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Fluorous biphasic catalysis with dirhodium(II) perfluorocarboxylates: selective silylation of alcohols under fluorous biphasic conditions

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Abstract—Dirhodium(II) perfluorocarboxylates bearing C7–C13 perfluoroalkyl chains have been prepared and used as catalysts under fluorous biphasic conditions. They were found to be active and recyclable catalysts for the silylation of alcohols with triethylsilane. Hydrophobic, primary alcohols are preferentially silylated by the fluorous biphasic catalytic system in comparison with hydrophilic or secondary ones. This opens the way to the development of selective silylation protocols.

1. Introduction

The synthetic potential of dirhodium(II) carboxylates and carboamidates as catalysts for organic syntheses, most notably those involving diazocompounds, has been disclosed in the course of the last years.[1] There is an impressive variety of chemical transformations that can be mediated by such compounds, including cyclopropanations, insertions into C–H and N–H bonds, ylide formations and dipolar cycloaddition reactions; efficient asymmetric variants of many of these reactions have been developed as well.[1,2] The chemo-, regio- and stereoselectivity of these processes is chiefly influenced by the nature of the coordination sphere surrounding the metal centre.[3] In particular, dirhodium(II) perfluoroacetates and perfluorobutyrates have been shown to be exceptionally useful for insertions in C–H bonds[3,4] and for the synthesis of (*Z*)-α,β-unsaturated carbonyl compounds.[5] Furthermore, *tetrakis* dirhodium(II) perfluorobutyrate, introduced by Doyle towards the end of the eighties, proved to be an excellent catalyst not only for reactions involving diazocompounds, but also for a series of other processes involving silanes, such as silylcarbonylations of alkynes,[6] hydrosilylations of alkynes and alkenes,[7,8] as well as silylations of alcohols.[9]

In spite of the potential of these catalysts, one of the fundamental problems for their industrial application is the need for efficient catalyst recovery and recycling. In this connection, a novel approach has been recently developed, based on the use of biphasic systems in which the catalyst is soluble in one phase whereas reagents and products are soluble in the other; in this case, simple phase separation allows the isolation and recycling of the catalysts.[10] The major successes (two large-scale industrial applications) have been so far achieved with aqueous biphasic catalysis, in which the catalyst is dissolved in an aqueous phase and reagents and products in an organic phase.[11] However, such a strategy is neither applicable to substrates and reactions which are water-sensitive, nor to hydrophobic reagents which react too slowly with the water-confined catalyst. A recently proposed alternative system is given by the so-called fluorous biphasic catalysis.[12–14] In this case, the aqueous phase is substituted for by a perfluorinated solvent immiscible with the major part of organic solvents, in which the catalyst is made soluble by functionalisation with suitable perfluoroalkyl chains.

Dirhodium(II) pefluorocarboxylates appear particularly suitable for fluorous biphasic catalysis. A simple extension of the ligand perfluoroalkyl chain should in fact be sufficient to impart the complex the proper solubility in a fluorous phase. According to the current literature, suitable catalysts for fluorous biphasic catalysis should contain a weight percentage of fluorine of at least 60%. In the case of dirhodium perfluorocarboxylates, this percentage is already achieved with perfluoroalkyl chains six carbon atoms long. In comparison with the known dirhodium catalysts with short-chain perfluorinated carboxylate substituents, the elongation of the perfluorinated chain should have minimal influence on the electronic properties of the ligand as well as on the steric constraints around the active centre of the catalyst (the free apical position). Therefore, large variations in the catalytic performance of these compounds are

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not expected. Indeed, very recently it was demonstrated that dirhodium(II) perfluorooctanoate was an active catalyst for olefin cyclopropanations and that it could be easily recovered by extraction into a fluorous phase after reaction completion.[15]

In this paper, we aim at evaluating the reactivity of these catalysts under fluorous biphasic conditions. For this purpose, we have chosen as test reaction the silylation of alcohols with silanes:

$$R_3SiH + R'OH \quad R_3SiOR' + H_2$$

This reaction has practical interest as a valuable alternative to the more classical silylation via stoichiometric reaction of alcohols with chlorosilanes, which necessitates the presence of a base and produces a stoichiometric amount of salt as byproduct. Previous work by Doyle[9] showed that *tetrakis* dirhodium(II) perfluorobutyrate is a very efficient catalyst for this reaction. On the basis of spectroscopic and stereochemical evidence, the following reaction mechanism was proposed,[9] in which the catalyst activates the silane for nucleophilic attack by the alcohol at silicon to give a dirhodium hydride complex and the protonated silyl ether; subsequent protonation of the hydride forms the observed products and releases the catalyst. The alcohol acts as an inhibitor by competing with the silane for coordination to the active site of the catalyst.

$$ROH + Rh_2L_4 \leftrightarrow Rh(L)_4Rh(ROH)$$

$$Et_3SiH + Rh_2L_4 \leftrightarrow Rh(L)_4Rh(H\text{–}SiEt_3)$$

$$Rh(L)_4Rh(H\text{–}SiEt_3) + ROH \rightarrow [Rh(L)_4Rh\text{–}H]^-$$

$$+Et_3SiO^+(H)R \rightarrow Rh_2L_4 + Et_3SiOR + H_2$$

2. Results and discussion

The preparation of the rhodium perfluorocarboxylate catalysts is straightforward.[15] The necessary perfluorocarboxylic acids RfCOOH (Rf=perfluoroalkyl chain) are among the most common perfluorinated compounds and are commercially available with a chain length up to 17 carbon atoms. Simple ligand exchange reactions with dirhodium(II) acetate readily yield the catalyst of interest.

$$Rh_2(OAc)_4 + 4RfCOOH \quad Rh_2(OOCRf)_4 + 4AcOH$$

In this way, we have prepared three catalysts bearing perfluorinated chains with seven ($Rh_2(pfo)_4$, with pfo=perfluorooctanoate), nine ($Rh_2(pfd)_4$, with pfd=perfluorodecanoate) and 13 ($Rh_2(pft)_4$, with pft=perfluorotetradecanoate) carbon atoms, respectively.

Initial experiments were performed in a dichloromethane/fluorous solvent biphasic system using 1 mol% catalyst and an equimolar mixture of 1-octanol and triethylsilane as reagent (Table 1). All catalysts were found to be active. However, with $Rh_2(pfo)_4$ and $Rh_2(pfd)_4$ an appreciable amount of catalyst was invariably extracted into the dichloromethane phase in the course of the reaction. Leaching into the dichloromethane phase, which became coloured, took place irrespective of the fluorous solvent employed and was found to be irreversible. On the contrary, with $Rh_2(pft)_4$ the dichloromethane phase remained perfectly colourless. Since $Rh_2(pft)_4$ was the only catalyst to remain satisfactorily confined in the fluorous phase under the conditions employed, we concentrated our investigations on the reactivity of this complex.

Table 1. Silylation of 1-octanol with triethylsilane under fluorous biphasic conditions

Entry	Catalyst	Fluorous solvent	Alcohol/silane ratio	Yield (%)[a]
1	$Rh_2(pfo)_4$	Perfluorodecaline	1:1	82
2	$Rh_2(pfd)_4$	Perfluorodecaline	1:1	69
3	$Rh_2(pft)_4$	Perfluorodecaline	1:1	52
4	$Rh_2(pft)_4$	Perfluoro-methylcyclohexane	1:1	68
5	$Rh_2(pft)_4$	Fluorinert® FC-77	1:1	68
6	$Rh_2(pft)_4$	Fluorinert® FC-77	1:2	64
7	$Rh_2(pft)_4$	Fluorinert® FC-77	2:1	87
8[b]	$Rh_2(pft)_4$	Fluorinert® FC-77	1:1	60
9[c]	$Rh_2(pft)_4$	Fluorinert® FC-77	1:1	45

Reaction conditions: 1–2 mmols of each reagent, 0.01 mmol (1 mol%) catalyst, 5 mL dichloromethane+1 mL fluorous solvent, room temperature, 6 h.
[a] GC yield referred to the limiting reagent.
[b] Recycle of entry 5.
[c] recycle of entry 8.

The activity of the catalysts was significantly decreased in comparison with the corresponding homogeneous system studied by Doyle (96% yield in 3 h).[9] This is not surprising, since it generally occurs when homogeneous catalysts are employed under biphasic conditions. In this connection, the higher reaction yields obtained with $Rh_2(pfo)_4$ and $Rh_2(pfd)_4$ are probably due to the contribution of catalytically active species dissolved in the dichloromethane phase. The reaction yield with $Rh_2(pft)_4$ can be increased by a proper choice of the fluorous phase (Table 1, entries 3–5), as well as by using an excess of alcohol (Table 1, entries 5–7). The reason for this behaviour will be discussed later.

The $Rh_2(pft)_4$ catalyst can be conveniently recycled by removing the dichloromethane phase after the reaction and subsequently feeding the reactor with fresh reagent solution. However, a decrease in the reaction yield, more pronounced in the second recycle, was recorded (Table 1, entries 8 and 9). This is most likely attributable to catalyst decomposition. We have been able to detect by GC/MS the presence of the triethylsilyl ester of the perfluorotetradecanoic acid ligand in the reaction mixture, which suggests the existence of a decomposition pathway of the catalyst by reductive elimination of the ester from a silylated intermediate. The formation of traces of a brown deposit, possibly metallic rhodium, at the liquid–liquid interphase supports this hypothesis. We are currently trying to optimise the reaction procedure (by e.g. controlled addition of the silane to the reaction mixture) in order to minimize the decomposition.

We have extended our observations to other alcohol substrates. The results are listed in Table 2. Interestingly, the biphasic catalytic system with $Rh_2(pft)_4$ shows a marked preference for primary alcohols; 1-octanol or benzyl alcohol

Table 2. Silylation of different alcohols with $Rh_2(pft)_4$ under fluorous biphasic conditions

Entry	Alcohol	Alcohol/silane ratio	Yield (%)[a]
1	1-Octanol	1:1	68
2	1-Octanol	1:2	64
3	1-Octanol	2:1	87
4	2-Octanol	1:1	22
5	2-Octanol	1:2	22
6	2-Octanol	2:1	33
7	Benzyl alcohol	1:1	81
8	Cyclohexanol	1:1	28
9	Propargyl alcohol	1:1	0

Reaction conditions: 1–2 mmol of each reagent, 0.01 mmol (1 mol%) catalyst, 5 mL dichloromethane+1 mL Fluorinert® FC-77, room temperature, 6 h.
[a] GC yield referred to the limiting reagent.

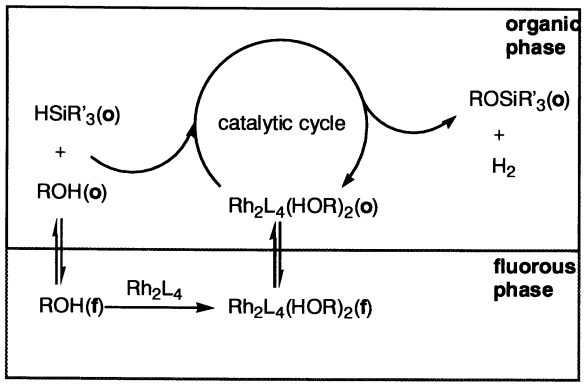

Figure 2. A possible reaction mechanism of the silylation of alcohols under fluorous biphasic conditions.

are much more readily silylated than 2-octanol or cyclohexanol. Furthermore, hydrophilic alcohols, like propargyl alcohol, are not reactive under biphasic conditions, presumably because they are not able to diffuse in the fluorous phase.

The reported results suggest the possibility to perform selective silylations of mixtures of alcohols with different hydrophilicity and/or different degrees of branching at the α position. The latter possibility has been tested by reacting a 1:1 mixture of 1-octanol and 2-octanol; the extent of silylation of the primary alcohol greatly exceeded that of the secondary one (Fig. 1).

The homogeneous catalyst investigated by Doyle also showed higher activity with primary alcohols. However, even if the reaction with secondary alcohols was slower, high yields could be reached in the homogeneous system at properly long reaction times (94% yield in 14 h for 2-octanol).[9] In contrast, in the fluorous biphasic system the reaction almost completely stops slightly above 20% conversion for 2-octanol, whereas for 1-octanol it slows down only above 70% conversion. This difference in behaviour can be explained in terms of a reaction mechanism in which the alcohol not only acts as a reagent, but also as a phase-transfer agent towards the catalyst (Fig. 2). According to this hypothesis, the alcohol has first to diffuse in the fluorous phase where it binds to the rhodium catalyst. The resulting complex adduct is less fluorous, hence more prone to be partially transferred to the dichloromethane phase, where it catalyzes the reaction homogeneously; when the concentration of alcohol falls below a certain value, the catalyst-alcohol adduct is no longer stable and the catalyst diffuses back in the fluorous phase. The efficiency of the phase-transfer process depends on the stability constant of the catalyst–alcohol complex. This appears to be greater for primary alcohols, probably because of lower steric limitations to coordination. A simple demonstration of the higher coordination ability of primary alcohols is given by the observation that addition of an excess of 1-octanol causes solubilisation of the perfluorinated catalysts even in dichloromethane, whereas this is not the case with 2-octanol. Consequently, the phase-transfer effect is expected to be more pronounced for primary alcohols.

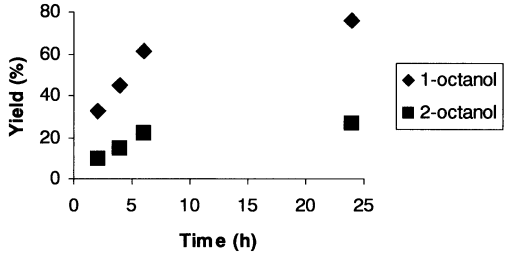

Figure 1. Competitive silylation of 1- and 2-octanol under fluorous biphasic conditions.

The hypothesis illustrated above is further supported by the consideration that the presence of an excess of alcohol invariably results in higher product yields. We have already pointed out this for 1-octanol (Table 1, entries 5–7), but this is also true for 2-octanol (Table 2, entries 4–6). In the latter case, the reaction yield increases by about 50%, on going from a stoichiometric 1:1 mixture to a 2:1 excess of the alcohol.

3. Conclusions

We have shown that silylations of alcohols catalyzed by dirhodium(II) perfluorocarboxylates can be carried out in a fluorous biphasic system, and that the utilization of fluorous biphasic conditions results in a peculiar selectivity of the catalytic process. Hydrophobic, primary alcohols are in fact preferentially silylated in comparison with hydrophilic or secondary ones. We are currently engaged in the optimisation of the performance of this catalytic system as well as in its application to other reactions of practical interest.

4. Experimental

All reagents and perfluorinated solvents were purchased from Aldrich or ABCR and used as received. Nonfluorinated solvents (Carlo Erba RPE) were dried and distilled according to standard procedures prior to use.

4.1. Preparation of the catalysts

4.1.1. *tetrakis*-Dirhodium(II)-perfluorooctanoate, $Rh_2(pfo)_4$. The compound was prepared following a procedure similar

to that adopted by Endres and Maas.[15] 0.750 g (1.81 mmol) of perfluorooctanoic acid are suspended in 40 mL of dry toluene under N_2. A suspension of 0.200 g (0.452 mmol) of dirhodium(II) acetate in 40 mL of absolute ethanol is then added, and the resulting mixture is heated at reflux. The solvent is azeotropically removed down to a volume of about 25 mL. The resulting solution is cooled to room temperature and the residual solvent is stripped off in vacuo. The waxy green residue is treated with a little acetonitrile. The resulting suspension is filtered and the isolated purple solid (the complex-acetonitrile adduct) is heated at 100°C in vacuo for 5 h to liberate the product. Anal. calcd for $Rh_2C_{32}F_{60}O_8$: C 20.69, H absent; found C 20.49, H absent. IR(KBr, cm^{-1}): 1651, 1424, 1244, 1204, 1146, 1018 (all s).

4.1.2. *tetrakis*-Dirhodium(II)-perfluorodecanoate, $Rh_2(pfd)_4$. The compound was prepared from 0.465 g (0.905 mmol) of perfluorodecanoic acid and 0.100 g (0.23 mmol) of dirhodium(II) acetate following a procedure fully analogous to that reported above. Anal. calcd for $Rh_2C_{40}F_{76}O_8$: C 21.28, H absent; found C 21.57, H absent. IR(KBr, cm^{-1}): 1634, 1424, 1207, 1150, 804 (all s). MS (MALDI-TOF, dihydroxybenzoic acid matrix): *m/z* 2648 (M^++2dihydroxybenzoic acid+$2K^+$).

4.1.3. *tetrakis*-Dirhodium(II)-perfluorotetradecanoate, $Rh_2(pft)_4$. 1.29 g (1.81 mmol) of perfluorotetradecanoic acid are suspended in 45 mL of dry toluene under N_2. A suspension of 200 mg (0.452 mmol) of dirhodium(II) acetate in 40 mL of absolute ethanol is then added, and the resulting mixture is heated at reflux. The solvent is azeotropically removed down to a residual volume of about 30 mL. The resulting suspension is cooled to room temperature, filtered, and the isolated solid green product is dried in vacuo. Anal. calcd for $Rh_2C_{56}F_{108}O_8$: C 21.99, H absent; found C 21.64, H absent. IR (KBr, cm^{-1}): 1634, 1424, 1204, 1150, 804 (all s). MS (MALDI-TOF, dihydroxybenzoic acid matrix): *m/z* 3252 (M^++dihydroxybenzoic acid+K^+).

4.2. General procedure for the silylation reactions

The catalyst (0.01 mmol) is dissolved in 1 mL of fluorous solvent in a glass vial under Ar. Dry dichloromethane (5 mL) and the two reagents (1–2 mmol each) are then added, and the resulting system is vigorously stirred at room temperature. 0.5 mL samples of the dichloromethane phase are withdrawn at regular intervals, diluted 1:1 with dichloromethane, and analysed by gas chromatography (25m OV-1701 capillary column; 100°C isotherm for 60 s followed by heating at 16°C min^{-1} to 200°C). The GC system was previously calibrated by determining the retention times and the response factors of the alcohol reagents and of the silylated products. The latter were separately prepared by reaction of the alcohol with chlorotriethylsilane and pyridine in diethylether (1 h, rt) followed by filtration, solvent evaporation and distillation under reduced pressure.

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