Enantioselective Friedel-Crafts Alkylation of Indoles with Nitroalkenes Catalyzed by Bifunctional Tridentate Bis(oxazoline)-Zn(II) Complex

Shao-Feng Lu, Da-Ming Du,* Jiayi Xu

*Beijing National Laboratory for Molecular Sciences (BNLMS), Key Laboratory of Bioorganic Chemistry
and Molecular Engineering, College of Chemistry and Molecular Engineering, Peking University,
Beijing 100871, P. R. China*

dudm@pku.edu.cn

Supporting Information

Contents

General remarks.....	S2
Preparation of ligand 4	S2
General procedure for the catalytic enantioselective Friedel-Crafts reaction.....	S3
Characterization of nitroalkylated indoles.....	S3
Reference.....	S7
Copies of HPLC profiles of nitroalkylated indoles.....	S8
Copies of ¹ H NMR and ¹³ C NMR of nitroalkylated indoles 7g , 7j , 7k , 7l and 7m	S21
Copies of ¹ H NMR and ¹³ C NMR of ligand 4	S31

General remarks

Commercially available compounds were used without further purification. Solvents were dried according to standard procedures. Column chromatography was carried out using silica gel (200-300 mesh). Melting points were measured on an XT-4 melting point apparatus and uncorrected. The ^1H NMR spectra were recorded on Mercury 300 and Bruker 400 MHz spectrometers, while the ^{13}C NMR spectra were recorded at 75 and 100 MHz respectively. Elemental analyses were carried out on an Elementar Vario EL instrument. Infrared spectra were obtained on a Nicolet AVATAR 330 FT-IR spectrometer. Mass spectra were obtained on a VG-ZAB-HS (EI) mass spectrometer. Optical rotations were measured on a Perkin-Elmer 341 LC spectrometer. The enantiomeric excess (ee) of the products was determined by chiral HPLC (2-propanol/hexane as the eluent). The nitroalkenes are commercial available or prepared according to literature.¹

Experimental Procedures

Preparation of ligand 4

A solution of 2,2'-dicarboxyl diphenylamine (1.837 g, 7.0 mmol) and thionyl chloride (10 mL) was refluxed for 4 h. The excess SOCl_2 was removed under reduced pressure to afford the diacyl dichloride. The above diacyl dichloride in CH_2Cl_2 (70 mL) was added dropwise to a solution of (1*S*, 2*S*)-2-amino-1,2-diphenylethanol (2.986 g, 14.0 mmol) and Et_3N (4.9 mL, 35.0 mmol) in CH_2Cl_2 (20 mL) at 0 °C and stirred at room temperature for 24 h. The reaction mixture was successively washed with saturated NH_4Cl (aq), HCl (1 *N*), saturated NaHCO_3 (aq) and brine. The organic layer was dried over anhydrous Na_2SO_4 , concentrated and purified by silica gel column chromatography using ethyl acetate as the eluting solvent to afford the bis(hydroxyamide) in 67% yield. To an ice-cold solution of the bis(hydroxyamide) (1.192 g, 1.84 mmol) and Et_3N (1.1 mL, 8.07 mmol) in CH_2Cl_2 (15 mL) was added methanesulfonyl chloride (0.32 mL, 4.04 mmol) via syringe. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. Then saturated NH_4Cl solution (30 mL) was poured into the reaction mixture. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 $\times$ 15 mL). The combined extracts were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo* to afford the crude bismesylate. The crude bismesylate was dissolved in methanol (4.4 mL) and a solution of 0.162 g NaOH in water (4.4 mL) was added to it. The reaction mixture was refluxed for 4 h and cooled to room temperature. The methanol was removed under reduced pressure and the residue was extracted with CH_2Cl_2 (3 $\times$ 15 mL). The combined organic layer was washed with brine,

dried over anhydrous Na_2SO_4 , and concentrated *in vacuo* to give the crude product. Purification by column chromatography on silica gel using petroleum ether-ethyl acetate 10:1 as the eluent to afford 700 mg (62% yield) of **4** as a pale yellow solid. m.p. 175–177 °C. $[\alpha]_{\text{D}}^{20} = +114$ (c 0.67, CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3): δ = 11.28 (s, 1H), 7.96 (dd, J = 7.8, 1.6 Hz, 2H), 7.60 (d, J = 8.2 Hz, 2H), 7.38–7.32 (m, 2H), 7.29–7.27 (m, 6H), 7.18–7.14 (m, 10H), 7.06–7.03 (m, 4H), 6.96–6.93 (m, 2H), 5.08 (d, J = 7.6 Hz, 2H), 4.92 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ = 163.3, 143.4, 142.0, 140.4, 131.6, 130.6, 128.6, 128.4, 128.1, 127.2, 126.4, 125.7, 119.9, 118.4, 115.7, 87.7, 78.7. IR (neat): 3061, 3030, 1641, 1580, 1518, 1455, 1269, 1052, 762, 747, 698 cm^{-1} . MS (70 eV, EI): m/z (%) 611 (M^+ , 100), 504 (22), 444 (22), 309 (33), 282 (20), 249 (15), 206 (30), 179 (32), 105 (11). Anal. Calcd for $\text{C}_{42}\text{H}_{33}\text{N}_3\text{O}_2$: C, 82.46; H, 5.44; N, 6.87. Found: C, 82.32; H, 5.56; N, 6.82.

General Procedure for the Catalytic Enantioselective Friedel-Crafts reaction.

(R)-3-(2-Nitro-1-phenylethyl)-1H-indole (7a). To a dried Schlenk tube were added $\text{Zn}(\text{OTf})_2$ (9.3 mg, 0.025 mmol) and ligand **4** (15.3 mg, 0.025 mmol) under nitrogen followed by addition of the toluene (2 mL). The solution was stirred at room temperature for 30 min and the *trans*- β -nitrostyrene **6a** (74.5 mg, 0.5 mmol) was added. The mixture was stirred for 10 min and cooled to -20 °C before the indole **5a** (57 mg, 0.5 mmol) was added.

After stirring for 15 h at -20 °C, the solvent was removed under vacuum. Purification by column chromatography (20% AcOEt in petroleum ether) afforded the desired product 3-(2-nitro-1-phenylethyl)-1H-indole **7a** (125.4 mg, 95% yield) as an oil. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 70:30, 0.9 mL/min, $t_{\text{minor}} = 20.7$ min, $t_{\text{major}} = 24.7$ min). $[\alpha]_{\text{D}}^{20} = -21.3$ (c 0.54, CH_2Cl_2 , 94% ee). ^1H NMR (300 MHz, CDCl_3): δ = 8.02 (s, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.31–7.15 (m, 7H), 7.06 (t, J = 7.6 Hz, 1H), 6.95 (d, J = 2.4 Hz, 1H), 5.16 (t, J = 8.1 Hz, 1H), 5.02 (dd, J = 12.4, 7.6 Hz, 1H), 4.90 (dd, J = 12.4, 8.6 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ = 139.1, 136.4, 128.9, 127.7, 127.5, 126.0, 122.6, 121.6, 119.9, 118.8, 114.2, 111.4, 79.5, 41.5. Lit.² $[\alpha]_{\text{D}}^{20} = +25.3$ (c 0.9, CH_2Cl_2 , 84% ee) for (*S*) configuration.

5-Methoxy-3-[2-nitro-1-phenylethyl]-1H-indole (7b). Prepared according to the general procedure using *trans*- β -nitrostyrene **6a** (74.5 mg, 0.50 mmol) and 5-methoxyindole **5b** (73.6 mg, 0.5 mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 142.2 mg (96%) of **7b** as an oil. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 85:15, 1.0 mL/min, $t_{\text{major}} = 27.7$ min, $t_{\text{minor}} = 33.5$ min). $[\alpha]_{\text{D}}^{20} = +33.1$ (c 1.15, CH_2Cl_2 , 98% ee). ^1H NMR (300 MHz, CDCl_3): δ = 7.99 (s, 1H), 7.34–7.19 (m, 6H), 6.96 (d, J = 2.4 Hz, 1H), 6.86 (d, J = 2.4 Hz, 1H), 6.83 (d, J = 1.5 Hz, 1H), 5.12 (t, J = 8.0 Hz, 1H), 5.02 (dd, J = 12.3, 7.5 Hz, 1H), 4.91 (dd, J = 12.3, 8.1 Hz, 1H), 3.76 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ = 154.1, 139.1, 131.5, 128.9, 127.7, 127.5, 126.5, 122.2, 114.0, 112.6, 112.1, 100.7, 79.4, 55.8, 41.5.

Lit.² $[\alpha]_D^{20} = -25.6$ (*c* 1.1, CH₂Cl₂, 79% ee).

5-Chloro-3-[2-nitro-1-phenylethyl]-1*H*-indole (7c). Prepared according to the general procedure using *trans*- β -nitrostyrene **6a** (74.5 mg, 0.50 mmol) and 5-chloroindole **5c** (75.8 mg, 0.5 mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 132.4 mg (88%) of **7c** as an oil. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 70:30, 0.9

mL/min, $t_{\text{major}} = 13.6$ min, $t_{\text{minor}} = 14.8$ min). $[\alpha]_D^{20} = +26.8$ (*c* 1.11, CH₂Cl₂, 81% ee). ¹H NMR (300 MHz, CDCl₃): $\delta = 8.12$ (s, 1H), 7.37 (d, *J* = 2.1 Hz, 1H), 7.35–7.21 (m, 6H), 7.12 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.05 (d, *J* = 2.4 Hz, 1H), 5.11 (t, *J* = 8.0 Hz, 1H), 5.01 (dd, *J* = 12.3, 8.1 Hz, 1H), 4.90 (dd, *J* = 12.3, 8.1 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): $\delta = 138.7, 134.7, 129.0, 127.7, 127.6, 127.1, 125.6, 123.0, 122.8, 118.3, 114.0, 112.4, 79.3, 41.3$. Lit.³ $[\alpha]_D^{20} = +18$ (*c* 0.370, CHCl₃, 71% ee).

(*R*)-1-Methyl-3-[2-nitro-1-phenylethyl]-1*H*-indole (7d). Prepared according to the general procedure using *trans*- β -nitrostyrene **6a** (74.5 mg, 0.50 mmol) and 1-methylindole **7d** (65.6 mg, 0.5 mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 130.0 mg (93%) of **4a** as an oil. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 85:15, 1.0 mL/min, $t_{\text{major}} = 49.9$ min, $t_{\text{minor}} = 52.8$ min). $[\alpha]_D^{20} = -23.5$ (*c* 1.37, CH₂Cl₂, 90% ee). ¹H NMR (300 MHz, CDCl₃): $\delta = 7.45$ –7.41 (m, 1H), 7.33–7.18 (m, 7H), 7.08–7.02 (m, 1H), 6.82 (s, 1H), 5.15 (t, *J* = 8.0 Hz, 1H), 5.00 (dd, *J* = 12.4, 7.6 Hz, 1H), 4.89 (dd, *J* = 12.3, 8.4 Hz, 1H), 3.67 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): $\delta = 139.3, 137.1, 128.8, 127.7, 127.4, 126.4, 126.3, 122.1, 119.4, 118.9, 112.6, 109.5, 79.4, 41.4, 32.7$. Lit.² $[\alpha]_D^{20} = +10.8$ (*c* 0.6, CH₂Cl₂, 31% ee) for (*S*) configuration.

3-[1-(2-Methoxyphenyl)-2-nitroethyl]-1*H*-indole (7e). Prepared according to the general procedure using 2-methoxy- β -nitrostyrene **6b** (89.6 mg, 0.50 mmol) and indole **5a** (57.0 mg, 0.5 mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 145.1 mg (99%) of **7e** as an oil. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 70:30, 0.9 mL/min, $t_{\text{major}} = 12.7$ min, $t_{\text{minor}} = 14.5$ min). $[\alpha]_D^{20} = -49.9$ (*c* 1.00, CH₂Cl₂, 77% ee). ¹H NMR (300 MHz, CDCl₃): $\delta = 7.96$ (s, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.26–6.99 (m, 6H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.79 (t, *J* = 7.2 Hz, 1H), 5.58 (dd, *J* = 8.6, 7.0 Hz, 1H), 5.03–4.89 (m, 2H), 3.85 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): $\delta = 156.8, 136.3, 128.8, 128.6, 127.1, 126.4, 122.3, 121.9, 120.7, 119.6, 119.0, 113.7, 111.2, 110.7, 78.0, 55.4, 35.4$. Lit.² $[\alpha]_D^{20} = +49.6$ (*c* 0.75, CH₂Cl₂, 61% ee).

3-[1-(2-Chlorophenyl)-2-nitroethyl]-1H-indole (7f). Prepared according to the general procedure using 2-chloro- β -nitrostyrene **6c** (96.8 mg, 0.50 mmol) and indole **5a** (57.0 mg,

0.5 mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 153.1 mg (99%) of **7f** as an oil. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 70:30, 0.9 mL/min, $t_{\text{major}} = 16.1$ min, $t_{\text{minor}} = 25.4$ min). $[\alpha]_{\text{D}}^{20} = -52.1$ (c 1.45, CH_2Cl_2 , 73% ee). ^1H NMR (300 MHz, CDCl_3): $\delta = 8.08$ (s, 1H), 7.42 (m, 2H), 7.33 (d, $J = 8.1$ Hz, 1H), 7.24–7.04 (m, 6H), 5.73 (t, $J = 8.0$ Hz, 1H), 5.03–4.91 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 136.4$, 133.8, 130.1, 128.9, 128.8, 127.2, 126.1, 122.7, 121.9, 120.5, 119.9, 118.8, 113.1, 111.4, 77.6, 37.9. Lit.² $[\alpha]_{\text{D}}^{20} = +79.4$ (c 0.95, CH_2Cl_2 , 72% ee).

3-[1-Naphth-2-yl-2-nitroethyl]-1H-indole (7g). Prepared according to the general procedure using 2-(2-nitrovinyl)naphthalene **6d** (99.6 mg, 0.50 mmol) and indole **5a** (57.0 mg, 0.5 mmol). Purified by column chromatography

(20% AcOEt in petroleum ether) to yield 156.0 mg (99%) of **7g** as an oil. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 70:30, 0.9 mL/min, $t_{\text{major}} = 23.6$ min, $t_{\text{minor}} = 28.8$ min). $[\alpha]_{\text{D}}^{20} = -15.6$ (c 1.32, CH_2Cl_2 , 89% ee). ^1H NMR (300 MHz, CDCl_3): $\delta = 8.24$ (d, $J = 7.8$ Hz, 1H), 7.90 (s, 1H), 7.85 (m, 1H), 7.74 (t, $J = 4.6$ Hz, 1H), 7.52–7.11 (m, 7H), 7.01 (t, $J = 7.4$ Hz, 1H), 6.84 (s, 1H), 6.03 (t, $J = 7.8$ Hz, 1H), 5.05–4.98 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 136.4$, 134.5, 134.1, 131.0, 129.1, 128.2, 126.8, 126.0, 125.9, 125.3, 124.6, 122.60, 122.56, 119.9, 118.7, 114.0, 111.4, 78.4, 36.9. IR (neat): 3433, 3056, 1550, 1458, 1377, 777, 737 cm^{-1} . MS (70 eV, EI): m/z (%) 316 (M^+ , 60), 269 (100), 256 (70), 241 (14), 153 (78), 127 (23), 115 (20). HRMS (EI) calcd for $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_2$: 316.12118, found: 316.12139.

3-[1-Furan-2-yl-2-nitroethyl]-1H-indole (7h). Prepared according to the general procedure using 2-(2-nitrovinyl)furan **6e** (69.6 mg, 0.50 mmol) and indole **5a** (57.0 mg, 0.5 mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 107.6 mg (85%) of **7h** as an oil. The ee was

determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 70:30, 0.9 mL/min, $t_{\text{major}} = 14.6$ min, $t_{\text{minor}} = 20.2$ min). $[\alpha]_{\text{D}}^{20} = +37.9$ (c 1.04, CH_2Cl_2 , 81% ee). ^1H NMR (300 MHz, CDCl_3): $\delta = 8.03$ (s, 1H), 7.53 (d, $J = 7.8$ Hz, 1H), 7.34–7.04 (m, 4H), 6.99 (d, $J = 1.5$ Hz, 1H), 6.27 (dd, $J = 1.8$, 3.0 Hz, 1H), 6.12 (d, $J = 3.3$ Hz, 1H), 5.21 (t, $J = 7.6$ Hz, 1H), 5.01 (dd, $J = 12.4$, 8.2 Hz, 1H), 4.86 (dd, $J = 12.6$, 7.5 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 152.1$, 142.2, 136.2, 125.5, 122.7, 122.5, 119.9, 118.6, 111.5, 111.3, 110.4, 107.3, 77.8, 35.6. Lit.² $[\alpha]_{\text{D}}^{20} = -78$ (c 1.0, CH_2Cl_2 , 78% ee).

3-[1-Nitromethylbutyl]-1H-indole (7i). Prepared according to the general procedure using

1-nitropent-1-ene **6f** (57.6 mg, 0.50 mmol) and indole **5a** (57.0 mg, 0.5 mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 106.4 mg (91%) of **7i** as an oil. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 90:10, 1.0 mL/min, $t_{\text{major}} = 31.8$ min, $t_{\text{minor}} = 34.8$ min). $[\alpha]_{\text{D}}^{20} = +39.6$ (c 1.12, CH_2Cl_2 , 92% ee). ^1H NMR (300 MHz, CDCl_3): $\delta = 7.99$ (s, 1H), 7.60 (d, $J = 7.8$ Hz, 1H), 7.27 (d, $J = 8.1$ Hz, 1H), 7.20–7.08 (m, 2H), 6.88 (d, $J = 1.0$ Hz, 1H), 4.65–4.53 (m, 2H), 3.79–3.74 (m, 1H), 1.84–1.68 (m, 2H), 1.32–1.22 (m, 2H), 0.84 (t, $J = 7.4$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 136.3$, 126.0, 122.2, 121.9, 119.5, 118.5, 113.7, 111.5, 80.5, 36.0, 34.5, 20.2, 13.7. Lit.² $[\alpha]_{\text{D}}^{20} = -51.1$ (c 0.45, EtOH, 70% ee).

3-[1-Nitromethyldecyl]-1H-indole (7j). Prepared according to the general procedure using

1-nitroundec-1-ene **6g** (99.6 mg, 0.50 mmol) and indole **5a** (57.0 mg, 0.5 mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 134.2 mg (91%) of **7j** as an oil. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 90:10, 1.0 mL/min, $t_{\text{major}} = 23.0$ min, $t_{\text{minor}} = 26.4$ min). $[\alpha]_{\text{D}}^{20} = +22.9$ (c 1.29, CH_2Cl_2 , 89% ee). ^1H NMR (300 MHz, CDCl_3): $\delta = 8.05$ (s, 1H), 7.62 (d, $J = 8.1$ Hz, 1H), 7.34 (d, $J = 7.8$ Hz, 1H), 7.23–7.10 (m, 2H), 6.98 (d, $J = 2.4$ Hz, 1H), 4.70–4.58 (m, 2H), 3.82–3.73 (m, 1H), 1.90–1.72 (m, 2H), 1.27–1.20 (m, 14H), 0.86 (t, $J = 6.8$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 136.4$, 126.1, 122.3, 121.9, 119.7, 118.7, 114.0, 111.5, 80.5, 36.3, 32.4, 31.8, 29.5, 29.4, 29.2, 27.1, 22.6, 14.1. IR (neat): 3422, 2925, 2854, 1548, 1458, 1425, 1380, 741 cm^{-1} . MS (70 eV, EI): m/z (%) 316 (M^+ , 46), 270 (21), 256 (16), 157 (46), 143 (80), 130 (100), 115 (10). HRMS (EI) calcd for $\text{C}_{19}\text{H}_{28}\text{N}_2\text{O}_2$: 316.21508, found: 316.21541.

3-[1-Nitromethyl-3-phenylpropyl]-1H-indole (7k). Prepared according to the general

procedure using 1-nitro-4-phenylbut-1-ene **6h** (88.6 mg, 0.50 mmol) and indole **5a** (57.0 mg, 0.5 mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 140.0 mg (88%) of **7k** as an oil. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 85:15, 1.0 mL/min, $t_{\text{major}} = 32.5$ min, $t_{\text{minor}} = 38.6$ min). $[\alpha]_{\text{D}}^{20} = +19.8$ (c 1.61, CH_2Cl_2 , 93% ee). ^1H NMR (300 MHz, CDCl_3): $\delta = 8.05$ (s, 1H), 7.59 (d, $J = 7.8$ Hz, 1H), 7.35 (d, $J = 7.8$ Hz, 1H), 7.29–7.11 (m, 5H), 7.07 (d, $J = 6.9$ Hz, 2H), 7.00 (d, $J = 2.1$ Hz, 1H), 4.69–4.57 (m, 2H), 3.84–3.74 (m, 1H), 2.67–2.48 (m, 2H), 2.24–2.06 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 141.2$, 136.5, 128.4, 128.3, 126.00, 125.96, 122.4, 122.2, 119.8, 118.7, 113.3, 111.6, 80.4, 35.9, 33.9, 33.2. IR (neat): 3422, 2920, 1546, 1457, 1381, 743, 701 cm^{-1} . MS (70 eV, EI): m/z (%) 294 (M^+ , 90), 247 (30), 232 (13), 156 (14), 143 (100), 130 (70), 117 (50), 91 (87). HRMS (EI) calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_2$: 294.13683, found: 294.13690.

3-(1-Cyclohexyl-2-nitroethyl)-1H-indole (7l). Prepared according to the general procedure using 2-nitrovinylcyclohexane **6i** (77.6 mg, 0.50 mmol) and indole **5a** (57.0 mg, 0.5mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 125.2 mg

(92%) of **7l** as an oil. The ee was determined by chiral HPLC on Daicel Chiracel AD column (hexane: 2-propanol 90:10, 1.0 mL/min, $t_{\text{major}} = 13.7$ min, $t_{\text{minor}} = 17.4$ min). $[\alpha]_{\text{D}}^{20} = +40.4$ (c 1.36, CH_2Cl_2 , 84% ee). ^1H NMR (300 MHz, CDCl_3): $\delta = 8.02$ (s, 1H), 7.60–7.57 (m, 1H), 7.31–7.28 (m, 1H), 7.21–7.08 (m, 2H), 6.89 (d, $J = 2.4$ Hz, 1H), 4.79 (dd, $J = 12.0$, 6.3 Hz, 1H), 4.69 (dd, $J = 11.8$, 9.4 Hz, 1H), 3.69–3.61 (m, 1H), 1.83–1.61 (m, 6H), 1.29–0.88 (m, 5H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 136.1$, 126.7, 122.2, 122.1, 119.5, 119.0, 113.0, 111.4, 78.4, 41.8, 40.4, 31.1, 30.3, 26.2, 26.09, 26.07. IR (neat): 3420, 2925, 2852, 1548, 1457, 1383, 1100, 743 cm^{-1} . MS (70 eV, EI): m/z (%) 272 (M^+ , 20), 225 (4), 210 (4), 189 (6), 157 (3), 143 (100), 130 (36), 115 (11), 90 (4), 77 (4). HRMS (EI) calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_2$: 272.15248, found: 272.15221.

3-(1-tert-butyl-2-nitroethyl)-1H-indole (7m). Prepared according to the general procedure using 3,3-dimethyl-1-nitrobut-1-ene **6j** (57.6 mg, 0.50 mmol) and indole **5a** (57.0 mg, 0.5mmol) at 30°C for 144h. Purified by column chromatography (20% AcOEt in petroleum ether) to yield 104.8 mg (85%) of **7m** as a pale yellow solid. m.p. 125–127°C. The ee was determined by chiral HPLC on Daicel Chiracel OD-H column (hexane: 2-propanol 90:10, 1.0 mL/min, $t_{\text{major}} = 17.5$ min, $t_{\text{minor}} = 28.7$ min). $[\alpha]_{\text{D}}^{20} = -16.1$ (c 0.56, CH_2Cl_2 , 87% ee). ^1H NMR (300 MHz, CDCl_3): $\delta = 8.06$ (s, 1H), 7.61 (d, $J = 7.5$ Hz, 1H), 7.29 (d, $J = 7.5$ Hz, 1H), 7.19–7.09 (m, 2H), 6.98 (d, $J = 2.4$ Hz, 1H), 4.87–4.71 (m, 2H), 3.77 (dd, $J = 11.1$, 4.8 Hz, 1H), 0.99 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = 135.7$, 128.2, 122.1, 121.9, 119.6, 119.3, 112.9, 111.1, 78.0, 45.5, 34.4, 28.0. IR (neat): 3422, 2962, 1549, 1458, 1380, 1340, 1230, 1103, 743 cm^{-1} . MS (70 eV, EI): m/z (%) 246 (M^+ , 17), 189 (6), 143 (100), 130 (8), 115 (9), 57 (17). HRMS (EI) calcd for $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_2$: 246.13683, found: 246.13663.

Reference:

- (1) (a) Lucet, D.; Sabelle, S.; Kostelitz, O.; Gall, T. L.; Mioskowski, C. *Eur. J. Org. Chem.* **1999**, 2583. (b) Denmark, S. E.; Marcin, L. *J. Org. Chem.*, **1995**, 60, 3221. (c) Denmark, S. E.; Marcin, L. *J. Org. Chem.* **1993**, 58, 3580.
- (2) Jia, Y.-X.; Zhu, S.-F.; Yang, Y.; Zhou, Q.-L. *J. Org. Chem.* **2006**, 71, 75.
- (3) Herrera, R. P.; Sgarzani, V.; Bernardi, L.; Ricci, A. *Angew. Chem. Int. Ed.* **2005**, 44, 6576.

Copies of HPLC profiles of nitroalkylated indoles

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.721	BB	0.7036	2.07271e4	458.37210	49.5585
2	24.842	PB	0.8541	2.10963e4	383.30325	50.4415

Totals : 4.18234e4 841.67535

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.474	BB	0.6691	1475.95679	34.50072	3.1662
2	24.992	BB	0.8833	4.51395e4	791.54016	96.8338

Totals : 4.66154e4 826.04088

Results obtained with enhanced integrator!

Area Percent Report

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.480	BB	0.9519	1.32345e4	214.47308	49.9849
2	34.723	PB	1.2893	1.32425e4	154.29637	50.0151

Totals : 2.64771e4 368.76945

Results obtained with enhanced integrator!

*** End of Report ***

OD-H, 85:15, 1.0, 25%

5-MeO

Area Percent Report

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000

Signal 1: DAD1 D, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.687	BB	0.9708	4.31540e4	692.68738	99.1694
2	33.523	BP	0.8609	361.44012	5.40025	0.8306

Totals : 4.35154e4 698.08763

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.240	BV	0.4340	7142.53369	257.21518	48.4964
2	14.072	VB	0.5323	7585.42822	215.68085	51.5036

Totals : 1.47280e4 472.89603

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.618	BV	0.4683	9917.46387	328.41275	90.5248
2	14.753	VB	0.5368	1038.05420	29.47754	9.4752

Totals : 1.09555e4 357.89029

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.505	BV	1.4107	8688.95020	96.29340	49.7919
2	50.185	VB	1.4024	8761.56836	95.49699	50.2081

Totals : 1.74505e4 191.79038

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	49.892	BV	1.4466	1.51484e4	159.13583	94.8256
2	52.785	VP	1.1899	826.61707	8.79996	5.1744

Totals : 1.59750e4 167.93579

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.030	VV	0.4453	2.24968e4	787.56287	51.5605
2	14.506	VV	0.5062	2.11350e4	645.19171	48.4395

Totals : 4.36318e4 1432.75458

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=235,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.705	BV	0.4274	2.20270e4	804.60199	88.7076
2	14.513	VV	0.4970	2804.02368	87.71545	11.2924

Totals : 2.48310e4 892.31744

Results obtained with enhanced integrator!

*** End of Report ***

=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.987	BB	0.5900	2.06068e4	539.07513	55.1138
2	25.589	BB	0.8936	1.67827e4	290.68869	44.8862

Totals : 3.73895e4 829.76382

Results obtained with enhanced integrator!

*** End of Report ***

=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.103	PB	0.5700	2.35452e4	638.81201	86.5780
2	25.447	BB	0.9036	3650.15698	63.41178	13.4220

Totals : 2.71953e4 702.22379

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.379	BB	0.9071	6677.96631	114.71877	52.9190
2	29.370	BB	1.0922	5941.25684	83.89746	47.0810

Totals : 1.26192e4 198.61623

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.621	BB	0.9018	2.08501e4	357.84937	94.3585
2	28.767	BB	1.0351	1246.59644	18.20060	5.6415

Totals : 2.20967e4 376.04997

Results obtained with enhanced integrator!

*** End of Report ***

=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.707	BB	0.4682	1.38458e4	458.68143	50.2272
2	20.200	BB	0.6577	1.37205e4	325.52484	49.7728

Totals : 2.75664e4 784.20627

Results obtained with enhanced integrator!
*** End of Report ***

=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.646	BB	0.4710	1.79608e4	593.68585	90.3718
2	20.155	BB	0.6466	1913.54919	46.06454	9.6282

Totals : 1.98743e4 639.75039

Results obtained with enhanced integrator!
*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.291	BV	0.8663	6056.06104	108.65150	50.0334
2	33.735	VB	0.9435	6047.97363	98.88667	49.9666

Totals : 1.21040e4 207.53816

Results obtained with enhanced integrator!

Last changed: 07/100 11:39:33 AM By: 115114

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.823	BB	0.9194	9026.92480	153.75169	96.0676
2	34.804	BP	0.8697	369.50934	5.97726	3.9324

Totals : 9396.43414 159.72896

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.353	BB	0.6891	1.49660e4	340.27036	50.0626
2	25.501	BB	0.7842	1.49286e4	297.11310	49.9374

Totals : 2.98946e4 637.38345

Results obtained with enhanced integrator!

*** End of Report ***

90:10, 254, 30, 1.0

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.020	BB	0.7145	1.34358e4	293.25708	94.5247
2	26.367	BB	0.7796	778.25818	15.09191	5.4753

Totals : 1.42140e4 308.34899

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.921	BB	1.1571	1.31052e4	177.14226	49.9450
2	40.188	BB	1.4952	1.31341e4	125.26562	50.0550

Totals : 2.62393e4 302.40788

Results obtained with enhanced integrator!

*** End of Report ***

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.454	BB	1.1137	1.01523e4	140.71471	96.6608
2	38.612	BB	0.9639	350.71747	4.31644	3.3392

Totals : 1.05030e4 145.03115

Results obtained with enhanced integrator!

*** End of Report ***

=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	s	Height [mAU]	Area %
1	13.909	VB	0.4596	7777.46338		261.13794	49.8694
2	17.671	BB	0.5630	7818.20264		214.79980	50.1306

Totals : 1.55957e4 475.93774

Results obtained with enhanced integrator!

*** End of Report ***

=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: VWD1 A, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	s	Height [mAU]	Area %
1	13.723	PB	0.4811	1.69212e4		547.95819	92.1225
2	17.374	BB	0.5423	1446.95532		40.89856	7.8775

Totals : 1.83681e4 588.85675

Results obtained with enhanced integrator!

*** End of Report ***

Last changed : 3/8/06 5:50:34 PM by Duam
 DAD1 B, Sig=254,8 Ref=360,100 (LVSHF00000061.D)

Area Percent Report

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000

Signal 1: DAD1 B, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.477	PB	0.5724	2.23795e4	595.49835	93.6827
2	28.687	BB	0.8577	1509.12292	27.52111	6.3173

Totals : 2.38886e4 623.01946

Results obtained with enhanced integrator!

*** End of Report ***

Copies of ^1H NMR and ^{13}C NMR of nitroalkylated indoles **7g**, **7j**, **7k**, **7l**, and **7m**

Copies of ^1H NMR and ^{13}C NMR of ligand **4**

4