Supporting Information

Indium-mediated tandem radical addition-cyclization-trap reactions in aqueous media

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Typical procedure for radical reaction of (1). To a micro tube containing **1** (50 mg, 0.18 mmol), RI (0.90 mmol) and indium (51 mg, 0.36 mmol) was added dropwise H₂O (0.5 mL) at 20 °C. After the reaction mixture was stirred at the same temperature for 1 h, RI (0.90 mmol) was added to the reaction mixture. After being stirred at the same temperature for 1 h, the reaction mixture was diluted with aqueous 36% potassium sodium (+)-tartrate and then extracted with CH₂Cl₂. The organic phase was dried over MgSO₄ and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane:AcOEt=5:1) afforded **2a-c** and **3a-c** in the yields shown in Table 1.

Representative characterization data:

trans-4-Iodomethyl-3-(2-methylpropyl)-1-diphenylmethyl-2-pyrrolidinone (trans-2a). a colorless crystal: mp 109.5-110.5 °C (hexane). IR (CHCl₃) 3007, 2960, 1678, 1496 cm⁻¹. ¹H NMR (CDCl₃) δ 7.38-7.14 (10H, m), 6.60 (1H, s), 3.34 (1H, dd, *J*=10.5, 8 Hz), 3.33 (1H, dd, *J*=10, 4.5 Hz), 3.13 (1H, dd, *J*=10, 9 Hz), 2.86 (1H, dd, *J*=10.5, 6.5 Hz), 2.34 (1H, ddd, *J*=8, 7.5, 6 Hz), 2.27-2.21 (1H, m, 4-H), 1.90-1.84 (1H, m), 1.76 (1H, ddd, *J*=14, 8.5, 6 Hz), 1.35 (1H, ddd, *J*=14, 8.5, 6 Hz), 0.96 (6H, d, *J*=6.5 Hz). ¹³C NMR (CDCl₃) δ 175.3, 138.7, 138.4, 128.7, 128.6, 128.5, 128.4, 127.7, 127.6, 58.5, 48.7, 44.7, 39.8, 33.7, 25.7, 22.8, 22.3, 5.1. HRMS calcd for C₂₂H₂₆INO (M⁺) 447.1058, Found : 447.1074. Anal. calcd for C₂₂H₂₆INO: C, 59.07; H, 5.86; N, 3.13. found: C, 59.11; H, 5.85; N, 3.11.

cis-4-Iodomethyl-3-(2-methylpropyl)-1-diphenylmethyl-2-pyrrolidinone (cis-2a). a white solid: IR (CH₃Cl) 3009, 2960, 1679, 1496 cm⁻¹. ¹H NMR (CDCl₃) δ 7.36-7.18 (10H, m), 6.60 (1H, s), 3.30 (1H, dd, *J*=10, 6 Hz), 3.24 (1H, dd, *J*=10, 4.5 Hz), 3.14 (1H, dd, *J*=10, 4 Hz), 2.95 (1H, dd, *J*=11, 10.5 Hz), 2.76-2.69 (1H, m), 2.61 (1H, dt, *J*=9, 7 Hz),

1.84-1.76 (1H, m), 1.56 (1H, dt, $J=15, 7$ Hz), 1.31 (1H, ddd, $J=15, 8.5, 6$ Hz), 0.98, 0.93 (each 3H, d, $J=6.5$ Hz); ^{13}C NMR (CDCl_3) δ : 175.9, 138.4, 138.3, 128.8, 128.6, 128.5, 128.2, 127.7, 127.5, 58.5, 49.3, 46.9, 41.0, 40.1, 25.7, 23.1, 22.2, 9.6; HRMS calcd for $\text{C}_{22}\text{H}_{26}\text{INO}$ (M^+) 447.1058, found : 447.1064.

NOESY data for **2a**

4-Methyl-N-diphenylmethyl-N-2-propenyl pentanamide (3a). The presence of rotamers precluded a comprehensive assignment of all protons and carbons. a colorless oil: IR (CH_3Cl) 3009, 2959, 1634, 1496 cm^{-1} . ^1H NMR (CDCl_3) δ 7.32-7.18 (10H, m), 6.31 (1/3H, br s) 5.33 (2/3H, br s) 5.08-5.02 (2/3H, br m) 4.84-4.81 (4/3H, m) 4.74-4.63 (1H, br m) 3.97 (2H, br s) 2.44-2.40 (2H, br m) 1.62-1.60 (3H, br m) 0.91 (12/3H, br d, $J=4.5$ Hz) 0.84 (6/3H, br m); ^{13}C NMR (CDCl_3) δ : 174.3, 139.6, 134.3, 129.0, 128.8, 128.5, 128.4, 127.8, 127.3, 120.7, 116.3, 116.0, 60.7, 48.0, 34.3, 31.9, 27.9, 22.4; HRMS calcd for $\text{C}_{22}\text{H}_{27}\text{NO}$ (M^+) 321.2091, found : 321.2099.

Typical procedure for radical reaction of (4). To a micro tube containing **4** (50 mg, 0.16 mmol), RI (0.80 mmol) and indium (45 mg, 0.32 mmol) was added dropwise H_2O (0.5 mL) at 20 $^\circ\text{C}$. After the reaction mixture was stirred at the same temperature for 2 h, RI (0.80 mmol) was added to the reaction mixture. After being stirred at the same temperature for 2 h, the reaction mixture was diluted with aqueous 36% potassium sodium (+)-tartrate and then extracted with CH_2Cl_2 . The organic phase was dried over MgSO_4 and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane:AcOEt=7:1) afforded **5a-c** in the yields shown in Table 2.

Representative characterization data:

trans-4-Iodomethyl-5-(2-methylpropyl)-2-diphenylmethyl-isothiazolidine 1,1-dioxide (trans-5a). a colorless crystal: mp 148-149.5 $^\circ\text{C}$ (Et_2O -hexane). IR (CHCl_3) 3030, 2962, 1210 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.38-7.27 (10H, m), 6.03 (1H, s), 3.30 (1H, dd, $J=10.5, 4.5$ Hz), 3.21 (1H, dd, $J=10, 7.5$ Hz), 3.09 (1H, dd, $J=10.5, 7.5$ Hz), 2.99 (1H, td, $J=9.5, 4.5$ Hz), 2.75 (1H, dd, $J=10, 7.5$ Hz), 2.24-2.16 (1H, m), 2.02-1.88 (2H, m), 1.41-1.35 (1H, m), 1.00, 0.99 (each 3H, d, $J=6.5$ Hz); ^{13}C NMR (CDCl_3) δ 138.6, 138.3, 129.04, 128.98,

128.6, 128.5, 128.4, 128.0, 127.8, 61.6, 61.3, 48.4, 39.9, 37.6, 25.3, 23.2, 21.8, 6.6; HRMS calcd for $C_{21}H_{26}INO_2S$ (M^+): 483.0727, found: 483.0730.

***cis*-4-Iodomethyl-5-(2-methylpropyl)-2-diphenylmethyl-isothiazolidine 1,1-dioxide (*cis*-5a).** a colorless oil: IR ($CHCl_3$) 1303, 1221, 1210 cm^{-1} ; 1H NMR ($CDCl_3$) δ 7.38-7.27 (10H, m), 6.02 (1H, s), 3.36 (1H, t, $J=11$ Hz), 3.31-3.23 (2H, m), 3.19 (1H, dd, $J=9.5$, 6 Hz), 3.08 (1H, dd, $J=9.5$, 4.5 Hz), 2.88-2.81 (1H, m), 1.97-1.89 (1H, m), 1.71-1.65 (1H, m), 1.39-1.33 (1H, m), 0.99, 0.95 (each 3H, d, $J=6.5$ Hz); ^{13}C NMR ($CDCl_3$) δ 138.5, 138.4, 128.8, 128.61, 128.56, 128.51, 128.46, 127.87, 61.1, 59.7, 48.4, 39.0, 32.6, 25.4, 22.9, 21.9, 2.6; HRMS calcd for $C_{21}H_{26}INO_2S$ (M^+): 483.0728, found: 483.0725.

NOESY data for **5a**

Typical procedure for radical reaction of (6). To a micro tube containing **6** (50 mg, 0.12 mmol), RI (0.62 mmol), indium (174 mg, 1.23 mmol) and MeOH (0.2 mL) was added dropwise H_2O (0.4 mL) at 20 $^{\circ}C$. After the reaction mixture was stirred at the same temperature for 2 h, RI (0.62 mmol) was added to the reaction mixture. After being stirred at the same temperature for 3 h, the reaction mixture was diluted with aqueous 36% potassium sodium (+)-tartrate and then extracted with CH_2Cl_2 . The organic phase was dried over $MgSO_4$ and concentrated at reduced pressure. Purification of the residue by preparative TLC (Benzene:AcOEt=40:1) afforded **7a-c** in the yields shown in Table 3.

Representative characterization data:

***trans*-5-(2-Methylpropyl)-4-(2,2-diphenylhydrazino)-2-phenylmethyl-isothiazolidine 1,1-dioxide (*trans*-7a).** a colorless oil: IR ($CHCl_3$) 3020, 1209, 1221 cm^{-1} ; 1H NMR ($CDCl_3$) δ 7.34-6.99 (15H, m), 4.25 (1H, d, $J=14$ Hz), 4.11 (1H, d, $J=14$ Hz), 3.48-3.45 (1H, m), 3.29-3.24 (1H, m), 3.08 (1H, dd, $J=10$, 6.5 Hz), 2.96 (1H, dd, $J=10$, 4.5 Hz), 1.86 (1H, ddd, $J=14$, 8.5, 6.5 Hz), 1.79-1.71 (1H, m), 1.31 (1H, ddd, $J=14$, 8.5, 6.5 Hz), 0.90, 0.86 (each 3H, d, $J=6.5$ Hz); ^{13}C NMR ($CDCl_3$) δ 147.8, 135.2, 129.4, 128.7, 128.6, 127.9, 123.4, 120.5, 59.8, 57.2, 48.7, 47.9, 37.8, 25.5, 22.8, 21.9; HRMS calcd for $C_{26}H_{31}N_3O_2S$ (M^+): 449.2133, found: 449.2144.

***cis*-5-(2-Methylpropyl)-4-(2,2-diphenylhydrazino)-2-phenylmethyl-isothiazolidine**

1,1-dioxide (*cis*-7a). a colorless oil: IR (CHCl₃) 3035, 1589, 1497 cm⁻¹; ¹H NMR (CDCl₃) δ 7.30-7.05 (15H, m), 4.25 (1H, d, *J*=15 Hz), 4.15 (1H, d, *J*=15 Hz), 3.77 (1H, ddd, *J*=6, 5.5, 2.5 Hz), 3.38-3.33 (1H, m), 3.21 (1H, dd, *J*=10, 2.5 Hz), 3.03 (1H, dd, *J*=10, 5 Hz), 1.97-1.92 (1H, m), 1.87-1.79 (1H, m), 1.74-1.68 (1H, m), 0.97, 0.96 (each 3H, d, *J*=2 Hz); ¹³C NMR (CDCl₃) δ 148.0, 135.5, 129.4, 128.6, 127.8, 123.3, 120.6, 59.1, 53.1, 50.0, 48.7, 31.9, 25.6, 22.7, 22.1; HRMS calcd for C₂₆H₃₁N₃O₂S (M⁺): 449.2135, found: 449.2130.

NOESY data for 7a

Pulse Sequence: s2pul

Pulse Sequence: s2pul

KPNN-4264

H-1

Pulse Sequence: s2pul

cis-2b

KFNN-4261
H-1

Pulse Sequence: s2pul

KFNN-4263
H-1

Pulse Sequence: s2pul

S10

trans-5a

cis-5a

S15

cis-5c

S18

KEN-4283
H-1

Pulse Sequence: s2pul

KFNN-4284
H-1

Pulse Sequence: s2pul

0.000

KFNN-4285
H-1

Pulse Sequence: s2pul