Anal. Calcd. for $C_{15}H_{12}O_4S$: C, 62.49; H, 4.20. Found: C, 62.27; H, 4.17.

(b) **With Sodium Hydrosulfite and Alkali.**—A solution of 1.0 g. of sodium hydrosulfite and 1.0 g. of sodium hydroxide in 10 ml. of water was added to a suspension of 0.60 g. of thiaxanthone-5-dioxide in 10 ml. of ethanol, and the mixture was warmed to *ca.* 50° under a nitrogen atmosphere for ten minutes. The resultant dark blue solution was cooled to room temperature, acidified with hydrochloric acid, and diluted with 100 ml. of water. The yellow precipitate was collected, washed with water, and dried *in vacuo* over calcium chloride; yield, 0.40 g. (66%) of yellow powder, m. p. 167–171°. Recrystallization of this material from chloroform afforded pale yellow crystals which melted at 181–183° and showed no depression in melting point when mixed with the acid-reduction product described above.

Reduction of Thiaxanthone-5-dioxide (I) to Thiaxanthene-5-dioxide (IV).—A mixture of 1.22 g. (0.0050 mole) of thiaxanthone-5-dioxide, 3 g. of amalgamated zinc dust, 15 ml. of acetic acid, and 3 ml. of hydrochloric acid was refluxed under nitrogen for three hours. Another 1 ml. of hydrochloric acid was added during the refluxing, and at the end of the three-hour period the unreacted zinc was filtered off and the filtrate as diluted with 100 ml. of water. The precipitate was collected, washed with water, and dried; yield, 1.08 g. (94%) of pale yellow microcrystalline powder, m. p. 150–155°, which gave a blue color on treatment with aqueous-alcoholic sodium hydroxide. After repeated recrystallization from ethanol, the pure product was obtained as almost colorless crystals, m. p. 171–172°, which gave *no color* on treatment with aqueous-alcoholic sodium hydroxide and which failed to depress the melting point of authentic thiaxanthene-5-dioxide prepared by the oxidation of thiaxanthene. This product exhibited a blue fluorescence on exposure to ultraviolet light.

Reduction of Thiaxanthenol-5-dioxide (III) to Thiaxanthene-5-dioxide (IV).—When an acetic acid solution of 1.23 g. (0.0050 mole) of thiaxanthenol-5-dioxide was treated with amalgamated zinc and hydrochloric acid in the same manner as in the preceding example, 0.85 g. (74%) of pale yellow powder, m. p. 139–144°, was obtained, which crystallized from ethanol in the form of almost colorless needles melting at 169–171°. No depression of the melting point was observed when this material was mixed with authentic thiaxanthene-5-dioxide.

Air Oxidation of Thiaxanthenol-5-dioxide (III).—A suspension of 0.62 g. of thiaxanthenol-5-dioxide in 10 ml. of ethanol was treated with 10 ml. of 10% aqueous sodium hydroxide, and air was blown into the mixture through a sintered glass gas-dispersion tube until the blue color was completely discharged (five to ten minutes). The resultant yellow suspension was diluted with water and filtered, thus affording 0.55 g. (90%) of yellow microcrystalline powder, m. p. 185–186°, which gave a blue color with aqueous-alcoholic alkali only after the addition of zinc dust or sodium hydrosulfite. This product failed to depress the melting point of thiaxanthone-5-dioxide prepared by the oxidation of thiaxanthone.

When a saturated solution of thiaxanthenol-5-dioxide in 95% ethanol was shaken with air for ten days in a mechanical shaker, a small amount of yellow insoluble material was precipitated which melted at 182–185° and showed no melting point depression when mixed with authentic thiaxanthone-5-dioxide.

Air Oxidation of Thiaxanthene-5-dioxide (IV).—A suspension of 0.20 g. of freshly purified thiaxanthene-5-dioxide in 10 ml. of 10% aqueous sodium hydroxide was refluxed for ten minutes while a stream of air was bubbled through the boiling mixture. Although the thiaxanthene-5-dioxide used in this experiment gave no color with alkali and sodium hydrosulfite, the yellow solid filtered out of the above suspension gave the characteristic blue color test for thiaxanthone-5-dioxide on treatment with these reagents.

When neutral, saturated solutions of pure thiaxanthene-5-dioxide in 95% ethanol were similarly aerated and refluxed for periods of several hours, addition of aqueous sodium hydroxide and sodium hydrosulfite resulted in the formation of a dark blue color. If the refluxing was carried out under nitrogen and no air was bubbled through the solution, no color test could be obtained even after four hours.

Summary

The color reactions of thiaxanthone-5-dioxide in the presence of alkaline reducing agents have been studied and shown to be similar to the familiar vatting reactions of anthraquinone. The intermediate reduction product responsible for the characteristic color reactions has been isolated and identified as thiaxanthenol-5-dioxide, which dissolves in alkali with the formation of a highly colored, readily oxidizable anion analogous to the anthrahydroquinone anion. On the basis of the assumption that sulfur is capable of expanding its valence shell, the thiaxanthone dioxide–thiaxanthenol dioxide–thiaxanthene dioxide oxidation–reduction system is formulated as the sulfone series counterpart of the anthraquinone–anthrahydroquinone–anthrone system.

SWARTHMORE, PA. RECEIVED SEPTEMBER 8, 1948

[CONTRIBUTION FROM THE INSTITUTE OF PAPER CHEMISTRY]

Reactions of Vanillin and its Derived Compounds. VII.[1] Some New Esters of Vanillic Acid and Related Acids[2,3]

BY IRWIN A. PEARL AND DONALD L. BEYER

Several esters of vanillic acid were recently shown[4,5] to have high toxicity toward representative microörganisms and to be of value as food preservatives. These results led to the synthesis of the new esters of vanillic acid, orthovanillic acid, and 5-chlorovanillic acid described in Table I.

The new esters of vanillic acid reported herein comprise esters of polyhydric alcohols, their chlorohydrins, and their ethers. Most of these were prepared by the various methods described earlier.[4] The chlorohydrin esters were prepared by reaction of the chlorohydrin with vanillic

[1] For paper VI of this series, see THIS JOURNAL, **70**, 2008 (1948).

[2] Presented before The Division of Organic Chemistry at the 113th meeting of The American Chemical Society, Chicago, Illinois, April 19–23, 1948.

[3] This paper represents a portion of the results obtained in the research program sponsored by the Sulphite Pulp Manufacturers' Research League and conducted for the League by The Institute of Paper Chemistry. Acknowledgment is made by the Institute for permission on the part of the League to publish these results.

[4] Pearl and McCoy, THIS JOURNAL, **69**, 3071 (1947).

[5] Pearl and McCoy, *Food Industries*, **17**, 1458 (1945).

TABLE I

ESTERS OF VANILLIC, ORTHOVANILLIC AND 5-CHLOROVANILLIC ACIDS

Ester	Yield, %	B. p.[a] °C.	B. p. Mm.	n^t_D	t, °C.	M. p.,[b] °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Inhibiting concn.,[c] % *Aero. aero.*	*Bac. myc.*	*Asper. niger*
Vanillic acid[d]														
$MeOCH_2CH_2$[e]	61	160	4			39[f]	$C_{11}H_{14}O_5$	58.40	58.13	6.24	6.29	>0.21	>0.21	>0.21
$EtOCH_2CH_2$[g]	50	142	3	1.5345	21.8		$C_{12}H_{16}O_5$	59.99	59.38	6.71	6.58	> .21	> .21	.21
$BuOCH_2CH_2$	38	176	4	1.5099	21.8		$C_{14}H_{20}O_5$	62.67	62.10	7.51	7.95	.09	.03	.09
$Et_2CHCH_2OCH_2CH_2$[h]	73	200	3	1.5161	24		$C_{16}H_{24}O_5$	64.84	64.65	8.16	8.27	> .21	.003	> .21
$PhOCH_2CH_2$[h]	81					113	$C_{16}H_{16}O_5$	66.66	66.65	5.60	5.67	> .21	> .21	> .21
$MeOCH_2CH_2OCH_2CH_2$[h]	40	216–219	3	1.5398	23		$C_{13}H_{18}O_6$	57.77	56.65	6.71	6.43			
$EtOCH_2CH_2OCH_2CH_2$[h]	61	209	3	1.5305	23		$C_{14}H_{20}O_6$	59.14	58.34	7.09	7.12			
CH_2ClCH_2	74[i]	161	3			58–59	$C_{10}H_{11}O_4Cl$	52.07	52.20	4.81	4.78	> .21	> .21	.21
$MeCHClCH_2$[j]	57	162	2			49	$C_{11}H_{13}O_4Cl$	54.00	54.06	5.35	5.44	.09	.03	.09
$CH_2ClCH_2CH_2$[k]	52	192–204	4			67–68	$C_{11}H_{13}O_4Cl$	54.00	54.27	5.35	5.48	.09	.09	.09
$CH_2ClCHClCH_2$	63[l]	195	3			42–43[f]	$C_{11}H_{12}O_4Cl_2$	47.33	47.54	4.33	4.34	.03	.015	.21
$(CH_2Cl)_2CH$	49	190	0.2	1.5513	24		$C_{11}H_{12}O_4Cl_2$	47.33	46.94	4.33	4.45	.09	.009	.21
CCl_3CMe_2[m]	10					138–139	$C_{12}H_{13}O_4Cl_3$	44.00	44.87	4.00	4.00	> .21	.009	> .21
CH_2OHCH_2[n]	52[o]	198	2			85–86[p]	$C_{10}H_{12}O_5$	56.60	56.67	5.70	5.82	> .21	> .21	> .21
C_2H_4-bis[q]	33[r]					144[s]	$C_{18}H_{18}O_8$	59.67	59.64	5.01	5.01	> .21	> .21	> .21
$MeCHOHCH_2$[n]	42	175	1				$C_{11}H_{14}O_5$	58.40	58.09	6.24	6.24	> .21	> .21	> .21
Orthovanillic acid[t]														
Me[u]	87					64–65[f]						.09	.09	.09
Et[u]	75	121	3	1.5342	20							.21	.15	.09
Pr	91					52[s]	$C_{11}H_{14}O_4$	62.84	62.85	6.71	6.76	.15[v]	.15	.009
iso-Bu	52	139	3.5			52–53	$C_{12}H_{16}O_4$	64.27	64.41	7.19	7.25	.21	.03	> .21
Bu	80	131	1.5			39–40	$C_{12}H_{16}O_4$	64.27	64.01	7.19	7.18	> .21	.009	> .21
iso-Am	85	147	2	1.5160	22		$C_{13}H_{18}O_4$	65.53	65.32	7.61	7.64	> .21	.009	> .21
Am	94					55–56	$C_{13}H_{18}O_4$	65.53	65.39	7.61	7.62	.21[v]	.09	> .21
Et_2CHCH_2	83	144	2	1.5174	22		$C_{14}H_{20}O_4$	66.64	66.40	7.99	7.99	> .21	.003	> .21
$EtOCH_2CH_2$	60	157–163	4			31[f]	$C_{12}H_{16}O_5$	59.99	60.14	6.71	6.75	.15[v]	.09	.09
$PhOCH_2CH_2$[h]	86					93	$C_{16}H_{16}O_5$	66.66	66.65	5.60	5.74	> .21	.21	> .21
Ph[w]	35					66[s]	$C_{14}H_{12}O_4$	68.84	68.62	4.95	4.97	.21[v]	.009	> .21
5-Chlorovanillic acid[t]														
Me	95					136–137	$C_9H_9O_4Cl$	49.90	49.90	4.19	4.19	> .21[v]	.15	.15
Et	91.5					119–120	$C_{10}H_{11}O_4Cl$	52.07	52.05	4.81	4.84	> .21[v]	.15	> .21
Pr	92					117–118	$C_{11}H_{13}O_4Cl$	54.00	54.09	5.35	5.36	> .21[v]	> .21	> .21
Bu	84					109–110	$C_{12}H_{15}O_4Cl$	55.71	55.76	5.84	5.89	> .21[v]	> .21	> .21

[a] All melting points and boiling points are uncorrected. [b] All compounds were recrystallized from petroleum ether (b. p. 65–110°) except where indicated. [c] Inhibiting concentrations were determined in accordance with the method described earlier.[4] Abbreviations used: *Aero. aero.* = *Aerobacter aerogenes; Bac. myc.* = *Bacillus mycoides; Asper. niger* = *Aspergillus niger.* [d] See Pearl, THIS JOURNAL, 68, 429, 1110, 2180 (1946). [e] Prepared by the reaction of vanillic acid with 2-methoxyethanol in the presence of sulfuric acid. All esters were prepared by this general method unless otherwise indicated. [f] Recrystallized from petroleum ether (b. p. 30–60°). [g] Monohydrate from petroleum ether (b. p. 30–60°), m. p. 47–48°. *Anal.* Calcd. for $C_{12}H_{18}O_6$: C, 55.80; H, 7.02. Found: C, 55.81; H, 7.02. [h] Prepared by reaction of acid with corresponding alcohol in presence of hydrogen chloride. [i] 59% by hydrogen chloride method from ethylene glycol. [j] Hydrogen chloride method from propylene glycol. [k] Hydrogen chloride method from trimethylene glycol. [l] 60% by hydrogen chloride method from glycerol. [m] Prepared by refluxing trichloro-*t*-butyl alcohol with vanillic acid in toluene under a water separatory head. Wolffenstein, German Patent 267,980 (Dec. 6, 1913), reported a m. p. of 130° for a compound prepared by heating trichloro-*t*-butyl alcohol with vanillic acid in the presence of zinc chloride. Wolffenstein's results could not be repeated. [n] Prepared by the reaction of potassium vanillate with the corresponding chlorohydrin. [o] 25% yield by refluxing vanillic acid with excess ethylene glycol without a condensing agent; 30% by reaction of carbethoxyvanilloyl chloride with ethylene glycol (see Pearl and McCoy).[4] [p] Recrystallized from chloroform. [q] Prepared by reaction of carbethoxyvanilloyl chloride with ethylene glycol through the intermediate, ethylene glycol biscarbethoxy vanillate, m. p. 139°. *Anal.* Calcd. for $C_{24}H_{26}O_{12}$: C, 56.91; H, 5.18. Found: C, 56.37; H, 5.24. [r] 20% yield by refluxing vanillic acid with excess ethylene glycol without a condensing agent (together with 2-hydroxyethyl vanillate). [s] Recrystallized from dilute ethanol. [t] See Pearl, *J. Org. Chem.*, 12, 85 (1947). [u] This is a previously reported compound. [v] Dissolved in ethanol for all microbiological analyses. [w] Prepared by reaction of orthovanillic acid with phenol in the presence of phosphorus oxychloride. Method patterned after preparation of phenyl salicylate by Seifert, *J. prakt. Chem.*, [2] 31, 472 (1885).

acid and by reaction of the parent glycols with vanillic acid in the presence of anhydrous hydrogen chloride. The structure of the dichloropropyl vanillate resulting from the reaction of glycerol with vanillic acid and anhydrous hydrogen chloride was established by its identity with 2,3-dichloropropyl vanillate prepared unequivocally from vanillic acid and glycerol 1,2-dichlorohydrin. Glycol esters were prepared by the carbethoxy route, reaction of the chlorohydrin with potassium vanillate, and by refluxing glycol with vanillic acid without a condensing agent. Esters of 5-chlorovanillic and orthovanillic acids were prepared by similar methods.

The inhibiting concentrations of these esters were determined for the three representative aerobic microörganisms—namely, non-sporeforming (*Aerobacter aerogenes*) and sporeforming (*Bacillus mycoides*) bacteria and molds (*Aspergillus niger*). Most of the vanillates were found to inhibit *Bacillus mycoides* and *Aspergillus niger* in low concentrations. The chlorohydrin esters, in addition, possessed remarkable toxicity toward *Aerobacter aerogenes*. This property was also characteristic of 2-butoxyethyl vanillate, but was not exhibited by trichloro-*t*-butyl vanillate. The esters of orthovanillic acid appear to be less specific in their toxicity. Of the 5-chlorovanillic acid esters, only the methyl and ethyl esters exhibited any toxicity whatsoever. Toxicity data are given in Table I.

Acknowledgment.—The authors are indebted to John F. McCoy and to Virginia West Martin, respectively, for the microbiological and chemical analyses reported in this paper.

Summary

A large number of new esters of vanillic acid and the closely related acids, orthovanillic and 5-chlorovanillic, were prepared. The inhibiting concentrations of these esters were determined for representative microörganisms.

RECEIVED OCTOBER 19, 1948

[CONTRIBUTION FROM THE SHELL DEVELOPMENT COMPANY]

Infrared and Ultraviolet Spectroscopic Studies on Ketones[1]

BY R. S. RASMUSSEN, D. D. TUNNICLIFF AND R. ROBERT BRATTAIN

The infrared, Raman, and ultraviolet spectra of aldehydes and ketones have been the subjects of numerous studies in the literature.[2] Some further investigations, which were made in connection with the OSRD program on penicillin structure, are reported here. These studies were made in order to gain a better insight into the influence of structure on the spectra of carbonylic compounds.

The infrared spectra, from 2 μ to 15 μ, of the compounds studied are shown in tabular form in Table I; the ultraviolet spectra, from 2200 to 3500 Å., are given in Figure 1. All spectra are of pure liquids or solutions. The sources of samples and further spectroscopic experimental details are given at the end of this paper. Discussion of the infrared spectra is limited to the 3 μ region (NH, OH, and CH stretching vibrations) and 6 μ region (double-bond stretching vibrations). These were the regions actually used on the penicillin structure work and are the ones having an obvious correlation with structure. Thompson and Torkington, however, have noted several interesting regularities at longer wave lengths,[2] and such regularities are also present in Raman spectra.[2]

Infrared Work

Unconjugated Ketones.—Previous published infrared and Raman work[2] together with unpublished work from this laboratory, indicates that unconjugated ketones exhibit their C=O absorption very near 5.83 μ (1715 cm.$^{-1}$). The only compound of this type discussed here in detail, diacetone alcohol, was examined to determine the effect of simple hydrogen bonding on the band position. Badger and Bauer[3] have given evidence, based on studies of the third harmonic of the OH stretching fundamental, that intramolecular hydrogen bonding is present in this compound. The band at 5.84 μ (1712 cm.$^{-1}$) indicates that the effect of hydrogen bonding on the C=O band is small, in contrast to the large effects noted by many investigators on the OH band position (*e. g.*, the shifts of 0.1–0.2 μ noted by Gordy[4] between CH$_3$OD in benzene and in ketones and other proton acceptor solvents). An auxiliary experiment was carried out by examining a 10% (vol.) solution of methyl ethyl ketone in methanol. Under these conditions, where a large amount of hydrogen bonding of the type CH$_3$OH $\cdots$ O=CR$_2$ is to be expected, the observed C=O band position was 5.86 μ (1706 cm.$^{-1}$), again indicating only a small effect.

The strong OH band is present in the diacetone alcohol spectrum at 2.87 μ (3484 cm.$^{-1}$), the usual position for hydrogen-bonded alcoholic OH groups.

Conjugated Ketones.—Two examples of ketone C=O conjugated to C=C, namely, isophorone and acetophenone, were examined. The strong bands at 5.98 μ and 5.93 μ, respectively, (1672 and 1686 cm.$^{-1}$) are to be attributed to the C=O vibration. These positions are in the range found by others from Raman[5] and infrared[6] work for this band type (roughly 1670–1690 cm.$^{-1}$). The factors influencing the exact amount of this conjugation shift are not yet understood, due to lack of data on a sufficient number of compounds. It is clear, however, that conjugation with C=C effects a shift of the order of 30 cm.$^{-1}$.

Other features of interest in the spectrum of isophorone are: (1) The weak band at 5.83 μ (1715 cm.$^{-1}$) which is probably caused by an unconjugated ketonic impurity (1 or 2% impurity would be sufficient to give a band of this intensity);

---

(1) The major part of this work was done under contract between the Office of Scientific Research and Development, and the Shell Development Company (Contract OEM-cmr-445).

(2) *Infrared:* H. W. Thompson and P. Torkington, *J. Chem. Soc.*, 640 (1945); R. B. Barnes, R. C. Gore, U. Liddel and V. Z. Williams, "Infrared Spectroscopy," Reinhold, New York, 1944; R. N. Jones, V. Z. Williams, M. J. Whalen and K. Dobriner, THIS JOURNAL, **70**, 2024 (1948). *Raman:* See J. H. Hibben, "The Raman Effect and its Chemical Applications," A. C. S. Monograph, Reinhold Publishing Corp., New York, N. Y., 1939. *Ultraviolet:* See H. Sponer and E. Teller, *Rev. Mod. Phys.*, **13**, 75 (1941).

(3) R. M. Badger and S. H. Bauer, *J. Chem. Phys.*, **5**, 839 (1937).

(4) W. Gordy, *J. Chem. Phys.*, **7**, 93 (1939).

(5) *E. g.*, K. W. F. Kohlrausch and A. Pongratz, *Z. physik. Chem.*, **B27**, 176 (1934).

(6) *E. g.*, Thompson and Torkington, ref. 2.