spectrum was entirely consistent with a long-chain saturated ester.

Characterization of Recovered Olefins. Dodecene-1.—After carbonation of the metalation mixtures at the time intervals shown in Table I, the acidic and neutral fractions were separated in the usual manner. Distillation of the organic layer provided a dodecene fraction with an infrared spectrum showing intense bands at 10.1 and 11.0 μ with no absorption at 10.3 (*trans*) or 14.2 μ (*cis*).[27] This spectrum is identical with that of the starting material and it was therefore concluded that no isomerization had occurred.

During the course of this work several reactions had been run for periods of approximately 20 hr. In some cases slight amounts of isomerization were indicated by a very weak infrared band at 10.3 μ (*trans*). In all cases very intense bands indicative of the terminal double bond were obtained. One experiment which was conducted for 48 hr. showed approximately 20% isomerization by infrared, while another run in which the metalation mixture was allowed to stand for 450 hr. showed approximately 40% isomerization as estimated from the infrared spectrum. In all these runs β,γ-unsaturated C_{13} acid products were obtained upon carbonation as described above. While the amounts of isomerization do not appear to be entirely reproducible in these heterogeneous reactions, these results justify the conclusion that isomerization is a relatively slow process in alkylpotassium systems.[7,13]

Hexene-1, *trans*-Hexene-2, and Mixtures Thereof.—Hexene-1, 2-hexene, and a 1:1 mixture of these two olefins were metalated as described above and carbonated after 2 and 18 hr. There was obtained an acid product with an infrared spectrum indicative of α-vinylbutyric acid (10.1 and 10.9 μ) and *trans*-3-heptenoic acid (10.3 μ). G.l.c. analyses of the corresponding esters showed two products with appropriate retention times. The infrared spectra of the recovered organic phases show that the relative intensities of the 10.1-, 10.3-, and 11.0-μ absorption were unchanged from those of the starting materials. It was therefore concluded that relatively little, if any, isomerization had occurred.

Preparation of 1-Bromo-1-dodecene.—This preparation was described previously.[7]

Reaction of 1-Bromo-1-dodecene with Potassium Dispersion.—A dispersion of potassium (3.9 g., 0.1 g.-atom) in 200 ml. of octane[10] was prepared and 1-bromo-1-dodecene (10 g., 0.04 mole) was added dropwise at room temperature. Stirring was continued and 40-ml. portions of the reaction mixture were removed after 15 min., 1 hr., and 4 hr. These were carbonated by pouring over excess solid carbon dioxide. The remaining reaction mixture was allowed to stir an additional 25 hr. and then carbonated. All operations were conducted under an atmosphere of dry nitrogen. The usual work-up, esterification, and analyses gave the results recorded in Table II. In a separate experiment, using the same amounts of materials, in which the entire reaction mixture was carbonated after stirring for 1 hr., 4.1 g. (47%) of C_{13} acids was obtained. In an analogous experiment using sodium metal 5.4 g. (62%) of C_{13} acids was obtained.

Addition of 1-Octene to 1-Potassio-1-dodecene.—A preparation of 1-potassio-1-dodecene using 7.8 g. (0.2 g.-atom) of potassium dispersed in octane and 10.0 g. (0.04 mole) of 1-bromo-1-dodecene was carried out as described above. This reaction mixture was stirred 0.5 hr. and a portion carbonated. The acid product was esterified and analyzed by g.l.c. It contained C_{13} α,β-unsaturated acids and no detectable amount of C_{13} β,γ-unsaturated acids. To the remaining reaction mixture was added 1-octene (46 g., 0.4 mole) and stirring was continued for an additional 3.5 hr. The entire reaction mixture was then poured over excess dry ice. Esterification with methyl alcohol and a catalytic amount of sulfuric acid, followed by g.l.c. analysis, showed the presence of C_9 β,γ-unsaturated acids (28%), by comparison with the acidic product obtained from carbonation of the metalation of 1-octene with butylsodium for 24 hr., C_{13} β,γ-unsaturated acids (10%), C_{13} α,β-unsaturated acids (34%), tridecanoic acid (12%), and 2-tridecynoic acid (15%).

A separate run was made in which 1-potassio-1-dodecene was generated from 1-bromo-1-dodecene (4.0 g., 0.016 mole) and potassium metal (1.5 g., 0.04 g.-atom) as described above. Octene-1 (17.9 g., 0.16 mole) was added immediately after completion of addition of the alkenyl bromide and the mixture stirred for 1.5 hr. Carbonation provided 1.1 g. (33%) of crude acid product. Esterification with methanol and a catalytic amount of sulfuric acid provided an ester product whose gas chromatogram showed the same peaks as those cited above.

---

[27] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, pp. 45-51.

Coordination in Solutions. II. Acid Dissociation Constants in Water and Structural Reassignments of the Isomeric Chlorosalicylaldehydes[1,2]

Clarence Postmus, Jr.,[3a] Irving Allan Kaye,[3b] Carolyn A. Craig,[3a] and Richard S. Matthews[3b,c]

Chemistry Division, Argonne National Laboratory, Argonne, Illinois, and Department of Chemistry,
Brooklyn College of the City University of New York, Brooklyn 10, New York

Received April 7, 1964

When the Reimer–Tiemann reaction with *m*-chlorophenol was repeated, using the procedure of Hodgson and Jenkinson, all three of the theoretically possible products were isolated and identified. The isomer, designated as "4-chlorosalicylaldehyde" by Hodgson and Jenkinson, is shown to be 6-chlorosalicylaldehyde. The pK values for acid dissociation, in molar concentration units, of 3-, 4-, 5-, and 6-chlorosalicylaldehyde and that of 2-chloro-4-hydroxybenzaldehyde are 6.61, 7.18, 7.41, 8.26, and 6.60, respectively, in aqueous soution at 25.0° and μ of 0.100 maintained with sodium perchlorate. The change in acidity caused by a chloro substituent in each ring position can be correlated with that observed in the corresponding phenol, anion stabilities, and intramolecular hydrogen bond strengths. Changes in the latter were also measured by n.m.r. spectroscopy and ultraviolet spectral shifts upon methylation. The unusually low acidity of 6-chlorosalicylaldehyde can be explained by the proximity of the *o*-chloro substituent to the carbonyl group.

A study of the four chloro derivatives of salicylaldehyde[4] was undertaken to determine the dependence of the chelating ability of the ligand upon the ring position of the substituent and, by comparison with the nitro derivatives,[2] upon the π-electron acceptor (nitro) or donor (chloro) characteristics of the substituent.[5,6] The acid dissociation constants in aqueous solution are presented in this paper as measures of the

---

[1] Based on work performed under the auspices of the U. S. Atomic Energy Commission. Work performed at Brooklyn College was supported by research and development subcontract no. 31-109-38-889 of the Argonne National Laboratory.

[2] Part I of this series: L. B. Magnusson, C. Postmus, Jr., and C. A. Craig, *J. Am. Chem. Soc.*, **85**, 1711 (1963).

[3] (a) Argonne National Laboratory; (b) Brooklyn College; (c) National Science Foundation Undergraduate Research Participant, Brooklyn College, 1961-1962.

[4] The salicylaldehydes are numbered with the carbonyl group in the 1-position and the hydroxyl group in the 2-position.

[5] J. G. Jones, J. B. Poole, J. C. Tomkinson, and R. J. P. Williams, *J. Chem. Soc.*, 2001 (1958).

[6] K. Clarke, R. A. Cowen, G. W. Gray, and E. H. Osborne, *ibid.*, 245 (1963).

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA OF SOME HYDROXYBENZALDEHYDES[a]

Compound[b]	λ_{max}, mμ	λ_{min}, mμ	λ_{max}, mμ	λ_{min}, mμ	λ_{max}, mμ
2-OH	210 (17.2)[c]	231 (2.45)	255 (11.3)	281 (0.67)	324 (2.99)
3-Cl-2-OH	214 (20.4)	234 (2.08)	257 (11.1)	285 (0.43)	333 (3.00)
4-Cl-2-OH[d]	214 (18.3)	235 (2.10)	264 (16.6)	288 (1.43)	322 (4.41)
5-Cl-2-OH	222 (24.1)	236 (4.36)	255 (9.12)	278 (0.18)	337 (3.25)
6-Cl-2-OH[e]	218 (13.7)	236 (1.26)	266 (9.86)[f]	293 (0.61)	337 (3.18)
4-OH		209 (3.80)	221 (11.5)	238 (0.12)	283 (15.8)
2-Cl-4-OH	207 (14.0)	218 (7.78)	229 (12.9)	246 (1.80)	281 (14.0)

[a] Measured in acidic aqueous solution, $\mu = 0.100$. [b] Compounds listed are named as derivatives of benzaldehyde. [c] Figures in parentheses refer to molar absorptivity and should be multiplied by 10^3. [d] This chlorosalicylaldehyde melted at 47°. [e] This product melted at 52°. [f] Bunnett, *et al.* (ref. 12), found λ_{max} 265 mμ (10.1×10^3).

relative strengths of proton chelation.[7] The acid strengths of some chlorosalicylaldehydes in aqueous dioxane have been determined previously,[5,6,8] but some of the measurements[5,6] have been made on compounds of uncertain structure (*vide infra*).

When this program was initiated, only the 5-chlorosalicylaldehyde was commercially available; the 3-[9] and 4-chloro[10] isomers had been reported as products of the Reimer–Tiemann reaction with *o*- and *m*-chlorophenol, respectively. The 4-chloro isomer had also been reported in a patent.[11] The 6-chloro compound has recently been prepared by two independent investigators,[6,12] who reported slightly differing melting points; no derivatives of either product were reported. Since the reported 3-, 4-, and 6-chlorosalicylaldehydes all melt within a few degrees of each other, melting point alone is insufficient to distinguish among them.

The two different preparations[10,11] of 4-chlorosalicylaldehyde gave products which differed slightly in melting point, but whose oxime derivatives melted 16° apart. The assignment of the chloro position in both preparations may be subject to criticism. Group migration may have occurred in the high temperature displacement reaction[11] or the Reimer–Tiemann product may be 6-chlorosalicylaldehyde,[10] a possible product. While the characterization of the Reimer–Tiemann product *via* its methoxy derivative appears irrefutable, the similarity of its melting point with that of 6-chlorosalicylaldehyde[6,12] and the isolation of 6-nitrosalicylaldehyde from a similar Reimer–Tiemann reaction with *m*-nitrophenol[13] cast doubt upon the "4-chlorosalicylaldehyde" designation. Despite the uncertainties, the designation of the Reimer–Tiemann product from *m*-chlorophenol as "4-chlorosalicylaldehyde" has gone unchallenged.[5,6]

To resolve these literature discrepancies in the assignment of the chloro position, which is of prime importance in this investigation, the Reimer–Tiemann reaction with *m*-chlorophenol was thoroughly reinvestigated and its salicylaldehyde products were compared with 4- and 6-chlorosalicylaldehyde prepared by less ambiguous methods.

Results and Discussion

Structural Assignments of 4- and 6-Chlorosalicylaldehydes.—Three isomeric aldehydes, 4- and 6-chlorosalicylaldehyde and 2-chloro-4-hydroxybenzaldehyde, were isolated from the Reimer–Tiemann reaction with *m*-chlorophenol. The two lower melting compounds were identified as salicylaldehydes by their strong metal chelation and the similarity of their ultraviolet spectra with those of salicylaldehyde and its known chloro derivatives which are distinctly different from those of *p*-hydroxybenzaldehydes (see Table I). The identification of the lower melting, 47°, chlorosalicylaldehyde as the 4-chloro and the higher melting, 52°, as the 6-chloro isomer was made from a comparison of melting points, mixture melting points, p*K* values, and infrared and ultraviolet spectra with those of the independently prepared aldehydes.

Our assignment is based upon the independent synthesis of both salicylaldehydes from compounds where the chloro positions are known. The melting points of the 4- and 6-chlorosalicylaldehydes agree with others reported in the literature.[11,12] In addition, several known derivatives of both aldehydes were prepared and their melting points confirmed this assignment. Furthermore, the infrared and n.m.r. spectra show that the position of the aryl protons are correctly designated. This assignment is further confirmed by the p*K* values and the n.m.r. data on the formyl and hydroxylic protons which will be discussed later.

In contrast to this work, Hodgson and Jenkinson[10] isolated, from their Reimer–Tiemann reaction, 2-chloro-4-hydroxybenzaldehyde and only *one* chlorosalicylaldehyde, which they designated as 4-chlorosalicylaldehyde. This designation, unchallenged by subsequent investigators, can no longer be accepted since the melting point of the aldehyde and its oxime derivatives as well as the p*K* value (see p*K* discussion) identify it as 6-chlorosalicylaldehyde. Although Hodgson and Jenkinson prepared derivatives of both 4-chloro- (the methoxy) and 6-chlorosalicylaldehyde (the oxime) from their aldehyde, their designation was based upon only one derivative (the methoxy). The conclusion appears inescapable that, although Hodgson and Jenkinson prepared both salicylaldehydes, their purified aldehyde is 6-chlorosalicylaldehyde and not the 4-chloro isomer.

While this work was in progress, Clarke, *et al.*,[6] reported the preparation of both 4- and 6-chlorosalicyl-

---

(7) The metal complexing results will be presented in a subsequent publication.

(8) M. Calvin and K. W. Wilson, *J. Am. Chem. Soc.*, **67**, 2003 (1945).

(9) W. Davies and L. Rubenstein, *J. Chem. Soc.*, 2839 (1923).

(10) H. H. Hodgson and T. A. Jenkinson, *ibid.*, 1740 (1927).

(11) W. Müller, W. Möllering, and W. Schommer, German Patent 942,808 (May 9, 1956) and British Patent 775,312 (May 22, 1957); *Chem. Abstr.*, **52**, 433 (1958). These authors prepared their 4-chlorosalicylaldehyde, m.p. 49°, by a high temperature displacement of the sulfonic acid function in 5-chloro-2-formylbenzene sulfonic acid with a hydroxyl group. Its oxime melted at 138–140°.

(12) J. F. Bunnett, J. H. Miles, and K. V. Nahabedian, *J. Am. Chem. Soc.*, **83**, 2512 (1961). These authors prepared 6-chlorosalicylaldehyde by a replacement of a fluoro substituent with a hydroxyl group in 2-chloro-6-fluorobenzaldehyde.

(13) D. R. Mehta and P. Ramaswami Ayyar, *J. Univ. Bombay*, **8**, part 3, 176 (1939); *Chem. Abstr.*, **34**, 2814 (1940).

TABLE II

ACID DISSOCIATION CONSTANTS OF SOME HYDROXYBENZALDEHYDES[a]

Compound[b]	Water[c]	Water-dioxane[d] (1:1)	Water-dioxane[e] (1:1)	Water-dioxane[f] (1:3)
2-OH	8.14[g]	9.5	9.35	10.35
3-Cl-2-OH	6.61	7.8	7.72	8.70
4-Cl-2-OH	7.18			
5-Cl-2-OH	7.41	8.6	8.47	9.35
6-Cl-2-OH	8.26		9.42[h] (8.99)[i]	10.50[h]
4-OH	7.45[g]			
2-Cl-4-OH	6.60			

[a] As p*K* values measured at 25.0°. Aqueous dioxane mixtures are given as water–dioxane (v./v.). [b] Named as derivatives of benzaldehyde. [c] This work; μ = 0.100 with sodium perchlorate as the inert electrolyte. Values are given as $pK = -\log[H^+][L^-]/[HL]$, where the concentrations of all species are given in moles/liter. [d] Results of ref. 8. [e] Results of ref. 6. [f] Results of ref. 5. [g] Results of ref. 2. [h] This compound was incorrectly designated as "4-chlorosalicylaldehyde" in the references cited. [i] The designation of this compound as 6-chlorosalicylaldehyde in ref. 6 is incorrect.

TABLE III

CHLORO SUBSTITUENT EFFECTS[a]

	Hydroxybenzaldehydes					Phenols
Compound[b]	Water[c]	Water-dioxane[d] (1:1)	Water-dioxane[e] (1:1)	Water-dioxane[f] (1:3)	Chloro position[g]	Water[h]
3-Cl-2-OH	1.53	1.7	1.63	1.65	*ortho*	1.47
4-Cl-2-OH	0.96				*meta*	0.87
5-Cl-2-OH	0.73	0.9	0.88	1.00	*para*	0.58
6-Cl-2-OH	−0.12		−0.07[i]	−0.15[i]	*meta*	0.87
			(+0.36)[j]			-
2-Cl-4-OH	0.85				*meta*	0.87

[a] The substituent effect is defined as the difference in the following equation, p*K* (of unsubstituted parent) − p*K* (of substituted parent). Aqueous dioxane mixtures are given as water–dioxane (v./v.). [b] Compounds are listed as derivatives of benzaldehyde. [c] Calculated from the results obtained in this study; μ = 0.100. The p*K* values of salicylaldehyde and *p*-hydroxybenzaldehyde, used in these calculations, were taken from ref. 2. [d] Calculated from values given in ref. 8. [e] Calculated from values given in ref. 6. [f] Calculated from values given in ref. 5. [g] The position of the chloro substituent in these compounds is given in relation to the hydroxyl group in phenol and the hydroxybenzaldehydes. [h] Calculated from the results of A. I. Biggs and R. A. Robinson, *J. Chem. Soc.*, 388 (1961), at μ = 0.000 in aqueous solutions. [i] This compound was incorrectly designated as "4-chlorosalicylaldehyde" in the references cited. [j] The designation of this compound as "6-chlorosalicylaldehyde" in ref. 6 is incorrect.

aldehyde. Since the former, prepared by the method of Hodgson and Jenkinson, has a melting point and p*K* value (see p*K* discussion) which identifies it as 6-chlorosalicylaldehyde, both compounds should have identical physical properties. Although there is close agreement in the melting points, the large difference in the p*K* values clearly demonstrates that their "6-chlorosalicylaldehyde" is erroneously designated.

Acid Dissociation Constants.—The acid dissociation constants as p*K* values in aqueous solution, at μ of 0.100, maintained with sodium perchlorate, and 25.0°, are given in Table II for the isomeric monochloro derivatives of salicylaldehyde and for 2-chloro-4-hydroxybenzaldehyde. These values are the average of at least two determinations which agreed to within ±0.01 log unit with a maximum estimated error of ±0.02 log unit.[2] The thermodynamic p*K* values can be approximated by the addition of 0.18 log unit to the values at 0.100 μ as shown previously for salicylaldehyde and similar organic acids.[2] Previous values in aqueous dioxane are included in Table II, where the aldehyde, prepared by the method of Hodgson and Jenkinson[10] and designated as "4-chlorosalicylaldehyde" in ref. 5 and 6, has been entered as 6-chlorosalicylaldehyde. Although p*K* values in different solvents cannot be directly compared, the substituent effect, defined as the p*K* of the unsubstituted compound minus the p*K* of the substituted compound, should be independent of solvent.[14,15] Table III lists the chloro substituent effects in various solvents and confirms the reassignment of Hodgson and Jenkinson's "4-chlorosalicylaldehyde" as 6-chlorosalicylaldehyde.

It has been shown that a nitro group weakens the intramolecular hydrogen bond in salicylaldehyde.[16] The weakening of the intramolecular hydrogen bond by an electronegative substituent may be expected to result in a larger substituent effect for an intramolecularly hydrogen-bonded species than for a nonintramolecularly hydrogen-bonded species.[2] As expected, Table III shows that the chloro substituent effects, compared with those of the corresponding phenols, are the same for the nonintramolecularly hydrogen-bonded species, *p*-hydroxybenzaldehyde, but larger for the intramolecular hydrogen-bonded 3-, 4-, and 5-chlorosalicylaldehydes. The increase, 0.06, 0.09, and 0.15 log unit, respectively, indicates that the intramolecular hydrogen bond is weakened least by chloro substitution in the 3-position of salicylaldehyde and most in the 5-position.

The *m*-chloro substituent effect for 6-chlorosalicylaldehyde is markedly different from that observed for *m*-chlorophenol, 4-chlorosalicylaldehyde, and 2-chloro-4-hydroxybenzaldehyde; in the 6-position of salicylaldehyde, the chloro substituent actually *decreases* the acidity of the parent. The obvious difference between these compounds is the position of the chlorosubstituent *ortho* to the carbonyl group in 6-chlorosalicylaldehyde. In the anion form of the latter, the negativity of the chloro group will oppose the rotation of the carbonyl group away from the negative phenoxide oxygen.[17] This destabilization of the anion will increase the p*K* value. In addition, infrared measurements of the carbonyl vibrational frequency of 6-

---

(14) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd Ed., Reinhold Publishing Corp., New York, N. Y., 1958, p. 682.

(15) L. G. Van Uitert, C. G. Haas, W. C. Fernelius, and B. E. Douglas, *J. Am. Chem. Soc.*, **75**, 455 (1953).

(16) C. J. W. Brooks and J. F. Morman, *J. Chem. Soc.*, 3372 (1961).

(17) R. N. Jones, W. F. Forbes, and W. A. Mueller [*Can. J. Chem.*, **35**, 504 (1957)] have shown by electrostatic considerations that a carbonyl oxygen is oriented away from an *ortho* halogen substituent. The steric considerations discussed in this reference do not apply to salicylaldehyde derivatives.

chlorosalicylaldehyde (1666 cm.$^{-1}$) show a stronger intramolecular hydrogen bond than that of 4-chlorosalicylaldehyde (1672 cm.$^{-1}$).[16] The stronger intramolecular hydrogen bond in 6-chlorosalicylaldehyde will be confirmed by other measurements. The increased intramolecular hydrogen bond strength may be attributed to the smaller average distance between the carbonyl oxygen and the hydroxylic proton as the torsional motion of the carbonyl group about the carbon–carbon bond is damped by the proximity of the negative chloro substituent. The effects of the proximity of the chloro group to the carbonyl group have more than offset the expected *m*-chloro substituent effect.

Methylation Shifts.—The increase in the intramolecular hydrogen bonding in 6-chlorosalicylaldehyde can be confirmed in several ways. The magnitude of the shift of the longest wave-length peak (*ca.* 325 mμ) of *o*-carbonyl phenols towards shorter wave lengths upon methylation has been used as a measure of the strength of intramolecular hydrogen bonding.[18–20] In ethanol, the methylation shifts of salicylaldehyde, 4-chloro-, and 6-chlorosalicylaldehyde are 6,[18] 4, and 17 mμ, respectively. In water, the corresponding shifts are decreased to 2, 1, and 11 mμ. Although the difference between salicylaldehyde and 4-chlorosalicylaldehyde may not be significant, the much larger methylation shift of 6-chlorosalicylaldehyde indicates a much stronger intramolecular hydrogen bond.

N.m.r. Formyl Proton.—The n.m.r. peak locations of the formyl and hydroxylic protons in chlorosalicylaldehydes and related compounds are given in Table IV. The similarity of the formyl proton peaks indicates that this proton has a similar environment in benzaldehyde, salicylaldehyde and the 3-, 4-, and 5-chlorosalicylaldehydes. However, the formyl peak in both *o*-chlorobenzaldehyde and 6-chlorosalicylaldehyde are shifted downfield by *ca.* 0.54 p.p.m. In both these compounds, the formyl proton is oriented towards the chloro substituent. It is believed that this large shift results from the short-range interaction between the electron clouds of the chloro substituent and the formyl proton. We will call this the *proximity effect.*[21] Although a proximity effect for the formyl proton in salicylaldehydes might be expected from interaction with the *ortho* hydroxyl group, intramolecular hydrogen bond formation between the carbonyl oxygen and the hydroxyl group orients the formyl proton away from the latter.

TABLE IV

PROTON MAGNETIC RESONANCE SPECTRA OF SOME CHLOROSALICYLALDEHYDES AND RELATED COMPOUNDS[a]

Compound	-CHO absorbance	-OH absorbance
Benzaldehyde	10.00	
o-Chlorobenzaldehyde	10.55	
Salicylaldehyde	10.00	11.12
3-Chlorosalicylaldehyde[b]	10.03	11.62
4-Chlorosalicylaldehyde[b]	9.88	11.25
5-Chlorosalicylaldehyde	9.94	11.06
6-Chlorosalicylaldehyde[b]	10.53	12.02

[a] Values are given as the separation in parts per million of the peak from that of tetramethylsilane in deuteriochloroform. [b] The absorption bands associated with the aryl protons are included in Experimental.

N.m.r. Hydroxylic Proton.—Substituent shifts, defined as the location of a given n.m.r. peak in the substituted compound minus that in the unsubstituted compound, of hydroxylic protons have been ascribed solely to hydrogen bond formation.[22,23] However, shifts are still observed at infinite dilution, where intermolecular hydrogen bonding has been eliminated, for the nonintramolecularly hydrogen-bonded species, *m*- and *p*-chlorophenols.[23] Similar shifts have been observed for aryl fluorines[24] and protons[25,26] and correlated with the Hammett δ-values of the substituent.[25,27] These shifts may be ascribed to changes in the electron density of the primary proton bond because of the resonance and inductive effects of the substituent and will be called the *primary effect.* A plot of the substituent shift of *p*-chlorophenol (0.5 p.p.m.[23]) and that of *p*-hydroxyacetophenone (1.6 p.p.m. from phenol[28]) *vs.* the corresponding substituent effects upon acidity (0.58 and 1.91[2] units, respectively) yields a line passing through the origin. Since the ΔpK values are proportional to Hammett σ-values, this correlation shows the existence of the primary effect for the *para* position, and it can be assumed to occur in all positions.

From the n.m.r. data of the present work, salicylaldehydes are monomeric (intramolecularly hydrogen bonded but not intermolecularly hydrogen bonded), since the hydroxylic proton peak location is independent of concentration (0.42 to 0.1 *M*). The reduction of intermolecular hydrogen bonding to a negligible amount by competitive intramolecular hydrogen bonding has also been observed at 0.6 *M* for *o*-chlorophenol.[23] Since the primary effect of a substituent should be the same in phenol and salicylaldehyde, differences in the substituent shifts may be attributed to changes in the intramolecular hydrogen bonding in the latter. The observed chloro substituent shifts for 4- and 5-chlorosalicylaldehyde (0.13 and -0.06 p.p.m., respectively) are smaller than in the corresponding phenols (0.3 and 0.5 p.p.m.[23]) by 0.17 and 0.56 p.p.m. These differences indicate that chloro substitution into salicylaldehyde has a greater weakening effect upon the intramolecular hydrogen bond in the 5-position than in the 4-, as was inferred from the pK discussion. In 6-chlorosalicylaldehyde, the primary effect should be the same as in *m*-chlorophenol. However, the very large positive difference in the substituent shifts (0.9 p.p.m. for 6-chlorosalicylaldehyde and 0.3 p.p.m. for *m*-chlorophenol[23]) indicates that the intramolecular hydrogen

---

(18) R. A. Morton and A. L. Stubbs, *J. Chem. Soc.*, 1347 (1940).

(19) V. C. Farmer, N. F. Hayes, and R. H. Thomson, *ibid.*, 3600 (1956).

(20) T. A. Geissman and J. B. Harborne, *J. Am. Chem. Soc.*, **78**, 832 (1956).

(21) W. F. Forbes, *Can. J. Chem.*, **40**, 1891 (1962). Although Forbes observed a similar downfield shift of a formyl proton, his assignment to a steric displacement will not explain the effect in these compounds.

(22) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, Chapter 15.

(23) C. M. Huggins, G. C. Pimentel, and J. N. Shoolery, *J. Phys. Chem.*, **60**, 1311 (1956).

(24) H. S. Gutowsky, D. W. McCall, B. R. McGarvey, and L. H. Meyer, *J. Am. Chem. Soc.*, **74**, 4809 (1952).

(25) A. A. Bothner-By and R. E. Glick, *ibid.*, **78**, 1071 (1956).

(26) P. L. Corio and B. P. Dailey, *ibid.*, **78**, 3043 (1956).

(27) R. W. Taft, Jr., *ibid.*, **79**, 1045 (1957).

(28) The substituent shift, 1.6 p.p.m., was calculated as the difference between a value of 6.0 p.p.m. observed for *p*-hydroxyacetophenone upon extrapolation to infinite dilution and a corrected phenol value of 4.4 p.p.m. The corrected phenol value was obtained from the value of 2.8 p.p.m. (ref. 23) measured with cyclohexane as a standard and the difference, 1.6 p.p.m., between cyclohexane and tetramethylsilane given in ref. 22, p. 89.

bond is strengthened by chloro substitution in the 6-position of salicylaldehyde. This conclusion is consistent with the designation of this compound as 6-chlorosalicylaldehyde.

The substituent shift for 3-chlorosalicylaldehyde cannot be compared directly with that of *o*-chlorophenol, since intramolecular hydrogen bonding to the chloro substituent occurs in the latter but is precluded in the former by the stronger competitive intramolecular hydrogen bonding to the carbonyl group. The primary effects of an *o*-chloro substituent can be estimated from the observed shift in 3-chlorosalicylaldehyde (0.5 p.p.m.) by the addition of 0.1 p.p.m.[29] to compensate for the shift due to the weakening of the intramolecular hydrogen bond by 3-chloro substitution. The observed substituent shift in *o*-chlorophenol (1.3 p.p.m.[23]) can now be attributed to a primary effect of 0.6 p.p.m. and the remainder, 0.7 p.p.m., to the formation of an intramolecular hydrogen bond to the chloro substituent.[30]

Experimental[31]

Materials. ***o*- and *m*-Chlorophenols, 3- and 5-chloro-2-methylanilines, and 5-chlorosalicylaldehyde** were obtained commercially; the first four compounds were used without further purification. 5-Chlorosalicylaldehyde was recrystallized from petroleum ether (b.p. 65–110°), m.p. 99–99.5° (H.). Inorganic chemicals were prepared and standardized as described in part I of this series.[2]

3-Chlorosalicylaldehyde.—This compound, m.p. 53.7–54.5° (lit.[9] m.p. 55°), was prepared from *o*-chlorophenol by the Reimer–Tiemann reaction.[9] The resonance peaks of the aromatic protons were found in the n.m.r. spectrum as double doublets centered at 7.66 (J = 8.0 and 2.0 c.p.s., C-4 proton), 7.13 (J = 8.0 and 8.0 c.p.s., C-5 proton), and 7.80 p.p.m. (J = 8.0 and 2.0 c.p.s., C-6 proton).

4-Chlorosalicylaldehyde.—5-Chloro-2-methylaniline was converted[32] to 5-chloro-2-methylphenol, m.p. 71.5–73° (lit.[33] m.p. 73–74°). The phenol was oxidized[34] to 4-chlorosalicylaldehyde triacetate, which was isolated as a crude oil by evaporation of an ether extract of the diluted reaction mixture. The unpurified triacetate was hydrolyzed[35] and the aldehyde recovered by evaporation of an ether extract, which had been washed with aqueous bicarbonate. The crude aldehyde was purified by washing its sodium bisulfite adduct with ethanol, followed by ether. Decomposition of the adduct with 4 M hydrochloric acid, followed by recrystallization from dilute acetic acid and then from petroleum ether (b.p. 30–60°), gave 4-chlorosalicylaldehyde, m.p. 47.0–47.8° (lit.[11] m.p. 49°), λ_{max} 322 and 262 mμ (95% ethanol).

Absorption peaks in the infrared were observed at 5.98 s (aryl aldehyde st.); 6.18 s, 6.36 s, and 6.72 s (aromatic skeletal in-plane vibrations); 7.61 s and 8.15 s (aryl aldehyde); 8.40 s, 8.89 m, 9.30 s, and 9.82 w (1,2,4-substituted on benzene); 10.81 s (CHO-H def.?); 11.58 m (CH out-of-plane def., one free H on benzene); 12.54 s (CH out-of-plane def., two adjacent hydrogens on benzene); and 7.94 m, 13.58 m (broad), and 14.05–14.10 μ m (broad).

The aromatic proton peaks were found in the n.m.r. spectrum as a doublet centered at 7.15 (J = 1.8 c.p.s., C-3 proton), a double doublet centered at 7.13 (J = 9.0 and 1.8 c.p.s., C-5 proton), and a doublet centered at 7.64 p.p.m. (J = 9.0 c.p.s., C-6 proton).

Anal. Calcd. for $C_7H_5ClO_2$: C, 53.70; H, 3.21; Cl, 22.65. Found: C, 53.81; H, 3.41; Cl, 22.60.

The oxime melted at 140–141° (H.) after recrystallization from aqueous ethanol. The melting point agrees with a melting point of 138–140° reported in ref. 11 and contrasts with that of 155° reported in ref. 10.

Anal. Calcd. for $C_7H_6ClNO_2$: C, 49.00; H, 3.52; Cl, 20.66; N, 8.16. Found: C, 48.89; H, 3.58; Cl, 20.75; N, 8.17.

The 2,4-dinitrophenylhydrazone, after three recrystallizations from ethyl acetate, was obtained as orange-red crystals: m.p. (vac.) 277.0–277.8°; λ_{max} 239, 308, and 394 mμ; λ_{min} 284 and 325 mμ (95% ethanol). This derivative was more insoluble in ethyl acetate than were the corresponding derivatives of 6-chlorosalicylaldehyde and 2-chloro-4-hydroxybenzaldehyde.

Anal. Calcd. for $C_{13}H_{19}ClN_4O_5$: C, 46.37; H, 2.70. Found: C, 46.69; H, 2.70.

The copper salt was prepared by treating a methanolic solution of the aldehyde with a filtered saturated solution of cupric acetate in methanol. The crystalline dull green precipitate, which appeared in about 1 min., was separated by filtration and washed well with cold methanol. It was very insoluble in the common laboratory solvents and did not melt at temperatures below 340°, but sintered slightly at about 296°.

Anal. Calcd. for $C_{14}H_{18}Cl_2CuO_4$: C, 44.88; H, 2.15. Found: C, 44.46; H, 2.36.

The methyl ether, obtained in about 70% yield by reaction with dimethyl sulfate in an alkaline aqueous medium, had m.p. 73–73.5° (H.) (lit. m.p. 74°[10] and 73.5°[36]) after recrystallization from aqueous ethanol, λ_{max} 318 and 261 mμ (95% ethanol).

6-Chlorosalicylaldehyde.—The procedure for the preparation of this compound from 3-chloro-2-methylaniline, *via* the phenol, m.p. 85.5–86° (H.) (lit.[37a,b] m.p. 86°), paralleled that of the 4-chloro isomer. 6-Chlorosalicylaldehyde had m.p. 51.5–52° (H.) (lit.[12] m.p. 50–52°) after recrystallization from petroleum ether (b.p. 30–60°), λ_{max} 338 and 262 mμ (95% ethanol). A Nujol mull absorbed in the infrared at 6.19 s, 6.32 m, and 6.82 s (aromatic C=C); 6.00 s, 7.65 m, and 8.34 w (aryl aldehyde); 8.51 s, 12.67 m, and 14.02 s (three adjacent aromatic hydrogens); 10.30 s (CHO-H def. ?); and 7.76 m, 12.28 m, and 13.00–13.05 μ m (broad).

In the n.m.r. spectrum, the C-3, C-4, and C-5 protons could be related with double doublets centered at 7.02 (J = 8.8 and 1.8 c.p.s.), 7.57 (J = 8.0 and 8.0 c.p.s.), and 7.09 p.p.m. (J = 8.0 and 1.8 c.p.s.), respectively.

Anal. Found: C, 53.63; H, 3.14; Cl, 22.52.

After recrystallization from aqueous ethanol, the oxime melted at 155–155.5°, which agrees with the melting point reported in ref. 10 for "4-chlorosalicylaldehyde."

Anal. Found: C, 48.99; H, 3.65; Cl, 20.45; N, 7.90.

The 2,4-dinitrophenylhydrazone was obtained as an orange powder which had m.p. (vac.) 244–245° after two recrystallizations from ethyl acetate; λ_{max} 239–240, 306, and 386 mμ; λ_{min} 285 and 325 mμ (95% ethanol). This derivative was more soluble in ethyl acetate than was 2-chloro-4-hydroxybenzaldehyde 2,4-dinitrophenylhydrazone.

Anal. Found: C, 46.62; H, 2.73.

---

(29) In the pK discussion it was concluded that a chloro substituent in the 3-position of salicylaldehyde weakens the intramolecular hydrogen bond less than in the 4-position. Since, in the latter, the weakening causes an n.m.r. shift of −0.17 p.p.m., a value of −0.1 p.p.m. was assumed for intramolecular hydrogen bond weakening in 3-chlorosalicylaldehyde.

(30) Although the n.m.r. substituent shifts are very different for 3-chlorosalicylaldehyde and *o*-chlorophenol, the substituent effects upon acidity are very similar. Since the n.m.r. differences are due to the formation of an intramolecular hydrogen bond to the chloro substituent in *o*-chlorophenol, it must be concluded that this weak intramolecular hydrogen bond is broken in the aqueous medium of pK measurements by competitive intermolecular hydrogen bonding to the water.

(31) All melting points are corrected and, unless otherwise specified, were determined in open Pyrex capillary tubes, except for those designated "vac.," which were observed in evacuated (to about 15 mm.) capillary tubes. "H." refers to melting points observed between cover slips on a hot stage. Infrared spectra were recorded on a Perkin-Elmer Model 21 spectrophotometer with sodium chloride optics using the Nujol mull technique. The ultraviolet spectra of the phenylhydrazones were obtained with a Beckman Model DU spectrophotometer; all others were recorded with an Applied Physics (Cary) Model 14 PM spectrophotometer. N.m.r. spectra were determined at a concentration of 0.42 M in deuteriochloroform solutions and were recorded on a Varian A-60 spectrometer operating at 60 Mc. Frequencies were obtained relative to tetramethylsilane as internal standard. Coupling constants were taken as the separation at peaks and chemical shifts as the mid-distances of multiplets. Microanalyses were performed by Dr. Alfred Bernhardt, Mülheim, Germany, and Micro-Tech Laboratories, Skokie, Ill.

(32) H. E. Ungnade and E. F. Orwoll, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 130.

(33) T. Zincke and O. Preiss, *Ann. Chem.*, **417**, 207 (1918); *Chem. Abstr.*, **13**, 1830 (1919).

(34) T. Nishimura, *Org. Syn.*, **36**, 58 (1956).

(35) S. M. Tsang, E. H. Wood, and J. R. Johnson, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 641.

(36) R. Kuhn and H. R. Hensel, *Chem. Ber.*, **84**, 557 (1951).

(37) (a) E. Noelting, *ibid.*, **37**, 1015 (1904); (b) M. S. Carpenter and W. M. Easter, *J. Org. Chem.*, **20**, 401 (1955).

The copper salt was prepared by adding 0.2 *M* aqueous cupric acetate to a saturated methanolic solution of the aldehyde. The chartreuse salt, on recrystallization from ethanol, precipitated as dull green crystals, m.p. (vac.) 265.7–266.4°.

Anal. Found: C, 44.86; H, 2.35.

The methyl ether was prepared in the same manner as the 4-chloro analog and in approximately the same yield. On recrystallization from aqueous ethanol, 6-chloro-2-methoxybenzaldehyde had m.p. 59.5° (H.), λ_{max} 321 and 285 mμ (95% ethanol).

Anal. Calcd. for $C_8H_7ClO_2$: C, 56.32; H, 4.14; Cl, 20.78. Found: C, 56.22; H, 4.09; Cl, 20.40.

6-Chloro-2-methoxybenzoic Acid.—Alkaline permanganate oxidation of 6-chloro-2-methoxybenzaldehyde afforded the corresponding benzoic acid which melted at 140–141° (H.) (lit.[38] m.p. 141°) after recrystallization from aqueous ethanol.

Anal. Calcd. for $C_8H_7ClO_3$: C, 51.49; H, 3.78. Found: C, 51.26; H, 3.91.

Decarboxylation occurred readily with the formation of *m*-chlorophenol when an attempt was made to cleave 6-chloro-2-methoxybenzoic acid by refluxing in 55% hydriodic acid.[39]

2-Chloro-4-hydroxybenzaldehyde, 4- and 6-Chlorosalicylaldehyde *via* the Reimer–Tiemann Reaction with *m*-Chlorophenol.—To a stirred mixture of 49.2 g. (0.38 mole) of *m*-chlorophenol, 122 g. of calcium hydroxide, 139.4 g. of anhydrous sodium carbonate, and 872 ml. of water, under nitrogen in a 3-l. flask, was added 90.6 g. (0.76 mole) of chloroform at such a rate that a reaction temperature of 70–75° could be maintained. The addition required 80 min. The reaction mixture was stirred, without external heating, for another half hour, while the reaction temperature reached a maximum of 82°. The stirred mixture was then heated under reflux for 2 hr. before acidification with 325 ml. of concentrated hydrochloric acid. The yellow reaction mixture was steam distilled until 5700 ml. of distillate had been collected; the steam distillate contained the chlorosalicylaldehydes, while the less volatile 2-chloro-4-hydroxybenzaldehyde remained in the steam-distillation flask.

Crude 2-chloro-4-hydroxybenzaldehyde (11.5 g. after washing with water) was isolated by filtration of the chilled residue in the steam distillation flask. The precipitate was dissolved in ether and treated with a large amount of decolorizing charcoal. After 100 ml. of carbon tetrachloride had been added, the solution was concentrated to incipient crystallization (vapor temperature 71.5°). 2-Chloro-4-hydroxybenzaldehyde precipitated (5.45 g.) and, after another recrystallization from the same solvent mixture, melted at 146.2–146.9°.

The infrared spectrum had absorption bands at 6.00 s (intermolecularly H-bonded C=O st.); 6.25 s, 6.42 s, and 6.66 s (aromatic C=C); 7.11 m (phenol?); 7.60 m and 8.05–8.09 s (broad) (aromatic aldehyde); 8.38 s, 8.86 m, and 9.64 m (1,2,4-substituted on benzene); 10.90 m (CHO–H def.?); 11.09 w (CH out-of-plane def., one free H on benzene); and 11.74 s, 11.96 w, and 12.36 μ s (CH out-of-plane def., two adjacent hydrogens on benzene). In chloroform solution the spectrum showed peaks at 2.77 w (OH st.) and 5.92 μ s (nonbonded C=O).

The crude salicylaldehydes were obtained as an amber oil by continuous liquid–liquid extraction[40] of the steam distillate with benzene and evaporation of the solvent. The sodium bisulfite adduct, formed by shaking the oil with 80 ml. of saturated aqueous sodium bisulfite, was purified by washing with absolute ethanol, followed by ether. Sodium bicarbonate, 8.7 g., was added in small portions to a stirred suspension of the adduct (24.2 g. in 100 ml. of water) at 60–70° and stirred for 7 hr. at room temperature. This treatment divides the adduct into two fractions, one of which is decomposed to form a soluble aldehyde (at the pH of aqueous bicarbonate) and another which is not decomposed. The latter was recovered by filtration of the chilled suspension and washed with small amounts of ice–water and large amounts of ether.

The filtrate was saturated with sodium chloride and the aldehyde extracted into several portions of ether. After drying the combined ether extracts with anhydrous sodium sulfate, the ether was removed *in vacuo*. The residual oil was dissolved in a mixture of ether and hexane and concentrated to a volume of 40 ml. (vapor temperature 65°). On chilling, there was isolated an additional 0.28 g. (total yield 9.6%) of 2-chloro-4-hydroxybenzaldehyde, m.p. 146.9–147.4°. The ether–hexane filtrate was evaporated to dryness and the residue, after crystallization from pentane, afforded 3.75 g. (6.3%) of white needles, m.p. 41–47°. After repeated recrystallizations, the melting point was constant at 46.8–47.8°. The melting point was not depressed on admixture with authentic 4-chlorosalicylaldehyde; in contrast, a mixture with authentic 6-chlorosalicylaldehyde was liquid at room temperature. The infrared and ultraviolet spectra as well as the p*K* were identical with those of authentic 4-chlorosalicylaldehyde.

Anal. Found: C, 53.80; H, 3.22; Cl, 22.54.

The bisulfite adduct recovered from the bicarbonate treatment (see above) was decomposed by stirring for several hours with 50 ml. of 4 *M* hydrochloric acid until sulfur dioxide was no longer evolved. The liberated 6-chlorosalicylaldehyde was recovered as a dark oil by evaporation of an ether extract, which had been dried with anhydrous sodium sulfate. The oil crystallized on standing and was recrystallized from aqueous methanol yielding 5.07 g. (8.5%) of long white needles, m.p. 51.3–52.2°. The ultraviolet absorption spectrum and the p*K* were indistinguishable from those of authentic 6-chlorosalicylaldehyde. A mixture melting point of the two products was sharp at 51.5° (H.).

Anal. Found: C, 53.78; H, 3.37; Cl, 22.50.

Measurement of p*K*.—The acid dissociation constants were evaluated from spectrophotometric measurements as a function of pH. The total concentration of the organic acids was *ca.* 10^{-4} *M*, the ionic strength was maintained at 0.100 μ by sodium perchlorate, and the temperature was 25.0°. The procedure and instruments were described in part I of this series.[2] Since all the organic acids, except 2-chloro-4-hydroxybenzaldehyde, were volatile from aqueous solution, separate aliquots of a stock solution were used for each pH measurement.

Calculations.—The acid dissociation constant is defined by eq. 1, where $[L^-]$ and [HL] are the molar concentrations of the

$$K = [H^+][L^-]/[HL] \qquad (1)$$

anion and acid, respectively. The actual value obtained experimentally was K' which differs from K in that the hydrogen ion concentration in the above expression is replaced by a'_H, where a'_H is defined as antilog (–pH). The evaluation of K' from the experimental data was made using either eq. 4 or 5 of ref. 2. K' was converted to K using the empirical relationship between a'_H and $[H^+]$ found previously in 0.100 *M* sodium perchlorate solutions.[2]

Acknowledgment.—The authors wish to thank Dr. Lawrence Magnusson of the Argonne National Laboratory for his helpful discussions, Dr. Youval Shvo of the Weizmann Institute of Science, Rehovoth, Israel, for help in recording and interpreting some of the nuclear magnetic resonance spectra, and Miss Grace Molko, National Science Foundation Undergraduate Research Participant (1962), for assistance in part of this investigation.

---

[38] F. Ullmann and L. Panchaud, *Ann. Chem.*, **350**, 108 (1906); *Chem. Abstr.*, **1**, 846 (1907).

[39] P. Cohn [*Chem. Zentr.*, **72** [II], 925 (1901)] has shown that 6-chlorosalicylic acid is decarboxylated readily while the 4-chloro isomer is stable.

[40] I. A. Kaye, *Chemist-Analyst*, **41**, 95 (1953).