Na^+: 1.17×10^{-2} (5×10^{-5}), 1.52×10^{-2} (1×10^{-4}), 2.05×10^{-2} (2×10^{-4}), 3.04×10^{-2} (5×10^{-4}), 4.49×10^{-2} (1×10^{-3}), 6.00×10^{-2} (2×10^{-3}), 7.38×10^{-2} (5×10^{-3}), 9.27×10^{-2} (1×10^{-2}), 8.97×10^{-2} (2×10^{-2}), 8.81×10^{-2} (5×10^{-2}), 8.13×10^{-2} (0.1), 7.78×10^{-2} (0.2); $r = 0.9882$.

K^+: 1.11×10^{-2} (1×10^{-4}), 1.19×10^{-2} (2×10^{-4}), 1.45×10^{-2} (5×10^{-4}), 1.92×10^{-2} (1×10^{-3}), 2.31×10^{-2} (2×10^{-3}), 3.67×10^{-2} (5×10^{-3}), 4.68×10^{-2} (1×10^{-2}), 5.39×10^{-2} (2×10^{-2}), 5.77×10^{-2} (5×10^{-2}), 5.76×10^{-2} (0.1), 5.72×10^{-2} (0.2); $r = 0.9611$.

Rb^+: 1.18×10^{-2} (5×10^{-4}), 1.39×10^{-2} (1×10^{-3}), 1.56×10^{-2} (2×10^{-3}), 2.25×10^{-2} (5×10^{-3}), 2.96×10^{-2} (1×10^{-2}), 3.30×10^{-2} (2×10^{-2}), 3.49×10^{-2} (5×10^{-2}), 3.72×10^{-2} (0.1), 3.74×10^{-2} (0.2); $r = 0.9485$.

Cs^+: 1.27×10^{-2} (2×10^{-3}), 1.52×10^{-2} (5×10^{-3}), 1.70×10^{-2} (1×10^{-2}), 1.95×10^{-2} (2×10^{-2}), 2.15×10^{-2} (5×10^{-2}), 2.17×10^{-2} (0.1), 2.06×10^{-2} (0.2); $r = 0.9902$.

Reaction 1, $x = 7$; $k_i = 6.15 \times 10^{-3}$ s^{-1}. Li^+: 2.30×10^{-3} (2×10^{-3}), 1.24×10^{-3} (5×10^{-3}), 7.77×10^{-4} (1×10^{-2}), 4.34×10^{-4} (2×10^{-2}), 1.92×10^{-4} (5×10^{-2}); $r = 0.9997$.

Na^+: 5.56×10^{-3} (5×10^{-4}), 5.04×10^{-3} (1×10^{-3}), 4.24×10^{-3} (2×10^{-3}), 3.11×10^{-3} (5×10^{-3}), 2.77×10^{-3} (1×10^{-2}), 2.52×10^{-3} (2×10^{-2}), 2.13×10^{-3} (5×10^{-2}), 1.85×10^{-3} (0.1), 1.62×10^{-3} (0.2); $r = 0.9816$.

K^+: 7.78×10^{-3} (2×10^{-4}), 1.08×10^{-2} (5×10^{-4}), 1.69×10^{-2} (1×10^{-3}), 2.24×10^{-2} (2×10^{-3}), 3.20×10^{-2} (5×10^{-3}), 3.81×10^{-2} (1×10^{-2}), 4.00×10^{-2} (2×10^{-2}), 4.55×10^{-2} (5×10^{-2}), 4.20×10^{-2} (0.1), 4.28×10^{-2} (0.2); $r = 0.9939$.

Rb^+: 7.31×10^{-3} (1×10^{-4}), 1.14×10^{-2} (2×10^{-4}), 1.84×10^{-2} (5×10^{-4}), 2.83×10^{-2} (1×10^{-3}), 4.57×10^{-2} (2×10^{-3}), 7.06×10^{-2} (5×10^{-3}), 8.53×10^{-2} (1×10^{-2}), 9.40×10^{-2} (2×10^{-2}), 0.109 (5×10^{-2}), 9.66×10^{-2} (0.1), 0.101 (0.2); $r = 0.9796$.

Cs^+: 8.01×10^{-3} (1×10^{-4}), 9.31×10^{-3} (2×10^{-4}), 1.84×10^{-2} (5×10^{-4}), 2.64×10^{-2} (1×10^{-3}), 4.38×10^{-2} (2×10^{-3}), 6.77×10^{-2} (5×10^{-3}), 0.101 (1×10^{-2}), 0.112 (2×10^{-2}), 0.122 (5×10^{-2}), 0.150 (0.1), 0.150 (0.2); $r = 0.9719$.

Me_4N^+: 5.81×10^{-3} (5×10^{-2}).

Et_4N^+: 5.44×10^{-3} (0.2).

Reaction 1, $x = 10$; $k_i = 3.27 \times 10^{-3}$ s^{-1}. Li^+: 1.71×10^{-3} (1×10^{-3}), 7.22×10^{-4} (5×10^{-3}), 3.92×10^{-4} (1×10^{-2}), 2.14×10^{-4} (2×10^{-2}), 6.32×10^{-5} (0.1); $r = 0.9984$.

Na^+: 2.58×10^{-3} (5×10^{-4}), 2.37×10^{-3} (1×10^{-3}), 1.88×10^{-3} (2×10^{-3}), 1.13×10^{-3} (5×10^{-3}), 9.27×10^{-4} (1×10^{-2}), 7.25×10^{-4} (2×10^{-2}), 5.27×10^{-4} (5×10^{-2}), 4.38×10^{-4} (0.1), 3.69×10^{-4} (0.2); $r = 0.9857$.

K^+: 3.60×10^{-3} (1×10^{-3}), 3.69×10^{-3} (2×10^{-3}), 4.44×10^{-3} (5×10^{-3}), 5.14×10^{-3} (1×10^{-2}), 5.50×10^{-3} (2×10^{-2}), 6.83×10^{-3} (5×10^{-2}), 8.60×10^{-3} (0.1), 1.08×10^{-2} (0.2).

Rb^+: 4.85×10^{-3} (1×10^{-3}), 6.15×10^{-3} (2×10^{-3}), 7.79×10^{-3} (5×10^{-3}), 9.38×10^{-3} (1×10^{-2}), 1.06×10^{-2} (2×10^{-2}), 1.15×10^{-2} (5×10^{-2}), 1.19×10^{-2} (0.1), 1.37×10^{-2} (0.2); $r = 0.9961$.

Cs^+: 3.95×10^{-3} (1×10^{-3}), 4.52×10^{-3} (2×10^{-3}), 5.07×10^{-3} (5×10^{-3}), 5.98×10^{-3} (1×10^{-2}), 6.59×10^{-3} (2×10^{-2}), 6.63×10^{-3} (5×10^{-2}), 6.90×10^{-3} (0.1), 6.83×10^{-3} (0.2); $r = 0.9468$.

Et_4N^+: 3.29×10^{-3} (0.2).

Reaction 1, $x = 16$; $k_i = 1.48 \times 10^{-3}$ s^{-1}. Li^+: 1.70×10^{-4} (1×10^{-2}), 1.02×10^{-4} (2×10^{-2}), 5.26×10^{-5} (5×10^{-2}); $r = 0.99999$.

Na^+: 1.22×10^{-3} (5×10^{-4}), 1.05×10^{-3} (1×10^{-3}), 8.58×10^{-4} (2×10^{-3}), 6.19×10^{-4} (5×10^{-3}), 4.20×10^{-4} (1×10^{-2}), 3.03×10^{-4} (2×10^{-2}), 2.17×10^{-4} (5×10^{-2}), 1.71×10^{-4} (0.1), 1.35×10^{-4} (0.2); $r = 0.9980$.

K^+: 1.28×10^{-3} (1×10^{-3}), 1.20×10^{-3} (2×10^{-3}), 1.06×10^{-3} (5×10^{-3}), 1.04×10^{-3} (1×10^{-2}), 9.20×10^{-4} (2×10^{-2}), 8.39×10^{-4} (5×10^{-2}), 7.42×10^{-4} (0.1), 6.80×10^{-4} (0.2).

Rb^+: 1.32×10^{-3} (5×10^{-3}), 1.26×10^{-3} (1×10^{-2}), 1.22×10^{-3} (2×10^{-2}), 1.12×10^{-3} (5×10^{-2}), 1.10×10^{-3} (0.1), 1.04×10^{-3} (0.2).

Cs^+: 1.41×10^{-3} (5×10^{-3}), 1.27×10^{-3} (1×10^{-2}), 1.23×10^{-3} (2×10^{-2}), 1.25×10^{-3} (5×10^{-2}), 1.23×10^{-3} (0.1), 1.17×10^{-3} (0.2).

Me_4N^+: 1.48×10^{-3} (5×10^{-3}), 1.42×10^{-3} (5×10^{-2}).

Et_4N^+: 1.68×10^{-3} (0.2).

Acknowledgment. The authors wish to thank Professor Gabriello Illuminati for critically reading the manuscript.

Registry No. *o*-$^-OC_6H_4(OCH_2CH_2)_3Br$, 87494-76-6; *o*-$^-OC_6H_4(OCH_2CH_2)_4Br$, 87494-77-7; *o*-$^-OC_6H_4(OCH_2CH_2)_6Br$, 87494-78-8; *o*-$^-OC_6H_4(OCH_2CH_2)_9Br$, 87494-79-9; *o*-$^-OC_6H_4(OCH_2CH_2)_{15}Br$, 87494-80-2; B12C4, 14174-08-4; B15C5, 14098-44-3; B18C6, 14098-24-9; B21C7, 67950-78-1; B30C10, 77963-50-9; B48C16, 87494-81-3; Li^+, 17341-24-1; Na^+, 17341-25-2; K^+, 24203-36-9; Rb^+, 22537-38-8; Cs^+, 18459-37-5.

Selective Syntheses Using Cyclodextrins as Catalysts. 2. Para-Oriented Carboxylation of Phenols[1]

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Abstract: 4-Hydroxybenzoic acid and 4-hydroxy-3-methylbenzoic acid are synthesized in virtually 100% selectivities and high yields from the corresponding phenols and carbon tetrachloride by using β-cyclodextrin (β-CD) as catalyst. The selective syntheses are successfully achieved by a small molar ratio, even 0.03, of β-CD to phenols and are hardly suppressed by oxygen. Kinetic study shows that the selective catalyses by β-CD originate from both promotion of the para carboxylation and almost complete inhibition of the ortho carboxylation. Heptakis(2,6-di-*O*-methyl)-β-cyclodextrin in contrast decreases the para selectivity, showing the importance of the hydroxyl groups of β-CD in its selective catalysis. The selective catalysis by β-CD proceeds via formation of a molecular complex with the active species, probably the trichloromethyl cation. In the electrophilic attack of the active species at phenols, β-CD regulates the mutual molecular conformation between them through noncovalent interactions, resulting in highly selective para carboxylation.

Cyclodextrins (CDs), cyclic oligomers of 6-8 glucoses, have been widely used as a model of enzymes. This is mostly due to the fact that the catalyses by CDs proceed via the formation of molecular complexes of them with substrates prior to chemical transformation. This process is identical with those of enzymatic catalyses. High substrate specificities were reported in many bond cleavage reactions such as ester hydrolyses, phosphate hydrolyses, and decarboxylation.[2,3]

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Table I. Reactions between Various Phenols and Carbon Tetrachloride in the Presence and the Absence of β-CD as Catalyst[a]

phenols	β-CD	yield,[b,c] mol % para-carboxylated phenol	yield,[b,c] mol % ortho-carboxylated phenol	selectivity for para-carboxylated phenol, %
phenol	present	59 (92)	0.6 (0.9)	99
	absent	8.6 (53)	7.1 (44)	55
	present[d]	0.0 (0.0)	0.0 (0.0)	
	present[e]	6.8 (38)	6.3 (35)	52
2-methylphenol	present	58 (62)	1.9 (2.0)	97
	absent	21 (45)	20 (43)	51
3-methylphenol	present	58 (59)	29 (30)	67
	absent	42 (61)	20 (29)	68
4-methylphenol	present	0.0 (0.0)	5.4 (92)	0
	absent	0.0 (0.0)	1.8 (86)	0

[a] Reaction conditions: phenol, 1.5 g; β-CD, 1.5 g (1.3 mmol); copper powder, 0.1 g (1.6 mmol); carbon tetrachloride, 3.0 mL (31.0 mmol); in 20 mL of 20% aqueous sodium hydroxide solution at 80 °C for 15 h under nitrogen. [b] The averages of the values for duplicate runs, which coincide with each other within 5%. [c] The numbers in parentheses are the values calculated in consideration of recovered phenols. [d] Without copper powder. [e] 1.6 mmol of copper sulfate is used in place of copper powder.

However, the examples of product specificities in bond formation reactions, exhibited by CDs, are rather few. Thus, application of CDs as selective catalysts for organic syntheses has been limited to a small number of reactions as yet.[1,4-12]

Previously,[12] the authors succeeded in selective syntheses of 4-hydroxybenzaldehydes from phenols and chloroform in alkaline aqueous solutions with CDs as catalysts.

This paper describes selective syntheses of 4-hydroxybenzoic acids from phenols and carbon tetrachloride by using CDs as catalysts. Dependence of the selectivity on the structures of phenols as well as the catalytic activities of various CDs and their derivatives are shown. Kinetic studies on the selective reactions are also made. Furthermore, the functions of CDs are discussed.

Experimental Section

Materials. Hexakis(2,6-di-*O*-methyl)-α-cyclodextrin and heptakis-(2,6-di-*O*-methyl)-β-cyclodextrin were synthesized from CDs and dimethyl sulfate by following the literature procedures.[13] Copper powder was obtained from the Yoneyama Chemical Co. and was used without further purification. All other chemicals were purified in the usual ways.

The authentic samples of 4-hydroxybenzoic acid, 2-hydroxybenzoic acid, 2-hydroxy-3-methylbenzoic acid, 2-hydroxy-4-methylbenzoic acid, and 2-hydroxy-5-methylbenzoic acid for HPLC analyses were obtained by repeated recrystallization of commercial products from ethanol–water: mp 215.1–215.4 °C (lit.[14] mp 212–213 °C), 158.7–159.3 °C (lit.[15] mp 159 °C), 163.6–164.0 °C (lit.[16] mp 163–164 °C), 177.2–177.5 °C (lit.[17] mp 177 °C), 151.6–152.0 °C (lit.[18] mp 151 °C), respectively. The specimens of 4-hydroxy-3-methylbenzoic acid and 4-hydroxy-2-methylbenzoic acid were synthesized by following the methods in the literature:[19] mp 174.5–174.9 °C (lit.[19] mp 174–175 °C) and 178.2–178.6 °C (lit.[19] mp 176–178 °C), respectively.

Selective Syntheses Using CDs as Catalysts. The typical reaction procedure is as follows. To 20 mL of 20 wt % aqueous sodium hydroxide solution, 1.5 g of phenol, various amounts of CDs or their derivatives, and 0.1 g of copper powder were added. The reaction was started with the addition of 3 mL of carbon tetrachloride and was continued at 80 °C for 15 h with vigorous stirring under nitrogen.

After the reaction was complete, the reaction mixture was acidified with hydrochloric acid, followed by extraction with ethyl ether. The ether layer was washed with water twice and evaporated. The product analyses were made with HPLC by using the absorbance at 254 nm: Toyo Soda LS410K, MeOH-100 column (silica gel octadecylsulfonate), 30 cm, 25 °C; eluent, 1:1 ethanol–water.

Kinetic Study. To 20 mL of a 3:2 water–ethanol mixture containing 2.0 g of sodium hydroxide, 1.5 g of phenol, 1.5 g of β-CD, 0.1 g of copper powder, and 0.05 mL of carbon tetrachloride were added. The reaction was carried out at 25 °C under nitrogen. The concentration of residual carbon tetrachloride was determined with GLPC (Porapak Q column, 2 m, 170 °C). The product analysis was made with HPLC as described above.

Results

Selective Syntheses of 4-Hydroxybenzoic Acids Using CDs as Catalysts. Table I shows the yields and selectivities for the formation of 4-hydroxybenzoic acids from phenols and carbon tetrachloride.

In the presence of β-CD, the selectivities for 4-hydroxybenzoic acids are virtually 100%, and their yields are satisfactorily high for both phenol and 2-methylphenol. In its absence, however, large amounts of the ortho-carboxylated phenols are produced, resulting in the selectivities for the desired compounds around 50%. Thus, the selective syntheses are successfully achieved by using β-CD as catalyst.

Quite importantly, the selective catalysis of β-CD is highly suppressed when phenol has a methyl substituent at the meta position. The selectivity for the formation of 4-hydroxy-2-methylbenzoic acid from 3-methylphenol in the presence of β-CD is almost identical with the value in its absence. This remarkably high substrate specificity indicates the participation of molecular complex between phenols and β-CD in the selective catalyses.

For 4-methylphenol, the carboxylation at the para-carbon atom does not take place even in the presence of β-CD.

Copper powder is absolutely required for the selective reaction to proceed. Although carboxylation also occurs in the presence of copper sulfate in place of copper powder, β-CD exhibits no selective catalysis there.

In Table II, the activities of various CDs and their derivatives as catalysts for selective syntheses of 4-hydroxybenzoic acid are listed. γ-CD exhibits selective catalysis as well as β-CD. The activity of β-CD is much larger than that of γ-CD. α-CD shows no increase in selectivity, although it slightly accelerates the reaction.

In contrast, hexakis(2,6-di-*O*-methyl)-α-cyclodextrin and heptakis(2,6-di-*O*-methyl)-β-cyclodextrin, in which all of the

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Table II. Catalytic Activities and Selectivities of CDs and Their Derivatives for Selective Synthesis of 4-Hydroxybenzoic Acid[a]

CD or its deriv	yield,[b,c] mol %		selectivity for 4-hydroxybenzoic acid, %
	4-hydroxybenzoic acid	2-hydroxybenzoic acid	
none	8.6 (53)	7.1 (44)	55
α-CD	12 (54)	10 (45)	55
β-CD	59 (92)	0.6 (0.9)	99
γ-CD	12 (58)	4.0 (19)	75
hexakis(2,6-di-*O*-methyl)-α-cyclodextrin	1.2 (35)	1.9 (55)	39
heptakis(2,6-di-*O*-methyl)-β-cyclodextrin	1.9 (33)	2.0 (35)	49

[a] Reaction conditions: phenol, 1.5 g (15.9 mmol); CDs or their derivatives, 1.5 g; copper powder, 0.1 g (1.6 mmol); carbon tetrachloride, 3.0 mL (31.0 mmol); in 20 mL of 20% aqueous sodium hydroxide solution at 80 °C for 15 h under nitrogen. [b] The averages of the values for duplicate runs, which coincide with each other within 5%. [c] The numbers in parentheses are the values calculated in consideration of recovered phenol.

Table III. Consumption Rates of Carbon Tetrachloride and Formation Rates of Products in the Mixtures Containing Carbon Tetrachloride Together with Various Additives[a-c]

additives	initial rate of consumption of CCl_4, 10^{-4} mol/h	initial rate of formation, 10^{-4} mol/h	
		4-hydroxybenzoic acid	2-hydroxybenzoic acid
none	0.00		
phenol	0.00	0.00	0.00
phenol + β-CD	0.00	0.00	0.00
phenol + Cu	0.30	0.07	0.06
phenol + Cu + β-CD	0.37	0.36	0.00
phenol + Cu + β-CD + styrene	0.36	0.36	0.00

[a] In 20 mL of a 3:2 water–ethanol mixture containing 2.0 g of sodium hydroxide at 25 °C under nitrogen. [b] Charged amount: phenol, 15.9 mmol; β-CD, 1.3 mmol; copper powder, 1.6 mmol; carbon tetrachloride, 0.52 mmol; styrene, 0.02 mmol. [c] All the values are averages of the values for duplicate runs, which coincide with each other within 3%.

hydroxyl groups at the 2 and 6 positions are methylated, show suppression of the reaction with respect to both yield and selectivity. This result definitely confirms the importance of the hydroxyl groups of CDs in their selective catalyses.

In all the selective syntheses, neither chloroform nor hexachloroethane was detected at all in the reaction mixtures throughout the reaction time. The GLC analyses employed should be able to detect these haloalkanes, if they had been formed in 0.03 mol % yields or more with respect to the charged carbon tetrachloride.

Effect of the Amount of β-CD on the Yield and Selectivity for 4-Hydroxybenzoic Acid. Figure 1 depicts the plots of the yield and the selectivity for 4-hydroxybenzoic acid vs. the initial molar ratio of β-CD to phenol in the reaction between phenol and carbon tetrachloride. The yield increases almost linearly with the increasing molar ratio in the range investigated.

The selectivity remains virtually constant at 100% in a wide range of the molar ratio. The decrease in the selectivity is detected only at the molar ratio smaller than 0.025. It is important that the selective catalysis by β-CD is achieved by a quite small amount of β-CD with respect to the charged phenol and carbon tetrachloride.

Effect of Oxygen on the Selective Catalysis by β-CD. The solid circles and squares in Figure 1, which refer to the yields and selectivities, respectively, for the reactions under air, almost perfectly superimpose on the open circles and squares for the reactions under nitrogen. Thus, oxygen exhibits no measurable effects on the selective catalysis by β-CD.

Kinetics in a Water–Ethanol Mixture. Table III lists the rates of consumption of carbon tetrachloride and those of formation of products in the alkaline mixtures containing carbon tetrachloride together with phenol, β-CD, and copper powder. The reactions are carried out in a 3:2 water–ethanol mixture, which perfectly dissolves all the components except for copper powder. In the absence of copper powder, carbon tetrachloride is not consumed at a measurable rate.

In the presence of phenol and copper powder, carbon tetrachloride is consumed at a considerable rate even in the absence of β-CD. However, only 43% ((0.07 + 0.06)/0.30) of the consumed carbon tetrachloride is incorporated to the reaction with phenol. In addition, the reaction takes place at the ortho and the para positions of phenol at almost identical rates.

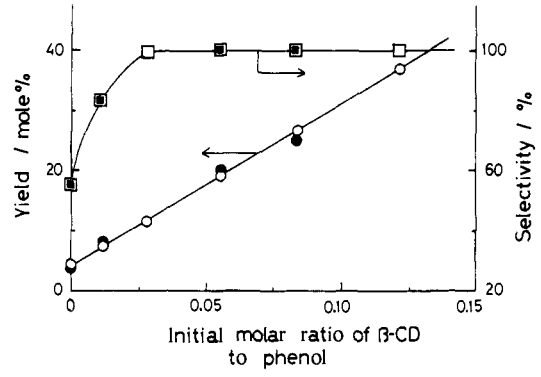

Figure 1. Plots of yield and selectivity vs. the initial molar ratio of β-CD to phenol for the selective synthesis of 4-hydroxybenzoic acid with use of β-CD as catalyst: ○ and □, for the reactions under nitrogen; ● and ■, for the reactions under air; phenol, 1.5 g; carbon tetrachloride, 3 mL; copper powder, 0.1 g; in 20 mL of 20% aqueous sodium hydroxide solution for 1 h at 80 °C.

In the presence of β-CD together with phenol and copper powder, however, almost all of the consumed carbon tetrachloride reacts with phenol. Furthermore, the reaction occurs overwhelmingly at the para position. The rate of the total consumption of carbon tetrachloride is slightly larger than the value in the absence of β-CD.

Thus, the selective catalysis by β-CD is attributable to both the promotion of the reaction at the para position and virtually total suppression of the reaction at the ortho position.

Styrene, a powerful quencher for the trichloromethyl radical,[20] shows no measurable effect on the selective synthesis at the initial molar ratio 0.04 to carbon tetrachloride.

Discussion

Active Species for CD-Catalyzed Selective Syntheses of 4-Hydroxybenzoic Acids. The selective syntheses of 4-hydroxybenzoic acids using β-CD as catalyst probably proceed with trichloromethyl cations, formed in situ from carbon tetrachloride by the catalysis of copper powder, as the active species.

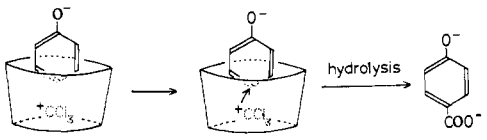

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Figure 2. Proposed mechanism of the selective syntheses of 4-hydroxybenzoic acids from phenol and 2-methylphenol with β-CD as catalyst.

The mechanism involving trichloromethyl radicals is unlikely due to the following reasons:

(1) Styrene, which strongly quenched trichloromethyl radicals and thus totally inhibited reactions involving them at the initial molar ratio 0.01 to carbon tetrachloride according to a literature,[20] showed no measurable retardation in the present reactions at the initial molar ratio 0.04 (see Table III).

(2) Oxygen, which exhibited significant retardation in the reactions involving trichloromethyl radicals according to the literature,[21] showed no measurable effect either on the rate or on the selectivity in the present reactions (see Figure 1).

(3) Chloroform and hexachloroethane, which were produced in high yields in the reactions involving trichloromethyl radicals according to the literature,[21] were not formed at measurable rates in the present reactions.

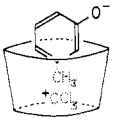
Almost all the trichloromethyl cations should form molecular complexes with β-CD prior to the attack at phenols, since the selective syntheses are achieved at quite a small molar ratio of β-CD to phenol or carbon tetrachloride (see Figure 1). Trichloromethyl cations can be trapped in the cavity of β-CD immediately after being formed on the surface of copper powder. Alternatively, the trichloromethyl cation can be formed predominantly from the carbon tetrachloride included in the cavity, also with catalysis by copper powder, and thus be trapped in the cavity. Otherwise a much larger amount of β-CD should be required for the selective syntheses, so that the β-CD-catalyzed selective reaction could proceed predominantly over the uncatalyzed less-selective reaction.

Effective trapping of the active species trichloromethyl cation by β-CD prior to attack at phenols is due to the large equilibrium constant for the formation of the molecular complex between trichloromethyl cation and β-CD. There, the electrostatic attraction between the positive charge of the cation and the negative charges of β-CD is cooperatively functioning with the apolar interaction between the cation and the β-CD. In the alkaline reaction media, the secondary hydroxyl groups of β-CD are mostly in the anionic forms, since their pK_a is around 12.[2] If the active species were trichloromethyl radicals rather than trichloromethyl cations, such an effective trapping of the active species by a small amount of β-CD would be hardly expected.

The above argument is consistent with the previous finding that molecular complex formation between positively charged modified CDs and negatively charged guest compounds was enhanced in considerable magnitudes by the cooperation of an electrostatic interaction and an apolar interaction.[22,23]

Participation of the molecular complex between trichloromethyl cation and β-CD in the selective catalyses is further supported by the fact that α-CD shows no measurable increase in selectivity. The CPK molecular model study indicates that the trichloromethyl cation as well as carbon tetrachloride can be almost totally accommodated in the cavity of β-CD but not in the cavity of α-CD.

Selective Catalyses by CDs. The mechanism of the selective syntheses of 4-hydroxybenzoic acids from phenol and 2-methylphenol using β-CD as catalyst is proposed as shown in Figure 2. First, a ternary molecular complex **1** is formed from the trichloromethyl cation, β-CD, and phenols. Here, the cavity of β-CD is largely occupied by the trichloromethyl cation, and phenols in their anionic form are shallowly included in the cavity from the apolar side involving the C-4 atoms. The inclusion of this apolar side in the apolar cavity of β-CD is energetically much more favorable than the inclusion of the polar side involving the phenoxide oxygen atom. Furthermore, the penetration from the polar side is largely inhibited by the electrostatic repulsion between the negative charge at the phenoxide oxygen atom and the negative charges at the ionized hydroxyl groups of β-CD.



2

Figure 3. Conformation of the ternary molecular complex **2** composed of 3-methylphenolate ion, β-CD, and trichloromethyl cation.

Then, the trichloromethyl cation should attack overwhelmingly at the para-carbon atom of phenols, which is located in close proximity. 4-Hydroxybenzoic acids are formed by the hydrolyses of the C–Cl bonds in the resulting intermediates.[24] The attack of the trichloromethyl cation at the ortho position of phenols in **1** is highly unfavorable. Thus, the selective catalysis by β-CD is attributable to the regulation of the mutual conformation between phenolates and the active species through noncovalent interactions.

The proposed mechanism is based on a previous NMR study[11,12] showing that phenolate ion is included in the cavity of α- or β-CD from the side involving the C-4 carbon atom in the molecular complex. Furthermore, formation of a ternary molecular complex composed of phenolate, chloroform, and α- or β-CD has been confirmed. The conformation of the ternary molecular complex is qualitatively identical with that of **1** except for the replacement of the trichloromethyl cation with chloroform.

The above mechanism is consistent with the kinetic results showing that the reaction at the ortho position is almost totally inhibited by β-CD and the reaction at the para position is promoted by β-CD (Table III). The active species, the trichloromethyl cations, are effectively incorporated into the reaction in Figure 2 without being wasted by hydrolysis, since almost all of them are trapped in the cavity as discussed above. Stabilization of unstable species by CDs, attributable to steric and/or microsolvent effects, has been well-known.[2]

The proposed mechanism is also in good agreement with the importance of the hyroxyl groups of β-CD in the selective catalysis, vividly shown by no catalytic activity of heptakis(2,6-di-*O*-methyl)-β-cyclodextrin (Table II). The smaller activity of γ-CD than that of β-CD is ascribed to the smaller magnitude of the conformational restriction between phenolates and the trichloromethyl cation, due to the larger size of the cavity.

The mechanism is further supported by the fact that the selective catalysis is suppressed by the methyl substitution at the meta position in phenol in spite of no suppression by the methyl substitution at the ortho position. In the reaction of 3-methylphenol, a ternary molecular complex **2** in Figure 3 is formed from trichloromethyl cation, β-CD, and 3-methylphenol instead of **1** as for the case of unsubstituted phenol or 2-methylphenol. 3-Methylphenolate is included in the cavity with the *m*-methyl group first.[25,26] Under this situation, the geometrical discrimination between the para and the ortho positions with respect to the attack by the trichloromethyl cation is so small that the selectivity for the para reaction is low as observed. The alkyl substituents at the meta position of phenol also exhibited a large suppression of selectivity in the β-CD-catalyzed selective syntheses of 4-hydroxybenzaldehydes from phenols.[12]

The proposed mechanism does not necessarily require the formation of a ternary molecular complex composed of the tri-

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chloromethyl cation, β-CD, and phenolates as a stable species. Instead, the regulation of the mutual conformation between phenolates and the trichloromethyl cation can be achieved by β-CD only in the transition state, also through noncovalent interactions.

Comparison of Selective Catalysis by CDs in Carboxylation with That in Formylation. As shown above, one of the functions of β-CD in the selective carboxylation is the regulation of the mutual conformation between phenolates and the trichloromethyl cation. This is identical with the function of β-CD in the selective syntheses of 4-hydroxybenzaldehydes from phenols and chloroform.[12] There, β-CD regulates the mutual conformation between phenolates and chloroform (and thus that between phenolates and the active species, dichlorocarbene), resulting in the reaction at the para position in high selectivity.

In the present selective carboxylation, β-CD additionally functions as a trapping and protecting agent for the active species. Thus, only a small amount of β-CD is required for the selective catalyses to proceed efficiently. In the selective formylation, however, the molar ratio of chloroform to β-CD must be carefully controlled below unity throughout the reaction, so that almost all of the chloroform is in the complexing state with β-CD.[12] Otherwise, the reaction involving free chloroform takes place competitively with the β-CD-catalyzed reaction, resulting in a decreased selectivity. This difference is due to the fact that the inclusion of the trichloromethyl cation in the cavity is much more favorable than the inclusion of dichlorocarbene in the cavity.

Acknowledgment. The authors would like to thank Makoto Yoshida for his technical assistance. This work is partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education in Japan. The support by the Kawakami Foundation is also ackowledged.

Registry No. Phenol, 108-95-2; 2-methylphenol, 95-48-7; 3-methylphenol, 108-39-4; 4-methylphenol, 106-44-5; 4-hydroxybenzoic acid, 99-96-7; 4-hydroxy-3-methylbenzoic acid, 499-76-3; 4-hydroxy-2-methylbenzoic acid, 578-39-2; 2-hydroxybenzoic acid, 69-72-7; copper, 7440-50-8; copper sulfate, 7758-98-7; β-CD, 7585-39-9; α-CD, 10016-20-3; γ-CD, 17465-86-0; hexakis(2,6-di-*O*-methyl)-α-CD, 51166-72-4; heptakis(2,6-di-*O*-methyl)-β-CD, 51166-71-3; CCl_4, 56-23-5; $^+CCl_3$, 27130-34-3.

cis-1-Methylcyclopropylcarbinyl Cation. Preparation and Facile Interconversion with the 1-Ethylallyl Cation

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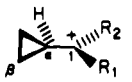
Abstract: The preparation of the previously unknown *cis*-1-methylcyclopropylcarbinyl cation **3** is reported. Cation **3** rearranges rapidly at −100 °C to the stable trans isomer, but instead of a direct rotation of the Cα–C1 bond, **3** finds a lower energy route involving at least seven intermediates, including the observable 1-ethylallyl cation **5**.

Of the simple "bisected" cyclopropylcarbinyl cations **1–4**, only



1, $R_1 = R_2 = H$

2, $R_1 = H$, $R_2 = CH_3$

3, $R_1 = CH_3$, $R_2 = H$

4, $R_1 = R_2 = CH_3$

the cis secondary ion **3** is unreported. However, the obvious precursers of **3**, e.g., 1-cyclopropylethanol, are reported[1] to yield only the trans ion **2** on addition to strong acids and this, and other evidence, strongly suggests that **2**, is the thermodynamically preferred member of this $C_5H_9^+$ pair.

The existance of **3**, as distinct from the trans isomer **2**, would seem to depend only on the magnitude of the rotation barrier about the C1–Cα bond, also an unknown experimental quantity. In Table I, we have tabulated what is presently known concerning the apparent C1–Cα rotation barriers in **1–4**. Barriers calculated by MO procedures are also listed and in the single case where a comparison with experimental can be made, the agreement is quite good. It is sufficient to note at this point that were the rotation barrier is **3** 19 kcal/mol, this would readily permit the observation of **3** ($t_{1/2}$ ca. 1 h at −21 °C).

Table I. C1–Cα Rotation Barriers for Cyclopropylcarbinyl Cations **1–4**

cation	designation	experimental barrier, E_a, kcal/mol	calculated barrier,[a] ΔE, kcal/mol
1	primary	⩾11.4[b]	26.3
2	secondary	?	20.8
3	secondary	?	19.0
4	tertiary	13.7[c]	13.2

[a] See ref 2. The data for **3** were calculated subsequently by using the same procedure. [b] This ion is stable to about −60 °C.[1] The absence of line broadening ($k < s^{-1}$) at this temperature was used to calculate a minimum $\Delta G^{\ddagger}$. [c] Reference 3.

This paper reports on the first preparation of **3**, the subsequent rearrangement of **3** to **2**, and the fact that the **3** → **2** rearrangement does not, as assumed above, take place by a direct C1–Cα bond rotation, involving instead the 1-ethylallyl cation as a key observable intermediate. This in turn allows one to study certain mechanistic aspects of the little investigated cyclopropylcarbinyl ⇄ allyl cation interconversion process.

Results

Cyclopropylcarbinyl–cyclobutyl cation interconversions are known to be highly stereospecific, and this suggests that a cyclobutane system would be a logical precurser to **3**. In fact, we

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