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Isomer specific syntheses of chlorinated catechols and guaiacols relevant to pulp bleaching

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Abstract

A variety of chlorinated catechols and guaiacols relevant to pulp bleaching were synthesized by employing fundamental differences in the acidities of phenolic hydroxyl groups in chlorinated catechols, and directive effects in guaiacols. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Chlorocatechols; Chloroguaiacols; Pulp bleaching

1. Introduction

Chlorinated catechols, guaiacols and syringols are by-products of pulp bleaching with chlorine (Lindström and Nordin, 1976; Kachi et al., 1980; Voss et al., 1980; McKague, 1981; Knuutinen, 1982). Recent changes in bleaching technology, particularly the implementation of chlorine dioxide bleaching, have minimized formation of the more highly chlorinated derivatives so that concentrations of these compounds in bleaching effluent are now in the low or sub parts per billion range (NCASI, 1994; Servos et al., 1996; Dence and Reeve, 1996). The Cluster Rule recently introduced in the United States (US Environmental Protection Agency, 1998) regulates levels of the 12 chlorophenols shown in Fig. 1. Other countries do not have specific regulations for chlorophenols, however the elimination of chlorine bleaching in many countries has minimized formation of the more highly chlorinated phenols anyway.

Other lesser chlorinated chlorophenols which have also been found frequently in effluent from chlorine bleaching are shown in Fig. 2 (Knuutinen, 1982; Knuutinen et al., 1982).

During the late 1980s and early 1990s, the demand for analytically pure samples of chlorinated catechols and guaiacols increased sharply in anticipation of forthcoming regulations and concern about their environmental properties. Although some of the compounds shown in Fig. 1, such as tetrachlorocatechol **7**,4,5,6-trichloroguaiacol **10**, tetrachloroguaiacol **11** and trichlorosyringol **12** can be prepared easily by direct chlorination of catechol, guaiacol and syringol, others cannot be prepared so readily. For example, the limited methylation of 3,4,5-trichlorocatechol **5**, which itself was not that easily prepared at that time, employed to prepare 3,4,5-trichloroguaiacol **8** is difficult and gives a low yield (Knuutinen, 1984; Lindström and Österberg, 1980). Also, the preparation of 3,4-dichlorocatechol **13** by the Reimer–Tiemann reaction of 2,3-dichlorophenol gives a low yield. This makes its use in the preparation of 3,4-dichloroguaiacol **14** by the limited methylation method reported (Knuutinen and Tarhanen, 1981) impractical. In this paper, isomer specific syntheses developed by employing differences in acidities of different phenolic hydroxyl groups in chlorocatechols, and directive effects of guaiacol substituents are reported. The synthesis of all possible isomers of the chlorosyringols was reported previously (McKague, 1993).

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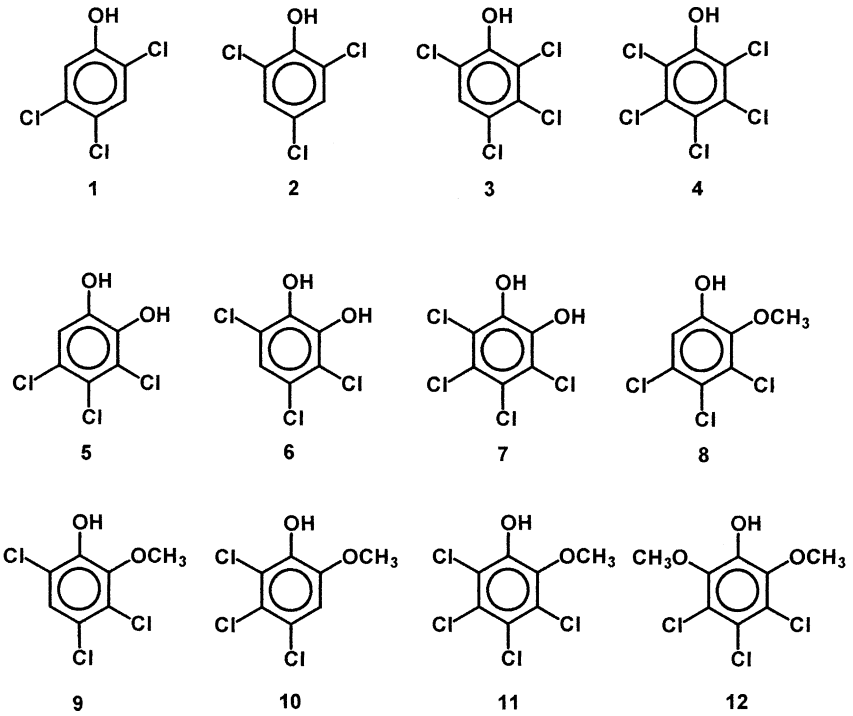


Fig. 1. Chlorophenols regulated by the Cluster Rule.

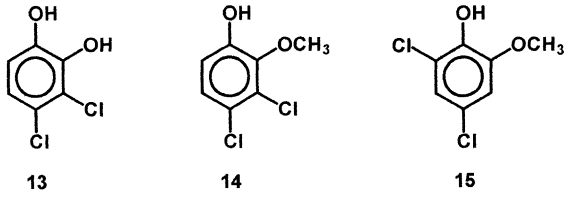


Fig. 2. Other chlorophenols reported in bleaching effluent.

2. Experimental

Reactions were monitored and product purities determined by gas chromatography (GC) using a Hewlett Packard HP5890 Gas Chromatograph equipped with a 25 m HP-1 capillary column. Guaiacols were analyzed without derivatization while catechols were converted to their acetate derivatives *in situ* by injection of solutions in acetic anhydride into the gas chromatograph. Products were characterized by comparison of their melting points, NMR and mass spectra with data from the literature.

2.1. Syntheses

2.1.1. 3,4-Dichlorocatechol (*13*)

Three drops of H_2SO_4 were added to a stirred solution of 6-chloroguaiacol **17** (Fig. 8) (15.8 g, 0.1 mol) in acetic anhydride (50 ml). The solution was stirred at 50°C for 1 h. The product was cooled, poured into cold water and extracted with ether. The extracts were washed with water, dried and concentrated to give 6-chloroguaiacol acetate as a yellow oil (20 g, 100% yield). The chloroacetate was dissolved in acetic acid (100 ml) and a solution of chlorine (7.7 g, 0.11 mol) in acetic acid (100 ml) added with stirring. After stirring for 15 min at room temperature, the product was poured into cold water with stirring. Filtration gave crude 5,6-dichloroguaiacol acetate (20 g). Crystallization from hexane gave yellow prisms (15 g, 64% yield), m.p. 86–88°C. The dichloroacetate was dissolved in methanol (100 ml), 10% KOH in methanol:water, 9:1 (100 ml) added and the solution stirred at 50°C for 20 min. The product was cooled, water (400 ml) added, acidified with dilute hydrochloric acid and extracted with ether. The extracts were washed with water, dried and concentrated to give 5,6-dichloroguaiacol (12 g, 63% yield) as a yellow oil. The 5,6-dichloroguaiacol was dissolved in dichloroethane (40 ml) and added to 1 M boron tribromide in CH_2Cl_2 (73 ml, 0.073 mol). The mixture was refluxed for 1 h, then cooled, water added cautiously with stirring and the product extracted with ether. The extracts were washed with water, dried and concentrated to give crude 3,4-dichlorocatechol **13** (10.6 g) as a grey solid. Crystallization from toluene gave off-white crystals of **13** (8 g, 45% yield), m.p. 98–99°C (Lit. 99°C; Azouz et al., 1955).

*2.1.2. 3,4,5-Trichlorocatechol (**5**)*

1 M Boron tribromide in CH_2Cl_2 (48 ml, 0.048 mol) was added over 10 min to a stirred solution of 4,5,6-trichloroguaiacol (9.0 g, 0 04 mol) in dichloroethane (35 ml). The mixture was refluxed 4 h then cooled, water added cautiously with stirring and the product extracted with ether. The extracts were washed with water, dried and concentrated to give the crude product (8 g). Crystallization from toluene (25 ml) gave colourless crystals of **5** (6 g, 71% yield), m.p. 131–134°C (Lit. 134–135°C; Cousin, 1898).

*2.1.3. 6-Chloroguaiacol (**17**)*

Guaiacol (62 g, 0.5 mol) was dissolved in a solution of NaOH (26 g, 0.65 mol) in water (600 ml). Commercial bleach (700 ml, 0.5 mol) was added with stirring over 20 min keeping the temperature below 25°C. After stirring another 20 min, the solution was acidified with hydrochloric acid and the product extracted with ether. The extracts were washed with water, dried and concentrated to give the crude product (80 g). Fractional distillation through a 10 cm Vigreux column gave 6-chloroguaiacol **17** (35 g) having 80% purity. Crystallization from hexane gave colourless needles of **17**, (30 g, 38% yield), m.p. 51–52°C (Lit. 54°C; Brown and McCall, 1955).

*2.1.4. 3,4-Dichloroguaiacol (**14**)*

A mixture of 3,4-dichlorocatechol **13** (5.3 g, 0.03 mol), K_2CO_3 (4.1 g, 0.03 mol) and methyl iodide (5.3 g, 0.04 mol) in acetone (50 ml) was refluxed 3 h with stirring. The product was cooled and partitioned between 5% NaOH and ether. The aqueous layer was acidified and extracted with ether. The ether extracts were washed with water, dried and concentrated to give a yellow oil (4.5 g). Purification on SiO_2 (150 g) and elution with hexane:ethyl acetate, 5:1, gave 3,4-dichloroguaiacol **14** (3.8 g) which was crystallized from hexane to give colourless needles (3 g, 52% yield), m.p. 50–51°C.

*2.1.5. 4,6-Dichloroguaiacol (**15**)*

4-Chloroguaiacol (Fig. 7) (Brown and McCall, 1955), (64 g, 0.4 mol) was dissolved in a solution of NaOH (20 g, 0.5 mol) in water (500 ml). Commercial bleach (500 ml, 0.36 mol) was added with stirring over 20 min keeping the temperature below 25°C. After stirring another 20 min, ether (400 ml) was added and the mixture acidified with 10% hydrochloric acid. The ether layer was separated and the aqueous layer extracted twice more with ether. The ether extracts were combined, washed with water, dried and concentrated to give the crude product (70 g) as a dark oil. Partial purification by passing through SiO_2 (400 g) and elution with hexane:ether 4:1 (1200 ml) gave 4,6-dichloroguaiacol **15** (40 g) 90% purity. Trituration followed by crystallization from hexane gave **15** as pale yellow crystals (30 g, 39% yield), m.p. 63–64°C (Lit. 64–65°C; Brown and McCall, 1955).

*2.1.6. 3,4,5-Trichloroguaiacol (**8**)*

Three drops of H_2SO_4 were added to a stirred solution of 4,5-dichloroguaiacol (Fig. 6) (Matell, 1955), (19.2 g, 0.1 mol) in acetic anhydride (50 ml). The solution was stirred at 50°C for 1 h then cooled and poured into cold water with stirring. After a few minutes, the product was filtered and washed with water giving 4,5-dichloroguaiacol acetate (23 g, 100 % yield). m.p. 64–66°C. The dichloroacetate was dissolved in acetic acid (140 ml) in a round bottom flask by warming to 40°C. A solution of chlorine (21 g, 0.3 mol) in acetic acid (250 ml) was added, the flask stoppered and the solution stirred at 40–50°C for 6 h. The product was cooled and poured into cold water with stirring. Filtration gave crude 3,4,5-trichloroguaiacol acetate (23 g) which was crystallized from hexane (70 ml) to give colourless needles (15 g, 56 % yield), m.p. 69–70°C. The trichloroacetate was dissolved in methanol (160 ml), 10% KOH in methanol:water, 9:1 (160 ml) added and the solution stirred at 50°C for 20 min. The product was cooled, water (700 ml) added and acidified with dilute hydrochloric acid. After stirring for 20 min, filtration gave crude 3,4,5-trichloroguaiacol **8** (11 g). Crystallization from hexane (120 ml) gave colourless needles of **8** (10 g, 74% yield), m.p. 85–86°C (Lit. 81–83°C; Lindström and Österberg, 1980).

*2.1.7. 3,4,6-Trichloroguaiacol (**9**)*

Sulfuryl chloride (3.0 g, 0.022 mol) was added to a solution of 3,4-dichloroguaiacol **14** (3.8 g, 0.02 mol) in acetic acid (40 ml) with stirring. The solution was stirred 1 h at 50°C then cooled and poured into cold water. Filtration and crystallization from hexane containing a little acetone gave pale yellow needles of **9** (3.2 g, 71% yield), m.p. 103–104°C (Lit. 103–104°C; Knuutinen, 1984; Smith et al., 1994).

3. Results and discussion

Catechols and guaiacols are interconvertable by limited methylation/demethylation (Fig. 3). Mixtures of isomeric guaiacols may be obtained from catechols containing substituents R (unless the symmetry of the catechol is maintained by the presence of more then one identical substituent in the appropriate positions, e.g. 4,5-, 3,4,5,6-, etc). This is the basis of the previously reported preparation of 3,4-dichloroguaiacol **14** (Knuutinen and Tarhanen, 1981) and 3,4,5-trichloroguaiacol **8** (Lindström and Österberg, 1980), two chlorinated guaiacols of interest in the present study.

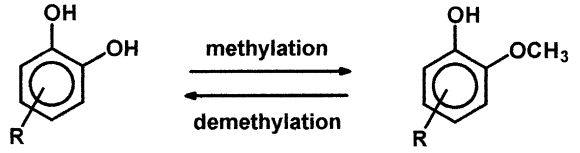


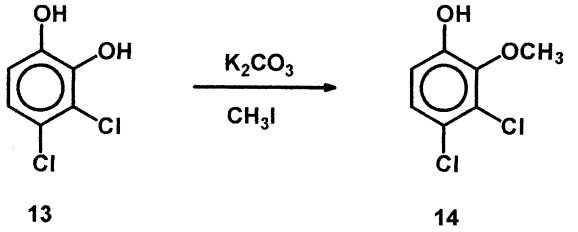
Fig. 3. Inconversion of catechols and guaiacols by methylation/demethylation.

Demethylation of substituted guaiacols gives only one isomer of the corresponding catechol, however, isomer specific synthesis of the starting substituted guaiacol is a prerequisite. The present work exploits differences in acidities of different hydroxyl groups in unsymmetrical catechols, and directive effects of substituents in guaiacols to achieve isomer specific syntheses of chlorinated catechols and guaiacols.

3.1. Syntheses of chlorinated guaiacols by selective methylation of unsymmetrically substituted catechols

The acidity of chlorophenols depends on the relative positions of the chlorine atom and hydroxyl group. This is illustrated by the pKa values for the simplest chlorophenols shown in Table 1 (Shiu et al., 1994).

The order of acidity *ortho>meta>para* was used to advantage to selectively methylate only one of the phenolic hydroxyl groups in chlorocatechols. By using one equivalent of potassium carbonate to selectively ionize the more acidic hydroxyl group in 3,4-dichlorocatechol **13**, it was possible to obtain 3,4-dichloroguaiacol **14** in 52% yield after crystallization (Fig. 4). Very little 5,6-dichloroguaiacol was formed, the main by-products being 3,4-dichloroveratrole and unreacted 3,4-dichlorocatechol which are readily separated. This method has also been used to prepare other chloroguaiacols with similar selectivity.



13 14

Fig. 4. Preparation of 3,4-dichloroguaiacol by selective methylation of 3,4-dichlorocatechol.

3.2. Syntheses of chlorinated guaiacols by employing directive effects

The chlorination of guaiacol normally proceeds as shown in Fig. 5, the substitution pattern being governed by the directive effects of the phenolic hydroxyl and methoxyl groups. Demethylation of 4,5,6-trichloroguaiacol **10** provides an easy synthesis of 3,4,5-trichlorocatechol **5**. The preparation of **5** by the chlorination of catechol is difficult because the reaction gives a mixture of di-, tri- and tetrachlorocatechol from which **5** is hard to separate in good yield.

When guaiacol is acetylated, the directive effect of the hydroxyl group is removed and substitution occurs para to the methoxyl group as shown in Fig. 6 (Hindmarsh et al., 1917). Since the acetylation/deacetylation procedure proceeds in essentially quantitative yield, this provides a very good synthesis of 5-chloroguaiacol **16** (Brown and McCall, 1955). A much more valuable application of this change in directive effect is for the synthesis of 3,4,5-trichloroguaiacol **8**. Chlorination of 4,5-dichloroguaiacol acetate gave 3,4,5-trichloroguaiacol acetate which was saponified to give **8** in 41% overall yield (Fig. 6). The procedure easily allows the preparation of 10–20 g quantities of **8**, and avoids the separation from 4,5,6-trichloroguaiacol **10** required when limited

Table 1
pKa values of simple chlorophenols

Compound	Structure	pKa
2-Chlorophenol		8.49
3-Chlorophenol		8.85
4-Chlorophenol		9.18

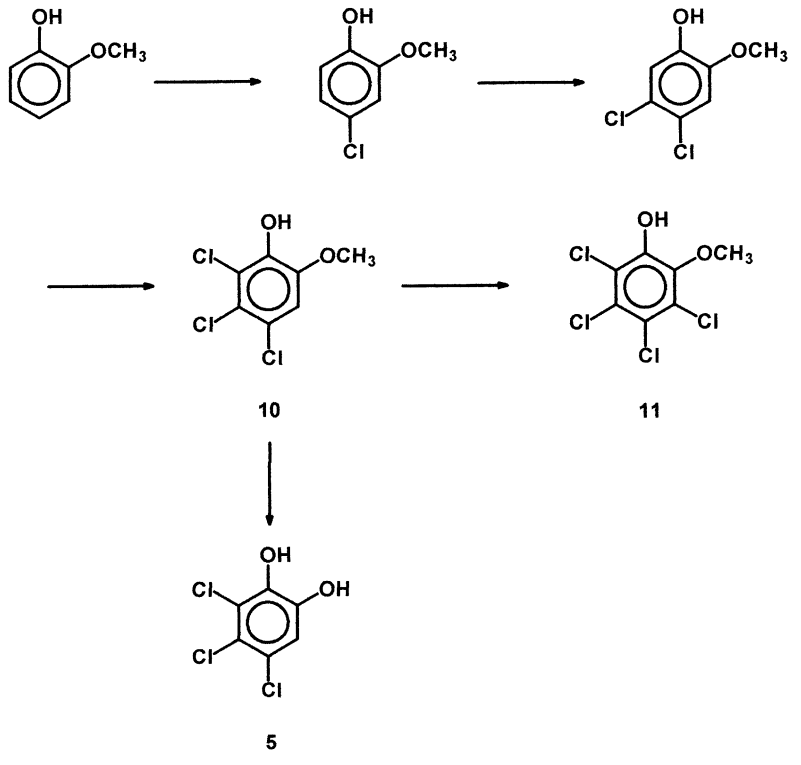


Fig. 5. Chlorination of guaiacol and preparation of 3,4,5-trichlorocatechol **5**.

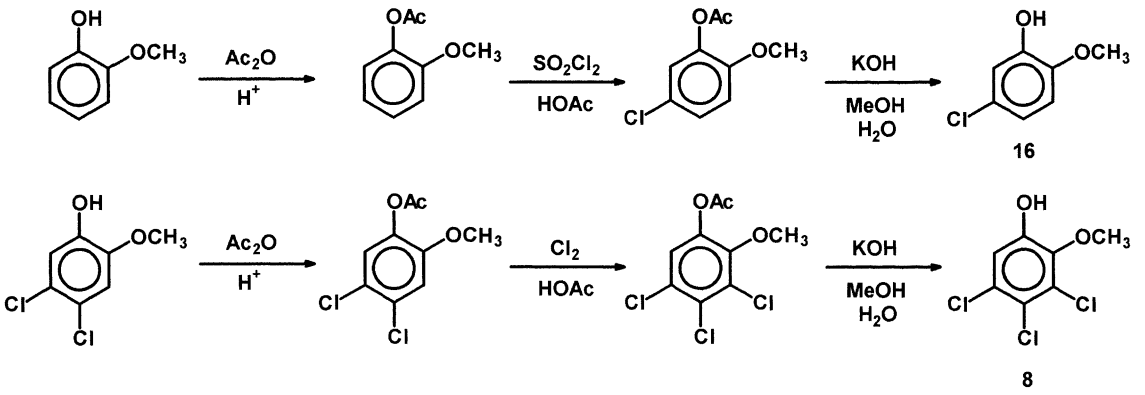


Fig. 6. Use of acetylation to direct the chlorination of guaiacols.

methylation of 3,4,5-trichlorocatechol **5** is used (Knuutinen, 1984; Lindström and Österberg, 1980).

A different type of directive tactic was used to prepare 6-chloroguaiacol **17**, a key intermediate in the preparation of a variety of chlorinated catechols and guaiacols. The chlorination of guaiacol, which normally gives 4-chloroguaiacol as shown in Fig. 5, gives a 4:1 ratio of 6-chloroguaiacol:4-chloroguaiacol when performed in alkaline solution (Fig. 7). The 6-chloro and 4-chloroguaiacols can be separated by countercurrent distribution between dichloromethane and aqueous sodium phosphate by virtue of the greater acidity of 6-chloroguaiacol (cf. Table 1). Similar reaction of 4-chloroguaiacol in alkaline solution provided a convenient synthesis of 4,6-dichloroguaiacol **15** (Fig. 7). This directive technique was also used in the preparation of 4-chlorosyringol (McKague, 1993).

The importance of 6-chloroguaiacol as a synthetic intermediate in the overall scheme of the present work is illustrated by the conversions shown in Fig. 8.

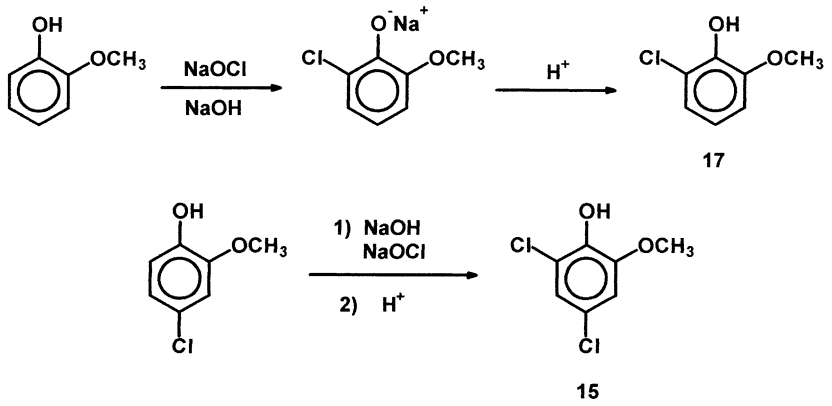


Fig. 7. Preparation of 6-chloroguaiacol and 4,6-dichloroguaiacol.

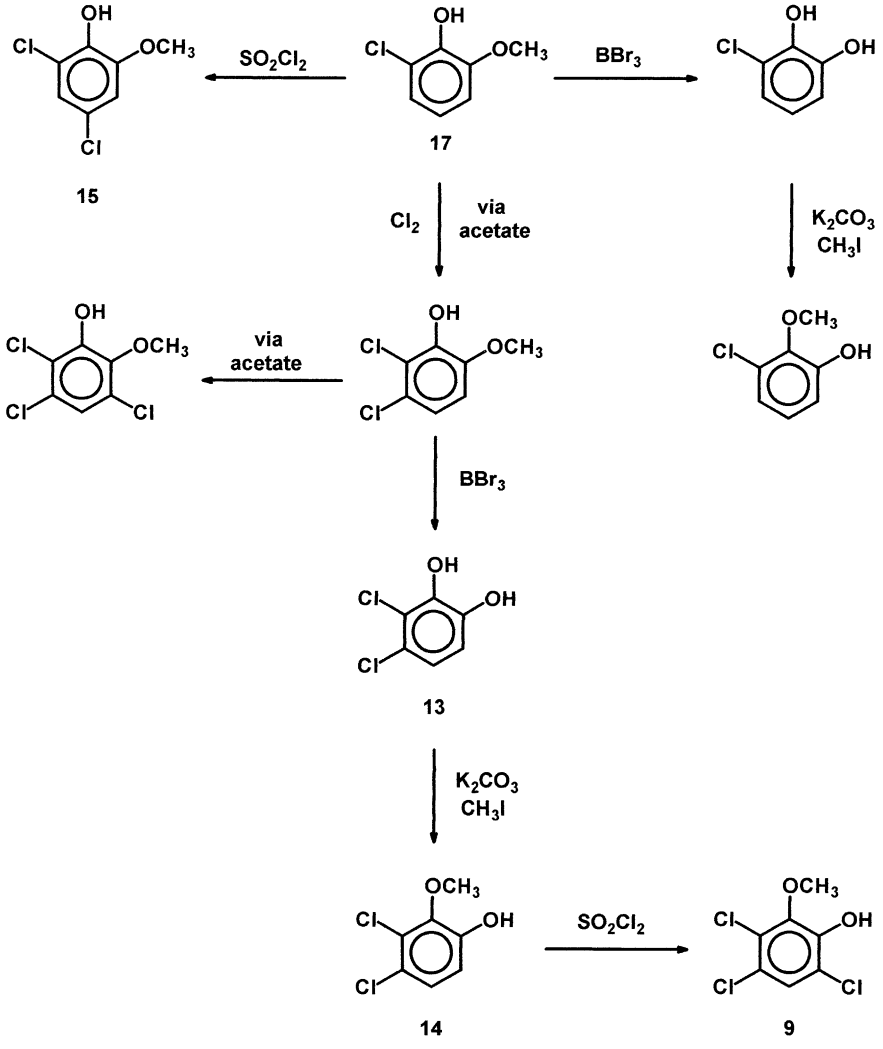


Fig. 8. Conversions of 6-chloroguaiacol **17** to other chlorocatechols and chloroguaiacols.

Chlorination gives 4,6-dichloroguaiacol **15** while demethylation with boron tribromide gives 3-chlorocatechol. Selective methylation of the more acidic hydroxyl group in 3-chlorocatechol as previously discussed gives 3-chloroguaiacol. Chlorination of 6-chloroguaiacol acetate gives 5,6-dichloroguaiacol and, if the chlorination is continued, 3,5,6-trichloroguaiacol. Demethylation of 5,6-dichloroguaiacol gives 3,4-dichlorocatechol **13** which can be selectively methylated to give 3,4-dichloroguaiacol **14**. Chlorination of 3,4-dichloroguaiacol gives 3,4,6-trichloroguaiacol **9**.

The synthetic procedures described in this paper take advantage of the fundamental differences in acidities of different phenolic hydroxyl groups in chlorocatechols, and directive effects in guaiacols. Application of the procedures allows significantly improved preparations of many of the isomeric chlorinated catechols and guaiacols.

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