[A CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Hydrogenation of Esters to Alcohols at 25–150°

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The discovery of the effectiveness of a high ratio of catalyst to ester, in lowering the temperature for reaction with hydrogen, is one of the important recent advances in the art of hydrogenation. The observation was first reported from the laboratory of P. A. Levene, in the Rockefeller Institute for Medical Research.[2] The importance of the discovery was recognized and utilized in This Laboratory in 1940.[3,4] Mozingo and Folkers have recently reported the successful hydrogenation of malonates, acetoacetates[5] and benzoates,[6] using a rather high ratio of copper–chromium oxide to ester.

In the case of nickel it was necessary to considerably improve the procedure[7,8] for the preparation of the Raney nickel catalyst before it could be consistently and effectively used for the hydrogenation of esters. However, with copper chromium oxide no improvement in the catalyst as used since 1930 is necessary, in order to take full advantage of the effectiveness of a high ratio of catalyst in lowering the temperature for the hydrogenation of esters 75–100° below that required with the conventional amount of catalyst. One of the advantages in the lower temperature for the hydrogenation of esters is that 1,3-glycols have now been prepared in almost quantitative yields by the hydrogenation of malonates, β-keto and β-hydroxy esters. With the conventional ratio of catalyst, glycols of this type could not be prepared by hydrogenation as the esters underwent cleavage with the formation of alcohols.

The effectiveness of a high ratio of catalyst is not dependent upon a proportional increase in the rate of hydrogenation. There is, for example, with a laurate no significant amount of hydrogenation at 200–210° with 5% as much catalyst as ester, no matter how long the period of exposure. However, with as much catalyst as ester the hydrogenation proceeds to completion at 150° within a few hours. The effects of ratio of catalyst, temperature of reaction and pressure of hydrogen for the hydrogenation of ethyl lactate and piperidinoacetate over W-6 Raney nickel, have been presented in another paper.[9]

In order to secure the maximum rate of hydrogenation, it appeared advisable to use a weight of catalyst as great or greater than the weight of ester. In the results reported in Tables I, II and III the weight of catalyst is 1.5 times the weight of ester. In some, if not in all, cases this ratio of catalyst is excessive. Mozingo and Folkers[5,6] used 20 to 50% as much catalyst as ester in the hydrogenation of four acetoacetates and three mal-

TABLE I

HYDROGENATION OF ESTERS OVER COPPER–CHROMIUM OXIDE

10 g. of ester in 75 ml. of dry ethanol with 15 g. of catalyst at 5000 p. s. i.

Ester	Time, hours	Yield[a] of products
Ethyl lactate	0.2[b]	1,2-Propanediol
Diethyl tartrate	9.0[b]	1,2,3,4-Butanetetrol
Diethyl malate	3.0[c]	67% 1,2,4-Butanetriol 20% 1,4-Butanediol
Ethyl mandelate	0.2[b]	1-Phenyl-1,2-ethanediol
Ethyl α-hydroxy-isobutyrate	0.2[b]	1,1-Dimethyl-1,2-ethanediol
Ethyl acetoacetate	8.5[c]	1,3-Butanediol
Ethyl α-acetobutyrate	6.5[c]	2-Ethyl-1,3-butanediol
Ethyl α-benzoylacetate	6.5[c]	3-Phenyl-1-propanol
Diethyl acetone-dicarboxylate	5.0[c]	60% 1,3,5-Pentanetriol 12% Ethyl β-hydroxyglutarate
Diethyl succinate	4.0[c]	1,4-Butanediol
Diethyl glutarate	10.0[c]	1,5-Pentanediol
Diethyl adipate	12.0[c]	1,6-Hexanediol
Methyl laurate	13.5[c]	1-Dodecanol
Ethyl piperidinoacetate	2.2[b]	2-Piperidino-1-ethanol
Diethyl malonate	11.0[c]	40% 1,3-Propanediol
Diethyl methylmalonate	4.5[c]	2-Methyl-1,3-propanediol
Diethyl ethylmalonate	6.5[c]	2-Ethyl-1,3-propanediol
Diethyl *n*-propylmalonate	8.0[c]	2-(*n*-Propyl)-1,3-propanediol
Diethyl *n*-butylmalonate	9.0[c]	2-(*n*-Butyl)-1,3-propanediol
Diethyl *n*-heptylmalonate	11.0[c]	2-(*n*-Heptyl)-1,3-propanediol
Diethyl phenylmalonate	1.0[c]	50% 2-Phenyl-1,3-propanediol 32% 2-Phenyl-1-ethanol
Diethyl benzalmalonate	5.5[c]	2-Benzyl-1,3-propanediol
Diethyl ethoxymethylenemalonate	5.0[c]	2-Methyl-1,3-propanediol
Diethyl ethyl-*n*-butylmalonate	13.0[c]	45% 2-Ethyl-2-(*n*-butyl)-1,3-propanediol 28% Ethyl 2-hydroxymethyl-2-ethyl-*n*-caproate

[a] Except as noted only a single product was apparently formed; however, due to losses on the catalyst and in distillation the yield actually isolated was approximately 80% of the theoretical. [b] at 125°. [c] at 150°.

(1) Monsanto Chemical Co. Fellow, 1946 and 1947.

(2) Christman and Levene, *J. Biol. Chem.*, **124**, 453 (1938); Ovakimian, Kuna and Levene, *ibid.*, **134**, 151 (1940); **135**, 91 (1940).

(3) Albert A. Pavlic, Ph.D. Thesis, University of Wisconsin, 1942.

(4) Adkins and Pavlic, THIS JOURNAL, **69**, 3039 (1947).

(5) Mozingo and Folkers, *ibid.*, **70**, 227 (1948).

(6) Mozingo and Folkers, *ibid.*, **70**, 229 (1948).

(7) Pavlic and Adkins, *ibid.*, **68**, 1471 (1946).

(8) Adkins and Billica, *ibid.*, **70**, 695 (1948).

(9) Adkins and Billica, *ibid.*, **70**, 000 (1948).

TABLE II

HYDROGENATION OF α-AMINO ESTERS OVER RANEY NICKEL

10 g. of ester in 35 ml. of dry ethanol with 15 g. of catalyst at 100° and 5000 p. s. i.

Ester	Time, hours	Yield[a] of products
Ethyl piperidinoacetate	1.7[b]	2-Piperidino-1-ethanol
Ethyl piperidinoacetate	10.0[c]	2-Piperidino-1-ethanol
5-Carbethoxy-2-pyrrolidone	14.0[d]	5-Hydroxymethyl-2-pyrrolidone
1-Amino-1-carbethoxycyclohexane	0.8[e]	1-Amino-1-hydroxymethylcyclohexane
1-Amino-1-carbethoxycyclopentane	1.0[e]	1-Amino-1-hydroxymethylcyclopentane
Ethyl α-amino-α-phenylpropionate	4.0[e]	2-Amino-2-cyclohexyl-1-propanol
Ethyl α-amino-isobutyrate	0.8[e]	2-Amino-2-methyl-1-propanol
Ethyl α-amino-α-methylisocaproate	0.8[b]	2-Amino-2,4-dimethyl-1-pentanol
Ethyl sarcosinate	1.5[e]	63% 2-(N-Methylamino)-1-ethanol
Ethyl N-phenylglycinate	3.0[e]	2-(N-Cyclohexylamino)-1-ethanol
Ethyl N-phenylglycinate	25.0[c]	2-(N-Cyclohexylamino)-1-ethanol
Diethyl oximinomalonate	0.5[b]	2-Amino-1,3-propanediol
Ethyl oximinoacetoacetate	0.2[b]	2-Amino-1,3-butanediol
Ethyl alaninate	2.5[e]	2-Amino-1-propanol
Ethyl β-phenylalaninate	9.0[e]	2-Amino-3-cyclohexyl-1-propanol
Ethyl hippurate	4.0[e]	2-(N-Hexahydrobenzoylamino)-1-ethanol
Ethyl tyrosinate	6.0[b]	2-Amino-3-(4-hydroxycyclohexyl)-1-propanol
Diethyl aminomethylenemalonate	1.0[b]	Diethyl methylmalonate
Ethyl β-piperidinopropionate	3.0[b]	5–10% 3-Piperidino-1-propanol, 72% piperidine and ethyl propionate

[a] Except as noted; only a single product was apparently formed; however, due to losses on the catalyst and in distillation the yield actually isolated was approximately 80% of the theoretical. [b] W-6 Raney nickel. [c] This hydrogenation was at 26° with W-6 Raney nickel. [d] W-4 Raney nickel. [e] W-5 Raney nickel.

onates, at about 160° for periods averaging about thirteen hours. They have reported yields of glycols averaging about 40%. A comparison of their results with those reported in Table III shows the very considerable advantage in yields, and in a lower temperature of reaction and in more rapid hydrogenations, of the higher ratio of catalyst to ester recorded in Table III.

The feasibility of hydrogenating an α-hydroxy ester, over copper chromium oxide at 125° to the corresponding glycol, was demonstrated some time ago in the case of ethyl benzilate.[10] Other examples have not been reported although N. R. Trenner and F. A. Bacher of the Merck Laboratories deserve credit and priority for achieving in 1940 the hydrogenation of a tartrate to 1,2,3,-4-butanetetrol. The data in Table I show that a variety of β-keto and α- and β-hydroxy esters and variously substituted malonates are rapidly and almost quantitatively converted to the corresponding glycols, triols or tetrols over copper chromium oxide at 125–150°. The yields from five other esters averaged 60%. A high ratio of catalyst to ester is so effective that diethyl succinate, glutarate and adipate and methyl laurate were quantitatively hydrogenated after four to thirteen hours at 150°, even though these esters carry no activating group.

The data given in Table II show that a variety of α-amino and oximino esters may be hydrogenated rapidly and quantitatively to the corresponding amino alcohols over W-6 and W-5 Raney nickel. The more active W-6 Raney nickel catalyst had not been developed at the time certain of the esters were studied; however, the results with the W-5 catalyst are not susceptible to much improvement. The temperature used (100°) is unnecessarily high as the hydrogenation of at least some of the esters proceeds to completion at a feasible rate even at 25°. It would be safer, particularly with the W-6 catalyst, to carry out the hydrogenations in the range 25–75°. The hydrogenation of ethyl N-phenylglycinate went with almost explosive violence at 100° with the W-6 catalyst.

One of the limitations on the procedure described with Raney nickel is the fact that all attempts to avoid the hydrogenation of a phenyl group failed. Thus the phenyl substituted esters gave cyclohexyl substituted amino alcohols. There was no alkylation of amino groups or hydrogenolysis, except in the case of diethyl aminomethylenemalonate. The amide linkages in a carbethoxy pyrrolidone and a hippurate were not hydrogenated while the ester group was being converted to carbinol group. The β-substituted amino ester ethyl β-piperidinopropionate underwent cleavage as the chief reaction with only a low yield of the desired piperidino alcohol. Another β-substituted amino ester, ethyl nipecotate, did not react with hydrogen over the W-5 catalyst at 100° and 5000 p.s.i.

Several α-hydroxy esters (see Table III) were hydrogenated over W-6 Raney nickel to the corresponding glycols at 25 to 100°. The yields from ethyl lactate, diethyl tartrate, ethyl β,β-dimethyl-α-hydroxybutyrate and ethyl α-hydroxy-

(10) Adkins, Wojcik and Covert, THIS JOURNAL, 55, 1673 (1933).

TABLE III

HYDROGENATION OF α- AND β-OXYGEN SUBSTITUTED ESTERS OVER W-6 RANEY NICKEL

10 g. ester in 25–75 ml. of dry ethanol with 15 g. catalyst at 5000 p. s. i.

Ester	Time, hours	Yield[a] of products
Ethyl lactate[e]	1.5[b]	1,2-Propanediol
Ethyl lactate[e]	13.0[c]	1,2-Propanediol
iso-Propyl lactate[e]	5.5[b]	1,2-Propanediol
Diethyl tartrate	10.0[b]	1,2,3,4-Butanetetrol
Diethyl malate	14.0[b]	48–53% 1,2,4-Butanetriol 25–30% 1,4-Butanediol and ethyl β,γ-dihydroxybutyrate
Ethyl mandelate	1.3[b]	32–53% 1-Cyclohexyl 1,2-ethanediol 24–12% 2-Cyclohexyl-1-ethanol 24–16% Ethyl cyclohexylacetate
Ethyl benzilate	6.0[b]	60% Ethyl dicyclohexylacetate 12% 1,1-Dicyclohexyl-1,2-ethanediol
Diethyl hydroxymethylenemalonate	5.0[b]	Diethyl methylmalonate
Ethyl α,β-dioxobutyrate	4.0[b]	80% 1,2,3-Butanediol
Diethyl oxomalonate	5.5[b]	50% Glycerol 16% Diethyl malonate
Ethyl α-hydroxy-β,β-dimethylbutyrate	15.0[b]	3,3-Dimethyl-1,2-butanediol
Diethyl ethoxymethylenemalonate	11.0[d]	32% 2-Methyl-1,3-propanediol 14% Diethyl methylmalonate
Diethyl ethylmalonate	24[d]	34% 2-Ethyl-1,3-propanediol
Diethyl *n*-propylmalonate	23[d]	11% 2-(*n*-Propyl)-1,3-propanediol
Diethyl *n*-butylmalonate	24[d]	7% 2-(*n*-Butyl)-1,3-propanediol
Diethyl *n*-heptylmalonate	21[d]	4% 2-(*n*-Heptyl)-1,3-propanediol
Diethyl ethyl-*n*-butylmalonate	24[d]	No reaction
Ethyl α-hydroxy-isobutyrate[e]	2.0[b]	1,1-Dimethyl-1,2-ethanediol
Ethyl acetoacetate[e]	6.0[d]	48% 1,3-Butanediol 27% Ethyl-β-hydroxybutyrate
Ethyl α-acetobutyrate[e]	13.0[d]	Ethyl α-ethyl-β-hydroxybutyrate
Ethyl acetone-dicarboxylate[e]	24.0[d]	36% Ethyl β-hydroxyglutarate 30% 1,3,5-Pentanetriol

[a] Except as noted, only a single product was apparently formed; however, due to losses on the catalyst and in distillation the yield actually isolated was approximately 80% of the theoretical. [b] at 100°. [c] at 25°. [d] at 125°, see warning in reference 8. [e] The reaction mixture contained 1–2 ml. of triethylamine.

isobutyrate were practically quantitative. From a malate, mandelate, α,β-dioxobutyrate and oxomalonate, the yields were 40–80% with considerable hydrogenolysis of hydroxyl groups. Certain β-oxygenated esters including substituted malonates, α-acetobutyrate and acetonedicarboxylate also underwent hydrogenation over W-6 Raney nickel but the yield of the corresponding hydroxy compounds was rather low due to hydrogenolysis. The difficulty of hydrogenating substituted malonates increased as the size of the substituent increased. However, as good, and in most cases much better, yields can be obtained from the esters referred to in this paragraph, through the use of copper chromium oxide instead of Raney nickel.

Experimental Part

The hydrogenations were carried out in the standard steel reaction tubes with rocking. One of those used had a void of 98 ml. and the other 270 ml. One or the other was used depending upon the hydrogen requirement of the amount of compound to be hydrogenated, a pressure drop of 700–1000 p. s. i. being desirable. The reaction mixture was made up either to 50 or 100 ml. with commercial absolute alcohol, depending upon which of the bombs was to be used. The procedure for the preparation of the Raney nickel has been recently published,[8] while the copper–chromium oxide catalyst was made by the usual procedure.

The esters of the amino acids were prepared by the following procedure: dry ethanol stored over magnesium ethoxide was distilled into a flask containing 50 g. of the amino acid, until the volume of the reaction mixture was 200–250 ml. Dry hydrogen chloride, with cooling, was passed into the ethanol until it was saturated, and the mixture allowed to stand overnight at room temperature, and was then refluxed for six to eight hours. The excess ethanol and hydrogen chloride was distilled out under reduced pressure. The crude ester hydrochloride was suspended in a mixture of 80 ml. of dry ethanol; and 700 ml. of dry ether, 200 g. of anhydrous barium oxide was added and the mixture rapidly stirred for thirty to forty hours. The mixture was then filtered and the solid washed once by trituration with absolute ether. The desired ester was distilled under reduced pressure after the distillation of the ether.

5-Carbethoxy-2-pyrrolidone was prepared from the crude hydrochloride of diethyl glutamate; as obtained in the procedure described above. The sirup from the esterification was diluted with 200 ml. of commercial absolute alcohol, the acid neutralized by potassium hydroxide in ethanol, the potassium chloride filtered off and the ethanol distilled off under reduced pressure. The crude diethyl glutamate was heated to 140–150° under reduced pressure for an hour or until frothing and bubbling ceased. The desired ester was distilled through a Vigreux column 6–8 cm. in length at 152–153° (3 mm.). The ester crystallized to colorless needles, m. p. 51–53°.[11]

Five α-amino acids were prepared from ketones through hydantoins by the method of Bucherer and Lieb.[12] The hydantoins were hydrolyzed in 60% sulfuric acid at 140–150°. The hydrosulfates of the amino acids crystallized out when the reaction mixtures were cooled, and the free amino acids were obtained after removal of the sulfate ion with barium carbonate. The acids were esterified by the procedure described above. The yields and properties of the hydantoins, amino acids and ethyl esters were as follows:

5-Pentamethylhydantoin (150 g.), m. p. 213–215°, from cyclohexanone (98 g.).

5,5-Dimethylhydantoin (100 g.), m. p. 173–175°, from acetone (60 g.).

5-Methyl-5-isobutylhydantoin (155 g.), m. p. 144–144.5°, from methyl isobutyl ketone (120 g.). *Anal.* Calcd. for $C_8H_{14}O_2N_2$: N, 16.45. Found: N, 16.60.

5-Methyl-5-phenylhydantoin (104 g.), m. p. 195–196°, from acetophenone (150 g.).

5-Tetramethylenehydantoin (167 g.), m. p. 203° dec., from cyclopentanone (105 g.). *Anal.* Calcd. for $C_7H_{10}O_2N_2$: N, 18.17. Found: N, 18.50.

1-Amino-cyclohexane-1-carboxylic acid was obtained in plates (65 g., 52% yield), m. p. 318–319°.[13]

The ethyl ester (25 g., 45% yield) distilled 78–79° (4 mm.), $n^{20}D$ 1.4603, neut. equiv. 171.4 (calcd. 171.2), hydrochloride m. p. 194–195°. *Anal.* Calcd. for $C_9H_{17}O_2N$: N, 8.18. Found: N, 8.12.

α-Amino-isobutyric acid (92% yield) was obtained in crystals which sublime over 280° and decompose explosively upon rapid heating. The ethyl ester (32 g., 50% yield) was distilled 43–44° (12 mm.), $n^{20}D$ 1.4167,[14,15]

(11) Fischer and Boehner, *Ber.*, **44**, 1333 (1911).

(12) Bucherer and Lieb, *J. prakt. Chem.*, **141**, 5 (1934).

(13) Zelinsky, Annenkow and Kulikow, *Z. physik. Chem.*, **73**, 466 (1910).

(14) Barker and Skinner, THIS JOURNAL, **46**, 405 (1924).

(15) Zelinsky, Annenkow and Kulikow, *Z. physik. Chem.*, **73**, 461 (1910).

neut. equiv. 132.6 (calcd. 131.2), hydrochloride m. p. 158–159°, picrate m. p. 184.5°.

α-Amino-α-methylisocaproic acid was obtained in needles (69.5 g., 66% yield) which sublime above 203°. *Anal.* Calcd. for $C_8H_{15}O_2N$: N, 9.65. Found: N, 9.47. The ethyl ester (38.7 g., 65% yield) distilled 78–80° (12 mm.), $n^{20}D$ 1.4290, d^{20} 0.9145, neut. equiv. 173.4 (calcd. 173.3), chloroplatinate m. p. 162–163°, hydrochloride m. p. 85–86° with softening above 83°. *Anal.* Calcd. for $C_9H_{19}O_2N$: N, 8.10. Found: N, 8.4.

α-Amino-α-phenylpropionic acid (50.5 g., 58% yield), sublimes above 225°. *Anal.* Calcd. for $C_9H_{11}O_2N$: N, 8.49. Found: N, 8.52. The ethyl ester (24 g. 45% yield) distilled 90–91° (1 mm.), $n^{20}D$ 1.5100, d^{20} 1.0598, picrate m. p. 179.5–180.5°, hydrochloride m. p. 143–144°, with softening 139°. *Anal.* Calcd. for $C_4H_{15}O_2N$: N, 7.25. Found: N, 7.17.

1-Aminocyclopentane-1-carboxylic acid was obtained in plates (111 g., 88% yield), m. p. 320–330° in a sealed tube. The ethyl ester (17 g. 26% yield) distilled 110–112° (36 mm.), $n^{20}D$ 1.4535,[16] hydrochloride m. p. 198–200°, picrate m. p. 166–167°.

Other esters submitted to hydrogenation were prepared from the corresponding acids or by other standard methods. Certain data on these esters are summarized below.

Ethyl piperidonoacetate (45 g. 80% yield), distilled at 93–94° (11 mm.) 109–111° (25 mm.), 104–106° (20 mm.), $n^{25}D$ 1.4518, picrate m. p. 118–119°.

Ethyl β-phenylalaninate distilled at 113–114° (3 mm.) picrate m. p. 155–156°.

Ethyl alaninate distilled at 34–35° (5 mm.), $n^{20}D$ 1.4487.

Ethyl tyrosinate (38 g., 66% yield) had a m. p. 105–107° when recrystallized from ethyl acetate.

Diethyl ethoxymethylenemalonate (60% yield), b. p. 137–140° mm., $n^{20}D$ 1.4626, and diethyl aminomethylenemalonate, m. p. 65.5–66.5°, and diethyl hydroxymethylenemalonate (83% yield), b. p. 92–93° (6 mm.), were prepared as described by Claisen.[17]

Ethyl mandelate (54 g., 92% yield) from mandelic acid, distilled at 98–99° (2 mm.) and 252–254° (745 mm.).[18]

Ethyl benzilate (29 g., 51% yield) from benzilic acid distilled at 138–140° (1 mm.)[19] and gave crystals, m. p. 23–28°.

Diethyl tartrate (57 g., 84% yield), from tartaric acid, distilled at 131–131.5° (5 mm.), $n^{25}D$ 1.4454.[20]

Diethyl malate (34 g., 60% yield) from *l*-malic acid distilled at 91–92° (1 mm.), 103–105° (2–3 mm.), $n^{25}D$ 1.4340, $n^{20}D$ 1.4361.

Diethyl oxomalonate, b. p. 68–71° (2 mm.), 2,4-dinitrophenylhydrazone, m. p. 117–118.5, was prepared by Dox's procedure.[21]

Ethyl α,β-diketobutyrate (6 g.), b. p. 80–90° (20–25 mm.), was obtained by a similar procedure in very low yield from acetoacetic ester. The reaction went with almost explosive violence.

The products of hydrogenation were isolated and characterized as described below:

5-Hydroxymethyl-2-pyrrolidone distilled 175–176° (1 mm.) and crystallized at m. p. 86–87°.[22]

5-Piperidino-1-ethanol distilled at 90–91.5° (17 mm.), $n^{25}D$ 1.4749, neut. equiv. 130 (calcd. 129.2).

1-Amino-1-hydroxymethyl-cyclohexane distilled at 117–118 (27 mm.), $n^{20}D$ 1.4970, neut. equiv. 129 (calcd. 129.2), hydrochloride m. p. 158–159°. *Anal.* Calcd. for $C_7H_{15}ON$: N, 10.83. Found: N, 10.71.

1-Amino-1-hydroxymethyl-cyclopentane distilled at 68–69° (1 mm.), $n^{20}D$ 1.4899, $n^{25}D$ 1.4879 (partially solidified to colorless needles), neut. equiv. 115 (calcd. 115), hydrochloride m. p. 130–131.5° with softening at 127°, picrate m. p. 106–107.5°. *Anal.* Calcd. for $C_6H_{13}ON$: N, 12.16. Found: N, 11.92.

2-Amino-2-cyclohexyl-1-propanol distilled at 103–104° (2 mm.), solidified to needles, m. p. 79.5–80.5°, after recrystallization from ether, neut. equiv. 157 (calcd. 157), hydrochloride m. p. 201.5–202°. *Anal.* Calcd. for $C_9H_{19}ON$: N, 8.91. Found: N, 9.12.

2-Amino-2-methyl-1-propanol distilled at 68–69°(10 mm.), $n^{20}D$ 1.4486, d^{20} 0.9316, neut. equiv. 89.8 (calcd. 89.2), hydrochloride m. p. 204–205°.[23] *Anal.* Calcd. for $C_4H_{11}ON$: N, 15.70. Found: N, 15.53.

2-Amino-2,4-dimethyl-1-pentanol distilled at 98–98.5° (12 mm.), $n^{20}D$ 1.4563, d^{20} 0.9060, neut. equiv. 131.3 (calcd. 131.2), chloroplatinate m. p. 169–169.5°. *Anal.* Calcd. for $C_7H_{17}ON$: N, 10.66. Found: N, 10.57.

2-(N-Methylamino)-1-ethanol distilled at 55.7° (11 mm.), $n^{20}D$ 1.4385,[24] picrate m. p. 147–148°.

2-(N-Cyclohexylamino)-1-ethanol distilled at 96.5–97° (3 mm.), 128–129° (16 mm.), $n^{20}D$ 1.4862, $n^{25}D$ 1.4859, d^{20} 0.9788, neut. equiv. 143.1 (calcd. 143.2), picrate m. p. 129–130°. *Anal.* Calcd. for $C_9H_{17}ON$: N, 9.78. Found: N, 9.86.

2-Amino-1,3-propanediol distilled at 115–116° (1 mm.), $n^{20}D$ 1.4891, neut. equiv. 91.3 (calcd. 91.1), hydrochloride m. p. 96–97.5°. The compound could be best isolated as the oxalate from dry ethanol. The oxalate recrystallized from ethanol–water had m. p. 199–201°.[25]

2-Amino-1-propanol distilled at 79.5–80° (18 mm.), $n^{20}D$ 1.4502, $n^{25}D$ 1.4482, neut. equiv. 75.3 (calcd. 71.1), picrate m. p. 112–114°.

2-Amino-3-cyclohexyl-1-propanol distilled at 107–108° (1 mm.), $n^{20}D$ 1.4989, $n^{25}D$ 1.4968, neut. equiv. 160.8 (calcd. 157.3), hydrochloride m. p. 190–192° with softening 185°, chloroplatinate m. p. 175–176° dec. *Anal.* Calcd. for $C_9H_{19}ON$: N, 8.91. Found: N, 8.88.

2-(N-Hexahydrobenzoylamino)-1-ethanol solidified, m. p. 80–80.5°, recrystallized from ether. *Anal.* Calcd. for $C_9H_{17}O_2N$: N, 8.18. Found: N, 8.15. After hydrolysis of the compound with 10% sulfuric acid, hexahydrobenzoic acid, m. p. 29.5–30°, and ethanolamine as the picrate, m. p. 159.5–160°, were obtained.

2-Amino-3-(4-hydroxycyclohexyl)-1-propanol distilled at 190–195° (1–2 mm.) as clear, colorless pitch-like material, neut. equiv. 173.4 (calcd. 173.2), neutral oxalate, m. p. 199.5–200.5°. *Anal.* of oxalate. Calcd. for $(C_9H_{19}O_2N)_2\cdot(CO_2H)_2$: N, 6.4. Found: N, 6.3.

2-Amino-1,3-butanediol distilled at 112–113° (2 mm.), $n^{21}D$ 1.4833, neut. equiv. 104.9 (calcd. 105.2), oxalate m. p. 195–195.5° dec. *Anal.* Calcd. for $C_4H_{11}O_2N$: N, 13.32. Found: N, 13.49.

1,2-Propanediol distilled at 97° (20 mm.),[26] $n^{20}D$ 1.4305,[27] phenylurethan m. p. 150°.[28]

1,2,3,4-Butanetetrol (erythritol) crystallized, m. p. 88–89° after recrystallization from ethanol, dibenzylidene derivative m. p. 204° after recrystallization from ethanol.[29]

1,2,4-Butanetriol[30] distilled at 132–133.5° (1 mm.), $n^{20}D$ 1.4688, triphenylurethan m. p. 146–149°.[31]

1-Cyclohexyl-1,2-ethanediol distilled at 110–112° (1 mm.), solidified to crystalline mass, m. p. 42–43°,[32] phenylurethan m. p. 100.5–101.2°.

2-Cyclohexyl-1-ethanol distilled at 82–90° (1–2 mm.), $n^{25}D$ 1.4640, $n^{20}D$ 1.4647,[33] phenylurethan m. p. 119.5–120.5°.

Ethyl cyclohexylacetate distilled at 71–74° (2 mm.),[34]

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$n^{20}D$ 1.4500.[35] After saponification cyclohexylacetic acid, b. p. 155–157° (40 mm.), m. p. 27°, was obtained.[36]

1-Phenyl-1,2-ethanediol crystallized, m. p. 67.5–68.5°[37] after recrystallization from petroleum ether, phenylurethan m. p. 149–150°.

Ethyl dicyclohexylacetate distilled at 127.5–130° (1 mm.), $n^{20}D$ 1.4809, $n^{25}D$ 1.4791, d^{20} 0.9859. Analysis for active hydrogen with methylmagnesium iodide indicated one carbonyl group per molecule. The ester resisted saponification. *Anal.* Calcd. for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 75.91; H, 11.47.

1,1-Dicyclohexyl-1,2-ethanediol distilled at 132–135° (2 mm.), $n^{20}D$ 1.4840, d^{20} 0.9957. Two active hydrogens and no carbonyl group per molecule were indicated by Grignard analysis. *Anal.* Calcd. for $C_{14}H_{26}O_2$: C, 74.30; H, 11.54. Found: C, 74.7; H, 11.16.

Diethyl malonate of characteristic odor distilled at 55–57° (3 mm.), $n^{20}D$ 1.4170, and gave malonic acid, m. p. 131–135°.

Glycerol distilled at 130–131° (2 mm.), $n^{20}D$ 1.4701, phenylurethan m. p. 181.2°.

2-Methyl-1,3-propanediol distilled at 83.5–84°[38] (3 mm.), $n^{25}D$ 1.4430, phenylurethan m. p. 125–125°.

1,2,3-Butanetriol distilled at 83–85° (2 mm.), $n^{21.4}D$ 1.4527.[39]

3,3-Dimethyl-1,2-butanediol distilled at 57–61° (2 mm.), solidified[40] to colorless plates, m. p. 48–49°.

1,1-Dimethyl-1,2-ethanediol distilled at 79–80° (12 mm.), 117° (743 mm.),[41] $n^{25}D$ 1.4340, d^{25} 0.9896, phenylurethan, m. p. 136.7°.

Ethyl β-hydroxybutyrate distilled at 77–80° (15 mm.),[42] $n^{25}D$ 1.4200, d^{25} 1.0052, M_R calcd. 33.65, found 33.27.

1,3-Butanediol distilled at 106–108° (14 mm.),[43] $n^{25}D$ 1.4381, d^{25} 1.0002, phenylurethan m. p. 115–116°, M_R calcd. 23.72, found 23.66.

Ethyl α-ethyl-β-hydroxybutyrate distilled at 95–100° (14–15 mm.),[44] $n^{25}D$ 1.4290, d^{25} 0.9714, M_R calcd. 42.39, found 42.51.

2-Ethyl-1,3-butanediol distilled at 86–88° (2 mm.), $n^{25}D$ 1.4473, d^{25} 0.9677, M_R calcd. 32.95, found 32.65, phenylurethan m. p. 134–135°. *Anal.* Calcd. for $C_6H_{14}O_2$: C, 60.98; H, 11.94. Found: C, 60.74; H, 11.77.

5-Phenyl-1-propanol distilled at 86–88° (2 mm.),[45] $n^{25}D$ 1.5218, phenylurethan m. p. 48°.

Diethyl β-hydroxyglutarate[46] distilled at 98–101° (1–2 mm.), $n^{25}D$ 1.4371, d^{25} 1.0814, M_R calcd. 49.23, found 49.47, phenylurethan m. p. 146.5–148°.

1,3,5-Pentanetriol distilled at 138–140° (1 mm.),[47] $n^{25}D$ 1.4594, d^{25} 1.1036, M_R calcd. 29.87, found 29.77, phenylurethan m. p. 151–152°.

2-Ethyl-1,3-propanediol distilled at 83–86° (1–2 mm.), $n^{20}D$ 1.4480, $n^{25}D$ 1.4471, d^{20} 0.9970, phenylurethan m. p. 123–123.5°, 3,5-dinitrobenzoate m. p. 129–130°. *Anal.* Calcd. for $C_5H_{12}O_2$: C, 57.66; H, 11.62. Found: C, 57.43; H, 11.47.

2-(*n*-Propyl)-1,3-propanediol distilled at 96–98° (3 mm.), $n^{25}D$ 1.4480, d^{25} 0.9636, M_R 32.83, calcd. 32.95, phenylurethan m. p. 124.5–125.5°. *Anal.* Calcd. for $C_6H_{14}O_2$: C, 60.98; H, 11.94. Found: C, 60.96; H, 11.88.

2-(*n*-Butyl)-1,3-propanediol distilled at 98–100° (2 mm.), $n^{25}D$ 1.4492, d^{25} 0.9461, M_R 37.49, calcd. 37.57, phenylurethan m. p. 130–131°. *Anal.* Calcd. for $C_7H_{16}O_2$: C, 63.59; H, 12.02. Found: C, 63.59; H, 12.02.

2-(*n*-Heptyl)-1,3-propanediol distilled at 128–130° (2 mm.), $n^{25}D$ 1.4488; solidified to fibrous crystals, m. p. 32.0–32.1°, phenylurethan m. p. 107–108.5°. *Anal.* Calcd. for $C_{10}H_{22}O_2$: C, 68.91; H, 12.75. Found: C, 68.87; H, 12.66.

2-Ethyl-2-(*n*-butyl)-1,3-propanediol distilled at 110–110.5° (2 mm.), $n^{25}D$ 1.4587, solidified to needles m. p. 38.5–39.5°. *Anal.* Calcd. for $C_9H_{20}O_2$: C, 67.45; H, 12.58. Found: C, 67.39; H, 12.69.

Ethyl 2-hydroxymethyl-2-ethyl-caproate distilled at 95–96° (2 mm.), $n^{25}D$ 1.4350, d^{25} 0.9359, M_R found 56.03, calcd. 56.08. *Anal.* Calcd. for $C_{11}H_{22}O_3$: C, 65.03; H, 10.96. Found: C, 65.12; H, 10.78.

Diethyl cyclohexylmalonate distilled at 95–98° (1 mm.), $n^{25}D$ 1.4550. After saponification cyclohexylmalonic acid, m. p. 175–177° was obtained.[48]

Ethyl cyclohexylacetate distilled at 64–70° (1 mm.),[52] $n^{25}D$ 1.4465,[53] and gave cyclohexylacetic acid, b. p. 156° (40 mm.),[55] m. p. 27°.[54]

2-Phenyl-1,3-propanediol distilled at 136–137° (2 mm.),[49] $n^{25}D$ 1.5348, solidified to fibrous crystals, m. p. 48.5–49°, with softening at 46°, phenylurethan m. p. 136.5–138°.

2-Phenylethanol distilled at 73–76° (2–3 mm.),[50] $n^{25}D$ 1.5251,[51] phenylurethan m. p. 79–80°.

2-Benzyl-1,3-propanediol distilled at 155–156° (3 mm.), crystallized to hexagonal plates, m. p. 67–68°, softening above 65°, phenylurethan, m. p. 68–70°. *Anal.* Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.36; H, 8.14.

1,4-Butanediol distilled at 102° (2 mm.), m. p. 16–17.5°,[56] $n^{25}D$ 1.4445, phenylurethan m. p. 183–183.5°.

1,5-Pentanediol distilled 122–127 (7 mm.),[57] $n^{25}D$ 1.4490, phenylurethan 172–172°.

1,6-Hexanediol distilled 124–125° (5 mm.), crystallized m. p. 42–43°,[45] phenylurethan m. p. 170–171°

1-Dodecanol distilled 117° (4 mm.), solidified to needles, m. p. 23–24°, phenylurethan m. p. 73–74°.

Summary

The effectiveness of a high ratio of catalyst in achieving the hydrogenation of esters to glycols or amino-alcohols has been shown for numerous esters. A high ratio of catalyst permits a much lower temperature of hydrogenation, so that hydrogenolysis of even 1,3-glycols may be avoided. W-6 Raney nickel is an effective catalyst at 25–100° for the hydrogenation of α-amino and -hydroxy esters to the corresponding aminoalcohols or glycols. Copper–chromium oxide is effective against many α-substituted esters and also against β-keto and -hydroxy esters and malonates in the temperature range 125–150°. It is the preferred catalyst unless hydrogenation at temperatures below 100° is advisable.

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