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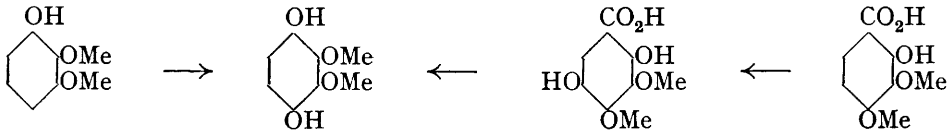
303. *Derivatives of* 1 : 2 : 3 : 4-*Tetrahydroxybenzene. Part V. The Synthesis of Parsley Apiole and Derivatives.*

By Wilson Baker and R. I. Savage.

The paper describes the synthesis for the first time of parsley apiole (2 : 5-dimethoxy-3 : 4-methylenedioxy-1-allylbenzene) and its degradation products apiolic acid and apione. The synthesis was made possible by the discovery of a practical method for the preparation of pyrogallol methylene ether, and by application in the pyrogallol series of the method of converting a phenol into a quinol by oxidation with alkaline potassium persulphate.

Earlier papers of this series have described the preparation of a number of derivatives of 1 : 2 : 3 : 4-tetrahydroxybenzene, including the naturally occurring substances dill apiole (2 : 3-dimethoxy-4 : 5-methylenedioxy-1-allylbenzene) and 2 : 3 : 4 : 5-tetramethoxy-1-allylbenzene (Baker, Jukes, and Subrahmanyam, J., 1934, 1681). The present paper describes the complete synthesis of parsley apiole (2 : 5-dimethoxy-3 : 4-methylenedioxy-1-allylbenzene) (XIII) and a number of its more important derivatives, including parsley apiolic acid (X), and parsley apione (VIII). The successful outcome of the present work has depended, firstly, upon the application to derivatives of pyrogallol of that little-used reaction whereby a monohydric phenol with a free *p*-position is converted into a derivative of quinol by oxidation with a persulphate in alkaline solution (see *e.g.*, Elbs, *J. pr. Chem.*, 1893, **48**, 179; D.R.-PP. 81068, 81297; Neubauer and Flatow, *Z. physiol. Chem.*, 1907, **52**, 375; Bargellini and Aureli, *Atti R. Accad. Lincei*, 1911, **20**, ii, 118; Bargellini and Monti, *Gazzetta*, 1915, **45**, i, 90; Bargellini, *Gazzetta*, 1916, **46**, 249; Wessely and Demmer, *Ber.*, 1929, **62**, 120; Hodgson and Beard, J., 1927, 2339), and secondly, upon the development of a satisfactory method for the preparation of pyrogallol methylene ether (2 : 3-methylenedioxyphenol) (VI). Preliminary oxidation experiments were carried out in the pyrogallol dimethyl ether series rather than with the less accessible methylene ethers.

Pyrogallol 1 : 2-dimethyl ether (I) was converted by oxidation in alkaline solution with potassium persulphate into 2 : 3-dimethoxyquinol (II), whose diacetate was shown to be identical with the product obtained by reduction and acetylation of 2 : 3-dimethoxy-*p*-benzoquinone (Baker and Smith, J., 1931, 2542). Methylation of (II) readily yielded 1 : 2 : 3 : 4-tetramethoxybenzene. Oxidation of 2-hydroxy-3 : 4-dimethoxybenzoic acid (IV) with alkaline persulphate gave 2 : 5-*dihydroxy*-3 : 4-*dimethoxybenzoic acid* (III). This acid loses carbon dioxide smoothly at 200°, forming 2 : 3-dimethoxyquinol (II), and on complete methylation gives 2 : 3 : 4 : 5-tetramethoxybenzoic acid, which has previously only been prepared from natural sources (see experimental section).



(I.) (II.) (III.) (IV.)

The methylene analogue of (I), pyrogallol methylene ether (VI), was previously obtained in traces (0·1% yield) (Baker, Jukes, and Subrahmanyam, *loc. cit.*) by the direct methylenation of pyrogallol with methylene bromide and potassium carbonate in acetone. The present method started with pyrogallolcarboxylic acid, which was converted into 2-*hydroxy*-3 : 4-*methylenedioxybenzoic acid* (V) by treatment with methylene sulphate and aqueous sodium hydroxide. Decarboxylation of this acid in quinoline solution with a "copper chromite" catalyst readily yielded pyrogallol methylene ether (VI), which thus becomes a moderately accessible compound. Oxidation of (VI) with alkaline persulphate yielded *methylenedioxyquinol* (VII), best characterised as its *diacetate*. Methylation of (VII) with methyl sulphate gave methylenedioxyquinol dimethyl ether (VIII), m. p. 77°, which was proved by mixed melting-point determination to be identical with parsley apione prepared from apiole. The structure (VII) assigned to the oxidation product of

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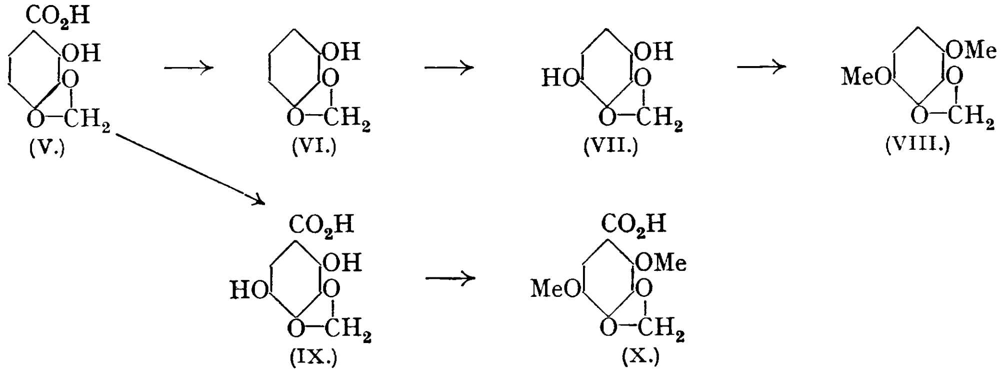
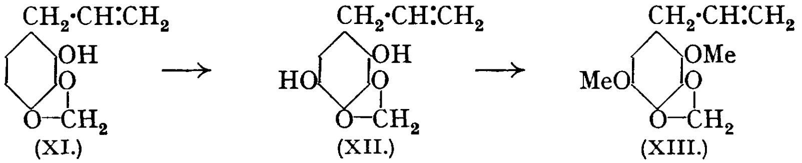
pyrogallol methylene ether is proved by the facts that its dimethyl ether is not identical with the isomeric dill apione (a liquid substance and the only alternative), 3 : 4-dimethoxy-1 : 2-methylenedioxybenzene, which has been synthesised by two unambiguous methods (Baker and Smith, *loc. cit.*; Baker, Jukes, and Subrahmanyam, *loc. cit.*), but is identical with parsley apione, a compound of known constitution.



A synthesis of apiolic acid (X) was readily effected by alkaline persulphate oxidation of 2-hydroxy-3 : 4-methylenedioxybenzoic acid (V) to 2 : 5-*dihydroxy*-3 : 4-*methylenedioxybenzoic acid* (IX); methylation of this afforded (X), identified with natural parsley apiolic acid (mixed m. p.). Further, both the synthetical and the natural acid were converted into the same dibromoapione, 1 : 2-dibromo-3 : 6-dimethoxy-4 : 5-methylenedioxybenzene.

The final synthesis of parsley apiole (XIII) followed naturally from the preceding experiments. Pyrogallol methylene ether (VI) was converted into 2 : 3-*methylenedioxyphenyl allyl ether* by the action of allyl bromide and potassium carbonate in acetone, and this substance underwent molecular rearrangement on heating with production of 2-*hydroxy*-3 : 4-*methylenedioxy*-1-*allylbenzene* (XI). The position of the allyl group in (XI) is established by its conversion into parsley apiole, as well as by other considerations. Oxidation of (XI) with potassium persulphate gave 2 : 5-dihydroxy-3 : 4-methylenedioxy-1-allylbenzene (XII) (uncharacterised), and when this compound was methylated it gave directly almost pure parsley apiole. The purified apiole, m. p. 28·5—29°, was shown to be identical with the natural product by means of a mixed melting-point determination, and also by a direct comparison of specimens of bromoapiole dibromide prepared from the synthetical and the natural apiole.



This synthesis of parsley apiole and derivatives fully confirms the work of Ciamician and Silber (*Ber.*, 1888, **21**, 913, 1621, 2129; 1889, **22**, 119, 2481; 1890, **23**, 2283; 1891, **24**, 2608) and of Thoms (*Ber.*, 1903, **36**, 1714) on the structure of the natural product.

A few other compounds prepared during the course of this work are described in the experimental section. The monobenzoylpyrogallol of Einhorn and Hollandt (*Annalen*, 1898, **301**, 105) is proved to be the 1-*O*-benzoyl derivative because, when treated with methyl iodide and alkali or with diazomethane, it yields 2 : 3-dimethoxyphenyl benzoate. A considerably improved method for the preparation of pyrogallol 1-monomethyl ether by the oxidation of *o*-vanillin with hydrogen peroxide is described, and conflicting statements in the literature with regard to the related 2 : 3-dihydroxy-4-methoxybenzaldehyde are corrected. The following compounds have been prepared: 2-hydroxy-3 : 4-dimethoxybenzoic acid (improved preparation); 2-*acetoxy*-3 : 4-*methylenedioxybenzoic acid*;

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5-*bromo*-2-*hydroxy*-3 : 4-*methylenedioxybenzoic acid*; 5-*nitro*-2-*hydroxy*-3 : 4-*methylenedioxybenzoic acid*; 4-*methyldaphnetin methylene ether*; 5(or 6)-*nitro*-4-*methyldaphnetin dimethyl ether.*

EXPERIMENTAL.

2-*Hydroxy*-3 : 4-*dimethoxybenzoic Acid* (IV).—The following preparation is an improvement upon other methods. To a stirred mixture of pyrogallolcarboxylic acid (50 g.), methyl alcohol (50 c.c.), 10% sodium hydroxide (150 c.c.), and methyl sulphate (80 c.c.), 10% sodium hydroxide (450 c.c.) was added in a thin stream, and the solution was then heated on the water-bath for 1 hour, cooled, and acidified; after 1 hour, the product was collected, washed, and dried (yield 44 g.) (cf. Mauthner, *J. pr. Chem.*, 1914, **89**, 304). Decarboxylation yielded pyrogallol 1 : 2-dimethyl ether (I) (Baker and Smith, *loc. cit.*).

Oxidation of Pyrogallol 1 : 2-*Dimethyl Ether with Potassium Persulphate.*—The ether (I) (5 g.), dissolved in a solution of sodium hydroxide (1·5 g.) in water (25 c.c.), was stirred during the addition (½ hour) from separate dropping funnels of (*a*) potassium persulphate (10 g.) in water (120 c.c.) and (*b*) sodium hydroxide (5 g.) in water (25 c.c.), added so that the solution remained alkaline. Considerable rise of temperature occurred, and after standing for 36 hours, the solution was made just acid to Congo-red, and unchanged pyrogallol 1 : 2-dimethyl ether removed by extracting it twice with ether. The solution was now acidified with concentrated hydrochloric acid (20 c.c.), heated to boiling, cooled, filtered, and extracted thrice with ether. After being dried and distilled, the extracts yielded crude 2 : 3-dimethoxyquinol (II) (*ca.* 1 g.) as a dark oil, which when methylated with methyl sulphate and alkali gave 1 : 2 : 3 : 4-tetramethoxybenzene, which separated from light petroleum (b. p. 60—80°) in slightly coloured prisms, m. p. 84—89° (0·8 g.). Recrystallisation gave the pure compound, m. p. 88—89°, not depressed on admixture with an authentic specimen of 1 : 2 : 3 : 4-tetramethoxybenzene of the same m. p. In another similar experiment the crude 2 : 3-dimethoxyquinol was refluxed for 4 hours with acetic anhydride (5 c.c.) and anhydrous sodium acetate, and poured into water. 2 : 3-Dimethoxyquinol diacetate was obtained from light petroleum (b. p. 40—60°) as prisms, m. p. 54°, unaltered on admixture with an authentic specimen prepared by the method of Baker and Smith (*loc. cit.*).

2 : 5-*Dihydroxy*-3 : 4-*dimethoxybenzoic Acid* (III).—2-Hydroxy-3 : 4-dimethoxybenzoic acid (IV) (24 g.) in a solution of sodium hydroxide (12 g.) in water (100 c.c.) was oxidised as in the preceding case by the addition of solutions of (*a*) potassium persulphate (40 g.) in water (480 c.c.) and (*b*) sodium hydroxide (20 g.) in water (60 c.c.). The subsequent steps were carried out as before, the oxidised product being isolated by four extractions with ether and crystallised from hot water (charcoal). It was obtained as colourless needles (6·5 g.), m. p. 171° (Found : C, 50·5; H, 4·7. $C_9H_{10}O_6$ requires C, 50·5; H, 4·7%). 2 : 5-*Dihydroxy*-3 : 4-*dimethoxybenzoic acid* gives a blue coloration with alcoholic ferric chloride.

2 : 3-*Dimethoxyquinol* (II).—2 : 5-Dihydroxy-3 : 4-dimethoxybenzoic acid (2 g.) was heated (oil-bath at 200°) until evolution of carbon dioxide ceased. The residue was distilled under diminished pressure, and solidified in the receiver as a very pale yellow mass, which separated from light petroleum (b. p. 40—60°) in colourless plates (1 g.), m. p. 84—85° (Found : C, 56·4; H, 6·0. Calc. for $C_8H_{10}O_4$: C, 56·4; H, 5·9%). This product was identified as 2 : 3-dimethoxyquinol by conversion into the diacetate, m. p. and mixed m. p. 54° (see above). 2 : 3-Dimethoxyquinol was previously described by Baker and Smith (*loc. cit.*) as an oil. In aqueous solution it gives a reddish-brown coloration with ferric chloride and is oxidised to 2 : 3-dimethoxy-*p*-benzoquinone.

2 : 3 : 4 : 5-*Tetramethoxybenzoic Acid.*—Some difficulty was experienced in the complete methylation of 2 : 5-dihydroxy-3 : 4-dimethoxybenzoic acid (III). The acid (III) (2 g.) in a little acetone was methylated in the usual manner by the alternate addition with shaking of potassium hydroxide (10 g.) in water (30 c.c.) and methyl sulphate (8 c.c.). The solution was heated on the water-bath for ½ hour, then cooled, diluted, acidified, and extracted with ether. The extracts yielded crude tetramethoxybenzoic acid, which solidified on scratching and after several crystallisations from light petroleum (b. p. 60—80°) had m. p. 81—82° and gave a weak blue ferric chloride reaction. It was accordingly remethylated under the same conditions as before, and then separated from light petroleum in long, colourless prisms, m. p. 87—88° (1 g.), which gave no ferric chloride reaction (Found : C, 54·9; H, 5·8; OMe, 49·0. Calc. for $C_{11}H_{14}O_6$: C, 54·5; H, 5·8; OMe, 51·2%). 2 : 3 : 4 : 5-Tetramethoxybenzoic acid, m. p. 87·5°, has been previously obtained by oxidation of the naturally occurring 2 : 3 : 4 : 5-tetramethoxyallylbenzene (Thoms, *Ber.*, 1908, **41**, 2753; Bignami and Testoni, *Gazzetta*, 1900,

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30, 245; see also Baker, Jukes, and Subrahmanyam, *loc. cit.*), and prepared from parsley apiole and fraxetin dimethyl ether (Wessely and Demmer, *Ber.*, 1928, **61**, 1279).

2-Hydroxy-3 : 4-methylenedioxybenzoic Acid (V).—Many experiments were carried out in order to determine the best conditions for the preparation and isolation of this acid. 2 : 3 : 4-Trihydroxybenzoic acid (pyrogallolcarboxylic acid) (80 g.) was dissolved in a solution of sodium hydroxide (80 g.) in water (700 c.c.) in an atmosphere of coal-gas, and, after cooling, acetone (100 c.c.) and methylene sulphate (80 g.) were added and the whole stirred at room temperature for 3 hours in coal-gas. The temperature was now raised slowly during 2 hours on a water-bath, which was finally allowed to boil. The resulting solution was cooled, acidified with excess of hydrochloric acid, and, after 12 hours, the solid product, which was partly crystalline and partly a hard tar, was collected, washed thoroughly with water, dried on the steam-bath, and powdered. The product, a brown powder (*ca.* 80 g.), was extracted twice with boiling ethyl acetate, the filtrates on distillation leaving a dark, crystalline residue. The solid was dissolved in boiling water with the addition of a 50% alcohol–acetic acid mixture and charcoal, the solution filtered, and evaporated under diminished pressure to remove the alcohol and some of the acetic acid and water. After standing for 12 hours, the *2-hydroxy-3 : 4-methylenedioxybenzoic acid* was collected, washed, and dried (yield 9—10 g.). An alternative but tedious method of isolation is to extract the powdered reaction product mixed with sand in a Soxhlet apparatus with benzene; the acid thus obtained is slightly purer, but the yield is in general only 5—6 g. The substance crystallised from acetic acid and then from dilute alcohol in prismatic needles, m. p. 235° (with evolution of carbon dioxide) (Found, in material dried at 120° : C, 52·7; H, 3·4; equiv., 179. $C_8H_6O_5$ requires C, 52·8; H, 3·3%; equiv., 182). Its solution in dilute alcohol develops an intense violet coloration with ferric chloride. The *acetyl* derivative was prepared by boiling the acid (2 g) with acetic anhydride (10 c.c.) and anhydrous sodium acetate (1 g.) for 6 hours. The solid obtained on addition of water was crystallised from benzene, and formed prismatic needles, m. p. 165° (Found: C, 53·6; H, 3·5. $C_{10}H_8O_6$ requires C, 53·6; H, 3·6%).

Pyrogallol Methylene Ether (VI).—2-Hydroxy-3 : 4-methylenedioxybenzoic acid (10 g.) in quinoline (40 c.c.) and a "copper chromite" catalyst (2 g.; Adkins and Connor, *J. Amer. Chem. Soc.*, 1931, **53**, 1092) were heated in an oil-bath at 180° for 2 hours, steady evolution of carbon dioxide occurring. To the product were added water (100 c.c.), concentrated hydrochloric acid (50 c.c.), sodium chloride (45 g.), and ether (100 c.c.), and, after being shaken, the whole was filtered, and the residue washed with a little ether. The ethereal layer was separated, and the aqueous layer extracted twice with ether. The combined extracts were shaken with dilute hydrochloric acid, then with sodium bicarbonate solution, dried with sodium sulphate, and distilled, leaving pyrogallol methylene ether as a pale brown oil (6 g.) which solidified completely on seeding. The bicarbonate solution yielded the unchanged acid (1 g.). The pyrogallol methylene ether was crystallised from light petroleum (b. p. 40—60°) and obtained in long prismatic needles, m. p. 65° (Found: C, 60·8; H, 4·4. Calc. for $C_7H_6O_3$: C, 60·9; H, 4·4%); a mixed m. p. established its identity with the compound prepared by direct methylenation of pyrogallol (Baker, Jukes, and Subrahmanyam, *loc. cit.*).

Methylenedioxyquinol (VII).—Pyrogallol methylene ether (4 g.), in a solution of sodium hydroxide (1·5 g.) in water (20 c.c.), was stirred during the simultaneous addition (20 minutes) of (*a*) potassium persulphate (10 g.) in water (120 c.c.), and (*b*) sodium hydroxide (6 g.) in water (15 c.c.). After 36 hours the methylenedioxyquinol (0·9 g.) was isolated by the usual procedure as a brown, crystalline crust, and unchanged pyrogallol methylene ether (1·5 g.) was also obtained. *Methylenedioxyquinol* is difficult to crystallise, and the solutions darken owing to oxidation. It separates from xylene in minute needles, m. p. *ca.* 180° (some decomp.) (Found: C, 54·6; H, 3·9. $C_7H_6O_4$ requires C, 54·5; H, 3·9%) The *diacetate*, prepared by refluxing it for 6 hours with acetic anhydride and sodium acetate, and pouring the mixture into water, separated from light petroleum (b. p. 100—120°) in clusters of flat prisms, m. p. 104° (Found: C, 55·4; H, 4·4. $C_{11}H_{10}O_6$ requires C, 55·4; H, 4·2%).

Methylenedioxyquinol Dimethyl Ether (*Parsley Apione*) (VIII).—(A) *Synthetical.* Methylenedioxyquinol, dissolved in a little methyl alcohol, was methylated in the usual way with methyl sulphate and aqueous potassium hydroxide, and the apione isolated from the alkaline liquid by steam-distillation. It solidified in the receiver, and was crystallised from light petroleum (b. p. 40—60°), and then from very dilute alcohol, being obtained in thin prisms, m. p. 77—77·5° (Found: C, 59·2; H, 5·5. Calc. for $C_9H_{10}O_4$: C, 59·3; H, 5·5%).

(B) *From natural apiole.* Apiole is most conveniently prepared by bromination of either apiolic acid or apiolic aldehyde (Fabinyi and Széki, *Ber.*, 1917, **50**, 1338) to dibromoapione

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(below), and removal of the bromine atoms with sodium amalgam. To dibromoapione (0·8 g.) in alcohol (20 c.c.) were added excess 3% sodium amalgam and insufficient water to produce turbidity. The mixture was warmed gently, left overnight, and the apione which separated on dilution was crystallised from light petroleum (b. p. 40—60°) (cf Ciamician and Silber, *Ber.*, 1891, **24**, 2608). It formed thin prisms, m. p. 77°, either alone or when mixed with the synthetical specimen.

2 : 5-*Dihydroxy*-3 : 4-*methylenedioxybenzoic Acid* (IX).—2-Hydroxy-3 : 4-methylenedioxybenzoic acid (6 g.) in a solution of sodium hydroxide (3 g.) in water (25 c.c.) was stirred during the addition (20 minutes) of (*a*) potassium persulphate (10 g.) in water (120 c.c.), and (*b*) sodium hydroxide (5 g.) in water (20 c.c.), the solutions being added so that the liquid remained alkaline. After 36 hours, the solution was made just acid to Congo-red, unchanged 2-hydroxy-3 : 4-methylenedioxybenzoic acid (3·1 g.) removed by filtration, and the filtrate shaken once with ether. The aqueous solution was now acidified with concentrated hydrochloric acid (20 c.c.), heated to boiling, cooled, extracted thrice with ether, and the extracts dried and distilled. The residue was triturated with a small quantity of water, collected, and crystallised from hot water. 2 : 5-*Dihydroxy*-3 : 4-*methylenedioxybenzoic acid* (0·3 g.) was obtained in very pale yellow, microcrystalline needles, m. p. 250° (decomp.) (Found : C, 48·2; H, 3·3. $C_8H_6O_6$ requires C, 48·5; H, 3·1%). The acid gives a deep blue ferric chloride reaction.

2 : 5-*Dimethoxy*-3 : 4-*methylenedioxybenzoic Acid* (*Parsley Apiolic Acid*) (X).—The preceding acid, dissolved in a little acetone, was shaken with a very large excess of methyl sulphate and aqueous potassium hydroxide, first at about 50° then at the b. p. The cooled, acidified solution deposited crude apiolic acid (m. p. 171°; no ferric chloride reaction), which was crystallised first from alcohol and then from water and obtained in colourless needles, m. p. 173° (Found : C, 52·9; H, 4·4. Calc. for $C_{10}H_{10}O_6$: C, 53·1; H, 4·4). A specimen of apiolic acid, obtained by degradation of parsley apiole (Ciamician and Silber, *Ber.*, 1888, **21**, 1624), was identical in appearance and m. p. with the synthetical acid; the mixed m. p. of the two specimens was also 173°, and both dissolved in warm concentrated sulphuric acid to yellow solutions, changing through green to blue.

1 : 2-*Dibromo*-3 : 6-*dimethoxy*-4 : 5-*methylenedioxybenzene* (*Dibromo Parsley Apione*).—Synthetical parsley apiolic acid was warmed in acetic acid solution with excess of bromine, water added, and the solid dibromo-compound collected, washed, and recrystallised from alcohol. It formed needles, m. p. 97—98° (Found : C, 31·7; H, 2·5; Br, 44·0. Calc. for $C_9H_8O_4Br_2$: C, 31·8; H, 2·4; Br, 47·1%). The same compound was similarly prepared from apiolic acid derived from natural apiole (Ciamician and Silber, *Ber.*, 1888, **21**, 2131); it melted at 97—98° either alone or when mixed with the synthetical specimen.

2 : 3-*Methylenedioxyphenyl Allyl Ether*.—Pyrogallol methylene ether (9 g.), pure acetone (200 c.c.), allyl bromide (24 g.), and anhydrous potassium carbonate (40 g.) were refluxed for 8 hours with constant stirring, and then allowed to distil almost to dryness. Water and a little sodium hydroxide were now added, and the *allyl ether* extracted with ether. It was obtained as a faintly yellow oil with a geranium-like odour, b. p. 139—140°/24 mm. (Found : C, 67·2; H, 5·7. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·6%). Yield 10 g.

2-*Hydroxy*-3 : 4-*methylenedioxy*-1-*allylbenzene* (XI).—2 : 3-Methylenedioxyphenyl allyl ether (8 g.) was heated in an oil-bath. At about 220° an exothermic reaction set in, as indicated by a rapid rise of temperature inside the flask (to 240°), and when no further reaction was apparent the bath was allowed to cool. The product was shaken with dilute sodium hydroxide and ether, the aqueous layer acidified, extracted with ether, and the extracts dried with sodium sulphate and distilled. 2-*Hydroxy*-3 : 4-*methylenedioxy*-1-*allylbenzene* (6·3 g.) distilled as a colourless oil, b. p. 155—156°/20 mm. (Found : C, 67·2; H, 5·6. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·6%).

2 : 5-*Dihydroxy*-3 : 4-*methylenedioxy*-1-*allylbenzene* (XII).—2-Hydroxy-3 : 4-methylenedioxy-1-allylbenzene (XI) (3·5 g.) in a solution of sodium hydroxide (1·6 g.) in water (20 c.c.) was stirred during the addition (15 minutes) of solutions of (*a*) potassium persulphate (6 g.) in water (70 c.c.) and (*b*) sodium hydroxide (2·7 g.) in water (10 c.c.). The reaction mixture was worked up in the usual manner, and yielded unchanged starting material (1·3 g.; distilled) and 2 : 5-dihydroxy-3 : 4-methylenedioxy-1-allylbenzene (XII) (0·14 g.) as a reddish oil which became crystalline on the addition of a little water. The substance was extremely difficult to crystallise.

Parsley Apiole (2 : 5-*Dimethoxy*-3 : 4-*methylenedioxy*-1-*allylbenzene*) (XIII).—The foregoing crude substance (XII), dissolved in a little methyl alcohol, was treated with methyl sulphate (2 c.c.) and a solution of potassium hydroxide (2·5 g.) in water (5 c.c.) added in portions with shaking. The mixture was warmed, and finally heated under reflux on the water-bath for ½

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hour; it was then diluted and steam-distilled till a clear distillate was obtained. The oily drops in the distillate solidified when seeded with natural apiole, and, after cooling in ice, the solid was collected, washed, and dried (yield 0·08 g.; m. p. 26—27°). The apiole was dissolved in a little light petroleum (b. p. 40—60°) at about 25°, the solution decanted from a little flocculent material, cooled to 0°, and seeded. After some time the mother-liquor was decanted from the crystals, which were then washed twice with ice-cold light petroleum. The synthetical apiole was thus obtained as long, blunt-ended, prismatic needles, m. p. 28·5—29° (Found: C, 65·0; H, 6·6. Calc. for $C_{12}H_{14}O_4$: C, 64·8; H, 6·4%). A specimen of natural apiole was crystallised as above, and was identical in appearance with the synthetical product; its m. p., either alone or when mixed with the synthetical specimen, was 28·5—29°.

Bromoapiole Dibromide.—Both synthetical and natural apiole were converted into bromoapiole dibromide by the action of excess bromine in carbon disulphide (Ginsberg, *Ber.*, 1888, **21**, 2514). The synthetical material had m. p. 79°, undepressed when mixed with the specimen, m. p. 79—80°, prepared from natural apiole. Ginsberg records m. p. 88—89°, but after many recrystallisations from alcohol and light petroleum we have been unable to raise the m. p. above 80—80·5° (Found, in the substance from natural apiole: Br, 52·4. Calc. for $C_{12}H_{13}O_4Br_3$: Br, 52·1%).

1-O-*Benzoylpyrogallol.*—Following the directions of Einhorn and Hollandt (*loc. cit.*) for the benzoylation of pyrogallol with benzoyl chloride in pyridine, and also by varying the conditions, we have been able to obtain from 40 g. of pyrogallol only 14 g. of the pure recrystallised compound, m. p. 140°. These authors claim a very much higher yield of slightly crude material, but do not give the yield of the pure compound; they make no suggestion about the position of the benzoyl group. Monobenzoylpyrogallol is described by Zetzsche and Loosli (*Annalen*, 1925, **445**, 296) as a " white, insoluble powder without melting-point "; no reference is made to earlier work. The pure substance gives a green ferric chloride reaction in alcoholic solution, and the solution in aqueous sodium hydroxide rapidly darkens on exposure to the air.

2 : 3-*Dimethoxyphenyl Benzoate.*—(A) A mixture of 1-*O*-benzoylpyrogallol (3 g.), acetone (30 c.c.), methyl iodide (20 c.c.), and anhydrous potassium carbonate (15 g.) was refluxed for 40 minutes, diluted with water, and extracted with ether. The extracts were shaken with dilute sodium hydroxide, then with water, dried, and distilled, and the oily residue triturated with ether–light petroleum (b. p. 40—60°). After 12 hours, the sticky material was pressed on porous earthenware and recrystallised from light petroleum (b. p. 40—60°) by cooling the solution saturated at room temperature to 0°. 2 : 3-Dimethoxyphenyl benzoate (0·6 g.) separated in stout rhombic prisms, m. p. 56° (Found: C, 69·9; H, 5·1. Calc. for $C_{15}H_{14}O_4$: C, 69·8; H, 5·4%). The same substance was also produced in poor yield by the action of excess diazomethane upon a methyl-alcoholic solution of monobenzoylpyrogallol. (B) Pyrogallol 1 : 2-dimethyl ether was warmed in pyridine with benzoyl chloride (1 mol.), poured into dilute hydrochloric acid, the solid collected and recrystallised as above, yielding prisms, m. p. 56° either alone or mixed with the specimen prepared by method (A) (cf. Herzig and Pollak, *Monatsh.*, 1904, **25**, 515).

Pyrogallol 1-*Monomethyl Ether.*—To a solution of *o*-vanillin (60 g.) in 2N-sodium hydroxide (200 c.c.) was added, from a tap-funnel in an atmosphere of coal-gas, 6% aqueous hydrogen peroxide (284 c.c.; 1·25 mols.) in several portions. After the solution had cooled, it was made faintly acid with sulphuric acid, then alkaline with a little sodium bicarbonate, saturated with sodium chloride, extracted 4 times with ether, the extracts dried with sodium sulphate, and distilled. Pyrogallol 1-monomethyl ether was obtained as a very pale yellow oil, b. p. 151°/24 mm. (44·7 g.), which solidified on cooling, and then had m. p. 41—42° (cf. Baker, Montgomery, and Smith, J., 1932, 1282; Baker, Jukes, and Subrahmanyam, *loc. cit.*, p. 1683).

2 : 3-*Dihydroxy*-4-*methoxybenzaldehyde.*—The production of an aldehyde by application of the Gattermann synthesis to pyrogallol 1-monomethyl ether has been described by Mauthner (*J. pr. Chem.*, 1936, **145**, 316) and by Baker and Evans (this vol., p. 373). The first author recorded m. p. 118—119° for the substance and described it as 3 : 4-dihydroxy-2-methoxybenzaldehyde, but has now shown (private communication) that it is the 2 : 3-dihydroxy-compound. The other authors correctly described the substance but recorded the erroneous m. p. of 69·5°. Repetition of the experiment has now confirmed the accuracy of the m. p. given by Mauthner.

5-*Bromo*-2-*hydroxy*-3 : 4-*methylenedioxybenzoic Acid.*—A solution of 2-hydroxy-3 : 4-methylenedioxybenzoic acid (V) in acetic acid was warmed with excess of bromine for 5 minutes. The solid which separated on cooling was collected, and crystallised twice from acetic acid. It separated in flat, obliquely truncated prisms containing acetic acid of crystallisation which is

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lost at 100°; m. p. 255° (decomp.) (Found, in material dried at 150°: Br, 30·8. $C_8H_5O_5Br$ requires Br, 30·7%).

5-*Nitro-2-hydroxy-3 : 4-methylenedioxybenzoic Acid.*—2-Hydroxy-3 : 4-methylenedioxybenzoic acid (0·2 g.) was dissolved in boiling acetic acid (2·5 c.c.), and the solution evaporated to about half its bulk. A solution of concentrated nitric acid (*d* 1·42; 1·5 mols.) in an equal volume of acetic acid was now added drop by drop, and the mixture stirred and warmed to 40°. The clear solution obtained after several minutes rapidly deposited a yellow solid, and after the addition of water (5 c.c.), the solid was collected, washed, and dried (yield 0·07 g.). After crystallising twice from glacial acetic acid, it formed very pale yellow crystalline aggregates, m. p. when rapidly heated 295° (decomp.) (Found: C, 42·3; H, 2·0; N, 5·9. $C_8H_5O_7N$ requires C, 42·3; H, 2·2; N, 6·2%). The *acid* dissolves in aqueous sodium bicarbonate to a yellow solution, which turns to bright orange on the addition of sodium hydroxide. Its alcoholic solution gives a red coloration with ferric chloride.

4-*Methyldaphnetin Methylene Ether.*—4-Methyldaphnetin (50 g.; von Pechmann and Duisberg, *Ber.*, 1883, **16**, 2127) in 10% sodium hydroxide (500 c.c.) and acetone (100 c.c.) was stirred with methylene sulphate (35 g.) while the temperature was slowly raised to 70° (4 hours). The solution was diluted, cooled, and acidified, and, after standing, the solid was collected, washed with dilute sodium carbonate solution to remove unchanged starting material, boiled with water, collected, and dried. The *methylene ether* (4 g.) separates from light petroleum (b. p. 100—120°) or from alcohol in minute, pale yellow, almost regular triangular plates, m. p. 226° (Found: C, 64·4; H, 3·8. $C_{11}H_8O_4$ requires C, 64·7; H, 3·9%).

5(or 6)-*Nitro-4-methyldaphnetin Dimethyl Ether.*—4-Methyldaphnetin dimethyl ether (5 g.; Shakai and Cota, *J. Pharm. Soc. Japan*, 1935, **55**, 691) was dissolved in acetic acid (5 c.c.), and fuming nitric acid (1·5 g.; *d* 1·5) added. The mixture was cautiously warmed, and, when the vigorous reaction had abated, was heated on the water-bath for ½ hour, and poured into water. The solid *nitro*-compound was collected, and crystallised from light petroleum (b. p. 100—120°), in which it was very sparingly soluble, or methyl alcohol. It formed pale yellow needles, m. p. 138—139° (Found: C, 54·6; H, 4·1; N, 5·4. $C_{12}H_{11}O_6N$ requires C, 54·3; H, 4·2; N, 5·3%).

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