1352 cm^{-1}. Anal. Calcd for $C_{11}H_9NO_2$: C, 70.58; H, 4.85; N, 7.50. Found: C, 70.32; H, 4.76; N, 7.24.

2-Nitro-1,3-benzenediacetic Acid, Bis(methyl ester) (19). A suspension of 2-nitro-1,3-benzenedicarboxylic acid[3] (25 g, 0.118 mol) in 1,1,2,2-tetrachloroethane (100 mL) was treated with thionyl chloride (30 mL), and the mixture was refluxed for 7 h. The mixture was concentrated at reduced pressure, and after crystallization from *n*-heptane yielded pure 2-nitro-1,3-benzenedicarbonyl chloride (mp 129-131.5 °C), which was used immediately. A solution of diazomethane (4.2 g, 0.1 mol) in diethyl ether (500 mL) was cooled to 0 °C, and 2-nitro-1,3-benzenedicarbonyl chloride (2.93 g, 0.0118 mol) was added in portions. The mixture was stirred for 17 h and concentrated at reduced pressure to yield 2-nitro-1,3-diazoacetylbenzene as a tan solid. This compound was dissolved in methanol (250 mL), and the solution was added to freshly prepared silver oxide (synthesized by the reaction of 5 mL of a 10% silver nitrate solution with sodium hydroxide). The mixture was stirred at 0 °C for 1 h and at 55-60 °C for 2 h. The solution was filtered and concentrated to yield crude **20**. Recrystallization from *n*-heptane afforded pure **19** (1.83 g, 58% yield): mp 144-145 °C; ^{1}H NMR (DMSO-d_6) 7.46 (3 H, m, aromatic), 3.81 (4 H, s, CH_2), 3.56 (6 H, s, CH_3); IR (KBr) 2950, 1740, 1612, 1528, 1436, 1347 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_6$: C, 53.93; H, 4.90; N, 5.24. Found: C, 53.81; H, 4.68; N, 5.01.

2,3-Dihydro-2-oxo-1*H*-indole-7-acetic Acid, Methyl Ester (20). A solution of **19** (5.98 g, 02.022 mol) in tetrahydrofuran and methanol (2:1, 100 mL) was treated with hydrogen gas in the presence of 20% Pd/C for 18 h. The mixture was filtered and concentrated at reduced pressure to yield 2,3-dihydro-2-oxo-1*H*-indole-7-acetic acid methyl ester. Final purification was accomplished using flash chromatography on silica (elution with 1:19 methanol-dichloromethane) and resulted in pure **20** (4.01 g, 89% yield): mp 156-157 °C; ^{1}H NMR ($CDCl_3$) 9.15 (1 H, br s, NH), 7.15-6.85 (3 H, m, aromatic), 3.68 (3 H, s, CH_3), 3.60 (2 H, s, CH_2CO), 3.05 (2 H, s, CH_2CO); IR (KBr) 3180, 3050, 1722, 1703, 1619, 1600, 1458 cm^{-1}. Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.44; H, 5.39; N, 6.73.

2,3-Dihydro-2-oxo-1*H*-indole-7-acetic Acid (21). A solution of **20** (2.05 g, 0.01 mol) in methanol (50 mL) was treated with 1 N sodium hydroxide (10 mL, 0.01 mol), and the mixture was heated at 60 °C for 1 h. The reaction was concentrated at reduced pressure to yield the sodium salt of 2,3-dihydro-2-oxo-1*H*-indole-7-acetic acid. The sodium salt was dissolved in 2:1 water-methanol, and the solution was passed over a Dowex 50X-8 ion exchange resin. The eluant was concentrated at reduced pressure to yield pure **21** (1.60 g, 84% over Dowex 50×8 234-236 °C; ^{1}H NMR ($CDCl_3$ + DMSO-d_6) 9.95 (1 H, br s, NH), 7.10-6.75 (3 H, m, aromatic), 3.55 (2 H, s, CH_2CO), 3.40 (2 H, s, CH_2CO); IR (film) 3290, 3072, 2960, 1749, 1690, 1545, 1458, 1440 cm^{-1}. Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.75; N, 7.33. Found: C, 62.55; H, 5.00; N, 7.21.

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Registry No. **1**, 18356-28-0; **2**, 99320-61-3; **3**, 99320-60-2; **4**, 124201-47-4; **7**, 16578-60-2; **8**, 99641-32-4; **9**, 99320-77-1; **10**·Na, 99320-78-2; **6**, 21161-11-5; **11**, 1127-59-9; **12**, 99320-70-4; **13**, 99320-71-5; **14**, 99320-72-6; **15**, 99320-74-8; **16**, 124201-48-5; **17**, 124201-49-6; **18**, 124201-50-9; **19**, 99641-28-8; **20**, 99641-02-8; **21**, 99641-03-9; **21**·Na, 124201-51-0; **10**, 99320-79-3; 22, 69498-64-2; **23**, 91240-16-3; 2-nitro-1,3-benzenedialdehyde, 99320-75-9; chloral hydrate, 302-17-0; *o*-methylaniline, 95-53-4; *o*-isonitrosoacetotoluidide, 1132-03-2; dimethyl malonate, 108-59-8; 2-nitro-1,3-benzenedicarbonyl chloride, 57053-00-6; 2-nitro-1,3-bis(diazoacetyl)benzene, 99641-27-7; 2-((*tert*-butyldimethylsiloxy)methyl)benzeneamine, 68847-33-6.

Asymmetric Halogenation and Hydrohalogenation of *trans*-2-Butenoic Acid in a Crystalline α-Cyclodextrin Complex

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trans-2-Butenoic acid was asymmetrically hydrohalogenated and halogenated in a crystalline α-cyclodextrin complex. Exposure to gaseous hydrogen bromide at 20 °C and to hydrogen chloride at 0 °C gave (*S*)-(+)-3-bromobutanoic acid in 58% and (*S*)-(-)-3-chlorobutanoic acid in 64% enantiomeric excesses, respectively. At 45-50 °C, the guest in the cavity of the cyclodextrin reacted with gaseous bromine or chlorine to produce erythro-dihalides with extremely low optical activities; no products were obtained on treatment with bromine for 50 h at the lower temperature of 20 °C. The crystal structure of the complex was determined to be: $C_{36}H_{60}O_{30}\cdot C_4H_6O_2\cdot 5H_2O$; FW = 1149.0; orthorhombic; space group, $P2_12_12_1$; Z = 4; a = 14.406 (5), b = 38.174 (12), and c = 9.430 (3) Å; V = 5185.9 Å^3; D_X = 1.472, D_m = 1.475 g/cm^2. A mechanism for the observed chiral induction in the present gas-solid reaction is discussed in terms of the crystal structure of the complex.

Introduction

The inclusion phenomenon in cyclodextrin enables guest molecules to exhibit different and sometimes new properties relative to those of the free molecules. Some of these properties, including physical, chemical, and biological phenomena, have been studied over the recent years.[1] Asymmetric reactions catalyzed by cyclodextrin are of particular interest, as a quick and easy method for the synthesis of chiral compounds from achiral materials would thus be made available. In this regard, some asymmetric reactions have been attempted in solution in the presence of cyclodextrin, but all of these reactions have afforded the products in low optical yields.[1]

Recently, we achieved high enantioselectivity in the chlorination of methacrylic acid in crystalline cyclodextrin complexes.[2] Moreover, we have observed asymmetric additions of gaseous halogens and hydrogen halides to *trans*-cinnamic acid, ethyl *trans*-cinnamate, and styrene included in crystalline cyclodextrins.[3-5] This paper describes the asymmetric halogenation and hydro-

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halogenation of *trans*-2-butenoic acid or crotonic acid in crystalline cyclodextrin complexes and discusses the reaction mechanism on the basis of the X-ray crystal structure of the complex.

Experimental Section

Materials. α- and β-cyclodextrins were purchased from Sanraku-Ocean Co., Ltd., and further purified by one recrystallization from 1-propanol and two from water. Crotonic acid (*trans*-2-butenoic acid) and other solid and liquid reagents were reagent grade and were used after purification by ordinary methods.[6] Chlorine and hydrogen chloride were obtained from Komatsugawa Sanso and Tsurumi Soda Co., Ltd., respectively, and passed through a sulfuric acid trap prior to use. Hydrogen bromide was prepared by the procedure given in the literature.[7]

Preparation of Inclusion Complexes. To 100 mL of an aqueous solution containing α-cyclodextrin ($(1.2–1.7) \times 10^{-1}$ M) or β-cyclodextrin ($(2.8–3.0) \times 10^{-2}$ M) were added equimolar amounts of *trans*-2-butenoic acid and dissolved by mixing at 40 °C for 30 min. After stirring for 2 h at room temperature, the resulting white precipitates were filtered and dried in vacuo at room temperature for 1 day. Then the dried powders were washed with dichloromethane to remove any guest molecule not included and dried again. Thus, the white crystalline powders were obtained as a 1:1 molar complex of *trans*-butenoic acid with α-cyclodextrin in 86% yield.

X-ray diffraction, thermogravimetric (TG), and differential scanning calorimetric (DSC) analyses were used to establish complex formation. The amounts of acid in the complexes were determined by proton nuclear magnetic resonance (^{1}H NMR) spectroscopy in deuterated dimethyl sulfoxide (DMSO-d_6) and by elemental analysis. No complexation of the acid was observed with β-cyclodextrin.

Halogenation and Hydrohalogenation of the Crystalline Inclusion Complex. A typical experimental procedure follows: *trans*-2-Butenoic acid and its inclusion complex with α-cyclodextrin (ca. 2 g or 2 mmol) was exposed to gaseous hydrogen bromide (ca. 2 mol; 10 mol % excess) in a desiccator (ca. 600 mL) in the dark under air at the desired temperature. After exposure for 10–25 h, excess gas was removed by evacuation and the complex was dissolved in water containing sodium thiosulfate as a reducing agent for the excess bromine. The resulting aqueous layer was stirred vigorously with diethyl ether at room temperature to extract the reacted and unreacted guests. After 3 h, the organic layer was separated, dried over anhydrous magnesium sulfate, and concentrated to give a colorless oil. The extract was recovered in 95–98% yield and was chromatographed on Wako C-300 silica gel with dichloromethane containing 1% methanol to give 170 mg of 3-bromobutanoic acid, as identified by ^{1}H NMR and infrared (IR) spectra. A similar procedure was followed for hydrochlorination, bromination, and chlorination of the *trans*-acid and its inclusion complex in the solid state.

Bromination and Hydrobromination in Solution. The bromination of *trans*-2-butenoic acid was also carried out in solution without α-cyclodextrin in the dark at room temperature: To 0.5 mL of a carbon tetrachloride solution containing 43 mg (0.5 mmol) of the acid was added 0.03 mL (ca. 0.58 mmol) of liquid bromine, and formation of the product was monitored by ^{1}H NMR spectroscopy. The dibromide was obtained in 10 and 90% yields after 72 and 96 h, respectively.

The *trans*-acid was hydrobrominated in a 5% solution of hydrogen bromide in acetic acid with 2,6-di-*tert*-butylphenol under nitrogen in the dark, or without the radical inhibitor under air, with UV irradiation at 25 °C for 1 h. In both cases, no 2-bromobutanoic acid was formed; instead, the 3-bromobutanoic acid, with no optical activity, was produced in 100% yield.

(*S*)-(+)-3-Bromobutanoic Acid. As described above, *trans*-2-butenoic acid was hydrobrominated in the cavity of α-cyclodextrin to give optically active 3-bromobutanoic acid in 60% yield: mp 17–18 °C (lit.[8] mp 17 °C); bp_{25} 131 °C (lit.[8] bp_{25} 130 °C); ^{1}H NMR (60 MHz, $CDCl_3$) δ 8.97 (1 H, s), 4.43 (1 H, m), 2.93 (2 H, d, J = 7 Hz), 1.73 (3 H, d, J = 7 Hz); IR (KBr) 3300–2500, 2900, 1700, 1410, 1290 cm^{-1}, no absorption peaks corresponding to olefinic bond; $[\alpha]^{25}_D$ +20.2° (*c* 1.00, diethyl ether), 58.4% enantiomeric excess (ee) (*S* predominates) based on $[\alpha]^{25}_D$ +17.3° (1, 0.5 dm), *S*-(+).[9]

(*S*)-(−)-3-Chlorobutanoic Acid. Exposure of *trans*-2-butenoic acid included in α-cyclodextrin to hydrogen chloride gas at 0 °C for 65 h gave 3-chlorobutanoic acid in 23% yield: bp_{20} 110–112 °C (lit.[10] $bp_{0.35}$ 67–70 °C); ^{1}H NMR (60 MHz, $CDCl_3$) δ 11.08 (1 H, s), 4.45 (1 H, m), 2.82 (2 H, d, J = 7 Hz), 1.62 (3 H, d, J = 7 Hz); IR (KBr) 3300–2500, 2950, 1700, 1405, 1280 cm^{-1}, no absorption peaks corresponding to olefinic bond; $[\alpha]^{25}_D$ −7.4° (*c* 0.25, diethyl ether), 64.4% ee (*S* predominates) based on $[\alpha]^{23}_D$ +11.5° (*c* 10, diethyl ether) of *R*-(+).[10]

***erythro*-(+)-2,3-Dibromobutanoic Acid.** Exposure of *trans*-2-butenoic acid included in α-cyclodextrin to bromine vapor at 45 °C for 50 h resulted in the formation of 2,3-dibromobutanoic acid in 16% yield: mp 84.5 °C (lit.[11] mp 84 °C); ^{1}H NMR (60 MHz, $CDCl_3$) δ 12.20 (1 H, s), 4.43 (1 H, m), 4.23 (1 H, d, J = 16 Hz), 1.93 (3 H, m); IR (KBr) 3300–2500, 2970, 1705, 1425, 1375 cm^{-1}, no absorption peaks corresponding to olefinic bond; $[\alpha]^{25}_D$ +0.2° (*c* 1.00, methanol).

***erythro*-(+)-2,3-Dichlorobutanoic Acid.** Solid *trans*-2-butenoic acid, with and without α-cyclodextrin, gave no reaction with chlorine gas, but the reaction proceeded rapidly when catalyzed by gaseous hydrogen chloride. Exposure of the α-cyclodextrin complex at 20 °C for 50 h to chlorine gas in the presence of a very small amount of hydrogen chloride gas gave 2,3-dichlorobutanoic acid in 8% yield: mp 62–63 °C (lit.[12] mp 62.5–63 °C); bp_{20} 123–124.5 °C (lit.[12] bp_{20} 124–125 °C); ^{1}H NMR (60 MHz, $CDCl_3$) δ 9.3 (1 H, s), 4.30 (1 H, m), 4.15 (1 H, d, J = 13 Hz), 1.67 (3 H, m); IR (KBr) 3300–2500, 2900, 1700, 1400, 1380 cm^{-1}, no absorption peaks corresponding to olefinic bond; $[\alpha]^{25}_D$ + 2.8° (*c* 0.5, methanol).

Analytical Methods. Optical rotations were measured in diethyl ether or methanol on a Perkin-Elmer 241 photoelectric spectropolarimeter using 1 dm cell at 25 °C. The infrared (IR) absorption spectra were measured in the region 650–4000 cm^{-1} on a Hitachi Model 285 spectrometer. The sample was prepared either neat on a KBr plate or as a KBr pellet. The proton nuclear magnetic resonance (^{1}H NMR) spectra were obtained at 60 MHz in deuterated dimethyl sulfoxide, deuterated chloroform, and carbon tetrachloride with tetramethylsilane (TMS) as the internal reference standard on a JEOL-PMX 60 spectrometer. The X-ray diffraction patterns of the powdered samples were measured in the region of 5–37° by a Rigaku Denki Model DC-8 X-ray diffractometer, using Ni-filtered Cu Kα radiation. The thermal behavior of the specimens was observed with a Rigaku Denki TG-DSC standard analyzer, which had been previously calibrated with standard substances, at a fixed heating rate of 10 °C/min.

Crystal Structure of the α-Cyclodextrin Complex with *trans*-2-Butenoic Acid. Plate-shaped single crystals, longer than 7 mm, were grown from an aqueous solution of α-cyclodextrin and *trans*-2-butenoic acid in a 1:1 molar ratio at room temperature. Lattice parameters and diffraction intensities were measured on a Nicolet P3/F diffractometer with monochromatic Cu Kα radiation. The structure was determined by the isomorphous replacement method, using for the coordinates of the cyclodextrin molecule those found for an α-cyclodextrin complex of methanol by Hingerty and Saenger,[13] and was refined by the least-squares method up to an R value of 0.077 for 3217 observed reflections. Full details of the crystal and molecular structures will be published elsewhere.[14] Crystallographic data: $C_{36}H_{60}O_{30}\cdot C_4H_6O_2$.

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Table I. Asymmetric Hydrohalogenation and Halogenation of *trans*-3-Butenoic Acid in a Crystalline α-Cyclodextrin Complex[a]

cyclodextrin	reagent	temperature, °C	time, h	product[b] butanoic acid	yield,[c] %	$[\alpha]^{25}_D$, deg	ee,[d] %	ref
α-CD	HBr	20	25	(*S*)-3-bromo	60	+20.2	58.4	9, 10
α-CD	HBr	25	20	(*S*)-3-bromo	28.6	+5.0	29.0	9, 10
none	HBr	20	20	3-bromo	90	0.0	0.0	
α-CD	HCl	0	65	(*S*)-3-chloro	23	−7.4	64.4	11
α-CD	HCl	20	20	(*S*)-3-chloro	41	−3.7	32.2	11
none	HCl	20	20	none	0	–	–	
α-CD	Br_2	20	50	none	0	–	–	
α-CD	Br_2	45	50	*erythro*-2,3-dibromo	16	+0.2	–	
α-CD	Br_2	50	15	*erythro*-2,3-dibromo	90	0.0	–	
none	Br_2	20	25	*erythro*-2,3-dibromo	95	0.0	–	
α-CD	Cl_2	20	50	*erythro*-2,3-dichloro	8	+2.8	–	
α-CD	Cl_2	45	20	*erythro*-2,3-dichloro	6	+0.9	–	
α-CD	Cl_2	50	20	*erythro*-2,3-dichloro	17	0.0	–	
none	Cl_2	20	15	*erythro*-2,3-dichloro	85	0.0	–	

[a] Crystalline *trans*-butenoic acid, free or complexed with α-cyclodextrin, was treated with gaseous reagents; a small amount of hydrogen chloride gas was added with chlorine gas. [b] Butanoic acid derivatives produced; configurations were previously determined on the dates given in the references. [c] Isolated yields. [d] Calculated from the reported specific rotation values given in the references.

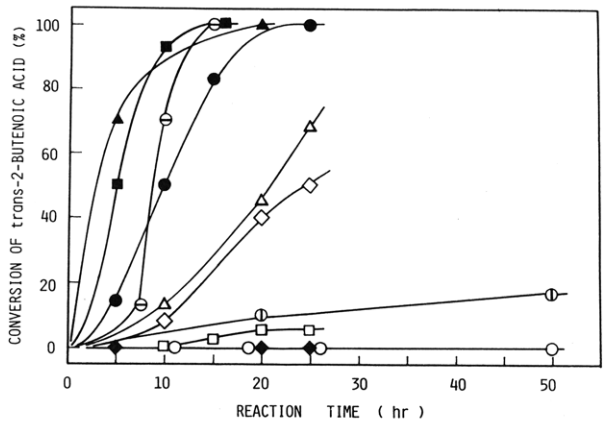

Figure 1. Solid-state hydrohalogenation and halogenation of *trans*-2-butenoic acid and its inclusion complex with α-cyclodextrin by gaseous hydrogen halides and halogens:

	inclusion complex			without cyclodextrin
	20 °C	45 °C	50 °C	20 °C
hydrobromination	△			▲
hydrochlorination	◇			●
bromination	○	⊕	⊖	●
chlorination	□			■

$5H_2O$; FW = 1149.0; orthorhombic; space group, $P2_12_12_1$; $Z = 4$; $a = 14.406$ (5), $b = 38.174$ (12), and $c = 9.430$ (3) Å; $V = 5185.9$ Å^3; $D_X = 1.472$, $D_m = 1.475$ g/cm^3.

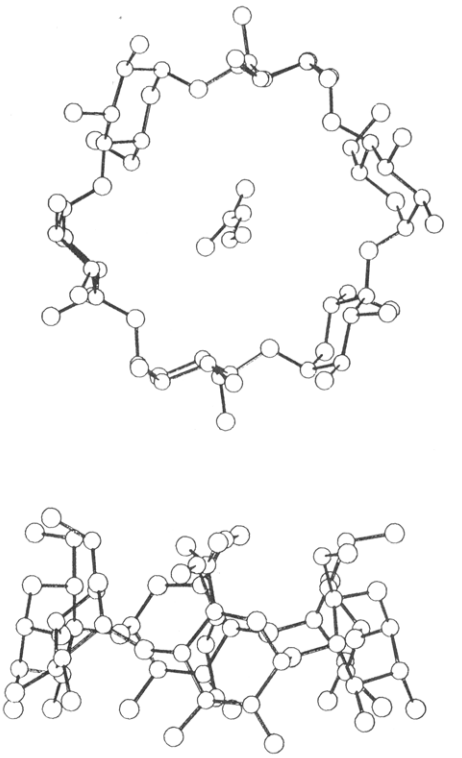

Figure 2. Molecular structure of crystalline α-cyclodextrin complex of *trans*-2-butenoic acid. The guest molecule is represented by a full circle.

Results

When platelets of the *trans*-2-butenoic acid complex with α-cyclodextrin are placed under a polarizing microscope in an enclosure maintained at 45–50 °C through which a stream of bromine gas is passed, a slow change is observed at the sides of the crystal while the top face remains clear. The region of disorder then spreads over the sample as the bromination reaction proceeds, although the outer shape of the crystal does not change in any way.

Table I shows the results of the halogenation and hydrohalogenation reactions of *trans*-2-butenoic acid, with and without α-cyclodextrin. As a guest in the cavity of cyclodextrin, this compound gives no reaction at all with bromine, and very little with chlorine at 20 °C, but does react with both hydrogen bromide and hydrogen chloride. These latter, being smaller molecules than the first two attacking reagents, give the corresponding 3-halo acids in high chemical yields of 60–90 and 23–41% with 58 and 32–64% e.e., respectively. On the other hand, the *trans*-acid is hydrochlorinated only when complexed by cyclodextrin. Thus, the cavity of α-cyclodextrin constitutes an important, possibly catalytic, environment in this hydrochlorination reaction, perhaps through the formation of a ternary molecular complex composed of the *trans*-acid, cyclodextrin, and hydrogen chloride.

These reaction behaviors are depicted graphically in Figure 1. The time-conversion behavior without cyclodextrin is similar to that reported by Hadjoudis et al.[11] for the bromination of 2,3-unsaturated acids, and the reaction rates are faster than those found with cyclodextrin. The temperature effect on this gas–solid bromination of *trans*-2-butenoic acid in the cavity of α-cyclodextrin was examined in order to determine the limitations of the topochemical factor in this two-phase reaction, and the results are shown in Table I and Figure 1. The *trans*-acid included in α-cyclodextrin does not react with bromine at all at 20 °C but does so rapidly at 50 °C to give the racemic *erythro*-dibromide in quantitative yield. However, bro-

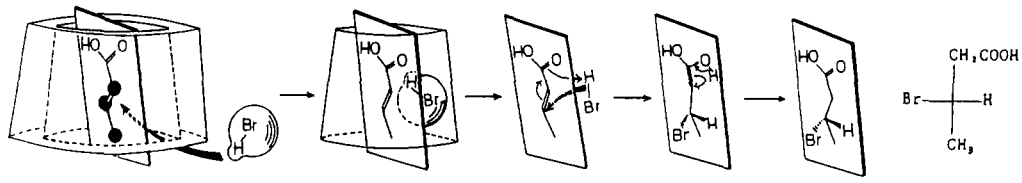

Figure 3. Reaction mechanism of asymmetric addition of hydrogen bromide to *trans*-2-butenoic acid included in α-cyclodextrin.

mination of the *trans*-acid without α-cyclodextrin proceeds more rapidly in the gas–solid reaction than it does in chloroform or carbon tetrachloride solutions at 20 °C. This result is consistent with the findings of Hajoudis et al.[11]

Discussion

Schmitt[15] showed in 1863 that solid cinnamic acid reacts with bromine vapor to give cinnamic acid dibromide or 2,3-dibromo-3-phenylpropanoic acid. Since that time, many examples of this type of reaction have appeared as a method for the synthesis of dibromides.[11,16-23] Solid 2,3-unsaturated acids, amides, and ketones yield, on exposure to bromine vapor at room temperature, the trans adduct quantitatively or near-quantitatively even where addition of bromine in solution has been reported to be difficult. Polymorphic forms of several compounds are also found to differ in their rates of bromine uptake and addition, but the stereo structure of the product is independent of the crystal structure of the reactant. In our experiments, 2,3-dibromo- and 2,3-dichlorobutanoic acids are obtained as erythro isomers or trans adducts.

A full description of the mechanism of asymmetric induction in these gas–solid reactions requires detailed knowledge concerning the environment of the reaction center. Figure 2, in which only the heavy atoms are shown, depicts the structure of the α-cyclodextrin complex of *trans*-2-butenoic acid. The guest molecule, *trans*-2-butenoic acid, is entirely included within the cavity of α-cyclodextrin, with the carboxyl group located at the narrower opening site involving the primary hydroxy groups of the host molecule. The mean plane of the carbon–carbon double bond of the guest seems to be somewhat inclined with respect to the pseudo-6-fold axis of the cyclodextrin, where the nonpolar side is expected to have a largely asymmetric environment.

As the data in Table I and Figure 1 show that the asymmetric hydrohalogenation of trans-2-butenoic acid should occur on the inside of the cavity, the mechanism depicted in Figure 3 then follows and is also possible on the basis of the crystal structure. In the crystalline complex of α-cyclodextrin, the guest acid is tightly anchored by the hydrogen bond between the primary hydroxyl group of the cyclodextrin and the doubly bonded oxygen of the guest acid. The olefinic bond of *trans*-2-butenoic acid penetrates to the chiral environment in the middle of the cavity. Thus, a reagent molecule, such as bromine or hydrogen halide, or an ionized species, consisting of proton and a halide anion, apparently attacks enantioselectively on the inclined plane of the carbon–carbon double bond from the side facing the wider opening site, as shown in Figure 2.

The exact nature of the hydrohalogenation process remains in doubt. Thus Gould[24] has proposed π-complex formation at the ethenyl bond to account for the predominantly trans-hydrohalogenation,[25] whereas Dewar[26] has suggested that 1,4-addition to the conjugated system of the unsaturated acids is more reasonable. The mechanism of the hydrohalogenation, especially with hydrogen iodide, of 2-substituted 2-propenoic acids should be distinct from that of normal electrophilic addition to simple olefins. Protonation of a 2-propenoic acid derivative would be expected to occur mostly easily at the carbonyl oxygen. The resulting ion could then add halide ion in the rate-determining step, followed by a migration of the proton to the second carbon atom through ketonization of the enol, resulting in a net 1,2-addition to the olefinic π-bond.[26,27]

A similar mechanism for the addition reaction could be proposed for the hydrohalogenation of crystalline *trans*-2-butenoic acid included in α-cyclodextrin, as shown in Figure 3. At first, the doubly bonded oxygen atom of the carboxyl group of the guest molecule is protonated by attack of hydrogen ion from the hydrogen halide, at which time the guest molecule may move along the longitudinal or *Z* axis of the cavity through simultaneous hydrogen bond cleavage. The halide anion can enter the cavity much more easily from the wider side of the secondary hydroxyl groups than from the narrower side of the primary hydroxyl groups of the cyclodextrin, and should therefore attack readily at the third carbon atom of the guest, located in the wider opening side of the host. Thus, a chiral center is formed in this step, and the attack of halide anions on the plane from the side facing the wider opening site (located at the lower left as shown in Figure 2) becomes more advantageous than from the side facing the narrower opening site.

A space-filling representation of the complex of *trans*-2-butenoic acid with α-cyclodextrin also reveals that the sinister-face of the olefinic plane (at the left space in Figure 2) is wider than the other side. Thus, predominant attack of the halide species at this enantio-face of the olefinic bond should result in the observed chiral induction, to give (*S*)-(+)-3-bromo- and (*S*)-(+)-3-chlorobutanoic acids in 58.4 and 64.4% ee., respectively.

Registry No. *trans*-2-Butenoic acid α-cyclodextrin complex (1:1), 124287-17-8; β-cyclodextrin, 7585-39-9; (*S*)-(+)-3-bromobutanoic acid, 77790-08-0; (*S*)-(−)-3-chlorobutanoic acid, 25139-77-9; *erythro*-(+)-2,3-dibromobutanoic acid, 90429-42-8; *erythro*-(+)-2,3-dichlorobutanoic acid, 81236-52-4; *trans*-2-butenoic acid, 107-93-7; *erythro*-(±)-2,3-dibromobutanoic acid, 90429-42-8; (±)-3-bromobutanoic acid, 77732-34-4.

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