lowed to stand overnight (0°) the crystalline 2-keto-D-galactonic acid was recovered, washed with aqueous dioxane and recrystallized from water: m. p. 170–171°; $[\alpha]^{20}D$ −6.0° (*c*, 2 in water), and on titration with alkali showed 99.9% purity.

*Anal.* Calcd. for $C_6H_{10}O_7$: C, 37.12; H, 5.19. Found: C, 37.02; H, 5.30.

**Methyl 2-Keto-D-galactonate.**—The acid (5 g.) was dissolved in 100 cc. of freshly distilled methanol containing 0.15% hydrogen chloride. The mixture was refluxed for two hours, and evaporated by repeated concentration *in vacuo* with methanol. Crystals of methyl 2-keto-D-galactonate were washed and recrystallized from alcohol–chloroform mixtures: m. p. 138–139° and $[\alpha]^{20}D$ −11.3° (*c*, 1.2 in water). D-Ascorbic acid m. p. 192° and $[\alpha]^{20}D$ −23° was made from this ester by the method of Maurer and Schiedt,[7] and this served to establish further the constitution of 2-keto-D-galactonic acid.

**Sodium 2-Keto-D-glucoheptonate Monohydrate.**—A hot solution of α-D-glucohepto-γ-lactone[8] (416 g.) was neutralized with 106 g. sodium carbonate, cooled, diluted to 4.2 liters and 73 g. of sodium chlorate, 40 cc. of 85% phosphoric acid and 20 g. of vanadium pentoxide were added. After stirring for two days, the reaction was complete; it was filtered, treated with enough calcium ferrocyanide to precipitate the $V^{+++}$, filtered again, the $PO_4^{---}$ precipitated with calcium hydroxide, and the excess $Ca^{++}$ removed with oxalic acid. The colorless solution containing only sodium salts was concentrated to 2 liters and an equal volume of methanol added dropwise with stirring during thirty-six hours. The crude crystalline sodium 2-keto-D-glucoheptonate (yield 38%) was recrystallized twice from 40% aqueous methanol: $[\alpha]^{20}D$ +45.5° (*c*, 2 in water).

*Anal.* Calcd. for $Na(C_7H_{11}O_8)\cdot H_2O$: Na, 8.70; C, 31.82; H, 4.96. Found: Na, 8.60; C, 31.87; H, 5.10.

The constitution of the 2-keto acid was established by preparing D-glucoascorbic acid from it. The free acid liberated from the sodium salt (26.4 g.) by sulfuric acid and precipitation with methanol was repeatedly evaporated *in vacuo* with methanol. The final residue was dissolved in 100 cc. of absolute methanol, treated with a measured quantity of diazomethane and concentrated *in vacuo* to 50 cc. The ester solution was stirred with 50 cc. of sodium methylate (containing 2.42 g. of sodium) at 45° under a current of nitrogen. When the suspension thinned out, it was treated with 10 cc. of 51.5% sulfuric acid, filtered, evaporated to dryness *in vacuo*, the residue dissolved in methanol, Norite was added and filtered. The filtrate was concentrated *in vacuo* to 25 cc. and allowed to stand several days at 0°. D-Glucoascorbic acid monohydrate recrystallized twice from methanol–acetone showed m. p. 140°, $[\alpha]^{20}D$ −22.0° (*c*, 1 in water) and iodine titration 99.7% which values agree with those obtained by Haworth, Hirst and Jones[9] who prepared D-glucoascorbic acid through the addition of hydrogen cyanide to glucosone.

**Potassium 2-Keto-D-galactoheptonate.**—A mixture of α- and β-D-galactoheptonic acids prepared by the addition of hydrogen cyanide to galactose, was neutralized with potassium carbonate. The dehydrogenation procedure described above for the isomeric acid was followed. However, the potassium 2-keto-D-galactoheptonate crystallized very readily on the addition of methanol to the aqueous solution of the potassium salts (yield about 65%). The crude potassium salt was recrystallized from water until a constant rotation was obtained; $[\alpha]^{20}D$ +67.5° (*c*, 2 in water).

*Anal.* Calcd. for $KC_7H_{11}O_8$: K, 14.91; C, 32.06; H, 4.23. Found: K, 14.90; C, 32.08; H, 4.37.

The constitution of 2-keto-D-galactoheptonic acid was established by preparing *d*-galactoascorbic acid from it by employing the procedure described above for 2-keto-D-glucoheptonic acid. Recrystallization from methanol–acetone yields the monohydrate. There is an evolution of gas at its m. p. 109° and a blackening at 190°, which observations are in agreement with those of Haworth,[10] *et al.*, who prepared D-galactoascorbic acid through the addition of hydrogen cyanide to galactosone.

## Summary

1. A general method is described for the catalytic dehydrogenation of α-hydroxy groups of six- and seven-carbon membered polyhydroxy acids.

2. Of the six-membered polyhydroxy acids, the previously unknown 2-keto-D-galactonic acid is described, and the properties of calcium 2-keto-gluconate trihydrate are noted.

3. In the seven-membered polyhydroxy acids, 2-keto-D-glucoheptonic and 2-keto-D-galactoheptonic acids have been prepared and described, and from these keto acids, corresponding ascorbic acid analogs were made.

(7) Maurer and Schiedt, *Ber.*, **66**, 1054 (1933).

(8) Hudson, Hartley and Purves, THIS JOURNAL, **56**, 1248 (1934).

(9) Haworth, Hirst and Jones, *J. Chem. Soc.*, 549 (1937).

(10) Baird, Haworth, Herbert, Hirst, Smith and Stacey, *ibid.*, 62, (1934).

BROOKLYN, N. Y. RECEIVED JULY 10, 1943

---

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

# A Method for the Preparation of Calcium D-Altronate[1]

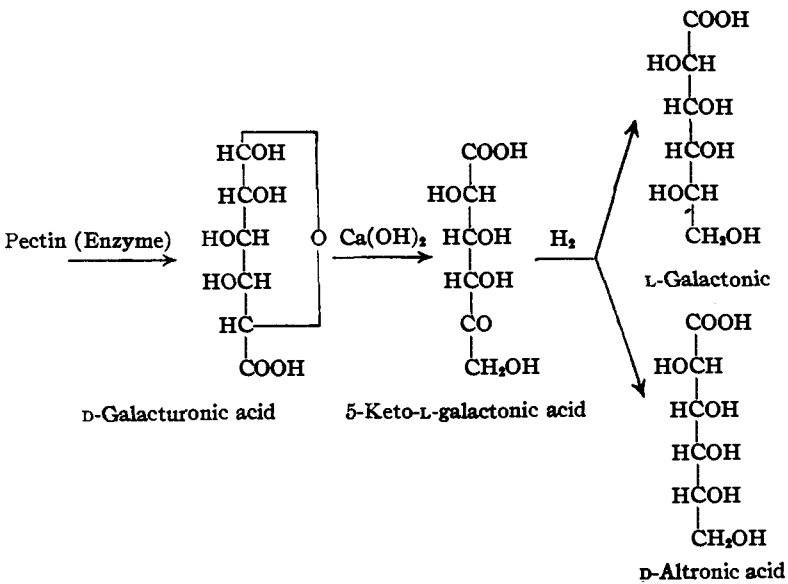
BY PETER P. REGNA[2] AND B. P. CALDWELL

In the course of work being carried out in this Laboratory in connection with the rates of transformation of 2-ketopolyhydroxy acids[3] into their ascorbic acid analogs, 2-ketoaltronic acid was needed. For this purpose we were interested in catalytically dehydrogenating either allonic or altronic acid in attempts to prepare the last remaining unknown 2-ketoaldonic acid. Accordingly we have produced D-altronic acid in large quantities by the following series of reactions: pectin → sodium calcium D-galacturonate → calcium 5-keto-L-galactonate → calcium D-altronate and calcium L-galactonate. The steps in the procedure, indicated by the acids of the foregoing salts, are represented by the configurational formulas

(1) Presented before the Division of Organic Chemistry of the American Chemical Society, Pittsburgh meeting, September, 1943.

(2) This paper is constructed from a thesis presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry, June, 1942. Present address: Chas. Pfizer & Co., Inc., Brooklyn, N. Y.

(3) Regna and Caldwell, THIS JOURNAL, **65**, 246 (1943).




The simplicity of this method provides a convenient source of D-altronic acid for the preparation of D-ribose.[4] In addition the procedure yields about equal quantities of the isomeric L-galactonic acid as a by-product. The heretofore almost unavailable L-galactonic acid may also be prepared by direct hydrogenation of sodium calcium D-galacturonate.

The existing methods for obtaining altronic acid are of limited applicability. Levene and Jacobs[5] made use of the addition of hydrogen cyanide to the costly sugar D-ribose, while the difficultly obtainable D-talonic acid is required for a method reported by Steiger and Reichstein.[6] The recent procedure of Richtmyer, Hann and Hudson[7] starting from *Sedum spectabile* was ineffectual because of the low yields of altronic acid.

The D-altronic acid prepared by the authors was readily oxidized by the procedure previously described[8] for the catalytic dehydrogenation of $\alpha$-hydroxy groups of polyhydroxy acids. Although a number of salts of D-altronic acid were oxidized to the 2-ketoaltronates, none was found to be crystalline.

## Experimental

**Sodium Calcium-D-Galacturonate Hexahydrate.**—D-Galacturonic acid was prepared by a modification of the joint methods of Pigman[9] and Mottern and Cole.[10] To six liters of distilled water was added 35 g. of Rohm and Haas Pectinol 46 AP, standardized with diatomaceous earth 100 D. The suspension was mechanically stirred and 600 g. of commercial citrus pectin was added in small portions. The viscous solution was covered with a thin layer of toluene to prevent mold growth, stoppered and allowed to stand for fourteen days at room temperature. At the end of this time a portion of the solution was titrated with standard alkali and showed 433 g. of D-galacturonic acid. An analysis by Fehling solution and calculated on the basis of galacturonic acid, indicated 487 g.

The main solution was treated with norite and filtered. Then two-thirds of the galacturonic acid in solution was neutralized with 77 g. of calcium carbonate, and the remaining one-third with 41 g. of sodium carbonate. There was an immediate precipitation of the double salt of galacturonic acid upon stirring the solution. This crop was filtered off and washed with water. Succeeding crops were obtained as the filtrates were repeatedly evaporated *in vacuo*. The combined crops after drying at about 50° weighed 464 g. A small sample of the double salt recrystallized from water was found upon analysis to have a composition corresponding to the hexahydrate, $[\alpha]^{20}D$ +33.0 (*c*, 1 in water), corresponding to $[\alpha]^{20}D$ +38.6° for the anhydrous salt.

*Anal.* Calcd. for $NaCa(C_6H_9O_7)_2 \cdot 6H_2O$: Ca, 5.33; Na, 3.07, uronic acid by $CO_2$ determination, 77.6. Found: Ca, 5.33; Na, 2.98; uronic acid by $CO_2$ determination, 78.1.

**Calcium 5-Keto-L-galactonate.**—Ehrlich and Guttmann,[11] found that in saturated limewater D-galacturonic acid undergoes the usual Lobry de Bruyn interconversion reaction by isomerizing the end CH(OH)CHO group into $COCH_2OH$. This produces the basic calcium salt of 5-keto-L-galactonic acid which is sparingly soluble in water, and consequently, the equilibrium shifts continuously in favor of the insoluble salt. The normal calcium 5-keto-L-galactonate was prepared from the basic calcium salt which, in turn, was produced by a modification of the method of Ehrlich and Guttmann.

In a typical run, 8.2 g. of calcium chloride was added to ten liters of filtered limewater containing 16.2 g. of calcium hydroxide. Sodium calcium D-galacturonate hexahydrate (111 g.) was then dissolved in this solution with stirring until it was clear. After about six days the basic calcium salt of 5-keto-L-galactonate, $(C_6H_9O_7) \cdot Ca(OH) \cdot 2H_2O$, precipitated in pale yellow crystals. These were separated from the large volume of water by a suction filter, washed with water and dried (110 g.). The salt was not further purified, but was suspended in water, neutralized with oxalic acid to a *p*H of 6.0 and the precipitated calcium oxalate filtered off. The filtrate was treated with norite, warmed, refiltered, and the filtrate evaporated *in vacuo*.

Erhlich and Guttmann were unable to crystallize sufficient of the normal calcium 5-keto-L-galactonate to obtain its analysis and physical properties. In the present case, however, after long standing a seed was obtained which caused the ready crystallization of the main solution. Normal calcium 5-keto-L-galactonate pentahydrate is a moderately soluble white salt: $[\alpha]^{20}D$ −14.0 (*c*, 1.15 in water), corresponding to $[\alpha]^{20}D$ −17.0 for the anhydrous salt. The specific rotation on the amorphous salt was obtained by Ehrlich and Guttmann as −15.25°, perhaps due to a less hydrated salt.

*Anal.* Calcd. for $Ca(C_6H_9O_7)_2 \cdot 5H_2O$; Ca, 7.76. Found: Ca, 7.80.

**Calcium D-Altronate.**—Reichstein and Bossard[12] catalytically hydrogenated diacetone-D-tagaturonic acid (diacetone-5-keto-L-galactonic acid) for the preparation of L-galactonic acid, but they did not report the isolation of D-altronic acid. In German Patent 618,907[13] is described the hydrogenation of free 5-keto-L-galactonic acid in aque-

(4) Hudson and Richtmyer, U. S. Patent 2,162,721, June 20, 1939.
(5) Levene and Jacobs, *Ber.*, **43**, 3141 (1910).
(6) Steiger and Reichstein, *Helv. Chim. Acta*, **19**, 195 (1936).
(7) Richtmyer, Hann and Hudson, THIS JOURNAL, **61**, 343 (1939).
(8) Regna and Caldwell, *ibid.*, **65**, 243 (1943).
(9) Pigman, *J. Research Natl. Bur. Standards*, **25**, 301 (1940).
(10) Mottern and Cole, THIS JOURNAL, **61**, 2701 (1939).
(11) Ehrlich and Guttmann, *Ber.*, **67**, 573 (1934).
(12) Reichstein and Bossard, *Helv. Chim. Acta*, **17**, 760 (1934).
(13) German Patent 618,907, Sept. 19, 1935.

ous acetic acid using platinum oxide catalyst at 50 atm. and 120–140° to a mixture of L-galactonic and D-altronic acids, which were isolated as the cadmium and calcium salts, respectively.

The authors hydrogenated 100 g. of the normal calcium 5-keto-L-galactonate by suspending it in about one liter of water in a stainless steel, high-pressure autoclave containing about 10 g. of Raney nickel catalyst. The reduction was carried out by slowly heating the mixture to 80° under 2300 lb. pressure. At the end of the hydrogenation period the nickel was removed by filtration. The filtrate showed no reduction of Fehling solution, indicating a fully hydrogenated mixture of the calcium salts of L-galactonic and D-altronic acids. The hot solution after removal of the nickel catalyst was concentrated under diminished pressure to about 200 cc. It was allowed to stand several days after which 45 g. of calcium L-galactonate was obtained. The solution was evaporated further and 2 g. more of calcium L-galactonate was gained.

The mother liquor containing chiefly calcium D-altronate could not be made to crystallize readily. Seeds were finally obtained by keeping a few cc. of the solution on a watch glass in an evacuated desiccator over barium oxide for several days. These were then used to inoculate the original solution and with the aid of stirring, 32 g. of calcium D-altronate·$3^1/_2H_2O$ was finally obtained. One recrystallization from water yielded pure calcium D-altronate·$3^1/_2H_2O$ which was identified by its analysis and its mutarotation in *N* hydrochloric acid. Table I shows the observations on the rotation of the salt made by the authors and the corresponding values obtained by Richtmyer, Hann and Hudson[7] for this compound prepared from sedoheptulose.

TABLE I

MUTAROTATION OF CALCIUM D-ALTRONATE·$3^1/_2H_2O$ IN *N* HCl (*c*, 3) AT 20°

| Time, min. | $[\alpha]^{20}D$ from sedoheptulose | $[\alpha]^{20}D$ from 5-keto-L-galactonic acid |
|---|---|---|
| 5 | +11.5 | +11.8 |
| 10 | 13.8 | 14.0 |
| 15 | 15.9 | 16.0 |
| 20 | 17.3 | 18.0 |
| 30 | 19.6 | 20.4 |
| 45 | 21.9 | 22.0 |
| 60 | 23.1 | 23.2 |
| 90 | 24.2 | 24.3 |
| Constant | 24.8 | 25.0 |

By concentrating the mother liquor and cautiously adding methanol, 9.2 g. more of the salt was gained. From 100 g. of the normal calcium 5-keto-L-galactonate·$5H_2O$, a total of 47 g. of calcium L-galactonate·$5H_2O$ and 41.2 g. of calcium D-altronate·$3^1/_2H_2O$ was obtained.

The separation of calcium L-galactonate from calcium D-altronate was relatively simple before seeds of the latter salt were obtained. But as we worked with these calcium salts in the laboratory, we found it increasingly more difficult to effect the fractionation of the calcium salts. Hence, recourse was made to separating their cadmium salts. This was readily done by removing the calcium ions from the mixture following the high pressure hydrogenation. The solution of the free acids was heated and neutralized with a suspension of freshly precipitated cadmium hydroxide. The separation of the cadmium salts was effected as described above for the calcium salts.

**Acknowledgment.**—One of the authors (P. P. R.) wishes to express his indebtedness to Dr. Richard Pasternack, with whom he collaborated in a separate investigation during which was developed the convenient method of isolating D-galacturonic acid by means of precipitation as its sodium calcium salt.

## Summary

A new preparation for large quantities of D-altronic acid is reported and two intermediate products, sodium calcium D-galacturonate hexahydrate and calcium 5-keto-L-galactonate pentahydrate, are described.

BROOKLYN, N. Y. RECEIVED JULY 23, 1943

---

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

# Kinetics of Transformation of 2-Ketopolyhydroxy Acids

BY PETER P. REGNA[1] AND B. P. CALDWELL

Ohle[2] and Maurer and Schiedt[3] were first to show that weak alkaline agents and alkoxides convert methyl 2-keto-D-gluconate into D-araboascorbic acid. Reichstein[4] recognized that this procedure was general for the rearrangements of 2-keto-3,4-dihydroxy acids and utilized the reaction for the enolization and lactonization of its isomer methyl 2-keto-L-gulonate into L-ascorbic acid (vitamin C). In addition he showed that hydrochloric acid can also bring about this transformation, but that the continued action of the hydrochloric acid results in decomposition of the L-ascorbic acid.

In the course of previous work, one of the authors had noted marked differences in the effect of hydrochloric acid on the rates of rearrangement of the isomers of 2-ketogluconic and 2-ketogulonic acids although similar intramolecular processes are involved. This observation led the present investigators to study the rates of the transformation of a series of 2-ketohydroxy acids into their ascorbic acid analogs and the rates at which the corresponding ascorbic acid analogs decompose.

Prefatory experiments showed the action of hydrochloric acid on L-ascorbic acid to be essentially a constant pseudo-unimolecular or first-order reaction. An analytical examination of the end product corroborated the observations of Hirst[5] and his collaborators, who showed that when ascorbic acid is heated with 12% hydro-

(1) This paper is constructed from a thesis presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry, June, 1942. Present address: Chas. Pfizer & Co., Inc., Brooklyn, New York.

(2) Ohle, *Angew. Chem.*, **46**, 399 (1933).

(3) Maurer and Schiedt, *Ber.*, **66**, 1054 (1933).

(4) Reichstein and Grüssner, *Helv. Chim. Acta*, **17**, 311 (1934).

(5) Herbert, Hirst, Percival, Reynolds and Smith, *J. Chem. Soc.*, 1270 (1933).