

# Homogeneous Catalysis of Mixed-Metal Systems. Highly Regioselective Hydroformylation-Amidocarbonylation of a Fluoro Olefin Catalyzed by Co-Rh Mixed-Metal Systems. Observation of $\text{CoRh}(\text{CO})_7$ Catalysis

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**Abstract:** The hydroformylation-amidocarbonylation of a fluoro olefin,  $\text{C}_6\text{F}_5\text{CH}=\text{CH}_2$ , catalyzed by  $\text{Co}_2(\text{CO})_8$ -rhodium carbonyl systems proceeds with excellent regioselectivity. The process includes a unique Co-Rh mixed-metal complex,  $\text{CoRh}(\text{CO})_7$ , as an active catalyst species whose presence is revealed by the high-pressure IR study in the actual reaction system. The mechanism of this novel mixed-metal complex catalyzed process is discussed. The relative catalytic activities of  $\text{CoRh}(\text{CO})_7$ , rhodium carbonyl, and cobalt carbonyl are estimated on the basis of the kinetic measurements as well as the analysis of regioselectivities attained by these three catalyst species.

One of the most fascinating goals in catalysis is to create effective multicatalyst systems that can promote sequential multistep reactions cooperatively, giving useful chemical substances from simple starting materials. Actually, bioorganisms use a variety of enzymes as catalysts and produce sophisticated biochemicals from simple molecules such as carbon dioxide, water, and nitrogen. Accordingly, it is a challenge for chemists to design multifunctional multicatalyst systems, which enable us to carry out multistep synthesis in one pot in a highly organized manner.

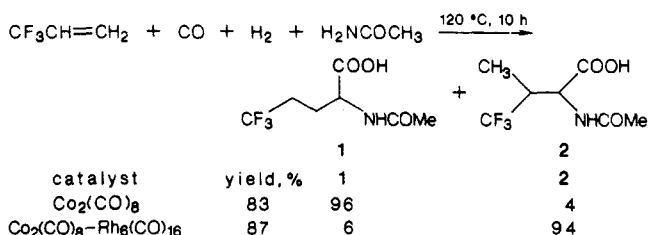
As a fundamental approach to this challenging goal, we have been designing and examining the efficiency of homogeneous bimetallic catalyst systems for amino acid synthesis, which can sequentially promote catalytic processes including carbonylation as one of the unit reactions.

Transition-metal complex catalyzed carbonylations of olefins, acetylenes, halides, alcohols, amines, nitro compounds, etc., have been extensively studied for a long time, and some of these reactions have been established as commercial processes.<sup>2</sup> There are, however, still strong demands for the development of new and efficient catalytic processes for the utilization of carbon monoxide in both industrial and laboratory organic synthesis. Among a variety of carbonylation reactions, we have been focusing on the exploitation of the cobalt-catalyzed amidocarbonylation of aldehydes as a key reaction since this reaction can produce biochemicals, i.e., *N*-acyl- $\alpha$ -amino acids from an aldehyde, amide, carbon monoxide, and hydrogen. This reaction was found in 1971 by Wakamatsu et al.<sup>3</sup> and developed by Ajinomoto's research group and later reinvestigated in more detail by Pino et al. in 1979 with regard to the synthetic potential and the reaction mechanisms.<sup>4</sup> Further applications of this reaction, e.g., to the synthesis of heterocyclic compounds, are being developed by Izawa et al.<sup>5</sup>

We already reported the first successful examples of isomerization-amidocarbonylation, which gives *N*-acyl- $\alpha$ -amino acids directly either from allylic alcohols<sup>6,7</sup> or from oxiranes.<sup>7</sup>

Since amidocarbonylation requires both  $\text{H}_2$  and CO, the reaction conditions are similar to those of hydroformylation except for the presence of an amide. Thus, it is logically possible to combine two reactions. If we could achieve excellent regioselectivities in the hydroformylation of olefins for the production of straight chain (*n*) as well as branched (*iso*) aldehydes, we should be able to synthesize *N*-acyl- $\alpha$ -amino acids highly regioselectively. In fact, we demonstrated the first example of highly regioselective hydroformylation-amidocarbonylation of trifluoropropene (TFP)

## Scheme I



catalyzed by  $\text{Co}_2(\text{CO})_8$  and  $\text{Co}_2(\text{CO})_8\text{-Rh}_6(\text{CO})_{16}$ . The  $\text{Co}_2(\text{CO})_8$ -catalyzed reaction gave *N*-acetyltrifluoronorvaline (**1**) in 96% selectivity while the reaction catalyzed by the  $\text{Co}_2(\text{CO})_8\text{-Rh}_6(\text{CO})_{16}$  binary system [ $\text{Co}_2(\text{CO})_8/\text{Rh}_6(\text{CO})_{16} = 50$ ] gave *N*-acetyltrifluorovaline (**2**) in 94% selectivity<sup>7</sup> (Scheme I). The latter result implies that the rhodium-catalyzed hydroformylation takes place exclusively in the first step to give 2-(trifluoromethyl)propanol highly selectively, which is effectively incorporated to the subsequent cobalt-catalyzed amidocarbonylation.

However, the attempted highly regioselective hydroformylation-amidocarbonylation of pentafluorostyrene (PFS) catalyzed by Co-Rh binary system as well as  $\text{Co}_2(\text{CO})_8$  under

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(2) (a) Pino, P.; Piacenti, F.; Bianchi, M. In *Organic Syntheses via Metal Carbonyls*; Wender, I., Pino, P., Eds.; Wiley-Interscience: New York, 1977; Vol. 2, pp 43-231. (b) Cornils, B. In *New Syntheses with Carbon Monoxide*; Falbe, J., Ed. Springer-Verlag: Berlin, 1980; pp 1-225.

(3) Wakamatsu, H.; Uda, J.; Yamakami, N. *J. Chem. Soc., Chem. Commun.* 1971, 1540.

(4) Parnaud, J. J.; Camperi, G.; Pino, P. *J. Mol. Catal.* 1979, 6, 341.

(5) (a) Nishi, S.; Asada, S.; Izawa, K. 31st Symposium on Organometallic Chemistry, Tsukuba, Japan, Oct 30-31, 1984; Abstract 202. (b) Izawa, K.; Nishi, S.; Asada, S. 10th International Congress of Heterocyclic Chemistry, Ontario, Canada, Aug 11-16, 1985; Abstract P8-207. (c) Nishi, S.; Asada, S.; Izawa, K. 3rd IUPAC Symposium on Organometallic Chemistry Directed Toward Organic Synthesis, Kyoto, Japan, July 11-15, 1985; Abstract 85. (d) Izawa, K.; Nishi, S.; Asada, S. 3rd International Kyoto Conference on New Aspects of Organic Chemistry, Kyoto, Japan, Nov 18-22, 1985; Abstract 187. (e) Izawa, K.; Nishi, S.; Asada, S. 32nd Symposium on Organometallic Chemistry, Osaka, Japan, Nov 5-6, 1985; Abstract 166. (f) Izawa, K. *J. Mol. Catal.* 1987, 41, 135.

(6) For a preliminary communication, see: Hirai, K.; Takahashi, Y.; Ojima, I. *Tetrahedron Lett.* 1982, 23, 2491.

(7) Ojima, I.; Hirai, K.; Fujita, M.; Fuchikami, T. *J. Organomet. Chem.* 1985, 279, 203.

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**Table I.**  $\text{Co}_2(\text{CO})_8$ -Catalyzed Hydroformylation of PFS<sup>a</sup>

entry	CO, psi	$\text{H}_2$ , psi	temp, °C	time, h	additive	aldehyde <sup>b</sup>		hydrogenation product yield, % <sup>c</sup>
						iso/n	yield, %	
1	600	600	80	16		40/60	4 (88)	0.5 (12)
2	600	600	100	20		28/72	40 (60)	4 (6.0)
3	600	600	125	15		26/74	67	26
4	1150	600	125	6		33/67	58	27
5	400	400	125	15		15/85	60	22
6	600	600	125	15	$\text{Me}_2\text{NCHO}^e$	26/74	23	75
7	600	600	125	15	$\text{H}_2\text{NCOCF}_3^e$	71/29	19	36
8	600	600	125	15	$\text{H}_2\text{NCO}_2\text{Me}^e$	61/39	21	29
9	1150	750	120	15	$\text{H}_2\text{NCOMe}^f$	8/92 <sup>d</sup>	30 <sup>d</sup>	

<sup>a</sup> All reactions were run with 1.0 mmol of PFS and 0.05 mmol of  $\text{Co}_2(\text{CO})_8$  in 1.0 mL of dioxane. <sup>b</sup> The products ratio and the yield were determined by GLC analysis. <sup>c</sup> The values in the parentheses are the conversion yield based on the consumed PFS. <sup>d</sup> For the corresponding amino acids. <sup>e</sup> 1.0–1.3 equiv of additive to PFS was used. <sup>f</sup> 2.0 equiv of additive to PFS was used.

**Table II.**  $\text{Rh}_6(\text{CO})_{16}$ -Catalyzed Hydroformylation of PFS<sup>a</sup>

entry	PFS/cation	solvent	CO, psi	$\text{H}_2$ , psi	temp, °C	time, h	additive	aldehyde <sup>b</sup> iso/n ratio
1	1000	dioxane	600	600	90	3		98/2
2	1000	dioxane	600	600	90	3	acetamide	98/2
3	1200	benzene	800	400	90	3		98/2
4	1200	dioxane	800	400	90	3		98/2
5	1000	dioxane	600	600	70	5		99/1 <sup>c</sup>
6	1000	dioxane	600	600	60	5		99.5/0.5 <sup>d</sup>

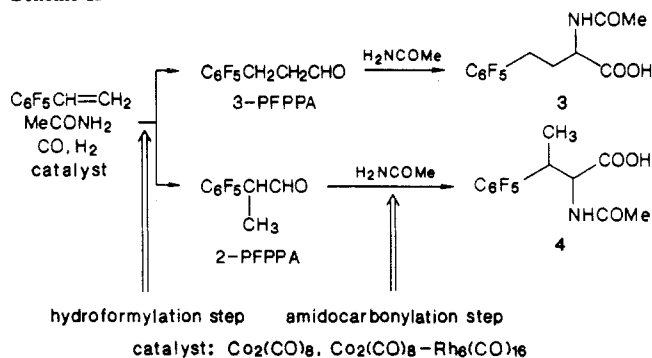
<sup>a</sup> All reactions were run with 1.0 mmol of PFS in 1.0 mL of solvent. <sup>b</sup> Conversion is >98% unless otherwise noted. <sup>c</sup> 74% conversion. <sup>d</sup> 17% conversion.

similar conditions to those for TFP gave unexpected results. The close investigation of the reaction revealed an interesting mechanistic aspect of Co–Rh mixed-metal catalyst systems as well as the existence of a novel  $\text{CoRh}(\text{CO})_7$ -catalyzed process. We describe here our approach to the analysis of multicatalyst systems and the application of such systems to the highly regioselective synthesis of *N*-acylfluoroamino acids.

## Results and Discussion

The hydroformylation–amidocarbonylation of pentafluorostyrene (PFS) catalyzed by  $\text{Co}_2(\text{CO})_8$  was carried out at 120 °C [1900 psi (131 bar) of CO and  $\text{H}_2$  (CO/ $\text{H}_2$  = 1.6)] with acetamide (2.0 equiv) in dioxane to give *N*-acetyl-4-(pentafluorophenyl)-homoalanine (**3**) with 90–92% regioselectivity (ca. 30% yield), which was much higher than the regioselectivity (79%) of the simple hydroformylation in benzene. The reaction catalyzed by Co–Rh binary system [ $\text{Co}_2(\text{CO})_8/\text{Rh}_6(\text{CO})_{16}$  = 50; CO, 1150 psi (79.3 bar);  $\text{H}_2$ , 750 psi (51.8 bar); 120 °C; acetamide, 2.0 equiv; dioxane] gave *N*-acetyl-3-(pentafluorophenyl)homoalanine (**4**; Scheme II) with only ca. 80% regioselectivity (70% yield), which is much lower than the excellent regioselectivity (98%) of the simple hydroformylation in benzene.<sup>8,9</sup>

To accommodate the observed results, we initially considered three possibilities: (i) The regioselectivity of the cobalt-catalyzed hydroformylation of PFS is affected by acetamide and/or dioxane to give 3-PFPPA (3-pentafluorophenyl)propanal in much higher selectivity (90–92%) since an amide could conceivably coordinate to the cobalt carbonyl to modify its regioselectivity; a similar solvent effect of dioxane can be considered as well. (ii) There is a kinetic selection of the *n*-aldehyde (3-PFPPA) in preference to the iso-aldehyde (2-(pentafluorophenyl)propanal; 2-PFPPA) in the amidocarbonylation step; viz., a considerable amount of 2-PFPPA should remain unreacted provided that 2-PFPPA is not consumed by side reaction(s). (iii) In the Co–Rh binary system, the rhodium catalyst is somewhat deactivated by forming less active or inactive Rh–Co mixed cluster(s) or the cobalt catalyst acquires special activation for the hydroformylation so that the Co–Rh binary system gives much lower iso/*n* ratio than the single rhodium catalyst since there should be  $10^3$ – $10^4$  difference between the activity of rhodium catalysts and  $\text{Co}_2(\text{CO})_8$  for the hydroformylation as far as the two catalysts work independently.<sup>2</sup> We

**Scheme II**

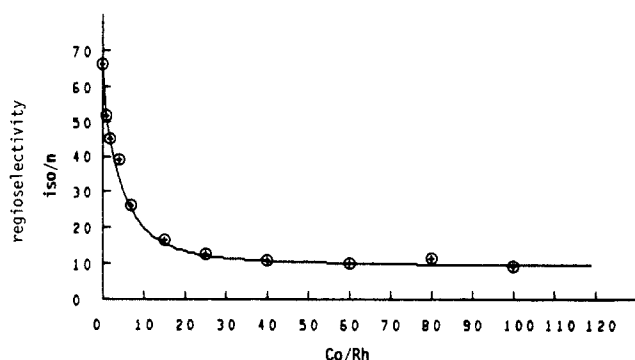
carried out a series of experiments to clarify these anomalies.

**Hydroformylation of PFS Catalyzed by  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_6(\text{CO})_{16}$ .** We found that (i) the cobalt-catalyzed hydroformylation of PFS was substantially slower than the amidocarbonylation of the aldehydes since no trace of 2-PFPPA or 3-PFPPA was detected at all in the GLC analysis of the reaction mixture even at low conversion and (ii) dioxane did not have any favorable solvent effects on the increase of *n* selectivity for the hydroformylation of PFS. Thus, it became evident that the hydroformylation was the regioselectivity-determining step, and the presence of acetamide to  $\text{Co}_2(\text{CO})_8$  substantially increased the *n* selectivity possibly by forming an active species like  $\text{HCo}(\text{CO})_n(\text{CH}_3\text{CONH}_2)_m$ . Actually, Izawa et al. also found that the addition of acetamide to  $\text{Co}_2(\text{CO})_8$  changed the regioselectivity in the hydroformylation of isobutene.<sup>10</sup> However, the addition of acetamide seemed to enhance the hydrogenation and polymerization of PFS. We also observed remarkable effects of other amides added to the reaction system on the regioselectivity of the reaction. It was also found that the *n* selectivity of PFPPA could be increased by elevating the temperature and lowering the CO pressure and vice versa, and a considerably large amount of hydrogenation product,  $\text{C}_6\text{F}_5\text{C}_2\text{H}_5$ , was formed (25–50%) at higher temperatures. Results of the

(8) Fuchikami, T.; Ojima, I. *J. Am. Chem. Soc.* **1982**, *104*, 3527.

(9) Ojima, I.; Fuchikami, T. U.S. Patent 4 370 504, 1983.

(10) Izawa et al. found that the hydroformylation of isobutene catalyzed by  $\text{Co}_2(\text{CO})_8$  in the absence of acetamide followed by amidocarbonylation with acetamide gave 60% of *N*-acetyl-leucine and 1.6% of *N*-acetyl-*tert*-butylglycine whereas the hydroformylation–amidocarbonylation of isobutene, which included hydroformylation in the presence of acetamide, gave 17% of *N*-acetyl-leucine and 22% of *N*-acetyl-*tert*-butylglycine. Izawa, K., private communication.



**Figure 1.** Dependence of regioselectivity on the Co/Rh ratio for the reactions in dioxane at 80 °C [1200 psi ( $\text{CO}/\text{H}_2 = 1$ )]. The concentration of  $\text{Rh}_4(\text{CO})_{12}$  is kept at  $1.0 \times 10^{-3}$  M, and the amount of  $\text{Co}_2(\text{CO})_8$  is changed. The Co/Rh ratio indicated is based on the metals; i.e., the Co/Rh ratio of 100 is equal to the  $\text{Co}_2(\text{CO})_8/\text{Rh}_4(\text{CO})_{12}$  ratio of 200.

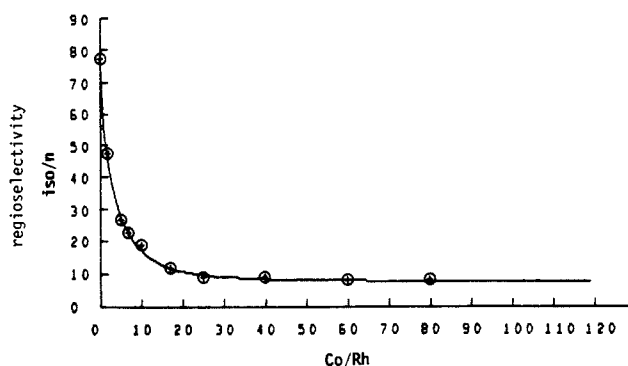
$\text{Co}_2(\text{CO})_8$ -catalyzed reactions are summarized in Table I.

In the  $\text{Rh}_6(\text{CO})_{16}$ -catalyzed hydroformylation of PFS, it was found that (a) neither acetamide nor dioxane had any appreciable effect on the regioselectivity, (b) the iso/n ratio was clearly dependent on the reaction temperature, the lower the temperature, the higher the selectivity (e.g., iso/n = 98/2 at 95 °C; iso/n = 99.5/0.5 at 60 °C), and (c) the formation of the hydrogenation product was negligible and thus the aldehyde selectivity is extremely high. Results of the  $\text{Rh}_6(\text{CO})_{16}$ -catalyzed reactions are summarized in Table II.

**Kinetic Selection of 2-PFPPA and 3-PFPPA in Amidocarbonylation.** In a competitive reaction of iso-aldehyde (2-PFPPA, 1.0 equiv) and *n*-aldehyde (3-PFPPA, 1.0 equiv) with 0.25 equiv of acetamide carried out in the presence of  $\text{Co}_2(\text{CO})_8$  (0.1 equiv) in dioxane at 125 °C, it was found that 3-PFPPA reacts 2.5 times faster than 2-PFPPA. Accordingly, it turned out that there was, actually, a kinetic selection of the aldehydes. However, this kinetic selection does not affect the iso/n ratio of amino acids, 3 and 4, in the  $\text{Co}_2(\text{CO})_8$ -catalyzed reaction since the hydroformylation step is considerably slower than the amidocarbonylation step as mentioned above. In the Co-Rh mixed-metal system, this kinetic selection could somewhat affect the iso/n ratio at low conversion since  $\text{CoRh}(\text{CO})_7$ -catalyzed and  $\text{Rh}_4(\text{CO})_{12}$ -catalyzed hydroformylation is much faster than the  $\text{Co}_2(\text{CO})_8$ -catalyzed amidocarbonylation. However, the kinetic selection should not affect the final iso/n ratio since the 2-PFPPA should be consumed eventually. Actually, no remaining aldehydes were detected after the reaction unless the reaction was quenched at an early stage. Consequently, we can rule out the possibility of the kinetic selection being responsible for the observed anomalies.

**Dependence of Regioselectivity on the Co/Rh Ratio.** Next, we looked closely at the hydroformylation of PFS in dioxane catalyzed by the Co-Rh mixed-metal system with various Co/Rh ratios. The reactions were run with the Co/Rh atomic ratio of 1–100 with the use of  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_4(\text{CO})_{12}$  or  $\text{Rh}_6(\text{CO})_{16}$ . The Co-Rh mixed clusters,  $\text{Co}_2\text{Rh}_2(\text{CO})_{12}$  and  $\text{Co}_3\text{Rh}(\text{CO})_{12}$ , were also used.

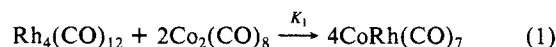
We examined the regioselectivities by carrying out the reactions at 95 °C [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 1$ )] with  $\text{Co}_2(\text{CO})_8/\text{Rh}_6(\text{CO})_{16}$  ratios of 10, 50, and 200, respectively. If the cobalt and rhodium catalysts worked independently, the ratio of *n*-aldehyde formation should increase at higher Co/Rh ratios and eventually the *n*-aldehyde should become a major product. However, contrary to this assumption, an interesting leveling phenomenon of regioselectivity was observed. Namely, the iso/n ratio decreased from 94/6 at  $\text{Co}_2/\text{Rh}_6 = 10$  to 88/12 at  $\text{Co}_2/\text{Rh}_6 = 50$ , but the ratio did not continue to decrease, significantly, with a further increase of Co/Rh ratio; the iso/n was 87/13 even at  $\text{Co}_2/\text{Rh}_6$  ratio of 200(!). Under the same reaction conditions, the reaction catalyzed by  $\text{Co}_3\text{Rh}(\text{CO})_{12}$  (Co/Rh = 3) gave the iso/n ratio of 96/4 and the reaction catalyzed by  $\text{Co}_2\text{Rh}_2(\text{CO})_{12}$  (Co/Rh = 1) gave a 98/2 ratio.



**Figure 2.** Dependence of regioselectivity on the Co/Rh ratio for the reactions in hexane at 80 °C [1200 psi ( $\text{CO}/\text{H}_2 = 1$ )]. For other conditions, see the caption for Figure 1.

This leveling phenomenon of the regioselectivity is best interpreted by taking into account the formation of and the catalysis by a Co-Rh mixed-metal complex. Namely,  $\text{Rh}_6(\text{CO})_{16}$  and  $\text{Co}_2(\text{CO})_8$  form a mixed-metal complex, which compete with the rhodium catalyst(s) in the system up to a point where practically almost all the rhodium catalyst(s) is converted to the Co-Rh mixed-metal complex in the presence of a large excess of  $\text{Co}_2(\text{CO})_8$ . The Co-Rh complex then becomes the most efficient catalyst species and governs the reaction and the regioselectivity.<sup>11</sup>

When we almost reached the conclusion that "some Co-Rh mixed-metal complex" was the active catalyst species in the hydroformylation of PFS, Horváth, Bor, and Pino<sup>12,13</sup> reported the synthesis, equilibrium study, isolation, characterization, and some reactions of an interesting coordinatively unsaturated Co-Rh mixed-metal complex,  $\text{CoRh}(\text{CO})_7$ , previously postulated as an active catalyst species in the hydroformylation of diketene.<sup>13</sup> This exciting report inspired us to closely reexamine the dependence of the regioselectivity of the PFS-hydroformylation on the Co/Rh ratio in order to obtain unambiguous evidence for the mixed-metal complex catalysis, i.e.,  $\text{CoRh}(\text{CO})_7$  catalysis, with  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_4(\text{CO})_{12}$  as catalyst precursors, since the equilibrium constant,  $K_1$ , for eq 1 was estimated to be  $3.5 \times 10^{-3}$  M at 84 °C in hexane.<sup>13</sup>

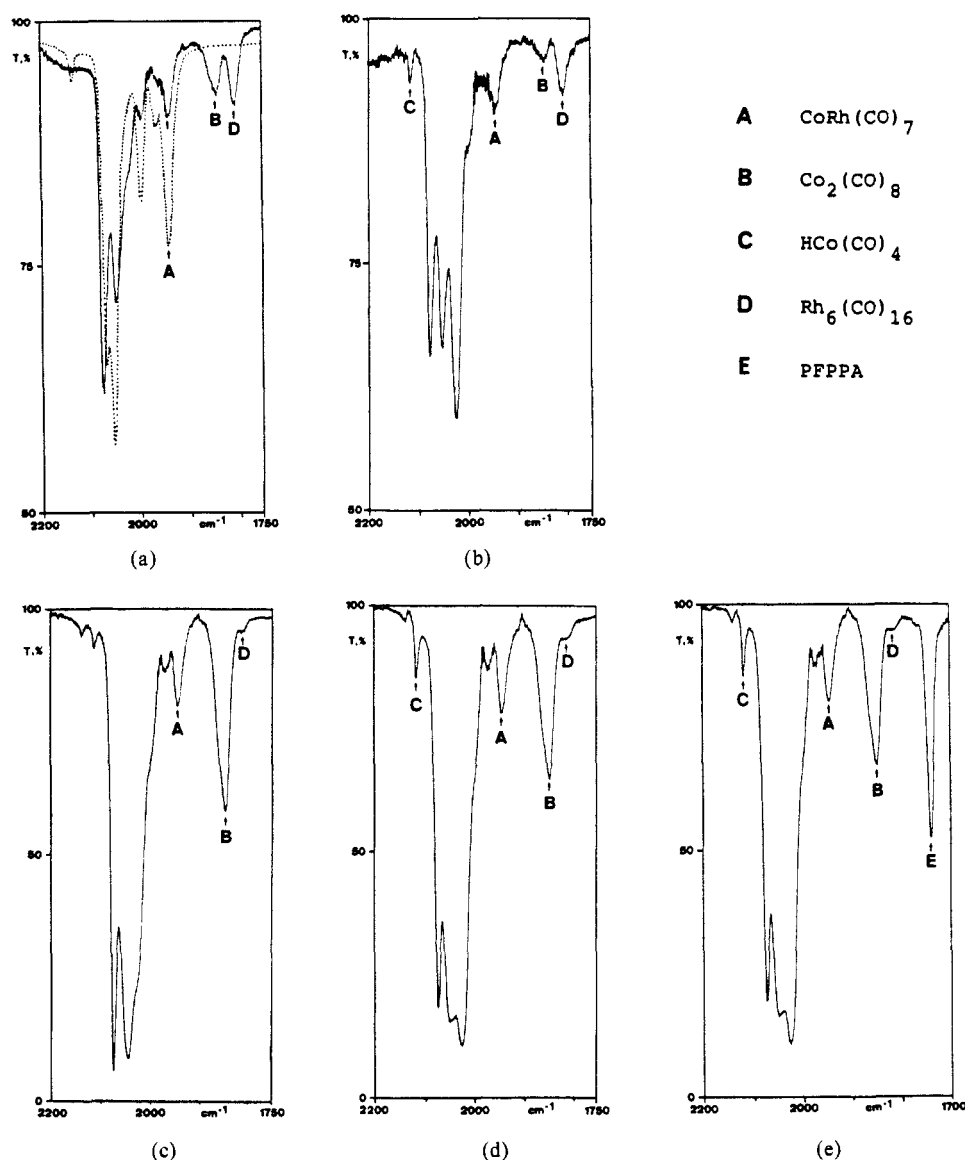


All reactions were run by mixing  $\text{Co}_2(\text{CO})_8$ ,  $\text{Rh}_4(\text{CO})_{12}$ , and PFS in dioxane or hexane, in advance, at 80 °C [600 psi (41.4 bar) of CO] for 12 h and then starting the reaction by introducing

(11) One might consider also the possibility that  $\text{HCo}(\text{CO})_4$  can act as an excellent hydrogen donor in the  $\text{Rh}_6(\text{CO})_{16}$ -catalyzed reaction for the cleavage of an acyl-rhodium complex, competing with the oxidative addition of molecular hydrogen followed by the reductive elimination, and thus the regioselectivity is changed up to a point at which the hydridocobalt-promoted cleavage becomes a virtually exclusive process. Beyond this point the regioselectivity would be constant provided that the cleavage is the selectivity-determining step. However, this possibility is very unlikely since the *n*/iso ratio of the complex should already be determined at the stage of the acyl-rhodium complex. If the cleavage by the hydridocobalt is faster than that by  $\text{H}_2$ , the regioselectivity should not change from that of the simple rhodium-catalyzed hydroformylation in a manner that favors the straight-chain aldehyde since it is known that the isomerization of a branched acyl-rhodium complex to a straight-chain acyl-rhodium complex is almost negligible in the rhodium-catalyzed hydroformylation of olefins in general.<sup>2b</sup> Consequently, this possibility is eliminated. Also, the possible special activation of the cobalt catalyst by the rhodium catalyst, which was considered as a possibility in the beginning (vide supra), is ruled out because of the finding of the leveling of regioselectivity.

(12) (a) Horváth, I. T.; Bor, G.; Garland, M.; Pino, P. *Organometallics* **1986**, 5, 1441. (b) Horváth, I. T.; Bor, G.; Pino, P. 12th International Conference on Organometallic Chemistry, Vienna, Austria, Sept 9–13, 1985; Abstract 336. (c) Bor, G. *Pure Appl. Chem.* **1986**, 58, 543.

(13) Spindler, F.; Bor, G.; Dietler, U.; Pino, P. *J. Organomet. Chem.* **1981**, 213, 303. As for the hydroformylation of *tert*-butylethene catalyzed by  $\text{CoRh}(\text{CO})_7$ , see: Horváth, I. T.; Bor, G.; Garland, M.; Pino, P. *Abstracts of Papers*, 193rd National Meeting of the American Chemical Society, Denver, CO, April 5–10, 1987; American Chemical Society: Washington, DC, INOR 353.



**Figure 3.** High-pressure IR spectra of the Co-Rh mixed-metal systems in dioxane: (a) mixture of  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_4(\text{CO})_{12}$  (2:1 molar ratio; 1:1 metal ratio) at 80 °C [600 psi of CO] (bold line) (system 1) and the reference spectrum of  $\text{CoRh}(\text{CO})_7$ , which is generated from  $\text{Co}_2\text{Rh}_2(\text{CO})_{12}$  at 25 °C [600 psi of CO] (dotted line); (b) mixture of  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_4(\text{CO})_{12}$  (1:1 molar ratio) at 80 °C [1200 psi ( $\text{CO}/\text{H}_2 = 1$ )], i.e., system 1 plus hydrogen (system 2); (c) mixture of  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_4(\text{CO})_{12}$  (80:1 molar ratio; 40:1 metal ratio) at 80 °C [1200 psi of CO] (system 3); (d)  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_4(\text{CO})_{12}$  (40:1 metal ratio) at 80 °C [1200 psi ( $\text{CO}/\text{H}_2 = 1$ )], i.e., system 3 plus hydrogen (system 4); (e) mixture of  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_4(\text{CO})_{12}$  (40:1 metal ratio) at 80 °C [1200 psi ( $\text{CO}/\text{H}_2 = 1$ )] at a 1-h period after the addition of PFS to the system 4 (system 5).

$\text{H}_2$  (600 psi; 41.4 bar) so that the Co-Rh mixed-metal system reached equilibrium before the hydroformylation began.<sup>14</sup> In the controlled experiments, the iso/n ratios for the  $\text{Rh}_4(\text{CO})_{12}$ -catalyzed reaction were 66 in dioxane and 76 in hexane; those for the  $\text{Co}_2(\text{CO})_8$ -catalyzed reaction were 0.67 in dioxane and 0.47 in hexane at 80 °C [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 1$ )]. Under the given conditions, the cobalt-catalyzed reaction was very slow so that the formation of the aldehydes was only 4.1% yield at a 16-h period in dioxane ( $4.0 \times 10^{-2}$  M of  $\text{Co}_2(\text{CO})_8$ ) and 6.0% at a 6-h period in hexane (0.10 M of  $\text{Co}_2(\text{CO})_8$ ) in 1.0 M PFS.

(14) When the reaction is initiated before the equilibrium is complete, e.g., by introducing  $\text{H}_2$  and CO simultaneously or by introducing  $\text{H}_2$  at less than a 2-h period after the mixing of  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_4(\text{CO})_{12}$  at 80 °C, the regioselectivity observed is close to that obtained by using the rhodium catalyst only. Since the regioselectivity is dependent on the relative amounts of the rhodium catalyst and  $\text{CoRh}(\text{CO})_7$  in the system, the reproducibility of those experiments tends to be low. For example, at the Co/Rh ratios of 40 and 60, the observed iso/n ratios for a control experiment in which hydrogen gas was introduced at a 30-min period after the mixing at 80 °C in dioxane were 44.3 (iso/n = 97.8/2.2) and 35.5 (iso/n = 97.3/2.7), respectively. This iso selectivity is much higher than that obtained under the standard conditions we used in which the equilibrium is complete (see Figure 1).

The results are shown in Figures 1 (solvent dioxane) 2 (solvent hexane).

As Figure 1 (solvent dioxane) shows, there is a clear leveling phenomenon, which is essentially the same as that observed for  $\text{Co}_2(\text{CO})_8$ - $\text{Rh}_6(\text{CO})_{16}$ . Namely, the iso/n ratio sharply decreases from 66 (Rh 100%) to 16 (Co/Rh = 15), the decrease slows down at higher Co/Rh ratios and becomes nearly constant, 10, at Co/Rh = 40, and the ratio is 9.5 at Co/Rh = 100. Accordingly, we made a working hypothesis at this stage that the catalyst species giving an iso/n ratio of 10 would be  $\text{CoRh}(\text{CO})_7$  and started collecting supporting evidence.

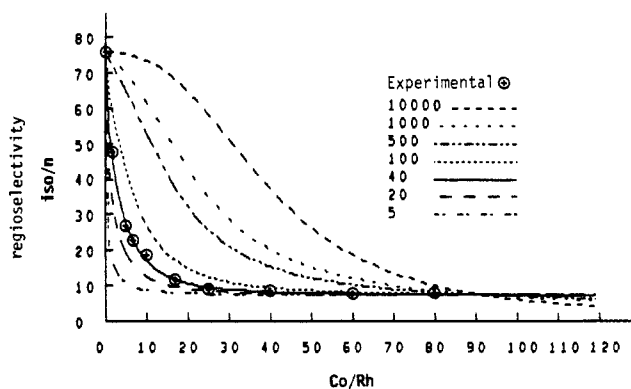
In hexane, as Figure 2 shows, the same type of clear saturation phenomenon of regioselectivity was observed as well. In this case, the regioselectivity that the catalyst species, assumed to be  $\text{CoRh}(\text{CO})_7$  gives is 7.5. Thus, it is apparent that there is a solvent effect on the regioselectivity. As mentioned above, the ETH group obtained all the data for the equilibrium between  $\text{Co}_2(\text{CO})_8$ ,  $\text{Rh}_4(\text{CO})_{12}$ , and  $\text{CoRh}(\text{CO})_7$  in hexane on the basis of the high-pressure IR studies, and these three species were found to be the only predominant species in hexane under carbon monoxide pressure.<sup>12,13</sup> Therefore, it is possible to consider that these three species are either the active catalyst species or the direct precursors

of the active catalyst species in hexane.<sup>15</sup>

Although it seemed reasonable to assume that the three major species existing in the Co–Rh mixed-metal system in dioxane under carbon monoxide pressure were the same as those in hexane, there might be some solvent effects that would change the major species.<sup>17</sup> Therefore, we carried out the high-pressure IR study of the  $\text{Co}_2(\text{CO})_8$ – $\text{Rh}_4(\text{CO})_{12}$  system in dioxane in order to directly observe active catalyst species in the actual reaction system.

**High-Pressure IR Study of the Co–Rh Mixed-Metal System in the Presence of Carbon Monoxide and Hydrogen.** As shown in Figure 3, the IR spectrum of the reaction mixture of  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_4(\text{CO})_{12}$  (2:1 molar ratio; i.e., 1:1 metal ratio) in dioxane at 80 °C [600 psi (41.4 bar) of carbon monoxide] displays the clear formation of  $\text{CoRh}(\text{CO})_7$  together with  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_6(\text{CO})_{16}$  (system 1) (Figure 3a, bold line). The bands at 1850 (B) and 1808  $\text{cm}^{-1}$  (D) are assigned to  $\text{Co}_2(\text{CO})_8$  and  $\text{Rh}_6(\text{CO})_{16}$ , respectively. The band at 1940  $\text{cm}^{-1}$  (A) is attributed to  $\text{CoRh}(\text{CO})_7$ , as evidently shown in the IR spectrum of  $\text{CoRh}(\text{CO})_7$  obtained quantitatively from the reaction of  $\text{Co}_2\text{Rh}_2(\text{CO})_{12}$  with carbon monoxide at 25 °C [600 psi (41.4 bar)] (Figure 3a, dotted line). The IR spectrum of  $\text{CoRh}(\text{CO})_7$  measured previously in *n*-hexane<sup>12</sup> is almost superimposable to that in dioxane, which indicates no change in the structure of this Co–Rh mixed complex in those two solvents. It should also be noted that  $\text{Rh}_4(\text{CO})_{12}$  disappeared virtually completely when it was dissolved in dioxane at 80 °C [600 psi (41.4 bar) of carbon monoxide] for 20 h although  $\text{Rh}_4(\text{CO})_{12}$  is stable in dioxane at 25 °C [600 psi (41.4 bar) of carbon monoxide]: The result clearly indicates a solvent effect on the structure of the major species of rhodium carbonyls as we suspected before the high-pressure IR study. Under the same conditions,  $\text{Co}_2\text{Rh}_2(\text{CO})_{12}$  shows exactly the same spectrum to system 1. When hydrogen (600 psi; 41.4 bar) was introduced to system 1, the spectrum of the reaction mixture displays new intense absorption of  $\text{HCo}(\text{CO})_4$  in place of the substantially diminished  $\text{Co}_2(\text{CO})_8$ ,  $\text{CoRh}(\text{CO})_7$ , and  $\text{Rh}_6(\text{CO})_{16}$  (system 2) (Figure 3b): The band at 2114  $\text{cm}^{-1}$  is assigned to  $\text{HCo}(\text{CO})_4$ .

Next, the high-pressure IR study of the Co–Rh mixed-metal systems was carried out with the Co/Rh metal ratio of 40, i.e.,  $\text{Co}_2(\text{CO})_8/\text{Rh}_4(\text{CO})_{12} = 80$ , under the same conditions as described above, i.e., in dioxane at 80 °C [600 psi (41.4 bar) of carbon monoxide] (system 3). At this Co/Rh ratio,  $\text{CoRh}(\text{CO})_7$  should become the predominant catalyst species on the basis of the results depicted in Figure 1. Indeed, as shown in Figure 3c,  $\text{Rh}_6(\text{CO})_{16}$  diminishes to a trace amount and  $\text{CoRh}(\text{CO})_7$  and  $\text{Co}_2(\text{CO})_8$  become the two major components in this system. The addition of hydrogen (600 psi; 41.4 bar) to system 3 brings about the formation of  $\text{HCo}(\text{CO})_4$  without affecting  $\text{CoRh}(\text{CO})_7$  concentration (Figure 3d) (system 4), which are the real reaction conditions. Finally, PFS was added to system 4, and the IR



**Figure 4.** Calculated dependence of regioselectivity on the Co/Rh ratio for the reactions in hexane with several hypothetical relative catalytic activity ratios for  $\text{Rh}_4(\text{CO})_{12}$  versus  $\text{CoRh}(\text{CO})_7$ . The regioselectivity of each catalyst used for the calculation is 76 for  $\text{Rh}_4(\text{CO})_{12}$ , 7.5 for  $\text{CoRh}(\text{CO})_7$ , and 0.47 for  $\text{Co}_2(\text{CO})_8$ . The  $y$  value in eq 3 for this display is 8400.

spectrum of this real reaction system was measured at 1-h periods after the addition of PFS. As Figure 3e shows, an intense aldehyde peak (E) appears together with those of  $\text{CoRh}(\text{CO})_7$ ,  $\text{HCo}(\text{CO})_4$ ,  $\text{Co}_2(\text{CO})_8$ , and a trace amount of  $\text{Rh}_6(\text{CO})_{16}$ : The ratio and the appearance of the metal carbonyl peaks did not change at all during the reaction.

Consequently, the IR study provides strongly supporting evidence for the working hypothesis regarding the  $\text{CoRh}(\text{CO})_7$  catalysis based on the regioselectivity dependence described above.

**Evaluation of Relative Catalytic Activities of the Cobalt Carbonyl, Rhodium Carbonyl, and Co–Rh Mixed Complexes Based on the Analysis of Regioselectivities.** (A) For Reactions in Hexane. On the basis of the equilibrium constant  $K_1$  ( $3.5 \times 10^{-3}$  M at 84 °C) reported for eq 1,<sup>13</sup> the relative concentrations of  $\text{CoRh}(\text{CO})_7$ ,  $\text{Co}_2(\text{CO})_{12}$ , and  $\text{Rh}_4(\text{CO})_{12}$  at a given Co/Rh ratio can be calculated by eq 2, where  $a$  = concentration of  $\text{CoRh}(\text{CO})_7$ ,  $b$  = initial concentration of  $\text{Co}_2(\text{CO})_8$ , and  $c$  = initial concentration of  $\text{Rh}_4(\text{CO})_{12}$ .

$$K_1 = \frac{[\text{CoRh}(\text{CO})_7]^4}{[\text{Rh}_4(\text{CO})_{12}][\text{Co}_2(\text{CO})_8]^2} = \frac{a^4}{(c - a/4)(b - a/2)^2} = 0.0035 \quad (2)$$

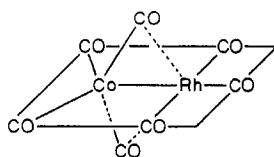
For example, the ratios of the three species  $[\text{CoRh}]/[\text{Rh}_4]/[\text{Co}_2]$  at Co/Rh ratios of 5, 40, and 100 are 1.00/0.0948/2.95, 1.00/2.91  $\times 10^{-3}$ /19.7, and 1.00/4.63  $\times 10^{-4}$ /50.1, respectively, provided that the initial concentration of  $\text{Rh}_4(\text{CO})_{12}$  is  $1.00 \times 10^{-3}$  M in every case. The relative catalytic activity of  $\text{Rh}_4(\text{CO})_{12}$  vs  $\text{CoRh}(\text{CO})_7$  as well as  $\text{Co}_2(\text{CO})_8$  can be estimated on the basis of the calculated relative concentrations of these three species and the observed iso/*n* ratios of PFPPA.

The results of the calculations and the computer plotting for the iso/*n* ratio vs Co/Rh ratios with several given relative catalytic activities are shown in Figure 4. The calculations were performed on the basis of the following assumptions and treatments.

(a) The rate constants,  $k_1$ ,  $k_2$ , and  $k_3$ , are defined for the unit reactions that give iso-aldehyde (2-PFPPA) catalyzed by  $\text{Rh}_4(\text{CO})_{12}$ ,  $\text{CoRh}(\text{CO})_7$ , and  $\text{Co}_2(\text{CO})_8$  respectively. Similarly,  $k_1'$ ,  $k_2'$ , and  $k_3'$  are defined as the rate constants for the unit reactions giving *n*-aldehyde (3-PFPPA) catalyzed by  $\text{Rh}_4(\text{CO})_{12}$ ,  $\text{CoRh}(\text{CO})_7$ , and  $\text{Co}_2(\text{CO})_8$  respectively.

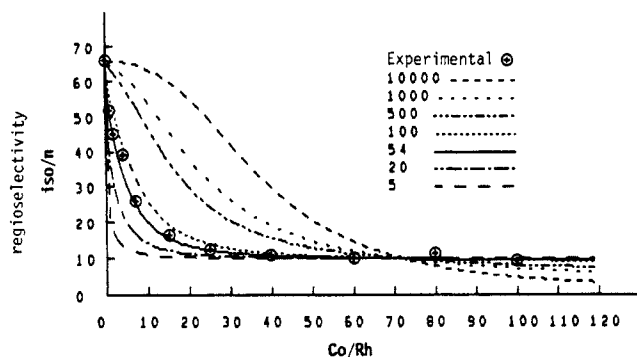
(b) The observed iso/*n* ratios should be described with the relative concentrations of the three catalyst species as follows on the basis of the observed iso/*n* ratios ( $k_{\text{iso}}/k_n$ ) for each catalyst species, i.e., 76 for  $\text{Rh}_4(\text{CO})_{12}$  ( $k_1/k_1'$ ), 7.5 for  $\text{CoRh}(\text{CO})_7$  ( $k_2/k_2'$ ), and 0.47 for  $\text{Co}_2(\text{CO})_8$  ( $k_3/k_3'$ ), and also on the basis of the assumption that the rate of the reaction is first order to the concentration of the catalyst in each case for the three catalysts

(15) It has been shown by Bor, Pino, Horváth, and their co-workers<sup>12,13</sup> that the Co–Rh mixed-metal systems, e.g.,  $\text{Co}_2(\text{CO})_8$ – $\text{Rh}_4(\text{CO})_{12}$ ,  $\text{Co}_2(\text{CO})_8$ – $\text{Rh}_6(\text{CO})_{16}$ ,  $\text{Co}_3\text{Rh}(\text{CO})_{12}$ , and  $\text{Co}_3\text{Rh}_2(\text{CO})_{12}$ , generate an equilibrium mixture under CO pressure in which  $\text{CoRh}(\text{CO})_7$ ,  $\text{Co}_2(\text{CO})_8$ , and  $\text{Rh}_4(\text{CO})_{12}$  are the three major components in hexane (eq 1) and  $\text{CoRh}(\text{CO})_7$  is an unusually stable complex. This forms a sharp contrast to other known mixed clusters such as  $\text{HCoRu}_3(\text{CO})_{13}$  and  $\text{H}_2\text{FeRu}_3(\text{CO})_{13}$ , which decompose easily to the corresponding homonuclear species under 1 atm of CO at 25–70 °C.<sup>16</sup> The proposed structure of  $\text{CoRh}(\text{CO})_7$  by Horváth et al. is



(16) Fox, J. R.; Gladfelter, W. L.; Geoffroy, G. L. *Inorg. Chim.* **1980**, *19*, 2574.

(17) In fact, it has been shown that  $\text{Co}_2\text{Rh}_2(\text{CO})_{12}$  reacts with various nucleophiles such as tetrahydrofuran, acetonitrile, and triethylphosphine to give the corresponding  $(\text{CO})_4\text{CoRh}(\text{CO})_2\text{Nu}$ . See: Horváth, I. T. *Organometallics* **1986**, *5*, 2333.



**Figure 5.** Calculated dependence of regioselectivity on the Co/Rh ratio for the reactions in dioxane with several hypothetical relative catalytic activity ratios for  $\text{Rh}_6(\text{CO})_{16}$  versus  $\text{CoRh}(\text{CO})_7$ . The regioselectivity of each catalyst used for the calculation is 66 for  $\text{Rh}_6(\text{CO})_{16}$ , 10 for  $\text{CoRh}(\text{CO})_7$ , and 0.67 for  $\text{Co}_2(\text{CO})_8$ . The  $y$  value in eq 3 for this display is 6600.

(eq 3),<sup>18</sup> where  $Z = (c - a/4) + a/x + (b - a/2)/y$ ,  $x = k_2/k_1$ , and  $y = k_3/k_1$ .

iso/n =

$$76(c - a/4)/Z + 7.5(a/x)/Z + 0.47[(b - a/2)/y]/Z \quad (3)$$

(c) The relative catalytic activities are defined as  $(k_1 + k_1')/(k_2 + k_2')$  for  $\text{Rh}_4(\text{CO})_{12}/\text{CoRh}(\text{CO})_7$  and  $(k_1 + k_1')/(k_3 + k_3')$  for  $\text{Rh}_4(\text{CO})_{12}/\text{Co}_2(\text{CO})_8$ . Since the observed iso/n ratios are 76 for  $\text{Rh}_4(\text{CO})_{12}$ , 7.5 for  $\text{CoRh}(\text{CO})_7$ , and 0.47 for  $\text{Co}_2(\text{CO})_8$ , we can derive the following equations:  $k_1 = 76k_1'$ ;  $k_2 = 7.5k_2'$ ;  $k_3 = 0.47k_3'$ . Thus, the relative catalytic activities can be described as follows:  $(77/8.5)k_1'/k_2'$  (9.06x) for  $\text{Rh}_4(\text{CO})_{12}/\text{CoRh}(\text{CO})_7$ ;  $(77/1.47)k_2'/k_3'$  (52.4y) for  $\text{Rh}_4(\text{CO})_{12}/\text{Co}_2(\text{CO})_8$ .

As is apparent from Figure 4, the relative catalytic activity of 40 for  $\text{Rh}_4(\text{CO})_{12}/\text{CoRh}(\text{CO})_7$ , i.e., 10 *per rhodium metal*, almost perfectly fits the experimental results. The relative catalytic activity for  $\text{Rh}_4(\text{CO})_{12}/\text{Co}_2(\text{CO})_8$  is calculated to be ca. 440 000, i.e., ca. 220 000 per metal, which indicates that  $\text{Co}_2(\text{CO})_8$  is nearly inactive under the given reaction conditions, i.e., at 80 °C [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 1$ )] this may well be partly ascribed to a low conversion of  $\text{Co}_2(\text{CO})_8$  to  $\text{HCo}(\text{CO})_4$ , which is the real active catalyst species, under these conditions besides the inherent activity difference between the rhodium catalyst and the cobalt catalyst (*vide infra*).

**(B) For Reactions in Dioxane.** As the high-pressure IR study revealed that the rhodium species existing in the catalytic reaction system in dioxane was  $\text{Rh}_6(\text{CO})_{16}$  instead of  $\text{Rh}_4(\text{CO})_{12}$ , eq 1 should be modified and an equilibrium constant for the modified equation be determined. Nevertheless, we may be able to assume that (i) the concentration of  $\text{Rh}_6(\text{CO})_{16}$  can be represented by  $\text{Rh}_4(\text{CO})_{12}$ , i.e.,  $[\text{Rh}_6(\text{CO})_{16}] = 2/3[\text{Rh}_4(\text{CO})_{12}]$ , since it has been shown<sup>12</sup> that  $\text{Rh}_6(\text{CO})_{16}$  should be converted to  $\text{Rh}_4(\text{CO})_{12}$  to react with  $\text{Co}_2(\text{CO})_8$  forming  $\text{CoRh}(\text{CO})_7$  and (ii) the  $K_1$  value in dioxane is not very different from that in hexane.

On the basis of this working hypothesis, the relative ratio of  $[\text{Co}(\text{Rh}(\text{CO})_7)]$ ,  $[\text{Rh}_6(\text{CO})_{16}]$ , and  $[\text{Co}_2(\text{CO})_8]$  at the given Co/Rh ratio can be calculated, and the relative catalyst activities for these three species can be estimated in a manner similar to the hexane case described above. The calculations were performed by a modified eq 3 in which only the numbers were changed on the basis of the iso/n ratio of 66 for the rhodium-catalyzed reaction ( $k_1/k_1'$ ), 10 for the  $\text{CoRh}(\text{CO})_7$ -catalyzed reaction ( $k_2/k_2'$ ), and

0.67 for the cobalt-catalyzed reaction ( $k_3/k_3'$ ) at 80 °C [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 1$ )]. The results of the calculations and the computer plotting for the iso/n ratio vs Co/Rh ratio with several given relative catalytic activities are shown in Figure 5. As Figure 5 shows, the relative catalytic activity of 54 for  $\text{Rh}_6(\text{CO})_{16}/\text{CoRh}(\text{CO})_7$  shows a very good agreement with the experimental results; i.e., the relative activity *per rhodium metal* is 9. The relative catalytic activity for  $\text{Rh}_6(\text{CO})_{16}/\text{Co}_2(\text{CO})_8$  is calculated to be ca. 400 000, i.e., 133 000 per metal. Thus, the results of the calculations are very similar to those of the hexane case.

**Kinetic Study of the Rhodium, Cobalt-Rhodium, and Cobalt Catalyst Systems.** Since the relative catalytic activities of  $\text{CoRh}(\text{CO})_7$ , rhodium carbonyl, and cobalt carbonyl were estimated on the basis of the analysis of the regioselectivity of the reactions, we carried out kinetic measurements of these catalyst systems to obtain another independent supporting evidence for our estimation of the relative catalytic activities.

**(A) For Reactions in Hexane.** The rhodium-catalyzed reaction was carried out with PFS ( $5.0 \times 10^{-2}$  M) and  $\text{Rh}_4(\text{CO})_{12}$  ( $5.0 \times 10^{-5}$  M) in hexane at 80 °C [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 1$ )]. The reaction is first order, and the *apparent* rate constant for  $\text{Rh}_4(\text{CO})_{12}$  is calculated to be  $6.1 \times 10^{-4} \text{ s}^{-1}$ ; i.e., the turnover number is estimated to be  $10980 \text{ h}^{-1}/\text{Rh}$ .

The cobalt-catalyzed reaction was carried out at 80 °C [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 1$ )] with PFS (1.0 M) and  $\text{Co}_2(\text{CO})_8$  ( $5.0 \times 10^{-2}$  M) in hexane. The formation of aldehydes at a 6-h period was 6.0%, and the calculated *apparent* rate constant is  $2.8 \times 10^{-6} \text{ s}^{-1}$ ; i.e., the turnover number is estimated to be  $5.0 \times 10^{-2} \text{ h}^{-1}/\text{Co}$ . Thus, the relative catalytic activity of  $\text{Rh}_4(\text{CO})_{12}$  vs  $\text{Co}_2(\text{CO})_8$  is calculated to be 439 000. The value estimated on the basis of the regioselectivity analysis is 440 000 (*vide supra*).

As  $\text{CoRh}(\text{CO})_7$  should become a predominant catalyst species at the Co/Rh ratio of 40 (see Figure 4), the reaction was carried out with PFS (0.25 M),  $\text{Rh}_4(\text{CO})_{12}$  ( $1.0 \times 10^{-3}$  M), and  $\text{Co}_2(\text{CO})_8$  ( $8.0 \times 10^{-2}$ ) in hexane at 80 °C [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 1$ )]. The reaction was first order like the cases of the rhodium carbonyl and cobalt carbonyl, and the *regioselectivity did not change throughout the reaction*. The calculated rate constant is  $6.8 \times 10^{-4} \text{ s}^{-1}$ ; i.e., the estimated turnover number per  $\text{CoRh}(\text{CO})_7$  is  $612 \text{ h}^{-1}$ . Accordingly, the relative activity ratio of  $\text{Rh}_4(\text{CO})_{12}$  to  $\text{CoRh}(\text{CO})_7$  *per rhodium* is 17.9. The estimated value based on the regioselectivity analysis is 10 (*vide supra*).<sup>19</sup>

**(B) For Reactions in Dioxane.** The rhodium-catalyzed reaction was carried out under the same conditions to those employed for the reaction in hexane except the solvent. The reaction is clearly first order, and the *apparent* rate constant for  $\text{Rh}_6(\text{CO})_{16}$  is calculated to be  $1.9 \times 10^{-4} \text{ s}^{-1}$ ; i.e., the turnover number is estimated to be  $3420 \text{ h}^{-1}/\text{Rh}$ .

The cobalt-catalyzed reaction was performed in two ways. First, the reaction was carried out at 80 °C [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 1$ )] with PFS (1.0 M) and  $\text{Co}_2(\text{CO})_8$  ( $5.0 \times 10^{-2}$  M) in dioxane. The conversion at a 16-h period was only 4.1%, and the calculated *apparent* rate constant is ca.  $7.1 \times 10^{-7} \text{ s}^{-1}$ ; i.e., the turnover number is estimated to be  $2.6 \times 10^{-2} \text{ h}^{-1}/\text{Co}$ . Thus, the relative catalytic activity of  $\text{Rh}_6(\text{CO})_{16}$  vs  $\text{Co}_2(\text{CO})_8$  is calculated to be 398 000. The estimated value based on the regioselectivity analysis is 400 000 (*vide supra*). Second, the reactions were carried out at 100 and 120 °C under 1200 psi (82.8 bar) of carbon monoxide and hydrogen ( $\text{CO}/\text{H}_2 = 1$ ) with PFS (0.20 M) and  $\text{Co}_2(\text{CO})_8$  ( $6.0 \times 10^{-3}$  M) in dioxane. The reaction is first order, and the estimated turnover numbers at 100 and 120 °C are 2.3 and 9.2  $\text{h}^{-1}/\text{Co}$ , respectively. The activation energy estimated on the basis

(18) As for the kinetics of cobalt- and rhodium-catalyzed hydroformylation of olefins, it has been shown that the equation

$$d(\text{aldehyde})/dt = k[\text{olefin}]^x[\text{catalyst}]^yP_{\text{H}_2}/P_{\text{CO}}$$

is basic, where  $x = y = 1$  for cobalt catalysts; when rhodium catalysts are used,  $x$  and  $y$  vary depending on the reaction conditions.<sup>23</sup> Under the reaction conditions used in our experiments, Heil and Markó reported that the rate is first order to the concentration of olefin and of  $\text{Rh}_4(\text{CO})_{12}$ .<sup>23b</sup> Accordingly, we assumed the first-order relation of the reaction rate with the catalyst concentration for  $\text{CoRh}(\text{CO})_7$  in the calculations.

(19) Although further detailed studies are necessary to understand the mechanism of  $\text{CoRh}(\text{CO})_7$  catalysis, our current working hypothesis is that the active site of  $\text{CoRh}(\text{CO})_7$  is the rhodium moiety since the rhodium moiety is coordinatively unsaturated and the cobalt moiety acts as a ligand for the rhodium moiety, which is responsible to the distinct regioselectivity of this mixed-metal complex in comparison with simple rhodium and cobalt complexes. In fact, Horváth<sup>17</sup> and Roberts et al.<sup>24</sup> isolated the phosphine complexes of the type  $(\text{CO})_4\text{CoRh}(\text{CO})_{3-n}(\text{PR}_3)_n$  ( $n = 1, 2$ ), which implies the feasibility of the rhodium moiety for ligand substitution and thus the rhodium moiety as the reaction site in catalysis.

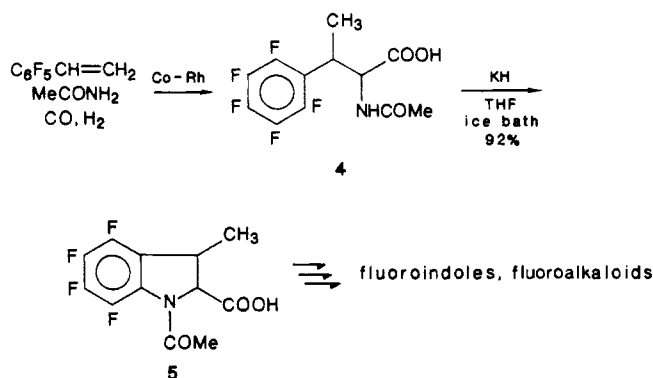
of Arrhenius plot is  $81.5 \text{ kJ}\cdot\text{mol}^{-1}$ , and the frequency factor is calculated to be  $3.5 \times 10^8 \text{ mol}^{-1}\cdot\text{L}\cdot\text{s}^{-1}$ . These results suggest that only a part of  $\text{Co}_2(\text{CO})_8$  is converted to  $\text{HCo}(\text{CO})_4$ , the active catalyst species, at  $80^\circ\text{C}$ , and thus the apparent rate constant and turnover number at  $80^\circ\text{C}$  is much smaller than the value expected from the given concentration of  $\text{Co}_2(\text{CO})_8$ . This observation corresponds well to the high-pressure IR study mentioned above. Namely, as shown in Figure 3c, only a partial conversion of  $\text{Co}_2(\text{CO})_8$  to  $\text{HCo}(\text{CO})_4$  was observed under almost the same conditions, i.e., at  $80^\circ\text{C}$  [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 1$ )] with  $\text{Co}_2(\text{CO})_8$  ( $4.0 \times 10^{-2} \text{ M}$ ) in dioxane.

The reaction with the Co/Rh ratio of 40 was carried out in dioxane under the same conditions to those employed for the reaction in hexane. The reaction was first order, and the regioselectivity did not change throughout the reaction, same as the reaction in hexane. The calculated rate constant is  $1.0 \times 10^{-3} \text{ s}^{-1}$ ; i.e., the estimated turnover number per  $\text{CoRh}(\text{CO})_7$  is  $900 \text{ h}^{-1}$ . Accordingly, the relative activity ratio of  $\text{Rh}_4(\text{CO})_{12}$  (or  $\text{Rh}_6(\text{CO})_{16}$ ) to  $\text{CoRh}(\text{CO})_7$  per rhodium is 3.8: The estimated value based on the regioselectivity analysis is 9 (vide supra).<sup>19</sup>

In order to investigate the catalysis of complicated mixed-metal systems like this, an introduction of a new scale besides the conventional kinetic measurements is necessary and powerful. We have demonstrated here a relevant example by successfully introducing "regioselectivity" as an excellent scale together with the equilibrium of components and the spectroscopic identification of catalyst species or their direct precursors in the actual reaction system:  $\text{CoRh}(\text{CO})_7$ ,  $\text{Rh}_4(\text{CO})_{12}$  (or  $\text{Rh}_6(\text{CO})_{16}$ ), and  $\text{Co}_2(\text{CO})_8$  have substantially different regioselectivities with respect to each other in the hydroformylation of PFS so that we can successfully analyze a rather complicated reaction. The estimated relative catalytic activity of  $\text{CoRh}(\text{CO})_7$  vs  $\text{Rh}_4(\text{CO})_{12}$  and  $\text{Rh}_6(\text{CO})_{16}$  based on the regioselectivity analysis showed a good agreement with that estimated by kinetic measurements in hexane as well as in dioxane in spite of several assumptions. Consequently, this study has provided a rare successful example of the elucidation of mixed-metal catalysis, in which actual active catalyst species and their direct precursors are detected spectroscopically and the observation corresponds almost perfectly to the mechanism proposed on the basis of the regioselectivity analysis.<sup>20</sup>

From the synthetic viewpoint, a highly regioselective production of the fluoroamino acids, **3** and **4**, is the ultimate goal. As for the synthesis of **4**, it can be said that the process is practical. For example, the  $\text{Co}_3\text{Rh}(\text{CO})_{12}$  catalyst (1.0 mol %) gives **4** in 74% yield with 92% regioselectivity at  $110^\circ\text{C}$  [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 3/1$ )], and the  $\text{Co}_2(\text{CO})_8$  (5.0 mol %)- $\text{Rh}_4(\text{CO})_{12}$  (0.05 mol %) catalyst system gives **4** in 80% yield with 98.2% regioselectivity at  $60^\circ$  for 6 h and then  $125^\circ\text{C}$  for 5 h under 1100 psi (75.9 bar) of CO and 700 psi (48.3 bar) of  $\text{H}_2$ . With regard to the synthesis of **3**, however, the single  $\text{Co}_2(\text{CO})_8$ -catalyzed process is not very efficient yet; although the regioselectivity of the reaction is high, 90–94%, the chemical yield is low, 30–35% mainly due to the hydrogenation of PFS (30–55%). Accordingly, we should search for another mixed-metal system that suppresses the hydrogenation without affecting high straight-chain selectivity of

Scheme III



cobalt carbonyl to overcome this problem.

*N*-Acetyl-3-(pentafluorophenyl)homocysteine (**4**; Scheme III) thus obtained can serve as a good precursor for fluoroindoles. Namely, the base-promoted cyclization of **5** gives *N*-acetyl-2-(hydroxycarbonyl)-3-methyl-2,3-dihydro-4,5,6,7-tetrafluoroindole (**5**) in 92% yield, which can be transformed to a variety of fluoroindoles and fluoroalkaloids.

In conclusion, the finding of novel  $\text{CoRh}(\text{CO})_7$ -catalyzed hydroformylation is worthy of note. It should also be noted that we have found a way to use any of the active catalyst species selectively among catalyst species in an equilibrium mixture like the one shown in eq 1 by choosing appropriate conditions such as metal-metal ratio, pressure, and temperature. The present approach has opened a new aspect of homogeneous catalysis and is applicable, in principle, to a variety of multistep catalytic processes.

## Experimental Section

**General Methods.** Boiling points and melting points are uncorrected. The  $^1\text{H}$  and  $^{19}\text{F}$  NMR spectra were measured on a Nicolet NT-300 with  $\text{Me}_4\text{Si}$  as the internal standard for  $^1\text{H}$  NMR and  $\text{CFCl}_3$  for  $^{19}\text{F}$  NMR. The IR spectra were recorded on a Perkin-Elmer 1310 or 1430 spectrophotometer. Analytical gas chromatography was carried out with a Hewlett-Packard 5830A or Perkin-Elmer 3920 with a Hewlett-Packard 3380A integrator with use of columns packed with OV-101, OV-17, or Dexsil 300. Preparative gas chromatography was performed with a Varian 90P with use of columns packed with 10% OV-17 or 30% SE-30. Analytical HPLC was carried out with a Waters HPLC system equipped with a Spectraphysics integrator with a reversed-phase column, Waters C18, and  $\text{MeOH}/\text{H}_2\text{O}/\text{AcOH}$  as eluting solvent.

**High-Pressure IR Spectroscopic Measurements.** High-pressure IR experiments were carried out with a 400-mL stainless-steel autoclave connected to a high-pressure IR cell of the type reported by Noack<sup>21</sup> equipped with a heating mantle modified by Dietler at ETH.<sup>22</sup> IR spectra were recorded on a Perkin-Elmer Model 983 spectrophotometer.

**Materials.** Pentafluorostyrene (PFS) was commercially available from SCM Chemicals, Inc., and was used as purchased. Dicobalt octacarbonyl and hexarhodium hexadecacarbonyl were purchased from Strem Chemicals, Inc. Tetrahydronium dodecacarbonyl was prepared by the literature method.

**Hydroformylation-Amidocarbonylation of PFS.** A typical reaction with  $\text{Rh}_4(\text{CO})_{12}$  and  $\text{Co}_2(\text{CO})_8$  is described. In a 300-mL stainless-steel autoclave was placed a Pyrex glass reaction vessel (20 mL) that contained a mixture of PFS (388 mg, 2.0 mmol), acetamide (236 mg, 4.0 mmol),  $\text{Rh}_4(\text{CO})_{12}$  (0.75 mg,  $1.0 \times 10^{-3}$  mmol),  $\text{Co}_2(\text{CO})_8$  (34.2 mg, 0.10 mmol) in degassed dioxane (3 mL), and a magnetic stirring bar under nitrogen. The autoclave was pressurized with carbon monoxide (100 psi; 6.9 bar), released three times to get rid of air, and then finally pressurized with 1100 psi (75.9 bar) of carbon monoxide. The autoclave was heated to  $60^\circ\text{C}$ , and hydrogen gas (700 psi; 48.3 bar) was introduced. After 6 h of reaction at  $60^\circ\text{C}$ , the autoclave was heated to  $125^\circ\text{C}$ , and the reaction was continued for an additional 5 h. Then, the autoclave was

(20) At this point, one may be curious about the reason why excellent regioselectivities were achieved in the hydroformylation-amidocarbonylation of TFP with  $\text{Rh}_6(\text{CO})_{16}$ - $\text{Co}_2(\text{CO})_8$  in which  $\text{CoRh}(\text{CO})_7$  should be generated as well. We did a preliminary study on the hydroformylation of TFP catalyzed by Co-Rh mixed-metal with  $\text{Rh}_4(\text{CO})_{12}$ - $\text{Co}_2(\text{CO})_{12}$  in a manner similar to the PFS case; all the reactions were run at  $80^\circ\text{C}$  [1200 psi (82.8 bar) ( $\text{CO}/\text{H}_2 = 1$ )] with a TFP/ $\text{Rh}_4(\text{CO})_{12}$  ratio of 1000 in dioxane by introducing  $\text{H}_2$  to the preheated and thus pre-equilibrated mixed-metal catalyst system with TFP. It was found that there was a clear dependency of regioselectivity on the Co/Rh ratio and a leveling phenomenon like the PFS case: e.g., iso/n = 29.7 at Rh 100; 14.2 at Co/Rh = 10; 8.6 at Co/Rh = 20; 5.7 at Co/Rh = 40; 4.7 at Co/Rh = 60; 3.3 at Co/Rh = 100. The observed iso/n ratio at relatively high Co/Rh ratio was substantially lower than the corresponding PFS case, which reflects a very small value of iso/n ratio (0.08) for the reaction catalyzed only by  $\text{Co}_2(\text{CO})_8$ . It is concluded that the high iso/n ratio (94/6) obtained in the hydroformylation-amidocarbonylation of TFP with  $\text{Rh}_6(\text{CO})_{16}$  (0.1 mol %)- $\text{Co}_2(\text{CO})_8$  (5 mol %) (vide supra)<sup>7</sup> is ascribed to the very fast hydroformylation of TFP by rhodium-catalyst species before the Co-Rh mixed-metal system reached an equilibrium.

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cooled to 0 °C with an ice bath, and the gases were purged carefully. The solvent was evaporated, and 10% aqueous sodium carbonate was added to the residue. After the resulting aqueous solution was washed with ether (GLC analysis showed the 3% formation of ethylpentafluorobenzene, hydrogenation product), the solution was acidified by phosphoric acid to pH 3 and extracted with ethyl acetate. The extract was dried over anhydrous magnesium sulfate, and the solvent was evaporated to give *N*-acetyl(pentafluorophenyl)homoalanine (498 mg) in 80% yield as colorless solid. The HPLC analysis with benzamide as the internal standard showed that the product consists of 98.2% of 3-pentafluorophenyl isomer (**4**; 65/35 diastereomeric mixture) and 1.8% of 4-pentafluorophenyl isomer (**3**). Pure **4** was obtained by recrystallization from CH<sub>2</sub>Cl<sub>2</sub>-hexane.

**4 (a mixture of diastereomers)**: colorless solid; mp 155–168 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>/CD<sub>3</sub>OD) δ 1.44 (d, *J* = 6.5 Hz, major), 1.46 (d, *J* = 6.5 Hz, minor) (3 H), 1.90 (s, minor), 2.02 (s, major) (3 H), 3.68 (m, 1 H), 4.88 (m, 1 H); <sup>19</sup>F NMR (acetone-*d*<sub>6</sub>) δ -141.1 (dd, *J* = 21.6, 6.9 Hz, minor), -141.6 (dd, *J* = 21.8, 6.1 Hz, major) (2 F), -158.1 (t, *J* = 20.5 Hz, major), -158.2 (t, *J* = 20.4 Hz, minor) (1 F), -164.1 (m, 2 F); IR (KBr disk) 3340 (ν<sub>NH</sub>), 1710, 1610 (ν<sub>C=O</sub>), 1545 (δ<sub>NH</sub>) cm<sup>-1</sup>. Anal. Calcd for C<sub>12</sub>H<sub>10</sub>F<sub>5</sub>NO<sub>3</sub>: C, 46.31; H, 3.24; N, 4.50. Found: C, 46.37; H, 3.34; N, 4.61.

Similarly, the reactions with Co<sub>2</sub>Rh<sub>2</sub>(CO)<sub>12</sub> and Co<sub>3</sub>Rh(CO)<sub>12</sub> were carried out.

The Co<sub>2</sub>(CO)<sub>8</sub>-catalyzed reaction was carried out in a similar manner at 125 °C [(600 psi) (CO/H<sub>2</sub> = 1)] for 15 h and at 125 °C [1800 psi (124.2 bar) (CO/H<sub>2</sub> = 5/1)] for 6 h with 5 mol % of the catalyst. The reaction gave *N*-acetyl(pentafluorophenyl)homoalanine in 30% yield: **3/4** = 93.5/6.5 based on HPLC analysis. Pure **3** was obtained by recrystallization from CH<sub>2</sub>Cl<sub>2</sub>-hexane.

**3**: colorless solid; mp 174–175 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>/CD<sub>3</sub>OD) δ 2.03 (s, 3 H), 2.10 (m, 2 H), 2.80 (t, *J* = 7.8 Hz, 2 H), 4.48 (m, 1 H); <sup>19</sup>F NMR (CDCl<sub>3</sub>/CD<sub>3</sub>OD) δ -144 (m, 2 F), -158 (m, 1 F), -163 (m, 2 F); IR (KBr disk) 3380 (ν<sub>NH</sub>), 1712, 1623 (ν<sub>C=O</sub>), 1556 (δ<sub>NH</sub>) cm<sup>-1</sup>. Anal. Calcd for C<sub>12</sub>H<sub>10</sub>F<sub>5</sub>NO<sub>3</sub>: C, 46.31; H, 3.24; N, 4.50. Found: C, 46.26; H, 3.40; N, 4.44.

**Hydroformylation of PFS**. The hydroformylation of PFS was carried out in a manner similar to that of the hydroformylation-amidocarbonylation. Typically, a solution of 1.0 mmol of PFS in 1.0 mL of dioxane in a 10-mL Pyrex glass reaction vessel was used. The reaction was allowed to start by introducing hydrogen to the reaction system, which was charged only with carbon monoxide, at the given reaction temperature. After the given period of time, the reaction was stopped by cooling to 0 °C and releasing the gases, and the reaction mixture thus obtained was immediately submitted to GLC analyses with tridecane as the internal standard.

The standard substrate/catalyst molar ratio used was 1000 for Rh<sub>4</sub>(CO)<sub>12</sub>, Rh<sub>6</sub>(CO)<sub>16</sub>, Co<sub>2</sub>Rh<sub>2</sub>(CO)<sub>12</sub>, and Co<sub>3</sub>Rh(CO)<sub>12</sub>.

Pure 2-(pentafluorophenyl)propanal (2-PFPPA) and 3-(pentafluorophenyl)propanal (3-PFPPA) were obtained from larger scale experiments catalyzed by Rh<sub>6</sub>(CO)<sub>16</sub> and Co<sub>2</sub>(CO)<sub>8</sub> respectively, through distillation.

**2-PFPPA**: bp 96 °C (21 mmHg); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.56 (d, *J* = 7.4 Hz, 3 H), 3.93 (q, *J* = 7.4 Hz, 1 H), 9.73 (t, *J* = 2.1 Hz, 1 H); <sup>19</sup>F NMR (acetone-*d*<sub>6</sub>) δ -142.4 (dd, *J* = 21.4 Hz, 7.2 Hz, 2 F), -156.9 (t, *J* = 20.3 Hz, 1 F), -163.4 (ddd, *J* = 21.4, 20.3, 7.2 Hz, 2 F); IR (neat) 1740 (ν<sub>C=O</sub>) cm<sup>-1</sup>; MS (*m/e*) 224 (4, M<sup>+</sup>), 195 (100). Anal. Calcd for C<sub>9</sub>H<sub>5</sub>F<sub>5</sub>O: C, 48.23; H, 2.25. Found: C, 48.00; H, 2.21.

**3-PFPPA**: <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.79 (t, *J* = 7.5 Hz, 2 H), 3.02 (t, *J* = 7.5 Hz, 2 H), 9.81 (br s, 1 H); <sup>19</sup>F NMR (acetone-*d*<sub>6</sub>) δ -144.0 (dd, *J* = 21.9, 7.9 Hz, 2 F), -159.2 (t, *J* = 20.3 Hz, 1 F), -164.3 (ddd, *J* = 21.9, 20.3, 7.9 Hz, 2 F); IR (neat) 1740 (ν<sub>C=O</sub>) cm<sup>-1</sup>; MS (*m/e*) 224 (15, M<sup>+</sup>), 181 (100). Anal. Calcd for C<sub>9</sub>H<sub>5</sub>F<sub>5</sub>O: C, 48.23; H, 2.25. Found: C, 47.91; H, 2.26.

**Competitive Amidocarbonylation of 2-PFPPA and 3-PFPPA**. A mixture of 2-PFPPA (135 mg, 0.6 mmol) and 3-PFPPA (135 mg, 0.6 mmol), acetamide (9.0 mg, 0.15 mmol), and Co<sub>2</sub>(CO)<sub>8</sub> (20 mg, 0.06 mmol) in dioxane (2.5 mL) in a Pyrex reaction vessel was placed in a 300-mL autoclave. The autoclave was charged with carbon monoxide (1200 psi, 82.8 bar) and hydrogen (300 psi, 20.7 bar) and heated at 115 °C for 17 h with stirring. After the gases were released, the reaction mixture was subjected to the standard workup for amidocarbonylation

(vide infra) to give a mixture of **3** and **4**. The yields of **3** and **4** based on acetamide were 65% and 26%, respectively, by HPLC analysis. Thus, the reactivity ratio of 2-PFPPA to 3-PFPPA is 2.5 based on the formation of the amino acids, **3** and **4**.

**Kinetic Study of the Hydroformylation of PFS**. The kinetic measurements were carried out in a 300-mL autoclave with periodic sampling at the given temperature. A mixture of a catalyst and PFS in degassed dioxane was transferred to the autoclave, and carbon monoxide was introduced. The mixture was heated to the given temperature, and the pressure of carbon monoxide was adjusted to 600 psi (41.4 bar). After the mixture was stirred a certain period of time, i.e., 30 min for Rh<sub>4</sub>(CO)<sub>12</sub> or Co<sub>2</sub>(CO)<sub>8</sub> and 24 h for the Rh-Co mixed system, hydrogen (600 psi; 41.4 bar) was introduced to the autoclave to start the reaction. For the Rh<sub>4</sub>(CO)<sub>12</sub>-catalyzed reaction, 5.0 × 10<sup>-2</sup> M PFS and 5.0 × 10<sup>-5</sup> M Rh<sub>4</sub>(CO)<sub>12</sub> in 50 mL of dioxane were used. For the Co<sub>2</sub>(CO)<sub>8</sub>-catalyzed reaction, 0.2 M PFS and 6.0 × 10<sup>-3</sup> M Co<sub>2</sub>(CO)<sub>8</sub> in 50 mL of dioxane were used. For the reaction catalyzed by the Co-Rh mixed-metal system, 0.25 M PFS, 1.0 × 10<sup>-3</sup> M Rh<sub>4</sub>(CO)<sub>12</sub>, and 8.0 × 10<sup>-2</sup> M Co<sub>2</sub>(CO)<sub>8</sub> in 50 mL of dioxane were used. In every case, the aldehyde formation gave clean first-order plots, and some induction periods were observed, which may well be ascribed to the time for saturation of hydrogen in the reaction system and for generation of active catalyst species, especially for the cobalt case, since hydrogen was separately added at the given reaction temperature.

The kinetic measurements for the reactions in *n*-hexane were performed in essentially the same manner under the same conditions as the dioxane case except the solvent.

As a side reaction associated with the hydroformylation of PFS, the hydrogenation of PFS giving C<sub>6</sub>F<sub>5</sub>C<sub>2</sub>H<sub>5</sub> was observed. The extent of the hydrogenation for the rhodium-catalyzed reaction in hexane or dioxane was negligible (<0.5%). However, for the cobalt-catalyzed reaction, the aldehyde/alkane ratios were 2.5 in hexane and 8.0 in dioxane, and for the Co-Rh mixed-metal catalyzed reaction (Co/Rh = 40), the aldehyde/alkane ratios were 1.53 in hexane and 1.94 in dioxane.

**Synthesis of 5 from 4 through Cyclization**. To a solution of **4** (112 mg, 0.36 mmol) in THF (20 mL) was added potassium hydride (119 mg, 2.99 mmol) at 0–5 °C, and the mixture was stirred vigorously for 20 h. The progress of the reaction was occasionally monitored by TLC. The reaction was quenched by water, and the reaction mixture was extracted with ethyl acetate to remove possible organic byproducts. Then, the aqueous layer was acidified with phosphoric acid to pH 3 and was extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate, treated with Norit, and concentrated to give a viscous oil (120 mg). The viscous oil thus obtained was submitted to a column chromatography on silica gel with chloroform-methanol (7/3) as eluant to give *N*-acetyl-2-(hydroxycarbonyl)-3-methyl-2,3-dihydro-4,5,6,7-tetrafluoroindole (**5**) (100 mg) in 95.4% yield. <sup>1</sup>H NMR analysis of **5** thus obtained showed that **5** was a mixture of two diastereomers (2,3-*trans*-**5**/2,3-*cis*-**5** = 55/45).

**5 (a mixture of diastereomers)**: colorless solid; mp 225–228 °C; <sup>1</sup>H NMR (acetone-*d*<sub>6</sub>) (2,3-*cis*-**5**) δ 1.50 (dd, *J* = 7.1, 0.6 Hz, 3 H), 2.25 (d, *J* = 3.1 Hz, 3 H), 4.32 (dq, *J* = 9.5, 7.1 Hz, 1 H), 5.28 (d, *J* = 9.5 Hz, 1 H); <sup>1</sup>H NMR (acetone-*d*<sub>6</sub>) (2,3-*trans*-**5**) δ 1.46 (d, *J* = 7.0 Hz, 3 H), 2.32 (d, *J* = 2.3 Hz, 3 H), 3.90 (dd, *J* = 7.0, 1.4 Hz, 1 H), 4.98 (d, *J* = 1.4 Hz, 1 H); <sup>19</sup>F NMR (acetone-*d*<sub>6</sub>) (2,3-*cis*-**5**) δ -163.9 (m, 1 F), -157.9 (m, 1 F), -147.5 (m, 1 F), -141.0 (m, 1 F); <sup>19</sup>F NMR (acetone-*d*<sub>6</sub>) (2,3-*trans*-**5**) δ -163.0 (m, 1 F), -157.3 (m, 1 F), -146.7 (m, 1 F), -140.2 (m, 1 F); IR (KBr disk) 3600–2800 (ν<sub>OH</sub>), 1645 (ν<sub>C=O</sub>) cm<sup>-1</sup>. Anal. Calcd for C<sub>12</sub>H<sub>9</sub>F<sub>4</sub>NO<sub>3</sub>: C, 49.49; H, 3.12. Found: C, 49.68; H, 3.41.

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