[Contribution from the Chemistry Department of Boston University]

A DIMER OF METHYLENEDIOXYBENZENE[1]

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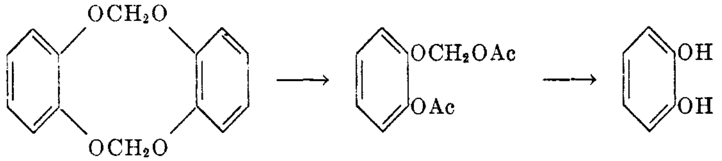
The reaction of catechol, alkali, and methylene chlorobromide leads not only to methylenedioxybenzene, but also to three minor products. In this paper an account is given of the nature of one of these products, a solid melting with decomposition at 261.6–262.6°.

The analytical figures for this material together with the Rast molecular weight determination served to fix the molecular formula as $(C_7H_6O_2)_2$, and thus to show that a dimer of methylenedioxybenzene was at hand. Cleavage experiments, as described below, led to the assignment of structure I to the dimer.

Treatment of the material with phosphorus pentachloride, according to the method of Barger (1) for the opening of the methylenedioxybenzene ring, afforded catechol, isolated as the dibenzoate. Although this result established the presence in the dimer of the unsubstituted catechol residue yet, because the yield of catechol was less than one mole per mole of starting material, no conclusion could be drawn concerning the presence of *two* such residues. Since acetic anhydride in the presence of zinc chloride is known to cleave ether linkages (2), it was thought likely that this reagent pair would act similarly on acetal linkages in the dimer. When the experiment was carried out, cleavage did occur but, instead of the expected diacetate of catechol, a different product was obtained.



I

II

Taking into account its mode of formation, its carbon and hydrogen content, and the fact that it could be hydrolyzed with alkali to catechol, it is difficult to write any structure for this cleavage product other than that of 1-acetoxy-2-acetoxymethoxybenzene (II). The derivation of a product having structure II under the cleavage conditions employed implies the presence of structural unit III in the starting material. Furthermore, because more than one mole of II was produced, this structural unit (III) must appear more than once and, accordingly,

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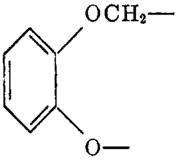
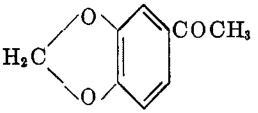
assignment of the ten-membered ring structure, I, to the dimer is directly indicated.[2]



III



IV

Attempts were made to prepare 1-acetoxy-2-acetoxymethoxybenzene (II) for comparison purposes by treating methylenedioxybenzene monomer with acetic anhydride and zinc chloride. The desired conversion appeared to be reasonable and straight-forward—particularly in the light of the analogous reaction of the dimer. However, no cleavage to compound II was observed. Instead, nuclear acetylation occurred with the formation of 3,4-methylenedioxyacetophenone (IV).[3]

Although this difference in behavior was not anticipated, consideration of the stereochemistry and the resonance possibilities in the monomer and in the dimer suggested a plausible explanation which is given below. The explanation received independent support from the differences in the ultraviolet absorption spectra of the two compounds.

Inspection of scale models of structure I shows that the molecule can assume a number of configurations all of which are strain-free, but none of which has the benzene rings and the bridge methylene groups in the same plane. The absence of coplanarity should result in damping of normal resonance coupling between the benzene ring and the attached oxygen atom — for when the valence bond from the oxygen to the methylene carbon does not lie in the plane of the ring, the p-orbital of the oxygen and the π-orbitals of the ring cannot be parallel and hence cannot be oriented for maximal interaction (4). As a consequence, the distribution of electrons from oxygen to the ring is, to a greater or lesser extent, hindered. On the other hand, in the rigidly planar methylenedioxybenzene monomer molecule no such damping effect is operative, and there is no steric restriction on the movement of the electrons from oxygen into the benzene ring. Keeping the fact in mind that these steric and resonance factors apply not only to the monomer and dimer molecules but also to the transition states for electrophilic attack on the ring or on the oxygen, the following conclusions may be drawn: (a) the monomer, with a relatively low electron density on the oxygen and a greater electron availability in the ring, would be attacked by positively charged acetylium ion[3] preferentially in the ring, with formation of compound

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[2] A report by K. Fuchs, appearing as a footnote in a paper by Mosettig and Jovanović (3), mentions the production of "dibrenzkatechin-dimethylenäther" in the reaction of chloromethyl sulfate with sodium catecholate. Quite possibly this is a reference to the same dimeric material.

[3] Burton and Prail, *J. Chem. Soc.*, 726 (1951) reported a similar reaction in the acetylation of anisole to p-methoxyacetophenone with acetic anhydride-zinc chloride.

IV, whereas (b) the dimer, with a relatively high electron density on the oxygen and a relatively low electron availability in the benzene ring, would be attacked preferentially on the oxygen (5) with subsequent formation of compound II.

If, in the dimer and the monomer, a significant difference does exist in degree of electronic interaction of the benzene rings and the substituent oxygen atoms, the absorption of the two compounds in the ultraviolet should be correspondingly different. This is indeed the case. Inspection of Fig. 1 shows that both the wave length and the intensity of the absorption maxima for the dimer (λ_{max} 269 mμ, ϵ 2495 and 275 mμ, ϵ 2330)[4] are lower than the corresponding values for the monomer (λ_{max} 283 mμ, ϵ 3300)[5] Therefore, inasmuch as a decrease in the in-

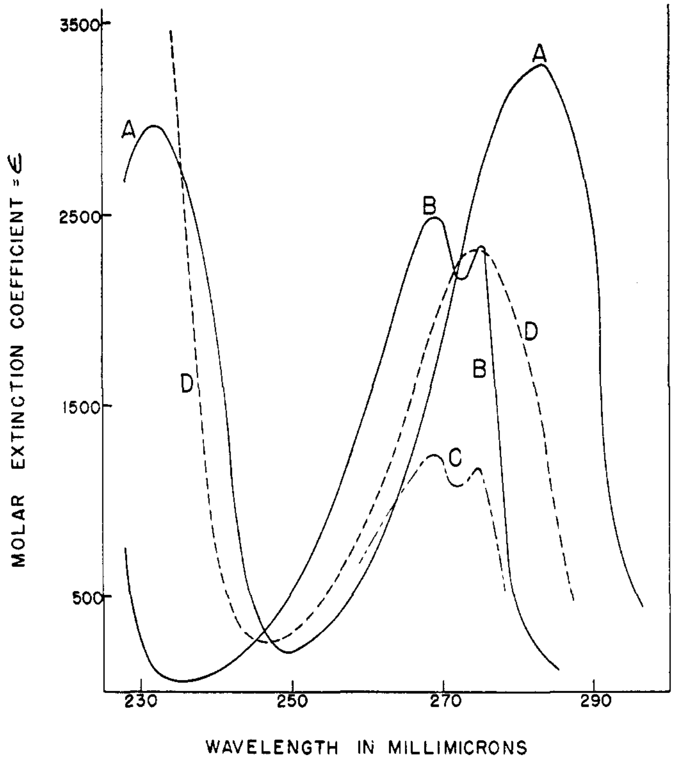

FIG. 1. ULTRAVIOLET SPECTRA. Curve A: methylenedioxybenzene (5 × 10^{-4} M in ethanol). Curve B: methylenedioxybenzene dimer (I) (2.5 × 10^{-4} M in ethanol). Curve C: plotted with ordinates one-half those of curve B (See footnote 5). Curve D: veratrole (5 × 10^{-4} M in ethanol).

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[4] The origin of the double absorption peak in the dimer is not clear.

[5] The comparison of absorption intensities should be made on the basis of absorption per comparable absorbing unit. Therefore, instead of comparing the molar extinction coefficients for the two compounds (*i.e.*, curves A and B), it would be actually more appropriate to compare the molar extinction coefficient for the monomer with *half* the molar extinction coefficient for the dimer (*i.e.*, curves A and C).

tensity at the absorption maxium (or a downward shift in both intensity and wave length) may be correlated with a decrease in the extent of resonance coupling (6), the spectral data agree with and support the interpretation in the preceding paragraph. It should be pointed out that analogous situations—in which the degree of electronic interaction of an aromatic ring with a substituent group depends on steric factors originating not in the van der Waals repulsion of neighboring groups but rather in the geometric requirements of the valence-bonded atoms of a ring—have been recognized before and have been treated in a related manner (7).

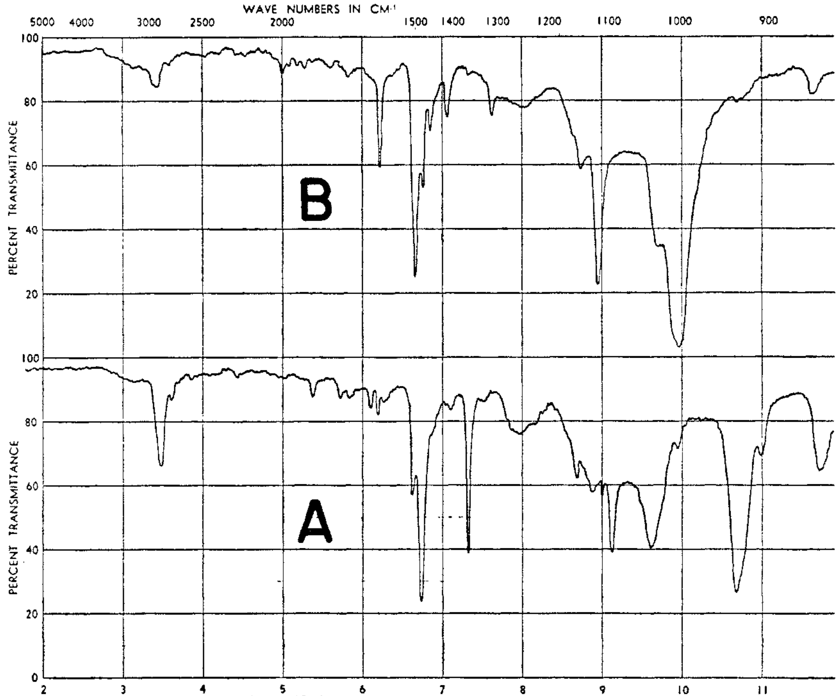

FIG. 2. INFRARED SPECTRA (carbon tetrachloride solutions). Curve A: methylenedioxybenzene (0.10 M). Curve B: methylenedioxybenzene dimer (I) (0.05 M).

The absorption of veratrol (Fig. 1, curve D) is included for comparison. On the basis of the position and the intensity of its absorption maximum (λ_{max} 275 mμ, ϵ 2320), the extent of oxygen-ring interaction is intermediate between that in the methylenedioxybenzene monomer and in the dimer.

Infrared absorption curves for the monomer and dimer are shown in Fig. 2. Although essentially the same functionality is present in both molecules, the two curves are more conspicuous in their differences than in their similarities. It is apparent that the vibrational modes of the planar and somewhat strained monomer molecule must be significantly different from those in the non-planar and strain-free dimer molecule.

EXPERIMENTAL[6]

Reaction of catechol, alkali, and methylene chlorobromide and the isolation of methylenedioxybenzene. A mixture of 220 g. (2.0 moles) of catechol, 272 (2.1 moles) of methylene chlorobromide, 220 g. (3.93 moles) of potassium hydroxide, and 1 l. of absolute alcohol was boiled for 72 hours. The top of the reflux condenser was connected to a mercury trap. The cooled, brown-colored, reaction mixture was filtered, and the solids were washed with ether. The ether washings were combined with the residue left after most of the alcohol solvent in the filtrate had been removed by distillation at atmospheric pressure through a 2-ft. Vigreux column. An additional 500 ml. of ether was added and the mixture was shaken vigorously with 1 l. of water plus at least 200 ml. of 20% aqueous sodium hydroxide. The solid dimer, which had collected at the ether-water interface, was removed by first draining the lower aqueous layer and then filtering the upper ether layer. The aqueous layer was extracted further with three 500-ml. portions of ether, and all the ether layers were combined. As much of the color as possible was removed from the ethereal solution by washing with several portions of water. After drying the yellow ethereal solution over calcium chloride, the solvent was removed by distillation, and the residual oil (124 g.) was distilled in a Claisen flask. The first fraction, which was nearly pure methylenedioxybenzene, was collected at b.p. 74–78° (23 mm.) and weighed 65.2 g. Redistillation afforded 63.5 g. (26%) of water-white product, b.p. 77.5° (27 mm.). In other smaller scale experiments 26–32% yields of methylenedioxybenzene were obtained.

The second fraction, weighing 10.2 g. and boiling at 80–84° (0.010 mm.), was treated as described below. The residue in the distillation flask was reserved for the isolation of the dimeric methylenedioxybenzene.

Isolation of the high-boiling products from the methylenation reaction. The combined higher boiling fractions (total weight, 16.5 g.) from several experiments were distilled through a small Vigreux column. The following fractions were taken: (a) 6.65 g. with b.p. 87.5–89° (0.5 mm.); (b) 7.2 g. with b.p. 89–97° (0.45 mm.); and (c) 1.1 g. with b.p. 97–102° (0.45 mm.). On redistilling fraction (a) in a small flask provided with a 2-inch vacuum-jacketed Vigreux column, 4.7 g. of a slightly yellow oil, b.p. 66–66.8° (0.009 mm.) and n_D^{18} 1.5162, was obtained.

Anal. Calc'd for $C_{19}H_{24}O_6$: C, 65.5; H, 6.9.
Calc'd for $C_{22}H_{28}O_7$: C, 65.3; H, 7.0.
Found: C, 65.6; H, 7.0.

On redistillation, fraction (b) furnished 4.0 g. of yellow liquid with b.p. 68–71° (0.010 mm.) and n_D^{18} 1.5112, and 2.0 g. of yellow liquid with b.p. 71–71.5° (0.010 mm.) and n_D^{18} 1.5052. The analytical figures for the 2.0-g. fraction are as follows:

Anal. Calc'd for $C_{14}H_{20}O_5$: C, 62.7; H, 7.5.
Calc'd for $C_{17}H_{24}O_6$: C, 63.0; H, 7.5.
Calc'd for $C_{20}H_{28}O_7$: C, 63.1; H, 7.4.
Found: C, 62.8; H, 7.3.

Both of the infrared absorption curves, taken with chloroform solutions of material from the two analytical samples, showed familiar peaks at 3.47 μ, but unusually weak peaks in the carbonyl region (5.8–6.0 μ).

Methylenedioxybenzene dimer (I)[7]. The isolation of the dimer formed in a one-fifth scale preparation, in which 44 g. (0.40 mole) of catechol was used as starting material, is described below.

An absolute alcohol solution of the residue left in the still after removal of the methylenedioxybenzene and the higher-boiling fractions was cooled at −5° overnight. The crystals were collected, washed with ether, and dried. The weight of the practically colorless ma-

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[6] Boiling points and melting points are corrected. The carbon and hydrogen analyses were performed by Carol K. Fitz, 115 Lexington Ave., Needham Heights 94, Massachusetts.

[7] We wish to acknowledge the kindness of Drs. J. L. Hartwell and J. Koo of the National Cancer Institute in supplying us with some of this partially purified material.

terial was 0.85 g. The dimer fraction which had been collected previously during the isolation of the methylenedioxybenzene was washed thoroughly with ether and with water and was dried in the air. The combined lots (1.05 g.) were dissolved in chloroform, and the solution, decolorized with carbon if necessary, was diluted with petroleum ether (b.p. 30–60°) and was cooled. The glistening colorless crystals obtained in this manner weighed 0.8 g., and melted with sublimation and some decomposition at 261.6–262.6°.

Anal. Calc'd for $(C_7H_6O_2)_2$: C, 68.8; H, 4.9; Mol. weight, 244.
Found: C, 68.6; H, 4.9; Mol. weight (Rast), 244.

Cleavage of methylenedioxybenzene dimer (I) *with phosphorus pentachloride* (1). A sealed tube containing 0.244 g. (0.0010 mole) of the dimer and 0.5 g. of phosphorus pentachloride was heated in an oil-bath at 175–185° for 35 minutes. The contents of the cooled tube were poured into ice-water, and the mixture was boiled for 30 minutes. The catechol present was transformed to catechol dibenzoate by treating the cold solution, made alkaline with sodium hydroxide, with benzoyl chloride. The alkaline reaction mixture, containing solid material, was extracted with chloroform. The chloroform solution was washed with water, dried over calcium chloride, decolorized with carbon, and finally warmed until no solvent remained.

The residue was distilled in a creased test tube under 0.01 mm. pressure and at an outside temperature of 130°. Three crystallizations of the distilled material from petroleum ether (b.p. 30–60°) at −10° resulted in 0.10–0.20 g. (15–30%) of product, m.p. 82–84°. The mixture melting point with authentic catechol dibenzoate, melting at 85.5–86.2°, was 84–85.5°.

Cleavage of methylenedioxybenzene dimer (I) *with acetic anhydride and zinc chloride.* A mixture of 2.0 g. (0.0082 mole) of the dimer, 25 ml. of acetic anhydride, and 1 g. of anhydrous zinc chloride was boiled for 15 minutes. The cooled solution, dark orange in color, was poured into water and the aqeuous mixture was neutralized with sodium carbonate and extracted with ether. After drying the ether solution over sodium carbonate, all solvent was removed by distillation. Distillation of the residual material in a creased test-tube under 0.05 mm. and at an outside temperature of 90–120° afforded 2.8 g. (76%) of colorless product. Further purification was effected by dissolving this material in ether, adding petroleum ether (b.p. 30–60°) and maintaining the solution at −10° overnight. Colorless crystals (2.15 g.) were removed by filtration. Concentration of the mother liquors followed by further dilution with petroleum ether and cooling, furnished an additional 0.25 g. of product which was combined with the first crop material. The total yield of 1-acetoxy-2-acetoxymethoxybenzene (II), m.p. 66–66.8°, was 2.4 g. (65.4%).

Anal. Calc'd for $C_{11}H_{12}O_5$: C, 58.9; H, 5.4.
Found: C, 58.9; H, 5.5.

Catechol from 1-acetoxy-2-acetoxymethoxybenzene (II). Saponification of this material was effected by heating 0.20 g. (0.000892 mole) under nitrogen with 20 ml. of 10% sodium hydroxide solution on the steam-bath for two hours. The homogeneous solution was acidified with dilute hydrochloric acid, and extracted several times with ether. The ether solution, dried over sodium carbonate, was decolorized with carbon, and was cooled. The resulting needle-like crystals of catechol, after collection and drying, weighed 60 mg. (61%) and melted at 102.5–103.5°. When mixed with authentic catechol, m.p. 103.5–104.5°, the melting point was 103–104°.

Methylenedioxybenzene with acetic anhydride and zinc chloride. A. Reaction at reflux temperature. No 1-acetoxy-2-acetoxymethoxybenzene (II), and only 0.25 g. (9.3%) of 3,4-methylenedioxyacetophenone (IV), m.p. 84–85°, could be obtained when the acetic anhydride-zinc cholride procedure used with the dimer was applied to 2.0 g. of the monomer. The isolation steps were the same with the exception of the distillation, which was eliminated.

B. Reaction at room temperature. A mixture of 2.0 g. (0.0162 mole) of methylenedioxybenzene, 25 ml. of acetic anhydride, and 1 g. of zinc chloride was allowed to stand at room temperature for two hours. The dark reddish-orange colored solution was poured into water, the mixture was neutralized with sodium carbonate, and was extracted with ether.

After drying the ether solution over sodium sulfate, some of the solvent was removed, the partially concentrated solution was decolorized with carbon, and the solution concentrated further. Two crops of colorless crystals were obtained by crystallization of the product first from ether-petroleum ether (b.p. 30–60°) and then from petroleum ether. The yield of 3,4-methylenedioxyacetophenone, m.p. 85.6–86.3°,[8] was 0.90 g. (33.5%).

Anal. Calc'd for $C_9H_8O_3$: C, 65.8; H, 4.9.

Found: C, 65.8; H, 5.0.

Approximately half of the starting material, methylenedioxybenzene, b.p. 172–173°, could be recovered from the mother liquors. The acetylation product was insoluble in 10% sodium hydroxide, and showed a positive iodoform test. A carbonyl absorption peak was observed at 5.72 μ.

SUMMARY

1. A solid dimer of methylenedioxybenzene, having a ten-membered ring structure, is formed in small amounts in the reaction of catechol and alkali with methylene chlorobromide.

2. Differences in the behavior of methylenedioxybenzene monomer and dimer toward acetic anhydride and zinc chloride are considered, and are correlated with absorption data.

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REFERENCES

(1) Barger, *J. Chem. Soc.*, **93**, 563 (1908).

(2) Wilson, *J. Chem. Soc.*, 48 (1945); Paul, *Bull. soc. chim.*, **53**, 417 (1933); Norris and Rigby, *J. Am. Chem. Soc.*, **54**, 2088 (1932); Meerwein and Maier-Hüser, *J. prakt. Chem.*, **134**, 51 (1932); Hamonet, *Ann. chim. phys.*, [9] **10**, 5 (1918).

(3) Mosettig and Jovanović, *Monatsh.*, **53**, 427 (1929).

(4) O'Shaughnessy and Rodebush, *J. Am. Chem. Soc.*, **62**, 2906 (1940); Dewar, *The Electronic Theory of Organic Chemistry*, Clarendon Press, Oxford, 1949, p. 200.

(5) Burwell, Elkin, and Maury, *J. Am. Chem. Soc.*, **73**, 2428 (1951); Meerwein and Maier-Hüser, *J. prakt. Chem.*, **134**, 51 (1932).

(6) *Cf.* Turner and Voitle, *J. Am. Chem. Soc.*, **73**, 1403 (1951).

(7) Arnold and Truett, *J. Am. Chem. Soc.*, **73**, 5508 (1951); Ramart-Lucas and Hoch, *Bull. soc. chim.*, [5] **2**, 327 (1935); Bicquard, *Bull. soc. chim.*, [5] **8**, 55 (1941); Remington, *J. Am. Chem. Soc.*, **67**, 1838 (1945); Brown, Widiger, and Letang, *J. Am. Chem. Soc.*, **61**, 2597 (1939); Baddeley, Chadwick, and Rawlinson, *Nature*, **164**, 833 (1949); Bartlett and Lewis, *J. Am. Chem. Soc.*, **72**, 1005 (1950) and earlier papers; Baddeley and Gordon, *J. Chem. Soc.*, 2190 (1952). Also, see Kadesch, *J. Am. Chem. Soc.*, **66**, 1207 (1944); Brown and Fried, *J. Am. Chem. Soc.*, **65**, 1841 (1943).

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[8] 3,4-Methylenedioxyacetophenone, m.p. 87–88°, has been reported as the product of the Friedel-Crafts reaction of acetyl chloride and methylenedioxybenzene (3). The orientation is fixed by virtue of the fact that the same compound has been derived from piperonylic acid [Mauthner, *J. prakt. chem.*, **116**, 32 (1927)].