Catalytic Hydrogenation. V.[1] The Reaction of Sodium Borohydride with Aqueous Nickel Salts. P-1 Nickel Boride, a Convenient, Highly Active Nickel Hydrogenation Catalyst

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Received October 24, 1969

The reaction of sodium borohydride with aqueous solutions of nickel salts immediately produces a finely divided black precipitate. This material (P-1 nickel) is a highly active catalyst for atmospheric pressure hydrogenations, more active than Raney nickel. The hydrogenations of a variety of alkenes have been examined and all but the most hindered double bonds were reduced successfully. Certain dienes were reduced cleanly to single olefinic products. P-1 nickel has marked advantages over Raney nickel: it is not pyrophoric; it is readily prepared *in situ;* it is highly reproducible.

During World War II Brown, Schlesinger, and coworkers[4] found that sodium borohydride reacted with certain first-row transition-metal salts to yield finely divided black precipitates, thought to be borides. The cobalt precipitate proved to have considerable activity as a catalyst for the hydrolysis of borohydride. In fact, the $NaBH_4$–cobalt system was investigated for the field generation of hydrogen.[5-7] Wartime pressure prevented further investigation of these black precipitates. However, in 1951 Paul and coworkers reported that the product of the reaction of nickel(II) salts with sodium borohydride was useful for catalytic hydrogenation. Activity was roughly equal to Raney nickel.[8,9]

We found that the reduction medium played an important role in the type of catalyst formed.[10,11] For example, in aqueous media a granular black material is formed from sodium borohydride and nickel(II) acetate. This material is at least as active as Raney nickel for double-bond hydrogenations.[10] However, in ethanol a nearly colloidal black suspension is produced which is much more sensitive to double-bond structure.[11,12] These materials, designated P-1 Ni and P-2 Ni, respectively,[13] are nonmagnetic and nonpyrophoric, unlike Raney nickel. Furthermore, they are easily reproducible and so readily prepared that detailed study of their characteristics as hydrogenation catalysts seemed warranted.

Therefore, as part of a systematic study of the uses of borohydride-reduced metal powders, we undertook a survey of hydrogenations using these nickel catalysts. This paper reports the results with P-1 Ni. A comparable study with P-2 Ni is in progress.

Results

The catalyst is prepared by treating an aqueous solution of nickel(II) salt with a threefold molar excess of sodium borohydride solution. After the excess borohydride has hydrolyzed, the water is decanted and the fine black granules are washed twice with absolute ethanol. We found that the presence of sodium acetate, sodium borate, ammonia, or sodium hydroxide during reduction had little effect on the activity of the catalyst for the hydrogenation of 1-octene. After reduction, two ethanol washings alone were sufficient. Washing of the catalyst with water, dilute acetic acid, dilute sodium hydroxide, or more ethanol had little or no effect on the activity.

Four nickel(II) salts were examined: nitrate, chloride, sulfate, and acetate. Nickel nitrate gave a precipitate which was too fine to be washed by decanting. Catalyst activity was slightly less for the chloride and sulfate than for the acetate, as shown by the times required for half-hydrogenation of cyclohexene: chloride, 22 min; sulfate, 18 min; acetate, 16 min. The acetate, $Ni(C_2H_3O_2)\cdot 4H_2O$, was chosen as standard. (In these studies 40 mmol of substrate and 5.0 mmol of catalyst was standard.)

Reproducibility was explored with the hydrogenation of 1-octene. In ten hydrogenations the time required for half-hydrogenation was between 6.0 and 7.0 min. During the course of the entire study, an occasional check run would require a maximum of 7.5 min for half-hydrogenation.

A comparison of the relative activity of the P-1 catalyst and W-2 Raney nickel[14] was made. The following results demonstrate the greater activity of P-1 nickel (olefin, relative time for half-hydrogenation of 40.0 mmol over P-1 nickel and W-2 Raney nickel): safrole, 1.0, 1.0; 1-octene, 1.0, 1.3; cyclopentene, 1.3, 2.0; cyclohexene, 2.5, 3.5; cyclooctene, 2.0, 5.3. These results are shown in detail in Table I.

The reaction plots for 1-octene show a noticeable, sharp decrease in rate toward the end. Glpc analysis at the rate break shows that only 2-octenes are present. Evidently the double bond isomerizes during hydrogenation; after the remaining 1-octene is consumed, 2-octenes

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[1] Part IV: C. A. Brown, *Anal. Chem.*, **39**, 1882 (1967).

[2] National Science Foundation Postdoctoral Fellow, 1968–1969.

[3] Institute of Organic Chemistry, Syntex Research, 3401 Hillview Ave., Palo Alto, Calif. 94304.

[4] H. C. Brown, H. I. Schlesinger, A. E. Finholt, J. R. Gilbreath, H. R. Hoekstra, and E. K. Hyde, *J. Amer. Chem. Soc.*, **75**, 215 (1953).

[5] H. C. Brown, personal communication.

[6] For a detailed discussion of such a gas generator, see A. Levy, J. B. Brown, and C. J. Lyons, *Ind. Eng. Chem.*, **52**, 211 (1960).

[7] Later studies have shown that several platinum metals react with sodium borohydride to produce even more active catalysts for the hydrolysis: H. C. Brown and C. A. Brown, *J. Amer. Chem. Soc.*, **84**, 1493 (1962).

[8] R. Paul, P. Buisson, and N. Joseph, *Compt. Rend.*, **232**, 627 (1951).

[9] R. Paul, P. Buisson, and N. Joseph, *Ind. Eng. Chem.*, **44**, 1006 (1952).

[10] C. A. Brown and H. C. Brown, *J. Amer. Chem. Soc.*, **85**, 1003 (1963).

[11] H. C. Brown and C. A. Brown, *ibid.*, **85**, 1004 (1963).

[12] (a) C. A. Brown, *Chem. Commun.*, 952 (1969); (b) C. A. Brown, research in progress.

[13] The designations are derived from Purdue University, where this work was initiated.

[14] A standard commercial sample of preformed Raney nickel was obtained from the Raney Catalyst Co., Inc., Chattanooga, Tenn. This catalyst is essentially the W-2 preparation and is that commonly stocked in many laboratories; thus it appeared representative. Although many preparations of Raney nickel have been reported, most procedures yield catalysts which differ little in activity in the hydrogenation of limonene: H. A. Smith, W. C. Bedoit, Jr., and J. R. Fuzek, *J. Amer. Chem. Soc.*, **71**, 3769 (1948).

TABLE I

HYDROGENATION OF REPRESENTATIVE OLEFINS OVER RANEY NICKEL AND P-1 NICKEL[a]

	Raney nickel[b]		P-1 nickel[b]	
Olefin	Initial[c] rate	$t_{50\%}$,[d] min	Initial[c] rate	$t_{50\%}$,[d] min
Safrole	75	6	69	6
1-Octene	59	8	72	6
Cyclopentene	36	12	56	8
Cyclohexene	23	21	31	16
Cyclooctene	17	32	42	12

[a] Hydrogenation of 40.0 mmol of substrate over 5 mmol of catalyst in ethanol at 25° (1 atm). [b] P-1 nickel based upon amount of nickel acetate used in preparation. Raney nickel based on volume of settled catalyst, which weighed *ca.* 0.3 g when dry. [c] Average rate from 0 to 20% reaction, in cubic centimeters of H_2 at STP per minute. Total hydrogen uptake (STP) = 896 cm^3. [d] Time for uptake of 20.0 mmol of hydrogen.

are hydrogenated at a slower rate.[15] The rate break occurs at an earlier point in the hydrogenation with Raney nickel, indicating more isomerization.

Isomerization during hydrogenation over the two catalysts was compared in the hydrogenations of 1-pentene. At 50% hydrogenation of 1-pentene, Raney nickel produced 3% *cis-* and 20% *trans*-2-pentene, a total of 23% isomerization. P-1 nickel produced 2% *cis-* and 5% *trans*-2-pentene, a total of 7%. The detailed comparison is shown in Table II.

TABLE II

ISOMERIZATION DURING HYDROGENATION OVER NICKEL CATALYSTS[a]

	Product, mmol[b,c]			
% Reaction	*n*-Pentane	1-Pentene	*trans*-2-Pentene	*cis*-2-Pentene
	A. Raney nickel W-2			
0	0.0	40.0	0.0	0.0
25	9.2	24.8	4.0	1.6
50	20.4	10.4	8.0	1.2
75	30.4	0.0	7.2	2.4
	B. P-1 nickel			
0	0.0	40.0	0.0	0.0
25	9.6	28.8	1.2	0.4
50	20.3	16.6	2.0	0.8
75	30.6	4.4	3.3	1.7

[a] Hydrogenation of 40.0 mmol of 1-pentene over 5.0 mmol of nickel catalyst at 25° (1 atm). [b] By glpc. [c] Normalized. Absolute yields 90–100%.

Next, the effect of olefin structure upon hydrogenation over P-1 nickel was systematically investigated.

Effect of Chain Length.—Four olefins from C_5 to C_{12} were hydrogenated to determine what effect moderate changes in length might have. All were reduced smoothly, and the relative times for half-hydrogenation follow: 1-pentene, 1.2; 1-hexene, 1.0; 1-octene, 1.0; 1-dodecene, 1.2. In all cases breaks in rate owing to isomerization of the olefin (*vide supra*) occurred in the vicinity of 90% hydrogenation.

Effect of Chain Branching.—Successive substitutions of methyl groups for the hydrogens α to the double bond produced very little change in the relative times for half-hydrogenation: 1-pentene, 1.0; 3-methyl-1-butene, 1.25; 3,3-dimethyl-1-butene, 1.05. The larger value for 3-methyl-1-butene is probably an artifact of its low boiling point (20°) and high vapor pressure; at 25°, the reaction temperature, the hydrogen partial pressure in the reactor is undoubtedly significantly below atmospheric. The first two compounds exhibit a rate break around 85% reaction; the last had a linear rate (isomerization by a simple shift of a hydrogen atom is not possible).

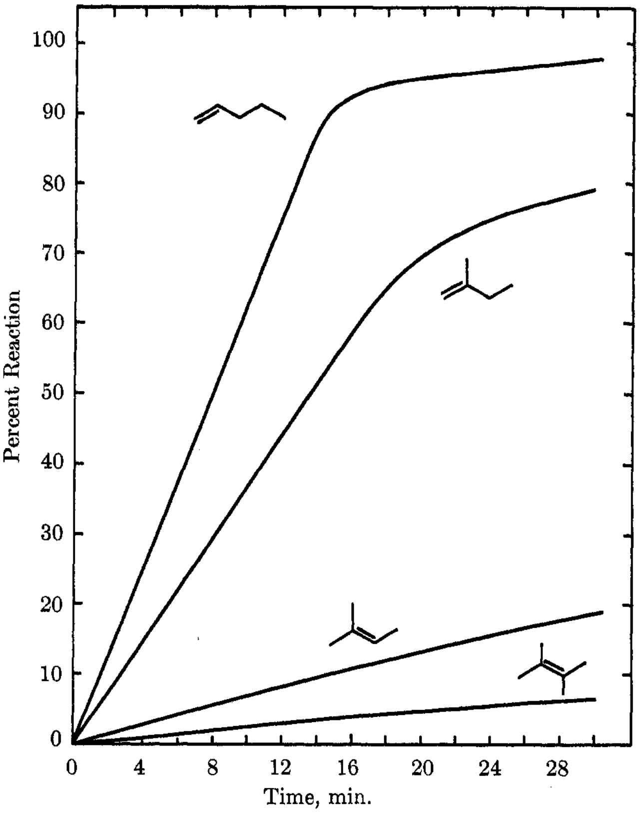

Figure 1.—Effect of substitution on rate of hydrogenation over P-1 nickel. Hydrogenation of 40.0 mmol of substrate over 5.0 mmol of catalyst at 25° (1 atm).

Effect of Increased Substitution.—Successively replacing the vinyl hydrogens with alkyl groups causes an appreciable decrease in reaction rate, as shown by the following relative half-hydrogenation times: 1-pentene, 1.0; 2-methyl-1-butene, 1.6; 2-methyl-2-butene, 16; 2,3-dimethyl-2-butene, *ca.* 45. Note that the big jump occurs between di- and trisubstitution. However, it is still significant that even the hindered tetrasubstituted olefin was still reduced under very mild conditions (25°, 1 atm). Figure 1 effectively demonstrates this effect of substitution.

Effect of Ring Size.—Cyclic olefins were readily reduced, with the order of reactivity being $C_5 > C_8 > C_6$. The relative times for half-hydrogenation follow: cyclopentene, 1.0; cyclooctene, 1.5; cyclohexene, 2.0 (1-octene, for comparison, is 0.8). The reactions slowed slightly toward the end. It is interesting to note that cyclohexene is the most reactive of these olefins over borohydride-reduced platinum metal catalysts.[15] Figure 2 reveals the effect of ring size on the rates of hydrogenation of cyclopentene, cyclohexene, and 1-octene over the two catalysts.

Phenyl Substituents.—Phenyl-substituted olefins are hydrogenated at least as readily as their aliphatic counterparts. For example, α-methylstyrene required only 70% as long as 2-methyl-1-butene for half-hy-

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[15] Similar double-bond migrations have been found with borohydride-reduced platinum metal catalysts: H. C. Brown and C. A. Brown, *Tetrahedron, Suppl. 8, Part I,* 129 (1966).

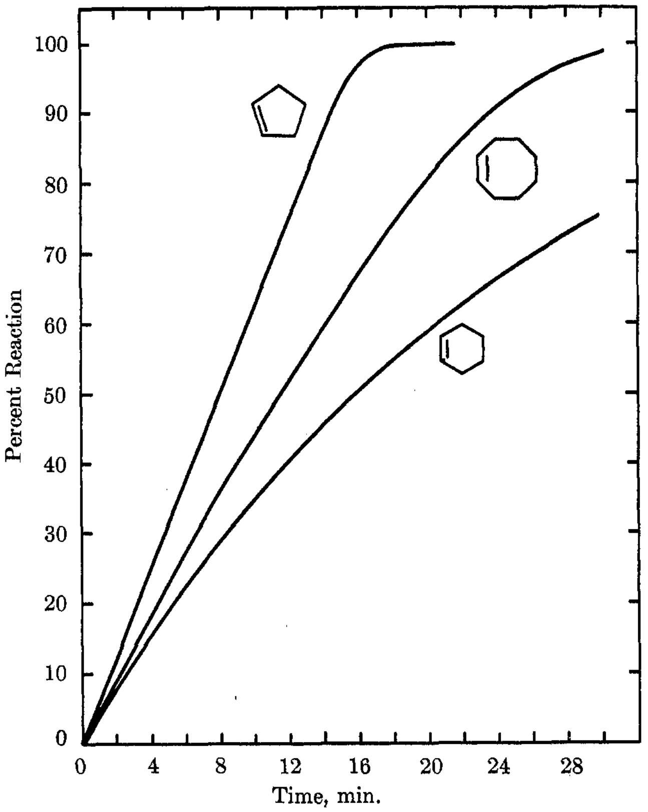


Figure 2.—Effect of ring size on rate of hydrogenation over P-1 nickel. Hydrogenation of 40.0 mmol of substrate over 5.0 mmol of catalyst at 25° (1 atm).

drogenation, while safrole took even less time than 1-octene. The relative half-hydrogenation times follow: safrole, 1.0; allyl benzene, 1.1; styrene, 1.2; α-methylstyrene, 1.6 (1-octene, 1.1).

Aromatic Nucleus.—In the cases above no evidence was found for reduction of the aromatic ring. In a separate experiment, benzene failed to reduce at all in 2 hr at atmospheric pressure and 25°. However, pyrocatechol is readily reduced to cyclohexanediol over P-1 Ni in an autoclave.[16]

The presence of benzene inhibits slightly the hydrogenation of simple olefins. Thus the addition of 40.0 mmol of benzene to the hydrogenation of 40.0 mmol of 1-octene resulted in an increase in half-hydrogenation time of 50% (10 min. *vs.* 6.5 min without benzene).

Effect of Bond Strain.—Reduction of norbornene proceeded smoothly and linearly. Time for half-hydrogenation was about 90% of that for 1-octene, and appreciably less than that for either cyclopentene or cyclohexene, its monocyclic analogs.

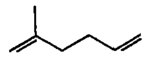
The above reductions are tabulated with initial rates and absolute half-hydrogenation times in Table III.

TABLE III

HYDROGENATION OF REPRESENTATIVE OLEFINS OVER THE P-1 NICKEL CATALYST[a]

Compd	Initial rate,[b] cm^3 of H_2 at STP/min	$t_{50\%}$,[c] min
1-Pentene	56	8
1-Hexene	71	6.5
1-Octene	72	6
1-Dodecene	54	8
3-Methyl-1-butene	45	10
3,3-Dimethyl-1-butene	56	8.5
2-Methyl-1-butene	36	13
2-Methyl-2-butene	7	130
2,3-Dimethyl-2-butene	2	~360
Cyclopentene	56	8
Cyclohexene	31	16
Cyclooctene	43	12
Safrole[d]	72	6
Styrene[d]	63	7.5
α-Methylstyrene[d]	49	9.5
Allylbenzene[d]	69	6.5
Norbornene	80	6.0

[a] Hydrogenation of 40.0 mmol of substrate over 5.0 mmol of P-1 nickel in ethanol at 25° (1 atm). [b] Average rate from 0 to 20% reaction. Total reaction is 896 cm^3 at STP. [c] Time for adsorption of 20 mmol of hydrogen. [d] Reduction of side chain only.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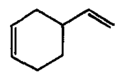
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Selective Hydrogenations.—Applications of this catalyst to selective hydrogenations were generally beyond the scope of this study; they are under investigation currently. However, two selective hydrogenations can be reported: 2-methyl-1,5-hexadiene (I) and 4-vinylcyclohexene (II). After uptake of 1.0 equiv of hydrogen, glpc analysis showed that the vinyl group had been almost completely reduced in both cases. Thus 2-methyl-1-hexene was obtained 93% pure, and 4-ethylcyclohexene 98% pure. Thus this catalyst does seem to have promise in this area.

Discussion

P-1 nickel is a very useful catalyst for a variety of carbon–carbon double bond hydrogenations. Even under the very mild reaction conditions employed in this study, only the hindered tri- and tetrasubstituted double bonds were sluggish. Increased hindrance α to the double bond does not seem to have much effect.

One point of some interest is the inhibition of 1-octene hydrogenation by benzene, even though benzene is not reduced noticeably under the typical reaction conditions. This suggests that the aromatic ring may physically adsorb onto the catalyst surface (interfering with olefin chemisorption) without actually bonding (chemisorbing) to the active metal sites. As noted, however, the use of more vigorous conditions (high pressure, elevated temperature) may permit the reduction of aromatic compounds.[16] Further work on this application is anticipated.

P-1 nickel is more active and produces less double-bond migration than standard Raney nickel. Furthermore, P-1 nickel is not pyrophoric.[17] It is also much more readily prepared than Raney nickel. The preparation of enough of the latter for a small-scale hydrogenation requires more than 1 hr. P-1 nickel may be prepared in 10–15 min merely by mixing two

(16) G. Zweifel, University of California, Davis, personal communication.

(17) (a) In contrast, a literature preparation[17b] of W-2 Raney nickel warns that "the product [catalyst] is highly pyrophoric and must be kept under a liquid at all times;" (b) R. Mozingo, "Organic Syntheses," Coll. Vol. III, John Wiley & Sohs, Inc., New York, N. Y., 1955, p 181.

reagents in the reactor.[18] Very possibly because P-1 nickel is always freshly prepared, we have realized consistently high reproducibility and reliability over a period of years and in several laboratories.

Extra activation of P-1 nickel-type catalysts have been reported by conducting the reduction of nickel salts in the presence of 2% chromium, molybdenum, tungsten, or vanadium salts.[9,19] Mears and Boudart[20] have shown that this increase in activity (as measured for dehydrogenation of isopropyl alcohol to acetone) is directly proportional to increases in catalyst surface area (presumably owing to the presence of a "foreign" material during catalyst precipitation).

In addition to high reproducibility, P-1 nickel is very resistant to poisoning in successive hydrogenations using the same batch of catalyst, considerably more so than Raney nickel.[9]

The nature of the catalyst itself remains unknown. The presence of boron has been shown by chemical analyses,[4,8,9,21] atomic absorption spectroscopy,[21] and electron-microprobe X-ray analysis (strong K_α line for boron).[21] The material was originally[4,8,9] postulated to be Ni_2B, formed as shown in eq 1. This reaction

$$2Ni(OAc)_2 + 4NaBH_4 + 9H_2O \longrightarrow Ni_2B + 4Na(OAc)_2 + 3B(OH)_3 + 12.5H_2(g) \quad (1)$$

yields 78% of the hydrogen theoretically obtainable from $4NaBH_4 (\rightarrow 16.0\ H_2)$. In fact the yield of hydrogen is 75–78%.[22–24] Chemical analyses have indicated as much as 7.7% boron (8.5% calculated for Ni_2B).[8,9] However, the boron content has been reported to vary with the ratio of reactants used in preparation.[25]

Films produced by similar borohydride–nickel salt reactions in nonelectrolytic plating baths are reported to be amorphous mixtures of nickel and boron containing 3–10% of the latter. At temperatures over 400°, these films yield crystalline nickel borides.[26,27]

In addition to hydrogenation and dehydrogenation,[18] P-1 nickel (or similarly prepared materials) has been reported highly useful for deuterium exchange[28] and selective desulfurizations.[29,30]

The P-1 nickel catalyst and similar materials should find considerable use in organic syntheses. We are currently studying further properties of these highly accessible and interesting materials, both for hydrogenation and other reactions.

Experimental Section

Apparatus.—The all-glass automatic borohydride hydrogenator described in earlier studies[1,31] was employed throughout.[32] This device greatly facilitates the preparation and use of P-1 nickel catalysts.

Reagents.—The following nickel salts were obtained from J. T. Baker Co. (Baker A.R. grade): $Ni(C_2H_3O_2)_2 \cdot 4H_2O$; $NiCl_2 \cdot 6H_2O$; $Ni(NO_3)_3 \cdot 6H_2O$; $NiSO_4 \cdot 6H_2O$.

Sodium borohydride, 98%, was produced and supplied by Ventron Corp. A stabilized solution for catalyst preparation is prepared by dissolving 1.0 g of sodium hydroxide and 9.45 g of sodium borohydride in 200 cm^3 of water. This is diluted to 250 cm^3 and filtered. It is best prepared freshly the day required.

The organic substrates were usually used directly from freshly opened bottles. If colored or if their refractive index varied significantly from literature values, they were distilled from sodium borohydride. Substrates and their sources are listed in Table IV.

TABLE IV

SUBSTRATES AND SOURCES

Compd	Source
1-Pentene	Phillips[a]
1-Hexene	Phillips
1-Octene	Phillips
1-Dodecene	HW[b]
3-Methyl-1-butene	Phillips
3,3-Dimethyl-1-butene	API[c]
2-Methyl-1-butene	Phillips
2-Methyl-2-butene	Phillips
2,3-Dimethyl-2-butene	Phillips
Cyclopentene	Phillips
Cyclohexene	Phillips
Cyclooctene	CS[d]
Safrole	Aldrich[e]
Styrene	MCB[f]
α-Methylstyrene	MCB
Allylbenzene	Columbia[g]
Benzene	Phillips
4-Vinylcyclohexene	Phillips
2-Methyl-1,5-hexadiene	Columbia

[a] Phillips Petroleum Co. (Pure Grade). [b] Humphrey–Wilkens Co. [c] American Petroleum Institute project at The Ohio State University. [d] Cities Service Petroleum Co. [e] Aldrich Chemical Co. [f] Matheson Coleman and Bell. [g] Columbia Chemical Co.

Catalyst Preparation and Use.—Nickel acetate tetrahydrate (1.24 g, 5.0 mmol) was dissolved in 50 cm^3 of water in a 125-ml erlenmeyer flask (modified for high-speed magnetic stirring). This flask was attached to the borohydride hydrogenator and flushed with nitrogen. With vigorous stirring 10.0 cm^3 of 1.0 *M* sodium borohydride solution in 0.1 *M* sodium hydroxide (*vide supra*) was injected over 30–45 sec. When gas evolution ceased, a further 5.0 cm^3 of solution was added. After gas evolution again subsided, stirring was discontinued and the flask was detached from the hydrogenator. The supernate was decanted from the catalyst (fine black granules); the catalyst was then washed twice with 50 cm^3 of ethanol by swirling and decanting. Then $(50 - n)$ cm^3 (n = volume of substrate to be added) of ethanol was added, the flask was attached to the hydrogenator, and the system was purged with hydrogen. Stirring was resumed and the reaction was initiated by injecting olefin.

Agitation was provided by a small LaPine magnetic stirrer and a 1.5-in. TFE-covered stirring bar fitted with an oversize spin ring.

Samples were withdrawn from reaction mixtures through an 8-mm port in the reactor closed with a serum stopper; using a syringe and stainless steel needle, 0.1-cm^3 samples were pulled at appropriate points. Blank runs showed that there was no

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(18) (a) Because of the time consumed, the preparation of Raney nickel is often carried out on a large scale, or the catalyst is purchased in 1-lb containers.[14] However, catalysts change on aging (generally for the worse).[18b] (b) R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, Inc., New York, N. Y., 1967.

(19) Similar activation has been reported for Raney nickel: R. Paul, *Bull. Soc. Chim. Fr.*, 208 (1946).

(20) D. E. Mears and M. Boudart, *Amer. Inst. Chem. Eng. J.*, **12**, 313 (1966).

(21) Ch.-Y. Chen, H. Yamamoto, and T. Kwan, *Chem. Pharm. Bull.* (Tokyo), **17**, 1287 (1969).

(22) C. A. Brown, unpublished observations.

(23) N. N. Mal'tseva, *et al.*, *Zh. Neorg. Khim.*, **11**, 720 (1966).

(24) N. N. Mal'tseva, *et al.*, *Dokl. Akad. Nauk SSSR*, **160**, 325 (1965).

(25) K. N. Mochalov, *et al.*, *Tr. Kazansk. Khim. Technol. Inst.*, **33**, 95 (1964); *Chem. Abstr.*, **64**, 18930*g* (1966).

(26) K. Lang, *Electroplating Metal Finishing*, **19**, 86 (1966).

(27) H. Narcus, *Plating*, **54**, 380 (1967).

(28) G. E. Colfand and J. L. Garnett, *J. Phys. Chem.*, **68**, 3887 (1964).

(29) W. E. Truce and F. E. Roberts, *J. Org. Chem.*, **28**, 961 (1963).

(30) W. E. Truce and F. M. Perry, *ibid.*, **30**, 1316 (1965).

(31) C. A. Brown and H. C. Brown, *J. Amer. Chem. Soc.*, **84**, 2829 (1962).

(32) A commercial model was obtained from Delmar Scientific Laboratories, Inc., Maywood, Ill.

detectable difference in reaction half-times in all-glass reactors or when sampling was being conducted.

Analyses.—Samples were analyzed by glpc and compared with known materials. The following liquid phases were used: adiponitrile on firebrick (1-pentene) and tetracyanoethylated pentaerythritol (TCEPA) on Chromosorb P (4-vinylcyclohexene, 2-methyl-1,5-hexadiene).

Registry No.—Sodium borohydride, 16940-66-2; nickel(II) acetate, 373-02-4; safrole, 14871-41-1; 1-octene, 111-66-0; cyclopentene, 142-29-0; cyclohexene, 110-83-8; cyclooctene, 931-88-4.

Acknowledgments.—This study was assisted in part by a Research Award (585 C) from the American Chemical Society Petroleum Research Fund, a grant from Parke, Davis and Co., and a fellowship from the National Science Foundation.

Diastereomers of Quinic Acid. Chemical and Nuclear Magnetic Resonance Studies

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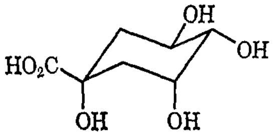
Received June 23, 1969

(±), (−), and (+)-*epi*-Quinides (γ-lactones of 34/15 and 45/13-tetrahydroxycyclohexanecarboxylic acids) have been prepared from their respective acetates. (+)-*epi*-Quinide triacetate separated by a spontaneous resolution in the crystallization of the optically impure (±) compound. *scyllo*-Quinic acid [*meso*-(4/135)-tetrahydroxycyclohexanecarboxylic acid] was also prepared from its acetate and its structure and conformation were determined. The 3.0- and 6.5-Hz splittings of the H-4 proton resonance in the 100-MHz nmr spectrum of the *epi*-quinic anion can most reasonably be assigned to *gauche* and *trans* splittings of a deformed chair (9), indicating that the H-4 and either H-3 or H-5 are axial. The magnitude of the *trans* coupling is considerably lower than that observed for other isomers. Ir and nmr (both ordinary and decoupled) spectra of *epi*-quinide triacetate verify a γ-lactone structure with the hydroxyls on C-4 and C-5 equatorial (11). Of particular interest in the nmr spectrum are the zero value of $J_{2(a),3(e)}$, the 1.0-Hz value for $J_{3(e),4(a)}$, and the 3.5-Hz long-range coupling between the equatorial methylene protons. The 9.0-Hz triplet splitting in H-4 in the nmr spectrum of *scyllo*-quinic acid clearly indicates that the three hydroxyls are equatorial (**13** or **14**). The formation of δ-lactone **16** on prolonged heating in acetic acid establishes that the carboxyl is *cis* to the 4-hydroxyl group and that *scyllo*-quinic acid has structure **14**.

(−)-Quinic acid, intimately involved in the "shikimic acid route" of the main pathway of aromatic biosynthesis, is one of eight diastereoisomeric 1,3,4,5-tetrahydroxycyclohexanecarboxylic acids. Of the eight such acids, only two, (−)-quinic acid (**1**) and its mirror image (**2**), (+)-quinic acid, are known.[1a] Gorin[2] isomerized (−)-quinic acid with acetic acid–sulfuric acid mixtures and obtained, after acetylation, three acetates. These were assigned the structure (−)-*epi*-quinide triacetate (**3**), (±)-*epi*-quinide triacetate, and *scyllo*-quinic acid tetraacetate, derived from one of the four *meso* acids. The structural assignments were based on the positions of the acetoxy protons in their respective nmr spectra and a series of reactions of the carboxyl-reduced derivatives, quinicols. Gorin favored **4** [*meso*-(35/14)-tetraacetoxycyclohexane-1-carboxylic acid] over **5** [the (4/135) isomer] for the structure of *scyllo*-quinic acid tetraacetate, mainly on the basis of extrapolated kinetic data. Since *epi*-quinic acid is the only isomer (pair) other than quinic acid which may be optically active, the structural recognition of *epi*-quinide triacetate was on a sound basis (although two of the *meso* acids can form optically active lactones).



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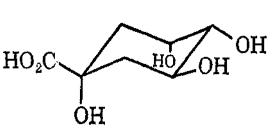

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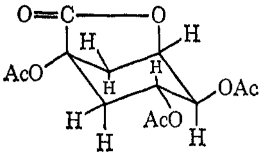

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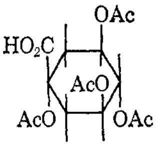

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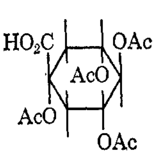

5

The nomenclature of the quinic acids is in a state of uncertainty. The "Tentative Rules for Cyclitol Nomenclature" proposes that the quinic acids be named according to cyclitol rules. In our opinion such an action would be premature without radical changes being made to avoid grave errors. In this paper the system currently in general use will be followed: the carboxyl will be numbered 1 and will be drawn above the ring; the numbering will be clockwise as in the Maquenne system.[1b] Thus (−)-quinic acid is (−)-(3/145)-tetrahydroxycyclohexane-1-carboxylic acid, and (+)-quinic acid is the (+)-(5/134) isomer. We realize that it is not immediately apparent that these two are enantiomers, but to give them the same Maquenne fraction requires both clockwise and counterclockwise numbering. This leads to a remarkable confusion in describing the reactions discussed in this paper and in relating the acids of aromatic biosynthesis from 5-dehydroquinic acid. The comparable confusion possible in the carbohydrates and inositols has been sidestepped by using trivial names *solely* as a basis of nomenclature. Hence the trivial names (±)-*epi*-quinic and *scyllo*-quinic acids introduced by Gorin will be retained because of their convenience. The Sequence Rule[3,4] nomenclature, although awkward in use, is a definitive nomenclature: (−)-quinic acid is (1*R*:3*R*:4*S*:5*R*)-3/145-tetrahydroxycyclohexane-3-car-

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(1) (a) T. Posternak, "The Cyclitols," Holden-Day, Inc., San Francisco, Calif., 1965, p 268 ff; (b) p 8 ff.

(2) P. A. J. Gorin, *Can. J. Chem.*, **41**, 2417 (1963).

(3) R. S. Cahn, *J. Chem. Educ.*, **41**, 116 (1964).

(4) R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956).