[CONTRIBUTION FROM WESTERN REGIONAL RESEARCH LABORATORY][1]

The Spectrophotometric Examination of Some Derivatives of Pyrogallol and Phloroglucinol

BY TOD W. CAMPBELL AND GALVIN M. COPPINGER

The ultraviolet spectra of a series of alkyl and acyl derivatives of pyrogallol and phloroglucinol have been determined in neutral, alkaline, and acid methanol solution. In alkaline solution, changes occur in the spectra which in the case of pyrogallol derivatives are irreversible. In the latter instance complex oxidative decomposition is indicated, although in some cases, alkaline oxidation appears to lead to discrete compound formation. Certain changes brought about by substitution have been noted. Spectral evidence has been obtained which shows that diaceto- and triacetophloroglucinol exist in solution in two forms, which are in equilibrium. In alkali one form predominates, while in acid the other does. Improved methods for the acylation of pyrogallol and the preparation of diacetophloroglucinol are described.

Studies being carried out in this Laboratory on the chemistry of humulone, lupulone,[2] and other naturally occurring derivatives of phloroglucinol and on derivatives of pyrogallol to be used as antioxidants[3,4,5] have made a collection of the spectra of model compounds of this type desirable to aid in determining structures of unknown derivatives. An examination of the literature showed that very few spectrophotometric data on these types of compounds are available, although a few studies[6] have used the spectra of certain phloroglucinol derivatives for comparison with spectra of naturally occurring compounds of unknown, or partially known, structure. To supplement existing data, a number of variously substituted models have been prepared and their spectra obtained under neutral, acid and alkaline conditions.

Experimental

Acylpyrogallols.—Pyrogallol (0.1 mole) was dissolved in ether (50 ml.), and 0.1 mole of the appropriate aliphatic acid was added. The resulting solution was saturated with boron trifluoride gas at 0°. The reaction mixture was allowed to stand one hour and was then poured into 500 ml. of water. The orange mixture which resulted was extracted thoroughly with ether and the ethereal solution was extracted with dilute (5%) sodium bicarbonate, which removed much of the color. The resulting ethereal solution was then washed twice with water, dried, and evaporated. Final purification was brought about by recrystallization from water, or from a benzene–hexane mixture if the side chain was more than four carbons in length. The results are shown in Table I.

4-Acetyl-6-*t*-butylpyrogallol.—Fifty grams of 4-acetylpyrogallol, 100 g. of *t*-butyl chloride, 500 cc. glacial acetic acid, and 8 g. of anhydrous ferric chloride were heated together for 72 hours on a steam-bath. The reaction mixture was poured into water and the solid filtered off and recrystallized from 50% *n*-propanol–water, to give 35 g. of nicely crystalline pearly scales, m.p. 174.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.3; H, 7.19. Found: C, 64.3; H, 7.29.

1,3-Diacetophloroglucinol.—Ten grams of phloroglucinol was dissolved in warm glacial acetic acid (50 cc.) and the solution was saturated with boron trifluoride gas, without cooling. When saturated, the reaction mixture was poured into 500 cc. of water, and the product allowed to crystallize (one hour). The product, 11.8 g. of an orange crystalline powder, was treated with 15 cc. of cold acetone. Under these conditions a small amount of triacetophloroglucinol remains undissolved. The acetone solution was easily decolorized and the pure product, m.p. 168°,[11] obtained by recrystallization from water.

TABLE I

BORON FLUORIDE CATALYZED ACYLATION OF PYROGALLOL

Derivative	M.p., °C.	Yield, %	Literature
4-Acetyl	171	90	(7)
4-Propyl	128	80	(7)
4-Butyryl	102	79	(7, 8)[a]
4-Valeryl	82	88	(7)
4-Isovaleryl	109	72	[b]
4-Diethylacetyl	111	71	[c]
4-Benzoyl	146	44	(9)
4-Ethyl-6-acetyl	141	78	(10)

[a] *Anal.* Calcd. for $C_{10}H_{12}O_3$: C, 61.21; H, 6.17. Found: C, 61.5; H, 6.22. [b] *Anal.* Calcd. for $C_{11}H_{14}O_4$: C, 62.8; H, 6.69. Found: C, 63.0; H, 6.78. [c] *Anal.* Calcd. for $C_{12}H_{16}O_4$: C, 64.3; H, 7.18. Found: C, 64.4; H, 7.27.

Additional Compounds.—Ethylpyrogallol and diethylpyrogallol were made by Clemmensen reduction of the appropriate ketone.[10] Di-*t*-butylpyrogallol was made according to the method of Rozycki, from *t*-butyl chloride, pyrogallol, and ferric chloride.[12] Pyrogallol trimethyl ether[13] and tribenzyl ether[14] were prepared conventionally. Pyrogallol 1,3-dimethyl ether was obtained from Eastman Kodak Co.[15]

Methylphloroglucinol was prepared by the zinc-dust-alkali reduction of methylenediphloroglucinol.[16] Dimethyl- and trimethyl-phloroglucinol were made from trinitro-*m*-xylene and trinitro-mesitylene, by the method of Weidel and Wenzel.[17] Ethyl phloroglucinol was made by the Clemmensen reduction of phloroacetophenone.[18] Monoacylphloroglucinols were made by the Hoesch synthesis from the appropriate nitrile and alkylphloroglucinol. They have all been described previously.[19] 1,3,5-Triacetophloroglu-

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(1) Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

(2) (a) V. Richter, "Organic Chemistry," or "Chemistry of the Carbon Compounds," Vol. II, Revised by Taylor and Mullidge, Nordemann, New York, N. Y., 1939. (b) J. C. Lewis, *et al.*, AIC-231, Western Regional Research Laboratory, Bureau of Agricultural and Industrial Chemistry, U. S. Department of Agriculture, 1949.

(3) S. G. Morris and R. W. Riemenschneider, *J. Am. Oil Chem. Soc.*, **26**, 638 (1949).

(4) E. M. Bickoff, T. W. Campbell and G. M. Coppinger, unpublished data.

(5) E. M. Bickoff, *J. Am. Oil Chem. Soc.*, **28**, 65 (1951).

(6) For example A. Russell, J. Todd and C. L. Wilson, *J. Chem. Soc.*, 1940 (1934), and R. H. Morton and Z. Sawires, *ibid.*, 1052 (1940).

(7) M. C. Hart and E. H. Woodruff, THIS JOURNAL, **58**, 1957 (1936).

(8) R. D. Haworth and D. Woodcock, *J. Chem. Soc.*, 999 (1946).

(9) E. Fischer and M. Rapaport, *Ber.*, **46**, 2394 (1913).

(10) E. Clemmensen, *ibid.*, **47**, 51 (1914).

(11) G. Heller, *Ber.*, **45**, 422 (1912).

(12) L. Rozycki, *ibid.*, **32**, 2428 (1899).

(13) E. Chapman, A. G. Perkin and R. Robinson, *J. Chem. Soc.*, 3028 (1927).

(14) R. A. Baxter, G. R. Ramage and J. A. Timson, *J. Chem. Soc.*, suppl. 30 (1949).

(15) Mention of this product does not imply that it is endorsed or recommended by the Department of Agriculture over others of a similar nature not mentioned.

(16) R. L. Shriner and C. J. Hull, *J. Org. Chem.*, **10**, 228 (1945).

(17) H. Weidel and F. Wenzel, *Monatsh.*, **19**, 249 (1898).

(18) G. Weisweiller, *ibid.*, **21**, 48 (1900).

(19) P. Karrer, *Helv. Chim. Acta*, **2**, 477 (1918); **3**, 392 (1919); K. C. Gulati, S. R. Seth and K. Venkataraman, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., p. 522; K. Hoesch, *Ber.*, **48**, 1129 (1915); P. Karrer and S. Rosenfeld, *Helv. Chim. Acta*, **4**, 707 (1921).

cinol was prepared by rearranging phloroglucinol triacetate in the presence of fused zinc chloride.[20] Phloroglucinol trimethyl ether was made by the method of Freudenberg.[21] Phloroglucinol carboxylic acids were synthesized[22] by carboxylation of the appropriate phloroglucinol with potassium bicarbonate. Phloroglucinol triacetate and trimethylphloroglucinol triacetate[17,19] were easily prepared by acetylation with acetic anhydride and pyridine. They hydrolyzed rapidly in dilute alkali.

Spectrophotometric Data.—These data were obtained from a Cary Recording Ultraviolet Spectrophotometer, Model 11,[23,24] on freshly crystallized samples[24] of the appropriate compound in pure methanol. The spectrum of each compound was obtained under three different conditions of hydrogen ion concentration, defined as follows:

1. "**Neutral.**"—Compound dissolved in methanol; nothing else added. The concentration was that which would give a solution of maximum absorbancy (optical density) of about 1.0–1.5, *i.e.*, 10^{-3} to 10^{-5} molar.
2. "**Basic.**"—One drop of 0.2 *M* sodium hydroxide added to 3 cc. of "neutral" solution. Tests showed no further change in spectra with greater amounts of alkali, except in the cases noted.
3. "**Acidic.**"—The above basic solutions were made acidic (*p*H about 2) with 0.2 *M* sulfuric acid.

The data so obtained are recorded in Table II and Figs. 1–12. It should be noted that the data for pyrogallol derivative in alkali solutions are not precisely reproducible because of rapid oxidative and/or other change. The data in the table and figures under the heading "alkaline" and "acidic" are thus merely representative, and should not be used for characterization. Essentially the same spectrum was obtained in all cases studied, except as noted, when the neutral solution was made acidic directly.

TABLE II

SPECTRA OF SOME DERIVATIVES OF PYROGALLOL AND PHLOROGLUCINOL

Compound	Neutral solution		Basic solution	
	λ_{max}	ϵ_{max}	λ_{max}	ϵ_{max}
Phloroglucinol	2675	450	2525	20000
	2710	388	3495	8730
Methylphloroglucinol	2715	835	2560	16400
	2780	769	3565	6650
Dimethylphloroglucinol	2750	1210	2610	16000
			3630	6100
Trimethylphloroglucinol	2710	900	2655	10500
	2740	885	2925	6300
			3675	3430
Ethyl phloroglucinol	2705	756	2570	16400
	2740	743	3570	6350
	2785	659		
Phloroacetophenone	2270	12400	3180	26400
	2855	14700		
Phlorobutyrophenone	2270	13100	3185	22400
	2850	15500		
Diacetophloroglucinol	2710	23900	2890	24900
Triacetophloroglucinol	2675	42100	2800	31300
Methylphlorobutyrophenone	2885	14100	3250	18400
Dimethylphlorobutyrophenone	2915	13500	3350	14900
Phloroglucinoltrimethyl ether	2650	482	2650	482
Phloroglucinol tri-acetate			2850	1740
	2615	361	3470	2560
Trimethyl phloroglucinol triacetate			2380	7650
	2615	231	2910	3740
Phloroglucinol carboxylic acid	2625	13100	2605	10400
	2975	2750	2750	8500
3,5-Dimethyl phloroglucinol carboxylic acid	2160	27500	2625	8810
	2600	10600	2875	7700
	3060	2920		
Phenol			2375	11200
	2730	1750	2895	4740
Resorcinol	2765	2140	2375	7160
	2830	1800	2875	2490
Pyrogallol	2675	682	2445	5440
			2750	4530
			3570	4680
Pyrogallol 1,3-dimethylether	2675	1090	2680	1350
Pyrogallol trimethylether	2670	655	2670	655
Pyrogallol tribenzylether	2580	1310	2580	1310
	2645	1380	2645	1380
	2680	1270	2680	1270
4-Ethyl pyrogallol	2695	735	3475	4780
4,6-Diethylpyrogallol	2730	978	3100	2210
4,6-Di-*t*-butylpyrogallol	2690	1000	2625	2230
			3190	4010
4-*t*-Butyl-6-acetopyrogallol	2965	13800	2495	7430
			3460	16000
4-Ethyl-6-acetopyrogallol	2195	16400	3180	12700
4-Acetopyrogallol	2370	8560	3090	12700
	2960	12500		
4-Propiopyrogallol	2365	9780	3100	13600
	2910	13100		
4-*n*-Butyropyrogallol	2370	1030	3120	14900
	2915	14300		
4-*n*-Valeropyrogallol	2365	10100	3110	14700
	2915	14200		
4-(Diethylacetyl)pyrogallol	2375	9400	3140	14800
	2930	14900		
4-iso-Valerylpyrogallol	2375	10800	3120	15600
	2930	15700		
4-Benzoyl pyrogallol	2270	17600	2275	15400
	2720	2400	2740	5000
			2800	4900
Gallic acid	2725	8720	2625	6470
			3350	6630
Ethyl gallate	2750	10000	2350	10300
			2790	11400
			3240	8500

Discussion of Spectra

Pyrogallol and Its Alkyl Derivatives.—Little change is made in the spectrum of pyrogallol by alkyl substituents, when the spectrum is obtained under neutral conditions. However, when these solutions are made alkaline, evidence of irreversible chemical changes may be readily observed (Figs. 1, 2, 3). It is well known that alkaline solutions of pyrogallol absorb oxygen readily to give dark-colored products of considerable complexity.

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(20) G. Heller, *Ber.*, **42**, 2736 (1909).

(21) K. Freudenberg, *ibid.*, **53**, 1425 (1920).

(22) (a) R. Boehm, *Ann.*, **302**, 174, 182 (1899); (b) A. Robertson and R. Robinson, *J. Chem. Soc.*, 2196 (1927).

(23) Applied Physics Corporation, Pasadena, California.

(24) The polyphenols studied, especially di- and tri-methylphloroglucinol and dimethylacylphloroglucinols, are susceptible to autoxidation in the solid state. The compounds used in this study were carefully purified and analyzed by combustion analysis. If any length of time (more than a few days) passed from time of preparation and purification to the time the spectra were obtained, they were recrystallized again just before use. It is interesting to note that Woodward and Blout, THIS JOURNAL, **65**, 562 (1943), have emphasized a similar observation regarding the susceptibility of alkyl substituted β-diketones to autoxidation.

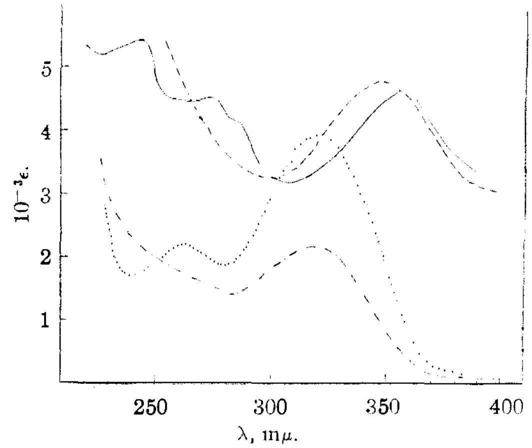

Fig. 1.—Alkaline solution: ——, pyrogallol; — — - - -, ethylpyrogallol; ...., di-*t*-butylpyrogallol; —·—·—, di-ethylpyrogallol.

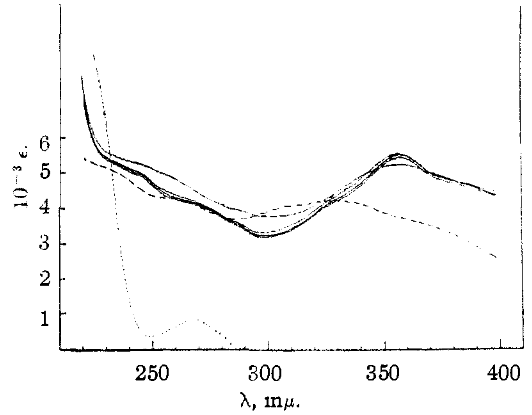

Fig. 2.—Pyrogallol: ....., neutral; ——, basic, showing shift downward with time (10-min. intervals); — — —, acid (after 45 min.).

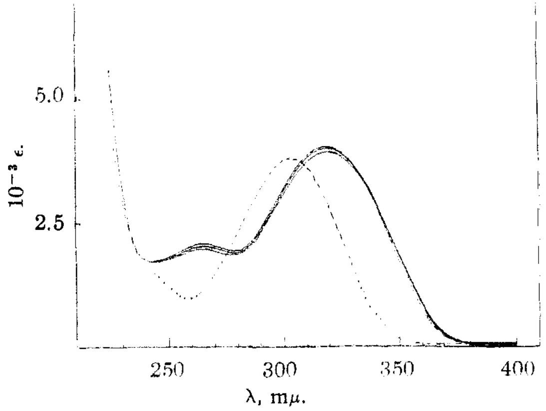

Fig. 3.—Di-*t*-butylpyrogallol: ——, basic, as in 4; — — —, acid (after 45 min.).

Harries,[25] using very mild conditions, obtained an identifiable product, hexahydroxybiphenyl, in good yield. Erdtmann[26] similarly obtained hexahydroxydiethylbiphenyl from 4-ethylpyrogallol, but obtained only ill-defined compounds from 4,6-diethylpyrogallol. This is not surprising, since biphenyl formation in the former compounds appears to take place through the 4 or 6 positions, both of which are blocked in the latter compound.

Examination of the spectral data for alkyl pyrogallols (Figs. 1, 2, 3, 4) can lead to certain conclusions concerning the oxidative processes involved. Pyrogallol (Figs. 1, 3) is profoundly and rapidly changed in alkali, as may be seen from

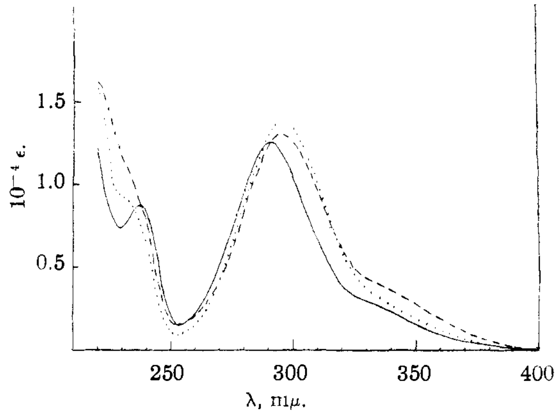

Fig. 4.—Neutral solution: ——, acetopyrogallol; — — —, ethylacetopyrogallol; ......, *t*-butylacetopyrogallol.

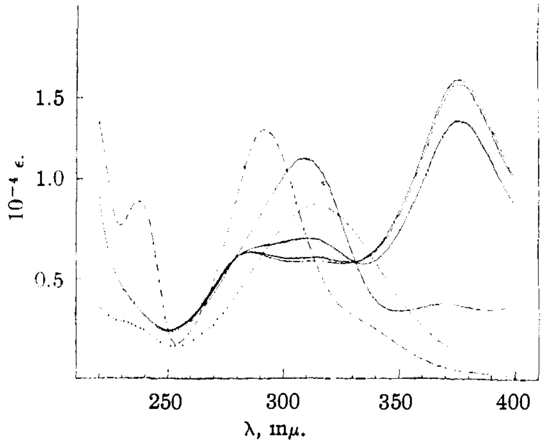

Fig. 5.—Acetopyrogallol: — — —, neutral; ——, basic, 0.01 *N* in NaOH, showing change at 5 min. intervals; ......, acid (after 25 min.).

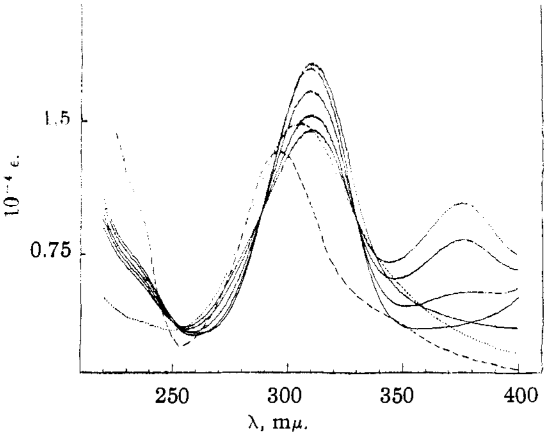

Fig. 6.—Acetopyrogallol: as in VII, except 0.001 *N* in NaOH.

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(25) C. Harries, *Ber.*, **35**, 2957 (1902).

(26) H. Erdtmann, *Ann.*, **513**, 240 (1934).

the complexity and lack of definition in the spectrum of the alkaline solution both before and after reacidification. Substitution of one ethyl group still gives an ill-defined spectrum; however, diethylpyrogallol, and especially di-*t*-butylpyrogallol, gives alkaline-oxidation spectra which have considerable definition, indicating that the oxidation of these compounds may lead to few and simple products.

Acyl Pyrogallols (Figs. 4, 5, 6).—Substitution of an acyl group in pyrogallol causes a significant shift in the wavelength of the principal maximum from about 2675 Å. to 2960 Å., and a large increase in the maximum molar extinction coefficient. As with the alkyl pyrogallols, significant though less profound changes occur in alkali in the presence of air. There is a gradual shift (see Figs. 5, 6) of the alkaline spectrum with time to longer wave lengths, until the spectrum eventually becomes rather stabilized. Discrete compound formation appears to have resulted, either by an oxidative process, or as a result of the action of alkali as a hydrolyzing or condensing agent. Reacidification gives a solution with maximum about 200 Å. farther toward the visible.

Figures 5 and 6 also indicate that relatively simple chemical changes are occurring, since as the 300 mμ band decreases with time, isobestic points occur at about 330 mμ and 280 mμ, indicating that only two absorbing species are present,[35] one of which must be starting material.

Phloroglucinol and its Alkyl Derivatives.—The neutral absorption of phloroglucinol and alkyl phloroglucinols (Fig. 7) is quite similar to that of phenol, substituted phenols,[27,28,29] resorcinol,[30] and pyrogallol.

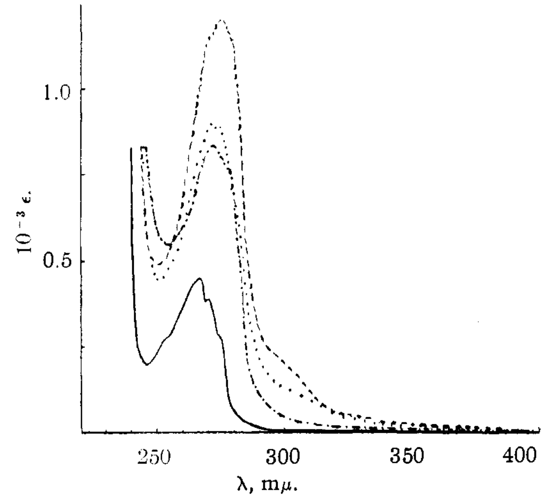

Fig. 7.—Neutral solution: ——, phloroglucinol; —·—, methylphloroglucinol; — —, dimethylphloroglucinol; ......, trimethylphloroglucinol.

In alkaline solution (Fig. 8) certain interesting regularities may be noted in the spectra with addition of methyl groups. The principal maximum now appears in the neighborhood of 2600 Å., in all cases at lower wave lengths than in neutral solution. A second maximum has appeared in the neighborhood of 3600 Å., both of these maxima have extinction coefficients about 20–50 times those in neutral solution. Furthermore, a third maximum develops gradually at ~2925 Å., as methyl groups are introduced into the nucleus. This orderly change in the spectrum of phloroglucinol with substitution of methyl groups may be due to hyperconjugative effects.[31]

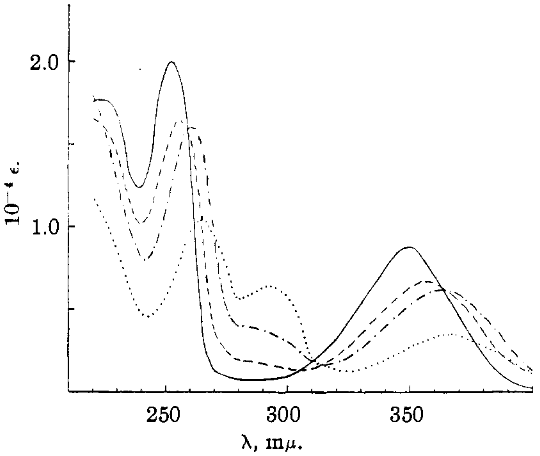

Fig. 8.—Basic solution: ——, phoroglucinol; — — —, methylphloroglucinol; —·—, dimethylphloroglucinol; ......, trimethylphloroglucinol.

Phloroglucinol trimethyl ether in neutral, acid, and basic solution, gives a spectrum virtually identical to that of phloroglucinol in neutral solution, as is to be expected. The triacetates are likewise similar, in neutral and acid solution, although ϵ_{max} is lowered by introducing methyl groups. This effect is the opposite to the one for un-acetylated compounds. In base, they hydrolyze too rapidly for a discrete spectrum of the triacetate to be obtainable.

Monoacylphloroglucinols.—Lemon[32] has examined the spectra of *p*-hydroxyacetophenone and similar compounds in neutral and alkaline solution, as Cram[30] has done for corresponding derivatives of resorcinol. The spectra they have recorded are similar to those of the phloroglucinol derivatives (Figs. 9, 10). The only differences appear to be somewhat larger molar extinction coefficients and a general shift of maxima toward higher wave lengths for the phloroglucinol derivatives. Acylphloroglucinols slowly decompose in alkali on standing, probably by hydrolysis.[33]

Polyacylphloroglucinols.—Successive substitution of acyl groups causes successive increases of the extinction coefficient of the principal maximum. At the same time, the wave length of the maximum is shifted toward shorter wave lengths (Fig. 11). The phenolic hydroxyl groups in the polyacetyl compounds undergo keto–enol tautom-

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(27) L. Doub and J. M. Vandenbelt, THIS JOURNAL, **69**, 2716 (1941).

(28) American Petroleum Institute Research Project 44, Collection of Ultraviolet Absorption Spectra.

(29) N. D. Coggeshall and C. M. Lang, THIS JOURNAL, **70**, 3283 (1948).

(30) D. J. Cram and F. W. Cranz, *ibid.*, **72**, 595 (1950).

(31) Compare G. W. Wheland, R. M. Brownell and E. C. Mayo, *ibid.*, **70**, 2492 (1948).

(32) H. W. Lemon, *ibid.*, **69**, 2998 (1947).

(33) G. Heller, *Ber.*, **45**, 422 (1912).

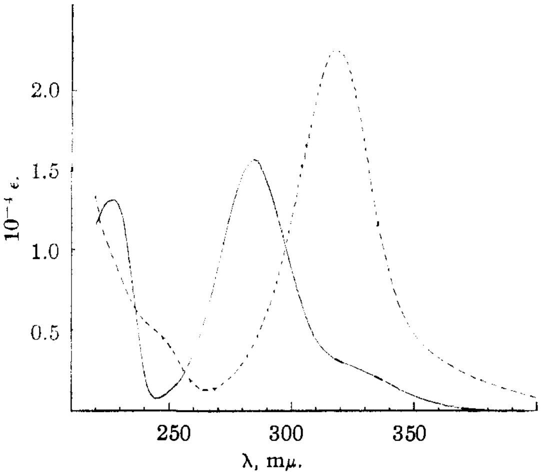

Fig. 9.—Phlorobutyrophenone: ——, acid and neutral; — — — —, basic.

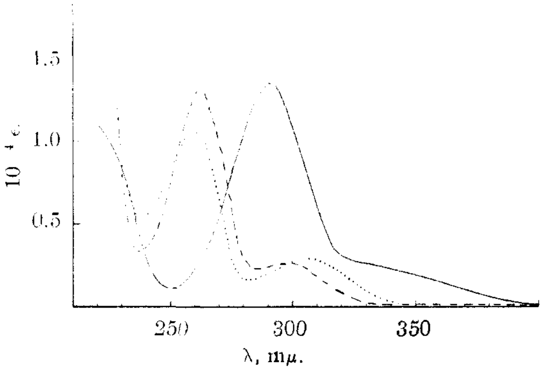

Fig. 10.—Neutral solution: ——, dimethylphlorobutyrophenone; ......, dimethylphloroglucin carboxylic; — —, phloroglucinol carboxylic acid.

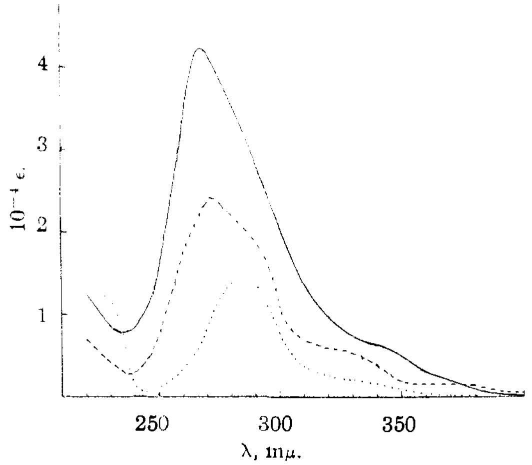

Fig. 11.—Neutral solution: ——, triacetophloroglucinol; — — —, diacetophloroglucinol; ....., monoacetophloroglucinol.

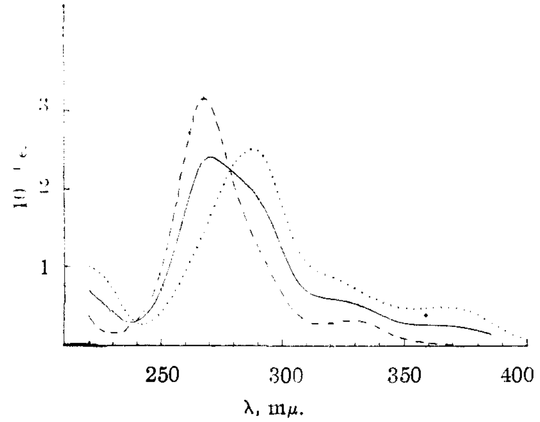

Fig. 12.— ——, Neutral solution of diacetophloroglucinol; ......, basic solution; — — —, acidic solution.

erism in which the keto form may predominate. Fig. 12 shows that diacetophloroglucinol has a spectrum affected not only by base but by acid. The occurrence of isobestic points[34] at about 244 and 279 mμ is good evidence that the spectrum is that of a mixture of only two absorbing forms in equilibrium.[35] In excess base, one form exists to the virtual exclusion of the other, while in acid the reverse is true. In neutral solution, however, the shape of the spectrum indicates an appreciable amount of both forms.[36] In view of the complexity of the molecule of diacetophloroglucinol no attempt has been made to assign structures to the components of the equilibrium on the basis of spectrophotometric evidence alone.

Acknowledgments.—We wish to thank Miss Geraldine Secor and Mrs. Mary Kilpatrick for ultimate analyses.

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(34) An isobestic point is a point at which a series of spectra intersect. The probability that more than two absorbing species shall have exactly the same absorption at two different points under conditions which change the spectrum as a whole (in this case changing of pH) is very low.

(35) Confirmation of the existence of an equilibrium was afforded by observing the effect of temperature on the neutral spectrum. At 10°, the ratio of the optical density at 2680 Å. to the optical density at 2890 Å. was 1.75, while at 50° the ratio was 1.52, the peak at 2890 Å. having developed at the expense of the peak at 2680 Å.

(36) The cyclic β-diketone, dimethyldihydroresorcinol, shows the same type of change with change in pH. E. R. Blout, V. W. Eager, and D. C. Silverman, This Journal, **68**, 566 (1946).