Direct Nucleophilic Acylation of Nitroalkenes Promoted by a Fluoride Anion/Thiourea Combination

Anita E. Mattson, Andrea M. Zuhl, Troy E. Reynolds and Karl A. Scheidt*

Department of Chemistry, Northwestern University, 2145 Sheridan Road, Evanston, Illinois, 60208

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General Information. All reactions were carried out under a nitrogen atmosphere in flame-dried glassware with magnetic stirring. THF, Et₂O, CH₂Cl₂, DMF and toluene were purified by passage through a bed of activated alumina.¹ CHCl₃ was purified by passage through a pad of alumina prior to use. Reagents were purified prior to use unless otherwise stated following the

1. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometal.* **1996**, *15*, 1518-1520.

guidelines of Perrin and Armarego.² Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and anisaldehyde, ceric ammonium nitrate stain, potassium permanganate, or phosphomolybic acid followed by heating. Melting points were obtained on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Bio-Rad Win FT-IR Pro spectrometer. ¹H-NMR spectra were recorded on a Varian Inova 500 (500 MHz) or Mercury 400 (400 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 7.26 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C-NMR spectra were recorded on a Varian Inova 500 (125 MHz) or Mercury 400 (100 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm). Laser desorption mass spectra were obtained with PE BioSystems time-of-flight MALDI mass spectrometer with 2,5-dihydroxybenzoic acid as matrix. Electrospray ionization mass spectra were obtained on a Thermo Finnigan lcms ion trap mass spectrometer.

Tetrabutylammonium triphenyldifluorosilicate (TBAT) and tetramethylammonium fluoride (TMAF) were purchased from Aldrich and used without further purification. Nitroalkenes (**2**) were prepared according to the procedure of Feringa et al.³ 1-Nitrocyclohexene was purchased from Aldrich and used with further purification. Thiocarbanilide was used as received from Aldrich. Thiourea **17** was prepared according to the procedure of Soos and coworkers.⁴

General Procedure for the Preparation of Protected Thiazolium Carbinols:

Synthesis of Carbinols:

A flame-dried round bottom flask under N₂ was charged with 4,5-dimethylthiazole (1 mL, 9.45 mmol). THF (45 mL) was added and the solution was cooled to 78 °C. *n*-Butyl lithium (1.9M, 6 mL, 11.3 mmol) was added dropwise to the cold reaction mixture. The resulting dark red solution was stirred for 45 min at 78 °C. The aldehyde (28.4 mmol) was then added, causing the solution to turn yellow, and the reaction was stirred for 1h at 78 °C. The reaction was warmed to room temperature and stirred for 2h. At this time, water (50 mL) was added to quench the reaction. The reaction mixture was diluted with ethyl acetate (200 mL) and washed with water (200 mL). The aqueous layer was extracted two additional times with ethyl acetate (100 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated *in vacuo*. The resulting residue was purified by recrystallization (ethyl acetate/hexanes).

Partial Characterization of Carbinols:

2. Perrin, D. D. and Armarego, W. L. *Purification of Laboratory Chemicals*; 3rd Ed., Pergamon Press, Oxford. 1988.
3. Duursma, A.; Minnaard, A.J.; Feringa, B.L. *Tetrahedron* **2002**, 58, 5773-5778.
4. Vakulya, B.; Varga, S.; Csampai, A.; Soos, T. *Org Lett* **2005**, 7, 1967-1969.

(4-Chlorophenyl)(4,5-dimethylthiazol-2-yl)methanol: Purified by recrystallization (ethyl acetate/hexanes), yielding 79% as a yellow solid. ^1H NMR (500 MHz, CDCl_3) δ 7.42 (m, 2H); 7.35 (m, 2H); 5.93 (s, 3H); 4.46 (s, 1H); 2.30 (s, 3H); 2.28 (s, 3H).

(4,5-Dimethylthiazol-2-yl)(phenyl)methanol: Purified by recrystallization (ethyl acetate/hexanes), yielding 1.94 g (84%) as a white solid. ^1H NMR (500 MHz, CDCl_3) δ 7.46 (m, 2H); 7.38 (m, 3H); 5.95 (s, 3H); 2.30 (s, 3H); 2.29 (s, 3H).

(4,5-Dimethylthiazol-2-yl)(naphthalen-3-yl)methanol: Purified by recrystallization (ethyl acetate/hexanes), yielding 1.99 g (78%) as an off white solid. ^1H NMR (500 MHz, CDCl_3) δ 7.98 (m, 1H); 7.87 (m, 1H); 7.86 (m, 1H); 7.86 (m, 1H); 7.59 (m, 1H); 7.57 (m, 1H); 7.51 (m, 1H); 6.14 (s, 1H); 2.32 (s, 3H); 2.30 (s, 3H).

(3-Methoxyphenyl)(4,5-dimethylthiazol-2-yl)methanol: Purified by recrystallization (ethyl acetate/hexanes), yielding 2.18 g (93%) as a yellow solid. ^1H NMR (500 MHz, CDCl_3) δ 7.30 (m, 1H); 7.06 (m, 2H); 6.88 (m, 1H); 5.93 (s, 1H); 3.82 (s, 3H); 2.30 (s, 3H); 2.28 (s, 3H).

(4-Bromophenyl)(4,5-dimethylthiazol-2-yl)methanol: Purified by recrystallization (ethyl acetate/hexanes), yielding 1.87 g (70%) as a yellow solid. ^1H NMR (500 MHz, CDCl_3) δ 7.51-7.50 (m, 2H); 7.37-7.35 (m, 2H); 5.90 (s, 3H); 2.31 (s, 3H); 2.30 (s, 3H).

Typical Protection and Alkylation of Carbinols:

To a flame-dried round bottom flask under N_2 was added the carbinol (7.3 mmol) followed by dichloromethane (75 mL). Next, triethylsilylchloride (22 mmol) was added followed by imidazole (8.0 mmol). The resulting suspension was then stirred overnight at room temperature. The reaction mixture was diluted with dichloromethane (100 mL) and washed three times with brine (200 mL). The combined aqueous layers were washed with dichloromethane. The combined organic layers were dried over Na_2SO_4 , filtered and concentrated *in vacuo*. The pale yellow oil was used in the next step without further purification.

To the protected carbinol in a flame-dried round bottom flask was added iodomethane (10 eq) and the reaction was heated at reflux at 80 $^\circ\text{C}$. After 12h the reaction was cooled to room temperature and concentrated *in vacuo*. Diethyl ether was then added to the yellow residue and the product precipitated. The solid was collected by vacuum filtration, washed with diethyl ether and dried under vacuum. The resulting product was used with further purification.

1a was isolated as a pale yellow solid in a 50% yield over the two steps. R_f = 0.49 (20% methanol/chloroform); Mp: 152-154°C; IR (film) 1951, 2876, 1600, 1242, 2083, 1101, 806, 735 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.62 (m, 2H); 7.42 (m, 2H); 7.05 (s, 1H); 4.01 (s, 3H); 2.52 (s, 3H); 2.44 (s, 3H); 0.89 (t, J = 8.0 Hz, 9H); 0.69 (m, 6H); ^{13}C NMR (500 MHz, CDCl_3) δ 177.0, 144.0, 136.4, 135.8, 130.7, 130.0, 72.4, 40.9, 13.3, 12.9, 7.0, 5.1; LRMS (MALDI-TOF): Mass calculated for $\text{C}_{19}\text{H}_{29}\text{NO}_2\text{SSi}$ $[\text{M-I}]^+$, 382.14. Found 382.75.

1b was isolated as a pale yellow solid in a 75% yield over the two steps. R_f = 0.50 (20% methanol/chloroform); Mp: 150-151°C; IR (film) 2953, 2875, 1604, 1455, 1073, 1008, 808, 735 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.56 (m, 2H); 7.44 (m, 3H); 6.86 (s, 1H); 3.95 (s, 3H); 2.51 (s, 3H); 2.43 (s, 3H); 0.87 (t, J = 7.6 Hz, 9H); 0.65 (m, 6H); ^{13}C NMR (500 MHz, CDCl_3) δ 177.0, 143.9, 137.0, 130.6, 129.7, 128.5, 73.4, 40.6, 13.5, 13.1, 6.9, 5.1; LRMS (MALDI-TOF): Mass calculated for $\text{C}_{19}\text{H}_{30}\text{NO}_2\text{SSi}$ $[\text{M-I}]^+$, 348.60. Found 348.80.

1c was isolated as a yellow solid in a 66% yield over the two steps. R_f = 0.55 (20% methanol/chloroform); Mp: 160-161 °C; IR (film) 2951, 2874, 1600, 1456, 1085, 1009, 807, 745 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.21 (s, 1H); 7.96 (m, 1H); 7.90 (m, 1H); 7.87 (m, 1H); 7.59 (m, 1H); 7.57 (m, 1H); 7.52 (m, 1H); 3.97 (s, 3H); 2.53 (s, 3H); 2.42 (s, 3H); 0.87 (t, J = 8.0 Hz, 9H); 0.68 (m, 6H); ^{13}C NMR (500 MHz, CDCl_3) δ 177.0, 144.0, 134.1, 133.9, 133.2, 130.7, 130.0, 128.7, 128.6, 128.1, 127.7, 127.3, 124.6, 73.6, 40.7, 13.4, 13.1, 6.9, 5.1; LRMS (MALDI-TOF): Mass calculated for $\text{C}_{23}\text{H}_{32}\text{NOSSi}$ $[\text{M-I}]^+$, 398.20. Found 398.70.

1d was isolated as a yellow solid in a 57% yield over the two steps. R_f = 0.55 (20% methanol/chloroform); Mp: 118-120 °C; IR (film) 2951, 2875, 1597, 1456, 1261, 1078, 1008, 806, 745 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.34 (m, 1H); 7.12 (s, 1H); 7.10 (s, 1H); 6.94 (m, 1H); 6.79 (s, 1H); 3.95 (s, 3H); 3.84 (s, 3H); 2.45 (s, 3H); 2.43 (s, 3H); 0.87 (t, J = 8.0 Hz, 9H); 0.65 (m, 6H) ppm; ^{13}C NMR (500 MHz, CDCl_3) δ 177.2, 160.4, 143.9, 138.5, 130.8, 130.5, 120.6, 115.9, 114.0, 73.3, 56.0, 40.7, 13.4, 12.9, 6.9, 5.1; LRMS (MALDI-TOF): Mass calculated for $\text{C}_{20}\text{H}_{34}\text{NOSSi}$ $[\text{M-I}]^+$, 378.19. Found 378.9.

1e was isolated as a yellow solid in a 44% yield over the two steps. R_f = 0.55 (20% methanol/chloroform); Mp: 170-172 °C; IR (film) 2955, 2876, 1597, 1486, 1242, 1080, 1010, 806, 731 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.56 (m, 4H); 7.04 (s, 1H); 4.00 (s, 3H); 2.52 (s, 3H); 2.44 (s, 3H); 0.87 (t, J = 7.9 Hz, 9H); 0.65 (m, 6H) ppm; ^{13}C NMR (500 MHz, CDCl_3) δ 176.2, 144.1, 136.2, 132.9, 130.8, 130.2, 124.6, 72.5, 40.8, 13.4, 13.0, 7.0, 5.1; LRMS (MALDI-TOF): Mass calculated for $\text{C}_{20}\text{H}_{34}\text{NOSSi}$ $[\text{M-I}]^+$, 424.4. Found 426.9.

Typical Procedure for the Nucleophilic Acylation of Nitroalkenes:

A dry screw-capped tube containing a magnetic stir bar was charged with thiourea **7** (76 mg, 0.335 mmol) in a nitrogen-filled glove box. Also in the box the protected thiazolium carbinol (260 mg, 0.510 mmol) and tetramethylammonium fluoride (TMAF, 48 mg, 0.510 mmol) were weighed into two separate dram vials. All items were removed from box and the tube was put under a positive N₂ pressure. Nitroalkene (52 mg, 0.335 mmol) was added to the thiourea in dichloromethane (1.6 mL). Reaction mixture was cooled to -40 °C. Next, carbinol was added in dichloromethane (0.5 mL) and the reaction was allowed to stir for 5 min. Last, TMAF was added in dichloromethane (0.5 mL). Reaction was allowed to stir at -40 °C for 2-24h until complete by thin layer chromatography (20% ether/hexanes). Upon completion reaction was quenched with water and diluted with dichloromethane then allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted two additional times with dichloromethane (30 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated *in vacuo*. The resulting orange residue was purified by flash column chromatography on silica gel.

2-Cyclohexyl-3-nitro-1-phenylpropan-1-one (5): Purified with 5% ether/hexanes, yielding 59 mg (59%) of **5** as a colorless oil. $R_f = 0.39$ (20% ether/hexanes); IR (film) 2929, 2854, 1679, 1551, 1375 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.00-7.98 (m, 2H); 7.63-7.60 (m, 1H); 7.52-7.49 (m, 2H); 5.09 (dd, $J = 14.5, 10.4$ Hz, 1H); 4.53 (dd, $J = 14.6, 3.3$ Hz, 1H); 4.20-4.16 (m, 1H); 1.72-1.62 (m, 6H); 1.25-1.06 (m, 4H); 0.96-0.91 (m, 1H); ¹³C NMR (500 MHz, CDCl₃) δ : 199.9, 136.8, 133.8, 129.1, 128.7, 73.9, 49.2, 39.5, 31.7, 29.8, 26.6, 26.4, 26.1; LRMS (ESI): Mass calculated for C₁₅H₁₉NO₃ [M]⁺, 261.32. Found [M+Na]⁺, 284.2.

1-(4-Chlorophenyl)-2-cyclohexyl-3-nitropropan-1-one (6): Purified with 5% ether/hexanes, yielding 78 mg (78%) of **6** as a white solid. $R_f = 0.39$ (20% ether/hexanes); Mp: 69.5-70.5 °C; IR (film) 2929, 1680, 1554, 1375 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.94-7.92 (m, 2H); 7.49-7.47 (m, 2H); 5.07 (dd, $J = 14.7, 10.4$ Hz, 1H); 4.53 (dd, $J = 15.0, 3.4$ Hz, 1H); 4.13-4.09 (m, 1H); 1.73-1.61 (m, 6H); 1.20-1.05 (m, 4H); 0.95-0.88 (m, 1H); ¹³C NMR (500 MHz, CDCl₃) δ 198.9, 140.4, 135.2, 130.1, 129.5, 73.9, 49.1, 39.5, 31.9, 29.9, 26.6, 26.4, 26.0; LRMS (ESI): Mass calculated for C₁₅H₁₈ClNO₃ [M]⁺, 295.8. Found [M+Na]⁺, 319.1.

1-(4-Chlorophenyl)-2-(nitromethyl)heptan-1-one (9): Purified with 5% ether/hexanes, yielding 65 mg (65%) of **9** as a colorless oil. $R_f = 0.42$ (20% ether/hexanes); IR (film) 2931, 2862, 1683, 1555, 1378 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.94-7.92 (m, 2H); 7.50-7.48 (m, 2H); 5.01 (dd, $J = 14.6, 9.5$ Hz, 1H); 4.49 (dd, $J = 14.6, 4.2$ Hz, 1H); 4.21-4.20 (m, 1H); 1.72-1.66 (m, 1H); 1.55-1.50 (m, 1H); 1.29-1.24 (m, 6H); 0.84-0.82 (m, 3H); ¹³C NMR (500 MHz, CDCl₃) δ 198.9, 140.6, 134.4, 130.2, 129.6, 75.2, 44.0, 31.8, 30.3, 26.6, 22.5, 14.1; LRMS (ESI): Mass calculated for C₁₄H₁₈ClNO₃ [M]⁺, 283.8. Found [M-NO₂]⁺, 236.3.

1-(4-Chlorophenyl)-3-methyl-2-(nitromethyl)butan-1-one (10): Purified with 5% ether/hexanes, yielding 73 mg (73%) of **10** as a colorless oil. $R_f = 0.32$ (20% ether/hexanes); IR (film) 2967, 2932, 1681, 1550, 1375 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.94-7.93 (m, 2H); 7.50-7.48 (m, 2H); 5.09 (dd, $J = 10.5, 4.0$ Hz, 1H); 4.54 (dd, $J = 11, 3.5$ Hz, 1H); 4.14-4.11 (m, 1H); 2.14-2.11 (m, 1H); 1.04 (d, $J = 7.0$ Hz, 3H); 0.88 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (500 MHz, CDCl_3) δ 198.8, 140.4, 135.0, 130.1, 129.5, 73.3, 49.5, 29.5, 21.2, 19.1;

3-(Benzyloxy)-1-(4-chlorophenyl)-2-(nitromethyl)butan-1-one (11):

Purified using a gradient from 5% to 40% ether/hexanes, yielding 80 mg (80%) of **11**, a non-separable mixture of diastereomers, as a colorless oil. $R_f = 0.20$ (20% ether/hexanes); IR (film) 2978, 2919, 2872, 1555, 1378 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.95-7.93 (m, 2H); 7.82-7.81 (m, 2H); 7.50-7.48 (m, 2H); 7.44-7.42 (m, 2H); 7.39-7.31 (m, 6H); 7.29-7.27 (m, 2H); 7.24-7.23 (m, 2H); 5.16 (dd, $J = 14.7, 10.2$ Hz, 1H); 5.70 (dd, $J = 15.0, 9.7$ Hz, 1H); 4.80 (dd, $J = 15.0, 3.5$ Hz, 1H); 4.71 (dd, $J = 14.8, 2.8$ Hz, 1H); 4.66 (d, $J = 12.1$ Hz, 1H); 4.58 (d, $J = 11.7$ Hz, 1H); 4.54 (m, 1H); 4.47 (d, $J = 11.9$ Hz, 1H); 4.37 (m, 1H); 4.34 (d, $J = 11.7$ Hz, 1H); 3.94 (m, 1H); 3.82 (m, 1H); 1.23 (d, $J = 6.2$ Hz, 3H); 1.13 (d, $J = 6.2$ Hz, 3H); ^{13}C NMR (500 MHz, CDCl_3) δ 197.5, 196.7, 140.6, 140.6, 137.6, 137.4, 135.0, 134.5, 130.3, 130.2, 129.5, 129.4, 128.9, 128.8, 128.4, 128.3, 128.1, 128.0, 73.7, 73.6, 72.8, 71.6, 71.4, 71.1, 50.3, 49.6, 18.2, 16.4; LRMS (ESI): Mass calculated for $\text{C}_{18}\text{H}_{18}\text{ClNO}_4$ $[\text{M}]^+$, 347.8. Found $[\text{M}+\text{M}]^+$, 696.2.

(4-Chlorophenyl)(2-nitrocyclohexyl)methanone (12):

Purified with 5% ether/hexanes, yielding 80 mg (80%) of **12**, the trans diastereomer, as a white solid. $R_f = 0.29$ (20% ether/hexanes); Mp: 78-79 $^\circ\text{C}$; IR (film) 2943, 2864, 1680, 1546, 1379 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.95-7.93 (m, 2H); 7.51-7.49 (m, 2H); 4.98 (ddd, $J = 11.9, 11.9, 3.3$ Hz, 1H); 3.96 (ddd, $J = 11.9, 11.9, 2.9$ Hz, 1H); 2.65-2.63 (m, 1H); 2.17-2.14 (m, 1H); 2.04-2.02 (m, 1H); 1.90-1.80 (m, 2H); 1.55-1.33 (m, 3H); ^{13}C NMR (500 MHz, CDCl_3) δ 198.9, 140.4, 133.7, 130.1, 129.4, 95.0, 84.9, 48.0, 31.8, 29.4, 25.0, 24.9. LRMS (ESI): Mass calculated for $\text{C}_{13}\text{H}_{14}\text{ClNO}_3$ $[\text{M}]^+$, 267.7. Found $[\text{M}+\text{M}+\text{Na}]^+$, 557.0. Diastereomer ratio was determined by 500MHz ^1H NMR.

Determination of Conformation of β -Nitroketone **12**:

Proton decoupling experiments were performed in order to determine the conformation of **12**.

Decoupled Proton	J - Values
H_a	$J \text{H}_b = 12.3, 2.9$ Hz
H_b	$J \text{H}_a = 11.9, 3.3$ Hz
H_c	$J \text{H}_a = 11.5, 11.5$ Hz

4-Chlorophenyl(1-(nitromethyl)cyclohexyl)methanone (13): Purified with 5% ether/hexanes, yielding 56 mg (56%) of **13** as a colorless oil. $R_f = 0.29$ (20% ether/hexanes); IR (film) 2936, 2862, 1682, 1551, 13378 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.51-7.49 (m, 2H); 7.41-7.39 (m, 2H); 4.96 (s, 2H); 1.76-1.74 (m, 2H); 1.60-1.58 (m, 3H); 1.50-1.43 (m, 2H); 1.36-1.33 (m, 1H); ^{13}C NMR (500 MHz, CDCl_3) δ 206.3, 137.5, 126.9, 128.8, 79.6, 51.8, 32.1, 25.4, 22.0; LRMS (ESI): Mass calculated for $\text{C}_{14}\text{H}_{16}\text{ClNO}_2$ $[\text{M}]^+$, 281.7. Found $[\text{M}-\text{NO}_2]^+$, 236.4.

2-Cyclohexyl-1-(naphthalen-3-yl)-3-nitropropan-1-one (14): Purified with 5% ether/hexanes, yielding 80 mg (80%) of **14** as a colorless oil. $R_f = 0.28$ (20% ether/hexanes); IR (film) 2928, 2854, 1674, 1551, 1375 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.52 (s, 1H); 8.05-8.00 (m, 2H); 7.94-7.89 (m, 2H); 7.64-7.56 (m, 2H); 5.15 (dd, $J = 14.5, 10.2$ Hz, 1H); 4.59 (dd, $J = 14.6, 3.1$ Hz, 1H); 4.35 (m, 1H); 1.81-1.61 (m, 6H); 1.21-0.96 (m, 5H); ^{13}C NMR (500 MHz, CDCl_3) δ 200.0, 136.0, 134.3, 132.8, 130.5, 130.0, 129.1, 129.0, 128.1, 127.2, 124.3, 74.1, 49.2, 39.7, 31.7, 30.0, 26.6, 26.5, 26.1; LRMS (ESI): Mass calculated for $\text{C}_{19}\text{H}_{21}\text{NO}_2$ $[\text{M}]^+$, 311.4. Found $[\text{M}+\text{H}]^+$, 312.4.

2-Cyclohexyl-1-(3-methoxyphenyl)-3-nitropropan-1-one (15): Purified with 5%-40% ether/hexanes, yielding 60 mg (60%) of **15** as a colorless oil. $R_f = 0.38$ (20% ether/hexanes); IR (film) 2930, 2854, 1680, 1554, 1266 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.59-7.58 (m, 1H); 7.52 (s, 1H); 7.45-7.42 (m, 1H); 7.18-7.16 (m, 1H); 5.09 (dd, $J = 14.5, 10.4$ Hz, 1H); 4.55 (dd, $J = 14.5, 2.9$ Hz, 1H); 4.2 (m, 1H); 3.89 (s, 3H); 1.73-1.63 (m, 6H); 1.23-1.08 (m, 4H); 0.98-0.93 (m, 1H); ^{13}C NMR (500 MHz, CDCl_3) δ 199.7, 160.2, 138.2, 130.1, 121.3, 120.2, 113.1, 73.9, 55.7, 49.3, 39.5, 31.7, 29.8, 26.6, 26.4, 26.1; LRMS (ESI): Mass calculated for $\text{C}_{16}\text{H}_{21}\text{NO}_4$ $[\text{M}]^+$, 291.3. Found $[\text{M}+\text{Na}+\text{H}]^+$, 315.5.

1-(4-Bromophenyl)-2-cyclohexyl-3-nitropropan-1-one (16): Purified with 2-6% ether/hexanes, yielding 81 mg (81%) of **16** as a colorless oil. $R_f = 0.29$ (20% ether/hexanes); Mp = 95.5-97 $^\circ\text{C}$; IR (film) 2929, 2854, 1680, 1554, 1375, 1250 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.87-7.86 (m, 2H); 7.67-7.65 (m, 2H); 5.09 (dd, $J = 15.0, 10.7$ Hz, 1H); 4.55 (dd, $J = 15.0, 3.4$ Hz, 1H); 4.13-4.10 (m, 1H); 1.74-1.62 (m, 6H); 1.26-1.06 (m, 4H); 0.97-0.89 (m, 1H); ^{13}C NMR (500 MHz, CDCl_3) δ 199.1, 135.6, 132.4, 130.2, 129.1, 73.9, 55.7, 49.1, 39.5, 31.7, 29.9, 26.6, 26.4, 26.0; LRMS (ESI): Mass calculated for $\text{C}_{18}\text{H}_{18}\text{BrNO}_2$ $[\text{M}]^+$, 340.2. Found $[\text{M}+\text{Na}]^+$, 363.5.

Asymmetric Nucleophilic Acylation of Nitroalkenes:

A dry screw-capped tube containing a magnetic stir bar was charged with thiourea **17** (200 mg, 0.335 mmol) in a nitrogen-filled glove box. Also in the box the protected thiazolium carbinol **1a** (260 mg, 0.510 mmol) and tetramethylammonium fluoride (TMAF, 48 mg, 0.510 mmol) were weighed into two separate dram vials. All items were removed from box and the tube was put

under a positive N₂ pressure. Nitroalkene (52 mg, 0.335 mmol) was added to the thiourea in dichloromethane (1.6 mL). Reaction mixture was cooled to -78 °C. Next, carbinol was added in dichloromethane (0.5 mL) and the reaction was allowed to stir for 5 min. Last, TMAF was added in dichloromethane (0.5 mL). Reaction was allowed to stir at -78 °C for 2-24h until complete by thin layer chromatography (20% ether/hexanes). Upon completion reaction was quenched with water and diluted with dichloromethane then warmed to room temperature. The layers were separated and the aqueous layer was extracted two additional times with dichloromethane (30 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated *in vacuo*. The resulting orange residue was purified by flash column chromatography on silica gel.

Enantiomeric excess determined by HPLC on a Chiralcel OD-H column. 10% IPA/Hexanes, 1mL/min.

Determination of Stereochemistry:

The absolute stereochemistry was determined by X-ray crystallography of **16**. The asymmetric nucleophilic acylation was carried out using the 4-Br-Ph thiazolium carbinol (**1e**) and nitroalkene **2a** to yield **16** with an enantiomeric excess of 70%. Enantiomeric excess determined by HPLC on a Chiralcel OD-H column. 10% IPA/Hexanes, 1mL/min. Recrystallized from ether/hexanes.

HPLC trace of racemic 6:

Data File C:\HPCHEM\2\DATA\ACHAN\AM000000.D

pCl, racemic

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Injection Date   : 6/2/2005 10:30:18 AM
Sample Name      :                               Location : Vial 1
Acq. Operator    : Anita                               Inj Volume : 5 µl
Acq. Method      : C:\HPCHEM\2\METHODS\ANITA.M
Last changed     : 3/7/2005 7:51:16 PM by Dave
Analysis Method  : C:\HPCHEM\2\METHODS\ANITA.M
Last changed     : 9/15/2005 3:48:24 PM by Anita
                  (modified after loading)

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Area Percent Report
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Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs

```

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.020	PV	0.2135	3976.90063	270.50851	50.5609
2	8.892	PB	0.2765	3888.66264	205.71507	49.4391

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Totals :                7865.56348  476.22359
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Results obtained with enhanced integrator!

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*** End of Report ***

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Data File C:\HPCHEM\1\DATA\ANITA\50-40003.D

Sample Name: 50-4

-78

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Injection Date   : 7/29/2005 11:56:33 AM
Sample Name      : 50-4                      Location : Vial 3
Acq. Operator    : Anita
Acq. Instrument  : Instrument 1              Inj Volume : 5 µl
Acq. Method      : C:\HPCHEM\1\METHODS\AM1.M
Last changed     : 7/29/2005 11:55:55 AM by Anita
                  (modified after loading)
Analysis Method  : C:\HPCHEM\1\METHODS\AM1.M
Last changed     : 9/15/2005 3:56:44 PM by Anita
                  (modified after loading)
=====
```

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Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.048	PE	0.2124	1002.51740	68.62119	87.0595
2	9.080	PP	0.2730	149.01405	8.01220	12.9405

Totals : 1151.53145 76.63338

Results obtained with enhanced integrator!

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*** End of Report ***

Data File C:\HPCHEM\1\DATA\ANITA\PBRRAC00.D

pBr racemic

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=====
Injection Date   : 9/23/2005 3:25:44 PM
Sample Name      :                               Location : Vial 31
Acq. Operator    : Anita
Acq. Instrument  : Instrument 1                   Inj Volume : 10 µl
Acq. Method      : C:\HPCHEM\1\METHODS\AM1.M
Last changed     : 9/23/2005 3:25:08 PM by Anita
                  (modified after loading)
Analysis Method  : C:\HPCHEM\1\METHODS\AM1.M
Last changed     : 9/23/2005 3:42:06 PM by Anita
                  (modified after loading)
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```

Area Percent Report

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=====
Sorted By       : Signal
Multiplier      : 1.0000
Dilution        : 1.0000
Use Multiplier & Dilution Factor with ISTDs
=====
```

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.382	NM	0.5138	222.86940	7.22898	49.3205
2	9.589	NM	0.5917	229.01047	6.45077	50.6795

Totals : 451.87987 13.67976

Results obtained with enhanced integrator!

*** End of Report ***

Data File C:\HPCHEM\1\DATA\ANITA\70-40000.D

pBr with quinine thiourea

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*****
Injection Date   : 9/2/2005 1:56:56 PM
Sample Name      :                               Location : Vial 31
Acc. Operator    : Anita
Acc. Instrument  : Instrument 1                   Inj Volume : 5 µl
Acc. Method      : C:\HPCHEM\1\METHODS\AM1.M
Last changed     : 9/2/2005 9:52:57 AM by Anita
                  (modified after loading)
Analysis Method  : C:\HPCHEM\1\METHODS\CHO S.M
Last changed     : 9/23/2005 4:24:03 PM by Anita
                  (modified after loading)
*****
```

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Area Percent Report
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```
Sorted By       :      Signal
Multiplier      :      1.0000
Dilution        :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.211	PB	0.1976	210.09106	15.75636	85.1250
2	9.295	PB	0.2471	36.71182	2.21782	14.8750

Totals : 246.80289 17.97418

Results obtained with enhanced integrator!

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*** End of Report ***

Data File C:\HPCHEM\1\DATA\ANITA\PBR00000.D

pBr crystal

```
*****
Injection Date : 9/23/2005 2:59:07 PM
Sample Name :
Location : Vial 31
Acq. Operator : Anita
Acq. Instrument : Instrument 1
Inj Volume : 5 µl
Acq. Method : C:\HPCHEM\1\METHODS\AM1.M
Last changed : 9/20/2005 4:00:11 PM by Rob
Analysis Method : C:\HPCHEM\1\METHODS\AM1.M
Last changed : 9/23/2005 3:23:23 PM by Anita
(modified after loading)
```

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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.303	FB	0.2108	70.76501	4.89014	100.0000

Totals : 70.76501 4.89014

Results obtained with enhanced integrator!

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*** End of Report ***