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Transition metal catalysis in fluorous media: extension of a new immobilization principle to biphasic and monophasic rhodium-catalyzed hydrosilylations of ketones and enones

Long V. Dinh[a,b] and J. A. Gladysz[a,b,*]

[a]*Department of Chemistry, University of Utah, Salt Lake City, Utah 84112, USA*
[b]*Institut für Organische Chemie, Friedrich-Alexander Universität Erlangen-Nürnberg, Henkestrasse 42, 91054 Erlangen, Germany*

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Abstract

The title protocol utilizes $CF_3C_6F_{11}$ solutions of $ClRh[P(CH_2CH_2(CF_2)_{n-1}CF_3)_3]_3$ (n=6, 8; 0.8–0.2 mol%) and toluene (biphasic conditions, 60°C) or hexanes or ether (monophasic conditions, 28–60°C) solutions of $PhMe_2SiH$ and cyclic enones or ketones. Samples are cooled to room temperature or −30°C, and simple organic/fluorous phase separations remove products from the catalyst, which can be directly reused without loss of activity.

Keywords: hydrosilylation; rhodium; catalyst recovery; fluorocarbon solvents.

The development of easily recovered reagents or catalysts is an important frontier of both synthetic organic and 'green' chemistry.[1] Towards this end, Horváth has introduced a conceptually innovative protocol, 'fluorous biphase chemistry'.[2–4] 'Fluorous' is utilized as an analog to aqueous for highly fluorinated alkane, ether, or tertiary amine solvents. These non-polar media give bilayers with most organic solvents at room temperature or slightly below. However, systems usually become miscible at higher temperatures, allowing the option of homogeneous reactions.[3] Most organic compounds have low affinities for fluorous media. However, when reagents and catalysts are derivatized with sufficient fluoroalkyl groups or 'pony tails' $(CH_2)_m(CF_2)_{n-1}CF_3$, exceptional fluorous affinities become possible.[3] Thus, reactions can be conducted under monophasic conditions (higher temperature) with the advantage of facile biphasic product separation (lower temperature).

We recently synthesized aliphatic fluorous phosphine analogs of Wilkinson's catalyst, $ClRh[P(CH_2CH_2(CF_2)_{n-1}CF_3)_3]_3$ (n=6, **1**; 8, **2**).[5] Complexes **1**–**2** were shown to be soluble in $CF_3C_6F_{11}$ and $CF_3C_6H_5$, insoluble in common organic solvents, and active catalysts for the hydroboration and hydrogenation of alkenes.[5,6] Reactions utilized $CF_3C_6F_{11}$ solutions of **1**–**2**, with or without added organic solvent. Rates were sufficiently rapid under biphasic conditions (40–45°C) that no efforts were made to reach monophasic regimes. Products were extracted into THF or toluene, leaving **1** and **2** behind

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[*] Corresponding author. Please address correspondence to the new Erlangen permanent address.

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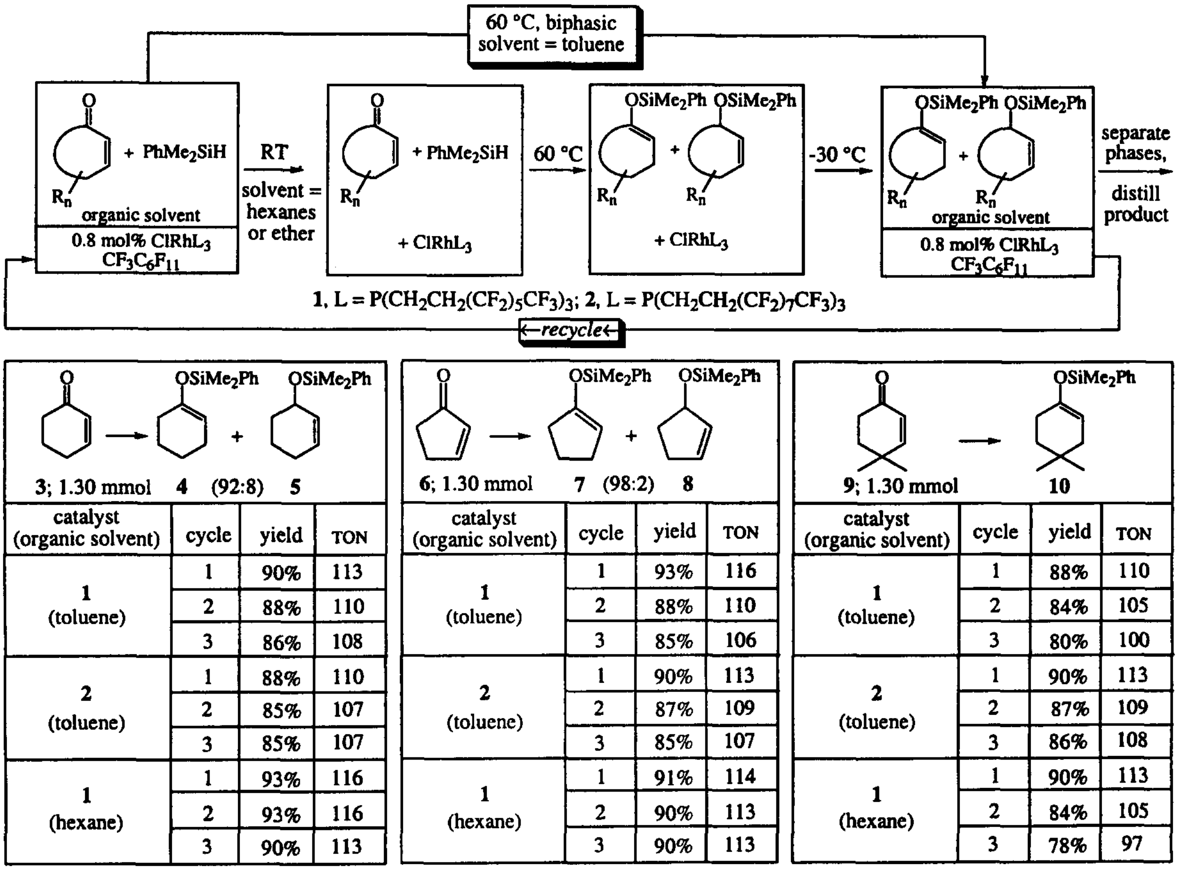

3; 1.30 mmol → 4 (92:8) + 5

catalyst (organic solvent)	cycle	yield	TON
1 (toluene)	1	90%	113
	2	88%	110
	3	86%	108
2 (toluene)	1	88%	110
	2	85%	107
	3	85%	107
1 (hexane)	1	93%	116
	2	93%	116
	3	90%	113

6; 1.30 mmol → 7 (98:2) + 8

catalyst (organic solvent)	cycle	yield	TON
1 (toluene)	1	93%	116
	2	88%	110
	3	85%	106
2 (toluene)	1	90%	113
	2	87%	109
	3	85%	107
1 (hexane)	1	91%	114
	2	90%	113
	3	90%	113

9; 1.30 mmol → 10

catalyst (organic solvent)	cycle	yield	TON
1 (toluene)	1	88%	110
	2	84%	105
	3	80%	100
2 (toluene)	1	90%	113
	2	87%	109
	3	86%	108
1 (hexane)	1	90%	113
	2	84%	105
	3	78%	97

Figure 1. Fluorous rhodium-catalyzed hydrosilylation: biphasic and monophasic conditions

for re-use. We sought to probe whether: (1) **1**–**2** could duplicate other useful reactions of Wilkinson's catalyst; (2) monophasic conditions involving different solvent combinations might be superior; and (3) turnover frequencies, which are an important measure of catalyst recovery and/or stability, remained constant as a function of cycle. In this communication, we report auspicious preliminary findings for hydrosilylations of cyclic enones and ketones.[7,8]

As detailed in Fig. 1 and representative procedure A,[9] $CF_3C_6F_{11}$ solutions of **1**–**2** (1.0 mL; 0.8 mol%), 2-cyclohexen-1-one (**3**; 1.30 mmol), $PhMe_2SiH$ (1.43 mmol), and toluene (1.0 mL) were combined. The partition coefficients of **3** (1.7:98.3; $CF_3C_6F_{11}$:toluene, 24°C)[3] and $PhMe_2SiH$ (3.6:96.4) translate into roughly equimolar concentrations of catalysts and educts in the $CF_3C_6F_{11}$ layer. Reactions went to completion over the course of 10 h under biphasic conditions at 60°C, as assayed by GC. The samples were cooled, and the upper toluene layers were carefully removed by syringe. The remaining $CF_3C_6F_{11}$ layers were extracted with toluene (1.0 mL). Distillation of the toluene phases gave the isomeric 1,4- and 1,2-hydrosilylation products **4** and **5** (92:8; Fig. 1) as a clear liquid in 90–88% yields (TON 113–110).

The $CF_3C_6F_{11}$ catalyst solutions were recharged with **3**, $PhMe_2SiH$, and toluene. A second reaction cycle gave **4** and **5** in 88–85% yields, and a third cycle gave similar results (Fig. 1). Analogous three-cycle sequences were conducted with 2-cyclopenten-1-one (**6**) and 4,4-dimethyl-2-cyclohexen-1-one (**9**). Hydrosilylation products (**7**/**8**, **10**) were isolated in comparable yields by distillation, as summarized in Fig. 1. The $^1H/^{13}C$ NMR spectra matched those previously reported, and 1,4/1,2 selectivities paralleled those of non-fluorous rhodium catalysts.[10–12] The partition coefficient of **10** ($CF_3C_6F_{11}$:toluene, 24°C) was 0.6:99.4.

The temperatures at which fluorous and organic solvents become miscible are strong functions of the molar proportions and solutes.[3] The $CF_3C_6F_{11}$/toluene reactions would become homogeneous with further heating.[2c] However, lower temperatures are preferable in synthesis. Hexanes and ether are among the few solvents miscible with $CF_3C_6F_{11}$ at room temperature, consistent with their low polarities and small volumes.[3] However, two phases form at 0°C. Accordingly, the above reactions were repeated with **1** in $CF_3C_6F_{11}$/hexanes under monophasic conditions at 60°C. GC analyses showed product formation to be complete on time scales of 1–2 h, as opposed to 4–10 h under biphasic conditions. The phases were separated at –30°C. Products were isolated in comparable yields (Fig. 1), and **1** could similarly be recycled.

Further optimization was conducted with cyclohexanone (**11**), a simple ketone that can only give a 1,2-addition product (**12**) and is thus better suited for mechanistic studies. First, **1** (0.2 mol%) catalyzed the addition of $PhMe_2SiH$ under monophasic conditions in $CF_3C_6F_{11}$/hexanes or $CF_3C_6F_{11}$/ether.[9] Reactions were complete after 8 h at 28°C, with TON values of 485–481 (cycle 2, 3, 4: 481–475; 465; 450–445). Second, as shown in Fig. 2, rates in $CF_3C_6F_{11}$/hexanes were monitored as a function of cycle at 40°C vs tridecane internal standard. The first cycle showed a brief induction period. Subsequent cycles showed no induction periods, and only slight diminutions in rates. Similar results were obtained under biphasic $CF_3C_6F_{11}$/toluene conditions at 40°C. However, each cycle required approximately twice as long, and rates noticeably declined after 70–80% completion. Regardless, these data show that only low levels of catalyst leaching or deactivation occur under both monophasic and biphasic conditions. Finally, a monophasic preparative reaction was conducted (13.0 mmol cyclohexanone, 28°C) with a lower catalyst loading (0.02 mol%). After 72 h, workup gave **12** in 88% yield (TON 4400).

From the preceding reactions, it can confidently be extrapolated that **1** and **2** are effective hydro-

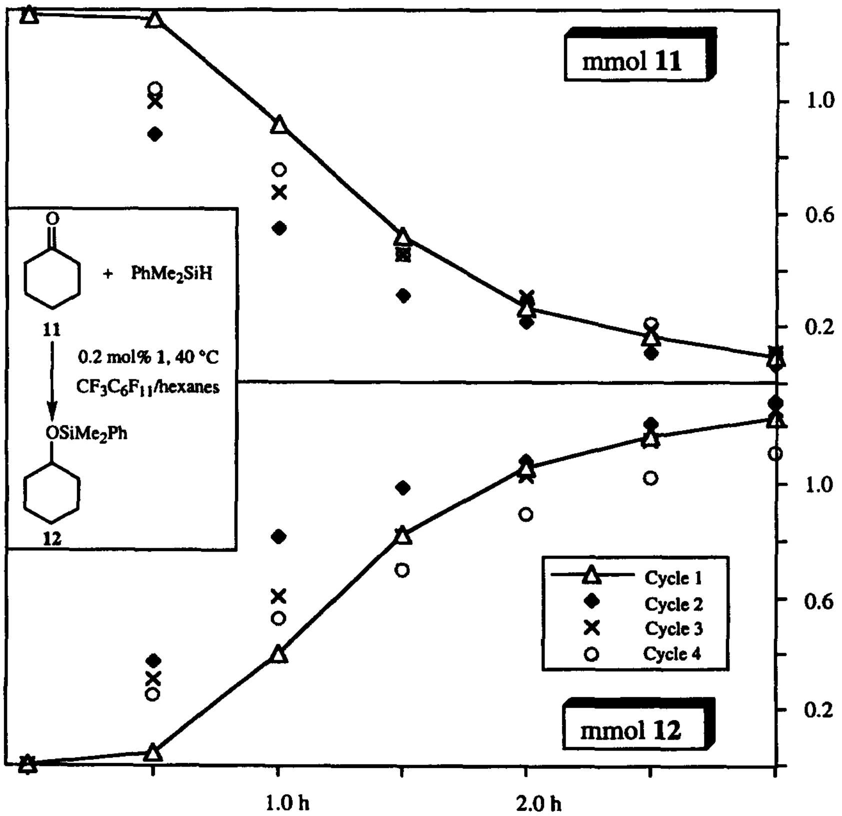

Figure 2. Reaction profile as a function of cycle

silylation catalysts for a variety of carbonyl compounds. We furthermore anticipate that they can effect hydrosilylations of other functional groups. From a reactivity standpoint, **1** and **2** are not superior to non-fluorous rhodium catalysts. However, from a recycling standpoint, they offer many attractive new features. In catalytic hydroborations, leaching levels (one cycle) correspond to 2–4 rhodium atoms for every 1 000 000 product molecules.[5b] In conclusion, we have demonstrated the applicability of fluorous catalysis, in both biphasic and monophasic modes, to an important laboratory scale transformation, hydrosilylation. To our knowledge, we are the first to show that solvents that are miscible at room temperature can be employed. Additional synthetic and mechanistic details will be supplied in our full paper, and other fluorous catalysts and reagents will be reported in the near future.

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9. Representative procedures. **A** (biphasic): A vial was charged with a $CF_3C_6F_{11}$ solution of **2** (1.0 mL, 0.0104 M, 0.8 mol%), $PhMe_2SiH$ (0.219 mL, 1.43 mmol), **3** (0.126 mL, 1.30 mmol), and toluene (1.0 mL). The mixture was vigorously stirred at 60°C and briefly cooled every 2 h. The toluene layer was analyzed by GC (complete reaction at 10 h). The toluene layer was removed by syringe, and the $CF_3C_6F_{11}$ layer extracted with toluene (1.0 mL). The products (Fig. 1) were isolated by Kugelrohr distillation of the combined toluene layers (0.266 g, 88%; TON=110). **B** (monophasic): A vial was similarly charged with a $CF_3C_6F_{11}$ solution of **1** (1.0 mL, 0.0026 M, 0.2 mol%), $PhMe_2SiH$ (0.219 mL, 1.43 mmol), **11** (0.135 mL, 1.30 mmol), tridecane (0.100 mL, 0.410 mmol), and hexanes (2.0 mL). The mixture was vigorously stirred at 40°C, analyzed every 0.5 h by GC, and after 3.5 h cooled to –30°C. After 4 h, the hexanes layer was removed by syringe, and the $CF_3C_6F_{11}$ layer extracted with hexanes (1.0 mL, –30°C). The product (Fig. 2) was isolated as in procedure A (0.274 g, 1.17 mmol, 90%).
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