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Catalytic Hydrogenation of Calcium D-Xylo-5-hexulosonate on Transition Metal Catalysts

CHAU-YANG CHEN, HARUHIKO YAMAMOTO
and TAKAO KWAN

Faculty of Pharmaceutical Sciences, University of Tokyo[1]

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Catalytic hydrogenation of calcium D-xylo-5-hexulosonate (5-keto-D-gluconate) has been investigated on transition metal catalysts with special interest in the selective formation of calcium L-idonate. The reaction completed usually within several hours under 20—100 kg/cm² hydrogen pressures at 80°. Initial rates on a Raney nickel catalyst were represented by $dC/dt = k'P_{H_2}^{0.5}$ where C is the degree of conversion.

Nickel, ruthenium and palladium gave rise to more L-idonate especially when prepared from their salts by treating with sodium borohydride. For example, 73% of the hydrogenated products was L-idonate on a "boron-modified-palladium" catalyst.

Introduction

Synthesis of L-ascorbic acid starting from D-glucose includes, according to Gray's method,[2] a process of catalytic hydrogenation of D-xylo-5-hexulosonate (5-keto-D-gluconate) to produce L-idonate. This catalytic hydrogenation reaction was investigated first by Pasternack and Brown[3] who found that the hydrogenation of calcium 5-keto-D-gluconate yields in the presence of a Raney nickel catalyst a mixture of L-idonate and D-gluconate under a high hydrogen pressure. In view of the importance for the industrial synthesis of L-ascorbic acid, similar investigations were carried out by a number of workers[4] and aimed to produce more L-idonate in the catalytic hydrogenation. Nevertheless, there still remains a question of interest as to catalyst's selectivity for the preferential formation of L-idonate or D-gluconate.

In the present paper we shall reinvestigate the catalytic hydrogenation of calcium 5-keto-D-gluconate by using group VIII transition metals as the catalysts. Special interest will be laid on rate law, catalyst activity and preferential formation of L-idonate. Since gas chromatographic analysis for L-idonate and D-gluconate has been recently established by us,[5] we would expect accurate information concerning to the competitive formation of the two diastereoisomers during the hydrogenation reaction.

Experimental

Materials——Calcium 5-keto-D-gluconate trihydrate of high purity, supplied by Takeda Pharmaceutical Co., was employed as the substrate. Commercial hydrogen was used without special purification. Iron,

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[1] Location: *7-3 Hongo, Bunkyo-ku, Tokyo.*

[2] B.E. Gray, U.S. Patent 2421611 (1947)(*Chem. Abstr.*, **41**, 5683).

[3] R. Pasternack and E.V. Brown, (Ch. Pfizer & Co.), U.S. Patent 2168878, 2168897 (1938).

[4] I. Hori and T. Karasaki, *J. Fermentation Technol.*, **26**, 84 (1949); M. Yamazaki and T. Miki, *J. Fermentation Technol.*, **31**, 39 (1953); K. Sato and T. Miki, (Pharmaceutical Researches Foundation), Japan Patent, 2157 (1959); T. Miki, T. Hasegawa and Y. Sahashi, *J. Vitaminol.*, **6**, 205 (1960); K. Asano and A. Matsumoto, (Daiichi Pharmaceutical Co.), Japan Patent 20016 (1961); R.M. Alieva, *Vestn. Leningr. Univ.*, **18**(21), Ser. Biol. No. 4, 148 (1963)(*Chem. Abst.*, **60**, 9346); Y. Nakajima and S. Taura, (Chugai Pharmaceutical Co.), Japan Patent 2331 (1965); T. Sato, I. Takahashi and T. Iida, (Takeda Pharmaceutical Co.), Japan Patent 20535 (1965).

[5] C.Y. Chen, T. Imanari, H. Yamamoto and T. Kwan, *Chem. Pharm. Bull.* (Tokyo), **16**, 755 (1968).

cobalt, copper, nickel, ruthenium, palladium, rhodium and platinum were respectively subjected to examination of their catalytic activities as well as selectivities. Two types of these catalysts were investigated. group A was commercially available one; iron, cobalt, nickel and copper were of Raney type (Kawaken Fine Chemical Co.), and ruthenium, palladium, rhodium and platinum were supported by 5% on active carbon (Japan Engelhard Co.). On the other hand, nickel, ruthenium, palladium and rhodium prepared from an aqueous solution of metal salt by treating with sodium borohydride were also investigated[6] as group B; the precipitated metal powder was repeatedly washed with distilled water until the filtrate became colorless for phenolphthalein test.

Hydrogenation Reaction——A sample of 2—20 g calcium 5-keto-D-gluconate (equivalent to 0.01—0.1 mole), suspended in 50—100 ml of water, was subjected to hydrogenation in the presence of 0.1—3.0 g of catalyst in an autoclave (200 ml). The reaction system was stirred electromagnetically (140 strokes/min) under hydrogen pressures of 20—100 kg/cm², the reaction temperature being from room temperature to 80°.

Analysis——Reaction products were analyzed by a gas chromatographic method[5] and by a polarimetric method respectively.[7] For the gas chromatographic analysis, the ratio of area under corresponding peaks was assumed, as usual, to give the ratio of L-idonate to D-gluconate. For the polarimetric analysis, the ratio of L-idonate to D-gluconate was given by the degree of optical rotation of complexes of L-idonate and D-gluconate with molybdate as well as with borate. This method also gave total amounts of L-idonate and D-gluconate. The ratio of L-idonate to D-gluconate, as determined by the two methods, agreed fairly well, although the latter method often gave rise to error when the sample contained some additives. The degree of conversion was determined in most cases by filtering off the unconverted insoluble calcium 5-keto-D-gluconate from soluble calcium L-idonate and calcium D-gluconate, and the calcium ion in the filtrate was then converted to calcium oxalate followed by back titration with potassium permanganate. The degree of conversion, as determined by the two methods, was in good agreement.

Results and Discussion

Since the solubility of calcium 5-keto-D-gluconate in water is very small (0.034M at 80°)[8] and that of hydrogenated products, calcium L-idonate and calcium D-gluconate, is fairly large,[9] it was possible to estimate an approximate degree of conversion through the appearance of the reacting system. Thus, the hydrogenation of calcium 5-keto-D-gluconate was completed usually within several hours on most catalysts under 60 kg/cm² hydrogen pressure at 80°. Gas chromatographic analysis indicated that products consisted exclusively of L-idonate and D-gluconate below 80°.

In order to compare relative catalytic activities of various catalysts, the degree of conversion was determined on each catalyst keeping reaction temperature, hydrogen pressure and the amount of substrate constant. The amount of catalyst was not kept constant; it ranged from 0.1 to 3.0 g. The degree of conversion C is defined by

$$C=\frac{(\mathrm{I})_t+(\mathrm{G})_t}{(\mathrm{KG})_0}\times 100$$

where $(\mathrm{I})_t$ and $(\mathrm{G})_t$ are the number of moles for L-idonate and D-gluconate at time t, and $(\mathrm{KG})_0$ is that for 5-keto-D-gluconate at time zero.

It was found that the degree of conversion was much lower on iron, cobalt and copper than on nickel, ruthenium, rhodium, palladium and platinum. Therefore, investigations were carried out primarily with respect to the latter metal catalysts.

Let us describe the result of investigation for catalysts of group A (commercial). It was noted that the degree of conversion, determined at a reactiom time 30 min, is the greatest on rhodium–carbon (0.25 g) and the least on Raney nickel (1.0 g) while this activity sequence does not hold along with the progress of conversion. The degree of conversion, measured during the course of 120 min reaction on each catalyst, is shown in Fig. 1.

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[6] H.C. Brown and C.A. Brown, *J. Am. Chem. Soc.*, **84**, 1493 (1962).
[7] Y. Asahi and F. Kasahara, *Japan Analyst*, **14**, 614 (1965).
[8] S. Teramoto and I. Hori, *J. Fermentation Technol.*, **26**, 7 (1948).
[9] "Kagaku Binran," ed. by Japan Chemical Society, 1966. p. 676.

It is apparent from the conversion–time curves of Fig. 1 that the catalysts are poisoned during the progress of hydrogenation. The platinum–carbon catalyst seems to be quite sensitive to poison whereas Raney nickel and ruthenium–carbon catalysts are so insensitive that nearly 100% conversion can be performed. Indeed, ruthenium–carbon is known to be a good catalyst for the hydrogenation of various carbohydrates.[10] Because of the poisoning effect, it was rather difficult to compare relative catalytic activity of the catalysts. However, rough estimation of the activity at the initial stage of reaction may lead to

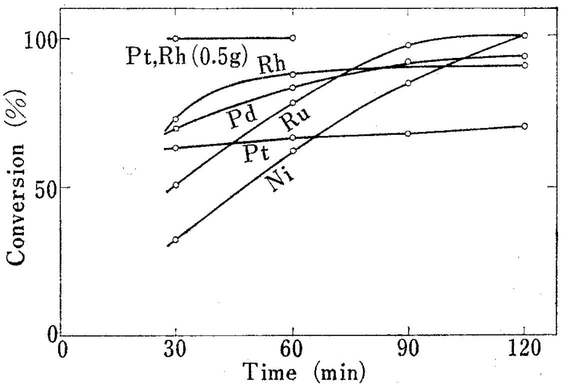

Fig. 1. The Rate of Conversion on Raney Nickel (1.0 g), Ruthenium–Carbon (0.5 g), Palladium–Carbon (0.5 g), Platinum–Carbon (0.25 g) and Rhodium–Carbon (0.25 g)

P_{H_2}: 60 kg/cm² T: 80° KG: 10 g

rhodium–carbon, platinum–carbon$\geq$palladium–carbon$\geq$ruthenium–carbon

$>$Raney nickel.

Similar investigations were carried out with catalysts of Group B and it was found that these catalysts are stable against poison in particular with nickel and palladium, and that the relative catalytic activity is palladium $>$nickel.

To get information on kinetic law for the hydrogenation of calcium 5-keto-D-gluconate, the degree of conversion was investigated on Raney nickel as function of hydrogen pressure, reaction temperature and the amount of substrate. The measurement of the degree of conversion was carried out within 30 min so that the "initial rates" could be obtained.

The initial rate of hydrogenation may generally be expressed by

$$\frac{dC}{dt}=k(\mathrm{KG})^{\alpha}(\mathrm{H_2})^{\beta}$$

Experimental results indicated that the rate is independent on the amount of calcium 5-keto-D-gluconate. This result may be quite reasonable because the concentration of the substrate is substantially constant during the reaction due to its low solubility in water. The rate of hydrogenation appeared to be not proportional to hydrogen pressure in the range from 20 to 100 kg/cm², but to 0.5 th power of hydrogen pressure at 80°. Consequently, the catalytic hydrogenation of calcium 5-keto-D-gluconate was expressed by

$$\frac{dC}{dt}=k'(\mathrm{H_2})^{0.5}$$

where k' is a constant. The temperature dependence of the hydrogenation was investigated in the temperature range from 30 to 80°, and found to be about 12 kcal.

Judging from the above kinetic features, it seems very probable that the rate is not determined by the physical processes such as dissolution or diffusion of hydrogen or calcium 5-keto-D-gluconate. Surface reaction would be rate-controlling.

Let us investigate the composition of hydrogenated products. It was found gas chromatographically that the products, obtained after 100% conversion, consisted, as mentioned

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[10] P.N. Rylander, "Catalytic Hydrogenation over Platinum Metals," Academic Press, New York and London 1967, p. 245; G. Gilman and G. Cohn, "Advances in Catalysts," Vol. IX, ed. by A. Farkas Academic Press Inc, New York, N.Y., 1957, p. 741.

already, exclusively of L-idonate and D-gluconate unless reaction temperature is higher than 80° and that the racemization does not proceed under the present experimental circumstance.

The selectivity, S, for the hydrogenation of calcium 5-keto-D-gluconate is defined by

$$S=\frac{(\mathrm{I})_t}{(\mathrm{G})_t}$$

S was now investigated on each catalyst during the course of hydrogenation. On the catalyst of group A, S appeared to decrease more or less along with the progress of hydrogenation. On the other hand, S was nearly constant over metal catalysts prepared by sodium borohydride (group B). Typical data for S are illustrated in Fig. 2.

General trend was that the catalyst, whose activity is poor, yielded more L-idonate than D-gluconate. The S-values for 100% conversion determined on several catalysts are listed in Table I.

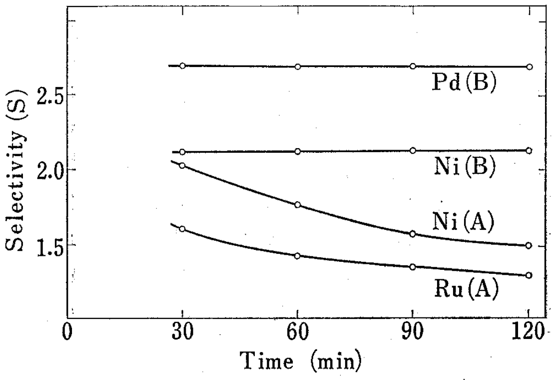

Fig. 2. Changes in the Selectivity during the Hydrogenation

Pd(B), Ni(B): sodium borohydride treated metals
Ni(A): Raney Nickel
Ru(A): Ruthenium-carbon
P_{H_2}: 60 kg/cm² T: 80°

Table I. Hydrogenation Selectivities Catalysed by Boron-modified (B) and Unmodified Metal (A) Catalysts

Metal / Group	Ni	Ru	Pd	Rh	Pt
A	1.5	1.4	1.2	1.0	0.9
B	2.0	2.0	2.7	0.9	0.7

The boron content of the catalyst precipitated by sodium borohydride was found, in the case of nickel, as $Ni_{2-3}B$ and in the case of palladium, as $Pd_{10}B$.[11] It is interesting to note that enhanced selectivity is obtainable for the formation of L-idonate when calcium 5-keto-D-gluconate is hydrogenated, for example, on boron-modified-palladium while selectivity is reversed on boron-modified-platinum. Thus, boron seems to play an important role in the preferential formation of the two diastereoisomers.

Boron-modified-metal was somewhat less active than unmodified metal, but it was resistive to catalyst poison. In view of the fundamental and practical importance of this reaction we further investigated the hydrogenation of 5-keto-D-gluconic acid. The result will be reported in a subsequent paper.

Acknowledgement The authors are indebted to Takeda Pharmaceutical Co. for providing them samples of pure calcium 5-keto-D-gluconate.

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11) C.Y. Chen, H. Yamamoto and T. Kwan, *Chem. Pharm. Bull.* (Tokyo), **17**, 1287 (1969).