[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF OREGON]

Cyclization Studies in the Syntheses of Methoxy-Substituted 1-Phenyl-4-hydroxy-2-naphthoic Acids. III.[1]

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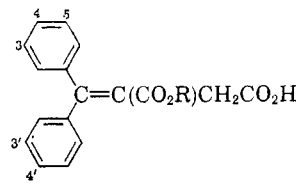
The Stobbe *t*-butyl half esters from 3-methoxy-, 3,3′-dimethoxy-, 3,4,3′,4′-tetramethoxy-, and 3,4,5,3′,4′-pentamethoxybenzophenones were cyclized (and subsequently hydrolyzed) to methoxy-substituted *t*-butyl 1-phenyl-4-hydroxy-2-naphthoates by heating with anhydrous sodium acetate in acetic anhydride. Complete product analyses were made on the reaction mixtures based on selective alkaline extractions of the various acidic components. In particular, separations were thus made between the cryptophenolic *t*-butyl hydroxynaphthoates bearing a methoxy group in the 5-position (*peri* isomers) and positional non-*peri* isomers (regular phenolic acidity). Structures of these compounds were assigned on the bases of OH-stretching frequencies in their IR spectra (ν_{max} = 3606 ± 3 cm.$^{-1}$ for 1-naphthol and non-*peri* isomers and 3400 ± 40 cm.$^{-1}$ for 8-methoxy-1-naphthol and *peri* isomers). In the dimethoxy case the ratio *para:ortho* for cyclization with respect to the methoxy group was 2.1:1. This ratio was raised to *ca.* 45:1 in the tetramethoxy case. The free methoxy-substituted 1-phenyl-4-hydroxy-2-naphthoic acids were obtained in yields of 90% or more by pyrolyses at 190–225° of the *t*-butyl esters—alone in the case of the non-*peri* isomers or with an added phenol in the case of the *peri* isomers. Theoretical implications of the results are presented.

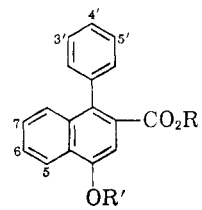
In a previous paper[4] it was reported that the crude product (Ia) from Stobbe condensation between 3-methoxybenzophenone and diethyl succinate was cyclized in the presence of acetic anhydride and anhydrous sodium acetate to mixed acetoxy esters (presumably VIa, VIIa, and VIIIa) and subsequently hydrolyzed with aqueous sodium hydroxide to mixed hydroxy acids (presumably VId, VIId, and VIIId). However, only two crystalline acids (of the three expected) were isolated from the hydrolysis mixture. In later work[5] the Stobbe product (IIIb) from 4,4′-dimethoxybenzophenone and di-*t*-butyl succinate was found to produce the hydroxy ester IXc by the same two-step cyclization-hydrolysis reaction sequence. Formation of the corresponding acid IXd (the only one expected) required an additional hydrolysis step conducted under more strenuous conditions.

In the present research the procedure employed with 4,4′-dimethoxybenzophenone has been extended to reaction of the ketones 3-methoxy-, 3,3′-dimethoxy-, 3,4,3′,4′-tetramethoxy-, and 3,4,5-3′,4′-pentamethoxybenzophenone and quantitative determination (by means of combined fractionation and infrared spectral analysis) of the ratios of isomeric *t*-butyl hydroxynaphthoates formed therefrom. Two such isomers (Xc and XIc; XIIc and XIIIc, respectively) are possible from the symmetrical di- and tetramethoxy ketones while three are possible (VIc, VIIc, and VIIIc; XIVc, XVc, and XVIc, respectively) from the unsymmetrical mono- and pentamethoxy ones. It should be noted



a. R = C_2H_5
b. R = *t*-C_4H_9

Position(s) of methoxy substituent(s) in derivatives
I. 3-CH_3O II. 3,3′-diCH_3O III. 4,4′-diCH_3O
IV. 3,4,3′,4′-tetraCH_3O V. 3,4,5,3′,4′-pentaCH_3O



a. R = C_2H_5, R′ = Ac
b. R = *t*-C_4H_9, R′ = Ac
c. R = *t*-C_4H_9, R′ = H
d. R = R′ = H

Position(s) of methoxy substituent(s) in derivatives
VI. 3′-CH_3O VII. 5-CH_3O VIII. 7-CH_3O
IX. 4′,6-diCH_3O X. 3′,5-diCH_3O XI. 3′,7-diCH_3O
XII. 3′,4′,5,6-tetraCH_3O XIII. 3′,4′,6,7-tetraCH_3O
XIV. 3′,4′,5′,5,6-pentaCH_3O XV. 3′,4′,5′,6,7-pentaCH_3O
XVI. 3′,4′,5,6,7-pentaCH_3O

that each of these ketones contains at least one methoxy group *meta* to the carbonyl group and is susceptible to the production of a *peri* (*i.e.* a 4-hydroxy-5-methoxy) isomer from cyclization *ortho* to this methoxy group as well as a non-*peri* (*i.e.* a 4-hydroxy-5-unsubstituted) isomer from cyclization *para* to this methoxy group. In the case of the pentamethoxybenzophenone only, a second *peri* isomer (XVI) would result from cyclization into the trimethoxyphenyl ring; while in the case of the monomethoxybenzophenone only, a second non-*peri* isomer (VI) would result from cyclization into the unsubstituted phenyl ring. The *peri* isomers may be considered derivatives of 1-hydroxy-8-methoxynaphthalene, a cryptophenolic com-

(1) This investigation was supported by research grant No. CY-3097 from the National Cancer Institute, U. S. Public Health Service.

(2) Research Associate, 1957–1960.

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(4) L. H. Klemm and T. Largman, *J. Am. Chem. Soc.*, **76**, 1688 (1954).

(5) L. H. Klemm and C. D. Lind, *J. Org. Chem.*, **21**, 258 (1956).

pound[6,7] (*i.e.*, one of masked phenolic acidity). In fact advantage was taken of the different acidities of the *peri* and non-*peri* isomers to effect chemical separation of them.

Stobbe condensations were conducted essentially in the manner described by Daub and Johnson.[8,9] Of the *t*-butyl esters formed (yields of 81–91%) only IVb, derived from 3,4,3′,4′-tetramethoxybenzophenone, was obtained in crystalline form. From the Stobbe reactions there were also isolated small quantities (<4%) of the self-condensation product of di-*t*-butyl succinate, *i.e.* di-*t*-butyl 2,5-cyclohexanedione-1,4-dicarboxylate or (on long standing in contact with air) its oxidation product di-*t*-butyl 2,5-dihydroxy-terephthalate. These by-products were identified by comparison with synthetic specimens of the same compounds.

In general, cyclizations of the Stobbe *t*-butyl half esters were run at 90° in the presence of anhydrous sodium acetate and acetic anhydride for varying lengths of time (usually 45–65 min.). In order to obtain quantitative data on the extent of cyclization and the isomeric composition of the cyclized materials, a scheme of successive alkaline treatments of the mixed reaction products was used. For the dimethoxy series, as a representative case, this consisted of (a) separation of unchanged Stobbe half ester (IIb, 5% recovery) from other reaction products by means of extraction with cold, dilute aqueous sodium hydroxide, (b) stirring residual mixed neutral *t*-butyl acetoxynaphthoates with warm, dilute aqueous sodium hydroxide to effect hydrolysis of the acetoxy function, and to a small extent hydrolysis of the *t*-butyl ester function, and to leave undissolved the cryptophenolic *peri* *t*-butyl hydroxynaphthoate isomer (Xc, 29%) thereby produced, (c) acidification of the preceding alkaline solution and stirring of the precipitated mixed compounds with dilute aqueous sodium bicarbonate to effect separation of soluble hydroxynaphthoic acids (Xd and XId, 7% total), from the less acidic, insoluble non-*peri* *t*-butyl hydroxynaphthoate isomer (XIc, 58%). The combined yield of products was nearly quantitative. The identity and composition of the mixed hydroxynaphthoic acids was ascertained by direct comparison with synthetic mixtures of the *bona fide* acids (*vide infra*) using infrared spectrophotometry. More definite structural assignments for the *t*-butyl hydroxynaphthoates Xc and XIc are considered later in the paper. Taking into account both the hydroxynaphthoates and their corresponding acids the ratio of non-*peri* products to *peri* isomeric products (*i.e.*, of cyclization *para* to the methoxy group *versus* cyclization *ortho* to the methoxy group) formed in the dimethoxy case was 2.1 ± 0.1:1. In fact this ratio was the same in three other runs under different conditions, one for 50 minutes at the same temperature but with mixed acetic acid–acetic anhydride as solvent, another for 20 minutes with acetic anhydride as solvent but at 140°, and a third for 7 hours with acetic anhydride as solvent and at steam bath temperature.

To avoid some of the experimental difficulties connected with low solubility of sodium salts and solubilization of *peri* isomers in alkaline solutions bulk separations of isomeric cyclized products in the tetramethoxy and pentamethoxy series were made by fractional crystallizations from organic solvents. In the tetramethoxy series the total yield of non-*peri* products (from *para* cyclization) was 91% while that of *peri* products (from *ortho* cyclization) was less than 2%, ratio 45:1. Since the electronic effect of changing from a 3-methoxyphenyl ring (in the dimethoxy series) to a 3,4-dimethoxyphenyl ring (in the tetramethoxy series) would not be expected to alter the *para:ortho* cyclization ratio, the greatly enhanced selectivity for *para* cyclization in the tetramethoxy series as compared to the dimethoxy series must be ascribed to steric factors, probably entirely to the buttressing effect[10] of the vicinal methoxy substituents. Despite expectations of the formation of two *peri* isomers in the pentamethoxy series, only one such crystalline isomer was isolated. Total yields in this series were 55% of crude non-*peri* products and 39% of *peri* products (ratio 1.4:1 in four identical runs). If one assumes that the ratio of *para:ortho* cyclization into the dimethoxyphenyl ring is the same in the pentamethoxy series as in the tetramethoxy series then not more than 1–2% of the total cyclized products should have structure XIV. On the basis of this argument only, the crystalline *peri* *t*-butyl hydroxynaphthoate isolated was assigned structure XVIc rather than XIVc. Any XIVc formed could easily have escaped detection by our method.

To check on the relative rates of substitution into the phenyl and 3-methoxyphenyl rings and to assist in isolation of both of the expected non-*peri* isomers cyclization in the monomethoxy series was conducted in two partial steps. Thus, after a reaction time of only 20 minutes, there resulted 31% of recovered half ester plus 16% of crystalline *peri* ester VIIc, m.p. 142°, and 21% of a crystalline non-*peri* ester, m.p. 195°, presumably VIIIc.

(6) H. Staudinger, E. Schlenker, and H. Goldstein, *Helv. Chim. Acta*, **4**, 334 (1921); N. P. Buu-Hoï and D. Lavit, *J. Chem. Soc.*, 2412 (1956).

(7) Though it now appears that cryptophenolic behavior is rather general for this type of structure, the acidic character of the phenolic group may not be decreased in the presence of strong electron-withdrawing substituents, as, *e.g.*, in the case of 2,4-dinitro-1-hydroxy-8-methoxynaphthalene described by F. Calvet and M. C. Carnero, *J. Chem. Soc.*, 556 (1936).

(8) G. H. Daub and W. S. Johnson, *J. Am. Chem. Soc.*, **70**, 418 (1948).

(9) G. H. Daub and W. S. Johnson, *J. Am. Chem. Soc.*, **72**, 501 (1950).

(10) F. H. Westheimer, *Steric Effects in Organic Chemistry*, M. S. Newman, ed., J. Wiley and Sons, Inc., New York, 1956, pp. 552–3.

None of the other crystalline non-*peri* ester was isolated. The 31% of recovered half ester was then re-subjected to cyclization conditions for 7 hours longer, whereupon only 0.3% of additional VIIc and 26% of total material soluble in 10% aqueous sodium hydroxide was produced. From the latter fraction there was obtained the second non-*peri* ester, m.p. 172°, presumably VIc, but none of the crystalline 195° isomer. It is to be expected that the yield of crystalline *peri* ester VIIc would be unaffected by the formation of the two non-*peri* esters and should be essentially quantitatively isolable. Assuming that the cyclization reaction is not reversible and that the *para:ortho* ratio of isomers for cyclization into the 3-methoxyphenyl ring would be the same as was found in the dimethoxy series then yields of 33% and 0.6% of VIIIc for the first and second parts of the cyclization, respectively, would have been expected. It is on this basis that the tentative assignments of structures to the non-*peri* esters as noted above is made. Such preference for cyclization into the 3-methoxyphenyl ring as compared to the phenyl ring would be consistent with an electrophilic (S_E) cyclization process.

There is a limited amount of evidence to show that neither geometric isomerization nor ester exchange occurs under the conditions of sodium acetate-acetic anhydride cyclization of Stobbe half esters. Thus Knott[11] was able to isolate Stobbe geometric isomers from condensation between phenyl 2-furyl ketone and diethyl succinate and to show that each isomer cyclized to a different product. Johnson and Goldman[12] likewise isolated geometric isomers from Stobbe reaction between 2-acetylnaphthalene and diethyl succinate and found that only one of the isomers (presumably that with the aryl and $-CH_2-CO_2H$ groups *cis*) cyclized at all. When, however, they synthesized the non-Stobbe positionally isomeric ester with the aryl and $-CO_2H$ groups *cis* ($-CH_3$ and $-CH_2CO_2C_2H_5$ also *cis*) an indone was formed under the cyclization conditions. The failure to isolate any identifiable indones from our reaction mixtures would indicate that ester exchange likewise fails to occur in our Stobbe *t*-butyl half esters during cyclization. Unfortunately, the complete lack of success in our efforts to separate *cis* and *trans* Stobbe half esters from the two unsymmetrically substituted benzophenones prevented direct checking for possible geometric isomerization during the cyclization process and for preferential formation of one of the two possible geometric isomers in the Stobbe condensation itself.[12a]

The series from the two symmetrically substituted benzophenones are free of questions regarding isomeric ratios of Stobbe products and geometric isomerization during cyclization. They are, therefore, appropriate systems for study of the ratio of *para:ortho* cyclization. Thus far, only ratios from reactions carried nearly to completion have been investigated, but the aforementioned observation that the *para:ortho* ratio in the dimethoxy series remains almost exactly 2.1:1 under a variety of reaction conditions may imply that steric hindrance to *ortho*-substitution remains unaltered by the conditions. Klages[13] has concluded from microwave studies of dipole relaxation that the methoxy group in anisole at room temperature is locked into coplanarity with the phenyl ring only 15% of the time. Dipole moment measurements on *p*-dimethoxybenzene are consistent with essentially free rotation of the methoxy group.[14] It is reasonable, therefore, to assume that the methoxy group is freely rotating in the dimethoxy Stobbe half ester under the cyclizing conditions used. For appreciable electrophilic activation (resonance effect) by the methoxy group this group may need to be in or close to the plane of the phenyl ring. Thus, cyclization might be expected to occur only at such times as the methoxy group has a conformation in the region $0° \pm \alpha$ or $180° \pm \alpha$, where α is an angle of rotation of unknown, but probably small, magnitude. Particularly for the cyclization in question, where one forms a six-membered aromatic ring, the transition state would be expected to require nearly coplanar geometry. For *para* cyclization neither the conformer ($0° \pm \alpha$) nor the conformer ($180° \pm \alpha$) would offer steric hindrance, while for *ortho* cyclization only the latter ($180° \pm \alpha$, methoxy group oriented *anti* to the substituting chain) is sterically unhindered. If one assumes that the conformer ($0° \pm \alpha$) completely inhibits *ortho* cyclization it is possible to rationalize the observed 2.1:1 isomeric ratio almost exactly. In the tetramethoxy series the vicinal methoxy groups can no longer be freely rotating but would prefer to assume conformations *anti* to one another, *i.e.* for *ortho* cyclization the methoxy group would show a strong preference for assuming the sterically hindering ($0° \pm \alpha$) conformation. The effect on *para* cyclization would again be unchanged. Again the *para:ortho* ratio observed seems consistent with this geometry.

Although the differing acidities of the *peri* and non-*peri* *t*-butyl hydroxynaphthoates were useful

(11) E. B. Knott, *J. Chem. Soc.*, 189 (1945).

(12) W. S. Johnson and A. Goldman, *J. Am. Chem. Soc.*, **66**, 1030 (1944); **67**, 430 (1945). See also W. S. Johnson and R. P. Graber, *J. Am. Chem. Soc.*, **72**, 925 (1950).

(12a) NOTE ADDED IN PROOF. Recently E. E. Smissman, P. S. Portoghese, and R. A. Mode [*J. Org. Chem.*, **26**, 3628 (1961)] reported the separation of Stobbe isomers from condensation of 3,4-methylenedioxy-3′,4′,5′-trimethoxybenzophenone with dimethyl succinate. Their studies, however, were not carried out to such extent as to provide clear answers to these questions.

(13) G. Klages, *Z. Naturforsch.*, **9A**, 366 (1954).

(14) G. E. K. Branch and M. Calvin, *The Theory of Organic Chemistry*, Prentice-Hall, Inc., New York, 1941, pp. 141–3; A. Aihara and M. Davies, *J. Colloid Sci.*, **11**, 671 (1956); S. Mizushima, *Structure of Molecules and Internal Rotation*, Academic Press, Inc., New York, 1954, pp. 90–3.

TABLE I

INFRARED ABSORPTION BANDS IN THE REGION 3200–3750 CM.$^{-1}$ FOR SOME METHOXY-SUBSTITUTED *t*-BUTYL 1-PHENYL-4-HYDROXY-2-NAPHTHOATES[a]

Compound	Position(s) of Methoxy Substituent(s)	OH-Stretching Band			Unassigned Absorption Band		
		ν_{max} cm.$^{-1}$	$\Delta\nu_{1/2}$[b] cm.$^{-1}$	Absorbance[c] A 10^7 cm.-mole^{-1}	ν_{max} cm.$^{-1}$	$\Delta\nu_{1/2}$[b] cm.$^{-1}$	Absorbance[c] A 10^7 cm.-mole^{-1}
			Non-*peri* Compounds[d]				
1-Naphthol	—	3609	23	1.67	No band	—	—
VIc	3′-	3604	24	1.76	3417	100	1.29
VIIIc	7-	3603	25	1.79	3418	92	0.88
XIc	3′,7-	3605	24	1.78	3419	94	1.06
XIIIc	3′,4′,6,7-	3606	23	1.65	3417	102	1.43
XVc	3′,4′,5′,6,7-	3604	23	1.67	3415	96	1.42
			Peri Compounds[e]				
8-Methoxy-1-naphthol	—	3440	58	4.28			
VIIc	5-	3434	63	5.02			
Xc	3′,5-	3431	64	5.03			
XIIc	3′,4′,5,6-	3361	76	5.45			
XVIc	3′,4′,5,6,7-	3378	73	5.55			

[a] Run in carbon tetrachloride solution. [b] Apparent value for width of absorption band at half intensity. [c] Calculated according to method I of D. A. Ramsay [*J. Am. Chem. Soc.*, **74**, 72 (1952)], using the formula $A = \frac{K\Delta\nu_{1/2}}{Cl} \ln \left(\frac{T_0}{T}\right)_{\nu_{max}}$ where C is concentration of compound in solution, l is the path length (10 cm.), T is the percentage transmission of light through the sample, T_0 is the percentage transmission without the sample, and K is taken as 1.57 for the *peri* compounds and 1.55 for the non-*peri* ones. [d] C is 3.24–3.30 × 10^{-4} moles/l. [e] C is 2.66–2.95 × 10^{-4} moles/l.

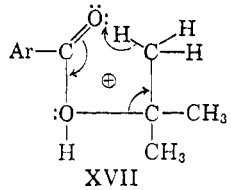
indications of their structures and highly valuable in effecting chemical separations of isomers, the various structural assignments made for these compounds rest principally on observations of the OH-stretching bands in their infrared absorption spectra. Data relative to these bands are listed in Table I, observation of which shows that in dilute solution in carbon tetrachloride 1-naphthol and the five hydroxynaphthoates which were soluble in 10% aqueous sodium hydroxide solution all have sharp OH-stretching bands at 3606 ± 3 cm.$^{-1}$, while 8-methoxy-1-naphthol and the four cryptophenolic hydroxynaphthoates have broader, considerably more intense (about three times as great) OH-stretching bands at 3400 ± 40 cm.$^{-1}$ The shift of OH-stretching bands to longer wave lengths (lower frequencies) and the intensification of absorption through hydrogen bonding have been noted by Tsubomura.[15] In addition to the OH-stretching band the non-*peri* isomers exhibited a much broader nonoverlapping band of somewhat lower intensity at 3417 ± 2 cm.$^{-1}$ This band which was shown neither by 1-naphthol nor by *t*-butyl 1-(3,4-dimethoxyphenyl)-4,6,7-trimethoxy-2-naphthoate could conceivably result from intermolecular hydrogen bonding between the phenolic OH-group of one molecule and an ester-group oxygen of another molecule. No evidence for the presence of this extra band was found in the band profiles of the *peri* compounds though observation of such a band would have been difficult at best.

The foregoing infrared spectral method clearly distinguishes *peri* isomers from non-*peri* ones. For the dimethoxy and tetramethoxy series where only one of each isomer is both possible and isolable, structural identification is complete. In the pentamethoxy series where two *peri* isomers (plus one non-*peri* isomer) are possible but only one was isolated the structural assignment XVIc rests on arguments based on an extension of observations from the tetramethoxy series (*vide supra*). In the monomethoxy series, where two non-*peri* isomers (plus one *peri* isomer) are possible the assignments of structures VIc and VIIIc to the 172°- and the 195°-hydroxynaphthoates, respectively, must be considered indefinite and tentative at this point. Additional evidence bearing on this assignment will be presented later.

For conversion of the *t*-butyl hydroxynaphthoates to the corresponding 1-phenyl-4-hydroxy-2-naphthoic acids the aqueous ethanolic barium hydroxide (sealed bomb) method of Klemm and Lind[5] was employed in one case (63% yield of XIIId). More generally, however, the esters were pyrolyzed at a temperature of 190–225° to give the acids in 90% yields or higher. Under such conditions the five non-*peri* esters, when heated by themselves, lost isobutene completely in 15 minutes. Contrariwise the *peri* esters (except XIIc which was not tried) were recovered unchanged and without evident loss of gas when subjected to the same conditions alone. Pyrolysis proceeded readily, however, when these *peri* esters were first admixed with a phenol such as 1-naphthol or *p*-bromophenol. Thus, it is apparent that the thermal dissociation is catalyzed by an acidic phenolic group. For the non-*peri* esters such groups are already present in the mole-

(15) H. Tsubomura, *J. Chem. Phys.*, **24**, 927 (1956).

cules themselves, while for the *peri* esters the cryptophenolic character of the hydroxy groups again becomes manifest. Consistent with these observations would be the transition state XVII for the catalyzed pyrolytic process.



XVII

Breslow, Baumgarten, and Hauser[16] have also noted the catalytic effect of *p*-toluenesulfonic acid in the thermal de-*t*-butylation of acyl-substituted ethyl *t*-butyl malonates in refluxing benzene solution. Acid catalysis is likewise important in the reverse process of esterification of simple carboxylic acids by isobutene.[17]

With the three possible monomethoxy 1-phenyl-hydroxy-2-naphthoic acids VId, VIId, and VIIId from the monomethoxy series in hand it now became possible to correlate our results with those of Klemm and Largman[4] who had isolated only two of the three possible acids. From a complete cyclization reaction these workers obtained isomers melting at 212° (44% yield) and 280° (15% yield). By our interrupted cyclization-isolation-pyrolysis process we obtained isomeric acids melting at 205°, 209°, and 278° (*via* the isomeric *t*-butyl esters melting at 142°, 172°, and 195°, respectively). Mixture melting points and comparative infrared spectra showed the identity of the 209°–212° and 278°–280° combinations. Our 205° compound clearly has the structure VIId for it was derived from pyrolysis of the *peri* ester VIIc (m.p. 142°) for which the structural assignment has herewith been presented. It is thus now clear that the wrong structure was assigned to the 280° isomer by Klemm and Largman who had based their interpretation on the infrared correlations for —COH and —COC— absorbancies at about 9 μ in the acids themselves rather than to use the more certain phenolic OH— stretching absorbancies in the esters, as was done here. Tentative structural assignments for our 209° and 278° acids, as based on yields of *t*-butyl hydroxynaphthoates in the interrupted cyclization process (*vide supra*), are VId and VIIId, respectively. These assignments are consistent with the observations of Klemm and Largman. Thus, only the 212° isomer of the earlier workers (our 209° isomer) gives an ultraviolet absorption spectrum nearly identical with that of 1-phenyl-4-hydroxy-2-naphthoic acid. Moreover, to rationalize the high yield (44%) of the 212° isomer and the failure to isolate any of the 205° isomer by Klemm and Largman in terms of the reverse structural assignments for these two isomers one would need to invoke such unexpected phenomena as preponderance of one Stobbe isomer over the other or of geometric isomerization during cyclization plus a *para:ortho* ratio of products different from ours. Such phenomena are indeed possible, but perhaps unlikely.

(16) D. S. Breslow, E. Baumgarten, and C. R. Hauser, *J. Am. Chem. Soc.*, **66**, 1286 (1944).

(17) H. Henecka, *Methoden der Organischen Chemie* (*Houben-Weyl*), 4th ed., Vol. VIII, E. Müller, ed., Georg Thieme Verlag, Stuttgart, 1952, pp. 534–5.

EXPERIMENTAL[18]

Preparation of ketones. 3-Methoxybenzophenone was prepared by interaction of benzonitrile with the Grignard reagent from *m*-bromoanisole,[19] distillation, and recrystallization from methanol, m.p. 36–38.5° (82% yield).

3,3′-Dimethoxybenzophenone, b.p. 174–176° (1 mm.), was prepared from 3,3′-dinitrobenzophenone by way of the corresponding diamino- and dihydroxybenzophenones as recorded previously,[20] but with the following modifications: The diamine was liberated from its chlorostannate salt by means of excess sodium hydroxide. Subsequent tetrazotization of this crude diamine in aqueous sulfuric acid thus furnished a clear solution (rather than a precipitated salt) which was added in 25-ml. portions (each derived from *ca.* 0.013 moles of dinitro compound) to an equal number of 90-ml. portions of boiling 3.6*N* sulfuric acid. When evolution of gas had ceased, all portions were combined, diluted with boiling water to three times the volume, treated with Norit, and allowed to crystallize; yield 70–80% (based on dinitro compound) of diol, m.p. 160–163°, changed to 162–164° on recrystallization from acidulated water. Methylation was effected by simultaneous, but separate, dropwise additions of dimethyl sulfate and 10% aqueous sodium hydroxide to a well-stirred solution of the diol in dilute alkali at such rates that the mixture was always somewhat basic and until its bright yellow color was discharged, yield 94%.

3,4,3′,4′-Tetramethoxybenzophenone (m.p. 142.5–145°, av. yield 70%) was prepared by condensation of veratrole with veratric acid in the presence of polyphosphoric acid according to the general procedure reported for the synthesis of 3,4,5,3′,4′-pentamethoxybenzophenone.[21]

Molecular compound of di-t-butyl succinate and phenol. Di-*t*-butyl succinate was prepared by alcoholysis of diphenyl succinate according to the procedure of Daub and Johnson[9] and was recrystallized from methanol m.p. 35.5–37°. In purification of the crude reaction mixture it was observed that, if phenol was not thoroughly removed by many washings with dilute alkali, the product isolated had a higher m.p. than that of the pure ester. Fractional crystallization of such material from 30–60° petroleum ether produced rods, m.p. 45.5–47°.

Anal. Calcd. for $C_{12}H_{22}O_4 \cdot C_6H_6O$: C, 66.64; H, 8.70. Found: C, 66.42; H, 8.71.

The same molecular compound (as based on m.p. and IR spectrum) was formed in 93% yield by cooling a warm solution of 6.67 mmoles each of phenol and di-*t*-butyl succinate in 5 ml. of 30–60° petroleum ether. Stirring of these crystals with dilute aqueous sodium hydroxide at 40° served to free the diester component, m.p. 35–36.5°.

Stobbe condensations. In general the procedure of Daub and Johnson[8,9] was followed. The reaction was conducted at *ca.* 50° with 0.05 mole of ketone, 0.063 mole of di-*t*-butyl

(18) Microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill. Melting points are uncorrected.

(19) S. Natelson and S. P. Gottfried, *J. Am. Chem. Soc.*, **61**, 1001 (1939).

(20) L. H. Klemm, R. Mann, and C. D. Lind, *J. Org. Chem.*, **23**, 349 (1958).

(21) L. H. Klemm and G. M. Bower, *J. Org. Chem.*, **23**, 344 (1958).

succinate, 0.188 mole of sodium hydride, 0.013 mole of anhydrous *t*-butyl alcohol, and sufficient anhydrous benzene (at least 1.7 l.) to dissolve the ketone and facilitate stirring. Reaction times were 5.5 hr. for the monomethoxy, 11 hr. for the dimethoxy and pentamethoxy, and 18 hr. for the tetramethoxy compounds. Excess sodium hydride was destroyed with glacial acetic acid in the first three cases and with ethanol (followed by dilute hydrochloric acid) in the tetramethoxy case. Organic layers containing the products were extracted with 5% sodium bicarbonate solutions and saved for further investigation (*vide infra*). Acidification of the alkaline extracts and isolation of the Stobbe *t*-butyl half esters gave 89–91% yields of amber vitreous products, Ib, IIb, and Vb, from the mono, di-, and pentamethoxybenzophenones, respectively (neut. equiv. for IIb, calcd., 398; found, 396). From the tetramethoxybenzophenone there resulted light yellow platelets of *3-(carbo-t-butoxy)-4,4-di-(3,4-dimethoxyphenyl)-3-butenoic acid* (IVb) hemihydrate on recrystallization of the product from aqueous acetone or aqueous methanol, m.p. 120–123.5° (81%). Further recrystallization from the same solvent furnished a sample for microanalysis, m.p. 121–122° (inserted in bath at 119°).[22]

Anal. Calcd. for $C_{25}H_{30}O_8 \cdot 1/2\ H_2O$: C, 64.24; H, 6.68. Found: C, 64.47; H, 6.74.

Upon slow evaporation to dryness of a methanolic solution of the hemihydrate there resulted faintly cream prisms of anhydrous product, m.p. 127–129°.

Anal. Calcd. for $C_{25}H_{30}O_8$: C, 65.49; H, 6.60. Found: C, 65.41; H, 6.66.

A dimorphic form of the anhydrous product, white prisms, m.p. 140–141°, was obtained on recrystallization from chloroform-ligroin (b.p. 90–120°). On seeding molten 129°-product with the 141°-modification the mixture solidified and remelted at the higher temperature.

Di-t-butyl 2,5-cyclohexanedione-1,4-dicarboxylate. (*a*). A mixture of 1.15 g. of di-*t*-butyl succinate, 0.5 g. of sodium hydride, and 5 drops of *t*-butyl alcohol was heated on a steam bath until the immediate vigorous evolution of hydrogen had ceased. Excess sodium hydride was treated with glacial acetic acid (added dropwise). The mixture was acidified and extracted with ether. The residue from evaporation of the ethereal extract was stirred with 5 ml. of petroleum ether (30–60°) and recrystallized from ethanol, yield 0.35 g. of yellow needles. Further recrystallization from dioxane and finally methanol afforded white needles, m.p. *ca.* 169° (dec.); cherry red coloration with ethanolic ferric chloride; $\lambda_{max}^{CHCl_3}$ (no sharp OH band), 6.01, 6.22 μ.

Anal. Calcd. for $C_{16}H_{24}O_6$: C, 61.52; H, 7.75. Found: C, 60.88; H, 7.85.

(*b*). Combined miscellaneous alkali-washed organic layers from the preceding Stobbe condensations were evaporated to dryness and the residue was recrystallized from ethanol to give a by-product (<4% yield based on total di-*t*-butyl succinate used) identical with the dione[23] from part (*a*), as based on m.p. and infrared spectrum.

Di-t-butyl 2,5-dihydroxyterephthalate. (*a*). In one instance the preceding Stobbe by-product was allowed to stand for a year before it was investigated. On repeated recrystallizations from ethanol and methanol it formed pale yellow needles, m.p. *ca.* 168° (dec.); soluble in warm 5% aqueous sodium hydroxide; brownish green coloration with ethanolic ferric chloride; $\lambda_{max}^{CHCl_3}$ 3.11, 5.95, 6.67 μ.

Anal. Calcd. for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 62.22, 62.13; H, 7.21, 7.40.

(*b*). Through a solution of 0.1 g. of di-*t*-butyl 2,5-cyclohexanedione-1,4-dicarboxylate in 1 ml. of 10% aqueous potassium hydroxide and 1 ml. of methanol was bubbled a stream of oxygen until the yellow color had just turned to brown (10 min.). The solid (14 mg.) which precipitated when the solution was acidified and cooled had an infrared spectrum identical with that in part (*a*).

Cyclization of the Stobbe half-ester from 3,3'-dimethoxybenzophenone. (*a*) *With acetic acid, at 90°.* To a stirred solution of 3.86 g. of fused sodium acetate in 118 ml. of acetic anhydride and 20 ml. of glacial acetic acid, kept at 90 ± 2° under an atmosphere of nitrogen, was added, all at once and in small pieces, 10 g. of half ester IIb. The half-ester dissolved immediately. After 50 min. the mixture was cooled to below 30°, stirred with 40 ml. of water, and 1 ml. of pyridine until cessation of the evolution of heat, and freed from volatile constituents by distillation under reduced pressure. The residue was treated with water and extracted with ether. The ethereal extract was washed successively with 10% hydrochloric acid, water, 5% aqueous sodium hydroxide, and water, and then evaporated. Acidification of the alkaline wash solution gave 1.69 g. of brown gum (presumably chiefly starting material). The residue from the ethereal layer was stirred on a steam bath for 1 hr. with 40 ml. of 10% aqueous sodium hydroxide (in order to de-acetylate the *t*-butyl acetoxynaphthoates) and then for 30 min. while 40 ml. of water (added to dissolve sodium salts of the resultant non-*peri* *t*-butyl hydroxynaphthoate and hydroxynaphthoic acids) was gradually added. Thereupon all oily product had dissolved and a crystalline precipitate (solubilized by the 10% aqueous sodium hydroxide) began to form. The mixture was refrigerated overnight and filtered to give 2.12 g. (22%) of the *peri* product *t*-butyl *1-(3-methoxyphenyl)-4-hydroxy-5-methoxy-2-naphthoate* (Xc), m.p. 136–138°. A sample for analysis was recrystallized from aqueous acetone as prisms, m.p. 137–138°.

Anal. Calcd. for $C_{23}H_{24}O_5$: C, 72.61; H, 6.36. Found: C, 72.61; H, 6.11.

Ether extraction of the filtrate from Xc followed by evaporation of the solvent and trituration of the residue with 3.3% aqueous sodium hydroxide gave an additional 0.32 g. (3.3%) of Xc (previously solubilized).

Acidification of combined sodium hydroxide extracts of Xc yielded a precipitate which was washed with water, stirred with 5% sodium bicarbonate (to remove any naphthoic acids formed by hydrolysis of the *t*-butyl ester grouping), dried, and washed with a few milliliters of boiling petrol (60–90°, removed 0.08 g. of crude Xc) to leave 4.92 g. (51%) of the non-*peri* product *t-butyl 1-(3-methoxyphenyl)-4-hydroxy-7-methoxy-2-naphthoate* (XIc), m.p. 178–179.5°. Two recrystallizations of a sample from acetone gave prisms, m.p. 178.5–180°, slow dec.

Anal. Calcd. for $C_{23}H_{24}O_5$: C, 72.61; H, 6.36. Found: C, 72.50; H, 6.51.

Acidification of the bicarbonate washings of XIc gave 0.19 g. (2.4%) of tan solid, identified as a mixture of the two acids Xd (20%) and XId (80%) by infrared examination (*vide infra*).

(*b*) *Without acetic acid, at 90°.* A suspension of 2.8 g. of powdered anhydrous sodium acetate in 118 ml. of acetic anhydride was stirred at 90 ± 2° for *ca.* 1 hr. before the half-ester (10.3 g.) was added. The reaction was allowed to proceed at 90° for 45 min. and the mixture was processed essentially as in preceding run (*a*), yields: 0.52 g. of "starting material," 2.82 g. (29%) of Xc, 5.73 g. (58%) of XIc, and 0.60 g. (7%) of a mixture of acids of the same composition as in (*a*).

(*c*) *Without acetic acid, at 140°.* This run differed from run (*b*) only in that it was conducted with 4.2 g. of sodium acetate and 10 g. of half-ester and at reflux temperature (140°) for 20 min., yields: 0.21 g. of "starting material," 2.73 g. (29%) of Xc, 6.03 g. (63%) of XIc, and 0.43 g. (5%) of mixed acids.

Cyclization of Stobbe half-ester from 3-methoxybenzophenone. Following the general procedure used in part (*b*) for cyclization of the dimethoxy analog, except that the reaction time was only 20 min., from a mixture of 17.6 g. of resinous half-

(22) One sample from aqueous methanol was found to melt at 115.5–116.5° when first prepared and at 121–123° after standing for some time.

(23) The very limited extent to which di-*t*-butyl succinate undergoes self-condensation in the Stobbe reaction has been noted previously.[9]

ester Ib, 5.8 g. of sodium acetate, and 280 ml. of acetic anhydride, there were isolated 5.49 g. (31%, presumably mainly recovered half-ester) of material soluble in 5% aqueous sodium hydroxide and 11.5 g. (62%) of material insoluble therein. Stirring the latter with warm 10% aqueous sodium hydroxide and then diluting the mixture to 3–5 volumes (to dissolve sodium salts of the alkali-soluble products) left 2.76 g. (16%) of alkali-insoluble *t-butyl 1-phenyl-4-hydroxy-5-methoxy-2-naphthoate* (VIIc), m.p. 137–141°. Recrystallization of a sample from methanol gave prisms, m.p. 141–142°.

Anal. Calcd. for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 75.13; H, 6.15.

Acidification of the alkaline filtrate from VIIc precipitated 6.74 g. (40%) of mixed solids from which was isolated, after repeated recrystallizations from ethanol, 3.54 g. (21%) of needles, *t-butyl 1-phenyl-4-hydroxy-7-methoxy-2-naphthoate* (VIIIc), m.p. *ca.* 195° dec.

Anal. Calcd. for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 75.33; H, 6.43.

The foregoing "recovered half-ester" (5.49 g.) was stirred at 90° with 87 ml. of acetic anhydride and 1.8 g. of sodium acetate for 7 hr. and re-processed as in the preceding paragraphs, yields (based on original 17.6 g. of starting material): 0.05 g. (0.3%) of alkali-insoluble product, 0.69 g. (3.9%) of product soluble in 5% sodium hydroxide, and 4.30 g. (26%) of product soluble in warm 10% aqueous sodium hydroxide (after dilution). Repeated recrystallization of the last of these from aqueous methanol gave *t-butyl 1-(3-methoxyphenyl)-4-hydroxy-2-naphthoate* (VIc) as prisms, m.p. 171.3–172.3°.

Anal. Calcd. for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 75.16; H, 6.26.

Cyclization of Stobbe half-ester from 3,4,5,3',4'-pentamethoxybenzophenone. Following the general procedure used in part (*b*) for cyclization of the dimethoxy analog a mixture of 10 g. of half-ester Vb, 3.5 g. of sodium acetate, and 93 ml. of acetic anhydride (reacted for 65 min.) gave 0.26 g. (2.6%) of "starting material." In order to circumvent solubility and solubilization difficulties encountered in fractionation of hydrolyzates from the foregoing monomethoxy and dimethoxy cyclization series two modifications in procedure were introduced here. First, to avoid the precipitation of difficultly soluble alkaline metal salts, the mixed acetates (residue from the etheral layer) were dissolved, instead, in 20 ml. of boiling methanol to which 40 ml. of 10% aqueous potassium hydroxide was added. Boiling was continued for 30 min. and then while the methanol was removed by a stream of nitrogen. Acidification of the resultant solution gave a precipitate which was washed with water and dissolved in chloroform. Extraction of the chloroform solution with 5% aqueous sodium bicarbonate followed by acidification of the alkaline extract gave 60 mg. (0.7%) of mixed acids XVd (56%) and XVId (44%) as determined by infrared examination. Second, bulk separation of the *peri* and non-*peri* isomers was effected by fractional crystallization from an organic solvent rather than by differential solubility in aqeous alkali. Thus, the chloroform solution was evaporated nearly to dryness, boiled briefly with 50 ml. of carbon tetrachloride and allowed to cool. The crystalline precipitate (4.74 g., 49%) which formed was washed with carbon tetrachloride, recrystallized (for analysis) from chloroform–carbon tetrachloride and then from ethyl acetate to give fine needles of *t-butyl 1-(3,4,5-trimethoxyphenyl)-4-hydroxy-6,7-dimethoxy-2-naphthoate* (XVc), molten in 30 sec. when inserted in a bath at 217° (dec.).

Anal. Calcd. for $C_{26}H_{30}O_8$: C, 66.37; H, 6.43. Found: C, 66.43; H, 6.55.

Repeated extraction with 3% aqueous potassium hydroxide of the organic mother liquor from which XVc had crystallized gave (on acidification) 0.52 g. (5.4%) more of less pure XVc. Subsequent evaporation of the organic layer to dryness left 3.75 g. (39%) of residue, m.p. 130–134°. Repeated recrystallizations of the residue from ethyl acetate and then once from methanol gave prisms of *t-butyl 1-(3,4-dimethoxyphenyl)-4-hydroxy-5,6,7-trimethoxy-2-naphthoate* (XVIc), m.p. 135–137°.

Anal. Calcd. for $C_{26}H_{30}O_8$: C, 66.37; H, 6.43. Found: C, 66.46; H, 6.50.

In one cyclization run lasting only 4 min., there were obtained yields of 55% of "starting material," 2% of cyclized mixed acids, 18% of XVc, and 20% of XVIc.

Cyclization of Stobbe half-ester from 3,4,3',4'-tetramethoxybenzophenone. The cyclization was conducted with 49.9 g. of half-ester IVb, 18 g. of sodium acetate, and 280 ml. of acetic anhydride in the manner used on the pentamethoxy analog. Mixed acetates, however, were first dissolved in benzene and extracted with excess 10% aqueous sodium hydroxide (to give 2.1 g., 4% of "starting material"). Then, in this case, bulk separation of isomeric cyclization products was made on the acetates. Thus, concentration of the benzene solution and addition of ether gave a white solid which was recrystallized once from ethanol, yield 42.1 g. (80%), m.p. 168.5–170.5°. Recrystallization of a sample once from ethanol and twice from methanol gave prisms of *t-butyl 1-(3,4-dimethoxyphenyl)-4-acetoxy-6,7-dimethoxy-2-naphthoate* (XIIIb), m.p. 170–171.5°.

Anal. Calcd. for $C_{27}H_{30}O_8$: C, 67.20; H, 6.27. Found: C, 66.80; H, 6.22.

The benzene-ether mother liquor from isolation of XIIIb was evaporated to dryness. The residue was dissolved in methanol and further processing was conducted as for the mixed acetates from cyclization of the pentamethoxy analog. There were obtained 0.2 g. (0.5%) of mixed cyclized acids (soluble in bicarbonate); 5.1 g. (11%) of tan solid precipitated by carbon tetrachloride—identified as XIIIc by its infrared spectrum (*vide infra*); and 0.63 g. (1.3%) of residue from evaporation of the carbon tetrachloride solution, m.p. 110–120°. Recrystallization to constant m.p. of this final residue from methanol gave *t-butyl 1-(3,4-dimethoxyphenyl)-4-hydroxy-5,6-dimethoxy-2-naphthoate* (XIIc), obtained as needles, m.p. 125–127°.

Anal. Calcd. for $C_{25}H_{28}O_7$: C, 68.17; H, 6.41. Found: C, 67.93; H, 6.76.

Hydrolysis of XIIIb with aqueous ethanolic sodium hydroxide according to the procedure of Klemm and Lind[5] gave a tan product which was recrystallized from ethanol to give white prisms of *t-butyl 1-(3,4-dimethoxyphenyl)-4-hydroxy-6,7-dimethoxy-2-naphthoate* (XIIIc), m.p. > 217°C. (dec.), yield 91%. Additional recrystallizations of this product from ethanol and acetone gave a sample for microanalysis, immediate melting (with gas evolution) when inserted in a bath at 225° (but not at 221°).

Anal. Calcd. for $C_{25}H_{28}O_7$: C, 68.17; H, 6.41. Found: C, 68.49; H, 6.28.

A mixture of 4.40 g of XIIIc, 80 ml. of acetone, 2.1 g. of powdered potassium carbonate, and 1.5 g. of dimethyl sulfate was refluxed for 15 min., diluted sufficiently to dissolve all salts, refluxed 15 min. more, allowed to stand overnight, and warmed with aqueous sodium hydroxide. The solid precipitate was washed and recrystallized from methanol to give 2.3 g. (51%) of *t-butyl 1-(3-4-dimethoxyphenyl)-4,6,7-trimethoxy-2-naphthoate,* m.p. 168–183°. Recrystallization first from ethanol containing a few drops of concentrated aqueous sodium hydroxide and then from pure ethanol gave prisms, m.p. 176–177.5°.

Anal. Calcd. for $C_{26}H_{30}O_7$: C, 68.70; H, 6.65. Found: C, 68.68; H, 6.76.

Methylation of XIIIc was likewise accomplished with dimethyl sulfate and dilute aqueous sodium hydroxide at room temperature as well as by excess diazomethane in ether.

Hydrolysis of the hydroxy ester XIIIc by means of aqueous ethanolic barium hydroxide in a sealed bomb was conducted in the manner described by Klemm and Lind[5] except that the resultant solid was first washed with ether and then treated with concentrated hydrochloric acid. The resultant solid product was washed with water and recrystal-

lized from methanol to give 5.5 g. (63%) of *1-(3,4-dimethoxyphenyl)-4-hydroxy-6,7-dimethoxy-2-naphthoic acid* (XIIId), obtained as needles, m.p. 224–225°, λ_{max}^{EtOH} 227 mμ (log ε 4.50), 257 (4.64), 301 (3.97).

Anal. Calcd. for $C_{21}H_{20}O_7$: C, 65.61; H, 5.24. Found: C, 65.42; H, 5.49.

Pyrolyses of non-peri t-butyl hydroxynaphthoates. A sample (0.729 g.) of XIIIc was heated in a bath maintained at 205–208°. It showed gradual sintering and yellowing, followed by melting and the evolution of gas, and finally resolidification. After 15 min. the temperature was raised to 215° for a brief period and then heating was discontinued. The evolved gas (0.094 g., determined by loss in weight) gave no precipitate with aqueous barium hydroxide solution but decolorized bromine in carbon tetrachloride and reduced aqueous permanganate solution (calcd. loss of weight for isobutene: 0.093 g.). The residue, presumably crude hydroxynaphthoic acid XIIId, was nearly completely soluble in 5% aqueous sodium bicarbonate and melted at *ca.* 270°, with charring. When a molten sample of the preceding acid XIIId (m.p. 222–224°) obtained from barium hydroxide hydrolysis of XIIIc was seeded with this higher melting form the entire mass solidified and remelted at *ca.* 270°, with charring.

Pyrolysis of 5 g. of XIc at 190–200° under reduced pressure in a nitrogen atmosphere until bubbling stopped (12 min.), extraction of the product with 5% aqueous potassium bicarbonate, and acidification of the alkaline extract gave a quantitative yield of *1-(3-methoxyphenyl)-4-hydroxy-7-methoxy-2-naphthoic acid* (XId), m.p. 206–209.5°. Recrystallization from aqueous methanol gave prisms, m.p. 208–209.5°.

Anal. Calcd. for $C_{19}H_{16}O_5$: C, 70.36; H, 4.98. Found: C, 70.42; H, 4.90.

Pyrolysis of XVc at 215–225° for 15 min. and recrystallization of the resultant residue from methanol gave a 90% yield of prisms of *1-(3,4,5-trimethoxyphenyl)-4-hydroxy-6,7-dimethoxy-2-naphthoic acid* (XVd), n.p. 219–221.5°, raised to 221–222° on further recrystallization. The analytical sample was dried for 12 hr. at room temperature and 1 hr. at 80°.

Anal. Calcd. for $C_{22}H_{22}O_8 \cdot H_2O$: C, 61.10; H, 5.59. Found: C, 60.83; H, 5.78.

Further drying (at 130°) to constant weight gave the anhydrous acid.

Anal. Calc. for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35. Found: C, 63.57; H, 5.38.

Pyrolysis of VIIIc and recrystallization of the residue from ethanol gave *1-phenyl-4-hydroxy-7-methoxy-2-naphthoic acid* (VIIId), m.p. 276–278° alone or 275–278° on admixture with a sample of "isomer A" (m.p. 273–276°) prepared by Klemm and Largman.[4] Similar pyrolysis of VIc and recrystallization of the residue from aqueous methanol gave *1-(3-methoxyphenyl)-4-hydroxy-2-naphthoic acid* (VId), m.p. 208–210°, unchanged on admixture with a sample of "isomer B" (m.p. 208–209.5°) prepared by Klemm and Largman.[4] The identities of these two pairs of acids were also checked by infrared spectra.

Pyrolysis of peri t-butyl hydroxynaphthoates. When VIIc was heated at 195–200° for 15 min. (pyrolysis conditions for the isomeric VIc and VIIIc) it was recovered unchanged. A mixture of 0.95 g. of VIIc and 0.5 g. of 1-naphthol was heated at 200–220° for 15 min. and the residue was shaken with a two-phase mixture of aqueous sodium bicarbonate and ether. Acidification of the aqueous extract gave 0.75 g. (94%) of *1-phenyl-4-hydroxy-5-methoxy-2-naphthoic acid* (VIId), m.p. 203–205°, raised to 203.5–205° after two recrystallizations from methanol, λ_{max}^{EtOH} 236 mμ (log ε 4.60), 311 (3.96).

Anal. Calcd. for $C_{18}H_{14}O_4$: C, 73.46; H, 4.80. Found: C, 73.44; H, 4.75.

Similar pyrolysis of Xc and recrystallization of the bicarbonate-soluble product from aqueous acetone, benzene-ethanol, and methanol gave prisms of *1-(3-methoxyphenyl)-4-hydroxy-5-methoxy-2-naphthoic acid* (Xd), m.p. 179.5–183.5°.

Anal. Calcd. for $C_{19}H_{16}O_5$: C, 70.36; H, 4.98. Found: C, 69.88; H, 5.13.

Pyrolysis of 10 g. of XVIc with the aid of 1 g. of *p*-bromophenol at 190–210° gave 8.3 g. (94%) of *1-(3,4-dimethoxyphenyl) - 4 - hydroxy - 5,6,7 - trimethoxy - 2 - naphthoic acid* (XVId), m.p. 166–169°. Recrystallization from ethanol, methanol, and acetone gave prisms, m.p. 168–169°.

Anal. Calcd. for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35. Found: C, 63.61; H, 5.42.

Infrared spectra of t-butyl 1-phenyl-4-hydroxy-2-naphthoates Infrared absorption spectra in the region 3200 cm.$^{-1}$ to 3750 cm.$^{-1}$ (OH-stretching region) used for assignment of *peri* and non-*peri* structures to analytical samples of *t*-butyl 1-phenyl-4-hydroxy-2-naphthoates were obtained by means of a Perkin-Elmer Model 21 spectrophotometer[24] using a lithium fluoride prism. Samples were dissolved in dry, purified carbon tetrachloride (2.6–3.4 × $10^{-4}M$ solutions) and instrument settings were maintained constant for all spectra measured. Ten-centimeter matched cells with sodium chloride windows were used. Zero per cent transmission was measured by means of a glass shutter. Each spectrum was calibrated against the rotational fine structure of the 3-μ ammonia band. Spectral data are presented in Table I.

All other infrared spectral data were obtained with a Perkin-Elmer Model 137 spectrophotometer fitted with sodium chloride optics. Analyses of mixed hydroxynaphthoic acids from cyclization studies were made by spectral comparisons of samples thereof with synthetic mixtures of the pure acids derived from pyrolyses of the *t*-butyl esters. Various other compounds were identified by direct comparisons of infrared spectra of two different samples.

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