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Supporting Information

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Three-Component Enantioselective Synthesis of Propargylamines Through Zr-catalysed Additions of Alkylzincs to Alkynylimines

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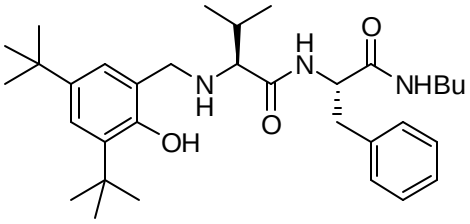
General. Infrared (IR) spectra are recorded on a Perkin Elmer 781 spectrophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m) or weak (w). ^1H NMR spectra are recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance resulting from incomplete deuteration as the internal standard ($CDCl_3$: 7.26). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants. ^{13}C NMR spectra are recorded on a Varian Unity INOVA 400 (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: 77.16). Enantiomer ratios were determined by chiral HPLC analysis (Chiral Technologies Chiralpak OD column (0.46 cm x 25 cm)) in comparison with authentic racemic materials. High resolution mass spectrometry was performed on a Micromass LCT ESI-MS (positive mode) at the Mass Spectrometry Facility, Boston College. Optical rotation values were recorded on a Rudolph Research Analytical Autopol IV polarimeter.

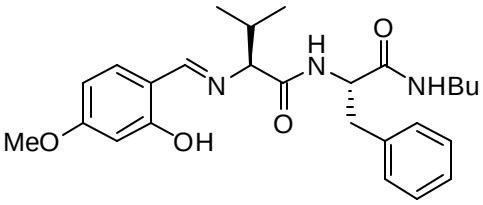
Unless otherwise stated, all reactions are conducted in oven- (135 °C) and flame-dried glassware under an inert atmosphere of dry nitrogen. Solvents are purified under a positive pressure of dry argon by a modified Advanced ChemTech purification system – toluene and benzene are purified through Cu and alumina columns; dichloromethane is purified through two alumina columns. Diethylzinc is purchased from Strem and dimethylzinc as a 2.0M solution in toluene from Aldrich. Both are used without purification. Other alkylzincs are prepared using known methods.[1] Zirconium *tert*-butoxide is purchased from Aldrich and distilled under vaccum, while zirconium isopropoxide (isopropanol complex, 1:1) is purchased from Aldrich and used without purification. Unless otherwise stated, substrates are synthesized from commercially available starting materials using known methods. EDC•HCl, HOBt•H_2O, piperidine, *n*-butylamine, Boc-protected amino acids, salicylaldehydes, alkynes and dimethylformamide are purchased from commercial sources and used without further purification. Butyllithium is purchased from Strem and titrated with *N*-pivaloyl-*o*-toluidine[2] prior to use. Propargyl aldehydes are synthesized through formylation of commercially available alkynes[3] and purified by simple distillation or silica gel chromatography. [3-(4-Fluorophenoxy)phenyl]-propynal (**14**) is synthesized from *o*-iodophenol through a Sonigashira coupling with propargyl alcohol[4], followed by copper-

[1] P. Knochel, R. D. Singer, *Chem. Rev.* **1993**, *93*, 2117-2188 and references cited therein.
[2] J. Suffert, *J. Org. Chem.* **1989**, *54*, 509-510.
[3] M. Journet, D. Cai, L. M. DiMichele, R. D. Larson, *Tetrahedron Lett.* **1998**, *39*, 6427-6428
[4] K. Sato, T. Yoshimura, M. Shindo, K. Shishido, *J. Org. Chem.* **2001**, *66*, 309-314.
[5] D. A. Evans, J. L. Katz, T. R. West, *Tetrahedron Lett.* **1998,** *39*, 2937-2940.
[6] D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155-4156; D. B. Dess, J. C. Martin *J. Am. Chem. Soc.* **1991**, *113*, 7277-7287.

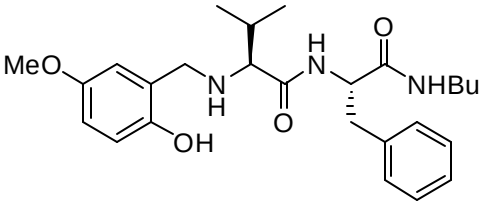
promoted phenol arylation[5], and oxidation with Dess-Martin periodinane.[6] Peptidic ligands were prepared according to previously reported procedures.[7]



***N*-(1-Butylcarbamoyl-2-phenylethyl)-2-(3,5-di-*tert*-butyl-2-hydroxybenzylamino)-3-methylbutyramide (6):** Previously reported procedures were followed to afford **6** as a white solid, mp = 152 °C. IR (solid thin film); 3280 (br), 3087 (w), 2959 (m), 2872 (m), 1637 (s), 1561 (s), 1456 (m), 1236 (m); ^{1}H NMR (400 MHz): δ 7.38-7.22 (6H, m), 6.72 (1H, s), 6.49 (1H, d, *J* = 7.6 Hz), 5.63 (1H, br s), 4.72 (1H, q, *J* = 6.4 Hz), 3.78-3.75 (1H, m), 3.47-3.44 (1H, m), 3.21-3.04 (4H, m), 2.74 (1H, br s), 2.26 (1H, br s), 1.86-1.82 (1H, m), 1.66 (1H, br s), 1.42 (9H, s), 1.33-1.16 (13H, m), 0.96 (3H, d, *J* = 6.8 Hz), 0.90-0.84 (6H, m); ^{13}C NMR (100MHz): δ 173.2, 170.4, 154.4, 140.9, 136.7, 136.2, 129.3, 128.9, 127.3, 123.7, 123.4, 122.0, 67.3, 54.8, 51.7, 39.4, 39.2, 35.0, 34.3, 31.8, 31.8, 31.5, 29.8, 20.0, 19.8, 19.0, 13.8; HRMS calcd for $C_{33}H_{52}N_3O_3$: 538.4009, Found: 538.3990; $[\alpha]_D^{20} = -20.3°$ (*c* = 0.73, $CHCl_3$).



***N*-(1-Butylcarbamoyl-2-phenylethyl)-2-[(2-hydroxy-4-methoxybenzylidene)-amino]-3-methylbutyramide (22)**: Previously reported procedures were followed to afford **22** as a yellow solid, mp = 199 °C. IR (thin film); 3294 (br), 2957 (w), 2933 (w), 2868 (w), 1646 (s), 1628 (m), 1514 (m), 1510 (m), 1222 (w); ^{1}H NMR (400 MHz): δ 8.15 (1H, s). 7.33-7.16 (6H, m), 6.54-6.48 (3H, m), 5.87 (1H, br s), 4.54 (1H, q, *J* = 8.4 Hz), 3.86 (3H, s), 3.58 (1H, d, *J* = 4.0 Hz), 3.23-3.02 (4H, m), 2.36-2.28 (1H, m), 1.57 (1H, br s), 1.37-1.30 (2H, m), 1.24-1.15 (2H, m), 0.84 (3H, t, *J* = 7.2 Hz), 0.78 (3H, d, *J* = 7.2 Hz), 0.62 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz): δ 171.9, 170.4, 167.3, 164.1, 163.3, 136.9, 133.5, 129.4, 129.0, 127.2, 112.4, 107.3, 101.3, 79.0, 55.7, 54.9, 39.4, 37.9, 32.0, 31.5, 20.1, 19.6, 16.7, 13.8; HRMS calcd for $C_{26}H_{36}N_3O_4$: 454.2706, Found: 454.2711; $[\alpha]_D^{20} = +24.8°$ (*c* = 0.5, $CHCl_3$).

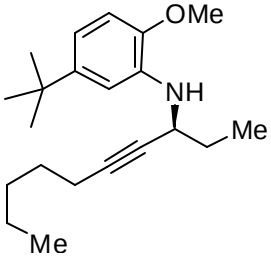


***N*-(1-Butylcarbamoyl-2-phenylethyl)-2-(2-hydroxy-5-methoxybenzylamino)-3-methylbutyramide (20):** For synthesis and full characterization of **20** see ref. 7.

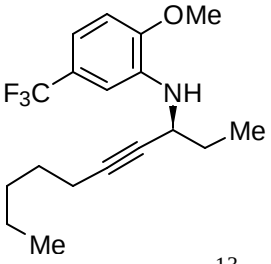
Representative experimental procedure for Zr-catalyzed addition of ethyl zinc to propargyl imines: To a 25 mL round bottom flask under an atmosphere of nitrogen in a glove box was added **6** (42 mg, 0.07 mmol), Zr(O*i*Pr)•HO*i*Pr (30 mg, 0.07 mmol), and 1 mL toluene. The solution stirred until the contents completely dissolved. *o*-Phenoxyaniline (140 mg, 0.76 mmol) and phenylpropargyl aldehyde **2** (94 mg, 0.76 mmol) were added in 2 mL of toluene. Following rinsing

[7] J. R. Porter, J. F. Traverse, A. H. Hoveyda, M. L. Snapper, *J. Am. Chem. Soc.* **2001**, *123*, 10409-10410.

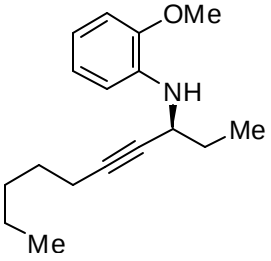
and dilution with an additional 9 mL of toluene, the reaction was sealed with a septum and teflon tape, removed from the glove box and cooled to 0 °C. Et_2Zn (470 μL, 4.56 mmol, caution, pyrophoric) was added dropwise to the stirred mixture under an atmosphere of nitrogen. The ice bath was removed and the solution warmed to 22 °C while stirring for four hours. The solution was poured into saturated aqueous NH_4Cl (15 ml), the layers separated and aqueous layer washed with Et_2O (3 x 5 ml). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The resulting orange oil was purified by silica gel chromatography (100:1 hexane:Et_2O) to yield **24** as a pale yellow oil (210 mg, 0.64 mmol, 84%).



(5-*tert*-Butyl-2-methoxyphenyl)-(1-ethyloct-2-ynyl)amine (7): The general procedure, as described earlier, was followed to afford 7 as a yellow oil. IR (neat): 3414 (w), 2955 (s), 2930 (s), 2860 (s), 1595 (m), 1526 (s), 1457 (m), 1419 (m), 1223 (m), 1224 (m); ^{1}H NMR (400 MHz): δ6.85 (1H, br s), 6.69-6.68 (2H, m), 4.24 (1H, br s), 4.02 (1H, br s), 3.81 (3H, s), 2.14 (2H, dt, *J* = 7.2, 4.0 Hz), 1.88-1.74 (2H, m), 1.49-1.42 (2H, m), 1.30 (13H, br s), 1.10 (3H, t, *J* = 8.0 Hz), 0.86 (3H, t, *J* = 8.0 Hz); ^{13}C NMR (100 MHz): δ 145.2, 143.9, 136.3, 113.4, 109.6, 109.0, 83.3, 80.7, 55.6, 47.2, 34.4, 31.7, 31.3, 29.3, 28.7, 22.3, 18.8, 14.0, 10.6; HRMS calcd for $C_{21}H_{34}NO$: 316.2640, Found: 316.2625.

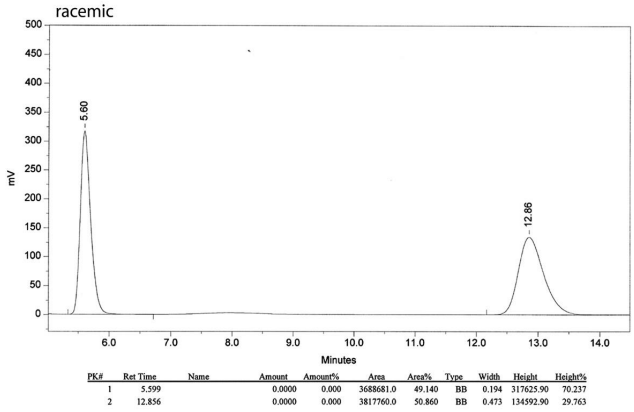


(1-Ethyloct-2-ynyl)-(2-methoxy-5-trifluoromethylphenyl)amine (8): The general procedure, as described earlier, was followed to afford 8 as a pale yellow oil. IR (neat): 3427 (w), 2961 (m), 2936 (m), 1608 (m), 1532 (m), 1451 (s), 1224 (s), 1318 (m), 1224 (s), 1117 (s); ^{1}H NMR (400 MHz): δ6.97-6.95 (2H, m), 6.79-6.77 (1H, m), 4.43 (1H, d, *J* = 7.2 Hz), 4.05-4.00 (1H, m), 3.88 (3H, s), 2.14 (2H, ddd, *J* = 7.2, 7.2, 2.0 Hz), 1.89-1.74 (2H, m), 1.48-1.41 (2H, m), 1.33-1.21 (4H, m), 1.10 (3H, t, *J* = 7.6 Hz), 0.85 (3H, t, *J* = 7.2); ^{13}C NMR (100 MHz): δ 149.3, 137.1, 124.9 (q, *J* = 274.0 Hz), 123.4 (q, *J* = 31.8 Hz), 108.7, 107.8 (q, *J* = 3.8 Hz), 114.3 (q, *J* = 4.5 Hz), 55.7, 46.9, 31.1, 29.2, 29.0, 22.3, 18.7, 14.0, 10.6, HRMS calcd $C_{18}H_{25}F_3NO$: 328.1888, Found: 328.1874.

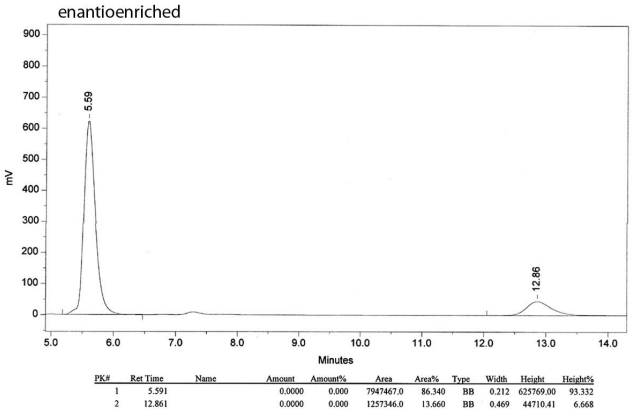


(1-Ethyl-oct-2-ynyl)-(2-methoxyphenyl)amine (5): The general procedure, as described earlier, was followed to afford 5 as an orange oil. IR (thin film): 3414 (w), 2958 (m), 2932 (s), 2861 (m), 1602 (m), 1511 (s), 1456 (m), 1241 (m), 1242 (m), ^{1}H NMR (400 MHz): δ 6.88 (1H, ddd, *J* = 7.6, 6.4, 1.6 Hz), 6.79-6.76 (2H, m), 6.69 (1H, ddd, *J* = 7.2, 6.4, 1.6 Hz), 4.36 (1H, br s), 4.01 (1H, ddt, *J* = 8.8, 5.6, 2.0 Hz), 3.84 (3H, s), 2.15 (2H, dt, *J* = 6.8, 2.4 Hz), 1.89-1.71 (2H, m), 1.5-1.4 (2H, m), 1.36-1.23 (4H, m), 1.09 (3H, t, *J* = 7.2 Hz), 0.87 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz): δ 147.2, 137.0, 121.2, 117.1, 111.6, 109.7, 83.3, 80.8, 55.6, 47.2, 31.3, 29.3, 28.7, 22.3, 18.8, 14.1, 10.6; HRMS calcd $C_{17}H_{26}NO$: 260.2014, Found: 260.2014; $[\alpha]_D^{20}$ = –36.7 ° (*c* = 0.85, $CHCl_3$).

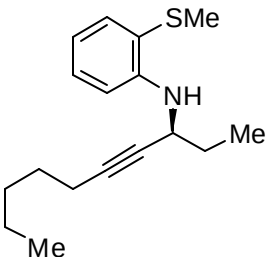
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 98.0:2.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 68% *ee*.



PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.599		0.0000	0.000	3688681.0	49.140	BB	0.194	317625.90	70.237
2	12.856		0.0000	0.000	3817760.0	50.860	BB	0.473	134592.90	29.763

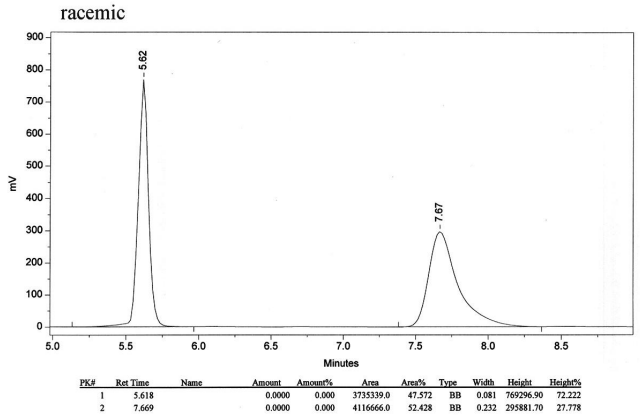


PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.591		0.0000	0.000	7947467.0	86.340	BB	0.212	625769.00	93.332
2	12.861		0.0000	0.000	1257346.0	13.660	BB	0.469	44710.41	6.668

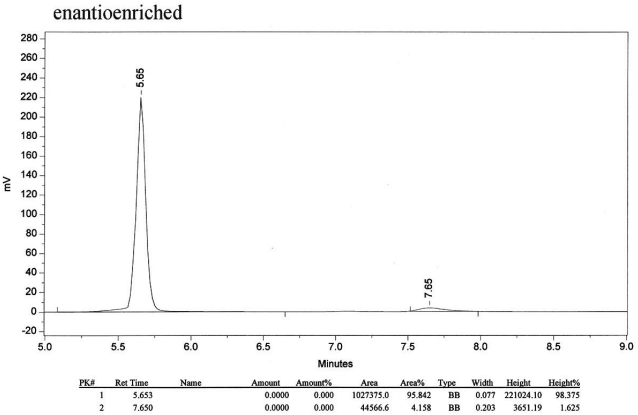


(1-Ethyloct-2-ynyl)-(2-methylsulfanylphenyl)amine (9): The general procedure, as described earlier, was followed to afford **9** as a yellow oil. IR (thin film); 3358 (w), 2961 (s), 2936 (s), 2860 (m), 1589 (s), 1495 (s), 1451 (m), 1318 (m); ^{1}H NMR (400 MHz): δ 7.39 (1H, dd, *J* = 7.6, 1.6 Hz), 7.19 (1H, dt, *J* = 8.4, 1.6 Hz), 6.79 (1H, dd, *J* = 8.0, 1.2 Hz), 6.68 (1H, dt, *J* = 7.6, 1.2), 5.00 (1H, d, *J* = 8.0 Hz), 4.05 (1H, tq, *J* = 8.0, 2.0 Hz), 2.32 (3H, s), 2.15 (2H, dt, *J* = 8.4, 1.2 Hz), 1.88-1.77 (2H, m), 1.48-1.42 (2H, m), 1.35-1.24 (4H, m), 1.10 (3H, t, *J* = 7.6 Hz), 0.87 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz): δ 147.5, 134.2, 129.41, 120.6, 117.7, 111.9, 83.4, 80.5, 47.4, 31.2, 29.4, 28.6, 22.3, 18.8, 18.5, 14.1, 10.6; HRMS calcd for $C_{17}H_{26}NS$: 276.1786, Found: 276.1785; $[\alpha]_D^{20} = -11.4$ ° (*c* = 0.6, $CHCl_3$).

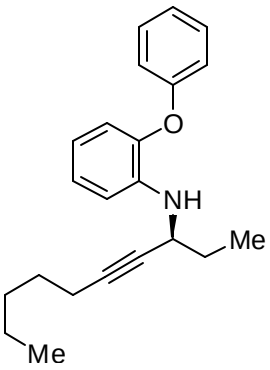
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 99.0:1.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 92% *ee*.



PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.618		0.0000	0.000	3735339.0	47.572	BB	0.081	769296.90	72.222
2	7.669		0.0000	0.000	4116666.0	52.428	BB	0.232	295881.70	27.778



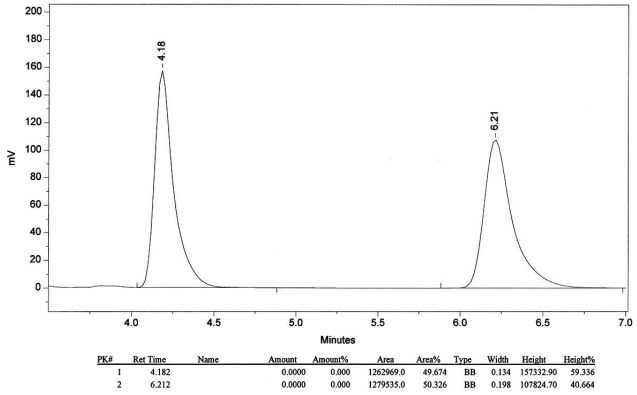
PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.653		0.0000	0.000	1027375.0	95.842	BB	0.077	221024.10	98.375
2	7.650		0.0000	0.000	44566.6	4.158	BB	0.203	3651.19	1.625



(1-Ethyloct-2-ynyl)-(2-phenoxyphenyl)amine (10): The general procedure, as described earlier, a was followed to afford **10** as a pale yellow oil. IR (thin film): 3420 (w), 3055 (w), 2961 (s), 2923 (s), 2860 (m), 1608 (s), 1513 (s), 1488 (s), 1438 (s), 1243 (s), 1218(s); ^{1}H NMR (400 MHz): δ7.32-7.28 (2H, m), 7.08-7.03 (2H, m), 6.99 (2H, m), 6.91 (1H, dd, *J* = 8.0, 1.6 Hz), 6.83 (1H, dd, *J* = 8.0, 1.2 Hz), 6.67 (1H, dt, *J* = 7.6, 1.6 Hz), 4.28 (1H, br s), 4.04 (1H, m), 2.14 (2H, dt, *J* = 2.0, 7.2 Hz), 1.83-1.65 (2H, m), 1.49-1.42 (2H, m), 1.34-1.23 (4H, m), 1.02 (3H, t, *J* = 7.6 Hz), 0.87 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz): δ 157.7, 143.8, 139.4, 129.8, 124.8, 122.9, 119.2, 117.8, 117.5, 113.4, 83.5, 80.5, 47.3, 31.1, 29.3, 28.6, 22.3, 18.8, 14.1, 10.5; HRMS calcd $C_{22}H_{28}NO$: 322.2183, Found: 322.2171; $[\alpha]_D^{20}$ = – 42.6° (*c* = 0.7, $CHCl_3$).

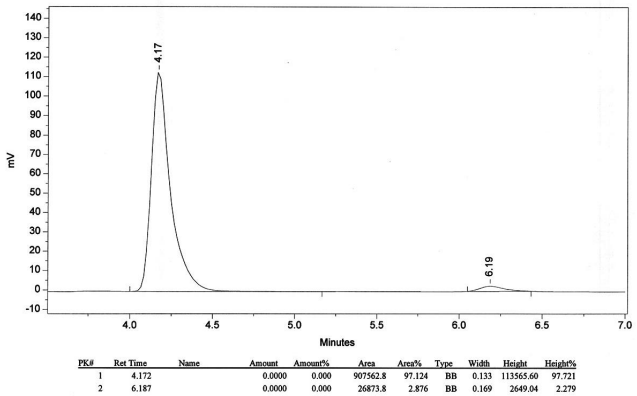
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 98.0:2.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 94% *ee*.

racemic



PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	4.182		0.0000	0.000	1262969.0	49.674	BB	0.134	157332.90	59.336
2	6.212		0.0000	0.000	1279535.0	50.326	BB	0.198	107824.70	40.664

enantioenriched



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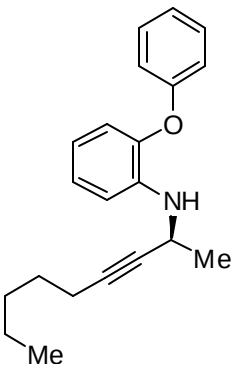
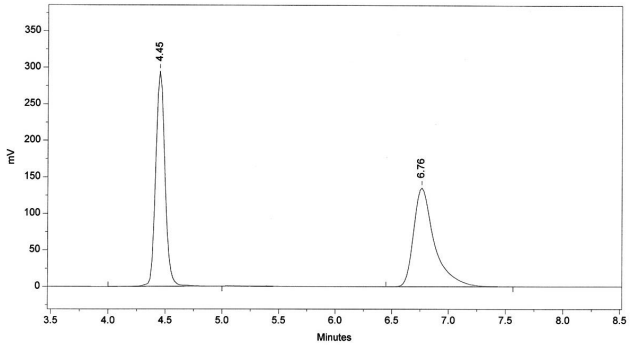
1	4.172		0.0000	0.000	907562.8	97.124	BB	0.133	113565.60	97.721
2	6.187		0.0000	0.000	26873.8	2.876	BB	0.169	2649.04	2.279



(1-Methyloct-2-ynyl)-(2-phenoxyphenyl)amine (15): The general procedure as described earlier, modified by a slow addition of Me_2Zn (2.0 M solution in toluene) to the reaction mixture over 1h, afforded **15** as a pale yellow oil. IR (thin film): 3408 (w), 3062 (w), 2974 (w), 1608 (m), 1489 (s), 1256 (m), 1218 (s), 1155 (m); ^{1}H NMR (400 MHz): δ 7.33-7.28 (2H, m), 7.08-7.03 (2H, m), 7.00-6.90 (2H, m), 6.91 (1H, dd, *J* = 8.0, 1.6 Hz), 6.82 (1H, dd, *J* = 8.0, 1.6 Hz), 6.67 (1H, ddd, *J* = 8.4, 7.6,1.6 Hz), 4.22 (1H, br s), 2.12 (2H, t, *J* = 7.2), 1.48-1.42 (5H, m), 1.30-1.26 (4H, m), 0.87 (3H, t, *J* = 6.8 Hz); ^{13}C NMR (100 MHz): δ 157.7, 143.8, 139.3, 129.8, 124.7, 122.9, 119.1, 117.9, 117.7, 113.5, 82.6, 81.7, 41.0, 31.1, 28.6, 22.9, 22.3, 18.7, 14.1, HRMS calcd for $C_{21}H_{26}NO$: 308.2014, Found: 308.2013; $[\alpha]_D^{20}$ = –5.3° (*c* = 0.3, $CHCl_3$).

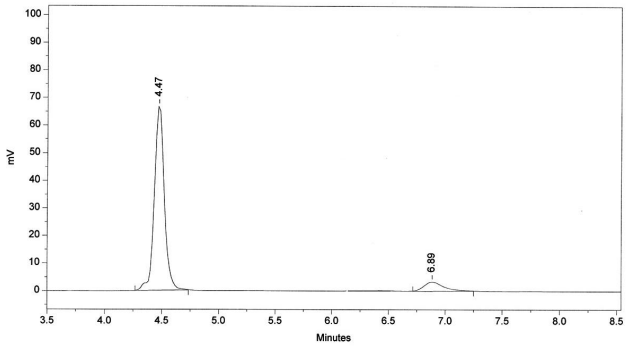
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 98.0:2.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 82% *ee*..

racemic

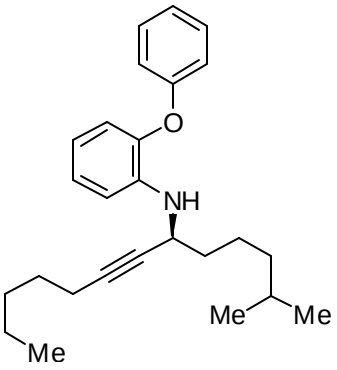


PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	4.451		0.0000	0.000	1678428.0	49.349	BB	0.095	294815.30	68.488
2	6.765		0.0000	0.000	1722735.0	50.651	BB	0.212	135646.00	31.512

enantioenriched



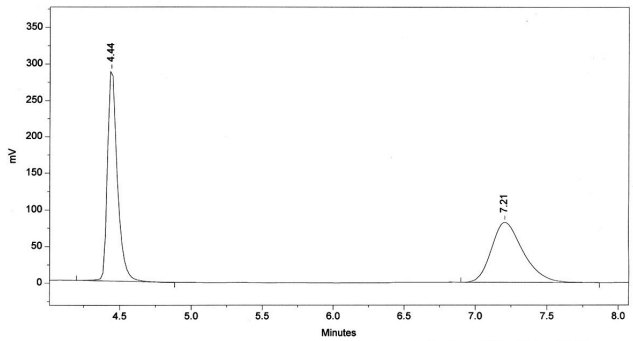
PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	4.473		0.0000	0.000	407623.3	90.914	BB	0.101	67404.12	95.238
2	6.888		0.0000	0.000	40738.9	9.086	BB	0.201	3369.98	4.762



[1-(4-Methylpentyl)oct-2-ynyl]-(2-phenoxyphenyl)amine (16): The general procedure, as described earlier, was followed to afford **16** as a pale yellow oil. IR (thin film): 3421 (w), 2954 (s), 2932 (s), 2862 (m), 1608 (m), 1511 (s), 1490 (m), 1432 (w), 1250 (w), 1218 (s); ^{1}H NMR (400 MHz): δ 7.32-7.28 (2H, m), 7.08-7.03 (2H, m), 7.0-6.96 (2H, m), 6.90 (1H, dd, *J* = 8.4, 1.2 Hz), 6.83 (1H, dd, *J* = 8.0, 1.6 Hz), 6.70-6.65 (1H, m), 4.22 (1H, d, *J* = 6.8 Hz), 4.08 (1H, d, *J* = 6.8 Hz), 2.13 (2H, dt, *J* = 7.2, 2.0 Hz), 1.70-1.15 (13 H, m), 1.50-1.18 (9H, m); ^{13}C NMR (100 MHz): δ 157.8, 143.7, 139.5, 129.8, 124.8, 122.9, 119.3, 117.8, 117.5, 113.3, 83.3, 80.8, 45.9, 38.6, 36.5, 31.1, 28.6, 28.0, 23.9, 22.7, 22.7, 22.3, 18.8, 14.1; HRMS calcd $C_{26}H_{35}NONa$: 400.2616, Found: 400.2613; $[\alpha]_D^{20}$= –1.7 ° (*c* = 0.8, $CHCl_3$).

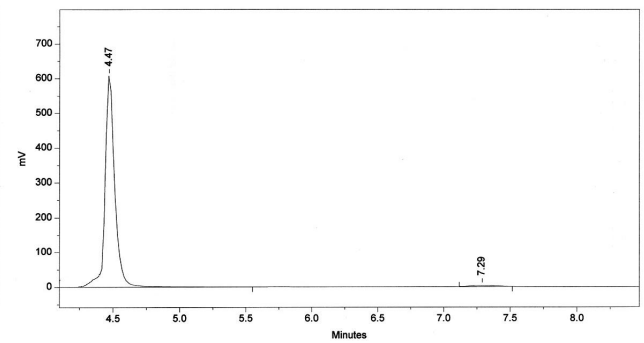
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 99.0:1.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 98% *ee*.

racemic

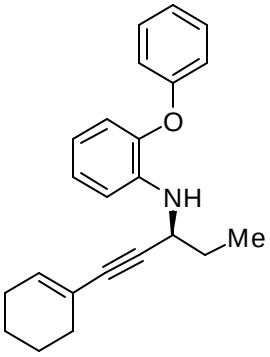


PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	4.441		0.0000	0.000	1386264.0	52.327	BB	0.078	297222.50	78.328
2	7.207		0.0000	0.000	1262945.0	47.673	BB	0.256	82234.15	21.672

enantioenriched

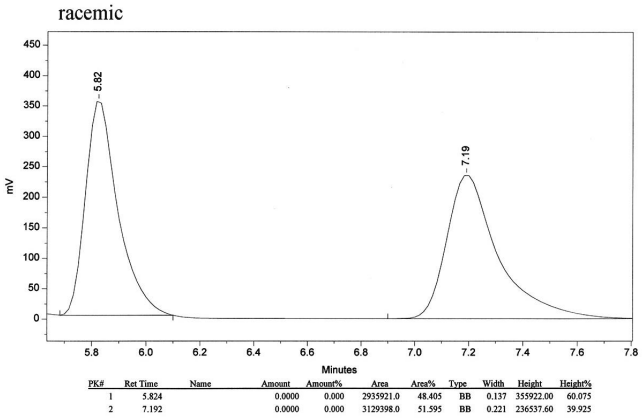


PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	4.471		0.0000	0.000	3822058.0	98.631	BB	0.103	616361.40	99.366
2	7.291		0.0000	0.000	53069.4	1.369	BB	0.225	3935.38	0.634

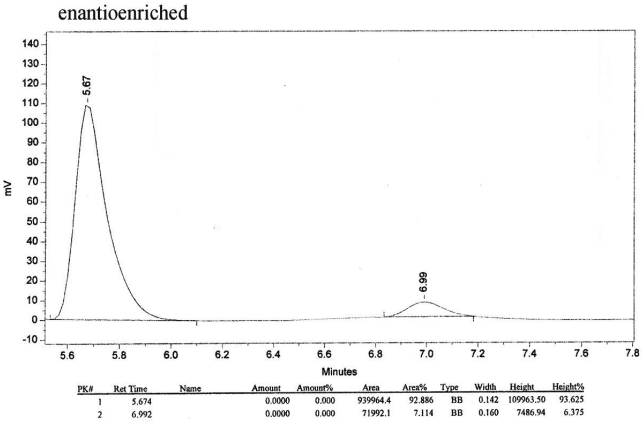


(3-Cyclohex-1-enyl-1-ethylprop-2-ynyl)-(2-phenoxyphenyl)amine (21): The general procedure, as described earlier, was followed to afford **21** as a pale yellow oil. IR (thin film): 3415 (w), 2930 (s), 1607 (s), 1510 (s), 1490 (s), 1435 (m), 1218 (s); ^{1}H NMR (400 MHz): δ 7.33-7.27 (2H, m), 7.08-7.03 (2H, m), 7.01- 6.97 (2H, m), 6.83 (2H, m), 6.67 (1H, dt, *J* = 7.6, 1.6 Hz), 6.02 (1H, dt, *J* = 4.0, 2.0 Hz), 4.29 (1H, br s), 4.18 (1H, t, *J* = 6.8 Hz), 2.07-2.03 (4H, m), 1.87-1.70 (2H, m), 1.63-1.52 (4H, m), 1.03 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz): δ 157.7, 143.8, 139.4, 134.6, 129.8, 124.8, 122.9, 120.6, 119.3, 117.8, 117.6, 113.3, 87.1, 84.9, 47.6, 29.5, 29.2, 25.7, 22.4, 21.6, 10.5; HRMS calcd $C_{23}H_{25}NONa$: 354.1834, Found: 354.1836; $[\alpha]_D^{20} = -6.1°$ (*c* = 0.4, $CHCl_3$).

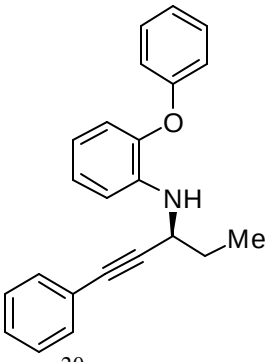
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 99.0:1.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 86% *ee*.



PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.824		0.0000	0.000	2935921.0	48.405	BB	0.137	355922.00	60.075
2	7.192		0.0000	0.000	3129398.0	51.595	BB	0.221	236537.60	39.925



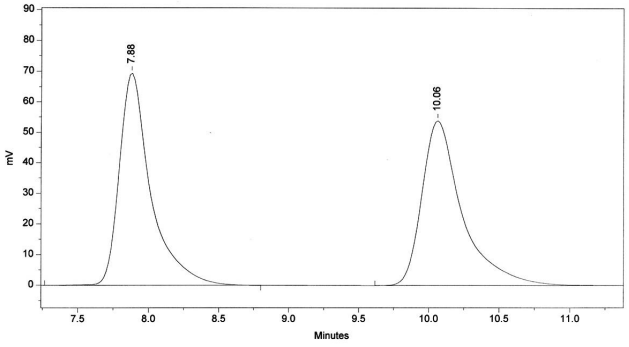
PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.674		0.0000	0.000	939964.4	92.886	BB	0.142	109963.50	93.625
2	6.992		0.0000	0.000	71992.1	7.114	BB	0.160	7486.94	6.375



(1-Ethyl-3-phenylprop-2-ynyl)-(2-phenoxyphenyl)-amine (24): The general procedure, as described earlier, was followed to afford 24 as a yellow solid, mp = 51 °C. IR (solid thin film): 3421 (w), 3043 (w), 2965 (s), (2928 (s), 2867 (m), 1608 (s), 1585 (s), 1509 (s), 1489 (s), 1436 (m), 1217 (m); ^{1}H NMR (400 MHz): δ 7.38-7.35 (2H, m), 7.32-7.26 (5H, m), 7.11-6.97 (2H, m), 7.02-6.97 (3H, m), 6.87-6.84 (1H, m), 6.72-6.68 (1H, m), 4.37 (1H, br s), 4.31 (1H, br s), 1.89 (2H, m), 1.12 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz): δ 157.7, 143.9, 139.2, 131.9, 129.8, 128.3, 128.2, 124.9, 123.3, 123.0, 119.3, 117.8, 113.4, 90.0, 83.1, 47.7, 29.2, 10.6; HRMS calcd $C_{23}H_{22}NO$: 328.1698, Found: 328.1701; $[\alpha]_D^{20} = -32.1$ ° (*c* = 0.5, $CHCl_3$).

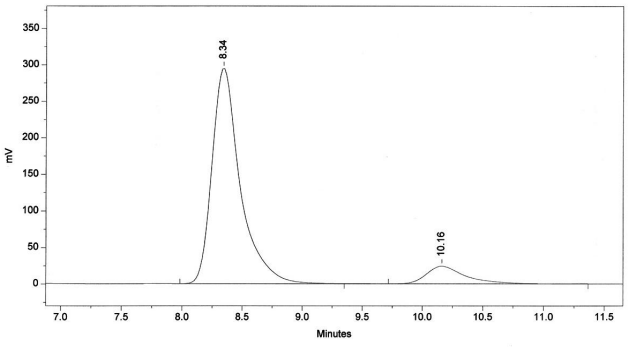
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 99.0:1.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 80% *ee*.

racemic

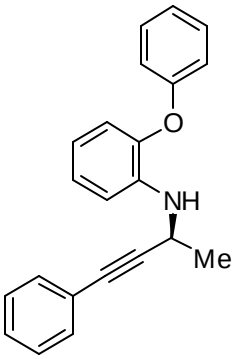


PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	7.878		0.0000	0.000	1071882.0	49.955	BB	0.257	69507.56	56.292
2	10.064		0.0000	0.000	1073821.0	50.045	BB	0.332	53969.67	43.708

enantioenriched



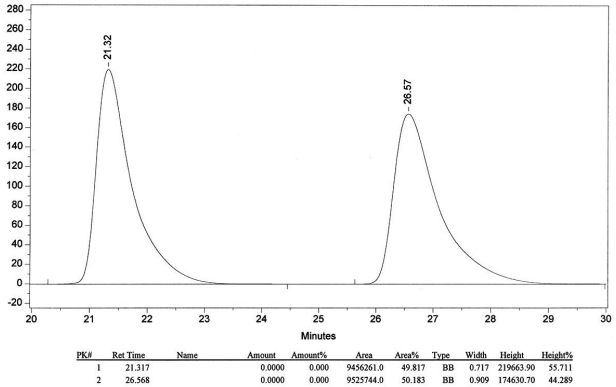
PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	8.342		0.0000	0.000	4815853.0	89.944	BV	0.272	295362.10	92.439
2	10.162		0.0000	0.000	538401.9	10.056	VB	0.371	24159.71	7.561



(1-Methyl-3-phenyl-prop-2-ynyl)-(2-phenoxyphenyl)amine (23): The general procedure as described earlier, modified by a slow addition of Me_2Zn (2.0 M solution in toluene) to the reaction mixture over 1h, afforded **23** as a tan solid, mp = 65 ^{o}C. IR (solid thin film): 3415 (w), 3056 (w), 2980 (w), 2930 (w), 1608 (s), 1508 (s), 1489 (s), 1250 (s), 1212 (s), 752 (s), 690 (s); ^{1}H NMR (400 MHz): δ7.36-7.63 (7H, m), 7.10-7.04 (2H, m), 7.02-6.98 (3H, m), 6.85-6.83 (1H, m), 6.72-6.68 (1H, m), 4.48 (1H, m), 4.34 (1H, d, J = 7.2 Hz), 1.60 (3H, t, J = 6.4 Hz); ^{13}C NMR (100 MHz): δ157.7, 144.0, 139.2, 131.9, 129.8, 128.3, 128.1, 124.8, 123.2, 123.0, 119.2, 118.0, 117.9, 113.6, 91.0, 82.2, 41.5, 22.5; HRMS calcd $C_{22}H_{19}NONa$: 336.1367, Found: 336.1364; $[\alpha]_D^{20}$ = –10.9° (c = 0.1, $CHCl_3$).

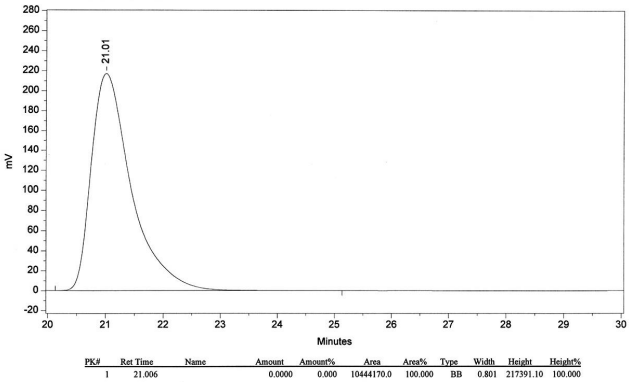
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 99.5:0.5 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, >98% *ee*.

racemic



PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	21.317		0.0000	0.000	9456261.0	49.817	BB	0.717	219663.90	55.711
2	26.568		0.0000	0.000	9525744.0	50.183	BB	0.909	174630.70	44.289

enantioenriched



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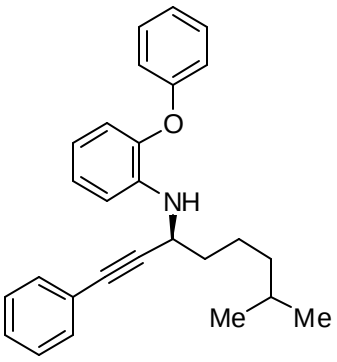
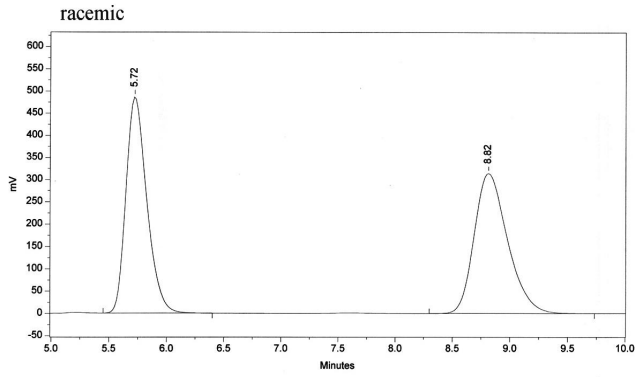
1	21.006		0.0000	0.000	10444170.0	100.000	BB	0.801	217391.10	100.000

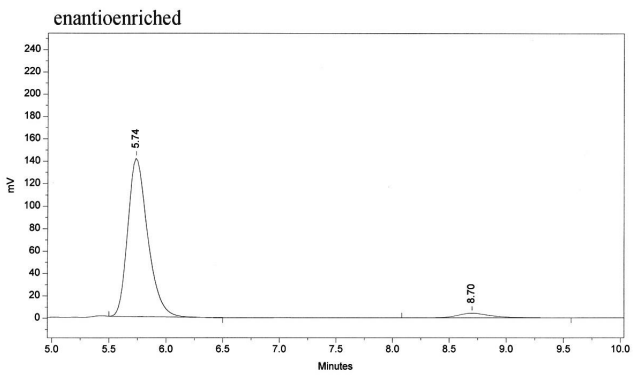


(5-Methyl-1-phenylethynylhexyl)-(2-phenoxyphenyl)amine (25): The general procedure, as described earlier, was followed to afford **25** as a pale yellow oil. IR (thin film): 3421 (w), 2952 (s), 2967 (m), 1607 (s), 1510 (s), 1489 (s), 1457 (w), 1217 (s); ^{1}H NMR (400 MHz): δ 7.28-7.17 (7H, m), 7.02-6.9 (5H, m), 6.68 (1H, dd, *J* = 8.0, 1.2 Hz), 6.64-6.6 (1H, m), 4.25 (2H, br s), 1.75-1.73 (2H, m), 1.50-1.42 (3H, m), 1.18-1.13 (2H, m), 0.80 (6H, d, *J* = 6.0 Hz); ^{13}C NMR (100 MHz): δ157.7, 143.8, 139.4, 131.8, 129.8, 128.3, 128.1, 124.9, 123.3, 122.9, 119.4, 117.9, 117.8, 113.4, 90.3, 83.0, 46.3, 38.6, 36.2, 28.0, 23.9, 22.8, 22.6; HRMS calcd $C_{27}H_{29}NONa$: 406.2147 Found: 406.2143; $[\alpha]_D^{20}$ = – 1.42 ° (*c* = 0.7 , $CHCl_3$).

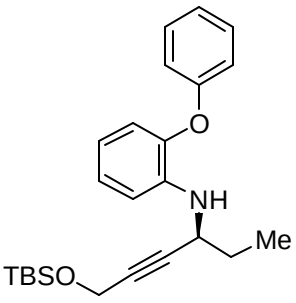
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 98.0:2.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 92% *ee*.



PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.721		0.0000	0.000	6099278.0	49.057	BB	0.209	486825.80	60.745
2	8.815		0.0000	0.000	6333778.0	50.943	BB	0.336	314594.40	39.255



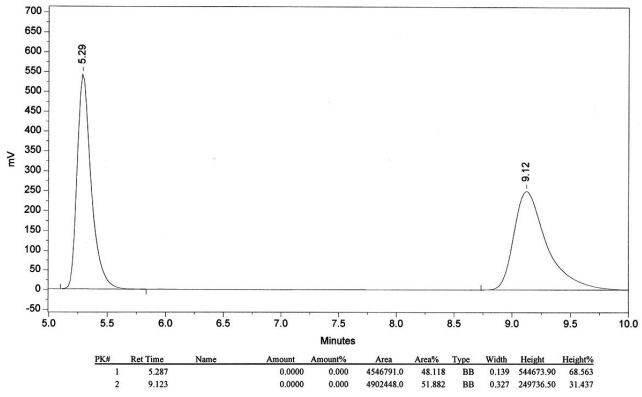
PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.736		0.0000	0.000	1712372.0	95.586	BB	0.202	141225.80	97.217
2	8.702		0.0000	0.000	79078.9	4.414	BB	0.326	4043.12	2.783



[4-(*tert*-Butyldimethylsilanyloxy)-1-ethylbut-2-ynyl]-(2-phenoxyphenyl)amine (18): The general procedure, as described earlier, was followed to afford **18** as a yellow oil. IR (thin film): 3421 (w), 2957 (s), 2929 (s), 2857 (s), 1608 (m), 1511 (s), 1490 (s), 1250 (m), 1218 (s), 1093 (s), 837 (s); ^{1}H NMR (400 MHz): δ 7.33-7.29 (2H, m), 7.09-7.03 (2H, m), 7.01-6.98 (2H, m), 6.90 (1H, dd, *J* = 8.4, 1.6 Hz), 6.84 (1H, dd, *J* = 8.0, 1.6 Hz), 6.68 (1H, dt, *J* = 7.2, 1.2 Hz), 4.30 (1H, d, *J* = 1.6 Hz), 4.10 (1H, dd, *J* = 7.2, 1.6), , 1.84-1.75 (2H, m), 1.04 (3H, t, *J* = 7.2 Hz), 0.89 (9H, s), 0.07 (6H, s); ^{13}C NMR (100 MHz): δ 157.7, 143.9, 139.3, 129.8, 124.9, 123.0, 119.3, 117.9, 117.8, 113.2, 85.3, 81.5, 52.0, 47.1, 29.0, 26.0, 10.5, 5.0; HRMS calcd $C_{24}H_{33}NO_2NaSi$: 418.2163, Found: 418.2178; $[\alpha]_D^{20}$ = –17.3° (*c* = 0.8, $CHCl_3$).

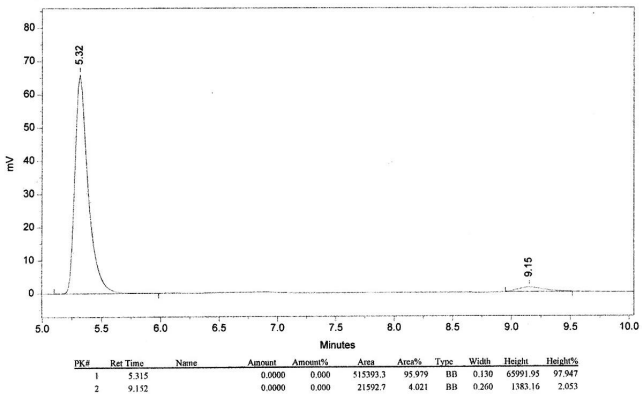
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 99.0:1.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 92% *ee*.

racemic

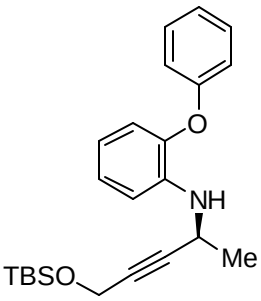


PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.287		0.0000	0.000	4546791.0	48.118	BB	0.139	544673.90	68.563
2	9.123		0.0000	0.000	4902448.0	51.882	BB	0.327	249736.50	31.437

enantioenriched



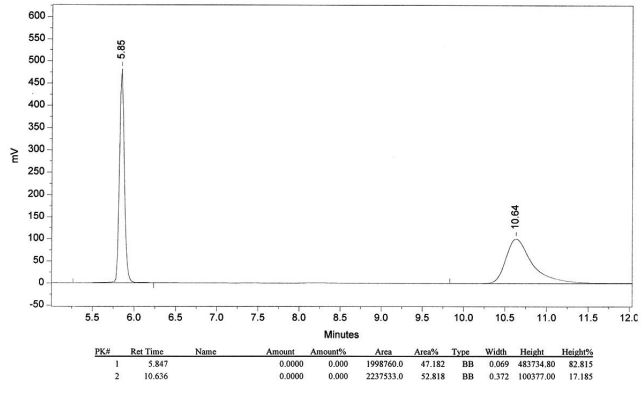
PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.315		0.0000	0.000	515393.3	95.979	BB	0.130	65991.95	97.947
2	9.152		0.0000	0.000	21592.7	4.021	BB	0.260	1383.16	2.053



[4-(*tert*-Butyldimethylsilanyloxy)-1-methylbut-2-ynyl]-(2-phenoxyphenyl)amine (17): The general procedure as described earlier, modified by a slow addition of Me_2Zn (2.0 M solution in toluene) to the reaction mixture over 1h, afforded **17** as a yellow oil. IR (thin film): 3408 (w), 2948 (m), 2930 (s), 2854 (m), 1583 (m), 1608 (m), 1508 (s), 1489 (s), 1249 (s), 1218 (s), 1073 (m), 834 (s). ^{1}H NMR (400 MHz): δ 7.31-7.27 (2H, m), 7.07-7.01 (2H, m), 6.98-6.96 (2H, m), 6.97 (1H, dd, *J* = 8.0, 1.2 Hz), 6.80 (1H, dd, *J* = 8.0, 1.2 Hz), 6.67 (1H, q, *J* = 7.2, 1.6 Hz), 4.27 (4H, br s), 1.50 (3H, d, *J* = 6.4 Hz), 0.88 (9H, s), 0.06 (6H, s); ^{13}C NMR (100 MHz): δ 157.6, 143.9, 139.0, 129.8, 124.8, 123,0, 119.0, 117.9, 117.9, 113.3, 86.3, 80.6, 51.9, 40.9, 26.0, 22.4, 18.4, -5.0; HRMS calcd $C_{23}H_{31}NO_2NaSi$: 403.1943, Found: 403.1941; $[\alpha]_D^{20} = -23.5°$ (*c* = 0.2, $CHCl_3$).

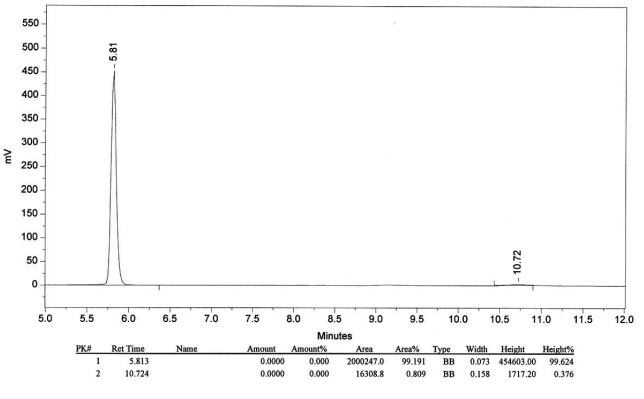
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 99.0:1.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 98% *ee*.

racemic



PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	5.847		0.0000	0.000	1998760.0	47.182	BB	0.069	483734.80	82.815
2	10.636		0.0000	0.000	2237533.0	52.818	BB	0.372	100377.00	17.185

enantioenriched



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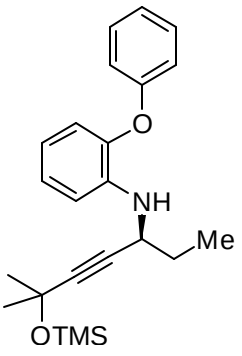
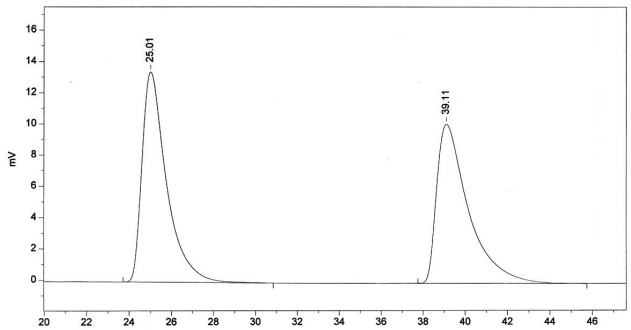
1	5.813		0.0000	0.000	2000247.0	99.191	BB	0.073	454603.00	99.624
2	10.724		0.0000	0.000	16308.8	0.809	BB	0.158	1717.20	0.376



(1-Ethyl-4-methyl-4-trimethylsilanyloxypent-2-ynyl)-(2-phenoxyphenyl)amine (19): The general procedure, as described earlier, was followed to afford **19** as a pale yellow solid, mp = 44 °C. IR (solid thin film): 3427 (w), 2974 (m), 2930 (m), 1608 (m), 1583 (m), 1508 (s), 1489 (s), 1438 (m), 1250 (s), 1218 (s), 1162 (s), 1035 (s), 841 (s); ^{1}H NMR (400 MHz): δ 7.32-7.28 (2H, m), 7.08-7.02 (2H, m), 7.00-6.96 (2H, m), 6.88 (1H, dd, *J* = 8.0, 1.6 Hz), 6.83 (1H, dd, *J* = 8.0, 1.6 Hz), 6.67 (1H, dt, *J* = 7.6, 1.2 Hz), 4.27 (1H, br s), 4.08 (1H, t, *J* = 6.8 Hz), 1.83-1.71 (2H, m), 1.41 (3H, s), 1.42 (3H, s), 1.03 (3H, t, *J* = 7.2 Hz), 0.11 (9H, s); ^{13}C NMR (100 MHz): δ 157.7, 143.7, 139.3, 129.8, 124.8, 122.9, 119.3, 117.8, 117.7, 113.3, 88.1, 83.3, 66.6, 47.0, 33.3, 29.0, 10.5, 2.0; HRMS calcd $C_{23}H_{31}NO_2NaSi$: 382.2202, Found: 382.2187; $[\alpha]_D^{20}$ = –9.4° (*c* = 0.2, $CHCl_3$).

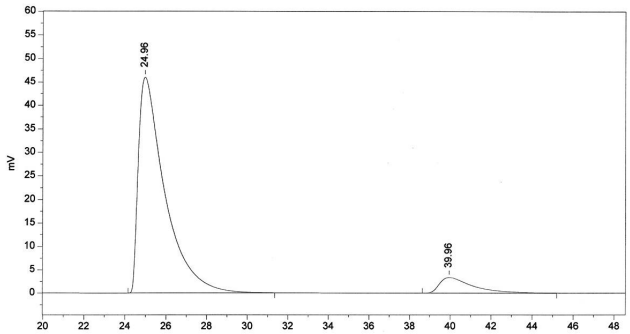
The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 100% hexanes, 1.0 mL/min, λ = 254 nm, 84% *ee*.

racemic



PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	25.012		0.0000	0.000	1080553.0	50.393	BB	1.339	13450.98	56.924
2	39.112		0.0000	0.000	1063715.0	49.607	BB	1.742	10178.71	43.076

enantioenriched



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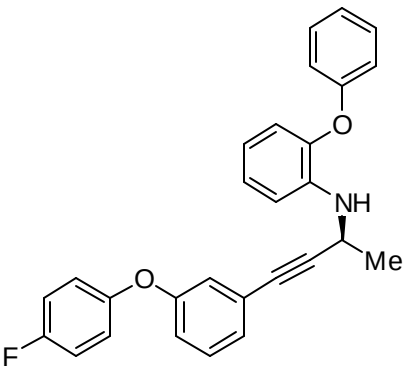
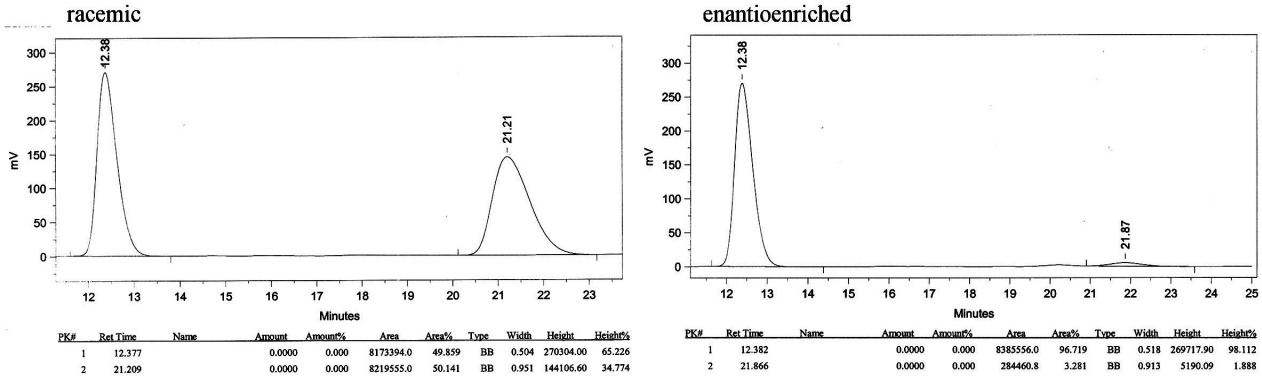
1	24.962		0.0000	0.000	4144750.0	91.773	BB	1.500	46038.52	93.234
2	39.955		0.0000	0.000	371573.0	8.227	BB	1.854	3340.84	6.766



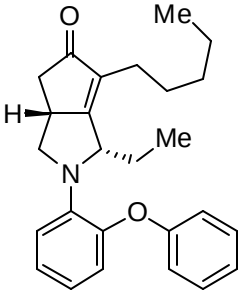
{3-[3-(4-Fluorophenoxy) phenyl]-1-methylprop-2-ynyl}-(2-phenoxyphenyl)amine (26): The general procedure as described earlier, modified by a slow addition of Me_2Zn (2.0 M solution in toluene) to the reaction mixture over 1h, afforded **26** as a yellow oil. IR (thin film): 3396 (w), 3069 (w), 2930 (w), 1608 (m), 1501 (s), 1218 (m), 1199 (s); ^{1}H NMR (400 MHz): δ 7.36-7.26 (10H, m), 7.10-7.04 (2H, m), 7.02-6.98 (3H, m), 6.84 (1H, dd, *J* = 8.0, 1.6 Hz), 6.70 (1H, dt, *J* = 7.6, 1.6 Hz), 4.50 (1H, m), 4.35 (1H, br s), 1.60 (3H, d, *J* = 6.8 Hz); ^{13}C NMR (100 MHz): δ 160.4, 157.7 (d, *J* = 4.5 Hz), 152.7, 144.0, 139.1, 129.9, 129.8, 126.8, 124.8, 123.1, 121.3, 121.0, 120.9, 119.2, 118.5, 118.1, 118.0, 116.7, 116.5, 113.6, 91.7, 81.6, 41.5, 22.5; HRMS calcd $C_{28}H_{23}FNO_2$: 424.1724, Found: 424.1713; $[\alpha]_D^{20}$ = –12.2 ° (*c* = 0.4, $CHCl_3$).

The optical purity of the alkylzinc addition adduct was determined by chiral HPLC: Chiracel OD (0.46 x 25 cm), 99.0:1.0 hexanes:isopropanol, 1.0 mL/min, λ = 254 nm, 94% *ee*.

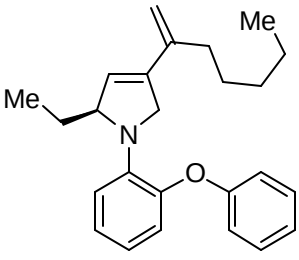


PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	12.377		0.0000	0.000	8173394.0	49.859	BB	0.504	270304.00	65.226
2	21.209		0.0000	0.000	8219555.0	50.141	BB	0.951	144106.60	34.774

PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	12.382		0.0000	0.000	8385556.0	96.719	BB	0.518	269717.90	98.112
2	21.866		0.0000	0.000	284460.8	3.281	BB	0.913	5190.09	1.888



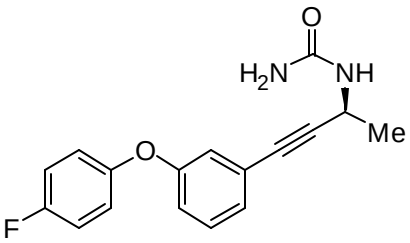
2-Ethyl-4-(1-methylenehexyl)-1-(2-phenoxyphenyl)-2,5-dihydro-1H-pyrrole (31): (1-Ethyl-oct-2-ynyl)-(2-phenoxyphenyl)amine (**10**) was allylated according to reported procedures.[8] In a glove box under an atmosphere of N_2, a 5 mL flask was charged with $Ti(Cp)_2(CO)_2$ (3.6 mg, 0.015 mmol) and allyl-(1-ethyloct-2-ynyl)-(2-phenoxyphenyl)amine (**28**) (24.8 mg, 0.08 mmol) in toluene (0.5 mL). The flask was fit with a condenser, sealed with a septum and teflon tape and removed from the glove box. The vessel was purged with CO and kept under an atmosphere of CO for the duration of the reaction. The mixture was heated to 90 ^oC in an oil bath for 12 h. After cooling to 22 ^oC, the mixture was diluted with Et_2O, filtered through a plug of silica, and concentrated. Silica gel chromatography (100:1 hexanes: Et_2O) afforded **31** as a pale yellow oil (24 mg, 0.06 mmol, 80%, 9:1 mixture of diastereomers). IR (thin film): 2958 (m), 2929 (m), 2857 (w), 1710 (s), 1671 (m), 1601 (w), 1489 (s), 1222 (s), 750 (m); ^1H NMR (400 MHz): δ 7.28-7.26 (2H, m), 7.10 (1H, m), 7.02-6.95 (3H, m), 6.88-6.84 (3H, m), 5.02 (0.13H, br s, minor diastereomer), 4.57 (1H, br s), 4.31 (1H, t, J = 8.0 Hz), 3.67 (0.13H, t, J = 7.2 Hz, minor diastereomer), 3.01-3.04 (1H, m), 2.62-2.54 (2H, m), 2.15 (1H, t, J = 8.0 Hz), 2.07 (1H, dd, J = 18, 2.5 Hz), 1.79-1.90 (1H, m), 1.67-1.56 (1H, m), 1.48-1.17 (7H, m), 0.85 (3H, t, 6.8 Hz), 0.75 (3H, t, J = 7.2 Hz), 0.51 (0.33 H, t, J = 7.2 Hz minor diastereomer); ^{13}C NMR (100 MHz): δ 209.5, 178.1, 158.4, 146.4, 140.2, 136.9, 129.7, 125.34, 123.3, 122.4, 120.8, 118.5, 116.8, 59.5, 55.8, 41.3, 40.1, 32.1, 27.8, 26.1, 24.4, 22.6, 14.1, 9.8; HRMS calcd $C_{26}H_{32}NO_2$: 361.2406, Found: 361.2402.



2-Ethyl-4-(1-methylene-hexyl)-1-(2-phenoxy-phenyl)-2,5-dihydro-1H-pyrrole (30): In a 10 mL round bottom flask, allyl-(1-ethyl-oct-2-ynyl)-(2-phenoxy-phenyl)-amine (**28**) (111.1 mg, 0.30 mmol) and catalyst (**29**) (9.4 mg, 0.015 mmol) were combined in 3 mL CH_2Cl_2. The reaction was allowed stir under an atmosphere of nitrogen for 3h. The resulting mixture was evaporated to dryness and passed through a plug of silica gel with 200:1 hexane:Et_2O to afford **30** as a pale orange

[8] J. Dolman, E. S. Sattely, A. H. Hoveyda, R. R. Schrock, *J. Am. Chem. Soc.* **2002**, *124*, 6991-6997.

oil (96.0 mg, 0.27 mmol, 90%). At this point, the catalyst was eluted with 1:2 hexanes:Et_2O (8.9 mg, .014 mmol, 95% recovery). IR (thin film): 2960 (m), 2930 (m), 2858 (m), 1602 (w), 1501 (s), 1451 (m), 1358 (w), 1222 (s); ^{1}H NMR (400 MHz): δ 7.27-7.23 (2H, m), 7.11-7.07 (1H, m), 6.99-6.93 (2H, m), 6.89-6.84 (3H, m), 6.71 (1H, ddd, *J* = 7.2, 7.2, 1.6 Hz), 5.82 (1H, br s), 5.17-5.16 (1H, m), 4.95 (2H, d, *J* = 6.0 Hz), 4.09-4.04 (1H, m), 2.33-2.13 (2H, m), 1.90-1.80 (1H, m), 1.74-1.64 (1H, m), 1.90-1.80 (1H, m), 1.74-1.65 (1H, m), 1.55-1.38 (2H, m), 1.32-1.23 (4H, m), 0.87 (3H, t, *J* = 7.2 Hz), 0.51 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz): δ 158.9, 143.45, 142.1, 141.2, 140.1, 129.7, 125.6, 123.3, 122.4, 121.8, 117.8, 116.4, 115.8, 112.5, 64.5, 58.3, 34.6, 31.9, 28.5, 24.1, 22.7, 14.2, 7.3. HRMS calcd $C_{26}H_{32}NO_2$: 390.2433, Found: 390.2403.



{3-[3-(4-Fluorophenoxy)phenyl]-1-methylprop-2-ynyl}urea (33): To a solution of $PhI(OAc)_2$ (50.0 mg, 0.16 mmol) in MeOH (2.5 mL), **26** in acetonitrile (1mL) was added, by a syringe pump, over 1h. A 1.0 N HCl (5.0 mL) was added and the mixture was allowed to stir for 2h. The aqueous layer was washed three times with CH_2Cl_2 being careful to remove all oxidant, and the organic layer washed with 0.1 N HCl. To the combined aqueous layers an equal volume of CH_2Cl_2 was added. Potassium cyanate (65 mg, 0.8 mmol) in water (14 mL) was added to the vigorously stirring biphasic solution, followed by dropwise addition of $NaHCO_3$ until a pH of 10 was achieved. The solution was allowed to stir one hour after which the layers were separated and the aqueous layer washed three times with CH_2Cl_2. Combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. **32** was isolated as a pale yellow oil (29 mg, 0.10 mmol, 61%). IR (solid thin film): 3413 (w), 3060 (w), 2980 (w), 2930 (w), 1655 (s), 1609 (s), 1508 (s), 1489 (s), 1250 (s), 1212 (s), 755 (s); ^{1}H NMR (400 MHz): δ?7.34-7.26 (8H, m), 3.93 (1H, m), 1.42 (3H, d, *J* = 6.8 Hz). HRMS calcd $C_{17}H_{15}FN_2O_2$: 298.1118, Found: 298.1112.