

Further experiments with the amount of Boc-L-Asn-ONp (I) below and the same polymer under similar conditions gave:

With 2 × 5 equiv. of I for 2 × 2.5 h	4 %
10 equiv. of I for 5 h	5 %
5 equiv. of I for 1 h in	DMF-methylene chloride
1:3.6	63 %

With Gly-L-Ala-polymer and 5 equiv. of I for 5 h 6 %

With L-Ile-L-Ala-polymer * and 5 equiv. of I for 5 h 5 %

B: Preparative experiment. 2.4 g of L-Leu-L-Ala-polymer, corresponding to about 0.6 mmole of dipeptide, were swollen in DMF. 1.06 g (3.0 mmole) of Boc-L-Asn-ONp in 5 ml of DMF were added and allowed to react for 5 h under rotation. The DMF solution was sucked off and the resin rinsed twice with DMF and twice with abs. ethanol (as before). A small sample was withdrawn and dried, and the amount of free amino groups still present as determined with the above procedure was found to be 3 %. Submitting the resin to a second condensation with 1.06 g of Boc-L-Asn-ONp in the same amount of DMF for a further 5 h and proceeding as just mentioned, reduced the amount of unreacted amino groups to 0.9 %.

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* L-Ile-L-Ala-polymer was reacted without prior drying.

Reactions between *p*-Benzoquinone and Pyrogallol

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The acid-catalysed reaction between *p*-benzoquinone and suitable benzene derivatives sometimes offers a convenient synthetic route to *p*-terphenyls.¹⁻⁴ Aluminium chloride has often been employed as a catalyst but other acids may also be used to effect this type of reaction. Pummerer and Huppman obtained a termolecular product on reacting *p*-benzoquinone and resorcinol in dilute sulphuric acid.⁵⁻⁶ However, this reaction has been shown to give an *m*-terphenyl derivative.⁷

This finding of the formation of an *m*-terphenyl prompted us to investigate similar reactions between *p*-benzoquinone and phenols in dilute sulphuric acid. In this paper, we wish to report some results obtained during an investigation of the reactions between *p*-benzoquinone and pyrogallol.

A mixture of *p*-benzoquinone and pyrogallol was treated with dilute sulphuric acid for two days. The dark reaction mixture was extracted with ethyl acetate and the extract treated with aqueous sodium dithionite. The phenolic mixture obtained by this procedure was methylated with dimethyl sulphate. The mixture of methyl ethers was steam-distilled in order to remove large amounts of pyrogallol trimethyl ether and hydroquinone dimethyl ether. The residue was distilled *in vacuo* and two fractions were obtained.

According to thin layer chromatography, the low-boiling fraction consisted of three compounds. These were separated by chromatography on a preparative scale. It was assumed that one of these compounds was formed by simple combination of *p*-benzoquinone and pyrogallol and this was found to be the case. 2,3,4,2',5'-Pentamethoxybiphenyl was synthesized by reacting *p*-benzoquinone with the diazonium salt from 2,3,4-trimethoxyaniline according to the

method of Brassard and L'Ecuyer.⁸ Reduction of the resulting quinone followed by methylation gave a compound, which was found to be identical with one of the components of the low boiling fraction.

The remaining two compounds were found to be dehydrogenation product derivatives namely 2,3,4,2',3',4'-hexamethoxybiphenyl and 2,3,4,3',4',5'-hexamethoxybiphenyl, by comparison with authentic specimens. 2,3,4,2',3',4'-Hexahydroxybiphenyl is a well-known dehydrogenation product of pyrogallol⁹ and its hexamethyl ether was prepared by a known procedure.¹⁰ 2,3,4,3',4',5'-Hexamethoxybiphenyl has been described by Haworth *et al.* in connection with their studies on pupurogallin formation from pyrogallol. It was prepared by a somewhat modified procedure.

The high-boiling fraction consisted of two compounds, which were separated by preparative thin layer chromatography. The mass spectra of these compounds indicated that they are terphenyls containing eight and nine methoxyl groups, respectively.

The structure of the octamethoxyterphenyl was elucidated in the following way. The melting point of this compound was not identical with that of the previously prepared 2,3,4,2',5',2'',3'',4''-octamethoxy-*p*-terphenyl. It was consequently assumed that the compound was a derivative of *m*-terphenyl in analogy with the resorcinol-*p*-benzoquinone coupling product. Its identity was verified by the synthesis of 2,3,4,2',5',2'',3'',4''-octamethoxy-*m*-terphenyl from 2,6-diiodohydroquinone dimethyl ether and 4-iodopyrogallol trimethyl ether, which were subjected to a mixed Ullmann coupling (*cf.* Ref. 11), giving a product identical with the octamethoxyterphenyl from *p*-benzoquinone and pyrogallol. It is interesting to note this formation of an *m*-terphenyl derivative by acid-catalysed coupling of *p*-benzoquinone and a phenol. The previously described coupling product from resorcinol is thus not an isolated case. However, the latter reaction gives a comparatively larger yield of termolecular product. The structure of the nonamethoxy terphenyl, a dehydrogenation product of pyrogallol, is presently under investigation.

Experimental. All melting points are uncorrected. Thin layer chromatography has been performed on Kieselgel HF₂₅₄ nach Stahl (E. Merck A. G., Darmstadt). For analytical

purposes (see R_F -values below) a thickness of 0.25 mm has been used and for preparative scale chromatography a layer of thickness 0.75 to 1 mm was found to be suitable. The chromatograms have been developed with isopropyl ether. The spots have been detected by UV-absorption and spraying with conc. sulphuric acid.

The reaction between p-benzoquinone and pyrogallol in sulphuric acid. A mixture of pyrogallol (226.8 g) and *p*-benzoquinone (39.6 g) was stirred in dilute sulphuric acid (2 M, 3300 ml) for 40 h. The reaction mixture was extracted thoroughly with ethyl acetate. The extract was treated with a saturated solution of sodium dithionite, washed with water and then dried over anhydrous sodium sulphate. The phenolic mixture, obtained by evaporating the solvent, was methylated with an excess of dimethyl sulphate and dry potassium carbonate in dry acetone in an inert atmosphere (argon). The reaction mixture was poured into water and subjected to steam distillation. Large amounts of pyrogallol trimethyl ether and hydroquinone dimethyl ether were obtained. The residue was extracted with ether and the ethereal extract dried over sodium sulphate. After evaporation of the solvent, a dark-brown oil (18.7 g) remained. The oil (14.2 g) was distilled *in vacuo* and the following fractions collected: 1. 7.1 g, b.p. 120–210°, 0.1 mm; 2. 1.8 g, b.p. 210–300°, 0.1 mm. The components of fraction 1 (2 g) were separated by means of thin layer chromatography:

Component 1a. R_F 0.42; 104 mg; The substance was recrystallised from methanol and sublimed *in vacuo*, m.p. 63–65°. The compound was found to be identical with 2,3,4,2',5'-pentamethoxybiphenyl (see below).

Component 1b. R_F 0.35; 134 mg; The compound was recrystallised from methanol, m.p. 123–124°. (Found: C 65.0; H 6.6. Calc. for $C_{18}H_{22}O_6$: C 64.7; H 6.6). M.p. of authentic 2,3,4,2',3',4'-hexamethoxybiphenyl¹⁰ 124–125°, mixed m.p. 123–125°. The IR-spectra of the two specimens were superimposable.

Component 1c. R_F 0.27; 240 mg; The compound was recrystallised from methanol and sublimed *in vacuo*. M.p. 104–105°. (Found: C 64.7; H 6.7; mol.wt. 334 [mass spectrometry]. Calc. for $C_{18}H_{22}O_6$: C 64.7; H 6.6; mol.wt. 334.4). The compound was found to be identical with 2,3,4,3',4',5'-hexamethoxybiphenyl (see below).

The components of fraction 2 (1.8 g) were separated by the same procedure as those of fraction 1.

Component 2a. R_F 0.23; 22 mg; The compound was recrystallised from methanol. M.p. 142–143°. The compound was found to

be identical with 2,3,4,2',5',2'',3'',4''-octamethoxy-*m*-terphenyl (see below).

Component 2b. R_F 0.13; 300 mg; The compound was recrystallised from ethanol and sublimed *in vacuo*. M.p. 154–155°. (Found: C 64.4; H 6.3; mol.wt. 500 [mass spectrometry]. Calc. for $C_{27}H_{22}O_8$; C 64.8; H 6.4; mol.wt. 500.5).

2,3,4,2',5'-Pentamethoxybiphenyl. An ether solution of crude 2,3,4-trimethoxyphenyl-*p*-benzoquinone, obtained from 2,3,4-trimethoxyaniline hydrochloride¹⁰ (14.4 g) and *p*-benzoquinone (8.7 g) according to Brassard and L'Ecuyer⁸ was reduced by shaking with an excess of saturated sodium dithionite solution. After drying over sodium sulphate, the solvent was removed and the crude reaction product was methylated with an excess of dimethyl sulphate and anhydrous potassium carbonate in dry acetone under an argon atmosphere. Yield 11.0 g. The compound was recrystallised from methanol and sublimed *in vacuo*. M.p. 64–65°. (Found: C 67.3; H 6.7; mol.wt. 304 [mass spectrometry]. Calc. for $C_{17}H_{20}O_5$; C 67.1; H 6.6; mol.wt. 304.3). Mixed m.p. with component 1a 63–65°. The IR-spectra of the two specimens were superimposable.

2,3,4,3',4',5'-Hexamethoxybiphenyl. 4-Iodopyrogallol trimethyl ether¹⁰ (7 g) and 5-iodopyrogallol trimethyl ether¹⁰ (7 g) were subjected to a mixed Ullmann coupling according to the method of Critchlow, Haworth and Pauson.¹² The crude reaction product was extracted with ethanol. After evaporation of the ethanol, there remained a brownish semi-solid mass (8 g). This mass (7.5 g) was chromatographed on a column of silica gel (Mallinckrodt, Silicic Acid, 100 mesh, 250 g, diameter of column 3 cm) constructed in isopropyl ether. The components were eluted with isopropyl ether in the following order: 2,3,4,2',3',4'-hexamethoxybiphenyl (1.6 g), m.p. 122–123° (lit.¹⁰ m.p. 122–123°); 2,3,4,3',4',5'-hexamethoxybiphenyl (1.4 g), m.p. 103–105° (after recrystallisation from methanol and sublimation *in vacuo*, lit.¹² m.p. 89°); 3,4,5,3',4',5'-hexamethoxybiphenyl (1.6 g), m.p. 129–130° (lit.¹⁰ m.p. 126°). A mixture of 2,3,4,3',4',5'-hexamethoxybiphenyl and component 1c had m.p. 102–104°. The IR-spectra of the two specimens were superimposable.

2,3,4,2',5',2'',3'',4''-Octamethoxy-*m*-terphenyl: 2,6-Diiodohydroquinone dimethyl ether¹³ (1.5 g), copper bronze (20 g) and 4-iodopyrogallol trimethyl ether¹⁰ (10.5 g) were thoroughly mixed and heated to 270° whereupon a vigorous

reaction started. After some minutes, the reaction mixture was allowed to cool and the organic products extracted with chloroform. The chloroform was removed and the residue was dissolved in isopropyl ether. The solution was filtered through a short column of aluminium oxide constructed in isopropyl ether. The solvent was removed from the filtrate and the residue (3.6 g) was subjected to thin layer chromatography on a preparative scale. The terphenyl derivative (350 mg, R_F 0.23) was isolated and purified by recrystallisation from methanol and sublimation *in vacuo*. M.p. 144–145° (Found: C 66.5; H 6.5; mol.wt. 470 [mass spectrometry]. Calc. for $C_{28}H_{20}O_8$; C 66.4; H 6.4; mol.wt. 470.5). A mixture of this compound and component 2a had m.p. 143–145°. The IR-spectra of the two specimens were superimposable.

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