From the experimental data in Table I the dissociation constants of BaCit$^-$ were calculated in the usual manner.[5] The values of the exchange constants and the dissociation constants of the salts of Ba^{++} and Sr^{++} are summarized in Table II. It should be noted that the concentrations of the carrier-free tracer cations in these experiments were less than 10^{-10} molar.

The exchange constants, $K_{ex.}$, were calculated from the relation[5,8]

$$[K_{ex.}]_{pH} = \lambda_0 \times (NH_4)^2/NH_4R \qquad (1)$$

where λ_0 is the ratio of the fraction of M^{++} in the resin and liquid phases, respectively.[4] The concentrations of NH$_4$$^+$ and NH$_4$R are expressed in moles per liter.

The data in Table II show that in ammonium citrate solution Ba^{++} is much less strongly bound by the citrate ion than is Sr^{++} while its affinity for the exchanger is slightly greater. The combination of these two factors enhances the difference in adsorbability between these elements just as is the case for the rare earths,[6f,9] except that the relation of atomic number to the adsorption and complex affinity of the latter are in reverse order as compared to the alkaline earths.

Fig. 1.—Adsorption of Ba^{140} and La^{140}, by the hydrogen form of the cation exchanger, Amberlite IR-1, from 5% (0.24 M) citric acid as a function of pH. The weight of resin was 0.50 g. air-dried and the volume of solution was 25 ml. The solution pH was adjusted by adding ammonium hydroxide. The molarity of the NH$_4$$^+$ at the different pH's was as follows:
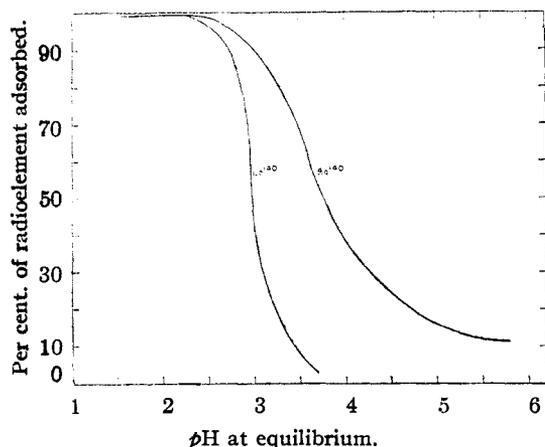
pH	Molarity of NH$_4$$^+$	pH	Molarity of NH$_4$$^+$
1.79	0.0	4.34	0.45
2.32	.075	4.73	.53
2.83	.15	5.09	.60
3.21	.23	5.56	.73
3.70	.30	5.82	.80
3.92	.38		

(8) G. E. Boyd, J. Schubert and A. W. Adamson, THIS JOURNAL, 69, 2818 (1947).

(9) E. R. Tompkins and S. W. Mayer, ibid., 69, 2859 (1947).

At a pH $\leq$ 2 citric acid exists principally in the undissociated form[10] and therefore contributes very little to the effective cation concentration of a solution. The complexing action of citric acid becomes less pronounced as the pH is decreased.[6a,9] It was found that concentrations of citric acid (or of acetic) as high as 0.8 M had no effect on the adsorption of Ba^{++} from salt solutions at a pH of 2. As the pH of a solution is increased the citric acid dissociates further and produces a greater concentration of the ions possessing the stronger complexing action. In Fig. 1 is shown the effect of pH on the adsorption of Ba^{140} and La^{140} from citric acid solutions. It is seen that at a pH of about 3 the adsorption of La^{+3} decreases very rapidly principally because of complex ion formation while the adsorption of Ba^{++} is nearly unchanged. This marked difference is responsible for the simple and effective manner in which the divalent fission product cations are separated from the trivalent rare earths.[6a]

Barium becomes appreciably complexed at a pH $\sim$ 4 (after discounting the effect of NH$_4$$^+$) as is indicated in Fig. 1 and it seems likely that a weak complex ion, Ba(HCit) exists. The formation of a complex Ca(HCit) in the pH region 3.6–5.2 is known.[11]

More exact measurements of the dissociation constants of complex ions by the ion exchange method than reported here can be made. The following factors should be considered: (a) a resin such as Dowex 50[12] whose capacity is independent of pH over a very wide range should be used and (b) the values for λ_0 should be kept between the approximate limits of 1–2 whenever possible because of the sensitivity of K_c to small errors in λ_0. For example, in Table I in the case in which λ_0 = 10.0, a 1% error in this value of λ_0 gives a 10% error in K_c.

(10) N. Bjerrum and A. Unmack, Kgl. Danske Videnskab. Selskab, Mat-fys. Medd., IX, 1 (1929).

(11) J. Muus and H. Lebel, Kgl. Dansk Veidenskab. Selskab Mat.-fys Medd., 13, No. 19 (1936).

(12) W. C. Bauman and J. Eichhorn, THIS JOURNAL, 69, 2830 (1947).

Note Concerning the Constitution of Chlorogenin

BY MILLARD SEELEY AND C. R. NOLLER

On the basis of molecular weight determinations in benzene, it was concluded[1] that the amorphous reaction product of hydrazine with the diketone obtained by the oxidation of chlorogenin (chlorogenone) and that with 3,6-cholestanedione were polymeric, and hence that the products were not dihydropyridazines and that their formation did not necessarily prove the 1,4 relation of the carbonyl groups postulated by Marker and Rohrmann.[2] Later Bursian[3] reported that there was

(1) Noller, THIS JOURNAL, 61, 2976 (1939).

(2) Marker and Rohrmann, ibid., 61, 946 (1939).

(3) Bursian, Ber., 73, 922 (1940).

some evidence of association in the case of the pyridazine derivative from 3,6-cholestanedione, but that if the results of determinations in cyclopentadecanone (Exaltone) are extrapolated to infinite dilution, a value for the molecular weight is obtained that is in good agreement with the value calculated for a monomolecular product. Since then we have repeated the preparation of the reaction product of hydrazine with chlorogenone and have obtained it in crystalline form. While the solubility in Exaltone is low, preventing an extended range of concentrations, molecular weight determinations in this solvent indicate that the product is monomolecular and hence is a pyridazine derivative.

The molecular weights determined in benzene solution and reported previously[1] are much higher than those obtained in Exaltone. However, the concentrations were higher in benzene, and the temperature at which the determinations was made was considerably lower. If the three determinations previously reported are plotted against the concentration, the points lie close to a straight line and extrapolation to infinite dilution gives a value comparable with that obtained in Exaltone (Fig. 1).
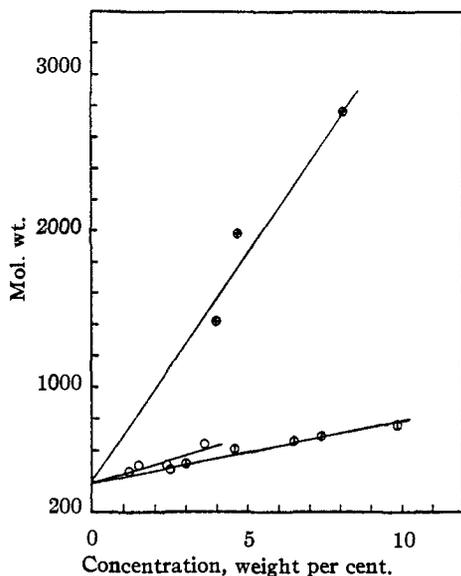
Fig. 1.—Variation of molecular weight with concentration: ⦵, pyridazine derivative from 3,6-cholestanedione in Exaltone[2]; ○, pyridazine derivative from chlorogenone in Exaltone; ⊗, pyridazine derivative from chlorogenone in benzene.[1]

With pure samples of the pyridazine derivative of 3,6-cholestanedione and of chlorogenone available, their ultraviolet absorption spectra were determined (Fig. 2). The spectra are practically identical, indicating that the compounds are similarly constituted.

Since the hydroxyl groups of chlorogenin are in the 3,6-positions,[2,4] dehydration should lead to

(4) Marker, Jones and Turner, THIS JOURNAL, 62, 2537 (1940).
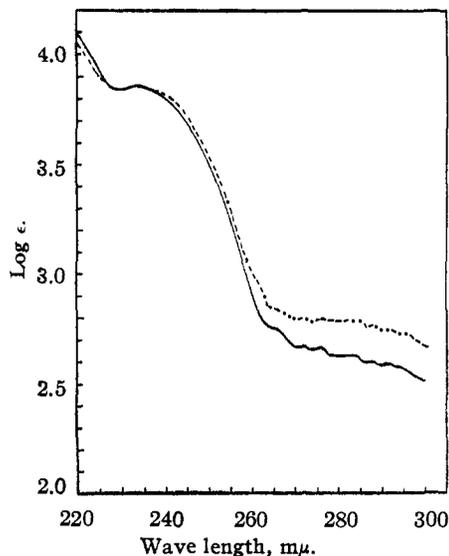
Fig. 2.—Ultraviolet absorption spectra: —, pyridazine derivative of 3,6-cholestandione; - - - -, pyridazine derivative of cholorogenone.

the formation of a diene having the same structure in rings I and II as 3,5-cholestadiene. While it was not possible to obtain a pure substance from the dehydration products of chlorogenin, a material was obtained which gave the same ultraviolet absorption spectrum as 3,5-cholestadiene and which appeared to contain approximately 50% of the expected diene (Fig. 3).
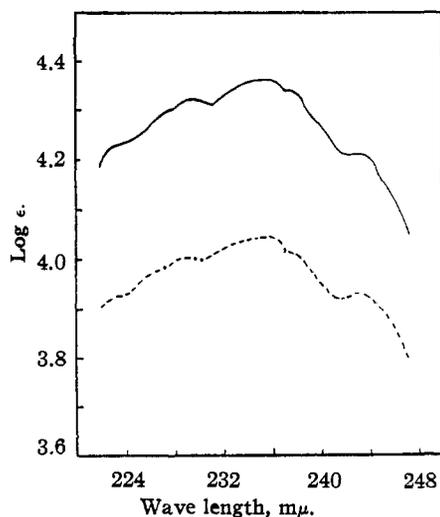
Fig. 3.—Ultraviolet absorption spectra: —, 3,5-cholestadiene; - - - -, dehydrated cholorogenin.

Experimental

Molecular Weight Determinations.—Micro determinations were made in capillary tubes according to the method of Pregl[5] using a Hershberg melting point apparatus[6] as a bath, and a Beckmann thermometer. The procedure

(5) Pregl and Roth, "Quantitative Organic Microanalysis," Blakiston's Son and Company, Philadelphia, Pa., 1937, p. 237.

(6) Hershberg, Ind. Eng. Chem., Anal. Ed., 8, 312 (1936).

was checked by duplicating the results of Bursian on the pyridazine derivative from 3,6-cholestanedione.

Dehydration of Chlorogenin.—Numerous procedures for the dehydration of chlorogenin were tried but none gave a product which absorbed light of $\lambda = 236$ mμ as strongly as 3,5-cholestadiene prepared by the dehydration of cholesterol.[7] The procedure yielding a product having the strongest absorption consisted in the decomposition of the dimethanesulfonate in methyl alcohol solution.

To a solution of 2 g. of chlorogenin, m. p. 272–275°, in 10 cc. of dry pyridine was added 1 cc. of methanesulfonyl chloride. After standing overnight, water was added and the precipitate was filtered and crystallized twice from methyl alcohol, and twice from benzene–ligroin (60–70°) mixture. The colorless needles decomposed with evolution of gas at about 180°. *Anal.* Calcd. for $C_{29}H_{48}O_8S_2$: S, 10.88. Found: S, 10.96.

A solution of 0.5 g. of the dimethanesulfonate in 30 cc. of methyl alcohol was heated in a sealed tube at 140° for four hours. Evaporation of the solvent gave a light brown oil which solidified in an ice-bath but could not be crystallized from solvents. Solution in alcohol and precipitation with water gave a product having log $\epsilon_{max.} = 4.04$ at 236 mμ. Since log $\epsilon_{max.} = 4.36$ at 236 mμ for 3,5-cholestadiene, the dehydration product of chlorogenin appears to contain about 50% of the diene. All absorption spectra were determined in 95% ethyl alcohol, using a Beckman Quartz Spectrophotometer.

(7) Mauthner and Suida, *Monatsh.*, **17**, 34 (1896).

DEPARTMENT OF CHEMISTRY
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The Preparation of 2,3-Disubstituted-4-thiazolidones. II. 3-Alkyl (and Aralkyl) 2-Aryl Derivatives

BY ALEXANDER R. SURREY

The reaction of thioglycolic acid with anils to give 2,3-disubstituted-4-thiazolidones[1] has been extended to include some 3-alkyl (and aralkyl)-2-aryl-4-thiazolidones,[2] I.
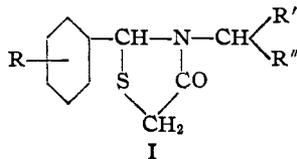
For this purpose the following anils were employed: benzylideneisopropylamine, 4-nitrobenzylidenephenethylamine and 4-ethoxy-3-methoxybenzylidenephenethylamine. In general, the reaction of thioglycolic acid with these anils is much faster than with the Schiff bases derived from an aromatic aldehyde and aromatic amine.[1] Two of the thiazolidones described were oxidized with potassium permanganate in acetic acid solution to yield the corresponding 1-dioxides.

(1) Surrey, THIS JOURNAL, **69**, 2911 (1947).

(2) After this work had been completed, a paper by Mr. H. D. Troutman and Dr. Loren M. Long on the synthesis of some 3-alkyl-(and aralkyl)-2-aryl-4-thiazolidones was presented before the Medicinal Division at the Chicago meeting of the American Chemical Society on April 21, 1948. These authors employed ethyl or methyl thioglycolate in their experimental work. The oxidation of several thiazolidones to the corresponding 1-dioxides by means of hydrogen peroxide was also reported.

Experimental

3-Isopropyl-2-phenyl-4-thiazolidone.—To a well-stirred solution of 10.6 g. of benzaldehyde in 100 ml. of dry benzene was added dropwise 9 g. of isopropylamine. After stirring for thirty minutes, the mixture was poured into a separatory funnel and allowed to stand overnight. The benzene layer was separated and refluxed with 18 g. of thioglycolic acid for eight hours (1.3 ml. of water collected). After removing the benzene, the solid which formed on cooling was recrystallized twice from a mixture of ether–Skellysolve A; 6.5 g. (29%) m. p. 100.4–101.8° cor.

Anal. Calcd. for $C_{12}H_{15}NOS$: S, 14.49; N, 6.33. Found: S, 14.74; N, 6.21.

3-Isopropyl-2-phenyl-4-thiazolidone-1-dioxide.—A solution of 19.4 g. of potassium permanganate in 360 ml. of water was added dropwise with stirring to 13.5 g. of 3-isopropyl-2-phenyl-4-thiazolidone in 270 ml. of acetic acid at 30–35°. When the addition was completed, sodium bisulfite was added until the solution was practically colorless. More water was then added with continued stirring. The tan-colored solid which precipitated was filtered off and recrystallized from methanol; 10 g. (65%), m. p. 163–165°. Another recrystallization gave a white product melting at 169.6–171° cor.

Anal. Calcd. for $C_{12}H_{15}NO_3S$: S, 12.66; N, 5.53. Found: S, 12.66; N, 5.42.

2-(4-Ethoxy-3-methoxyphenyl)-3-(2-phenethyl)-4-thiazolidone.—A mixture of 12 g. of phenethylamine and 18 g. of 4-ethoxy-3-methoxybenzaldehyde was heated for thirty minutes on the steam-bath in a flask connected to a water pump. After dissolving the product in 100 ml. of dry benzene, 11 g. of thioglycolic acid was added and the solution was refluxed for three hours. The water (1.8 ml.) which formed was collected in a separator connected to the apparatus. The benzene was distilled off and the residue was taken up in ether, washed with sodium carbonate solution, then water, and dried over Drierite. The product crystallized on spontaneous evaporation of the ether. The solid was triturated with Skellysolve A and filtered to yield 22.5 g. (63%) melting at 57–61°. After recrystallization from a mixture of ether–Skellysolve A and then from ether alone, the product melted at 60.7–62.5° cor.

Anal. Calcd. for $C_{20}H_{23}NO_3S$: S, 8.97; N, 3.92. Found: S, 9.04; N, 3.88.

4-Nitrobenzylidene Phenethylamine.—Equimolecular quantities of 4-nitrobenzaldehyde and phenethylamine were heated *in vacuo* on the steam-bath for thirty minutes. On cooling the residue solidified. It was recrystallized from Skellysolve B, m. p. 70.8–72.3° cor.

Anal. Calcd. for $C_{15}H_{14}N_2O_2$: $N_{(NO_2)}$, 5.51. Found: $N_{(NO_2)}$, 5.55.

2-(4-Nitrophenyl)-3-(2-phenethyl)-4-thiazolidone.—A solution of 25 g. of 4-nitrobenzylidenephenethylamine and 12.5 g. of thioglycolic acid in 150 ml. of dry benzene was refluxed for eight hours, while removing the water as it formed. After distilling the benzene *in vacuo* the residue was dissolved in warm ethanol. The product which precipitated on cooling was recrystallized three times from ethanol to yield 26.5 g. (81%) melting at 124.6–125.2° cor.

Anal. Calcd. for $C_{17}H_{16}N_2O_3S$: N, 8.53; S, 9.76. Found: N, 8.44; S, 9.59.

2-(4-Aminophenyl)-3-(2-phenethyl)-4-thiazolidone.—A well-stirred mixture of 10 g. of 2-(4-nitrophenyl)-3-(2-phenethyl)-4-thiazolidone, 40 g. of iron filings, 60 ml. of ethanol, 50 ml. of water and 1 ml. of acetic acid was refluxed on a steam-bath for four hours. After adding an equal volume of ethanol and an excess of solid sodium carbonate the reaction mixture was filtered hot. The solid which precipitated from the cooled filtrate was recrystallized from ethanol, 6 g. (66%), m. p. 143–144.2° cor.

Anal. Calcd. for $C_{17}H_{18}N_2OS$: N, 9.38; S, 10.74. Found: N, 9.14; S, 10.69.