

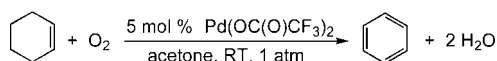
Oxidative Aromatization of Olefins with Dioxygen Catalyzed by Palladium Trifluoroacetate

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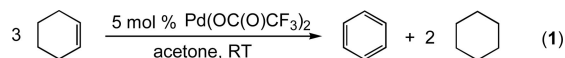
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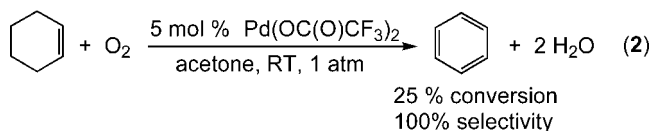
Molecular oxygen can replace sacrificial olefins as the hydrogen acceptor in the palladium trifluoroacetate catalyzed dehydrogenation of cyclohexene and related cyclic olefins into aromatics. One of the major drawbacks of the homogeneous system is the tendency of the palladium trifluoroacetate to precipitate as palladium(0) at elevated temperatures. The use of better ligands affords catalysts that can operate at higher temperatures, although they are less reactive than palladium trifluoroacetate.

Two of the major challenges in the functionalization of organic molecules are the activation of C–H bonds^{1–3} and the utilization of O₂ as a terminal oxidant in oxidative transformations.^{4–7} In both cases the development of practical methods could have a significant environmental and economic impact in a number of different areas. An early and intriguing example of facile C–H bond activation was a 1980 report by Trost and Metzner, that cyclohexene is catalytically disproportionated into 1 equiv of benzene and 2 equiv of cyclohexane (eq 1) or dehydrogenated to benzene using dimethyl fumarate or maleic acid as sacrificial hydrogen acceptors (giving dimethyl succinate or succinic acid, respectively) in the presence of an acetone solution of palladium trifluoroacetate.⁸ The reactions were proposed to be heterogeneously catalyzed⁹ and to involve an intermediate palladium hydride species. Recently, several reports have established similarities between the reactions of O₂ and olefins with palladium hydrides,^{10–14} suggesting that it might

be possible to replace the sacrificial olefin with O₂ in dehydrogenative reactions. Here, we report our findings about reactions between palladium trifluoroacetate and olefins in the presence of O₂.



Whereas precipitation of Pd occurs rapidly upon addition of cyclohexene to an acetone solution of palladium trifluoroacetate under inert atmosphere,⁸ the same procedure under 1 atm of O₂ resulted in a homogeneous orange solution. Analysis by ¹H NMR spectroscopy indicated that after 24 h only benzene had formed and no cyclohexane was present (eq 2). An additional broad resonance at δ 4.1 ppm, which grew in over the course of the reaction, is attributed to water (formed through the reduction of O₂), in exchange with free trifluoroacetic acid (formed through protonation of the trifluoroacetate ligand). In support of this assignment, addition of a small amount of water to the final solution caused the broad resonance to increase in intensity and shift slightly in position.



Further confirmation of the role of O₂ in the reaction was obtained by performing reactions with O₂ as the limiting reagent. In these experiments, initially the solution remained clear, and benzene was the only product detected by ¹H NMR spectroscopy. At later stages, once all of the O₂ had been consumed, a black solid precipitated out of solution and formation of cyclohexane occurred, as a result of the heterogeneous disproportionation reaction described by Trost.⁸ The ratio of direct conversion of cyclohexene to benzene compared with disproportionation was controlled by the amount of O₂ present. For reactions performed using the same amount of catalyst, solvent, and cyclohexene under 1 atm of O₂ in a J. Young NMR tube, the ratio of benzene to cyclohexane at the end of the reaction was approximately 1:1, whereas in a flask with a 10 mL headspace the ratio was 3.5:1. No disproportionation was observed so long as excess O₂ was present.

A number of lines of evidence indicate that the dehydrogenation with O₂ is homogeneously catalyzed. First, in the early stages of the reaction the solution appears completely homogeneous with no solid particles visible.¹⁵ Over time a fine precipitate starts to appear, but the formation of benzene is well underway before this begins; monitoring the reaction by ¹H NMR spectroscopy indicates no initiation period and no

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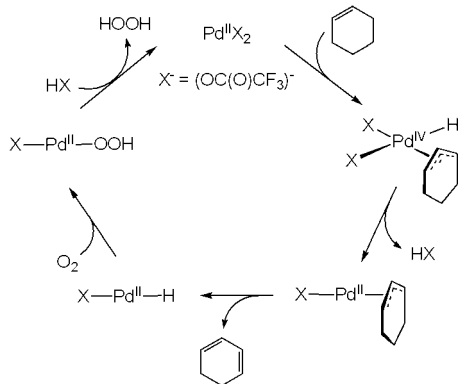
(15) Of course, this observation does not exclude the possibility of a colloidal heterogeneous catalyst. The usual “mercury drop” test is uninformative, as elemental Hg rapidly reduces palladium trifluoroacetate to Pd(0) under reaction conditions.

TABLE 1. Ratio of Benzene to Cyclohexane and Conversion at Different Temperatures in Reactions between Palladium Trifluoroacetate and Cyclohexene under 1 atm of O₂^a

temp (°C)	ratio C ₆ H ₆ :C ₆ H ₁₂	conversion (%)
25	no cyclohexane	25
40	0.96:1	37
60	0.82:1	85

^a Reactions contained 0.016 mmol of palladium trifluoroacetate, 0.32 mmol of cyclohexene, and 0.6 mL of *d*₆-acetone in a J. Young NMR tube under 1 atm of O₂.

SCHEME 1



evidence for autocatalytic kinetics. Most significantly, the heterogeneously catalyzed disproportionation of cyclohexene into benzene and cyclohexane is *inhibited* by O₂. When the precipitate from a reaction under inert atmosphere was isolated and added to a fresh solution of cyclohexene in acetone under O₂, no conversion of cyclohexene at all was observed, whereas under argon the same precipitate was highly active for disproportionation. Hence if the oxidative dehydrogenation is heterogeneously catalyzed, there would have to be *two different* solid catalysts present in the precipitate: one that converts cyclohexene directly to benzene using O₂ as the oxidant and a second that disproportionates cyclohexene to benzene and cyclohexane and is suppressed by O₂. It seems far more likely that the former reaction is homogeneous.

Consistent with this interpretation, when the reaction was carried out at higher temperatures in order to increase the rate of conversion, black solid precipitated out of solution almost immediately upon heating, and analysis of the reaction mixtures after 24 h by ¹H NMR spectroscopy showed that both benzene and cyclohexane had formed (Table 1). It appears that although at room temperature O₂ is able to keep the palladium catalyst almost completely in solution, as the temperature is raised, precipitation sets in and the heterogeneously catalyzed disproportionation becomes a viable side reaction even in the presence of O₂.

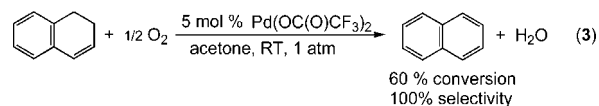
A plausible mechanism for the oxidative dehydrogenation is shown in Scheme 1, including C–H activation similar to that proposed by Trost for the heterogeneous case⁸ and oxidation related to that proposed by Muzart and Pete for the dehydrogenation of cyclohexanones using O₂ as the oxidant.¹⁶ Insertion of the highly electrophilic palladium into the allylic C–H bond of cyclohexene, followed by elimination of trifluoroacetic acid, gives an intermediate that undergoes β-hydride elimination to give 1,3-cyclohexadiene and a palladium hydride species.

Insertion of O₂ into the Pd–H bond (in the absence of O₂ the latter would quickly decompose to give Pd metal) then produces a peroxy intermediate that reacts with trifluoroacetic acid to regenerate the catalyst. In a similar cycle (not shown) 1,3-cyclohexadiene would react analogously to give benzene. Independent experiments using 1,3-cyclohexadiene as a substrate demonstrate that it is completely oxidized to benzene in 3 h, under conditions analogous to those described for cyclohexene, confirming that it is considerably more reactive and would not accumulate.

Likewise, the absence of detectable hydrogen peroxide could indicate either that it is a better oxidant than O₂ and is rapidly consumed by a related cycle or that the catalytic system efficiently decomposes it to O₂ and water.¹⁷ Addition of a stoichiometric (relative to cyclohexene) amount of hydrogen peroxide to a solution containing cyclohexene and palladium trifluoroacetate resulted in vigorous bubbling, and after 15 min little or no peroxide remained (iodide test). After 12 h palladium black had precipitated out of solution and cyclohexane and benzene had been formed in an approximately 2:1 ratio (cyclohexane was also still present), consistent with disproportionation but no oxidative aromatization having occurred. Clearly hydrogen peroxide is *not* a competitive oxidant but instead is rapidly decomposed under catalytic conditions.

In exploring the scope of the reaction, we found that 1,2-dihydronaphthalene behaves very similarly to cyclohexene: reaction under 1 atm of O₂ resulted in rapid conversion to naphthalene (eq 3), whereas the same reaction performed under argon gave disproportionation to tetralin and naphthalene. Substituted cyclohexenes exhibit reduced reactivity: none of 1-methylcyclohexene, 4-methylcyclohexene, or 3-chlorocyclohexene underwent any reaction at room temperature, but at 60 °C (where black solid precipitated) products consistent with both direct oxidation and disproportionation were observed.

For 1-methylcyclohexene and 4-methylcyclohexene the ratios of toluene to methylcyclohexane were 1.38 and 1.32 to 1, respectively, with conversions of around 80% (after 24 h). With 3-chlorocyclohexene the ratio of chlorobenzene to chlorocyclohexane was around 1.3 to 1, with competing dechlorination giving some benzene, cyclohexane, and cyclohexene. These results demonstrate that a direct oxidation pathway is feasible for substituted cyclohexenes, but because the reactions must be run at higher temperatures the heterogeneous disproportionation pathway becomes a significant side reaction.



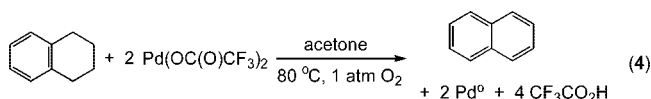
Linear olefins do not exhibit analogous chemistry. No reaction was observed between palladium trifluoroacetate and 20 equiv of 1-hexene under 1 atm of O₂ at room temperature. When the reaction mixture was heated a black precipitate crashed out of solution; when the mixture was maintained at 80 °C for 1 week, slow isomerization to a mixture of *cis*- and *trans*-2-hexene took place. This process is heterogeneously catalyzed, as the black solid could be isolated by filtration, washed with acetone, and then reused successfully to catalyze 1-hexene isomerization, as well as disproportionation of cyclohexene to benzene plus cyclohexane. As with the latter, isomerization was inhibited by O₂: it proceeded significantly faster under argon (reaction took

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around 3 days). Presumably, O₂ inhibits both reactions by covering the catalyst surface and blocking olefin coordination, which is consistent with the O₂ inhibition being less significant at higher temperatures. Surprisingly, neither *cis*- nor *trans*-2-hexene is isomerized by palladium trifluoroacetate at 80 °C. We believe this is because the sterically more hindered olefins cannot easily coordinate to the metal, which is presumably the first step in isomerization.

We also examined the behavior of 1,2,3,4-tetrahydronaphthalene (tetralin), which contains benzylic but no allylic C–H bonds. There was no reaction of palladium trifluoroacetate with 12 equiv of tetralin under 1 atm of O₂ at room temperature, but heating to 80 °C led to the formation of 0.5 equiv of naphthalene per palladium (eq 4), along with formation of black precipitate; the same result was obtained when the reaction was performed under argon. These results suggest that O₂ plays no role in the reaction and is consistent with the reaction being stoichiometric in palladium (2 equiv of palladium are required to convert tetralin to naphthalene). However, when maleic acid (1.5 equiv relative to tetralin) was added to the reaction mixture (under argon), the ratio of tetralin to naphthalene at the end of the reaction was 4:1 and a considerable amount of succinic acid had been generated. This suggests that hydride transfer from a palladium species to maleic acid is occurring and in this case the reaction is catalytic in palladium. The reaction with maleic acid appears to be heterogeneous and only occurs at elevated temperatures, presumably because it is more difficult to activate the C–H bonds in tetralin. The results shown above suggest that O₂ is unable to keep the catalyst in solution at elevated temperatures, and this may be why O₂ is unable to work as a sacrificial hydride acceptor in this reaction.



One approach to finding a palladium catalyst that is less likely to aggregate as Pd(0) at elevated temperatures is to use better ligands than trifluoroacetate. We have recently shown that complexes of the type [(diimine)Pd^{II}(μ₂-OH)]₂²⁺ (diimine = ArN=C(Me)–C(Me)=NAr; Ar = 3,5-^tBu₂C₆H₃ or 2,4,6-Me₃C₆H₂) can catalyze the conversion of cyclohexene to benzene under 1 atm of O₂ at 60 °C.⁹ This reaction appears to be homogeneous, indicating that the ligand stabilizes the intermediates at higher temperatures. Consistent with the proposal that O₂ and olefins may operate interchangeably as hydride acceptors, when we perform the reaction between cyclohexene and 5 mol % of [(diimine)Pd^{II}(μ₂-OH)]₂²⁺ (diimine = ArN=C(Me)–C(Me)=NAr; Ar = 3,5-^tBu₂C₆H₃) in the presence of maleic acid, we see conversion to benzene (approximately 71% after 4 days at 60 °C), in addition to succinic acid along with a small amount of cyclohexane. Presumably, cyclohexene can compete with maleic acid to act as the hydride acceptor. The greater stability of this N-ligated system also allows us to use O₂ as the oxidant for the conversion of tetralin to naphthalene at 110 °C, although with low conversion (4% conversion, 2 turnovers per Pd). Unfortunately, as indicated by the higher required reaction temperatures, these diimine complexes appear significantly less reactive than palladium trifluoroacetate.

We have demonstrated that O₂ can replace sacrificial olefins as the hydride acceptor in the palladium trifluoroacetate catalyzed dehydrogenation of cyclohexene and related species

into aromatics. This represents a significant improvement as O₂ is cheap and abundant and produces only water as a byproduct. It appears that catalysis using O₂ as the oxidant occurs homogeneously, whereas when a sacrificial olefin is used, the reaction is heterogeneous. One of the major drawbacks of the homogeneous system is the tendency of the palladium trifluoroacetate to precipitate as palladium(0) at elevated temperatures. The use of better ligands affords catalysts that can operate at higher temperatures; ongoing studies are aimed at finding ligands that stabilize the palladium complexes at higher temperatures without sacrificing activity. Sacrificial olefins are requisite co-reagents in many instances of low-temperature, homogeneously catalyzed alkane dehydrogenation;¹⁸ our ultimate goal is to be able to substitute O₂ for a much wider range of substrates.

Experimental Section

Palladium trifluoroacetate (purchased from Sigma Aldrich) and other organic compounds used in this work were reagent-grade commercial samples used without further purification. The hydroxy-bridged palladium dimer, [(diimine)Pd^{II}(μ₂-OH)]₂²⁺ (diimine = ArN=C(Me)–C(Me)=NAr; Ar = 3,5-^tBu₂C₆H₃), was synthesized using a literature procedure.⁹ ¹H NMR spectra were recorded at ambient temperature using a Varian Mercury 300 MHz spectrometer. GC analyses were performed on an HP model 6890N chromatograph equipped with a 10 m × 0.10 mm × 0.40 μm DB-1 column. GC/MS analyses were performed on an HP model 6890N chromatograph equipped with a 30 m × 25 mm × 0.40 μm HP5-1 column and equipped with an HP 5973 mass selective EI detector.

Standard Reaction Protocol. The following procedure was used for a standard reaction catalyzed by palladium trifluoroacetate. Palladium trifluoroacetate (5 mg, 0.016 mmol) was dissolved in *d*₆-acetone (0.6 mL) in a J. Young NMR tube. Cyclohexene (30 μL, 0.32 mmol, 20 equiv) was then added, and the solution immediately placed in liquid nitrogen. If an organic additive was used, it was added at the same stage as cyclohexene. The reaction mixture was degassed using three consecutive freeze–pump–thaw cycles and placed under 1 atm of O₂ using a Schlenk line (a similar procedure was used to perform control reactions under argon). Reactions were heated at the appropriate temperature and monitored using ¹H NMR spectroscopy. At the completion of the reactions the ratio of products was determined using both ¹H NMR spectroscopy and gas chromatography (GC). In reactions under 1 atm of O₂ at room temperature, solutions were initially orange (regardless of the substrate) and appeared homogeneous before a fine black precipitate formed over time (hours to days). When these reactions were heated, a black precipitate formed much faster (hours) and the solution gradually became colorless. The rate at which this process occurred increased as the temperature was raised. In reactions under argon, solutions were initially orange before a black precipitate formed and the solution became colorless in less than 15 min. In many cases the black precipitate was isolated through filtration and then washed with acetone and hexane before being dried under reduced pressures.

The following procedure was used for the reaction between [(diimine)Pd^{II}(μ₂-OH)]₂²⁺ (diimine = ArN=C(Me)–C(Me)=NAr; Ar = 3,5-^tBu₂C₆H₃), cyclohexene, and maleic acid. [(Diimine)-Pd^{II}(μ₂-OH)]₂²⁺ (3 mg, 0.002 mmol) was dissolved in a 6:1 mixture of *d*₄-dichloroethane (0.6 mL) and *d*₃-trifluoroethanol (0.1 mL) in a J. Young NMR tube. Cyclohexene (20 μL, 0.197 mmol, 22 equiv per Pd) and maleic acid (69 mg, 0.591 mmol, 3 equiv to cyclohexene) were then added, and the solution

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immediately placed in liquid nitrogen. The reaction mixture was degassed using three consecutive freeze–pump–thaw cycles and placed under 1 atm of O₂ using a Schlenk line. The reaction was heated at 60 °C and monitored using ¹H NMR spectroscopy. At the completion of the reactions the ratio of products was determined using both ¹H NMR spectroscopy and GC. A similar procedure was utilized for a reaction between [(diimine)Pd^{II}(μ₂-OH)]₂²⁺ (5 mg, 0.004 mmol) and tetralin (50 μL, 0.368 mmol, 45 equiv per Pd), which was heated for 8 days at 110 °C. At the

end of the reaction 4% of the tetralin had been converted to naphthalene, which corresponds to approximately two turnovers per palladium center.

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