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Highly selective hydroformylation of 3,3,3-trifluoropropene to 4,4,4-trifluorobutanal using Rh/Xantphos catalyst

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ABSTRACT

Synthesis of 4,4,4-trifluorobutanal by Rh-catalyzed hydroformylation of 3,3,3-trifluoropropene with bis(4,5-diphenylphosphino)xanthene as a ligand was investigated. The uses of $[Rh(OH)(cod)]_2$ (cod = 1,5-cyclooctadinene) and dimethylformamide in CO/H_2 = 75/25 mixed gas under atmospheric pressure at 80 °C for 15 h provided the highest aldehyde yield 90%. The molar ratio of linear aldehyde (4,4,4-trifluorobutanal) to branched aldehyde (3,3,3-trifluoro-2-methylpropanal) was 99/1. The successive addition of dimethylformamide solution of 3,3,3-trifluoropropene under atmospheric pressure revealed that 4,4,4-trifluorobutanal formation increased linearly with the reaction time and the total turnover number reached 500 after 10 h retaining 99% selectivity of 4,4,4-trifluorobutanal at 80 °C.

1. Introduction

4,4,4-Trifluorobutanal (TFB) is one of the most important raw materials in the syntheses of pharmaceuticals, and a numerous number of compounds have been synthesized using TFB in the last several years [1]. TFB is generally obtained by the oxidation of 4,4,4-trifluorobutanol using sodium hypochlorite in laboratory scale [2]; the reaction should be carried out at controlled low temperature owing to its exothermic property. The selective hydroformylation of 3,3,3-trifluoropropene (TFP) is one of the candidates for the practical production of TFB. To our best knowledge, only two examples of the hydroformylation of TFP have been reported. Ojima and co-workers reported various metal-catalyzed hydroformylation of TFP using PPh_3, $P(OPh)_3$, DPPB or DIOP as a ligand in the last 25 years [3]. Following their method, Ru or Rh-catalyzed hydroformylation afforded mainly the branched product, 3,3,3-trifluoro-2-methylpropanal (TFMP); the molar ratio of [TFB]/[TFMP] was 3/97–15/85. The use of Pt catalysts improved this ratio to 71/29. Satisfactory [TFB]/[TFMP] ratio, 91/9–93/7, was obtained using Co catalysts. However, the following conditions were required: a long reaction time, 20–41 h; a high pressure of 50/50 CO/H_2 mixed gas, 130 atm; and a large amount of $Co_2(CO)_8$ catalyst, 2.0 mol% of TFP. Hiyama and co-workers reported the Rh/(*R*,*S*)-BINAPHOS catalyzed asymmetric hydroformylation of TFP to (*R*,*S*)-TFMP [4]. Because the target of this reaction was asymmetric TFMP, [TFB]/[TFMP] ratio was low, 4/96–12/88.

In 1995, van Leeuwen and co-workers synthesized a series of bidentate diphosphines based on xanthene-like backbones and succeeded in the extremely selective formation of linear aldehydes in the Rh-catalyzed hydroformylation of terminal olefins [5]. Later, hydroformylation using these diphosphines, particularly the most simple bis(4,5-dipehnylphosphino)xanthene (Xantphos), as a ligand has been extended to the hydroformylation with various metal catalysts, substrates and medias [6]. Among them, we noticed that a Xantphos derivative is effective in the highly selective hydroformylation of propylene, which is the second sterically smallest olefin, to linear butanal [6i]. Thus, Rh complex supported on SiO_2 with Xantphos substituted by $-SO_3^-Na^+$ groups at the 2 and 7 positions provided 70/30–94/6 of [butanal]/[2-methylpropanal] ratio. This stimulated us to use Xantphos as a ligand in the Rh-catalyzed hydroformylation of TFP that is relatively small olefin. In addition, the hydroformylation of n-C_nF_{2n+1}-$CH{=}CH_2$ including TFP has not been examined using Xantphos and its derivatives. Herein, we reported TFB synthesis by the Rh-catalyzed hydroformylation of TFP using Xantphos. We successfully achieved the highly selective synthesis of TFB under mild reaction conditions.

2. Results and discussion

2.1. Hydroformylation of TFP

We performed successive two steps for the hydroformylation of TFP. In the hydroformylation using Xantphos, the catalytically active species for high selectivity of linear aldehyde, $[RhH(CO)_2$

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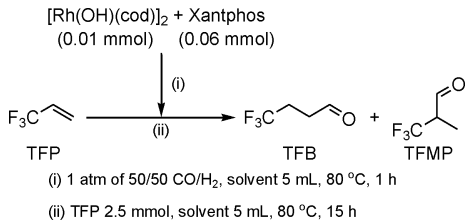
Table 1
Effect of solvents in hydroformylation of TFP on yield and selectivity of aldehydes.



Entry	Solvent	Aldehyde (%)[a]	[TFB]/[TFMP][a]
1	Toluene	66	98/2
2	DMF	81	99/1
3	DMAc	77	97/3
4	NMP	77	99.5/0.5
5	MeCN	65	98/2
6[b]	Me_2SO	80	98/2
7[c]	Toluene	45	97/3
8[c]	DMF	51	97/3

[a] Determined by ^{19}F NMR.
[b] 2.0 mmol of TFP was charged in the form of 10 mL of 0.2 mol/L DMSO solution.
[c] 48 mL (*ca.* 2.0 mmol) of gaseous TFP was charged using a gas-tight syringe through a septum.

(xantphos)], should be prepared in advance [6]. Therefore, we prepared this species in the absence of TFP before the start of the reaction (preparation step (i)). When dinuclear $[Rh(OH)(cod)]_2$ (cod = 1,5-cyclooctadinene) and Xantphos ([P]/[Rh] = 3) was dissolved in toluene at 80 °C for 1 h in an atmosphere of 1 atm 50/50 CO/H_2 mixed gas, the color of the solution turned from orange to yellow. This color change indicated the formation of the mononuclear $[RhH(CO)_2(xantphos)]$ complex. We confirmed the formation of $[RhH(CO)_2(xantphos)]$ using ^{31}P NMR of the other toluene solution, the concentration of $[Rh(OH)(cod)]_2$ and Xantphos in which was five times thicker than the reaction mixture. After this sample solution was heated at 80 °C for 1 h in an atmosphere of 1 atm 50/50 CO/H_2 mixed gas, the doublet peak ($J_{P\text{-}Rh}$ = 126.5 Hz) at δ 20.6 ppm appeared in ^{31}P NMR spectrum. Therefore, we concluded that $[RhH(CO)_2(xantphos)]$ was generated in preparation step (i). In preparation step (i), because the ratio of [CO] or $[H_2]$ relative to $[Rh(OH)(cod)]_2$ was *ca.* 2500 (see Section 4.2.2), the decrease in amounts of CO and H_2 consumed for the formation of $[RhH(CO)_2(xantphos)]$ was negligible. Therefore, the following reaction step (ii) was carried out without further addition of 50/50 CO/H_2 mixed gas. Next, a toluene solution of TFP was added to the reaction mixture; [CO] or $[H_2]$ relative to [TFP] were *ca.* 10, respectively. After this reaction mixture was heated at 80 °C for 15 h, the ^{19}F NMR analyses of the mixture revealed that the yield of the aldehydes, the sum of linear TFB and branched TFMP, was 66% (entry 1 in Table 1). The ratio of [TFB]/[TFMP], which corresponds to the selectivity of TFB, was 98/2 that is remarkably higher than those previous report [3]. To improve the yield of the aldehydes, the reactions in various solvents were examined. The results are listed in entries 2–6 of Table 1. Interestingly, satisfactory yields retaining high selectivity of TFB were obtained using nitrogen-containing aprotic solvents (entries 2–4), which are rarely used in hydroformylation. Of them, dimethylformamide (DMF) and *N*-methyl-2-pyrrolidone (NMP) provided the highest yield and selectivity, respectively (entry 2 and 4). Although dimethyl sulfoxide also gave satisfactory yield and excellent selectivity (entry 6), the solubilities of the catalyst and TFP was slightly lower than those in the other solvents. When gaseous TFP was charged into the gas phase of the reaction system after preparation step (i) in toluene and DMF solvents, the yields were declined with excellent selectivity (entry 7 and 8). This indicates that the yield of the aldehydes largely depends on the concentration of TFP in the reaction solution. Therefore, we used the DMF solution of TFP in reaction step (ii).

Since virtually the same [TFB]/[TFMP] ratios were obtained in all entries, the catalytically active $[RhH(CO)_2(xantphos)]$ may have generated in any solvents. The ^{19}F NMR and gas chromatography analyses of the liquid and gas phases in entry 1 and 2 of Table 1 revealed the formation of 1,1,1-trifluoropropane (TFPR) that may be formed by the hydrogenation of TFP. The formed amounts of TFPR in the liquid and gas phases were 15% and 10% in toluene (entry 1) and 11% and 4% in DMF (entry 2), respectively. Thus, the higher yield of the aldehydes in DMF as compared to toluene is certainly attributed to the suppression of the hydrogenation of TFP.

Fig. 1 shows the yield and [TFB]/[TFMP] ratio (in the parentheses) in the hydroformylation of TFP using $[Rh(OH)(cod)]_2$ and various bidentate phosphine ligands with [P]/[Rh] = 3. The use of Xantphos (**a**) resulted in 81% yield and 99/1 selectivity. The low charged amount of Xantphos, [P]/[Rh] = 1.5, afforded the slightly low yield and selectivity. On the other hand, almost the same yield and selectivity were maintained by increasing the ratio of [P]/[Rh] to 4.5. The slightly lower yield and selectivity using Xantphos derivatives, (**b**) and (**c**), than those using Xantphos indicate that a substituent on the phenyl ring did not affect the activity. The ligand with phenoxazine backbone (**d**) showed the excellent selectivity even though the yield was moderate. The bidentate phosphite (**e**), which was used as a ligand for the Rh-catalyzed highly selective hydroformylation of 1-dodecene to linear tridecanal [7], also gave the excellent selectivity and moderate yield. The other bidentate phosphines (**f**, **g**, and **h**) afforded poor yield and selectivity. In conclusion, the use of the most simple Xantphos (**a**) as a ligand resulted in the highest yield and selectivity.

Table 2 shows the results of the hydroformylation using various Rh precursors and Xantphos in DMF solvent. The use of the dinuclear complexes (entries 1–3) gave the yields over 70%. A poor selectivity was obtained only with $[RhCl(cod)]_2$ (entry 3) among the dinuclear complexes, indicating that catalytically active $[RhH(CO)_2(xantphos)]$ did not generate efficiently from $[RhCl(cod)]_2$. As shown in entries 4–8, mononuclear complexes also exhibited the satisfactory yield and the excellent selectivity irrespective of the oxidation number except $[RhCl(PPh_3)_3]$ (entry 6) and $RhCl_3{\cdot}3H_2O$ (entry 8); the former gave a moderate yield and slightly lower selectivity than those with other Rh precursors and the hydroformylation did not occur at all using the latter. It is interesting that polynuclear and zerovalent $[Rh_6(CO)_{16}]$ also showed the satisfactory yield and selectivity (entry 9).

All the Rh precursors which showed poor selectivity or no hydroformylation activity bear chloro ligand(s). The formation of mononuclear active complex $[RhH(CO)_2(xantphos)]$ from these complexes should require cleavage of Rh–Cl bond which may be strong for the formation of this active complex.

Next we optimized the conditions of preparation step (i) and reaction step (ii) with $[Rh(OH)(cod)]_2$, Xantphos and DMF solvent (Table 3). At first, the temperature and reaction time in preparation step (i) were examined. A lower temperature than 80 °C and shorter time than 1 h afforded low yield and selectivity (entries 2 and 3), indicating that the amount of catalytically active $[RhH(CO)_2(xantphos)]$ thus formed was insufficient for the hydroformylation. Since preparation step (i) for 2 h slightly affected the yield and selectivity (entry 4), the time of 1 h for preparation step (i) is enough to form $[RhH(CO)_2(xantphos)]$. Next, the temperature in reaction step (ii) was examined. The high selectivity was retained at 90 °C, whereas the yield was declined to 74% (entry 5). Almost 100% selectivity was obtained at 100 °C despite the low yield (entry 6). The poor yields and selectivites were obtained at the temperature lower than 80 °C (entries 7 and 8). In particular, the main product was TFMP in the reaction at

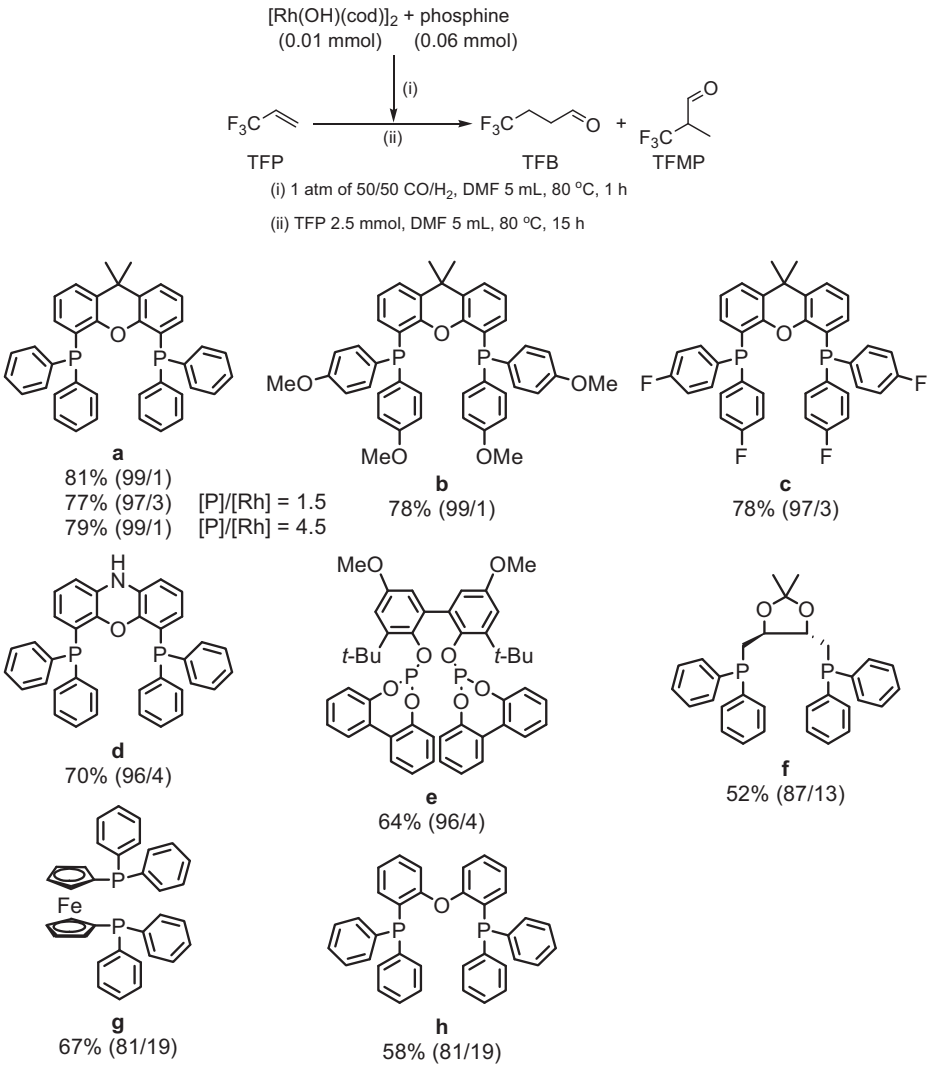
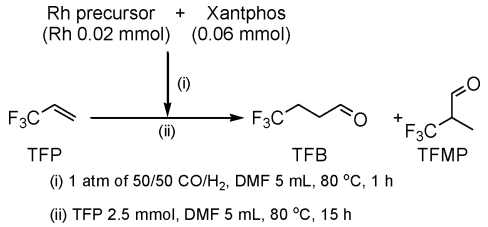


Fig. 1. Hydroformylation of TFP using various phosphine ligands.

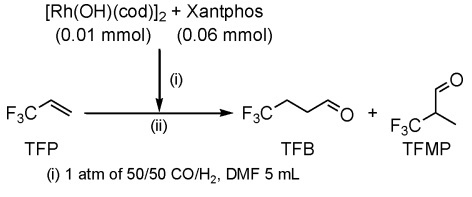
Table 2
Hydroformylation of TFP using various Rh precursors.



Entry	Rh precursor	Aldehyde (%)[a]	[TFB]/[TFMP][a]
1	$[Rh(OH)(cod)]_2$	81	99/1
2	$[Rh(OMe)(cod)]_2$	78	98/2
3	$[RhCl(cod)]_2$	71	78/22
4	$[RhH(CO)(PPh_3)_2]$	75	99/1
5	$[Rh(CO)_2(acac)]$	79	99/1
6	$[RhCl(PPh_3)_3]$	73	93/7
7	$[Rh(acac)_3]$	77	99/1
8	$RhCl_3{\cdot}3H_2O$	Trace	–
9	$[Rh_6(CO)_{16}]$	79	99/1

[a] Determined by ^{19}F NMR.

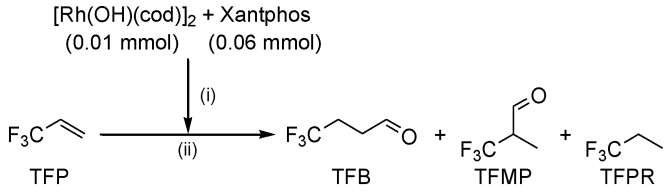
Table 3
Optimization of reaction conditions in preparation step (i) and reaction step (ii) in DMF solvent.



Entry	Temperature of step (i) (°C)	Time of step (i) (h)	Temperature of step (ii) (°C)	Aldehyde (%)[a]	[TFB]/[TFMP][a]
1	80	1	80	81	99/1
2	rt	1	80	74	94/6
3	80	0.25	80	71	93/7
4	80	2	80	79	99/1
5	80	1	90	74	99/1
6	80	1	100	62	>99.9/<0.1[b]
7	80	1	70	76	94/6
8	80	1	50	72	38/62

[a] Determined by ^{19}F NMR.
[b] TFMP was virtually not detected.

Table 4
Effect of ratio of CO/H_2 on yield and selectivity.



Entry	CO/H_2	Aldehyde (%)[a]	[TFB]/[TFMP][a]	Conversion of TFP (%)	TFPR (%)	
					Liquid[a]	Gas[b]
1	50/50	81	99/1	100	11	4
2	60/40	81	99/1	100	9	4
3	70/30	88	99/1	100	5	2
4	75/25	90	99/1	100	4	1
5	80/20	79	98/2	91	3	1

[a] Determined by ^{19}F NMR.
[b] Determined by gas chromatography.

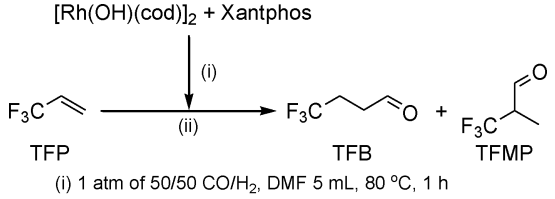
50 °C. From these results, we adopted the condition in entry 1 for further investigation.

As shown in entry 1 of Table 3, we now obtained the best yield and selectivity, 81% and 99/1, with approximately 100% conversion of TFP. On the other hand, 15% of TFPR that is the hydrogenated product of TFP was found in the liquid and gas phase under this condition as described above. The sum of the aldehydes and TFPR was 96% (81% + 15%), which was nearly equal to 100% conversion of TFP. This indicates that the suppression of the hydrogenation of TFP should be overcome to enhance the yield. Therefore, the amount of H_2 in the CO/H_2 mixed gas was decreased maintaining the same total volume. The results are listed in Table 4. As expected, the hydrogenation was suppressed and the yield of the aldehydes gradually increased maintaining the selectivity of 99/1 in the range from CO/H_2 = 50/50 to 75/25 (entries 1–4). In the reaction with 75/25 CO/H_2 mixed gas, the maximum yield of the aldehydes, 90%, was obtained. Although the amount of TFPR further decreased by the use of 80/20 CO/H_2 mixed gas, 9% of unreacted TFP was detected in the liquid (7%) and gas (2%) phase, respectively, resulting in the decline of the yield to 79% (entry 5). In the 80/20 CO/H_2 mixed gas, the amount of H_2 is *ca.* 7.5 equivalent to TFP. This small amount of H_2 may be disadvantageous for the hydroformylation. In entry 3 of Table 2, $[RhCl(cod)]_2$ showed moderate yield and poor selectivity, 71% and 78/22, respectively, and we concluded that the Rh–Cl bond cleavage is unfavorable for the catalytically active $[RhH(CO)_2$(xantphos)] formation. Interestingly, the use of 75/25 CO/H_2 mixed gas in the hydroformylation with $[RhCl(cod)]_2$ improved the yield to 83% and the selectivity to 95/5, respectively. Therefore, the use of 75/25 CO/H_2 mixed gas not only suppresses the hydrogenation of TFP but also accelerates the catalytically active $[RhH(CO)_2$(xantphos)] formation from $[RhCl(cod)]_2$.

Moreover, we examined the reduction in the amount of catalyst. As shown in Table 5, the aldehydes were obtained in 80% yields in the range from 0.01 mmol (0.8 mol% of TFP) to 0.0025 mmol (0.2 mol% of TFP) of Rh atom in $[Rh(OH)(cod)]_2$ with a slight decrease in selectivity (entries 1–3). While the turnover number (TON) is 101 in entry 1, it reached 400 in entry 3. Although the yield and selectivity fell into 38% and 93/7 with the use of 0.001 mmol (0.02 mol% of TFP) of $[Rh(OH)(cod)]_2$, the TON rose up to 475 (entry 4). This low yield was recovered by the addition of twice amount of Xantphos from 38% to 72%, resulting in the TON = 900, while declined selectivity was not improved (entry 5).

The reactions under atmospheric pressure described above are unfavorable on the vessel efficiency, because the huge volume of CO/H_2 mixed gas is required. For example, in the reaction in entry 1 of Table 5, the volume ratio of gas phase to liquid phase is *ca.* 240. From the view point of the practical use, we examined the hydroformylation under pressurized conditions using an autoclave. In this investigation, we found that the standard procedure consisting of preparation step (i) and reaction step (ii) afforded the low yield and selectivity (see Section 4.2.3). Therefore, we performed the reactions without preparation step (i). Thus, $[Rh(OH)(cod)]_2$, Xantphos and the DMF solution of TFP were charged together in an autoclave, and the initial pressure of 50/50 CO/H_2 mixed gas was set at 1.0 atm at room temperature; the [CO] or $[H_2]$/[TFP] ratio was *ca.* 1.2. The inside pressure increased up on heating at 80 °C and showed the maximum pressure of 1.1 atm at *ca.* 15 min. After that, the pressure gradually decreased along with the consumption of CO and H_2 by the hydroformylation and the pressure drop stopped after 2 h from the reaction start. Then, the autoclave was cooled in an ice bath and the inside pressure was 0.6 atm at that time. This pressure drop from 1.0 atm indicates that the consumption of CO and H_2 was *ca.* 0.7 mmol, respectively. Since the charged amount of TFP was 1.5 mmol, the yield of the aldehydes was estimated to be *ca.* 50% from this pressure drop. Indeed, the ^{19}F NMR analysis revealed 57% yield of the aldehydes (entry 1 of Table 6). This low yield is presumably unavoidable due

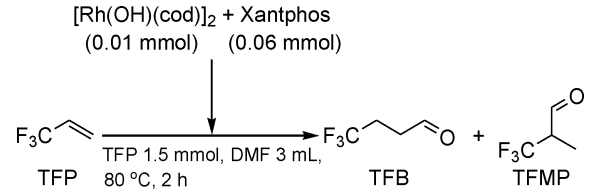
Table 5
Effect of amount of $[Rh(OH)(cod)]_2$ on yield and selectivity.



Entry	$[Rh(OH)(cod)]_2$ (mmol)	[P]/[Rh]	Aldehyde (%)[a]	TON	[TFB]/[TFMP][a]
1	0.01	3	81	101	99/1
2	0.005	3	80	200	97/3
3	0.0025	3	80	400	97/3
4	0.001	3	38	475	93/7
5	0.001	6	72	900	92/8

[a] Determined by ^{19}F NMR.

Table 6
Effect of reaction pressure on yield and selectivity.



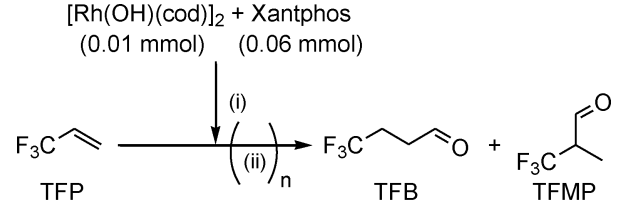
Entry	Ini. press.[a] (atm)	Max. press.[b] (atm)	Fin. press.[c] (atm)	Aldehyde (%)[d]	[TFB]/[TFMP][d]
1	1.0	1.1	0.6	57	84/16
2	1.5	1.7	1.2	48	63/37
3[e]	1.0	1.1	0.6	39	96/4

[a] Initial pressure.
[b] Maximum pressure.
[c] Final pressure.
[d] Determined by ^{19}F NMR.
[e] An NMP solution of TFP was used instead of a DMF solution.

to the very low ratio of [CO] or [H_2]/[TFP], *ca.* 1.2. Surprisingly, the ratio of [TFB]/[TFMP] were remarkably low, 84/16. The yield and selectivity were further declined in the reaction under the initial pressure of 1.5 atm (entry 2), even though the ratio of [CO] or [H_2]/[TFP], *ca.* 1.8, was somewhat higher than entry 1. To enhance the yield and selectivity under the pressurized condition, we examined the combined use of DMF and NMP as a solvent; the use of the latter solvent provides the highest selectivity as shown in entry 4 of Table 1. Although the yield was declined, the selectivity was improved from 84/16 to 96/4 (entry 1 *vs.* 3 of Table 6). Based on these results, we concluded that the present hydroformylation is unfavorable under the pressurized condition.

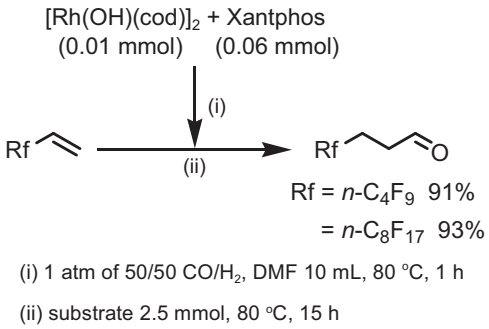
The poor selectivity under the pressurized conditions proved fatal to the practical use on the point of vessel efficiency. To overcome this disadvantage, we must develop the process to which the huge volume of CO/H_2 mixed gas is applicable under atmospheric condition. As a candidate of this process, we examined the successive addition of the DMF solution of TFP without extra addition of CO/H_2 mixed gas. Before the examination of this method, the hydroformylation in the shorter reaction time than 15 h was investigated. When the reaction of entry 1 of Table 4 was interrupted at 2 h, the same yield, 81%, selectivity, 99/1, and conversion, *ca.* 100%, were obtained (entry 1 of Table 7). Thus, the present hydroformylation completed within 2 h from the reaction start; the turnover frequency was remarkably improved from

Table 7
Successive addition of TFP in hydroformylation in DMF solvent.



Entry	*n*	Total reaction time (h)	Total yield of aldehyde (%)[a]	[TFB]/[TFMP][a]	TON	TOF (h^{-1})
1	1	2	81	99/1	101	51
2	3	6	78	99/1	293	49
3	5	10	80	99/1	500	50

[a] Determined by ^{19}F NMR.



Scheme 1. Hydroformylation of n-C_4F_9–CH=CH_2 and n-C_8F_{17}–CH=CH_2.

6.8 h^{-1} to 50 h^{-1}. After the 2 h reaction, a 5 mL of DMF solution of TFP was added to the reaction mixture again and the mixture was heated at 80 °C for another 2 h. This procedure was repeated once more; the total charged amount of TFP was 7.5 mmol (2.5 mmol × 3) and the total reaction time was 6 h (2 h × 3). The ^{19}F NMR of this mixture revealed a slight decrease in the yield, 78%, and the excellent selectivity, 99/1 (entry 2). Thus, the catalytically active species is intact during 6 h reaction at least. We repeated the same procedure for another two times. The total charged amount of TFP was 12.5 mmol (2.5 mmol × 5), and the total reaction time was 10 h (2 h × 5). The yield and selectivity also remained constant after these five times addition of the DMF solution (entry 3). As a result, the TON reached 500 after 10 h reaction (entry 3). As a matter of course, the TOF was constant, *ca.* 50 h^{-1}, during 10 h at least. Based on the long life of Rh/Xantphos catalyst observed in Table 7, the successive addition of the DMF solution of TFP is promising for the practical use.

2.2. Hydroformylation of other substrates

The present Rh-Xantphos catalyzed hydroformylation was effective for highly selective linear aldehyde formation from long-chained perfluoroalkyl substituted ethylene, n-C_nF_{2n+1}–CH=CH_2. As depicted in Scheme 1, the hydroformylation of n-C_4F_9–CH=CH_2 and n-C_8F_{17}–CH=CH_2 provided only linear aldehydes in excellent yields with *ca.*100% conversion of the substrates. This exclusive formation of the linear aldehyde is presumably because of the bulkiness of perfluoroalkyl group. The by-products observed were hydrogenated products (7% for Rf = n-C_4F_9 and 6% for Rf = n-C_8F_{17}).

The products in Scheme 1 are known as an intermediate in the syntheses of a separation material (Rf = n-C_4F_9) [8] or a medicine (Rf = n-C_8F_{17}) [9]. In the previous reports, these fluorinated aldehydes were synthesized by the reduction of chloride or iodide precursors, n-C_nF_{2n+1}–CH_2CH_2–Cl or –I; the chlorides are obtained from the reaction of n-C_nF_{2n+1}–CH_2CH_2COOH with thionyl chloride. In addition, $Rh_4(CO)_{12}$-catalyzed hydroformylation of n-C_nF_{2n+1}–CH=CH_2 including n-C_8F_{17}–CH=CH_2 afforded linear n-C_nF_{2n+1}–CH_2CH_2CHO in low selectivity, 3.4/96.6–27.2/72.8 [3b]. The present hydroformylation may be advantageous for practical use, because it is simple and gave the high selectivity.

3. Conclusion

TFB that is a raw material in the syntheses of pharmaceutical chemicals was obtained with high selectivity by Rh-catalyzed hydroformylation of TFP by the use of Xantphos ligand and DMF solvent. This method tolerates diverse fluorinated aldehydes. The selectivity was unsatisfactory at a low temperature and under the pressurized conditions. This is strikingly different from the hydroformylation of ordinary non-fluorinated alkenes and indicates that the mechanism is very unique. The mechanistic investigation is now in progress.

4. Experimental

4.1. General techniques

^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded in $CDCl_3$ on Bruker a DRX-500 (^{13}C 125 MHz) and a DRX-250 (^{1}H 250 MHz, ^{19}F 235 MHz) spectrometers using tetramethylsilane as an internal reference for ^{1}H and ^{13}C NMR and fluorotrichloromethane as an external reference for ^{19}F NMR. The chemical shifts are expressed in ppm (δ). The multiplicities are indicated by brs (broad singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). The ^{19}F NMR yields were calculated with 2,2,2-trifluoroethanol as an internal standard. Gas chromatography (GC) analyses were performed using a Shimadzu GC-14A with CP-Volamine (60 m × 0.32 mm). All the commercially available reagents were used without further purification.

4.2. Reaction procedures of hydroformylation

4.2.1. Quantitative analyses of product

The quantitative analyses of the starting material and products in the liquid phase were mainly carried out by the ^{19}F NMR spectral analyses. Prior to the analyses, the calibration curve was established with five authentic samples of TFB and TFMP; each of concentration was adjusted according to that in the reaction mixture, [TFB]/[TFMP] = 91, 95, 97, 99 and 99.5. We confirmed that the peak area ratio of TFB to TFMP in ^{19}F NMR spectrum is approximately equal to the molar ratio of the authentic samples. Furthermore, the quantitative analyses by GC also supported the accuracy of the ^{19}F NMR spectral analyses.

4.2.2. Hydroformylation in 1 atm of 50/50 CO/H_2 mixed gas

The reaction apparatus was equipped to a gas buret or a balloon. A Rh precursor (0.001–0.01 mmol), a ligand (0.006–0.06 mmol) and a solvent (5 mL) were charged in the reaction apparatus. After purging the apparatus with 50/50 CO/H_2 mixed gas, *ca.* 1.2 L of mixed gas was charged and sealed under atmospheric pressure. The amounts of CO and H_2 were *ca.* 25 mmol under the standard condition, respectively. The reaction mixture was stirred at 80 °C for 1 h (preparation step (i)) and then 5 mL of the solution of TFP (0.5 mol/L, TFP 2.5 mmol) was added through a septum using a syringe. [CO] or [H_2]/[TFP] was *ca.* 10. The mixture was further heated for 15 h (reaction step (ii)). After cooling to 0 °C, an aliquot of the mixture was analyzed by ^{19}F NMR spectroscopy. The analysis of gas phase was performed by GC. The aldehydes in the gas phase were confirmed to be very small (<0.1%). The reactions in Table 7 were carried out by the further addition of the DMF solution of TFP after 2 h reaction.

4.2.3. Hydroformylation in 1 atm of 60/40–80/20 CO/H_2 mixed gas

A reaction apparatus was equipped to a gas buret or a balloon. A Rh precursor (0.001–0.01 mmol), a ligand (0.001–0.01 mmol) and DMF (5 mL) were charged in the reaction apparatus. After perging the apparatus with CO/H_2 mixed gas, *ca.* 1.8 L of mixed gas was charged and sealed under atmospheric pressure. For example, 80/20 CO/H_2 mixed gas contains *ca.* 56.3 mmol of CO and 18.7 mmol of H_2 under the standard conditions, which correspond to [CO]/[TFP] = *ca.* 22 and [H_2]/[TFP] = *ca.* 7.5, respectively. The mixture was heated at room temperature or 80 °C for 1 h and then 5 mL of the DMF solution of TFP (0.5 mol/L, TFP 2.5 mmol) was charged through a septum using a syringe. The mixture was further heated for 15 h. After cooling to 0 °C, an aliquot of the mixture was analyzed by ^{19}F NMR spectroscopy and GC. The analysis of the gas phase was performed by GC. The aldehydes in the gas phase were confirmed to be very small (<0.1%).

4.2.4. Hydroformylation in an autoclave

$[Rh(OH)(cod)]_2$ (0.006 mmol), Xantphos (0.036 mmol), DMF (7 mL) and the DMF solution of TFP (3 mL, 0.5 mol/L, TFP 1.5 mmol) were charged together in a 100 mL autoclave. After purging the autoclave with 50/50 CO/H_2 mixed gas, the autoclave was sealed under 1.0 or 1.5 atm at room temperature. For example, the volume of CO or H_2 was *ca.* 45 mL under 1.0 atm, which corresponds to *ca.* 1.2 equivalent to TFP. The mixture was then heated at 80 °C for 2 h. After cooling to 0 °C, an aliquot of the mixture was analyzed ^{19}F NMR spectroscopy and GC. The same procedure as the reactions under atmospheric pressure, where the reaction was performed after preparation step (i) followed by step (ii), afforded lower yield and selectivity, 39% and 80/20, than entry 1 of Table 6.

4.3. Characterization of products

All the products are known compounds and are given a CAS number. These compounds except 4,4,5,5,6,6,7,7,7-nonafluoroheptanal have been already characterized by ^{1}H, ^{13}C and ^{19}F NMR [3b]. The NMR data agreed with this reported data.

4.3.1. 4,4,4-Trifluorobutanal (CAS No. 406–87-1)

Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 2.46 (m, 2H), 2.77 (t, J = 7.5 Hz, 2H), 9.81 (brs, 1H). ^{13}C NMR ($CDCl_3$) δ 26.4 (q, J_{CF} = 30.4 Hz), 36.3 (q, J_{CF} = 2.5 Hz), 126.4 (q, J_{CF} = 275.6 Hz), 198.0. ^{19}F NMR ($CDCl_3$) δ −66.7.

4.3.2. 3,3,3-Trifluoro-2-methylpropanal (S: CAS No. 189638-88-8, R: CAS No. 189638-87-7)

Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 1.33 (d, J = 7.2 Hz, 3H), 3.10 (m, 1H), 9.77 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 7.3 (q, J_{CF} = 2.6 Hz), 50.5 (q, J_{CF} = 25.9 Hz), 125.5 (q, J_{CF} = 279.7 Hz), 195.0 (q, J_{CF} = 3.0 Hz). ^{19}F NMR ($CDCl_3$) δ −68.5.

4.3.3. 4,4,5,5,6,6,7,7,7-nonafluoroheptanal (CAS No. 1262646-38-7)

Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 2.47 (m, 2H), 2.83 (t, J = 7.5 Hz, 2H), 9.84 (brs, 1H). ^{13}C NMR ($CDCl_3$) δ 23.4 (t, J_{CF} = 22.4 Hz, $-CH_2C_4F_9$), 34.5 (t, J_{CF} = 2.8 Hz, $-CH_2CHO$), 100–130 (m, $-C_4F_9$), 197.4 (−CHO). ^{19}F NMR ($CDCl_3$) δ −81.2 (m, 3F), −114.6 (m, 2F), −124.5 (m, 2F), −126.1 (m, 2F).

4.3.4. 4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecenal (CAS No. 42028-44-4)

Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 2.47 (m, 2H), 2.83 (t, J = 7.5 Hz, m), 9.84 (brs, 1H). ^{13}C NMR ($CDCl_3$) δ 23.5 (t, J_{CF} = 22.5 Hz, $-CH_2C_8F_{17}$), 34.5 ($-CH_2CHO$), 100–130 (m, $-C_8F_{17}$), 197.3 (−CHO). ^{19}F NMR ($CDCl_3$) δ −80.7 (t, J = 10.0 Hz, 3F), −114.7 (m, 2F), −121.7 (m, 2F), −121.9 (m, 4F), −122.7 (m, 2F), −123.5 (m, 2F), −126.1 (m, 2F).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2014.02.005.

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