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Direct synthesis of 3-methylbenzofuran from phenol and acetone over halide cluster catalysts taking advantage of acidic and metallic properties

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ABSTRACT

When a molecular tantalum halide cluster on silica gel, $[(Ta_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ (**1**)/SiO_2, is treated in a helium stream in the temperature range 150–300 °C, catalytic activity for the condensation of phenol with acetone to yield 2-isopropenylphenol develops. Above 350 °C, subsequent cyclodehydrogenation proceeds to afford 3-methylbenzofuran with 60% selectivity. Higher reaction temperatures promote the subsequent cyclodehydrogenation. The condensation is caused by weak Brønsted acidity of a hydroxo ligand, which is formed by elimination of hydrogen chloride from the chloro and aqua ligands in **1**. In contrast, the cyclodehydrogenation is catalyzed by a coordinatively unsaturated platinum-like metal atom developed in the cluster. Niobium, molybdenum, and tungsten clusters with the same metal framework also catalyze the reaction.

1. Introduction

Since the first report on molybdenum(II) chloride in 1859 [1], many halide clusters have been synthesized [2–6]. Studies on these clusters have focused mainly on syntheses and structures, whereas application of the clusters to catalysis has not been reported. The halide clusters have characteristic features such as multi-center and multi-electron systems, unique intermediate oxidation states of the metal atoms, high thermal stability, high melting point, and low vapor pressure as halide complexes. Taking these features into consideration, we have been studying the application of the clusters to catalysis. When the halide clusters were thermally treated in a gas stream, a hydroxo ligand and a coordinatively unsaturated site developed on the metal atom, as exemplified by Scheme 1 in the case of the tantalum cluster $[(Ta_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ (**1**) [7]. The hydroxo ligand acted as a Brønsted acid [8] to catalyze dehydration of alcohols [9], ring-attachment isomerization of dialkylbenzenes [10], methylation of toluene [8], and hydration of alkynes [11]. The metal atom, which accepts some electrons from the halogen ligands and can be isoelectronic with the platinum group metals [12], catalyzed hydrogenation of alkenes and alkynes [7,12], dehydrogenation of cyclohexene [12], and hydrogenolysis of ethylbenzene [13].

One of the most challenging subjects in catalysis is to develop new reactions over new catalysts. This paper describes the novel direct synthesis of 3-methylbenzofuran (**2**) from phenol and acetone (Scheme 2), in which Brønsted acidity and platinum-like metallic behavior operated concurrently. Benzofurans including **2** are used as raw materials for pharmaceuticals [14], fluorescent dyes [15], and photoreceptors [16]. Although more than 1100 reports on syntheses of benzofurans were published prior to 1973 [17], there have been no precedents for the direct synthesis of benzofurans from phenols and ketones.

2. Experimental

Crystals of molecular cluster complexes $[(Nb_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ [18], $(H_3O)_2[(Mo_6Cl_8)Cl_6]\cdot 6H_2O$ [19], $[(Ta_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ (**1**) [18], and $(H_3O)_2[(W_6Cl_8)Cl_6]\cdot 6H_2O$ [20] were synthesized according to the published procedures. The cluster Re_3Cl_9 was a commercial product (Furuya Metal Co. Ltd., Japan), and was used without further purification.

General procedure for the preparation of the silica-supported catalyst is described in detail for **1**. Methanol (330 mL) was added to a 1 L flask containing **1** (1.0 g). After dissolution of the cluster, silica gel (Nippon Aerosil, Tokyo, Aerosil 380 m^2/g, 19.0 g) was added and allowed to stand for 1 h with occasional shaking. Then the solvent was evaporated to dryness under vacuum at ambient temperature. Samples of the dried silica gel were crushed and screened to 150–200 mesh. All of the clusters were supported on the silica gel in the same way at 5.0% by weight. All of the organic compounds were

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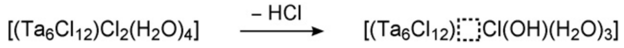
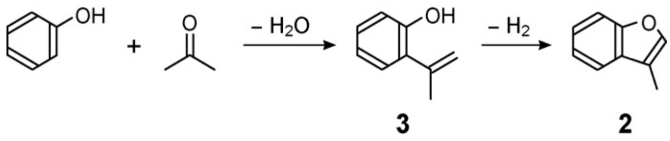


Scheme 1.



Scheme 2.

commercially available and used as received. The other chemicals were commercial products and used as received: silica–alumina, Catalysts & Chemicals Ind. Co., Ltd. (JRC-SHA-1, Catalysis Society of Japan); H-beta, Sud-Chemie Catalysts Japan, Inc. (JRC-Z-HB25(1), Catalysis Society of Japan); H-ZSM-5-25H, Mobil Catalysts Corporation of Japan (JRC-Z5-25H, Catalysis Society of Japan); H-mordenite, Tosoh Corporation (JRC-Z-HM20(4), Catalysis Society of Japan).

The general procedure for the catalytic reaction is described in detail for the system **1**/phenol/acetone. A conventional vertical glass fixed-bed microreactor with a continuous gas flow system was operated at atmospheric pressure [21]. In each experiment, a weighed fresh catalyst sample of **1** (100 mg) was packed in a borosilicate glass tube (6 mm i.d.) with the aid of quartz glass wool and placed in the center of an electric furnace. The catalyst was initially heated from room temperature to a fixed temperature between 100 and 450 °C for 1 h in a helium stream (600 mL/h). The temperature reached the set point in 15 min. The reaction was initiated by feeding a mixture of phenol (10 mg/h, 0.11 mmol/h) and acetone (40 μL/h, 0.55 mmol/h) into the helium stream using syringe pumps without changing the temperature. The reaction was monitored every 30 min by sampling the reaction gas (1 mL) with a six-way valve maintained at 200 °C, followed by analysis using an on-line GLC (methylsilicone G-column). The reactor effluent was frozen in a dry-ice trap for subsequent analyses with GLC (dimethylpolysiloxane capillary column) and GC/MS (dimethylpolysiloxane capillary column). Catalytic reactions using the other catalysts were performed in the same way. In this article, conversion and selectivity are defined as follows: conversion = products/(products + recovered phenol) × 100 (%), and selectivity = product/(total amount of products) × 100 (%) based on phenol.

3. Results and discussion

3.1. Catalytic reaction

The supported tantalum cluster, $[(Ta_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ (**1**)/SiO_2, was placed in a glass reaction tube and activated at 350 °C in a helium stream for 1 h. The reaction was initiated by introduction of a mixture of phenol with acetone in a mole ratio of 1:5 into the helium stream at 350 °C. The reaction profile is plotted in Fig. 1. The catalytic activity decreased with time, probably because of coke deposition on the catalyst. Coke formed from phenol has been reported to deactivate the Nafion-H catalyst in a gas–solid phase reaction [22]. Until 1.5 h, the catalytic activity of **1** sharply decreased, and the selectivity for **2** increased. At the beginning of the reaction, catalytic active sites with different strength could be developed. Coke would be formed preferentially on the stronger active sites, resulting in rapid disappearance of the activity, and then the weaker active sites would be resident. After a period of 1.5 h the selectivity remained steady, indicating that the nature of the catalytic active sites was not changed, though the number of the active sites decreased. 3-Methylbenzofuran (**2**) was obtained with 60% selectivity, along with 2-isopropenylphenol (**3**) with 34% selectivity. The turnover frequency per cluster during a period of 2–4 h was 24.8 h^{-1}, assuming that all of the cluster molecules were active. The material balance was 92% at 2–4 h based on phenol.

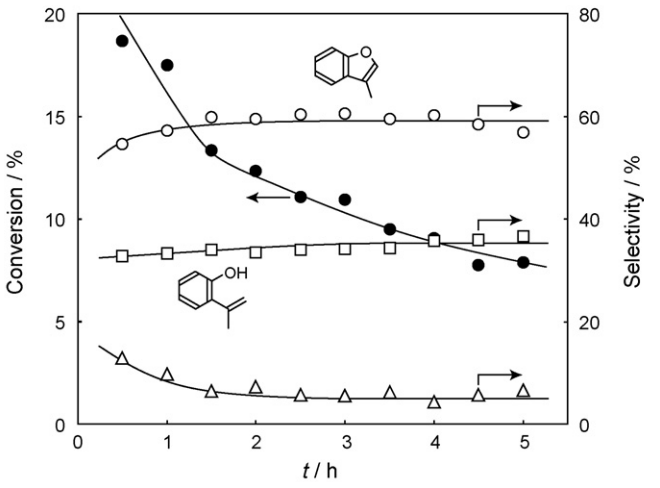


Fig. 1. A typical reaction profile of phenol with acetone catalyzed by $[(Ta_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ (**1**)/SiO_2 in a helium stream. Legend: conversion of phenol (closed circles); selectivity for 3-methylbenzofuran (open circles); selectivity for 2-isopropenylphenol (open squares); and selectivity for the other aromatic products such as cresol and ethylphenol (open triangles).

Table 1 lists the catalytic activities of various clusters of Group 5–7 metals and related compounds at 3 h after the reaction started at 350 °C. Supported chloride clusters of niobium (entry 1), molybdenum (entry 2), and tungsten (entry 8) also catalyzed the reaction. The supported bromide cluster of tantalum was also an active catalyst for the reaction (entry 7). In contrast, no catalytic activity was observed over the supported trinuclear rhenium chloride cluster (entry 9), which has no coordinated water to produce hydroxo ligands. When *p*-cresol was used in place of phenol over **1**/SiO_2, the corresponding benzofuran, 3,5-dimethylbenzofuran, was obtained with 64% selectivity (entry 6). Table 1 also shows that, when 15 times molar amount of acetone was added to phenol over **1**/SiO_2, the conversion was 40% with 48 % selectivity for **2** (entry 4), and then the yield of **2** based on phenol was 19 %. This yield was comparable to the overall yields for conventional multi-step stoichiometric syntheses of **2** from phenol: 36% for the route via 2-iodophenol and *O*-allyl-2-iodophenol [23,24], and 22–32% for that via sodium phenoxide, 3-oxo-2-phenoxybutanoic acid ethyl ester, and 3-methyl-2-benzofurancarboxylic acid [25].

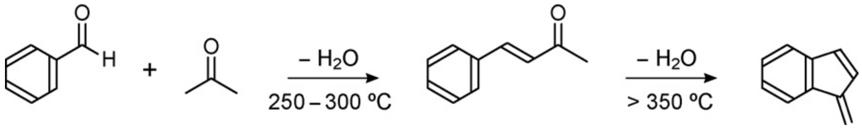
The effect of the reaction temperature on activity and selectivity over **1**/SiO_2 at 3 h after the start of the reaction is shown in Fig. 2, in which activation and successive reaction temperatures were changed concomitantly. The catalytic activity developed above 150 °C, and increased with increasing temperature, having a maximum around 300 °C. Above 350 °C, the activity decreased with increasing temperature. However, the catalytic activity at 30 min after the reaction started was reversed: the conversion was 12.8% at 300 °C, 18.6% at 350 °C, 62.3% at 400 °C, and 71.5% at 450 °C. These data indicate that the catalytic activity at higher temperatures was high at the initial stage of the reaction but rapidly decreased. The rapid deactivation at higher temperatures is probably due to coke deposition promoted by increasing temperature. We have reported a similar rapid deactivation of the halide clusters above 350 °C for the dehydration of alcohol [9].

Over the temperature range 150–300 °C, condensation yielding **3** selectively proceeded, as Fig. 2 shows. Above 350 °C, the main product changed to **2**, which would be formed by subsequent cyclodehydrogenation of **3** (Scheme 2). We have reported

Table 1
Synthesis of 3-methylbenzofuran over various halide clusters[a].

Entry	Catalyst	Conversion (%)	Selectivity (%)		
			2-Isopropenylphenol (**3**)	3-Methylbenzofuran (**2**)	Others[b]
1	$[(Nb_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O/SiO_2$	20.4	19.7	27.5	52.7
2	$(H_3O)_2[(Mo_6Cl_8)Cl_6]\cdot 6H_2O/SiO_2$	4.4	30.4	56.8	12.9
3	$[(Ta_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ (**1**)$/SiO_2$	10.9	34.1	60.4	5.5
4	$[(Ta_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ (**1**)$/SiO_2$[c]	39.7	26.4	48.0	25.6
5	$[(Ta_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ (**1**)[d]	16.1	50.1	15.8	34.1
6	$[(Ta_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ (**1**)$/SiO_2$[e]	3.6	11.2[f]	64.1[g]	24.7
7	$[(Ta_6Br_{12})Br_2(H_2O)_4]\cdot 4H_2O/SiO_2$	13.1	40.4	47.5	12.1
8	$(H_3O)_2[(W_6Cl_8)Cl_6]\cdot 6H_2O/SiO_2$	7.2	47.9	42.0	10.1
9	Re_3Cl_9/SiO_2	0.0			
10	Ta metal	0.0			
11	SiO_2	0.0			
12	SiO_2–Al_2O_3 (high alumina)	25.9	9.2	7.8	83.0
13	H-beta	8.6	1.1	1.4	97.5
14	H-ZSM-5-25H	7.0	1.5	0.9	97.6
15	H-mordenite	2.3	2.5	2.1	95.4
16	None	0.0			

[a] At 350 °C. At 3 h after the reaction started.
[b] Cresol, ethylphenol, etc.
[c] Fifteen molar amounts of acetone (120 μL/h, 1.65 mmol/h) was added to phenol (10 mg/h, 0.11 mmol/h).
[d] Unsupported crushed crystalline cluster.
[e] *p*-Cresol (12 mg/h, 0.11 mmol/h) was used in place of phenol.
[f] 2-Isopropenyl-4-methylphenol.
[g] 3,5-Dimethylbenzofuran.



Scheme 3.

that the reaction of benzaldehyde with acetone over the halide cluster catalysts selectively afforded the aldol condensation product, *E*-4-phenyl-3-penten-2-one, in the temperature range 250–300 °C, whereas subsequent cyclodehydration yielding indene proceeded above 350 °C (Scheme 3) [26]. According to Le Chatelier's principle, a reaction that increases the number of product molecules is thermodynamically favorable at higher temperatures under constant pressure. Thus, the higher reaction temperatures promoted the cyclodehydrogenation of **3** to **2**, similar to the cyclodehydration yielding indene. Above 350 °C, the selectivity for **2** decreased, and the selectivity for decomposition products such as cresol and ethylphenol increased. The decomposition increases the number of product molecules more than the cyclodehydrogenation to yield **2** does, and proceeds more favorably at higher temperatures. In the hydration of 1-hexyne over the tungsten cluster, the selectivity for decomposition yielding ethylene, propene, 1-butene, and 1-pentyne increased above 400 °C [11].

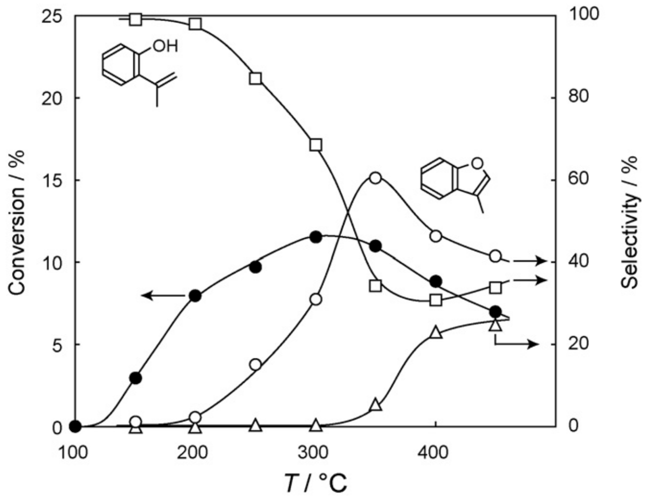
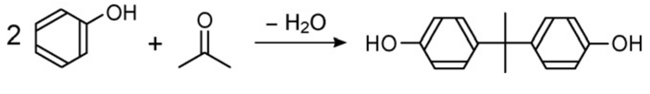


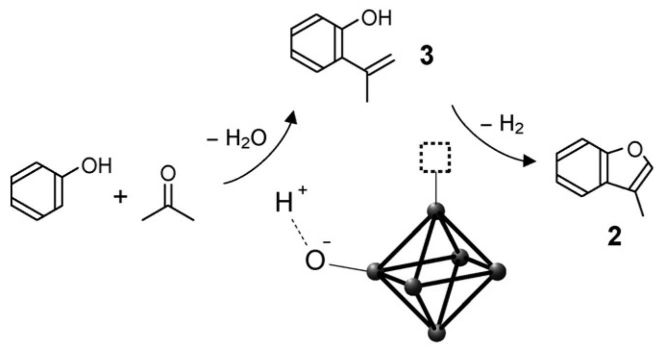
Fig. 2. Temperature effect on the reaction of phenol with acetone over $[(Ta_6Cl_{12})Cl_2(H_2O)_4]\cdot 4H_2O$ (**1**)$/SiO_2$ at 3 h after the reaction started. Both the initial treatment and reaction temperatures were altered concomitantly. Legend: conversion of phenol (closed circles); selectivity for 3-methylbenzofuran (open circles); selectivity for 2-isopropenylphenol (open squares); and selectivity for the other aromatic products such as cresol and ethylphenol (open triangles).

3.2. Active sites

Bisphenol A, 2,2-bis(4-hydroxyphenyl)propane, is commercially produced from phenol and acetone in the presence of HCl [27] or ion exchange resins [28] at around 70 °C (Scheme 4). SiO_2–Al_2O_3 [29], H-beta [30], H-mordenite [29], and $H_3PW_{12}O_{40}$ [31] are also reported to catalyze the reaction in the temperature range 90–180 °C. At 250 °C, bisphenol A is reported to be decomposed to phenol and *p*-isopropenylphenol in the presence of HCl [32]. On the other hand, the halide clusters had no catalytic activity below 100 °C, and no formation of bisphenol A was detected over the temperature range 150–450 °C (Fig. 2). Those acids for bisphenol A synthesis are strong acids with a Hammett acidity function (H_0) less than −8 [33,34]. In contrast, the acidity of the halide clusters is expected to be weak, because it is based on the hydroxo ligand [35]. Acid titrations [36–38], in fact, showed that H_0 values of the niobium and molybdenum clusters activated at around 300 °C



Scheme 4.



Scheme 5.

were +1.0. Thus, the acid strength of the catalysts would change the reaction pathway.

As Table 1 shows, formation of 3-methylbenzofuran scarcely proceeded over the conventional solid acids under identical conditions (entries 12–15). Moreover, there have been no reports on cyclodehydrogenation of alkenylphenols to benzofurans over solid Brønsted acid catalysts. On the other hand, the platinum group metal catalysts such as Pd metal [39] and $RuCl_3$ [40] are reported to catalyze cyclodehydrogenation of 2-allylphenol to yield 2-methylbenzofuran. Similar cyclodehydrogenation is reported for Pd/C, $PdCl_2$, and $Pd(OAc)_2$ [41]. Thus, the cyclodehydrogenation over the halide clusters would be attributed to the metal atom of the cluster, which behaved like the platinum group metals.

4. Conclusion

When phenol was allowed to react with acetone over the tantalum halide cluster (**1**) in the temperature range 150–200 °C, condensation yielding 2-isopropenylphenol (**3**) proceeded almost exclusively. The condensation activity is attributable to the weak Brønsted acidity of the hydroxo ligand. Above 350 °C, subsequent cyclodehydrogenation of **3** proceeded to afford 3-methylbenzofuran (**2**) as the main product. The cyclodehydrogenation was promoted by the coordinatively unsaturated platinum-like metal atom of the cluster. Thus, the halide clusters acted as acidic and metallic bifunctional catalysts, leading to direct synthesis of benzofurans from phenols and acetone (Scheme 5).

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