dihydroxychalcones to 2′-hydroxyflavanones, sodium borohydride reduction to flavan-4-ol epimeric mixtures, and then cyclization to the final heterocyclic. Bhatia, Mukerjee, and Seshardi[4] utilized a similar scheme to prepare (±)-trimethylcyanomaclurin (**2d**). This synthesis required a selective oxidation process of the intermediate flavanone to insert a hydroxyl group at the C-13. They also prepared (±)-trimethylcyanomaclurin acetate (**2e**) by direct acetylation of **2d** and by acetylation of the intermediate flavanone before reduction and cyclization.

CHART I

PREVIOUSLY REPORTED

6H,12H-6,12-METHANODIBENZO[*b,f*][1,5]DIOXOCINS



Compd	R_1	R_2	R_3	R_4
2a	OH	OH	OH	OH
2b	OCH_3	H	H	H
2c	OCH_3	OCH_3	H	H
2d	OCH_3	OCH_3	OCH_3	OH
2e	OCH_3	OCH_3	OCH_3	OAc

Structure Proof of Neutral Product from the Reaction of *o*-Vinylphenol and Salicylaldehyde.—A mixture of *o*-vinylphenol, salicylaldehyde, and dilute (5%) hydrobromic acid was heated at the reflux temperature for 12 hr. The neutral product was isolated after alkaline extraction of acidic components and purified (4.6% yield). Elemental analysis and molecular weight determination indicated the molecular formula $C_{15}H_{12}O_2$. The ir spectrum was characteristic for structure **1**. Intense absorption at 753 cm^{-1} with the distinctive pattern in the 1650–2000-cm^{-1} region was compatible with an *ortho*-substituted phenyl ring.

(1) G. Westöö, *Acta Chem. Scand.*, **13**, 679 (1959).

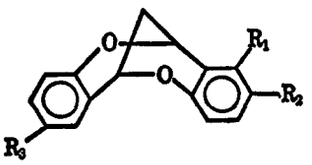
(2) (a) P. M. Nair and K. Venkataraman, *Tetrahedron Lett.*, No. 5, 317 (1963). (b) P. M. Nair, P. C. Parthasarathy, P. V. Radhakrishnan, and K. Venkataraman, *ibid.*, No. 44, 5357 (1966).

(3) A. G. Perkin and F. Cope, *J. Chem. Soc.*, 937 (1895).

(4) G. D. Bhatia, S. K. Mukerjee, and T. R. Seshardi, *Tetrahedron, Suppl.*, **8** (2), 531 (1966).

TABLE I

6H,12H-6,12-METHANODIBENZO[*b*,*f*][1,5]DIOXOCINS FROM *o*-COUMARIC ACID



Compd	R_1	R_2	R_3	Yield, %	Mp, °C	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
1	H	H	H	4.6	159–160.5	$C_{15}H_{12}O_2$				
3	H	Br	H	6.0	168–169	$C_{15}H_{11}BrO_2$[a]	59.41	3.63	59.2	3.47
4	H	NO_2	H	3.0	159–160	$C_{15}H_{11}NO_4$[b]	66.91	4.09	66.8	5.20
5	H	CH_3	H	5.3	128–128.5	$C_{15}H_{14}O_2$	80.67	5.92	80.9	5.93
6	*o*-C_6H_4[c]		H	3.6	128–131	$C_{19}H_{14}O_2$	83.21	5.11	83.4	5.15
7	*o*-C_6H_4[c]		CH_3	3.8	135–140	$C_{20}H_{16}O_2$	83.33	5.56	83.2	5.87

[a] Calcd: Br, 26.40. Found: Br, 26.3. [b] Calcd: N, 5.20. Found: N, 5.23. [c] *o*-Phenylene radical thus representing a naphthalene nucleus.

Several strong sharp bands in the 1000–1250-cm^{-1} region were characteristic for a cyclic ether. Absorptions at 1220 and 2970 cm^{-1} were indicative of phenyl–oxygen and aliphatic carbon–hydrogen bonds, respectively. The 60-Mcps nmr spectrum of **1** was also compatible with the proposed structure. The methylene and benzylic protons appear as triplets at τ 7.75 and 4.72, respectively. This compares favorably with the absorption at τ 7.87 and 4.81 reported for **2b**.[2b] The aromatic ring protons gave a complicated absorption centered at τ 2.95.

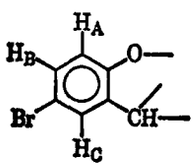
Compound **1** was also prepared from the reaction of *o*-coumaric acid and salicylaldehyde (also a 4.6% yield) under the same reaction conditions. Attempts to isolate **1** with a carboxylic acid group at C-13 were unsuccessful and it is tentatively concluded that the salicylaldehyde is reacting with *o*-vinylphenol formed, *in situ*, by the decarboxylation of *o*-coumaric acid.

Synthesis of Substituted 6H,12H-6,12-Methanodibenzo[*b*,*f*][1,5]dioxocins.—A yield of 4.6% was realized when either *o*-vinylphenol or *o*-coumaric acid was utilized. *o*-Vinylphenols are usually synthesized from *o*-coumaric acids. Therefore, this study was restricted to the reactions of *o*-coumaric acids and salicylaldehydes. The heterocyclics prepared in this study are tabulated in Table I. The reaction conditions were the same as described for the condensation of *o*-vinylphenol and salicylaldehyde.

Compounds **3** and **4** were prepared from the reaction of *o*-coumaric acid with 5-bromo- and 5-nitrosalicylaldehydes, respectively. Compound **5** was synthesized from the reaction of 2-hydroxy-5-methylcinnamic acid and salicylaldehyde. Reactions of 2-hydroxy-1-naphthaldehyde with *o*-coumaric and 2-hydroxy-5-methylcinnamic acids gave the heterocyclics **6** and **7**, thus illustrating the incorporation of a naphthalene nucleus into the molecule.

The yields are low because of polymerization side reactions. However, most of the starting materials are readily available and thus this is a practical way of obtaining this novel structure. Yield comparisons with previously reported methods are not possible because Nair, *et al.*,[2b] did not report yields, and the synthesis by Bhatia, *et al.*,[4] gave an understandably low yield because the preparation of a compound with a hydroxyl group at C-13 was much more difficult. Development work to improve the yields of our method is underway and preliminary results are very encouraging.

Chemistry of 6H,12H-6,12-Methanodibenzo[*b*,*f*][1,5]dioxocins. — 6H,12H-6,12-Methanodibenzo[*b*,*f*][1,5]dioxocin is stable in a basic environment but very unstable in the presence of acids. The benzylic ether linkages are easily cleaved by acids leading to polymeric products. The compound brominates in the presence of ferric oxide or aluminum chloride to produce 2,8-dibromo-6H,12H-6,12-methanodibenzo[*b*,*f*][1,5]dioxocin (**8**) in 47% yield (Scheme I). The structure of **8** was confirmed by nmr spectral analysis. The aromatic proton spectrum is a single ABC pattern establishing that both rings are substituted in the same manner. H_A, H_B, and H_C (partial structure A) have chemical



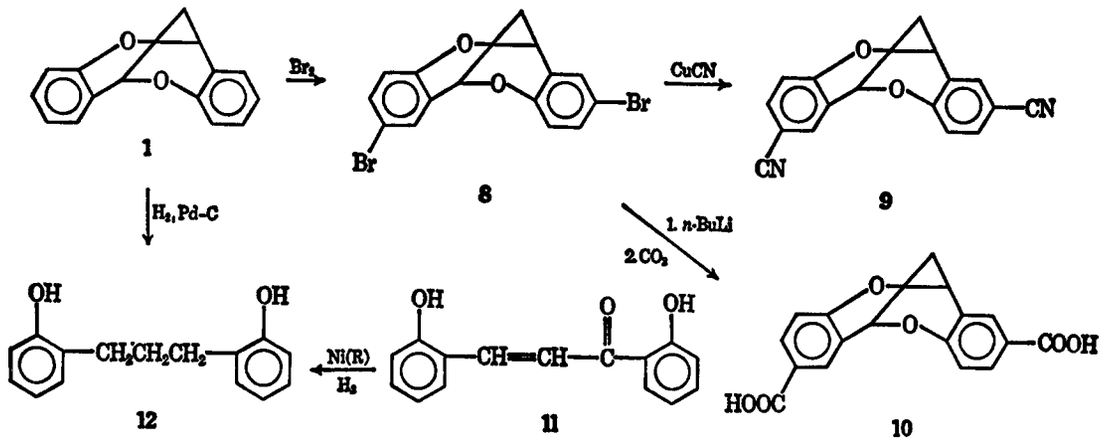
A

shifts of τ 3.37, 2.80, and 2.76, respectively. The coupling constants J_{AB}, J_{AC}, J_{BC} of 8.6 ± 0.1, 0 ± 0.3, and 2.4 ± 0.1 Hz, respectively, indicate that H_A is *ortho* to H_B and *para* to H_C and that H_B is *meta* to H_C. The methylene and methine protons appear as triplets at τ 7.87 and 4.90 indicating that the heterocyclic rings remained intact. This combination of restrictions establishes the structure of the brominated product as 2,8-dibromo-6H,12H-6,12-methanodibenzo[*b*,*f*][1,5]dioxocin. *ortho* substitution in all probability also occurred, but the less abundant *ortho*-substituted products would be lost in the purification of the 2,8-dibromo derivative by crystallization. The brominated heterocyclic was converted into the dicyano compound **9** by reaction with cuprous cyanide in 30% yield.

2,8-Dibromo-6H,12H-6,12-methanodibenzo[*b*,*f*][1,5]-dioxocin (**8**) in our hands was completely resistant to Grignard reagent formation. Repeated attempts using a variety of conditions including entrainment techniques and benzene–triethylamine solvent combination[5]

(5) E. C. Ashly, *J. Amer. Chem. Soc.*, **87**, 2506 (1965).

SCHEME I



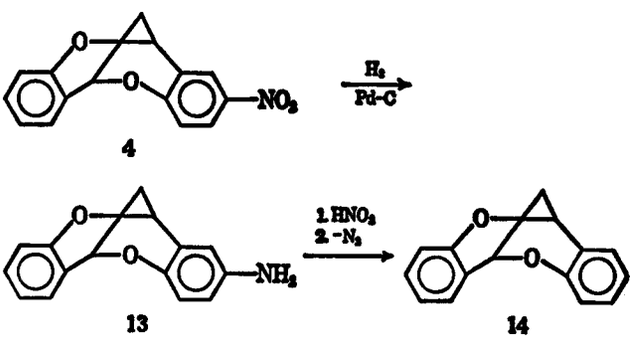
resulted only in almost quantitative recovery of starting material. The chemical was, however, successfully metalated with *n*-butyllithium. This dilithio derivative was carbonated to yield the dicarboxylic acid (**10**) in 63% yield. Similar reactions were conducted with 2-bromo-6H,12H-6,12-methanodibenzo[*b*,*f*][1,5]dioxocin (**3**), the product of the reaction of *o*-coumaric acid and 5-bromosalicylaldehyde. The compound was converted into the cyano derivative in 30% yield and into the carboxylic acid *via* the organolithium intermediate in only 2% yield. The dibromoheterocyclic was converted into the dicarboxylic acid in 63% yield as noted earlier. The disparity in yields is believed to be due to the difference in solubility of the aryllithium salts in the reaction solvent. The dilithio derivative precipitated from solution and was therefore isolated from possible side reactions so often observed with organolithium compounds.[6] The monolithio derivative was completely soluble and attempts to quickly convert it into the carboxylic acid failed to increase the yield.

Finally, 6H,12H-6,12-methanodibenzo[*b*,*f*][1,5]dioxocin was catalytically hydrogenolyzed to 2,2′-trimethylenediphenol (**12**) in 30% yield. 2,2′-Trimethylenediphenol, a known compound, was also prepared by the reduction of 2,2′-dihydroxychalcone (**11**).[7] The mixture melting point of **12** prepared from **1** and **11** was undepressed and their infrared (ir) spectra were superimposable. More vigorous conditions (75°, 200 lb/in.²) than anticipated were required to open the rings. In fact, the conditions were so vigorous that hydrogenation of the phenol rings to cyclohexanones and cyclohexanols was a serious side reaction resulting in only a 30% yield. Catalytic hydrogenolysis of benzyl ethers often occurs at room temperature in quantitative yields. The difficulty encountered is probably due to the rigidity and nonplanarity of the molecule making it difficult to align properly on the catalyst surface. This hydrogenolysis constituted an important proof of structure of 6H,12H-6,12-methanodibenzo[*b*,*f*][1,5]dioxocin.

Resolution of 2-Amino-6H,12H-6,12-methanodibenzo[*b*,*f*][1,5]dioxocin.—The asymmetry of these heterocyclic molecules was quickly recognized and nonsuperimposability of models of the mirror images was established. The rigidity of the [3.3.1] system prevents the heterocyclic rings from racemizing by turning inside out. The successful resolution of the enantiomers of 6H,12H-6,12-methanodibenzo[*b*,*f*][1,5]-dioxocin or a derivative would further confirm the proposed structure for the molecule. Also, it would be of interest to compare the specific rotation of this compound with that of the related natural product, cyanomaclurin, $[\alpha]^{26}D$ +204°.[8]

The chemistry involved in this investigation is outlined in Scheme II. 2-Nitro-6H,12H-6,12-methanodibenzo[*b*,*f*][1,5]dioxocin was hydrogenated to the amine **13** utilizing palladium-on-carbon catalyst at 60° and atmospheric pressure in 87% yield. The hydrogenation was followed by disappearance of the nitro group ir absorption peak at 1350 cm^{-1}. Disappearance

SCHEME II



of the cited peak required 4 hr. The high yield indicated that hydrogenolysis of the heterocyclic rings was not a problem.

Resolution utilizing (−)-malate salts was partially successful. Enriched optical isomers of $[\alpha]^{25}D$ +4 and −27° were obtained. Although these results were encouraging, a much better resolution was desired. The complete resolution was achieved using (+)-tartaric acid as the resolving agent. Several recrystallizations of the less soluble tartrate salt and restoration to the original amine yielded the dextrorotatory isomer, $[\alpha]^{25}D$ +389.0°. The tartrate salt in the mother liquor from the first crystallization was converted into the free amine. Recrystallization of the amine to a constant specific rotation yielded the levorotatory isomer, $[\alpha]^{25}D$ −393.3°. The ultraviolet (uv) absorption spectra of (+)- and (−)-2-amino-6H,12H-6,12-

(6) R. G. Jones, *Organic Reactions*, **6**, Chapter 7 (1951).

(7) A. T. Carpenter and R. F. Hunter, *J. Appl. Chem.* (London), **1**, 217 (1951).

(8) H. Appel and R. Robinson, *J. Chem. Soc.*, 752 (1935).

methanodibenzo[*b,f*][1,5]dioxocin were identical and their optical rotatory dispersion curves showed opposite Cotton effects with equal intensities centered at 279 mμ.

After considerable practice of converting (±)-2-amino-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (**5**) into **1** by reduction *via* the diazonium salt, the (+)-amino compound was converted into (+)-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (**14**), $[\alpha]^{25}D$ +266.7°, in 84% yield. The (−)-amino compound was not similarly treated to yield levorotatory parent compound because so little was isolated in the resolution.

The successful resolution of (±)-2-amino-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin confirms the rigidity of this heterocyclic molecule. The capability of resolution is consistent with the proposed structures for these compounds. The specific rotations of the optical isomers isolated compared favorably with the specific rotation of cyanomaclurin.

Experimental Section[9]

Starting Materials.—*o*-Coumaric acid,[10] *o*-vinylphenol,[10] 2-hydroxy-5-methylcinnamic acid,[11] and 5-bromosalicylaldehyde[12] were prepared by published procedures. Yields and physical properties were in good agreement with literature values. 5-Nitrosalicylaldehyde (Eastman) and 2-hydroxy-1-naphthaldehyde (Aldrich Chemical Co., Inc.) were purchased.

6H,12H-6,12-Methanodibenzo[*b,f*][1,5]dioxocin (1) from the Reaction of *o*-Vinylphenol and Salicylaldehyde.—A mixture of 5.2 g (0.043 mol) of *o*-vinylphenol, 7.5 g (0.062 mol) of salicylaldehyde, 50 ml of water, and 5 ml of concentrated (48%) hydrobromic acid was stirred and heated at the reflux temperature for 12 hr. Then 75 ml of 10% sodium hydroxide solution was added and heating was continued for 1 hr. The yellow undissolved solid was collected on a Büchner funnel and recrystallized from aqueous ethanol to yield 0.44 g (4.6%) of fine white needles: mp 160–160.5°; $\lambda_{max}^{isooctane}$ 277 mμ (ε 4310), 286 (3370).

Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.33; H, 5.40; mol wt, 224. Found: C, 80.28; H, 5.56; mol wt, 224 (mass spectrum).

General Procedure for the Preparation of 6H,12H-6,12-Methanodibenzo[*b,f*][1,5]dioxocins from *o*-Coumaric Acids.—The size of the runs ranged from 0.1 to 1 *M* quantities of starting materials. The ratios of reactants, solvents, etc., were kept constant in all the experiments. As a general procedure, a mixture of molar quantities of the *o*-coumaric acid and the salicylaldehyde, 1500 ml of water, and 100 ml of hydrobromic acid (48%) were stirred and heated at the reflux temperature for 12 hr. Sodium hydroxide solution (10%, 2000 ml) was added and heating was resumed at the reflux temperature for 1 hr. Insoluble crude yellow solid product was collected on a Büchner funnel, water washed, and recrystallized from ethanol–water mixtures. In this manner (Table I), the reaction of *o*-coumaric acid with salicylaldehyde, 5-bromosalicylaldehyde, 5-nitrosalicylaldehyde, and 2-hydroxy-1-naphthaldehyde gave compounds **1**, **3**, **4**, and **6**, respectively. The reaction of 2-hydroxy-5-methylcinnamic acid with salicylaldehyde and 2-hydroxy-1-naphthaldehyde gave compounds **5** and **7**, respectively.

2,8-Dibromo-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (8).—A mixture of 5.0 g (0.022 mol) of 6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (**1**), 100 ml of carbon tetrachloride, 7.2 g (0.045 mol) of bromine, and 0.1 g of ferric oxide was heated for 6 hr at the reflux temperature. Evaporation of the mixture to dryness left a reddish brown solid which was extracted two times with 75-ml portions of boiling ethanol. The crude product precipitated from the cooled ethanolic extracts. The mother liquors were diluted with water while hot and cooled to give second crops. The combined crude product fractions were recrystallized from ethanol to yield 4.09 g (47%) of product, mp 143–145°. An analytical sample recrystallized twice from ethanol gave white needles, mp 145–146.5°.

Anal. Calcd for $C_{15}H_{10}Br_2O_2$: C, 47.15; H, 2.16; Br, 41.83. Found: C, 47.36; H, 2.53; Br, 41.69.

The compound was also prepared in 49% yield under the same conditions utilizing 0.2 g of aluminum chloride as the catalyst instead of ferric oxide.

2,8-Dicyano-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (9).—A mixture of 1.00 g (0.00262 mol) of 2,8-dibromo-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (**8**), 1.0 g (0.011 mol) of cuprous cyanide, and 5 ml of pyridine was heated for 6 hr at 150°. The pyridine was removed by distillation under reduced pressure and the brown residue was heated with 10% hydrochloric acid for 30 min at reflux temperature. The acid-insoluble solid was collected, dissolved in hot acetone, and treated with Norit. Cooling of the acetone solution yielded a white solid, mp 284–289°. Three additional recrystallizations from acetone gave 0.215 g (30%) of white crystalline product, mp 309–312°.

Anal. Calcd for $C_{17}H_{10}N_2O_2$: C, 74.45; H, 3.65; N, 10.22. Found: C, 74.5; H, 3.63; N, 10.40.

2-Cyano-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin.—This compound was prepared from 2-bromo-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (**3**) and cuprous cyanide in pyridine and purified in the same manner as described for the 2,8-dicyano derivative (**9**) yielding white needles also in 30% yield: mp 152–154°; ν_{max}^{Nujol} 2220 cm^{-1} (C≡N).

Anal. Calcd for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.41; N, 5.62. Found: C, 76.9; H, 4.31; N, 5.99.

6H,12H-6,12-Methanodibenzo[*b,f*][1,5]dioxocin-2,8-dicarboxylic Acid (10).—To a solution of 9.00 g (0.236 mol) of 2,8-dibromo-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (**8**) in 100 ml of benzene under a nitrogen atmosphere was added 21 g (0.49 mol, 15% in *n*-hexane) of *n*-butyllithium and 60 ml of dry ether. A white precipitate formed after a short period of heating; copious amounts were present after 30 min at 50–60°. The mixture was poured over crushed Dry Ice. Ether (100 ml) was used to aid the transfer and water was added after carbonation completion. The layers were separated. Acidification of the aqueous layer with concentrated hydrochloric acid precipitated a white solid which was recrystallized from tetrahydrofuran to yield 4.6 g (63%) of white crystalline product: mp >300°; ν_{max}^{Nujol} 1730 cm^{-1} (C=O).

Anal. Calcd for $C_{17}H_{12}O_6$: C, 65.38; H, 3.85. Found: C, 65.6; H, 4.03.

6H,12H-6,12-Methanodibenzo[*b,f*][1,5]dioxocin-2-carboxylic Acid.—This compound was prepared from 2-bromo-6H,12H-6,12-methanodibenzo[*b,f*][1,5]dioxocin (**3**) and *n*-butyllithium followed by carbonation in the same manner as previously described for the 2,8-dicarboxylic acid derivative (**10**). The yield of white crystalline product, mp 178–181°, was only 2%.

Anal. Calcd for $C_{16}H_{12}O_4$: C, 71.34; H, 4.48. Found: C, 71.4; H, 4.49.

2,2′-Trimethylenediphenol (12).—6H,12H-6,12-Methanodibenzo[*b,f*][1,5]dioxocin (**1**, 2.0 g, 0.089 mol) was hydrogenolyzed in 250 ml of absolute ethanol in the presence of 5 g of palladium (5%) on charcoal in a Parr Series 4500 medium-pressure apparatus. Reaction conditions were 75° for 4 hr at 200 lb/in.² of pressure. The palladium catalyst was collected on a Büchner funnel and the ethanol was removed by distillation under reduced pressure (*ca.* 20 mm). The viscous, colorless, oily residue could not be induced to crystallize. The oil was mixed with 5% sodium hydroxide solution. The alkaline solution was extracted with carbon tetrachloride and then carbonated with Dry Ice. The flocculant white solid which separated was collected and recrystallized from Skellysolvent (bp 60–100°) to yield 0.61 g (30%) of 2,2′-trimethylenediphenol, mp 95.5–96° (lit.[7] mp 97–99°).

Authentic 2,2′-dihydroxychalcone (**12**) (lit. mp 161–163°,[7] 154–155°[13]) was prepared from the reaction of *o*-hydroxyacetophenone and salicylaldehyde,[7] mp 159–162°. This chalcone was hydrogenated to 2,2′-trimethylenediphenol, mp 96.5–97° (lit.[7] mp 97–99°), *via* the method of Carpenter and Hunter.[7] The

(9) Melting points were determined in a "Melt-Pointer" (Scientific Glass Apparatus Co., Inc.) and are corrected. Elemental analyses were done by the staff of Dr. P. Boyd, The Dow Chemical Co. Infrared spectra were recorded on a Perkin-Elmer spectrophotometer, Model 237, the ultraviolet spectra on a Cary recording spectrophotometer, Model 15, specific rotations and optical rotatory dispersion curves on a Cary 60 spectropolarimeter, and nmr spectra on a 60-Mcps Varian Associates instrument.

(10) I. H. Updegraff and H. G. Cassidy, *J. Amer. Chem. Soc.*, **71**, 407 (1947).

(11) T. J. Thompson and R. H. Edee, *ibid.*, **47**, 2556 (1925).

(12) A. Auwers and O. Bürger, *Ber.*, **37**, 3929 (1904).

(13) E. Shraufestatter and S. Deutch, *Chem. Ber.*, **81**, 489 (1949).

mixture melting point of a mixture of 2,2′-trimethylenediphenol (**12**) from **11** and **1** was 96.5–97°. The ir spectra of **12** prepared by both methods were superimposable.

(±)-2-Amino-6H,12H-6,12-methanodibenzo[b,f][1,5]dioxocin (13).—2-Nitro-6H,12H-6,12-methanodibenzo[b,f][1,5]dioxocin (**4**,2.60 g, 0.00967 mol) dissolved in 150 ml of benzene was placed in a flask equipped with a hydrogen sparger tube. Palladium-on-carbon catalyst (1.0 g) was added and a stream of hydrogen was sparged through the heated (60°) stirred mixture. Reaction progression was followed by periodically sampling the reaction mixture and observing the diminishment of the nitro group ir absorption at 1350 cm^{-1}. Four hours were required for complete disappearance of the peak and thus reaction completion. The catalyst was collected on a Büchner funnel and the filtrate solvent was removed by evaporation. The yellow residue was dissolved in hot ethanol, treated with Norit, and recrystallized twice from ethanol to yield 1.87 g (81%) of product as white needles: mp 208–210°; ν_{max}^{KBr} 1640, 3400 cm^{-1} (NH_2).

Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.31; H, 5.44; N, 5.86. Found: C, 75.8; H, 5.47; N, 5.81.

The acetamide was prepared from the reaction of **13** and acetic anhydride and purified by recrystallization from ethanol to yield white needles, mp 173–175°.

Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.60; H, 5.34; N, 4.98. Found: C, 72.7; H, 5.40; N, 5.03.

The benzamide was prepared by the reaction of **13** and benzoyl chloride and recrystallized from aqueous ethanol to give white needles, mp 160–162°.

Anal. Calcd for $C_{22}H_{17}NO_3$: C, 76.97; H, 4.96; N, 4.08. Found: C, 76.8; H, 5.02; N, 4.04.

The phenylthiourea derivative was synthesized by the reaction of **13** and phenylisothiocyanate and purified by recrystallization from ethanol to yield a white solid, mp 172–175°.

Anal. Calcd for $C_{22}H_{18}N_2O_2S$: C, 70.58; H, 4.81. Found: C, 70.2; H, 4.90.

Resolution of(±)-2-Amino-6H-12H-6,12-methanodibenzo[b,f]-[1,5]dioxocin.—A solution of 2.0 g (0.0084 mol) of (±)-2-amino-6H,12H-6,12-methanodibenzo[b,f][1,5]dioxocin in 100 ml of ethanol was mixed with 0.90 g (0.00625 mol) of (+)-tartaric acid. The solution was heated to achieve reaction and solution. Ethanol was removed by evaporation until 40 ml of solution remained. This solution was allowed to slowly cool. The salt which precipitated was collected. The filtrate was further reduced by evaporation to ~25 ml. A second crop of crystals were collected. The two crops were combined, recrystallized 10 times from ethanol, and then decomposed with warm 10% sodium hydroxide solution. The free amine was recrystallized twice from ethanol to yield 0.2 g of the dextrorotatory isomer as white needles: mp 238–240°; $[\alpha]^{25}D$ +389.0° (CH_3OH). The mother liquor from the second crop of tartrate salt crystals was made alkaline with 10% sodium hydroxide solution to pH 10. The free amine was collected and recrystallized several times from ethanol to a constant specific rotation to yield 0.05 g of the levorotatory isomer as white needles: mp 242–244°; $[\alpha]^{25}D$ −393.3° (CH_3OH). The uv absorption spectra of the enantiomers were superimposable: $\lambda_{max}^{CH_3OH}$ 301 mμ (ε 2120), 286 (2460), 277 (2420). The (+) and (−) isomers showed positive and negative Cotton effects, respectively, in the ORD curves centered at 279 mμ, $[\alpha]_{291}^{25}$ 7500° (CH_3OH).

(+)-6H,12H-6,12-Methanodibenzo[b,f][1,5]dioxocin from 13.—(+)-2-Amino-6H,12H-6,12-methanodibenzo[b,f][1,5]dioxocin (0.14 g, 0.000586 mol) was dissolved in 10 ml of 15% hydrochloric acid solution. Sodium nitrite (0.07 g, 0.001 mol) dissolved in 2 ml of water was added dropwise with stirring to the cold (0°) amine salt solution. Starch–iodide paper gave a positive nitrous acid test at the end of the addition. The reaction mixture was kept at 15° for 0.5 hr and then was added in 1-ml portions to a boiling solution of 0.2 g of cupric sulfate pentahydrate dissolved in 50 ml of ethanol. The reaction temperature was maintained between 70 and 80° and gas evolution was allowed to subside considerably between additions. Heating of the reaction mixture was continued for 0.5 hr after addition was complete. The ethanol was removed by distillation. The solid which precipitated in the cooled residue was collected on a filter, washed with water, and recrystallized from acetone to give 0.11 g (84%) of white needles: mp 153–154°; $\lambda_{max}^{CH_3OH}$ 277 mμ (ε 3790), 286 (3090). The uv absorption spectrum compares favorably with the racemate: $\lambda_{max}^{CH_3OH}$ 277 mμ (ε 4040), 286 (3160). The ir spectra of the (+) enantiomer and the racemic mixture were superimposable. Significant points in the ORD spectrum were $[\alpha]_{285}^{25}$ −8900, $[\alpha]_{290}^{25}$ +8900, $[\alpha]_{295}^{25}$ +4000, $[\alpha]_{300}^{25}$ +2800, $[\alpha]_{305}^{25}$ +1800, $[\alpha]_{310}^{25}$ +1100, and $[\alpha]_{315}^{25}$ +800° (CH_3OH).

Reduction of and Coupling Products of (±)-6H,12H-6,12-Methanodibenzo[b,f][1,5]dioxocin-2-diazonium Chloride.—(±)-2-Amino-6H,12H-6,12-methanodibenzo[b,f][1,5]dioxocin was converted into the corresponding diazonium chloride in the same manner as previously described for the dextrorotatory isomer. A portion was reduced as described for the (+) enantiomer to give (±)-6H,12H-6,12-methanodibenzo[b,f][1,5]dioxocin, mp 159–160°, which had an ir spectrum superimposable with that of an authentic compound. Another portion of the diazonium chloride was coupled with β-naphthol to form 1-{(6H,12H-6,12-methanodibenzo[b,f][1,5]dioxocin-2-yl)azo}-2-naphthol which was recrystallized from acetone to yield red needles, mp 260–261°.

Anal. Calcd for $C_{25}H_{18}N_2O_3$: C, 76.14; H, 4.57; N, 7.11. Found: C, 76.5; H, 4.70; N, 6.82.

Reaction of the diazonium salt with 2,6-dichlorophenol gave 2,6-dichloro-4-{(6H,12H-6,12-methanodibenzo[b,f][1,5]dioxocin-2-yl)azo}phenol which was recrystallized from acetone to yield yellow crystals, mp 208–209°.

Anal. Calcd for $C_{21}H_{14}N_2O_3Cl_2$: C, 61.02; H, 3.39; N, 6.78. Found: C, 61.3; H, 3.40; N, 6.31.

Registry No.—**1,** 7490-81-5; **3,** 19203-30-6; **4,** 19203-31-7; **5,** 19203-32-8; **6,** 19203-33-9; **7,** 19203-34-0; **8,** 19203-35-1; **9,** 19203-36-2; **10,** 19203-37-3; (±) **13,** 19206-21-4; (±) **13** (acetamide), 19206-22-5; (±) **13** (benzamide), 19206-23-6; (±) **13** (phenylthiourea derivative, 19206-24-7; (+) **13,** 19206-25-8; (−) **13,** 19206-26-9; (+) **14,** 19221-85-3; 2-cyano-6H-12H-6,12-methanodibenzo[b,f][1,5]dioxocin, 19221-84-2; 6H,12H-6,12-methanodibenzo-[b,f][1,5]dioxocin-2-carboxylic acid, 19203-38-4; 1-{(6H,12H-6,12-methanodibenzo[b,f][1,5]dioxocin-2-yl)azo}-2-naphthol, 19203-39-5; 2,6-dichloro-4-{(6H,12H-6,12-methanodibenzo[b,f][1,5]dioxocin-2-yl)azo}phenol, 19203-40-8.

Acknowledgment.—The authors wish to express their appreciation to Drs. Warren B. Crummett and Patrick J. Oriel for the uv and ORD measurements, respectively, Drs. E. B. Baker and Jerry P. Heeschen for nmr analyses, and H. J. Sloane for ir interpretation.