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Mechanistic Studies on Fluorobenzene Synthesis from 1,1-Difluorocyclohexane via Pd-Catalyzed Dehydrofluoro–Dehydrogenation

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The chemical reactivity and reaction mechanism of fluorobenzene synthesis via dehydrofluoro–dehydrogenation of 1,1-difluorocyclohexane was investigated. 1,1-Difluorocyclohexane reacted with molecular oxygen to give fluorobenzene in good yields in the presence of both Pd and metal fluoride catalysts. The reaction proceeded with dehydrofluorination of 1,1-difluorocyclohexane to yield 1-fluorocyclohexene as the sole intermediate species, followed by oxidative dehydrogenation. The present system offers a selective synthesis of fluorobenzene.

Fluoroaromatics are widely used in the synthesis of pharmaceuticals,[1] agrochemicals,[2] functional organic materials,[3] and high-performance polymers.[4] Fluorobenzene in particular is a common starting material for commercial-scale manufacturing processes. Although various synthetic methods have been reported for fluorobenzene,[5] most of them have drawbacks as follows. The Schiemann reaction typically involves unstable diazonium salts.[5a,6] Nucleophilic displacement of aryl chloride by fluoride is known to generate chloride as waste.[7] Direct fluorination of benzene using F_2 and some metal fluorides exhibits poor selectivity.[8] 1-Alkyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane salts (Selectfluor™) are applicable in fluorination of activated aromatics.[8,9] Copper(II) fluoride reacts directly with benzene, and is regenerated by treating the copper metal with hydrogen fluoride (HF) under molecular oxygen,[10] but its conversion is less than 30%.

Recently, transition-metal-promoted fluorinations have been developed using electrophilic N–F reagents. Sanford and co-workers[11] reported a palladium-mediated fluorination of aromatic C–H bonds. Ritter and co-workers[12] published a palladium-[12a–12c] or silver-mediated[12d–12f] fluorination of aryl boronic acids and aryl stannanes. However, substrates are limited to specific pyridine derivatives in the former reaction and stoichiometric amounts of transition metal are necessary in the latter reaction. More recently, Buchwald and co-workers[13] achieved a palladium-catalyzed nucleophilic conversion of aryl triflates into aryl fluorides using metal fluorides. Most recently, Knochel and co-workers[14] and Beller and co-workers[15] reported an electrophilic fluorination of aryl bromides or iodides via aryl magnesium reagent.

We have previously reported that 1,1-difluorocyclohexane was converted to fluorobenzene by catalytic oxidative dehydrofluoro–dehydrogenation.[16] Because 1,1-difluorocyclohexane is easily synthesized from cyclohexanone by various methods,[17,18] its dehydrofluoro–dehydrogenation can be an alternative synthesis of fluorobenzene. Although this method had been reported earlier,[16] the reaction mechanism had not yet been discussed. Herein, we report the chemical reactivity and reaction mechanism of the dehydrofluoro–dehydrogenation of 1,1-difluorocyclohexane in the presence of catalyst. 1,1-Difluorocyclohexane reacted with molecular oxygen to give fluorobenzene in good yields in the presence of both Pd and metal fluoride catalysts. It was proven that the reaction proceeded with dehydrofluorination of 1,1-difluorocyclohexane to yield 1-fluorocyclohexene as the sole intermediate species, and subsequent oxidative dehydrogenation gave fluorobenzene. Thus, this offers a selective synthesis of fluorobenzene.

Results and Discussion

Oxidative Dehydrofluoro–Dehydrogenation of 1,1-Difluorocyclohexane (1). We first characterized the catalytic oxidative dehydrofluoro–dehydrogenation of 1,1-difluorocyclohexane (**1**) in the presence of molecular oxygen as an oxidant. In the formation of fluorobenzene (**2**) from **1**, an effective catalyst must promote both dehydrofluorination and dehydrogenation. HF is formed as a result of dehydrofluorination, and therefore the catalyst should be acid resistant. Combinations of heterogeneous group VIII metals and metal fluorides were chosen for these reasons,[16] because the metal fluoride works as a dehydrofluorination catalyst, and the group VIII metal operates as a dehydrogenation catalyst. Gas-phase reaction of **1**

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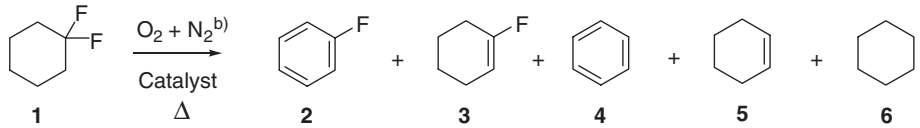
Table 1. Oxidative Dehydrofluoro–Dehydrogenation of 1,1-Difluorocyclohexane (**1**)[a)]



Entry	Group VIII metal (wt %)[d)]	Metal fluoride (wt %)[d)]	Temperature /°C	Time[e)] /h	Conversion[f)] /%	Selectivity[g)]/%					Catalyst activity[h)] /mmol m^{-2} h^{-1}
						2	**3**	**4**	**5**	**6**	
1	Pd-black (10)	AlF_3 (90)	370	0.31	72	8	91	0.2	0.1	0.1	2.0
2	Pt-black (10)	AlF_3 (90)	370	0.31	69	5	94	0.2	0.1	0.1	1.0
3	Ru-black (10)	AlF_3 (90)	370	0.31	70	1	98	0.3	0.1	0.2	0.1
4	Pd-black (10)	FeF_3 (90)	370	0.31	30	7	92	0.4	0.1	0.2	0.7
5	Pd-black (10)	GaF_3 (90)	370	0.31	9	6	93	0.2	0.1	0.1	0.2
6	Pd-black (10)	AlF_3 (90)	370	0.63	72	7	92	0.2	0.1	0.1	0.9
7	Pd-black (10)	AlF_3 (90)	410	0.63	99	15	84	0.3	0.1	0.1	2.5
8	Pd-black (10)	AlF_3 (90)	450	0.63	100	28	71	0.4	0.1	0.2	4.8
9	Pd-black (30)	AlF_3 (70)	450	0.63	100	61	38	0.4	0.1	0.1	2.6
10	Pd-black (60)	AlF_3 (40)	450	0.63	100	81	18	0.5	0.1	0.2	2.3

a) 8 g h^{-1} (Entries 1–5) or 4 g h^{-1} (Entries 6–10) of gaseous **1** was fed to a fixed bed flow reactor packed with the catalysts. b) Mixed gas [O_2: 20 cm^3 min^{-1} c); N_2: 200 cm^3 min^{-1} c) (Entries 1–5) or O_2: 50 cm^3 min^{-1} c); N_2: 450 cm^3 min^{-1} c) (Entries 6–10)] was used. c) Standard cubic centimeters per minute. d) Total amount of catalyst was 2.50 g. e) Residence time was calculated from a reciprocal of WHSV (weight hourly space velocity). f) Determined by gas-liquid chromatography. g) Based on **1**. h) Yield of **2** per unit metal surface area[i)] per hour. i) Metal surface area: Pt-black 30 m^2 g^{-1}; Ru-black 90 m^2 g^{-1}; Pd-black 25 m^2 g^{-1}.

with molecular oxygen was performed under atmospheric pressure over a fixed bed flow reactor packed with a mixture of a group VIII metal and metal fluoride catalysts as described earlier.[16] Reaction conditions and selected results are summarized in Table 1.

When the catalyst activities (yield of **2** per unit metal surface per hour) with AlF_3 were compared (Entries 1–3), Pd-black exhibited the highest activity (2.0 mmol m^{-2} h^{-1}). Although the major product was 1-fluorocyclohexene (**3**) (91–98% selectivity), this dehydrofluorination catalyst also produced **2** (1–8% selectivity) and benzene (**4**), cyclohexene (**5**), and cyclohexane (**6**) (less than 1% each). Among the dehydrofluorination catalysts (Entries 1, 4, and 5), AlF_3, the most acidic Lewis acid, was the most active catalyst in the presence of Pd-black. Table 1 also (Entries 6–8) shows that conversion of **1**, selectivity of **2**, and catalyst activity increased with higher temperature (conversion of **1**: 72–100%; selectivity of **2**: 7–28%; catalyst activity: 0.9–4.8 mmol m^{-2} h^{-1}). A relatively higher selectivity of **2** (28%) was observed at 450 °C (Entry 8). The increase in the ratio of Pd-black catalyst to AlF_3 catalyst enhanced the yield of **2** (28–81%, Entries 8–10), whereas the conversion of **1** remained 100%. Thus, a smaller amount of dehydrofluorination catalyst (AlF_3) is sufficient because the dehydrogenation catalyst (Pd-black) catalyzes the rate-controlling step.

Figure 1 indicates the time course of dehydrofluoro–dehydrogenation of **1**. Catalysts and reaction temperature were identical to those of Entry 10 in Table 1. A range of the residence time (from 0.078 to 1.25 h) was determined by varying the feed rate of the inlet gas (the mixture of **1**, O_2, and N_2). Because **3** (symbol □) increased with decreasing of **1** (symbol △), and **2** (symbol ○) increased with decreasing of **3**, simple consecutive first-order kinetics of **2** from **1** via **3** were assumed. The rate equations are

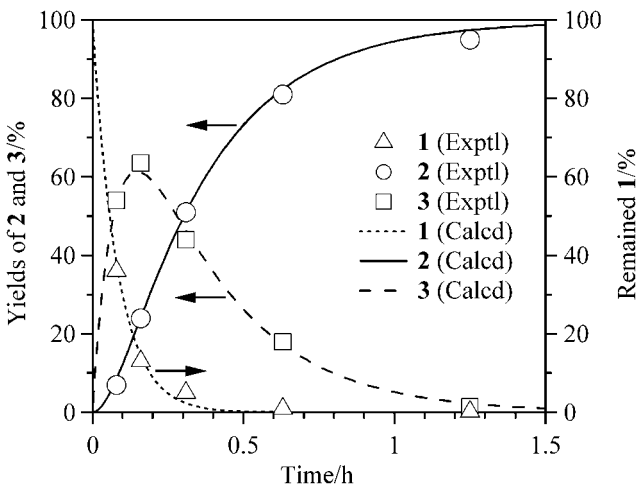


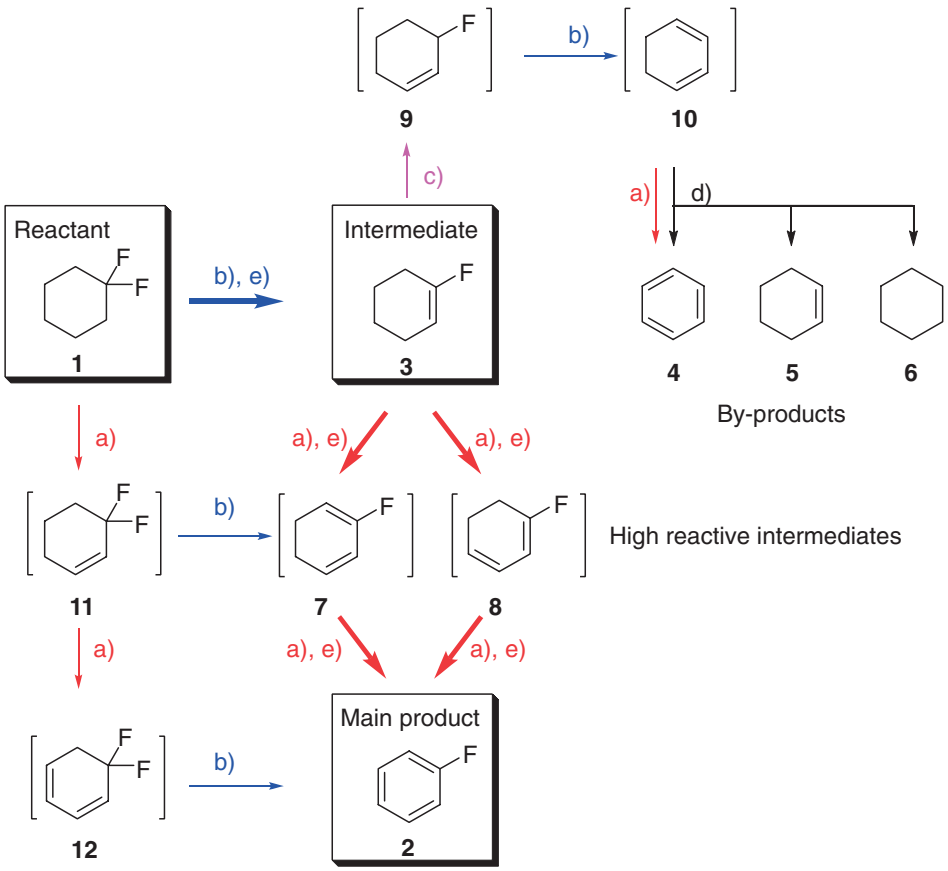
Figure 1. Time courses of oxidative dehydrofluoro–dehydrogenation of 1,1-difluorocyclohexane (**1**). Gaseous **1** was fed to a fixed bed flow reactor packed with catalyst (mixture of 1.5 g of Pd-black and 1.0 g of AlF_3) under mixed gas (O_2: 50 cm^3 min^{-1}; N_2: 450 cm^3 min^{-1}) at 450 °C, and residence time was calculated from a reciprocal of WHSV (weight hourly space velocity). Symbols (△, ○, and □) are experimental data and calculated lines are based on the assumption that **1** yields **2** via **3** consecutively.

$$d[\mathbf{1}]/dt = -k_1[\mathbf{1}] \quad (1)$$

$$d[\mathbf{3}]/dt = k_1[\mathbf{1}] - k_2[\mathbf{3}] \quad (2)$$

$$d[\mathbf{2}]/dt = k_2[\mathbf{3}] \quad (3)$$

where [**1**], [**2**], and [**3**] are concentrations in mole fractions of **1**, **2**, and **3**, respectively. The symbols k_1 and k_2 are rate constants of the reaction from **1** to **3** and **3** to **2**, which were obtained by



Scheme 1. Possible reaction sequence of **2** formation by dehydrofluoro–dehydrogenation of **1**. Conditions: a) Oxidative dehydrogenation. b) Dehydrofluorination. c) Isomerization. d) Disproportionation or simple dehydrogenation. e) Bold lines are possible main paths.

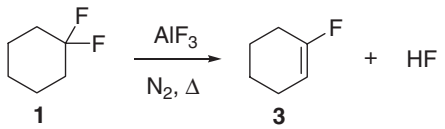
curve fitting of the experimental data.[19] The calculated lines based on this assumption were in good agreement with the experimental data, supporting that **3** is an intermediate to **2** from **1**. The fitted rate constant k_1 (12.1 h^{-1}) was larger than k_2 (3.3 h^{-1}), showing that the dehydrofluorination is faster than oxidative dehydrogenation under the present conditions.

Scheme 1 shows a possible reaction sequence including several dehydrofluorination and dehydrogenation pathways. At first, **1** yields **3** as shown in Figure 1. 2-Fluorocyclohexa-1,3-diene (**7**) or 1-fluorocyclohexa-1,3-diene (**8**) must be consecutively formed by dehydrogenation of **3**, but were not observed. The conjugated dienes **7** and **8** do not desorb and have high reactivities for further dehydrogenation to **2**. Besides fluorine-containing compounds **2** and **3**, small amounts of cyclic hydrocarbons **4**, **5**, and **6** are formed. It was confirmed that independently synthesized **9**[20] easily dehydrofluorinates to yield reactive cyclohexa-1,3-diene (**10**), which yields **4**, **5**, and **6** under oxidative conditions. Considering that the bond between the sp^2-carbon and fluorine atom is stable, this suggests that **3** isomerizes to 3-fluorocyclohexene (**9**). When the dehydrofluorination and dehydrogenation catalysts are mixed before use (Table 1), there is a possibility that dehydrogenation occurs prior to dehydrofluorination. The dehydrogenated product 3,3-difluorocyclohexene (**11**) might be further dehydrogenated to yield 5,5-difluorocyclohexa-1,3-diene (**12**). Both allyl difluorides **11** and **12** could be dehydrofluorinated to yield **7** and **2**, respectively. The reaction steps including **11** and **12** as shown in Scheme 1 are discussed below.

Dehydrofluorination of 1,1-Difluorocyclohexane (1). We conducted gas-phase dehydrofluorination of **1** in order to characterize the reaction path from **1** to **3** as shown in Scheme 1. Although gas-phase heterogeneous dehydrofluorination of **1** has been reported before using Al_2O_3[21a] or metal fluorides[21b] as catalysts, no detailed data was published. The reaction was carried out under atmospheric pressure over a fixed bed flow reactor packed with AlF_3. Detailed conditions and selected results are summarized in Table 2. Intermediate **3** was obtained as the single product only with AlF_3 (all entries). Because the dehydrofluorinated product **10** and further disproportionated products **4**, **5**, and **6** were not observed at all, it is evident that the Pd-black catalyzed an isomerization (Table 1). The activation energy E_a of the dehydrofluorination of **2**, determined by Arrhenius plot (Entries 2a–2d), was 136 kJ mol^{-1}, indicating that a high reaction temperature of up to 450 °C is necessary to attain the high conversion of **1**.

Oxidative Dehydrogenation of Cyclohexenes. The reactivities of fluorocyclohexenes **3** and **9** were examined in order to understand the reaction path from **3** to **2** as shown in Scheme 1. This reaction had been reported earlier,[22] but metal fluorides were not employed as catalysts. The oxidative dehydrogenation of fluorocyclohexenes was carried out in a

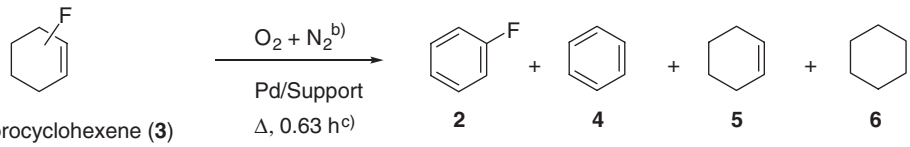
Table 2. Dehydrofluorination of **1** with AlF_3 Catalyst[a)]



Entry	Temperature /°C	Time[b)] /h	Conversion[c)] /%	Selectivity[d)]/%					k_1[e)] /h^{-1}	E_a[f)] /kJ mol^{-1}	A[f)] /h^{-1}
				2	**3**	**4**	**5**	**6**			
1	450	0.63	100	ND	>99	ND	ND	ND	—	—	—
2a	400	0.078	19.8	ND	>99	ND	ND	ND	2.83	136	9.3×10^{10}
2b	380	0.078	8.0	ND	>99	ND	ND	ND	1.07		
2c	360	0.078	3.7	ND	>99	ND	ND	ND	0.48		
2d	340	0.078	2.0	ND	>99	ND	ND	ND	0.26		

a) 4 g h^{-1} (Entry 1) or 32 g h^{-1} (Entries 2a–2d) of gaseous **1** and N_2 [200 cm^3 min^{-1} (Entry 1) or 500 cm^3 min^{-1} (Entries 2a–2d)] were fed to a fixed bed flow reactor packed with AlF_3 (2.5 g). b) Residence time was calculated from a reciprocal of WHSV. c) Determined by gas-liquid chromatography. d) Based on **1**. ND: Not detected. e) Calculated from the integral representation of the first-order reaction rate: $k_1 = -\ln([\mathbf{1}]/[\mathbf{1}]_0)/t$. f) Activation energy E_a and frequency factor A were determined by Arrhenius plot.

Table 3. Oxidative Dehydrogenation of Fluorocyclohexenes with/without Dehydrofluorination Catalyst[a)]



1-Fluorocyclohexene (**3**)
3-Fluorocyclohexene (**9**)

Entry	Substrate	Pd[d)] (wt %)	Support[d)] (wt %)	Temperature /°C	Conversion[e)] /%	Selectivity[f)]/%			
						2	**4**	**5**	**6**
1	**3**	Pd-black (60)	AlF_3 (40)	370	100	98	1.5	0	0.4
2	**3**	Pd-black (60)	AlF_3 (40)	200	34	98	1.5	0	0.3
3	**3**	Pd (5)	SiO_2 (95)	200	96	81	14	2	3
4	**3**	Pd-black (60)	Quartz (40)	200	51	98	1	0	0.6
5	**9**	Pd-black (60)	AlF_3 (40)	200	100	0.6	99	0	0.2

a) 3.3 g h^{-1} of gaseous **3** or **9** were fed to a fixed bed flow reactor packed with catalyst. b) Mixed gas (O_2: 50 cm^3 min^{-1}; N_2: 450 cm^3 min^{-1}) was used. c) Residence time was calculated from a reciprocal of WHSV. d) Mixed catalysts (Pd catalyst and support) were used in Entries 1, 2, 4, and 5, and SiO_2-supported Pd was used in Entry 3; total amount of catalysts was 2.5 g. e) Determined by gas-liquid chromatography. f) Based on **1**. g) Yield of **2** per unit metal surface area[h)] per hour. h) Metal surface area: Pd-black 25 m^2 g^{-1} and Pd–SiO_2 100 m^2 g^{-1}.

similar manner as described for Entry 1 of Table 1, except **3** or **9** was used instead of **1**.

Table 3 shows that the conversion of **3** was 100% and selectivity of **2** was 98% at 370 °C (Entry 1), but the conversion of **3** was suppressed at 200 °C (34%, Entry 2). When Pd/SiO_2 was employed, high conversion (96%) but low selectivity of **2** (81%) were observed (Entry 3). Because this is a common catalyst for dehydrogenation, the acidity of the SiO_2 might affect the reactivity of the palladium metal. Indeed, an inactive quartz support showed the same selectivity (98%) as that of AlF_3 at higher conversion (51%) in Entry 4. These results suggest that AlF_3 did not affect the selectivity of formation of **2** but somewhat affected the conversion of **3**. When allyl monofluoride **9**, a probable intermediate to **4**, **5**, and **6**, was used instead of **3**, **4** was mainly produced (99% selectivity) and only a small amount of **2** was obtained (0.6% selectivity) (Entry 5). Thus, **9** was found to be a precursor of **4** and Pd-black worked as a dehydrogenation catalyst. As described above, the Pd-black also worked as an isomerization catalyst of **3**. Thus, the main steps relating to the formation of by-products (**3** to **9**, and **9** to **4** via **10**) were catalyzed by Pd-black.

In comparing Entry 10 in Table 1 with Entry 1 in Table 3, the former gave a lower yield of **2** (81%) at 450 °C than the latter (98% yield) at 370 °C. Even if there might be some time-lag in the reaction of Entry 10, the formation rate of **2** from **1** at 450 °C seems lower than that from **3** at 370 °C. Because the former involved HF, the reaction kinetics of the oxidative dehydrogenation of **3** were evaluated in order to confirm that an effect from HF exists. Figure 2 illustrates the temperature dependency of the reaction rate of oxidative dehydrogenation of **3** with (symbol ■) and without (symbol □) HF. The Arrhenius plot based on the assumption of first-order kinetics of **2** formation gave reaction rate constants k_2 for each [with HF: $k_2 = 2.06 \times 10^4 \exp(-50000/RT)$; without HF: $k_2 = 3.42 \times 10^4 \exp(-43000/RT)$]. At 250 °C, the reaction rate in the presence of HF ($k_2 = 0.21$ h^{-1}) is 8 times slower than that in the absence of HF ($k_2 = 1.73$ h^{-1}). This suggests that the activity of the Pd catalyst is somewhat affected by HF, e.g., HF

Catalyst	E_a/kJ mol^{-1}	A/h^{-1}
□ Pd-black (60%) + AlF_3 (40%)	43	3.42×10^4
■ Pd-black (60%) + AlF_3 (40%) with HF	50	2.06×10^4

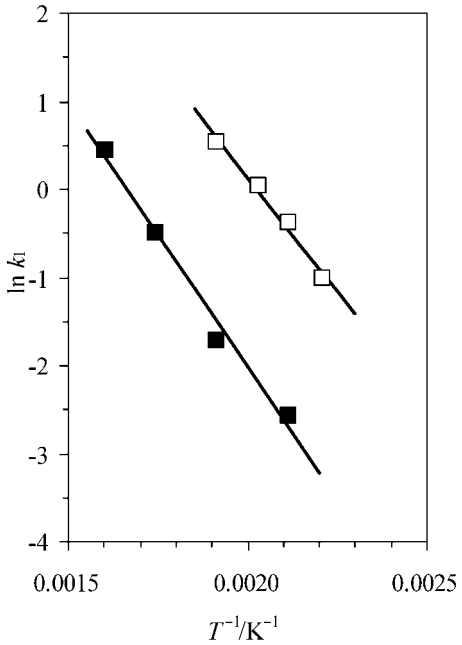
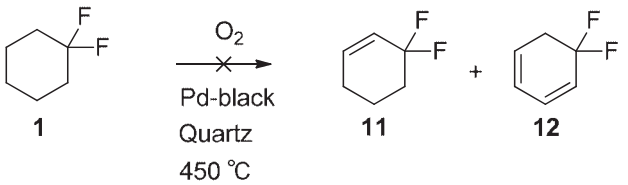


Figure 2. Temperature dependency of the reaction rate of oxidative dehydrogenation of **3**. 26.7 g h^{-1} of gaseous **3** was fed to a fixed bed flow reactor packed with catalyst (2.5 g) under mixed gas (O_2: 50 cm^3 min^{-1}; N_2: 450 cm^3 min^{-1}) in the absence (symbol □)/presence (symbol ■) of HF at 140 to 350 °C. Residence time calculated from a reciprocal of WHSV was 0.078 h. Activation energy E_a of the dehydrofluorination of **3** was determined by Arrhenius plot (first-order kinetics of **3** to **2** was assumed).

could adsorb on Pd-black and suppress the activity of active sites by surface-coating. Therefore, it is necessary to increase the reaction temperature to 450 °C and extend the residence time in order to achieve a high yield of **2** (Entry 10 of Table 1).

Oxidative Dehydrogenation of 1,1-Difluorocyclohexane (1). In order to examine the possibility of the pathway via **11** in Scheme 1, *gem*-difluoride **1** was reacted using Pd-black catalyst without AlF_3 catalyst (Scheme 2). However, no reaction proceeded, proving the absence of the pathway via **11** or **12**. Because **3** was dehydrogenated to yield **2** even at lower temperature (200 °C in Entry 4 of Table 3), it follows that **1** has low reactivity against dehydrogenation. The HOMO energy levels of the substrates were calculated, showing that the HOMO energy of **1** (−11.8 eV) is lower than that of **3** (−9.8 eV). This supports that **1** is more stable than **3** against dehydrogenation. It has become apparent that **1** can yield **2** only via reactive intermediate **3**. The HOMO energy level of unsubstituted cyclohexane **6** (−11.2 eV) is considerably higher than that of **1**. This is in agreement with the fact that **6** is known to dehydrogenate to benzene **4**.[23] The origin of the lower HOMO energy level of **1** is derived from the lower atomic orbital energy level of the fluorine's 2p orbital (−18.6 eV) compared to that of the proton's 1s orbital (−13.6 eV).[24]



Scheme 2. Oxidative dehydrogenation of **1** without dehydrofluorination catalyst.

Effect of Catalyst Configuration. Because the dehydrogenation of **1** is much more difficult than dehydrofluorination, as mentioned above, the main pathway of the dehydrofluoro–dehydrogenation of **1** should first experience dehydrofluorination of **1** to **3**, followed by dehydrogenation of **3** to **2**. In Table 4, when the dehydrofluorination and dehydrogenation catalysts were added separately in this order along the reaction gas flow, this was indicated as "separated catalyst." When both catalysts were added, this was indicated as "mixed catalyst." Table 4 shows that the separated catalyst configuration showed lower selectivity of **2** with larger amounts of by-products **4** and **6** (Entry 2) than the mixed catalyst configuration (Entry 1). The concentration of **3** in the mixed catalyst is lower than that in the separated catalyst, because the formed **3** immediately undergoes dehydrogenation in the mixed catalyst. In the separated catalyst configuration, formed **3** is accumulated during dehydrofluorination and is exposed all at once at its highest concentration to the Pd catalyst, causing by-product formation.

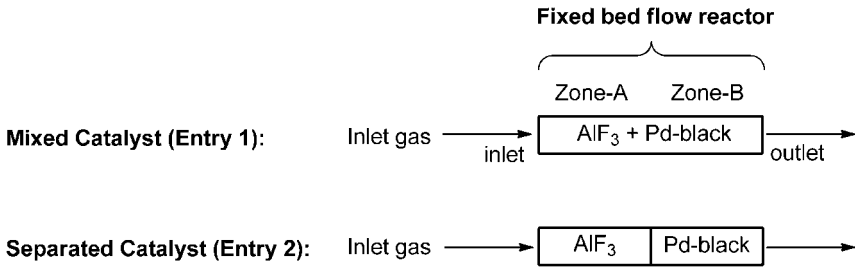
Conclusion

We have described the chemical reactivity and reaction mechanism of the one-step synthesis of fluorobenzene (**2**) by dehydrofluoro–dehydrogenation of 1,1-difluorocyclohexane (**1**). *gem*-Difluoride **1** reacted with molecular oxygen to give **2** in good yields in the gas phase in the presence of Pd and metal fluoride catalysts. Each possible reaction pathway was conducted separately to elucidate the reaction mechanism, showing that dehydrofluorination and dehydrogenation proceeded consecutively via 1-fluorocyclohexene (**3**). Examination of the catalyst configuration showed that the dehydrofluorination and dehydrogenation catalysts should be mixed to avoid lowering the selectivity resulting from a high concentration of intermediate **3**. It was also found that the formed HF suppressed the dehydrogenation to some extent, though a high yield of **2** was attained by increasing both the reaction temperature and residence time. Because 1,1-difluorocyclohexane is easily synthesized from cyclohexanone,[17] its dehydrofluoro–dehydrogenation is an alternative synthesis of fluorobenzene. From the viewpoint of industrial production, it offers a practical synthesis of fluorobenzene compared to direct fluorination of benzene and homogeneous-metal-complex-mediated fluorination of benzene derivatives. The present system exhibits high selectivity without any active electrophilic N–F reagent and/or highly specialized metal complexes. Furthermore, this is a clean reaction system, in which only water and recyclable HF are formed as by-products.

Experimental

General. Unless otherwise noted, chemical reagents were purchased from commercial sources and used without further

Table 4. Oxidative Dehydrofluoro–Dehydrogenation of **1**: Effect of Catalyst Configuration[a)]



Entry	Catalyst configuration		Conversion[d)] /%	Selectivity[e)]/%				
	Catalyst[b)] (zone-A)[c)]	Catalyst[b)] (zone-B)[c)]		**2**	**3**	**4**	**5**	**6**
1[f)]	Mixture of AlF_3 (1.0 g) and Pd-black (1.5 g)		100	81	18	0.5	0.1	0.2
2	AlF_3 (1.0 g)	Pd-black (1.5 g)	100	76	15	6	0.3	2

a) Gaseous **1** (4 g) and mixed gas (O_2: 50 $cm^3\,min^{-1}$; N_2: 450 $cm^3\,min^{-1}$) were fed to a fixed bed flow reactor packed with catalyst; residence time calculated from a reciprocal of WHSV was 0.63 h; reaction temperature was 450 °C. b) Total amount of catalyst was 2.50 g. c) Catalyst bed was divided into 2 zones, zone-A and zone-B, in this order along the reaction gas flow. d) Determined by gas-liquid chromatography. e) Based on **1**. f) Identical to Entry 10 of Table 1.

treatment. Group VIII metal catalysts were purchased from N.E. Chemcat Corporation. Metal surface areas of catalysts were: Pt-black 30 $m^2\,g^{-1}$; Ru-black 90 $m^2\,g^{-1}$; Pd-black 25 $m^2\,g^{-1}$; Pd-SiO_2 100 $m^2\,g^{-1}$. The unit of gas flow rate was standard cubic centimeters per minute ($cm^3\,min^{-1}$). Quantitative analysis was carried out on a gas chromatograph with a FID detector. The chemical structure of each product was identified by a combination of GC-MS spectroscopy (Hewlett Packard HP-5971 or Hitachi M-80) and ^{1}H NMR spectroscopy (JEOL GX-270).

Synthetic Procedure. 1,1-Difluorocyclohexane (1): Compound **1** was synthesized from cyclohexanone via 1,1-bis(trifluoroacetoxy)cyclohexane (**13**) according to literature procedures:[17g] Colorless liquid, bp 99–101 °C/760 mmHg (lit.[25b] 99–100 °C/760 mmHg). ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.9–2.3 (m, 10H). MS (EI): m/z 120 (M^+, 9%), 100 (63), 80 (12), 57 (98), 41 (100).

1-Fluorocyclohexene (3) (Method A: Dehydrofluorination of 1): Authentic sample **3** was synthesized from **1**.[25] To a magnetically stirred solution of *tert*-BuOK (0.3 mol) and 1,2-dimethoxyethane (200 mL), **1** (0.2 mol) was added slowly at room temperature under nitrogen atmosphere, and the mixture was stirred under reflux (85 °C) for 12 h. After three quarters of the solvent were evaporated under reduced pressure (550 mmHg) at an oil bath temperature of 90 °C, the reaction mixture was poured into a mixture of ice and saturated aq. $NaHCO_3$. The resulting mixture was extracted five times with diethyl ether. The combined extract was washed with water, dried over $MgSO_4$, and the solvent was evaporated. The crude product was distilled under atmospheric pressure to give **3**:[25c,26] yield 17.4 g (87%). Colorless liquid, bp 95–96 °C/760 mmHg (lit.[26] 95–96 °C/760 mmHg). MS (EI): m/z 100 (M^+, 47%). ^{1}H NMR (270 MHz, CCl_4): δ 1.7–2.0 (m, 4H), 2.1–2.4 (m, 4H), 5.1 (d, $J = 17.3$ Hz, 1H).

1-Fluorocyclohexene (3) (Method B: Dehydrobromination of *cis*-1-Bromo-2-fluorocyclohexane (14)): Another authentic sample **3** was synthesized according to literature procedures:[26,27] Cyclohexene oxide (1.22 mol), KHF_2 (1.81 mol), and diethylene glycol (230 g) were mixed in a 1-L flask equipped with a mechanical stirrer and a condenser. The mixture was stirred at 150 °C for 1.5 h, followed by vacuum distillation. The distillate was redistilled under reduced pressure to give *trans*-2-fluorocyclohexanol in 69% yield. Bp 77–78 °C/22 mmHg (lit.[27] bp 68–69 °C/14 mmHg), mp 19–20 °C (lit.[21] 19–20 °C). ^{1}H NMR (270 MHz, CCl_4): δ 0.6–2.4 (m, 8H), 3.33 (s, 1H), 3.2–4.8 (m, 2H). To a mixture of PBr_3 (0.9 mol) and NaBr (0.72 mol), *trans*-2-fluorocyclohexanol (0.9 mol) was added with stirring at 140 °C. After stirring at 140 °C for 5 h, the reaction mixture was poured into ice water and worked up as described above. The crude product was distilled under reduced pressure to give *cis*-1-bromo-2-fluorocyclohexane (**14**) in 46% yield. Colorless liquid, bp 68–70 °C/14 mmHg (lit.[27] bp 78 °C/16 mmHg). ^{1}H NMR (270 MHz, CCl_4): δ 1.0–2.6 (m, 8H), 3.8–5.1 (m, 2H). To the magnetically stirred solution of *tert*-BuOK (0.25 mol) and *tert*-BuOH (300 mL), **14** (0.25 mol) was added slowly at room temperature under nitrogen atmosphere, and the mixture was stirred at 70 °C for 4 h. The reaction mixture was worked up as described above. The crude product was distilled under atmospheric pressure to give **3** in 80% yield. Bp 95–96 °C/760 mmHg (lit.[27] bp 96 °C/760 mmHg). The obtained **1** had an identical ^{1}H NMR spectrum to that reported.[25c,26]

3-Fluorocyclohexene (9):[20] To diethylaminosulfur trifluoride (=(diethylamino)trifluoro-λ^4-sulfane, DAST, 0.05 mol) in a 50-mL polyethylene bottle cooled at −50 °C, 2-cyclohexen-1-ol (0.05 mol) was added slowly at −50 °C with stirring under nitrogen atmosphere, and the mixture was further stirred for 3 h while warming to room temperature. The reaction mixture was poured into a mixture of ice and saturated aq. $NaHCO_3$. The upper layer was separated, washed with ice water, and dried over $MgSO_4$ in a refrigerator to give crude **9** in 63% yield. ^{1}H NMR (270 MHz, CCl_4): δ 1.5–2.2 (m, 2H), 4.9 (m, 1H), 5.8 (m, 1H), 6.0 (m, 1H). The obtained product decomposed slowly at room temperature[20] to give HF and 1,3-cyclohexadiene (**10**), which was identified spectroscopically.

Caution: Because HF is corrosive, the reaction mixture containing HF should be handled in a well ventilated hood with protection.

Catalytic Reaction. Conversion of 1 to 2 by Oxidative Dehydrofluoro–Dehydrogenation (Table 1, Figure 1): The Group VIII metal (Pd-black, Pt-black, or Ru-black) and metal fluoride (AlF_3, FeF_3, or GaF_3) were mixed in advance. The mixed catalyst (2.5 g) was packed in a fixed bed flow reactor. To the reactor, the mixed gas [O_2: 20 $cm^3 min^{-1}$; N_2: 200 $cm^3 min^{-1}$ (Entries 1–5) or O_2: 50 $cm^3 min^{-1}$; N_2: 450 $cm^3 min^{-1}$ (Entries 6–10)], which was used as the carrier gas with oxidant, was fed. After the reactor was heated to the desired temperature, gaseous **1** was fed to the reactor. Residence time calculated from a reciprocal of WHSV (weight hourly space velocity) was 0.31 or 0.63 h. The reaction mixture gas, which contained HF, water, and organic compounds, was cooled and collected into a mixture of ice and saturated aq. $NaHCO_3$. After the resulting mixture was extracted with diethyl ether, the combined extracts were washed with water, dried over $MgSO_4$, and the solvent was evaporated. The crude products were analyzed with toluene as an internal standard using gas-liquid chromatography. The yields of **2**–**6** were based on converted **1**. Yields of **2** per unit metal surface area per hour were calculated using the metal surface area. Products **2** and **3** were separated by preparative gas-liquid chromatography. All products **2**–**6** were characterized spectroscopically and showed identical MS and ^{1}H NMR spectra to the commercial reagents (**2** and **4**–**6**) and **3** synthesized above.

Conversion of 1 to 3 by Dehydrofluorination (Table 2): AlF_3 (2.5 g) was packed in a fixed bed flow reactor instead of mixed catalyst. N_2 (500 $cm^3 min^{-1}$) was fed to the reactor instead of mixed O_2/N_2 gas. Compound **1** (4–32 $g h^{-1}$) was treated in a similar manner as above except for the elimination of dehydrofluorination catalyst and oxygen. Reaction temperature was 340–450 °C and residence time was 0.63 h.

Conversion of Fluorocyclohexenes (3 and 9) by Oxidative Dehydrogenation (Table 3): To a reactor, the mixed gas (O_2: 50 $cm^3 min^{-1}$; N_2: 450 $cm^3 min^{-1}$) was fed. After the reactor was heated to 200 °C, 3.3 $g h^{-1}$ of gaseous **3** or **9** were fed to a fixed bed flow reactor packed with catalyst [a mixture of a Pd catalyst and a support (Entries 1, 2, 4, or 5) or Pd-supported SiO_2 (Entry 3); total amount of catalyst was 2.5 g]. Residence time was 0.63 h.

Conversion of 3 to 2 by Oxidative Dehydrogenation with/without HF (Figure 2): Without HF: 26.7 $g h^{-1}$ of gaseous **3** was fed to a fixed bed flow reactor packed with catalyst (2.5 g) under mixed gas (O_2: 50 $cm^3 min^{-1}$; N_2: 450 $cm^3 min^{-1}$) at 140–350 °C, and residence time was 0.078 h. With HF: in the experiment (Symbol ■ in Figure 2), 32 $g h^{-1}$ of gaseous **1** was fed to a fixed bed flow reactor packed with AlF_3 (2.5 g) and heated at 450 °C. The reaction mixture gas, which contained HF and **3**, was fed as **3** accompanied by HF.

Oxidative Dehydrogenation of 1 (Scheme 2): 2.5 g of a mixture of Pd-black (60%) and quartz (40%) was packed in a fixed bed flow reactor. Mixed gas (O_2: 50 $cm^3 min^{-1}$; N_2: 450 $cm^3 min^{-1}$) was fed to the reactor. The compound **1** (4 $g h^{-1}$) was treated in a similar manner as above except for the elimination of the dehydrofluorination catalyst. Reaction temperature was 450 °C and residence time was 0.63 h. The reaction mixture was analyzed in the same manner as described above. However, it was confirmed that no reaction proceeded.

Conversion of 1 to 2 by Oxidative Dehydrogenation (Entry 2 of Table 4): The catalyst bed of the fixed bed flow reactor was divided into two zones, zone-A and zone-B, in this order along the reaction gas flow. AlF_3 (1.0 g) was placed at zone-A and Pd-black (1.5 g) was placed at zone-B. Compound **1** (4 $g h^{-1}$) was treated in a similar manner as above. Reaction temperature was 450 °C and residence time was 0.63 h. The reaction mixture was analyzed in the same manner as described above.

Computational Method. MOPAC 2002[28] in CS ChemBio3D Ultra (ver. 11.0)[29] was used to compute the HOMO energy levels of **1**, **3**, and **6**. The PM3 method was selected in MOPAC.

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19 The integral representations of the reaction rates are

$$\ln[\mathbf{1}] - \ln[\mathbf{1}]_0 = k_1 t \tag{1a}$$

$$[\mathbf{3}] = [\mathbf{1}]_0[k_1/(k_2 - k_1)][\exp(-k_1 t) - \exp(-k_2 t)] \tag{2a}$$

$$[\mathbf{2}] = [\mathbf{1}]_0[1 + 1/(k_1 - k_2)][k_2 \exp(-k_1 t) - k_1 \exp(-k_2 t)] \tag{3a}$$

where $[\mathbf{1}]_0$ is the initial concentration of **1**. First-order plot showed that the calculated ($\ln[\mathbf{1}] - \ln[\mathbf{1}]_0$) of eq 1a had a linear relationship with time. The rate constant k_1 was calculated from the slope of the linear plot to be 12.1 h^{-1}. The first-order rate constant k_2 was determined to be 3.3 h^{-1} by trial-and-error-method using eq 3a {A rough value of k_2 was obtained as an initial value for the trial-and-error method in the following manner. As shown in Figure 1, the concentration of **3** has a maximum, where $d[\mathbf{3}]/dt = k_1[\mathbf{1}]_m - k_2[\mathbf{3}]_m = 0$. $[\mathbf{1}]_m$ and $[\mathbf{3}]_m$ are the concentrations of **1** and **3** when **3** is maximum. The value of k_2 was calculated roughly to be 2.5 h^{-1} according to the relationship $k_2 = k_1[\mathbf{1}]_m/[\mathbf{3}]_m = 12.1 \times 0.13/0.635 = 2.5$ (h^{-1}) when $t = 0.16$ (h).}.

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