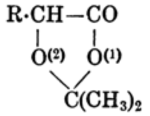
CATALYTIC HYDROGENATION OF ACETONE-COMPOUNDS OF α-HYDROXY-ACIDS.*

By **Haruomi ÔEDA.**

Received July 27th, 1935. Published November 28th, 1935.

In a previous communication,(1) preparation of acetone-compounds of some α-hydroxy-acids was reported. As already described in that paper, the manipulation for their preparations is simple and their yields are fairly good in almost all cases and there is the prospect that they can be favourably used as a starting material for several reactions.

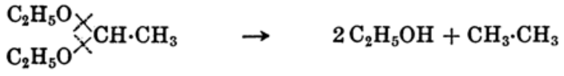
In the present communication studies on catalytic hydrogenation of these compounds under pressure are reported. Copper-chromium oxide was used as catalyzer, which had been proved by H. Adkins(2) to be very effective in the reduction of esters into alcohols.



In the heterocyclic ring of acetone-compounds of α-hydroxy-acids, one of the oxygen atoms (1) may functionate as ester, and on hydrogenation, it is probable that the cleavage of linking might occur in carbonyl side of the oxygen, as in the hydrogenation of esters:

$$R{\cdot}COOC_2H_5 \quad \rightarrow \quad R{\cdot}CH_2OH + HOC_2H_5$$

Another oxygen (2) in the ring may be compared with those in ethers or acetals. Several papers(3) are published on the hydrogenation of acetals and in every instance cleavage of the molecule occurs in the aldehyde side of the oxygen with regeneration of the alcohol, detaching the aldehyde as a hydrocarbon:



$$(C_2H_5O)_2CH{\cdot}CH_3 \quad \rightarrow \quad 2\,C_2H_5OH + CH_3{\cdot}CH_3$$

Recently K. Yoshikawa(4) obtained hexahydric alcohols in the hydrogenation of many hexoses. It may also be regarded as the same cleavage

---

* Studies on Hydroxy-Acids and their Derivatives. III.

(1) H. Ôeda, this Bulletin, **10** (1935), 187.

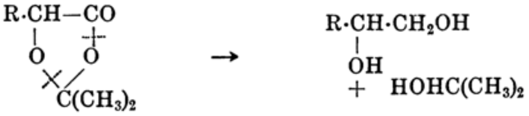
(2) H. Adkins, K. Folkers, *J. Am. Chem. Soc.*, **53** (1931), 1095; **54** (1932), 1145. H. Adkins, B. Wojcik, L. Covert, *ibid.*, **55** (1933), 1669.

(3) T. Kariyone, *J. Pharm. Soc. Japan*, **43** (1923), 51. M. Bergmann, N. Carter, *Z. physiol. Chem.*, **191** (1930), 211. L. Covert, R. Connor, H. Adkins, *J. Am. Chem. Soc.*, **54** (1932), 1651.

(4) K. Yoshikawa, *Bull. Inst. Phys. Chem. Research, Japan*, **13** (1934), 1045.

of acetal linking in the sugar molecules. These facts suggest that, through hydrogenation, cleavage in linking (2) may occur in isopropylidene side of the oxygen.

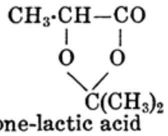
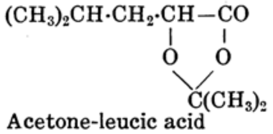
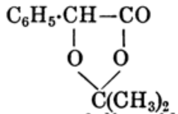
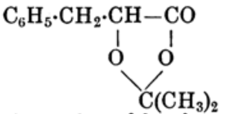
From the above consideration, the hydrogenation of these acetone-compounds may result in the formation of corresponding glycols as well as isopropyl alcohol.



The experimental results of the present study agree with the above expectation except in one case and they are summarized in Table 1.

H. Adkins has studied on the hydrogenation of ethyl lactate⁽⁵⁾ and ethyl mandelate⁽⁶⁾ in the presence of copper-chromium oxide and he found that the former yielded propylene glycol, while, it was not the case

Table 1.

Substance	Products	
 Acetone-lactic acid	$CH_3 \cdot CHOH \cdot CH_2OH$ Propylene glycol $+HOHC(CH_3)_2$ Isopropyl alcohol	—
 Acetone-leucic acid	$(CH_3)_2CH \cdot CH_2 \cdot CHOH \cdot CH_2OH$ Isohexylene glycol $+HOHC(CH_3)_2$ Isopropyl alcohol	$+ (CH_3)_2CH \cdot CH_2 \cdot CH_2 \cdot CH_2OH$ Isohexyl alcohol
 Acetone-mandelic acid	— $+HOHC(CH_3)_2$ Isopropyl alcohol	$+ C_6H_5 \cdot CH_2 \cdot CH_2OH$ β-Phenyl-ethyl alcohol + Aromatic hydrocarbon
 Acetone-phenyl-lactic acid	$C_6H_5CH_2 \cdot CHOH \cdot CH_2OH$ Benzyl-ethylene glycol $+HOHC(CH_3)_2$ Isopropyl alcohol	$+ C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_2OH$ γ-Phenyl-propyl alcohol $+ C_6H_5 \cdot CH_2 \cdot CHOH \cdot CH_3$ Benzyl methyl carbinol

---

(5) K. Folkers, H. Adkins, *J. Am. Chem. Soc.*, **54** (1932), 1145.

(6) H. Adkins, B. Wojcik, L. Covert, *J. Am. Chem. Soc.*, **55** (1933), 1669.

with the latter, which never yielded glycol, but gave a considerable amount of ethyl-benzene together with phenyl-ethyl alcohol. He concluded that hydroxyl attached to a carbon having benzenoid ring was very labile and hydrogenation of further advanced stage occurred in this case.*

The results obtained in the present study are in good agreement with the works of Adkins as shown in Table 1. Hydrocarbon yielded from mandelic ester was mentioned by Adkins as ethyl-benzene. Corresponding fraction in distillation has been also obtained from the acetone-compound.**

Expected course of hydrogenation was observed in the other two acetone-compounds. Both of them were found to give corresponding glycol and monohydric alcohol or alcohols which may be regarded as products of further hydrogenation of the glycol.

A viscous odourless liquid boiling at 111–113.5° under 15 mm. was obtained from acetone-leucic acid and it was found to be isohexylene glycol by the analysis as well as by the formation of bis-phenylurethane (m.p. 115–116°). No information of this glycol is found in literature.

By the action of phenyl magnesium bromide upon α-monochlorohydrine of glycerol, Grignard⁽⁷⁾ obtained a mixture of two isomeric glycols, which boils at 163–165° under 12 mm. Benzyl-ethylene glycol⁽⁸⁾ yielded from acetone-phenyl-lactic acid corresponds to one of the glycols of Grignard. Its bis-phenylurethane was prepared, which was isolated in two forms with different melting points. Neither of them contains solvent of crystallisation. The form, which was obtained by crystallisation from alcohol, is crystalline and melts at 108–109°, while the other obtained from benzene solution is amorphous and melts at 132–133°. They are interconvertible by changing the solvent in crystallisation. Monotropic change was also observed on heating, that is, the urethane melting at 108–109° was gradually transformed into the other form on prolonged heating at 100–110°.

---

* It was shown by Adkins that compounds of similar type respecting their hydroxyls such as benzyl alcohol, phenyl methyl carbinol, and diphenyl carbinol were readily hydrogenated with the same catalyzer to the corresponding hydrocarbons at 150 to 200°, temperature lower than that necessary for hydrogenation of esters.

** In the present study it could not be identified as ethyl-benzene, it yielded benzoic acid on oxidation and it corresponds to a mixture of toluene and ethyl-benzene with regards to its boiling point.

(7) V. Grignard, *Compt. rend.*, **141** (1905), 45; *Ann. chim. phys.*, (8), **10** (1907), 31.

(8) Recently this glycol was prepared by Hershberg, starting from allyl-benzene through the di-benzoic ester, *Helvetica Chim. Acta*, **17** (1934), 351.

Experimental Part.

Copper-chromium oxide catalyzer (containing a little barium) was prepared according to the description of Adkins(9) by the calcination of the precipitates formed by mixing ammoniacal solutions of copper and barium nitrates and of ammonium bichromate. Its composition is to be $2(0.9CuO + 0.1BaO) + Cr_2O_3$ when estimated from the proportion of reagents used.

Acetone-compound (prepared from hydroxy-acid and acetone by dehydration with conc. sulphuric acid) was mixed with 1/5–1/10 of its weight of the above catalyzer without any diluent. The hydrogenation was carried out at the temperature of 240–260° for 0.5–4.5 hours in an autoclave (capacity 250 c.c.) provided with shaking equipment, initial pressure of hydrogen being 100–120 atmospheres at room temperature.

Hydrogenated products were separated from catalyzer with glass filter and they were fractionated through Widmer column into several fractions under ordinary or reduced pressure.

Hydrogenation of Acetone-*dl*-lactic acid. Acetone-compound (b.p. 49.0–49.5° under 11 mm.) 30 g. (0.23 mol). Catalyzer 5.0 g. Time of hydrogenation 4.0 hours at 240–260°. Reaction product was fractionated into two parts.

I	79–81° under ordinary pressure	4.0 g.
II	82–85° under 11 mm.	10.2 g.

Fraction I was found to be isopropyl alcohol by converting it into naphthylurethane. *Naphthylurethane.* Mixture of the alcohol (1.0 g.) and α-naphthyl isocyanate (2.5 g.) was heated up to 150° (in glycerine bath) for one hour. On cooling, it turned to a hard cake, which was dissolved in hot ligroin and filtered. Naphthylurethane (0.8 g.) was obtained from the filtrate, which melted at 104–105° after repeated recrystallisation from ligroin (Table 2).

Fraction II distilled at 94–96° under 20 mm. after refractionation and it was found to be propylene glycol by converting it into bis-phenylurethane. *Bis-phenylurethane.* The glycol (1.0 g.) and phenyl isocyanate (2.0 g.) were mixed and heated at 120–140° for one hour. Five times of ligroin was added, the mixture well stirred, the ligroin was decanted off, and the remaining liquid was dissolved in benzene. The solution was evaporated to a small bulk, from which the crude urethane crystallized out (1.0 g., m.p. 120–135°). After repeated recrystallisation from ligroin and finally from alcohol it melted at 143–144° and showed no change of m.p. on further purification (Table 2).

Hydrogenation of Acetone-*l*-leucic acid. Acetone-compound (b.p. 84.5–85.5° under 13 mm.) 30 g. (0.175 mol). Catalyzer 4.0 g. Time of hydrogenation $4\frac{1}{3}$ hours at 240–260°. Fractionation (filtered solution, 24.6 g.):

I	80– 81°	under ordinary pressure	7.6 g.
II	140–150°	,,	4.4 g.
III	56–105°	under 15 mm.	1.1 g.
IV	110–116°	,,	9.3 g.

---

(9) R. Connor, K. Folkers, H. Adkins, *J. Am. Chem. Soc.*, **54** (1932), 1139. The above catalyzer is specified as No. 37 KAF in this paper.

Fraction II was treated with 10% NaOH to remove acetone-compound and the neutral part was collected by extracting with ether and the extract was refractionated. Main part (3.2 g.) boiled at 140–147°, which was found to be isohexyl alcohol by converting it into 3,5-dinitrobenzoic ester. The boiling point mentioned above is lower and extends in wider range than the value in literature (b.p. 153°) and the sample is suspected to be mixed with isomeric secondary alcohol (inactive form, b.p. 129–134°) but the latter could not be identified. *Dinitrobenzoic ester.* It was prepared by treating the alcohol with 3,5-dinitrobenzoyl chloride according to the description of Mulliken.(10) The ester obtained melted at 68–69° after repeated recrystallisation from 95% alcohol (Table 2).

Fraction IV. After treating with 10% NaOH it was refractionated, b.p. 111–113.5° under 15 mm., 7.7 g. It was found to be isohexylene glycol by analysis (Table 3). *Bis-phenylurethane.* Mixture of the glycol (0.5 g.) and phenyl isocyanate (1.0 g.) was heated at 120–130° for 0.5 hour. On cooling, it changed to a viscous fluid. Ligroin (1:5) was added, well stirred, and colourless amorphous powder gradually deposited. It melted at 115–116° after recrystallisation from mixture of ligroin and alcohol (5:1) (Table 2).

Hydrogenation of Acetone-*dl*-mandelic acid. Experiment A. Acetone-compound (m.p. 46–47°) 38.5 g. (0.20 mol). Catalyzer 6.0 g. Time of hydrogenation 1.5 hours at 240–260°. Fractionation (filtered solution, 28.0 g.):

I	78– 80° under ordinary pressure	13.4 g.
II	30– 35° under 17 mm.	2.7 g.
III	102–107° under 14 mm.	8.4 g.

Fractions I and II had the odour of aromatic hydrocarbon. Twice its volume of water was added to them to dissolve isopropyl alcohol and the part not miscible with water was separated, which (5.8 g.) was distilled over metallic sodium. Even after repeated fractionation with the aid of Widmer column, it was not possible to separate it into fractions of distinct boiling points:

(a)	up to 110°	1.3 g.
(b)	110–114°	0.5 g.
(c)	115–122°	1.1 g.

An attempt was made to prepare crystalline nitro-compounds with the object of identifying the hydrocarbons, nitration being carried out, regarding (b) as toluene, by the method of Mulliken,(11) (c) as ethyl-benzene, according to the description of Schultz.(12) But the products thereby obtained always remained as oil and could not be brought into crystallisation. *Oxidation of* (a). It (0.8 g.) was boiled with potassium permanganate solution (3.0 g of salt in 75 c.c. of water) for one hour. After filtration and evaporation, the solution was acidified with hydrochloric acid. Crystals (0.1 g) which melted at 121° after recrystallisation from water were obtained and identified as benzoic acid by the mixed melting point determination. These fractions which gave benzoic acid on oxidation can be assumed to be a mixture of toluene and ethyl-benzene.

---

(10) Mulliken, "Identification of Organic Compounds," Vol. I, 168.
(11) Mulliken, *ibid.*, Vol. I, 202.
(12) G. Schultz, *Ber.*, **42** (1909), 2634.

Fraction II. Boiling point of this fraction corresponds to that of phenyl-ethyl alcohol and it was identified as such by converting it into phenylurethane. *Phenylurethane.* The alcohol (1.0 g.) and phenyl isocyanate (1.0 g.) were mixed and heated at 100–120° for one hour. On cooling, the mixture became a semi-fluid, to which an equal volume of petroleum ether was added, well stirred, and filtered. The crude urethane (1.5 g.) thus prepared was repeatedly recrystallized from alcohol. It melted at 78–79° (Table 2) and showed no lowering of melting point when mixed with a specimen of urethane prepared from pure phenyl-ethyl alcohol (Takeda).

Experiment B. Acetone-compound 25.2 g. (0.13 mol). Catalyzer 4.0 g. Time of hydrogenation 0.75 hour at 240–260°. Fractionation:

I	78– 80°	under ordinary pressure	5.6 g.
II	105–106°	under 16 mm.	5.4 g.
III	over 110°	,,	3.0 g.

In this experiment hydrogenation was interrupted before the absorption of hydrogen has been completed. The yield of fraction I (isopropyl alcohol and hydrocarbon) was inferior to that in Exp. A, while a fraction of higher boiling point (III) was obtained, which was not met with in Exp. A.

Fraction III has a odour reminding of aromatic ester. After removing acid by treating with 10% sodium carbonate, it was hydrolyzed by boiling with sodium hydroxide (10%) for three hours. The reaction mixture was acidified and extracted with ether. From the ether extract crystals (0.7 g.) were obtained, which melted at 75–76° after recrystallisation from water and were identified as phenyl-acetic acid by mixed melting point determination.

Hydrogenation of Acetone-*l*-phenyl-lactic acid. Experiment A. Acetone-compound (m.p. 63–64°) 25.0 g. (0.12 mol). Catalyzer 4.0 g. Time of hydrogenation 1.5 hours at 240–260°. Fractionation (15.1 g.):

I	77– 80°	under ordinary pressure	2.5 g.
II	110–120°	under 16 mm.	2.8 g.
III	120–123°	,,	2.4 g.
IV	164–166°	,,	6.3 g.

Fractions II and III and corresponding ones in the next experiment were combined and treated as follows. The substance has a pleasant odour reminding of cinnamic ester. It was boiled with 10% sodium hydroxide for one hour to hydrolyze the ester and was extracted with ether. The ether extract was separated into three fractions by fractionation:

(a)	up to 100°	under 9 mm.	2.4 g.
(b)	100–108°	,,	2.6 g.
(c)	108–109°	,,	6.2 g.

These fractions were found to be a mixture of phenyl-propyl alcohol (b.p. 120–121° under 13 mm.) and benzyl methyl carbinol (active form, b.p. 125° under 25 mm.) by converting them into phenylurethanes. *Phenylurethanes.* Though the differentiation of isomeric alcohols by above fractionation never seemed complete, their phenylurethanes could be obtained separately from fractions rich in corresponding alcohols, as solubilities of the phenylurethanes in ethyl alcohol are markedly different from each other. The alcohol from fraction (a) (1.2 g.) and phenyl isocyanate (1.2 g.) were mixed and heated at 130° for two hours. On cooling, an equal volume of petroleum ether was added and the phenylurethane thus separated was filtered (1.2 g.). It melted at 88–89° after recrystallisations from alcohol (Table 2).

The alcohol from fraction (c) (1.0 g.) was treated with phenyl isocyanate just in the same way as above. On cooling, it was dissolved in alcohol, filtered and was concentrated. Phenylurethane gradually deposited after long standing. It melted at 45–46° after recrystallisations from little alcohol (Table 2) and showed no lowering when mixed with a specimen of urethane prepared from pure phenyl-propyl alcohol (Takeda, b.p. 110–113° under 9 mm.).

The alkaline solution used for hydrolysis of ester was acidified and extracted with ether. A small amount of crystals was obtained from the extract after long standing in the desiccator. It melted at 46–47° and was identified as hydrocinnamic acid by the mixed melting point determination.

Fraction IV. After treating with 10% sodium hydroxide it was extracted with ether. The extract was fractionated, and the main part distilled at 168–170° under 17 mm., which was found to be benzyl-ethylene glycol by analysis (Table 3) as well as by the formation of bis-phenylurethane (Table 2). *Bis-phenylurethane.* The glycol (1.0 g.) and phenyl isocyanate (2.0 g.) were mixed and heated at 120–130° for 0.5 hour. After cooling, twice its volume of ligroin was added, well stirred, from which crude urethane (2.6 g.) crystallized out on standing. It can be recrystallized from either alcohol or benzene. *Recrystallisation from alcohol.* Half amount of the crude urethane was dissolved in hot alcohol and filtered. The filtrate was concentrated to a syrup which gradually changed to crystalline mass. It melted at 108.5–109.5° after recrystallisation from the same solvent (A) (Table 2). *Recrystallisation from benzene.* Another half of the crude urethane was treated with benzene instead of alcohol just in the same way. The phenylurethane thus purified was amorphous powder and melted at 132–133° after recrystallisation from benzene (B) (Table 2).

Samples A and B showed the same nitrogen content corresponding to bis-phenylurethane, while their melting points were distinctly apart from each other. Sample A can be converted into B (melting at 129–131°) after one recrystallisation from benzene and the reverse change was observed when sample B was treated with alcohol (melting 109–110°). The monotropic transformation from A to B takes place on mere heating. Sample A was put in Abderhalden drying apparatus and maintained at 100° in vacuum for three hours and then at 110° for seven hours, during which the weight and melting point were determined from time to time. The loss of weight was never observed during whole operation, while melting point gradually changed and finally reached a constant value 131–133°, which shows that the sample was completely changed into B. The sample thus prepared can be reconverted into A (melting at 108–109°) by twice recrystallizing from alcohol.

Experiment B. Acetone-compound 25.0 g. (0.12 mol). Catalyzer 4.0 g. Time of hydrogenation 4.5 hours at 240–260°. Fractionation (19.3 g.):

I	79– 82° under ordinary pressure	7.5 g.
II	100–120° under 11 mm.	10.1 g.

Fraction I smelt of aromatic hydrocarbon as in the case of acetone-mandelic acid and when put into water, it did not dissolve completely, but the part insoluble in water was too minute to test its boiling point.

Fraction II was combined with the corresponding fraction in experiment A as already mentioned. In the present experiment higher boiling fraction corresponding to glycol was lacking. The glycol seemed to have been completely hydrogenated to monohydric alcohols in prolonged hydrogenation in this experiment.

Table 2.

Alcohol and glycol	Derivative prepared	N		
		Found*	Calc.	for
$CH_3 \cdot CH(OH) \cdot CH_3$	α-Naphthylurethane, m.p. 104–105°	6.07	$C_{14}H_{15}O_2N$,	6.11%
$(CH_3)_2CH \cdot CH_2 \cdot CH_2 \cdot CH_2OH$	3, 5-Dinitrobenzoic ester,(13) m.p. 68–69°	9.64	$C_{13}H_{16}O_6N_2$,	9.46%
$C_6H_5 \cdot CH_2 \cdot CH_2OH$	Phenylurethane, m.p. 78–79°	5.77	$C_{15}H_{15}O_2N$,	5.81%
$C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_2OH$	Phenylurethane, m.p. 44–45°	5.63	$C_{16}H_{17}O_2N$,	5.49%
$C_6H_5 \cdot CH_2 \cdot CH(OH) \cdot CH_3$ (active)**	Phenylurethane,(14) m.p. 88–89°	5.48	$C_{16}H_{17}O_2N$,	5.49%
$CH_3 \cdot CH(OH) \cdot CH_2OH$ (*dl*)	Bis-phenylurethane,(15) m.p. 143–144°	8.87	$C_{17}H_{18}O_4N_2$,	8.90%
$(CH_3)_2CH \cdot CH_2 \cdot CH(OH) \cdot CH_2OH$ (active)**	Bis-phenylurethane, m.p. 115–116°	7.79	$C_{20}H_{24}O_4N_2$,	7.87%
$C_6H_5 \cdot CH_2 \cdot CH(OH) \cdot CH_2OH$ (active)**	Bis-phenylurethane, {m.p. 108–109° (A) {m.p. 132–133° (B)	7.18 7.13	$C_{23}H_{22}O_4N_2$,	7.18%

---

* Nitrogen was estimated by micro-Kjeldahl method except in case of nitro-compound.

** The activities were not examined. During hydrogenation they might be subjected to racemisation to some extent. E. Bowden, H. Adkins, *J. Am. Chem. Soc.*, **56** (1934), 689.

(13) G. B. Malone, E. E. Reid, *J. Am. Chem. Soc.*, **51** (1929), 3426.

(14) Phenylurethane of active alcohol is unknown. That of *dl*-alcohol melts at 92°. M. Tiffeneau, *Compt. rend.*, **146** (1908), 698.

(15) G. S. Walpole, *Proc. Roy. Soc. London* (B), **83** (1911), 272. Walpole gives the m.p. 152.5–153.5° for the same bis-phenylurethane of *dl*-glycol, but in the present study it could not be raised above 144°. That of active glycol, m.p. 145–146°, P. A. Levene, A. Walti, *J. Biol. Chem.*, **73** (1927), 263.

Table 3.

Glycol	Analytical results	
	Found	Calc. for
Isohexylene glycol, b.p. 111–113.5° under 15 mm.	C, 60.82; H, 11.84	$C_6H_{14}O_2$: C, 60.95; H, 11.96%
Benzyl-ethylene glycol, b.p. 168–170° under 17 mm.	C, 70.94; H, 8.11	$C_9H_{12}O_2$: C, 71,01; H, 7.96%

The present study was carried out in the Chemical Institute, Faculty of Science, Imperial University of Tokyo. The author wishes to express his sincere thanks to Prof. K. Matsubara for the kind inspection of this paper. His best thanks are also due to Dr. Y. Takayama for the constant encouragements during this study.