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Rhodium-catalyzed interconversion between acid fluorides and thioesters controlled using heteroatom acceptors

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ABSTRACT

A rhodium complex catalyzed the equilibrium acyl transfer reaction between acid fluorides and thioesters. In the presence of fluoride or thiolate acceptors, the reaction could be shifted to either product. $RhH(PPh_3)_4$-dppe catalyzed the reaction of acid fluorides and diorgano disulfides in the presence of triphenylphosphine giving thioesters, which was accompanied by triphenylphosphine difluoride. The same complex catalyzed the reaction of aryl thioesters and hexafluorobenzene giving acid fluorides, which was accompanied by 1,4-di(arylthio)-2,3,5,6-tetrafluorobenzenes.

1. Introduction

A catalyst is a substance that changes the reaction course without affecting the relative stability of substrates and products. The development of an efficient catalyst, which decreases the activation energy of the reaction, results in equilibrium when the relative thermodynamic stabilities of the substrates and products are close. We found that a transition-metal complex could be used as a catalyst in the synthesis and transformation of organosulfur and organophosphorus compounds,[1] and that, in some cases, such reactions exhibit equilibrium. For example, organothio groups are exchanged among disulfides,[2] thioalkynes,[3] thioesters,[4] and thioketones.[5] Therefore, the control of equilibrium reactions to provide desired products with high efficiency has become a subject of interest.

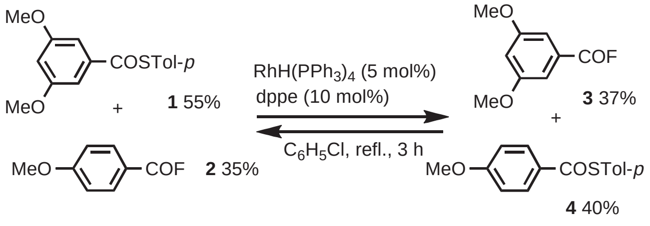
We found that the acyl transfer reaction between thioesters and acid fluorides could be catalyzed by a rhodium catalyst. When *S*-(*p*-tolyl) 3,5-dimethoxybenzothioate **1** and *p*-methoxybenzoyl fluoride **2** were treated with $RhH(PPh_3)_4$ (5 mol %) and dppe (10 mol %) in refluxing chlorobenzene for 3 h, a mixture of 3,5-dimethoxybenzoyl fluoride **3** (37%) and *S*-(*p*-tolyl) *p*-dimethoxybenzothioate **4** (40%) was obtained with the recovery of **1** (55%) and **2** (35%) (Scheme 1). No reaction occurred in the absence of the rhodium catalyst.

In order that thioesters or acid fluorides can be obtained effectively, a device for shifting the equilibrium reaction is required. In this work, it has been shown that acid fluorides could be converted to thioesters in the presence of triphenylphosphine, and the reverse reaction could be conducted in the presence of hexafluorobenzene (Scheme 2). The use of sulfur or fluoride acceptors effectively shifted the equilibrium reaction.

Benzoyl fluoride (1 equiv), di(*p*-tolyl) disulfide (0.5 equiv), and triphenylphosphine (0.5 equiv)[6] were reacted in refluxing THF for 3 h in the presence of $RhH(PPh_3)_4$ (0.1 mol %) and dppe (0.2 mol %), and *S*-(*p*-tolyl) benzothioate was obtained with a 88% yield (Table 1, entry 1). The yield increased to 100% using 1 mol % of the rhodium complex. The formation of triphenylphosphine difluoride was confirmed by ^{19}F NMR δ −42.9 and ^{31}P NMR δ −55.0 absorptions of the crude products.[6]

The method was applied to the synthesis of various acid fluorides and disulfides (Table 1). For the reaction of aroyl fluorides and diaryl disulfides, a small effect of the aromatic *p*-substituents was observed for both aroyl and arylthio moieties (entries 1–4 and 8–10). The reaction of aliphatic disulfides also proceeded smoothly (entries 5–7). Aliphatic acid fluorides could react with di(*p*-tolyl) disulfide (entries 11–14). In some cases, the catalyst loading could be reduced to 0.1 mol % (entries 1–5).

The synthesis of thioesters has generally been conducted using acid chlorides or anhydrides and thiols in the presence of a base. It is notable that the present method produces thioesters from acid fluorides without using a strong base under transition-metal catalysis.[7] It was then considered interesting to compare the reactivities of benzoyl fluoride and chloride, which revealed the notable



Scheme 1.

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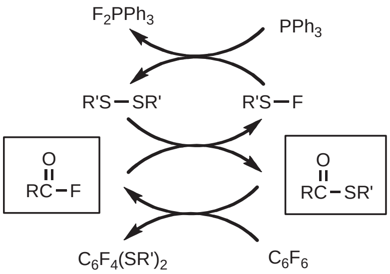
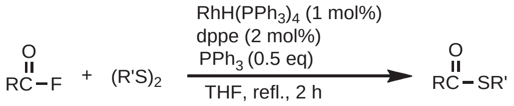


Scheme 2.

Table 1
Rhodium-catalyzed reaction of acid fluorides and disulfides



Entry	R	R′	Yield (%)
1	Ph	*p*-Tol	88,[a] 100
2		*p*-ClC$_6$H$_4$	22,[a] 88[b]
3		*p*-MeOC$_6$H$_4$	85[a]
4		Ph	91[a]
5		PhCONH(CH$_2$)$_2$	89[a]
6		PhCOO(CH$_2$)$_3$	86[c]
7		*n*-C$_8$H$_{17}$	63[c]
8	*p*-ClC$_6$H$_4$	*p*-Tol	99
9	*p*-MeOC$_6$H$_4$	*p*-Tol	86
10	*p*-MeC$_6$H$_4$	*p*-Tol	88
11	*n*-C$_{11}$H$_{23}$	*p*-Tol	92
12	Ph(CH$_2$)$_2$	*p*-Tol	90
13	(*n*-Pr)$_2$CH	*p*-Tol	80
14	*n*-PrMe$_2$C	*p*-Tol	82

[a] RhH(PPh$_3$)$_4$ (0.1 mol %), dppe (0.2 mol %), reaction time 5 h.
[b] RhH(PPh$_3$)$_4$ (0.5 mol %), dppe (1 mol %).
[c] RhH(PPh$_3$)$_4$ (5 mol %), dppe (10 mol %).

Table 2
Reaction of benzoyl fluoride and chloride with di(*p*-tolyl) disulfide

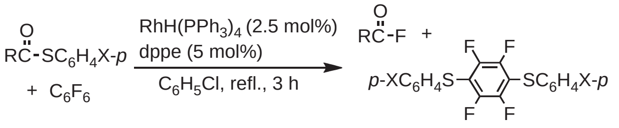
Entry	Catalyst	PPh$_3$	Temp	Yield (%)	
				X = F	X = Cl
1	None	None	Refl.	ND	ND
2	None	0.5 Equiv	rt	ND	13
3	RhH(PPh$_3$)$_4$ (1 mol %) dppe (2 mol %)	0.5 Equiv	rt	45	20

ND: Not detected.

reactivity of the acid fluoride under rhodium catalysis (Table 2). It was first confirmed that no reaction occurred when benzoyl fluoride or chloride was reacted with di(*p*-tolyl) disulfide under THF reflux for 2 h (entry 1). In the presence of triphenylphosphine (0.5 equiv), the acid chloride gave a small amount of thioester (13%) at room temperature, but the acid fluoride did not, which revealed the lower reactivity of the latter (entry 2). When RhH(PPh$_3$)$_4$ (1 mol %) and dppe (2 mol %) were added to the mixtures, the reaction of the acid chloride slightly improved, giving a thioester with 20% yield, whereas the acid fluoride gave the same product with 45% yield. It was shown that the acid fluoride is specifically activated by the rhodium complex.

The reverse reaction for the synthesis of acid fluorides from thioesters was then examined in the presence of an organothio acceptor. The reaction of *S*-(*p*-tolyl) *p*-methoxybenzothioate **4** and hexafluorobenzene[6] (2 equiv) in the presence of RhH(PPh$_3$)$_4$ (2.5 mol %) and dppe (5 mol %) in refluxing chlorobenzene for 3 h gave *p*-methoxybenzoyl fluoride **2** and 1,4-di(*p*-tolylthio)-2,3,5,6-tetrafluorobenzene[7] with 94% and 99% yields, respectively (Table 3, entry 1). No reaction occurred in the absence of the rhodium complex or dppe. Hexafluorobenzene is a reactive organosulfur acceptor compared with *p*-fluoronitrobenzene, which gave **2** with 85% yield along with 4-(*p*-tolylthio)nitrobenzene (87%). The reaction also proceeded under THF reflux conditions, that is, thioester synthesis conditions, giving a modest yield (42%) of product **2**.

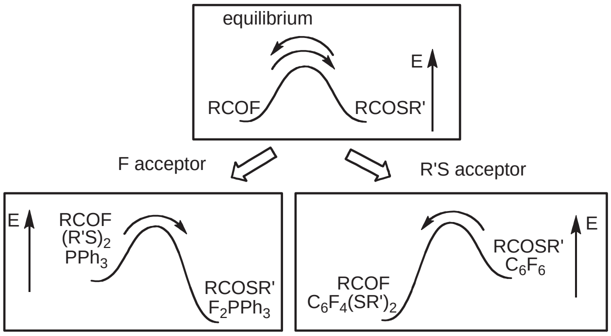
Table 3
Rhodium-catalyzed reaction of thioesters and hexafluorobenzene



Entry	R	X	Yield (%)
1	*p*-MeOC$_6$H$_4$	Me	94
2		OMe	83
3		H	83
4		Cl	85
5	*p*-EtOC$_6$H$_4$	Me	88
6	3,5-(MeO)$_2$C$_6$H$_3$	OMe	73
7	*p*-Me$_2$NC$_6$H$_4$	OMe	90
8	*p*-ClC$_6$H$_4$	OMe	30
9	*n*-C$_9$H$_{19}$	OMe	65
10	PhCH$_2$CH$_2$	OMe	72
11	4-(*t*-Butyl)cyclohexyl	OMe	80
12	1-Adamantyl	OMe	82

A notable *p*-substituent effect of the aroyl moiety was shown by a higher yield of *p*-methoxybenzothioate than that of *p*-chlorobenzothioate (entries 2 and 6–8). The aromatic substituent effect at the arylthio moiety was small in this reaction (entries 1–4). *S*-Octyl *p*-methoxybenzoate gave a very small amount of acid fluoride under the conditions used. The slightly different effects of the substituents in the thioester formation (Table 1) and acid fluoride formation (Table 3) may be due to the difference in efficiency between the CO–S and CO–F bond cleavages. Acid fluorides were generally synthesized from carboxylic acids by treating them with reactive fluorinating reagents such as DAST or cyanuric fluoride;[8,9] however, the transition-metal-catalyzed synthesis of acid fluorides from thioesters using a stable fluorinating reagent may also be an interesting approach.

The rhodium catalyst equilibrated the acyl transfer reaction between acid fluorides and thioesters, and the use of fluoride or thiolate acceptors shifted the reaction for the synthesis of either product. The use of triphenylphosphine promoted the formation



Scheme 3.

of thioesters, and hexafluorobenzene promoted that of acid fluorides (Scheme 3). The acceptors were employed to change the relative thermodynamic stabilities of the substrates and products. The conversion of triphenylphosphine to difluoride promoted the formation of thioesters and that of hexafluorobenzene to aryl sulfide promoted the formation of acid fluorides.

2. Typical experimental procedures

In a two-necked flask equipped with a reflux condenser were placed benzoyl fluoride (620 mg, 5.0 mmol), *p*-tolyl disulfide (615 mg, 2.5 mmol), $RhH(PPh_3)_4$ (5.8 mg, 0.1 mol %), 1,2-bis(diphenylphosphino)ethane (4.0 mg, 0.2 mol %), and triphenylphosphine (655 mg, 50 mol %) in tetrahydrofuran (2 mL) under an argon atmosphere, and the solution was stirred under reflux for 2 h. The solvent was removed under reduced pressure, and $RhH(PPh_3)_4$ was removed by short flash column chromatography on silica gel. The eluents were concentrated under reduced pressure, and the residue was purified by flash column chromatography on silica gel giving *S*-(*p*-tolyl) benzothioate (1.006 g, 88%).

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.09.009.

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