Asymmetric Michael Addition of Nitroalkanes to Nitroalkenes Catalyzed by C₂-Symmetric Tridentate Bis(oxazoline) and Bis(thiazoline) Zinc Complexes

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General

Unless otherwise indicated, all commercially available compounds were used without further purification. Solvents were dried according to standard procedures. Nitroalkane was freshly distilled before use. Et₂Zn (10 wt % solution in hexane) was purchased from Strem. Nitroalkenes were prepared according to the literature.¹ 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 200 and Mercury 300 MHz spectrometers, while the ¹³C NMR spectra were recorded at 50 and 75 MHz respectively. 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 were determined by chiral HPLC (2-propanol/hexane as the eluent).

Experimental Procedures

1. Enantioselective Michael addition for synthesis of 1,3-dinitroalkanes

General Procedure. A 25 mL Schlenk tube equipped with a stirring bar was flame dried under vacuum. After cooling to room temperature, the flask was flushed with N₂, and nitroalkene (0.50 mmol), ligand **1c** (23.0 mg, 0.05 mmol), toluene (1.2 mL), hexane (0.8 mL), nitroethane (150 μ L, 4.0 equiv) and Ti(OiPr)₄ (120 μ L, 0.40 mmol) were added under nitrogen. The reaction mixture was cooled to 0 °C and stirred for 0.5 h. Then, Et₂Zn (220 μ L, 0.125 mmol) was added and the reaction mixture was warmed to 30 °C. After 72 h, the reaction was quenched with aqueous 1N HCl (2 mL) and extracted with CH₂Cl₂ (5 mL $\times$ 3). The combined organic phase was dried (Na₂SO₄), concentrated in vacuo, and purified by column chromatography on silica gel.

***syn*-1,3-Dinitro-2-phenylbutane (4a).**² Prepared according to the general procedure using β -nitrostyrene **3a** (75.0 mg, 0.50 mmol). Purified by column chromatography (20 % AcOEt in petroleum ether) to yield 97.6 mg (87 %) of diastereoisomers (*syn:anti* 5.8:1). *syn*-isomer: White solid, mp 89–90 °C. The ee was determined through its derivative **6a** by chiral HPLC. [α]_D²⁰ = +21.6 (*c* 1.12, CH₂Cl₂, 90 % ee). ¹H NMR(CDCl₃): δ = 7.40–7.33 (m, 3H), 7.20–7.15 (m, 2H), 4.98–4.90 (m, 2H), 4.83 (dd, *J* = 13.8, 8.3 Hz, 1H), 4.06–3.99 (m, 1H), 1.58 (d, *J* = 6.9 Hz, 3H). ¹³C NMR (CDCl₃): δ = 133.4, 129.3, 129.1, 127.9, 84.0, 76.0, 47.3, 16.7.

***syn*-1,3-Dinitro-2-(4-methylphenyl)butane (4b).** Prepared according to the general procedure using 4-methyl- β -nitrostyrene **3b** (81.6 mg, 0.50 mmol). Purified by column chromatography (20 % AcOEt in petroleum ether) to yield 99.3 mg (83%) of diastereoisomers (*syn:anti* 6.1:1). *syn*-isomer: White solid, mp 43–44 °C. The ee was determined by chiral HPLC on OJ column (hexane: 2-propanol 85:15, 1.0 mL/min, *t*_{major}=54.0 min, *t*_{minor}=61.9 min). [α]_D²⁰ = +12.5 (*c* 1.08, CH₂Cl₂, 91 % ee). ¹H NMR(CDCl₃): δ = 7.16 (d, *J* = 8.1 Hz, 2H), 7.03 (dd, *J* = 8.1, 1.8 Hz, 2H),

4.96–4.88 (m, 2H), 4.80 (dd, $J = 13.5, 8.4$ Hz, 1H), 4.01–3.94 (m, 1H), 2.32 (s, 3H), 1.56 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (CDCl_3): $\delta = 139.0, 130.3, 129.9, 127.8, 84.1, 76.2, 47.0, 21.0, 16.6$. IR (neat): 1548, 1381, 814, 724 cm^{-1} . MS (70 eV, EI): m/z (%) 238 (M^+ , 8), 191 (30), 145 (100), 131 (53), 117 (55), 105 (51), 91 (44). HRMS (EI) calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_4$: 238.09536, found: 238.09507.

***syn*-1,3-Dinitro-2-(4-methoxyphenyl)butane (4c).** Prepared according to the general

procedure using 4-methoxy- β -nitrostyrene **3c** (89.6 mg, 0.50 mmol). Purified by column chromatography (20 % AcOEt in petroleum ether) to yield 105.6 mg (83 %) of diastereoisomers (*syn:anti* 6.5:1). *syn*-isomer: White solid, mp 82–84 °C. The ee was determined through its derivative **6c** by chiral HPLC. $[\alpha]_{\text{D}}^{20} = +18.2$ (c 1.14, CH_2Cl_2 , 89 % ee). ^1H NMR(CDCl_3): $\delta = 7.09\text{--}7.06$ (m, 2H), 6.90–6.86 (m, 2H), 4.94–4.87 (m, 2H), 4.79 (dd, $J = 13.5, 8.4$ Hz, 1H), 3.78 (s, 1H), 1.56 (d, $J = 6.6$ Hz, 3H).

^{13}C NMR (CDCl_3): $\delta = 159.9, 129.1, 125.1, 114.6, 84.1, 76.3, 55.2, 46.7, 16.7$. IR (neat): 1613, 1555, 1516, 1380, 1257, 1184, 1032, 835 cm^{-1} . MS (70 eV, EI): m/z (%) 254 (M^+ , 41), 207 (44), 161 (99), 134 (100), 121 (85), 91 (96). HRMS (EI) calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_5$: 254.09027, found: 254.09078.

***syn*-1,3-Dinitro-2-(2-methoxyphenyl)butane (4d).** Prepared according to the general

procedure using 2-methoxy- β -nitrostyrene **3d** (89.6 mg, 0.50 mmol). Purified by column chromatography (20 % AcOEt in petroleum ether) to yield 114.7 mg (90 %) of diastereoisomers (*syn:anti* 5.8:1). *syn*-isomer: White solid, mp 62–64 °C. The ee was determined by chiral HPLC on OJ column (hexane:2-propanol 85:15, 1.0 mL/min, $t_{\text{minor}}=47.6$ min, $t_{\text{major}}=55.2$ min). $[\alpha]_{\text{D}}^{20} = +9.3$ (c 1.00, CH_2Cl_2 , 91 % ee). ^1H

NMR(CDCl_3): $\delta = 7.34\text{--}7.27$ (m, 1H), 7.06 (dd, $J = 7.6, 1.4$ Hz, 1H), 6.94–6.90 (m, 2H), 5.24–5.14 (m, 1H), 4.90–4.88 (m, 2H), 4.31 (dd, $J = 14.4, 7.5$ Hz, 1H), 3.87 (s, 3H), 1.59 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (CDCl_3): $\delta = 157.1, 130.2, 129.9, 121.8, 121.1, 111.2, 83.0, 75.0, 55.4, 43.8, 17.0$. IR (neat): 1556, 1496, 1380, 1250, 1026, 758 cm^{-1} . MS (70 eV, EI): m/z (%) 254 (M^+ , 47), 177 (8), 161 (100), 147 (27), 134 (44), 119 (25), 91 (59). HRMS (EI) calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_5$: 254.09027, found: 254.08904.

***syn*-1,3-Dinitro-2-(3,4-dimethoxyphenyl)butane (4e).** Prepared according to the general

procedure using 3,4-dimethoxy- β -nitrostyrene **3e** (104.6 mg, 0.50 mmol). Purified by column chromatography (30 % AcOEt in petroleum ether) to yield 94.6 mg (67 %) of diastereoisomers (*syn:anti* 9.6:1). *syn*-isomer: White solid, mp 86–88 °C. The ee was determined through its derivative **6e** by chiral HPLC. $[\alpha]_{\text{D}}^{20} = +11.7$ (c 1.27, CH_2Cl_2 , 86 % ee). ^1H NMR (CDCl_3): $\delta = 6.83$ (d, $J = 8.4$ Hz, 1H), 6.72 (dd, $J = 8.3, 2.0$ Hz, 1H), 6.63 (d, $J = 2.1$ Hz, 1H), 4.97–4.89 (m, 2H), 4.81 (dd, $J = 13.5, 8.4$ Hz, 1H),

3.98–3.93 (m, 1H), 3.86 (s, 6H), 1.59 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (CDCl_3): $\delta = 149.5, 149.3, 125.5, 120.1, 111.4, 111.0, 84.1, 76.3, 55.9, 55.8, 47.1, 16.7$. IR (neat): 1562, 1521, 1381, 1268, 1149, 1026, 688 cm^{-1} . MS (70 eV, EI): m/z (%) 284 (M^+ , 90), 237 (44), 208 (52),

192 (100), 177 (45), 164 (80), 151 (54), 91 (44), 77 (36). HRMS (EI) calcd for C₁₂H₁₆N₂O₆: 284.10084, found: 284.10049.

***syn*-1,3-Dinitro-2-(4-fluorophenyl)butane (4f).** Prepared according to the general procedure

using 4-fluoro- β -nitrostyrene **3f** (83.6 mg, 0.50 mmol). Purified by column chromatography (20 % AcOEt in petroleum ether) to yield 96.3 mg (80 %) of diastereoisomers (*syn:anti* 3.9:1). *syn*-isomer: White solid, mp 129–131 °C. The ee was determined through its derivative **6f** by chiral HPLC. $[\alpha]_D^{20} = +6.1$ (*c* 1.11, CH₂Cl₂, 90 % ee). ¹H NMR(CDCl₃): $\delta = 7.18\text{--}7.14$ (m, 2H), 7.09–7.03 (m, 2H), 4.99–4.88 (m, 2H), 4.92 (dd,

$J = 13.5, 6.3$ Hz, 1H), 4.80 (dd, $J = 13.5, 8.5$ Hz, 1H), 4.04–3.97 (m, 1H), 1.59 (d, $J = 6.6$ Hz, 3H). ¹³C NMR (CDCl₃): $\delta = 162.9$ (d, $J = 247.5$ Hz), 129.7 (d, $J = 8.3$ Hz), 129.2 (d, $J = 3.5$ Hz), 116.4 (d, $J = 21.4$ Hz), 84.0, 76.2, 46.7, 16.8. IR (neat): 1557, 1549, 1512, 1385, 1220, 834 cm⁻¹. MS (70 eV, EI): m/z (%) 242 (M⁺, 4), 195 (28), 149 (100), 135 (63), 122 (42), 109 (84). HRMS (EI) calcd for C₁₀H₁₁N₂O₄F: 242.07029, found: 242.07034.

***syn*-1,3-Dinitro-2-(2-fluorophenyl)butane (4g).** Prepared according to the general procedure

using 2-fluoro- β -nitrostyrene **3g** (83.6 mg, 0.50 mmol). Purified by column chromatography (20 % AcOEt in petroleum ether) to yield 105.9 mg (87 %) of diastereoisomers (*syn:anti* 6.2:1). *syn*-isomer: Brown oil. The ee was determined through its derivative **6g** by chiral HPLC. $[\alpha]_D^{20} = +21.7$ (*c* 1.17, CH₂Cl₂, 90 % ee). ¹H NMR (CDCl₃): $\delta = 7.38\text{--}7.31$ (m, 1H), 7.16–7.08 (m, 3H), 5.11–5.02 (m, 1H), 4.92 (dd, $J = 13.8, 6.4$ Hz,

1H), 4.85 (dd, $J = 13.8, 8.1$ Hz, 1H), 4.92 (dd, $J = 13.8, 6.4$ Hz, 1H), 4.32 (dd, $J = 14.4, 7.2$ Hz, 1H), 1.61 (d, $J = 6.6$ Hz, 3H). ¹³C NMR (CDCl₃): $\delta = 160.7$ (d, $J = 245.1$ Hz), 130.9 (d, $J = 8.9$ Hz), 129.6 (d, $J = 3.6$ Hz), 125.0 (d, $J = 3.6$ Hz), 121.0 (d, $J = 13.6$ Hz), 116.2 (d, $J = 22.0$ Hz), 83.2, 75.0 (d, $J = 2.3$ Hz), 42.0, 16.9. IR (neat): 1559, 1494, 1380, 762 cm⁻¹. MS (70 eV, EI): m/z (%) 242 (M⁺, 12), 195 (4), 165 (11), 149 (100), 135 (48), 122 (35), 109 (76). HRMS (EI) calcd for C₁₀H₁₁N₂O₄F: 242.07029, found: 242.06980.

***syn*-1,3-Dinitro-2-(2-chlorophenyl)butane (4h).** Prepared according to the general procedure

using 2-chloro- β -nitrostyrene **3h** (91.8 mg, 0.50 mmol). Purified by column chromatography (20 % AcOEt in petroleum ether) to yield 107.0 mg (83 %) of diastereoisomers (*syn:anti* 3.8:1). *syn*-isomer: Yellow oil. The ee was determined by chiral HPLC on OJ column (hexane: 2-propanol 85:15, 1.0 mL/min, $t_{\text{major}} = 54.9$ min, $t_{\text{minor}} = 66.2$ min). $[\alpha]_D^{20} = +12.7$ (*c* 1.39, CH₂Cl₂, 91 % ee). ¹H NMR(CDCl₃): $\delta = 7.47\text{--}7.44$ (m,

1H), 7.32–7.25 (m, 2H), 7.16–7.13 (m, 1H), 5.21–5.12 (m, 1H), 4.97–4.84 (m, 2H), 4.71 (dd, $J = 13.4, 6.8$ Hz, 1H), 1.62 (d, $J = 6.6$ Hz, 3H). ¹³C NMR (CDCl₃): $\delta = 134.4, 131.4, 130.7, 130.1, 128.1, 127.7, 82.9, 74.9, 43.0, 16.4$. IR (neat): 1553, 1378, 1361, 1040, 759 cm⁻¹. MS (70 eV, EI): m/z (%) 258 (M⁺, 16), 165 (100), 151 (19), 139 (23), 130 (38), 125 (42), 115 (42), 103 (27), 91 (16). HRMS (EI) calcd for C₁₀H₁₁N₂O₄³⁵Cl: 258.04073, found: 258.04082.

***syn*-1,3-Dinitro-2-(2-naphthyl)butane (4i).** Prepared according to the general procedure

using 2-(2-nitrovinyl)naphthalene **3i** (99.6 mg, 0.50 mmol). Purified by column chromatography (20 % AcOEt in petroleum ether) to yield 113.4 mg (83 %) of diastereoisomers (*syn:anti* 3.8:1). *syn*-isomer: *syn*-isomer: Yellow oil. The ee was determined through its derivative **6i** by chiral HPLC. $[\alpha]_D^{20} = -26.1$ (*c* 1.00, CH₂Cl₂, 88 % ee). ¹H NMR (CDCl₃): δ = 8.18 (d, *J* = 8.4 Hz, 1H), 7.92–7.83 (m, 2H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 6.9 Hz, 1H), 5.21–5.12 (m, 2H), 4.98 (d, *J* = 6.9 Hz, 2H), 1.56 (d, *J* = 6.6 Hz, 3H). ¹³C NMR (CDCl₃): δ = 134.1, 131.0, 130.0, 129.5, 129.3, 127.3, 126.3, 125.1, 123.8, 121.8, 83.7, 75.0, 40.7, 15.6. IR (neat): 1556, 1379, 1261, 1093, 1020, 799, 780 cm⁻¹. MS (70 eV, EI): *m/z* (%) 274 (M⁺, 86), 198 (28), 182 (56), 181 (100), 167 (72), 153 (91), 141 (28). HRMS (EI) calcd for C₁₄H₁₄N₂O₄: 274.09536, found: 274.09485.

syn-1,3-Dinitro-2-(2-furyl)butane (4j). Prepared according to the general procedure using 2-(2-nitrovinyl)furan **3j** (69.6 mg, 0.50 mmol). Purified by column chromatography (20% AcOEt in petroleum ether) to yield 71.7 mg (67 %) of diastereoisomers (*syn:anti* 6.7:1). *syn*-isomer: Yellow oil. The ee was determined through its derivative **6j** by chiral HPLC. $[\alpha]_D^{20} = +38.8$ (*c* 1.14, CH₂Cl₂, 88 % ee). ¹H NMR (CDCl₃): δ = 7.39 (dd, *J* = 0.8, 2.0 Hz, 1H), 6.34 (dd, *J* = 3.3, 2.1 Hz, 1H), 6.28 (d, *J* = 3.4 Hz, 1H), 4.96–4.81 (m, 3H), 4.26–4.22 (m, 1H), 1.60 (d, *J* = 6.6 Hz, 3H). ¹³C NMR (CDCl₃): δ = 147.0, 143.4, 110.7, 109.5, 82.4, 74.1, 41.1, 16.2. IR (neat): 1562, 1379, 1151, 1017, 754 cm⁻¹. MS (70 eV, EI): *m/z* (%) 214 (M⁺, 16), 167 (54), 138 (32), 121 (69), 107 (58), 94 (72), 83 (100), 39 (60). HRMS (EI) calcd for C₈H₁₀N₂O₅: 214.05897, found: 214.05942.

syn-1,3-Dinitro-2-(4-chlorophenyl)butane (4k). Prepared according to the general procedure using 4-chloro- β -nitrostyrene **3k** (91.8 mg, 0.50 mmol). Purified by column chromatography (20 % AcOEt in petroleum ether) to yield 87.7 mg (68 %) of diastereoisomers (*syn:anti* 5.2:1). *syn*-isomer: White solid, mp 98–100 °C. $[\alpha]_D^{20} = +17.1$ (*c* 1.11, CH₂Cl₂). ¹H NMR (CDCl₃): δ = 7.36–7.32 (m, 2H), 7.13–7.08 (m, 2H), 4.96–4.87 (m, 2H), 4.79 (dd, *J* = 13.6, 8.6 Hz, 1H), 4.03–3.96 (m, 1H), 1.59 (d, *J* = 6.9 Hz, 3H). ¹³C NMR (CDCl₃): δ = 135.2, 131.8, 129.6, 129.3, 83.8, 76.0, 46.8, 16.8. IR (neat): 1555, 1392, 1381, 1090, 1014, 830 cm⁻¹. MS (70 eV, EI): *m/z* (%) 258 (M⁺, 6), 211 (30), 165 (100), 151 (25), 138 (38), 125 (53), 115 (43), 103 (25), 91 (16). HRMS (EI) calcd for C₁₀H₁₁N₂O₄³⁵Cl: 258.04073, found: 258.04069.

syn-4-Nitro-3-nitromethyl-1-phenylpentane (4l). Prepared according to the general procedure using 1-nitro-4-phenyl-1-butene **3l** (88.6 mg, 0.50 mmol). Purified by column chromatography (petroleum ether:ethyl acetate 10:1) to yield 102 mg (80 %) of diastereoisomers (*syn:anti* 3.4:1). *syn*-isomer: pale yellow oil, 72 % ee. The ee was determined through its derivative **6k**. ¹H NMR (CDCl₃): δ = 7.34–7.14 (m, 5H), 4.75–4.60 (m, 2H), 4.49–4.40 (m, 1H), 2.83–2.56 (m, 3H), 1.87–1.76 (m, 2H), 1.53 (d, *J* =

6.9 Hz, 3H). ^{13}C NMR (CDCl_3): δ = 139.6, 128.7, 128.2, 126.6, 83.2, 74.9, 40.3, 32.7, 29.1, 16.0. IR (neat): 1551, 1496, 1455, 1392, 750, 701 cm^{-1} . MS (70 eV, EI): m/z (%) 252 (M^+), 204, 191, 159, 143, 129, 117, 104, 91. HRMS (EI) calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}_4$: 252.11101, found: 252.11084.

***syn*-1,3-Dinitro-2-phenylpentane (4m).** Prepared according to the general procedure using

β -nitrostyrene **3a** (75.0 mg, 0.50 mmol) and 1-nitropropane (178 μL , 4.0 equiv). Purified by column chromatography (20 % AcOEt in petroleum ether) to yield 105 mg (88%) of diastereoisomers (*syn:anti* 4.1:1). *syn*-isomer: colorless solid, m.p. 65–66 $^{\circ}\text{C}$. The ee was determined chiral HPLC on OJ column (hexane:2-propanol 85:15, 0.9 mL/min, t_{major} =53.5 min, t_{minor} =76.1 min). $[\alpha]_{\text{D}}^{20}$ = +12.4 (c 0.84, CH_2Cl_2 , 88 % ee). ^1H NMR (CDCl_3): δ = 7.39–7.30 (m, 3H), 7.18–7.13 (m, 2H), 4.88 (dd, J = 6.3, 13.5 Hz, 1H), 4.81–4.72 (m, 1H), 4.04 (q, J = 7.2 Hz, 1H), 2.04–1.95 (m, 1H), 1.91–1.84 (m, 1H), 1.01 (t, J = 7.2 Hz). ^{13}C NMR (CDCl_3): δ = 133.8, 129.1, 128.9, 127.8, 91.0, 76.2, 46.4, 24.2, 10.1. IR (neat): 1552, 1457, 1377, 1088, 810, 701 cm^{-1} . MS (70 eV, EI): m/z (%) 238 (M^+ , 4), 191 (18), 161 (12), 145 (100), 131 (45), 117 (50), 104 (62), 91 (69), 77 (30). HRMS (EI) calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_4$: 238.09536, found: 238.09565.

2. Preparation of substituted thioureas

Typical Procedure. To a solution of *syn*-1,3-dinitro-2-phenylbutane **4a** (64.2 mg, 0.29 mmol) in EtOH (5 mL) was added 10 wt % Pd/C (61.5 mg, 20 mol %). The mixture was stirred under hydrogen at room temperature for 36 h. After filtration, the filtrate was concentrated in vacuo to afford colorless oil. The oil was redissolved in THF (5 mL) and refluxed with CS_2 (27 μL , 1.5 equiv) for 24 h. The mixture was cooled to room temperature and concentrated in vacuo. Purification by column chromatography on silica gel afforded 21.9 mg (37 %) of **6a** as a white solid.

***syn*-4-Methyl-5-phenyl-tetrahydropyrimidine-2-thione (6a).** Prepared according to the typical procedure using *syn*-1,3-dinitro-2-phenylbutane **4a** (64.2 mg, 0.29 mmol). Purified by column chromatography (30 % petroleum ether in AcOEt) to yield 21.9 mg (37 %) of **6a** as a white solid, mp 194–196 $^{\circ}\text{C}$. The ee was determined by chiral HPLC on OF column (hexane: 2-propanol 70:30, 0.9 mL/min, t_{minor} =31.8 min, t_{major} =40.7 min). $[\alpha]_{\text{D}}^{20}$ = +121.2 (c 0.96, CHCl_3 , 90 % ee). ^1H NMR (CDCl_3): δ = 7.34–7.29 (m, 3H), 7.19–6.66 (m, 2H), 6.77 (br s, 1H), 6.66 (br s, 1H), 3.88–3.79 (m, 1H), 3.63 (dd, J = 6.0, 2.6 Hz, 2H), 3.25 (dd, J = 10.6, 5.8 Hz, 1H), 1.00 (d, J = 6.9 Hz, 3H). ^{13}C NMR (CDCl_3): δ = 176.0, 137.7, 128.7, 127.9, 127.4, 50.5, 43.0, 39.2, 17.6. IR (neat): 3178, 2968, 1561, 1550, 1450, 1324, 1246, 1210, 766, 742, 700 cm^{-1} . MS (70 eV, EI): m/z (%) 206 (M^+ , 86), 117 (12), 104 (100), 91 (10), 81 (26), 69 (45), 44 (50). HRMS (EI) calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{S}$: 206.08777, found: 206.08747.

***syn*-4-Methyl-5-(4-methylphenyl)-tetrahydropyrimidine-2-thione (6b).** Prepared according to the typical procedure using *syn*-1,3-dinitro-2-(4-methylphenyl)butane **4b** (57.4

mg, 0.24 mmol). Purified by column chromatography (30 % petroleum ether in AcOEt) to yield 28.3 mg (53 %) of **6b** as a white solid, mp 216–218 °C. The *ee* was determined by chiral HPLC on OF column (hexane:2-propanol 70:30, 0.9 mL/min, $t_{\text{minor}}=31.4$ min, $t_{\text{major}}=38.2$ min). $[\alpha]_{\text{D}}^{20} = +104.8$ (c 1.05, CHCl_3 , 91 % *ee*). ^1H NMR (CDCl_3): δ = 7.16 (d, J = 8.1 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 6.88 (br s, 1H), 6.77 (br s, 1H), 3.84–3.79 (m, 1H), 3.60 (dd, J = 6.3, 2.7 Hz, 2H), 3.21 (dd, J = 10.5, 6.0 Hz, 1H), 2.34 (s, 3H), 0.99 (d, J = 6.9 Hz, 3H). ^{13}C NMR (CDCl_3): δ = 176.3, 137.1, 134.6, 129.4, 127.8, 50.6, 43.3, 38.9, 21.0, 17.6. IR (neat): 3174, 2967, 1552, 1514, 1322, 1211, 817, 737 cm^{-1} . MS (70 eV, EI): m/z (%) 220 (M^+ , 68), 118 (100), 115 (15), 91 (16), 44 (35). HRMS (EI) calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{S}$: 220.10342, found: 220.10315.

syn-4-Methyl-5-(4-methoxyphenyl)-tetrahydropyrimidine-2-thione (6c).

Prepared according to the typical procedure using *syn*-1,3-dinitro-2-(4-methoxyphenyl)butane **4c** (67.0 mg, 0.26 mmol). Purified by column chromatography (30 % petroleum ether in AcOEt) to yield 24.6 mg (40 %) of **6c** as a white solid, mp 198–200 °C. The *ee* was determined by chiral HPLC on OF column (hexane:2-propanol 70:30, 0.9 mL/min, $t_{\text{minor}}=52.5$ min, $t_{\text{major}}=66.3$ min). $[\alpha]_{\text{D}}^{20} = +93.5$ (c 0.83, CHCl_3 , 89 % *ee*). ^1H NMR (CDCl_3): δ = 7.44 (br s, 1H), 7.27 (br s, 1H), 7.11–7.06 (m, 2H), 6.90–6.86 (m, 2H), 3.84–3.77 (m, 4H), 3.57 (dd, J = 6.3, 2.7 Hz, 2H), 3.19 (dd, J = 10.6, 6.2 Hz, 1H), 0.98 (d, J = 6.6 Hz, 3H). ^{13}C NMR (CDCl_3): δ = 175.8, 158.7, 129.7, 128.9, 114.0, 55.1, 50.5, 43.2, 38.4, 17.5. IR (neat): 3203, 2968, 1548, 1514, 1250, 1200, 1181, 1032, 910, 831, 729 cm^{-1} . MS (70 eV, EI): m/z (%) 236 (M^+ , 41), 134 (100), 119 (13), 91 (13), 44 (11). HRMS (EI) calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{OS}$: 236.09834, found: 236.09804.

syn-4-Methyl-5-(3,4-dimethoxyphenyl)-tetrahydropyrimidine-2-thione (6e).

Prepared according to the typical procedure using *syn*-1,3-dinitro-2-(3,4-dimethoxyphenyl)butane **4e** (81.4 mg, 0.29 mmol). Purified by column chromatography (15 % petroleum ether in AcOEt) to yield 30.0 mg (39%) of **6e** as a white solid, mp 171–173 °C. The *ee* was determined by chiral HPLC on OF column (hexane:2-propanol 50:50, 0.6 mL/min, $t_{\text{minor}}=73.6$ min, $t_{\text{major}}=104.3$ min). $[\alpha]_{\text{D}}^{20} = +80.2$ (c 0.97, CHCl_3 , 86 % *ee*). ^1H NMR (CDCl_3): δ = 7.09 (br s, 1H), 6.91 (br s, 1H), 6.87–6.82 (m, 1H), 6.71–6.64 (m, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.84–3.80 (m, 1H), 3.65–3.53 (m, 2H), 3.17 (dd, J = 10.6, 5.2 Hz, 1H), 1.00 (d, J = 6.9 Hz, 3H). ^{13}C NMR (CDCl_3): δ = 176.4, 149.0, 148.3, 130.2, 120.1, 111.2, 111.1, 56.0, 55.8, 50.6, 43.8, 38.8, 17.7. IR (neat): 3203, 2963, 1518, 1463, 1269, 1251, 1202, 1146, 1026, 752 cm^{-1} . MS (70 eV, EI): m/z (%) 266 (M^+ , 39), 164 (100), 149 (15), 91 (13). HRMS (EI) calcd for $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$: 266.10890, found: 266.10869.

syn-4-Methyl-5-(4-fluorophenyl)-tetrahydropyrimidine-2-thione (6f). Prepared according to the typical procedure using *syn*-1,3-dinitro-2-(4-fluorophenyl)butane **4f** (58.1 mg, 0.24 mmol). Purified by column chromatography (30 % petroleum ether in AcOEt) to yield 18.8 mg (35 %) of **6f** as a white solid, mp 202–204 °C. The *ee* was determined by chiral HPLC on

OF column (hexane:2-propanol 70:30, 0.9 mL/min, $t_{\text{minor}}=26.3$ min, $t_{\text{major}}=33.3$ min). $[\alpha]_{\text{D}}^{20} = +94.5$ (c 1.20, CHCl_3 , 90 % ee). ^1H NMR (CDCl_3): δ = 7.36–7.00 (m, 5H), 6.91 (br s, 1H), 3.88–3.79 (m, 1H), 3.67–3.51 (m, 2H), 3.21 (dd, J = 10.8, 5.1 Hz, 1H), 0.99 (d, J = 6.9 Hz, 3H). ^{13}C NMR (CDCl_3): δ = 176.0, 162.0 (d, J = 244.5 Hz), 133.5 (d, J = 3.6 Hz), 129.5 (d, J = 8.3 Hz), 115.6 (d, J = 20.9 Hz), 50.3, 43.4, 38.6, 17.6. IR (neat): 3175, 2969, 1567, 1544, 1511, 1208, 833 cm^{-1} . MS (70 eV, EI): m/z (%) 224 (M^+ , 67), 192 (10), 136 (15), 122 (100), 44 (45). HRMS (EI) calcd for $\text{C}_{11}\text{H}_{13}\text{N}_2\text{FS}$: 224.07835, found: 224.07898.

syn-4-Methyl-5-(2-fluorophenyl)-tetrahydropyrimidine-2-thione (6g). Prepared according

to the typical procedure using *syn*-1,3-dinitro-2-(2-fluorophenyl)butane **4g** (45.0 mg, 0.19 mmol). Purified by column chromatography (30 % petroleum ether in AcOEt) to yield 12.4 mg (29 %) of **6g** as a white solid, mp 210–212 °C. The ee was determined by chiral HPLC on OF column (hexane: 2-propanol 75:25, 0.9 mL/min, $t_{\text{minor}}=30.6$ min, $t_{\text{major}}=38.6$ min). $[\alpha]_{\text{D}}^{20} = +106.9$ (c 1.24, CHCl_3 , 90 % ee). ^1H NMR (CDCl_3): δ = 7.51 (br s, 1H), 7.31–7.04 (m, 5H), 3.93–3.91 (m, 1H), 3.64–3.62 (m, 3H), 1.02 (d, J = 6.6 Hz, 3H). ^{13}C NMR (CDCl_3): δ = 176.1, 160.7 (d, J = 244.5 Hz), 128.9 (d, J = 8.3 Hz), 128.3 (d, J = 58.9 Hz), 126.5 (d, J = 264.7 Hz), 124.9 (d, J = 13.7 Hz), 115.2 (d, J = 22.6 Hz), 49.4, 43.1, 31.4, 17.5. IR (neat): 3207, 2972, 1564, 1547, 1493, 1218, 757 cm^{-1} . MS (70 eV, EI): m/z (%) 224 (M^+ , 90), 206 (14), 146 (4), 122 (100), 104 (20). HRMS (EI) calcd for $\text{C}_{11}\text{H}_{13}\text{FN}_2\text{S}$: 224.07835, found: 224.07864.

syn-4-Methyl-5-(2-naphthyl)-tetrahydropyrimidine-2-thione (6i). Prepared according to

the typical procedure using *syn*-1,3-dinitro-2-(2-naphthyl)butane **4i** (77.1 mg, 0.28 mmol). Purified by column chromatography (30 % petroleum ether in AcOEt) to yield 30.6 mg (43 %) of **6i** as a white solid, mp 260–262 °C. The ee was determined by chiral HPLC on OF column (hexane:2-propanol 70:30, 0.9 mL/min, $t_{\text{minor}}=39.1$ min, $t_{\text{major}}=67.3$ min). $[\alpha]_{\text{D}}^{20} = +234.7$ (c 0.77, CHCl_3 , 88 % ee). ^1H NMR (CDCl_3): δ = 8.03 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 8.1 Hz, 1H), 7.62–7.52 (m, 2H), 7.47 (t, J = 7.8 Hz, 1H), 7.25 (d, J = 7.5 Hz, 1H), 6.94 (br s, 2H), 4.20–4.14 (m, 1H), 4.09–4.06 (m, 1H), 3.99–3.92 (m, 1H), 3.64–3.58 (m, 1H), 0.96 (d, J = 6.6 Hz, 3H). ^{13}C NMR (CDCl_3): δ = 175.7, 133.8, 133.2, 131.5, 129.1, 128.0, 126.6, 125.8, 125.2, 123.6, 122.5, 49.8, 41.4, 34.7, 17.6. IR (neat): 3201, 2971, 1549, 1511, 1280, 1202, 908, 780, 729 cm^{-1} . MS (70 eV, EI): m/z (%) 256 (M^+ , 44), 165 (5), 154 (100), 141 (4), 128 (4), 115 (4). HRMS (EI) calcd for $\text{C}_{15}\text{H}_{16}\text{N}_2\text{S}$: 256.10342, found: 256.10334.

syn-4-Methyl-5-(2-furyl)-tetrahydropyrimidine-2-thione (6j). Prepared according to the typical procedure using *syn*-1,3-dinitro-2-(2-furyl)butane **4j** (43.0 mg, 0.20 mmol). Purified by column chromatography (30 % petroleum ether in AcOEt) to yield 7.3 mg (19 %) of **6j** as a white solid, mp 226–228 °C. The ee was determined by chiral HPLC on OF column (hexane: 2-propanol 80:20, 0.9 mL/min, $t_{\text{minor}}=47.3$ min, $t_{\text{major}}=53.5$ min). $[\alpha]_{\text{D}}^{20} = +61.6$ (c 0.69,

CHCl₃, 88 % ee). ¹H NMR (CDCl₃): δ = 7.37 (d, *J* = 1.2 Hz, 1H), 6.86 (br s, 1H), 6.67 (br s, 1H), 6.36 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.17 (d, *J* = 3.3 Hz, 1H), 3.89–3.84 (m, 1H), 3.61 (ddd, *J* = 12.4, 5.0, 2.7 Hz, 1H), 3.52 (ddd, *J* = 12.6, 6.6, 3.0 Hz, 1H), 3.39–3.33 (m, 1H), 1.06 (d, *J* = 6.6 Hz, 3H). ¹³C NMR (CDCl₃): δ = 176.5, 151.3, 141.7, 110.6, 106.9, 49.7, 42.6, 33.9, 17.9. IR (neat): 3187, 2970, 1575, 1541, 1333, 1299, 1243, 1207, 1020, 736 cm⁻¹. MS (70 eV, EI): *m/z* (%) 196 (M⁺, 64), 108 (10), 94 (100), 79 (10), 66 (16), 44 (35). HRMS (EI) calcd for C₉H₁₂N₂OS: 196.06703, found: 196.06720.

***syn*-4-Methyl-5-phenylethyl-tetrahydropyrimidine-2-thione (6l).** Prepared according to the

typical procedure using *syn*-4-nitro-3-nitro- methyl-1-phenylpentane **4l** (100 mg, 0.4 mmol). Purified by column chromatography (30 % petroleum ether in AcOEt) to yield 42 mg (45 %) of **6l** as a colorless solid, mp 120–122 °C, 72 % ee. The ee was determined by chiral HPLC on OJ column (hexane:2-propanol 85:15, 0.8 mL/min, *t*_{minor}=30.4 min, *t*_{major}=25.5 min). ¹H NMR (CDCl₃): δ = 7.32–7.18 (m, 5H), 6.65 (br s, 2H), 3.60–3.55 (m, 1H), 3.31–3.24 (m, 1H), 3.20–3.10 (m, 1H), 2.73–2.55 (m, 2H), 2.04–1.94 (m, 1H), 1.70–1.50 (m, 2H), 1.14 (d, *J* = 6.9 Hz, 3H). ¹³C NMR (CDCl₃): δ = 176.3, 140.9, 128.6, 128.2, 126.3, 49.6, 42.8, 33.1, 32.8, 29.2, 16.8. IR (neat): 3209, 2969, 2937, 2681, 1551, 1496, 1453, 1379, 1288, 1205, 751, 701 cm⁻¹. MS (70 eV, EI): *m/z* (%) 234 (M⁺, 100), 143 (14), 130 (76), 115 (53), 104 (10), 91 (74). HRMS (EI) calcd for C₁₃H₁₈N₂S: 234.11907, found: 234.11870.

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- (2) (a) Alcántara, M. D.; Escribano, F. C.; Gómez-Sánchez, A.; Diáñez, M. J.; Estrada, M. D.; López-Castro, A.; Pérez-Garrido, S. *Synthesis* **1996**, 64–70. (b) Alcántara, M. D.; Escribano, F. C.; Gómez-Sánchez, A. *Tetrahedron Lett.* **1988**, 29, 6001–6004.

3. Determination of absolute configuration of 1,3-dinitroalkanes

The absolute configuration of major *syn*-isomer of 1,3-dinitroalkanes were assigned to be 2*R*, 3*R* from the crystal structure of **4f** and **4k**. CCDC 294471 & 294472 contains the supplementary crystallographic data for these two compounds. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. The crystal structure of **4f** and **4k** are given in Figure 1 and Figure 2, respectively.

Figure S1. The ORTEP diagram of (*R,R*)-1,3-dinitro-2-(4-fluorophenyl)butane **4f**

Figure S2. The ORTEP diagram of (*R,R*)-1,3-dinitro-2-(4-chlorophenyl)butane **4k**

4. Proposed transition state for asymmetric Michael addition

Figure S3. Possible transition state for asymmetric Michael addition

HPLC spectra of 1,3-dinitroalkanes and substituted thioureas

rac-syn-1,3-dinitro-2-phenylbutane

syn-1,3-dinitro-2-phenylbutane

rac--syn-1,3-dinitro-2-(2-methoxyphenyl)butane

syn-1,3-dinitro-2-(2-methoxyphenyl)butane

rac-syn-1,3-dinitro-2-(2-chlorophenyl)butane

syn-1,3-dinitro-2-(2-chlorophenyl)butane

rac-syn-4-methyl-5-(4-methylphenyl)-tetrahydropyrimidine-2-thione

syn-4-methyl-5-(4-methylphenyl)-tetrahydropyrimidine-2-thione

rac-syn-4-methyl-5-(4-methoxyphenyl)-tetrahydropyrimidine-2-thione

syn-4-methyl-5-(4-methoxyphenyl)-tetrahydropyrimidine-2-thione

rac-syn-4-methyl-5-(3,4-dimethoxyphenyl)-tetrahydropyrimidine-2-thione

syn-4-methyl-5-(3,4-dimethoxyphenyl)-tetrahydropyrimidine-2-thione

rac-syn-4-methyl-5-(4-fluorophenyl)-tetrahydropyrimidine-2-thione

syn-4-methyl-5-(4-fluorophenyl)-tetrahydropyrimidine-2-thione

rac-syn-4-methyl-5-(2-fluorophenyl)-tetrahydropyrimidine-2-thione

syn-4-methyl-5-(2-fluorophenyl)-tetrahydropyrimidine-2-thione

rac-syn-4-methyl-5-(2-naphthyl)-tetrahydropyrimidine-2-thione

syn-4-methyl-5-(2-naphthyl)-tetrahydropyrimidine-2-thione

rac-syn-4-methyl-5-(2-furyl)-tetrahydropyrimidine-2-thione

syn-4-methyl-5-(2-furyl)-tetrahydropyrimidine-2-thione

rac-syn-4-Methyl-5-phenylethyl-tetrahydropyrimidine-2-thione (containing *anti*-isomer)

syn-4-Methyl-5-phenylethyl-tetrahydropyrimidine-2-thione

Copies of ^1H NMR and ^{13}C NMR of 1,3-dinitroalkanes

1v050713-07
 Archive directory: /export/home/vmr1/vmr-sys/data
 Sample directory:
 File: PR010N
 Pulse Sequence: szpul

1v050713-07-C
Pulse Sequence: szpu1

1V050224-01
p-MeO addition

1v051106-01

1W051207-01

1v051207-01-C

1w050716-01

Archive directory: /export/home/vnmr1/vnmr/sys/data
Sample directory:
File: PROTON

Pulse Sequence: szpul

E

lv050716-01-C
Pulse Sequence: szpu1

1v050623-01-C
Pulse Sequence: zgpg30

1W050110-01

1w060401-01

Copies of ^1H NMR and ^{13}C NMR of substituted thioureas

1v051104-01

1v050810-02

2.176

0.991
0.969

1v051136-07

1W051208-01

1.435

0.970
0.948

-0.000

1W051204-01