# XLIII.—*The Variation of Phenol Coefficients in Homologous Series of Phenols.*

By Charles Edward Coulthard, Joseph Marshall, and Frank Lee Pyman.

The introduction into medicine of the antiseptic, hexylresorcinol, was the outcome of work by Johnson and Lane (*J. Amer. Chem. Soc.*, 1921, **43**, 348) and Dohme, Cox, and Miller (*ibid.* 1926, **48**, 1688) in which the influence of alkyl substituents upon the germicidal value of resorcinol was studied. It was shown that the germicidal value of 4-*n*-alkylresorcinols rose to a maximum at 4-*n*-hexylresorcinol, which had a phenol coefficient of 50, the values for *n*-amyl- and *n*-heptyl-resorcinol being 33 and 30 respectively. It was further shown that the antiseptic values of the *n*-alkylresorcinols were greater than those of branched-chain alkylresorcinols having the same number of carbon atoms.

Exact information as to the effect of alkyl substituents upon the antiseptic value of phenol and its homologues is somewhat scanty and therefore it appeared to be of interest to make a systematic study of the variation of the phenol coefficients in the homologous series of *n*-alkylphenols, *n*-alkylcresols, and *n*-alkylguaiacols.

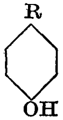
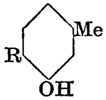
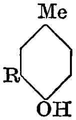
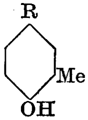
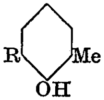
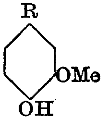
For the determination of phenol coefficients, the Rideal–Walker technique was closely followed, but owing to the sparing solubility of most of the compounds in water, solutions in dilute aqueous sodium hydroxide were employed, care being taken to keep the concentration of sodium hydroxide below lethal strength. In most cases, initial solutions of 0·1% of the compound in *N*/100-sodium hydroxide were used. The results are in Table I.

Comparing the vertical columns in this table, it will be seen that the phenol coefficients of the *p*-*n*-alkylphenols are, in general, considerably less than those of the corresponding *n*-alkylcresols, and the values of the *n*-alkylguaiacols are comparatively trivial. In comparing the horizontal columns, it will be noticed that the antiseptic value of the compounds increases generally with the number of carbon atoms in the side chain up to the *n*-amyl derivative and then diminishes.

Of the *n*-amylcresols, 4-*n*-amyl-*m*-cresol has been studied in some detail, and has been found to have high phenol coefficients (200 to 300), not only when tested against *Bacillus typhosus* (which is employed in the Rideal–Walker method), but also against various strains of *Streptococcus* and *Staphylococcus*. Since, in addition, its toxicity is comparatively low, it may prove to be of value in medicine.

TABLE I.

*Phenol coefficients.*

| R. | *p*-*n*-Alkylphenols.<br> | 4-*n*-Alkyl-*m*-cresols.<br> | 3-*n*-Alkyl-*p*-cresols.<br> | 5-*n*-Alkyl-*o*-cresols.<br> | 3-*n*-Alkyl-*o*-cresols.<br> | 4-*n*-Alkylguaiacols.<br> |
|---|---|---|---|---|---|---|
| $CH_3$ | 2·5 | — | — | — | — | 2·7 |
| $C_2H_5$ | 7·5 | 12·5† | 12·5 | 15 | — | 2 |
| $n$-$C_3H_7$ | 20 | 34 | — | — | — | 5 |
| $n$-$C_4H_9$ | 70* | 100 | 95 | 110 | 60 | 25 |
| $n$-$C_5H_{11}$ | 104 | 280 | 250 | 300 | 250 | 25 |
| $n$-$C_6H_{13}$ | 90 | 275 | 175 | 100 | 180 | 9 |
| $n$-$C_7H_{15}$ | 20 | 30 | — | — | — | — |

* The phenol coefficient of *o*-*n*-butylphenol was 75.

† The phenol coefficient of 6-ethyl-*m*-cresol (Me : OH : Et = 1 : 3 : 6) was 15.

### *Preparation of* n-*Alkylphenols,* n-*Alkylcresols, and* n-*Alkylguaiacols.*

All the alkyl derivatives were prepared by reduction of the corresponding ketones by Clemmensen's method. The ketones were prepared by four methods : (1) the Nencki condensation of acid and phenol using zinc chloride, (2) the Fries isomerisation of phenyl esters by means of aluminium chloride, (3) the isomerisation of phenyl esters by zinc chloride, and (4) condensation of acids with phenols by means of phosphorus oxychloride.

(1) The Nencki reaction is well known to give good yields of 4-acylresorcinols or 2-acylquinols when resorcinol or quinol is condensed with fatty acids and zinc chloride. Goldzweig and Kaiser (*J. pr. Chem.*, 1891, **43**, 86) state that pyrocatechol does not react when employed in the Nencki reaction and it would appear that this statement has been accepted, although Neitzel (*Ber.*, 1891, **24**, 2863) mentions that acetylpyrocatechol is " apparently " produced by this method. He did not, however, obtain it in a pure state owing to the similarity in solubility of pyrocatechol and acetylpyrocatechol. We are able to confirm the formation of acetylpyrocatechol and other acylpyrocatechols by the Nencki method, and have separated them from unchanged pyrocatechol in each case by distillation under diminished pressure.

Attempts to apply the Nencki reaction to monoalkyl ethers of dihydroxybenzenes have given poor yields, but positive results were obtained in the formation of pæonol from resorcinol monomethyl ether and acetic acid, and in the preparation of acetovanillone and its homologues from guaiacol and fatty acids. Attempts to condense quinol monomethyl ether with acetic acid, however, gave a negative result. The Nencki reaction has been little used for the condensation of monohydric phenols with fatty acids, but Michael and Palmer (*Amer. Chem. J.*, 1885, **7**, 275) obtained *p*-acetylphenol in this manner, and Goldzweig and Kaiser (*loc. cit.*) obtained *p*-propionylphenol similarly, although the yield is not stated in either case. We have condensed a series of fatty acids with phenol by this method and have obtained the *p*-acylphenols in poor yield, *viz.*, 2—10% of the theoretical, and have observed that small quantities of the *o*-acylphenols are formed simultaneously. The sole products obtained from *m*-cresol in the Nencki reaction were the 4-acyl-*m*-cresols, as would be expected from the well-known fact that an alkyl group in the meta-position to the hydroxyl induces substitution in the neighbourhood of the hydroxyl (Auwers and Mauss, *Annalen*, 1928, **464**, 293), but here again the yields are poor.

(2) A considerable number of acylphenols and acylcresols have been made by the Fries isomerisation under the conditions described

by Rosenmund and Schnurr (*Annalen*, 1928, **460**, 56), *viz.*, heating the appropriate ester with 1·1 molecules of aluminium chloride. Attempts to prepare acylguaiacols similarly were unsuccessful, but the publication of a paper by Pfeiffer and Haack (*Annalen*, 1927, **460**, 156) on the combination of aluminium bromide with ethers in molecular proportion led us to suspect that a similar combination occurred between aluminium chloride and guaiacol esters, and that this prevented the aluminium chloride from producing isomerisation. In later experiments, two molecular proportions of aluminium chloride were consequently added to guaiacol esters and 4-acylguaiacols were then produced together with a proportion of the corresponding acylpyrocatechols. The position taken up by the acyl group was proved by the facts (1) that guaiacyl acetate gave acetovanillone, (2) that guaiacyl butyrate gave a ketone which was reduced to a butylguaiacol identical with that obtained by Nomura and Hotta (*Sci. Rep. Tôhoku Imp. Univ.*, 1925, **14**, 119) by the reduction of zingerone, and (3) that the propylguaiacol obtained in the same manner from guaiacyl propionate was identical with dihydroeugenol.

(3) Pope (Brit. Pat. 287,967) has described a method for the preparation of 4-*n*-alkylresorcinols by isomerisation of resorcinol monoacyl esters by heating with zinc chloride. We have found that, although this method gives good yields (80—90%) of resacetophenone and 4-*n*-hexoylresorcinol when applied to resorcinol monoacetate and mono-*n*-hexoate, it gives only poor yields of acylphenols when applied to esters of phenol, *m*-cresol, and guaiacol.

(4) The condensation of guaiacol and acetic acid by means of phosphorus oxychloride gave *iso*acetovanillone (5-acetylguaiacol), which was obtained previously by Schneider and Kraft (*Ber.*, 1922, **55**, 1892) by condensing guaiacol and acetic anhydride by means of sulphuric acid. Propionic and butyric acids were also condensed with guaiacol by means of phosphorus oxychloride, and gave compounds isomeric with 4-propionylguaiacol and 4-*n*-butyrylguaiacol, which are doubtless 5-*propionylguaiacol* and 5-n-*butyrylguaiacol.*

## EXPERIMENTAL.

(1) *The Nencki Reaction.—*o- *and* p-*Acetylphenols.* Phenol (150 g.) was added to a hot solution of anhydrous zinc chloride (200 g.) in glacial acetic acid (100 c.c.) and the mixture was boiled for 1 hour. After the mass had cooled, water was added and the product was distilled with steam. The oil separated from the distillate was dissolved in excess of warm 5*N*-sodium hydroxide, and from this solution, on cooling, pale yellow crystals were deposited which after decomposition with dilute hydrochloric acid gave

*o*-acetylphenol (5 g.; yield, 2%*) having b. p. 110°/15 mm. and m. p. 28° (Found: C, 70·5; H, 5·8. Calc.: C, 70·6; H, 5·9%). The oxime melted at 112°. Auwers (*Ber.*, 1925, **58**, 36) gives b. p. 218° and m. p. of oxime 112°. The non-volatile oil remaining after the steam distillation was distilled under diminished pressure and gave *p*-acetylphenol (7 g.; yield, 3%) having b. p. 190°/15 mm. and m. p. 106—107°. Michael and Palmer (*loc. cit.*) give m. p. 108° and Perkin (J., 1897, **71**, 805) gives m. p. 107°.

The great difference in boiling point exemplified in the case of the *o*- and *p*-acetylphenols is found generally for *o*- and *p*-acylphenols and their methyl homologues. The *o*-hydroxyketones differ further from *p*-hydroxyketones in being volatile in steam and in giving red to violet colorations with ferric chloride. Moreover, the sodium salts of the *o*-acylphenols are readily obtained in yellow crystals freely soluble in water, and are easily precipitated by a small excess of alkali, whereas the sodium salts of the *p*-compounds are colourless and are easily soluble in water and in dilute sodium hydroxide solution.

As a general rule, the phenylhydrazones of the *o*-compounds are more readily made than the *p*-compounds, as is known to be the case with the oximes.

*p*-Propionylphenol was prepared by the method of Goldzweig and Kaiser (*loc. cit.*) in 10% yield.

p-n-*Valerylphenol* was obtained in 5% yield accompanied by the *o*-compound, of which the presence was indicated through the production of a violet colour on the addition of ferric chloride to an alcoholic solution of the steam-distillate of the reaction product. *p*-*n*-Valerylphenol has b. p. 210°/15 mm. and crystallises from benzene–light petroleum in cubes, m. p. 62—63° (Found: C, 74·0; H, 7·9. $C_{11}H_{14}O_2$ requires C, 74·2; H, 7·8%).

p-n-*Hexoylphenol* (yield, 8%) forms colourless plates, m. p. 63—64°, from benzene (Found: C, 75·1; H, 8·4. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%).

p-n-*Heptoylphenol* (yield, 9%; b. p. 220°/15 mm.) crystallises from benzene in well-formed prisms, m. p. 93—94° (Found: C, 75·9; H, 8·6. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

p-*Heptoylphenyl benzoate* crystallises from alcohol in needles, m. p. 92—93° (Found: C, 77·0; H, 7·1. $C_{20}H_{22}O_3$ requires C, 77·4; H, 7·1%).

4-Propionyl-*m*-cresol was isolated from the product of the fusion of propionic acid and *m*-cresol with zinc chloride by distillation with steam and rectification of the oil obtained in a vacuum. The

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* Yields are given in % of the theoretical, and the substances are colourless except where it is otherwise stated.

fraction, b. p. 125—135°/15 mm., was crystallised from dilute alcohol, giving needles or plates, m. p. 45—46° (yield, 11%). It did not depress the melting point of 4-propionyl-*m*-cresol, prepared by the isomerisation of *m*-tolyl propionate, for which Auwers (*Annalen*, 1924, **439**, 132) gives m. p. 45—46°.

4-*n*-Butyryl-*m*-cresol was similarly obtained from *m*-cresol and butyric acid (yield, 17%) and identified as the oxime, m. p. 74—75° (see page 288).

*Pæonol.* To zinc chloride (40 g.), dissolved in hot glacial acetic acid (40 c.c.), resorcinol monomethyl ether (25 g.) was added. The mixture was brought to the boiling point, allowed to cool in an oil-bath, and distilled with steam. The oil which distilled was separated by fractional distillation under diminished pressure into about 10 g. of unchanged resorcinol monomethyl ether and a fraction of higher boiling point from which 6 g. (29%) of pæonol, m. p. 50°, were obtained.

4-*Acetylpyrocatechol.* Pyrocatechol (25 g.), glacial acetic acid (50 g.), and zinc chloride (100 g.) were fused together in the usual manner. The mass was poured into water, and the solution extracted with ether. After distillation under diminished pressure, pyrocatechol and a fraction of b. p. about 180° (15 g.) were obtained. This was dissolved in hot benzene and allowed to cool; the crystals which separated were recrystallised and gave 8 g. (20%) of 4-acetylpyrocatechol, m. p. 116°. 4-*n*-Butyrylpyrocatechol and 4-*n*-hexoylpyrocatechol were obtained by exactly similar methods of procedure. Each was compared and found to be identical with the corresponding product obtained from the guaiacol ester by treatment with aluminium chloride.

*Acetovanillone.* To zinc chloride (100 g.) in hot glacial acetic acid (200 c.c.), guaiacol (100 g.) was added. The mixture was boiled gently under reflux for 3 hours, and acetic acid then distilled off under diminished pressure. After cooling, the residue was poured into water and extracted with ether. The extract was distilled under diminished pressure; a fraction, b. p. 170—190°, solidified and after recrystallisation from ether gave acetovanillone (5 g.; 4%), m. p. 113—114°.

4-*n*-Butyrylguaiacol and 4-*n*-hexoylguaiacol were prepared similarly and proved to be identical with the products, described later, obtained by the isomerisation of guaiacol esters with aluminium chloride; in each case considerable quantities of pyrocatechol and of the corresponding acylpyrocatechols were obtained as by-products.

(2) *The Fries Isomerisation.*—Phenyl butyrate, hexoate, and heptoate were converted into mixtures of *o*- and *p*-acylphenols by

heating with 1·1 mols. of aluminium chloride at 160—180° for 1—2 hours, and separated by distillation with steam or under diminished pressure.

o-n-*Butyrylphenol* (yield, 60%) had b. p. 124—126°/14 mm. and m. p. 8° (Found: C, 72·9; H, 7·3. $C_{10}H_{12}O_2$ requires C, 73·2; H, 7·3%). Its *phenylhydrazone* is yellow and melts at 85—87° (Found: N, 11·0. $C_{16}H_{18}ON_2$ requires N, 11·0%). *p*-Butyrylphenol (yield, 19%) has b. p. 200°/15 mm. and m. p. 91°. Perkin (J., 1889, **55**, 546) gives m. p. 91°. p-*Butyrylphenyl benzoate* crystallises from alcohol in platelets, m. p. 106—107° (Found: C, 75·8; H, 6·0. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%).

o-n-*Hexoylphenol* (yield, 50%) has b. p. 145—147°/15 mm. and crystallises from alcohol in prisms, m. p. 22° (Found: C, 74·8; H, 8·4. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%). Its *phenylhydrazone* crystallises from alcohol in yellowish leaflets, m. p. 102—103° (Found: N, 9·6. $C_{18}H_{22}ON_2$ requires N, 9·9%).

o-n-*Heptoylphenol* (yield, 58%) has b. p. 172—174°/20 mm. and separates from alcohol in prisms, m. p. 24° (Found: C, 75·3; H, 8·7. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%). Its phenylhydrazone separates from alcohol in yellow plates, m. p. 91—92°.

The isomerisation of *o*-tolyl acetate has been described by Auwers (*Ber.*, 1925, **58**, 36) and by Rosenmund and Schnurr (*Annalen*, 1927, **460**, 56).

5-*Acetyl*-o-*tolyl benzoate* separates from dilute spirit in fine silky needles, m. p. 79—80° (Found: C, 75·5; H, 5·3. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%).

*o*-Tolyl butyrate, valerate, and hexoate were isomerised by heating the ester with 1·1 mols. of aluminium chloride at 160—180° for ½ hour, and the *o*- and *p*-ketones were separated by distillation under diminished pressure.

3-n-*Butyryl*-o-*cresol* (yield, 60% at 160—180°; 40% at 100°) has b. p. 143°/11 mm. and solidifies in a freezing mixture (Found: C, 73·9; H, 7·9. $C_{11}H_{14}O_2$ requires C, 74·2; H, 7·8%). Its oxime forms needles, m. p. 87—88°, from alcohol, and its *phenylhydrazone* separates from alcohol in yellow needles, m. p. 157—158° (Found: N, 10·3. $C_{17}H_{20}ON_2$ requires N, 10·4%).

5-n-*Butyryl*-o-*cresol* (yield, 30% at the ordinary temperature in 2 days; 55% at 100°; and 30% at 160—180°), b. p. 195—200°/15 mm., forms prisms, m. p. 132—133°, from benzene (Found: C, 74·0; H, 7·8. $C_{11}H_{14}O_2$ requires C, 74·2; H, 7·8%). The phenylhydrazone separates in yellowish plates, m. p. 110°.

3-n-*Valeryl*-o-*cresol* (yield, 46%) has b. p. 143—145°/15 mm. and m. p. 18° (Found: C, 74·6; H, 8·5. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%). The *phenylhydrazone* forms pale yellow leaflets, m. p.

116—118°, from alcohol (Found : N, 9·8. $C_{18}H_{22}ON_2$ requires N, 9·9%).

5-n-*Valeryl*-o-*cresol* (yield at 160°, 30%), b. p. 205°/15 mm., forms rhombic prisms, m. p. 103—104°, from benzene (Found : C, 74·8; H, 8·5. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%). 5-n-*Valeryl*-o-*tolyl benzoate* separates from alcohol in small plates, m. p. 72—73° (Found : C, 77·0; H, 7·1. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·7%). 5-n-*Valeryl*-o-*cresol phenylhydrazone* forms very pale yellow needles, m. p. 120—121° (Found : N, 9·8. $C_{18}H_{22}ON_2$ requires N, 9·9%).

3-n-*Hexoyl*-o-*cresol* (yield, 60%), b. p. 152—154°/15 mm., separates from cold alcohol in prisms, m. p. 23° (Found : C, 75·9; H, 9·0. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%). Its *phenylhydrazone* separates from alcohol in leaflets, m. p. 93—94° (Found : N, 9·3. $C_{19}H_{24}ON_2$ requires N, 9·5%).

5-n-*Hexoyl*-o-*cresol* (yield at 160°, 25%), b. p. 200—205°/15 mm., separates from benzene in plates which fall to powder on drying at 50°; it then melts at 79—80° (Found : C, 75·7; H, 8·9. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%). The *benzoate* crystallises from alcohol in shining leaflets, m. p. 59—60° (Found : C, 77·2; H, 6·9. $C_{20}H_{22}O_3$ requires C, 77·4; H, 7·1%).

The ketones obtained by isomerisation of *p*-tolyl esters with 1·1 mols. of aluminium chloride for 2 hours at 160° were purified by steam distillation, crystallisation of the sodium salts, and subsequent distillation under reduced pressure.

3-n-*Butyryl*-p-*cresol oxime* forms needles, m. p. 96—97°, from light petroleum (Found : N, 7·3. $C_{11}H_{15}O_2N$ requires N, 7·3%). 3-n-*Butyryl*-p-*cresol phenylhydrazone* separates from alcohol in rhombic prisms, m. p. 141—142° (Found : N, 10·15. $C_{17}H_{20}ON_2$ requires N, 10·4%).

3-n-*Valeryl*-p-*cresol* (yield, 65%), made but not characterised by Wittig (*Annalen*, 1925, **446**, 155), has b. p. 144—145°/15 mm. and separates from light petroleum in fine needles, m. p. 32—33° (Found : C, 74·9; H, 8·5. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%). Its *phenylhydrazone* separates from alcohol in yellowish plates, m. p. 113—115° (Found : N, 9·7. $C_{18}H_{22}ON_2$ requires N, 9·9%).

3-n-*Hexoyl*-p-*cresol* (yield, 80%), b. p. 150—152°/15 mm., crystallises from light petroleum in fine needles, m. p. 19° (Found : C, 75·3; H, 8·9. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%). The *phenylhydrazone* separates from alcohol in platelets, m. p. 110—112° (Found : N, 9·2. $C_{19}H_{24}ON_2$ requires N, 9·5%).

Although there is the possibility of the production of both 4- and 6-acyl-*m*-cresols in the isomerisation of *m*-tolyl esters, if the reaction is carried out at the ordinary temperature in nitrobenzene solution as described by Rosenmund the yield of the 6-compound is negligible, being only 2% in the case of *m*-tolyl butyrate. The ketones of this class were purified by steam distillation, followed by distillation under reduced pressure.

4-*Propionyl*-m-*cresol oxime* separates from light petroleum in needles, m. p. 103—104° (Found : N, 7·7. $C_{10}H_{13}O_2N$ requires N, 7·8%).

6-n-*Butyryl*-m-*cresol* separates from benzene in colourless plates, m. p. 97—98° (Found : C, 73·9; H, 7·8. $C_{11}H_{14}O_2$ requires C, 74·2; H, 7·9%).

4-n-*Butyryl*-m-*cresol* (yield, 88%) has b. p. 142—144°/15 mm. and m. p. 17° (Found : C, 74·0; H, 7·6. $C_{11}H_{14}O_2$ requires C, 74·2; H, 7·9%). Its *oxime* forms needles, m. p. 74—75°, from light petroleum (Found : N, 7·3. $C_{11}H_{15}O_2N$ requires N, 7·3%). Its *phenylhydrazone* forms pale yellowish leaflets, m. p. 95—97°, from alcohol (Found : N, 10·2. $C_{17}H_{20}ON_2$ requires N, 10·4%).

4-n-*Valeryl*-m-*cresol* (yield, 85%) has b. p. 152—154°/15 mm. and m. p. 16° (Found : C, 74·8; H, 8·2. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%).

4-n-*Hexoyl*-m-*cresol* (yield, 93%), b. p. 162—164°/15 mm., separates from alcohol in prismatic needles, m. p. 23—24° (Found : C, 75·5; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%). Its *phenylhydrazone* separates from alcohol in leaflets, m. p. 92—93° (Found : N, 9·3. $C_{19}H_{24}ON_2$ requires N, 9·5%).

4-n-*Heptoyl*-m-*cresol* (yield, 84%) has b. p. 172—174°/15 mm. and m. p. 18° (Found : C, 76·0; H, 9·1. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%).

The best conditions for the preparation of 4-acylguaiacols were found to be as follows : Aluminium chloride (270 g.; 2 mols.) was dissolved in nitrobenzene (600 c.c.) by heating at 100°, the solution cooled to 10°, and the ester (1 mol.) added quickly; the solution, which was at first clear, changed to a very viscous mass. On gentle warming, hydrogen chloride was evolved and the viscous mass became micro-crystalline. After remaining at about 80° for ½—1 hour, the product was kept over-night; the crystals were then collected out of contact with moist air and washed successively with benzene, benzene–light petroleum, and light petroleum.

The aluminium chloride compound was thus obtained as a cream-coloured sandy powder. It was added gradually to an excess of dilute hydrochloric acid; the almost pure 4-acylguaiacol then separated as an oil, which quickly solidified and was obtained in a yield of upwards of 50% of the theoretical. The nitrobenzene filtrate from the aluminium compound was distilled with steam to remove nitrobenzene and the remaining oil was distilled under diminished pressure; a further quantity of the 4-acylguaiacol was thus obtained, followed at a temperature some 30° higher by the corresponding acylpyrocatechol.

The 4-acylguaiacols and 4-acylpyrocatechols are easily crystallisable compounds, the acylguaiacols being more soluble in organic solvents but less soluble in water than the corresponding acylpyrocatechols. The solubility of 4-acetylpyrocatechol in water is such as to render water unsuitable for its recrystallisation, but this solvent may very conveniently be employed for recrystallising 4-propionyl- and 4-*n*-butyryl-pyrocatechols, both of which are, with difficulty, soluble in benzene. 4-*n*-Valerylpyrocatechol and 4-*n*-hexoylpyrocatechol are easily soluble in hot benzene.

4-Acylguaiacols and acylpyrocatechols give green and very deep bluish-green colorations, respectively, with alcoholic ferric chloride. Certain constants of these compounds, with analyses, are given below :—

| | | B. p. | Found. | | | Required. | |
|---|---|---|---|---|---|---|---|
| | M. p. | (15 mm.). | % C. | % H. | Formula. | % C. | % H. |
| 4-*Propionylguaiacol* ...... | 61—62° | 180—185° | 66·5 | 6·6 | $C_{10}H_{12}O_3$ | 66·7 | 6·7 |
| 4-n-*Butyryl* ,, ...... | 54—55 | 185—195 | 67·9 | 7·2 | $C_{11}H_{14}O_3$ | 68·0 | 7·2 |
| 4-n-*Valeryl* ,, ...... | 60—62 | 195—197 | 69·0 | 7·6 | $C_{12}H_{16}O_3$ | 69·2 | 7·7 |
| 4-n-*Hexoyl* ,, ...... | 60—62 | 212—215 | 70·1 | 8·1 | $C_{13}H_{18}O_3$ | 70·3 | 8·1 |
| 4-n-*Valerylpyrocatechol* ... | 143—144 | 230—240 | 68·0 | 7·0 | $C_{11}H_{14}O_3$ | 68·0 | 7·2 |
| 4-n-*Hexoyl* ,, ... | 93—94 | 240—250 | 69·1 | 7·6 | $C_{12}H_{16}O_3$ | 69·2 | 7·7 |

4-Propionylpyrocatechol and 4-*n*-butyrylpyrocatechol had b. p. 210—220° and 220—230°/15 mm. respectively. The m. p. of each was identical with that given by Rosenmund and Lohfert (*Ber.*, 1928, **61**, 2601).

The following derivatives of the acylguaiacols have been prepared :—

4-*Propionylguaiacyl benzoate*, m. p. 108—110° (Found : C, 71·6; H, 5·8. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%). 4-*Propionylguaiacol* p-*nitrophenylhydrazone*, yellowish needles, m. p. 151—152°, from alcohol (Found : N, 13·3. $C_{16}H_{17}O_4N_3$ requires N, 13·3%). 4-n-*Butyrylguaiacyl benzoate*, m. p. 75—77° (Found : C, 72·0; H, 6·0. $C_{18}H_{18}O_4$ requires C, 72·5; H, 6·0%). 4-n-*Butyrylguaiacol phenylhydrazone*, pale yellow needles, m. p. 91—92°, from dilute alcohol (Found : N, 9·6. $C_{17}H_{20}O_2N_2$ requires N, 9·9%). 4-n-*Valerylguaiacyl benzoate*, m. p. 85—87° (Found : C, 73·0; H, 6·3. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4%). 4-n-*Hexoylguaiacyl benzoate*, m. p. 54—55° (Found : C, 73·4; H, 6·8. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·7%).

(3) *Isomerisation of Esters with Zinc Chloride.*—(*a*) Phenyl acetate (100 g.) and powdered zinc chloride (15 g.) were heated at 125° for 3 hours. The product gave *o*-acetylphenol (4 g.; yield, 4%) and *p*-acetylphenol (8 g.; yield, 8%).

(*b*) *m*-Tolyl propionate (75 g.) and powdered zinc chloride (37·5 g.) were heated at 150—160° for 1 hour. The product was dissolved in dilute hydrochloric acid and distilled with steam. Extraction of the distillate with ether and distillation of the extract under low pressure gave 15 g. of pure 4-propionyl-*m*-cresol (yield, 20%).

(*c*) To guaiacyl acetate (20 g.) at 200°, powdered zinc chloride (5 g.) was added. Vigorous ebullition took place, and after 1 minute the melt was poured into water and boiled with dilute hydrochloric acid. Ether then extracted an oil, which was distilled under reduced pressure. A fraction, b. p. 180—200°/15 mm., solidified on cooling, and after crystallisation from benzene gave acetovanillone (5 g.), m. p. 113—114° (yield, 25%).

(4) *Condensation of Guaiacol with Fatty Acids by Means of Phosphorus Oxychloride.*—Guaiacol (100 g.) and glacial acetic acid (200 g.) were mixed, and phosphorus oxychloride (200 g.) was added slowly. After being warmed gently on the steam-bath until the evolution of hydrogen chloride ceased (3 hours), the product was poured into water, and the guaiacol distilled with steam. The non-volatile oil was extracted with ether and distilled under diminished pressure. The fraction, b. p. 180—200°/15 mm., solidified, and after crystallisation from benzene gave *iso*acetovanillone (26 g.), m. p. 91—92° (yield, 20%) (Found: C, 65·4; H, 6·3. Calc.: C, 65·1; H, 6·1%). It crystallised from water in long needles (m. p. 59—60°) containing water of crystallisation (Schneider and Kraft, *loc. cit.*, gave m. p. 91°, and 66—69° for the hydrate). iso*Acetovanillone phenylhydrazone* melts at 102° (Found: N, 10·8. $C_{15}H_{16}O_2N_2$ requires N, 10·9%), and iso*acetovanillone benzoate* at 141—142° (Found: C, 70·7; H, 5·3. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%).

5-*Propionylguaiacol* was prepared similarly (yield, 25%). It melts at 93—94°, and is moderately easily soluble in hot water or benzene (Found: C, 66·4; H, 6·7. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·77%). The *benzoate* melts at 96—98° (Found: C, 71·6; H, 5·8. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%).

5-n-*Butyrylguaiacol*, prepared similarly, melts at 81—82° (Found: C, 67·9; H, 7·2. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%).

### *Reduction of Acylphenols to Alkylphenols.*

For the conversion of the carbonyl group into the methylene group in the series of hydroxyketones, the usual procedure was to boil the ketone (1 part) under reflux on the steam-bath for 12—20 hours with amalgamated zinc (3 parts) and dilute hydrochloric acid (1 : 1) (6 parts) to which alcohol (2 parts) had been added. (When *o*-hydroxyketones were being reduced, the end of the reaction was clearly indicated by the failure of the colour reaction with ferric chloride.) The alcohol was removed by distillation with steam and the lower phenols were separated by continued distillation with steam, but the rate of distillation became too slow with the higher members of the series to permit of their being separated by this method. They were therefore extracted from the reaction mixture, distilled in a vacuum, and recrystallised wherever possible from light petroleum. The following table shows the new phenols which were prepared and certain constants and analytical data :—

| Phenol. | B. p. (15 mm.). | M. p. | Found. % C. | Found. % H. | Formula. | Calc. % C. | Calc. % H. |
|---|---|---|---|---|---|---|---|
| p-n-*Hexylphenol* | 155° | 29° | 80·8 | 10·1 | $C_{12}H_{18}O$ | 80·9 | 10·1 |
| o-n-*Heptyl* ,, | 163—165 | — | 80·9 | 10·5 | $C_{13}H_{20}O$ | 81·3 | 10·4 |
| p-n-*Heptyl* ,, | 165 | 24 | 81·2 | 10·3 | $C_{13}H_{20}O$ | 81·3 | 10·4 |
| 3-n-*Butyl*-o-*cresol* | 117—119 | 14 | 80·3 | 9·7 | $C_{11}H_{16}O$ | 80·4 | 9·8 |
| 5-n-*Butyl* ,, | 127—129 | 24 | 80·1 | 10·1 | $C_{11}H_{16}O$ | 80·4 | 9·8 |
| 3-n-*Amyl* ,, | 127—129 | 32 | 80·5 | 10·3 | $C_{12}H_{18}O$ | 80·9 | 10·1 |
| 5-n-*Amyl* ,, | 137—139 | 28 | 80·6 | 10·2 | $C_{12}H_{18}O$ | 80·9 | 10·1 |
| 3-n-*Hexyl* ,, | 139—141 | 8 | 80·9 | 10·5 | $C_{13}H_{20}O$ | 81·3 | 10·4 |
| 5-n-*Hexyl* ,, | 147—149 | 5 | 81·4 | 10·7 | $C_{13}H_{20}O$ | 81·3 | 10·4 |
| 4-n-*Butyl*-m-*cresol* | 132—134 | 18 | 80·5 | 9·9 | $C_{11}H_{16}O$ | 80·4 | 9·8 |
| 4-n-*Amyl* ,, | 137—139 | 24 | 80·6 | 10·2 | $C_{12}H_{18}O$ | 80·9 | 10·1 |
| 4-n-*Hexyl* ,, | 147—149 | 17 | 81·5 | 10·6 | $C_{13}H_{20}O$ | 81·3 | 10·4 |
| 4-n-*Heptyl* ,, | 153—155 | 24 | 81·3 | 10·8 | $C_{14}H_{22}O$ | 81·6 | 10·7 |
| 3-n-*Butyl*-p-*cresol* | 124—126 | 19 | 80·3 | 9·7 | $C_{11}H_{16}O$ | 80·4 | 9·8 |
| 3-n-*Amyl* ,, | 135—137 | 10 | 80·5 | 10·3 | $C_{12}H_{18}O$ | 80·9 | 10·1 |
| 3-n-*Hexyl* ,, | 148—150 | 30 | 81·0 | 10·5 | $C_{13}H_{20}O$ | 81·3 | 10·4 |
| 5-*Ethylguaiacol* | 130—132 | 35—36 | 71·2 | 8·0 | $C_9H_{12}O_2$ | 71·1 | 7·9 |
| 5-n-*Propyl* ,, | 132—134 | 21—22 | 72·1 | 8·3 | $C_{10}H_{14}O_2$ | 72·3 | 8·4 |
| 4-n-*Amyl* ,, | 155—157 | — | 74·0 | 9·3 | $C_{12}H_{18}O_2$ | 74·2 | 9·3 |
| 4-n-*Hexyl* ,, | 165—167 | — | 74·7 | 9·6 | $C_{13}H_{20}O_2$ | 75·0 | 9·6 |

A number of the phenols prepared in the course of this work were known previously, but had not been obtained crystalline, namely, *p*-*n*-butylphenol, m. p. 12°; *p*-*n*-amylphenol, m. p. 18°; 4-*n*-propyl-*m*-cresol, m. p. 16°; and 4-*n*-propylguaiacol, m. p. 16°. *p*-*n*-Propylphenol had m. p. 24°; Clemmensen (*Ber.*, 1914, **47**, 51) gives m. p. 21—22°. Aqueous solutions of sodium *o*- and *p*-butylphenoxides are colourless, contrary to the statements of Read and Mullen (*J. Amer. Chem. Soc.*, 1928, **50**, 1764). 4-*n*-Butylguaiacol, prepared by the reduction of 4-*n*-butyrylguaiacol, had b. p. 140—142°/15 mm. and its benzoate had m. p. 91·5°; Nomura and Hotta (*loc. cit.*) give b. p. of the reduction product of zingerone as 141—142°/13·5 mm. and m. p. of its benzoate as 92—93°.

The following benzoates of the above phenols are new :—

| Benzoate. | M. p. | Found. % C. | Found. % H. | Formula. | Calc. % C. | Calc. % H. |
|---|---|---|---|---|---|---|
| p-n-*Propylphenyl* | 37—38° | 79·6 | 6·8 | $C_{16}H_{16}O_2$ | 80·0 | 6·7 |
| p-n-*Butylphenyl* | 24—25 | 80·1 | 7·0 | $C_{17}H_{18}O_2$ | 80·3 | 7·1 |
| p-n-*Hexylphenyl* | 24 | 80·4 | 7·9 | $C_{19}H_{22}O_2$ | 80·8 | 7·8 |
| p-n-*Heptylphenyl* | 32—33 | 80·6 | 8·3 | $C_{20}H_{24}O_2$ | 81·0 | 8·1 |
| 4-*Ethylguaiacyl* | 58—59 | 74·7 | 6·3 | $C_{16}H_{16}O_3$ | 75·0 | 6·2 |
| 5-*Ethylguaiacyl* | 53 | 74·8 | 6·4 | $C_{16}H_{16}O_3$ | 75·0 | 6·2 |
| 4-n-*Hexylguaiacyl* | 82—83 | 76·8 | 7·9 | $C_{20}H_{24}O_3$ | 76·9 | 7·7 |

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Research Laboratories, Messrs. Boots Pure Drug Co., Ltd.,
Nottingham.
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