time. New procedures for preparing *o*-fluorostyrene, *o*-methoxystyrene and *o*-cyanostyrene are described.

Two more examples of the disproportionation of phenylmethylcarbinols to ethylbenzenes under the influence of activated alumina have been observed in the dehydration of *p*-benzylphenylmethylcarbinol and *o*-methoxyphenylmethylcarbinol.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MISSOURI]

The Hydrogenation of Phenolic Acids

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The catalytic reduction of phenolic acids has been investigated in the hope of obtaining a reasonably simple method for the preparation of acids of the type (I).

I

Previous attempts to prepare the methoxy acid (I, R = CH_3, R' = H) by catalytic reduction of the corresponding aromatic acid with platinum catalyst have been unsuccessful.[1] In numerous other investigations the catalytic reduction of phenolic acids has been reported to give low yields of hydroxycyclohexane acids due to side reactions. Low pressure hydrogenation, particularly in acid medium, causes considerable hydrogenolysis of the carbon–oxygen linkage with resultant loss of the hydroxyl group[2,3,4] whereas high pressure hydrogenation with nickel catalyst leads largely to decarboxylation[5] regardless of whether the acids or their sodium salts are reduced.[4] The hydrogenolysis reaction in the low pressure hydrogenation with platinum can be repressed by reducing in the presence of alkali. Good yields of 4-hydroxycyclohexanecarboxylic acid have thus far been reported only for the hydrogenation of *p*-hydroxybenzoic acid in ethyl acetate over palladium-on-strontium carbonate under high pressure.[4]

It has been shown in the present investigation that phenolic acids can be reduced smoothly to the hexahydro compounds by high pressure hydrogenation of their esters in alcoholic solution with W-2 Raney nickel catalyst[6] in the presence of approximately 0.3 mole % of the sodium salts of these compounds. The reduction products are pure substances which consist of mixtures of *cis*- and *trans*-isomers and which are formed in nearly quantitative yield. A direct separation of the isomers is rather difficult. A partial separation can be effected by adsorption of the esters on alumina. The *trans*-isomer is more strongly adsorbed.

The best method for the preparation of the pure *cis*- and *trans*-isomers consists in the reduction of the keto acids by specific reduction methods. Sodium and alcohol or sodium amalgam gives fairly pure *trans*-alcohols while the catalytic reduction with Raney nickel at room temperature yields predominantly *cis*-isomers.[3]

Experimental[7,8]

The phenolic acids used in this investigation were commercial products with the exception of α-(*p*-hydroxyphenyl)-butyric acid which was prepared according to Wilds and Biggerstaff.[9,10]

The ethyl esters of the phenolic acids were prepared by esterification of the acids with ethyl alcohol and sulfuric acid or by the method of Thielepape.[11] They were distilled under reduced pressure prior to reduction.

Hydrogenation of the Phenolic Esters.—The phenolic esters (0.2–1.0 mole) were dissolved in 100 cc. of absolute ethyl alcohol containing 0.3 mole % (on the basis of phenolic ester) of sodium ethoxide. Raney nickel (3–6 g.) was added and the mixture was immediately hydrogenated at between 160–220° (240–270 atm.) until the pressure remained constant. The catalyst was filtered off, the solvent was removed and the residue was distilled under reduced pressure. The constants of the products are given in Table I.

Preparation of the Keto Acids.—The hydroxycyclohexane esters described above were hydrolyzed by refluxing for two hours with four volumes of 10–20% aqueous sodium hydroxide solution and one volume of ethyl alcohol. The resultant solution was acidified with hydrochloric acid and extracted continuously with benzene. Most of the water and benzene were removed by distillation from a water-bath, the last traces under reduced pressure. The residual acids were used for the preparation of the keto acids without further purification. The mixtures of the isomeric acids were oxidized with chromic anhydride in aqueous acetic acid below 15°. Ethyl 4-hydroxycyclohexanecarboxylate was oxidized without previous hydrolysis. The resulting keto ester was purified through its bisulfite addition compound and was hydrolyzed on regeneration. The experimental data are given in Table II.

The keto acids were isolated by dilution of the reaction mixture with water and continuous extraction of the resultant solution with ether. The ether was removed by

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[1] Ruggli, Leupin and Businger, *Helv. Chim. Acta*, **24**, 339 (1941).

[2] Balas and Kosik, *Časopis Českoslov. Lékárnictva*, **7**, 105 (1927); Balas and Srol, *Coll. Czescoslov. Chem. Commun.*, **1**, 658 (1929); Edson, *J. Soc. Chem. Ind.*, **53**, 138T (1934); Long and Burger, *J. Org. Chem.*, **6**, 852 (1941); Price, Enos and Kaplan, THIS JOURNAL, **69**, 2261 (1947).

[3] Hardegger, Plattner and Blank, *Helv. Chim. Acta*, **27**, 793 (1944).

[4] Levin and Pendergrass, THIS JOURNAL, **69**, 2436 (1947).

[5] Ipatiew and Razuvajew, *Ber.*, **59B**, 306 (1926); Mitsuii, *Mem. Coll. Sci. Kyoto Imp. Univ.*, **A18**, 329 (1935); Martin and Robinson, *J. Chem. Soc.*, 491 (1943).

[6] Adkins and Pavlic, THIS JOURNAL, **69**, 3040 (1947).

[7] All temperatures uncorrected.

[8] Analyses by Karl Zilch.

[9] Wilds and Biggerstaff, THIS JOURNAL, **67**, 789 (1945).

[10] The authors are indebted to Dr. V. H. Wallingford of the Mallinckrodt Chemical Works for a generous supply of diethyl ethylphenylmalonate from which this acid was prepared.

[11] Thielepape, *Ber.*, **66**, 1454 (1933).

TABLE I

HYDROGENATION PRODUCTS OF THE PHENOLIC ACIDS

Ethyl ester	B. p. °C.[a]	Mm.	Yield,[b] %	n^{20}_D	d^{20}_4	M_D Calcd.	M_D Found
2-Hydroxycyclohexanecarboxylate	98.5–100	7	85	1.4625	1.0505	44.74	45.11
3-Hydroxycyclohexanecarboxylate	133–138	9	75[c]	1.4665	1.0564	44.74	45.22
4-Hydroxycyclohexanecarboxylate	136	8	87	1.4698	1.0667	44.74	44.96
4-Hydroxycyclohexaneacetate[d]	138–142	7	89	1.4705	1.0533	49.36	49.38
α-(4-Hydroxycyclohexane)-butyrate[e]	147	6	83	1.4710	1.0083	58.58	59.50

[a] The products boiled without forerun. [b] On the basis of purified products. [c] The low yield in this case was due to mechanical losses. [d] *Anal.* Calcd. for $C_{10}H_{18}O_3$: C, 64.50; H, 9.72. Found: C, 64.41; H, 9.91. [e] *Anal.* Calcd. for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.29; H, 10.24.

TABLE II

CHROMIC ACID OXIDATION OF THE HYDROXY ACIDS

Hydroxy compound	G.	CrO_3, g.	HOAc, cc.	H_2O, cc.	Yield, %[a]	M. p., °C.
Ethyl 4-hydroxycyclohexanecarboxylate	8.0	4.0	400	10	45.7	66–68
4-Hydroxycyclohexaneacetic acid	17.0	4.0	50	3	34.4	67–68
α-(4-Hydroxycyclohexane)-butyric acid	5.8	2.4	38	2	55	73–75

[a] The yields are based on crystallized products.

distillation, the residual acids were dried by removing the benzene–water azeotrope and were crystallized from Skellysolve B. The purification of the acids proved tedious since several weeks were required for the crystallization of the reaction products. Analyses of the acids and their semicarbazones are given in Table III.

TABLE III

KETO ACIDS

4-Ketocyclohexane acid	Calcd. %C	Calcd. %H	Found %C	Found %H	Semicarbazones M. p., °C.	Calcd. %C	Calcd. %H	Found %C	Found %H
R—COOH	[12]				196 (dec.)	[12]			
$R—CH_2—COOH$	61.52	7.76	61.29	8.07	175–176 (dec.)	50.69	7.09	50.33	7.12
$\mathrm{R—\underset{C_2H_5}{\underset{\mid}{CH}}—COOH}$	65.20	8.76	65.54	9.06	208–210 (dec.)	54.75	7.94	55.00	8.03

***cis*-4-Hydroxycyclohexaneacetic Acid.**—The keto acid (0.45 g.), dissolved in 11 cc. of 1 *N* aqueous sodium hydroxide solution, was reduced with 1.5 g. of Raney nickel under 50 mm. of hydrogen. The calculated amount of hydrogen was taken up in thirty-five minutes. The solution was filtered from the catalyst, acidified with concentrated hydrochloric acid and extracted continuously with ether for fourteen hours. The residue obtained after removing the solvent was dried by distillation with benzene. The remaining solid material (0.46 g.), m. p. 115–123°, was purified by crystallization from ethyl acetate. The pure acid melted at 133.5–134°.

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.47; H, 9.09. Found: C, 60.64; H, 9.14.

***trans*-4-Hydroxycyclohexaneacetic Acid.**—Sodium amalgam (75 g., 4%) was added in small pieces over a period of two hours with stirring to a solution of 2.3 g. of 4-ketocyclohexaneacetic acid in 140 cc. of 2 *N* aqueous sodium carbonate solution. The mixture was allowed to stand for fifteen hours. Sodium bicarbonate (10 g.) was then added to the mixture with stirring and stirring was continued for six hours. The mercury was removed by decantation and the aqueous solution was acidified with hydrochloric acid. Continuous extraction of the water solution with ether gave 2.4 g. of crude acid, m. p. 134–136°, which melted at 139.5–140° after repeated crystallization from ethyl acetate. The mixture with the *cis*-acid melted at 110–120°.

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 9.09. Found: C, 60.48; H, 9.08.

***cis*-α-(4-Hydroxycyclohexane)-butyric Acid.**—The catalytic reduction of the keto acid (0.4 g.) was carried out as described for *cis*-4-hydroxycyclohexaneacetic acid. The crude product (0.4 g., m. p. 102–107°) was crystallized from ethyl acetate. The pure hydroxy acid melted at 110.5–111°.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.50; H, 9.72. Found: C, 64.47; H, 9.95.

***trans*-α-(4-Hydroxycyclohexane)-butyric Acid.**—The mixture of isomeric hydroxy esters (3.73 g.) from the high pressure hydrogenation of ethyl α-(*p*-hydroxyphenyl)-butyrate was adsorbed on alumina from Skellysolve A solution. The less strongly adsorbed *cis*-isomer was eluted with the same solvent, the *trans*-compound was eluted with benzene. A portion of the benzene eluate (0.82 g.) was refluxed for three hours with 25 cc. of 10% aqueous sodium hydroxide solution and 10 cc. of ethyl alcohol. The solution was acidified with hydrochloric acid and extracted with ether in a continuous extractor. The ether was displaced with benzene, the latter removed by distillation, the last traces under reduced pressure. The residue (0.62 g.) solidified on standing and melted at 93–107°. Three crystallizations from benzene–Skellysolve B mixtures raised the melting point to 123.5–124°. The substance depressed the melting point of the *cis*-isomer.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.50; H, 9.72. Found: C, 64.35; H, 9.75.

Summary

The ethyl esters of the three hydroxybenzoic acids, *p*-hydroxyphenylacetic acid and α-(*p*-hydroxyphenyl)-butyric acid, have been reduced in good yield to the hexahydro compounds by high pressure hydrogenation over Raney nickel catalyst in alcoholic solution containing 0.3 mole % of sodium ethoxide. A method has been described for the conversion of these reduction products to the corresponding keto acids. The *cis*- and *trans*-isomers of 4-hydroxycyclohexaneacetic acid and α-(4-hydroxycyclohexane)-butyric acid have been prepared.

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(12) Perkins, *J. Chem. Soc.*, **85**, 427 (1904).