A class of N–O type oxidants to access high-valent palladium species

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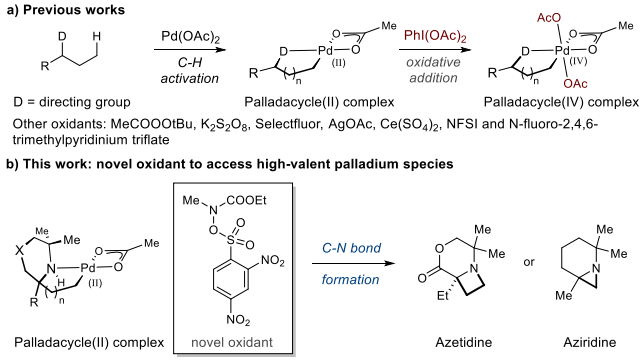
ABSTRACT: This article presents a new class of mild reagents that is capable of oxidizing palladacycle(II) complexes to high-valent palladium species, promoting the formation of C–N bonds in stoichiometric and catalytic conditions. The weak N–O bond and the extremely electron withdrawing benzenesulfonate group on the oxygen atom of the oxidant are crucial moieties to ensure the desired activity. The oxidation mechanism could involve outer-sphere single electron transfer (SET) processes, opening the possibility for a complementary reactivity of Pd(IV) species.

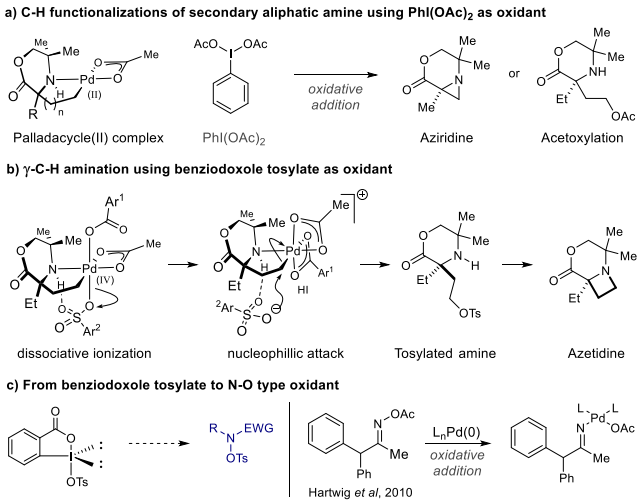
Palladium-catalyzed processes represent essential tools for the synthetic chemist. A myriad of distinct Pd-catalyzed transformations is routinely found as key steps in target-oriented syntheses, affording complex natural products, pharmaceutical lead compounds, fluorescent compounds, functional advanced materials and other high-value commercial products. The involvement of Pd(IV) complexes in C(sp^3)–H functionalization protocols have been implicated in several new synthetic methodologies and many important advances have been made in the last 20 years.[1,2] Typically, strong oxidants such as hypervalent iodonium salts (e.g. $PhI(OAc)_2$),[3] MeCOOOtBu,[4] $K_2S_2O_8$,[5] Selectfluor,[6] AgOAc,[7] $Ce(SO_4)_2$,[8] NFSI[9] and N-fluoro-2,4,6-trimethylpyridinium triflate[8] are used in stoichiometric amounts to promote the formation of Pd(IV) intermediates through oxidation of [Pd(II)] palladacycle complexes (Scheme 1a), allowing the development of several carbon–heteroatom bond-forming methodologies.

Scheme 1. Oxidants to access high-valent palladium species in C(sp^3)–H functionalization reactions.



The innately strong and unselective reactivity of the hypervalent iodonium salts and other oxidants can sometimes limit the scope of Pd(IV)-catalyzed C–H functionalization to substrates that are not susceptible to oxidative degradation. Therefore, the design of milder oxidative conditions to obtain Pd(IV) intermediate would be beneficial.[10,11,12] Herein, we report the discovery of a mild reagent capable of oxidizing palladacycle(II) complexes to high-valent palladium species, triggering the formation of C–N bonds in stoichiometric and catalytic conditions. The weak N–O bond and the electron withdrawing benzenesulfonate group on the oxygen atom of the oxidant are crucial moieties to ensure the desired activity (Scheme 1b).

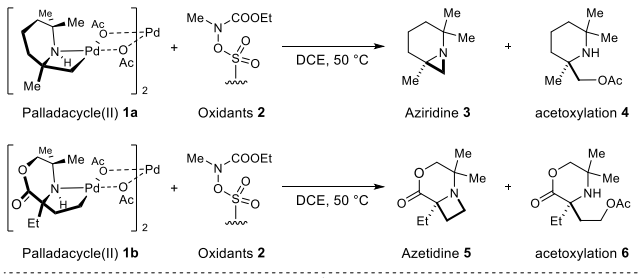
Scheme 2. Use of Pd(IV) chemistry in C(sp^3)–H functionalizations of secondary aliphatic amines.



In recent years, our group has developed a series of Pd-catalyzed C(sp^3)–H functionalization methods for aliphatic amines, exploiting the innate coordinating ability of the amine nitrogen to mediate substrate-catalyst interactions.[13,14,15,16,17] In case of Pd(IV) methodologies, $PhI(OAc)_2$ was successfully employed for the formation of C–N and C–O bonds delivering aziridines and acetoxylation products, depending on the substrates and conditions used (Scheme 2a).[13] Recently, we reported a palladium(II)-catalyzed γ-C–H amination process in which cyclic secondary alkyl amines are converted to highly substituted azetidines.[17] The use of a benziodoxole tosylate as

an oxidant, in combination with AgOAc, was crucial in delivering the azetidines. We proposed that the dissociative ionization and subsequent nucleophilic attack of the tosylate at the carbon atom bearing the palladium(IV) group forms the C–OTs bond, which in turn is displaced by the proximal amino group to form the azetidine (Scheme 2b). Guided by the discovery of the dissociative ionization mechanism, we wondered if a novel class of oxidant containing the tosylate group could be used to prompt the C–N bond formation. In particular, we speculated that the key I–O bond of the benziodoxole can be replaced with an N–O bond contained in the N-hydroxyl derivatives (Scheme 2c). Oxidative insertions of Pd(0) complexes to N–O bonds have been previously reported in the functionalization of N-acetoxyimine derivatives by Hartwig and others.[18] Therefore, we speculated that an electron withdrawing N-tosylate carbamate could promote the formation of high-valent Pd(IV) species through the oxidative insertion of the palladacycle(II) complexes into the reactive N–O bond.

Table 1. Stoichiometric studies on the new N–O type oxidants.

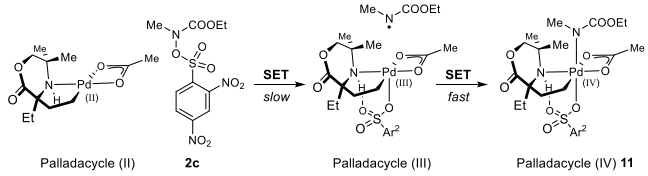


Entry	Pdcycle	Oxidant	N-heterocycles (yield [%][a])	-OAc (yield [%][a])
1	**1a**	**2a**	**3** (0)	**4** (0)
2	**1b**	**2a**	**5** (0)	**6** (0)
3	**1a**	**2b**	**3** (10)	**4** (15)
4	**1a**	**2c**	**3** (83)	**4** (0)
5	**1b**	**2c**	**5** (80)	**6** (0)

[a] Yields determined by ^{1}HNMR spectroscopy using 1,1,2,2-tetrachloroethane (TCE) as an internal standard.

We began our investigation by synthesizing N-tosylate carbamate derivative **2a** and conducting stoichiometric studies on the palladacycle(II) complexes (**1a** and **1b**) previously reported in our group (Table 1).[13,17] Unfortunately, none of the desired N-heterocycle products were observed (entries 1,2). We reasoned that decreasing the electron density of the aromatic ring would weaken the N–O bond and therefore we prepared and tested the 4-nitrobenzenesulfonate derivative **2b**. Pleasingly, when palladacycle **1a** was used, aziridine **3** was obtained in 10% along with 15% of the acetoxylated adduct **4** (entry 3). This is first time intramolecular C–H amination has been achieved for piperidine-type scaffolds. Indeed, when $PhI(OAc)_2$ was previously employed as oxidant, acetoxylated products were exclusively observed. Next, we synthesized the carbamate derivative **2c**, which contains an additional nitro group in *ortho* position of the benzenesulfonate moiety. Under mild reaction conditions, we were delighted to observe the exclusive formation of the desired aziridine **3** and azetidine **5** in very good yields, from palladacycles **1a** and **1b** respectively (entries 4,5). Significantly, no acetoxylation adducts were detected. From the reaction mixture we could also isolated a series of carbamate-containing by-products. In particular, ethyl *N*-methyl carbamate **7** was isolated in 27% yield, along with dimers **8** (15% yield), **9** (14% yield) and **10** (3% yield, Scheme 3). The formation of these compounds was also observed when similar N-halo carbamates were exposed to electrochemical reduction conditions, via two consecutive outer-sphere single electron transfers processes.[19] Since the 2,4-dinitrobenzenesulfonate oxidant **2c** has also been used as source of nitrogen center radical via single electron reduction in photochemistry[20] and due the formation of the dimeric byproducts in the reaction conditions, we wondered if outer-sphere single electron transfer processes are involved in the formation of our high-valent Pd intermediates. A possible mechanism is described in Scheme 3. A first slow single electron transfer could occur between carbamate **2c** and a palladacycle(II) complex. The radical anion of the oxidant would immediately undergo mesolytic fragmentation, yielding the 2,4-dinitrobenzenesulfonate and the reactive nitrogen centered radical. The sulfonate will stabilize the palladium (III) while a second fast single electron transfer would then afford the Pd(IV) complex and the corresponding carbamate anion (reduction potential of a general amidyl radical to the corresponding anion is very high),[21] which will immediately coordinate with the palladium and yield the Pd(IV) intermediate **11**. This outer-sphere mechanism can be seen as a formal oxidative insertion into the N–O bond. Finally, azetidine **5** is obtained via a similar dissociative ionization mechanism described in Figure 2b.

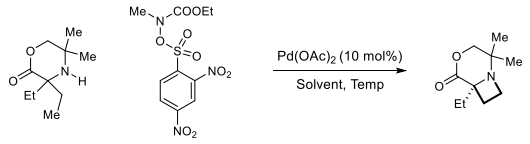
Scheme 3. Possible oxidation mechanism involving SET.



To understand if the first single electron transfer between 2,4-dinitrobenzenesulfonate oxidant **2c** and palladacycle **1b** is feasible, we conducted cyclic voltammetry studies (See SI for details). As expected, the reduction potentials of the oxidants presented a trend. The tosylated derivative **2a** showed a reduction wave around -1.2 V in MeCN (vs AgCl/Ag electrode, 3M KCl), while the 4-nitro (**2b**) and 2,4-dinitrobenzenesulfonate (**2c**) carbamates could be irreversibly reduced at only -0.40 V and -0.25 V respectively, confirming that compound **2c** is the best oxidant. Next, electron rich palladacycle **1b** was submitted to CV studies with two different tetrabutylammonium salts as support electrolytes. Using 0.1M solution of NBu_4PF_6, the electrochemical experiment showed one irreversible oxidation with onset potential at +0.83 V. When the same studies were performed using NBu_4OAc as electrolyte, the oxidation wave shifted to more negative value, showing an onset potential of +0.57 V. This changing oxidation potential can be explained by the different stabilization of the newly-formed high-valent Pd complexes, as also observed by Sanford and colleagues[12,22] (better nucleophiles, such as acetate, will better stabilize the Pd(IV) species). However, in case of outer-sphere oxidation, ethyl *N*-methyl carbamate anion will be formed (via 2-electrons reduction), which normally displays a very high nucleophilicity in comparison to the acetate anion. Therefore, even though the cyclic voltammetry studies suggest an endergonic

single electron transfer, it is possible that the real oxidation potential of palladacycle **1b** in the reaction conditions would be lower than +0.57 V (due to a better stabilization of the high-valent palladium species by the carbamate anion), enabling the first slow single electron transfer to oxidant **2c**. Obviously, the classical inner-sphere oxidative insertion mechanism cannot be ruled out.

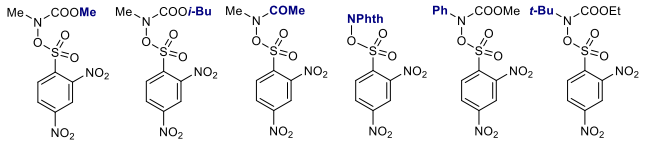
Table 2. Catalytic studies on the use of new N–O type oxidants.



12 **2c** **5**

Entry	2 (equiv)	Solvent	Temp [°C]	Additive (equiv)	5 yield [%][a]
1	**2c** (1.5)	HFIP	60	-	18
2	**2c** (1.5)	HFIP	90	-	25
3	**2c** (1.5)	Toluene	120	-	34
4	**2c** (2)	Toluene	105	-	42
5	**2c** (2)	Toluene	90	-	45
6	**2c** (3)	Toluene	90	-	51
7	**2c** (4)	Toluene	90	-	55
8	**2c** (4)	Toluene	90	AgOAc (2)	61
9	**2d** (2)	Toluene	90	-	41
10	**2e** (2)	Toluene	90	-	42
11	**2f** (2)	Toluene	90	-	23

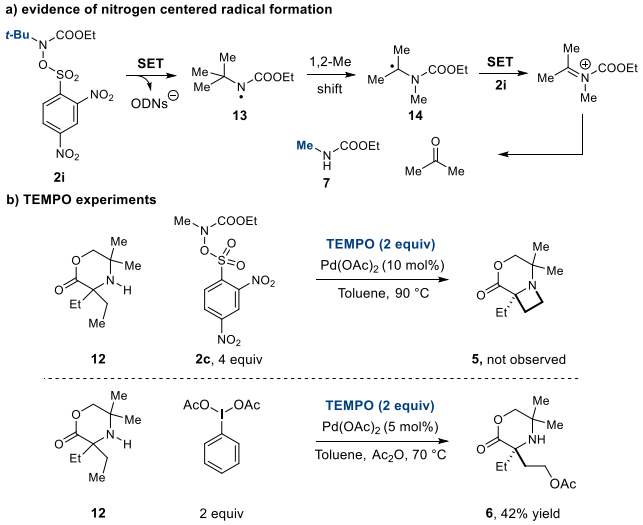
[a] Yields determined by ^{1}HNMR spectroscopy using 1,1,2,2-tetrachloroethane (TCE) as an internal standard.



2d **2e** **2f** **2g** **2h** **2i**

Intrigued by the reactivity of our novel N–O type oxidants, we next attempted a catalytic reaction for the formation of N-heterocycles. Initial experiments with stoichiometric amount of $Pd(OAc)_2$ showed promising results for azetidine **5** formation (60% yield using HFIP as a solvent), while aziridine **3** was only obtained in moderated yield (30% in dioxane, see experimental section for details). Therefore, we focused our attention on morpholinone substrate **12** (Table 2). Solvent, temperature and stoichiometry of the carbamate **2c** were crucial parameters in the optimization studies. Indeed, the reaction in toluene, at 90 °C with 4 equivalents of oxidant **2c** and 10 mol% of $Pd(OAc)_2$ provided the desired azetidine **5** in 55% yield (entry 7; 2.5 equivalents of the oxidant can be recovered at the end of the reaction and reused). Subsequent screening of additives showed AgOAc as a good candidate, improving the yield to 61% (entry 8). It is noteworthy that, while the use of silver additive was not fundamental in this case, traces of azetidine were obtained in absence of AgOAc in our previous methodology.[17] In an attempt to improve the reaction outcome, different carbamate derivatives were prepared and tested. Variations on the carbamate group showed little difference in the yield (entries 9,10), while amide **2f** provided the product in only 23% yield (entry 11). None of the azetidine was obtained when phthalimide (**2g**), N-phenyl (**2h**) or the N-*tert*-butyl (**2i**) derivatives were used as oxidant. Surprisingly, from the reaction mixture of the N-*tert*-butyl oxidant **2i**, we could isolate ethyl N-methyl carbamate **7** in 62% of yield. A plausible explanation for the formation of carbamate **7** in the reaction conditions is described in Scheme 4a. After the first single electron transfer between palladacycle **1b** and oxidant **2i** and mesolytic fragmentation of the corresponding radical anion, the newly-formed unstable nitrogen centered radical **13** undergoes 1,2-methyl shift to form the stable α-amino radical **14**. Another equivalent of carbamate **2i** immediately oxidizes the α-amino radical **14** to the corresponding iminium ion (E_{red} around +1.0 V),[23] which will hydrolyze to yield ethyl N-methyl carbamate **7** and acetone. Since the second electron transfer, and hence the formation of the carbamate anion, could not happen (no dimeric byproducts were detected in this case), the key Pd(IV) complex **11** was not formed, preventing the synthesis of the desired azetidine via the dissociative ionization mechanism. Consequently, the formation of carbamate **7** can be considered as a positive evidence for the presence of nitrogen centered radical **13** and therefore for the single electron transfer between oxidant **2i** and palladacycle **1b**.

Scheme 4. Evidence for the formation of N-centered radicals.



Moreover, when 2 equivalents of TEMPO were introduced in the standard reaction conditions, no azetidine product was observed (Scheme 4b). As a control experiment, the same amount of TEMPO was added to the standard acetoxylation reaction with $PhI(OAc)_2$ as oxidant. In this case, acetoxylated product **6** was obtained in 42% yield (62% yield without TEMPO), suggesting that in the previous experiment TEMPO inhibited the reaction through the quenching of radical species.

In conclusion, we have discovered a new class of oxidants to access high-valent palladium species. The weak N–O bond and the extremely electron withdrawing benzenesulfonate group on the oxygen atom of the oxidant are crucial moieties to ensure the desired activity. Palladacycle (II) complexes could be stoichiometrically oxidized to Pd(IV) species, which promoted the synthesis of N-heterocycles such as azetidine and aziridine. A preliminary catalytic version is also presented, where the azetidine product is obtained in good yield. Cyclic voltammetry experiments and the isolation of carbamate byproduct in the reaction conditions suggests the possibility of outer-sphere single electron transfer (SET) processes involved in the oxidation mechanism. Overall, we believe that these mild oxidants will find important application to other C–H functionalization

processes, especially in case of substrates that are susceptible to oxidative degradation.

EXPERIMENTAL SECTION

General information. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at ambient temperature on a Bruker AM 400 (400 MHz) or an Avance 500 (500 MHz) spectrometer. Chemical shifts (δ) are reported in ppm and quoted to the nearest 0.01 ppm relative to the residual protons in CDCl3 (7.26 ppm) and coupling constants (*J*) are quoted in Hertz (Hz). Data are reported as follows: Chemical shift (multiplicity, coupling constants, number of protons). Coupling constants were quoted to the nearest 0.1 Hz and multiplicity reported according to the following convention: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sp = septet, m = multiplet, bs = broad. Where coincident coupling constants have been observed, the apparent (app) multiplicity of the proton resonance has been reported. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded at ambient temperature on a Bruker AM 400 (100 MHz) or an Avance 500 (125 MHz) spectrometer. Chemical shift (δ) was measured in ppm and quoted to the nearest 0.1 ppm relative to the residual solvent peaks in $CDCl_3$ (77.16 ppm). Toluene was dried and distilled using standard methods. 1,1,2,2-Tetrachloroethane, 1,2-Dichloroethane (DCE), 1,1,1,3,3,3-Hexafluoropropan-2-ol (HFIP) were purchased from Acros and Sigma-Aldrich. $Pd(OAc)_2$ (Pd 45.9-48.4%, needles) and AgOAc were purchased from Alfa Aesar. All reagents were purchased at the highest commercial quality and used without further purification. Reactions were carried out under an atmosphere of air. Palladacycles **1a**,**1b** and morpholinone **12** were prepared according literature procedures.[13,17] Cyclic voltammetry studies were performed using electrasyn 2.0 IKA.

Typical procedure for the synthesis of oxidants 2.[20] To a stirred suspension of N-methylhydroxylamine hydrochloride (5.0 g, 60 mmol, 1.0 equiv) in THF (100 mL) and H_2O (10 mL) were added $NaHCO_3$ (10.0 g, 120 mmol, 2.0 equiv) and ethyl chloroformate (6 mL, 63 mmol, 1.05 equiv). The resulting clear suspension was stirred overnight at room temperature, then diluted with H_2O (50 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo to yield ethyl hydroxy(methyl)carbamate (7.1 g, 99% yield) as a colorless oil that was used without further purification. To a stirred solution of ethyl hydroxy(methyl)carbamate (3.4 g, 28.5 mmol, 1.0 equiv) in CH_2Cl_2 (200 mL) at 0 °C was added NEt_3 (5.1 mL, 37.1 mmol, 1.3 equiv) and 2,4-dinitrobenzenesulfonyl chloride (8.0 g, 29.9 mmol, 1.05 equiv). The resulting orange solution was stirred at 0 °C for 3 h, then diluted with 0.5 M aqueous citric acid (100 mL) and extracted with CH_2Cl_2 (2 x 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL), dried ($MgSO_4$) and concentrated in vacuo. The resultant orange solid was collected by filtration on a sintered funnel, then triturated and washed with Et_2O (2 x 100 mL) to provide oxidant **2c.** When necessary, the product was purified by flash chromatography using petroleum ether/ethyl acetate as eluent.

Ethyl (((2,4-dinitrophenyl)sulfonyl)oxy)(methyl)carbamate **2c** (76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.65 (d, *J* = 2.3 Hz, 1H), 8.55 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H), 8.42 (d, *J* = 8.7 Hz, 1H), 4.04 (q, *J* = 7.1 Hz, 2H), 3.39 (s, 3H),1.1 (t, *J* = 7.1 Hz, 3H).

Ethyl methyl(tosyloxy)carbamate **2a** (87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.86 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 8.7 Hz, 2H), 3.93 (q, *J* = 7.1 Hz, 2H), 3.26 (s, 3H), 2.46 (s, 3H), 1.0 (t, *J* = 7.1 Hz, 3H).

Methyl methyl(((4-nitrophenyl)sulfonyl)oxy)carbamate **2b** (82% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.40 (d, *J* = 8.9 Hz, 2H), 8.19 (d, *J* = 8.9 Hz, 2H), 3.51 (s, 3H), 3.34 (s, 3H).

Methyl (((2,4-dinitrophenyl)sulfonyl)oxy)(methyl)carbamate **2d** (74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.67 (d, *J* = 2.2 Hz, 1H), 8.56 (dd, *J* = 8.5 Hz, *J* = 2.2 Hz, 1H), 8.42 (d, *J* = 8.5 Hz, 1H), 3.61 (s, 3H), 3.39 (s, 3H).

Isobutyl (((2,4-dinitrophenyl)sulfonyl)oxy)(methyl)carbamate **2e** (77 yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.64 (d, *J* = 2.2 Hz, 1H), 8.55 (dd, *J* = 8.6 Hz, *J* = 2.2 Hz, 1H), 8.42 (d, *J* = 8.6 Hz, 1H), 3.8 (d, *J* = 6.7 Hz, 2H), 3.38 (s, 3H), 1.89-1.72 (m, 1H), 0.84 (d, *J* = 6.7 Hz, 6H).

N-(((2,4-dinitrophenyl)sulfonyl)oxy)-N-methylacetamide **2f** (52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.66 (d, *J* = 2.2 Hz, 1H), 8.60 (dd, *J* = 8.5 Hz, *J* = 2.2 Hz, 1H), 8.43 (d, *J* = 8.5 Hz, 1H), 3.37 (s, 3H), 2.13 (s, 3H). 1,3-dioxoisoindolin-2-yl 2,4-dinitrobenzenesulfonate **2g** (66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.75 (d, *J* = 2.2 Hz, 1H), 8.62 (dd, *J* = 8.6 Hz, *J* = 2.2 Hz, 1H), 8.47 (d, *J* = 8.6 Hz, 1H), 7.91-7.82 (m, 4H).

Methyl (((2,4-dinitrophenyl)sulfonyl)oxy)(phenyl)carbamate **2h** (48% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.67 (d, *J* = 2.2 Hz, 1H), 8.47 (dd, *J* = 8.5 Hz, *J* = 2.2 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.45-7.38 (m, 2H), 7.37-7.32 (m, 1H), 7.18-7.10 (m, 1H), 3.65 (s, 3H).

Ethyl *tert*-butyl(((2,4-dinitrophenyl)sulfonyl)oxy)carbamate **2i** (61% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.64 (d, *J* = 2.3 Hz, 1H), 8.55 (dd, *J* = 8.7 Hz, *J* = 2.3 Hz, 1H), 8.37 (d, *J* = 8.7 Hz, 1H), 4.04 (q, *J* = 7.1 Hz, 2H), 1.45 (s, 9H),1.1 (t, *J* = 7.1 Hz, 3H).

Stoichiometric studies using palladacycles. A suspension of the palladacycle **1** (0.025 mmol, 1 equiv), oxidant **2** (0.05 mmol, 2 equiv) in 1,2-dichloroethane (0.5 mL) was heated in a sealed tube at 50 °C and stirred for 16 hours. The reaction mixture was cooled to room temperature, filtered through Celite and elute with dichloromethane. In case of palladacycle **1a**, the solution was extracted with water (3x 10 mL) and concentrated in vacuo to deliver aziridine **3** as 2,4-dinitrobenzenesulfonate salt. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.42-8.34 (m, 3H), 8.19-8.02 (bs, 1H), 3.03 (dd, *J* = 7.4 Hz, *J* = 3.7 Hz, 1H), 2.52 (dd, *J* = 4.1 Hz, *J* = 3.7 Hz, 1H), 2.06-1.98 (m, 2H), 1.73 (s, 3H), 1.72-1.65 (m, 1H), 1.63 (s, 3H), 1.55-1.49 (m, 2H), 1.46 (s, 3H), 1.49-1.45 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 148.3, 148.2, 143.1, 132.0, 126.0, 118.8, 56.2, 48.9, 36.3, 32.3, 27.6, 27.1, 27.0, 23.1, 14.4. When palladacycle **1b** was used, the solution was basified by the addition of a saturated aqueous solution of $NaHCO_3$. The aqueous solution was further extracted with dichloromethane (3 x 10 mL) and the combined organic extracts were dried (MgSO4), filtered and concentrated in vacuo to deliver azetidine **5**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.52 (d, *J* = 11.5 Hz, 1H), 4.04 (d, *J* = 11.5 Hz, 1H), 3.38-3.28 (m, 1H), 3.23 (td, *J* = 8.3, 4.7 Hz, 1H), 2.35-2.22 (m, 2H), 1.90-1.74 (m, 2H), 1.11 (s, 3H), 1.04 (t, *J* = 7.5 Hz, 3H), 1.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.7, 73.2, 66.2, 49.9, 42.7, 32.5, 25.9, 25.1, 21.1, 8.1.

Ethyl (((ethoxycarbonyl)amino)methyl)(methyl)carbamate **8**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.65 (d, *J* = 7.3 Hz, 2H), 4.23-4.08 (bs, 4H), 3.00 (s, 3H), 1.27 (t, *J* = 7.0 Hz, 6H).

Diethyl methylenebis(methylcarbamate) **9**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.94-4.81 (bs, 2H), 4.23-4.08 (m, 4H), 2.95-2.81 (bs, 6H), 1.28 (t, *J* = 7.0 Hz, 6H).

Diethyl methylenedicarbamate **10**. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.55-4.47 (m, 2H), 4.17-4.09 (m, 4H), 1.30-1.22 (m, 6H).

Stoichiometric studies using $Pd(OAc)_2$. In a 10 mL vial equipped with stir bar, $Pd(OAc)_2$ (11 mg, 0.05 mmol) and oxidant **2c** (17 mg, 0.05 mmol) were combined, followed by the addition of the solvent (0.5 mL) and 2,2,6,6-tetramethylpiperidine (0.009 ml, 0.05 mmol) or 3,3-diethyl-5,5-dimethylmorpholin-2-one **12** (18.5 mg, 0.05 mmol). Then the vial was sealed under air with a screw cap and Teflon septum, placed in a pre-heated oil bath at 60 °C and stirred for 16 hours. The reaction mixture was cooled to room temperature, filtered through Celite, elute with dichloromethane and concentrated in vacuo. TCE (0.053 ml, 0.05 mmol) was added as an internal standard and the yields were determined by ^{1}HNMR spectroscopy. DCE: **3** = 13% yield, **5** = 25% yield; HFIP: **3** = traces, **5** = 60%; Dioxane: **3** = 30%, **5** = 56%; Toluene: **5** = 46%; AcOEt : **5** = 26%.

Typical procedure for catalytic studies. In a 10 mL vial equipped with stir bar, $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), oxidant **2c** (140 mg, 0.4 mmol), AgOAc (34 mg, 0.2 mmol) were combined, followed by the addition of toluene (1.0 mL) and 3,3-diethyl-5,5-dimethylmorpholin-2-one **12** (18.5 mg, 0.1 mmol). Then the vial was sealed under air with a screw cap and Teflon septum, placed in a pre-heated oil bath at the described temperature and stirred for 16 hours. The reaction mixture was cooled to room temperature, filtered through Celite, eluting with ethyl acetate, and then basified by the

addition of a saturated aqueous solution of $NaHCO_3$. The aqueous solution was further extracted with ethyl acetate (3 x 10 mL) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. TCE (0.0105 ml, 0.1 mmol) was added as an internal standard and the yields were determined by ^{1}HNMR spectroscopy.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

NMR traces and cyclic voltammetry studies (PDF)

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