physical constants as reported by Knorr.[24] Compound 43 was prepared according to Michaelis.[25]

The preparation of compounds 15, 17, 20, 33, 34, 35, 53, and 54 are given below.

***n*-Propyl Benzoylpyruvate and Hydrazines. A.**—A solution of equimolar quantities of *n*-propyl benzoylpyruvate[26] (mp 63–64°) and hydrazine hydrate in *n*-propyl alcohol was heated on a steam bath for 0.5 hr to give 3(5)-phenyl-5(3)-carbo-*n*-propoxypyrazole (53), mp 117–118°.

Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.83; H, 6.16; N, 12.00.

B.—A solution of equimolar quantities of *n*-propyl benzoylpyruvate and methyl hydrazine in *n*-propyl alcohol was heated on a steam bath for 0.5 hr. The product was distilled by heating under reduced pressure to give 15 and 20 in the ratio of 3:1.

1-Methyl-3-phenyl-5-carbo-*n*-propoxypyrazole (15) boiled at 195° at 10 mm.

Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.49; H, 6.52; N, 11.30.

1-Methyl-5-phenyl-3-carbo-*n*-propoxypyrazole (20) boiled at 205° at 10 mm.

Anal. Found: C, 68.83; H, 6.90; N, 11.22.

Ethyl 1-(3,5-Dimethylpyrazolyl)acetate (Compound 33).—A solution of equimolar quantities of 3,5-dimethylpyrazole, sodium ethoxide and ethyl bromoacetate in ethanol was treated according to the method used by Jones[27] for the preparation of compound 34. The yield of 33, bp 135° at 15 mm, was very low.

5-Amino-1-methyl-3-phenylpyrazole (Compound 17).—Equimolar quantities of benzoyl acetonitrile and methyl hydrazine dissolved in ethanol was heated under reflux for 1 hr. The product was recrystallized from benzene–methylcyclohexane mixture, mp 129–131°. From the nmr data the material was assigned structure 17.

Anal. Calcd for $C_{10}H_{11}N_3$: N, 24.26. Found: N, 24.03.

In a similar procedure benzoyl acetonitrile and hydrazine hydrate gave 3(5)-amino-5(3)-phenylpyrazole (54), mp 123–125° (lit.[28] mp 125°).

1-Methylcarbamoyl-3,5-dimethylpyrazole (Compound 35).—A solution of 0.1 mole of 3,5-dimethylpyrazole, 0.1 mole of methyl isocyanate, and 0.5 g of triethylenediamine dissolved in 100 ml of dry dioxane was allowed to stand at room temperature for 4 days. The solvent was removed by evaporation and the residue was recrystallized from petroleum ether (bp 60–70°) to give a nearly quantitative yield of 35, mp 75° (lit.[29] mp 71°).

Acknowledgment.—Several of the compounds evaluated had been prepared in our laboratory previous to this study by Nelson R. Easton and associates. The nmr spectra were determined by L. Spangle and J. Klemm. We also wish to acknowledge helpful discussions with P. W. Landis, Kevin T. Potts, D. M. Grant, and J. C. Martin.

[24] L. Knorr and J. Macdonald, *Ann.*, **279**, 217 (1894).

[25] A. Michaelis and A. Lachwitz, *Ber.*, **43**, 2106 (1910).

[26] M. Freri, *Gazz. Chim. Ital.*, **68**, 612 (1938).

[27] R. G. Jones, M. J. Mann, and K. C. McLaughlin, *J. Org. Chem.*, **19**, 1428 (1954).

[28] O. Seitel, *J. Prakt. Chem.*, **58**, 129 (1898).

[29] H. J. Becker, *Rec. Trav. Chim.*, **34**, 187 (1915).

Synthesis of the 1,8-Naphthalic Anhydride Obtained by Degradation of Trimethylherqueinone B[1]

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Starting material for the successful synthesis of 7-methyl-2,3,4,5-tetramethoxy-1,8-naphthalic anhydride (**2**) was 3,4,5-trimethoxybenzoic acid. This acid was converted to its homolog, whose ester (**5**) was condensed with methyl crotonate to give the glutaric acid derivative, **6**. Cyclization of the substituted glutaric acid with polyphosphoric acid yielded the tetralone **7**, which has the oxygen function and the methyl group in the positions required for the synthesis. The route chosen for eventual introduction of carboxyl groups in the *peri* positions involved initial decarboxylation of tetralone **7** to yield 3-methyl-6,7,8-tetramethoxy-1-tetralone (**8**). Dehydrogenation yielded the corresponding naphthol **9**, which was methylated and subjected to reaction with diphenyloxalimide chloride. The resultant acenaphthenequinone, **10**, was readily oxidized with alkaline hydrogen peroxide to yield the desired 1,8-naphthalic anhydride **2**. The synthetic anhydride proved identical with that previously obtained by a degradative sequence from trimethylherqueinone B.

The copper-red pigment from *Penicillium herquei*, first reported by Stodola and co-workers,[2] was subsequently named herqueinone.[3] The herqueinone structure has proved so sensitive to rather deep-seated changes that some aspects of this structure remain uncertain. In contrast, the structure of one of the ethers of herqueinone,[4] designated trimethylherqueinone B, has been established with reasonable firmness. The structure assigned[5] to trimethylherqueinone B is that shown in formula **1**. The alicyclic features of the ring system were established by a combination of chemical and spectroscopic methods, while the structure of the basic naphthalene nucleus was assigned from isolation of the degradation product shown in formula **2**. Since the degradation anhydride was formulated to a major extent on the basis of spectral interpretations, verification by synthesis of this key structure is

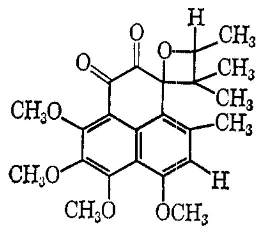
[1] This investigation was supported in part by a research grant (G-9766) from the National Science Foundation.

[2] F. H. Stodola, K. B. Raper, and D. I. Fennell, *Nature*, **167**, 773 (1951).

[3] R. H. Harman, J. Cason, F. H. Stodola, and A. L. Adkins, *J. Org. Chem.*, **20**, 1260 (1955).

[4] J. A. Gallaraga, K. G. Neill, and H. Raistrick, *Biochem. J.*, **61**, 456 (1955).

[5] J. Cason, J. S. Correia, R. B. Hutchison, and R. F. Porter, *Tetrahedron*, **18**, 839 (1962).



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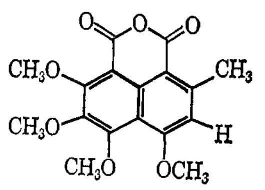

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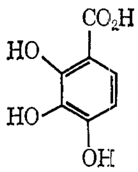
desirable. This synthesis is the subject of the present paper.

Since the degradation anhydride **2** is such a highly substituted 1,8-naphthalic anhydride, any synthetic approach depending on substitution in an available naphthalene derivative seems implausible. On the other hand, *vic*-trihydroxybenzene derivatives are available and should be useful starting materials. Pyrogallolcarboxylic acid (**3**) is readily obtained by a Kolbe–Schmitt reaction on pyrogallol,[6] while trimethylgallic acid (**4**) is commercially available. Convenient utilization of **3** as starting material for the projected synthesis requires a Friedel-Crafts or related reaction with the methyl trimethoxybenzoate. No difficulty in securing such a reaction was anticipated, for compounds such as *o*-nitroanisole have been acylated,[7] although in poor yield. There was developed a satisfactory method for converting **3** to the triether ester, using dimethyl sulfate and sodium methoxide in methanol; however, all efforts to acylate methyl 2,3,4-trimethoxybenzoate failed. The acylation procedures which were investigated included succinic anhydride or β-methoxycarbonylpropionyl chloride with aluminum chloride, methyl hydrogen succinate with polyphosphoric acid, and β-methoxycarbonylpropionyl chloride with ferric chloride. The last combination was used in the hope that this Lewis acid would not complex so strongly with the ester as does aluminum chloride. Methyl 2-furoate was acylated successfully with ferric chloride,[8] while the reaction using aluminum chloride failed.



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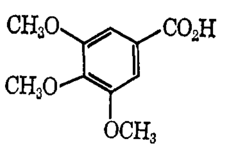

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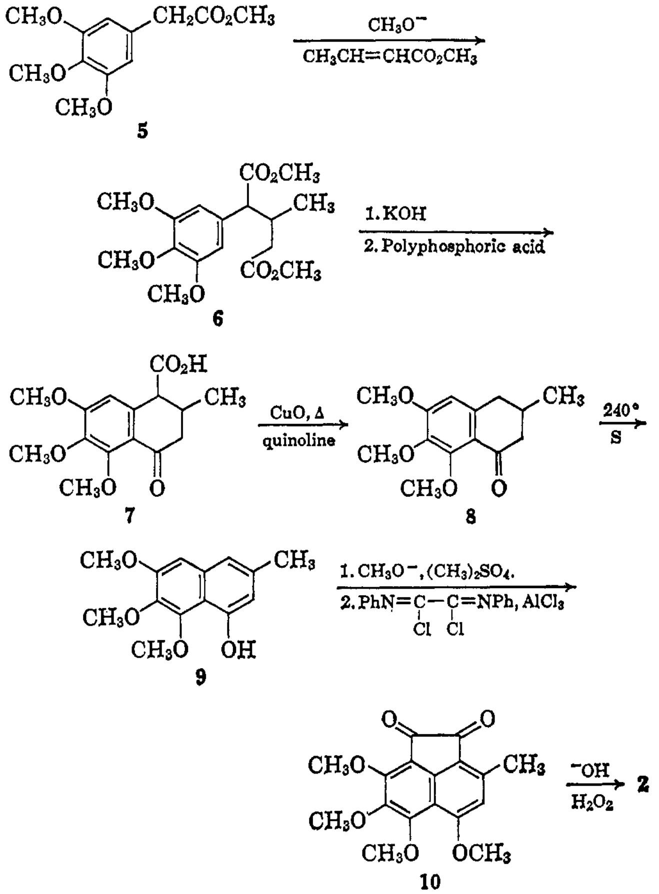
In the unsuccessful acylations just described, principal products recovered were starting ester ether and methyl 2-hydroxy-3,4-dimethoxybenzoate. The ratio of the latter increased under more strenuous conditions. Selective demethylation adjacent to a carbonyl group has been previously reported.[9] Presumably, this process depends on formation of a cyclic complex involving the carbonyl, the Lewis acid, and the ether oxygen. With ferric chloride, demethylation was not so specific for the 2-methoxy; an additional monohydroxy compound was isolated.

In contrast with methods depending on **3** as starting material, compound **4** was utilized in a successful synthesis. The method of Munch-Petersen[10] for conjugated addition of benzylmagnesium chloride to *sec*-butyl crotonate will give a side chain with the desired substitution; however, this method suffers from the requirement of excess of Grignard reagent. Therefore, an alternative approach was used, in which 3,4,5-trimethoxybenzoic acid **4** was converted to its homolog, and the homologous ester **5** was condensed with methyl crotonate. The Michael addition product, **6**, was converted to 3-methyl-6,7,8-trimethoxy-1-naphthol (**9**) according to Scheme I, which is patterned after the analogous conversion published for methyl 3,4-dimethoxyphenylacetate.[11]

SCHEME I



Diester **6** and keto acid **7** were obtained as mixtures of diastereoisomers, which were used for subsequent steps in the synthesis; however, it was possible to separate and characterize one pure isomer of **6**. A pure isomer of keto acid **7** could not be separated, but the stereoisomeric mixture gave good analytical figures and the infrared spectrum was that expected for the structure. Tetralone **8** also gave crystalline material of broad melting range, in spite of the fact that geometric isomerism appears impossible. This behavior was eventually established as nothing more than polymorphism. One pure polymorph, mp 89.0–90.5°, was secured, while the best sample of the other form melted at 94–97°. The

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[6] St. von Kostanecki, *Ber.*, **18**, 3202 (1885).

[7] F. Stockhausen and L. Gatterman, *ibid.*, **25**, 3521 (1892).

[8] H. Gilman and N. O. Calloway, *J. Am. Chem. Soc.*, **55**, 4197 (1933).

[9] P. C. Mitter and S. De, *J. Indian Chem. Soc.*, **16**, 35 (1939); P. C. Mitter and L. K. De, *ibid.*, 16, 199 (1939).

[10] J. Munch-Petersen, *J. Org. Chem.*, **22**, 170 (1957); *Acta Chem. Scand.*, **12**, 967 (1958). In connection with the present investigation, the nmr spectrum of the product from benzylmagnesium chloride and *sec*-butyl crotonate was examined. This verified the structure as that previously reported, where addition has occurred at the side-chain position rather than in the ring to give an *o*-tolyl derivative.

[11] J. D. Edwards, Jr., and J. L. Cashaw, *J. Am. Chem. Soc.*, **76**, 6188 (1954).

two forms were interconvertible and had identical infrared and nmr spectra, as well as the same behavior in gas chromatography.

Fortunately, no methyl migration occurred during the dehydrogenation of tetralone **8**, at the relatively low temperature possible with sulfur. The nmr spectra of both naphthol **9** and its methyl ether (each of sharp melting point) showed the three aromatic hydrogens as sharp peaks except for fine structure due to long-range coupling. Any structure resulting from methyl migration would have aromatic hydrogens on adjacent carbons.

An obvious synthetic route from keto acid **7** to the desired anhydride **2** would involve conversion of **7** to 2-methyl-4,5,6,7-tetramethoxynaphthoic acid, followed by homologation and cyclization to the corresponding acenaphthenone. In other syntheses in this laboratory, however, preparation of acenaphthenones by cyclization has proved quite unsatisfactory; therefore, the alternate route proceeding through the acenaphthenequinone **10** was chosen. Condensation of 6-methyl-1,2,3,8-tetramethoxynaphthalene with diphenyloxalimide chloride proved to give a 42% yield of quinone **10**, more satisfactory than normal for this reaction. The relatively good yield in the present instance may be ascribed to the unavailability of unhindered α positions for intermolecular condensation.

The synthetic anhydride (**2**) proved to have the same melting point and infrared spectrum as the anhydride which had been obtained from degradation,[5] and there was no depression in melting point on mixing the two samples. Thus, the orientation of substituents in the degradation anhydride, which was deduced by spectral interpretations, has been verified.

Experimental Section[12]

2,3,4-Trihydroxybenzoic Acid (3).—A mixture of 50 g of commercial pyrogallol (mp 43–46°), 220 g of potassium bicarbonate and 440 ml of water was heated under reflux for 1.5 hr. After the cooled and acidified solution had been allowed to stand overnight at 0° there crystallized 33 g (49%) of gray needles (dried *in vacuo* at 70°), mp 195–197° dec. The yield appeared to be improved slightly if a rapid stream of carbon dioxide was passed through the solution during reflux.

Normally, crude acid was used for methylation; however, purification of the material obtained as above was readily effected by charcoal treatment in about 300 ml of boiling water and crystallization at 0°. This treatment yielded 18.4 g of white needles, mp 200–202°, lit.[6] mp 200° dec.

Methyl 2,3,4-Trimethoxybenzoate.—Although methylation was carried out with dimethyl sulfate in presence of methanolic potassium hydroxide, aqueous potassium bicarbonate, and aqueous sodium hydroxide, the yield was much better when methanolic sodium methoxide was utilized.

In a typical run, a suspension of 16 g of crude 2,3,4-trihydroxybenzoic acid in a solution of 20.4 g of commercial sodium methoxide in 185 ml of absolute methanol was stirred as there was added dropwise, over a period of about 15 min, 47.5 g of distilled dimethyl sulfate. Gentle reflux was maintained during the addition, at the end of which the very dark reaction mixture was at about pH 8. Next, dimethyl sulfate (71 g) and a solution of 30.5 g of sodium methoxide in 150 ml of absolute methanol were added concurrently during about 25 min in a ratio of about 1:3 as gentle reflux was maintained. At the end of the addition, the pH of the solution was about 8 and remained there during a subsequent hour of reflux. The cooled reaction mixture was filtered with suction, and the precipitate was washed with methanol and discarded The filtrate was diluted with about 2.5 l. of water and extracted with 400 ml of ether, then extracted four times with 200-ml portions of ether. The combined ether layers were extracted with four 20-ml portions of cold 1 *N* aqueous sodium hydroxide, washed with four portions of cold water, and dried. Removal of solvent left 7.5 g (35%) of crude ether ester as a yellow oil, which was purified as described below.

The alkaline extract from the above ether ester was acidified and cooled to yield 1.92 g of tan crystals, mp 73–79°. Recrystallization from ethanol yielded 1.08 g of white crystals, mp 75–78°; lit. (for methyl 3,4-dimethoxy-2-hydroxybenzoate)[13] mp 75–78°. Infrared absorption for this compound was at 3.14, 5.96, and 6.17 μ, while the nmr spectrum was that expected[14] for the designated compound. Remethylation by the above-described procedure of 15.2 g of the partially methylated material yielded 13.4 g of the crude triether ester.

For purification of the crude methyl 2,3,4-trimethoxybenzoate, a 39.6-g sample was distilled at 7-mm pressure through a 2-ft Podbielniak column containing a simple wire spiral. In addition to a residue of 1.2 g of black tar, three fractions were obtained: (a) 791 mg, bp 98.5–100°; (b) 306 mg, bp 145–147.5°; (c) 36.6 g, bp 147.5–149°. The first fraction crystallized on scratching, and after recrystallization from ethanol–water had mp 43–46° (no depression on admixture with authentic pyrogallol trimethyl ether). Gas chromatography of the second fraction (column 10 ft × $^3/_8$ in., packed with 20% GE-SF-96 silicone on Chromosorb, temperature 186°, helium flow rate 102 cc/min) showed it to be a mixture of three compounds: 40% pyrogallol trimethyl ether (retention time 7.6 min), 20% unidentified substance (retention time 13.2 min), and 40% of the desired ester (retention time 22.8 min). The third fraction showed only a single peak in gas chromatography of the retention time of the desired ester, infrared absorption at 5.79 μ (no hydroxyl absorption), lit.[15] bp 281°.

Attempted Acylation of Methyl 2,3,4-Trimethoxybenzoate.—Among the various methods of acylation that were attempted, one of the more strenuous involved conditions similar to those used[7] for acylation of *o*-nitroanisole. For this purpose, 2.00 g of the ether ester and 1.50 g of β-methoxycarbonylpropionyl chloride [bp 69–71° (4 mm), containing about 5% dimethyl succinate] were dissolved in 20 ml of carbon disulfide (distilled from phosphorus pentoxide). This solution was stirred at room temperature as there was added over a period of 10 min 3.83 g of anhydrous aluminum chloride. The reaction mixture was then heated under reflux for 2 hr, at the end of which time ice–water and hydrochloric acid were added, and the mixture was worked up by ether extraction. Acidic products were removed by three extractions with cold aqueous sodium hydroxide solution (bicarbonate failed to extract any acid).

The extracted acidic material, 1.03 g (54% yield), melted at 73–77° and had the infrared spectrum of methyl 3,4-dimethoxy-2-hydroxybenzoate. One crystallation from ethanol yielded 722 mg, mp 75–78°, showing no depression in melting point on admixture with samples isolated from methylation of the trihydroxy acid.

Neutral material recovered after extraction of acids amounted to 374 mg (20% recovery) of a yellow oil exhibiting an infrared spectrum identical with that of the starting ether ester.

In a run of the same size with *ferric chloride as catalyst*, and with a reaction time of 21 hr at room temperature, there was recovered only 178 mg of starting ether ester. The yellow-orange oil extracted with sodium hydroxide, 1.07 g, contained at least three compounds which were not separated by adsorption chromatography on Woelm alumina, activity III, except for a first fraction of 33 mg of methyl 2-hydroxy-3,4-dimethoxybenzoate. By gas chromatography (column as in preceding section, temperature 209°, helium flow rate 88 cc/min) there were separated three compounds (ratio of 1:7:6) whose retention times were, respectively, 13.6, 15.9, and 22.9 min. The compound of shortest retention time was identified as methyl 2-hydroxy-3,4-dimethoxybenzoate.

The compound collected in gas chromatography at 15.9 min had mp 88–91°, after crystallation from benzene–hexane, while an analytical sample had the constant melting point of 88.5–89.5°.

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[12] Melting points are corrected. Infrared spectra were recorded on a Perkin-Elmer Infracord; nmr spectra, determined in about 10% solution in carbon tetrachloride, were recorded on a Varian A-60 instrument, with TMS as internal reference. Microanalyses were by the Microanalytical Division, Department of Chemistry, University of California, Berkeley.

[13] J. Herzig and J. Pollak, *Monatsh.*, **25**, 512 (1904).

[14] Nmr data to which reference is made in this paper are recorded in the Ph.D. Dissertation of D. M. Lynch, University of California, Berkeley, 1964.

[15] W. Will, *Ber.*, **21**, 2024 (1888).

Anal. Calcd for $C_{10}H_{12}O_5$: C, 56.6; H, 5.7. Found: C, 56.0; H, 5.5.

Infrared absorption was at 2.86 and 5.84 μ, while the nmr spectrum (in $CDCl_3$) showed Ar–H, two at τ 2.35 and 2.59 (J = 9 cps); Ar–OH, one at τ 4.23; Ar–OCH_3, six at τ 6.05; and Ar–CO_2–CH_3, three at τ 6.08. These data leave little doubt that this compound is methyl hydroxydimethoxybenzoate, where hydroxyl is at either the 3 or 4 position. Distinction between these isomers was not attempted since the corresponding acids have nearly the same melting points.[16]

The compound of longest retention time (analytical sample from benzene–hexane, mp 106–107°) was not the expected third isomeric hydroxydimethoxy ester, but an unidentified compound containing a higher ratio of oxygen (*Anal.* Found: C, 49.0, 48.9; H, 4.6, 4.8.). This compound had infrared absorption at 2.85 and 5.79 μ, while the nmr spectrum (in $CDCl_3$) showed only a singlet (ratio of 1) at τ 3.35, and a singlet with a shoulder (ratio of 9) at τ 6.06, with no resonance lines in the aliphatic region.

Methyl 3,4,5-Trimethoxyphenylacetate (5).—Commercial 3,4,5-trimethoxybenzoic acid (mp 171.5–5–173°) was reduced with lithium aluminum hydride in tetrahydrofuran, according to the procedure which has been published.[17] The distilled alcohol was converted to the chloride according to the procedure of the same investigators,[17] using thionyl chloride in presence of dimethylaniline. Distillation of the chloride [bp 141–142° (2.6 mm)] gave a white solid, mp 60–63°, lit.[17] mp 60–61°. This compound showed infrared absorption at 3.38, 3.44, 3.58, and 6.30 μ. Conversion to the nitrile was adapted from a procedure which has been applied to anisyl chloride.[18] When there were used 29.6 g of 3,4,5-trimethoxybenzyl chloride, 10.05 g of sodium cyanide, and 1.37 g of sodium iodide in 70 ml of dried acetone, there was obtained after one crystallization from benzene-hexane a 24.7-g yield (88%), mp 69–74°. Efforts at further purification by crystallization were without avail. Test with silver nitrate indicated that the nitrile was contaminated with the benzyl chloride. By sublimation at 3.5 mm, a small sample of pure nitrile was obtained as white fernlike crystals, mp 78–80°, weak absorption in the infrared at 4.45 μ which is characteristic of nitriles, lit.[19] mp 78°.

Hydrolysis of 3,4,5-trimethoxybenzyl cyanide in aqueous solution of sulfuric and acetic acids failed (decomposition to tar), but concentrated hydrochloric acid, in the manner that has been reported for a dimethoxybenzyl cyanide,[20] was satisfactory. For this purpose, a mixture of 12.4 g of once-crystallized nitrile and 50 ml of concentrated hydrochloric acid was stirred at room temperature for 3 hr; then the dark solution was stirred an additional 2 hr at about 50°. Finally, 175 ml of water was added to the reaction mixture, and heating was continued under reflux for 7 hr. At reflux, a yellow solution resulted, with a little dark liquid on the bottom (possibly the chloride). The cooled reaction mixture was extracted with four portions of ether (200 ml, then 100 ml), and the combined ether extracts were extracted with four portions of 5% aqueous bicarbonate (50 ml, then 30 ml). Removal of solvent from the washed ether solution left 0.88 g of yellow-red tar whose infrared spectrum suggested the presence of the benzyl chloride and a carboxylic acid. Acidification and work-up of the alkaline extracts yielded 9.35 g (69%) of white crystals, mp 117.5–120.5°, lit.[21] mp 120°. Infrared absorption in chloroform was at 5.87 μ, with typical carboxylic acid absorption above 3 μ.

A 23.6-g sample of the phenylacetic acid was esterified by heating under reflux for 2 hr with a solution of 2.2 ml of concentrated sulfuric acid in 64 ml of methanol. Dilution of the reaction mixture with 320 ml of water, extraction with ether, and removal of acidic material by bicarbonate extraction yielded 21.2 g of an amber oil. Distillation yielded 19.2 g (77%) of colorless oil, bp 157–158° (2.3 mm), lit.[22] bp 172–182° (10 mm); infrared absorption was at 5.78 μ.

Dimethyl 3-Methyl-2-(3,4,5-trimethoxyphenyl)glutarate (6).—To a solution of 1.78 g of sodium in 20 ml of anhydrous methanol, in an atomosphere of nitrogen, there was added at room temperature a mixture of 18.65 g of methyl 3,4,5-trimethoxyphenylacetate and 8.34 g of distilled (bp 120–123°) methyl crotonate. After the reaction mixture had been heated under reflux with stirring for 12 hr, the dark mass was cooled to room temperature and added to a stirred solution of 9.4 ml of glacial acetic acid in 175 ml of water. Work-up by ether extraction, washing with bicarbonate solution and water, then removal of solvent, yielded 15.8 g of yellow oil that slowly crystallized. A single recrystallization from benzene–hexane gave 13.5 g (51%) of the glutaric ester of mp 51–79°. After several recrystallizations, there was isolated one diastereoisomer of mp 83.5–84.5°.

Anal. Calcd for $C_{17}H_{24}O_7$: C, 60.0; H, 7.1. Found: C, 60.2; H, 7.0.

Infrared absorption was at 5.82 μ, and the nmr spectrum[14] showed the number of hydrogens, locations, and coupling expected for the structure.

The bicarbonate extracts from the above product contained 7.6 g of a viscous oil whose infrared spectrum suggested a mixture of hydrolyzed starting material and product; it was not further investigated.

4-Carboxy-3-methyl-6,7,8-trimethoxy-1-tetralone (7).—Ester 6 (13.5 g) was hydrolyzed by heating under reflux for 6 hr with a solution of 13.5 g of potassium hydroxide pellets in 85 ml of water. Filtration of the nearly homogeneous reaction mixture was followed by acidification and ether extraction, then removal of solvent to yield 12.7 g of a viscous oil which could not be induced to crystallize. Infrared absorption was at 5.89 μ.

To the crude glutaric acid (12.7 g) was added, with stirring at 70°, 95 g of polyphosphoric acid which had been heated to about 70°. After the reaction mixture had been stirred for 25 min at about 70° it was poured on 350 g of crushed ice. The viscous reaction complex was broken up by prolonged working by hand with a stirring rod; then the product was extracted with three 100-ml portions of chloroform. The chloroform extracts were extracted with three 50-ml portions of 5% aqueous bicarbonate solution, then water, and finally dried. Removal of chloroform left only a trace of dark residue. Acidification of the alkaline extracts yielded an oil which could be induced to crystallize. After standing overnight in a refrigerator, there was collected by suction filtration 7.13 g (61%) of white keto acid **7**, mp 151.5–169°. A sharp-melting isomer could not be secured by crystallization; material of mp 175–182° was used for analysis.

Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.2; H, 6.2. Found: C, 61.05; H, 6.05.

In the infrared spectrum, the acid has typical carboxyl absorption above 3 μ and bands at 5.88 (carboxyl) and 5.99 μ (aromatic carbonyl).

3-Methyl-6,7,8-trimethoxy-1-tetralone (8).—A mixture of 3.0 g of keto acid **7**, 32 mg of cupric oxide, and 5 ml of distilled quinoline [bp 112–113° (16 mm)] was heated at 200° for 1 hr. The cooled reaction mixture was added to 190 ml of 1 N hydrochloric acid, and the product was extracted with three 70-ml portions of chloroform. The combined chloroform extracts were washed with aqueous bicarbonate, 1 N hydrochloric acid, and water, then dried. Removal of solvent left 3.4 g of a dark red oil. Acidification of the bicarbonate extract yielded no product.

The crude oil, in 5 ml of benzene, was applied to a column of 90 g of Woelm alumina, activity III, and eluted with 70 ml of 50% acetone-benzene. A dark red band remained at the top of the column as a dark yellow band was eluted. Removal of solvent from the eluent yielded 2.4 g of a yellow oil which crystallized readily. Recrystallization from diethyl ether yielded 1.7 g of light amber crystals of mp 87–96°. A second crop, obtained by concentration of the mother liquor, was recrystallized to yield an additional 166 mg of mp 87–90° (68% total yield).

The polymorphic character of tetralone **8** was demonstrated by its behavior in melting and crystallization. When material initially melting at 87–90° was heated to 99°, then cooled rapidly until crystallization set in, the remelting point was 88–91°. Another sample treated similarly remelted at 88–90°, but one sample recovered from a dehydrogenation reaction (see below) melted at 93–97°. When this latter material was used to seed a molten sample at 86°, the resultant crystalline material melted at 94–97°. The infrared absorption of the samples with different melting points were identical, with carbonyl absorption at 6.02 μ, while material of the broadest melting point gave one sharp

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(16) E. Pacsu, *Ber.*, **56**, 407 (1923); D. Caunt, W. D. Crow, and R. D. Haworth, *J. Chem. Soc.*, 1313 (1951).

(17) N. L. Drake and W. B. Tuemmler, *J. Am. Chem. Soc.*, **77**, 1206 (1955).

(18) K. Rorig, J. D. Johnston, R. W. Hamilton, and T. J. Telinski, *Org. Syntheses*, **36**, 50 (1956).

(19) A. Dornow and G. Petsch, *Arch. Pharm.*, **285**, 323 (1952).

(20) W. Wenner, *J. Org. Chem.*, **15**, 548 (1950).

(21) J. Hadacek, J. Michalsky, and L. Macholan, *Chem. Listy*, **49**, 271 (1955).

(22) F. W. Semmler, *Ber.*, **41**, 1919 (1908).

peak in gas chromatography. Material of mp 88–90° was submitted for analysis.

Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.2; H, 7.25. Found: C, 67.5; H, 7.2.

In the ultraviolet spectrum, the tetralone showed λ_{max}, in mμ (ε), as follows: 219 (sh) (18,400), 229 (19,000), and 277 (15,800). The nmr spectrum was that expected,[14] with the three aromatic methoxyls at τ 6.18, 6.24, and 6.28.

3-Methyl-6,7,8-trimethoxy-1-naphthol (**9**).—An intimate mixture of 925 mg of tetralone **8** and 239 mg of sulfur was heated in a nitrogen atmosphere at 235–237° for 30 min. A solution of the cooled product in 175 ml of ether was filtered to remove a trace of black material, then extracted with three 30-ml portions of Claisen's alkali (aqueous alkali did not extract the phenol). Acidification of the alkaline extract and work-up *via* ether extraction yielded 0.6 g of a dark oil which was applied to 47 g of Woelm alumina, activity III, in dry benzene solution. Elution with about 95 ml of benzene washed a yellow-orange band through the column. The eluent yielded 0.5 g of orange-red oil which was sublimed at 90° and 1-mm pressure. After about 15 hr, 387 mg of sublimate had been collected. Crystallization from hexane yielded 361 mg (39%) of white prisms, mp 81–83°.

Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.7; H, 6.5. Found: C, 67.4; H, 6.6.

In the infrared spectrum, hydroxyl absorption was at 3.00 μ. In the ultraviolet, λ_{max}, in mμ (ε), were as follows: 228 (37,000), 247 (45,800), and 305 (4400). In the nmr spectrum, the phenolic hydrogen was at τ 0.76, the three aromatic hydrogens were in singlets at τ 3.28 and 3.38 and a doublet at 3.62 (J = 2.5 cps), while the methoxyl hydrogens were at τ 5.95, 6.16, and 6.21 and the methyl hydrogens were at τ 7.68.

6-Methyl-1,2,3,8-tetramethoxynaphthalene.—To a stirred solution of 611 mg of naphthol **9** and 135 mg of sodium methoxide in 4 ml of methanol was added, during about 1.5 min, 0.33 g of distilled dimethyl sulfate. Next, 0.46 g of dimethyl sulfate and a solution of 200 mg of sodium methoxide in 4 ml of methanol were added concurrently in a ratio of about 1:11, during about 3 min. After the resultant solution had been heated under reflux for about 1 hr it was cooled and added to 80 ml of water. The aqueous solution was extracted with three 20-ml portions of ether, and the combined ether extracts were extracted with three 10-ml portions of Claisen's alkali, followed by two 10-ml portions of water. Removal of solvent from the ether phase left 244 mg of light yellow oil which was crystallized from ether–pentane to yield 196 mg of yellow crystals, mp 81–87°. Recrystallization gave 169 mg of white crystals, mp 85–88°.

From the Claisen's alkali extract was recovered 315 mg of a yellow-orange oil whose infrared spectrum indicated starting naphthol. Remethylation by the same procedure and a similar work-up yielded 236 mg of crude starting material and 44 mg of white crystals of tetramethoxy compound, mp 85–88° (total yield, 39%). Recrystallization gave an analytical sample of mp 87–89°.

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.7; H, 6.9. Found: C, 68.3; H, 7.0.

The hydroxyl and carbonyl regions of the infrared spectrum were clear, and there was aromatic absorption at 6.18, 6.23, and 6.37 μ. The nmr spectrum[14] was that expected for the structure, with singlet aromatic hydrogens at τ 3.13, 3.37, and 3.62.

8-Methyl-3,4,5,6-tetramethoxyacenaphthenequinone (**10**).—In 2.5 ml of dry benzene was dissolved 200 mg of 6-methyl-1,2,3,8-tetramethoxynaphthalene and 212 mg of diphenyloxalimide chloride[23] (mp 116–118°). This solution was added during about 1 hr to a stirred suspension of 103 mg of finely pulverized technical aluminum chloride in 2 ml of dry benzene. The resultant dark mixture was stirred overnight, then poured on 5 g of ice. After 0.3 ml of concentrated hydrochloric acid had been added, the benzene was indirectly steam distilled. The gummy precipitate which separated from the cooled distillation residue was crystallized from 95% ethanol to give 77 mg of orange needles, mp 193–196°. A second crop of 29 mg was recrystallized to give an additional 23 mg, mp 193–196° (total yield, 42%). A final recrystallization yielded material of mp 197–199°.

Anal. Calcd for $C_{17}H_{16}O_6$: C, 64.6. Found:[24] C, 64.4.

Quinone **10** displayed a single strong carbonyl band in the infrared at 5.84 μ, in contrast with unsubstituted acenaphthenequinone which has a weak band at 5.63 μ and a strong one at 5.77 μ. The ultraviolet spectrum of quinone **10** is quite similar to that of the unsubstituted quinone except for a small shift to longer wavelengths. For quinone **10**, λ_{max}, in mμ (log ε), were 222 (4.39), 255 (5.13), 278 (4.13), and 335 (3.81).

7-Methyl-2,3,4,5-tetramethoxy-1,8-naphthalic Anhydride (**2**).—A condensation identical with that described above was carried out, and the gummy solid obtained as the initial product after steam distillation of benzene was added to 20 ml of 95% ethanol containing 6.3 ml of 4 N sodium hydroxide. To this suspension was added with swirling 6.3 ml of 30% hydrogen peroxide solution, whereupon a part of the solid dissolved. This reaction mixture was allowed to stand at room temperature for 30 min with occasional shaking, after which there was removed by filtration 32 mg of dirty white solid, mp 252–257° (no depression on admixture with oxanilide).

Acidification of the filtrate with concentrated hydrochloric acid and dilution with water gave a yellow-brown precipitate which was recrystallized from 95% ethanol. There separated 33 mg (15% from the methyltetramethoxynaphthalene) of light yellow needles, mp 207.0–208.5°. An authentic sample of the degradation anhydride[5] had mp 206–208°, and the melting point of the mixture of the two was unchanged. The infrared spectra of the two samples were identical in all respects.

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(23) This reagent was prepared by addition of 21.8 g of phosphorus pentachloride to a swirled suspension of 10 g of oxanilide in 33 ml of dry toluene. After this mixture had been heated under reflux for 3 hr, 22 ml of toluene was distilled slowly; then the residual solution was allowed to cool. The dark yellow crystallizate which separated was recrystallized from hexane to yield 4.54 g (40%) of yellow crystals, mp 116–118°. R. Bauer [*Ber.*, **40**, 2650 (1907)] reported mp 115°.

(24) Considerable difficulty was experienced in securing accurate analytical values for this compound, using classical methods of combustion analysis. Carbon values were usually more than 0.5% low. We are indebted to Dr. C. W. Koch of this department for the reported analysis, which was performed by a method depending on combustion in a sealed tube and volumetric determination of combustion products. The method is described by C. W. Koch and E. Jones, *Mikrochem. Acta*, **4**, 734 (1963).