[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, QUEEN'S UNIVERSITY]

Hindered Phenols Related to Metameconine[1]

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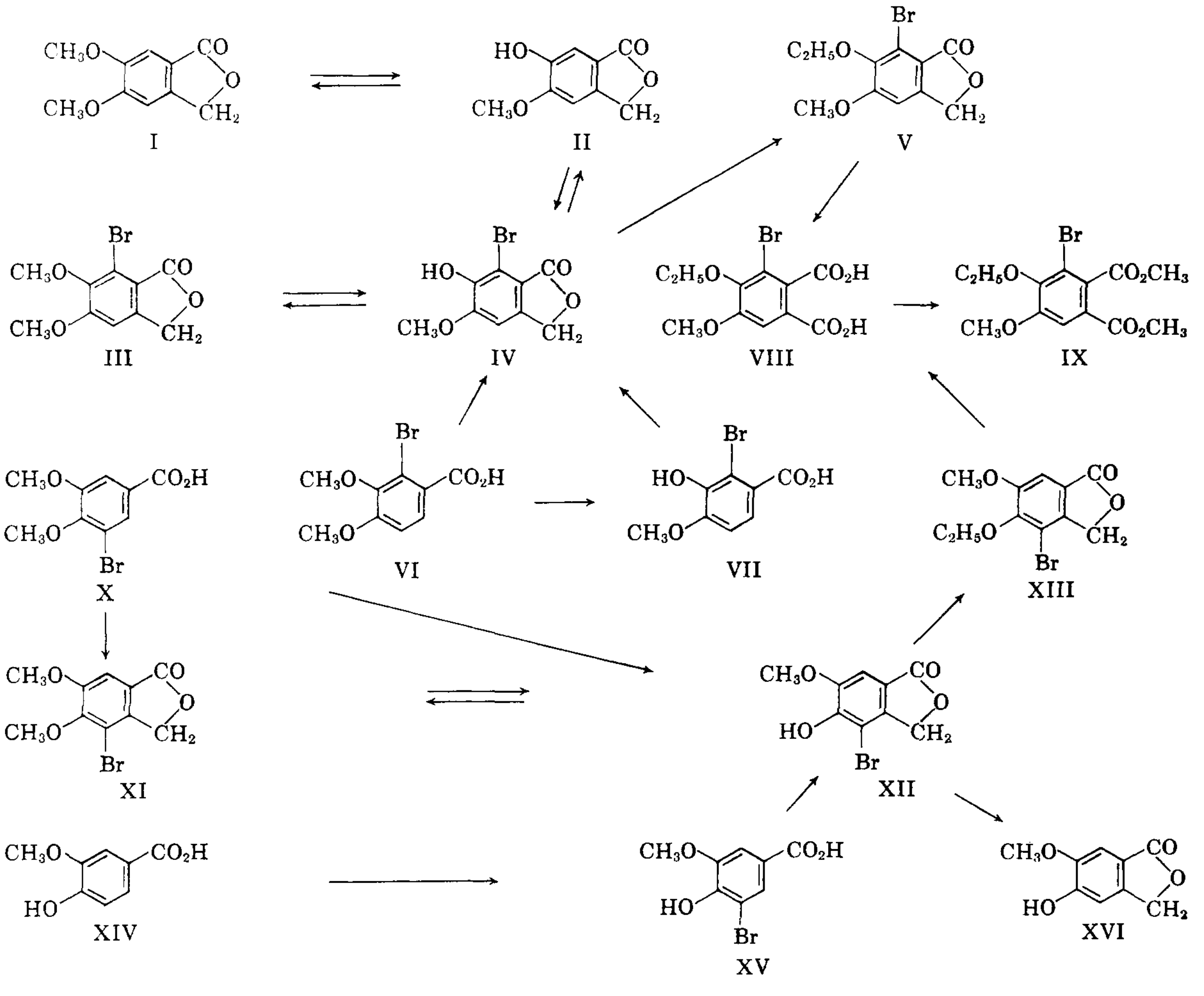
The reaction of 2-bromoveratric acid with acidified formaldehyde gave 5-methoxy-6-hydroxy-7-bromophthalide (IV) but no 7-bromometameconine (III). Some demethylation occurred during the reaction of 5-bromoveratric acid with formaldehyde. The investigation of these reactions led to the preparation of a series of hindered phenols needed in projected syntheses of highly hindered diphenyl ethers.



Only two isomers (III and XI) can arise when a hydrogen atom attached to the benzene ring of metameconine (I) is replaced by a bromine atom. Three have been described. Previous papers[4-6] of this series have shown that the isomer melting at 207° is 7-bromometameconine[7] (III), that the isomer melting at 183° is 4-bromometameconine[7] (XI), and therefore that the remaining "isomer" melting at 223°[8] cannot be a metameconine. The

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[2] Holders of Canadian Industries', Limited, Fellowships: (a) 1958–1959 and 1959–1960 and (b) 1942–1943.

[3] Ernest Mahler Fellow, 1950–1951.

[4] J. A. McRae, R. B. VanOrder, F. H. Griffiths, and T. H. Habgood, *Can. J. Chem.*, **29**, 482 (1951).

[5] R. H. Manske, J. A. McRae, and R. Y. Moir, *Can. J. Chem.*, **29**, 526 (1951).

[6] J. A. McRae, R. Y. Moir, J. J. Ursprung, and H. H. Gibbs, *J. Org. Chem.*, **19**, 1500 (1954).

[7] The numbering scheme used in our earlier papers differed from that of *Chem. Abstr.*, followed in the later papers.

[8] J. N. Rây and R. Robinson, *J. Chem. Soc.*, **127**, 1618 (1925).

present paper shows that the spurious "isomer" is the partially demethylated product 5-methoxy-6-hydroxy-7-bromophthalide (IV). Demonstration of the structure required the formation of a series of hindered phenols which are also needed in our studies of steric effects in highly substituted diphenyl ethers.[6,9]

The preparation of an adequate sample was the most difficult part of our work. The spurious "isomer" was formerly[4,8] only available from the reaction of formaldehyde upon 2-bromoveratric acid (VI), a method[4,8] which at best gave a 4% yield of a product accompanied by large amounts of tars. Purification was difficult, and all our early samples were contaminated with an impurity which had little effect upon the melting-point, although it very confusingly brought the analytical values close to those of a bromometameconine. These difficulties were finally solved by following the progressive elimination of the impurity with infrared spectroscopy, and by the discovery of new and more practical methods of preparing the material.

Proof of structure was then straightforward. Analysis showed the presence of one methoxyl group, and the presence of one phenolic group was shown by the formation of a monoacetate, by the presence of an O—H stretching band in the infrared spectrum, and by the solubility of the substance in weak alkalis. Methylation gave 7-bromometameconine (III), from which the spurious "isomer" could be regenerated, in preparative yields and in an easily purified form, by selective demethylation with sulfuric acid. These reactions left undetermined only the position of the free phenolic group, and this point was quickly settled when the spurious "isomer" was found to be formed by the action of formaldehyde upon 2-bromoisovanillic acid (VII). It must therefore have had the structure IV.

This demonstration quickly led to the correct structure of another unknown compound formed in our previous work. The action of formaldehyde upon 5-bromoveratric acid (X) had been shown[5] to give 4-bromometameconine (XI) and a new compound melting at 242° (raised in the present work to 248°). Clearly the new compound was 4-bromo-5-hydroxy-6-methoxyphthalide (XII), as it had the correct analyses, formed a monoacetate, showed the O—H stretching band in the infrared, gave 4-bromometameconine (XI) on methylation, and could itself be formed either by the action of sulfuric acid upon 4-bromometameconine (XI) or by the action of formaldehyde upon 5-bromovanillic acid (XV).

The weight of the proofs rested on the correct orientation of 2-bromoisovanillic acid (VII),[10] and of 5-bromovanillic acid (XV).[11] A new method of preparing the former, and a new method of preparing the 2-bromovanillic acid needed as a check, are given in the experimental part.

As a final check on the proofs, the structures offered for the new phenolic compounds (IV and XII) were shown to be consistent with each other. Ethylation and oxidation of each of the new compounds gave the same 2-bromo-3-ethoxy-4-methoxyphthalic acid (VIII) and further methylation gave the same ester (IX). The acid and its ester have been reported previously by King,[12] derivation of their structures being an essential part of his proof of the structures of the alkaloids bebeerine[13] and tubocurarine.[14] However, the proof offered for the position of the bromine atom in VIII and IX rested on the (undoubtedly reasonable) assumption that bromination of a precursor of VIII had occurred *ortho* to a free phenolic group rather than *ortho* to the methoxyl group (the phenolic group afterwards being ethylated). Our work gave a double confirmation of the correctness of this assumption as shown by the indirect formation of VIII and IX from each of VII and XV.

Selective demethylations with sulfuric acid were used several times in the course of the work, giving good yields of products essentially free from the unwanted isomers. The method was suggested to us by the selective demethylation of trimethoxybenzaldehyde to syringaldehyde reported by Pearl and Beyer.[15] Application of the method to metameconine (I) itself gave 5-methoxy-6-hydroxyphthalide (II) in good yield, and no trace could be found of its isomer (XVI) by fractional crystallization. There could be no doubt as to the structure of the isolated product, since on bromination it easily gave the spurious "isomer" (IV), from which it could be regenerated by reductive bromination. (Selective demethylation at the position *meta* to the carbonyl group had previously been noted[16] with veratric acid and with veratraldehyde.) As a final check upon the orientation of the demethylated product (II), the isomeric 5-hydroxy-6-methoxyphthalide (XVI) was made by reductive debromination of XII. A fourth method for the preparation of the spurious "isomer" had therefore been found, and the pleasing network of interrelations shown on the chart had been completed.

EXPERIMENTAL

Physical methods. All identities claimed in this paper were checked by comparison of the infrared spectra. The spectra

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[9] M. Allen and R. Y. Moir, *Can. J. Chem.*, **37**, 1799 (1959).

[10] L. C. Raiford and M. F. Ravely, *J. Org. Chem.*, **5**, 204 (1940).

[11] F. Misani and M. T. Bogert, *J. Org. Chem.*, **10**, 347 (1945).

[12] H. King, *J. Chem. Soc.*, 1165 (1939).

[13] H. King, *J. Chem. Soc.*, 1157 (1939).

[14] H. King, *J. Chem. Soc.*, 265 (1948).

[15] I. A. Pearl and D. L. Beyer, *J. Am. Chem. Soc.*, **74**, 4262 (1952).

[16] A. Lovecy, R. Robinson, and S. Sugasawa, *J. Chem. Soc.*, 817 (1930).

were usually obtained using potassium bromide disks containing 0.8% by weight of sample, but chloroform solutions were used for the compounds exhibiting dimorphism. Most melting points were determined in an instrument of high precision[17] and the rest were performed on a Koffler Micro Hot Stage and lowered 3-5° to agree with precision capillary melting points within less than 1° up to 250°.

Intermediates. Metameconine (I)[5,18] was made from veratraldehyde, *4-bromometameconine* (XI)[5] from 5-bromoveratric acid, *7-bromometameconine* (III)[4,6] *via* the nitration of metameconine, and *5-bromovanillic acid* (XV) by bromination of vanillic acid[19] according to the directions of Misani and Bogert.[11]

2-Bromoisovanillic acid (VII). 2-Bromoveratric acid (VI)[20] (3.0 g. crude) was heated with concd. sulfuric acid (15 ml.) at 60° for 3 days. The product (0.92 g.) precipitated when the cooled reaction mixture was poured onto ice, was recovered by filtration, washed with water and dried. The melting point was raised from 212-215° to 217.8-218.8° by three crystallizations from water. The recorded[10] value is 216.5°-218°.

Anal. Calcd. for $C_8H_7BrO_4$: C, 38.89; H, 2.86; Br, 32.34. Found: C, 39.27, 39.11; H, 2.90, 3.12: Br, 32.30, 32.40.

This compound was of decisive importance in our structure proof. In order to show beyond doubt that demethylation had occurred in the expected direction, the other possible isomer was prepared for comparison.

2-Bromovanillic acid. 2-Bromovanillin[21] was oxidized by the silver oxide method used by Pearl[19] for vanillic acid. The product after crystallization from water had a melting point of 164-165°. The recorded[22] melting point is 163-164°.

5-Methoxy-6-hydroxyphthalide (II). Metameconine (I) (2.0 g., m.p. 156.5-157°) was demethylated as described above for 2-bromoveratric acid. The product (0.5 g.) was crystallized once from ethyl alcohol and thrice from water to yield long fluffy white needles with a melting point of 208.4-209°.

Anal. Calcd. for $C_9H_8O_4$: C, 59.98; H, 4.48; —OCH_3, 17.22. Found: C, 60.25, 60.05; H, 4.54, 4.36; —OCH_3, 17.30.

5-Methoxy-6-hydroxy-7-bromophthalide (IV). (a). 7-Bromometameconine (III) (3.67 g., m.p. 203-204°), from 7-aminometameconine[4,6] and concentrated sulfuric acid (17 ml.) were heated at 60° for 4 days. The cooled solution was poured onto ice, the precipitate recovered and washed with water. One crystallization from water gave white needles (2.6 g., m.p. 220-221°) and two recrystallizations raised the melting point to 220-222°. A mixed melting point with the reference sample (see later) was 220-223°.

(b) 5-Methoxy-6-hydroxyphthalide (II) (1.63 g., m.p. 206-208°), glacial acetic acid (30 ml.), and bromine (1 ml.) were heated at 70° for 6 hr. Crystals separated from the cooled reaction mixture; they were recovered and washed with cold water to remove all the color. The product (1.45 g., m.p. 215-220°) after two recrystallizations from ethyl alcohol had a melting point of 220.6-221.2° and did not depress the melting point of the reference sample.

(c) 2-Bromoisovanillic acid (VII) (0.62 g., m.p. 214-216°), glacial acetic acid (20 ml.), hydrochloric acid (10 ml. concd.), and formaldehyde (4 ml., 36-38%) were heated under reflux at 75° for 20 hr. The cooled pale yellow solution was poured onto ice, and the resulting thick white precipitate recovered by filtration and washed with water. Two crystallizations from ethyl alcohol gave the product with a melting point of 220.8-222.4° and a mixed melting point with the reference sample of 220.6-222.4°.

(d) 2-Bromoveratric acid (VI)[20] (10.0 g.) was dissolved in glacial acetic acid (225 ml.) and heated to 80° in an oil bath. Hydrochloric acid (150 ml., concd.) and formaldehyde (50 ml., 37%) were slowly added, and the heating continued for 13 hr. at 80 ± 3°. More hydrochloric acid (50 ml.) and formaldehyde (50 ml.) were added, and the solution heated for another 17 hr. The reaction mixture was poured into water (500 ml.) and left to stand overnight. The mixture was filtered to remove unchanged 2-bromoveratric acid (20%) and the filtrate evaporated to dryness under reduced pressure. The tarry residue was washed with methanol and crystallized successively from 50% aqueous ethyl alcohol, butanol, and methanol. Long white needles resulted, melting with discoloration at 221-222°, the average yield from thirty-six preparations being 4%. Analytical results for this material and for the products obtained in repeated preparations were variable, the carbon and hydrogen results being usually more than 1% high.

Anal. Calcd. for $C_9H_7BrO_4$: Mol. wt., 259. Found: 289, 267.

The material (2.0 g., m.p. 216-221°) from several similar preparations was sublimed at 0.2 mm and 160-170°. The sublimate (1.9 g., m.p. 220.4-221.8°) was purified by conversion into the acetyl derivative (see later) followed by hydrolysis to regenerate 5-methoxy-6-hydroxy-7-bromophthalide, which after two recrystallizations from ethyl alcohol had a melting point of 220.8-222.4°. This sample was used as a *reference sample* for infrared spectra and mixed melting points.

Anal. Calcd. for $C_9H_7BrO_4$: C, 41.72; H, 2.72; Br, 30.83; —OCH_3, 11.97. Found: C, 41.62; H, 2.74; Br, 30.80; —OCH_3 12.60.

Most of the infrared spectrum from 4000-600 cm.$^{-1}$ is identical for all samples of 5-methoxy-6-hydroxy-7-bromophthalide, but in the region of 850 cm.$^{-1}$ there are small differences. The products prepared by methods (c) and (d) show a small peak at 850 cm.$^{-1}$ which is absent in the spectrum of the product from (a) and only present as a weak shoulder in the spectrum of the product from (b).

The products from the four methods of preparation were developed on paper chromatograms with a neutral solvent (ethyl alcohol, butyl alcohol, water, 9:3:3). The presence of phenolic components was revealed by the procedure described by Ames and Mitchell.[23] All the products appeared identical with an RF value of 0.66 and no impurities were detected.

5-Methoxy-6-acetoxy-7-bromophthalide. 5-Methoxy-6-hydroxy-7-bromophthalide (IV) (1.9 g., m.p. 220.4-221.8° from method d), acetic anhydride (20 ml.), and a trace of sulfuric acid were heated gently until a solution was formed and then left to stand at room temperature for 24 hr. The solution was diluted with water (100 ml.) and heated until all the acetic anhydride had decomposed. The cooled reaction mixture deposited crystals (2.3 g.) of melting point 161-163°. Three crystallizations from ethyl alcohol gave the analytical sample with a melting point of 162.5-163°.

Anal. Calcd. for $C_{11}H_9BrO_5$: C, 43.87; H, 3.01; Br, 26.54; —OCH_3, 10.34. mol. wt., 301. Found: C, 44.23, 44.50; H, 3.02, 3.13; Br, 25.90, 26.25; —OCH_3, 10.34; and on another sample: mol. wt., 294, 304, 302.

For hydrolysis 5-methoxy-6-acetoxy-7-bromophthalide (0.75 g.) dissolved in aqueous sodium hydroxide (25 ml. 5%) was left to stand for 3 hr. at room temperature, then diluted with water and acidified with hydrochloric acid. The white precipitate was recovered, washed with water, and dried. The product had a melting point of 217-218°, which was raised to 220.8-222.4° by two crystallizations

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(17) F. C. Merriam, *Anal. Chem.*, **20**, 1246 (1948).

(18) G. A. Edwards, W. H. Perkin, and F. W. Stoyle, *J. Chem. Soc.*, **127**, 195 (1925).

(19) I. A. Pearl, *J. Am. Chem. Soc.*, **68**, 429 (1946).

(20) L. C. Raiford and R. P. Perry, *J. Org. Chem.*, **7**, 354 (1942).

(21) L. C. Raiford and W. C. Stoesser, *J. Am. Chem. Soc.*, **49**, 1077 (1927).

(22) L. C. Raiford and D. J. Potter, *J. Am. Chem. Soc.*, **55**, 1682 (1933).

(23) B. N. Ames and H. K. Mitchell, *J. Am. Chem. Soc.*, **74**, 252 (1952).

from ethyl alcohol to give the *reference sample* described in method (d) above.

7-Bromometameconine (III). 5-Methoxy-6-hydroxy-7-bromophthalide (IV) (m.p. 221–222°) when treated with diazomethane in ether solution yielded 7-bromometameconine, which had a melting point at 205–206° after two recrystallizations from ethyl alcohol. This product did not depress the melting point of authentic 7-bromometameconine.[4,5]

5-Methoxy-6-ethoxy-7-bromophthalide (V). 5-Methoxy-6-hydroxy-7-bromophthalide (IV) (0.9 g., m.p. 218–220°), ethyl iodide (10 ml.), Drierite (1.0 g.) and dry acetone (25 ml.) were refluxed and stirred under very dry conditions. At intervals of 1 hr. freshly prepared silver oxide (5 g.) was added in portions (1 g.); after the additions the reaction was allowed to continue for another 4 hr., and then left to stand overnight. The reaction mixture was filtered to remove silver compounds and the clear solution was evaporated to dryness to leave a white residue which was crystallized from methyl alcohol. The product (0.72 g.) had a melting point of 165.6–166.2° which two more crystallizations only slightly changed to 166–166.8°.

Anal. Calcd. for $C_{11}H_{11}BrO_4$: C, 46.00; H, 3.83; Br, 27.87. Found: C, 46.52, 46.21; H, 4.31, 4.16; Br, 27.85, 27.55.

Diethyl sulfate gave the same product, but with a poorer melting point and in a reduced yield. This product appeared to exist in dimorphic forms, and in order to avoid confusion infrared spectra were obtained using chloroform solutions.

4-Bromo-5-hydroxy-6-methoxyphthalide (XII). (a). Formaldehyde and 5-bromoveratric acid (X) (72 g., m.p. 192.5–193°) were caused to react as previously described[5] and there were obtained: 4-bromo-5-hydroxy-6-methoxyphthalide (XII) (0.35 g., m.p. 248–248.5°), 4-bromometameconine (XI) (10.74 g., m.p. 180.4–181°) and unchanged 5-bromoveratric acid (X) (31.2 g., m.p. 189–190°).

(b). 4-Bromometameconine (XI) (5 g., m.p. 180.4–181°) was demethylated with sulfuric acid as previously described for 2-bromoveratric acid to yield a product which after crystallization from ethyl alcohol gave white needles (2.3 g.) with a melting point of 247–248°. Two more crystallizations gave the analytical sample, but did not alter the melting point. A mixed melting point with the product from method (a) was 247–247.5°.

Anal. Calcd. for $C_9H_7BrO_4$: C, 41.72; H, 2.72; Br, 30.83; —OCH_3, 11.97. Found: C, 41.61, 41.65; H, 2.86, 2.90; Br, 31.10, 30.90; —OCH_3, 11.80.

When this product was treated with diazomethane, 4-bromometameconine (XI) was regenerated, as shown by a mixture melting point and infrared spectrum.

(c). 5-Bromovanillic acid (XV) (1.0 g., m.p. 232–233°), glacial acetic acid (40 ml.), hydrochloric acid (20 ml., concd.), and formaldehyde (8 ml., 36–38%) were heated at 80–85° for 48 hr. The cooled solution was poured onto ice (100 g.) the white precipitate recovered, washed with water, and crystallized from ethyl alcohol. The product (0.27 g.) had a melting point of 246–247°, which was raised by a second crystallization to 249.2–250°. A mixed melting point with the product from method (a) showed no depression.

The infrared spectra of all samples of 4-bromo-5-hydroxy-6-methoxyphthalide were identical throughout the range 4000 cm.$^{-1}$ to 600 cm.$^{-1}$

4-Bromo-5-acetoxy-6-methoxyphthalide. 4-Bromo-5-hydroxy-6-methoxyphthalide (XII) (1.0 g., m.p. 247–248°) was heated on the steam bath for 30 min. with acetic anhydride (10 ml.) and a drop of sulfuric acid, and then allowed to stand at room temperature for 2 hr. The solution was diluted with water (100 ml.), heated until all the acetic anhydride had decomposed, and then cooled. The product separated out originally as fluffy needles, but in contact with solvent they gradually changed, over 7 days, into heavy needles. Four crystallizations from dilute acetic acid (1:1) gave the product with a melting point of 166.4–167.2°.

Anal. Calcd. for $C_{11}H_9BrO_5$: C, 43.87; H, 3.01; Br, 26.54; —OCH_3, 10.34. Found: C, 44.15, 43.91; H, 3.02, 3.15; Br, 26.65, 26.65; —OCH_3, 10.08.

A mixed melting point with 5-methoxy-6-acetoxy-7-bromophthalide gave a considerable depression.

The infrared spectrum of this acetyl derivative showed a small peak at approximately 3560 cm.$^{-1}$ which is in the region of OH stretching vibrations, suggesting that the acetylation was not complete or that the acetyl derivative had undergone partial hydrolysis. A second preparation was carried out in anhydrous conditions. The product was allowed to crystallize out of the acetic anhydride reaction mixture and was purified by two crystallizations from ethyl acetate. The pure product melted at 166.4–167.4°, and a mixed melting point with the previous product was 166.4–167.9°. The infrared spectrum was identical with that of the first product and the peak at approximately 3560 cm.$^{-1}$ appeared with unchanged amplitude. This peak is probably an overtone of the carbonyl peak at 1775 cm.$^{-1}$

4-Bromo-5-ethoxy-6-methoxyphthalide (XIII). 4-Bromo-5-hydroxy-6-methoxyphthalide (XII) (0.5 g., m.p. 247–248°) was ethylated with ethyl iodide using the method described above for 5-methoxy-6-hydroxy-7-bromophthalide. The product (0.42 g.) after crystallization from methyl alcohol had a melting point of 149–151°. Two more crystallizations from the same solvent gave the analytical sample with a melting point of 151.2–151.6°.

Anal. Calcd. for $C_{11}H_{11}BrO_4$: C, 46.00; H, 3.83; Br, 27.87. Found: C, 46.32; H, 3.95; Br, 28.10.

A sample of this ethoxy compound (m.p. 151.2–151.6°) crystallized from ethyl alcohol as long needles, but on standing in the solution for 14 days these crystals gradually changed to heavy cubes with a melting point of 152.2–153.2°. The two crystalline forms gave different infrared spectra in potassium bromide disks, but identical spectra in chloroform solution.

Diethyl sulfate gave an impure sample of the same product in a reduced yield.

4-Methoxy-5-ethoxy-6-bromophthalic acid (VIII). (a). 5-Methoxy-6-ethoxy-7-bromophthalide (V) (0.4 g., m.p. 165–165.5°), potassium permanganate (1.0 g.) and potassium hydroxide solution (40 ml., 5%) were vigorously stirred and heated on a steam bath for 30 min. Sulfur dioxide was passed into cooled reaction mixture until a colorless solution was obtained, then sulfuric acid (1 ml., concd.) was added. White crystals (0.23 g.) with a very poor melting point were deposited. Crystallization from water gave needles with a melting point of 204–205° and a second melting point due to the anhydride of 144.4–145.2°. The recorded[12] melting points are 206° for the acid and 147° for the anhydride.

(b) 4-Bromo-5-ethoxy-6-methoxyphthalide (XIII) (0.8 g., m.p. 150.5–151°) was oxidized as above to give a product (0.61 g.) which after two crystallizations from water had a melting point of 204–204.6° and a second melting point of 145–145.6°. As usual with phthalic acids, the analytical results were poor, and attention was concentrated on purifying the corresponding dimethyl ester. The infrared spectra of these two products were identical.

Dimethyl 4-methoxy-5-ethoxy-6-bromophthalate (IX). (a). 4-Methoxy-5-ethoxy-6-bromophthalic acid (VIII) (0.12 g., m.p. 204–205°, from part (a) above) was added to an ether solution of diazomethane (10 ml., 2%). After standing overnight the solution was evaporated to dryness and the residue crystallized from petroleum ether (b.p. 30–60°) to yield a product of melting point 80.8–82.0°.

(b) 4-Methoxy-5-ethoxy-6-bromophthalic acid (VIII) (0.39 g., m.p. 202–203°, from part (b) above) gave a white product (0.3 g.) with a melting point of 77–78°. Two crystallizations from petroleum ether gave the analytical sample with a melting point of 82–82.6°. A mixed melting point with the product from (a) was 81.4–82.6°. The recorded[12] melting point is 83–84°.

Anal. Calcd. for $C_{13}H_{15}BrO_6$: C, 44.96; H, 4.32; Br, 23.06. Found: C, 44.99, 45.19; H, 4.33, 4.27; Br, 23.00, 23.10.

The infrared spectra of these two products were identical.

Debromination of 5-methoxy-6-hydroxy-7-bromophthalide (IV). 5-Methoxy-6-hydroxy-7-bromophthalide (IV) (0.43 g., m.p. 221–222°) was heated under reflux with zinc (2.0 g.) and aqueous potassium hydroxide (40 ml. 10%) for 8 hr. The cooled reaction mixture was filtered to remove excess zinc and acidified. A white precipitate (0.3 g.) settled out which melted over a range 190–208°. Three crystallizations from benzene raised the melting point to 209–209.5°. A mixed melting point with 5-methoxy-6-hydroxyphthalide (II) obtained by demethylation of metameconine showed no depression.

5-Methoxy-6-acetoxyphthalide. 5-Methoxy-6-hydroxyphthalide (II) was acetylated with acetic anhydride in the usual way to give the acetyl derivative with a melting point of 184–186° which was raised to 186–186.6° by two crystallizations from dilute acetic acid (1:1).

Anal. Calcd. for $C_{11}H_{10}O_5$: C, 59.46; H, 4.54; $—OCH_3$, 13.96. Found: C, 59.77, 59.44; H, 4.50, 4.52; $—OCH_3$, 13.96.

5-Hydroxy-6-methoxyphthalide (XVI). 4-Bromo-5-hydroxy-6-methoxy-phthalide (XII) (0.2 g., m.p. 246–247°) was debrominated with zinc (1.0 g.) and aqueous potassium hydroxide (20 ml. 10%) by the method above for 5-methoxy-6-hydroxyphthalide. The product after three crystallizations from benzene melted at 177–177.6°.

Anal. Calcd. for $C_9H_8O_4$: C, 59.98; H, 4.48. Found: C, 60.04; H, 4.35.

The infrared spectrum was very similar to the spectrum of the isomeric 5-methoxy-6-hydroxyphthalide (II) in the range 4000–600 cm.$^{-1}$, a further confirmation of the structure suggested. Most of the peaks in the two spectra occurred in the same positions and a few varied by less than 10 cm.$^{-1}$. An extra peak was given by 5-methoxy-6-hydroxyphthalide at 1190 cm.$^{-1}$ and one by 5-hydroxy-6-methoxyphthalide at 1630 cm.$^{-1}$

Acknowledgment. We wish to pay tribute to Professor J. A. McRae, who began our work on the metameconines, and whose interest, encouragement, and help continued over a period of nearly twenty years, ending only with the completion of the present problem just before his death in April, 1960.

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KINGSTON, ONTARIO, CAN.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUQUESNE UNIVERSITY]

Chemistry of Aromatic Iodoso Salts. I. Reaction with Aralkyl Sulfides

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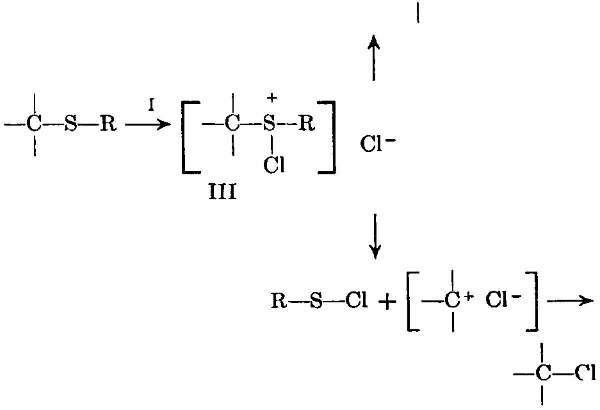
The reaction of iodobenzene dichloride (I) with dibenzyl, benzylphenyl, benzhydrylphenyl, and benzhydrylbenzyl sulfides has been investigated. The reaction proceeds with chlorination of the benzyl carbon with the first two compounds with cleavage to benzhydryl chloride and benzenesulfenyl chloride with benzhydrylphenyl sulfide and apparently by a combination of the two reaction paths in the case of benzhydryl benzyl sulfide. Reaction of iodobenzene diacetate with benzyl phenyl sulfide and dibenzyl sulfide gave the corresponding sulfoxides in 51 and 22% yield respectively.

While iodobenzene dichloride (I) has been known for over seventy years,[1] its reaction with sulfides has not been reported. It therefore appeared of interest to investigate the behavior of I with some sulfides.

The reactions of I with the sulfides studied can be summarized by the following schematic reaction path.



The formation of the chlorosulfonium chloride (III) is postulated as the first intermediate, as in the reactions of sulfides with chlorine studied by Bordwell and Pitt.[2] Decomposition of III can occur in one of two ways depending upon the nature of the organic groups attached to the sulfur atom. When one group is phenyl, benzyl, or methyl, and the other is methyl or benzyl, the intermediate reacts with the evolution of hydrogen chloride to give the α-chloro sulfide.[2] A second path by which the chlorosulfonium ion could decompose is by ionization of the intermediate to the sulfenyl halide and the carbonium ion. It should be noted here that factors that stabilize a carbonium ion greatly favor this path or reaction. It is for this

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(1) C. Willgerodt, *J. prakt. Chem.*, [2] **33**, 154 (1886).

(2) F. G. Bordwell and B. M. Pitt, *J. Am. Chem. Soc.*, **77**, 575 (1955).