ACETONE-COMPOUNDS OF SOME α-HYDROXY-ACIDS AND THEIR RAMAN SPECTRA.*

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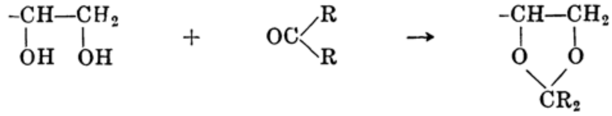
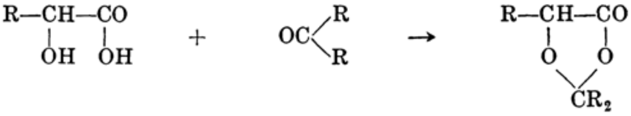
Polyhydric compounds, which contain two hydroxyls in α-positions, condense with a carbonyl compound producing cyclic acetals in the presence of dehydrating agents.



It is known that some α-hydroxy-acids behave similarly towards carbonyl and form compounds having a heterocyclic ring of the same type.



The preparation of such derivatives of α-hydroxy-acids was reported by Wallach,⁽¹⁾ Leipen,⁽²⁾ van Ekenstein,⁽³⁾ and several other investigators. Formaldehyde, benzaldehyde, and acetone can be mentioned as the reactants on α-hydroxy-acids. Restricting to the acetone compounds, following works are cited from the literature.

In 1923 Willstätter⁽⁴⁾ prepared acetone compounds of glycollic acid (b.p. 41° under 11 mm.), mandelic acid (m.p. 47.5–48°), and benzilic acid (m.p. 48°). In 1927 those of tartaric acids (*l* and *d*, m.p. 102°; *r*, 88.5°; *i*, 96–97°) and of quinic acid (m.p. 141°) were synthesized by H. O. L. Fischer.⁽⁵⁾ As the dehydrating agent, Willstätter used concentrated sulphuric acid or anhydrous copper sulphate, while zinc chloride and

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* Studies on Hydroxy-acids and their Derivatives. II.

(1) O. Wallach, Th. Heymer, *Ber.*, **9** (1876), 545.

(2) R. Leipen, *Monatsh.*, **9** (1888), 45.

(3) W. A. Ekenstein, C. A. Lobry de Bruyn, *Rec. trav. chim.*, **18** (1899), 305; **20** (1901), 331; **21** (1902), 310.

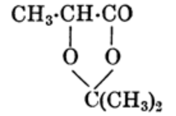
(4) R. Willstätter, Fr. Königsberger, *Ber.*, **56** (1923), 2107.

(5) H. O. L. Fischer, C. Taube, *Ber.*, **60** (1927), 485.

phosphorus pentoxide were recommended by H. O. L. Fischer and Smith(6) respectively.

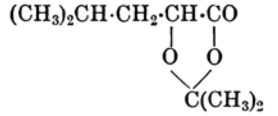
The present author tried the preparation of acetone compounds of other α-hydroxy-acids and isolated the following:

Acetone-lactic acid



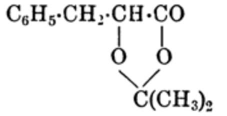
b.p. 49–49.5° under 11 mm.

Acetone-leucic acid



b.p. 84.5-85.5° under 13 mm.

Acetone-phenyl-lactic acid



m.p. 63-64°.

The latter two are formed by dehydration either with sulphuric acid or zinc chloride (better yield is obtained with the former), but the acetone compound of lactic acid is very sensitive to hydrolysis and can be prepared only with sulphuric acid under the special precautions that it never come in contact with water during its isolation.

Little was studied on the properties of acetone-hydroxy-acids and the only fact hitherto described is their instability towards warm dilute alkali. The author intends to carry out some investigations on the compounds of this class and the Raman spectra were first studied.

Raman Spectra. The acetone compounds of lactic acid and leucic acid were selected as materials. At room temperature, they are liquid, which provides every facility for the study of Raman spectra.

On the Raman spectra of compounds having five-membered saturated ring, informations are few except cyclopentane and its derivatives(7) and some of the anhydrides of dibasic acids.(8) From the Raman spectra of two above-mentioned compounds photographed by the author, the following conclusion can be derived.

(a) C·H-Frequencies. In both of the spectra, the frequencies close up and over 2900 cm.$^{-1}$ (2869, 2940, 2993 in acetone-lactic acid (I) and

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(6) L. Smith, J. Lindberg, *Ber.*, **64** (1931), 505.

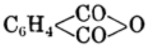
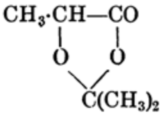
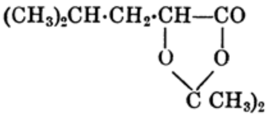
(7) Weiler, *Z. Physik*, **69** (1931), 586; Canal, *Compt. rend.*, **194** (1932), 1574. L. Piaux, *Compt. rend.*, **197** (1933), 1647; **198** (1934), 1496.

2868, 2902, 2939, 2994 in acetone-leucic acid (II)) are lines usually assigned as "C·H-valency-frequencies". No C·H-frequency which exceeds 3000 cm.$^{-1}$ is found in the spectra. The frequencies 1448 cm.$^{-1}$ in I and 1446 cm.$^{-1}$ in II are assigned as "C·H-deformation-frequencies".

(b) C:O-Frequency. The present compounds contain a carbonyl group in the molecules. The frequencies 1790 cm.$^{-1}$ in I and 1787 cm.$^{-1}$ in II can be attributed to this group, although the values observed here seem rather high for such frequencies.

According to the detailed study of Kohlrausch,(8) the C:O-frequency is said to be sensible to the constitutive effect of adjacent groups. It shows minimum value in free acids (mean 1660 cm.$^{-1}$) and it increases in ketones, aldehydes, and esters (mean of esters 1732 cm.$^{-1}$) in the order mentioned. In acid anhydrides, which show some similarity in structure with the present compounds, the value increases furthermore; 1740–1754 cm.$^{-1}$ are observed in six kinds of anhydrides of monobasic acids and 1774–1782 cm.$^{-1}$ in four kinds of anhydrides of dibasic acids (inner anhydrides). In addition to these, it was pointed out also by Kohlrausch that the more sensitive the compound to hydrolysis, the higher is the value of C:O-frequency, Table 1.

Table 1.

Phthalide	 $C_7H_4{<}\substack{CO\\CH_2}{>}O$	1753
Phthalic anhydride	 $C_6H_4{<}\substack{CO\\CO}{>}O$	1775
Benzoic anhydride	$C_6H_5{\cdot}CO{\cdot}O{\cdot}OC{\cdot}C_6H_5$	1776
Benzoyl peroxide	$C_6H_5{\cdot}CO{\cdot}O{\cdot}O{\cdot}OC{\cdot}C_6H_5$	1781
Acetone-lactic acid		1790
Acetone-leucic acid		1787

The present compounds have the similar cyclic structure as anhydrides of dibasic acids and show marked sensitivity to hydrolysis and it is easily understood from the study of Kohlrausch that the C:O-frequencies in these compounds show the values as high as 1787–1790 cm.$^{-1}$.

(c) Other frequencies. Among other frequencies, the two adjacent ones, 623, 706 cm.$^{-1}$ in I and 623, 700 cm.$^{-1}$ in II are sharp and strong and are very conspicuous in each of two spectra.

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(8) K. Kohlrausch, A. Pongratz, R. Seka, *Ber.*, **66** (1933), 1.

Experimental Part.

Preparation of acetone-compounds of α-hydroxy-acids.

Acetone-lactic acid. Lactic acid (Takeda; 100 g.) was dissolved in dry acetone (400 c.c.). The solution was kept at -5–-10° and concentrated sulphuric acid (300 g.) was added with mechanical stirring in the course of two hours. Benzene was poured repeatedly (total volume, 1000 c.c.) to the above solution and the product was thoroughly extracted.

To the combined benzene solution freshly ignited sodium sulphate was added and dry ammonia was passed to neutralize the remaining acid. After standing overnight, the benzene was removed under reduced pressure and the residual oil was subjected to vacuum distillation, when the main part distilled at 57–58° under 18 mm. and it amounted to 43.2 g., corresponding to 30 mol% assuming that the lactic acid was pure. After refractionation, the part distilling at 49–49.5° under 11 mm. was taken for analysis. The acetone-compound is readily hydrolyzed with warm dilute alkali and the components can be determined as follows: The weighed sample was completely hydrolyzed with an excess of N/10-alkali by warming on water bath. After cooling, the remaining alkali was titrated with N/10-acid. (Found: Saponification equivalent, 130.6. Calc. for $C_6H_{10}O_3$: 130.1). The weighed sample was hydrolyzed with an excess of N-alkali in a tightly stoppered bottle. After cooling, acetone was determined by Messinger's method as usual. (Found: acetone, 44.07. Calc. for $C_6H_{10}O_3$: 44.65%.)

Acetone-leucic acid. (a) *By sulphuric acid method.* Leucic acid (40 g., 0.30 mol) (m.p. 73°, prepared from natural leucine) was dissolved in acetone (110 c.c.) and the solution was cooled at -10–-20°. Concentrated sulphuric acid (25 g.) was gradually added with constant stirring. After 30 minutes, the reaction product was poured into an excess of ice-cooled 10% sodium carbonate solution to remove acid, whereupon an oil gradually accumulated on the surface of the solution. The oily layer was separated and the carbonate solution was thoroughly extracted with ether, to which the above oil was put together. After removing ether, the residual oil was distilled in vacuum; the part distilling at 90–92.5° under 18 mm. amounted to 33.7 g., corresponding to 64 mol%. (Found: Saponification equivalent, 173.6; acetone, 33.32. Calc. for $C_9H_{16}O_3$: sap. equ., 172.1; acetone, 33.72%.)

(b) *By zinc chloride method.* Leucic acid (20 g., 0.15 mol.) was dissolved in dry acetone (50 c.c.), to which a suspension of zinc chloride (40 g.) in acetone (100 g.) was gradually added. After standing overnight, acetone was distilled off in vacuum and ether (500 c.c.) was added and the mixture was extracted with water to remove zinc chloride. After drying, ether was expelled and the residual oil was subjected to distillation. The part distilling at 91–95° under 21 mm. (3.9 g., corresponding to 15 mol%) was collected, but it was contaminated with mesityl oxide. It required repeated fractionation to remove the impurity completely.

Acetone-phenyl-lactic acid. (a) *By sulphuric acid method.* Phenyl-lactic acid (40 g., 0.24 mol) (m.p. 124°; prepared from natural phenylalanine) was put into acetone (110 c.c.) and was treated with concentrated sulphuric acid (24 g.) just in the same manner as in the case of leucic acid. The solution was poured into an excess of ice-cooled 10% sodium carbonate solution and the acetone compound separated as crystals. It amounted to 43 g. after drying overnight. Yield, 88 mol%. It melted at 63–64° after recrystallisation from alcohol. (Found: saponification equivalent, 206.4; acetone, 27.82. Calc. for $C_{12}H_{14}O_3$: sap. eq., 206.1; acetone, 28.17%.)

(b) *By zinc chloride method.* From 15 g. of the hydroxy-acid, 50 c.c. of dry acetone, and 23 g. of zinc chloride; 5.2 g. of the acetone-compound was obtained, yield 28 mol%.

Raman Spectra.

The Raman spectra were taken in the laboratory of Prof. Mizushima by his and his collaborators' courtesy. Every appliance for Raman spectrum here used is of

Table 2. Acetone-lactic acid.

No.	Intensity	$\Delta\nu$ in cm.$^{-1}$	No. in which $\Delta\nu$ is equal
1	m.	k- 114	1-15
2	w.	k- 258(q-2941)	2-26-31
3	w.	k- 310(q-2993)	3-27-32
4	w.	k- 348(p-2996)	4-27-32
		(o-2936)	4-26-31
5	w.	k- 412(o-3000)	5-27-32
6	w.	k- 526	6-18
7	v.s.	k- 623	7-19
8	s.	k- 705	8-20
9	s.	k- 786	9-21
10	w.	k- 813(i- 624)	10- 7-19
11	w.	k- 883	11-22
12	w.	k- 934	12-23
13	w.	k- 984	13-24
14	m. b.	k-1449	14-28
15	s.	e- 115	15- 1
16	w.	e- 250	—
17	m.	e- 329	—
18	w.	e- 529	18- 6
19	v.s.	e- 622	19- 7
20	s.	e- 707	20- 8
21	s.	e- 784	21- 9
22	w.	e- 884	22-11
23	w.	e- 933	23-12
24	w.	e- 987	24-13
25	m.	e-1099(k-2868)	25-30
26	v.s.	e-1176(k-2943)	26-31
27	v.s.	e-1227(k-2994)	27-32
28	s. b.	e-1447	28-14
29	m.	e-1790	—
30	m.	e-2870	30-25
31	v.s.	e-2937	31-26
32	v.s.	e-2992	32-27

$\Delta\nu$: 115(s.), 250(w.), 329(m.), 528(w.), 623(v.s.), 706(s.), 785(s.), 884(w.), 934(w.), 986(w.), 1448(s. b.), 1790(m.), 2869(s.), 2940(v.s.), 2993(v.s.).

Table 3. Acetone-leucic acid.

No.	Intensity	$\Delta\nu$ in cm.$^{-1}$	No. in which $\Delta\nu$ is equal
1	w.	k- 223(p-2871)	1-26-32
2	m.	k- 258(q-2941)	2-28-34
3	w.	k- 278(o-2866)	3-26-32
4	m.	k- 317(q-3000)	4-29-35
5	w.	k- 352(o-2940)	5-28-34
		(p-3000)	5-29-35
6	w.	k- 415(o-3003)	6-29-35
7	w.	k- 518	7-19
8	v.s.	k- 623	8-20
9	s.	k- 699	9-21
10	w.	k- 808(i- 619)	10- 8-20
11	s.	k- 828	11-22
12	w.	k- 925	12-23
13	w.	k- 958	13-24
14	w.	k-1009	14-25
15	w.	k-1141(e+ 626)	15- 8-20
16	s. b.	k-1447	16-30
17	w.	e- 359	—
18	w.	e- 429	—
19	w.	e- 524	19- 7
20	v.s.	e- 622	20- 8
21	s.	e- 700	21- 9
22	s.	e- 829	22-11
23	w.	e- 928	23-12
24	m.	e- 957	24-13
25	w.	e-1001	25-14
26	s.	e-1103(k-2870)	26-32
27	s.	e-1136(k-2903)	27-33
28	v.s.	e-1172(k-2939)	28-34
29	v.s.	e-1229(k-2996)	29-35
30	s. b.	e-1444	30-16
31	m.	e-1787	—
32	s.	e-2865	32-26
33	s.	e-2901	33-27
34	v.s.	e-2939	34-28
35	v.s.	e-2992	35-29

$\Delta\nu$: 359(w.), 429(w.), 521(w.), 623(v.s.), 700(s.), 829(s.), 927(w.), 958(m.), 1005(w.), 1446(s. b.), 1787(m.), 2868(s.) 2902(s.), 2939(v.s.), 2994(v.s.).

their own construction.(9) 1. Light source: two mercury lamps, 30 cm. long (100 v.–10 amp.). 2. Spectrograph: an apparatus with large aperture (1:5) having a dispersion of 12 Å per mm. at 4000 Å. 3. The breadth of the slit: 0.1 mm. 4. Photographic plates: "Agfa Isochromplatten." 5. Time of exposure: 2.5 hours (3.5 hrs. in the case when quinine sulphate filter was used). 6. The relative intensity of Raman spectra was classified into four grades (by visual estimation), namely, very strong (v.s.), strong (s.), medium (m.) and weak (w.). 7. The Raman apectra were taken twice for each sample, once with the filter, and the mean value of the frequencies in both plates are shown in Tables 2 and 3. 8. Materials: purified by repeated fractionation in vacuum through a 6 cm. Widmer column, in each experiment, 25 c.c. of the pure sample was put into the scattering tube.

Acetone-lactic acid,	b.p. 58.0–58.5°C. under 18 mm.
Acetone-leucic acid,	b.p. 84.5–85.5°C. under 13 mm.

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 Prof. S. Mizushima and Mr. Y. Morino for their valuable instructions in the study of Raman spectrum and to Dr. Y. Takayama for his constant encouragements during this work.

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(9) The detailed description of the apparatus is given by Mizushima, Morino, and Higasi, *Scientific Papers of the Institute of Physical and Chemical Research, Japan,* **25** (1934), 159–221; *Physik. Z.*, **35** (1934), 905–911.