Thermomorphic fluorous imine and thioether palladacycles as precursors for highly active Heck and Suzuki catalysts; evidence for palladium nanoparticle pathways

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p-Iodobenzaldehyde is elaborated to the fluorous alcohol *p*-$R_{f8}(CH_2)_3C_6H_4CH(OH)(CH_2)_2R_{f8}$ (three steps/80%; R_{f8} = *n*-C_8F_{17}), which is converted to imine *p*-$R_{f8}(CH_2)_3C_6H_4C(=N(CH_2)_3R_{f8})(CH_2)_2R_{f8}$ (**6**, two steps/93%) and thioether *p*-$R_{f8}(CH_2)_3C_6H_4CH(S(CH_2)_3R_{f8})(CH_2)_2R_{f8}$ (**12**, 64%). Reactions with $Pd(OAc)_2$ (AcOH, 95 °C) give palladacycles with $[RC_6H_3CR'=N(R)Pd(\mu\text{-}OAc)]_2$ (**7**, 87%) and $[RC_6H_3CHR'S(R)Pd(\mu\text{-}OAc)]_2$ (**13**, 84%) cores. The former reacts with LiCl and LiI to give the corresponding bridging halide complexes (**8**, **9**); LiCl/PPh_3 affords monomeric $RC_6H_3CR'=N(R)Pd(Cl)(PPh_3)$ (**10**). Palladacycles **7**–**9** and **13** are poorly soluble or insoluble in many solvents at 20–24 °C, but much more soluble at higher temperatures. The $CF_3C_6F_{11}$/toluene partition coefficients of **6**, **7**, **12**, and **13** are >91:<9 (24 °C). Both **7** and **13** are excellent catalyst precursors for Heck reactions of aryl halides. Turnover numbers exceed 10^6 with phenyl iodide under homogeneous conditions in DMF at 140 °C. The palladacycles precipitate as bridging halides upon cooling, and can in theory be recovered by liquid/solid phase separations. However, since the quantities are small, the solvent $C_8F_{17}Br$ is added for recycling. Induction periods in both the first and second cycles, and progressively lower activities, are noted. Transmission electron microscopy indicates the formation of soluble palladium nanoparticles. Together with other data, it is proposed that the nanoparticles are the active catalysts, for which the recyclable palladacycles constitute a steady state source, until exhausted. Complex **7** similarly catalyzes the Suzuki reaction (K_3PO_4, toluene, 130 °C).

Introduction

Fluorous biphase catalysis is now a well established technique for catalyst/product separation and recycling that exploits the temperature-dependent miscibility of organic and fluorous phases.[1–3] Fig. 1A shows the most common protocol. Catalysts

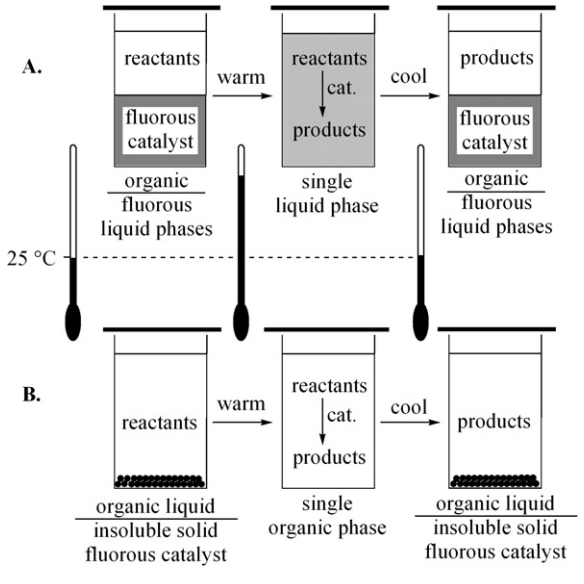
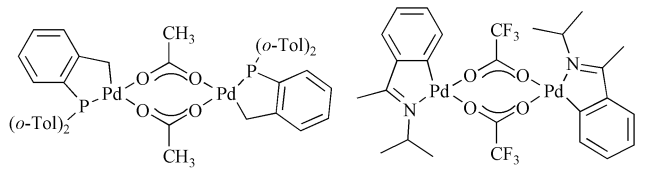


Fig. 1 Traditional (A) and fluorous-solvent-free (B) fluorous biphase catalysis.

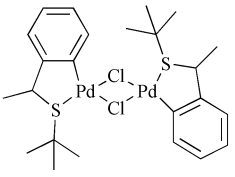
are derivatized with "pony tails" or $(CH_2)_m(CF_2)_{n-1}CF_3$ ($(CH_2)_mR_{fn}$) segments that provide high fluorous solvent affinities. Reactions can be conducted under homogeneous conditions at the one-phase, high temperature limit. Products normally have much greater affinities for the non-fluorous solvent, and are easily separated at the two-liquid-phase, low temperature limit. A newer-generation protocol is shown in Fig. 1B.[4,5] This dispenses with the fluorous solvent, and instead exploits the temperature-dependent solubility of the fluorous catalyst in the organic solvent. Such "thermomorphic"[6] behavior allows homogeneous reaction conditions at higher temperatures, with catalyst recovery *via* liquid/solid phase separation at lower temperatures.

Many fluorous transition-metal catalysts are now known. They have given impressive results in metal-catalyzed hydroformylations,[7] hydrogenations,[8] hydroborations,[9] hydrosilylations,[10] oxidations,[11] carbon–carbon bond forming reactions of aryl halides,[12–14] additions of Et_2Zn to carbonyl compounds,[15] and other processes.[16] Surprisingly, there have been no attempts to develop fluorous versions of palladacycle catalysts,[17] some examples of which are given in Fig. 2.[18–21] These are particularly effective for sp^2–sp^2 carbon coupling processes such as the Heck[22] and Suzuki[23] reactions. One contributing factor may be that most palladacycles contain multiple aromatic rings, which typically require three R_{f8} "pony tails" for effective immobilization in fluorous solvents.[2,8b,24] However, since Heck reactions normally require elevated temperatures, we thought it might be feasible to employ the newer protocol in Fig. 1B, which reduces the dependence upon a high fluorous/organic solvent partition coefficient.

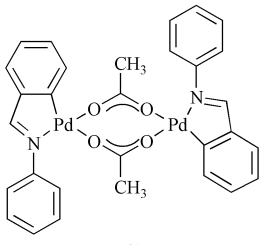


A[17b,18]
Herrmann/Beller catalyst

B[19]
Milstein catalyst



C[20]
Dupont catalyst



D[21]
Blackmond/Pfaltz catalyst

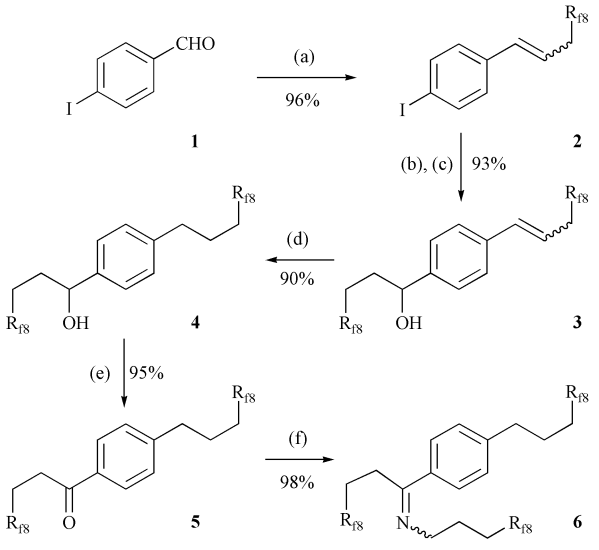
Fig. 2 Representative palladacycle catalyst precursors for the Heck reaction.

Our attention was drawn to two types of cyclopalladated complexes. The first was an imine-based system reported by Milstein (**B**, Fig. 2), with just one arene per palladium.[19] The second was a similar thioether-derived family described by Dupont (**C**, Fig. 2).[20] Both have been applied to the Heck reaction, and the latter to the Suzuki coupling. We independently became interested in palladium complexes of simple fluorous thioethers $(R_{f8}(CH_2)_n)_2S$ ($n = 2$, 3), which are also catalyst precursors for Suzuki coupling reactions.[13d] Hence, we set out to synthesize fluorous analogs of **B** and **C**, evaluate their efficacies as catalyst precursors, and attempt their recovery and reuse. A portion of this work has previously been communicated.[25]

Results

1. Synthesis and characterization of catalyst precursors

We first sought a fluorous imine containing at least three pony tails. As shown in Scheme 1, a synthesis was developed starting from commercial *p*-iodobenzaldehyde (**1**). We have previously shown that aromatic aldehydes undergo high-yield Wittig reactions with the ylide derived from the readily available phosphonium salt $R_{f8}CH_2CH_2PPh_3{}^+I^-$.[24,26] An analogous procedure with **1** gave the alkene **2** in 96% yield after workup (90:10 Z/E mixture). All new compounds gave satisfactory microanalyses, and were characterized by ^1H and ^{13}C NMR, and often additional means, as summarized in the experimental section.



Scheme 1 Synthesis of fluorous imine **6**. Conditions: (a) $R_{f8}CH_2CH_2PPh_3{}^+I^-$, K_2CO_3, *p*-dioxane/H_2O, 95 °C; (b) *i*-PrMgCl, THF; (c) $R_{f8}CH_2CH_2CHO$; (d) $(Ph_3P)_3RhCl$, H_2 (75 psi), EtOH/$CF_3C_6H_5$, 40 °C; (e) Dess–Martin periodinane, $CF_3C_6H_5$; (f) $NH_2CH_2CH_2CH_2R_{f8}$, $SnCl_2(H_2O)_2$, toluene, reflux, Dean Stark.

To our initial surprise, we were unable to hydrogenate the alkene moiety in **2** or closely related compounds such as the analogous bromide without simultaneous partial hydrogenolysis of the aryl halide (Pd/C, $(Ph_3P)_3RhCl$ catalysts). The resulting arene was also very difficult to separate from the target aryl iodide. Accordingly, *i*-PrMgCl was used to effect iodine/magnesium exchange,[27] and subsequent addition of the readily available fluorous aldehyde $R_{f8}CH_2CH_2CHO$[28] gave the benzylic alcohol **3** in 93% yield after workup. The alkene moiety of this two-pony-tail system could be hydrogenated (7 mol% $(Ph_3P)_3RhCl$) without competing carbon–oxygen bond hydrogenolysis, affording **4** in 90% yield.

Oxidation of **4** with the Dess–Martin periodinane[29] gave the aryl ketone **5** in 95% yield. Subsequent condensation with the readily available fluorous amine $H_2NCH_2CH_2CH_2R_{f8}$[28] in the presence of $SnCl_2(H_2O)_2$ (20 mol%) simultaneously introduced the third pony tail and generated the imine **6**, which was isolated in 98% yield (35:65 Z/E mixture). Although the synthesis of **6** required five steps, product purifications—often the most important consideration in fluorous syntheses—were easy and the overall yield was good. The $CF_3C_6F_{11}$/toluene partition coefficients of **5** and **6** were measured by GC as described in the experimental section. As summarized in Table 1, the fluorous phase affinity of **6** was very high (98.7:1.3), but that of **5** was—as expected from the number of pony tails—lower.

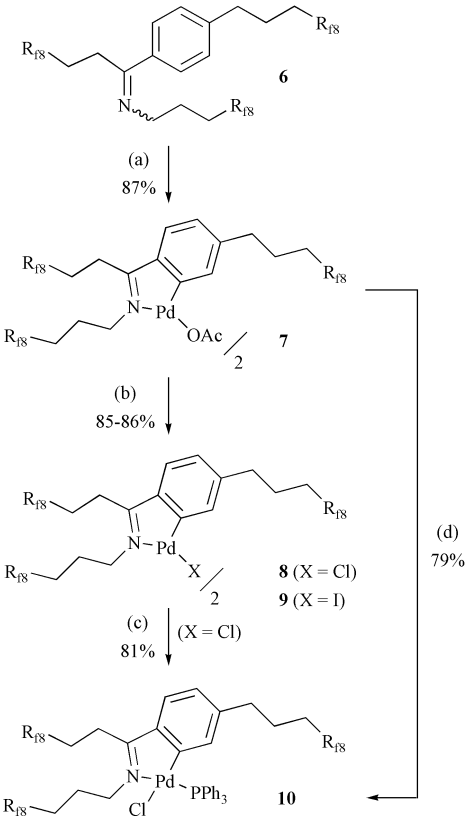
As shown in Scheme 2, **6** underwent cyclopalladation under standard conditions ($Pd(OAc)_2$, AcOH, 95 °C). Workup gave the yellow dimeric N-donor palladacycle **7** in 87% yield. A crystallized sample melted at 78–80 °C and was thermally stable to 225 °C, as assayed by DSC and TGA measurements.[30] When DMF or $CF_3C_6H_5$ solutions of **7** were kept at 140 °C (2 h) or 100 °C (16 h), no decomposition was detected visually or by NMR. Reactions of **7** with LiCl or LiI gave the corresponding dimeric palladacycle halides **8** and **9** in 85–86% yields. We thought that monomeric species might be better suited for X-ray crystallography. Accordingly, reactions of (1) the palladacycle chloride **8** with PPh_3, and (2) the palladacycle acetate **7** with LiCl/PPh_3, gave the phosphine complex **10** in 79–81% yields. However, all crystals diffracted poorly. The thermal stabilities of **8**–**10** were similar to that of **7**.

The N-donor palladacycles **7**–**10** showed IR $\nu_{C=N}$ bands at lower frequencies than the imine **6** (1583–1587 *vs.* 1657 cm^{-1}). Complex **7** gave IR $\nu_{C=O}$ values (1571, 1424 cm^{-1}) close to those of other palladacycle bridging acetates.[20c,31] The ^1H and ^{13}C NMR spectra clearly indicated a trisubstituted arene ring. Palladacycle bridging acetates exhibit structures that are sharply folded about each O_2C–CH_3 axis.[18b,20c] This renders the protons of each methylene group in **7** diastereotopic, and exchange is slow on the ^1H NMR time scale. Interestingly,

Table 1 Partition coefficients (24 °C)

Analyte	$CF_3C_6F_{11}$:toluene	$C_8F_{17}Br$:DMF
Ketone **5**[a]	84.6:15.4	—
Imine **6**[a]	98.7:1.3	—
Imine palladacycle **7**[a]	95.5:4.5	95.9:4.1
Thioether **12**[b]	99.5:0.5	—
Thioether palladacycle **13**[b]	90.7:9.3	91.4:8.6

[a] Measured by GC. [b] Measured by HPLC.



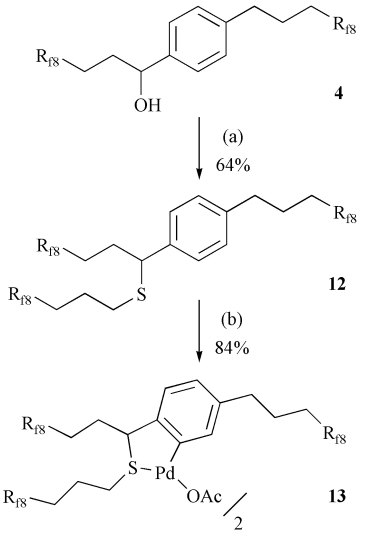
Scheme 2 Synthesis of fluorous N-donor palladacycles. Conditions: (a) $Pd(OAc)_2$, AcOH, 95 °C; (b) LiX (X = Cl, I), $CF_3C_6H_5$/MeOH; (c) PPh_3, CH_2Cl_2; (d) LiCl, PPh_3, THF.

the chemical shifts of the $=NCH_2$ ^1H NMR signals of the palladacycle halides **8** and **9** vary significantly from those of **7** (**7**, 2.98–3.05 (m, 1H), 3.22–3.29 (m, 1H); **8**, 3.84–3.91 (m, 2H); **9**, 4.15–4.18 (m, 2H).

At room temperature, **7** was soluble in fluorinated solvents such as $CF_3C_6F_{11}$, $C_8F_{17}Br$, $CF_3C_6F_5$, and $CF_3C_6H_5$, poorly soluble in common organic solvents such as CH_2Cl_2, $CHCl_3$, acetone, and THF, and insoluble in DMF. Complexes **8** and **9** were completely insoluble in organic solvents, and poorly soluble in the preceding fluorinated solvents. However, solubilities in $CF_3C_6F_5$ were much higher above 50 °C, allowing NMR spectra to be recorded. Complex **10** was much more soluble than **7** in CH_2Cl_2, $CHCl_3$, acetone, and THF, and was very soluble in $CF_3C_6F_{11}$, $CF_3C_6F_5$, and $CF_3C_6H_5$ as well. The $CF_3C_6F_{11}$/toluene partition coefficient of **7** could be determined by HPLC, but **8** and **9** were too insoluble. As shown in Table 1, the value was slightly lower than that of imine **6**, and was little changed in $C_8F_{17}Br$/DMF, a biphase system employed below.

We next turned our attention to fluorous thioethers that could serve as precursors to palladacycles similar to **C** (Fig. 2). Thiols are known to condense with benzylic alcohols in the presence of Lewis acids.[32] Accordingly, the known fluorous thiol $R_{f8}CH_2CH_2CH_2SH$[33] was synthesized by a "new" route (previously applied to other fluorous thiols)[34] involving thiourea and the fluorous iodide $R_{f8}CH_2CH_2CH_2I$.[11a] As shown in Scheme 3, reaction with the fluorous benzylic alcohol **4** gave the triply pony-tailed fluorous thioether **12** in 64% yield. Cyclopalladation under conditions analogous to those in Scheme 2 afforded the dimeric S-donor palladacycle **13** in 84% yield.

Unlike the imine **6**, thioether **12** is chiral. Accordingly, the dimeric palladacycle **13** contains two carbon stereocenters—as well as two sulfur stereocenters not present in the free ligand. Mixtures of diastereomers are therefore possible, and



Scheme 3 Synthesis of a fluorous S-donor palladacycle. Conditions: (a) $R_{f8}CH_2CH_2CH_2SH$ (**11**), ZnI_2, $CF_3C_6H_5$, 60 °C; (b) $Pd(OAc)_2$, AcOH, 95 °C.

NMR spectra were much more complex than those of **7**. Analogs of **C** with *n*-alkyl sulfur substituents also exist as mixtures of diastereomers.[20c] The palladacycle **13** exhibited solubilities similar to those of **7**. However, the partition coefficient was slightly lower (Table 1), and only a single HPLC peak was observed.

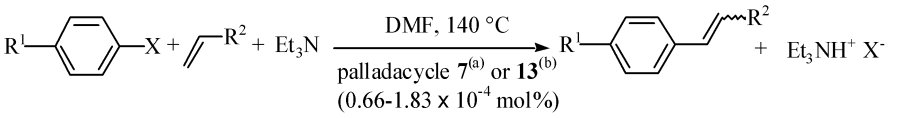
2. Catalysis

We first sought to demonstrate that the fluorous N-donor and S-donor palladacycle acetates **7** and **13** were viable catalyst precursors for Heck couplings of aryl halides. Note that halide ions are generated under the reaction conditions—for example in the form of the ammonium salts $Et_3NH^+X^-$ when Et_3N is used as the base. Thus, given the rapid reactions with LiCl and LiI in Scheme 2, both **7** and **13** should be converted to bridging halide complexes after the first turnover (even, foreshadowing a point below, if catalysis is effected by an entirely different species). In this context, it is often overlooked that the properties of the catalyst rest state, not the catalyst precursor, are of greatest relevance to recycling.[35]

Hence, a solution of an aryl halide in freshly distilled DMF was sequentially treated with an alkene, Et_3N, and a standard solution of **7** or **13** in $CF_3C_6H_5$, as summarized in Table 2. In order to maximize turnover numbers (TON), the catalyst loadings were kept low ($0.66–1.83 \times 10^{-4}$ mol%). The apparently homogeneous samples were reacted at 140 °C, and then cooled. GC analyses showed the expected coupling products in 49–100% yields, corresponding to TON values of 266 000 to 1 510 000. In accord with most other studies involving dimeric palladacycles, these are based upon the molecular structure (two palladium atoms). The values place **7** and **13** among the best high-turnover Heck catalyst precursors.[21] For the less reactive aryl bromide (entries 5 and 6), GC monitoring showed that the lower conversions are due to catalyst deactivation.

Similar reactions were conducted in which **7** was introduced as a solid, and at much higher loadings (0.5 mol%). The initially insoluble **7** dissolved as the DMF was warmed. Upon cooling, palladium complexes precipitated. In reactions of phenyl iodide, NMR analyses showed palladacycle iodide **9** to be the dominant species (> 95%). The reaction products and all other materials remained soluble. These observations raised the possibility of catalyst recovery by a simple liquid/solid phase separation of the type in Fig. 1B. However, the catalyst quantities involved were impracticably small—a problem that would be ameliorated on industrial process-chemistry scales.

Table 2 Heck reactions under high turnover conditions



Entry	X	R^1	R^2	Catalyst, mmol	*t*/h	Conv.[c] (%)	Yield[c] (%)	TON
1	I	H	CO_2CH_3	**7**, 0.00000344	14	100	100[d]	1 460 000
2				**13**, 0.0000415	18	100	100[d]	1 510 000
3	I	H	C_6H_5	**7**, 0.00000344	24	94	88[e]	1 270 000
4				**13**, 0.0000415	48	100	100[e]	1 510 000
5	Br	CH_3CO	CO_2CH_3	**7**, 0.00000917	48	77	49[d]	266 000
6				**13**, 0.0000831	48	66	50[d]	301 000

[a] Conditions for **7**: ArX (*ca.* 5.000 mmol), alkene (*ca.* 1.25 equiv), Et_3N (*ca.* 2 equiv), DMF (6.00 mL). [b] Conditions for **13**: ArX (*ca.* 5.000–6.279 mmol), alkene (*ca.* 2 equiv), NEt_3 (*ca.* 2 equiv), DMF (8.00 mL). [c] Determined by GC. [d] *trans* only. [e] *trans*:*cis* 87:13.

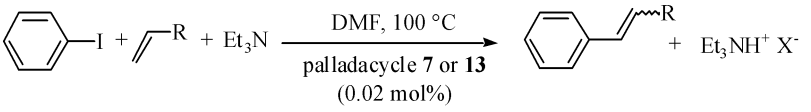
Accordingly, the reactions shown in Table 3 were conducted with 0.02 mol% of **7**, and with periodical monitoring by GC. Since the catalyst loading was higher than in Table 2, a lower temperature (100 °C) could be used. After cooling, $C_8F_{17}Br$ was added as a "catalyst carrier", giving a liquid/liquid biphasic sample. This fluorous solvent best dissolves the palladacycle iodide **9**. Pictures of a reaction sequence are given in Fig. 3, using 0.5 mol% of **7** for better visualization. The upper DMF phase was separated, and the $C_8F_{17}Br$ phase washed with DMF. The combined DMF phases were analyzed to give the data in Table 3. The $C_8F_{17}Br$ was removed under vacuum, and the residue charged with fresh educts and DMF for a second reaction cycle.

The results of four cycles are given in Table 3. The data show a gradual loss of activity or turnover frequency. With **7** and methyl acrylate, conversion and yield drop in the third cycle. Only by extending the duration of the fourth cycle from 2 to 10 h are quantitative yields restored. With styrene, activity loss is evident in the second cycle (15 *vs.* 5 h), and then drops further. The same protocol was applied to the S-donor palladacycle **13**. With methyl acrylate, reaction times must again be continually lengthened to maintain quantitative yields. With styrene, no catalyst remains after three cycles. Thus, **13** is consumed at a faster rate than **7**. However, additional GC data showed that **13** gave higher TOF values than **7** in the first two cycles with methyl acetate.

These observations are consistent with several scenarios. One would be that the active catalyst is efficiently recycled, but is of limited stability, resulting in progressively slower rates. Another would be that catalyst recycling is not as efficient as anticipated—due, for example, to retention in the DMF phase. Another would be that the active catalysts are non-recyclable decomposition products of **7** or **13**. The remaining palladacycle would then be recycled (as the bridging halide), with the diminishing activity representing progressively smaller quantities available for catalyst generation.

In the latter context, many metallic palladium catalysts for the Heck reaction are known.[22,36–41] These include organic-solvent-soluble colloidal palladium nanoparticles,[36,42] and two varieties of fluorous-solvent-soluble nanoparticles—one type imbedded in a fluorous dendrimer, and the other stabilized by absorbed fluorous molecules.[37,38] Also, close relatives of the catalyst **B** (Fig. 2) upon which **7** is based decompose to active metallic palladium.[39] Furthermore, colloidal palladium nanoparticles often impart a reddish-orange tint to DMF,[36a] and a similar hue is apparent in Fig. 3. We therefore considered the possibility that **7**, **13**, and the analogous bridging halides serve mainly as recyclable sources of soluble *non*-fluorous colloidal nanoparticle catalysts. To probe this model, the rate of reaction of phenyl iodide and methyl acrylate was monitored under the conditions summarized in Fig. 4.

Table 3 Heck reactions under recycling conditions[a]



		Data for **7**				Data for **13**			
R	Cycle	*t*/h	Conv.[b] (%)	Yield[b] (%)	TON[c]	*t*/h	Conv.[b] (%)	Yield[b] (%)	TON[c]
CO_2Me	1	2	100	100[d]	5100	1	100	100[d]	5100
	2	2	100	100[d]	10 200	1.5	100	100[d]	10 200
	3	2	77	55[d]	13 300	6.5	100	100[d]	15 300
	4	10	100	100[d]	18 100	16	100	100[d]	20 400
C_6H_5	1	5	92	85[e]	4 340	5	87	85[e]	4 340
	2	15	88	80[e]	8 420	24	79	72[e]	8 010
	3	24	86	74[e]	12 190	55	81	81[e]	12 140
	4	24	74	52[e]	14 840	132	0	0[e]	12 140

[a] Conditions: **7** or **13** (0.0014 g or 0.0015 g, 0.00044 mmol), phenyl iodide (0.250 mL, 2.24 mmol), alkene (*ca.* 1.25 equiv), Et_3N (0.625 mL, 4.48 mmol), DMF (4.00 mL). [b] Determined by GC. [c] Cumulative. [d] *trans* only. [e] *trans*:*cis* 87:13.

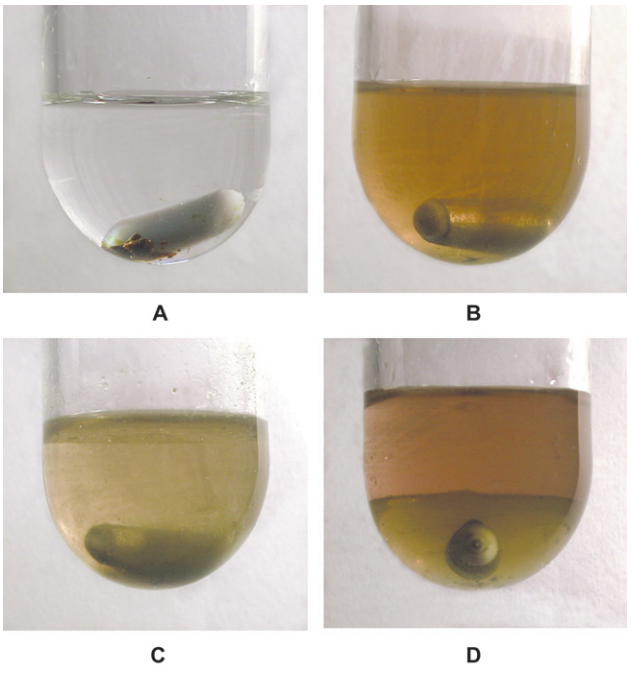


Fig. 3 Photographs of a recycling sequence analogous to the first entry in Table 3 (**7**, methyl acrylate) but with 0.5 mol% **7**. **A**, before heating, with undissolved **7**; **B**, after 2 h at 100 °C; **C**, after cooling to room temperature, with precipitated palladium complexes; **D**, after addition of $C_8F_{17}Br$. Reprinted from ref. 25 with permission from the American Chemical Society.

Importantly, both the first and second cycles with **7** in Table 3 (Fig. 4, top; red and blue traces) appeared to show an induction period, and the second cycle was slightly slower. An induction period for the first cycle could be rationalized under any circumstances, but an induction period for the second suggests that the active catalyst is not being recycled. In order to improve the time resolution, reactions were repeated at 80 °C (Fig. 4, bottom; green and orange traces). The induction periods and rate differences were markedly enhanced. The palladacycle iodide **9** showed identical activity (purple trace). In all

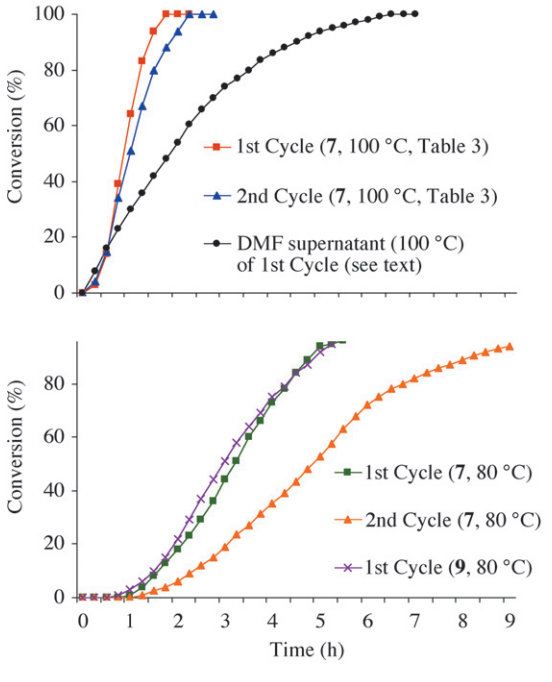


Fig. 4 Conversion as a function of time for Heck reactions of phenyl iodide and methyl acrylate.

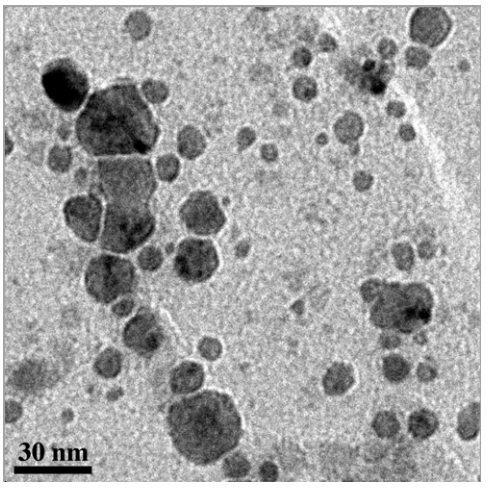


Fig. 5 Transmission electron microscopy (TEM) image taken from panel B in Fig. 3.

cases, reddish-orange tints became apparent near the end of the induction period.

The first cycle with **7** in Table 3 was repeated (100 °C), and the DMF separated from the DMF/$C_8F_{17}Br$ mixture (see panel **D**, Fig. 3). The $C_8F_{17}Br$ layer was washed with DMF (50% of original DMF volume). The DMF phases were combined, charged with additional educts, and heated to 100 °C. As shown in Fig. 4 (top, black trace), reaction now occurred without an induction period, indicating a leached catalyst. Although the activity is somewhat less than for the first or second cycles (red and blue traces), it should be noted that all concentrations are *ca.* 67% lower.

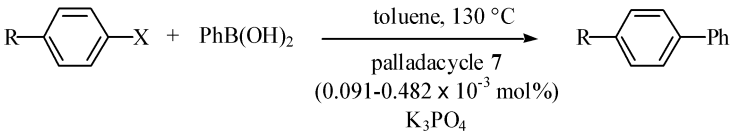
Next, aliquots from the first cycle in Table 3, at the stage of panel **B** in Fig. 3, were examined by transmission electron microscopy. This is one of the best methods for detecting palladium nanoparticles.[36,38] As shown in Fig. 5, a distribution of sizes was found, with an average diameter of *ca.* 10 nm. Given the above data, and as further elaborated in the discussion section, we assign the bulk of the activity of palladacycle catalyst precursors **7**, **9**, and **13** to DMF-soluble, non-fluorous palladium nanoparticles.

During the course of the above studies, but before the nature of the active catalyst was appreciated, we also conducted a variety of Suzuki reactions, some of which are summarized in Table 4. We note in passing that the insoluble nature of the base K_3PO_4, which is customarily used in excess, renders these reactions less suitable for catalyst recovery by liquid/solid phase separation (Fig. 1B). Although palladacycle **7** gave high TON values in the single-cycle experiments in Table 4, attempted recycling with $C_8F_{17}Br$ always gave dramatically lower yields and activities. Indeed, many types of metallic palladium are known to catalyze the Suzuki reaction, as discussed further below.[36a,38a,41]

Discussion

Despite the careful design of the highly fluorophilic, thermomorphic palladacycle catalyst precursors **7** and **13**, the preceding data clearly indicate that a *non-molecular* catalyst is responsible for the Heck and Suzuki reactions in Tables 2–4. All evidence is consistent with the generation, during the induction periods illustrated in Fig. 4, of highly active soluble colloidal palladium nanoparticles—which are physically detected in Fig. 5. Since the palladacycles are otherwise stable in DMF and $CF_3C_6H_5$ at 100–140 °C, this process must be triggered by one of the reactants (*e.g.*, phenyl iodide, alkene, or Et_3N in Table 3). As **7** and **13** or the corresponding bridging

Table 4 Selected Suzuki reactions[a]



X	R	ArX/mmol	**7**/mmol	*t*/h	Conv.[b] (%)	Yield[b] (%)	TON
I	H	5.023	0.00000458	38	65	40	440 000
Br	CH_3CO	5.000	0.00000458	24	67	31	337 000
Br	H	2.374	0.0000115	24	98	82	170 000
Br	CH_3	2.374	0.0000115	24	96	76	157 000
Br	CH_3O	2.391	0.0000115	24	90	83	174 000

[a] Conditions: *ca.* 1.0/1.5/2.0 ArX/$PhB(OH)_2$/K_3PO_4, toluene (8.00–13.00 mL). [b] Determined by GC.

halide complexes are progressively consumed in each cycle, catalysis slows and ultimately ceases.

Interestingly, the nanoparticles preferentially partition into non-fluorous solvents, as shown by the retention of activity in DMF after extraction with $C_8F_{17}Br$. This suggests, in accord with much precedent,[36a,42] that they are stabilized by the by-product $Et_3NH^+X^-$. However, as noted above, palladium nanoparticles can also be stabilized by certain fluorous molecules, such as **E**–**G** in Fig. 6.[38] Such nanoparticles exhibit high fluorous phase affinities, and those stabilized by **E** are highly active and easily recycled catalysts for the Heck and Suzuki reactions.[38a] Unfortunately, the types of fluorous molecules that are able to stabilize palladium nanoparticles can, at present, only be determined empirically. Certainly the fluorous ligands of **7** and **13**, which must be extruded en route to nanoparticles, *could* have provided the requisite stabilization. It therefore remains possible that ligand modifications might reverse the phase affinity, giving recyclable fluorous catalysts.

What do our and other data suggest regarding the active Heck catalyst derived from the Milstein palladacycle **B** (Fig. 2)? Detailed kinetic studies of the closely related Blackmond/Pfaltz catalyst precursor **D** clearly establish homogeneous pathways, with rates dependent upon concentrations of dissolved palladium complexes.[43] However, Nowotny has found that the similar polystyrene-supported palladacycle **H** (Fig. 7) exhibits characteristics comparable to **7** and **13**.[39] These include an induction period for the first cycle, little or no activity in subsequent cycles, and complete retention of activity in the supernatant after removal of the insoluble polystyrene support. Bedford has reported similar behavior for the silica-bound palladacycles **I**/**I′** in Suzuki reactions.[41a] Hence, the nature of the catalytically active species appears to be an extremely sensitive function of structure.

In this regard, it is worth emphasizing that no nanoparticles are detected during Heck reactions with the Herrmann/Beller P-donor palladacycle **A**.[36a] For this reason, we had thought that sulfur, another second-row donor atom, might give more robust fluorous palladacycles. However, the S-donor palladacycle **13** appears to be slightly more labile than **7**. There are no data at present suggesting that Dupont's similar catalyst precursor **C** also functions as a palladium nanoparticle source. However, several other palladium adducts of sulfur donor ligands have been evaluated as catalyst precursors for Heck and Suzuki reactions. In many cases, such as we have described for the fluorous complexes $[(R_{f8}(CH_2)_n)_2S]_2PdCl_2$ (n = 2,3),[13b] there is good evidence that the active catalyst is a form of metallic palladium.

In view of the above data, it is in our opinion worth critically examining whether any of the fluorous palladium catalysts so far applied in carbon–carbon bond forming reactions of aryl halides[12–14] are truly *molecular*. As pointed out in a recent commentary,[35] activity losses of the type in Table 3 can be masked in several ways. One is to use a high catalyst loading. Another is to select a reaction time for the first few cycles that is much longer than required (*e.g.*, 10 h for the **7**/methyl acrylate runs in Table 3). This can allow high yields to be maintained, even when (for example) 90% of the catalyst has been lost. Rate experiments of the type in Fig. 4 unambiguously indicate the degree of retained activity and catalyst, but for some reason are not as frequently conducted. Despite these question marks, we continue to believe that highly active and easily recycled molecular fluorous catalysts for the Heck and Suzuki reactions are realistic objectives. Other types of chelate ligands appear to offer enhanced stabilities, and are currently under active investigation in our laboratory.[44]

This work, together with related studies mentioned above,[39,41a] illustrates the valuable insight that recoverable

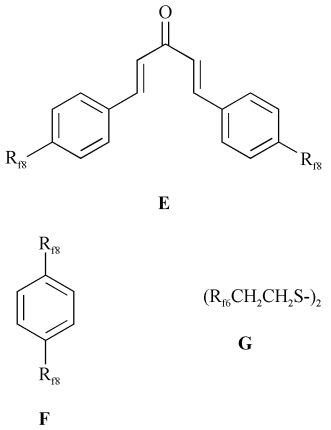


Fig. 6 Representative fluorous compounds that stabilize palladium nanoparticles.[38]

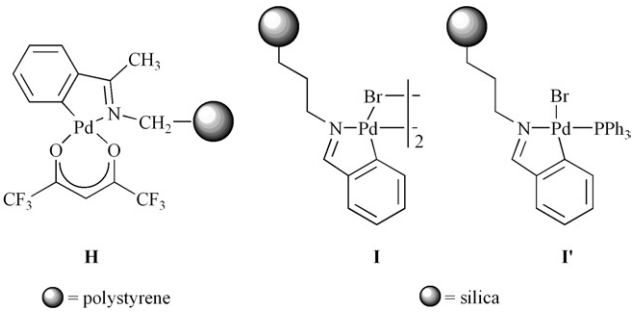


Fig. 7 Other immobilized palladacycles that have been evaluated as catalyst precursors for Heck and Suzuki reactions.[39,41a]

and/or immobilized compounds can offer in the elucidation of mechanism.[45,46] In order to rationally design a recoverable catalyst, a model for the active species is necessary. The success or failure of the recoverable catalyst in turn bears upon the accuracy of the model. Whenever (1) induction periods are observed, *and* (2) activity remains in a phase different from that of the recovered "catalyst", *and* (3) the recovered material continues to exhibit induction periods, together with reduced activity, it is highly probable that the immobilized species bears little relationship to the active catalyst. Naturally, there are a variety of related scenarios, such as simultaneous catalysis by an immobilized species and a leached species. Regardless, such "phase tests"[45,46] deserve more frequent use in the study of catalyst mechanisms.

Conclusion

This study has established new catalyst systems for the Heck and Suzuki reactions (Tables 2–4) based upon the novel fluorous palladacycle catalyst precursors **7** and **13**. From the standpoint of TON values, the Heck reactions rank with the best in the literature. Complexes **7** and **13** represent new examples of thermomorphic fluorous compounds, with little or no solubility in organic solvents at room temperature but significant solubility at elevated temperatures, thus enabling homogeneous reactions in the absence of fluorous solvents.[4,5] However, in apparent contrast to closely related non-fluorous palladacycles, they act mainly as steady-state sources of extremely reactive, soluble colloidal palladium nanoparticles. Such species are of great current interest,[36–42] but those obtained from **7** and **13** are not amenable to fluorous recycling protocols. Fluorous analogs of existing Heck catalysts that are expected to show greater stabilities with respect to nanoparticles, and function as molecular catalysts, will be described in future reports.[44]

Experimental

General

All reactions were conducted under N_2. Chemicals were treated as follows: THF, ether, toluene, hexanes, distilled from Na/benzophenone; Et_3N, distilled from Na; $CF_3C_6F_{11}$ (Oakwood or ABCR), distilled from P_2O_5; $CF_3C_6H_5$ (ABCR), distilled from CaH_2; *i*-PrMgCl (2.0 M in ether, Aldrich), standardized;[47] $C_8F_{17}Br$ (Fluorochem), $(Ph_3P)_3RhCl$, $Pd(OAc)_2$ (2 × Strem), PPh_3, phenyl iodide (2 × Fluka), bromobenzene, *p*-bromotoluene, *p*-bromoacetophenone, *p*-bromoanisole, methyl acrylate, $PhB(OH)_2$, *p*-iodobenzaldehyde, aliquat 336 (8 × Aldrich), styrene (Acros), $CDCl_3$ (Cambridge Isotope or Aldrich) and other solvents, used as received. NMR spectra were recorded on 400 MHz spectrometers at ambient probe temperatures unless noted and referenced to residual internal $CHCl_3$ (^1H, δ 7.27) or $CDCl_3$ (^{13}C, δ 77.2). IR spectra were measured on an ASI React-IR spectrometer. GC data were acquired using a ThermoQuest Trace GC 2000 instrument fitted with a capillary column (OPTIMA-5-0.25 μm; 25 m × 0.32 mm). HPLC was conducted on a Thermoquest instrument package (pump/autosampler/detector P4000/AS3000/UV6000LP). DSC and TGA data were recorded with a Mettler-Toledo DSC821 instrument and treated by standard methods.[30] TEM data were obtained with a Philips CM 300 UT instrument. Elemental analyses were conducted with a Carlo Erba EA1110 instrument (in-house).

p-$R_{f8}CH_2CH{=}CHC_6H_4I$ (2)

A flask was sequentially charged with *p*-iodobenzaldehyde (**1**; 0.724 g, 3.12 mmol), $R_{f8}CH_2CH_2PPh_3^+I^-$ (3.91 g, 4.68 mmol),[24a] K_2CO_3 (0.646 g, 4.68 mmol), *p*-dioxane (15 mL), and water (0.5 mL), fitted with a condenser, and placed in a 95 °C oil bath. The mixture was stirred and monitored by TLC (1:9 v/v EtOAc/hexanes). After 24 h, reaction was complete. The solvent was removed by rotary evaporation. Water (25 mL) was added to the yellow oil, and the mixture extracted with CH_2Cl_2 (2 × 50 mL). The extracts were dried ($MgSO_4$) and the solvent removed by rotary evaporation. The oily residue was chromatographed on a silica gel column (eluent hexane) to give **2** as a colorless oil that solidified upon standing (1.994 g, 3.011 mmol, 96%, 90:10 *Z*/*E*).[48] Calcd for $C_{17}H_8F_{17}I$: C, 30.83; H, 1.21. Found: C, 31.08; H, 1.08%.

NMR ($CDCl_3$): ^1H 2.97–3.21 (2 overlapping dt, $^3J_{HF}$ = 18 Hz, $^3J_{HH}$ = 7 Hz, CF_2CH_2, *Z*/*E*), 5.78 (dt, $^3J_{HH}$ = 11 Hz, $^3J_{HH}$ = 7 Hz, $CH_2CH{=}$, *Z*), 6.16 (dt, $^3J_{HH}$ = 16 Hz, $^3J_{HH}$ = 7 7 Hz, $CH_2CH{=}$, *E*), 6.55 (d, $^3J_{HH}$ = 16 Hz, $=CHC_6H_4$, *E*), 6.72 (d, $^3J_{HH}$ = 11 Hz, $=CHC_6H_4$, *Z*), 6.97 and 7.77 (2d, $^3J_{HH}$ = 8 Hz, C_6H_4, *Z*), 7.13 and 7.68 (2d, $^3J_{HH}$ = 8 Hz, C_6H_4, *E*); $^{13}C\{^1H\}$ (partial, *Z*) 30.7 (t, $^2J_{CF}$ = 22 Hz, CF_2CH_2), 119.0 (t, $^3J_{CF}$ = 5 Hz, $CH_2CH{=}$), 128.4, 130.4, 134.7, 135.5, 138.0 (5s, $=CHC_6H_4$).

p-$R_{f8}CH_2CH{=}CHC_6H_4CH(OH)(CH_2)_2R_{f8}$ (3)

A Schlenk flask was charged with **2** (0.795 g, 1.200 mmol) and THF (10 mL). Then *i*-PrMgCl (2.4 M in ether, 0.60 mL, 1.44 mmol) was added with stirring over the course of 5 min (room temperature). The mixture warmed slightly and turned yellow. After 30 min, a solution of $R_{f8}CH_2CH_2CHO$ (0.686 g, 1.44 mmol)[28] in THF (10 mL) was added over 10 min. After an additional 2 h, aqueous HCl (0.1 M, 25 mL) was added. The mixture was extracted with ether (2 × 50 mL). The extracts were dried ($MgSO_4$) and the solvent removed by rotary evaporation. The yellow oil was chromatographed on a silica gel column (1:9 v/v ether/hexanes) to give **3** as a colorless oil that solidified upon standing (1.131 g, 1.117 mmol, 93%, 90:10 *Z*/*E*).[48] Calcd for $C_{28}H_{14}F_{34}O$: C, 33.22; H, 1.39. Found: C, 33.08; H, 1.28%.

NMR ($CDCl_3$): ^1H 1.92 (br s, OH), 1.99–2.38 (m, $CH_2CH_2CF_2$, *E*/*Z*), 3.14–2.98 (2 overlapping dt, $^3J_{HF}$ = 18 Hz, $^3J_{HH}$ = 7 Hz, $CF_2CH_2CH{=}$, *Z*/*E*), 4.81 (t, $^3J_{HH}$ = 6 Hz, CHOH), 5.78 (dt, $^3J_{HH}$ = 11 Hz, $^3J_{HH}$ = 7 Hz, $CH_2CH{=}$, *Z*), 6.16 (dt, $^3J_{HH}$ = 16 Hz, $^3J_{HH}$ = 7 Hz, $CH_2CH{=}$, *E*), 6.63 (d, $^3J_{HH}$ = 16 Hz, $=CHC_6H_4$, *E*), 6.83 (d, $^3J_{HH}$ = 11 Hz, $=CHC_6H_4$, *Z*), 7.25 and 7.37 (2d, $^3J_{HH}$ = 8 Hz, C_6H_4, *Z*), 7.33 and 7.41 (2d, $^3J_{HH}$ = 8 Hz, C_6H_4, *E*); $^{13}C\{^1H\}$ (partial, *Z*) 27.5 (t, $^2J_{CF}$ = 22 Hz, $CH_2CH_2CF_2$), 29.5 (br s, $CH_2CH_2CF_2$), 30.7 (t, $^2J_{CF}$ = 22 Hz, $CF_2CH_2CH{=}$), 73.1 (s, CHOH), 118.6 (t, $^3J_{CF}$ = 5 Hz, $=CHCH_2$), 126.1, 129.0, 135.2, 136.0, 143.0 (5s, $=CHC_6H_4$).

p-$R_{f8}(CH_2)_3C_6H_4CH(OH)(CH_2)_2R_{f8}$ (4)

A Fisher–Porter bottle was charged with **3** (0.770 g, 0.761 mmol), $(Ph_3P)_3RhCl$ (0.053 g, 0.057 mmol), and $CF_3C_6H_5$/EtOH (20 mL, 1:1 v/v). The system was purged with H_2 and pressurized to 75 psig. The bottle was placed in a 40 °C oil bath and the mixture stirred. After 14 h, the bath was removed, the system vented, and the solvents removed by rotary evaporation. The residue was chromatographed on a silica gel column (1:9 v/v ether/hexanes) to give **4** as a white solid (0.695 g, 0.685 mmol, 90%), mp 89 °C (capillary), 89.8 °C (DSC). Calcd for $C_{28}H_{16}F_{34}O$: C, 33.15; H, 1.59. Found: C, 32.76; H, 1.31%.

NMR (4:1 v/v $CDCl_3/CF_3C_6F_5$): ^1H 1.88 (br s, OH), 1.90–2.39 (m, $2CH_2CH_2CF_2$), 2.76 (t, $^3J_{HH}$ = 7 Hz, $CH_2C_6H_4$), 4.77 (t, $^3J_{HH}$ = 6 Hz, CHOH), 7.22 and 7.33 (2d, $^3J_{HH}$ = 8 Hz, C_6H_4); $^{13}C\{^1H\}$ (partial) 22.0 (br s, $CF_2CH_2CH_2CH_2$), 27.6 (t, $^2J_{CF}$ = 22 Hz, $CH(OH)CH_2CH_2CF_2$), 29.6 (br s, $CH(OH)$-$CH_2CH_2CF_2$), 30.7 (t, $^2J_{CF}$ = 22 Hz, $CF_2CH_2CH_2CH_2$), 34.9

(s, $CH_2C_6H_4$), 73.3 (s, *C*HOH), 126.3, 129.0, 141.0, l42.0 (4s, C_6H_4).

p-$R_{f8}(CH_2)_3C_6H_4C(=O)(CH_2)_2R_{f8}$ (5)

A Schlenk flask was charged with **4** (0.642 g, 0.632 mmol), the Dess–Martin periodinane (0.322 g, 0.759 mmol),[29] and $CF_3C_6H_5$ (20 mL). The solution was stirred overnight. Ether (50 mL) was added, and the white suspension poured into a solution of Na_2SO_3 (1.31 g, 5.31 mmol) in saturated aqueous $KHCO_3$ (50 mL). The biphasic mixture was vigorously stirred until the organic phase appeared clear. The organic phase was washed with saturated aqueous $KHCO_3$ (50 mL) and dried ($MgSO_4$). The solvent was removed by rotary evaporation. The residue was chromatographed on a silica gel column (3:17 v/v $CHCl_3$/hexanes) to give **5** as a white solid (0.608 g, 0.600 mmol, 95%), mp 112–113 °C (capillary), 110.9 °C (DSC). Calcd for $C_{28}H_{14}F_{34}O$: C, 33.22; H, 1.39. Found: C, 33.42; H, 1.38%. IR (cm^{-1}, thin film) $\nu_{C=O}$ 1683.

NMR (4:1 v/v $CDCl_3/CF_3C_6F_5$): ^1H 1.96–2.15 (m, $CF_2CH_2CH_2CH_2$), 2.54–2.68 (m, $C(=O)CH_2CH_2$), 2.80 (t, $^3J_{HH} = 7$ Hz, $CH_2C_6H_4$), 3.30 (t, $^3J_{HH} = 7$ Hz, $C(=O)CH_2$), 7.32 and 7.95 (2d, $^3J_{HH} = 8$ Hz, C_6H_4); $^{13}C\{^1H\}$ (partial) 21.7 (br s, $CF_2CH_2CH_2CH_2$), 25.8 (t, $^2J_{CF} = 22$ Hz, $C(=O)CH_2CH_2CF_2$), 29.6 (s, $C(=O)CH_2CH_2CF_2$), 30.5 (t, $^2J_{CF} = 22$ Hz, $CF_2CH_2CH_2CH_2$), 35.2 (s, $CF_2CH_2CH_2CH_2$), 128.8, 129.1, 134.9, l47.3 (4s, C_6H_4), 196.3 (s, C=O).

p-$R_{f8}(CH_2)_3C_6H_4C(=N(CH_2)_3R_{f8})(CH_2)_2R_{f8}$ (6)

A flask was charged with **5** (0.522 g, 0.516 mmol), $H_2NCH_2CH_2CH_2R_{f8}$ (0.492 g, 1.031 mmol),[28] $SnCl_2(H_2O)_2$ (0.017 g, 0.10 mmol), and toluene (50 mL), fitted with a Dean–Stark trap, and placed in a 140 °C oil bath. After 14 h, the mixture was cooled and the solvent was removed by oil pump vacuum. The residue was flash chromatographed (silica gel dried for a minimum of 5 days at 120 °C) using dry hexanes/THF (3:1 v/v). The solvent was removed by rotary evaporation to give **6** as a colorless oil that solidified upon standing (0.744 g, 0.506 mmol, 98%, 35:65 *Z*/*E*).[49] Calcd for $C_{39}H_{20}F_{51}N$: C, 31.83; H, 1.37. Found: C, 32.06; H, 1.47%. IR (cm^{-1}, thin film) $\nu_{C=N}$ 1657.

NMR ($CDCl_3$):[50] ^1H 1.81–2.30 (m, $2CH_2CH_2CH_2CF_2$, *Z*/*E*, $N=CCH_2CH_2CF_2$, *Z*), 2.49–2.60 (m, $N=CCH_2CH_2CF_2$, *E*), 2.74 (t, $^3J_{HH} = 8$ Hz, $CH_2C_6H_4$, *E*), 2.75 (t, $^3J_{HH} = 8$ Hz, $CH_2C_6H_4$, *Z*), 2.82 (t, $^3J_{HH} = 8$ Hz, $N=CCH_2$, *E*), 3.01 (t, $^3J_{HH} = 8$ Hz, $N=CCH_2$, *Z*), 3.30 (t, $^3J_{HH} = 8$ Hz, NCH_2, *E*), 3.61 (t, $^3J_{HH} = 8$ Hz, NCH_2, *Z*), 7.07 and 7.25 (2d, $^3J_{HH} = 8$ Hz, C_6H_4, *E*), 7.24 and 7.70 (2d, $^3J_{HH} = 8$ Hz, C_6H_4, *Z*); $^{13}C\{^1H\}$ (partial) 19.3 (s, $CH_2C{=}N$, *Z*), 21.7 (s, NCH_2CH_2, *Z*), 21.8 (s, NCH_2CH_2, *E*), 22.1 (br s, $CH_2CH_2C_6H_4$, *Z*/*E*), 27.0 (t, $^2J_{CF} = 22$ Hz, $N=CCH_2CH_2$, *E*), 28.8 (t, $^2J_{CF} = 22$ Hz, $CH_2CH_2CH_2C_6H_4$, *Z*/*E*), 29.0 (t, $^2J_{CF} = 22$ Hz, $N=CCH_2CH_2$, *Z*), 30.3 (t, $^2J_{CF} = 22$ Hz, $NCH_2CH_2CH_2$, *Z*), 30.4 (t, $^2J_{CF} = 22$ Hz, $NCH_2CH_2CH_2$, *E*), 31.7 (s, $CH_2C{=}N$, *E*), 34.8 (s, $CH_2C_6H_4$, *Z*), 34.9 (s, $CH_2C_6H_4$, *E*), 50.0 (s, $C{=}NCH_2$, *Z*), 51.4 (s, $C{=}NCH_2$, *E*), 126.7 (s, C_6H_4, *E*), 127.2 (s, C_6H_4, *Z*), 129.0 (s, C_6H_4, *Z*/*E*), 136.3 (s, C_6H_4, *E*), 136.8 (s, C_6H_4, *Z*), 141.7 (s, C_6H_4, *E*), 143.3 (s, C_6H_4, *Z*), 166.0 (s, C=N, *Z*), 168.8 (s, C=N, *E*).

Imine palladacycle acetate 7

A Schlenk flask was charged with **6** (1.019 g, 0.692 mmol), $Pd(OAc)_2$ (0.155 g, 0.692 mmol), and AcOH (12 mL), and placed in a 95 °C oil bath. The mixture was stirred (1.5 h) and cooled to room temperature. The solvent was removed by rotary evaporation, and $CF_3C_6H_5$ (10 mL) was added. This was poured on top of a short column of silica gel in $CF_3C_6H_5$ (10 cm × 2.5 cm Ø). The column was washed with $CF_3C_6H_5$ (*ca.* two times the column volume) and then eluted with $CF_3C_6H_5$/EtOH (9:1 v/v). The solvent was removed from the last fraction by rotary evaporation. The residue was dried by oil pump vacuum to give **7** as a dark yellow gum (0.986 g, 0.301 mmol, 87%). A solution of **7** (0.070 g), in $CF_3C_6H_5$ (2 mL) was layered with toluene (10 mL) and kept at 4 °C. This gave yellow needles of **7**, mp 78–80 °C (capillary), 78.5 °C (DSC). Calcd for $C_{82}H_{44}F_{102}N_2O_4Pd_2$: C, 30.10; H, 1.35. Found: C, 30.15; H, 1.13%. IR (cm^{-1}, thin film) $\nu_{C=N}$ 1587, $\nu_{C=O}$[20c,31] 1571, 1424.

NMR (4:1 v/v $CDCl_3/CF_3C_6F_5$):[50] ^1H 1.35–1.45 (m, $N=CCH_2CHH'$), 1.70–1.81 (m, NCH_2CHH', $N=CCH_2CHH'$), 1.87–1.94 (m, $CH_2CH_2C_6H_3$), 2.08–2.25 (m, $NCH_2CH_2CH_2$, $CH_2CH_2CH_2C_6H_3$), 2.17 (s, CH_3), 2.40–2.45 (m, NCH_2CHH'), 2.50–2.55 (m, $N=CCHH'$), 2.61–2.73 (m, $N=CCHH'$, $CH_2C_6H_3$), 2.98–3.05 (m, $NCHH'$), 3.22–3.29 (m, $NCHH'$), 6.88, 6.92 (2d, $^3J_{HH} = 8$ Hz, C_6H_3), 6.98 (s, C_6H_3); $^{13}C\{^1H\}$ (partial) 18.7 (s, $N=CCH_2$), 21.5 (s, NCH_2CH_2), 22.3 (s, $CH_2CH_2C_6H_3$), 24.0 (s, CH_3), 28.8, 31.0 (2t, $^2J_{CF} = 22$ Hz, $CH_2CH_2CH_2C_6H_3$, $NCH_2CH_2CH_2$), 29.4 (t, $^2J_{CF} = 22$ Hz, $N=CCH_2CH_2$), 35.8 (s, $CH_2C_6H_3$), 52.2 (s, NCH_2), 124.3, 126.2, 128.7, 129.1 132.9, 157.1[51] (6s, C_6H_3), 179.9 (s, C=N), 181.9 (s, C=O).

Imine palladacycle chloride 8

A Schlenk flask was charged with a solution of **7** (0.358 g, 0.109 mmol) in $CF_3C_6H_5$ (8 mL). Then a solution of LiCl (0.070 g, 2.19 mmol) in CH_3OH (5 mL) was added with stirring. After 1 h, solvent was removed from the cloudy mixture by oil pump vacuum. The yellow residue was triturated with CH_3OH (10 mL), collected by filtration, washed with CH_3OH (3 × 10 mL) and ether (2 × 5 mL), and dried by oil pump vacuum. This gave **8** as a beige powder (0.300 g, 0.0093 mmol, 85%), mp 176 °C (capillary), 179.0 °C (DSC). Calcd for $C_{78}H_{38}F_{102}Cl_2N_2Pd_2$: C, 29.05; H, 1.19. Found: C, 29.18; H, 1.69%. IR (cm^{-1}, thin film) $\nu_{C=N}$ 1583.

NMR (1:1 v/v $CDCl_3/CF_3C_6F_5$, 57 °C): ^1H 1.99–2.57 (m, $2CH_2CH_2CH_2CF_2$, $N=CCH_2CH_2CF_2$), 2.78, 2.84 (2t, $^3J_{HH} = 7$ Hz, $CH_2C_6H_3$), 3.12–3.16 (m, $N=CCH_2$), 3.84–3.91 (m, NCH_2), 7.07–7.23 (m, C_6H_3); $^{13}C\{^1H\}$ (partial) 19.6, 22.0, 22.3 (3s, $3CH_2CH_2CF_2$), 29.2, 30.3, 31.3 (3t, $^2J_{CF} = 22$ Hz, $3CH_2CF_2$), 36.0 (s, $CH_2C_6H_3$), 53.0 (s, CH_2N), 125.5, 127.3, 134.1, 134.3, 145.1, 156.0[51] (6s, C_6H_3), 182.7 (s, C=N).

Imine palladacycle iodide 9

Complex **7** (0.240 g, 0.073 mmol), $CF_3C_6H_5$ (8 mL), LiI (0.200 g, 1.49 mmol), and CH_3OH (5 mL) were combined in a procedure analogous to that given for **8**. An identical workup gave **9** as a yellow powder (0.215 g, 0.063 mmol, 86%), mp 182 °C (capillary), 188.5 °C (DSC). Calcd for $C_{78}H_{38}F_{102}I_2N_2Pd_2$: C, 27.49; H, 1.12. Found: C, 27.54; H, 1.20%. IR (cm^{-1}, thin film) $\nu_{C=N}$ 1583.

NMR (1:1 v/v $CDCl_3/CF_3C_6F_5$, 57 °C): ^1H 2.00–2.75 (m, $2CH_2CH_2CH_2CF_2$, $N=CCH_2CH_2CF_2$), 2.80–2.85 (m, $CH_2C_6H_3$), 3.15–3.19 (m, $N=CCH_2$), 4.15–4.18 (m, NCH_2), 7.10–7.16, 7.22–7.24, and 7.71 (m/m/s, C_6H_3); $^{13}C\{^1H\}$ (partial) 20.0, 22.0, 22.6 (3s, $3CH_2CH_2CF_2$), 28.7, 30.4, 31.3 (3t, $^2J_{CF} = 22$ Hz, $3CH_2CF_2$), 36.0 (s, $CH_2C_6H_3$), 54.6 (s, CH_2N), 125.2, 128.0, 128.2, 139.4, 146.5, 159.7[51] (6s, C_6H_3), 183.1 (s, C=N).

Imine palladacycle phosphine 10

A. A Schlenk flask was charged with **7** (0.450 g, 0.137 mmol), LiCl (0.058 g, 1.38 mmol), and PPh_3 (0.079 g, 0.302 mmol). THF (10 mL) was added with stirring, and **7** dissolved over *ca.* 0.5 h. After 1 h, the solvent was removed by oil pump

vacuum. The yellow powder was extracted with CH_2Cl_2 (2×10 mL). The extract was filtered under N_2 into a new Schlenk flask and taken to dryness by oil pump vacuum. The residue was triturated with hexanes (5 mL, 15–20 min), collected by filtration, washed with hexanes (2×10 mL) and dried by oil pump vacuum. This gave **10** as a beige powder (0.408 g, 0.217 mmol, 79%). **B**. A Schlenk flask was charged with **8** (0.269 g, 0.083 mmol), PPh_3 (0.048 g, 0.18 mmol), and CH_2Cl_2 (10 mL). The suspension was vigorously stirred. After 1 h, the solvent was removed from the light yellow solution by oil pump vacuum. Hexanes (5 mL) was added to the solid, which was isolated by filtration, washed with hexanes (2×10 mL), and dried by oil pump vacuum to give **10** as a beige powder (0.254 g, 0.135 mmol, 81%), mp 135 °C (capillary), 138.4 °C (DSC). T_i, 228.4 °C (TGA). Calcd for $C_{57}H_{34}ClF_{51}NPPd$: C, 36.52; H, 1.82. Found: C, 36.61; H, 1.89%. IR (cm^{-1}, thin film) $\nu_{C=N}$ 1586.

NMR ($CDCl_3$):[50] ^1H 1.17–1.25 (m, $CH_2CH_2C_6H_3$), 1.63–1.74 (m, $CH_2CH_2CH_2C_6H_3$), 2.03 (t, $^3J_{HH} = 8$ Hz, $CH_2C_6H_3$), 2.10–2.18 (m, NCH_2CH_2), 2.23–2.36 (m, $NCH_2CH_2CH_2$), 2.40–2.49 (m, $N{=}CCH_2CH_2$), 3.06–3.10 (m, $N{=}CCH_2$), 4.20 (br s, NCH_2), 6.35 (d, $^3J_{PH} = 5$ Hz, 1H of C_6H_3), 6.77 and 7.14 (2d, $^3J_{HH} = 8$ Hz, 2H of C_6H_3), 7.36–7.47 (m, 9H of $P(C_6H_5)_3$), 7.72–7.77 (m, 6H of $P(C_6H_5)_3$); $^{13}C\{^1H\}$ (partial) 19.4 (s, $N{=}CCH_2$), 21.3 (s, $CH_2CH_2C_6H_3$), 22.1 (s, NCH_2CH_2), 28.3 (t, $^2J_{CF} = 22$ Hz, $NCH_2CH_2CH_2$), 29.4 (t, $^2J_{CF} = 22$ Hz, $N{=}CCH_2CH_2$), 30.3 (t, $^2J_{CF} = 22$ Hz, $CH_2CH_2CH_2C_6H_3$), 35.1 (s, $CH_2C_6H_3$), 51.0 (s, NCH_2), 124.4, 127.0 (2s, 2C of C_6H_3), 128.4 (d, $^2J_{PC} = 11$ Hz, *m*-PPh), 131.1 (s, *p*-PPh), 131.2 (d, $^1J_{PC} = 50$ Hz, *i*-PPh), 135.6 (d, $^3J_{PC} = 13$ Hz, *o*-PPh), 139.5 (d, $^3J_{PC} = 11$ Hz, 1C of C_6H_3), 143.8, 146.5, 159.9[51] (3s, 3C of C_6H_3), 181.6 (s, C=N); $^{31}P\{^1H\}$ 42.9 (s, PPh_3).

$R_{f8}CH_2CH_2CH_2SH$ (11)[33]

A round bottomed flask was charged with $R_{f8}CH_2CH_2CH_2I$ (5.02 g, 8.53 mmol),[11a] thiourea (0.973 g, 12.8 mmol), phase transfer catalyst aliquat 336 (0.221 g, 0.546 mmol), and water (15 mL), fitted with a condenser, and placed in a 100 °C bath. The mixture was stirred and a precipitate slowly formed. After 20 h, aqueous KOH (50 mL, 0.1 M) was added. After 0.5 h, the mixture was allowed to cool to room temperature. Concentrated HCl was added until the sample was acidic. The mixture was extracted with CH_2Cl_2 (2×50 mL). The extract was dried ($MgSO_4$), and the solvent was removed by rotary evaporation. The light brown oil was chromatographed (silica gel column, hexanes) to give **11** as a clear oil (3.30 g, 6.68 mmol, 78%). Calcd for $C_{11}H_7F_{17}S$: C, 26.73; H, 1.42. Found: C, 26.83; H, 1.42%.

NMR ($CDCl_3$): ^1H 1.36 (t, $^3J_{HH} = 8$ Hz, SH), 1.87–1.95 (m, $CF_2CH_2CH_2CH_2$), 2.14–2.27 (m, $CF_2CH_2CH_2CH_2$), 2.61 (dt, $^3J_{HH} = 8$ Hz, $^3J_{HH} = 7$ Hz, $CF_2CH_2CH_2CH_2$); $^{13}C\{^1H\}$ (partial) 23.8 (s, $CF_2CH_2CH_2CH_2$), 24.6 (s, $CF_2CH_2CH_2CH_2$), 29.5 (t, $^2J_{CF} = 22$ Hz, $CF_2CH_2CH_2CH_2$).

p-$R_{f8}(CH_2)_3C_6H_4CH(S(CH_2)_3R_{f8})(CH_2)_2R_{f8}$ (12)

A Schlenk flask was charged with **4** (1.00 g, 0.987 mmol), **11** (0.763 g, 1.54 mmol), ZnI_2 (0.315 g, 0.986 mmol), and $CF_3C_6H_5$ (15 mL), and placed in a 60 °C bath. The solution was stirred. After 16 h, water (50 mL) was added. The mixture was extracted with ether (2×50 mL). The extract was dried ($MgSO_4$), and the solvents were removed by rotary evaporation. The residue was placed on the top of a silica gel column packed with hexanes. The column was eluted with hexanes (removing excess **11**) and then hexanes/ether (20:1 v/v). The solvents were removed from the latter fractions by oil pump vacuum to give **12** as a white solid (0.929 g, 0.632 mmol, 64%), mp 48 °C (capillary), 47.8 °C (DSC). Calcd for $C_{39}H_{21}F_{51}S$: C, 31.42; H, 1.42. Found: C, 31.42; H, 1.34%.

NMR ($CDCl_3$): ^1H 1.68–1.72 (m, $CHCH_2CH_2CF_2$), 1.89–2.19 (m, $CF_2CH_2CH_2CH_2$, $SCH_2CH_2CH_2$, $SCHCH_2CH_2CF_2$), 2.32 and 2.42 (2 quint, $^2J_{HH} = 13$ Hz, $^3J_{HH} = 7$ Hz, $SCHH'CH_2CH_2$ and $SCHH'CH_2CH_2$), 2.69 (t, $^3J_{HH} = 7$ Hz, $CF_2CH_2CH_2CH_2$), 3.74 (t, $^3J_{HH} = 7$ Hz, $CHCH_2CH_2CF_2$), 7.14 and 7.22 (2d, $^3J_{HH} = 8$ Hz, C_6H_4); $^{13}C\{^1H\}$ (partial) 19.9 (s, $CHCH_2CH_2CF_2$), 21.6, 27.0 (2s, $CF_2CH_2CH_2CH_2$, $SCH_2CH_2CH_2$), 29.1, 29.4, 30.1 (3t, $^2J_{CF} = 22$ Hz, CF_2CH_2), 30.2 (s, $SCH_2CH_2CH_2$), 34.5 (s, $CF_2CH_2CH_2CH_2$), 48.6 (s, $CHCH_2CH_2CF_2$), 127.7, 128.8, 139.0, l40.3 (4s, C_6H_4).

Thioether palladacycle acetate 13

Complex **12** (0.740 g, 0.496 mmol), $Pd(OAc)_2$ (0.111 g, 0.496 mmol), and AcOH (15 mL) were reacted in a procedure analogous to that given for **7** (2 h). A similar workup (15 cm × 2.5 cm Ø column) gave **13** as a dark yellow gum (0.695 g, 0.210 mmol, 84%). Calcd for $C_{82}H_{46}F_{102}S_2O_4Pd_2$: C, 29.75; H, 1.40; S, 1.94. Found: C, 30.54; H, 1.55; S, 1.80%. IR (cm^{-1}, thin film) $\nu_{C=O}$[20c,31] 1567, 1424.

NMR (4:1 v/v $CDCl_3/CF_3C_6F_5$; see text regarding isomers): ^1H 1.28–2.66 (m, 14H), 2.12 (br s, CH_3) 2.85–4.50 (m, $CHSCHH'$), 6.66–7.20 (m, C_6H_3); $^{13}C\{^1H\}$ (partial) 14.1, 20.3, 22.1, 24.2 (4br s, CH_2), 29.6–30.9 (br t, $3CH_2CF_2$), 30.1, 30.4 (2s, CH_3, SCH_2), 35.2 (br s, $CH_2C_6H_3$), 58.3 (br s, SCH_2), 181.2 (br s, C=O).

Partition coefficients (Table 1)

The following are representative. **A**. A 10 mL vial was charged with **6** (0.0236 g, 0.0160 mmol), $CF_3C_6F_{11}$ (2.000 mL), and toluene (2.000 mL), fitted with a mininert valve, and vigorously shaken (2 min). After 12 h (24 °C), a 0.400 mL aliquot of each layer was added to a hexane solution of eicosane (2.000 mL, 0.0273 M). GC analysis (average of 7–8 injections) showed 0.00304 mmol of **6** in the $CF_3C_6F_{11}$ aliquot and 0.000040 mmol in the toluene aliquot (98.7:1.3; a 2.000/0.400 scale factor gives a mass balance of 0.0226 g, 96%). **B**. A 10 mL vial was charged with **7** (0.0104 g, 0.0031 mmol), $CF_3C_6F_{11}$ (2.000 mL), and toluene (2.000 mL), fitted with a mininert valve, and vigorously shaken (2 min). After 2 h (24 °C), a 0.250 mL aliquot of the fluorous phase and a 0.750 mL aliquot of the non-fluorous phase were removed. The solvents were evaporated and the residues dried by oil pump vacuum (1 h). Each residue was taken up in $CF_3C_6H_5$/EtOH (9:1 v/v; 0.500 mL) and analyzed by HPLC (average of 5 injections, 200 × 4 mm Nucleosil 100-5 column, UV/visible detector). The relative peak intensities were (after normalization to the aliquot volumes) 95.5:4.5.

Heck and Suzuki reactions

The following are representative. Table 2: A Schlenk tube was sequentially charged with DMF (6 mL), phenyl iodide (0.560 mL, 5.02 mmol), methyl acrylate (0.565 mL, 6.28 mmol), Et_3N (1.400 mL, 10.05 mmol), and a solution of **7** in $CF_3C_6H_5$ (0.000229 M; 0.015 mL, 3.44×10^{-6} mmol), fitted with a condenser, and placed in a 140 °C oil bath. The solution was vigorously stirred (14 h), removed from the bath to cool, and diluted with ether to 25.00 mL. An aliquot (0.500 mL) was added to a toluene solution of tridecane (0.250 mL, 0.100 M). GC analysis showed only *trans*-methyl cinnamate (100%, TON 1 460 000). The aliquot was recombined with the mother solution. A standard basic aqueous workup and flash chromatography on silica gel (9:1 v/v hexanes/EtOAc) gave *trans*-methyl cinnamate in 98% yield (0.797 g, 4.914 mmol). Table 3: A Schlenk tube was sequentially charged with **7** (0.0014 g, 0.00043 mmol), DMF (4 mL), phenyl iodide (0.250 mL, 2.24

mmol), methyl acrylate (0.250 mL, 2.78 mmol), and Et_3N (0.625 mL, 4.48 mmol), and placed in a 100 °C oil bath. The solution was vigorously stirred (2 h), and removed from the bath to cool (0.5 h). Then $C_8F_{17}Br$ (1 mL) was added to give a biphasic system. The upper DMF layer was removed by syringe, and the $C_8F_{17}Br$ phase extracted with DMF (2 mL). The combined DMF extracts were diluted with ether to 20.00 mL. An aliquot (0.5 mL) was added to a toluene solution of tridecane (0.250 mL, 0.100 M). GC analysis showed only *trans*-methyl cinnamate (100%; TON 5100 (rounded digits included)). The $C_8F_{17}Br$ phase was taken to dryness by oil pump vacuum (0.5 h). The tube was recharged with identical quantities of DMF and all reactants except **7**. A second cycle was analogously conducted. Table 4: A Schlenk tube was sequentially charged with $PhB(OH)_2$ (1.455 g, 7.534 mmol), K_3PO_4 (2.132 g, 10.05 mmol), toluene (13 mL), phenyl iodide (0.560 mL, 5.023 mmol), and a solution of **7** in $CF_3C_6H_5$ (0.000229 M; 0.020 mL, 4.58×10^{-6} mmol), fitted with a condenser, and placed in a 130 °C oil bath. The suspension was vigorously stirred (38 h), removed from the bath to cool, and diluted with ether to 25.00 mL. An aliquot (0.5 mL) was added to a solution of tridecane (0.250 mL, 0.100 M). GC analysis showed the partial consumption of phenyl iodide (65%) and formation of biphenyl (40%, TON 440 000).

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References

1 (*a*) I. T. Horváth, *Acc. Chem. Res.*, 1998, **31**, 641; (*b*) E. de Wolf, G. van Koten and B.-J. Deelman, *Chem. Soc. Rev.*, 1999, **28**, 37; (*c*) M. Cavazzini, F. Montanari, G. Pozzi and S. Quici, *J. Fluorine Chem.*, 1999, **94**, 183; (*d*) E. G. Hope and A. M. Stuart, *J. Fluorine Chem.*, 1999, **100**, 75; (*e*) J. Yoshida and K. Itami, *Chem. Rev.*, 2002, **102**, 3693.
2 Survey of practical considerations and underlying physical principles: L. P. Barthel-Rosa and J. A. Gladysz, *Coord. Chem. Rev.*, 1999, **190–192**, 587.
3 J. A. Gladysz and D. P. Curran, *Tetrahedron*, 2002, **58**, 3823 and following papers in this special issue devoted to "fluorous chemistry".
4 M. Wende, R. Meier and J. A. Gladysz, *J. Am. Chem. Soc.*, 2001, **123**, 11 490.
5 (*a*) K. Ishihara, S. Kondo and H. Yamamoto, *Synlett*, 2001, **9**, 1371; (*b*) J. Xiang, A. Orita and J. Otera, *Adv. Synth. Catal.*, 2002, **344**, 84.
6 D. E. Bergbreiter, P. L. Osburn, A. Wilson and E. M. Sink, *J. Am. Chem. Soc.*, 2000, **122**, 9058.
7 (*a*) I. T. Horváth, G. Kiss, R. A. Cook, J. E. Bond, P. A. Stevens, J. Rábai and E. J. Mozeleski, *J. Am. Chem. Soc.*, 1998, **120**, 3133; (*b*) D. F. Foster, D. Gudmunsen, D. J. Adams, A. M. Stuart, E. G. Hope, D. J. Cole-Hamilton, G. P. Schwarz and P. Pogorzelec, *Tetrahedron*, 2002, **58**, 3901.
8 (*a*) D. Rutherford, J. J. J. Juliette, C. Rocaboy, I. T. Horváth and J. A. Gladysz, *Catal. Today*, 1998, **42**, 381; (*b*) B. Richter, A. L. Spek, G. van Koten and B.-J. Deelman, *J. Am. Chem. Soc.*, 2000, **122**, 3945; (*c*) E. de Wolf, A. L. Spek, B. W. M. Kuipers, A. P. Philipse, J. D. Meeldijk, P. H. H. Bomans, P. M. Frederik, B.-J. Deelman and G. van Koten, *Tetrahedron*, 2002, **58**, 3911.
9 J. J. J. Juliette, D. Rutherford, I. T. Horváth and J. A. Gladysz, *J. Am. Chem. Soc.*, 1999, **121**, 2696.
10 (*a*) L. V. Dinh and J. A. Gladysz, *Tetrahedron Lett.*, 1999, **40**, 8995; (*b*) E. de Wolf, E. A. Speets, B.-J. Deelman and G. van Koten, *Organometallics*, 2001, **20**, 3686.
11 (*a*) J.-M. Vincent, A. Rabion, V. K. Yachandra and R. H. Fish, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2346; J.-M. Vincent, A. Rabion, V. K. Yachandra and R. H. Fish, *Angew. Chem.*, 1997, **109**, 2438; (*b*) S. Quici, M. Cavazzini, S. Ceragioli, F. Montanari and G. Pozzi, *Tetrahedron Lett.*, 1999, **40**, 3647; (*c*) G. Pozzi, M. Cavazzini, F. Cinato, F. Montanari and S. Quici, *Eur. J. Org. Chem.*, 1999, 1947; (*d*) T. Nishimura, Y. Maeda, N. Kakiuchi and S. Uemura, *J. Chem. Soc., Perkin Trans. 1*, 2000, 4301; (*e*) S. Colonna, N. Gaggero, F. Montanari, G. Pozzi and S. Quici, *Eur. J. Org. Chem.*, 2001, 181; (*f*) G. Ragagnin, B. Betzemeier, S. Quici and P. Knochel, *Tetrahedron*, 2002, **58**, 3985.
12 Heck reactions: (*a*) J. Moineau, G. Pozzi, S. Quici and D. Sinou, *Tetrahedron Lett.*, 1999, **40**, 7683; (*b*) L. Xu, W. Chen, J. F. Bickley, A. Steiner and J. Xiao, *J. Organomet. Chem.*, 2000, **598**, 409; (*c*) Y. Nakamura, S. Takeuchi, S. Zhang, K. Okumura and Y. Ohgo, *Tetrahedron Lett.*, 2002, **43**, 3053.
13 Suzuki reactions: (*a*) S. Schneider and W. Bannwarth, *Helv. Chim. Acta*, 2001, **84**, 735; (*b*) C. Rocaboy and J. A. Gladysz, *Tetrahedron*, 2002, **58**, 4007.
14 Stille, Sonogashira, and other reactions: (*a*) S. Schneider and W. Bannwarth, *Angew. Chem., Int. Ed.*, 2000, **39**, 4142; S. Schneider and W. Bannwarth, *Angew. Chem.*, 2000, **112**, 4293; (*b*) C. Markert and W. Bannwarth, *Helv. Chim. Acta*, 2002, **6**, 1877; (*c*) B. Betzemeier and P. Knochel, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2623; B. Betzemeier and P. Knochel, *Angew. Chem.*, 1997, **109**, 2736; (*d*) S. Saito, Y. Chounan, T. Nogami, O. Ohmori and Y. Yamamoto, *Chem. Lett.*, 2001, 444.
15 (*a*) Y. Tian, Q. C. Yang, T. C. W. Mak and K. S. Chan, *Tetrahedron*, 2002, **58**, 3951; (*b*) Y. Nakamura, S. Takeuchi, K. Okumura, Y. Ohgo and D. P. Curran, *Tetrahedron*, 2002, **58**, 3963; (*c*) see also H. Kleijn, E. Rijnberg, J. T. B. H. Jastrezebski and G. van Koten, *Org. Lett.*, 1999, **1**, 853.
16 (*a*) M. Cavazzini, S. Quici and G. Pozzi, *Tetrahedron*, 2002, **58**, 3943; (*b*) A. Endres and G. Maas, *Tetrahedron*, 2002, **58**, 3999; (*c*) K. Mikami, Y. Mikami, H. Matsuzawa, Y. Matsumoto, J. Nishikido, F. Yamamoto and H. Nakajima, *Tetrahedron*, 2002, **58**, 4015; (*d*) Q. Zhang, Z. Luo and D. P. Curran, *J. Org. Chem.*, 2000, **65**, 8866; (*e*) R. Kling, D. Sinou, G. Pozzi, A. Choplin, F. Quignard, S. Busch, S. Kainz, D. Koch and W. Leitner, *Tetrahedron Lett.*, 1998, **39**, 9439.
17 (*a*) J. Dupont, M. Pfeffer and J. Spencer, *Eur. J. Inorg. Chem.*, 2001, 1917; (*b*) W. A. Herrmann, V. P. W. Böhm and C.-P. Reisinger, *J. Organomet. Chem.*, 1999, **576**, 23.
18 (*a*) A. Zapf and M. Beller, *Chem. Eur. J.*, 2001, **7**, 2908; (*b*) V. P. W. Böhm and W. A. Herrmann, *Chem. Eur. J.*, 2001, **7**, 4191.
19 M. Ohff, A. Ohff and D. Milstein, *Chem. Commun.*, 1999, 357.
20 (*a*) A. S. Gruber, D. Zim, G. Ebeling, A. L. Monteiro and J. Dupont, *Org. Lett.*, 2000, **2**, 1287; (*b*) D. Zim, A. S. Gruber, G. Ebeling, J. Dupont and A. L. Monteiro, *Org. Lett.*, 2000, **2**, 2881; (*c*) J. Dupont, A. S. Gruber, G. S. Fonseca, A. L. Monteiro and G. Ebeling, *Organometallics*, 2001, **20**, 171.
21 (*a*) D. G. Blackmond, T. Rosner and A. Pfaltz, *Org. Proc. Res. Dev.*, 1999, **3**, 275; (*b*) additional N-donor palladacycles that are effective catalyst precursors: I. P. Beletskaya, A. N. Kashin, N. B. Karlstedt, A. V. Mitin, A. V. Cheprakov and G. M. Kazankov, *J. Organomet. Chem.*, 2001, **622**, 89.
22 Recent reviews: (*a*) I. P. Beletskaya and A. V. Cheprakov, *Chem. Rev.*, 2000, **100**, 3009; (*b*) N. J. Whitcombe, K. K. Hii and S. E. Gibson, *Tetrahedron*, 2001, **57**, 7449.
23 Recent reviews: (*a*) A. Suzuki, *J. Organomet. Chem.*, 2002, **653**, 83; (*b*) N. Miyaura, *J. Organomet. Chem.*, 2002, **653**, 54.
24 (*a*) C. Rocaboy, D. Rutherford, B. L. Bennett and J. A. Gladysz, *J. Phys. Org. Chem.*, 2000, **13**, 596; (*b*) C. Rocaboy, F. Hampel and J. A. Gladysz, *J. Org. Chem.*, 2002, **67**, 6863.
25 C. Rocaboy and J. A. Gladysz, *Org. Lett.*, 2002, **4**, 1993.
26 T. Soós, B. L. Bennett, D. Rutherford, L. P. Barthel-Rosa and J. A. Gladysz, *Organometallics*, 2001, **20**, 3079.
27 M. Rottländer, L. Boymond, L. Bérillon, A. Leprêtre, G. Varchi, S. Avolio, H. Laaziri, G. Quéguiner, A. Ricci, G. Cahiez and P. Knochel, *Chem. Eur. J.*, 2000, **6**, 767.
28 C. Rocaboy, W. Bauer and J. A. Gladysz, *Eur. J. Org. Chem.*, 2000, 2621.
29 (*a*) D. B. Dess and J. C. Martin, *J. Am. Chem. Soc.*, 1991, **113**, 7277; (*b*) M. Frigerio, M. Santagostino and S. Sputore, *J. Org. Chem.*, 1999, **64**, 4537.
30 H. K. Cammenga and M. Epple, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1171; H. K. Cammenga and M. Epple, *Angew. Chem.*, 1995, **107**, 1284.
31 H. Onoue and I. Moritani, *J. Organomet. Chem.*, 1972, **43**, 431.
32 Y. Guindon, R. Frenette, R. Fortin and J. Rokach, *J. Org. Chem.*, 1983, **48**, 1357.

33 (*a*) C. Naud, P. Calas, H. Blancou and A. Commeyras, *J. Fluorine Chem.*, 2000, **104**, 173; (*b*) N. Mureau, F. Guittard and S. Géribaldi, *Tetrahedron Lett.*, 2000, **41**, 2885.
34 F. Szonyi and A. Cambon, *J. Fluorine Chem.*, 1989, **42**, 59.
35 J. A. Gladysz, *Pure Appl. Chem.*, 2001, **73**, 1319.
36 (*a*) M. T. Reetz and E. Westermann, *Angew. Chem., Int. Ed.*, 2000, **39**, 165; M. T. Reetz and E. Westermann, *Angew. Chem.*, 2000, **112**, 170, and earlier papers referenced therein; (*b*) J. Le Bars, U. Specht, J. S. Bradley and D. G. Blackmond, *Langmuir*, 1999, **15**, 7621.
37 (*a*) V. Chechik and R. M. Crooks, *J. Am. Chem. Soc.*, 2000, **122**, 1243; (*b*) L. K. Yeung and R. M. Crooks, *Nano Lett.*, 2001, **1**, 14; (*c*) R. M. Crooks, M. Zhao, L. Sun, V. Chechik and L. K. Yeung, *Acc. Chem. Res.*, 2001, **34**, 181.
38 (*a*) M. Moreno-Mañas, R. Pleixats and S. Villarroya, *Organometallics*, 2001, **20**, 4524; (*b*) see also M. Moreno-Mañas, R. Pleixats and S. Villarroya, *Chem. Commun.*, 2002, 60.
39 M. Nowotny, U. Hanefeld, H. van Koningsveld and T. Maschmeyer, *Chem. Commun.*, 2000, 1877.
40 (*a*) K. Köhler, R. G. Heidenreich, J. G. E. Krauter and J. Pietsch, *Chem. Eur. J.*, 2002, **8**, 622; (*b*) F. Zhao, B. M. Bhanage, M. Shirai and M. Arai, *Chem. Eur. J.*, 2000, **6**, 843.
41 Related data for the Suzuki reaction: (*a*) R. B. Bedford, C. S. J. Cazin, M. B. Hursthouse, M. E. Light, K. J. Pike and S. Wimperis, *J. Organomet. Chem.*, 2001, **633**, 173; (*b*) S.-W. Kim, M. Kim, W. Y. Lee and T. Hyeon, *J. Am. Chem. Soc.*, 2002, **124**, 7642; (*c*) C. Ramararo, S. V. Ley, S. C. Smith, I. M. Shirley and N. DeAlmeida, *Chem. Commun.*, 2002, 1132.
42 For incisive overviews of nanoparticle catalysts, see: (*a*) S. Özkar and R. G. Finke, *J. Am. Chem. Soc.*, 2002, **124**, 5796; (*b*) A. Roucoux, J. Schulz and H. Patin, *Chem. Rev.*, 2002, **102**, 3757.
43 (*a*) T. Rosner, J. Le Bars, A. Pfaltz and D. G. Blackmond, *J. Am. Chem. Soc.*, 2001, **123**, 1848; (*b*) T. Rosner, A. Pfaltz and D. G. Blackmond, *J. Am. Chem. Soc.*, 2001, **123**, 4621.
44 L. Dinh and R. C. Costa, research in progress, Universität Erlangen-Nürnberg.
45 I. W. Davies, L. Matty, D. L. Hughes and P. J. Rieder, *J. Am. Chem. Soc.*, 2001, **123**, 10 139.
46 J. Rebek, *Tetrahedron*, 1979, **35**, 723.
47 S. C. Watson and J. F. Eastham, *J. Organomet. Chem.*, 1967, **9**, 165.
48 The *Z*/*E* HC=CH assignments were based upon well established trends in the $^3J_{HH}$ values (*Z*, *ca.* 11 Hz; *E*, *ca.* 16 Hz).
49 The *Z*/*E* C=N assignment is tentative.
50 These NMR assignments were confirmed by COSY and HETCOR experiments.
51 This signal is assigned to the palladated aryl carbon.