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Hydroalkylation of Phenol to Cyclohexylphenol in the Presence of Pd–Al_2O_3 and NaCl–$AlCl_3$ under Hydrogen Pressure

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The hydroalkylation of phenol (**1**) in the presence of palladium catalyst and fused salt (NaCl–$AlCl_3$) under hydrogen pressure was carried out. By using 1% Pd–Al_2O_3 (1 g) and the fused salt (1 : 1 mol ratio, 6 g), 4-cyclohexylphenol (**6**) was obtained selectively from **1** (30 g) in a yield of 31.9% at 120 °C for 4.5 h. Cyclohexylphenols were formed by way of 2-cyclohexen-1-ol and **1**.

Keywords——hydroalkylation; palladium catalyst; fused salt; phenol; 2-cyclohexylphenol; 4-cyclohexylphenol; 2-cyclohexylcyclohexanone

Cyclohexylphenols are useful intermediates for pharmaceutical and agricultural chemicals and as carriers for dyeing. Conventionally, cyclohexylphenol has been prepared by the alkylation of phenol (**1**) with cyclohexanol (**2**) or cyclohexene (**7**) in the presence of a large amount of anhydrous aluminum chloride, though undesirable side reactions also occur.[1] The hydroalkylation of **1**, using a bifunctional catalyst of nickel on silica-alumina, has also, been reported.[2]

In previous papers, we have reported the hydroalkylation of benzene to cyclohexylbenzene,[3,4] and of aniline to *N*-cyclohexylaniline and *p*-cyclohexylaniline[5] in the presence of palladium catalyst and fused salt (NaCl–$AlCl_3$). This catalyst system was applied to the hydroalkylation of **1** in an attempt to prepare 4-cyclohexylphenol (**6**).

In this paper, the reaction conditions were examined to obtain the optimum yield and selectivity for **6**.

Results and Discussion

Hydroalkylation of Phenol

The reaction was carried out using a bifunctional catalyst system consisting of a hydrogenation catalyst (1% Pd–Al_2O_3) and various alkylation catalysts under hydrogen pressure. The results are summarized in Table I. The hydrogenation of **1** gave **2** in 95.4% yield in the presence of 1% Pd–Al_2O_3 at 160 °C for 3 h. The addition of a Lewis acid ($AlCl_3$, $FeCl_3$, or $ZnCl_2$) to Pd–Al_2O_3, completely inhibited the hydrogenation of **1** and no hydroalkylation occurred. Although the addition of P_2O_5 or BF_3 gave the hydroalkylated products in poor yields, large amounts of these catalysts disturbed the hydrogenation. However, a fused salt, prepared from NaCl and $AlCl_3$, accelerated the hydroalkylation of **1** without disturbing the hydrogenation, as has been observed in the hydroalkylation of benzene[4] and of aniline.[5]

We compared the activities of aluminium halogenides themselves with those of several fused salts for the hydroalkylation in the presence of Pd–Al_2O_3. It is known that in Friedel–Crafts type alkylation the activity increases in the order of $AlCl_3 < AlBr_3 < AlI_3$.[6] In our reaction system, these compounds completely inhibited the hydrogenation. On the other hand, the fused salt, NaCl–$AlCl_3$, gave the hydroalkylated products, and the activities were

Table I. Hydroalkylation of Phenol in the Presence of 1% Pd–Al_2O_3 and Various Alkylation Catalysts

Alkylation cata. (g)	Conversion (%)	Yield (%) 4	5	6
—	95.4[a)]	0	0	0
P_2O_5 (4)	40.0	24.7	1.1	10.1
P_2O_5 (6)	16.8	2.4	5.3	6.3
BF_3 (1.2)	10.4	0	0.2	9.5
BF_3 (3.0)	4.3	0	0	2.9
NaCl–$FeCl_3$[b)] (4)	0	0	0	0
NaCl–$AlCl_3$[b)] (4)	37.7	4.6	7.3	15.8
NaBr–$AlBr_3$[c)] (4)	7.5	0	0	6.9
NaI–AlI_3[b)] (4)	0	0	0	0

Phenol (30 g) and 1% Pd–Al_2O_3 (1 g) were used for all experiments. The reaction was carried out at 160 °C for 3 h. *a)* Phenol was converted to cyclohexanol in a yield of 95.4%. *b)* Fused salt (1 : 1 mol ratio) was used. *c)* Fused salt (2 : 1 mol ratio) was used.

Table II. Distribution of the Hydroalkylated Products of Phenol at Various Reaction Temperatures

Temp. (°C)	Conversion (%)	Yield (%) 2	3	4	5	6
110	42.3	1.2	22.3	7.5	1.6	8.8
120[a)]	40.2	1.1	5.4	2.8	1.8	28.4
120[b)]	36.4	0.5	1.5	0.4	2.1	31.9
140	54.3	3.1	18.8	21.4	1.4	9.3
160	53.9	4.8	17.8	13.9	5.1	11.9
210	46.7	2.0	8.5	11.3	9.7	14.5
240	41.4	0.1	4.8	8.2	11.6	16.3
280	24.8	0	2.1	3.2	8.4	9.3

In each run, 30 g of phenol, 1 g of 1% Pd–Al_2O_3, and 2 g of the fused salt (1 : 1 mol ratio) were used. The reaction was carried out for 3 h. *a)* The amount of the fused salt used was 6 g. *b)* The reaction time was 4.5 h and 6 g of the fused salt was used.

higher than with NaBr–$AlBr_3$ or NaI–AlI_3. Then, we examined in detail the selectivity for **6** by using 1% Pd–Al_2O_3 and NaCl–$AlCl_3$. The distribution of products obtained by the hydroalkylation of **1** in the presence of Pd–Al_2O_3 and the fused salts at various reaction temperatures is shown in Table II.

The hydrogenation at 110 °C gave cyclohexanone (**3**) as the major product. Increase in the amount of the fused salt increased the yield of **6** (31.9%) at 120 °C for 4.5 h. At 140 °C, **3** and 2-cyclohexylcyclohexanone (**4**) was formed in almost equal yields. At higher temperatures, the yield of **3** was decreased and those of hydroalkylated products, 2-cyclohexylphenol (**5**) and **6**, were increased. At more elevated temperature (280 °C), the yields of the series of compounds, **2** to **6**, were decreased owing to the decomposition of the catalysts. Therefore, the fused salt effectively gave the hydroalkylated products at reaction temperatures between 160 and 240 °C. Further, the use of a larger amount of the fused salt (6 g) increased the yields of **5** and **6** at 120 °C. Therefore, the effect of the amount of the fused salt (NaCl–$AlCl_3$, 1 : 1 mol ratio) on the yields of **5** and **6** was examined (Table III).

At 160 °C, the yields of **5** and **6** increased with increasing amount of the fused salt, and then saturated at 20% of the fused salt with respect to **1**. When a larger amount (25 to 33%) of the fused salt was used for **1**, five to six times more **6** than **5** was obtained.

TABLE III. The Effect of the Amount of the Fused Salt on the Yields of **5** and **6** in the Hydroalkylation of Phenol

NaCl–AlCl$_3$ (g)	Conversion (%)	Yield (%) **2**	**3**	**4**	**5**	**6**
0	95.4	95.4	0	0	0	0
1.0	50.5	4.8	22.1	12.0	4.7	6.9
2.0	53.6	4.8	17.8	13.1	5.1	11.9
3.0	38.5	1.8	8.2	4.6	7.3	15.8
5.0	43.3	1.6	9.2	4.0	7.7	19.9
6.0	44.9	2.4	4.8	3.1	10.5	23.9
7.5	24.1	0.7	0	1.6	2.7	17.1
10.0	22.7	1.8	0	0.5	2.9	15.5

Phenol (30 g), 1% Pd–Al$_2$O$_3$ (1 g), and NaCl–AlCl$_3$ (1 : 1 mol ratio) were used. The reaction was carried out at 160 °C for 3 h.

TABLE IV. Alkylation of **1** with Possible Intermediates in the Presence of NaCl–AlCl$_3$

Compound (1 g)	Yield (%) **4-1**	**5**	**5-1**	**6**	**6-1**
2	0	2.8	0	0.3	0
3	4.5	0	0.1	0	0.7
7	0	7.1	0	2.1	0
8	0	0	11.8	0	8.3

Phenol (5 g), NaCl–AlCl$_3$ (1 : 1 mol ratio, 1 g), and cyclohexane (30 g) as a solvent were used. The reaction was carried out at 160 °C for 3 h.

Therefore, substitution at the *para* position was favored by either the use of a large amount (20 to 33% for **1**) of the fused salt or reaction temperatures around 120 °C.

Reaction Scheme for the Hydroalkylation of Phenol

Previously, we considered that **7** is the most likely intermediate species in the hydroalkylation of benzene[4] and cyclohexenylamine or cyclohexylimine in the hydroalkylation of aniline.[5] In this reaction, partially hydrogenated products of **2**, **3**, **7**, and 2-cyclohexene-1-ol (**8**) were considered as possible intermediates. These compounds were treated with **1** in the presence of the fused salt (Table IV). A possible reaction scheme is shown in Chart 1. A mixture of **5** and **6** was obtained by heating **1** and **7** in the presence of the fused salt in the absence of hydrogen.

On the other hand, 2-(1-cyclohexenyl)-cyclohexanone (**4**-1) was obtained from **1** and **3** as the main product. Compound **4** was also formed by the aldol condensation of two molecules of **3** with the loss of one molecule of water (acid catalyst), followed by hydrogenation.[2] When **8**, another hypothetical intermediate, was treated with **1**, a mixture of 2-(2-cyclohexenyl)-phenol (**5**-1) and 4-(2-cyclohexenyl)-phenol (**6**-1) was obtained in the presence of the fused salt. These compounds, **5**-1 and **6**-1, were hydrogenated to **5** and **6**, respectively, on Pd–Al$_2$O$_3$ with H$_2$. These results suggest that **8** may be the intermediate in the hydroalkylation of **1**.

Previously, it has been observed that the intermediates in the hydroalkylation are **7** for benzene and cyclohexylimine for aniline. In the case of **1**, the key intermediate was **8**. Therefore, partially hydrogenated derivatives of aromatic compounds may be common intermediates in hydroalkylation reactions.

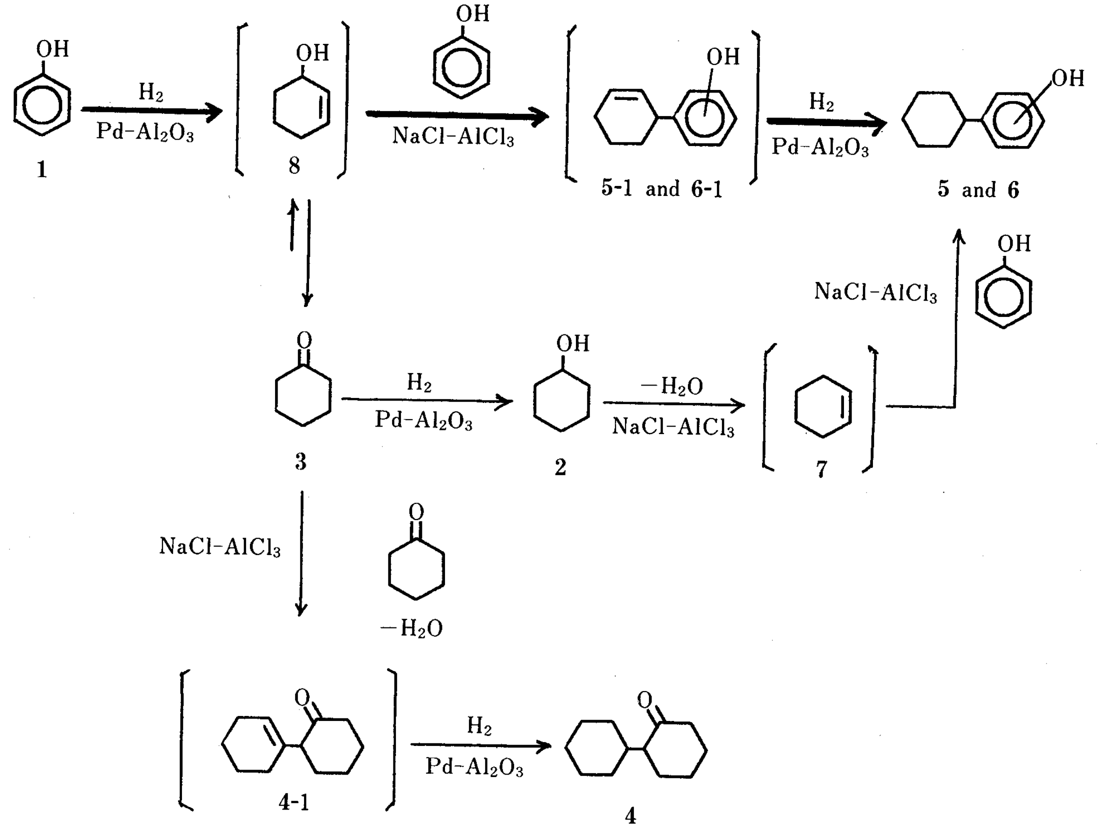

Chart 1

Experimental

All melting points were recorded on a Yanagimoto micro melting point apparatus and are uncorrected. Gas-liquid chromatography (GLC) was carried out on a Shimadzu GC-3BF gas chromatography by using a column packed with 25% Apiezon grease M on C-22 (30—60 mesh) (3 m) for the analyses of hydroalkylated products. Hydrogenated products and unreacted phenol were also analyzed in the same gas chromatograph (column packing; 20% silicone DC-550 on Shimalite, 80—100 mesh, 2 m). The proton nuclear magnetic resonance (^{1}H-NMR) spectra were obtained on a Hitachi R-600 instrument in $CDCl_3$ with tetramethylsilane as an internal standard. The abbreviations used are: s (singlet), d (doublet) and m (multiplet).

Preparation of Catalysts——Palladium supported on alumina and fused salts were prepared according to the previously reported method.[4)]

General Procedures and Products Analyses——Phenol, 1% $Pd–Al_2O_3$, and the fused salt ($NaCl–AlCl_3$) were placed in a stainless steel 100 ml autoclave (Sakashita, SUS-32) equipped with a magnetic stirrer. Hydrogen (130—150 kg/cm^2) was introduced at room temperature. Stirring was started, then the autoclave was heated to the desired temperature. Hydrogen was pressurized until hydrogen uptake ceased. After the reaction, products and unreacted phenol were washed with diluted hydrochloric acid, and extracted with ether. Ether was removed by evaporation, and the products were analyzed by GLC.

2-Cyclohexylcyclohexanone (4)——Phenol (30 g) was reacted with 1% $Pd–Al_2O_3$ (1 g) in the presence of the fused salt (2 g) at 140 °C for 4 h under hydrogen pressure. The resulting products were isolated by fractional gas chromatography to give **4** (21.4% yield). *Anal.* Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.19. Found: C, 79.65; H, 11.27. IR $\nu^{\mathrm{neat}}\mathrm{cm}^{-1}$: 1705 (C=O).

2-(1-Cyclohexenyl)-cyclohexanone (4-1)——A mixture of phenol (5 g) and cyclohexanone (1 g) in cyclohexane (30 g) was heated in the presence of the fused salt (1 g) at 160 °C for 3 h. After the reaction, the solvent was evaporated off, and the residue was isolated by preparative thin layer chromatography (TLC) using 2-propanol and *n*-hexane (1 : 1) as a developing solvent to give **4-1**. *Anal.* Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 81.11; H, 10.09. IR $\nu^{\mathrm{neat}}\mathrm{cm}^{-1}$: 1700 (C=O).

2-Cyclohexylphenol (5) and 4-Cyclohexylphenol (6)——Phenol (30 g) was hydroalkylated in the presence of 1% $Pd–Al_2O_3$ (1 g) and the fused salt (6 g) at 160 °C for 3 h. The resulting products including **5** (10.5% yield) and **6** (23.9% yield) were also separated by fractional gas chromatography. **5**: *Anal.* Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.43; H, 8.85. ^{1}H-NMR ($CDCl_3$) δ: 1.00—2.05 (11H, m), 4.38 (1H, s), 6.92—7.30 (4H, m). IR $\nu^{\mathrm{KBr}}\mathrm{cm}^{-1}$: 3300

(O–H), 1600 (C–H). mp 55.5—56.0 °C (lit.[1] 57.0 °C). **6**: *Anal.* Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 82.06; H, 9.14. ^{1}H-NMR ($CDCl_3$) δ: 1.10—2.10 (11H, m), 4.54 (1H, s), 6.80 (2H, d), 7.01 (2H, d). IR ν^{KBr} cm^{-1}: 3200 (O–H), 1595 (C–H). mp 132.0—132.5 °C (lit.[1] 132.0—133.0 °C).

2-(2-Cyclohexenyl)-phenol (5-1) and 4-(2-Cyclohexenyl)-phenol (6-1)——A mixture of phenol (5 g) and 2-cyclohexene-1-ol (1 g) in cyclohexane (30 g) was stirred in the presence of the fused salt (1 g) at 160 °C for 3 h. The resulting products were also isolated by fractional gas chromatography, then purified by preparative TLC using benzene as a developing solvent to give **5**-1 and **6**-1. **5**-1: ^{1}H-NMR ($CDCl_3$) δ: 1.20—2.25 (9H, m), 3.20 (1H, m), 4.50 (s, 1H), 5.54 (1H, dd), 5.85 (1H, m), 6.85—7.45 (4H, m). **6**-1: *Anal.* Calcd for $C_{12}H_{14}O$: C, 82.75; H, 8.10. Found: C, 82.55; H, 8.13. ^{1}H-NMR ($CDCl_3$) δ: 1.25—2.45 (9H, m), 3.35 (1H, m), 4.70 (1H, s), 5.70 (1H, dd), 5.90 (1H, m), 6.80 (2H, d), 7.10 (2H, d). mp 69—70 °C.

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