Efficient Palladium-Catalysed Enamide Synthesis from Enol Triflates and Enol Tosylates

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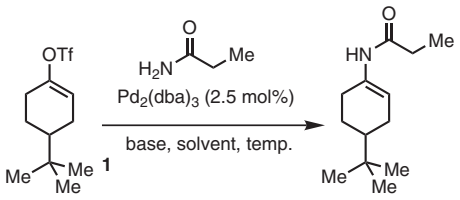
Dedicated to Professor Steven Ley on the occasion of his 60th birthday

Abstract: Catalysts generated from $Pd_2(dba)_3$ and biphenyl ligands **4** and **7** efficiently promote the coupling of amides and carbamates with unactivated vinyl triflates and tosylates, to provide enamides in good to excellent yields.

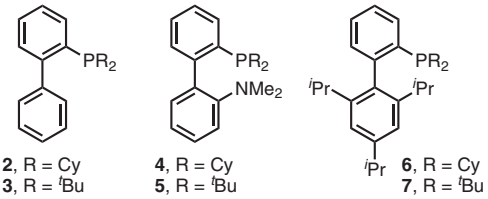
Key words: enamides, palladium, catalysis, enol triflates, enol tosylates

Enamides are important functional groups found in many natural products,[1] designed medicinal agents and synthetic intermediates.[2] Their use as substrates for enantioselective hydrogenations, allowing the preparation of enantiomerically enriched amines and amino acid derivatives, is particularly notable and represents an area of considerable activity.[3] The synthesis of enamides from the corresponding carbonyl compounds and amides is a difficult transformation, requiring harsh conditions and often producing mixtures of products.[4] Although several alternative syntheses are available,[5] the use of palladium- and copper-catalysed C–N coupling reactions have recently emerged as attractive methods to prepare these functional groups.[6] Although the palladium-based methods, involving the union of enol triflates or tosylates with amides and carbamates, have been shown to be fairly broad ranging, delivering a variety of enamide systems in good yields, they are limited in that the enol triflate or tosylate group must feature an electron-withdrawing or aryl substituent in the β-position.[7] While the copper-based methods do not suffer this limitation they are not applicable to enol triflate and tosylate coupling partners and instead require the use of vinyl halides.[8] The sulfonate substrates are more attractive as they can be readily prepared, in a regio- and stereoselective manner from the corresponding carbonyl compounds.[9] In this paper we document a palladium-based enamide synthesis that combines the attractive features of employing enol triflate and tosylate substrates, while eliminating the need for an activating functional group.

We selected the union of triflate **1** and propionamide as a suitably challenging coupling process to evaluate potential catalyst systems (Scheme 1 and Table 1). We had previously shown that the ligand BINAP used in combination Cs_2CO_3 was effective in promoting the coupling of amines with unactivated vinyl triflates;[10] however when applied to the trial amide coupling this combination proved to be poorly effective (entry 1). Palladium-catalysed aromatic C–N bond forming reactions have been considerably advanced by the discovery of a number of highly effective phosphine ligands-based on a biphenyl scaffold;[11] we elected to explore the use of several of these ligands in our test reaction. Both simple mono-substituted ligands were ineffective, as was the NMe_2/PCy_2 substituted ligand (entries 2–4). However, the $NMe_2/P(t\text{-}Bu)_2$ variant (**5**; Figure 1), used in combination with Cs_2CO_3 delivered the required enamide with a 29% conversion (entry 5). Similarly, the *tert*-butyl version of the two tri(isopropyl)-substituted ligands (**6** and **7**; Figure 1) was the most successful, providing a 52% conversion to enamide (entries 6 and 7). Employing the same ligand in combination with K_2CO_3 in *t*-BuOH increased the yield to 66% (entry 8).[12] Lowering the reaction temperature from 110 °C to 80 °C and reducing the reaction time to ten hours allowed a 98% yield of enamide to be obtained (entry 9). The increase in yield obtained with the lower reaction temperature implies product degradation under the higher temperature conditions. Useful yields can be achieved at even lower temperatures (60 °C), however the reaction required significantly longer to achieve reasonable conversion (entry 10). These final two experiments were performed using only 1.25 mol% of $Pd_2(dba)_3$.



Scheme 1



2, R = Cy
3, R = ^{t}Bu
4, R = Cy
5, R = ^{t}Bu
6, R = Cy
7, R = ^{t}Bu

Figure 1

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Table 1 Reaction Optimization[a]

Entry	Ligand	Base	Solvent	Temp. (°C)	Time (h)	Yield (%)[b]
1	BINAP	Cs_2CO_3	dioxane	115	18	10[c]
2	**2**	Cs_2CO_3	dioxane	100	20	0
3	**3**	Cs_2CO_3	dioxane	100	20	0
4	**4**	Cs_2CO_3	dioxane	100	20	0
5	**5**	Cs_2CO_3	dioxane	100	20	29[c]
6	**6**	Cs_2CO_3	dioxane	100	20	35[c]
7	**7**	Cs_2CO_3	dioxane	100	20	52[c]
8	**7**	K_2CO_3	*t*-BuOH	110	14	66
9	**7**	K_2CO_3	*t*-BuOH	80	10	98[d]
10	**7**	K_2CO_3	*t*-BuOH	60	38	78[d]

[a] Reaction conditions: triflate (1.0 equiv), amide (1.2 equiv), base (1.4 equiv), Pd:L (1:1.5) except for ligand **7** which was 1:1.3.
[b] Isolated yields.
[c] Conversion.
[d] $Pd_2(dba)_3$ (1.25 mol%).

With optimised conditions available we explored the scope of the reaction with respect to amide and triflate structure (Table 2): We first evaluated variation of the amide (and derivatives) in combination with triflate **1**. Pleasingly, alkyl, aryl and alkenyl amides all coupled with triflate **1** in good to excellent yields (entries 1–3). The presence of a potential coordinating group in the amide, as demonstrated by the reaction employing nicotinamide, had minimal effect on the coupling efficiency, with the desired enamide being obtained in 98% yield (entry 4). Using carbamates in the place of amides was also tolerated well, with the common ethyl, benzyl and *tert*-butyl carbamates all undergoing smooth coupling with triflate **1** (entries 5–7). The final variation with respect to the *N*-reaction component was to demonstrate that amines could also be coupled using the same catalyst system; the morpholine-derived enamine was obtained in 65% yield after bulb-to-bulb distillation (> 95% conversion, entry 8). Variation of the alkenyl coupling partner was investigated next; in all cases *tert*-butyl carbamate was used as the *N*-coupling partner. The two isomeric triflates generated from 2-methyl cyclohexanone both underwent smooth coupling, with no isomerisation being observed (entries 9 and 10). The cycloheptanone derived triflate also performed well (entry 11). Using the standard conditions the enol triflate used in entry 12, featuring an α-quaternary carbon centre, failed to react, however the use of ligand **4** and Cs_2CO_3 allowed the enamide to be obtained in an excellent yield. Enol tosylates generally display greater stability than their triflate counterparts, and also have the added advantage of being prepared from much lower cost reagents.[7c] The final three entries demonstrate that enol tosylates are also effective substrates for enamide synthesis; application of the standard reaction conditions allowed enamides and an enamine to be obtained in good to excellent yields (entries 13–15).

In conclusion, we have demonstrated that catalysts generated using $Pd_2(dba)_3$ and either biphenyl ligands **4** or **7** allow the efficient preparation of a range of enamides from the corresponding enol triflate or enol tosylate. Significantly, it is possible to use enol sulfonates that do not feature an activating substituent; the utility of the developed conditions has been demonstrated by the successful use of several substrates previously considered inert to amide coupling.[7b,c] Finally, the same catalyst systems can also be used to combine triflate or tosylate substrates with amines to deliver enamine products. Application of the methodology to heterocycle synthesis is underway and will be reported in due course.

NMR spectra were obtained on a Bruker Avance 300 spectrometer, with TMS as an internal standard. *J* values are given in Hz. IR spectra were recorded on a Perkin-Elmer 1600 FT IR spectrophotometer, using NaCl discs. Mass spectrometry measurements were performed at the EPSRC National Mass Spectrometry Service Centre, University of Wales Swansea. All anhydrous solvents were freshly distilled under N_2 prior to use. Dioxane was distilled over CaH_2 and stored over 4 Å molecular sieves, *t*-BuOH was distilled before use. All glassware was dried in an oven and allowed to cool under N_2 prior to use. Column chromatographic separation was carried out using silica gel (35–70 mesh) pre-washed with 5% Et_3N–petroleum ether. Light petroleum ether (PE) with bp range 40–60 °C was used. All commercial reagents were used as obtained. Phosphine ligands were purchased from Aldrich chemical company. Enol triflate **1**,[13] and those used in entries 9 and 10,[14] and entries 11 and 12[15] and enol tosylates used in entries 13 and 14[7c] were prepared according to literature procedures.

Table 2 Variation of *N*- and Alkenyl-Coupling Partner[a]

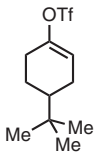
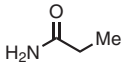
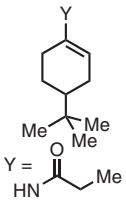
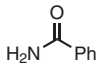
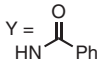
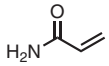
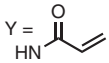
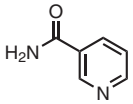
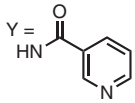
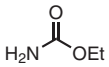
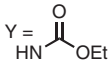
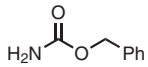
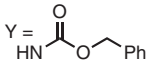
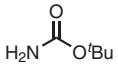
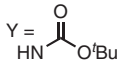
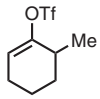
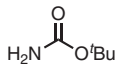
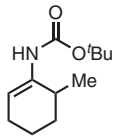
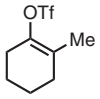
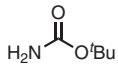
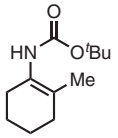
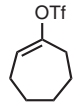
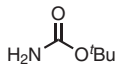
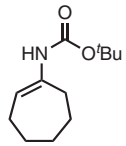
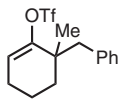
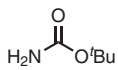
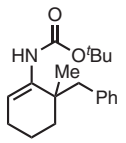
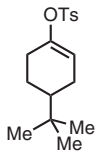
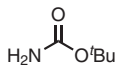
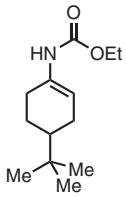
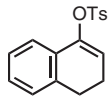
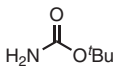
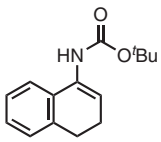
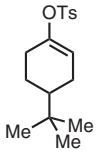
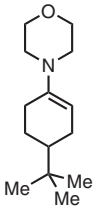
Entry	Alkene	*N*-group	Product	Yield (%)[b]
1[c]				98
2[d]	**1**			97
3	**1**			76
4[d]	**1**			98
5	**1**			93
6[d]	**1**			90
7[d]	**1**			88
8	**1**			66[e]
9				80
10				88
11[f]				61
12[g]				75
13				83

Table 2 Variation of *N*- and Alkenyl-Coupling Partner[a] (continued)

Entry	Alkene	*N*-group	Product	Yield (%)[b]
14				93
15				54[e]

[a] Reaction conditions: triflate/tosylate (1.0 equiv), amide/amine (1.2 equiv), K_2CO_3 (2.0 equiv), $Pd_2(dba)_3$ (1.25 mol%), ligand **7** (3.35 mol%), *t*-BuOH, 80 °C.
[b] Isolated yields.
[c] K_2CO_3 (1.40 equiv) used.
[d] K_2CO_3 (2.50 equiv) used.
[e] Conversion > 95%.
[f] K_2CO_3 (2.5 equiv), $Pd_2(dba)_3$ (2.50 mol%), ligand **7** (6.70 mol%) used.
[g] Ligand **4** (3.75 mol%), Cs_2CO_3 (1.4 equiv), dioxane, 100 °C.

Cross-Coupling of Enol Triflates and Tosylates with *N*-Compounds; Typical Procedure

N-(4-*tert*-Butylcyclohexen-1-yl)-*tert*-butylcarbamate (Table 2, Entry 7)

K_2CO_3 (179 mg, 1.298 mmol) and *tert*-butylcarbamate (73 mg, 0.6230 mmol) were added to an oven-dried flask charged with $Pd_2(dba)_3$ (6 mg, 6.490 μmol) and ligand **7** (7.4 mg, 17.43 μmol) under N_2. The flask was flushed with N_2 and the reagents suspended in *t*-BuOH (1.04 mL). 4-*tert*-Butylcyclohexen-1-yl triflate (**1**, 149 mg, 0.5192 mmol) was added and the reaction was heated at 80 °C for 5 h under N_2. After cooling, the reaction mixture was diluted with Et_2O (5 mL) and filtered through a celite pad and washed with Et_2O (30 mL). The filtrate was reduced in vacuo. The product was purified via flash column chromatography (1% Et_2O–PE) to yield the carbamate (116 mg, 88%); viscous, pale amber oil; R_f 0.27 (5% Et_2O–petroleum ether).

IR (Nujol): 3446, 3343, 1716, 1678, 1512 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.86 (s, 9 H, *t*-Bu), 1.16–1.33 (m, 2 H), 1.46 (s, 9 H, O*t*-Bu), 1.78–1.91 (m, 2 H), 1.99–2.29 (m, 3 H), 5.49–5.62 (br s, 1 H, NH), 5.77–5.86 (m, 1 H, C=CH).

^{13}C NMR ($CDCl_3$): δ = 23.8, 25.3, 27.2, 28.3, 29.4, 32.1, 43.8, 79.7, 109.2, 132.1, 153.0.

CI–MS: *m*/*z* (%) = 254.2 (45) $[M + H]^+$, 215.2 (10), 154.0 (100) $[M + 2 H - CO_2t\text{-}Bu]^+$, 52.2 (10).

HRMS (ES^+): *m*/*z* calcd for $C_{15}H_{28}NO_2$: 254.2115; found: 254.2110.

N-(4-*tert*-Butylcyclohexen-1-yl)propionamide (Table 2, Entry 1)

Prepared following the general procedure, using propionamide (46 mg, 0.6230 mmol) and K_2CO_3 (100 mg, 0.7969 mmol), heating for 10 h. The product was isolated via flash column chromatography (40% Et_2O–PE) to yield the enamide (107 mg, 98%); off-white solid; mp 107.5–110 °C; R_f 0.15 (50% Et_2O–PE).

IR (Nujol): 3292, 1659, 1552, 1530 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.86 (s, 9 H, *t*-Bu), 1.16 (t, *J* = 7.5 Hz, 3 H), 1.21–1.30 (m, 2 H), 1.77–1.93 (m, 2 H), 2.05–2.33 (m, 3 H), 2.23 (q, *J* = 7.5 Hz, 2 H), 6.05–6.12 (m, 1 H, C=CH), 6.18–6.35 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 9.8, 23.7, 25.4, 27.2, 29.5, 30.6, 32.1, 43.6, 112.7, 132.3, 171.9.

CI–MS: *m*/*z* (%) = 227.2 (15) $[M + NH_4]^+$, 210.1 (100) $[M + H]^+$, 154.1 (10) $[M + 2 H - COEt]^+$, 91.0 (10), 52.2 (50).

HRMS (ES^+): *m*/*z* calcd for $C_{13}H_{24}NO$: 210.1852; found: 210.1851.

N-(4-*tert*-Butylcyclohexen-1-yl)benzamide (Table 2, Entry 2)

Prepared following the general procedure, using benzamide (75 mg, 0.6230 mmol), heating for 13 h. The product was isolated via flash column chromatography (10% Et_2O–PE) to yield the enamide (130 mg, 97%); off-white solid; mp 107.5–110.2 °C; R_f 0.23 (25% Et_2O–PE).

IR (Nujol): 3318, 1649, 1602 (w), 1581 (w), 1540 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.89 (s, *t*-Bu, 9 H), 1.19–1.41 (m, 2 H), 1.81–2.00 (m, 2 H), 2.11–2.46 (m, 3 H), 6.19–6.26 (m, 1 H, C=CH), 6.91–7.05 (br s, 1 H, NH), 7.39–7.53 (m, 3 H, ArH), 7.72–7.78 (m, 2 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 22.8, 25.5, 27.2, 29.5, 32.2, 43.6, 113.9, 126.8, 128.6, 131.4, 132.6, 135.4, 165.7.

CI–MS: *m*/*z* (%) = 258.2 (100) $[M + H]^+$, 154.1 (10) $[M + 2 H - COPh]^+$, 52.2 (75).

HRMS (ES^+): *m*/*z* calcd for $C_{17}H_{24}NO$: 258.1852; found: 258.1851.

N-(4-*tert*-Butylcyclohexen-1-yl)acrylamide (Table 2, Entry 3)

Prepared following the general procedure, using acrylamide (44 mg, 0.6230 mmol) and K_2CO_3 (144 mg, 1.038 mmol), heating for 20 h. The product was isolated via flash column chromatography (40% Et_2O–PE) to yield the enamide (82 mg, 76%); off-white solid; mp 117.5–120 °C; R_f 0.22 (50% Et_2O–petroleum ether).

IR (Nujol): 3281, 1662, 1627 (w), 1558 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.87 (s, 9 H, *t*-Bu), 1.20–1.35 (m, 2 H), 1.79–1.95 (m, 2 H), 2.10–2.38 (m, 3 H), 5.65 (dd, *J* =1.5, 10.1 Hz, 1 H, *cis*-CH=CH*H*), 6.09 (dd, *J* = 10.1, 16.9 Hz, 1 H, C*H*=CHH), 6.16–6.23 (m, 1 H, C=CH), (dd, *J* = 1.0, 16.9 Hz, 1 H, *trans*-CH=C*H*H), 6.37–6.53 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 23.8, 25.3, 27.2, 29.5, 32.1, 43.6, 113.7, 126.8, 131.4, 132.2, 163.4.

CI–MS: *m*/*z* (%) = 225.2 (25) $[M + NH_4]^+$, 208.2 (100) $[M + H]^+$, 154.1 (15) $[M + 2\,H - COCH{=}CH_2]^+$, 52.2 (53).

HRMS (ES^+): *m*/*z* calcd for $C_{13}H_{22}NO$: 208.1696; found: 208.1696.

***N*-(4-*tert*-Butylcyclohexen-1-yl)nicotinamide (Table 2, Entry 4)**
Prepared following the general procedure, using nicotinamide (76 mg, 0.6230 mmol), heating for 24 h. The product was isolated via flash chromatography (EtOAc) to yield the enamide (132 mg, 98%); off-white solid; mp 92–95 °C; R_f 0.37 (2.5% MeOH–EtOAc).

IR (Nujol): 3363, 1670, 1657, 1588 (w), 1551 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.89 (s, 9 H, *t*-Bu), 1.26–1.40 (m, 2 H), 1.85–1.99 (m, 2 H), 2.13–2.47 (m, 3 H), 6.17–6.26 (m, 1 H, C=CH), 7.05–7.16 (br s, 1 H, NH), 7.38 (ddd, *J* = 0.8, 4.8, 7.9 Hz, 1 H, ArH), 8.09 (ddd, *J* = 1.7, 2.3, 7.9 Hz, 1 H, ArH), 8.70 (app. dd, *J* = 1.5, 4.8 Hz, 1 H, ArH), 8.95 (d, *J* = 1.7 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 23.8, 25.6, 27.2, 29.4, 32.2, 43.5, 114.9, 123.5, 131.0, 132.4, 135.1, 147.6, 152.1, 163.7.

CI–MS: *m*/*z* (%) = 259.2 $[M + H]^+$ (100), 244.2 (10), 154.1 (5) $[M + 2\,H - COC_5H_4N]^+$, 123.0 (10), 100.1 (10), 52.2 (32).

HRMS (ES^+): *m*/*z* calcd for $C_{16}H_{23}N_2O$: 159.1805; found: 259.1807.

***N*-(4-*tert*-Butylcyclohexen-1-yl)ethylcarbamate (Table 2, Entry 5)**
Prepared following the general procedure, using urethane (56 mg, 0.6230 mmol) and K_2CO_3 (144 mg, 1.038 mmol), heating for 22 h. The product was isolated via flash column chromatography (4% Et_2O–PE) to yield the carbamate (109 mg, 93%); pale amber oil; R_f 0.09 (5% Et_2O–PE).

IR (liquid film): 3326, 1713, 1681, 1538 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.86 (s, 9 H, *t*-Bu), 1.17–1.34 (m, 2 H), 1.25 (t, *J* = 7.1 Hz, 3 H), 1.75–1.94 (m, 2 H), 2.04–2.31 (m, 3 H), 4.12 (q, *J* = 7.1 Hz, 2 H), 5.59–5.74 (br s, 1 H, NH), 5.75–5.84 (m, 1 H, C=CH).

^{13}C NMR ($CDCl_3$): δ = 14.6, 23.8, 25.3, 27.2, 29.3, 32.1, 43.7, 60.7, 110.0, 132.0, 153.8.

CI–MS: *m*/*z* (%) = 226.2 (100) $[M + H]^+$, 154.2 (50) $[M + 2\,H - CO_2Et]^+$, 61.2 (17).

HRMS (ES^+): *m*/*z* calcd for $C_{13}H_{24}NO_2$: 226.1802; found: 226.1800.

***N*-(4-*tert*-Butylcyclohexen-1-yl)benzylcarbamate (Table 2, Entry 6)**
Prepared following the general procedure, using benzylcarbamate (94 mg, 0.6.230 mmol), heating for 24 h. The product was isolated via flash column chromatography (1% Et_2O–PE) to yield the carbamate (134 mg, 90%); off-white solid; mp 72.2–74.8 °C; R_f 0.15 (10% Et_2O–PE).

IR (Nujol): 3350, 1728, 1708, 1546, 1497 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.87 (s, 9 H, *t*-Bu), 1.16–1.34 (m, 2 H), 1.76–1.93 (m, 2 H), 2.04–2.31 (m, 3 H), 5.11 (s, 2 H, CH_2Ar), 5.69–5.89 (br m, 2 H), 7.28–7.39 (m, 5 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 23.8, 25.3, 27.2, 29.2, 32.1, 43.7, 66.5, 110.2, 128.2, 128.2, 128.5, 131.8, 136.3, 153.4.

CI–MS: *m*/*z* (%) = 288.2 (100) $[M + H]^+$, 244.2 (10), 154.1 (90) $[M + 2\,H - CO_2Bn]^+$, 126.1 (10), 108.0 (10).

HRMS (ES^+): *m*/*z* calcd for $C_{18}H_{26}NO_2$: 288.1958; found: 288.1961.

***N*-(4-*tert*-Butylcyclohexen-1-yl)morpholine (Table 2, Entry 8)**
Prepared following the general procedure, using morpholine (54 mg, 0.6230 mmol), heating for 20 h. The product was isolated via Kugelrohr distillation (collecting between 125–135 °C/3.5 mmHg) to yield the enamine (76 mg, 66%); white solid; mp 42–44.5 °C.

IR (Nujol): 2924, 2854, 1652 cm^{-1}.

^{1}H NMR (C_6D_6): δ = 0.87 (s, 9 H, *t*-Bu), 1.09–1.25 (m, 2 H), 1.68–1.79 (m, 1 H), 1.82–2.01 (m, 3 H), 2.04–2.17 (m, 1 H), 2.54 (app. ddd, *J* = 4.7, 5.0, 11.8 Hz, 2 H), 2.64 (app. ddd, *J* = 4.6, 5.1, 11.8 Hz, 2 H), 3.59 (app. t, *J* = 4.8 Hz, 4 H), 4.58–4.62 (m, 1 H, C=CH).

^{13}C NMR (C_6D_6): δ = 25.4, 26.9, 28.0, 29.0, 32.8, 45.4, 49.6, 67.7, 100.7, 146.4.

***N*-(6-Methylcyclohexen-1-yl)-*tert*-butylcarbamate (Table 2, Entry 9)**
Prepared following the general procedure, using 6-methylcyclohexen-1-yl triflate (127 mg, 0.5192 mmol) and K_2CO_3 (144 mg, 1.038 mmol), heating for 14 h. The carbamate (88 mg, 80%) was obtained in an essentially pure form following filtration through a celite pad, washing with hexane; amber oil; R_f 0.14 (5% Et_2O–PE).

IR (Nujol): 3327, 1732, 1668, 1513 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.07 (d, *J* = 7.0 Hz, 3 H, Me), 1.46 (s, 9 H, O*t*-Bu), 1.49–1.67 (m, 3 H), 1.72–1.84 (m, 1 H), 2.03–2.11 (m, 2 H), 2.16–2.32 (m, 1 H), 5.45–5.61 (br s, 1 H, NH), 5.81–5.91 (m, 1 H, C=CH).

^{13}C NMR ($CDCl_3$): δ = 18.9, 19.3, 24.4, 28.3, 30.7, 31.4, 79.6, 109.9, 136.2, 153.6.

***N*-(2-Methylcyclohexen-1-yl)-*tert*-butylcarbamate (Table 2, Entry 10)**
Prepared following the general procedure, using 2-methylcyclohexen-1-yl triflate (127 mg, 0.5192 mmol) and K_2CO_3 (144 mg, 1.038 mmol), heating for 5 h. The product was isolated via flash column chromatography (2.5% Et_2O–PE) to yield the carbamate (96 mg, 88%); off-white solid; mp 68–70.5 °C; R_f 0.12 (5% Et_2O–PE).

IR (Nujol): 3322, 1736, 1691, 1508 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.45 (s, 9 H, O*t*-Bu), 1.51–1.69 (m, 7 H), 1.96–2.05 (m, 2 H), 2.15–2.25 (m, 2 H), 5.36–5.58 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 18.1, 22.6, 23.2, 28.3, 30.9, 79.3, 124.3, 126.6.

CI–MS: *m*/*z* (%) = 229.1 (10) $[M + NH_4]^+$, 212.1 (30) $[M + H]^+$, 173.1 (100) $[M + H + NH_4 - t\text{-Bu}]^+$, 112.0 (90) $[M + 2\,H - CO_2t\text{-Bu}]^+$, 90 (20).

HRMS (ES^+): *m*/*z* calcd for $C_{12}H_{22}NO_2$: 212.1645; found: 212.1645.

***N*-Cyclohepten-1-yl-*tert*-butylcarbamate (Table 2, Entry 11)**
Prepared following the general procedure, using cyclohepten-1-yl triflate (127 mg, 0.5192 mmol) and a 5 mol% catalyst loading, heating for 5 h. The product was isolated via flash column chromatography (1% Et_2O–PE) to yield the carbamate (67 mg, 61%); pale amber solid; mp 49–52.5 °C; R_f 0.20 (5% Et_2O–PE).

IR (Nujol): 3315, 1737, 1690, 1507 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.45 (s, 9 H, O*t*-Bu), 1.45–1.63 (m, 4 H), 1.65–1.76 (m, 2 H), 2.10 (app. dd, *J* = 6.8, 10.9 Hz, 2 H), 2.23–2.29 (m, 2 H), 5.62–5.73 (br s, 1 H, NH), 5.91 (t, *J* = 6.7 Hz, 1 H, C=CH).

^{13}C NMR ($CDCl_3$): δ = 26.0, 26.5, 27.1, 28.3, 32.0, 33.9, 79.7, 114.6, 138.9, 153.2.

CI–MS: *m*/*z* (%) = 212.2 (60) $[M + H]^+$, 112.0 (100) $[M + 2\,H - CO_2t\text{-Bu}]^+$, 58.1 (15).

HRMS (ES^+): *m*/*z* calcd for $C_{12}H_{22}NO_2$: 212.1645; found: 212.1648.

N-(6-Benzyl-6-methylcyclohexen-1-yl)-*tert*-butylcarbamate (Table 2, Entry 12)

Prepared using a modified version of the general procedure, using 6-benzyl-6-methylcyclohexen-1-yl triflate (174 mg, 0.5192 mmol), ligand **4** (7.7 mg, 19.47 μmol) and Cs_2CO_3 as the base (237 mg, 0.7269 mmol), heating in dioxane (1.04 mL) at 100 °C for 17 h. The product was isolated via flash column chromatography (1% Et_2O–PE) to yield the carbamate (118 mg, 75%); off-white solid; mp 64–66 °C; R_f 0.17 (5% Et_2O–PE).

IR (Nujol): 3400, 1737, 1706, 1514 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.05 (s, 3 H, Me), 1.23–1.38 (m, 1 H), 1.46 (s, 9 H, O*t*-Bu), 1.50–1.70 (m, 3 H), 2.05–2.15 (m, 2 H), 2.69 (d, *J* = 13.4 Hz, 1 H), 2.76 (d, *J* = 13.4 Hz, 1 H), 5.34–5.46 (br s, 1 H, NH), 6.00 (t, *J* = 4.0 Hz, 1 H), 7.13–7.18 (m, 2 H, ArH), 7.18–7.31 (m, 3 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 18.4, 24.8, 25.3, 28.3, 35.4, 37.8, 45.2, 79.5, 114.4, 126.2, 127.9, 130.4, 137.3, 138.1, 153.8.

CI–MS: *m*/*z* (%) = 302.3 (55) $[M + H]^+$, 263.2 (15), 202.1 (90) $[M + 2\ H - CO_2t\text{-Bu}]^+$, 112.1 (25).

HRMS (ES^+): *m*/*z* calcd for $C_{19}H_{28}NO_2$: 302.2115; found: 302.2114.

Coupling of 4-*tert*-Butylcyclohexen-1-yl Tosylate with *tert*-Butylcarbamate (Table 2, Entry 13)

Prepared following the general procedure, using 4-*tert*-butylcyclohexen-1-yl tosylate (160 mg, 0.5192 mmol), heating for 5 h. The product was isolated via flash column chromatography (1% Et_2O–PE) to yield the carbamate (109 mg, 83%); viscous pale amber oil. All the spectroscopic data were as above.

N-(3,4-Dihydronaphthalen-1-yl)-*tert*-butylcarbamate (Table 2, Entry 14)

Prepared following the general procedure, using 1,2-dihydro-4-naphthyl tosylate (156 mg, 0.5192 mmol), heating for 16 h. The product was isolated via flash column chromatography (3% Et_2O–PE) to yield the carbamate (119 mg, 93%); pale yellow solid; mp 60.5–62.8 °C; R_f 0.19 (10% Et_2O–PE).

IR (Nujol): 3315, 1740, 1699, 1527 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.50 (s, 9 H, O*t*-Bu), 2.30–2.39 (m, 2 H), 2.72–2.79 (m, 2 H), 5.95–6.08 (br s, 1 H, NH), 6.25–6.37 (m, 1 H, C=CH), 7.13–7.23 (m, 4 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 22.1, 27.8, 28.3, 80.1, 115.9, 120.4, 126.4, 127.4, 127.8, 131.6, 131.8, 137.0, 153.9.

CI–MS: *m*/*z* (%) = 246.2 (50) $[M + H]^+$, 172.0 (100) $[M - O t\text{-Bu}]^+$, 146.0 (95) $[M + 2\ H - CO_2t\text{-Bu}]^+$, 52.2 (50).

HRMS (ES^+): *m*/*z* calcd for $C_{15}H_{20}NO_2$: 246.1489; found: 246.1491.

Coupling of 4-*tert*-Butylcyclohexen-1-yl Tosylate with Morpholine (Table 2, Entry 15)

Prepared following the general procedure, using 4-*tert*-butylcyclohexen-1-yl tosylate (160 mg, 0.5192 mmol) and morpholine (54 mg, 0.6.230 mmol) and a 5 mol% catalyst loading, heating for 36 h. The product was isolated via Kugelrohr distillation (collecting between 105–120 °C/0.8 mmHg) to yield the enamine (63 mg, 54%) as a white solid. All the spectroscopic data were as above.

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