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A CONVENIENT, HIGH-YIELDING METHOD FOR THE METHYLENATION OF CATECHOLS

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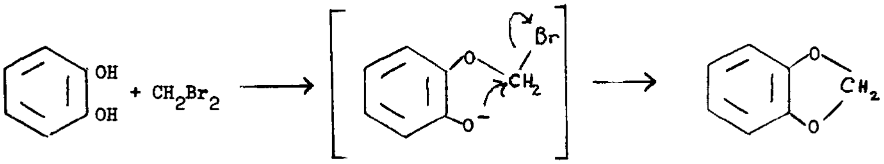
The methylenedioxy group occurs in many natural products[1] and, in addition, has been suggested as a protecting group for catechols[2]. However, synthetically, the methylenation of catechols [FIG 1] has never been easy and high yields difficult to obtain[3].

FIG 1



Bonthrone and Cornforth have shown[4] that if the reaction is carried out using dichloromethane in a dipolar aprotic solvent such as dimethylsulphoxide, coupled with the slow addition of a mixture of solid sodium hydroxide and the catechol, good yields of the methylenated catechol may be obtained. Several substituted catechols have been methylenated in high yield using dichloromethane in dimethylformamide or dimethylsulphoxide in the presence of a bronze[5], cupric oxide[6] or nickel oxide[7] catalyst.

However, all these methods suffer from the disadvantage that they must be effected in aprotic solvents under anhydrous conditions.

We now wish to report a simple synthetic procedure, using phase transfer catalysis[8,9] which gives high yields of methylenated catechol. In methylenation reactions the methylenating agent of choice is normally diiodomethane; however due to the known role of iodide ion as a catalyst poison in phase transfer catalysis[10] dibromomethane was used. The phase transfer catalyst selected was Adogen 464[11], which fulfils the required criteria for effective phase transfer catalysis.

A mixture of water (20 cm^3), dibromomethane (.15 mole) and Adogen 464 (1 mmole) was vigorously stirred and heated to reflux. The air in the system was displaced by nitrogen. A solution of the appropriate o-dihydroxybenzene (.1 mole) and sodium hydroxide (.25 mole) in water (50 cm^3) was added at such a rate that the addition was complete after 2 hours. After the addition was complete, the reaction mixture was stirred and refluxed for a further hour. The product was then isolated[4] and identified. Yields obtained are shown in the table.

	Reactant	Product	Yield*
1.	Catechol	Benzo-1,3-dioxole	76%
2.	2,3-Dihydroxynaphthalene	Naphtho[2,3-d][1,3] dioxole	82%
3.	2,3-Dihydroxybenzaldehyde	Piperonal	80%
4.	4-Methylcatechol	4-Methyl-benzo-1,3-dioxole	86%

*Yields shown above are calculated from the amount of purified product and are the average yields obtained in a series of experiments

Phase transfer catalysis has recently been applied with considerable success to the methylation of some hindered phenols[12] and from the table it can be seen that using this technique high yields can be easily obtained in the methylenation of catechols. It is, however, important to ensure (i) an adequate stirring rate[8] and (ii) to add slowly the solution of catechoxide dianion to the reaction mixture, so as to avoid the possibility of intermolecular reaction[4].

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