Notes

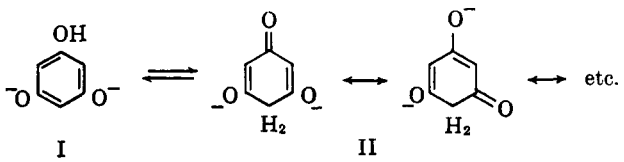
The Structure of the Phloroglucinol Dianion

R. J. Highet and T. J. Batterham

Laboratory of Metabolism, National Heart Institute, and Laboratory of Physical Biology, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda 14, Maryland

Received August 21, 1963

It has long been known that phloroglucinol reacts readily in the keto form.[1] Baeyer observed in 1886 that the compound forms a trioxime with hydroxylamine,[2] and alkylation in alkali gives either C- or O-alkylation, according to the specific conditions.[3] Recently, Fray has made the interesting observation that sodium borohydride reduces phloroglucinol to resorcinol.[4] The occurrence of a peak at 350 mμ in the ultraviolet spectrum of an alkaline solution has been repeatedly observed and cited as support for the existence of a keto form by its resemblance to that of dihydroresorcinol or filicinic acid.[5] In particular, the careful work of Scheibe and Kohler[5d] has shown that the dianion exists much more in tautomeric form II than the other ionic forms exist in corresponding forms. However, none of these observations can reveal ac-



I II

curately the extent to which the equilibrium of the various anions favors keto structures, for the equilibrium is displaced by subsequent irreversible reactions to form the products observed, while ignorance of the extinction coefficient expected of such structures as II prevents assay by spectrophotometric means.

This question has now been investigated by examining the n.m.r. spectrum of aqueous solutions of phloroglucinol and its sodium salts.

Experimental

Commercial phloroglucinol (The Matheson Co.), m.p. 217–219° (lit.[6] 217–218°), was treated with the appropriate quantity of 50% sodium hydroxide and was diluted to provide the solutions described in Table I. Spectra were determined in a Varian A-60 n.m.r. spectrometer equipped with a variable temperature probe. To distinguish the resonance peaks of the carbon-bound protons from the spinning side bands of the solvent, each spectrum was run at two different spin speeds; the peaks reported are those whose positions were not affected by this procedure. Positions are noted relative to the position of the main peak of sodium trimethylsilyl propanesulfonate (Eastman Kodak Co.), added in approximately 1% concentration.[7] Temperatures were measured by noting the difference in chemical shift of the two peaks of ethylene glycol, and were determined from a graph of the equation, $T = 188 - 1.66\ \Delta$, in which Δ is expressed in c.p.s.[8]

The rapid exchange between the salts and the solvent made it impossible to determine their spectra in deuterium oxide solution; the only peak observed was that of water. The insolubility of the salts in organic solvents precluded use of the other solvents common in n.m.r. spectroscopy.

Disodium phloroglucinolate was prepared for the infrared spectrum by evaporating the aqueous solution to dryness and holding the solid under high vacuum for several hours. The spectra of Nujol mulls were determined on a Perkin-Elmer Model 21 infrared spectrometer by Mrs. K. S. Warren.

Table I

Nuclear Magnetic Resonance Spectra of Phloroglucinol Solutions

	Aromatic, τ	Olefinic τ, Width[a]		Alicyclic τ, Width[a]		Temp., ±2°C.
Phloroglucinol, 0.062 *M*	3.95					35
Monosodium phloroglucinolate, 0.2 *M*	3.98					35
Disodium phloroglucinolate, 1.0 *M*		4.92	2.4	6.95	2.8	35
1.0 *M*		4.95	2.6	6.97	4.6	50
1.0 *M*		4.93	3.6	6.95	7.0	61
0.2 *M*		4.97	1.4	7.00	1.2	35
0.05 *M*		4.98		7.03	0.9	35
Trisodium phloroglucinol,[b] 0.20 *M*		4.92		6.95	5.5	35

[a] Width of the peak at half height in c.p.s. [b] *I.e.*, a solution of phloroglucinol treated with 3 equiv. of sodium hydroxide and diluted to the specified molarity.

Discussion

The n.m.r. spectrum of an aqueous solution of phloroglucinol shows a single peak for the aromatic protons at τ 3.95, which is slightly shifted by the addition of one mole of sodium hydroxide to τ 3.98. However, addition of 2 equiv. of sodium hydroxide produces a solution whose spectrum shows no aromatic peak, but contains an olefinic peak at τ 4.97, and a peak at τ 7.00 corresponding to the methylene group between two carbonyl groups. Integration of the two peaks by tracing, cutting, and weighing showed them to be of equal area, while an equimolar mixture of sodium

(1) *Cf.* W. J. Hickinbottom, "The Chemistry of Carbon Compounds," Vol. IIIA, E. H. Rodd, Ed., Elsevier Publishing Co., New York, N. Y., 1954, pp. 483–484.

(2) A. Baeyer, *Ber.*, **19**, 159 (1886).

(3) A. Spitzer, *Monatsh.*, **11**, 104, 287 (1890); J. Herzig and F. Wenzel, *ibid.*, **27**, 786 (1906).

(4) G. I. Fray, *Tetrahedron*, **3**, 316 (1958).

(5) (a) A. Lambrechts, *Compt. rend.*, **198**, 1852 (1934); (b) N. A. Valyasko and E. M. Voroshin, *Trudy Kharkov Khim. Tekhnol. Inst. in. S. M. Kirova*, **5**, 15 (1945); *Chem. Abstr.*, **43**, 2598 (1949); (c) T. W. Campbell and G. M. Coppinger, *J. Am. Chem. Soc.*, **73**, 2708 (1951); (d) H. Köhler and H. Scheibe, *Z. anorg. allgem. Ch m.*, **285**, 221 (1956).

(6) A. Baeyer, *Ber.*, **19**, 2187 (1886).

(7) G. V. D. Tiers and A. Kowalsky, Abstracts, 137th National Meeting of the American Chemical Society, Cleveland, Ohio, April, 1960, p. 17R.

(8) "Preliminary Instruction Manual, V-6057, Variable Temperature System for A-60 Analytical Spectrometers," Varian Associates, Palo Alto, Calif., p. 29.

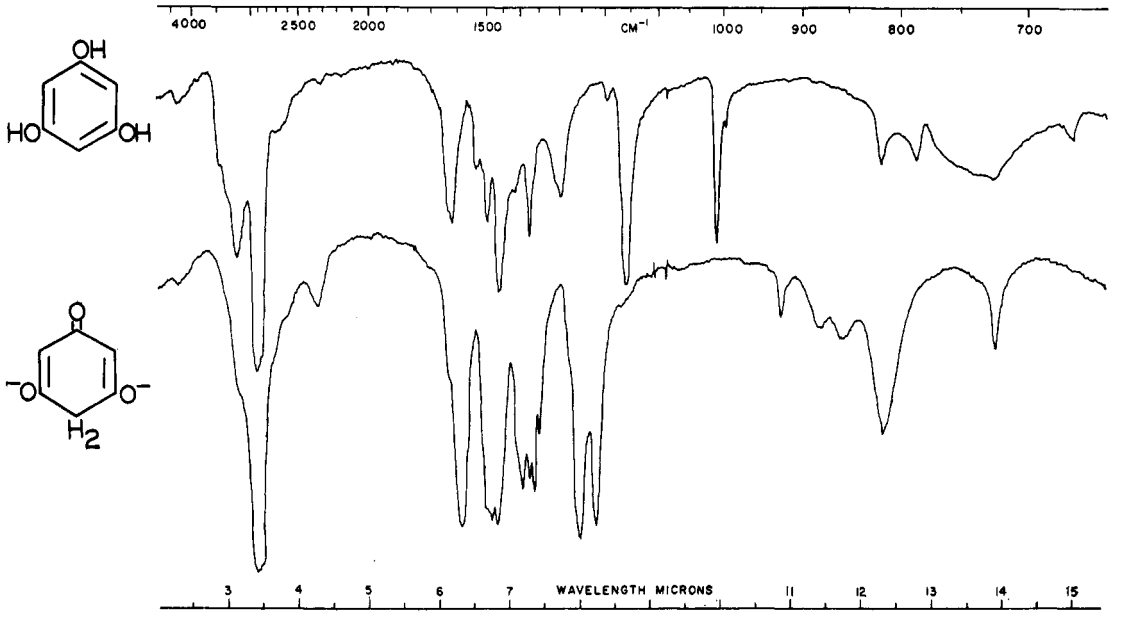


Figure 1.

benzoate and disodium phloroglucinolate shows peaks near τ 2.5 and 6.93 in the anticipated ratio of 5:2.

The chemical shift of the observed peaks is relatively insensitive to changes in concentration and temperature. Warming, however, produced the broadening to be expected of the increased rate of exchange, with the eventual disappearance of the separate peaks into the solvent peak at about 75°.[9] Addition of further sodium hydroxide increased the rate of exchange at room temperature, with the eventual disappearance of the C–H proton peak.

TABLE II

DISSOCIATION CONSTANTS OF SELECTED DIBASIC PHENOLS[a]

	$K_1 \times 10^9$	$K_2 \times 10^{12}$
Phloroglucinol	3.56	1320
Pyrogallol	9.67	2.30
Resorcinol	0.71	4.78
Catechol	0.75	0.84
Hydroquinone	0.12	0.92

[a] C. T. Abichandani and S. K. Jatkar, *J. Indian Inst. Sci.*, **A21**, 417 (1938).

These observations demonstrate clearly that phloroglucinol and its monosodium salt exist in an aromatic structure, while the disodium salt exists as the alicyclic tautomer (II).

The infrared spectra of Nujol mulls of phloroglucinol and the disodium salt both show strong absorption near 1600 cm.$^{-1}$ but differ markedly at lower frequencies (see Fig. 1). The strong aromatic oxygen peaks of the phloroglucinol are absent in the spectrum of the disalt, which evidently also exists in the alicyclic form (II) in the solid state.

The unusual structure of the dianion is associated with unusual acidity. As Table II shows, the second dissociation constant of resorcinol is approximately 300 times smaller than that of phloroglucinol, while those of other polyphenols are even smaller.

(9) *Cf.* 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, p. 218.

The Ionization Constants, Ultraviolet and Infrared Spectra of Some Substituted Benzimidazoles

DOROTHY J. RABIGER AND MADELEINE M. JOULLIÉ

Department of Chemistry, University of Pennsylvania, Philadelphia 4, Pennsylvania

Received August 2, 1962

The benzimidazole ring is of considerable chemical and biological interest and has been the subject of many papers. Review articles on benzimidazoles may be consulted for leading references in this field.[1a-c] A considerable amount of work on benzimidazole chemistry has been carried out in this laboratory by several workers. This interest in benzimidazole chemistry has prompted us to start a systematic study of various physical properties of substituted benzimidazoles in order to observe the effect of substituents on the physical properties of the ring. Because of the importance of the benzimidazole ring, more data on the ionization constants and spectroscopic characteristics of substituted benzimidazoles appeared desirable.

Experimental and Results

The benzimidazoles used in this study were either available commercially or prepared by well-known procedures. All compounds were recrystallized from the appropriate solvents to constant melting points. All melting points are uncorrected. Melting points and appropriate references are shown in Table I. The ionization constants of various substituted benzimidazoles are also listed in Table I.

The pK_a values shown in Table I were determined by potentiometric titration. A Leeds and Northrup pH meter equipped with glass and saturated calomel electrodes was used to follow the pH of each solution during its titration. The pH meter was calibrated against two buffers: (1) 0.05 *M* potassium phthalate

(1) (a) J. B. Wright, *Chem. Rev.*, **48**, 437 (1951); (b) K. Hofmann, "The Chemistry of Heterocyclic Compounds," A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1953, p. 379; (c) E. S. Schipper and A. R. Day, "Heterocyclic Compounds," Vol. 5, Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1957, p. 194.