In one of the two cases investigated the action of free oxygen on the magnesium derivative resulted in the formation of equimolar quantities of an unsaturated ketone and a new type of oxanol. In the other case the oxidation product was an alpha hydroxy ketone.

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[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY, UNIVERSITY OF WISCONSIN]

HYDROGENOLYSIS OF OXYGENATED ORGANIC COMPOUNDS

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This paper deals with the cleavage of carbon to carbon or carbon to oxygen bonds accompanied by the addition of hydrogen. This type of reaction applied to hydrocarbons has been referred to by Ellis[2] as "hydrogenolysis," since it is clearly analogous to the reactions commonly termed hydrolysis, alcoholysis and ammonolysis which involve the *cleavage* of a bond *accompanied* by the *addition* of water, alcohol or ammonia.

$$CH_3COCR_2COOC_2H_5 \xrightarrow{H_2O} \underset{\text{Hydrolysis}}{CH_3COOH + R_2CHCOOH + C_2H_5OH} \qquad (I)$$

$$CH_3CHOHCR_2COOC_2H_5 \xrightarrow{H_2} \underset{\text{Hydrogenolysis}}{2C_2H_5OH + R_2CHCH_2OH} \qquad (II)$$

The cleavage of oxygenated organic compounds with addition of hydrogen has been observed several times to occur as the result of the action of hydrogen in the presence of a catalyst. Recently the use of higher pressures of hydrogen and especially of the copper–chromium oxide catalyst has greatly extended the field of operation and rendered more important the application of hydrogenolysis as a tool in the transformation of organic compounds.

Previous work in this Laboratory has shown that the linkages indicated by dotted lines in the formulas I to VII are susceptible to hydrogenolysis over a copper–chromium oxide catalyst.

$$\underset{\text{I}^{3}}{C_6H_5CHR....OH} \quad \underset{\text{II}^{4}}{C_6H_5CHRCH_2....OH} \quad \underset{\text{III}^{5}}{HO....CHRCH_2COOEt} \quad \underset{\text{IV}^{4}}{RC(=O)....OC_2H_5}$$

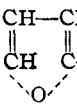
[1] The authors are indebted to E. I. du Pont de Nemours and Company for the support of a fellowship enjoyed by Dr. Connor during the academic year 1931–1932.

[2] C. Ellis, "Hydrogenation of Organic Substances," 3d ed., D. Van Nostrand Company, New York, 1930, p. 564.

[3] Adkins and Connor, THIS JOURNAL, **53**, 1091 (1931).

[4] Adkins and Folkers, *ibid.*, **53**, 1095 (1931).

[5] Folkers and Adkins, *ibid.*, **54**, 1145 (1932).



V[3]

$CH_3C(OH)....C(CH_3)_2COOEt$

VI[4]

$C_6H_5CH_2....CH(C_6H_5)_2$

VII[6]

The cleavage of similar linkages through the action of hydrogen in the presence of a catalyst has been observed by earlier investigators, among which may be cited the following. Sabatier and Murat[7] noted that the hydrogenation of benzyl alcohol over nickel gave toluene. Sabatier and Mailhe[8] isolated ethyl butyrate, acetone, isopropyl alcohol, propionic acid and dehydroacetic acid from the hydrogenation of acetoacetic ester over nickel. The opening of the furan ring by a platinum catalyst was reported by Adams and Kaufmann.[9] The formation of ethers from acetals was accomplished by nickel catalysts.[10,11] Propanediol-1,2 has been obtained from mannitol over a member of the iron or platinum group.[12]

It was the purpose of the investigation herewith described to increase the information available with regard to the relationship of structure to ease of cleavage with hydrogen, of carbon to oxygen and of carbon to carbon linkages. To this end a number of glycols, β-hydroxy and malonic esters, and furan derivatives have been subjected to the action of hydrogen under pressure in the presence of a copper–chromium–barium oxide catalyst.[13]

In Table I are listed the results of the hydrogenolysis of several glycols, hydroxy esters, substituted malonic esters, and furan derivatives and of certain hydrogenations incidental to the work. The products were characterized in many cases by the preparation of solid derivatives in addition to the usual determination of boiling or melting points or analysis. The iodoform reaction was extensively used for the detection of methyl monalkyl carbinols and the method of Wright for methanol.[14] (For the sake of economy in publication, almost twenty pages describing the experi-

[6] Zartman and Adkins, THIS JOURNAL, **54**, 1668 (1932).

[7] Sabatier and Murat, *Ann. chim.*, [9] **4**, 258 (1915).

[8] Sabatier and Mailhe, *Bull. soc. chim.*, [4] **3**, 232 (1908).

[9] Adams and Kaufmann, THIS JOURNAL, **45**, 3029 (1923).

[10] Sigmund and Marchart, *Monatsh.*, **48**, 267 (1927); Sigmund and Uchaan, *ibid.*, **51**, 234 (1929); Cabanac, *Compt. rend.*, **188**, 1257 (1929).

[11] Covert, Connor and Adkins, THIS JOURNAL, **54**, 1651 (1932).

[12] I. G. Farbenind., German Patent 541,326, October 25, 1927 [*C. A.*, **26**, 1939 (1932)].

[13] The authors believe that the data herewith presented are for the present to be interpreted only as a measure of the influence of various structures upon the ratio of competitive reactions under specified conditions. An attempt to apply these results to the influence of the substituent group upon the strength of bonds (in an electrochemical sense) is not justified because the ratio of rates of competitive reactions may not be at all the same as the ratio of the forces binding the atoms together at the various linkages which are undergoing rupture. *Cf.* Adkins, *J. Chem. Education*, **9**, 1865 (1932).

[14] Wright, *Ind. Eng. Chem.*, **19**, 750 (1927).

TABLE I

HYDROGENATION AND HYDROGENOLYSIS OF VARIOUS ORGANIC COMPOUNDS[a]

No.	Compound	Moles	Catalyst, g.	Time, hrs.	Products
1	Cyclohexanediol-1,3	0.30	3[c]	3.0	Cyclohexanol 95%
2	Cyclohexanediol-1,3	.30	6[c]	0.0	Cyclohexanol 80%
3	Cyclohexanediol-1,2	.25	3[c]	6.3	Cyclohexanol 20%; cyclohexanediol-1,2
4	Cyclohexanediol-1,4	.25	3[c]	8.5	Cyclohexanediol-1,4 96%
5	Propanediol-1,3	.50	3[c]	1.2	Propanol-1 74% (94%)
6	Butanediol-1,3	.50	3[c]	4.5	Butanol-2 65%; butanol-1 17%; butanediol-1,3 9%
7	Butanediol-1,3	.50	3[c]	0	Butanol-2 56%; butanol-1 32%
8	2-Methyl-pentanediol-2,4	.50	3[c]	0.5	Propanol-2 86%; 2-methylpentanol-4 13%
9	2-Methyl-pentanediol-2,4	.29	5[c]	0	Propanol-2 62%; 2-methylpentanol-4 10%
10	Aldol	1.13	2[f]	1.0	Butanediol-1,3 39%; ethanol, butanol and condensation products
11	Aldol	0.82	2[f]	1.2	Butanediol-1,3 41%; ethanol, butanol and condensation products
12	Aldol[h]	1.13	3[b]	4.3	No hydrogenation
13	Diacetone alcohol	0.80	2.0[b]	0.5	2-Methyl-pentanediol-2,4 41%; 2-methyl-pentanol-4, propanol-2
14	Diacetone alcohol	.80	2.0[b]	0.07	2-Methyl-pentanediol-2,4 59%; 2-methyl-pentanol-4 6%; propanol-2 25%
15	Diacetone alcohol	.80	0.5[b]	6.0	2-Methyl-pentanediol-2,4 41%; acetone, propanol-2 42%; diacetone alcohol 0%
16	Diacetone alcohol	.88	3[f]	4.0	2-Methyl-pentanediol-2,4 89%; 2-methyl-pentanol-4 6%
17	Pentanediol-1,2	.50	5[c]	10.0	Pentanediol-1,2 73%; amyl alcohols, traces of butanol and methanol 26%
18	Pinacol	.50	5[c]	10.0	Propanol-2 17%; dimethylisopropylcarbinol 16%; pinacol 63%
19	Glycerol (98%)	.50	5[c]	4.0	Propanediol-1,2 85%; condensation products 12%
20	Pentaerythritol	.75	10[c]	5.0	Isobutanol and methanol 99%
21	Mannitol	.25	5[c]	9.0	Propanediol-1,2 24%; alcohols 22%; condensation products 20%
22	α-Methyl-*d*-glucoside	.25	5[c]	8.0	Propanediol-1,2 23%; alcohols 10%
23	4-Methyl-2,6-dimethylolphenol[i]	.30	6[b]	0.2	Mesitol (2,4,6-trimethylphenol) 50%; di-(2-hydroxy-3,5-dimethylphenyl)methane 25%
24	4-Methyl-2,6-dimethylolphenol[h]	.40	8[b]	5.0	Tar
25	Ethyl acetoacetate	.50	3[c]	8	Ethanol, butanol-1, butanol-2, ethyl butyrate 86%
26	Hexahydrobenzyl β-hydroxybutyrate	.32	5[c]	6	Butanol-1 and butanol-2 (cyclohexylcarbinol) 75%
27	Ethyl hexahydrosalicylate	.20	3[c]	3	2-Methyl-cyclohexanol-1 92%
28	Ethyl α-ethylacetoacetate	.20	3[c]	8	*n*-Butanol 41%; diethylcarbinylcarbinol (containing 7% residual ester) 41%
29	Ethyl α-ethylacetoacetate	.30	5[c]	5	*n*-Butanol 50%; diethylcarbinylcarbinol (containing 2% ester) 47%
30	Ethyl α-isopropylacetoacetate	.30	5[c]	13	Isoamyl alcohol 60%; 3-methyl-2-ethylbutanol-1 27%; ester 2%
31	Ethyl α-*n*-butylacetoacetate	.30	13[c]	26.5	*n*-Hexanol 43%; ethyl caproate 10%; 2-ethyl-butanol-1 21%; loss 18%
32	Ethyl α-hexahydrobenzyl-β-hydroxybutyrate	.20	5[c]	5	3-Cyclohexylpropanol-1 96%
33	Ethyl α-benzylacetoacetate	.20	5[c]	5	3-Phenylpropanol-1 89%
34	Ethyl α-(β-phenethyl)-acetoacetate	.20	5[c]	4.5	4-Phenylbutanol-1 97%
35	Ethyl α-methyl-β-ketovalerate	.18	3[c]	8	Propanol-1 46%
36	Diethyl β-methyl-α,γ-diacetylglutarate	.20	13[c]	16	A di-primary glycol 96%
37	Diethyl β-phenyl-α,γ-diacetylglutarate	.10	8[c]	17	A di-primary glycol 92%
38	Ethyl α,α-diethylacetoacetate	.20	3[c]	8	Diethylcarbinylcarbinol 99%
39	Ethyl α,α-di-*n*-butylacetoacetate	.20	3[c]	10	Di-*n*-butylcarbinylcarbinol 99%
40	Ethylmalonic ester	.50	15[c]	8	Butanol-1 18%; 2-methylbutanol-1 72%
41	Butylmalonic ester	.44	6[c]	9	Hexanol-1 26%; 2-methylhexanol-1 64%
42	Benzylmalonic ester	.31	10[c]	8	3-Phenylpropanol-1 19%; 2-benzylpropanol-1 68%
43	Phenylmalonic ester	.30	10[c]	8	Ethylbenzene 71%; β-phenylethanol 9%
44	Dimethylmalonic ester	2.39	30[c]	4	Isobutanol 88%; 2,2-dimethylpropanediol-1,3 5%
45	Methylethylmalonic ester	1.22	15[c]	5	2-Methylbutanol-1 80%; slightly impure 2-methylbutanol-1 16%
46	Methylisopropylmalonic ester	1.43	20[c]	23	2,3-Dimethylbutanol-1

TABLE I (*Concluded*)

No.	Compound	Moles	Catalyst, g.	Time, hrs.	Products
47	Diethylmalonic ester	0.50	10[e]	12	Diethylcarbinylcarbinol 94%
48	*n*-Propylmethylcarbinylethylmalonic ester	.82	15[c]	30	3-Methyl-2-ethylhexanol-1 80%; *n*-propylmethylcarbinylethylmalonic ester 18%
49	*n*-Propylmethylcarbinylethylmalonic ester	.30	5[c]	20	3-Methyl-2-ethylhexanol-1 78%; *n*-propylmethylcarbinylethylmalonic ester 8%
50	Isoamylethylmalonic ester	.30	10[e]	7	5-Methyl-2-ethylhexanol-1 91%
51	Isoamylethylmalonic ester	.30	10[e]	2.3	5-Methyl-2-ethylhexanol-1 87%; isoamylethylmalonic ester 9%
52	Isoamylethylmalonic ester	.68	10[e]	6.5	5-Methyl-2-ethylhexanol-1 90%; isoamylethylmalonic ester 6%
53	Ethyl α-phenylbutyrate	.50	8[e]	1.7	Hydrocarbons 8%; ethyl α-phenylbutyrate 25%; 2-phenylbutanol-1 60%
54	Ethyl α-phenylbutyrate	.10	3[e]	2.5	*Sec.*-butylbenzene 28%
	2-Phenylbutanol-1	.25			2-Phenylbutanol-1 66%
55	Furfuryl alcohol	5.1	10[e]	57.5	Methylfuran 20%; pentanol-1 10%; furfuryl and tetrahydrofurfuryl alcohols 17%; pentanediol-1,2 14%; pentanediol-1,5 15%; intermediates and residue 10%
56	Furfuryl alcohol	5.1	10[e]	4	*n*-Pentane 0.3%; pentanol-1 36%; furfuryl and tetrahydrofurfuryl alcohols 13%; pentanediol-1,2 14%; pentanediol-1,5 15%; intermediates and residue 11%; methylfuran 36%
57	Methylfuran	1.0	4[e]	4	*n*-Pentane 4%; methyltetrahydrofuran 15%; pentanol-2 33%; pentanol-1 30%; intermediates, residue and loss by drying 15%
58	Ethyl salicylate	0.86	5[f]	8	Ethyl hexahydrosalicylate 58%; high boiling product 28%
59	Methyl salicylate	.33	10	9	Ethyl hexahydrobenzoate 8%; ethyl hexahydrosalicylate 79%
60	Methyl salicylate	.82	...	6.5	Methyl salicylate 96%
61	Heptaldehyde	4.63	3[e]	5.0	Heptanol-1, water and condensation products 78%
62	Ethyl acetoacetate + cyclohexylcarbinol	0.38	2[c]	0.4	Ethyl β-hydroxybutyrate and cyclohexylcarbinol 76%; hexahydrobenzyl β-hydroxybutyrate 21%
63	Ethyl acetoacetate + cyclohexylcarbinol	.38	2[c]	0.5	Hexahydrobenzyl β-hydroxybutyrate 29%
64	Ethyl acetoacetate + cyclohexylcarbinol	.38	2[c]	2.0	Hexahydrobenzyl β-hydroxybutyrate 36%
65	Cyclohexyl carbinol + ethyl β-hydroxybutyrate	(134.5 g.)	...	9.0	Hexahydrobenzyl β-hydroxybutyrate (3.9 g.); unchanged material (127.5 g.)
66	Ethyl α,α-diethylacetoacetate	0.11	1[b]	1.0	Ethyl α,α-diethyl-β-hydroxybutyrate 89%
67	Ethyl cinnamate	.85	2[b]	1.0	Ethyl β-phenylpropionate 97%
68	Benzoin	.64	6[d]	8.0	Diphenyl ethylene glycol
69	Ethyl benzalacetoacetate	.27	3[f]	5.0	Ethyl α-hexahydrobenzyl-β-hydroxybutyrate 98%
70	Diacetylmethane	.33	3[f]	1.3	Pentanediol-2,4 39%; low boiling material 52%
71	Diacetylmethane	.48	1[e]	3.5	Diacetylmethane 74%; low boiling material 26%
72	Tetrahydrofurfuryl alcohol	1.0	10[e]	11	Methyltetrahydrofuran and water 5%; tetrahydrofurfuryl alcohol 77%; pentanediol-1,5 13%
73	Methylfuran	0.61	5[f]	2	Methyltetrahydrofuran 83%; methylfuran 6%
74	Methyltetrahydrofuran	.5	5[e]	6	Methyltetrahydrofuran 74%

[a] The pressure was 175 ± 35 atmospheres and the temperature 250° except that it was 200° in Nos. 1, 6, 8, 12, 23, 24, 55, 59, 60 and 68; 190° in 58 and 69, 175° in 61, 66 and 70; 175 to 200° in 71; 135 to 165° in 14; 150° in 16, 62, 63, 64, 65 and 67; 125° in 10 and 11 and 120° in 15.

[b] A copper–chromium oxide catalyst made according to the directions first published.[3]

[c] A nickel catalyst prepared by the precipitation of nickel carbonates ("B method") using sodium carbonate as a precipitant.[15]

[15] Adkins and Covert. *J. Phys. Chem.*, **35**, 1684 (1932).

[d] Catalyst No. 28 RAC was a copper–chromium–barium oxide catalyst, previously described.[16]

[e] Copper–chromium–barium oxide catalysts prepared like catalyst 37 KAF.[16]

[f] A nickel catalyst prepared by the use of ammonium carbonate as a precipitant.[17]

[h] The catalyst was red and inactive after runs 12, 24, 25 and 71.

[i] The authors are greatly indebted for certain compounds to Dr. H. A. Shonle of Eli Lilly and Company, to Dr. V. H. Wallingford of the Mallinckrodt Chemical Works and to Messrs. C. F. Koelsch, B. W. Howk, Rudolph Nagy and E. F. Struss of this Laboratory.

mental details of characterization, etc., were deleted from the original manuscript of this paper.)

Correlation of Results

Hydrogenolysis of Glycols and Corresponding Carbonyl Containing Compounds.—The formation from esters of good yields of propanediol-1,2 and pentanediol-1,5, of fair yields of butanediol-1,4, and the failure to obtain 1,3-glycols, indicated that 1,3-glycols are most susceptible to hydrogenolysis.[5] This hypothesis was borne out by the fact that cyclohexanediol-1,3 was completely converted to cyclohexanol by the time the temperature of the bomb reached 250°. However, the relative stability of the cyclohexanediols-1,2 and -1,4 was found to be the reverse of that observed for propanediol-1,2 and butanediol-1,4. Cyclohexanediol-1,4 was perfectly stable at 250° while a 20% yield of cyclohexanol was obtained from the 1,2-glycol after six hours.

The 1,3-glycols (or corresponding carbonyls) may undergo hydrogenolysis to give four sets of reaction products as illustrated below. The

$$\left.\begin{array}{l} \\ R_2COH \\ | \\ CH_2 \\ | \\ R_2'COH \end{array}\right. \begin{array}{l} \xrightarrow{H_2} \\ \xrightarrow{H_2} \\ \xrightarrow{H_2} \\ \xrightarrow{H_2} \end{array} \begin{array}{ll} R_2CHCH_2C(OH)R_2' + H_2O & \text{(III)} \\ R_2C(OH)CH_2CH_2R_2' + H_2O & \text{(IV)} \\ R_2CHOH + R_2'C(OH)CH_3 & \text{(V)} \\ R_2'CHOH + R_2C(OH)CH_3 & \text{(VI)} \end{array}$$

results of the hydrogenolysis of three glycols of this type, *i. e.*, $HOCH_2CH_2CH_2OH$, $CH_3CHOHCH_2CH_2OH$, and $(CH_3)_2CHOHCH_2CHOHCH_3$, indicated the effect of branching of the chain upon the ease of and the point of cleavage of the carbon chain as well as upon the relative stability of primary and secondary hydroxyl groups. That branching of the chain greatly facilitated hydrogenolysis is shown by the fact that the reaction of propanediol-1,3 required 1.2 hours at 250°, while the reaction of butanediol-1,3 was complete by the time the temperature of the bomb reached 250°, or in 4.5 hours at 210°. The reaction of the more labile 2-methylpentanediol-2,4 was complete within a half hour at 200°.

[16] Connor, Folkers and Adkins, THIS JOURNAL, **54**, 1139 (1932).

[17] Covert, Connor and Adkins, *ibid.*, **54**, 1651 (1932).

Propanediol-1,3 and butanediol-1,3 showed no carbon to carbon cleavage, while the more branched chain 2-methylpentanediol-2,4 underwent cleavage giving from 62 to 86% of propanol-2, the point of cleavage being nearer the more branched end of the glycol molecule. It was surprising to find that the hydroxyl group on a primary carbon atom was in the case of these glycols more labile toward hydrogenolysis than was a hydroxyl on a secondary carbon atom, yet this was true in the hydrogenolysis of butanediol-1,3, from which almost twice as much butanol-2 as butanol-1 was produced. The greater lability of the primary as contrasted with the secondary hydroxyl is further evidenced by the formation of 2-methylcyclohexanol-1, rather than of cyclohexylcarbinol, from ethyl hexahydrosalicylate. Moreover, unpublished work by Wojcik in this Laboratory indicates that this is not simply a function of the character of the carbinol group, for substitution on the 2 carbon atom appears to be more effective in labilizing oxygen to carbon linkages than when the substitution is on the 1 (or carbinol) carbon atom. However, it should be noted that in the monosubstituted β-hydroxybutyric esters the secondary rather than the primary hydroxyl group was eliminated.

Sufficient branching of the chain made possible the hydrogenolysis of the carbon–carbon bond even in the case of the relatively stable 1,2-glycols. Although pentanediol-1,2 gave a 26% yield of alcohols, there was present only a trace of methanol. With pinacol, however, 17% of isopropyl alcohol and 16% of dimethylisopropylcarbinol were formed.

The cleavage of 2-methylpentanediol-2,4 and of 2-methyl-4-ketopentanol-2 (diacetone alcohol) appeared to occur so readily that diacetone alcohol could not be hydrogenated to the glycol without the formation of considerable isopropyl alcohol. The temperature of the hydrogenation appeared to make little difference, for yields of 41, 59 and 41% of 2-methylpentanediol-2,4 were obtained in the runs on diacetone alcohol at 120, 135–165 and 150°, respectively. Furthermore, the amount of catalyst did not seem to be the deciding factor for the above runs were made in the presence of 0.5, 2.0 and 2.0 g. of the same catalyst, respectively. On the basis of the data at hand it seems that a rapid hydrogenation is the most favorable condition for a good yield of the glycol, for the times for the hydrogenations were six hours, four minutes and thirty minutes in the order named.

It is possible that the oxide catalyst is alkaline enough to act as a catalyst for the reversal of the reaction by which diacetone alcohol is formed.

$$2CH_3COCH_3 \rightleftharpoons CH_3COCH_2COH(CH_3)_2 \qquad \text{(VII)}$$

This hypothesis is borne out by the fact that a nickel catalyst made by precipitation with ammonium carbonate and which should contain no alkali gave no isopropyl alcohol, but an 89% yield of the glycol accompanied by a 6% yield of 2-methylpentanol-4.

Aldol behaved similarly in that it did not give a high yield of the glycol

by hydrogenation. It is worth noting that with nickel as a catalyst 39 and 41% yields of the glycol were obtained irrespective of whether freshly distilled or the technical aldol was used. The copper–chromium oxide catalyst induced no hydrogenation, even at 200°, and was itself reduced to the inactive form.

Only a few compounds containing more than two hydroxyl groups were investigated. Glycerol gave a good yield of propanediol-1,2. Mannitol and α-methyl-*d*-glucoside were hydrogenated with surprising ease. The reaction products were not investigated thoroughly, but in both cases some of the lower alcohols (including ethanol and methanol) and propanediol-1,2 were obtained. The presence of much water caused high losses and may have prevented the detection of some products. The complexity of these cases can be seen from the fact that each of the hydroxy groups in mannitol is beta (*i. e.*, labile) to another and that two of them are beta to two others. Pentaerythritol underwent a very smooth cleavage to give methyl and isobutyl alcohols. Hydrogenation of 4-methyl-2,6-dimethylolphenol gave a 50% yield of mesitol (2,4,6-trimethylphenol) and a 25% yield of di-(2-hydroxy-3,5-dimethylphenyl)-methane. This hydrogenation, to be successful, must be rapid, for when the material is subjected to slow hydrogenation the product is a tar.

The Hydrogenolysis of β-Hydroxy Esters.—The compounds subjected to the action of hydrogen were in most cases β-keto esters. However, since hydrogenation of the carbonyl group takes place at much lower temperatures than does cleavage or hydrogenation of the carbethoxy group, the compounds actually undergoing hydrogenolysis were β-hydroxy esters or 1,3-glycols. The possible reactions involved are as follows

$$\begin{array}{lcll} CH_3 & (CH_3) & \xrightarrow{H_2} & C_2H_5OH + R_2CHCH_2OH \quad \text{(VIII)} \\ CHOH & (CHOH) & \xrightarrow{H_2} & CH_3CHOHCR_2CH_3 + H_2O \quad \text{(IX)} \\ CR_2 & (CR_2) & \xrightarrow{H_2} & CH_3CHOHCHR_2 + CH_3OH \quad \text{(X)} \\ COC_2H_5 & (CH_2OH) & \xrightarrow{H_2} & CH_3CH_2CR_2CH_2OH + H_2O \quad \text{(XI)} \end{array}$$

In the case of unsubstituted acetoacetic ester only reactions IX and XI occurred. With monosubstituted esters, reactions VIII and XI occurred chiefly with enough of IX to give a trace of a secondary alcohol. A test for methanol gave such a slight color that considering the delicacy of the test it is doubtful if reaction X occurred at all. With disubstituted acetoacetic esters only reaction VIII was found to take place.

Although the work on butanediol-1,3 previously mentioned indicated that the 2,3-carbon–carbon bond in acetoacetic ester did not cleave, additional proof was obtained by the hydrogenation of hexahydrobenzyl β-hydroxybutyrate. In this case ethanol could come only from cleavage and not from hydrogenation of a carbethoxy group. No ethanol was found.

The ratio of carbon–carbon cleavage to carbon–oxygen cleavage in monosubstituted derivatives of acetoacetic ester is a function of the substituent group. This is shown in Table II.

TABLE II

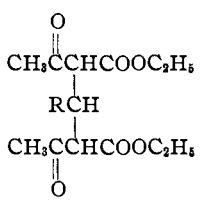
THE HYDROGENOLYSIS OF MONOSUBSTITUTED ACETOACETIC ESTER DERIVATIVES

Compound	% Carbon–carbon cleavage (± 5%)
Ethyl acetoacetate	0
Ethyl hexahydrosalicylate	0
Ethyl α-ethylacetoacetate	50
Ethyl α-isopropylacetoacetate	60
Ethyl α-butylacetoacetate	71
Ethyl α-hexahydrobenzylacetoacetate	100
Ethyl α-benzylacetoacetate	100
Ethyl α-(β-phenethyl)-acetoacetate	100
Ethyl α,γ-dimethylacetoacetate	100

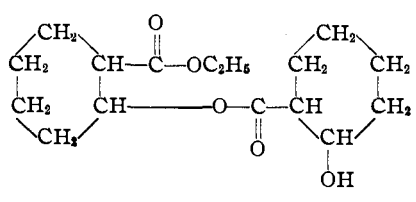
These data indicate that the weight and chemical character of the substituent group are important factors in determining the ease of cleavage of the carbon–carbon linkage.

It also appears that the hydrogenolysis of carbon–carbon linkages differed according not only to the substituent group α to the carbethoxy group, but also according to the substituent γ to it. For, with the α-monosubstituted acetoacetic esters, there was 50 to 100% cleavage to give the primary alcohol and ethanol, while ethyl α,γ-dimethylacetoacetate underwent complete carbon–carbon cleavage to give *n*-propanol. These facts indicate that the ease of hydrogenolysis of the carbon–carbon linkage was enhanced more by the group CH_3CH_2CHOH— than by the group CH_3CHOH—. The —CH_2OH group facilitated carbon to carbon cleavage less than did these groups for only traces of methanol were produced from monosubstituted acetoacetic esters, and there was less carbon to carbon cleavage with the monosubstituted malonic than with the corresponding acetoacetic esters.

A marked difference in the type of hydrogenolysis occurring was observed in the case of two more complex monosubstituted acetoacetic esters, *i. e.*, diethyl α,γ-diacetyl-β-methylglutarate, or the corresponding β-phenyl compound, as illustrated in formula VIII where R is methyl or phenyl



VIII



IX

In the case of these compounds there occurred little or no carbon to carbon cleavage but only hydrogenolysis of the carbon to oxygen linkage with the formation of primary glycols.

In the hydrogenation of β-hydroxy esters it has not been possible to isolate the glycol. In those cases in which hydrogenation was not complete there was present, besides the alcohols normally expected, only the esters of the acids corresponding to the alcohols—*never* a glycol or hydroxy ester. When 0.5 mole of acetoacetic ester had absorbed only 60% of the amount of hydrogen theoretically necessary for reduction of the carbonyl and carbethoxy groups, followed by hydrogenolysis, there was present neither glycol or hydroxy ester, but only butyl alcohols and butyric ester. Therefore it seems that hydrogenolysis of the β-hydroxy ester (or 1,3-glycol) is so much easier than hydrogenation of the carbethoxy group that the glycol cannot ordinarily be obtained. In only one case noted below was a 1,3-glycol isolated from the hydrogenation of a β-oxygenated ester.

The hydrogenolysis of monosubstituted acetoacetic esters, as a preparational method for alcohols is doubtless impractical because of the diversity of products and the similarity of the boiling points of some of them. The catalytic cleavage of disubstituted acetoacetic esters might, on the other hand, be of some synthetic value, for these undergo carbon–carbon scission smoothly. The disubstituted malonic esters give the same products, however, and would probably be the ones oftenest used because of their greater ease of preparation.

The Hydrogenolysis of Malonic Esters.—It had previously been observed that *n*-propanol and ethyl propionate were formed by the hydrogenation of malonic ester and that 2-methylbutanol-1 (XII) was obtained from ethylmalonic ester.[5] In this investigation it has been found, however, that the monosubstituted malonic esters also undergo some carbon–carbon cleavage, with the formation of methanol (XIII).

$$\begin{array}{l} \mathrm{C_2H_5CH(COOC_2H_5)_2} + 4\mathrm{H_2} \longrightarrow \mathrm{C_2H_5CH(CH_2OH)_2} \xrightarrow{\mathrm{H_2}} \mathrm{C_2H_5CH(CH_3)CH_2OH} + \mathrm{H_2O} \quad \text{(XII)} \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad \xrightarrow{\mathrm{H_2}} \mathrm{C_2H_5CH_2CH_2OH} + \mathrm{CH_3OH} \quad \text{(XIII)} \end{array}$$

This has been verified by the isolation of *n*-butanol from the products from ethylmalonic ester, qualitative tests for methanol, and by quantitative determination of the amount of methanol present on the basis of the density and refractive indices of the alcohol fractions.

The results indicated that 29% of the butylmalonic, 22% of the benzylmalonic and 20% of the ethylmalonic ester had cleaved to give methanol. Considering the possible errors involved, one may say that these groups all cause approximately the same amount of carbon–carbon cleavage. However, phenylmalonic ester gave no cumene, so far as it was possible to tell

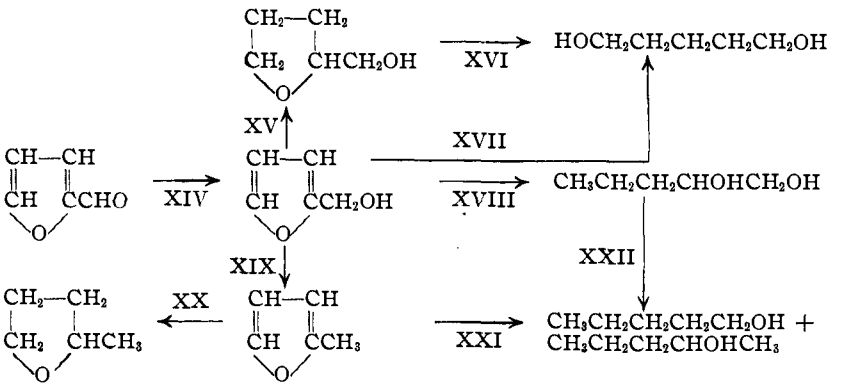
by fractionation, but only ethylbenzene, indicating complete carbon–carbon as well as carbon to oxygen cleavage.

The disubstituted malonic esters form the most practical intermediates for preparation of alcohols of all the groups of compounds subjected to hydrogenolysis. These reacted smoothly and so far as was possible to ascertain underwent 100% cleavage of the carbon–carbon bond to methanol and a dialkyl carbinyl carbinol. Six disubstituted malonic esters were hydrogenated and all behaved satisfactorily. Among these was the only case in which a 1,3-glycol was obtained from the hydrogenation of an ester. From 450 g. of dimethylmalonic ester there was obtained 12 g. of 2,2-dimethylpropanediol-1,3, corresponding to a 5% yield. This small yield indicates the futility of attempting to isolate the glycol in runs of an ordinary size.

Dehydration as a Possible Step in Carbon to Oxygen Cleavage.—In the cases reported in this paper where an hydroxyl group is replaced by a hydrogen, it is perhaps significant that dehydration is always possible. In the cases where dehydration is impossible (the disubstituted malonic esters) only carbon–carbon cleavage occurred. The converse, *i. e.*, that cleavage of carbon–oxygen takes place whenever dehydration is possible, is not true, for the disubstituted acetoacetic ester derivatives underwent carbon–carbon scission entirely while the monosubstituted malonic and acetoacetic esters and some glycols also had the carbon–carbon bond broken to varying extents. There is therefore the possibility (although in the opinion of the authors not a probability) that the cleavage of the carbon–oxygen linkage involves first dehydration and then hydrogenation. This mechanism could not be applied to the breaking of the furan ring to be discussed later. In the case of carbon–carbon cleavage, on the other hand, no plausible speculation as to the mechanism can be formulated at present.

The Reported Cleavage of Ethyl α-Phenylbutyrate.—It has been reported that ethylbenzene is formed in the hydrogenation of ethyl α-phenylbutyrate.[5] Inasmuch as this would seem to be an unusual type of cleavage it was further investigated. The result of these experiments indicated that the ethylbenzene previously obtained was probably formed from ethyl phenylacetate, present as an impurity in the sample of ethyl α-phenylbutyrate formerly available.

Hydrogenolysis of Furan Derivatives.—The hydrogenolysis of the carbon–oxygen bond had been noted earlier in the hydrogenation of furfuryl alcohol with a copper–chromium oxide catalyst.[3] Since this fell so clearly in line with the present work the reaction was further investigated upon a larger scale and for tetrahydrofurfuryl alcohol, methylfuran, methyltetrahydrofuran and pentanediol-1,2. The data on these compounds (Table I) indicate very clearly that the reactions follow the paths indicated in reactions XIV to XXII.



The chief reactions are the direct hydrogenolysis of furfuryl alcohol, cleavage occurring at each of the three oxygen to carbon linkages as indicated by reactions XVII, XVIII and XIX. Hydrogenation in the sense of reactions XV and XX does occur at 200 to 250° over the copper–chromium oxide catalyst but to a relatively small extent. Both reactions proceed almost quantitatively over a nickel catalyst. In contrast to the ease of hydrogenolysis of the unsaturated furfuryl alcohol was the relative stability of the saturated tetrahydrofurfuryl alcohol. Reaction XVI did occur but at only a small fraction of the rates of reactions XVII and XVIII. Furthermore, tetrahydrofurfuryl alcohol underwent hydrogenolysis to give pentanediol-1,5 almost exclusively, instead of the mixture of glycols produced from furfuryl alcohol. Pentanediol-1,2 as well as methylfuran underwent hydrogenolysis to give mixtures of pentanols, while pentanediol-1,5 and methyltetrahydrofuran did not react under similar conditions. It is thus clear that furan derivatives are much more readily hydrogenolyzed than are the corresponding tetrahydro compounds.[18]

Miscellaneous Hydrogenations.—In Table I the results of several hydrogenations not previously reported are recorded which do not require additional comment, except to note the aldolization that occurred in the hydrogenation of heptaldehyde, the formation of hexahydrobenzyl β-hydroxybutyrate from acetoacetic ester and cyclohexylcarbinol, and the behavior of ethyl salicylate. When the latter was subjected to hydrogenation, there was produced a high molecular weight compound which apparently had the structure indicated in formula IX. The compound was not produced if the hydrogenation was carried out in an ethanol solution. This behavior is understandable if it is noted that a molecule of ethyl salicylate has within it the same structure as the enol of a beta keto ester.

[18] Attention should be called to an error [Connor, Folkers and Adkins, THIS JOURNAL, **54**, p. 1140, line 5 (1932)] in which tetrahydrofurfuryl is printed where furfuryl was meant. The former alcohol is not produced from furfural under the conditions there described.

It has been previously reported that when acetoacetic ester is hydrogenated a condensation product results which is not formed if the hydrogenation is carried out in an ethanol solution. The analogy of ethyl salicylate to an enol of a β-keto ester is also evidenced by the fact that phenols are the only compounds in which a benzenoid ring has apparently been hydrogenated over a copper–chromium oxide catalyst.[5] It seems probable that the hydrogenation of ethyl salicylate over this catalyst actually proceeds through the β-keto ester of which salicylic ester is the enol.

TABLE III

ANALYTICAL DATA AND PHYSICAL CONSTANTS OF NEW COMPOUNDS

	Compound	B. p., °C.	Mm.
1	2-Ethyl-5-methylhexanol-1	84– 86	10
2	2-Ethyl-3-methylhexanol-1	83– 86	10
3	Ethyl hexahydrosalicylhexahydrosalicylate	192–196	6
4	Ethyl α-hexahydrobenzyl-β-hydroxybutyrate	147–148	10
5	Hexahydrobenzyl β-hydroxybutyrate	149–150	17
6	Ethyl α,α-diethyl-β-hydroxybutyrate	87– 89	9

	Formula	n_D^{25}	d_{25}^{25}	MR'D Found	MR'D Calcd.	C, % Found	C, % Calcd.	H_2, % Found	H_2, % Calcd.
1	$C_9H_{20}O$	1.4304	0.8232	45.33	45.05	74.93	75.00	13.92	13.89
2	$C_9H_{20}O$	1.4356	.8383	44.85	45.05	74.51	75.00	13.92	13.89
3	$C_{16}H_{26}O_5$	1.4781	1.1024	76.53	76.80	64.48	64.43	8.73	8.73
4	$C_{13}H_{24}O_3$	1.4600	0.9882	63.18	63.23	68.27	68.42	10.51	10.52
5	$C_{11}H_{20}O_3$	1.4565	1.0150	53.58	53.96	65.87	66.00	10.20	10.00
6	$C_{10}H_{20}O_3$	....	....	...	...	63.69	63.83	10.78	10.64

Summary

A number of glycols, hydroxy and malonic esters and derivatives of furan have been subjected to the action of hydrogen, over a copper–chromium oxide catalyst, in studying the effect of structure upon the hydrogenolysis of carbon to carbon and carbon to oxygen linkages. The particular points of interest have been the effect of branching of the carbon chain and of the position of substituents upon the ease of cleavage, especially of the ratio of cleavage, of C to C to that of C to O. It has been observed that 1,3-glycols undergo hydrogenolysis at a lower temperature, or more rapidly, than do 1,2- or 1,4-glycols. There is competition in the cleavage of C to C and C to O, the cleavage of the former being facilitated by branching or prolongation of the carbon chain, not only for 1,3- but also for 1,2-glycols.

The unsubstituted β-hydroxybutyric esters and 2-carbethoxycyclohexanol-1 showed C to O but no C to C cleavage. Other α-monosubstituted β-hydroxybutyric esters showed an amount of C to C cleavage which increased, apparently with increase in weight of the substituent. γ-Methyl-β-hydroxyvaleric ester also showed complete cleavage of C to C. The α,α-dialkyl-β-hydroxybutyric esters showed 100% C to C cleavage.

The monoalkyl malonic esters underwent a varying ratio of C to C as compared to C to O cleavage, depending upon the nature of the substituent. Six dialkylmalonic esters cleaved smoothly and completely to give methanol and dialkylcarbinylcarbinols. In contrast with this is the fact that α,γ-diacetyl-β-methyl(or phenyl)glutaric esters showed little if any C to C cleavage.

It appears that the C to O linkage in a primary carbinol group is in many cases more readily cleaved than in a secondary alcohol. The presence of a carbon to carbon double bond facilitates the cleavage of C to O linkages.

A considerable amount of information in regard to the hydrogenation and hydrogenolysis of a variety of organic compounds has been presented in tabular form and cannot be more briefly summarized here.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

THE REDUCING ACTION OF THE GRIGNARD REAGENT. III. HYDROCARBONS FORMED DURING REDUCTION

BY C. R. NOLLER, W. E. GREBE AND L. H. KNOX

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Of the various types of reduction that may take place during the reaction of an aldehyde or ketone with a Grignard reagent,[1] the type most frequently encountered occurs only when a hydrogen bearing carbon atom is adjacent to the carbon atom that *is combined with magnesium*. This may be represented by the equation

$$R_2C{=}O + R_2CH{-}C(MgX)R_2 \longrightarrow R_2C(OMgX)H + R_2C{=}CR_2$$

where R may be either hydrogen or a radical.

Thus far no careful investigation has been made of the hydrocarbon formed during the reduction. Hess and Wustrow[2] reported that primary addition products of ethylmagnesium bromide, isobutylmagnesium bromide, and isobutylmagnesium chloride with cinnamic aldehyde had been isolated in a pure state and that on heating they lost in weight an amount equivalent to one mole of unsaturated hydrocarbon. Meisenheimer[3] was unable to confirm these results and also pointed out that while Hess and Wustrow claim the quantitative loss of isobutylene from the addition product of isobutylmagnesium bromide and cinnamic aldehyde, they actually isolated from the addition product of isobutylmagnesium chloride and cinnamic aldehyde only 8.5% of the theoretical amount of isobutylene as the dibromide. It should be mentioned that in Hess and Wustrow's

[1] For a summary of the different types of reduction and references to previous work on this subject, see the first article of this series, THIS JOURNAL, **53**, 635 (1931).

[2] Hess and Wustrow, *Ann.*, **437**, 256 (1924).

[3] Meisenheimer, *ibid.*, **442**, 180 (1925).