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Evidence for Single-Electron Pathways in the Reaction between Palladium(II) Dialkyl Complexes and Alkyl Bromides under Thermal and Photoinduced Conditions

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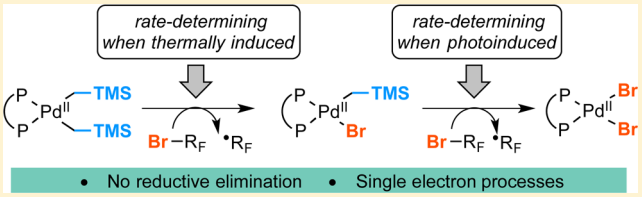
Supporting Information

ABSTRACT: Palladium(II) dialkyl complexes have previously been studied for their formation of alkanes through reductive elimination. More recently, these complexes, especially $L_2Pd(CH_2TMS)_2$ derived from $Pd(COD)(CH_2TMS)_2$, have found general use as palladium(0) precursors for stoichiometric formation of oxidative addition complexes through a two-electron reductive elimination/oxidative addition sequence. Herein, we report evidence for an alternative pathway, proceeding through single-electron elementary steps, when $DPEPhosPd(CH_2TMS)_2$ is treated with an α-bromo-α,α-difluoroacetamide. This new pathway does not take place through a palladium(0) intermediate, neither does it afford the expected oxidative addition complexes. Instead, stoichiometric amounts of carbon-centered alkyl radicals are formed, which can be trapped in high yields either by TEMPO or by an arene, leading to α-aryl-α,α-difluoroacetamides. The same overall transformation takes place under both thermal conditions (70 °C) and irradiation with a household light bulb (at 30 °C). It is also demonstrated that $DPEPhosPdMe_2$, made in situ from $Pd(TMEDA)Me_2$, displays a similar initial reactivity. Finally, electronically and structurally different alkyl bromides were evaluated as reaction partners.



INTRODUCTION

Palladium catalysis is one of the most widely used synthetic tools in both the chemical industry and academia for the construction of carbon−carbon and carbon−heteroatom bonds.[1] A typical catalytic cycle is initiated by oxidative addition of a palladium(0) species into a carbon−halogen bond. Unfortunately, many palladium(0) catalysts are not air-stable, and instead it is common practice to employ palladium(II) precatalysts. These precatalysts are usually air-stable but can be readily transformed into a catalytically active palladium(0) species under the reaction conditions.[2] The activation from palladium(II) to palladium(0) as well as the remainder of the catalytic cycle is usually represented as proceeding via two-electron processes (Figure 1).

The palladium(II) complex $Pd(COD)(CH_2TMS)_2$ (**1**) is typically used as a precursor for in situ formation of $L_2Pd(0)$-type complexes.[3,4] Combining this complex with mono- or bidentate L-type (dative) ligands has been exploited both for catalyst generation and for the formation of oxidative addition complexes at room temperature.[5] The activation pathway is believed to proceed via rapid substitution of COD for the added ligand followed by reductive elimination of $(CH_2TMS)_2$ to generate $L_2Pd(0)$ (eq 1). Frequent isolation of oxidative addition complexes (e.g., eq 2) in combination with a few reports on the observation of $(CH_2TMS)_2$ indicates a mechanism involving these two-electron elementary steps.[5,6] A few examples of ligand exchange of a single CH_2TMS group on $Pd(COD)(CH_2TMS)_2$ or $L_2Pd(CH_2TMS)_2$ without reductive elimination have also been reported; however, no

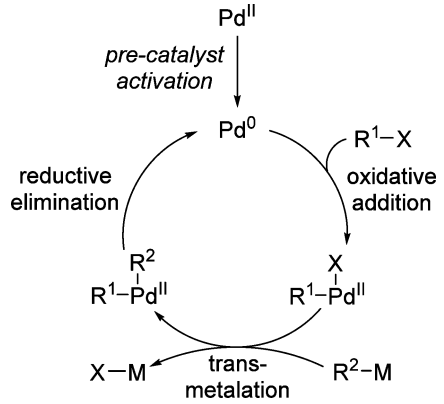


Figure 1. General catalytic cycle for palladium-catalyzed cross-couplings. Ligands have been omitted for the sake of simplicity. M = metal; X = halide.

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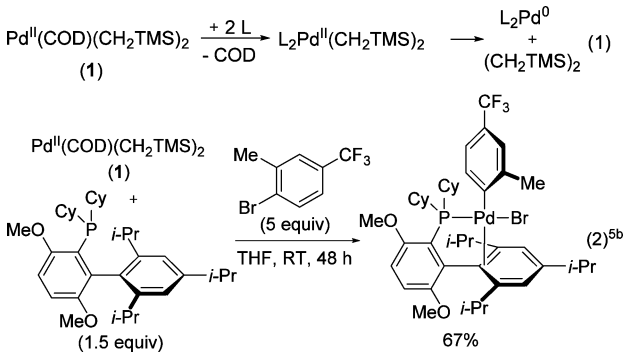


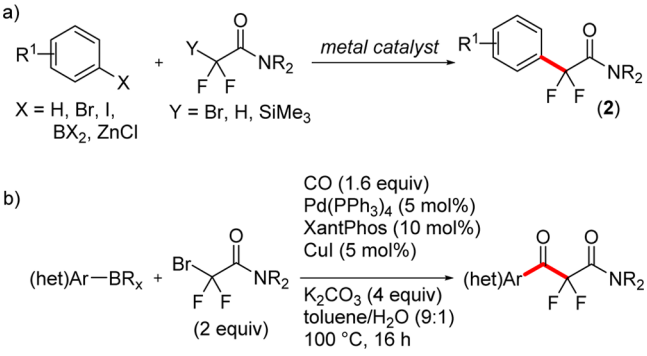
comments on the mechanistic path for this exchange were mentioned.[7] In fact, none of the reports utilizing Pd(COD)-$(CH_2TMS)_2$ contain evidence for or suggest the alternative possibility of a single-electron pathway involving free radicals.

Herein, we report clear evidence for an alternative pathway to the commonly accepted reductive elimination/oxidative addition sequence for an $L_2Pd(II)(CH_2TMS)_2$ complex. The unexpected reactivity is established through the first study of reactions between alkyl bromides and an $L_2Pd(II)$ $(CH_2TMS)_2$ complex. The alternative pathway proceeds through single-electron elementary steps and involves the formation of free radicals. The implication of similar modes of reactivity for a palladium(II) dimethyl complex as well as different alkyl bromides is also presented.

RESULTS AND DISCUSSION

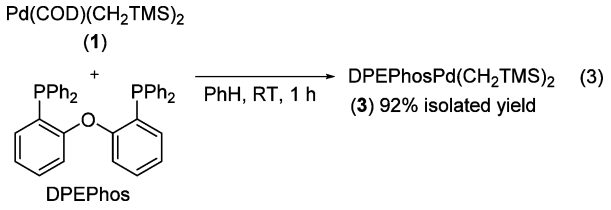
Aryldifluoroamides **2** have recently received significant attention due to their important pharmacological properties.[8] Several reports on the synthesis of aryldifluoroamides have appeared including examples starting from bromodifluoroacetamides (Scheme 1a).[9] In certain cases using palladium(0) or

Scheme 1. (a) Synthesis of α-Aryl-α,α-difluoroacetamides; (b) Our Synthesis of α-(Hetero)aryl α,α-Difluoro-β-ketoamides Using a Carbonylative Protocol



photoredox catalysts with these *gem*-difluorobromides, the generation of radical intermediates, which can be trapped by unsaturated carbon−carbon moieties, has been invoked.[10]

Recently, we and others reported the use of bromodifluoroacetamides and -acetates for the synthesis of α-(hetero)aryl α,α-difluoro-β-ketoamides and α,α-difluoro-β-ketoesters using a palladium-catalyzed carbonylative protocol (Scheme 1b).[11] During our preliminary studies on the mechanism of this reaction, we attempted to prepare oxidative addition complexes starting from $Pd(COD)(CH_2TMS)_2$ as a palladium(0) precursor. Mixing $Pd(COD)(CH_2TMS)_2$ with bidentate phosphine ligands, such as DPEPhos, led to rapid and clean displacement of the COD ligand as expected, forming complex **3** (eq 3).[12] However, when mixing bromodifluoroacetamide **4**,



$Pd(COD)(CH_2TMS)_2$, and DPEPhos in benzene, we did not obtain the desired oxidative addition complex (Scheme 2a). Instead, aryldifluoroacetamide **2a** was obtained along with the palladium(II) monobromide complex **5**. Repeating the reaction with two equivalents of the bromide led to the palladium(II) dibromide complex **6** (Scheme 2b). The structures of the comlexes **3**, **5**, and **6** were identified by X-ray analysis (Figure 2). The presence of further equivalents of the bromodifluoroacetamide remained untouched even after prolonged reaction time (Scheme 2c).[13] These results show that the thermally induced reaction is a stepwise process whereby the first CH_2TMS ligand is replaced at a much higher rate than the second and that the consumption of the bromodifluoroacetamide **4** corresponds to the conversion of palladium complex.

Due to the formation of aryldifluoroacetamide **2a** under the thermal conditions, it seems likely that the reaction goes through a palladium−carbon bond homolysis or a related radical pathway.[14,15] Hence, we were curious if the same transformation could be performed under milder conditions when irradiated by light. Indeed, when the reaction in Scheme 2b was repeated under irradiation of a household 26 W CFL, the same transformation proceeded at 30 °C (Scheme 2d). In contrast to the thermal reaction, only trace amounts of the intermediate monobromide **5** were observed when following the reaction by ^{31}P NMR spectroscopy, demonstrating that the second substitution is now faster than the first. A possible explanation for this divergence can be made when comparing the UV−vis absorption spectra of the starting palladium complex, $DPEPhosPd(CH_2TMS)_2$, with the intermediate complex **5** (Figure 3). While $DPEPhosPd(CH_2TMS)_2$ absorbs only in the UV region, the intermediate has additional absorption shifted into the visible region, which is where the 26 W CFL is emitting predominantly. This shift should favor the excitation and hence further reaction of $DPEPhosPdBr(CH_2TMS)$ over $DPEPhosPd(CH_2TMS)_2$. In contrast, the thermally induced reactions were performed in the dark, and the change in absorption will play no role in this case.

In order to examine the influence of light irradiation on the reaction progress, we performed light on/off cycles (Figure 4). It was observed that the conversion rapidly ceases when the irradiation is switched off. Although this does not exclude a radical chain mechanism, it clearly demonstrates the pivotal role of the light irradiation throughout the reaction.[16]

Next, we performed relative reactivity experiments to examine the influence on the reaction rate of electronic effects on the arene reaction partner (Scheme 3). Both an arene bearing an electron-withdrawing substituent (CN) and an arene bearing an electron-donating substituent (OMe) react faster than benzene. These results are consistent with the addition of a free radical to the arene; however, they are inconsistent with pathways involving electrophilic aromatic substitution and

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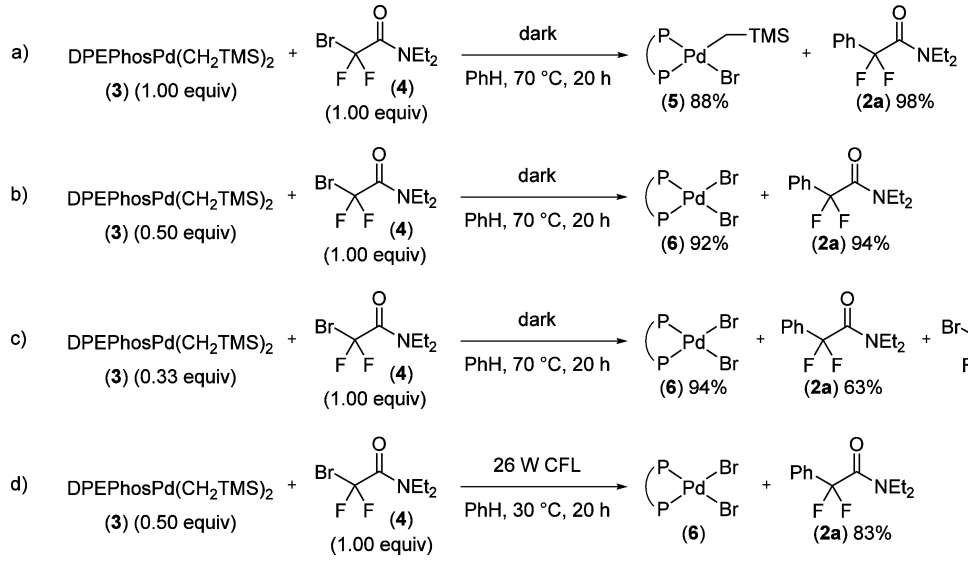
Scheme 2. Reactions of DPEPhosPd(CH_2TMS)$_2$ with Varying Equivalents of Bromodifluoroacetamide 4 under both Thermal (Dark) and Light-Irradiation Conditions[a]



[a]Yields of **2a** were determined by HPLC analysis with the aid of a calibrated internal standard, and the findings are in accordance with intensities in ^{19}F NMR. Yield of **5** is based on ^{1}H NMR analysis with the aid of an internal standard. Yields of **6** are isolated yields relative to the amount of palladium complex added. In all cases, the remainder of the mass balance is hydro-debrominated starting material. The same reaction outcomes, albeit with slightly inferior yields, were observed when starting from Pd(COD)(CH_2TMS)$_2$ and DPEPhos instead of the premade complex.

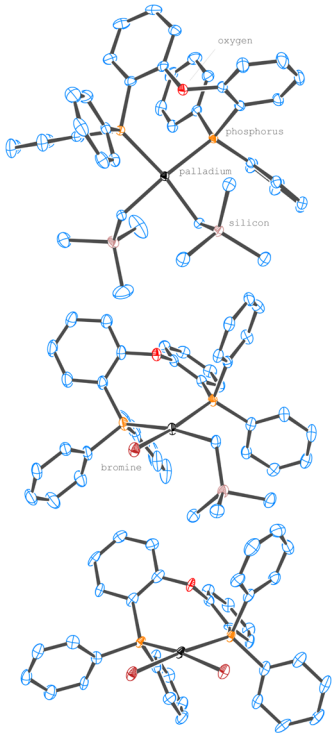


Figure 2. X-ray crystal structures of DPEPhosPd(CH_2TMS)$_2$ (top), DPEPhosPd(CH_2TMS)Br (middle), and DPEPhosPdBr_2 (bottom) (ellipsoids are shown at 50% probability, and hydrogens are omitted for clarity).

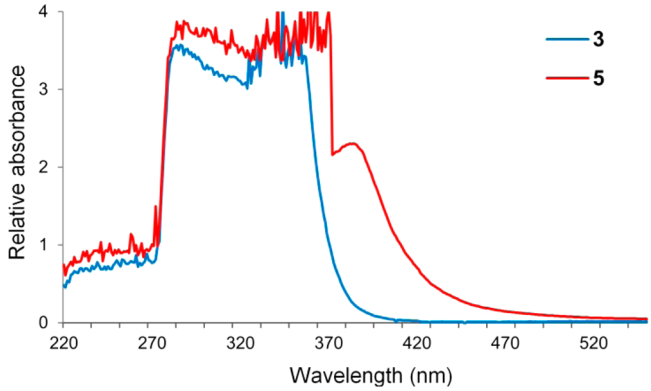


Figure 3. UV−vis absorption spectra for DPEPhosPd(CH_2TMS)$_2$ (**3**) and DPEPhosPd(CH_2TMS)Br (**5**), both recorded in benzene.

electrophilic palladation. The observed regioselectivities are also in accordance with those previously reported for the addition of electrophilic radicals to arenes.[17] Importantly, the ratios in the competition experiments are very similar for the thermal and the light-induced reactions, supporting the suggestion that they follow a similar mechanism.

While arenes are not typically used as radical traps, 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) is usually the reagent of choice for this purpose. In order to trap potential radical intermediates, some of the reactions were accordingly repeated in the presence of TEMPO (Scheme 4). Both the thermal and the photoinduced reaction led to the TEMPO adduct **7** being formed as the major product. These observations further support the intermediacy of a free alkyl radical under both sets of conditions. Interestingly, under the thermal conditions, the presence of TEMPO led to an acceleration of the second step, as the intermediate monobromide **5** only started to appear once the majority of TEMPO had been consumed (Scheme 4c).[18]

Neither heating at 70 °C in the dark nor irradiation of the bromodifluoroacetamide **4** at 35 °C in the presence of TEMPO afforded more than a trace (<1%) of the TEMPO adduct **7**, thus indicating that unassisted homolysis of the bromide **4** is unlikely to be the first step under either set of conditions.[20] The presence of the palladium complex is pivotal for the reactivity of the bromodifluoroacetamide. Further control experiments

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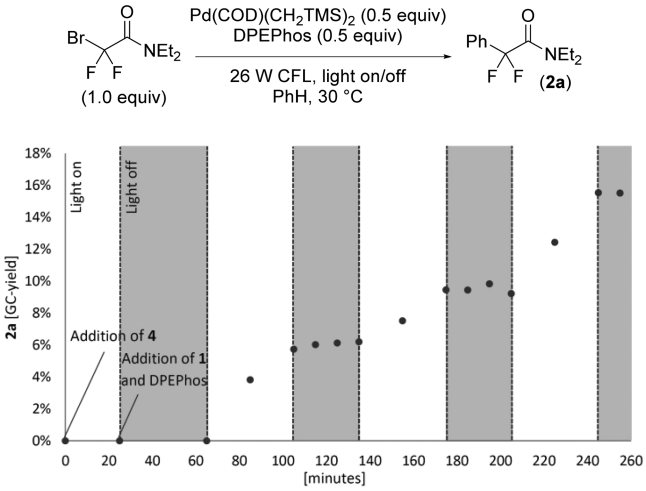
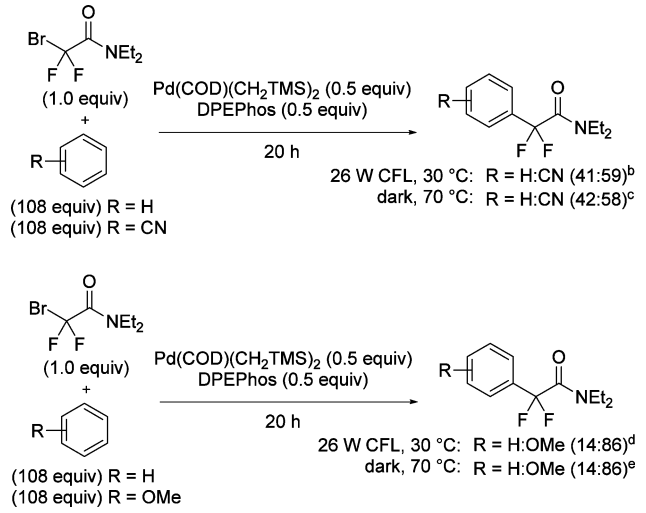


Figure 4. Influence of light irradiation on reaction progress by light on/off cycles. Yields were determined by GC-FID analysis with the aid of a calibrated internal standard.

Scheme 3. Intermolecular Competition Experiments between Benzene and an Electron-Poor Arene and an Electron-Rich Arene, Respectively[a]

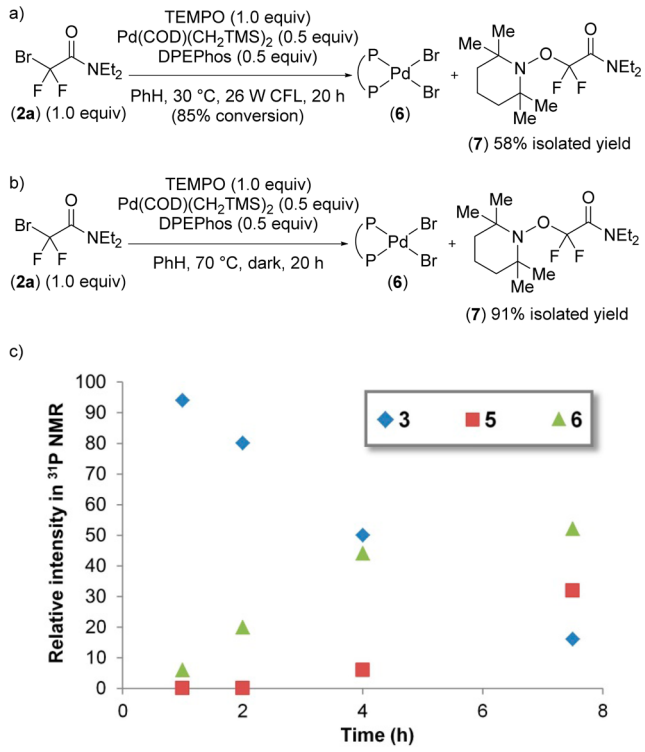


[a]The reported product ratios were determined by ^{19}F NMR. Regioselectivities observed for monosubstituted substrates (o:m:p): [b](4.7:1.0:4.5). [c](4.5:1.0:4.2). [d](3.1:2.0:1.0). [e](2.9:2.3:1.0).

showed that the palladium complex is stable, in both the presence and absence of the bromodifluoroacetamide **4**, in solution at 35 °C in the dark for at least 24 h. However, in the absence of bromodifluoroacetamide **4**, it decomposes within 6 h under irradiation of a 26 W CFL, and decomposition is also observed within 2 h in the dark at 70 °C. Consistent with the lack of reaction at 35 °C in the dark, the oxidation/reduction potentials measured by cyclic voltammetry also indicated that it is unlikely that bromodifluoroacetamide **4** acts as an outer-sphere single-electron oxidant for the oxidation of Pd(II) to Pd(III) with concurrent formation of the radical anion of **4** (irreversible oxidation of DPEPhosPd$(CH_2TMS)_2$ observed at $E_{p/2}$ = +1.23 V vs Ag/AgI in DMF; irreversible reduction of bromide **4** observed at $E_{p/2}$ = −1.25 V vs Ag/AgI in DMF).[21]

On the basis of the results presented so far, it seems plausible that the elementary steps for the substitution of the first and the second CH_2TMS are the same. Furthermore, this also appears

Scheme 4. Reactions Performed in the Presence of TEMPO under (a) Light Irradiation Conditions and (b) Thermal Conditions; (c) Reaction under Thermal Conditions in the Presence of TEMPO Monitored Over Time[19]



to be the case for both the thermally and the light-induced reactions; however, the relative rates depend on the applied conditions. Under thermal conditions, the slowest step is found during the substitution of the second CH_2TMS, while the slowest step for the light-irradiated reaction occurs during substitution of the first CH_2TMS. A mechanistic proposal for the substitution of the first CH_2TMS for a bromide under light irradiation is shown in Scheme 5a. The reaction starts with excitation of DPEPhosPd$(CH_2TMS)_2$ (**3**).[22,23] The excited complex **3*** can now follow one of two pathways. In the first pathway (step B), homolysis of the Pd−C bond occurs, affording a CH_2TMS radical and the Pd(I) complex **8**. This highly reactive intermediate can rapidly abstract a bromide from the bromodifluoroacetamide **4**, leading to Pd(II) complex **5** and a carbon-centered alkyl radical (step C). Addition of this radical to benzene generates an aryl radical, which, upon hydrogen abstraction, can rearomatize, producing **2a** (vide infra).[24] Alternatively, the excited complex **3*** can directly abstract the bromide, leading to Pd(III) intermediate **9** and the carbon-centered alkyl radical (step D).[25−27] Loss of a CH_2TMS radical from **9** leads to the monobromide complex **5** (step E).

Since no photoexcitation can occur under the thermal conditions, it is possible that heating provides sufficient energy for the starting complex **3** to undergo either homolysis or bromide abstraction (Scheme 5b). The subsequent steps are likely highly related to the light-induced pathways.

When following the light-irradiated reactions by ^{31}P NMR spectroscopy, very little of the intermediate **5** is observed. Instead, complexes **3** and **6** are major species, suggesting that one of the steps A (excitation of **3**), B (loss of the alkyl radical from **3***), or D (bromide abstraction from R_F−Br by **3***) is overall rate-limiting (Figure 5e). Under thermal conditions with

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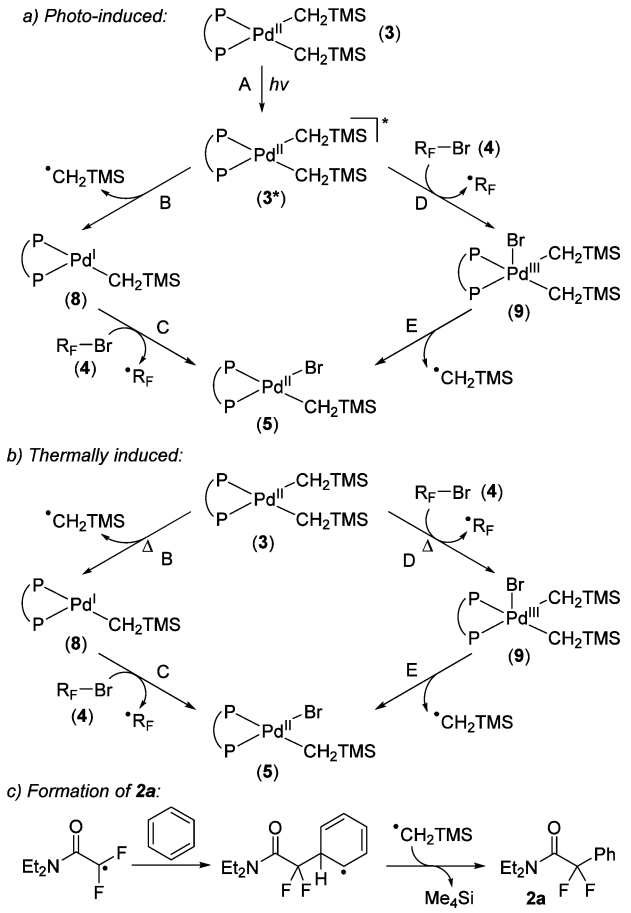
Scheme 5. Mechanistic Proposal for the Formation of DPEPhosPd(CH_2TMS)Br under Light Irradiation and Thermal Conditions; Similar Steps are Presumed for the Formation DPEPhosPdBr_2 from 5



one equivalent of the bromodifluoroacetamide **4**, only complexes **3** and **5** are observed, while complexes **3**, **5**, and **6** are observed during the reaction with two equivalents of the bromodifluoroacetamide (Figure 5d). Accordingly, the overall rate-limiting step under thermal conditions takes place during the substitution of the second CH_2TMS group.

The selective substitution of one CH_2TMS ligand on $L_2Pd(CH_2TMS)_2$ complexes has been demonstrated previously with carboxylic acids and a protonated phosphine; however, no comments on the mechanism were mentioned except for the observation of the formation of Me_4Si in a single example.[7a] Next, we set out to investigate the fate of the CH_2TMS ligands under our reaction conditions. At the end of the reactions in Scheme 2a–c, the dimerized ligand, $(CH_2TMS)_2$, was observed by GC-FID in 41%, 31%, and 27% calibrated yields, respectively.[28] This product could originate from reductive elimination; however, taking the nature and the yield of the obtained palladium(II) complexes **5** and **6** into account, it is difficult to imagine a feasible mechanism via palladium(0) intermediates formed by the reductive elimination. It seems more likely that the CH_2TMS dimer arises from radical dimerization of CH_2TMS radicals, either free or through attack of a free CH_2TMS radical on a metal-bound CH_2TMS.[29] Importantly, under the photoinduced reaction conditions (Scheme 2d) no $(CH_2TMS)_2$ was observed, but the palladium(II) complex **6** is still formed in a high yield. The absence of

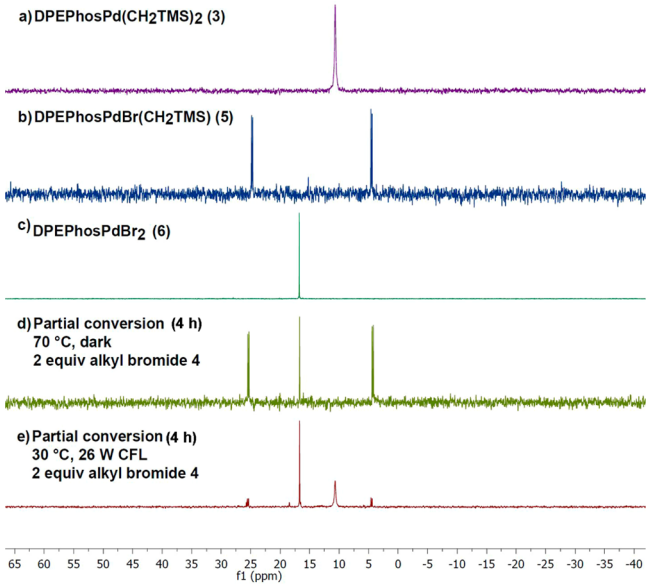
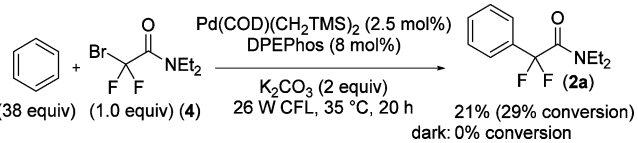


Figure 5. ^{31}P NMR of the different complexes and reactions in Scheme 2: (a) DPEPhosPd$(CH_2TMS)_2$. (b) DPEPhosPdBr-(CH_2TMS) observed in the crude reaction mixture with 1.0 equiv of [Pd] under thermal conditions (Scheme 2a). (c) DPEPhosPdBr_2. (d) Reaction at partial conversion under thermal conditions (Scheme 2b). (e) Reaction at partial conversion under light irradiation (Scheme 2d).

$(CH_2TMS)_2$ under these conditions was further confirmed by ^1H NMR spectroscopy of the reaction mixture, when the reaction was repeated in C_6D_6. Instead of the dimer, only a peak at 0 ppm was observed, indicating the formation of Me_4Si. Overall, these results are consistent with the mechanistic proposals with the addition that the predominant fate of the liberated CH_2TMS radical is hydrogen abstraction (Scheme 5c).

In the presence of a base such as K_2CO_3, we observed that the conversion of the palladium complex and bromodifluoroacetamide **4** did not correlate. Repeating the reaction with a large excess of bromodifluoroacetamide relative to palladium, we observed a 21% yield of **2a** with only 2.5 mol % Pd(COD)$(CH_2TMS)_2$ and 8 mol % DPEPhos (Scheme 6).

Scheme 6. Reactions with Substoichiometric Amounts of Palladium Complex Performed in the Presence of Base[a]



[a]Yields were determined by GC-FID analysis with the aid of a calibrated internal standard.

However, at the end of this reaction, the only observed peak in the ^{31}P NMR spectrum corresponds to the oxidized phosphine, making the intermediacy of a Pd(0) species likely. It appears that in the presence of K_2CO_3 a new species is formed, which can consume superstoichiometric amounts of **4**.[30,31] Other bases, such as Cs_2CO_3 and LiO*t*Bu provided similar results.

To examine the generality of the observations made with DPEPhosPd$(CH_2TMS)_2$, we performed preliminary studies on the related dialkyl palladium complex, Pd(TMEDA)Me_2 (**10**).

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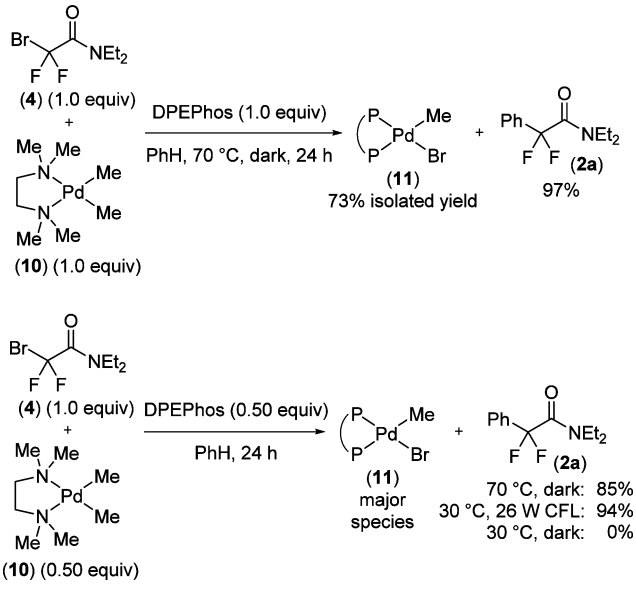
Such a comparison will also be valuable in terms of evaluating the necessity of β-silicon atoms on the alkyl substituents as a prerequisite for the enclosed reactivity.[32,33] Thermolysis of **10** has been reported to lead to the formation of a mixture of ethane and methane, the latter suggested deriving from a unimolecular α-elimination.[34a] Also, Pd(TMEDA)Me_2 has been reported to undergo two-electron oxidative addition to R–X-type electrophiles, mostly Me–X, providing Pd(IV) intermediates, which collapse with concomitant and quantitative release of ethane.[34] Sanford et al. reported on the mechanism for the formation of ethane from (t-Bu_2bpy)$PdMe_2$ in the presence of the one-electron oxidant $[Cp_2Fe]PF_6$.[35] It was discovered that following the initial formation of Pd(III), a disproportion to Pd(II)/Pd(IV) takes place followed by reductive elimination of ethane from the Pd(IV) species to form Pd(II).[36,37] However, later studies indicate that this high-valent pathway is only operating when diamine ligands are employed and that bis-phosphine ligands instead lead to oxidation-induced Pd–C bond homolysis, producing methane along with a substantial amount of ethane.[38] Photodecomposition of a bis-phosphine-ligated complex, (dppe)$PdMe_2$, has also been studied briefly.[39] Interestingly, while photolysis of (dppe)PdMeCl was found to proceed through radical pathways, a nonradical pathway was indicated for photodecomposition of (dppe)$PdMe_2$, although the presence of several simultaneously operating mechanisms complicated the conclusions.

When we subjected Pd(TMEDA)Me_2 to thermal conditions corresponding to Scheme 2a in the presence of one equivalent of DPEPhos, aryldifluoroacetamide **2a** was again obtained in a near-quantitative yield (Scheme 7). Examining the crude reaction mixture by $^{31}P\{H\}$ NMR spectroscopy revealed a single set of doublet signals resonating at δ = 28.8 and 6.8 ppm

Scheme 7. Reactions of Pd(TMEDA)Me_2 in the Presence of DPEPhos with Varying Equivalents of Bromodifluoroacetamide 4 under Both Thermal (Dark) and Light-Irradiation Conditions[a]

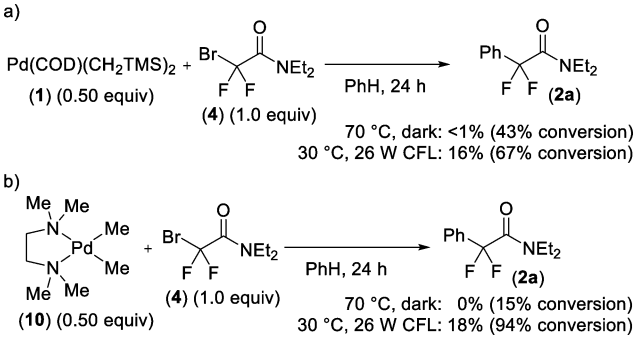


[a]Unless otherwise specified, yields were determined by HPLC analysis with the aid of a calibrated internal standard, and the findings are in accordance with intensities in ^{19}F NMR.

with equal integration and with a common P,P coupling constant of 30.4 Hz. Isolation of this phosphine species as a colorless solid was possible and ^1H NMR analysis of the obtained compound was consistent with the palladium(II) monobromide complex (**11**).[40] The result suggests that a stepwise substitution on palladium via a radical pathway similar to the one for DPEPhosPd($CH_2TMS)_2$ could be operating under thermal conditions. In order to examine if the substitution of the second methyl group was feasible, the reactions were repeated in the presence of excess bromodifluoroacetamide **4** similar to the reactions in Scheme 2b and d. Under these conditions, high yields of fluoroalkylated benzene were obtained as expected. However, DPEPhosPdMeBr (**11**) was still observed as the major phosphine species by ^{31}P NMR with only trace amounts of DPEPhosPdBr_2.[41] Possibly, the presence of TMEDA, which can serve as a base similar to K_2CO_3 (Scheme 6), can account for the discrepancy between the yield of **2a** and formation of DPEPhosPdMeBr. Overall, these findings suggest that DPEPhosPdMe_2 could follow a similar single-electron pathway as described for DPEPhosPd($CH_2TMS)_2$ under both thermal and photochemical conditions, consuming one equivalent of bromodifluoroacetamide **4**, affording DPEPhosPdMeBr (**11**). However, unlike the related monobromide **5**, this complex does not react further under our reaction conditions.

The influence of the phosphine ligand on the pathway taken by dialkyl palladium complexes **1** and **10** in their reaction with bromodifluoroacetamide **4** was also assessed (Scheme 8). For

Scheme 8. Reactions of Pd(TMEDA)Me_2 in the Absence of Added Phosphine Ligand under Both Thermal (Dark) and Light-Irradiation Conditions[a]



[a]Yields and conversions were determined by HPLC analysis with the aid of a calibrated internal standard. Conversion refers to conversion of bromodifluoroacetamide **4**. Palladium-black was observed in all the reactions.

both complexes, essentially none of the aryldifluoroacetamide **2a** could be detected under thermal conditions in the absence of DPEPhos. In contrast, under the photoinduced reaction conditions, **2a** is observed for both complexes albeit in low yields. In all the reactions the conversion of bromodifluoroacetamide **4** was found to be significantly higher than the formation of **2a** due to undetermined side reactions. In the reactions with Pd(COD)($CH_2TMS)_2$ (**1**), formation of the dimer, ($CH_2TMS)_2$, occurred in a 58% yield for the thermal and a 14% yield for the photoinduced reaction.[42] On the basis of these results, the presence of the phosphine ligand seems crucial for selectively accessing the new reactivity.

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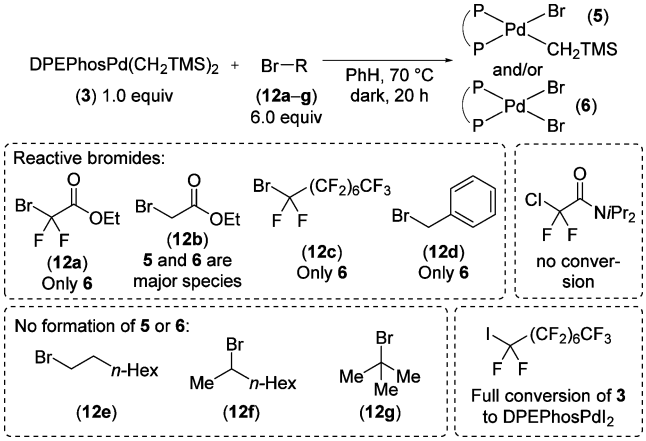
Having examined the influence of the β-silicon groups, we turned our attention to the alkyl bromide reaction partner. Interestingly, for reactions with DPEPhosPd(CH_2TMS)$_2$ (**3**), the bromodifluoroacetate (**12a**), perfluoroalkyl bromide (**12c**), and benzyl bromide (**12d**) all led to clean formation of palladium(II) dibromide complex **6** (Scheme 9). For

Scheme 9. Examination of Formation of 5 and 6 from Other Alkyl Bromides (12a–g) and of the Reactivity of an Alkyl Chloride and an Alkyl Iodide[a]



[a]The reported complex formation is based on observation in the ^{31}P NMR spectrum of the crude reaction mixture.

bromoacetate **12b**, the major peaks observed by ^{31}P NMR spectroscopy corresponded to a mixture of palladium(II) monobromide **5** and palladium(II) dibromide **6**. Importantly, the fate of the alkyl moieties of **12a–d** was consistent with the formation of free alkyl radicals: For **12a**, addition to benzene producing ethyl phenyldifluoroacetate was observed exclusively by ^{19}F NMR spectroscopy. For **12b**, addition to benzene producing ethyl phenylacetate was observed in small amounts by ^{1}H NMR spectroscopy. Exclusive formation of Ph(CF_2)$_7$$CF_3$ was observed by ^{1}H and ^{19}F NMR spectroscopy for **12c**. Finally, for **12d**, significant formation of 1,2-diphenylethane was observed by ^{1}H NMR spectroscopy. A series of unfunctionalized alkyl bromides (**12e–g**) did not lead to any formation of **5** or **6**. These results indicate that a functional group stabilizing the generated carbon-centered radical is necessary for accessing the disclosed reaction pathway; however, once this requirement is met, different alkyl bromide substrates successfully undergo the new transformation.

A preliminary investigation of other halide-containing substrates as well as other phosphine ligands was also undertaken. An α-chloro-α,α-difluoroacetamide was recovered quantitatively when subjected to the reaction conditions represented in Scheme 9.[21] In contrast, the iodide analogue of **12c** reacted smoothly, leading to clean formation of DPEPhosPdI_2 and Ph(CF_2)$_7$$CF_3$, both consistent with the disclosed reactivity. No conversion of (PPh_3)$_2$Pd(CH_2TMS)$_2$ was observed in the presence of the alkyl bromide **4** under the conditions in Scheme 9. However, under the same conditions, XantPhosPd(CH_2TMS)$_2$ led to 20% conversion to XantPhosPdBr_2 along with a corresponding 40% yield of **2a** relative to the palladium complex. Accordingly, the new reactivity is also accessible with XantPhosPd(CH_2TMS)$_2$, albeit to a lesser extent.

CONCLUSIONS

In summary, we report evidence for an alternative pathway to the commonly proposed two-electron reductive elimination for the often used $L_2Pd(CH_2TMS)_2$ complexes, when ligated to the bidentate ligand DPEPhos and in the presence of an α-bromo-α,α-difluoroacetamide. The same overall transformation takes place under both thermal and photoinduced conditions, leading to either DPEPhosPd(CH_2TMS)Br or DPEPhosPdBr_2 instead of DPEPhosPd(0) or a Pd(II) oxidative addition species derived thereof. In spite of the different conditions, the mechanistic studies indicate that the processes are taking place by similar pathways albeit with different overall rate-determining steps. During the reaction, stoichiometric amounts of a carbon-centered alkyl radical are formed, which can be trapped in high yields either by the arene solvent, leading to aryldifluoroacetamides, or by TEMPO. A similar reactivity was also observed for the replacement of the first methyl group for DPEPhosPdMe_2, suggesting that this type of reactivity could be a general reaction pathway for palladium dialkyl complexes. Finally, this novel reactivity was also observed across a series of alkyl bromides, which can form stabilized radicals, thus indicating the discovered pathway may be of a more general nature. This was further corroborated by preliminary investigations with other alkyl halides and phosphine ligands.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.6b00893.

Experimental procedures and compound characterization data (PDF)

Crystallographic data (CIF)

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All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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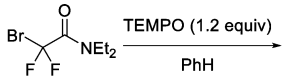
(18) TEMPO can accordingly not be considered an innocent bystander for these reactions.
(19) For (a), 15% hydro-debrominated starting material was observed. For (c), reaction monitored over time by ^{31}P NMR was performed with 0.33 equiv of DPEPhosPd(CH_2TMS)$_2$, 0.40 equiv of TEMPO, and 1.0 equiv of bromodifluoroacetamide **4**.
(20)



Conditions	Observation
70 °C, dark, 5 h	no conversion
35 °C, 26 W CFL, 5 h	no conversion
35 °C, 26 W CFL, 23 h	<1% of **7**

Data based on ^{19}F NMR of the crude reaction mixture.

(21) See Supporting Information for additional details.
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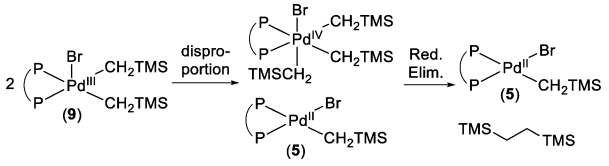
(36) Although our reactions are not performed in the presence of a ferrocenium oxidant, a related mechanism via Pd(III) species **9** can be hypothesized in the cases where $(CH_2TMS)_2$ is observed (see below). Due to the limited amount of $(CH_2TMS)_2$ formed, this cannot be the major pathway when two or more equivalents of **4** are used. Under the photoinduced conditions, the absence of $(CH_2TMS)_2$ excludes this pathway.



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(40) Crystals of sufficient quality for X-ray analysis have not been obtained. However, the formation of complex **11** is in line with the reactivity displayed by complex **3** and correlates well with the concomitant formation of **2a**.

(41) Under these conditions and in contrast to the reactions with DPEPhosPd$(CH_2TMS)_2$ several other species, which are unknown at this stage, were observed in the ^{31}P NMR spectrum of the crude reaction mixture.

(42) The yield of dimer is relative to the amount of palladium added.

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