(0b)(a, e); 1015[a](0)(a, e); 1091(15)(a, b, e); 1172(15)(a, b, e); 1203(15)(a, b, e); 1398(1)(a, e); 1589[a](20)(a, c, e); 1739[b](8b)(b, e); 1780[b](6b)(b, e); 3075[a](12)(a).

[a] Differ from Kohlrausch, Pongratz and Stockmair by more than 2 cm.$^{-1}$. [b] By more than 6 cm.$^{-1}$.

Lines reported by Kohlrausch, Pongratz and Stockmair not found: 1295($^1/_2$). Lines not reported by Kohlrausch, Pongratz and Stockmair but found: 115(0b).

o-NITROBENZOYL CHLORIDE

Previous investigators: None. Prepared from *o*-nitrobenzoic acid + $SOCl_2$. Distilled 4 times *in vacuo;* b. p. 128.2 ± 0.05° at 5 mm. [Excitation by blue light only. Violet light completely absorbed. No Raman lines of longer wave length than 4916 Å. measured because of low dispersion and large number of weak Hg lines there.]

Plate	Filter	Type plate	Time	Continuous Background	Spectrograph
14	Q. S.	I-G	20	Weak	Hilger C.D.
XXI	None	"Gaevaert Sensima"	4	Strong	Zeiss
77	Q. S.	I-G	2	Strong	Hilger E-439
85	Q. S.	I-G	1.25	Medium	Hilger E-439
126	Satd. $NaNO_2$	I-G	4	Faint	Hilger E-439

$\Delta\nu$ = 49(1)(e); 98(1)(e); 125(0)(e); 168(1)(e); 474(2)(e); 552(0)(e); 646(2b)(e); 854(2)(e); 1043(5)(e); 1085(1)(e); 1152(1)(e); 1170(2)(e); 1205(4)(e); 1352(20b)(e); 1449(1)(e); 1540(2)(d, e); 1581(5)(c, e); 1608(1)(e); 1800(1)(e).

m-NITROBENZOYL CHLORIDE

Previous investigators: None. Eastman "White Label," crystallized from carbon tetrachloride and petroleum ether. Distilled *in vacuo* 4 times; b. p. 120.2–120.4° at 2.5 mm. [Absorbed violet light completely treated as *o*-nitro-.]

Plate	Filter	Type plate	Time	Background
78	Q. S.	I-G	1	Dark
79	Q. S.	I-G	2	Very dark
124	Satd. $NaNO_2$	I-G	4	Weak

$\Delta\nu$ = 48(1)(e); 192(0)(d, e); 387(1)(e); 437(1)(e); 491(0)(e); 518(0)(e); 656(2)(e); 700(0)(e); 843(0)(e); 928(00)(e); 1005(5)(e); 1091(1)(e); 1203(6)(e); 1284(0)(e); 1352(10)(e); 1437(1)(e); 1540(2)(e); 1586(2)(e); 1618(1)(e); 1760(3)(e); 2500(0)(e).

p-NITROBENZOYL CHLORIDE

Previous investigators: None. Eastman "White Label," crystallized from carbon tetrachloride 4 times, but still yellow. [Dissolved in acetone. Absorbed all Raman light of shorter wave length than 4579 Å.]

$\Delta\nu$ = 1109(1)(e); 1353(6)(e); 1534(0)(e); 1601(6)(e); 1772(1)(d, e).

Summary

The Raman spectra of the monomethoxy and mononitro (incomplete) substitution products of benzoyl chloride have been determined for the first time. The spectra of benzoyl chloride, its monomethyl and monochloro derivatives have been determined and compared with the data of Kohlrausch, Pongratz and Stockmair.

CAMBRIDGE, MASS. RECEIVED JULY 17, 1936

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, THE UPJOHN COMPANY]

Alkyl Phenols. I. The 4-*n*-Alkylpyrogallols[1]

BY MERRILL C. HART AND E. H. WOODRUFF

Since Johnson and Lane[2] demonstrated that the introduction of an alkyl group into resorcinol increased its germicidal activity, a vast amount of work has been done on the alkyl mono- and dihydroxy phenols and their derivatives. The literature of the past fifteen years is so voluminous in this respect that no attempt will be made to list it here.

However, during this time the alkylated trihydroxyphenols have received only a haphazard attention. Hurd and Parrish[3] recently reported the phenol coefficients of dihexenyl (2 forms), heptenyl and diheptenylpyrogallol, using *S. Aureus* as the test organism, to be 20 and 250, 120 and 20, respectively. Niederl, Natelson and Beekman[4] prepared diisobutylpyrogallol but have not reported its phenol coefficient. Klarmann[5] gives the phenol coefficients of *n*-hexyl, phenylmethyl, phenethyl and phenylpropyl phloroglucinol as 8 by the Hygienic Laboratory test.

In view of the wide divergence of the phenol coefficients as well as the lack of definite information concerning the variation of activity with structure in the trihydroxy phenols, it was thought to be of interest to prepare a homologous series of alkylpyrogallols and determine their activity as germicides. As is readily seen from Fig. 1, the phenol coefficients vary regularly with increasing length of the alkyl group attached in a manner quite similar to those series already investigated.

Since the maximum germicidal activity against

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[1] Presented at the Pittsburgh meeting of The American Chemical Society, September, 1936.

[2] Johnson and Lane, THIS JOURNAL, **43**, 348 (1921).

[3] Hurd and Parrish, *ibid.*, **57**, 1731 (1935).

[4] Niederl, Natelson and Beekman, *ibid.*, **55**, 2571 (1933).

[5] Klarmann, *ibid.*, **48**, 2359 (1926).

gram negative organisms reaches a maximum with a side chain of five carbon atoms in the monohydroxy phenols and with six carbon atoms in the dihydroxy phenols, it might be expected that the maximum would not occur until a side chain of seven carbons in the trihydroxy phenols. This is not the case, the maximum occurring with a six carbon side chain as in the dihydroxy phenols. In the case of gram positive organisms as indicated by the tests with *S. Aureus* the phenol coefficient continues to rise with the length of the side chain as in the case of other alkylated phenols. The reversal of effectiveness against gram positive and gram negative bacteria occurs with the *n*-hexyl derivative. Thus the "quasi specific" effect as noted by Klarmann[6] in other series is evidenced by the alkylpyrogallols.

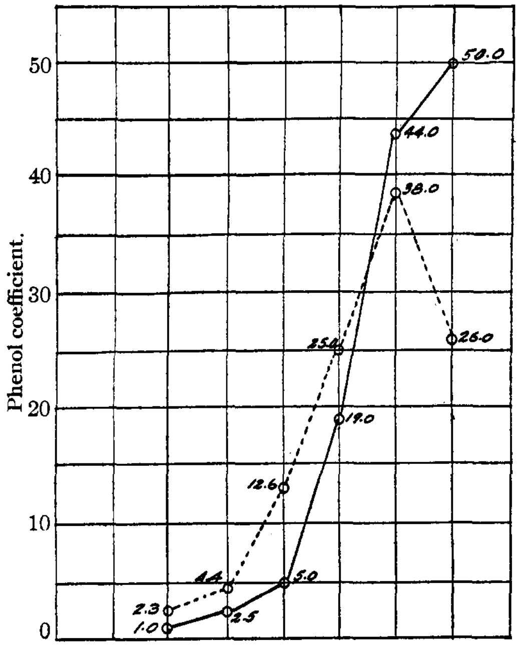

Fig. 1.– – – – –, *B. Coli*; ———, *S. Aureus*.

While the alkylpyrogallols are effective germicides they are not as effective as the alkyl mono- or dihydroxy phenols. The comparison is easily seen in Fig. 2,[7] the comparison being against gram negative organisms. Just why the phenol coefficient should diminish with the increase in number of phenolic hydroxyls, the group presumably responsible for the germicidal property of the molecule, is not clear, and in view of the conflicting theories as to the mode of action of the phenolic germicides, no attempt will be made to elucidate this point.

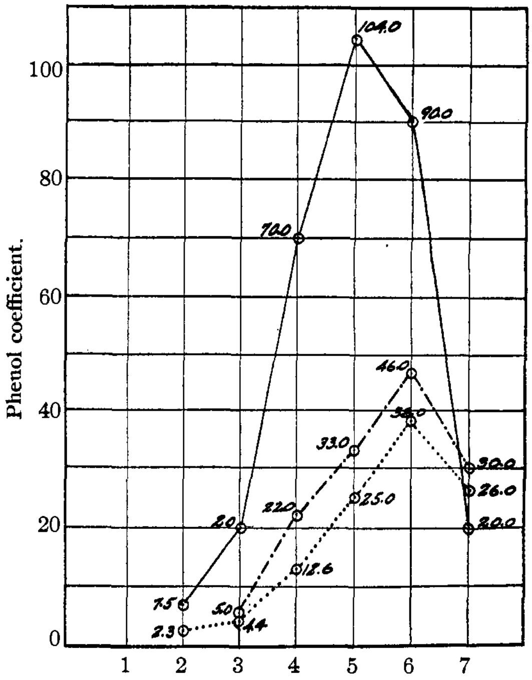

Fig. 2.————, Alkyl phenols, Coulthard, Marshall and Pyman, *J. Chem. Soc.*, 280, (1930); —·—·, alkyl resorcinols [Ref. 8]; ······, alkyl pyrogallols.

None of the alkylpyrogallols are stable in alkaline solution although the rate of oxidation is diminished as the length of the alkyl group attached is increased.

The 4-*n*-alkylpyrogallols were prepared by the reduction of the corresponding ketone by the method of Clemmensen.[8] The ketones were prepared by the method of Nencki, as given by Johnson and Lane[2] and Dohme, Cox and Miller.[9] Difficulty was encountered in the preparation of the C_5 and C_7 ketones and alkylpyrogallols, the yields being appreciably lower than the other members of the series. A similar lowering of the yield was noted by Stoughton, Baltzly and Bass[10] in the case of *n*-amylhydroquinone. Whether the lower yield was due to experimental conditions or a peculiarity of the odd numbered side chain was not investigated.

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(6) Klarmann, Shternov and Gates, THIS JOURNAL, 55, 2576 (1933).

(7) The bacteriological data from the literature, as recorded in Fig. 2, were obtained by the Hygienic Laboratory method. This is a somewhat different test than the F.D.A. method used here for the alkylpyrogallols. It is not believed that this difference would change the relative order of effectiveness of the alkylpyrogallols with respect to the other two series.

(8) Clemmensen, *Ber.*, 47, 51–63 (1914).

(9) Dohme, Cox and Miller, THIS JOURNAL, 48, 1688 (1926).

(10) Stoughton, Baltzly and Bass, *ibid.*, 56, 2007 (1934).

TABLE I

Compound	Cryst. form	Solvent	M. p.,[d] uncorr., °C.	Yield, %	Calcd., % C	Calcd., % H	Found, % C	Found, % H
Gallacetophenone		[a]	170	58		[e]		
Gallpropiophenone		[a]	128–129	35		[f]		
Gallbutyrophenone		[a]	101–102	36		[g]		
Gallvalerophenone	Yellow needles	[b,c]	84–84.5	14	62.82	6.71	62.89	6.60
Gallcaprophenone	White needles	[b,c]	86.5–87	32	64.25	7.19	64.19	7.59
Gallheptophenone	Small lemon-yellow needles	[b,c]	78–78.5	11	65.52	7.62	65.39	7.65

[a] Chloroform. [b] Benzene. [c] Petroleum ether (b. p. 30–60°). [d] All melting points are on air-dried material. [e] "Organic Syntheses," Vol. XIV, p. 40. [f] Beilstein, Erganzungsband III, p. 115. [g] *Ibid.*, p. 119.

TABLE II

4-*n*-Alkylpyrogallol	Cryst. form	Solvent	Yield, %	M. p., °C.	Analyses (micro) Calcd., % C	Analyses (micro) Calcd., % H	Analyses (micro) Found, % C	Analyses (micro) Found, % H
Ethyl		[a]	48	108.5		(8)		
Propyl	White rods	[a]	45	110–111	64.25	7.14	64.07	6.96
Butyl	Light tan needles	[b]	56	88–89	65.89	7.75	65.97	7.55
Amyl	White rods	[b]	25	90–91	67.30	8.33	66.94	7.95
Hexyl	White needles	[b]	54	104–105	65.52	8.64	65.39	8.75
Heptyl	Silvery needles	[c]	30	116–117	69.55	8.99	69.33	8.80

[a] Chloroform. [b] Benzene. [c] Petroleum ether (b. p. 30–60°).

Experimental

2,3,4-Trihydroxyphenyl *n*-Amyl Ketone (Gallcaprophenone).—One hundred and thirty-six grams (1.0 mole) of anhydrous zinc chloride was dissolved in 250 g. (2.1 moles) of caproic acid with the aid of heat, whereupon 126 g. (1.0 mole) of pyrogallol was added. The mixture was heated at 130–140° for one and one-half hours. The unreacted caproic acid was removed by vacuum distillation. The heavy oil was washed several times with water and recrystallized from a mixture of toluene and petroleum ether; yield 68 g. or 32.1%, m. p. 83–85°. Further recrystallizations from the same mixed solvents gave white needles, m. p. 86.5–87°.

4-*n*-Hexylpyrogallol.—Fifty grams of gallcaprophenone was reduced by the method of Clemmensen[8] using 200 g. of amalgamated zinc and 500 cc. of dilute hydrochloric acid (1:1 concd. hydrochloric acid and water). After reduction the cooled solution was extracted with ether, the ether solution dried with anhydrous magnesium sulfate, filtered and the ether removed by distillation. The residual oil was poured into 1 liter of petroleum ether (b. p. 30–60°). The solid obtained melted at 102–103° and weighed 25 g. or 53.4% of the theoretical. After several recrystallizations from a mixture of benzene and petroleum ether (b. p. 30–60°) white needles, m. p. 104–105°, were obtained.

The phenol coefficients were determined by the F. D. A. technique at 37.5° using *S. Aureus* and *B. Coli* as test organisms. The authors wish to thank Dr. John F. Norton and Mr. E. A. Gibson of the Bacteriological Laboratory of The Upjohn Company for the determination of the phenol coefficients, and Mr. C. H. Emerson for the micro analyses given.

Summary

1. The 4-*n*-alkylpyrogallols from C_2H_5 through C_7H_{15} have been prepared and their phenol coefficients determined.

2. The phenol coefficients varied with increasing size of the attached alkyl group in a similar manner to the alkyl mono and dihydroxyphenols.

3. The "quasi specific" effect was found to exist in the alkyl pyrogallols.

4. The phenol coefficient of compounds having the same alkyl group tends to diminish as the number of phenolic hydroxyl groups in the molecule increases.

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