Supporting Information

Synthesis of Cyclic Enones via Direct Palladium-Catalyzed Aerobic Dehydrogenation of Ketones

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Table of Contents

1. General considerations.

All commercially available compounds were used as received and purchased from Sigma Aldrich except for $Pd(OAc)_2$ and $Pd(TFA)_2$ which were donated by Eli Lilly. Substrates that were not commercially available were prepared according to literature procedures: 5a-androstane-3,17-dione (Table 2, entry 9),[1] (*R*)-1-oxo-2-methyl-2-ethyl-cyclohexanepropanoate (eq 1),[2] 2-hydroxy-5-methyl-5-(2-propen-1-yl)-2-cyclopenten-1-one (eq 2).[3]

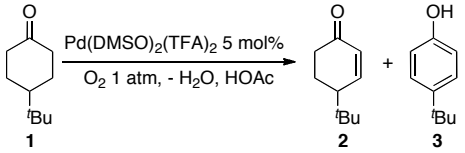
^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 MHz or a Varian Mercury-300 MHz spectrometer. The chemical shifts (δ) are given in parts per million and referenced to residual solvent peaks or a TMS internal standard. Gas chromatography was performed on a Shimadzu GC-17A using a Stabilwax®-DB column (15 m) and referenced to an internal standard (tetradecane). Flash column chromatography was performed on an Isco Combiflash system using silica gel 60 (Silicycle) and eluted with ethyl acetate/hexane. Melting points were recorded on a Melt-Temp® apparatus.

CAUTION: The combination of organic solvents and O_2 creates the risk of an explosion. To minimize risks, all reactions carried out at pressures above 1 atm utilized a dilute oxygen gas mixture (9% O_2 in N_2) to ensure that the O_2 content remains below the lower explosive limit of O_2/organic mixtures.[4] All reactions should be performed with care and

carried out behind a blast shield.

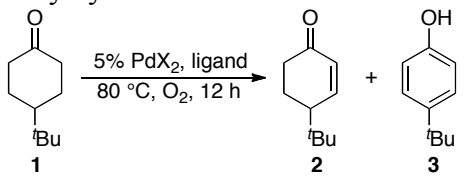
2. General procedure for catalyst optimization.

Catalytic aerobic oxidation reactions were performed using a custom reaction apparatus that enabled several reactions to be performed simultaneously under a constant pressure of O_2 (approx 1 atm) with controlled temperature and orbital agitation. Control experiments demonstrated that similar results can be obtained using a standard round-bottom flask equipped with a stir bar and a balloon of O_2 (see below), or using a stainless steel (or Hastelloy) Parr pressure vessel for reactions carried out under elevated pressures of O_2.



To a disposable 13 mm thick-walled culture tube was added $Pd(TFA)_2$, (1.65 mg, 0.005 mmol, 0.05 equiv), DMSO (0.7 μL, 0.01 mmol, 0.1 equiv), and 0.25 ml acetic acid. The reaction tubes were placed in a 48-well parallel reactor mounted on a Glas-Col large capacity mixer. The headspace was purged with O_2 for 10 min, after which a solution of 4-*tert*-butylcyclohexanone (15.4 mg, 0.1 mmol, 1 equiv) in acetic acid (0.25 ml) was added via syringe. The solution was agitated vigorously at 80 °C for 12 h. After 12 h, the reaction vessel was vented. External standard (tetradecane, 10 μl, 0.038mmol) was added. The solution was then diluted with CH_2Cl_2 and analyzed by GC.

Table S1. Additional Catalyst Optimization Data for the Aerobic Oxidative Dehydrogenation of 4-*tert*-Butylcyclohexanone **1**.[a]



entry	Pd	ligand (mol%)	solvent	additive	**2** (%)[b]	**3** (%)[b]
1	$Pd(OAc)_2$		DMSO		63	14
2	$Pd(TFA)_2$		DMSO		34	56
3	$Pd(TFA)_2$	2-Me_2Npy (10)	DMSO	TsOH (20%)	23	33
4	$Pd(TFA)_2$	5,5-Me_2bpy (5)	PhCl	4Å MS, 50 mg	19	0
5	$Pd(TFA)_2$	5,5-Me_2bpy (5)	PhCl		23	0
6	$Pd(OAc)_2$		AcOH		13	0
7	$Pd(TFA)_2$		AcOH		24	1
8	$Pd(OAc)_2$	DMSO (10)	AcOH		86	8
9	$Pd(TFA)_2$	DMSO (10)	AcOH		91	8
10	$Pd(TFA)_2$	DMSO (10)	AcOH	4Å MS, 50 mg	6	0
11	$Pd(TFA)_2$	DMSO (10)	Toluene		67	3
12	$Pd(TFA)_2$	DMSO (10)	Mesitylene		86	6
13	$Pd(TFA)_2$	DMSO (10)	THF		66	8
14	$Pd(TFA)_2$	DMSO (10)	Dioxane		84	10
15	$Pd(TFA)_2$	DMSO (10)	EtOAc		30	6
16	$Pd(TFA)_2$	DMSO (10)	DMF		27	2
17	$Pd(TFA)_2$	DMSO (10)	DMA		47	5

18	$Pd(TFA)_2$	DMSO (10)	PhCN		16	2
19	$Pd(TFA)_2$	DMSO (10)	PhCl		11	0
20	$Pd(TFA)_2$	DMSO (10)	PhCl	4Å MS, 50 mg	12	0
21	$Pd(TFA)_2$	MePhSO (10)	AcOH		22	0
22	$Pd(TFA)_2$	tetramethylenesulfoxide (10)	AcOH		65	4
23	$Pd(TFA)_2$	trimethylenesulfoxide (10)	AcOH		7	0
24	$Pd(TFA)_2$	Pyridine (10)	HOAc		55	2
25	$Pd(TFA)_2$	2-MeOpy (10)	AcOH		8	0
26	$Pd(TFA)_2$	2-Me_2Npy (10)	AcOH		3	1
27	$Pd(TFA)_2$	4-NH_2py (10)	AcOH		79	4
28	$Pd(TFA)_2$	2-NH_2py (10)	AcOH		1	0
29	$Pd(TFA)_2$	2-F py (10)	AcOH		37	2
30	$Pd(TFA)_2$	3-Nitropy (10)	AcOH		4	0
31	$Pd(TFA)_2$	bpy (5)	AcOH		0	0
32	$Pd(TFA)_2$	6,6'-Me_2bpy (5)	AcOH		31	3
33	$Pd(TFA)_2$	5,5'-Me_2bpy (5)	HOAc		0	0
34	$Pd(TFA)_2$	4,4'-Me_2bpy (5)	AcOH		0	0
35	$Pd(TFA)_2$	4,4'-di*tert*butyl-bpy (5)	AcOH		11	0
36	$Pd(TFA)_2$	phenanthroline (5)	AcOH		0	0
37	$Pd(TFA)_2$	6,6'-dimethylphen (5)	AcOH		26	2
38	$Pd(TFA)_2$	bipyrimidine (5)	AcOH		6	0
39	$Pd(TFA)_2$	Bissulfoxide (5)	HOAc		9	4
40	$Pd(TFA)_2$	DMSO (10)	AcOH	NaOAc (10%)	85	6
41	$Pd(TFA)_2$	DMSO (10)	AcOH	NaOBn (10%)	82	4
42	$Pd(TFA)_2$	DMSO (10)	AcOH	Na_2CO_3 (10%)	83	5
43	$Pd(TFA)_2$	DMSO (10)	AcOH	pentamethylpiperidine (10%)	83	6
44	$Pd(TFA)_2$	DMSO (10)	AcOH	TsOH (10%)	5	20

[a] Reaction conditions: see procedure above. [b] GC yield.

3. General procedure for dehydrogenation of cyclohexanones and product isolation. Good gas-liquid mixing is critical for these reactions, and analysis of different reaction format revealed that the best results are obtained with orbital agitation. Nevertheless, the reactions could be carried out in a round-bottom flask equipped with a balloon of O_2, with magnetic stirring, or by using high-pressure diluted O_2 (9% in N_2) in a Parr pressure vessel, with magnetic stirring. Representative procedures employing each of these formats is described below.

*Dehydrogenation of **1** with orbital agitation.* To two disposable 13 mm thick-walled culture tubes were added $Pd(TFA)_2$ (6.6 mg, 0.02 mmol, 0.05 equiv), DMSO (2.8 μL, 0.01 mmol, 0.1 equiv), and acetic acid (1 ml). The reaction tubes were placed in a 48-well parallel reactor mounted on a Glas-Col large capacity mixer. The headspace was purged with O_2 for 10 min, after which a solution of 4-*tert*-butyl cyclohexanone (61.6 mg, 0.4 mmol, 1 equiv) in acetic acid (1 ml) was added via syringe. The solution was agitated vigorously at 80 °C for 12 h. After 12 h, the reaction was cooled down, and O_2 was vented from the reactor. The two reaction mixtures were combined and acetic acid was removed under vacuum using a rotovap. Silica gel was saturated with 1% triethylamine in hexane, and loaded onto a column. The column was then washed with hexane to remove excess triethylamine. The reaction mixture was loaded onto the column

and flushed with 10% ethyl acetate in hexane. The cyclohexenone product **2** was obtained in 91% yield as a colorless liquid, and the phenol byproduct **3** was obtained as a white solid in 8% yield.

*Dehydrogenation of **1** in a round-bottom flask.* To a 25 ml round-bottom flask equipped with a stir bar was added $Pd(TFA)_2$ (13 mg, 0.04 mmol, 0.05 equiv) and 4-*tert*-butyl cyclohexanone (123 mg, 0.8 mmol). A reflux condenser was place on the flask and sealed with a septum. A balloon was attached via a needle. The flask and balloon were purged and filled with O_2, followed by addition of DMSO (5.6 μL, 0.02 mmol, 0.1 equiv) and acetic acid (4 ml). The flask was stirred at 80 °C for 12 h. After 12 h, O_2 was vented from the flask. Acetic acid was removed under vacuum using a rotovap. Products **2** and **3** were isolated as described above and obtained in 90% and 6% yield, respectively.

Dehydrogenation of 5α-Cholestan-3-one (Table 2, entry 8) in a round-bottom flask. To a 25 ml round-bottom flask equipped with a stir bar was added $Pd(TFA)_2$ (3.3 mg, 0.01 mmol, 0.05 equiv) and 5α-Cholestan-3-one (78 mg, 0.2 mmol). A reflux condenser was place on the flask and sealed with a septum. A balloon was attached via a needle. The flask and balloon were purged and filled with O_2, followed by addition of DMSO (1.4 μL, 0.02 mmol, 0.1 equiv) and acetic acid (1 ml). The stock solution of NMR internal standard, 1,3,5-trimethoxybenzene (0.001 mmol, in DMSO-d_6), was added. The mixture was then neutralized with saturated $NaHCO_3$ aqueous solution and extracted with $CDCl_3$. The organic layer was transferred to an NMR tube via a pipet and analyzed by ^1H NMR spectroscopy, which revealed the enone product was formed in 90% NMR, comparable to the yield obtained from the reaction carried out with orbital agitation.

Dehydrogenation of unsubstituted cyclohexanone in a Parr pressure vessel. The oxidation of cyclohexanone in acetic acid afforded cyclohexenone in only modest yield (~50%) with poor mass balance. Improved mass balance was observed when the reaction was carried out in ethyl acetate. A good yield (72%) could be obtained with 1 atm O_2 when the reaction was mixed via orbital agitation; however, attempts to perform the oxidation in a round-bottom flask with an O_2 balloon failed, due to fast decomposition of the Pd catalyst (the use of AcOH as the solvent appears to stabilize the catalyst). We speculated that the catalyst would be more stable with elevated pressures of O_2 and the reaction was analyzed under different pressures of O_2 (Figure S1). Low O_2 pressure led to low conversion and observation of signficant amounts of Pd black. Elevated O_2 pressure resulted in a significant increase in product formation. A typical protocol for this reaction format is as follows:
To a 45 mL Hastelloy Parr pressure vessel equipped with a stir bar was added $Pd(TFA)_2$ (13.2 mg, 0.04 mmol, 0.05 equiv), DMSO (5.6 μL, 0.02 mmol, 0.1 equiv), ethyl acetate (1 ml) and cyclohexanone (80 μl, 0.8 mmol). The vessel was sealed and 70 atm of 9% O_2 in N_2 (6.3 atm partial pressure of O_2) was supplied to the vessel. The reaction was heated to 60 °C with vigorous stirring for 24 h. After 24 h, the O_2 was vented from the vessel. The product was purified as described above, and afforded a 70% yield of cyclohexenone and 20% phenol.

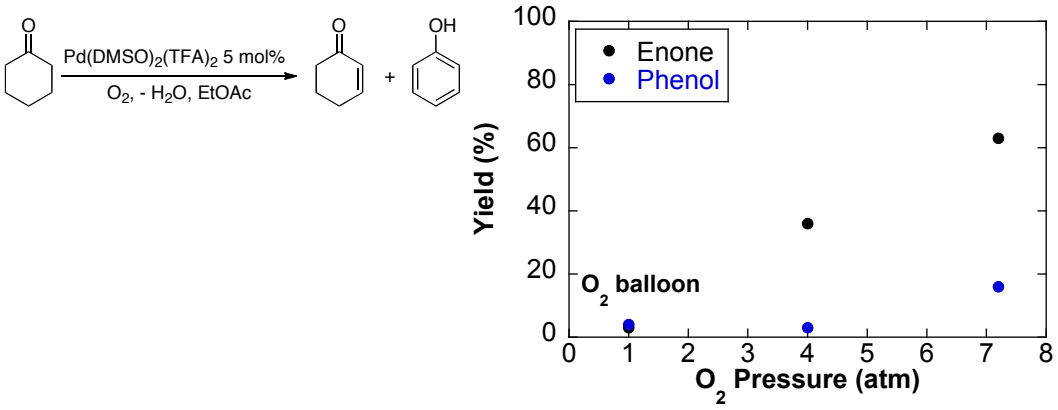


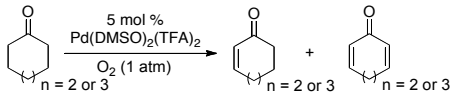
Figure S1. O_2 Pressure Dependence. Conditions: [cyclohexanone] = 0.8 M (0.8 mmol), 5% $Pd(TFA)_2$ (0.04 mmol), 10% DMSO (0.08 mmol), Ethyl acetate (1 mL).

4. Procedure for aerobic dehydrogenation of cyclohexanone 1 in a flow reactor.
The flow reactor used in these studies has been described previously.[5] The total volume of the tube reactor is 66 mL. An oil bath set to 100 °C was used to regulate the reaction-zone temperature of the flow reactor. The flow reactor was first rinsed with toluene and dried by passing nitrogen gas through the tubing at 100 °C. The reactor was pressurized with a 500 psig of dilute O_2 gas (8% O_2 in N_2). Four sequential metering valves connected to the O_2 outlet were adjusted to obtain the desired gas flow rate. The total gas flow out of the vapor-outlet valve was maintained around 1.6 sccm. The reactor was then purged with the dilute oxygen gas for 10-15 minutes (8% O_2 in N_2; 500 psig). Two syringe pumps were used for delivery of the reagents and catalyst. The first syringe pump was charged with $Pd(DMSO)_2(TFA)_2$ stock solution in acetic acid (0.02 M, 180 ml), and the second syringe pump was charged with 4-*tert*-butylcyclohexanone stock solution in acetic acid (0.4 M, 180 ml). The feed rates of both pumps were adjusted to 0.014 ml/min (residence time = 12 h). Both syringe pumps were started to initiate the flow of liquid solution with continuous delivery of dilute oxygen gas through the reactor. After starting the pumps (t = 0), the time when liquid started to accumulate in the liquid product tank was recorded as the actual liquid residence time. The product was analyzed by GC and isolated as described above (88% GC yield; 78% isolated yield). The discrepancy between GC and isolated yield was due to loss of material when the acetic acid solvent was removed under vacuum.

5. Acquisition of time course data and fitting of data in Figure 1.
The reactions were performed using orbital shakers under standard conditions, as described above. The catalyst was heated to 80 °C and the temperature was allowed to equilibrate for 5 min. A stock solution of internal standard (1,4-dimethoxybenzene) was injected via syringe. Injection of substrates dissolved in solvent established the t = 0 point. After various time intervals, aliquots were withdrawn from the reaction mixture via pipet, diluted with CH_2Cl_2 and analyzed by GC. Time course data were imported into the kinetic simulation software COPASI,[6] and a simple sequential first-order kinetic model, A → B → C, was used to fit the data in COPASI using Levenberg-Marquardt numerical methods.

6. Oxidation of cycloheptanone and cyclooctanone

Table S2. Oxidation of cycloheptanone and cyclooctanone.[a]

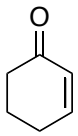


entry	substrate	solvent	Enone (%)[b]	dienone (%)[b]
1	cycloheptanone	AcOH	5	8
2	cycloheptanone	Toluene	1	26
3	cyclooctanone	AcOH	2	24
4	cyclooctanone	Toluene	9	9

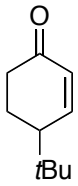
[a] Reaction conditions: see procedure above. [b] NMR yield. Products were confirmed by GC-MS spectroscopy.

7. ^{1}H NMR Spectroscopic Data.

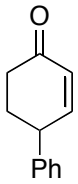
All compounds in Table 2 and eqs 1 and 2 have been reported previously. In all cases, the product identities were established by comparison of the ^{1}H NMR spectra with previously reported data. In one case (Table 2, entry 8), full characterization was not previously reported; these data are included below.



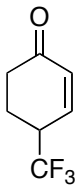
(Table 2, Entry 1): Prepared as described above. Purified by silica gel column chromatography using a 0-20% EtOAc in hexane gradient elution to give 72% yield of the product as a colorless oil. ^{1}H NMR data match previously reported data.[7] ^{1}H NMR ($CDCl_3$): δ 7.000 (dt, 1H, J = 10.1, 4.1 Hz), 6.03 (d, 1H, J = 10.1, 2.0 Hz), 2.44 (t, 2H, J = 6.4 Hz), 2.40-2.30 (m, 2H), 2.09-1.97 (m, 2H).



(Table 2, Entry 2): Prepared as described above. Purified by silica gel column chromatography that has been saturated with 1% Et_3N using a 0-10% EtOAc in hexane gradient elution to give 91% yield of the product as a colorless liquid. ^{1}H NMR data match previously reported data.[8] ^{1}H NMR ($CDCl_3$): 7.02 (dd, 1H, J = 10.4, 2.0 Hz), 6.04 (dd, 1H, J = 10.4, 2.8 Hz), 2.53 (dt, 1H, J = 16.6, 3.6 Hz), 2.34 (ddd, 1H, J = 16.6, 14.2, 4.8 Hz), 2.45-2.16 (m, 1H), 2.16-2.03 (m, 1H), 1.82-1.66 (m, 1H), 0.98 (s, 9H).

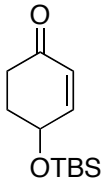


(Table 2, Entry 3): Prepared as described above. Purified by silica gel column chromatography that has been saturated with 1% Et_3N using a 0-10% EtOAc in hexane gradient elution to give 83% yield of the product as a white solid. ^{1}H NMR data match previously reported data.[9] ^{1}H NMR ($CDCl_3$): δ 7.40-7.32 (m, 2H), 7.32-7.27 (m, 1H), 7.25-7.19 (m, 2H), 7.00 (ddd, 1H, J = 10.2, 2.9, 1.4 Hz), 6.17 (ddd, 1H, J = 10.2, 2.5, 0.6 Hz), 3.78-3.68 (m, 1H), 2.62-2.45 (m, 2H), 2.45-2.30 (m, 1H), 2.13-1.98 (m, 1H).

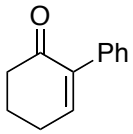


(Table 2, Entry 4): Prepared as described above. Purified by silica gel column

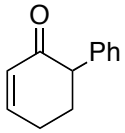
chromatography using a 0-20% EtOAc in hexane gradient elution to give 81% yield of the product as a colorless oil. ^{1}H NMR data match previously reported data.[10] ^{1}H NMR ($CDCl_3$): δ 6.88 (ddd, 1H, J = 10.3, 2.5, 1.5), 6.22 (dd, 1H, J = 10.3, 2.6 Hz), 3.30-3.11 (m, 1H), 2.65 (dt, 1H, J = 17.4, 4.6 Hz), 2.51-2.40 (m, 1H), 2.36-2.28 (m, 1H), 2.21-2.06 (m, 1H).



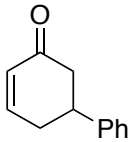
(Table 2, Entry 5): Prepared as described above. Purified by silica gel column chromatography using a 0-15% EtOAc in hexane gradient elution to give 76% yield of the product as a slightly yellow oil. ^{1}H NMR data match previously reported data.[11] ^{1}H NMR ($CDCl_3$): δ 6.84 (dt, 1H, J = 10.3, 2.1 Hz), 5.93 (ddd, 1H, J = 10.3, 1.8, 1.0 Hz), 4.56-4.49 (m, 1H), 2.58 (dt, 1H, J = 17.1, 5.1 Hz), 2.35 (ddd, 1H, J = 17.1, 12.7, 4.4 Hz), 2.21 (dqd, J = 14.4, 4.4, 1.8 Hz), 2.00 (tdd, J = 12.7, 9.0, 4.4 Hz), 0.92 (9H, s), 0.13 (3H, s), 0.12 (3H, s).



(Table 2, Entry 6): Prepared as described above. Purified by silica gel column chromatography using a 0-20% EtOAc in hexane gradient elution to give 63% yield of the product as a colorless oil. ^{1}H NMR data match previously reported data.[12] ^{1}H NMR ($CDCl_3$): δ 7.39-7.24 (m, 5H), 7.03 (t, 1H, J = 4.4 Hz), 2.64-2.48 (m, 4H), 2.17-2.05 (m, 2H).

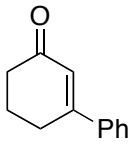


(Table 2, Entry 6): Prepared as described above. Purified by silica gel column chromatography using a 0-20% EtOAc in hexane gradient elution to give 21% yield of the product as a colorless oil. ^{1}H NMR data match previously reported data.[13] ^{1}H NMR ($CDCl_3$): δ 7.38-7.22 (m, 3H), 7.20-7.12 (m, 2H), 7.04 (dt, 1H, J = 10.1, 4.2 Hz), 6.17 (dt, 1H, J = 10.1, 1.8 Hz), 3.61 (t, 1H, J = 8.1 Hz), 2.53-2.43 (m, 2H), 2.34-2.23 (m, 2H).

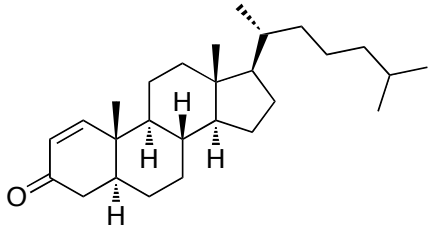


(Table 2, Entry 7): Prepared as described above. Purified by silica gel column chromatography using a 0-20% EtOAc in hexane gradient elution to give 63% yield of the product as a colorless oil. ^{1}H NMR data match previously reported data.[14] ^{1}H NMR

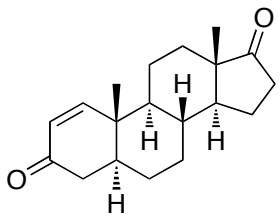
($CDCl_3$): δ 7.41-7.31 (m, 2H), 7.31-7.15 (m, 3H), 7.05 (ddd, 1H, J = 9.9, 5.5, 2.4 Hz), 6.13 (ddt, 1H, J = 9.9, 2.4, 0.6 Hz), 3.36 (h, 1H, J = 5.3 Hz), 2.73-2.65 (m, 2H), 2.65-2.60 (m, 1H), 2.56 (dt, 1H, J = 10.7, 2.4 Hz)



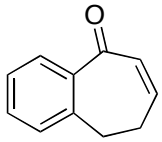
(Table 2, Entry 7): Prepared as described above. Purified by silica gel column chromatography using a 0-20% EtOAc in hexane gradient elution to give 23% yield of the product as a colorless oil. ^{1}H NMR data match previously reported data.[15] ^{1}H NMR ($CDCl_3$): δ 7.57-7.52 (m, 2H), 7.45-7.38 (m, 3H), 6.43 (t, 1H, J = 1.4 Hz), 2.78 (td, 2H, J = 5.8, 1.4 Hz), 2.53-2.44 (m, 2H), 2.22-2.11 (m, 2H).



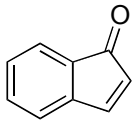
(Table 2, Entry 8): Prepared as described above. Purified by silica gel column chromatography using a 0-15% EtOAc in hexane gradient elution to give 94% yield of the product as a white solid. This compound has been reported previously;[16] however, full characterization data have not been reported. ^{1}H NMR ($CDCl_3$): δ 7.14 (d, 1H, J = 10.0 Hz), 5.85 (d, 1H, J = 10.0 Hz), 2.37 (dd, 1H, J = 17.4, 13.8 Hz), 2.21 (dd, 1H, J = 17.4, 4.2 Hz), 2.05 (dt, 1H, J = 12.6, 3.4 Hz), 1.99-1.77 (m, 2H), 1.77-1.65 (m, 2H), 1.63-0.95 (m, 20H), 1.00 (s, 3H), 0.91 (d, 3H, J = 6.9 Hz), 0.87 (d, 3H, J = 6.5 Hz), 0.86 (d, 3H, J = 6.5 Hz), 0.69 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 200.5, 158.9, 127.6, 56.6, 56.4, 50.2, 44.5, 42.9, 41.2, 40.0, 39.7, 39.2, 36.3, 36.0, 35.9, 31.5, 28.4, 28.2, 27.9, 24.3, 24.0, 23.0, 22.8, 21.5, 18.9, 13.2, 12.4. HRMS (ESI) [M + Na^+]/z calcd. 384.3387, found 384.3376. M.P. = 99–100 °C.



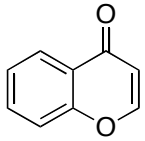
(Table 2, Entry 9): Prepared as described above. Purified by silica gel column chromatography using a 20-40% EtOAc in hexane gradient elution to give 93% yield of the product as a white solid. ^{1}H NMR data match previously reported data.[17] ^{1}H NMR ($CDCl_3$): δ 7.14 (d, 1H, J = 10.5 Hz), 5.87 (d, 1H, J = 10.5 Hz), 2.53-2.32 (m, 2H), 2.24 (ddd, 1H, J = 17.7, 4.3, 0.8 Hz), 2.17-2.06 (m, 1H), 2.02-1.81 (m, 5H), 1.67 (qd, 1H, J = 10.6, 4.2 Hz), 1.60-1.27 (m, 6H), 1.15-0.99 (m, 2H), 1.05 (s, 3H), 0.91 (s, 3H).



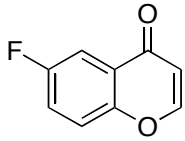
(Table 2, Entry 10): Prepared as described above. 50% DMSO was used as ligand and toluene was the solvent. The reaction was heated to 60 °C for 24 h, then 80 °C for another 24 h. Purified by silica gel column chromatography using a 0-10% EtOAc in hexane gradient elution to give 81% yield of the product as a slightly yellow oil. ^{1}H NMR data match previously reported data.[18] ^{1}H NMR ($CDCl_3$): δ 7.75 (dd, 1H, J = 7.5, 1.4 Hz), 7.42 (td, 1H, J = 7.5, 1.4 Hz), 7.31 (td, 1H, J = 8.8, 1.4 Hz), 7.19 (d, 1H, J = 7.5 Hz), 6.75 (dt, 1H, J = 12.2, 4.9 Hz), 6.28 (dt, 1H, J = 12.2, 2.0 Hz), 3.11-2.98 (m, 2H), 2.65-2.53 (m, 2H).



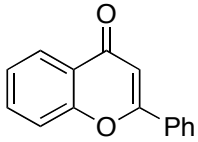
(Table 2, Entry 11): Prepared as described above. 50% DMSO was used as ligand and toluene was the solvent. Purified by silica gel column chromatography using a 0-20% EtOAc in hexane gradient elution to give 54% yield of the product as a yellow oil. ^{1}H NMR data match previously reported data.[19] ^{1}H NMR ($CDCl_3$): δ 7.57 (d, 1H, J = 6.2 Hz), 7.43 (d, 1H, J = 7.0 Hz), 7.35 (t, 1H, J = 7.0 Hz), 7.23 (t, 1H, J = 7.0 Hz), 7.06 (d, 1H, J = 7.0 Hz), 5.89 (d, 1H, J = 6.2 Hz).



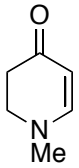
(Table 2, Entry 12): Prepared as described above. Purified by silica gel column chromatography using a 20-40% EtOAc in hexane gradient elution to give 80% yield of the product as a white solid. ^{1}H NMR data match previously reported data.[20] ^{1}H NMR ($CDCl_3$): δ 8.22 (dd, 1H, J = 8.0, 1.4 Hz), 7.87 (d, 1H, J = 6.1 Hz), 7.68 (ddd, 1H, J = 8.6, 8.0, 1.4 Hz), 7.47 (d, 1H, J = 8.6 Hz), 7.42 (t, 1H, J = 8.0 Hz), 6.36 (d, 1H, J = 6.1 Hz).



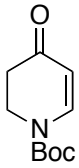
(Table 2, Entry 13): Prepared as described above. Purified by silica gel column chromatography using a 30% EtOAc in hexane gradient elution to give 78% yield of the product as a white solid. ^{1}H NMR data match previously reported data.[21] ^{1}H NMR ($CDCl_3$): δ 7.87 (d, 1H, J = 6.0 Hz), 7.85 (dd, 1H, J = 8.2, 3.2 Hz), 7.48 (dd, 1H, J = 9.0, 4.4 Hz), 7.40 (ddd, 1H, J = 9.0, 7.5, 3.2 Hz), 6.34 (d, 1H, J = 6.0 Hz).



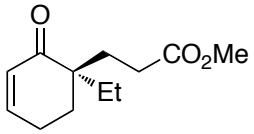
(Table 2, Entry 14): Prepared as described above. The reaction mixture was washed with water and extracted with ethyl acetate. The mixture was purified by silica gel column chromatography using a gradient 0%-30% EtOAc in hexane elution to give 88% yield of the product as a white solid. ^{1}H NMR data match previously reported data.[22] ^{1}H NMR ($CDCl_3$): δ 8.25 (dd, 1H, J = 8.0, 1.6 Hz), 7.99-7.89 (m, 2H), 7.72 (ddd, 1H, J = 8.6, 7.1, 1.6 Hz), 7.59 (dd, 1H, J = 8.6, 1.0 Hz), 7.57-7.49 (m, 3H), 7.44 (ddd, 1H, J = 8.0, 7.1, 1.0), 6.88 (s, 1H).



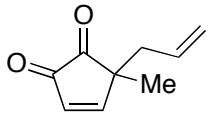
(Table 2, Entry 15): Prepared as described above. Purified by filtration through a pipette of Al_2O_3, eluted with pure ethyl acetate to give 74% yield of the product as a colorless oil. ^{1}H NMR data match previously reported data.[23] ^{1}H NMR ($CDCl_3$): δ 6.98 (d, 1H, J = 7.4 Hz), 4.92 (d, 1H, J = 7.4 Hz), 3.44 (t, 2H, J = 7.7 Hz), 2.48 (t, 2H, J = 7.7 Hz).



(Table 2, Entry 16): $Pd(TFA)_2$ in DMSO was used for this substrate. No ligand was added. Purified by silica gel column chromatography using a 30-40% EtOAc in hexane gradient elution to give 72% yield of the product as a white solid. ^{1}H NMR data match previously reported data.[24] ^{1}H NMR ($CDCl_3$): δ 7.82 (br, 1H), 5.31 (d, 1H, J = 8.3 Hz), 3.98 (t, 2H, J = 7.4 Hz), 2.55 (t, 2H, J = 7.4 Hz), 1.54 (s, 9H).



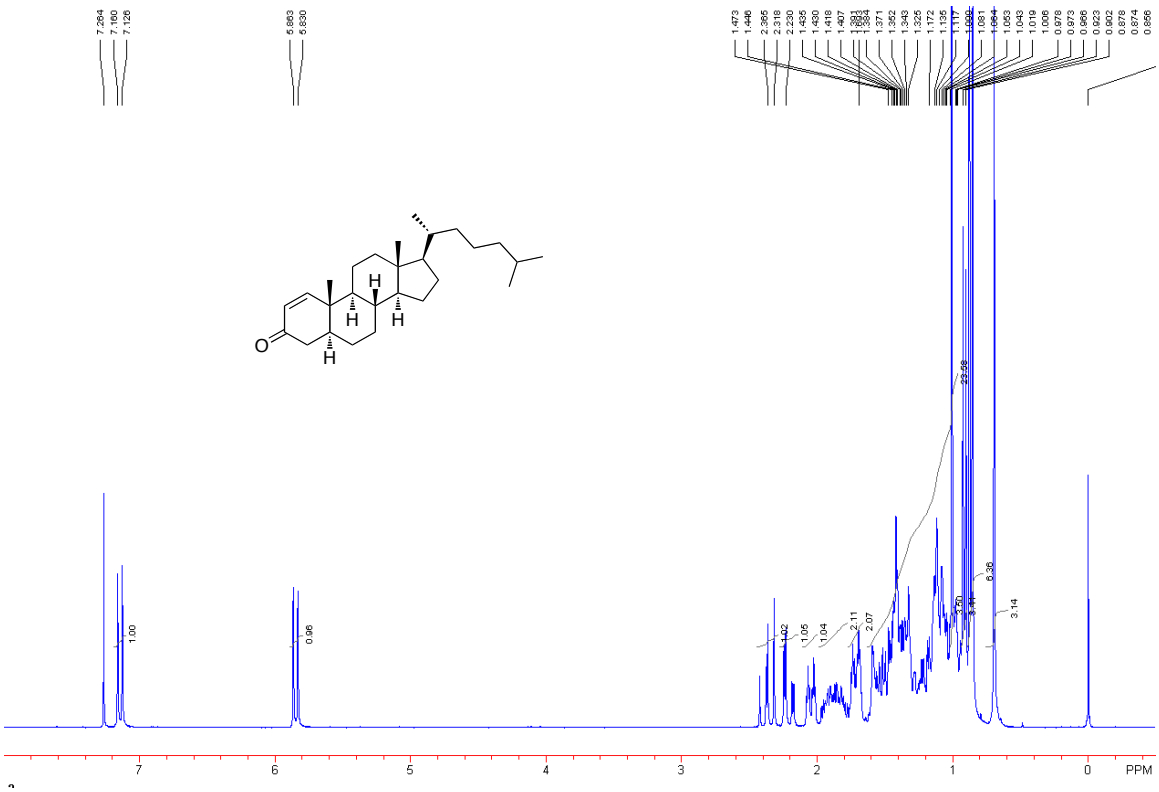
(eq 1): Prepared as described above. Purified by silica gel column chromatography using a 10-20% EtOAc in hexane gradient elution to give 85% yield of the product as a pale yellow oil. ^{1}H NMR data match previously reported data.[25] ^{1}H NMR ($CDCl_3$): δ 6.85 (dt, 1H, J = 10.0, 4.0 Hz), 5.90 (dt, 1H, J = 10.0, 2.0 Hz), 3.66 (s, 3H), 2.45-2.35 (m, 2H), 2.35-2.16 (m, 2H), 1.98-1.77 (m, 4H), 1.70-1.46 (m, 2H), 0.84 (t, 3H, J = 7.7 Hz).

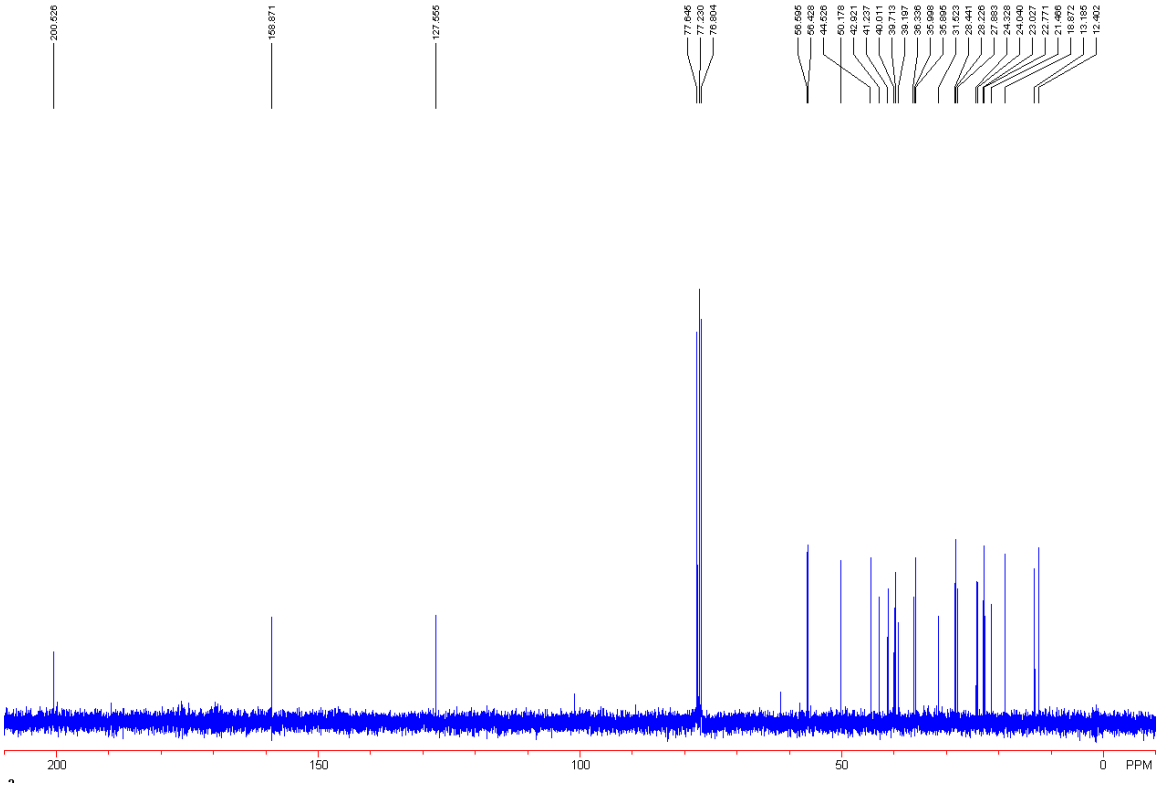


(eq 2): Prepared as described above. Good gas-liquid mixing is very crucial to this

substrate to prevent catalyst decomposition. After catalyst and solvent were mixed and purged with O_2, the substrate was added via syringe while agitating. Reaction conditions: [substrate] = 0.025 M, [$Pd(TFA)_2$] = 0.0025 M (10%), [DMSO] = 0.0075 M (30%), 1 atm O_2. Purified by silica gel column chromatography using a 0-20% EtOAc in hexane gradient elution to give 90% yield of the product as a yellow oil. ^{1}H NMR data match previously reported data.[26] ^{1}H NMR ($CDCl_3$): δ 7.83 (d, 1H, J = 7.3 Hz), 6.88 (d, 1H, J = 7.3 Hz), 5.59 (dddd, 1H, J = 17.5, 10.4, 7.9, 7.3 Hz), 5.16-5.01 (m, 2H), 2.47 (dd, 1H, J = 13.8, 7.9 Hz), 2.36 (ddt, 1H, J = 13.8, 7.1, 1.0 Hz), 1.28 (s, 3H).

7. ^{1}H and ^{13}C NMR Spectra for Enone from Table 2, Entry 8.





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