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CARBONYLATION OF 1-PERFLUOROALKYL-SUBSTITUTED 2-IODOALKANES CATALYZED BY TRANSITION-METAL COMPLEXES

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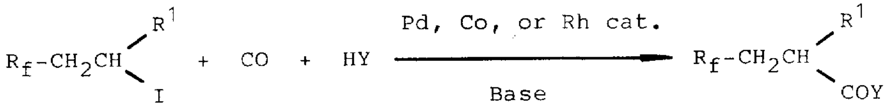
Abstract: *Carboxylic acids and esters with perfluoroalkyl substituent at β position were synthesized in good yields from 1-perfluoroalkyl-substituted 2-iodoalkanes and carbon monoxide with water or alcohols in the presence of base by using group VIII transition-metal complexes as catalysts.*

We have already reported that palladium-catalyzed carbonylation of perfluoroalkyl iodides with terminal alkynes or alkenes under carbon monoxide pressure in the presence of potassium carbonate in alcohols, namely "carbo-carbonylation reactions", directly affords β-perfluoroalkyl-substituted alkenoates or alkanoates, respectively.1) We have proposed that β-perfluoroalkyl-substituted alkenyl- and alkyl-palladium species may be formed as the key intermediates in these carbonylations and they readily undergo insertion of carbon monoxide faster than β-hydrogen elimination of the organopalladium species. These findings strongly suggest us that the similar alkyl-metal species may be generated by oxidative addition of 1-perfluoroalkyl-substituted 2-iodoalkanes, which can be easily prepared from perfluoroalkyl iodides and olefins,2) to low valent transition-metal complexes. If β-hydrogen elimination from the intermediates are slower than CO insertion as observed in the carbo-carbonylation, a variety of fluorine-containing carboxylic acid derivatives can be synthesized by transition-metal catalyzed carbonylations3-5) of these iodides.

Here, we wish to report carbonylations of 1-perfluoroalkyl-substituted 2-iodoalkanes (**1**) with water and alcohols in the presence of base catalyzed with palladium, cobalt, and rhodium complexes producing the corresponding carboxylic acids and esters, respectively (Eq. 1).

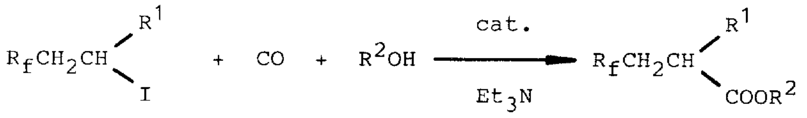


$$R_f\text{-}CH_2CH(R^1)I + CO + HY \xrightarrow[\text{Base}]{\text{Pd, Co, or Rh cat.}} R_f\text{-}CH_2CH(R^1)COY \qquad (1)$$

1

R_f = perfluoroalkyl group; HY = R^2OH, H_2O

Table 1. Esterification of **1** Catalyzed by Transition-Metal Complexes



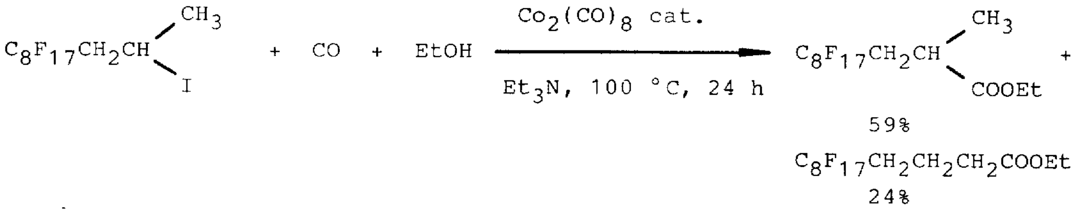
$$\mathrm{R_fCH_2CH}\genfrac{}{}{0pt}{}{\mathrm{R^1}}{\mathrm{I}} + \mathrm{CO} + \mathrm{R^2OH} \xrightarrow[\mathrm{Et_3N}]{\mathrm{cat.}} \mathrm{R_fCH_2CH}\genfrac{}{}{0pt}{}{\mathrm{R^1}}{\mathrm{COOR^2}}$$

1

Run	R_f	R^1	R^2	cat[a]/mol%	CO/atm	Temp./°C	Time/h	Yield/%
1	n-C_8F_{17}	Bu	Et	A/5	30	80	12	73
2				B/5	30	80	12	83
3				D/5	30	80	12	48
4			Me	A/5	30	80	12	68
5			Bu	A/5	30	80	12	53
6		H	Et	A/5	30	80	12	74
7				C/10	50	100	24	85
8				E/1.9	50	100	24	66
9				F/5	50	100	24	10
10		Me	Et	A/5	50	100	24	88
11				C/10	50	100	24	83[b]
12				E/0.8	50	100	24	70
13	n-C_6F_{13}	H	Et	A/10	30	100	12	57
14	n-C_4F_9	H	Bu	A/5	30	80	12	44
15		Hex	Et	A/5	30	80	12	54
16	CF_3	H	Et	A/10	30	80	24	93
17				C/10	50	100	24	65

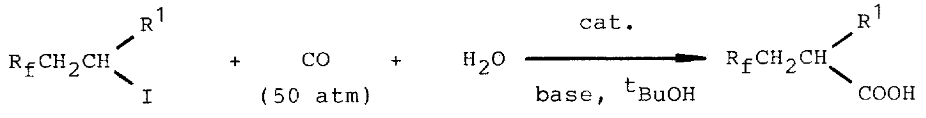
a) A: $(Ph_3P)_2PdCl_2$, B: $(dppf)PdCl_2$ (dppf=1,1'-bis(diphenylphosphino)-ferrocene), C: $Co_2(CO)_8$, D: $RhCl(PPh_3)_3$, E: $Rh_6(CO)_{16}$, F: $(Ph_3P)_2PtCl_2$.
b) A mixture of regioisomers (see Eq. 2).

Initially, we investigated esterification of 1-perfluorooctyl-2-iodohexane under the similar conditions to the carbo-carbonylation,[1] using $(Ph_3P)_2PdCl_2$ catalyst under CO pressure (30 atm) in the presence of K_2CO_3 in ethanol. However, ethyl 3-perfluorooctylpropionate was obtained in only 9% yield, the main product being 1-perfluorooctyl-1-hexene, which can be formed by elimination of hydrogen iodide from the starting iodide. On the other



$$\mathrm{C_8F_{17}CH_2CH}\genfrac{}{}{0pt}{}{\mathrm{CH_3}}{\mathrm{I}} + \mathrm{CO} + \mathrm{EtOH} \xrightarrow[\mathrm{Et_3N,\ 100\ ^\circ C,\ 24\ h}]{\mathrm{Co_2(CO)_8\ cat.}} \underset{59\%}{\mathrm{C_8F_{17}CH_2CH}\genfrac{}{}{0pt}{}{\mathrm{CH_3}}{\mathrm{COOEt}}} + \underset{24\%}{\mathrm{C_8F_{17}CH_2CH_2CH_2COOEt}} \quad (2)$$

Table 2. Carboxylation of **1** Catalyzed by Transition-Metal Complexes



1

Run	R_f	R^1	cat[a]/mol%	base/eq.	Temp./°C	Time/h	Acid/%
1	C_8F_{17}	H	A/10	Et_3N/1	80	48	58
2			A/10	KF/2	80	48	85
3			A/10	$Ca(OH)_2$/1	80	48	42[b]
4			B/0.8	$Ca(OH)_2$/1	120	24	60
5			C/5	KF/2	80	15	89
6	C_8F_{17}	Bu	A/10	Et_3N/1	80	48	63[c]
7			A/10	KF/2	80	48	84[c]
8			A/10	$Ca(OH)_2$/2	120	24	46[c]
9	CF_3	H	A/10	Et_3N/1	80	48	61

a) A: $Co_2(CO)_8$, B: $Rh_6(CO)_{16}$, C: $(Ph_3P)_2PdCl_2$. b) α-Keto acid was also formed in 16% yield. c) $C_8F_{17}(CH_2)_6COOH$ was also produced in 10% (Run 6), 2% (Run 7), and 22% (Run 8) yields, respectively.

hand, the desired ester was produced in 73% yield when triethylamine was employed as the base. To our knowledge, this is the first example of palladium-catalyzed effective carbonylation of alkyl iodides. The conversion of the iodide as well as the yield of ester was very low when aromatic amine such as pyridine or 2,6-lutidine was used as the base. We found that not only Pd but also Co and Rh catalysts exhibit high catalytic activities in the present esterification, whereas Pt-phosphine complex is much less active toward these fluorinated iodides (Run 9).[5] Representative results are summarized in Table 1. Interestingly, a mixture of regioisomers of the ester was obtained from secondary alkyl iodides only in the case of Co catalyst (Run 10) as shown in Eq. 2. This result shows that the CO insertion into initially formed *sec*-alkyl-cobalt intermediate and its isomerization to *n*-alkyl-cobalt species can compete with each other.

The next approach was carboxylic acids synthesis by the reaction of **1** and CO with water in the presence of transition-metal catalyst and base. Among the group VIII transition-metal complexes examined as a catalyst, Co, Pd, and Rh complexes were effective for the carboxylation of **1** in ^tBuOH at 80-120 °C. It is noteworthy that the selection of base is also very important in the present reaction. By using $Ca(OH)_2$ as the base[6], doubly carbonylated product, α-keto acid, as well as singly carbonylated acid were observed in the reaction of primary alkyl iodides (R^1 = H) catalyzed by $Co_2(CO)_8$ (Run 3).[7] Under the similar reaction conditions as above, however, double carbonylation did not proceed at all when secondary alkyl iodide (R^1 = Bu) was used as the starting material (Run 8). In this case, the formation of isomeric linear acid $C_8F_{17}(CH_2)_6COOH$ was observed in 22% yield with the desired acid (46%). Potassium fluoride was the most suitable base from a viewpoint of the selectivity of the products.

As shown here, various types of transition-metal catalyzed carbonylations of 1-perfluoroalkyl-substituted 2-iodoalkanes easily proceed in the presence of appropriate base in moderate to good yields. These results suggest that the introduction of perfluoroalkyl groups into organic molecules can modify their reactivities and selectivities toward transition-metal catalyzed reactions. Further applications and precise mechanistic studies of these reactions are in progress.

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