Development of Oxidative Formylation and Ketonylation Reactions

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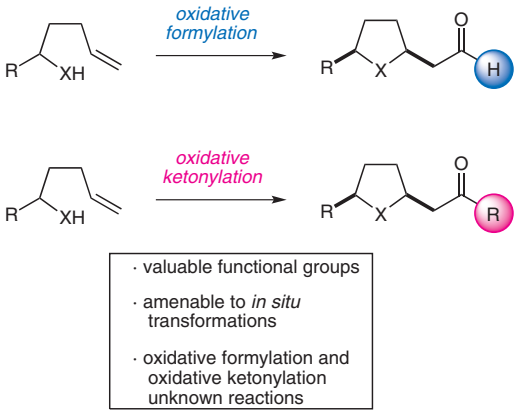
Abstract: The first oxidative formylation and oxidative ketonylation of alkenylamines and alkenyl alcohols is demonstrated. A range of substrates that participate in this process are provided. Oxidative formylation was found to proceed optimally with the use of triphenylsilane as the hydride source. Oxidative ketonylation was feasible with a number of organometallic partners, especially dialkylzinc or organostannanes. An interesting finding regarding the fate of various acylpalladium intermediates is discussed.

Key words: oxidative carbonylation, palladium, multicomponent reaction, formylation, ketonylation

One-pot, multi-transformation processes offer significant advantages in terms of synthetic efficiency, yield, time, and waste reduction. Our research group is interested in exploring such strategies to advance the capacity to rapidly generate valuable molecular architectures.[1] A major strategy in this regard is to invent new methodologies that produce reactive functionalities amenable to facile in situ derivatization, which may then serve as linchpin transformations for highly productive multicatalytic[2] or telescopic[3] processes.

As a platform for the development of linchpin methods, we have been attracted to the palladium(II)-catalyzed intramolecular oxidative carbonylation chemistry developed by Semmelhack[4] and Hegedus.[5] Intramolecular oxidative carbonylation reactions produce substantial increases in molecular complexity and accordingly have found impressive application in natural product synthesis.[6] We believe the utility of these reactions would be further increased if alternative, more reactive carbonyl functionalities could be generated from this process in addition to the traditional ester or amide linkages.[7] In this context, we recently reported an oxidative aminochlorocarbonylation reaction that generates acid chlorides, which we employed in tandem with Friedel–Crafts acylation to produce complex α-pyrrolidinyl aryl ketones.[1a]

As a result of the broad synthetic versatility of aldehydes and ketones, we viewed the development of intramolecular oxidative carbonylation reactions that would generate these functionalities as an especially attractive goal (Scheme 1). To the best of our knowledge, no examples of *oxidative* carbonylation of alkenyl alcohols or alkenylamines to generate aldehydes (oxidative formylation) or ketones (oxidative ketonylation) have been disclosed. This report describes our invention of such processes.



Scheme 1 Oxidative formylation and ketonylation reactions

In contemplating the development of palladium(II)-mediated oxidative formylation and ketonylation reactions, we noted that these proposed transformations should be mechanistically identical to traditional oxidative carbonylations except in the fate of the acylpalladium species (Scheme 2). Thus, instead of termination of acylpalladium intermediate **2** with an equivalent of alcohol to produce an ester product **3** as in the traditional Semmelhack-type carbonylation, generation of an aldehyde or ketone product **4** would require transmetalation with a suitable organometallic reagent followed by reductive elimination.

Of course, cross-coupling reactions of acylpalladium species are well known in Pd(0)–Pd(II) catalytic cycles. However, the feasibility of achieving this type of reaction under oxidative carbonylation conditions was not clear, especially given that during the generation of acylpalladium intermediates **2** an equivalent of strong acid is produced. Given the substantial potential benefit of achieving reactions of the type engendered by **1** → **4**, we decided to investigate whether this type of reaction was feasible.

To begin, we decided to examine quenching of an acylpalladium intermediate with a hydride source to generate aldehyde products. In these reactions, the substrate **5** and one equivalent of $PdCl_2(PhCN)_2$ were stirred in α,α,α-trifluorotoluene under an atmosphere of carbon monoxide for one hour, after which time a hydride source was added (Table 1). Using this protocol, tributyltin hydride (1 equiv) resulted in the production of aldehyde **6** in 21% yield, but also induced rapid palladium black formation

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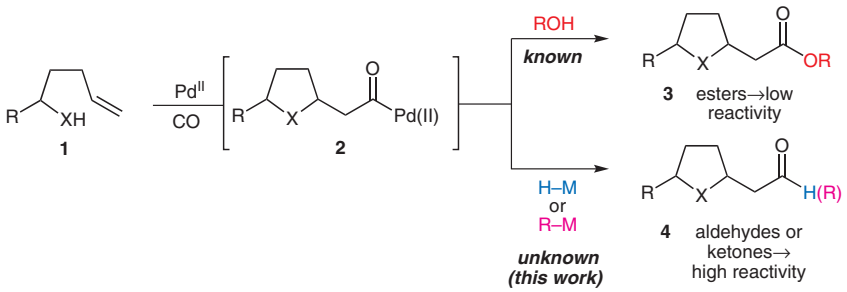


Scheme 2 Design of an oxidative formylation reaction

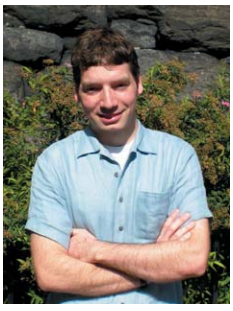
and significant substrate decomposition (entry 1). Alternatively, triethylsilane (1 equiv) resulted in a significant increase of yield of **6** to 49%, albeit still with accompanying palladium black formation and a relatively complex product mixture (entry 2).

On the other hand, triphenylsilane provided a comparable yield (43%) of **6** to triethylsilane but suppressed palladium black formation and proved to be more reproducible (entry 3). The use of additional equivalents of the silane increased the yield significantly (entries 4 and 5), presumably by helping to outcompete acid chloride formation, which tended to be the major side product in this process.

Further improvements in yield were observed with the addition of molecular sieves (entry 6), lowering of the temperature to –15 °C (entry 7), and dilution of the reaction medium (entry 8). Finally, optimal conditions were achieved through the use of a slight excess of palladium reagent (1.05 equiv) and by presaturating the solvent with carbon monoxide (entry 9). Under these conditions, the oxidative formylation product **6** was produced in 78% yield (as its ethylene acetal **6′**) as a >20:1 mixture of *syn*/*anti* isomers. To the best of our knowledge, this represents the first report of oxidative formylation of an alkenyl amine derivative.

Biographical Sketches

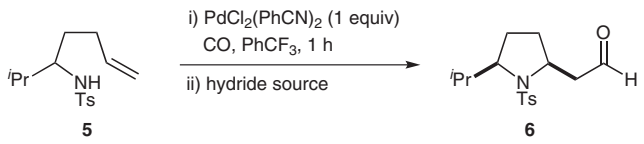
Lisa Ambrosini was born in New Brunswick, New Jersey in 1983. She received her B.S. degree in biochemistry at Providence College in 2006. She also conducted summer research at The Memorial Sloan-Kettering Cancer Center with Derek Tan. In 2006 she began her graduate studies under the mentorship of Tristan Lambert. Her graduate studies have been focused on the development of new methods to enable multicatalytic reactions.



Tim Cernak was born in Montreal, Québec in 1980. He received a B.Sc. in 2002 from Okanagan University College and a Ph.D. in 2007 from McGill University under the supervision of Jim Gleason. From 2007 to 2009, Tim worked with Tristan Lambert at Columbia University as a FQRNT Postdoctoral Fellow developing carbonylation reactions as a platform for multicatalysis. In 2009, he joined the Medicinal Chemistry team at Merck in Rahway, New Jersey.

Tristan Lambert was born in Madison, Wisconsin in 1976 and received his B.S. from the University of Wisconsin at Platteville in 1998. That year he began graduate studies with David MacMillan at the University of California at Berkeley, and moved with MacMillan to Caltech in 2000 where he received his Ph.D. in 2004. From 2004–2006 he was an NIH postdoctoral fellow with Samuel Danishefsky at the Memorial Sloan-Kettering Cancer Center. Since 2006 he has been an assistant professor at Columbia University. His research group is interested in the development of new multicatalytic processes and the design of reaction methods using aromatic ions.

Table 1 Optimization Screen for Oxidative Formylation



5 6

Entry	Hydride source (equiv)	Additive	Temp (°C)	Molarity	Yield[a] (%)
1	Bu_3SnH (1)	–	0	0.12	21
2	Et_3SiH (1)	–	0	0.12	49
3	Ph_3SiH (1)	–	0	0.12	43
4	Ph_3SiH (2)	–	0	0.12	55
5	Ph_3SiH (3)	–	0	0.12	59
6	Ph_3SiH (3)	4 Å MS	0	0.12	65
7	Ph_3SiH (3)	4 Å MS	–15	0.12	70
8	Ph_3SiH (3)	4 Å MS	–15	0.05	71
9[b]	Ph_3SiH (3)	4 Å MS	–15	0.05	78[c]

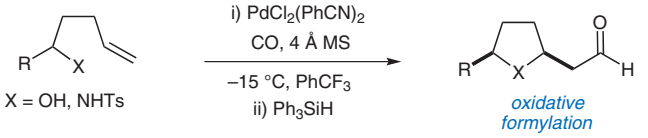
[a] Yields determined by ^1H NMR analysis using Bn_2O as an internal standard. The dr was >20:1 *syn*/*anti* in all cases.
[b] $PdCl_2(PhCN)_2$ (1.05 equiv) was used and the solvent was saturated with CO before reaction.
[c] The isolated yield for this reaction for **6** as its ethylene acetal **6′** was also 78%.

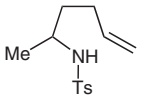
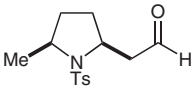
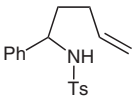
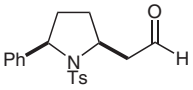
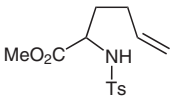
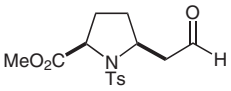
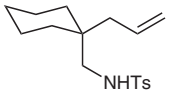
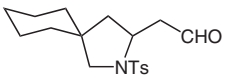
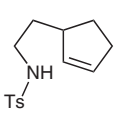
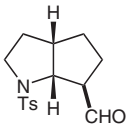
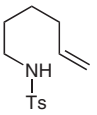
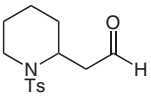
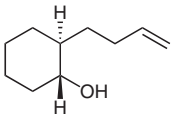
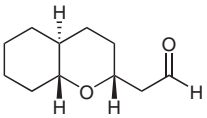
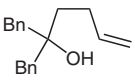
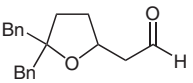
An examination of the substrate scope of this reaction is shown in Table 2. Both α-alkyl and α-aryl amino substrates were found to participate efficiently in this process (entries 1 and 2). In addition, use of an α-amino ester substrate led to the generation of a proline ester derivative (entry 3). Substitution in the β-position was also well tolerated (entry 4). Notably, oxidative formylation of an internal olefin proved possible, as with the production of the bicyclic aldehyde shown in entry 5. We found cyclization to form piperidine adducts to be more difficult, although *N*-tosylhex-5-en-1-amine was employed with reasonable success (entry 6).

Alcohol substrates present an additional challenge due to the potential for carbonylative dimerization (acylation of the starting material by the acylpalladium intermediate). Nevertheless, we found that certain substrates were viable in this process. Thus the cyclohexenol substrate shown in entry 7 led to the formation of an octahydrochromenyl aldehyde in good yield. In addition, a tertiary alcohol substrate reacted efficiently to produce the tetrahydrofuranyl aldehyde shown in entry 8.

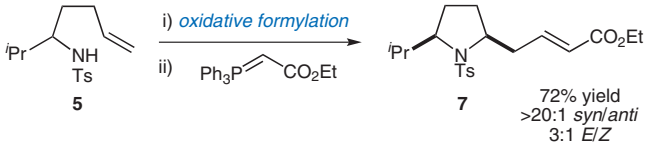
As a demonstration of the utility of this oxidative formylation reaction for one-pot, multi-transformation synthesis, we conducted the following experiment. Thus alkenylamine **5** was subjected to oxidative formylation followed by addition to the reaction mixture of ethyl (triphenylphosphoranylidene)carboxylate, which produced the α,β-unsaturated ester **7** in 72% yield as a single observable diastereomer (Equation 1).

Table 2 Substrate Scope for Intramolecular Oxidative Formylation[a]



Entry	Substrate	Product	Yield[b] (%)	dr[c]
1			77	>20:1
2			81	>20:1
3			66	18:1
4			74	
5			66	>20:1
6			63	>20:1
7			70	
8			72	–

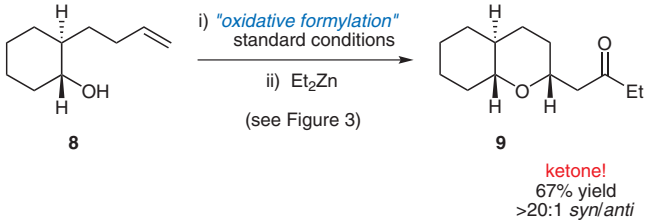
[a] Reactions were performed using the optimal conditions described in the text.
[b] Determined on the 1,3-dioxolane derivatives as isolated and purified products.
[c] Determined by ^1H NMR analysis on crude reaction mixtures.



5 7

Equation 1

We were also interested in employing aldehyde products of oxidative formylation as substrates for in situ nucleophilic addition reactions. However, when alcohol **8** was subjected to our standard oxidative formylation conditions and then treated with diethylzinc, we were surprised to observe ketone **9** (67% yield, >20:1 *syn*/*anti*) and none of the expected secondary alcohol (Equation 2).



Equation 2

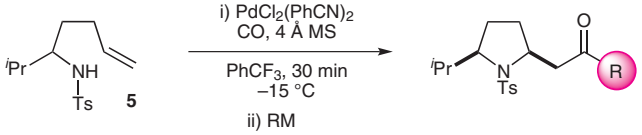
In an effort to understand how ketone **9** arose from this sequence, we independently prepared aldehyde **13** and subjected it to diethylzinc under a range of conditions, attempting to mimic those present in the reaction shown in Equation 2 (Scheme 3). Under no circumstances, however, was any nucleophilic addition product observed, suggesting that the reaction of diethylzinc to form **9** must have occurred prior to reductive elimination of the putative acylpalladium hydride intermediate **12**.

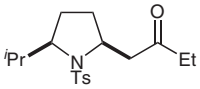
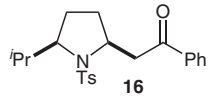
This finding was interesting, given that when methanol was added to the same intermediate, aldehyde **13** was generated without production of methyl ester **11**, which *is* produced if no hydride source is added (Semmelhack carbonylation). Thus we believe that acylpalladium hydride intermediate **12** is formed but does not undergo reductive elimination until workup, and that addition of diethylzinc to intermediate **12** results in production of an acylpalladium alkyl intermediate **14** that undergoes reductive elimination in complete preference to the corresponding hydride reductive elimination.

Given our goal of generating ketone products via oxidative carbonylation, we decided to investigate the same general reaction without the addition of silane (Table 3). Remarkably, when the acylpalladium intermediate produced from alkenylamine **5** was treated with three equivalents of diethylzinc, the ethyl ketone product **15** was produced in 95% yield as a single observable diastereomer (entry 1). Furthermore, we found that the equivalents of the zinc reagent could be reduced to as low as 0.5 without substantial detriment to product yield (entries 2–5), which is remarkable given that an equivalent of HCl is produced during acylpalladium formation. Other organometallic partners also proved viable for the production of the phenyl ketone product **16**, including phenylzinc chloride (entry 6) and tributyl(phenyl)stannane (entry 7). Notably, use of 1.5 equivalents of stannane resulted in the same yield as 3 equivalents (entries 7 and 8), and reasonable efficiency was still observed using only 1.1 equivalents (entry 9). A Grignard reagent provided the expected product, albeit with diminished yield (entry 10), while phenyllithium and phenylboronic acid proved to be poor participants in this process (entries 11 and 12).

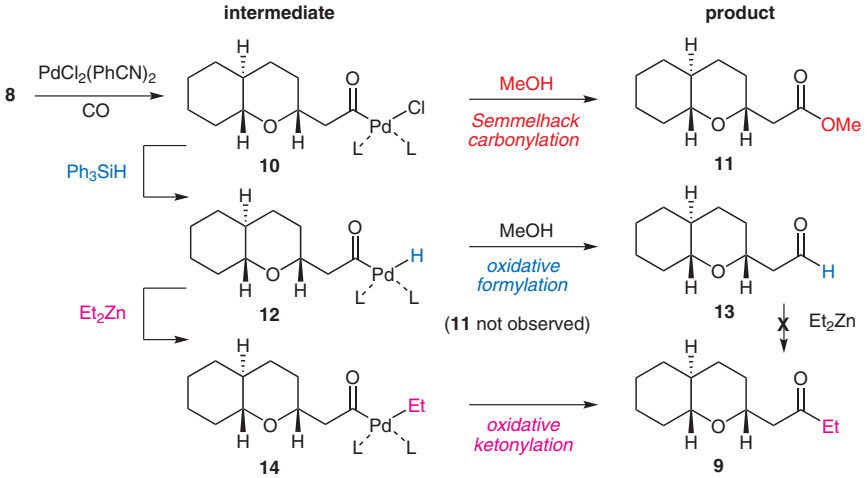
Next we conducted experiments to probe the substrate scope for this oxidative ketonylation reaction (Table 4). Thus both ethyl and methyl ketones could be accessed in

Table 3 Oxidative Ketonylation Using Various Organometallic Reagents[a]



Entry	RM	Equiv	Product	Yield[b] (%)
1	Et_2Zn	3.0		95
2	Et_2Zn	1.5		94
3	Et_2Zn	1.0		93
4	Et_2Zn	0.6		90
5	Et_2Zn	0.5		88
6	PhZnCl	1.1		85
7	$PhSnBu_3$	3.0		92
8	$PhSnBu_3$	1.5		92
9	$PhSnBu_3$	1.1		79
10	PhMgBr	2.2		64
11	PhLi	2.2		<15
12	$PhB(OH)_2$	2.0		35

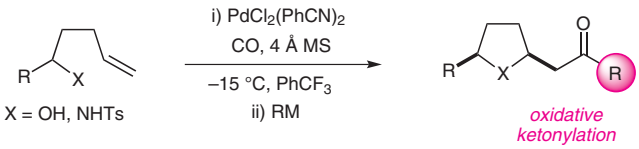
[a] Reactions conditions: substrate, $PdCl_2(PhCN)_2$ (1.05 equiv), 4 Å MS, $PhCF_3$ (0.075 M), CO, stirring, –15 °C, 30 min. Indicated organometallic reagent was then added and stirred at –15 °C for 20 min.
[b] Isolated yield.

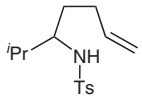
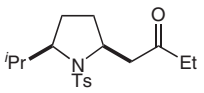
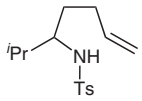
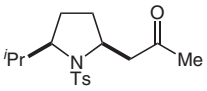
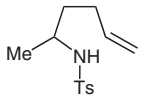
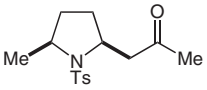
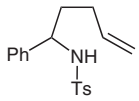
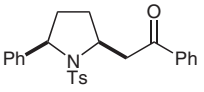
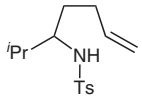
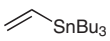
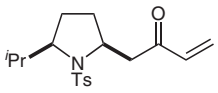
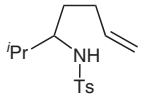
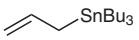
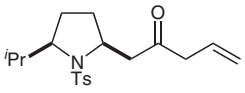
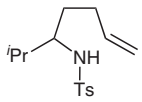
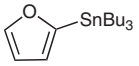
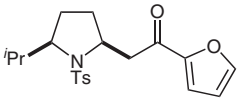
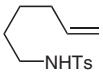
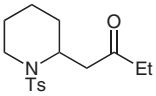
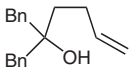
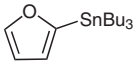
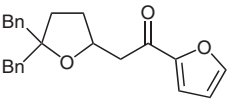
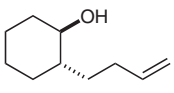
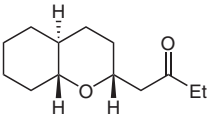


Scheme 3 Studies to determine fate of acylpalladium intermediates

high yield using commercially available dialkylzinc reagents (entries 1–3). A benzylic amine substrate was also a productive reactant, leading to a phenyl ketone product with the use of commercially available phenylzinc chloride (entry 4). Notably, use of tributyl(vinyl)stannane gave rise to an α,β-unsaturated ketone (entry 5), a synthetically versatile structural motif. Alternatively, allyltributylstannane furnished the corresponding β,γ-unsaturated ketone, albeit with somewhat diminished yield (entry 6). On the other hand, tributyl(furan-2-yl)stannane led to the generation of furanyl ketone products in high yield (entries 7 and 9). It should be noted that furans and unactivated benzenes (entries 4, 7, and 9) were not accessible using our previously reported multicatalytic chlorocarbonylation/Friedel–Crafts methodology, making the present technology a useful complement to that procedure.[1a] As observed before, cyclization to piperidine adducts was possible, though less efficient (entry 8). On the other hand, alcohol substrates could be employed with high ef-

Table 4 Substrate Scope Studies for Oxidative Ketonylation[a]

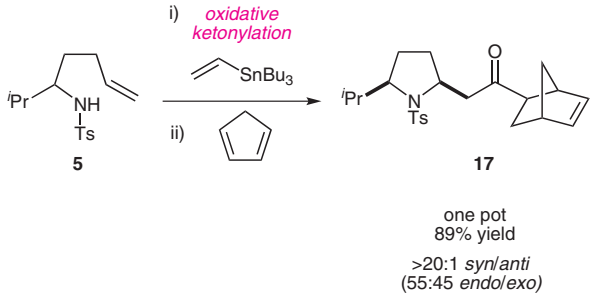


Entry	Substrate	RM (equiv)	Product	Yield[b] (%)	dr[c]
1		Et_2Zn (0.6)		90	>20:1
2		Me_2Zn (0.6)		82	>20:1
3		Me_2Zn (0.6)		76	>20:1
4		PhZnCl (1.1)		79	16:1
5		 (1.3)		94	>20:1
6		 (1.5)		58	18:1
7		 (1.3)		84	>20:1
8		Et_2Zn (0.6)		63 (82[d])	–
9		 (1.3)		93	–
10		Et_2Zn (0.6)		72	>20:1

[a] Reaction conditions: substrate, $PdCl_2(PhCN)_2$ (1.05 equiv), 4 Å MS, $PhCF_3$ (0.075 M), CO, stirring, –15 °C, 30 min. Indicated organometallic reagent was then added and stirred at –15 °C for 20 min.
[b] Isolated yield.
[c] Diastereomeric ratios were determined by ^1H NMR analysis on crude reaction mixtures.
[d] Based on recovered starting material.

ficiency, as with the tertiary and secondary alcohols shown in entries 9 and 10.

To demonstrate the ability of this oxidative ketonylation procedure to facilitate one-pot, multi-transformation processes, we subjected the alkenylamine substrate **5** to our standard conditions, using tributyl(vinyl)stannane as the organometallic reagent (Equation 3). Subsequent addition of cyclopentadiene to the resultant vinyl ketone then induced a Diels–Alder reaction to produce the complex ketone **17** in 89% yield.



Equation 3

In conclusion, we have developed the first examples of oxidative carbonylation reactions that generate aldehyde and ketone products. These transformations provide new synthetic tools with which to access these important heterocyclic architectures without the need for redox manipulations. Further development of this chemistry to achieve catalytic use of palladium represents an intriguing goal that we are currently contemplating.[8]

All reactions were performed using base-washed, oven-dried glassware under an atmosphere of argon (dried by passage through Drierite) or CO. Reagents and solvents were transferred under argon by syringe. Organic solns were concentrated under reduced pressure using a Buchi rotary evaporator. $PhCF_3$ purchased from Aldrich was distilled from K_2CO_3, degassed by freeze-pump-thaw method and stored under an atmosphere of CO. Et_2O, THF, and CH_2Cl_2 were dried using a J. C. Meyer solvent purification system. $PdCl_2(PhCN)_2$ was prepared according to a known procedure[9] from $PdCl_2$ purchased from Strem or Aldrich and PhCN purchased from TCI America. All other reagents were used as received unless specified. Flash column chromatography was performed employing 32–63 μm silica gel (Dynamic Adsorbents Inc) or basic alumina (Fluka, pH 9.5). TLC was performed on silica gel 60 F_{254} plates (EMD).

^1H and ^{13}C NMR were recorded in $CDCl_3$ on Bruker DRX-300 and DRX-400 as noted, and are internally referenced to the residual solvent peak. Data for ^{13}C NMR are reported in terms of chemical shift. IR spectra were recorded on a Nicolet Avatar 370 DTGS (Thermo) using NaCl salt plates.. LR-MS were acquired on a JEOL JMS-LCmate liquid chromatography mass spectrometer system using APCI+ ionization technique.

Oxidative Formylation; General Procedure A

An oven-dried round-bottom flask with a magnetic stir bar was charged with $PdCl_2(PhCN)_2$ (1.05 equiv) and flame-dried, ground 4 Å MS (500 mg/mmol of substrate). The flask was evacuated and backfilled with CO via balloon (3 ×) and $PhCF_3$ (9.2 mL/mmol) was added. The soln was cooled to –15 °C in a salt–ice bath and CO was bubbled through the soln for 30 min. A 0.24 M soln of the substrate in $PhCF_3$ (filtered through silica gel before use) cooled to –15 °C was added. The mixture was stirred until completion of the reaction (10–60 min). 0.45 M Ph_3SiH in $PhCF_3$ (3 equiv) cooled to –15 °C was added quickly and the mixture was stirred for 10 min. Ethylene glycol (5 equiv) was added and the mixture was warmed to 23 °C. After 3 h, the mixture was filtered through a plug of celite and concentrated in vacuo. The product was purified by flash chromatography (silica gel or alumina).

Oxidative Ketonylation; General Procedure

An oven-dried round-bottom flask with a magnetic stir bar was charged with $PdCl_2(PhCN)_2$ (1.05 equiv) and flame-dried, ground 4 Å MS (500 mg/mmol of substrate). The flask was evacuated and backfilled with CO via balloon (3 ×) and $PhCF_3$ (8.5 mL/mmol) was added. The soln was cooled to –15 °C in a salt–ice bath and CO was bubbled through the soln for 30 min. A 0.24 M soln of the substrate in $PhCF_3$ (filtered through silica gel before use) cooled to –15 °C was added. The mixture was stirred until completion of reaction (10–60 min). The required organometallic reagent at the indicated amount was then added at –15 °C and the mixture was stirred at this temperature for 20 min. The mixture was filtered through a plug of celite and concentrated in vacuo. The product was purified by flash chromatography (silica gel or alumina).

Troubleshooting

This reaction is sensitive to the saturation of the reaction solvent by CO. For best reproducibility, reactions are run in larger reactions vessels (25-mL and 50-mL round bottom flasks for 0.1–0.2 mmol reactions) to increase the surface area for CO absorption. After allowing the $PdCl_2(PhCN)_2$ to dissolve in the solvent and then cooling the reaction, bubble CO through the mixture before addition of the substrate to ensure maximum CO solubility. Finally, the solns of both the substrate and silane must be cooled to the reaction temperature before very quick additions to the reaction vessel. The best results have been obtained using $PdCl_2(PhCN)_2$ synthesized from $PdCl_2$ purchased from Strem.

1-Phenyl-*N*-tosylpent-4-en-1-amine (Table 2, Entry 2, Substrate)

A soln of 1-phenylpent-4-en-1-amine[10] (0.41 g, 2.5 mmol, 1.0 equiv), Et_3N (0.70 mL, 5.0 mmol, 2.0 equiv), and DMAP (30.5 mg, 0.25 mmol, 0.1 equiv) in CH_2Cl_2 (8 mL) was cooled to 0 °C. A soln of TsCl (572 mg, 3.0 mmol, 1.2 equiv) in CH_2Cl_2 (2 mL) was slowly added to the mixture, which was then stirred at r.t. overnight. The mixture was diluted with CH_2Cl_2 (10 mL), washed with 1 M HCl (1 × 10 mL), H_2O (1 × 10 mL), and brine (1 × 10 mL), dried (anhyd Na_2SO_4), and concentrated in vacuo. Column chromatography (silica gel, 5% EtOAc–hexanes) gave the title compound (459 mg, 58%) as a white solid.

IR: 3280, 3070, 3035, 2930, 2854, 1449, 1337, 1155, 1099, 924, 812, 708, 659 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.16–7.14 (m, 3 H, Ar-H), 7.11 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.01–6.98 (m, 2 H, Ar-H), 5.77–5.64 (m, 1 H, C*H*=CH_2), 4.97–4.90 (m, 3 H, TsN*H*, CH=CH_2), 4.33–4.26 (m, 1 H, PhC*H*), 2.35 (s, 3 H, ArCH_3), 2.03–1.72 (m, 4 H, CH_2CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.1, 140.8, 137.8, 137.3, 129.4, 128.6, 127.6, 127.2, 126.6, 115.7, 58.0, 36.8, 30.1, 21.6.

LR-MS (APCI+): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{22}NO_2S$: 316.4; found: 316.1.

Methyl 2-(Tosylamino)hex-5-enoate (Table 2, Entry 3, Substrate)

A soln of *N*-(diphenylmethylene)glycine methyl ester[11] (447 mg, 1.76 mmol, 1.0 equiv) in DMF (3 mL) was added to a 0 °C suspension of 60% NaH (74 mg, 1.85 mmol, 1.05 equiv) in DMF (10 mL).

The mixture was stirred for 30 min at 0 °C, NaI (26 mg, 0.176 mmol, 0.1 equiv) and 4-bromobut-1-ene (0.36 mL, 3.53 mmol, 2.0 equiv) were added. The mixture was stirred at 50 °C for 90 min. The mixture was cooled and diluted with Et_2O (30 mL) and washed with H_2O (5 × 20 mL) and brine (1 × 20 mL). The organic layer was dried (anhyd Na_2SO_4) and concentrated in vacuo. The crude product was then stirred overnight in a mixture of 1 M HCl (5 mL) and Et_2O (5 mL) at 23 °C. The layers were then separated and Na_2CO_3 was added to the aqueous layer until it reached pH 9. The aqueous layer was then extracted with 5% MeOH–CH_2Cl_2 (5 × 10 mL) and then the organic layer was washed with brine (1 × 20 mL). The soln was dried (anhyd Na_2SO_4) and concentrated in vacuo to give crude product that was used directly in the next reaction. A soln of the amino ester, Et_3N (0.29 mL, 1.64 mmol, 2.0 equiv), and DMAP (10 mg, 0.082 mmol, 0.1 equiv) in CH_2Cl_2 (3 mL) was cooled to 0 °C. A soln of TsCl (187 mg, 0.98 mmol, 1.2 equiv) in CH_2Cl_2 (1 mL) was slowly added to the mixture, which then stirred at r.t. for 6 h. The mixture was diluted with CH_2Cl_2 (5 mL), washed with H_2O (1 × 5 mL) and brine (1 × 5 mL), dried (anhyd Na_2SO_4), and concentrated in vacuo. Column chromatography (silica gel, gradient 10–20% EtOAc–hexanes) gave the title compound (241 mg, 46% over 3 steps) as a white solid.

IR: 3273, 2951, 2917, 1742, 1637, 1595, 1435, 1330, 1169, 1092, 812, 652 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.28 (d, *J* = 8.4 Hz, 2 H, Ar-H), 5.77–5.64 (m, 1 H, C*H*=CH$_2$), 5.24 (d, *J* = 9.3 Hz, 1 H, TsN*H*), 5.01–4.96 (m, 2 H, CH=C*H*$_2$), 3.95–3.88 (m, 1 H, TsNHC*H*), 3.48 (s, 3 H, OCH_3), 2.40 (s, 3 H, CH_3), 2.10 (q, *J* = 7.5 Hz, 2 H, CH_2), 1.86–1.63 (m, 2 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.2, 143.7, 136.8, 136.6, 129.7, 127.4, 116.1, 55.2, 52.5, 32.6, 29.1, 21.6.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{20}NO_4S$: 298.4; found: 298.2.

2-(Cyclopent-2-enyl)-*N*-tosylethanamine (Table 2, Entry 5, Substrate)

To a suspension of $LiAlH_4$ (1.51 g, 39.8 mmol, 2.5 equiv) in THF (80 mL) cooled to 0 °C, a soln of cyclopent-2-eneacetic acid (1.66 g, 14.8 mmol, 1.0 equiv) in THF (16 mL) was slowly added. The mixture was heated to reflux for 3 h and then cooled to 0 °C. The mixture was diluted with Et_2O (100 mL) and then H_2O (2 mL), 1 M NaOH (2 mL), and H_2O (4 mL) were added sequentially. The mixture was stirred for 1 h and then filtered over a short silica plug, dried (anhyd Na_2SO_4), and concentrated in vacuo to yield 2-(cyclopent-2-enyl)ethanol as a colorless oil (1.66 g, 93%). A soln of the alcohol, Et_3N (4.1 mL, 29.6 mmol, 2.0 equiv), and DMAP (90 mg, 0.74 mmol, 0.05 equiv) in CH_2Cl_2 (44 mL) was cooled to 0 °C. A soln of TsCl (3.39 g, 17.8 mmol, 1.2 equiv) in CH_2Cl_2 (12 mL) was slowly added to the mixture, which was stirred at r.t. overnight. The mixture was diluted with CH_2Cl_2 (40 mL), washed with H_2O (1 × 40 mL) and brine (1 × 40 mL), dried (anhyd Na_2SO_4), and concentrated in vacuo. Column chromatography (silica gel, gradient 5–10% EtOAc–hexanes) gave 3-[2-(tosyloxy)ethyl]cyclopentene (3.51 mg, 89%) as a colorless oil.

IR: 3056, 2924, 2854, 1609, 1372, 1176, 1099, 952, 903, 812, 652 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.34 (d, *J* = 8.1 Hz, 2 H, Ar-H), 5.72–5.69 (m, 1 H, C*H*=CH), 5.56–5.53 (m, 1 H, CH=C*H*), 4.07 (t, *J* = 6.0 Hz, 2 H, C*H*$_2$OTs), 2.73–2.66 (m, 1 H, CH), 2.45 (s, 3 H, ArC*H*$_3$), 2.37–2.16 (m, 2 H, CH=CHC*H*$_2$), 2.04–1.92 (m, 1 H, CH_2), 1.82–1.70 (m, 1 H, CH_2), 1.67–1.56 (m, 1 H, CH_2), 1.38–1.27 (m, 1 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.8, 133.6, 133.4, 131.5, 130.0, 128.0, 69.7, 41.9, 35.0, 32.0, 29.6, 21.7.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{19}O_3S$: 267.4; found: 267.0.

The tosylate synthesized above (2.0 g, 7.5 mmol, 1.0 equiv), K_2CO_3 (2.07 g, 15.0 mmol, 2.0 equiv), and $TsNH_2$ (1.93 g, 11.3 mmol, 1.5 equiv) in acetone (10 mL) were heated to reflux overnight. The mixture was then concentrated and diluted with EtOAc (30 mL), then washed with H_2O (1 × 20 mL) and brine (1 × 20 mL), dried (anhyd Na_2SO_4), and concentrated in vacuo. Column chromatography (silica gel, gradient 5–10% EtOAc–hexanes) gave the title compound (1.21 g, 56%) as a colorless oil.

IR: 3278, 2935, 2843, 1422, 1317, 1161, 1087, 752, 665 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.31 (d, *J* = 7.8 Hz, 2 H, Ar-H), 5.72–5.70 (m, 1 H, C*H*=CH), 5.57–5.54 (m, 1 H, CH=C*H*), 4.40 (t, *J* = 5.7 Hz, 1 H, TsN*H*), 2.97 (q, *J* = 7.2 Hz, 2 H, TsNHC*H*$_2$), 2.67–2.61(m, 1 H, CH), 2.43 (s, 3 H, ArC*H*$_3$), 2.33–2.20 (m, 2 H, CH=CHC*H*$_2$), 2.04–1.92 (m, 1 H, CH_2), 1.63–1.51 (m, 1 H, CH_2), 1.50–1.41 (m, 1 H, CH_2), 1.38–1.28 (m, 1 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.5, 137.7, 137.1, 133.9, 131.4, 129.8, 127.2, 42.9, 42.0, 35.8, 32.0, 29.6, 21.6.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{20}NO_2S$: 266.4; found: 266.0.

2-Benzyl-1-phenylhex-5-en-2-ol (Table 2, Entry 8, Substrate)

To soln of methyl pent-4-enoate (0.60 g, 5.3 mmol, 1.0 equiv) in THF (49 mL) cooled to –78 °C, 2.0 M BnMgCl in Et_2O (6.6 mL, 13.3 mmol, 2.5 equiv) was slowly added. The mixture was warmed to 23 °C and stirred for 2 h. The reaction was quenched at 0 °C with sat. NH_4Cl soln (30 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 20 mL). The organic layer was then washed with brine (1 × 20 mL), dried (anhyd Na_2SO_4), and concentrated in vacuo. Column chromatography (silica gel, 5% EtOAc–hexanes) gave the title compound (0.80 g, 59%) as a pale yellow oil.

IR: 3568, 3470, 3061, 3025, 2923, 1637, 1606, 1499, 1446, 1370, 1268, 1085, 1036, 903, 756, 725, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.28 (m, 10 H, Ar-H), 5.90–5.77 (m, 1 H, C*H*=CH$_2$), 5.11–4.98 (m, 2 H, CH=C*H*$_2$), 2.88 (s, 4 H, PhC*H*$_2$), 2.36–2.28 (m, 2 H, CH_2), 1.55–1.49 (m, 2 H, CH_2), 1.46 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.6, 137.3, 130.8, 128.3, 126.6, 114.6, 74.2, 45.6, 37.4, 28.4.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{23}O$: 267.4; found: 267.2.

***syn*-2-[(1,3-Dioxolan-2-yl)methyl]-5-isopropyl-1-tosylpyrrolidine (6′)**

Following general procedure A using 2-methyl-*N*-tosylhept-6-en-3-amine[1a] (**5**, 40.0 mg, 0.142 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (56.4 mg, 0.147 mmol, 1.05 equiv), 4 Å MS (70 mg), Ph_3SiH (111 mg, 0.426 mmol, 3.0 equiv), and ethylene glycol (40 μL, 0.71 mmol, 5.0 equiv) and flash chromatography (silica gel, gradient 1–5% EtOAc–hexanes) gave **6′** (39.1 mg, 78%) as a white solid.

IR: 2958, 2867, 1602, 1330, 1148, 1085, 1036, 994, 819, 658 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.29 (d, *J* = 8.4 Hz, 2 H, Ar-H), 4.95 [t, *J* = 5.1 Hz, 1 H, $CH_2CH(OR)_2$], 3.99–3.90 (m, 2 H, OCH_2), 3.90–3.84 (m, 2 H, OCH_2), 3.79–3.74 (m, 1 H, TsNC*H*), 3.40 (q, *J* = 6.9 Hz, 1 H, TsNC*H*), 2.41 (s, 3 H, ArC*H*$_3$), 2.29 [dt, *J* = 4.8, 13.8 Hz, 1 H, C*H*$_2$CH(OR)$_2$], 2.10–1.99 (m, 1 H, Me$_2$C*H*), 1.78–1.67 [m, 1 H, C*H*$_2$CH(OR)$_2$], 1.65–1.55 (m, 2 H, CH_2), 1.52–1.42 (m, 1 H, CH_2), 1.35–1.24 (m, 1 H, CH_2), 0.96 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.90 (d, *J* = 6.7 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.3, 135.1, 129.7, 127.8, 102.6, 67.3, 64.9, 64.7, 58.1, 41.1, 31.7, 30.3, 25.5, 21.6 20.2, 17.5.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{28}NO_4S$: 354.2; found: 354.0.

syn-2-[(1,3-Dioxolan-2-yl)methyl]-5-methyl-1-tosylpyrrolidine (Table 2, Entry 1, Product)

Following general procedure A using *N*-tosylhex-5-en-2-amine[12] (40.0 mg, 0.158 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (63.6 mg, 0.166 mmol, 1.05 equiv), 4 Å MS (79 mg), Ph_3SiH (123 mg, 0.474 mmol, 3.0 equiv), and ethylene glycol (44 μL, 0.79 mmol, 5.0 equiv) and flash chromatography (alumina, gradient 5–20% EtOAc–hexanes) gave the title compound (39.5 mg, 77%) as a white solid.

IR: 2968, 2922, 2871, 1604, 1340, 1157, 1099, 1036, 664 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.29 (d, *J* = 8.1 Hz, 2 H, Ar-H), 4.98 [t, *J* = 4.8 Hz, 1 H, $CH_2CH(OR)_2$], 4.00–3.90 (m, 2 H, OCH_2CH_2O), 3.88–3.81 (m, 2 H, OCH_2CH_2O), 3.79–3.74 (m, 1 H, TsNC*H*), 3.70–3.75 (m, 1 H, TsNC*H*), 2.42 (s, 3 H, $ArCH_3$), 2.32 [dt, *J* = 5.1, 13.8 Hz, 1 H, $CH_2CH(OR)_2$], 1.85–1.76 [m, 1 H, $CH_2CH(OR)_2$], 1.73–1.45 (m, 4 H, CH_2), 1.33 (d, *J* = 6.3 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.3, 135.1, 129.7, 127.7, 102.6, 64.9, 64.8, 58.3, 57.5, 41.4, 32.2, 20.4, 23.7, 21.6.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{24}NO_4S$: 326.1; found: 326.2.

syn-2-[(1,3-Dioxolan-2-yl)methyl]-5-phenyl-1-tosylpyrrolidine (Table 2, Entry 2, Product)

Following general procedure A using 1-phenyl-*N*-tosylpent-4-en-1-amine (40.0 mg, 0.127 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (51.1 mg, 0.133 mmol, 1.05 equiv), 4 Å MS (64 mg), Ph_3SiH (99.2 mg, 0.381 mmol, 3.0 equiv), and ethylene glycol (35 μL, 0.64 mmol, 5.0 equiv) and flash chromatography (silica gel, gradient 5–20% EtOAc–hexanes) gave the title compound (39.7 mg, 81%) as a white solid.

IR: 2970, 2883, 1600, 1487, 1439, 1335, 1152, 1087, 1035, 743, 665 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.37–7.20 (m, 7 H, Ar-H), 5.00 [t, *J* = 5.1 Hz, 1 H, $CH_2CH(OR)_2$], 4.71 (t, *J* = 6.6 Hz, 1 H, TsNC*H*Ph), 4.02–3.92 (m, 3 H, OCH_2CH_2O, TsNC*H*), 3.88–3.84 (m, 2 H, OCH_2CH_2O), 2.53 [dt, *J* = 4.8, 13.8 Hz, 1 H, $CH_2CH(OR)_2$], 2.43 (s, 3 H, $ArCH_3$), 1.97–1.84 [m, 3 H, $CH_2CH(OR)_2$, CH_2], 1.69 (q, *J* = 6.3 Hz, 2 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.5, 142.7, 135.1, 129.7, 128.5, 127.9, 127.1, 126.3, 102.7, 65.0, 64.8, 64.7, 58.6, 40.9, 34.4, 30.6, 21.7.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{26}NO_4S$: 388.2; found: 388.0.

Methyl _syn_-5-[(1,3-Dioxolan-2-yl)methyl]-1-tosylpyrrolidine-2-carboxylate (Table 2, Entry 3, Product)

Following general procedure A using methyl 2-(tosylamino)hex-5-enoate (40.0 mg, 0.135 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (54.2 mg, 0.141 mmol, 1.05 equiv), 4 Å MS (68 mg), Ph_3SiH (105 mg, 0.405 mmol, 3.0 equiv), and ethylene glycol (41 μL, 0.68 mmol, 5.0 equiv) and chromatography (silica gel, gradient 10–30% EtOAc–hexanes) gave the title compound (32.7 mg, 66%) as a pale yellow oil.

IR: 2951, 2881, 1763, 1595, 1344, 1197, 1155, 1015, 812, 666 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.31 (d, *J* = 8.1 Hz, 2 H, Ar-H), 4.96 [t, *J* = 4.8 Hz, 1 H, $CH_2CH(OR)_2$], 4.23 (t, *J* = 6.0 Hz, 1 H, TsNC*H*CO_2CH_3), 3.97–3.81 (m, 5 H, OCH_2CH_2O, TsNC*H*), 3.74 (s, 3 H, CO_2CH_3), 2.42 (s, 3 H, $ArCH_3$), 2.35 [dt, 1 H, $CH_2CH(OR)_2$], 1.99–1.65 [m, 5 H, $CH_2CH(OR)_2$, CH_2CH_2].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.7, 143.9, 135.2, 129.9, 127.8, 102.5, 65.0, 64.8, 61.7, 58.3, 52.7, 39.9, 31.1, 29.5, 21.7.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{24}NO_6S$: 370.1; found: 370.2.

3-[(1,3-Dioxolan-2-yl)methyl]-2-tosyl-2-azaspiro[4.5]decane (Table 2, Entry 4, Product)

Following general procedure A using *N*-tosyl(1-allylcyclohexyl)methylamine[5b] (40.0 mg, 0.130 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (52.4 mg, 0.137 mmol, 1.05 equiv), 4 Å MS (65 mg), Ph_3SiH (102 mg, 0.390 mmol, 3.0 equiv), and ethylene glycol (36 μL, 0.65 mmol, 5.0 equiv) and flash chromatography (silica gel, gradient 5–20% EtOAc–hexanes) gave the title compound (36.7 mg, 74%) as a colorless oil.

IR: 2924, 2847, 1595, 1449, 1337, 1162, 1085, 1043, 938, 819, 659 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.30 (d, *J* = 8.1 Hz, 2 H, Ar-H), 4.91 [dd, *J* = 4.2, 5.7 Hz, 1 H, $CH_2CH(OR)_2$], 3.99–3.89 (m, 2 H, OCH_2CH_2O), 3.85–3.81 (m, 2 H, OCH_2CH_2O), 3.66–3.58 (m, 1 H, TsNC*H*), 3.24 (d, 1 H, TsNCH_2), 3.10 (d, 1 H, TsNCH_2), 2.68–2.61 [m, 1 H, $CH_2CH(OR)_2$], 2.41 (s, 3 H, $ArCH_3$), 1.94–1.80 [m, 2 H, $CH_2CH(OR)_2$, CH_2], 1.56–1.50 (m, 1 H, CH_2), 1.42–1.13 (m, 8 H, CH_2), 0.80–0.73 (m, 1 H, CH_2), 0.64–0.60 (m, 1 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.3, 134.9, 129.6, 127.7, 102.8, 64.9, 58.6, 56.0, 45.2, 41.4, 41.0, 36.6, 34.3, 26.0, 23.8, 23.0, 21.7.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{30}NO_4S$: 380.2; found: 380.3.

syn-6-(1,3-Dioxolan-2-yl)-1-tosyloctahydrocyclopenta[*b*]pyrrole (Table 2, Entry 5, Product)

Following general procedure A using 2-(cyclopent-2-enyl)-*N*-tosylethanamine (35.0 mg, 0.132 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (60.7 mg, 0.158 mmol, 1.2 equiv), 4 Å MS (66 mg), Ph_3SiH (103 mg, 0.396 mmol, 3.0 equiv), and ethylene glycol (37 μL, 0.66 mmol, 5.0 equiv) and flash chromatography (alumina, gradient 2–15% EtOAc–hexanes) gave the title compound (29.4 mg, 66%) as a white solid.

IR: 2952, 2865, 1591, 1343, 1152, 1109, 1026, 813, 652 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.32 (d, *J* = 8.1 Hz, 2 H, Ar-H), 5.08 [d, *J* = 3.6 Hz, 1 H, $CH_2CH(OR)_2$], 4.04–3.84 (m, 4 H, OCH_2CH_2O), 3.77 (dd, 1 H, NTsC*H*), 3.50–3.42 (m, 1 H, TsNCH_2), 3.13–3.05 (m, 1 H, TsNCH_2), 2.66–2.61 [m, 1 H, C*H*CH(OR)$_2$], 2.50–2.42 (m, 1 H, CH_2), 2.42 (s, 3 H, $ArCH_3$), 1.89–1.73 (m, 2 H, CH_2), 1.69–1.41 (m, 4 H, CH_2, CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.4, 134.3, 129.7, 128.0, 104.9, 66.5, 65.3, 65.1, 50.1, 49.4, 44.3, 30.6, 30.4, 24.8, 21.7.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{24}NO_4S$: 338.1; found: 338.9.

2-[(1,3-Dioxolan-2-yl)methyl]-1-tosylpiperidine (Table 2, Entry 6, Product)

Following general procedure A using *N*-tosylhex-5-en-1-amine[12] (40.0 mg, 0.158 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (63.6 mg, 0.166 mmol, 1.05 equiv), 4 Å MS (79 mg), Ph_3SiH (123 mg, 0.474 mmol, 3.0 equiv), and ethylene glycol (44 μL, 0.79 mmol, 5.0 equiv) and flash chromatography (silica gel, gradient 5–20% EtOAc–hexanes) gave 2-[(1,3-dioxolan-2-yl)methyl]-1-tosylpiperidine (32.4 mg, 63%) as a white solid. This example suffers from a significant yield of acid chloride that was not able to be circumvented. The acid chlo-

ride is isolated as 2-hydroxyethyl 2-(1-tosylpiperidin-2-yl)ethanoate (12.4 mg, 23%) as a white solid.

2-[(1,3-Dioxolan-2-yl)methyl]-1-tosylpiperidine

IR: 2928, 2888, 1598, 1334, 1151, 1094, 922, 818 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.27 (d, *J* = 8.1 Hz, 2 H, Ar-H), 4.86–4.82 [m, 1 H, $CH_2CH(OR)_2$], 4.36–4.27 (m, 1 H, TsNC*H*), 3.98–3.90 (m, 2 H, OCH_2CH_2O), 3.88–3.78 (m, 3 H, OCH_2CH_2O, $NTsCH_2$), 3.03–2.93 (m, 1 H, $TsNCH_2$), 2.42 (s, 3 H, $ArCH_3$), 2.02–1.94 [m, 1 H, $CH_2CH(OR)_2$], 1.81–1.74 [m, 1 H, $CH_2CH(OR)_2$], 1.72–1.48 (m, 5 H, CH_2), 1.30–1.26 (m, 1 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.9, 138.9, 129.7, 127.2, 102.7, 65.0, 64.9, 49.6, 40.9, 34.2, 28.3, 24.7, 21.6, 18.6.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{24}NO_4S$: 326.1; found: 326.2.

2-Hydroxyethyl 2-(1-Tosylpiperidin-2-yl)ethanoate

^1H NMR (300 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.29 (d, *J* = 8.4 Hz, 2 H, Ar-H), 4.66–4.60 (m, 1 H, TsNC*H*), 4.33–4.14 (m, 2 H, $CO_2CH_2CH_2$), 3.88–3.72 (m, 3 H, CH_2OH, $NTsCH_2$), 3.12–3.03 (m, 1 H, $TsNCH_2$), 2.83–2.70 (m, 2 H, CH_2CO_2, OH), 2.50 (dd, *J* = 14.4, 6.3 Hz, 1 H, CH_2CO_2), 2.42 (s, 3 H, $ArCH_3$), 1.58–1.37 (m, 5 H, CH_2), 1.14–1.08 (m, 1 H, CH_2).

***trans*-2-[(1,3-Dioxolan-2-yl)methyl]octahydro-2*H*-chromene (Table 2, Entry 7, Product)**

Following general procedure A using *syn*-2-(but-3-enyl)cyclohexanol[13] (30.0 mg, 0.195 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (78.5 mg, 0.205 mmol, 1.05 equiv), 4 Å MS (98 mg), Ph_3SiH (152 mg, 0.585 mmol, 3.0 equiv), and ethylene glycol (54 μL, 0.98 mmol, 5.0 equiv) and flash chromatography (silica gel, gradient benzene to 2% EtOAc–benzene) gave the title compound (31.0 mg, 70%) as a colorless liquid.

IR: 2926, 2852, 1448, 1404, 1139, 1104, 1035, 943 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.04 [dd, *J* = 3.6, 6.6 Hz, 1 H, $CH_2CH(OR)_2$], 3.98–3.90 (m, 2 H, OCH_2CH_2O), 3.86–3.82 (m, 2 H, OCH_2CH_2O), 3.58–3.49 (m, 1 H, OCH), 2.96–2.89 (m, 1 H, OCH), 1.99–1.86 [m, 2 H, $CH_2CH(OR)_2$, CH_2], 1.76–1.57 [m, 6 H, $CH_2CH(OR)_2$, CH_2, CH), 1.43–1.07 (m, 6 H, CH_2), 1.00–0.88 (m, 1 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 102.4, 82.0, 74.4, 64.9, 64.8, 41.8, 41.1, 32.8, 32.7, 31.9, 31.0, 26.0, 25.2.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{23}O_3$: 227.2; found: 227.1.

2-[(5,5-Dibenzyltetrahydrofuran-2-yl)methyl]-1,3-dioxolane (Table 2, Entry 8, Product)

Following general procedure A using 2-benzyl-1-phenylhex-5-en-2-ol (35.0 mg, 0.132 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (53.2 mg, 0.139 mmol, 1.05 equiv), 4 Å MS (66 mg), Ph_3SiH (103 mg, 0.396 mmol, 3.0 equiv), and ethylene glycol (37 μL, 0.66 mmol, 5.0 equiv) and flash chromatography (silica gel, gradient CH_2Cl_2–hexanes 1:1 to 2:1) gave the title compound (31.8 mg, 72%) as a colorless liquid.

IR: 3070, 3021, 2914, 2870, 1495, 1450, 1085, 1032, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.23 (m, 10 H, Ar-H), 4.95 [dd, *J* = 4.2, 6.3 Hz, 1 H, $CH_2CH(OR)_2$], 3.99–3.95 (m, 2 H, OCH_2CH_2O), 3.92–3.83 (m, 3 H, OCH_2CH_2O, OCH), 2.95–2.71 (m, 4 H, $PhCH_2$), 1.92–1.79 (m, 3 H, CH_2, CH_2), 1.63–1.54 (m, 2 H, CH_2), 0.95–0.82 (m, 1 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.4, 138.2, 131.1, 130.9, 128.0, 127.8, 126.3, 102.9, 85.4, 75.7, 64.8, 46.8, 46.6, 40.0, 33.1, 32.4.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{27}O_3$: 339.5; found: 339.1.

Ethyl 4-(*syn*-5-Isopropyl-1-tosylpyrrolidin-2-yl)but-2-enoate (7)

Following general procedure A using 2-methyl-*N*-tosylhept-6-en-3-amine[1a] (**5**, 40.0 mg, 0.142 mmol, 1 equiv), $PdCl_2(PhCN)_2$ (56.4 mg, 0.147 mmol, 1.05 equiv), 4 Å MS (70 mg), and Ph_3SiH (111 mg, 0.426 mmol, 3.0 equiv), but instead of ethylene glycol, $Ph_3P{=}CHCO_2Et$ (148 mg, 0.426 mmol, 3.0 equiv) was added and the mixture was stirred at r.t. for 12 h. This modified procedure was followed by flash chromatography (silica gel, gradient 1–5% EtOAc–hexanes) to yield **7** (39.0 mg, 72%) as a white solid; ratio *E*/*Z* 3:1.

***E*-Isomer (major product)**

IR: 2951, 2868, 1714, 1665, 1477, 1344, 1253, 1162, 1085, 1029, 994, 812, 666 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.31 (d, *J* = 8.1 Hz, 2 H, Ar-H), 6.94–6.84 (m, 1 H, C*H*=$CHCO_2Et$), 5.90–5.86 (m, 1 H, CH=C*H*CO_2Et), 4.16 (q, *J* = 7.2 Hz, 2 H, $CO_2CH_2CH_3$), 3.71–3.62 (m, 1 H, NTsC*H*), 3.41 (q, *J* = 5.1 Hz, 1 H, NTsC*H*), 2.83–2.75 (m, 1 H, $CH_2CH{=}CH$), 2.43 (s, 3 H, $ArCH_3$), 2.48–2.35 (m, 1 H, $CH_2CH{=}CH$), 2.06–1.95 (m, 1 H, Me_2CH), 1.66–1.58 (m, 1 H, CH_2), 1.51 (q, *J* = 7.2 Hz, 2 H, CH_2), 1.31–1.20 (m, 1 H, CH_2), 1.29 (t, *J* = 7.2 Hz, 3 H, $CO_2CH_2CH_3$), 0.99 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.91 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4, 144.8, 143.6, 134.8, 129.8, 127.8, 124.0, 67.7, 60.5, 39.7, 31.5, 29.3, 25.5, 21.7, 20.2, 17.8, 14.4.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{30}NO_4S$: 380.5; found: 381.1.

***Z*-Isomer (minor product)**

IR: 2959, 2919, 2870, 1717, 1334, 1156, 1090, 1032, 743, 663 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.31 (d, *J* = 8.1 Hz, 2 H, Ar-H), 6.46–6.37 (m, 1 H, C*H*=$CHCO_2Et$), 5.90–5.86 (m, 1 H, CH=C*H*CO_2Et), 4.17 (q, *J* = 6.9 Hz, 2 H, $CO_2CH_2CH_3$), 3.83–3.72 (m, 1 H, NTsC*H*), 3.42 (q, *J* = 6.6 Hz, 1 H, NTsC*H*), 3.14–3.03 (m, 1 H, $CH_2CH{=}CH$), 2.94–2.83 (m, 1 H, $CH_2CH{=}CH$), 2.43 (s, 3 H, $ArCH_3$), 2.15–2.03 (m, 1 H, Me_2CH), 1.74–1.62 (m, 1 H, CH_2), 1.57–1.46 (m, 1 H, CH_2), 1.43–1.31 (m, 1 H, CH_2), 1.29 (t, *J* = 7.2 Hz, 3 H, $CO_2CH_2CH_3$), 1.31–1.18 (m, 1 H, CH_2), 0.97 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.91 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 146.1, 143.5, 135.1, 129.8, 127.9, 121.5, 67.7, 61.0, 60.1, 35.5, 31.7, 29.5, 25.5, 21.7, 20.3, 17.4, 14.4.

LR-MS (APCI+): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{30}NO_4S$: 380.5; found: 380.1.

(±)-1-(Octahydro-2*H*-chromen-2-yl)butan-2-one (9)

Following general procedure A: using *syn*-2-(but-3-enyl)cyclohexanol[13] (30.0 mg, 0.195 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (78.5 mg, 0.205 mmol, 1.05 equiv), 4 Å MS (98 mg), Ph_3SiH (152 mg, 0.585 mmol, 3.0 equiv), but instead of ethylene glycol, 1.0 M Et_2Zn in THF (0.59 mL, 0.585 mmol, 3.0 equiv) was added at –15 °C. The mixture stirred at –15 °C for 20 min and then quenched with sat. NH_4Cl soln (0.5 mL). The mixture was filtered through a celite plug using EtOAc, dried (anhyd Na_2SO_4), and concentrated in vacuo. This modified procedure was followed by flash chromatography (silica gel, gradient hexanes to 2% EtOAc–hexanes) to yield **9** (27.3 mg, 67%) as a colorless liquid.

Following general procedure B: syn-2-(but-3-enyl)cyclohexanol[7] (20.0 mg, 0.130 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (52.3 mg, 0.137 mmol, 1.05 equiv), 4 Å MS (65 mg), and 1.0 M Et_2Zn in hexanes

(78 μL, 0.078 mmol, 0.6 equiv) followed by flash chromatography (silica gel, gradient 1–2% EtOAc–hexanes) yielded the title compound as a colorless oil (19.7 mg, 72%). Spectra same as described above.

IR: 2932, 2856, 1708, 1446, 1357, 1103, 1072 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.81–3.74 (m, 1 H, OCH), 2.92–2.89 (m, 1 H, OCH), 2.66 [dd, *J* = 15.6, 7.5 Hz, 1 H, $CH_2C(O)CH_2$], 2.52–2.34 [m, 3 H, $CH_2C(O)CH_2$], 1.82–1.55 (m, 6 H, CH, CH_2), 1.35–1.08 (m, 6 H, CH, CH_2), 1.01 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.04–0.86 (m, 1 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 210.3, 82.1, 74.3, 49.3, 41.7, 37.2, 32.7, 32.4, 31.8, 30.8, 25.9, 25.2, 7.74.

LR-MS (APCI+): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{23}O_2$: 211.3; found: 211.0.

1-(*syn*-5-Isopropyl-1-tosylpyrrolidin-2-yl)butan-2-one (15)

Following general procedure B using 2-methyl-*N*-tosylhept-6-en-3-amine[1a] (**5**, 20.0 mg, 0.071 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (28.6 mg, 0.075 mmol, 1.05 equiv), 4 Å MS (36 mg), and 1.0 M Et_2Zn in hexanes (43 μL, 0.043 mmol, 0.6 equiv) and flash chromatography (silica gel, gradient 7–10% EtOAc–hexanes) gave **15** (21.7 mg, 90%) as a colorless oil.

IR: 2958, 2875, 1707, 1602, 1470, 1330, 1162, 1092, 994, 819, 666 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.31 (d, *J* = 8.1 Hz, 2 H, Ar-H), 3.99–3.89 (m, 1 H, TsNC*H*), 3.40–3.34 (m, 1 H, TsNC*H*), 3.22 [dd, *J* = 17.4, 3.3 Hz, 1 H, $CH_2C(O)$], 2.62–2.36 [m, 3 H, $CH_2C(O)$, $CH_2C(O)$], 2.44 (s, 3 H, $ArCH_3$), 2.07–1.95 [m, 1 H, $(CH_3)_2CH$], 1.81–1.70 (m, 1 H, CH_2), 1.64–1.54 (m, 1 H, CH_2), 1.47–1.36 (m, 1 H, CH_2), 1.27–1.18 (m, 1 H, CH_2), 1.06 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3), 0.99 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.91 (d, *J* = 6.9 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 209.9, 143.6, 134.6, 129.9, 127.9, 67.5, 57.6, 50.2, 36.7, 31.8, 30.9, 25.5, 21.7, 20.3, 17.8.

LR-MS (APCI+): *m*/*z* $[M]^+$ calcd for $C_{18}H_{28}NO_3S$: 338.5; found: 337.9.

2-(*syn*-5-Isopropyl-1-tosylpyrrolidin-2-yl)-1-phenylethanone (16)

Following general procedure B using 2-methyl-*N*-tosylhept-6-en-3-amine[1a] (**5**, 20.0 mg, 0.071 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (28.6 mg, 0.075 mmol, 1.05 equiv), 4 Å MS (36 mg), and 0.5 M PhZnCl in THF (160 μL, 0.078 mmol, 1.1 equiv) and flash chromatography (silica gel, benzene) gave **16** (23.3 mg, 85%) as a white solid.

IR: 2951, 2975, 1686, 1588, 1449, 1344, 1211, 1162, 1092, 1001, 666 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 7.5 Hz, 2 H, Ar-H), 7.72 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.62–7.47 (m, 3 H, Ar-H), 7.36–7.30 (m, 2 H, Ar-H), 4.17–4.13 (m, 1 H, TsNC*H*), 3.88 (dd, *J* = 17.1, 3.0 Hz, 1 H, TsNC*H*), 3.42 [q, *J* = 7.2 Hz, 1 H, $CH_2C(O)$], 3.07 [dd, *J* = 17.1, 10.5 Hz, 1 H, $CH_2C(O)$], 2.43 (s, 3 H, $ArCH_3$), 2.14–2.02 (m, 1 H, Me_2CH), 1.85–1.70 (m, 1 H, CH_2), 1.60–1.47 (m, 2 H, CH_2), 1.32–1.20 (m, 1 H, CH_2), 1.02 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.96 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.6, 143.6, 136.7, 134.6, 133.5, 129.9, 128.8, 128.3, 127.8, 67.5, 58.3, 46.9, 31.7, 30.6, 25.5, 21.7, 20.3, 17.6.

LR-MS (APCI+): *m*/*z* $[M]^+$ calcd for $C_{22}H_{28}NO_3S$: 386.5; found: 385.9.

1-(*syn*-5-Isopropyl-1-tosylpyrrolidin-2-yl)propan-2-one (Table 4, Entry 2)

Following general procedure B using 2-methyl-*N*-tosylhept-6-en-3-amine[1a] (**5**, 20.0 mg, 0.071 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (28.6 mg, 0.075 mmol, 1.05 equiv), 4 Å MS (36 mg), and 1.0 M Me_2Zn in heptane (43 μL, 0.043 mmol, 0.6 equiv) and flash chromatography (silica gel, gradient 7–10% EtOAc–hexanes) gave the title compound (18.8 mg, 82%) as a colorless oil.

IR: 2965, 2868, 1714, 1337, 1155, 1085, 1008, 812, 680 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.31 (d, *J* = 8.1 Hz, 2 H, Ar-H), 3.97–3.88 (m, 1 H, TsNC*H*), 3.40–3.34 (m, 1 H, TsNC*H*), 3.26 [dd, *J* = 17.7, 3.3 Hz, 1 H, $CH_2C(O)$], 2.60 [dd, *J* = 17.7, 9.9 Hz, 1 H, $CH_2C(O)$], 2.42 (s, 3 H, $ArCH_3$), 2.16 (s, 3 H, CH_3), 2.07–1.95 (m, 1 H, Me_2CH), 1.81–1.70 (m, 1 H, CH_2), 1.63–1.54 (m, 1 H, CH_2), 1.46–1.35 (m, 1 H, CH_2), 1.28–1.16 (m, 1 H, CH_2), 0.98 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.91 (d, *J* = 6.9 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.1, 143.6, 134.5, 129.8, 127.8, 67.4, 57.4, 51.4, 31.7, 30.8, 30.6, 25.5, 21.6, 20.2, 17.7.

LR-MS (APCI+): *m*/*z* $[M]^+$ calcd for $C_{17}H_{26}NO_3S$: 324.5; found: 323.9.

1-(*syn*-5-Methyl-1-tosylpyrrolidin-2-yl)propan-2-one (Table 4, Entry 3)

Following general procedure B using *N*-tosylhex-5-en-2-amine[12] (25.0 mg, 0.099 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (39.7 mg, 0.166 mmol, 1.05 equiv), 4 Å MS (50 mg), and 1.0 M Me_2Zn in heptane (60 μL, 0.059 mmol, 0.6 equiv) and flash chromatography (silica gel, gradient 7–10% EtOAc–hexanes) gave the title compound (22.1 mg, 76%) as a white solid.

IR: 2979, 2917, 2889, 1707, 1344, 1148, 1092, 987, 826, 666 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.31 (d, *J* = 8.0 Hz, 2 H, Ar-H), 3.94–3.87 (m, 1 H, TsNC*H*), 3.68–3.61 (m, 1 H, TsNC*H*), 3.29 [dd, *J* = 17.6, 3.6 Hz, 1 H, $CH_2C(O)$], 2.66 [dd, *J* = 17.6, 9.6 Hz, 1 H, $CH_2C(O)$], 2.42 (s, 3 H, $ArCH_3$), 2.17 (s, 3 H, CH_3), 1.82–1.73 (m, 1 H, CH_2), 1.56–1.38 (m, 3 H, CH_2CH_2), 1.32 (d, *J* = 6.4 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.2, 143.6, 134.4, 129.8, 127.7, 57.6, 57.5, 51.7, 31.8, 30.7, 30.6, 23.5, 21.6.

LR-MS (APCI+): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{22}NO_3S$: 296.4; found: 295.9.

1-Phenyl-2-(*syn*-5-phenyl-1-tosylpyrrolidin-2-yl)ethanone (Table 4, Entry 4)

Following general procedure B using 1-phenyl-*N*-tosylpent-4-en-1-amine (20.0 mg, 0.063 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (25.5 mg, 0.067 mmol, 1.05 equiv), 4 Å MS (32 mg), and 0.5 M PhZnCl in THF (140 μL, 0.069 mmol, 1.1 equiv) and flash chromatography (silica gel, benzene) gave the title compound (20.9 mg, 79%) as a white solid.

IR: 3070, 2937, 2868, 1679, 1595, 1351, 1169, 1085, 666 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.03 (dd, *J* = 8.1, 1.2 Hz, 2 H, Ar-H), 7.76 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.62–7.25 (m, 10 H, Ar-H), 4.73 (t, *J* = 5.1 Hz, 1 H, TsNC*H*), 4.36–4.27 (m, 1 H, TsNC*H*), 4.10 [dd, *J* = 16.8, 3.0 Hz, 1 H, $CH_2C(O)$], 3.24 [dd, *J* = 17.1, 10.5 Hz, 1 H, $CH_2C(O)$], 2.45 (s, 3 H, $ArCH_3$), 2.05–1.75 (m, 3 H, CH_2CH_2), 1.61–1.50 (m, 1 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.5, 143.9, 142.5, 136.7, 134.4, 133.6, 130.0, 128.9, 128.6, 128.3, 127.9, 127.3, 126.3, 64.7, 58.7, 46.6, 34.0, 30.8, 21.7.

LR-MS (APCI+): *m*/*z* $[M]^+$ calcd for $C_{25}H_{26}NO_3S$: 420.5; found: 419.8.

1-(*syn*-5-Isopropyl-1-tosylpyrrolidin-2-yl)but-3-en-2-one (Table 4, Entry 5)

Following general procedure B using 2-methyl-*N*-tosylhept-6-en-3-amine[1a] (**5**, 20.0 mg, 0.071 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (28.6 mg, 0.075 mmol, 1.05 equiv), 4 Å MS (36 mg), and tributyl(vinyl)stannane (27 μL, 0.092 mmol, 1.3 equiv) and flash chromatography (silica gel, gradient 7–10% EtOAc–hexanes) gave the title compound (22.4 mg, 94%) as a colorless oil.

IR: 2972, 2930, 2868, 1672, 1602, 1337, 1155, 1092, 994, 812, 666 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.31 (d, *J* = 8.1 Hz, 2 H, Ar-H), 6.33–6.30 (m, 2 H, CH=CH_2), 5.91 (dd, *J* = 7.5, 3.9 Hz, 1 H, C*H*=CH_2), 4.02–3.93 (m, 1 H, TsNC*H*), 3.46 [dd, *J* = 17.1, 3.3 Hz, 1 H, CH_2C(O)], 3.41–3.35 (m, 1 H, TsNC*H*), 2.74 [dd, *J* = 17.1, 10.5 Hz, 1 H, CH_2C(O)], 2.43 (s, 3 H, ArCH_3), 2.09–1.98 (m, 1 H, Me_2C*H*), 1.80–1.69 (m, 1 H, CH_2), 1.66–1.50 (m, 1 H, CH_2), 1.49–1.17 (m, 2 H, CH_2), 0.99 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.92 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.1, 143.6, 136.7, 134.4, 129.8, 129.1, 127.8, 67.4, 57.9, 47.4, 31.7, 30.6, 28.0, 27.0, 25.4, 21.6, 20.2, 17.7, 13.7.

LR-MS (APCI+): *m*/*z* $[M]^+$ calcd for $C_{18}H_{26}NO_3S$: 336.5; found: 335.9.

1-(*syn*-5-Isopropyl-1-tosylpyrrolidin-2-yl)pent-4-en-2-one (Table 4, Entry 6)

Following general procedure B using 2-methyl-*N*-tosylhept-6-en-3-amine[1a] (**5**, 20.0 mg, 0.071 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (28.6 mg, 0.075 mmol, 1.05 equiv), 4 Å MS (36 mg), and allyltributylstannane (33 μL, 0.107 mmol, 1.5 equiv) and flash chromatography (silica gel, gradient 2–7% EtOAc–hexanes) yielded the title compound (14.3 mg, 58%) as a colorless oil.

IR: 2958, 2868, 1721, 1344, 1162, 1085, 994, 819, 659 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.31 (d, *J* = 8.1 Hz, 2 H, Ar-H), 5.98–5.84 (m, 1 H, C*H*=CH_2), 5.22–5.13 (m, 2 H, CH=CH_2), 3.97–3.88 (m, 1 H, TsNC*H*), 3.40–3.34 (m, 1 H, TsNC*H*), 3.26 [dd, *J* = 17.7, 3.6 Hz, 1 H, CH_2C(O)], 3.22–3.18 (m, 2 H, CH_2CH=CH_2), 2.62 [dd, *J* = 17.7, 9.9 Hz, 1 H, CH_2C(O)], 2.43 (s, 3 H, ArCH_3), 2.06–1.95 (m, 1 H, Me_2C*H*), 1.81–1.70 (m, 1 H, CH_2), 1.63–1.54 (m, 1 H, CH_2), 1.46–1.35 (m, 1 H, CH_2), 1.27–1.15 (m, 1 H, CH_2), 0.99 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.91 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.1, 143.6, 134.5, 130.3, 129.8, 127.9, 127.8, 119.3, 67.4, 57.4, 50.1, 48.3, 31.8, 30.9, 25.5, 21.7, 20.2, 17.8.

LR-MS (APCI+): *m*/*z* $[M]^+$ calcd for $C_{19}H_{28}NO_3S$: 350.5; found: 349.9.

1-(Furan-2-yl)-2-(*syn*-5-isopropyl-1-tosylpyrrolidin-2-yl)ethanone (Table 4, Entry 7)

Following general procedure B using 2-methyl-*N*-tosylhept-6-en-3-amine[1a] (**5**, 20.0 mg, 0.071 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (28.6 mg, 0.075 mmol, 1.05 equiv), 4 Å MS (36 mg), and tributyl(furan-2-yl)stannane (29 μL, 0.092 mmol, 1.3 equiv) and flash chromatography (silica gel, 7–10% EtOAc–hexanes) gave the title compound (22.5 mg, 84%) as a white solid.

IR: 2958, 2868, 1686, 1470, 1351, 1155, 1092, 673 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.61 (d, *J* = 1.2 Hz, 1 H, Ar-H), 7.33–7.30 (m, 3 H, Ar-H), 6.57–6.55 (m, 1 H, Ar-H), 4.11–4.02 (m, 1 H, TsNC*H*), 3.64 [dd, *J* = 16.2, 3.3 Hz, 1 H, CH_2C(O)], 3.44–3.37 (m, 1 H, TsNC*H*), 3.07 [dd, *J* = 16.2, 10.5 Hz, 1 H, CH_2C(O)], 2.43 (s, 3 H, ArCH_3), 2.12–2.00 (m, 1 H, Me_2C*H*), 1.77–1.54 (m, 3 H, CH_2CH_2), 1.32–1.19 (m, 1 H, CH_2), 1.00 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.94 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 187.3, 152.6, 146.8, 143.6, 134.5, 129.9, 127.8, 118.0, 112.5, 67.5, 58.1, 46.4, 31.7, 30.4, 25.4, 21.7, 20.2, 17.7.

LR-MS (APCI+): *m*/*z* $[M]^+$ calcd for $C_{20}H_{26}NO_4S$: 376.5; found: 375.9.

1-(1-Tosylpiperidin-2-yl)butan-2-one (Table 4, Entry 8)

Following general procedure B, *N*-tosylhex-5-en-1-amine[12] (20.0 mg, 0.079 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (31.8 mg, 0.083 mmol, 1.05 equiv), 4 Å MS (40 mg), and 1.0 M Et_2Zn in hexanes (47 μL, 0.047 mmol, 0.6 equiv) and flash chromatography (silica gel, gradient 10–15% EtOAc–hexanes) gave the title compound (15.3 mg, 63%) as a colorless oil; starting material (4.9 mg, 0.019 mmol) recovered giving an 82% yield of product based on recovered starting material.

IR: 2930, 2868, 1707, 1330, 1155, 1099, 917, 826, 666 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.27 (d, *J* = 9.0 Hz, 2 H, Ar-H), 4.52–4.49 (m, 1 H, TsNC*H*), 3.80–3.75 (m, 1 H, NTsCH_2), 2.98–2.89 (m, 1 H, TsNCH_2), 2.76 [dd, *J* = 16.2, 9.3 Hz, 1 H, CH_2C(O)], 2.56 [dd, *J* = 16.2, 4.8 Hz, 1 H, CH_2C(O)], 2.41 (s, 3 H, ArCH_3), 2.41–2.35 [m, 2 H, CH_2C(O)], 1.62–1.25 (m, 6 H, CH_2), 1.01 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.9, 143.3, 138.2, 129.8, 127.2, 49.0, 42.7, 41.4, 36.5, 27.9, 24.8, 21.7, 18.5, 7.77.

LR-MS (APCI+): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{24}NO_3S$: 310.4; found: 309.9.

2-(5,5-Dibenzyltetrahydrofuran-2-yl)-1-(furan-2-yl)ethanone (Table 4, Entry 9)

Following general procedure B using 2-benzyl-1-phenylhex-5-en-2-ol (20.0 mg, 0.075 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (30.2 mg, 0.079 mmol, 1.05 equiv), 4 Å MS (38 mg), and tributyl(furan-2-yl)stannane (31 μL, 0.098 mmol, 1.3 equiv) and flash chromatography (silica gel, gradient 5–7% EtOAc–hexanes) gave the title compound (25.2 mg, 93%) as a white solid.

IR: 3028, 2924, 1665, 1567, 1470, 1078, 1015, 757, 701 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.71 (s, 1 H, Ar-H), 7.31–7.22 (m, 10 H, Ar-H), 7.14 (d, *J* = 3.3 Hz, 1 H, Ar-H), 6.56–6.55 (m, 1 H, Ar-H), 4.21–4.12 (m, 1 H, OCH), 3.05–2.70 [m, 5 H, PhCH_2, CH_2C(O)], 2.56 [dd, *J* = 15.3, 6.6 Hz, 1 H, CH_2C(O)], 1.86–1.82 (m, 2 H, CH_2), 1.68–1.58 (m, 1 H, CH_2), 0.93–0.80 (m, 1 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 187.4, 153.0, 146.5, 138.2, 131.2, 131.0, 128.1, 127.8, 126.3, 117.5, 112.3, 85.8, 75.5, 46.9, 46.6, 44.7, 32.8, 32.1.

LR-MS (APCI+): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{25}O_3$: 361.5; found: 360.9.

1-(Bicyclo[2.2.1]hept-5-en-2-yl)-2-(*syn*-5-isopropyl-1-tosylpyrrolidin-2-yl)ethanone (17)

Following general procedure B using 2-methyl-*N*-tosylhept-6-en-3-amine[1a] (**5**, 20.0 mg, 0.071 mmol, 1.0 equiv), $PdCl_2(PhCN)_2$ (28.6 mg, 0.075 mmol, 1.05 equiv), 4 Å MS (36 mg), and tributyl(vinyl)stannane (27 μL, 0.092 mmol, 1.3 equiv). Cyclopentadiene (17 μL, 0.213 mmol, 3.0 equiv) was added and the mixture stirred at –15 °C for 3 h. The mixture was then filtered through celite and purified by chromatography (silica gel, 5% EtOAc–hexanes) to yield **17** (25.5 mg, 89%) as a colorless oil; ratio *endo*/*exo* 55:45.

IR: 2958, 2868, 1700, 1344, 1162, 1092, 994, 805, 666 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.30 (d, *J* = 8.1 Hz, 2 H, Ar-H), 6.17–6.14 (m, 1 H, C*H*=CH), 5.94–5.91 (m, 1 H, CH=C*H*; one diastereomer), 5.78–5.75 (m, 1 H,

CH=C*H*; one diastereomer), 3.97–3.84 (m, 1 H, TsNC*H*), 3.41–3.33 (m, 1 H, TsNC*H*), 3.29 (br s, 1 H, C*H*CHCH), 3.23 (br s, 1 H, C*H*CHCH), 3.08–2.96 [m, 1 H, CH_2C(O)], 2.90 [br s, 1 H, C*H*C(O)], 2.66–2.55 [m, 1 H, CH_2C(O)], 2.42 (s, 3 H, ArCH_3), 2.06–1.95 (m, 1 H, Me_2C*H*), 1.79–1.53 (m, 3 H, CH_2), 1.52–1.16 (m, 5 H, CH_2), 1.01–0.89 (m, 7 H, CH_2, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 209.6, 209.3, 143.5, 138.3, 137.8, 134.6, 131.8, 131.0, 129.8, 127.9, 67.4, 57.8, 57.6, 52.4, 51.9, 50.2, 50.1, 49.9, 49.8, 46.2, 42.9, 42.8, 31.8, 31.7, 31.0, 30.9, 28.0, 27.6, 27.5, 27.0, 25.5, 21.7, 20.3, 17.8, 17.7, 13.8.

LR-MS (APCI+): *m*/*z* $[M]^+$ calcd for $C_{23}H_{31}NO_3S$: 402.6; found: 401.6.

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