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Catalytic Activity of an Octopus-type Calixarene on the Formation of Ethers¹⁾

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5,11,17,23,29,35-Hexa-p-tert-butyl-37,38,39,40,41,42-hexakis-(3,6,9-trioxadecyloxy)calix[6]arene catalyzes the formation of an ether and bisphenoxymethanes through the Williamson synthesis.

Calixarenes,²⁾ which are macrocyclic oligomers from base-catalyzed condensation of para-substituted phenols with formaldehyde, have lately attracted considerable attention because their potential as enzyme mimics has been suggested.³⁾

Shinkai and co-workers have synthesized water-soluble calixarenes, which serve not only as host molecules in an aqueous system but also as a new class of surfactants and acid catalysts.⁴⁾ Using the water-soluble calixarenes, they have also demonstrated the possibility of the selective extraction of uranyl ion from sea water.⁵⁾ Gutsche and co-workers have shown the interaction, in solution, between calixarenes and amines.⁶⁾ The existence of calixarene-organic solvent molecule clathrates⁷⁾ and calixarene-alkali cation complexes⁸⁾ has been shown by

other workers. In paticular, octopustype calixarenes(Fig.1) form complexes with alkali cations as crown ethers do.⁹⁾ These calixarenes have both hydrophobic moiety and hydrophilic moiety within one molecule; they have the same nature as surfactants. Their interesting features prompted us to use them as catalysts for organic reactions. Thus, we investigated the catalytic activity of 5,11,17,23,29,35hexa-p-tert-butyl-37,38,39,40,41,42hexakis(3,6,9-trioxadecyloxy)calix[6]-



Fig. 1. Octopus-type calixarene.

arene(1) for the formation of ethers through the Williamson synthesis.

The calixarene $\underline{1}$ was prepared by a modification of the literature procedure.¹⁰⁾

In order to assess the catalytic activity of $\underline{1}$ and to compare $\underline{1}$ with other various catalysts, we at first examined the reaction of phenol with benzyl bromide (Eq.1).¹¹⁾ After the reaction, the calixarene $\underline{1}$ could be easily removed by adsorption on silica gel. Moreover, the calixarene $\underline{1}$ could be used repeatedly as a

catalyst after recovery from the silica gel.¹¹⁾ Table 1 shows the results.

$$C_6H_5OH + C_6H_5CH_2Br \xrightarrow{Cat.-KOH} C_6H_5CH_2-O-C_6H_5$$
 (1)
CH₂Cl₂, 40 °C

Run	Cat.	PhOH/Cat ^b	Time/h	Yield of ether/% ^{c)}
1	<u>1</u>	35	2	100
2	PEG-DEE 456 ^d)	5.8	3	80
3	BTAC ^{e)}	4.8	20	100
4	none	-	20	30

Table 1. The reaction of benzyl bromide with phenol^{a)}

a) $C_6H_5OH(1.2 \text{ g}, 12.8 \text{ mmol})$, benzyl bromide(2.2 g, 12.5 mmol), KOH(2.5 g), a guaranteed grade of commercial $CH_2Cl_2(15 \text{ ml})$, temp at 40 °C. b) Molar ratio. c) We could not detect any by-product. d) Poly(ethylene glycol) diethyl ether(mol. wt.=456). e) Benzyltrimethylammonium chloride.

In this reaction, the catalyst $\underline{1}$ is the most excellent among the catalysts used. Within only 2 hours, the reaction was complete. Less efficient appear to be a quarternary ammonium salt and poly(ethylene glycol)diethyl ether. With the former a longer reaction time was required(20 h) than with the catalyst $\underline{1}$. With the latter the yield of the ether was lowered(80%). These findings suggest that the catalytic activity of the calixarene $\underline{1}$ is attributable to not only the hydrophilic moiety of $\underline{1}$ but also the hydrophobic moiety.



Quarternary ammonium salts are already known to be good catalysts for the formation of bisaryloxymethanes.¹²⁾ We have next applied the calixarene <u>1</u> as a catalyst to the formation of bisaryloxymethanes to assess its catalytic activity (Eq.2).¹³⁾ Substrates used in this investigation are <u>2a</u>, <u>2b</u>, and <u>2c</u>. Table 2 shows the results. When <u>2a</u> was used, the calixarene <u>1</u> catalyzed the reaction most excellently among the catalysts used to form bisphenoxymethane(<u>5a</u>). When the substrate was <u>2b</u> and dichloromethane saturated with water was used, the calixarene <u>1</u> catalyzed, as well as benzyltrimethylammonium chloride, to form the corresponding bisphenoxymethane(<u>5b</u>). In this case, the use of dried dichloromethane lowered the yield of <u>5b</u>(31%). A longer reaction time(144 h) was required to obtain a

yield of 19% of 5b in a two-phase system. When 2c was used, the calixarene 1 did not catalyze the reaction, whereas benzyltrimethylammonium chloride acted as a good catalyst. As described above, it was found that the catalytic activity of the calixarene 1 varied with kinds of phenols.

Run	Phenol	Cat.	PhOH/Cat ^{b)}	Time/h	Yield of $5/8^{c}$
1	<u>2a</u>	<u>1</u>	24	24	100 ^d)
2	<u>2a</u>	PEG-DEE 456 ^{e)}	5.8	24	85 ^a)
3	<u>2a</u>	PEG 600 ^{f)}	0.77	195	23 ^d)
4	<u>2a</u>	BTAC ^{g)}	4.7	24	86 ^{d)}
5	<u>2a</u>	none	-	24	0.3 ^{d)}
6	<u>2b</u>		48	96	
7	<u>2b</u>	<u>1</u>	48	96	311)
8	<u>2b</u>	1	48	144	19 ^{j)}
9	<u>2b</u>	BTAC ^{g)}	4.7	72	100 ^d)
10	<u>2c</u>	<u>1</u> .	48	168	trace
11	<u>2c</u>	BTAC ^{g)}	2.3	77	99 ^{d)}

Table 2. The reaction of phenols with dichloromethane^{a)}

a) Phenol(1.2 g, 12.8 mmol), KOH(2.5 g), $CH_2Cl_2(50 \text{ ml})$, temp at 40 °C. b) Molar ratio. c) We could not detect any by-product. d) A guaranteed grade of commercial CH_2Cl_2 was employed for the reaction. e) Poly(ethylene glycol)diethyl ether (mol. wt.=456). f) Poly(ethylene glycol)(mol. wt.=600). g) Benzyltrimethyl-ammonium chloride. h) Dichloromethane which was saturated with water was used. i) Dichloromethane dried over molecular sieves was used. j) The reaction was carried out in a two-phase system; $CH_2Cl_2(50 \text{ ml})$ and water(5 ml).

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- 11) The reaction was carried out in the following manner: A mixture of PhOH(1.2 g, 12.8 mmol), benzyl bromide(2.2 g, 12.5 mmol), KOH(2.5 g), and the calixarene $\underline{1}$ (0.7 g) was placed in a flask. To the flask, $CH_2Cl_2(15 \text{ ml})$ was added all at once. After stirring for 2 h at 40 °C, the reaction mixture was poured upon a Büchner funnel containing silica gel(ca. 10 g) and the silica gel was washed with $CH_2Cl_2(ca. 100 \text{ ml})$. Silica gel adsorbed the calixarene $\underline{1}$, which was extracted with EtOH and used repeatedly. The filtrate was evaporated to dryness to give a white solid(benzyl phenyl ether); mp 39 °C. Yield 100%.
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