Intramolecular Pd-Catalyzed Carboetherification and Carboamination. Influence of Catalyst Structure on Reaction Mechanism and Product Stereochemistry.

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Supporting Information

Experimental procedures for synthesis of substrates, characterization data for all new compounds, and descriptions of stereochemical assignments with supporting crystallographic structural data (38 pages).

Contents

General. All reactions were carried out under an argon or nitrogen atmosphere in oven- or flame-dried glassware. All reagents were purchased from commercial sources and were used as obtained unless otherwise noted. Tris(dibenzylideneacetone)dipalladium (0) and all phosphine ligands were

purchased from Strem Chemical Co. and used without further purification. 3-(2-bromophenyl)propanal (**S1**)[1] and *E*-7-(2-bromophenyl)hept-4-enoic acid ethyl ester (**S2**)[2] were prepared according to literature procedures. Toluene, diethyl ether, THF, and methylene chloride were purified using a Glass Contour solvent purification system. Aniline was purified by distillation from calcium hydride under nitrogen. The regiochemistry of the heterocyclic products was assigned on the basis of ^{1}H NMR 2-D COSY experiments; stereochemistry was assigned on the basis of x-ray crystallography and/or ^{1}H NMR nOe experiments. Ratios of diastereomers were determined by ^{1}H NMR and/or capillary GC analysis. Yields refer to isolated yields of compounds estimated to be ≥95% pure as determined by ^{1}H NMR, and either capillary GC or combustion analysis. The yields reported in the supporting information describe the result of a single experiment, whereas the yields reported in Tables 1–2, Schemes 2–3, and eq 2–7 are average yields of two or more experiments. Thus, the yields reported in the supporting information may differ from those shown in Tables 1–2, Schemes 2–3, and eq 2–7.

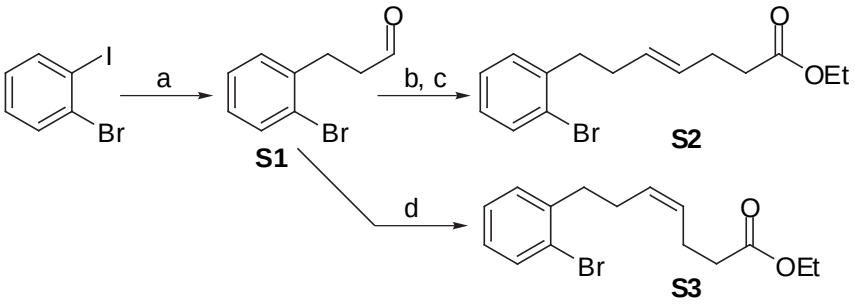
Synthesis of Substrates

Synthesis of Substrate Precursors S2 and S3

The substrates employed in these studies were generated from *E*-7-(2-bromophenyl)hept-4-enoic acid ethyl ester (**S2**) or *Z*-7-(2-bromophenyl)hept-4-enoic acid ethyl ester (**S3**), which served as common intermediates for the generation of all substrates employed in the intramolecular carboetherification and carboamination reactions. The esters were prepared from 3-(2-bromophenyl)propanal (**S1**),[1] which was synthesized via Heck-coupling of allyl alcohol with 1-bromo-2-iodobenzene. Aldehyde **S1** was elaborated to *E*-ester **S2** via vinyl Grignard

addition followed by orthoester Claisen rearrangement,[2] and the *Z*-ester **S3** was obtained via Wittig olefination of **S1** (Scheme S1).

Scheme S1. Synthesis of Substrate Precursors[a]



a. Conditions: (a) Allyl Alcohol, Bu_4NCl, $NaHCO_3$, cat. $Pd(OAc)_2$, DMF, 40 °C, 80%; (b) vinylmagnesium bromide, THF, 0 °C, 64%; (c) triethylorthoacetate, propionic acid, 80–150 °C, 70%; (d) $BrPh_3P(CH_2)_3CO_2Et$, KO*t*Bu, THF, 0 °C, 81%.

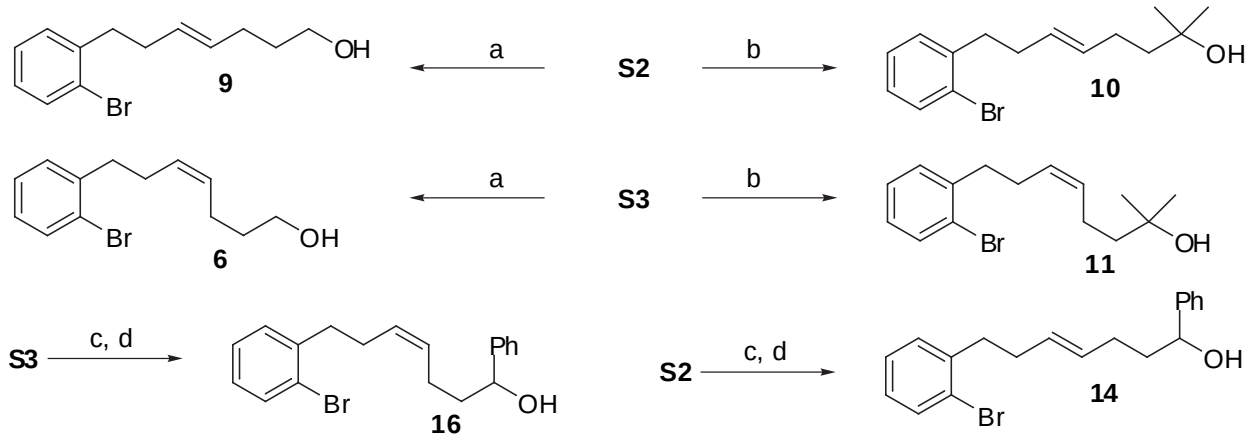
***Z*-7-(2-Bromophenyl)hept-4-enoic acid ethyl ester (S3).** A flame-dried flask equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with 4-(ethoxycarbonyl)butyltriphenylphosphonium bromide[3] (17.72 g, 38.77 mmol) and THF (180 mL). The flask was cooled to –78 °C, solid potassium *t*-butoxide (4.34 g, 38.77 mmol) was added, and the resulting yellow solution was stirred at –78 °C for 45 minutes. A solution of 3-(*o*-bromophenyl)propanal[2] (7.12 g, 33.43 mmol) in THF (20 mL) was then added and the reaction mixture was stirred for an additional 45 minutes at –78 °C then warmed to room temperature over several hours. After the starting aldehyde had been consumed as judged by TLC analysis

(ca. 8 h) the reaction mixture was quenched with water and extracted with ethyl acetate (3 x 200 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by flash column chromatography using 5% ethyl acetate/hexanes as the eluant to afford 8.46 g (81%) of the title compound as a colorless oil. The alkene configuration was judged to be >95% *Z* by NMR and GC analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.4 Hz, 1 H), 7.25–7.20 (m, 2 H), 7.07–7.03 (m, 1 H), 5.52–5.35 (m, 2 H), 4.12 (q, *J* = 7.2 Hz, 2 H), 2.80–2.76 (m, 2 H), 2.41–2.22 (m, 6 H), 1.25 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 141.2, 133.0, 130.8, 129.8, 128.9, 127.8, 127.5, 124.6, 60.5, 36.3, 34.5, 27.7, 23.0, 14.5; IR (film) 2978, 1734 cm^{-1}; MS (EI) 310.0562 (310.0568 calcd for $C_{15}H_{19}BrO_2$).

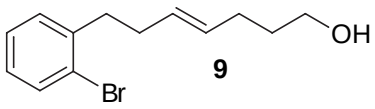
Synthesis of Substrates Bearing Tethered Alcohols.

Esters **S2** and **S3** were converted to substrates bearing tethered alcohol groups as shown in Scheme S2. Treatment of **S2** and **S3** with $LiAlH_4$ provided primary alcohols **9** and **6**. Tertiary alcohols **10** and **11** were prepared by treatment of **S2** and **S3** with methylmagnesium bromide. Secondary alcohols **14** and **16** were generated by oxidation of **9** and **6** with SO_3•pyr/dmso followed by treatment of the resulting aldehydes with phenylmagnesium bromide. Experimental procedures and characterization data are given below.

Scheme S2. Synthesis of Substrates Bearing Alcohol Nucleophiles[a]

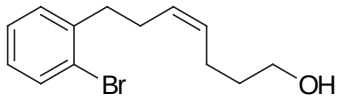


a. Conditions: (a) $LiAlH_4$, Et_2O, 69% from *E*-substrate, 80% from *Z*-substrate; (b) MeMgBr, THF, 0 °C-rt, 76% from *E*-substrate, 71% from *Z*-substrate; (c) SO_3•pyr, Et_3N, DMSO, CH_2Cl_2, 74% from *E*-substrate, 85% from *Z*-substrate; (d) PhMgBr, THF, 0 °C-rt, 96% from *E*-substrate, 70% from *Z*-substrate.



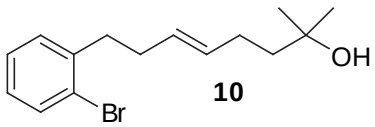
***E*-7-(2-Bromophenyl)hept-4-en-1-ol (9).** A flame-dried flask equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with *E*-7-(2-bromophenyl)hept-4-enoic acid ethyl ester (1.04 g, 3.34 mmol) and diethyl ether (15 mL). The solution was cooled to 0 °C, a solution of $LiAlH_4$ (6.6 mL, 6.6 mmol, 1 M in diethyl ether) was added dropwise, and the reaction mixture was warmed to room temperature and stirred for 8 h. The reaction mixture was then cooled to 0 °C and water (1 mL) was added dropwise followed by 10 M NaOH (2 mL) and additional water (3 mL). The resulting mixture was decanted, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was then purified by flash chromatography using 10% ethyl acetate/hexanes as the eluant to afford 620 mg (69%) of the title compound as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.0 Hz, 1 H),

7.24–7.18 (m, 2 H), 7.07–7.03 (m, 1 H), 5.55–5.41 (m, 2 H), 3.62 (app. q, J = 6.0 Hz , 2 H), 2.81–2.77 (m, 2 H), 2.34–2.28 (m, 2 H), 2.11–2.05 (m, 2 H), 1.65–1.57 (m, 2 H), 1.26–1.22 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 133.0, 130.6, 130.7, 129.9, 127.7, 127.5, 124.7, 62.7, 36.4, 32.9, 32.5, 29.0; IR (film) 3341, 2931, 1566 cm^{-1}. Anal calcd for $C_{13}H_{17}BrO$: C, 58.01; H, 6.37. Found: C, 58.21; H, 6.37.



6

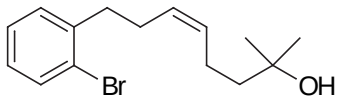
***Z*-7-(2-Bromophenyl)hept-4-en-1-ol (6).** Treatment of *Z*-7-(2-bromophenyl)hept-4-enoic acid ethyl ester (3.81 g, 12.25 mmol) with $LiAlH_4$ (24 mL, 24 mmol, 1 M in diethyl ether) using a procedure analogous to that described above for the synthesis of **9** afforded 2.64 g (80%) of the title compound as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.0 Hz, 1 H), 7.25–7.20 (m, 2 H), 7.07–7.03 (m, 1 H), 5.51–5.39 (m, 2 H), 3.58 (t, J = 6.4 Hz, 2 H), 2.80–2.76 (m, 2 H), 2.41–2.35 (m, 2 H), 2.11–2.05 (m, 2 H), 1.60–1.52 (m, 2 H), 1.24 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 132.9, 130.8, 130.3, 129.1, 127.7, 127.5, 124.6, 62.6, 36.3, 32.6, 27.7, 23.7; IR (film) 3336, 3005 cm^{-1}. Anal calcd for $C_{13}H_{17}BrO$: C, 58.01; H, 6.37. Found: C, 58.41; H, 6.48.



10

***E*-8-(2-Bromophenyl)-2-methyloct-5-en-2-ol (10).** A flame-dried flask equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with *E*-7-(2-bromophenyl)hept-4-enoic acid ethyl ester (0.723 g, 2.32 mmol) and diethyl ether (8 mL). The

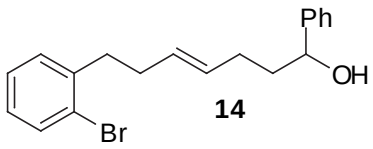
reaction mixture was cooled to 0 °C and methylmagnesium bromide (2.3 mL, 6.97 mmol, 3 M in THF) was added slowly. The resulting mixture was warmed to room temperature and stirred for 8 h. The reaction mixture was then quenched with aqueous NH_4Cl and transferred to a separatory funnel. The aqueous layer was extracted with ethyl acetate (3 x 100 mL) and the combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The crude reaction mixture was purified by flash chromatography using 5% ethyl acetate/hexanes as the eluant to afford 525 mg (76%) of the title compound as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 1 H), 7.24–7.18 (m, 2 H), 7.07–7.02 (m, 1 H), 5.56–5.44 (m, 2 H), 2.78 (t, *J* = 7.6 Hz, 2 H), 2.33-2.28 (m, 2 H), 2.12–2.05 (m, 2 H), 1.55–1.51 (m, 2 H), 1.31 (s, 1 H), 1.22 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 132.9, 131.4, 130.6, 129.3, 127.7, 127.5, 124.7, 71.2, 43.6, 36.4, 32.9, 29.5, 27.8; IR (film) 3380, 2966, 1566 cm^{-1}. Anal calcd for $C_{15}H_{21}BrO$: C, 60.61; H, 7.12. Found: C, 60.78; H, 7.21.



11

***Z*-8-(2-Bromophenyl)-2-methyloct-5-en-2-ol (11).** Treatment of 1.22 g (3.92 mmol) of *Z*-7-(2-bromophenyl)hept-4-enoic acid ethyl ester with methylmagnesium bromide (3.9 mL, 11.8 mmol, 3 M in Et_2O) using a procedure analogous to that described above for the synthesis of **10** afforded 827 mg (71%) of the title compound as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 1 H), 7.24–7.18 (m, 2 H), 7.07–7.02 (m, 1 H), 5.48–5.39 (m, 2 H), 2.79 (t, *J* = 7.6 Hz, 2 H), 2.42–2.36 (m, 2 H), 2.08–2.02 (m, 2 H), 1.43 (s, br, 1 H), 1.40–1.36 (m, 2 H), 1.18 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 133.0, 131.0, 130.9, 128.6, 127.8, 127.5,

124.7, 71.1, 43.7, 36.4, 29.4, 27.7, 22.5; IR (film) 3388, 2966, 1566 cm^{-1}. Anal calcd for $C_{15}H_{21}BrO$: C, 60.61; H, 7.12. Found: C, 60.80; H, 7.10.

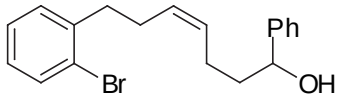


14

***E*-7-(2-Bromophenyl)-1-phenylhept-4-en-1-ol (14).** A flame-dried flask equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with alcohol **9** (2.19 g, 8.17 mmol), methylene chloride (20 mL), and triethylamine (5.1 mL, 36.8 mmol). The flask was cooled to 0 °C and DMSO (23.2 mL, 327 mmol) was added to the reaction mixture followed by SO_3·pyridine (4.03 g, 25.3 mmol). The resulting suspension was stirred at 0 °C for 1 h then warmed to room temperature and stirred for 7 h. The reaction mixture was quenched with aqueous $NaHCO_3$ and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 200 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography using 5% ethyl acetate/hexanes as the eluant to provide 1.63 g (74%) of *E*-7-(2-Bromophenyl)-1-phenylhept-4-en-1-al as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.75 (s, 1 H), 7.54–7.50 (m, 1 H), 7.25–7.16 (m, 2 H), 7.08–7.02 (m, 1 H), 5.58–5.38 (m, 2 H), 2.81–2.75 (m, 2 H), 2.51–2.46 (m, 2 H), 2.36–2.27 (m, 4 H).

A flame-dried flask equipped with a magnetic stirbar was charged with phenylmagnesuium bromide (12 mL, 12.0 mmol, 1 M in THF) and cooled to 0 °C. A solution of *E*-7-(2-bromophenyl)-1-phenylhept-4-en-1-al (965 mg, 3.61 mmol) in THF (10 mL) was added, and the reaction mixture was warmed to room temperature and stirred for 8 h. The reaction mixture was

quenched with aqueous NH_4Cl, and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography using 5% ethyl acetate/hexanes as the eluant to afford 1.19 g (96%) of the title compound as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 6.8 Hz, 1 H), 7.37–7.32 (m, 4 H), 7.29–7.27 (m, 1 H), 7.24–7.18 (m, 2 H), 7.06–7.02 (m, 1 H), 5.54–5.43 (m, 2 H), 4.65 (dd, *J* = 4.4, 6.0 Hz, 1 H), 2.80–2.77 (m, 2 H), 2.34–2.29 (m, 2 H), 2.14–2.02 (m, 2 H), 1.89–1.82 (m, 1 H), 1.79–1.72 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 141.3, 132.9, 130.6, 130.5, 129.9, 128.6, 127.7, 127.6, 127.4, 126.1, 124.6, 74.1, 38.8, 36.3, 32.9, 29.0; IR (film) 3365 cm^{-1}. Anal calcd for $C_{19}H_{21}BrO$: C, 66.09; H, 6.13. Found: C, 66.42; H, 6.15.



16

***Z*-7-(2-Bromophenyl)-1-phenylhept-4-en-1-ol (16).** Alcohol **6** (2.64 g, 9.85 mmol) was converted to *Z*-7-(2-Bromophenyl)-1-phenylhept-4-en-1-al (2.23 g, 85% yield, colorless oil) in a manner analogous to that described above for the synthesis of *E*-7-(2-Bromophenyl)-1-phenylhept-4-en-1-al. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1 H), 7.52 (d, *J* = 7.6 Hz, 1 H), 7.27–7.19 (m, 2 H) 7.07–7.03 (m, 1 H), 5.41–5.34 (m, 2 H), 2.80–2.76 (m, 2 H), 2.39–2.25 (m, 6 H).

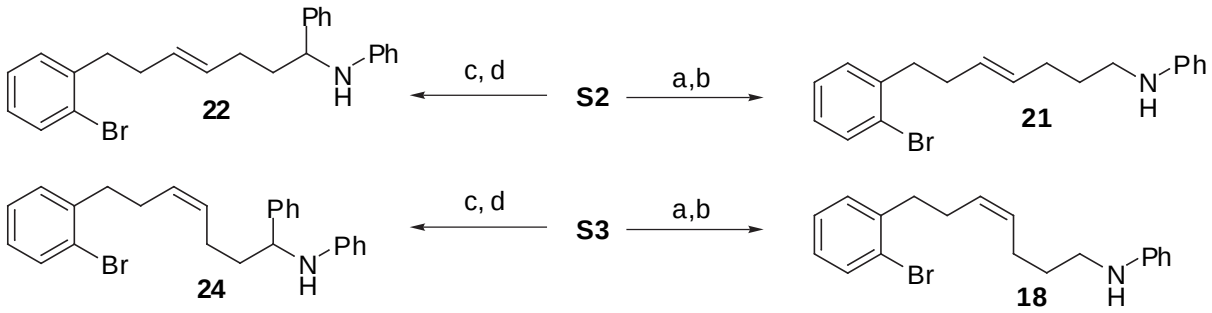
Z-7-(2-Bromophenyl)-1-phenylhept-4-en-1-al (1.63 g, 6.06 mmol) was converted to the title compound (1.46 g, 70% yield) in a manner analogous to that described above for the synthesis of

14. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.44 (m, 1 H), 7.30–7.26 (m, 2 H), 7.25–7.17 (m, 3 H) 7.15–7.10 (m, 2 H), 6.99–6.95 (m, 1 H), 5.45–5.34 (m, 2 H), 4.57–4.53 (m, 1 H), 2.72–2.67 (m, 2 H), 2.31–2.26 (m, 2 H), 2.06–1.96 (m, 2 H), 1.78–1.77 (m, 1 H), 1.76–1.67 (m, 1 H), 1.64–1.55 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 141.3, 132.9, 130.8, 130.3, 129.2, 128.6, 127.8, 127.7, 127.5, 126.1, 124.6, 74.3, 39.0, 36.4, 27.7, 23.9; IR (film) 3369, 2930, 1470 cm^{-1}. Anal calcd for $C_{19}H_{21}BrO$: C, 66.09; H, 6.13. Found: C, 66.39; H, 6.21.

Synthesis of Substrates Bearing Amine Nucleophiles

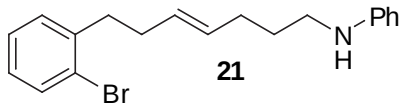
As shown in Scheme S3, unbranched aniline derivatives **18** and **21** were generated via amidation of **S2** and **S3** followed by reduction with $LiAlH_4$. Branched substrates **24** and **22** were prepared via conversion of esters **S2** and **S3** to the corresponding Weinreb Amides followed by addition of phenylmagnesium bromide to generate phenyl ketone derivatives. Conversion of these intermediates to *N*-aryl imines followed by reduction with $LiAlH_4$ generated **24** and **22**. Experimental procedures and characterization data are given below.

Scheme S3. Synthesis of Substrates Bearing Amine Nucleophiles[a]



a. Conditions: (a) $PhNH_2$, MeMgBr, THF, 0 °C–rt, 60% from *E*-substrate, 70% from *Z*-substrate; (b) $LiAlH_4$, Et_2O, 0 °C-rt, 70% from *E*-substrate, 89% from *Z*-substrate; (c) MeN(OMe)H•HCl, $AlMe_3$, toluene, 0°C–rt, 61% from *E*-

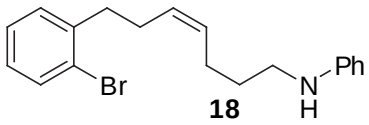
substrate, 68% from *Z*-substrate; (d) PhMgBr, THF, 0 °C, 69% from *E*-substrate, 71% from *Z*-substrate; (e) i) $PhNH_2$, TFA, benzene, reflux; ii) $LiAlH_4$, Et_2O, 0°C, 59% from *E*-substrate, 58% from *Z*-substrate.



21

***E*-[7-(2-Bromophenyl)hept-4-enyl]aniline (21).** A flame-dried flask was cooled under a stream of nitrogen and charged with aniline (0.6 mL, 6.52 mmol) and tetrahydrofuran (6 mL). The mixture was cooled to 0°C, a solution of methylmagnesium bromide (2.2 mL, 6.6 mmol, 3 M in diethyl ether) was added dropwise, and the reaction mixture was warmed to room temperature and stirred for 12 h. A solution of *E*-7-(2-bromophenyl)hept-4-enoic acid ethyl ester (1.03 g, 3.31 mmol) in tetrahydrofuran (6 mL) was added to the reaction mixture, and the resulting solution was stirred at room temperature for 12 h. The reaction was quenched with water, the layers were separated, and the aqueous layer was extracted with diethyl ether (3 x 200 mL). The combined organic extracts were washed sequentially with 2M HCl (2 x 100 mL) aqueous $NaHCO_3$, and brine, and were then dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography using 5%→10% ethyl acetate/hexanes as the eluant to afford 710 mg (60%) of *E*-7-(2-bromophenyl)hept-4-enoic acid phenyl amide as a gray solid, m.p. 80–85 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.50 (m, 3 H), 7.44–7.31 (m, 2 H), 7.22–7.18 (m, 3 H), 7.06–7.00 (m, 1 H), 5.64–5.55 (m, 2 H), 2.79 (t, *J* = 7.2 Hz, 2 H), 2.48–2.42 (m, 4 H), 2.36–2.32 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 141.2, 138.1, 132.8, 130.8, 130.6, 129.3, 129.1, 127.7, 127.5, 124.6, 124.4, 120.2, 37.5, 36.2, 32.8, 28.6; IR (film) 3296, 1652 cm^{-1}. Anal calcd for $C_{19}H_{20}BrNO$: C, 63.70; H, 5.63; N, 3.91. Found: C, 63.49; H, 5.67; N, 3.85.

A flame-dried flask was cooled under nitrogen and charged with *E*-7-(2-bromophenyl)hept-4-enoic acid phenyl amide (690 mg, 1.93 mmol) and diethyl ether (10 mL). The solution was cooled to 0 °C and $LiAlH_4$ (5.78 mL, 5.78 mmol, 1 M in diethyl ether) was added dropwise. The reaction mixture was warmed to room temperature and stirred for 10 h, then was cooled to 0 °C and water (1 mL) was added dropwise followed by 10 M NaOH (2 mL) and additional water (3 mL). The resulting mixture was decanted, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography using 5%→10% ethyl acetate/hexanes as the eluant to afford 523 mg (70%) of the title compound as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 6.0 Hz, 1 H), 7.24–7.16 (m, 4 H), 7.06–7.02 (m, 1 H), 6.70 (t, *J* = 7.2 Hz, 1 H), 6.61 (d, *J* = 7.6 Hz, 2 H), 5.56–5.42 (m, 2 H), 3.84 (s, br, 1 H), 3.09 (t, *J* = 7.2 Hz, 2 H), 2.82–2.78 (m, 2 H), 2.35–2.29 (m, 2 H), 2.13–2.08 (m, 2 H), 1.70–1.65 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 141.4, 132.9, 130.6, 130.5, 130.0, 129.4, 127.7, 127.5, 124.7, 117.4, 113.0, 43.6, 36.4, 32.9, 30.2, 29.3; IR (film) 3411, 2928, 1603 cm^{-1}. Anal calcd for $C_{19}H_{22}BrN$: C, 66.28; H, 6.44; N, 4.07. Found: C, 66.53; H, 6.40; N, 4.12.

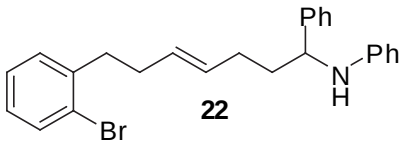


18

***Z*-[7-(2-Bromophenyl)hept-4-enyl]aniline (18).** *Z*-7-(2-bromophenyl)hept-4-enoic acid ethyl ester (941 mg, 3.02 mmol) was converted to *Z*-7-(2-bromophenyl)hept-4-enoic acid phenyl amide (755 mg, 70% yield, colorless oil) in a manner analogous to that described above for the synthesis of *E*-7-(2-bromophenyl)hept-4-enoic acid phenyl amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.48 (m, 3 H), 7.32–7.18 (m, 4 H), 7.10–7.03 (m, 2 H), 5.56–5.41 (m, 2 H), 2.79 (t, *J* = 8.0 Hz, 2 H), 2.44–2.36 (m, 4 H), 2.23–2.19 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 141.2,

138.1, 132.9, 131.0, 130.2, 129.2, 128.9, 127.8, 127.5, 124.6, 124.4, 120.0, 37.7, 36.2, 27.6, 23.5; IR (film) 3302, 1651 cm^{-1}.

Z-7-(2-bromophenyl)hept-4-enoic acid phenyl amide (585 mg, 1.63 mmol) was converted to the title compound (498 mg, 89% yield) in a manner analogous to that described above for the synthesis of **21**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.0 Hz, 1 H), 7.25–7.15 (m, 4 H), 7.06–7.03 (m, 1 H), 6.70–6.66 (m, 1 H), 6.58 (d, *J* = 8.0 Hz, 2 H), 5.51–5.40 (m, 2 H), 3.56 (s, br, 1 H), 3.07–3.05 (m, 2 H), 2.78 (t, *J* = 6.4 Hz, 2 H), 2.40–2.35 (m, 2 H), 2.12–2.07 (m, 2 H), 1.61–1.55 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 141.3, 133.0, 130.8, 130.2, 129.4, 129.2, 127.8, 127.5, 124.6, 117.3, 112.9, 43.7, 36.4, 29.6, 27.8, 25.0; IR (film) 3409, 2928, 1601 cm^{-1}. Anal calcd for $C_{19}H_{22}BrN$: C, 66.28; H, 6.44; N, 4.07. Found: C, 66.46; H, 6.62; N, 4.07.



22

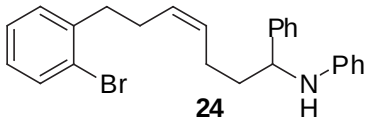
***E*-[7-(2-Bromophenyl)-1-phenylhept-4-enyl]aniline (22).** A flame-dried flask was cooled under a stream of nitrogen and charged with N,O-dimethylhydroxylamine hydrochloride (2.3 g, 23.6 mmol) and toluene (30 mL). The mixture was cooled to 0 °C, and a solution of trimethylaluminum (11.8 mL, 23.6 mmol, 2 M in toluene) was added dropwise. The resulting mixture was stirred at 0 °C for 10 min, then a solution of ester **S2** (2.94 g, 9.45 mmol) in toluene (16 mL) was added to the reaction mixture *via* cannula. The resulting solution was allowed to slowly warm to room temperature over 10 h with stirring. The reaction mixture was then cooled to 0 °C and 1M HCl was added dropwise. The resulting mixture was transferred to a separatory funnel, the layers were separated, and the aqueous layer was extracted with methylene chloride

(3 x 400 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography using 20% ethyl acetate/hexanes as the eluant to provide 1.88g (61%) of *E*-7-(2-bromophenyl)hept-4-enoic acid (methoxy)methylamide as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53–7.50 (m, 1 H), 7.24–7.17 (m, 2 H), 7.06–7.02 (m, 1 H), 5.58–5.44 (m, 2 H), 3.67 (s, 3 H), 3.18 (s, 3 H), 2.80–2.76 (m, 2 H), 2.49–2.45 (m, 2 H), 2.35–2.27 (m, 4 H).

A flame-dried flask was cooled under a stream of nitrogen and charged with *E*-7-(2-bromophenyl)-hept-4-enoic acid (methoxy)methylamide (1.88 g, 5.76 mmol) and THF (10 mL). The mixture was cooled to 0 °C, a solution of phenylmagnesium bromide (17.3 mL, 17.3 mmol, 1 M in THF) was added dropwise, and the reaction mixture was warmed to room temperature with stirring over 8 h. The reaction mixture was then cooled to 0 °C, water (5 mL) was added dropwise, and the reaction mixture was transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 300 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography using 10% ethyl acetate/hexanes as the eluant to provide 1.34 g (69%) of *E*-7-(2-bromophenyl)-1-phenylhept-4-en-1-one as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97–7.95 (m, 2 H), 7.61–7.43 (m, 4 H), 7.21–7.19 (m, 2 H) 7.05–7.01 (m, 1 H), 5.60–5.48 (m, 2 H), 3.04–3.00 (m, 2 H), 2.80–2.76 (m, 2 H), 2.46–2.41 (m, 2 H), 2.33–2.28 (m, 2 H).

A flame-dried flask equipped with Dean-Stark apparatus and reflux condenser was cooled under a stream of nitrogen and charged with *E*-7-(2-bromophenyl)-1-phenylhept-4-en-1-one (1.34 g,

3.90 mmol), benzene (20 mL), and trifluoroacetic acid (29.0 μL, 0.390 mmol). The mixture was heated to reflux under nitrogen for 48h with azeotropic removal of water. The reaction mixture was then cooled to room temperature, concentrated *in vacuo*, and diluted with diethyl ether. The resulting solution was cooled to 0 °C and a solution of lithium aluminum hydride (11.7 mL, 11.7 mmol, 1 M in ether) was added dropwise. The reaction mixture was then warmed to room temperature and stirred for 8 h. The reaction mixture was then cooled to 0°C, and H_2O (2 mL) followed by 10 M NaOH (3 mL) and additional water. The resulting suspension was decanted, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography using 10% ethyl acetate/hexanes as the eluant to afford 958 mg (59%) of the title compound as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53–7.51 (m, 1 H), 7.32–7.28 (m, 4 H), 7.24–7.20 (m, 1 H), 7.19–7.17 (m, 2 H), 7.10–7.02 (m, 3 H), 6.63 (t, *J* = 7.6 Hz, 1 H), 6.50 (d, *J* = 7.6 Hz, 2 H), 5.53–5.42 (m, 2 H), 4.30 (t, *J* = 6.8 Hz, 1 H), 4.06 (s, 1 H), 2.80–2.76 (m, 2 H), 2.33–2.28 (m, 2 H), 2.10–2.05 (m, 2 H), 1.89–1.81 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 144.2, 141.3, 133.0, 130.6, 130.32, 130.28, 129.3, 128.7, 127.7, 127.5, 127.1, 126.6, 124.7, 117.4, 113.4, 57.8, 38.6, 36.4, 32.9, 29.5; IR (film) 3412, 2929, 1600 cm^{-1}. Anal calcd for $C_{25}H_{26}BrN$: C, 71.43; H, 6.23; N, 3.33. Found: 71.44; H, 6.30; N, 3.35.



24

***Z*-[7-(2-Bromophenyl)-1-phenylhept-4-enyl]aniline (24).** *Z*-7-(2-bromophenyl)hept-4-enoic acid ethyl ester (1.44 g, 4.63 mmol) was converted to *Z*-7-(2-bromophenyl)hept-4-enoic acid (methoxy)methylamide (1.02 g, 68% yield, colorless oil) in a manner analogous to that described above for the synthesis of *E*-7-(2-bromophenyl)hept-4-enoic acid (methoxy)methylamide. ^{1}H

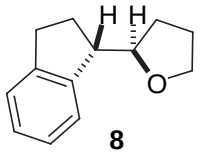
NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.6 Hz, 1 H), 7.25–7.16 (m, 2 H), 7.06–7.02 (m, 1 H), 5.51–5.40 (m, 2 H), 3.66 (s, 3 H), 3.17 (s, 3 H), 2.80–2.76 (m, 2 H), 2.42–2.39 (m, 3 H), 2.37–2.25 (m, 3 H).

Z-7-(2-bromophenyl)hept-4-enoic acid (methoxy)methylamide (1.02 g, 3.13 mmol) was converted to *Z*-7-(2-bromophenyl)-1-phenylhept-4-en-1-one (760 mg, 71% yield, colorless oil) in a manner analogous to that described above for the synthesis of *E*-7-(2-bromophenyl)-1-phenylhept-4-en-1-one. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.91 (m, 2 H), 7.58–7.44 (m, 4 H), 7.21–7.19 (m, 2 H) 7.04–7.00 (m, 1 H), 5.53–5.43 (m, 2 H), 2.91–2.87 (m, 2 H), 2.81–2.77 (m, 2 H), 2.45–2.38 (m, 4 H).

Z-7-(2-bromophenyl)-1-phenylhept-4-en-1-one (750 g, 2.19 mmol) was converted to the title compound (531mg, 58% yield, colorless oil) in a manner analogous to that described above for the synthesis of **22**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48–7.46 (m, 1 H), 7.24–7.20 (m, 4 H), 7.19–7.12 (m, 2 H), 7.07–6.97 (m, 4 H), 6.57 (dt, *J* = 1.0, 7.5 Hz, 1 H), 6.46 (d, *J* = 8.5 Hz, 2 H), 5.45–5.34 (m, 2 H), 4.23 (t, *J* = 6.5 Hz, 1 H), 3.97 (s, 1 H), 2.70–2.66 (m, 2 H), 2.30–2.21 (m, 2 H), 2.05–1.96 (m, 2 H), 1.70–1.63 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.5, 144.1, 141.2, 132.9, 130.8, 129.9, 129.4, 129.2, 128.7, 127.8, 127.4, 127.1, 126.5, 124.6, 117.3, 113.4, 57.9, 38.8, 36.3, 27.7, 24.3; IR (film) 3413, 2927 cm^{-1}. Anal calcd for $C_{25}H_{26}BrN$: C, 71.43; H, 6.23; N, 3.33. Found: C, 71.35; H, 6.21; N, 3.20

General Procedure for Pd-Catalyzed Cyclization Reactions

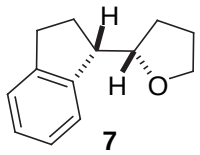
A flame-dried Schlenk tube equipped with a magnetic stirbar was cooled under a stream of nitrogen and charged with $Pd_2(dba)_3$ (1 mol % complex, 2 mol % palladium), ligand (4 mol %), and NaO*t*Bu (2.0 equiv). The tube was purged with nitrogen and a solution of the alcohol substrate in toluene (2.5 mL/0.5 mmol substrate) was added via cannula. An additional 1.0 mL of toluene was added and the resulting mixture was heated to 105 °C with stirring for 3–8 hours until the starting material had been consumed as determined by GC analysis. The reaction mixture was cooled to room temperature, aqueous NH_4Cl (2 mL) and ethyl acetate (10 mL) were added, and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL) and the combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was then purified by flash chromatography.



8

(±)-(1*S,2*R**)-2-Indan-1-yltetrahydrofuran (8).** The cyclization of **9** (150 mg, 0.56 mmol) following the general procedure using PCy_3•HBF_4 as the ligand afforded 54 mg (52%) of the title compound as a colorless oil. This compound was judged to be a >20:1 mixture of diastereomers by GC analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.49 (m, 1 H), 7.22–7.19 (m, 1 H), 7.18–7.13 (m, 2 H), 3.98–3.90 (m, 2 H), 3.82–3.77 (m, 1 H), 3.32–3.26 (m, 1 H), 2.98–2.83 (m, 2 H), 2.24–2.15 (m, 1 H), 2.00–1.83 (m, 3 H), 1.81–1.72 (m, 1 H), 1.64–1.54 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 144.4, 126.8, 126.3, 125.6, 124.5, 83.1, 68.3, 49.8, 31.8, 29.9, 28.3, 25.8; IR (film) 2952, 2858, 1474, 1457 cm^{-1}. Anal calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.07; H, 8.69.

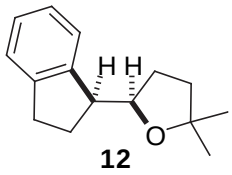
(±)-(1*S,2*R**)-2-Indan-1-yltetrahydrofuran (8).** The cyclization of **6** (190 mg, 0.71 mmol) following the general procedure using (±)–BINAP as the ligand afforded 79 mg (59%) of the title compound as a colorless oil. This compound was judged to be an 18:1 mixture of diastereomers by GC analysis. Spectroscopic data were identical to those given above.



7

(±)-(1*S,2*S**)-2-Indan-1-yltetrahydrofuran (7).** The cyclization of **6** (132 mg, 0.492 mmol) following the general procedure using $[(p\text{-MeO})C_6H_4]_3P$ as ligand afforded 48 mg (57%) of the title compound as a colorless oil. This compound was judged to be an 8:1 mixture of diastereomers by GC analysis. Data are for the major isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.29 (m, 1 H), 7.23–7.19 (m, 1 H), 7.17–7.15 (m, 2 H), 4.03–3.98 (m, 1 H), 3.91–3.85 (m, 1 H), 3.79–3.74 (m, 1 H), 3.38–3.33 (m, 1 H), 3.02–2.94 (m, 1 H), 2.89–2.81 (m, 1 H), 2.28–2.19 (m, 1 H), 2.08–1.97 (m, 2 H), 1.93–1.85 (m, 2 H), 1.68–1.59 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.7, 144.2, 126.9, 126.2, 125.0, 124.7, 81.7, 68.2, 49.8, 31.4, 29.5, 28.3, 26.4; IR (film) 2925 cm^{-1}; Anal calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.98; H, 8.25.

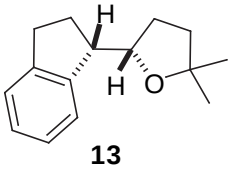
(±)-(1*S,2*S**)-2-Indan-1-yltetrahydrofuran (7).** The cyclization of **9** (70 mg, 0.26 mmol) following the general procedure using dpp-benzene as the ligand afforded 28 mg (58%) of the title compound as a colorless oil. This compound was judged to be a 15:1 mixture of diastereomers by GC analysis. Spectroscopic data were identical to those given above.



12

(±)-(1*S,5*R**)-2,2-Dimethyl-5-indan-1-yltetrahydrofuran (12).** The cyclization of **10** (150 mg, 0.51 mmol) following the general procedure using $[(p\text{-MeO})C_6H_4]_3P$ as ligand afforded 56 mg (51%) of the title compound as a colorless oil. This compound was judged to be a >20:1 mixture of diastereomers by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.47 (m, 1 H), 7.21–7.19 (m, 1 H), 7.18–7.13 (m, 2 H), 4.18–4.13 (m, 1 H), 3.37–3.31 (m, 1 H), 2.97–2.83 (m, 2 H), 2.22–2.14 (m, 1 H), 1.93–1.87 (m, 1 H), 1.85–1.79 (m, 1 H), 1.79–1.61 (m, 3 H), 1.30 (s, 3 H), 1.27 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.5, 144.5, 126.7, 126.2, 125.6, 124.4, 82.1, 80.9, 50.1, 38.6, 31.9, 29.6, 29.4, 28.4, 27.7; IR (film) 2966, 2865 cm^{-1}. Anal calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.01; H, 9.32.

(±)-(1*S,5*R**)-2,2-Dimethyl-5-indan-1-yltetrahydrofuran (12).** The cyclization of **11** (150 mg, 0.51 mmol) following the general procedure using PCy_3•HBF_4 as the ligand afforded 86 mg (79%) of the title compound as a colorless oil. This compound was judged to be a 14:1 mixture of diastereomers by ^{1}H NMR analysis. Spectroscopic data were identical to those given above.

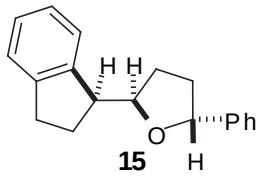


13

(±)-(1*S,5*S**)-2,2-Dimethyl-5-indan-1-yltetrahydrofuran (13).** The cyclization of **11** (200 mg, 0.673 mmol) following the general procedure using PMe_3•HBF_4 as ligand afforded 110 mg (76%) of the title compound as a colorless oil. This compound was judged to be a 9:1 mixture of

diastereomers by ^{1}H NMR analysis. Data are for the major isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 6.8 Hz, 1 H), 7.22 (d, *J* = 6.8 Hz, 1 H), 7.19–7.12 (m, 2 H), 4.13–4.08 (m, 1 H), 3.37–3.32 (m, 1 H), 3.01–2.93 (m, 1 H), 2.88–2.80 (m, 1 H), 2.28–2.19 (m, 1 H), 2.05–1.95 (m, 2 H), 1.72–1.61 (m, 3 H), 1.27 (s, 3 H), 1.25 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 145.1, 126.8, 126.0, 125.4, 124.6, 81.0, 80.5, 49.9, 38.9, 31.4, 29.4, 29.2, 28.6, 28.2; IR (film) 2967 cm^{-1}. Anal calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.03; H, 9.26.

(±)-(1*S,5*S**)-2,2-Dimethyl-5-indan-1-yltetrahydrofuran (13).** The cyclization of **10** (150 mg, 0.51 mmol) following the general procedure using (±)–BINAP as the ligand afforded 35 mg (32%) of the title compound as a colorless oil. This compound was judged to be a 6:1 mixture of diastereomers by ^{1}H NMR analysis. Spectroscopic data were identical to those given above.

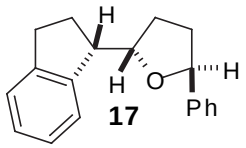


15

(±)-(1*S,2*R**,5*R**)-2-Indan-1-yl-5-phenyltetrahydrofuran (15).** The cyclization of **14** (150 mg, 0.434 mmol) following the general procedure using PCy_3•HBF_4 as ligand afforded 46 mg (40%) of the title compound as a yellow oil. This compound was obtained as a 92:5:2:1 mixture of diastereomers **15**:**S14**:**17**:**S15** as judged by ^{1}H NMR analysis. Data are for the major isomer. Structures and select data for isomers **S14** and **S15** are given below (Table S1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62–7.59 (m, 1 H), 7.38–7.31 (m, 4 H), 7.25–7.20 (m, 2 H), 7.18–7.14 (m, 2H), 5.14–5.11 (m, 1 H), 4.34–4.28 (m, 1 H), 3.44–3.38 (m, 1 H), 3.00–2.86 (m, 2 H), 2.44–2.38 (m, 1 H), 2.27–2.18 (m, 1 H), 2.12–2.06 (m, 1 H), 1.89–1.74 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.5, 144.5, 144.4, 128.5, 127.2, 126.8, 126.4, 125.8, 125.7, 124.5, 83.9, 80.8, 50.2, 35.4,

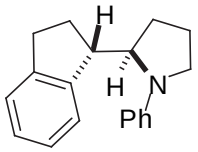
31.9, 31.0, 28.2; IR (film) 3024, 2958, 1602 cm^{-1}. Anal calcd for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.45; H, 7.65.

(±)-(1*S,2*R**,5*R**)-2-Indan-1-yl-5-phenyltetrahydrofuran (15).** The cyclization of **16** (122 mg, 0.35 mmol) following the general procedure using (±)–BINAP as the ligand afforded 23 mg (25%) of the title compound as a colorless oil. This compound was obtained as a 65:29:5:1 mixture of diastereomers **15**:**S14**:**17**:**S15** as judged by ^{1}H NMR analysis. Spectroscopic data for the major diastereomer (**15**) were identical to those given above.



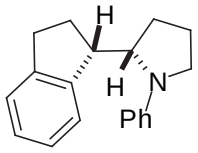
17

(±)-(1*S,2*S**,5*S**)-2-Indan-1-yl-5-phenyltetrahydrofuran (17).** The cyclization of **16** (182 mg, 0.529 mmol) following the general procedure using [(*p*-MeO)C_6H_4]$_3$P as ligand afforded 55 mg (40%) of the title compound as yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed that a 9:2:2:1 ratio of diastereomers **17**:**15**:**S15**:**S14** was formed. Upon purification the title compound was obtained as a 17:2:1:1 mixture of diastereomers **17**:**15**:**S15**:**S14** as judged by ^{1}H analysis. Data are for the major diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.37 (m, 1 H), 7.35–7.31 (m, 4 H), 7.26–7.23 (m, 2 H) 7.20–7.17 (m, 2 H), 5.02 (dd, *J* = 2.5, 8.5 Hz, 1 H), 4.39–4.35 (m, 1 H), 3.51–3.47 (m, 1 H), 3.04–2.97 (m, 1 H), 2.92–2.85 (m, 1 H), 2.38–2.31 (m, 1 H), 2.30–2.24 (m, 1 H), 2.15–2.09 (m, 2 H), 1.90–1.75 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.3, 144.2, 144.0, 128.5, 127.3, 127.0, 126.2, 125.8, 125.3, 124.7, 82.5, 80.9, 50.0, 36.0, 31.4, 30.3, 28.5; IR (film) 3026, 2942 cm^{-1}. Anal calcd for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.12; H, 7.61.



20

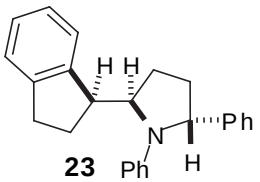
(±)-(1*S,2*R**)-*N*-Phenyl-2-indan-1-ylpyrrolidine (20).** The cyclization of **21** (150 mg, 0.436 mmol) following the general procedure using PCy_3•HBF_4 as ligand afforded 85 mg (74%) of the title compound as a colorless oil. This compound was judged to be a >20:1 mixture of diastereomers by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.17 (m, 4 H), 7.15–7.11 (m, 2 H), 6.68–6.63 (m, 3 H), 4.32–4.28 (m, 1 H), 3.85–3.80 (m, 1 H), 3.62–3.57 (m, 1 H), 3.31–3.25 (dd, *J* = 7.6, 16.8 Hz, 1 H), 2.98–2.91 (m, 1 H), 2.86–2.77 (m, 1 H), 2.09–1.99 (m, 2 H), 1.97–1.81 (m, 3 H), 1.69–1.63 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 145.2, 144.9, 129.2, 126.7, 126.4, 124.7, 124.4, 115.9, 112.6, 60.8, 50.1, 46.8, 31.8, 27.7, 27.3, 24.5; IR (film) 2960, 1597 cm^{-1}. Anal calcd for $C_{19}H_{21}N$: C, 86.65; H, 8.04; N, 5.32. Found: C, 86.42; H, 8.13; N, 5.34.



19

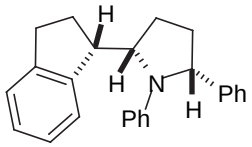
(±)-(1*S,2*S**)-*N*-Phenyl-2-indan-1-ylpyrrolidine (19).** The cyclization of **18** (155 mg, 0.450 mmol) following the general procedure using PCy_3•HBF_4 as ligand afforded 108 mg (92%) of the title compound as an orange oil. This compound was judged to be a >20:1 mixture of diastereomers by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.27 (m, 2 H), 7.21 (d, *J* = 7.6 Hz, 1 H), 7.17–7.14 (m, 1 H), 7.06 (d, *J* = 4.0 Hz, 2 H), 6.76 (d, *J* = 8.0 Hz, 2 H),

(6.73–6.69 (m, 1 H), 4.06–4.04 (m, 1 H), 3.93–3.89 (m, 1 H), 3.44 (dd, *J* = 4.0, 8.0 Hz, 1 H), 3.21–3.15 (m, 1H), 3.11–3.02 (m, 1 H), 2.95–2.88 (m, 1 H), 2.39–2.28 (m, 1 H), 1.96–1.85 (m, 2 H), 1.70–1.61 (m, 2 H), 1.32–1.27 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 145.1, 144.4, 129.4, 126.8, 126.2, 126.0, 124.4, 115.8, 112.6, 63.0, 50.3, 45.6, 32.0, 28.2, 27.6, 24.1; IR (film) 3063, 2942, 1597 cm^{-1}. Anal calcd for $C_{19}H_{21}N$: C, 86.65; H, 8.04; N, 5.32. Found: C, 86.44; H, 8.16; N, 5.31.



23

(±)-(1*S,2*R**,5*R**)-*N*,5-Diphenyl-2-indan-1-ylpyrrolidine (23).** The cyclization of **22** (123.8 mg, 0.295 mmol) following the general procedure using $PCy_3{\cdot}HBF_4$ as ligand afforded 59 mg (59%) of the title compound as yellow foam. This compound was judged to be a 5:1 mixture of diastereomers **23** and **S23** by ^{1}H NMR analysis. Data are for the major diastereomer; the structure of and selected data for the minor diastereomer **S23** are given below (Table S2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49–7.46 (m, 1 H), 7.41–7.36 (m, 2 H), 7.31–7.16 (m, 4 H), 7.14–7.10 (m, 4 H), 6.74–6.59 (m, 3 H), 5.17 (d, *J* = 6.8 Hz, 1 H), 4.87 (dd, *J* = 3.6, 8.0 Hz, 1 H), 4.14 (dt, *J* = 3.6, 7.2 Hz, 1 H), 2.98–2.90 (m, 1 H), 2.87–2.79 (m, 1 H) 2.65–2.54 (m, 1 H), 2.16–2.01 (m, 2 H), 1.97–1.90 (m, 1 H), 1.85 –1.80 (m, 1 H), 1.66–1.61 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.5, 145.3, 145.1, 144.9, 129.0, 128.6, 126.7, 126.6, 126.42, 126.39, 124.8, 123.9, 116.0, 115.0, 63.4, 61.1, 45.3, 35.3, 31.9, 27.4, 24.7; IR (film) 2963 cm^{-1}. Anal calcd for $C_{25}H_{25}N$: C, 88.45; H, 7.42; N, 4.13. Found: 88.16; H, 7.46; N, 4.13.



25

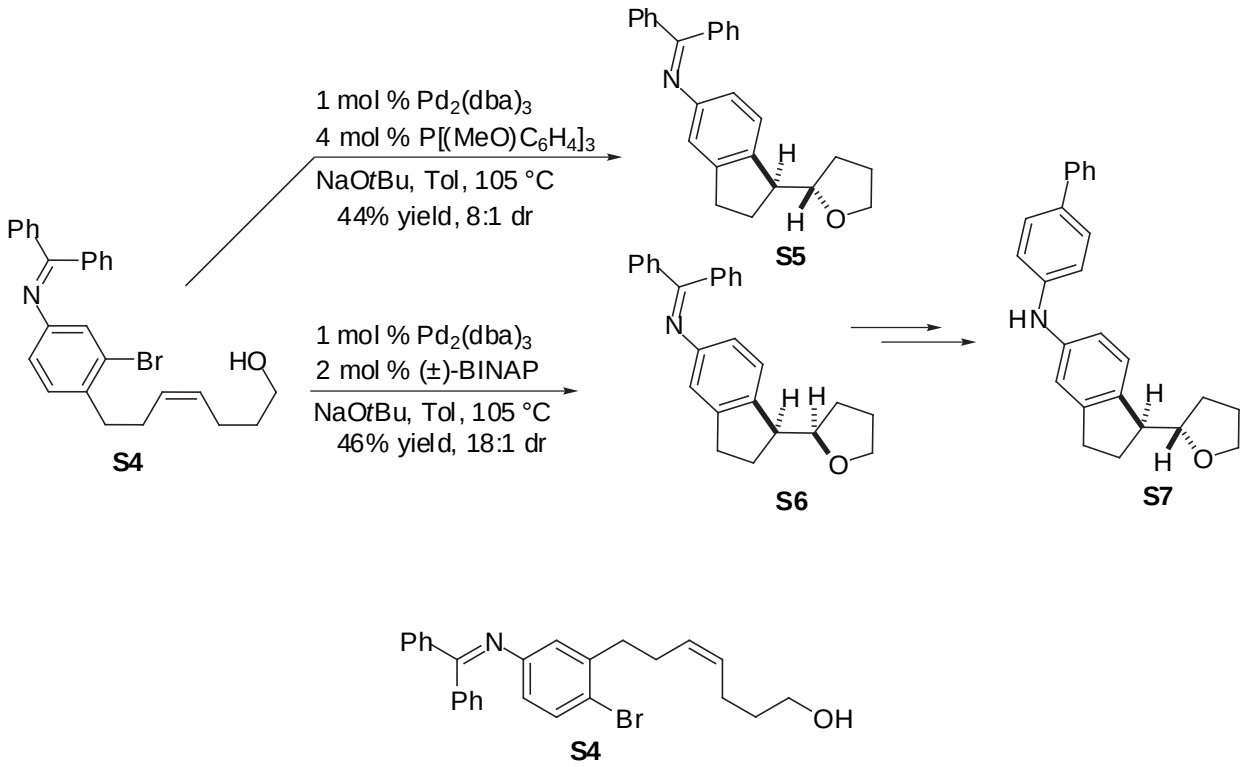
(±)-(1*S,2*S**,5*R**)-*N*,5-Diphenyl-2-indan-1-yl-pyrrolidine (25).** The cyclization of **24** (100 mg, 0.24 mmol) following the general procedure using $PCy_3 \cdot HBF_4$ as ligand afforded 60 mg (75%) of the title compound as an orange solid, m.p. 114–119 °C. This compound was judged to be a 2:1 mixture of diastereomers **25** and **S22** by ^1H analysis. Data are for the major diastereomer; the structure of and selected data for the minor diastereomer **S22** are given below (Table S2) ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.35 (m, 4 H), 7.34–7.29 (m, 2 H), 7.25–7.20 (m, 2 H), 7.16–7.13 (m, 3 H), 6.71 (t, *J* = 7.0 Hz, 1 H), 6.67 (d, *J* = 8.0 Hz, 2 H), 4.60 (t, *J* = 7.5 Hz, 1 H), 4.05 (dt, *J* = 2.0, 8.5 Hz, 1 H), 3.49 (dt, *J* = 3.5, 12.0 Hz, 1 H), 3.22–3.15 (m, 1 H), 2.95–2.89 (m, 1 H), 2.52–2.47 (m, 1 H), 2.44–2.40 (m, 1 H), 2.39–2.31 (m, 1 H), 2.10–2.06 (m, 1 H), 2.05–1.92 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.8, 145.5, 145.3, 144.9, 129.0, 128.9, 127.1, 126.8, 126.2, 125.8, 125.7, 125.0, 117.1, 113.8, 67.3, 64.8, 50.2, 35.0, 31.6, 29.8, 28.9. IR (film) 2941, 1598 cm^{-1}. Anal calcd for $C_{25}H_{25}N$: C, 88.45; H, 7.42; N, 4.13. Found: C, 88.39; H, 7.40, N, 4.17.

Determination of Stereochemistry

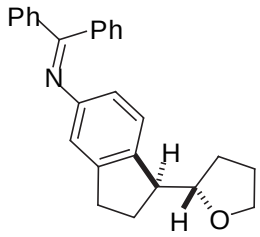
The stereochemistry of 2-(1-indanyl)tetrahydrofuran products **7** and **8** was assigned by preparing the related tetrahydrofurans **S5** and **S6** with subsequent conversion of **S6** to the crystalline solid **S7** (Scheme S3). Connectivity of **7**–**8** and **S5**–**S6** was determined by 2D-NMR COSY and HSQC experiments, and the stereochemical configuration of **S7** was established by x-ray crystallography. The unit cell contained both enantiomers of the racemic product.

Tetrahydrofuran derivatives **S5**–**S6** were prepared using a sequence of reactions similar to those described above for the synthesis of **7** and **8**.

Scheme S3.

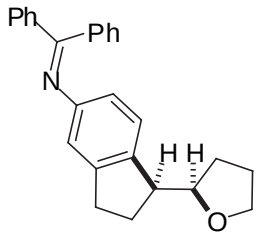


***Z*-7-[5-(Benzhydrilideneamino)-2-bromophenyl]hept-4-en-1-ol (S4)**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73–7.71 (m, 2 H), 7.49–7.46 (m, 1 H), 7.42–7.39 (m, 1 H) 7.33–7.26 (m, 5 H), 7.11–7.09 (m, 2 H), 6.60 (d, *J* = 2.5 Hz, 1 H), 6.43 (dd, *J* = 2.5, 8.5 Hz, 1 H), 5.37–5.30 (m, 2 H), 3.61–3.58 (m, 2 H), 2.63–2.60 (m, 2 H), 2.24–2.19 (m, 2 H), 2.09–2.05 (m, 2 H), 1.60–1.53 (m, 2 H), 1.49 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 150.6, 141.3, 139.6, 136.2, 132.8, 131.1, 130.2, 129.6, 129.5, 129.1, 129.0, 128.5, 128.3, 123.4, 120.7, 118.6, 62.7, 36.1, 32.8, 24.5, 23.8. IR (film) 3370, 2933, 1614 cm^{-1}; MS (ESI) 470.1093 (470.1095 calcd for $C_{26}H_{26}BrNO$, M + Na^+).



S5

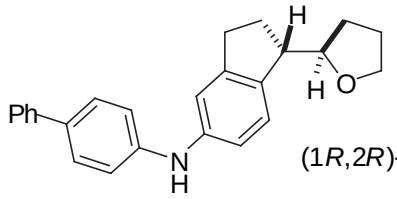
(±)-(1*S,2*R**)-Benzhydrilidene[1-(tetrahydrofuran-2-yl)indan-5-yl]amine (S5).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–7.71 (m, 2 H), 7.47–7.43 (m, 3 H), 7.40–7.36 (m, 2 H), 7.24–7.21 (m, 2 H), 7.13–7.11 (m, 2 H), 6.58 (s, 1 H), 6.49 (dd, *J* = 2.0, 8.0 Hz, 1 H), 3.91–3.85 (m, 2 H), 3.79–3.74 (m, 1 H), 3.22–3.16 (m, 1 H), 2.79–2.67 (m, 2 H) 2.16–2.04 (m, 1 H), 1.89–1.79 (m, 3 H), 1.74–1.65 (m, 1 H), 1.54–1.48 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 150.1, 144.8, 140.4, 140.2, 136.7, 130.7, 129.8, 129.5, 128.6, 128.3, 128.0, 125.2, 119.3, 117.2, 83.4, 68.3, 49.2, 31.8, 29.6, 28.3, 25.9; IR (film) 2953, 1652 cm^{-1}. Anal calcd for $C_{26}H_{25}NO$: C, 84.98; H, 6.86; N, 3.81. Found: C, 84.92; H, 6.84; N, 3.71.



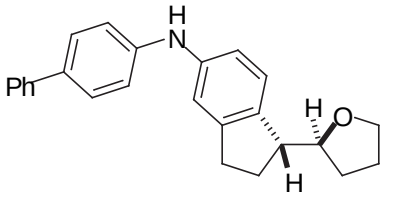
S6

(±)-(1*S,2*S**)-Benzhydrilidene[1-(tetrahydrofuran-2-yl)indan-5-yl]amine (S6).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.2 Hz, 2 H), 7.47–7.44 (m, 1 H), 7.41–7.37 (m, 2 H), 7.34–7.30 (m, 1 H), 7.27–7.24 (m, 2 H), 7.13–7.11 (m, 2 H), 7.03 (d, *J* = 7.6 Hz, 1 H), 6.61 (s, 1 H), 6.46 (d, *J* = 8.4 Hz, 1 H), 3.90–3.84 (m, 1 H), 3.84–3.79 (m, 1 H), 3.74–3.68 (m, 1 H),

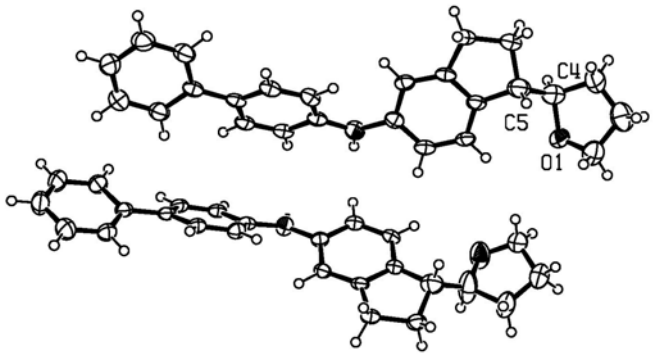
3.27–3.22 (m, 1 H), 2.82–2.77 (m, 1 H), 2.72–2.66 (m, 1 H), 2.20–2.15 (m, 1 H), 1.97–1.87 (m, 2 H), 1.86–1.77 (m, 2 H), 1.63–1.46 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 150.3, 145.6, 140.2, 138.9, 136.7, 130.7, 129.8, 129.5, 128.6, 128.4, 128.0, 124.9, 119.1, 117.4, 82.1, 68.1, 49.2, 31.4, 29.1, 28.7, 26.4; IR (film) 2942, 1652 cm^{-1}; MS (EI) 367.1942 (367.1936 calculated for $C_{26}H_{25}NO$).



(1*R*,2*R*)-**S7**

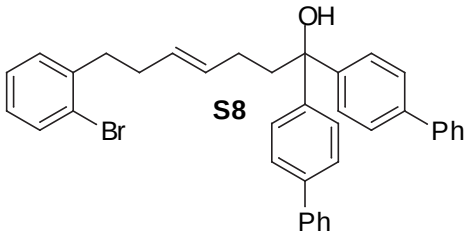


(1*S*,2*S*)-**S7**



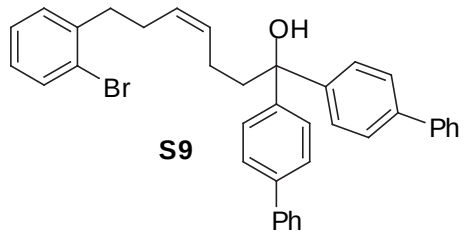
(±)-(1*S,2*S**)-Biphenyl-4-yl[1-(tetrahydrofuran-2-yl)indan-5-yl]amine (S7).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.55 (m, 2 H), 7.51–7.48 (m, 2 H), 7.44–7.40 (m, 3 H), 7.31–7.28 (m, 1 H), 7.12–7.08 (m, 2 H), 7.01 (s, 1 H), 6.95–6.93 (m, 1 H), 5.73 (s, br, 1 H), 4.00–3.94 (m, 1 H), 3.93–3.88 (m, 1 H), 3.83–3.78 (m, 1 H), 3.27–3.21 (m, 1 H), 2.95–2.81 (m, 2 H), 2.26–2.17 (m, 1 H), 2.03–1.85 (m, 3 H), 1.82–1.73 (m, 1 H), 1.65–1.56 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 143.6, 141.6, 141.2, 139.1, 133.2, 128.9, 128.1, 126.7, 126.6, 126.4, 117.5, 117.3, 114.8, 83.3, 68.3, 49.4, 32.0, 30.0, 28.7, 25.9; IR (film) 2951, 1605 cm^{-1}; MS (EI): 355.1924 (355.1936 calculated for $C_{25}H_{25}NO$); mp 87–90 °C.

The stereochemistry of the 2-(1-indanyl)tetrahydrofuran products **12** and **13** was established by comparison of the ^{1}H NMR spectra of **12** and **13** to the related tetrahydrofuran derivatives **S10** and **S11**, which were in turn assigned by x-ray crystallographic analysis of **S11**. The connectivity of these molecules was further confirmed by 2D-NMR COSY and HSQC experiments. Biphenyl tetrahydrofuran derivatives **S10**–**S11** were prepared using a sequence of reactions analogous to those described above for the synthesis of **12** and **13**.



S8

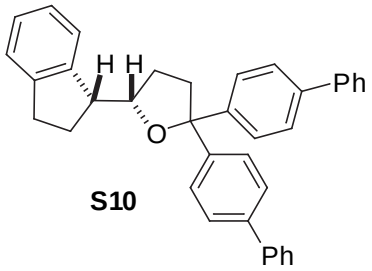
***E*-1,1-Bis(biphenyl-4-yl)-7-(2-bromophenyl)hept-4-en-1-ol (S8)**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63–7.59 (m, 8 H), 7.56–7.54 (m, 5 H), 7.47–7.46 (m, 4 H) 7.38–7.35 (m, 2 H), 7.26–7.20 (m, 2 H), 7.09–7.05 (m, 1 H), 5.58–5.50 (m, 2 H), 2.83–2.80 (m, 2 H), 2.45–2.42 (m, 2 H), 2.36–2.31 (m, 2 H), 2.12–2.10 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.1, 141.4, 140.9, 139.9, 132.9, 131.1, 130.6, 129.8, 128.9, 127.7, 127.5, 127.4, 127.2, 127.1, 126.6, 124.7, 78.4, 41.8, 36.4, 33.0, 27.3; IR (film) 3447, 2928 cm^{-1}. MS (EI) 572.1703 (572.1715 calcd for $C_{37}H_{33}BrO$).



S9

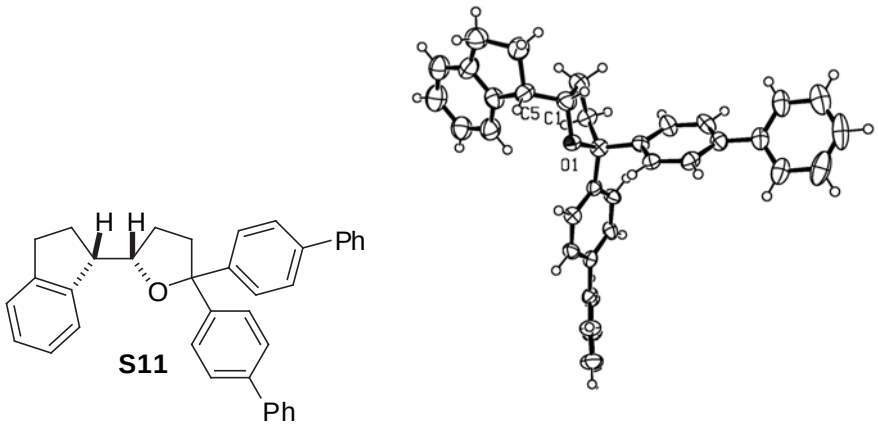
***Z*-1,1-Bis(biphenyl-4-yl)-7-(2-bromophenyl)hept-4-en-1-ol (S9)**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59–7.55 (m, 8 H), 7.51–7.44 (m, 5 H), 7.44–7.41 (m, 4 H) 7.35–7.32 (m, 2 H), 7.13–7.10 (m,

2 H), 7.00–6.96 (m, 1 H), 5.53–5.45 (m, 2 H), 2.73–2.70 (m, 2 H), 2.29–2.23 (m, 4 H), 2.08–2.03 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.0, 141.2, 140.9, 139.9, 132.9, 130.8, 130.6, 129.3, 128.9, 127.8, 127.4, 127.3, 127.2, 126.6, 124.6, 78.4, 42.0, 36.3, 27.7, 22.2 (one carbon signal is absent due to accidental equivalence); IR (film) 3563, 2928 cm^{-1}. Anal calcd for $C_{37}H_{33}BrO$: C, 77.48; H, 5.80. Found: C, 77.51; H, 5.61.



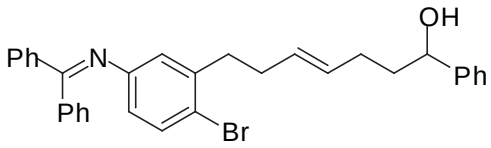
S10

(±)-(1*R,5*S**)-2,2-Bis(biphenyl-4-yl)-5-indan-1-yltetrahydrofuran (S10).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 6.8 Hz, 1 H), 7.62–7.50 (m, 12 H), 7.43–7.40 (m, 4 H), 7.34–7.31 (m, 2 H), 7.25–7.22 (m, 3 H), 4.30–4.25 (m, 1 H), 3.51–3.45 (m, 1 H), 2.99–2.87 (m, 2 H), 2.76–2.62 (m, 2 H), 2.26–2.18 (m, 1 H), 2.12–2.04 (m, 1 H), 1.88–1.72 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.6, 146.0, 145.7, 144.7, 141.11, 141.09, 139.8, 139.7, 128.9, 127.4, 127.3, 127.28, 127.23, 127.1, 126.9, 126.5, 126.46, 126.42, 126.1, 124.5, 88.4, 83.0, 50.6, 39.1, 31.9, 30.3, 28.7; IR (film) 3027, 2948 cm^{-1}; MS (EI): 492.2445 (492.2453 calculated for $C_{26}H_{25}NO$); m.p. 155–159 °C.



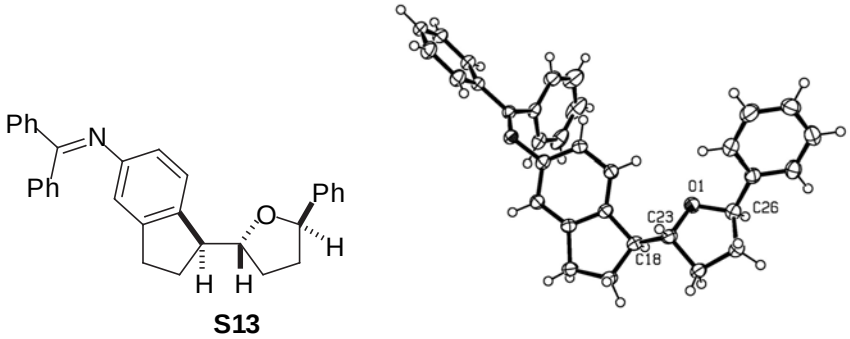
(±)-(1*S,5*S**)-2,2-Bis(biphenyl-4-yl)-5-indan-1-yltetrahydrofuran (S11).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64–7.55 (m, 13 H), 7.46–7.42 (m, 4 H), 7.36–7.28 (m, 3 H), 7.21–7.17 (m, 1 H), 7.14–7.11 (m, 1 H), 4.28–4.22 (m, 1 H), 3.52–3.47 (m, 1 H), 3.10–3.02 (m, 1 H), 2.95–2.87 (m, 1 H), 2.81–2.75 (m, 1 H), 2.62–2.55 (m, 1 H), 2.42–2.26 (m, 2 H), 2.15–2.07 (m, 1 H), 1.97–1.88 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.5, 146.0, 145.3, 144.1, 141.11, 141.08, 139.8, 139.6, 128.9, 127.4, 127.3, 127.27, 127.25, 127.1, 127.0, 126.5, 126.4, 126.1, 125.1, 124.7, 87.6, 81.2, 50.4, 39.2, 31.4, 29.9, 28.9; MS (EI) 492.2448 (492.2453 calcd for $C_{37}H_{32}O$); m.p. 145–147 °C.

The stereochemistry of the 2-(1-indanyl)tetrahydrofuran product **15** was established by comparison of the 1H NMR spectra of **15** to the related tetrahydrofuran derivative **S13**, which was in turn assigned by x-ray crystallographic analysis. The connectivity of these molecules was further confirmed by 2D-NMR COSY and HSQC experiments. Biphenyl tetrahydrofuran derivative **S13** was prepared using a sequence of reactions analogous to those described above for the synthesis of **15**.



S12

***E*-7-[5-(Benzhydrilideneamino)-2-bromophenyl]-1-phenylhept-4-en-1-ol (S12).** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60–7.60 (m, 2 H), 7.47–7.44 (m, 1 H), 7.38–7.29 (m, 8 H) 7.28–7.23 (m, 3 H), 7.07–7.05 (m, 2 H), 6.65 (d, *J* = 3.0 Hz, 1 H), 6.31 (dd, *J* = 2.5, 8.5 Hz, 1 H), 5.46–5.30 (m, 2 H), 4.52–4.48 (m, 1 H), 2.75–2.69 (m, 1 H), 2.63–2.57 (m, 2 H), 2.23–2.05 (m, 4 H), 1.87–1.80 (m, 1 H), 1.71–1.64 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.4, 150.2, 145.5, 141.3, 136.1, 132.7, 131.2, 130.8, 130.1, 129.64, 129.60, 129.1, 129.0, 128.6, 128.5, 128.4, 127.5, 126.1, 124.0, 120.3, 73.4, 38.7, 36.2, 32.8, 29.0; IR (film) 3392, 2926 cm^{-1}. MS (EI) 523.1506 (523.1511 calcd for $C_{32}H_{30}BrNO$).



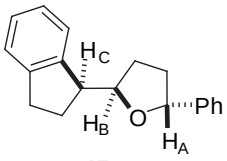
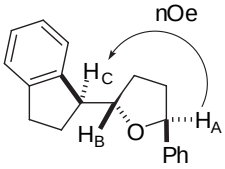
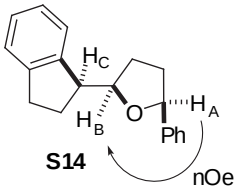
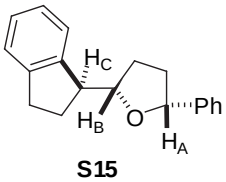
S13

(±)-(1*S,2*R**,5*R**)-Benzhydrilidene[1-(5-phenyltetrahydrofuran-2-yl)indan-5-yl]amine (S13).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.71 (m, 2 H), 7.47–7.44 (m, 1 H), 7.41–7.37 (m, 2 H), 7.33–7.30 (m, 5 H), 7.27–7.22 (m, 6 H), 7.21–7.12 (m, 2 H), 5.05–5.02 (m, 1 H), 4.28–4.23 (m, 1 H), 3.39–3.28 (m, 1 H), 2.80–2.73 (m, 2 H), 2.39–2.32 (m, 1 H), 2.20–2.12 (m, 1 H), 2.03–1.97 (m, 1 H), 1.86–1.70 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 150.2, 144.9,

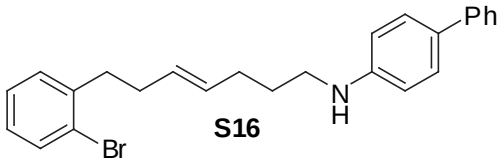
144.3, 140.4, 140.2, 136.7, 130.7, 129.8, 129.5, 128.6, 128.5, 128.4, 128.0, 127.2, 125.7, 125.4, 119.3, 117.2, 84.1, 80.8, 49.6, 35.4, 31.9, 29.9, 28.2; IR (film) 2926 cm^{-1}; MS (EI) 443.2255 (443.2249 calculated for $C_{32}H_{29}NO$); m.p. 117–121 °C.

The stereochemistry for the other three benzhydrilidene[1-(5-phenyltetrahydrofuran-2-yl)indan-5-yl] stereoisomers was assigned through a combination of ^1H NMR nOe experiments and correlation of NMR spectra to those obtained for **20**. A Table of relevant NMR data for the four benzhydrilidene[1-(5-phenyltetrahydrofuran-2-yl)indan-5-yl] stereoisomers (**15**, **17**, **S14**, and **S15**) is shown below. The chemical shift of H_B was downfield in molecules bearing *trans*-thf rings (**15** and **17**) relative to the chemical shift of H_B in *cis*-thf-containing products **S14** and **S15**. The chemical shift of H_c was downfield in molecules resulting from *anti*-addition across the *E*-alkene (**17** and **S15**) relative to molecules that derive from *syn*-addition across the *E*-alkene (**15** and **S14**). In addition, nOe enhancements were observed between H_A and H_C in **17** (evidence for *trans*-thf stereochemistry). The THF-ring stereochemistry of **S14** was further confirmed by NMR experiments that were conducted on the product mixture obtained by the Pd/BINAP-catalyzed cyclization of **16**. This transformation afforded a ~2:1 mixture of **15** and **S14**, with small amounts (ca 6% of total mixture) of **17** and **S15** also present. The resolution of the relevant signals was sufficient to observe nOe enhancements between H_A and H_B in **S14** (evidence for *cis*-stereochemistry).

Table S1

	 **15** *syn*-addition across *E*-alkene, *trans*-thf	 **17** *anti*-addition across *E*-alkene, *trans*-thf	 **S14** *syn*-addition across *E*-alkene, *cis*-thf	 **S15** *anti*-addition across *E*-alkene, *cis*-thf
δH_A	5.12	5.02	4.96	4.87
δH_B	4.31	4.37	4.18	4.13
δH_C	3.40	3.48	3.40	3.48

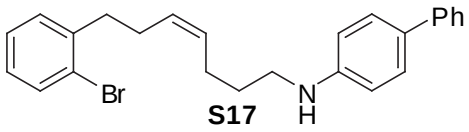
The stereochemistry of the 2-(1-indanyl)pyrrolidine products **20** and **19** was established by comparison of the ^{1}H NMR spectra of **20** and **19** to the analogous *N*-biphenyl pyrrolidine derivatives **S18** and **S19**, which were in turn assigned by x-ray crystallographic analysis. The connectivity of these four molecules was confirmed by 2D-NMR COSY and HSQC experiments. Biphenyl pyrrolidine derivatives **S18–S19** were prepared using a sequence of reactions analogous to those described above for the synthesis of **20** and **19**.



S16

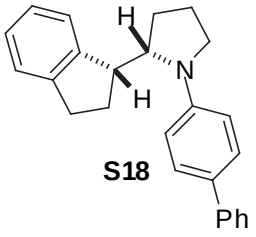
(*E*)-Biphenyl-4-yl-[7-(2-bromophenyl)hept-4-enyl)]amine (S16). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.55 (m, 3 H), 7.49–7.46 (m, 2 H), 7.44–7.40 (m, 2 H) 7.30–7.22 (m, 3 H), 7.09–7.05 (m, 1 H), 6.71–6.67 (m, 2 H), 5.60–5.46 (m, 2 H), 3.75 (s, 1 H), 3.16 (t, *J* = 5.6 Hz, 2 H), 2.86–2.82 (m, 2 H), 2.39–2.34 (m, 2 H), 2.18–2.12 (m, 2 H), 1.75–1.68 (m, 2 H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 148.0, 141.5, 141.4, 132.9, 130.6, 130.5, 130.2, 130.0, 128.8, 128.1, 127.7, 127.5, 126.4, 126.2, 124.7, 113.1, 43.5, 36.4, 32.9, 30.2, 29.3; IR (film) 3410, 2928, 1612 cm^{-1}; MS (ESI) 420.1333 (420.1327 calcd for $C_{25}H_{26}BrN$, M + H^+).

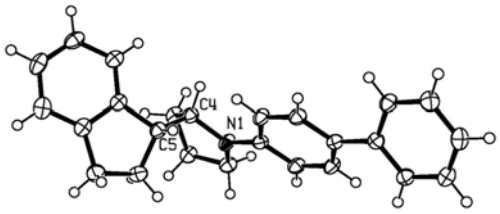


S17

(*Z*)-Biphenyl-4-yl-[7-(2-bromophenyl)hept-4-enyl)]amine (S17). ^1H NMR (400 MHz, $CDCl_3$) δ 7.56–7.53 (m, 3 H), 7.45 (d, *J* = 8.4 Hz, 2 H), 7.40 (t, *J* = 7.6 Hz, 3 H) 7.28–7.18 (m, 2 H), 7.08–7.04 (m, 1 H), 6.67 (d, *J* = 8.8 Hz, 2 H), 5.55–5.42 (m, 2 H), 3.72 (s, br, 1 H), 3.12 (t, *J* = 7.2 Hz, 2 H), 2.82–2.78 (m, 2 H), 2.43–2.37 (m, 2 H), 2.15–2.10 (m, 2 H), 1.65–1.57 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 141.5, 141.3, 133.0, 130.8, 130.23, 130.19, 129.3, 128.8, 128.1, 127.8, 127.5, 126.5, 126.2, 124.6, 113.2, 43.7, 36.4, 29.5, 27.8, 25.0; IR (film) 3411, 2859, 1612 cm^{-1}. Anal calcd for $C_{25}H_{26}BrN$: C, 71.43; H, 6.23; N, 3.33. Found: C, 71.67; H, 6.18; N, 3.39.

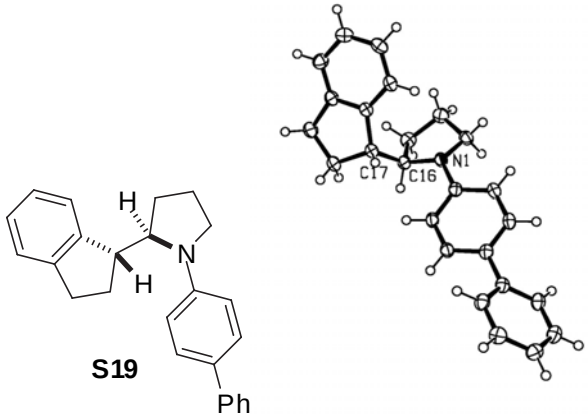


S18



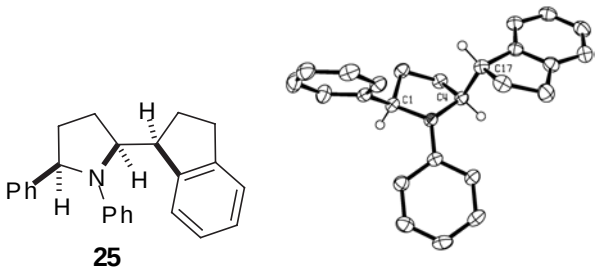
(±)-(1*R,2*S**)-*N*-(4-Phenyl)phenyl-2-indan-1-ylpyrrolidine (S18).** ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2 H), 7.50–7.48 (m, 2 H), 7.41 (t, *J* = 8.0 Hz, 2 H), 7.30–7.20 (m, 3 H), 7.20–7.14 (m, 2 H), 6.72 (d, *J* = 8.4 Hz, 2 H), 4.38–4.34 (m, 1 H), 3.90–3.85 (m, 1 H),

3.69–3.64 (m, 1 H), 3.39–3.32 (m, 1 H), 3.02–2.95 (m, 1 H), 2.90–2.82 (m, 1 H), 2.13–2.04 (m, 2 H), 2.02–1.87 (m, 3 H), 1.74–1.68 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 145.0, 144.9, 141.6, 128.8, 128.7, 127.9, 126.8, 126.4, 126.3, 126.0, 124.7, 124.4, 112.9, 60.9, 50.2, 46.9, 31.8, 27.8, 27.3, 24.5; IR (film) 2940, 1609 cm^{-1}; MS (EI): 339.1989 (339.1987 calcd for $C_{25}H_{25}N$); m.p. 103–110 °C.



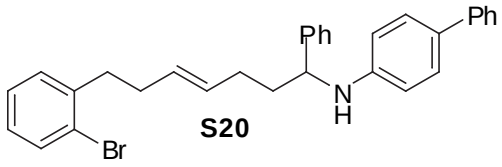
(±)-(1*R,2*R**)-*N*-(4-Phenyl)phenyl-2-indan-1-ylpyrrolidine (S19).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.54 (m, 4 H), 7.41 (t, *J* = 8.0 Hz, 2 H), 7.28–7.21 (m, 2 H), 7.18–7.14 (m, 1 H), 7.01–7.07 (m, 2 H), 6.83 (d, *J* = 8.8 Hz, 2 H), 4.11–4.08 (m, 1 H), 3.97–3.93 (m, 1 H), 3.51–3.45 (m, 1 H), 3.27–3.20 (m, 1 H), 3.10–3.04 (m, 1 H), 2.97–2.89 (m, 1 H), 2.39–2.31 (m, 1 H), 1.98–1.87 (m, 2 H), 1.72–1.55 (m, 2 H), 1.34–1.27 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 145.1, 144.2, 141.6, 128.8, 128.6, 128.0, 126.9, 126.4, 126.2, 126.0, 125.9, 124.5, 112.9, 63.0, 50.3, 45.6, 32.0, 28.2, 27.6, 24.1; IR (film) 2941, 1609 cm^{-1}; MS (EI): 339.1994 (339.1987 calculated for $C_{25}H_{25}N$); m.p. 93–98 °C.

The stereochemistry for (±)-(1*S**,2*S**,5*R**)-*N*,5-Diphenyl-2-indan-1-yl-pyrrolidine (**25**) was established by x-ray crystallographic analysis as shown below. Data are given above.



25

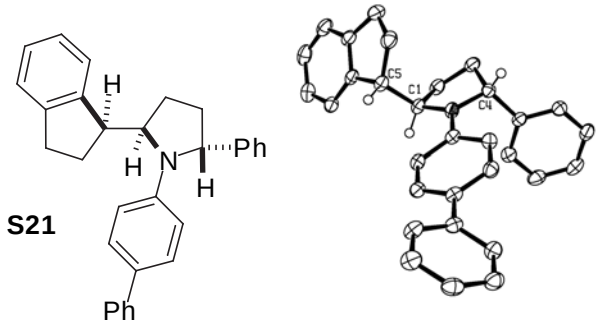
The stereochemistry of (1*S**,2*R**,5*R**)-*N*,5-Diphenyl-2-indan-1-ylpyrrolidine (**23**) was established by comparison of the ^{1}H NMR spectra of **23** to that obtained for the analogous *N*-biphenyl pyrrolidine derivative **S21**, which was in turn assigned by x-ray crystallographic analysis. Derivative **S21** was prepared using a sequence of reactions analogous to those described above for the synthesis of **23**.



S20

***E*-Biphenyl-4-yl[7-(2-bromophenyl)-1-phenylhept-4-enyl]amine (S20).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.51 (m, 1 H), 7.49–7.47 (m, 2 H), 7.37–7.31 (m, 8 H), 7.25–7.18 (m, 4 H), 7.06–7.02 (m, 1 H), 6.58–6.55 (m, 2 H), 5.55–5.43 (m, 2 H), 4.35 (t, *J* = 6.8 Hz, 1 H), 4.18 (s, br, 1 H), 2.80–2.77 (m, 2 H), 2.35–2.29 (m, 2 H), 2.15–2.03 (m, 2 H), 1.93–1.80 (m, 2 H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 147.0, 144.1, 141.4, 141.3, 132.9, 130.6, 130.3, 130.24, 130.19, 128.78, 128.77, 128.0, 127.7, 127.5, 127.2, 126.6, 126.4, 126.1, 124.7, 113.6, 57.8, 38.6, 36.4, 32.9, 29.5; IR (film) 3413, 2930, 1612 cm^{-1}. MS (ESI) 496.1646 (496.1640 calcd for $C_{31}H_{30}BrN$, M + H^+).

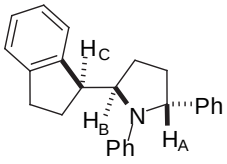
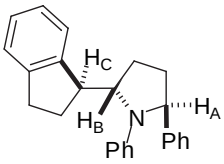
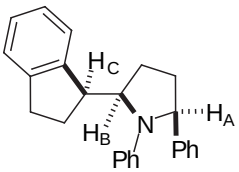
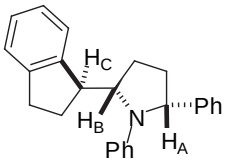


(1*S,2*R**,5*R**)-*N*-(Biphenyl-4-yl)-2-indan-1-yl-5-phenylpyrrolidine (S21).** ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.47 (m, 3 H), 7.38–7.32 (m, 6 H), 7.26–7.16 (m, 5 H), 7.13–7.11 (m, 2 H), 6.70 (d, *J* = 8.8 Hz, 2 H), 5.18 (d, *J* = 8 Hz, 1 H), 4.89–4.86 (m, 1 H), 4.17–4.12 (m, 1 H), 2.98–2.87 (m, 1 H), 2.86–2.78 (m, 1 H), 2.65–2.54 (m, 1 H), 2.13 –2.01 (m, 2 H), 1.96–1.89 (m, 1 H), 1.85–1.80 (m, 1 H), 1.66–1.61 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 145.1, 144.9, 144.8, 141.3, 128.8, 128.7, 127.6, 126.8, 126.7, 126.5, 126.4, 126.3, 126.0, 124.9, 123.9, 115.1, 114.5, 63.5, 61.2, 45.4, 35.3, 31.9, 27.5, 24.7; IR (film) 2918, 1609 cm^{-1}. MS (ESI) 416.2370 (416.2378 calcd for $C_{31}H_{29}N$, M + H^+); mp 148–152 °C.

The stereochemistry for the other two *N*,5-diphenyl-2-indan-1-ylpyrrolidine stereoisomers was assigned through correlation of NMR spectra to those obtained for **23** and **25**. A Table of

relevant NMR data for **23**, **25**, **S22**, and **S23** is shown below (Table S2). The chemical shift of H_B was downfield in molecules bearing *trans*-pyrrolidine rings (**23** and **S22**) relative to the chemical shift of H_B in *cis*-pyrrolidine-containing products **S23** and **25**.

Table S2

	 **23** *syn*-addition across *E*-alkene, *trans*-pyrrolidine	 **S22** *anti*-addition across *E*-alkene, *trans*-pyrrolidine	 **S23** *syn*-addition across *E*-alkene, *cis*-pyrrolidine	 **25** *anti*-addition across *E*-alkene, *cis*-pyrrolidine
δ H_A	5.17	4.92	4.66	4.60
δ H_B	4.87	4.51	4.39	4.05
δ H_C	4.14	4.19	3.95	3.49

References

[1] Wolfe, J. P.; Rennels, R. A.; Buchwald, S. L. *Tetrahedron* **1996**, *52*, 7525–7546.

[2] Bruyère, D.; Bouyssi, D.; Balme, G. *Tetrahedron* **2004**, *60*, 4007–4017.

[3] Matikainen, J.; Kaltia, S.; Hämäläinen, M.; Hase, T. *Tetrahedron* **1997**, *53*, 4531–4538.