Optical Isomer Effect on the Mechanochemical Interaction of Mandelic Acid with Talc Powder

Akiko IKEKAWA* and Sohachiro HAYAKAWA†
Faculty of Pharmaceutical Sciences, Showa University, Hatanodai, 1-5-8, Shinagawa-ku, Tokyo 142
†Laboratory of Applied Physics, Faculty of Engineering, Chiba University, Yayoi-cho 1-33, Chiba 260

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Mandelic acid was ball-milled with talc powder, and the optical isomer effect on the IR spectral change was investigated. The change showed that a complex was formed between talc and the hydroxyl group and the COOH group of mandelic acid. It was also shown that the covalent character in the bond of the C=O group with talc was greater for (*RS*)-mandelic acid than for the R-isomer and the S-isomer. The change in the region of the carbonyl-stretching vibration was affected by the humidity in the ball-milling atmosphere, and the effect on the R-isomer was greater than the effect on the S-isomer. Magnesium mandelate powder was obtained from an ethanolic suspension of the ball-milled mixture with talc. The IR spectra and the elemental analysis showed that the C=O group was covalently bonded to Mg in the complex of the (RS)-compound and that it was ionically bonded in the complex of the R-isomer and the S-isomer. The thermal analysis showed that the decomposition temperature for the complex of the R-isomer was different from the temperature for the complex of the S-isomer. It was suggested that talc powder had a chiral surface when it was mechanically treated.

The optical isomer effect on a chemical reaction is of great interest with regard to the origin of life. Furthermore, it is of practical importance in pharmaceutics. Kwan et al. reported that (S)-(+)-mandelic acid was adsorbed on starch from an aqueous solution of the racemate preferentially over the (R)-(−)-isomer.1) According to Nagwekar and Kastenbauder, the rate constant for the metabolism of the S-isomer in the human body was approximately twice the rate for the R-isomer.2)

Previously, the authors reported the optical isomer effect on the racemization of mandelic acid at the surface of talc powder.3) This paper will deal with the interaction of optically active and racemic mandelic acids with talc powder upon mechanical treatment.

Experimental

The materials used were (*S*)-(+)-mandelic acid [(*S*)-(+)-α-hydroxyphenylacetic acid] and (*R*)-(−)-mandelic acid purchased from the Aldrich Chemical Co, and (*RS*)-mandelic acid (guaranteed-grade), talc, and magnesium oxide (heavy, guaranteed-grade) of Wako Pure Chemicals Industries, Ltd. The ethanol, 2-propanol, 2-butanol, and formic acid were of a guaranteed grade. A 10-g portion of a mixture of mandelic acid with talc or a mixture with MgO was inserted into a stainless-steel mill (10 cm in diameter and with a capacity of 900 cm^3) containing ten stainless-steel balls (with a density of 8.2 g cm^{-3} and a diameter of 2.5 cm) and thirty balls 1.9 cm in diameter. The mill was rotated at a velocity of 95 rpm. This procedure will be called "ball-milling" hereafter. The ball-milling was carried out between December and February with a relative humidity of 45—55% or in June and July with a relative humidity of 75—85%. The ball-milled samples were kept in a desiccator containing silica gel.

Various samples were prepared from a mixture of talc containing 10 w/w% of mandelic acid, which had been ball-milled under a relative humidity of 45—55% for 10 h. A suspension of 1.6 g of this mixture in 80 ml of ethanol was stirred at 5 °C for 1 h at a velocity of 380 rpm. It was then centrifuged, and the supernatant, A, was evaporated to dryness at 60 °C under reduced pressure. The powder thus obtained, A′, was weighed, and then 3 ml of ethanol was added to this. This suspension was set aside at 5 °C for 1 h after having been shaken vigorously; a supernatant, B, and a precipitate, C, were obtained by centrifuging. The precipitate C was washed twice with ethanol, dried at 60 °C, and weighed (powder C). Powder C was washed with ethanol eight more times and then dried at 60 °C (powder C′). The supernatant B and the powders, A′, C, and C′, obtained from mixtures of the (RS)-compound and the R-isomer or the S-isomer are, respectively, expressed by B_{RS}, B_R, B_S, A'_{RS}, A'_R, A'_S, C_{RS}, C_R, C_S, C'_{RS}, C'_R, and C'_S. The powders M-Mg and M-Mg′ were prepared as follows. A suspension of MgO in an ethanolic solution of (*RS*)-mandelic acid was set aside for several hours at 60 °C in order to prepare the M-Mg powder and at 5 °C in order to prepare the M-Mg′ powder. These suspensions were then centrifuged, and the precipitates were washed with ethanol several times and dried at 60 °C. These samples were kept in a desiccator containing silica gel.

The IR spectra were measured with a JASCO infrared spectrophotometer (Model 810). The absorption spectra were measured with a Hitachi recording spectrophotometer (Model 340). The optical rotation of the solutions was measured with a JASCO digital polarimeter. The DTA and TG measurements were carried out using a thermal analyser (Model DT-20B and TG-30) of Shimadzu Seisakusho. The supernatant B was developed on a thin layer of silica gel with a solvent system of 2-butanol-2-propanol-formic acid-water (15 : 15 : 4 : 10).4)

Results and Discussion

IR Spectra. Figures 1 and 2 show the IR spectra of the ball-milled mixtures of mandelic acid and talc. The absorbances around 3400—3420 cm^{-1} and at 1700—1730 cm^{-1} decreased, while new peaks appeared in the 1600—1650 cm^{-1} region, on ball-milling. Under the relative humidity of 75—85%, new peaks appeared at 1610, 1630, and 1650 cm^{-1}, and the absorbance at 1650 cm^{-1} increased remarkably, at the first stage of ball-milling in the case of (*RS*)-mandelic acid. On the ball-milling of the mixture of the R-isomer or

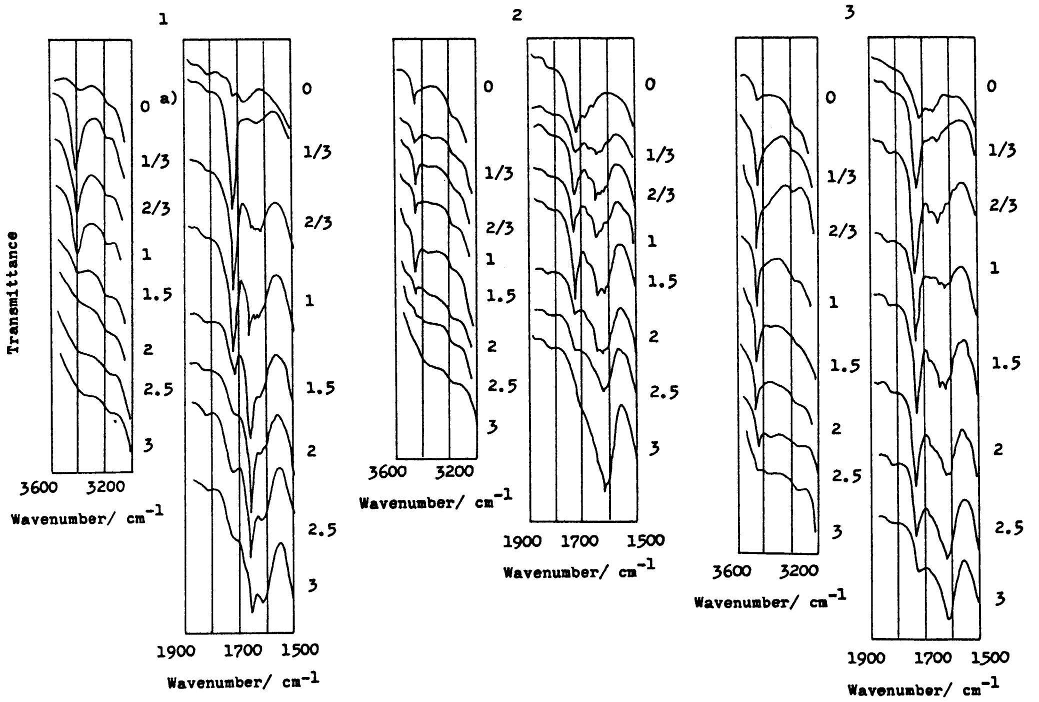


Fig. 1. Change in the IR spectra of mandelic acid upon ball-milling with talc in the atmosphere of high humidity. 1 (*RS*)-mandelic acid, 2 (*R*)-(−)-mandelic acid, 3 (*S*)-(+)-mandelic acid. Ball-milling conditions; the content of mandelic acid 10 w/w%, relative humidity 75—85%. a) Ball-milling time/h.

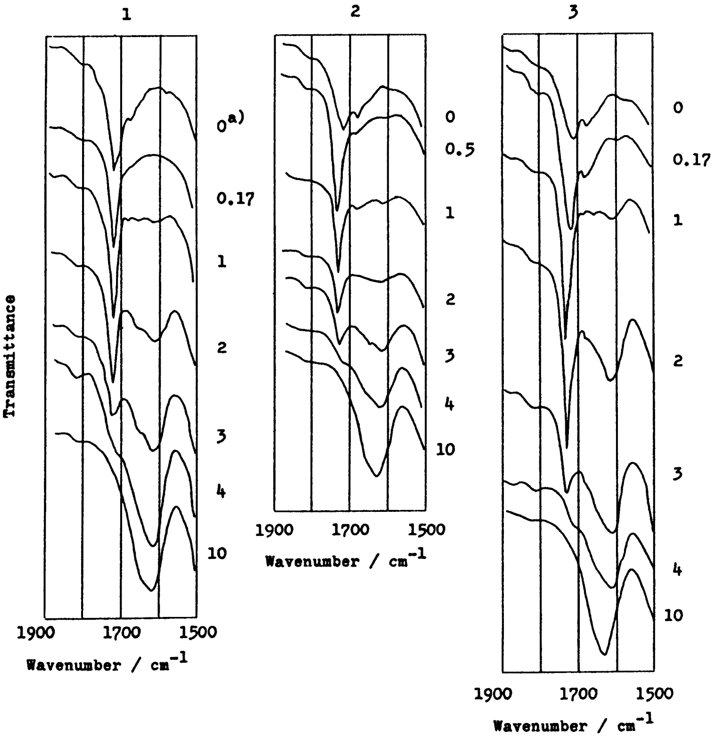


Fig. 2. Change in the IR spectra of mandelic acid upon ball-milling with talc in the atmosphere of low humidity. 1 (*RS*)-mandelic acid, 2 (*R*)-(−)-mandelic acid, 3 (*S*)-(+)-mandelic acid. Ball-milling conditions; the content of mandelic acid 10 w/w%, relative humidity 45—55%. a) Ball-milling time/h.

S-isomer, new peaks appeared at 1600, 1620, and 1640 cm^{-1}. These changes were greater for the R-isomer than those for the S-isomer at the first stage. Under the relative humidity of 45—55%, a new peak also appeared at 1650 cm^{-1} upon the ball-milling of a mixture containing 30 w/w% of the (RS)-compound. However a broad absorption band appeared at 1600—1700 cm^{-1} in the other mixtures, and the optical isomer effect was slight. Figure 3 shows the IR spectra of the ball-milled mixtures in the region between 1200 and 1800 cm^{-1}. In the spectra of the mixtures of the (RS)-compound, the absorbance at 1350 cm^{-1} was high and the absorbance at 1410 cm^{-1} was low when the absorbance at 1650 cm^{-1} was high and the absorbance at 1600—1620 cm^{-1} was low. In the spectra of a mixture of the R-isomer or the S-isomer, the absorbance at 1390 cm^{-1} was high and the absorbance at 1410—1430 cm^{-1} was low when the absorbance at 1640 cm^{-1} was high and the absorbance at 1600—1620 cm^{-1} was low. According to Khadikar et al.,[5] the absorption band of the hydroxyl group is around 3260 cm^{-1} and the COO^{-} band is around 1600 cm^{-1} in the spectra of the complex of mandelic acid and a bivalent metal ion. It is clear from the above results that a complex is formed between talc and the hydroxyl group and the carboxyl group of mandelic acid. The IR spectra of the complexes of α-hydroxy carboxylic acids, amino acids, or EDTA with such metals as Cu, Ni, and Co have been reported by many workers, and the following facts have been confirmed.[6] When the metal-carboxylato bond is ionic, the asymmetric stretching vibration of the C=O group is in the 1550—1600 cm^{-1} region, and an increase in the frequency occurs with an increase in the covalent character. When the bond is covalent, the band is found at 1650 cm^{-1}. The symmetric stretching vibration of the C=O group for the ionic bond is at 1400—1410 cm^{-1}, and the band shifts to a lower frequency with the increase in the covalent character. It is clear from the above facts that the band at 1640—1650 cm^{-1} is due to the C=O group bonded to talc highly covalently and that the band at 1600—1610 cm^{-1} is due to the C=O group bonded with talc highly ionically. It may also be concluded that the C=O group of the (RS)-compound is more highly covalently bonded with talc than that of the R-isomer or the S-isomer.

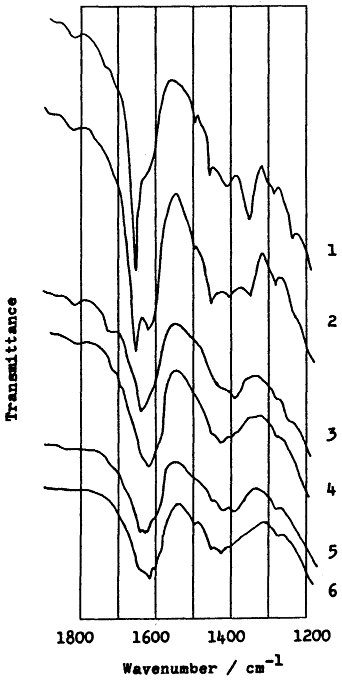


Fig. 3. Change in the symmetric and asymmetric stretching vibrations of the carbonyl group of mandelic acid upon ball-milling with talc.

	The type of mandelic acid	Ball-milling time/h
1	RS	1
2	RS	3
3	R	1
4	R	2.5
5	S	1.5
6	S	2.5

Ball-milling conditions; the content of mandelic acid 10 w/w%, relative humidity 75—85%.

The area surrounded by a straight line, passing through the transmittance at 1780 cm^{-1} and at 1550 cm^{-1}, and the transmittance-wavenumber curve was divided into five parts at the wavenumbers of 1620, 1640, 1660, and 1690 cm^{-1} for the (RS)-compound, and at the wavenumbers of 1610, 1630, 1660, and 1700 cm^{-1} for the R-isomer and the S-isomer. Only the four parts except the part between 1660—w cm^{-1} were discussed, where w is 1690 for the (RS)-compound and 1700 for the R-isomer and the S-isomer. S_Z and S_z' (Z=I, II, III, or IV) stand for the ratios of the area of each part to the total area for the (RS)-compound and for the R-isomer or the S-isomer respectively, where the wavenumber of part z, ν_z, is in the order of $\nu_{\mathrm{I}} \geqslant \nu_{\mathrm{II}} \geqslant \nu_{\mathrm{III}} \geqslant \nu_{\mathrm{IV}}$. As is

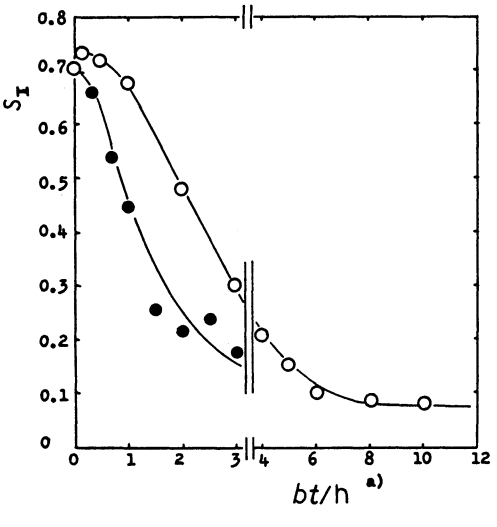


Fig. 4. Variation in S_{I} with ball-milling. Ball-milling conditions: the content of (*RS*)-mandelic acid 10 w/w%, relative humidity; 45—55% ○, 75—85% ●. a) *bt* is the ball-milling time.

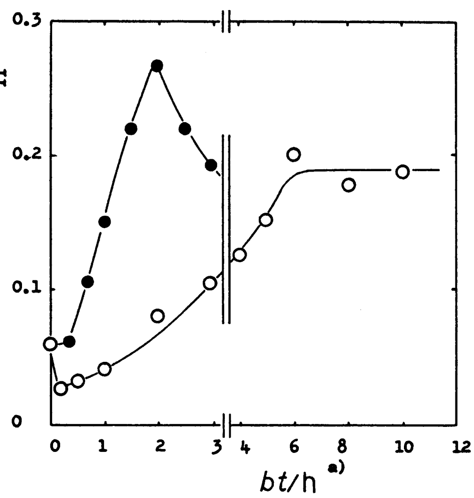


Fig. 5. Variation in S_{II} with ball-milling. Ball-milling conditions: the content of (*RS*)-mandelic acid 10 w/w%, relative humidity; 45—55% ○, 75—85% ●. a) *bt* is the ball-milling time.

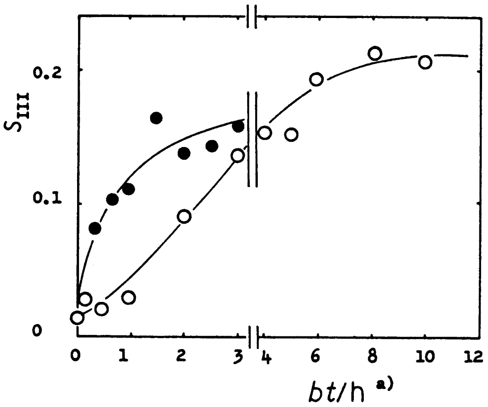


Fig. 6. Variation in S_{III} with ball-milling. Ball-milling conditions: the content of (*RS*)-mandelic acid 10 w/w%, relative humidity; 45—55% ○, 75—85% ● a) *bt* is the ball-milling time.

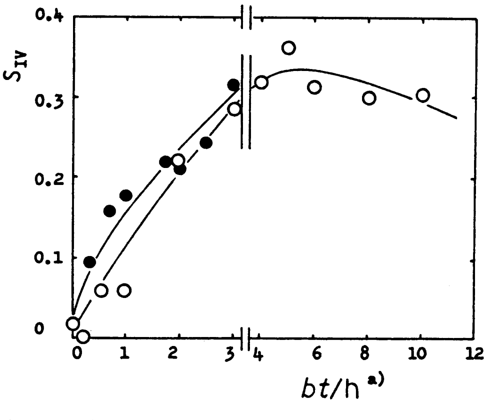


Fig. 7. Variation in S_{IV} with ball-milling. Ball-milling conditions: the content of (*RS*)-mandelic acid 10 w/w%, relative humidity; 45—55% ○, 75—85% ●. a) *bt* is the ball-milling time.

shown in Figs. 4—11, the change in these ratios at the first stage of ball-milling was greater under an atmosphere of high humidity. The effect of the humidity on S_{II} and S_{II}' was greater than the effect on the ratios for lower wavenumbers. The effect of the humidity on the mixture of the R-isomer was greater than the effect on the mixture of the S-isomer.

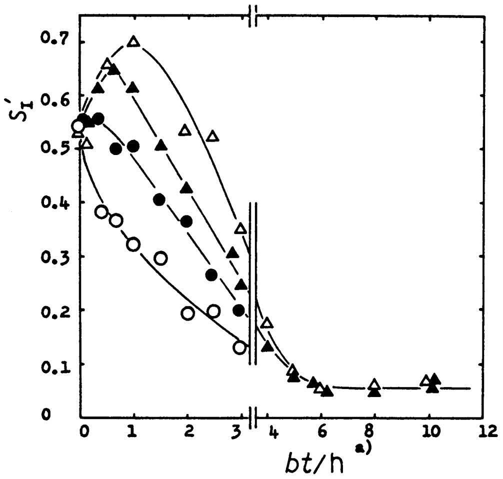


Fig. 8. Variation in S_I' with ball-milling. Ball-milling conditions: the content of mandelic acid 10 w/w%,

The kind of mandelic acid	Relative humidity/%
△ R	45—55
○ R	75—85
▲ S	45—55
● S	75—85

a) *bt* is the ball-milling time.

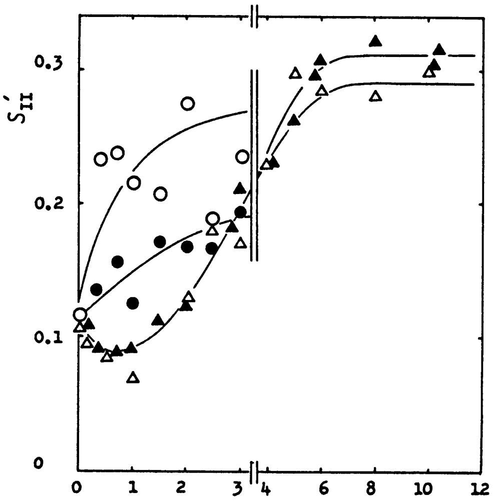


Fig. 9. Variation in S_{II}' with ball-milling. Ball-milling conditions; the content of mandelic acid 10 w/w%,

The kind of mandelic acid	Relative humidity/%
△ R	45—55
○ R	75—85
▲ S	45—55
● S	75—85

a) *bt* is the ball-milling time.

Magnesium Mandelate Powder. It was reported previously that mandelic acid was racemized when its anion was adsorbed very weakly at the surface of talc powder.[3] We have now measured the optical rotation and the absorption spectra for the supernatants of the ethanolic suspensions of the mixtures of mandelic acid with talc at the first stage of the ball-milling. It was clarified, from an analysis of these results, that the mandelic acid in the ball-milled mixture was not racemized, probably because of a strong interaction with talc. Table 1 shows the amounts of the A′ and C powders obtained from an ethanolic suspension of the ball-milled mixture. It is clear that the A'_R and A'_S powders contain more of an ethanol-soluble substance than A'_{RS}. According to many studies concerning the degradation of mandelic acid on γ-irradiation or oxidation, the main products are benzaldehyde, benzoic acid, and phenylglyoxylic acid.[7] By the thin-layer chromatography of B_R and B_S, mandelic acid, benzoic acid, and some substance other than the above three degradation products were detected, but mandelic acid was not detected for B_{RS}. A fine structure due to mandelic acid was observed in the absorption spectra of B_R and B_S, but a fine structure was not observed at all in the spectra of B_{RS}. It is considered that much of the ethanol-soluble substance in A'_R and A'_S powders is mandelic acid. In Table 1 are tabulated the amounts of mandelic acid in Solution A as inferred from the optical rotation of Solutions A and B.

In the IR spectra of C_R and C_S, the antisymmetric stretching vibration of C=O was around 1600 cm^{-1}, while it was at 1655 cm^{-1} in the spectra of C_{RS}. The spectra of C_{RS} were identical with those of M-Mg. In the spectra of M-Mg′ and the ball-milled mixture of mandelic acid with MgO, a broad band, which was a superposition of the bands at 1600 cm^{-1} and at 1655 cm^{-1}, was observed. Probably, powder C is the complex of mandelic acid and Mg, as M-Mg and M-Mg′ are considered to be the complexes of mandelic acid with MgO; this complex is also formed by ball-milling the mixture (Fig. 12).

Table 2 shows the contents of the C and H atoms in various C′ powders, as determined by the elemental

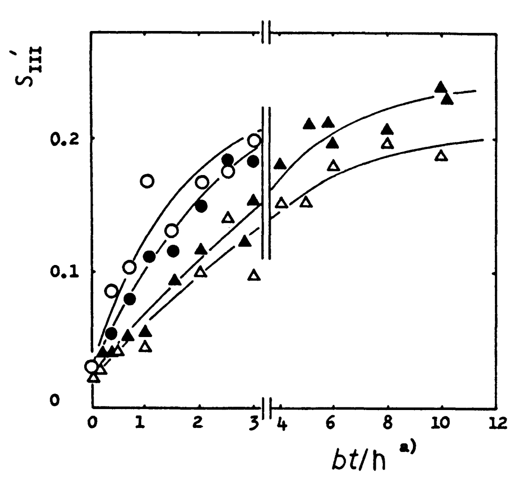


Fig. 10. Variation in S_{III}' with ball-milling. Ball-milling conditions; the content of mandelic acid 10 w/w%,

The kind of mandelic acid	Relative humidity/%
△ R	45—55
○ R	75—85
▲ S	45—55
● S	75—85

a) *bt* is the ball-milling time.

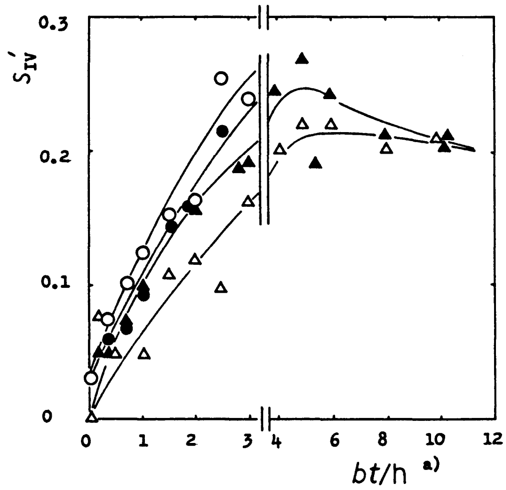


Fig. 11. Variation in S_{IV}' with ball-milling. Ball-milling conditions; the content of mandelic acid 10 w/w%,

The kind of mandelic acid	Relative humidity/%
△ R	45—55
○ R	75—85
▲ S	45—55
● S	75—85

a) *bt* is the ball-milling time.

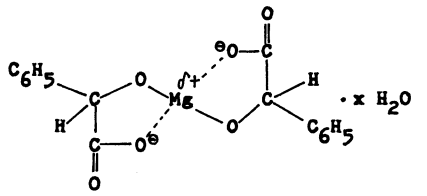
Table 1. Dissolution of Mandelic Acid from the Ball-Milled Mixture with Talc into Ethanol

Mandelic acid	RS		R		S	
$W_{A'}$/mg/80 ml[a]	29.3	34.6[c]	30.6	28.5	28.4	29.0
W_C/mg/80 ml[a]	27.1	30.8	21.9	24.6	20.6	19.8
$W_{A'}-W_C$/mg/80 ml	2.2	3.8	8.7	3.9	7.8	9.2
W_{MA}/mg/80 ml[b]	—	—	6.4—7.4	3.4—4.8	4.8—6.0	6.3—7.9

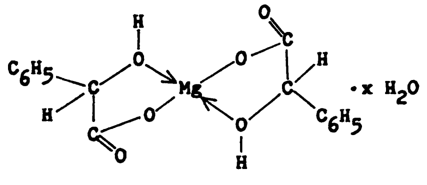
a) $W_{A'}$ and W_C are the weight amounts of A′ and C in 80 ml of A respectively. b) W_{MA} is the weight amount of mandelic acid in 80 ml of A obtained from the optical rotation of solutions A and B. The large values were obtained assuming that the optical rotation of B was all due to mandelic acid. The small values were obtained assuming that the optical rotation of B from that of A was due to mandelic acid. c) Each measurement was carried out twice.

Table 2. Elemental Analysis of Various C′ Powders

	Calcd/%					Found/%		
	K_A			K_B		C'_{RS}	C'_R	C'_S
x	0	1	2	0	1	—	—	—
C	59.21	56.10	53.29	58.84	55.77	57.84	55.74	55.22
H	3.73	4.12	4.47	4.32	4.68	4.21	4.13	4.22



K_A



K_B

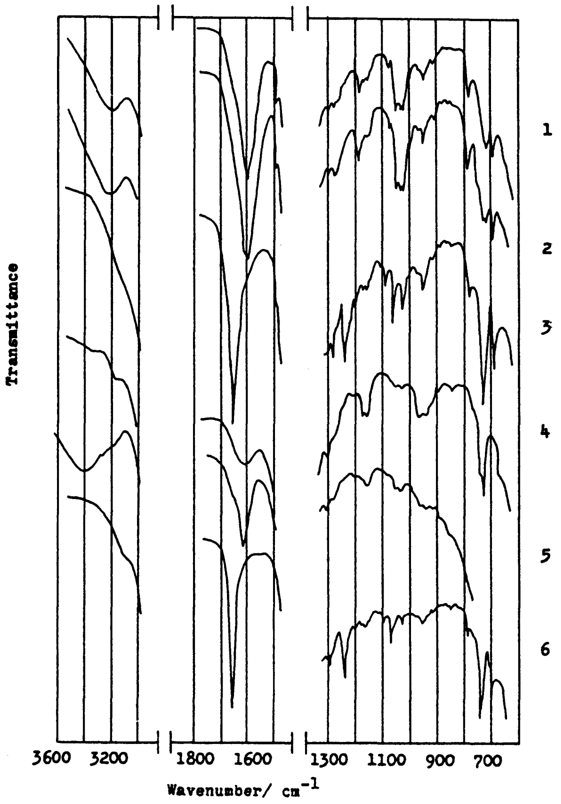


Fig. 12. IR spectra of various powders containing mandelic acid. 1 C_S, 2 C_R, 3 C_{RS}, 4 the ball-milled mixture of (*RS*)-mandelic acid and MgO (One g of mandelic acid and 9 g of MgO were ball-milled for 4 h.), 5 M-Mg′, 6 M-Mg.

analysis, and the values calculated for the substances of the molecular structures of K_A and K_B. A comparison between the found values and the calculated values suggests that the C'_{RS} powder is a substance with the molecular structure of K_B (x=0), mixed with a small amount of a substance with the molecular structure of K_A ($1<x<2$). The results also suggest that the C'_R and C'_S powders are substances with the molecular structure of K_A ($1<x<2$), mixed with only a small amount of a substance with the molecular structure of K_B (x=0).

Large exothermic peaks were observed at 300—400 °C and above 500 °C in the DTA thermograms of the C'_{RS} and C'_R powders. In addition, a small endothermic peak was observed at 280—320 °C in the thermogram of the C'_S powder. In the TG analysis, a mass loss was observed at these temperatures; the mass loss at 280—400 °C was 40—50%. It was determined from these measurements that the decomposition temperatures of the C'_{RS}, C'_R, and C'_S powders were 332, 320, and 282 °C respectively. A mass loss of approximately 4% was observed between room temperature and 100 °C in the case of the C'_S powder, but no mass loss was observed below the decomposition temperature in the cases of the C'_R and C'_{RS} powders. The water in these powders may be structural water, or it may coordinate with Mg, and the hydroxyl group and the COO^- group of mandelic acid may then bind with these coordinating water molecules.

Optical Isomer Effect. It is clear from the above results that the mechanochemical interaction of (*RS*)-mandelic acid with talc is different from the interaction of the R-isomer and the S-isomer. It is also clear that there is some difference between the interaction of the R-isomer and that of the S-isomer. The band of the free hydroxyl group is at 3515 cm^{-1} and this band shifts to a lower frequency upon hydrogen bonding.[8] The band of the hydroxyl group for the (RS)-compound is at 3400 cm^{-1}, while the bands for the R-isomer and the S-isomer are at 3420 cm^{-1}. This shows that intermolecular or intramolecular hydrogen bonds in the (RS)-compound are stronger than the bonds in the R-isomer or the S-isomer. Singurel[8] investigated the IR spectral change in mandelic acid upon interaction with proton acceptors. He pointed out that the C=O vibrations at 1718 cm^{-1} and 1762 cm^{-1} belonged to the dimer and to monomer mandelic acid respectively. When a proton acceptor complexed with the COOH group of mandelic acid, the C=O band appeared between the monomer band and the dimer band. The C=O band for the optically active mandelic acids at 1715 cm^{-1} shifted to a frequency higher by approximately 10 cm^{-1} at the first stage of ball-milling, but no shift was observed in the C=O band for the (RS)-compound. These facts show that the proton acceptors at the surface of talc powder form hydrogen bonds only with the optically active mandelic acids. Probably this causes the difference between the interactions of (*RS*)-mandelic acid and optically active mandelic acids with talc. The difference between the interaction of the R-isomer and that of the S-isomer also suggests that talc powder has a chiral surface when it is mechanically treated.

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