Supporting Information for the Paper

Efficient Entry to Highly Functionalized β-Lactams by Regio- and Stereoselective 1,3-Dipolar Cycloaddition Reaction of 2-Azetidinone-Tethered Nitrones. Synthetic Applications

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Nitrone (±)-3c. From 1.52 g (6.58 mmol) of aldehyde (±)-**1c**, 1.83 g (83%) of compound (±)-**3c** was obtained as a brown solid after purification by flash chromatography (hexanes/ethyl acetate 1/20). Mp: 176–177 ºC (hexanes/ethyl acetate). ^{1}H NMR: δ 3.78 (s, 1H), 4.31 (t, 1H, *J* = 6.3 Hz), 4.93 (s, 2H), 5.26 (dt, 1H, *J* = 10.3, 1.2 Hz), 5.31 (t, 1H, *J* = 6.3 Hz), 5.45 (dt, 1H, *J* = 17.2, 1.5 Hz), 5.65 (m, 1H), 6.82 (d, 2H, *J* = 9.0 Hz), 6.86 (d, 1H, *J* = 7.1 Hz), 7.25 (d, 2H,*J* = 9.0 Hz), 7.38 (m, 5H). ^{13}C NMR: δ 163.8, 156.4, 133.9, 132.3, 130.6, 129.3, 129.2, 128.9, 121.3, 117.7, 114.5, 70.2, 56.6, 55.5, 50.9. IR (KBr, cm^{-1}): ν 1750, 1516. MS (CI),*m/z* : 337 (M^+ + 1, 100), 336 (M^+, 16). (Anal. Calcd. for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.49; H, 5.95; N, 8.30).

Nitrone (±)-3d. From 100 mg (0.40 mmol) of aldehyde (±)-**1f**, 216 mg (77%) of compound (±)-**3d** was obtained as a colorless solid after purification by flash chromatography (hexanes/ethyl acetate 1/25). Mp: 159–160 ºC (hexanes/ethyl acetate). ^{1}H NMR: δ 0.67 (d, 3H, *J* = 6.5 Hz), 1.03 (d, 3H, *J* = 6.5 Hz), 1.70 (m, 1H), 3.18 (dd, 1H, *J* = 10.5, 5.7), 3.65 (s, 3H), 4.85 (s, 2H), 5.15 (dd, 1H, J = 7.7, 5.7 Hz), 6.65 (d, 2H, *J* = 9.0 Hz), 6.80 (d, 1H, *J* = 7.7 Hz), 7.10 (d, 2H, *J* = 9.0 Hz), 7.30 (m, 5H). ^{13}C NMR: δ 165.8, 156.1, 135.2, 132.5, 129.6, 129.5, 127.2, 125.8, 117.6, 114.5, 70.4, 62.7, 55.5, 49.9, 27.0, 21.6, 20.5. IR (KBr, cm^{-1}): ν 1751, 1514. MS (EI), *m/z* : 353 (M^+ + 1,

12), 352 (M^+, 100). (Anal. Calcd. for $C_{21}H_{24}N_2O_3$: C, 71.57; H, 6.86; N, 7.95. Found: C, 71.67; H, 6.83; N, 7.91).

Nitrone (±)-3g. From 50 mg (0.20 mmol) of aldehyde (±)-**1f**, 45 mg (81%) of compound (±)-**3g** was obtained as a colorless solid after purification by flash chromatography (hexanes/ethyl acetate 1/25). Mp: 167–170 ºC (hexanes/ethyl acetate). ^{1}H NMR: δ 0.85 (d, 3H, *J* = 6.5 Hz), 1.15 (d, 3H, *J* = 6.5 Hz), 1.90 (m, 1H), 3.25 (dd, 1H, *J* = 10.8, 5.7 Hz), 3.70 (s, 6H), 5.25 (dd, 1H, *J* = 7.6, 5.7 Hz), 6.80 (d, 2H, *J* = 8.9 Hz), 6.85 (d, 1H,*J* = 7.8 Hz), 7.20 (d, 2H, *J* = 8.9 Hz). ^{13}C NMR: δ 165.9, 156.2, 135.6, 130.8, 117.7, 114.5, 61.2, 55.5, 53.3, 49.9, 27.1, 21.7, 20.7. IR (KBr, cm^{-1}): ν 1737, 1514. MS (EI), *m/z* : 277 (M^+ + 1, 11), 276 (M^+, 100). (Anal. Calcd. for $C_{15}H_{20}N_2O_3$: C, 65.20; H, 7.30; N, 10.14. Found: C, 65.27; H, 7.33; N, 10.10).

Nitrone (±)-3h. From 438 mg (2.00 mmol) of aldehyde (±)-**1g**, 496 mg (100%) of compound (±)-**3h** was obtained as a colorless solid after purification by flash chromatography (hexanes/ethyl acetate 1/25). Mp: 171–172 ºC (hexanes/ethyl acetate). ^{1}H NMR: δ 1.25 (d, 3H, *J* = 7.6 Hz), 3.73 (dd, 1H, *J* = 7.6, 5.9 Hz), 3.76 (s, 3H), 3.78 (s, 3H), 5.23 (dd, 1H, *J* = 6.6, 5.9 Hz), 6.84 (d, 2H, *J* = 9.2 Hz), 6.87 (d, 1H, *J* = 6.6 Hz), 7.26 (d, 2H, *J* = 9.2 Hz). ^{13}C NMR: δ 166.9, 156.3, 134.9, 130.7, 117.7, 114.6, 55.5, 53.1, 50.8, 48.7, 9.9. IR (KBr, cm^{-1}): ν 1728, 1515. MS (EI), *m/z* : 249 (M^+ + 1, 7), 248 (M^+, 100). (Anal. Calcd. for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.94; H, 6.47; N, 11.32).

Oxime (±)-4a. From 50 mg (0.12 mmol) of aldehyde (±)-**1c**, 100 mg (81%) of compound (±)-**4a**, as a *E/Z* mixture (60:40) of isomers, was obtained as a colorless solid after purification by flash chromatography (ethyl acetate). ^{1}H NMR: δ 3.69 (s, 1.8H), 3.71 (s, 1.2H), 4.25 (m, 2H), 4.75 (dd, 0.6H, *J* = 8.1, 5.8 Hz), 5.29 (m, 2.4H), 5.44 (dt, 1H, *J* = 17.3, 1.5 Hz), 5.75 (m, 2H), 6.78 (m, 2H), 6.81 (d, 0.4H, *J* = 8.5 Hz), 7.26 (m, 2H), 7.38 (d, 0.6H, *J* = 8.1 Hz), 8.68 (brs, 0.6H), 9.06 (brs, 0.4H). ^{13}C NMR: δ 164.6 (M+m), 156.6 (M+m), 148.2 (M), 148.0 (m), 131.2 (M), 130.8 (m), 128.0 (M+m), 127.8 (M+m), 122.0 (M+m), 121.3 (M+m), 118.5 (m), 118.0 (M), 114.5 (m), 114.7 (M), 56.7 (M+m), 56.2 (M+m), 55.7 (M), 55.6 (m), 54.3 (M+m), 49.7 (M+m). IR (KBr, cm^{-1}): ν 3369, 1757, 1714. MS (EI), *m/z* : 247 (M^+ + 1, 9), 246 (M^+, 100).

Oxime (±)-4c. From 175 mg (0.72 mmol) of aldehyde (±)-**1e**, 150 mg (81%) of compound (±)-**4c**, as a *E/Z* mixture (52:48) of isomers, was obtained as a colorless solid after purification by

flash chromatography (ethyl acetate). ^{1}H NMR: δ 2.02 (s, 1H), 2.60 (m, 2H), 3.67 (m, 4H), 4.71 (dd, 0.52H, *J* = 7.4, 5.8 Hz), 5.23 (t, 0.48H, *J* = 5.9 Hz), 6.75 (m, 2H), 6.95 (d, 0.48H, *J* = 5.9 Hz), 7.26 (m, 2H), 7.60 (d, 0.52H, *J* = 7.4 Hz), 8.36 (brs, 0.52H), 9.12 (brs, 0.48H). ^{13}C NMR: δ 164.6 (M+m), 156.5 (M+m), 148.3 (m), 147.3 (M), 130.9 (M+m), 118.3 (M), 117.8 (m), 114.6 (m), 114.4 (M), 79.8 (M+m), 71.9 (m), 71.3 (M), 55.5 (M+m), 53.4 (M+m), 52.2 (M+m), 48.0 (M+m), 15.2 (M+m). IR (KBr, cm^{-1}): ν 3355, 3288, 1722, 1517. MS (EI), *m/z* : 259 (M^+ + 1, 10), 258 (M^+, 100).

Treatment of Oxime (±)-4b with Phenylselenyl Bromide and Triethylamine. From 124 mg (0.50 mmol) of oxime (±)-**4b**, and after flash chromatography eluting with ethyl acetate, 108 mg (52%) of the less polar compound (±)-**5b*M*** and 53 mg (26%) of the more polar compound (±)-**5b*m*** were obtained.

Bicyclic Nitrone (±)-5b*M*: yellow solid. Mp: 151–152 ºC (hexanes/ethyl acetate). ^{1}H NMR: δ 1.74 (s, 3H), 3.16 (d, 1H, *J* = 13.5 Hz), 3.57 (d, 1H, *J* = 13.5 Hz), 3.78 (s, 3H), 3.90 (d, 1H, *J* = 5.1 Hz), 4.89 (dd, 1H, *J* = 5.1 Hz, 1.2 Hz), 6.86 (d, 2H, *J* = 9.0 Hz), 7.26 (m, 5H), 7.55 (m, 2H). ^{13}C NMR: δ 161.6, 156.6, 132.8, 130.2, 129.4, 128.9, 127.7, 117.4, 114.5, 55.4, 55.3, 53.6, 37.4, 22.6. IR (KBr, cm^{-1}): ν 1734, 1515. MS (EI), *m/z* : 415 (M^+, 11), 179 (100). (Anal. Calcd. for $C_{20}H_{20}N_2O_3Se$: C, 57.84; H, 4.85; N, 6.74. Found: C, 57.76; H, 4.83; N, 6.77).

Bicyclic Nitrone (±)-5b*m*: yellow solid. Mp: 146–147 ºC (hexanes/ethyl acetate). ^{1}H NMR: δ 1.60 (s, 3H), 3.24 (d, 1H, *J* = 13.1 Hz), 3.50 (d, 1H, *J* = 13.1 Hz), 3.71 (s, 3H), 3.96 (d, 1H, *J* = 5.0 Hz), 4.87 (dd, 1H, *J* = 5.0 Hz, 1.7 Hz), 6.81 (m, 2H), 7.22 (m, 5H), 7.55 (m, 2H). ^{13}C NMR: δ 161.8, 156.8, 133.0, 130.4, 129.6, 129.1, 127.9, 117.6, 114.7, 76.3, 53.8, 53.5, 37.6, 22.8. IR (KBr, cm^{-1}): ν 1734, 1516. MS (EI), *m/z* : 415 (M^+, 14), 179 (100). (Anal. Calcd. for $C_{20}H_{20}N_2O_3Se$: C, 57.84; H, 4.85; N, 6.74. Found: C, 57.91; H, 4.83; N, 6.76).

Cycloadduct (±)-8b. From 84 mg (0.25 mmol) of nitrone (±)-**3c**, 90 mg (75%) of compound (±)-**8b** was obtained as a colorless oil after purification by flash chromatography (hexanes/ethyl acetate 2/1). ^{1}H NMR: δ 3.47 (dd, 1H, *J* = 6.3, 2.2 Hz), 3.78 (d, 1H, *J* = 13.2 Hz), 3.79 (s, 3H), 3.80 (s, 3H), 3.85 (s, 3H), 4.02 (m, 3H), 4.44 (dd, 1H, *J* = 10.6, 5.9 Hz), 5.02 (d, 1H, *J* = 6.3 Hz), 5.31 (dd, 1H, *J* = 9.9, 1.1Hz), 5.40 (d, 1H, *J* = 16.9 Hz), 5.84 (m, 1H), 6.85 (d, 2H, *J* = 9.2 Hz), 7.12 (m, 5H), 7.45 (d, 2H, *J* = 9.2 Hz). ^{13}C NMR: δ 171.4, 169.4, 165.0, 156.3, 135.2, 130.6, 128.9, 128.5,

128.0, 127.4, 122.4, 120.8, 113.4, 78.7, 77.2, 69.7, 59.9 56.6, 55.4, 54.7, 53.0. IR ($CHCl_3$, cm^{-1}): ν 1745, 1736. MS (EI), *m/z* : 481 (M^+ + 1, 1), 480 (M^+, 3), 91 (100). (Anal. Calcd. for $C_{26}H_{28}N_2O_7$: C, 64.99; H, 5.87; N, 5.83. Found: C, 64.91; H, 5.93; N, 5.78).

Treatment of Nitrone (–)-3e with Dimethyl Fumarate. From 50 mg (0.19 mmol) of nitrone (–)-**3e**, and after flash chromatography eluting with hexanes/ethyl acetate (1:1), 45 mg (60%) of the less polar compound (+)-**8c** and 8 mg (11%) of the more polar compound **9** were obtained. Compound **9** was not isolated in analytically pure form because it contained (20%) the major isomer (+)-**8c**.

Cycloadduct (+)-8c: colorless oil. $[\alpha]_D$ = +65.8 (*c* 1.0, $CHCl_3$). ^1H NMR: δ 2.50 (s, 3H), 3.33 and 3.35 (s, each 3H), 3.37 and 3.41 (s, each 3H), 3.73 (dd, 1H, *J* = 6.1, 3.6 Hz), 3.91 (dd, 1H, *J* = 9.6, 3.6 Hz), 4.27 (dd, 1H, *J* = 9.6, 5.5 Hz), 4.90 (d, 1H, *J* = 6.1 Hz), 4.93 (d, 1H, *J* = 5.5 Hz), 6.82 and 8.01 (d, each 2H, *J* = 9.3 Hz). ^{13}C NMR: δ 171.5, 169.6, 165.0, 156.3, 130.7. 119.6, 113.7, 82.1, 78.0, 72.3, 59.3, 59.2, 55.5, 55.3, 52.8, 52.6, 44.5. IR ($CHCl_3$, cm^{-1}): ν 1749. MS (CI), *m/z* : 409 (M^+ + 1, 100), 408 (M^+, 12). (Anal. Calcd. for $C_{19}H_{24}N_2O_8$: C, 55.88; H, 5.92; N, 6.86. Found: C, 55.96; H, 5.90; N, 6.89).

Cycloadduct 9: colorless oil. ^1H NMR: δ 2.88 (s, 3H), 3.42 (s, 3H), 3.48 (dd, 1H, *J* = 6.7, 2.7 Hz), 3.55 (s, 3H), 3.73 and 3.78 (s, each 3H), 4.36 (dd, 1H, *J* = 5.4, 2.7 Hz), 4.58 (d, 1H, *J* = 5.4 Hz), 4.71 (d, 1H, *J* = 6.7 Hz), 6.82 and 8.01 (d, each 2H, *J* = 9.3 Hz). MS (CI), *m/z* : 409 (M^+ + 1, 100), 408 (M^+, 6).

Cycloadducts 10b and 11b. From 100 mg (0.29 mmol) of nitrone (±)-**3c**, 108 mg (86%) of compound **10b**, containing *ca*. 48% of its epimer **11b**, was obtained as a colorless oil after purification by flash chromatography (hexanes/ethyl acetate 1/1). ^1H NMR: δ 2.18 (ddd, 0.5H, *J* = 13.4, 5.7, 2.5 Hz), 2.36 (ddd, 0.5H, *J* = 13.4, 9.0, 1.9 Hz), 2.83 (m, 1H), 3.47 (ddd, 0.5H, *J* = 10.7, 8.5, 2.5 Hz), 3.56 (m, 0.5H), 3.62 (d, 1H *J* = 13.5), 3.78 (s, 1.5H), 3.80 (s, 1.5H), 3.81 (s, 1.5H), 3.82 (s, 1.5H), 3.90 (d, 0.5H J = 13.0 Hz), 3.99 (d, 0.5H, *J* = 6.1 Hz), 4.02 (d, 0.5H, *J* = 6.1 Hz), 4.08 (d, 0.5H *J* = 13.5 Hz), 4.24 (dd, 0.5H, *J* = 10.2, 6.1 Hz), 4.44 (dd, 0.5H, *J* = 10.5, 6.1 Hz), 4.65 (dd, 0.5H, *J* = 8.5, 7.8 Hz), 4.75 (dd, 0.5H, *J* = 9.5, 5.7 Hz), 5.42 (m, 2H), 5.81 (m, 1H), 6.80 (m, 4H), 7.09 (m, 3H), 7.45 (m, 2H). ^{13}C NMR: δ 172.6, 171.1, 165.2, 165.1, 156.3, 156.2, 136.4, 135.9, 130.9, 128.7, 128.6, 128.5, 128.3, 128.1, 128.0, 127.4, 127.2, 122.5, 122.3, 120.6, 120.5,

113.5, 76.6, 74.5, 67.0, 66.8, 61.9, 60.7, 57.2, 56.4, 55.4, 54.6, 54.5, 52.6, 52.5, 35.4, 34.5. IR ($CHCl_3$, cm^{-1}): ν 1745, 1728. MS (CI), *m/z*: 423 (M^+ + 1, 100), 422 (M^+, 7).

Cycloadducts 10c and 11c. From 75 mg (0.28 mmol) of nitrone (–)-**3e**, 73 mg (74%) of compound **10c**, containing *ca*. 40% of its epimer **11c**, was obtained as a colorless oil after purification by flash chromatography (hexanes/ethyl acetate 1/1). $[\alpha]_D$ = +151.5 (*c* 1.6, $CHCl_3$). ^1H NMR: δ 2.25 (ddd, 0.6H, *J* = 13.4, 5.8, 3.9 Hz), 2.41 (ddd, 0.4H, *J* = 13.6, 8.8, 3.4 Hz), 2.50 (s, 1.8H), 2.56 (s, 1.2H), 2.89 (m, 1H), 3.35 (m, 0.6H), 3.46 (m, 0.4H), 3.62 (s, 1.8H), 3.63 (s, 1.2H), 3.77 (s, 3H), 3.78 (s, 1.8H), 3.81 (s, 1.2H), 4.16 (dd, 0.4H, *J* = 9.3, 5.6 Hz), 4.30 (dd, 0.6H, *J* = 9.5, 5.6 Hz), 4.53 (d, 0.6H, *J* = 5.6 Hz), 4.55 (d, 0.4H, *J* = 5.6 Hz), 4.58 (dd, 0.4H, *J* = 8.8, 7.3 Hz), 4.70 (dd, 0.6H, *J* = 9.0, 5.8 Hz), 6.83 (m, 2H), 7.60 (m, 2H). ^{13}C NMR: δ 172.4 (m), 171.5 (M), 165.5 (M), 165.4 (m), 156.4 (M), 156.3 (m), 131.2 (M + m), 119.7 (M), 119.6 (m), 113.8 (m), 113.7 (M), 82.2 (M + m), 75.8 (m), 74.0 (M), 68.9 (M), 68.7 (m), 59.9 (M), 59.5 (m), 59.4 (m), 59.3 (M), 55.4 (M +m), 52.6 (M), 52.5 (m), 45.9 (m), 44.9 (M), 35.9 (M), 35.5 (m). IR ($CHCl_3$, cm^{-1}): ν 1739, 1718. MS (CI), *m/z*: 351 (M^+ + 1, 100), 350 (M^+, 9).

Cycloadduct (±)-12c. From 160 mg (0.45 mmol) of nitrone (±)-**3d**, 65 mg (40%) of compound (±)-**12c** was obtained as a colorless oil after purification by flash chromatography (hexanes/ethyl acetate 2/1). ^1H NMR (acetone-d_6): δ 1.11 and 1.12 (d, each 3H, *J* = 6.9 Hz), 2.44 (m, 1H), 3.29 (m, 1H), 3.80 (s, 3H), 3.94 and 4.09 (d, 1H, *J* = 13.2 Hz), 4.22 (d, 1H, *J* = 8.3 Hz), 4.30 (d, 1H, *J* = 9.3 Hz), 4.49 (dd, 1H, *J* = 9.3, 5.8 Hz), 5.14 (d, 1H, *J* = 8.3 Hz), 6.85 (m, 4H), 7.15 (m, 5H), 7.45 (m, 5H). ^{13}C NMR: δ 174.3, 173.6, 166.6, 156.4, 134.6, 131.2, 130.7, 129.5, 129.2, 129.1, 128.4, 125.5, 121.1, 113.5, 78.3, 67.8, 63.4, 58.0, 56.2, 55.5, 53.3, 24.2, 24.0, 21.0. IR ($CHCl_3$, cm^{-1}): ν 1748, 1723. MS (CI), *m/z*: 526 (M^+ + 1, 100), 525 (M^+, 14). (Anal. Calcd. for $C_{31}H_{31}N_3O_5$: C, 70.84; H, 5.94; N, 7.99. Found: C, 70.77; H, 5.89; N, 8.03).

Cycloadduct (±)-12e. From 200 mg (0.77 mmol) of nitrone (±)-**3f**, 233 mg (70%) of compound (±)-**12e** was obtained as a colorless solid after purification by flash chromatography (hexanes/ethyl acetate 2/1). Mp: 104–106 ºC (hexanes/ethyl acetate). ^1H NMR: δ 2.70 (s, 3H), 3.78 (d, 1H, *J* = 7.7 Hz), 3.80 (s, 3H), 3.97 (d, 1H, *J* = 8.8 Hz), 4.14 and 4.34 (dd, each 1H, *J* = 8.8, 5.9 Hz), 4.87 (d, 1H, *J* = 7.7 Hz), 5.55 (m, 2H), 6.21 (m, 1H), 6.86 (d, 2H, *J* = 9.2 Hz), 7.23 (m, 2H), 7.49 (m, 5H). ^{13}C NMR: δ 173.9, 173.4, 165.1, 156.5, 131.1, 130.6, 129.4, 129.1, 128.4, 125.5,

123.1, 120.5, 113.8, 77.5, 72.2, 57.0, 55.4, 52.9, 46.7. IR (KBr, cm^{-1}): ν 1750, 1720. MS (EI), *m/z* : 434 (M^+ + 1, 5), 437 (M^+, 16), 84 (100). (Anal. Calcd. for $C_{24}H_{23}N_3O_5$: C, 66.50; H, 5.35; N, 9.69. Found: C, 66.58; H, 5.31; N, 9.65).

Cycloadduct (±)-12f. From 120 mg (0.43 mmol) of nitrone (±)-**3g**, 100 mg (51%) of compound (±)-**12f** was obtained as a colorless oil after purification by flash chromatography (hexanes/ethyl acetate 2/1). ^1H NMR: δ 1.10 and 1.29 (d, each 3H, *J* = 6.6 Hz), 2.45 (m, 1H), 2.73 (s, 3H), 3.18 (dd, 1H, *J* = 8.4, 5.5 Hz), 3.79 (s, 3H), 3.82 (dd, 1H, *J* = 8.1, 1.1 Hz), 4.03 (dd, 1H, *J* = 5.9, 1.1 Hz), 4.31 (dd, 1H, *J* = 5.9, 5.5 Hz), 4.43 (d, 1H, *J* = 8.1 Hz), 6.86 (d, 2H,*J* = 8.8 Hz), 7.21 (m, 3H), 7.37 (m, 2H), 7.45 (m, 2H). ^{13}C NMR: δ 174.5, 173.6, 166.9, 156.6, 131.1, 130.3, 129.4, 129.1, 125.6, 121.3, 117.5, 113.9, 77.9, 70.3, 59.2, 57.7, 55.4, 46.9, 24.4, 23.2, 20.8. IR ($CHCl_3$, cm^{-1}): ν 1753, 1718. MS (EI), *m/z* : 450 (M^+ + 1, 9), 449 (M^+, 30), 231 (100). (Anal. Calcd. for $C_{25}H_{27}N_3O_5$: C, 66.80; H, 6.09; N, 9.35. Found: C, 66.88; H, 6.04; N, 9.30).

Cycloadduct (±)-12g. From 100 mg (0.40 mmol) of nitrone (±)-**3h**, 132 mg (78%) of compound (±)-**12g** was obtained as a colorless oil after purification by flash chromatography (hexanes/ethyl acetate 1/1). ^1H NMR: δ 1.51 (d, 3H, *J* = 7.7 Hz), 2.66 (s, 3H), 3.47 (m, 1H), 3.68 (d, 1H, *J* = 8.3 Hz), 3.76 (s, 3H), 3.89 (d, 1H *J* = 9.3 Hz), 4.17 (dd, 1H, *J* = 9.3, 5.8 Hz), 4.90 (d, 1H, *J* = 8.3 Hz), 6.83 (d, 2H, *J* =9.3 Hz), 7.24 (m, 3H), 7.47 (m, 4H). ^{13}C NMR: δ 174.0, 173.7, 168.3, 156.2, 131.1, 131.0, 129.2, 129.0, 125.5, 120.4, 113.4, 77.8, 71.7, 56.2, 55.4, 53.1, 46.7, 45.8, 9.8. IR ($CHCl_3$, cm^{-1}): ν 1745, 1724. MS (CI), *m/z* : 422 (M^+ + 1, 100), 421 (M^+, 17). (Anal. Calcd. for $C_{23}H_{23}N_3O_5$: C, 65.55; H, 5.50; N, 9.97. Found: C, 65.64; H, 5.54; N, 9.91).

Cycloadduct (+)-13b. From 50 mg (0.12 mmol) of nitrone (–)-**3b**, 50 mg (75%) of compound (+)-**13b** was obtained as a colorless oil after purification by flash chromatography (hexanes/ethyl acetate 2/1). $[\alpha]_D$ = +251.6 (*c* 1.0, $CHCl_3$). ^1H NMR: δ 3.61 (s, 3H), 3.76 (s, 3H), 3.80 (s, 3H), 4.11 (AB, 2H, *J* = 14.0 Hz), 4.69 (d, 1H, *J* = 1.5 Hz), 4.97 (dd, 1H,*J* = 5.1, 1.5 Hz), 5.40 (d, 1H,*J* = 5.1 Hz), 6.79 (d, 2H, *J* = 9.0 Hz), 7.10 (m, 3H), 7.30 (m, 9H). ^{13}C NMR: δ 163.2, 162.6, 158.2, 157.0, 156.7, 153.4 , 135.3, 129.8, 129.2, 128.4, 127.8, 122.6, 120.3, 115.4, 114.1, 104.8, 79.1, 68.0, 63.1, 58.3, 55.5, 52.7, 52.2. IR ($CHCl_3$, cm^{-1}): ν 1753, 1700, 1654. MS (CI), *m/z* : 545 (M^+ + 1, 100), 544 (M^+, 100). (Anal. Calcd. for $C_{30}H_{28}N_2O_8$: C, 66.17; H, 5.18; N, 5.14. Found: C, 66.24; H, 5.14; N, 5.18).

Treatment of Nitrone (–)-3e with Methyl Propiolate. From 75 mg (0.28 mmol) of nitrone (–)-**3e**, and after flash chromatography eluting with hexanes/ethyl acetate (1:1), 60 mg (60%) of the less polar compound (+)-**14b** and 11 mg (11%) of the more polar compound (+)-**15b** were obtained.

Cycloadduct (+)-14b: colorless solid. Mp: 153–154 ºC (hexanes/ethyl acetate). $[\alpha]_D$ = +275.0 (*c* 1.0, $CHCl_3$). ^1H NMR: δ 2.64 (s, 3H), 3.66 (s, 3H), 3.77 (s, 3H), 3.84 (s, 3H), 4.11 (dd, 1H, *J* = 8.8, 2.9 Hz), 4.24 (dd, 1H, *J* = 8.8, 5.4 Hz), 4.54 (d, 1H, *J* = 5.4 Hz), 5.86 (d, 1H, *J* = 2.9 Hz), 6.83 and 7.71 (d, each 2H, *J* = 9.0 Hz). ^{13}C NMR: δ 165.0, 159.2, 156.5, 146.0, 130.9, 119.8, 113.8, 106.4, 81.9, 75.2, 60.0, 59.3, 55.6, 52.4, 46.5. IR (KBr, cm^{-1}): ν 1739, 1710. MS (EI), *m/z* : 349 (M^+ + 1, 7), 348 (M^+, 100). (Anal. Calcd. for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.70; N, 8.04. Found: C, 58.71; H, 5.75; N, 7.99).

Cycloadduct (+)-15b: colorless solid. Mp: 127–129 ºC (hexanes/ethyl acetate). $[\alpha]_D$ = +214.8 (*c* 1.1, $CHCl_3$). ^1H NMR: δ 2.87 (s, 3H), 3.63 (s, 3H), 3.77 (s, 3H), 3.80 (s, 3H), 4.24 (s, 1H), 4.56 (d, 1H, *J* = 5.4 Hz), 4.70 (d, 1H, *J* = 5.4 Hz), 6.77 (d, 2H,*J* = 8.7 Hz), 6.90 (s, 1H), 7.24 (d, 2H, *J* = 8.7 Hz). ^{13}C NMR: δ 165.5, 164.3, 156.4, 154.4, 130.4, 120.0, 113.7, 104.7, 82.3, 68.2, 59.2, 57.4, 55.4, 51.5, 46.6. IR (KBr, cm^{-1}): ν 1741, 1709. MS (EI), *m/z* : 349 (M^+ + 1, 13), 348 (M^+, 100). (Anal. Calcd. for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.70; N, 8.04. Found: C, 58.53; H, 5.76; N, 8.08).

Compound (+)-18b. From 75 mg (0.215 mmol) of adduct (+)-**14b**, 30 mg (40%) of compound (+)-**18b** was obtained as a colorless oil after purification by flash chromatography (hexanes/ethyl acetate 1/1). $[\alpha]_D$ = +18.0 (*c* 1.0, $CHCl_3$). ^1H NMR: δ 2.17 (t, 1H, *J* = 7.0 Hz), 2.52 (s, 3H), 3.39 (d, 1H, *J* = 7.0 Hz), 3.59 (s, 3H), 3.80 (s, 3H), 3.95 (s, 3H), 4.17 (dd, 1H, *J* = 7.0, 5.4 Hz,), 4.39 (d, 1H, *J* = 5.4 Hz), 6.91 and 7.32 (d, each 2H, *J* = 8.7 Hz). ^{13}C NMR: δ 190.1, 164.3, 162.7, 156.6, 131.2, 118.5, 114.6, 81.9, 58.9, 56.7, 55.5, 53.2, 48.8, 45.5. IR ($CHCl_3$, cm^{-1}): ν 1750, 1735. MS (CI), *m/z* : 349 (M^+ + 1, 100), 348 (M^+, 7). (Anal. Calcd. for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.79; N, 8.04. Found: C, 58.68; H, 5.74; N, 8.00).

Isoxazolidinyl β-amino ester (+)-21b. From 46 mg (0.09 mmol) of cycloadduct (+)-**8a**, 35 mg (74%) of compound (+)-**21b** was obtained as a yellow oil. $[\alpha]_D$ = +4.8 (*c* 1.8, $CHCl_3$). ^1H NMR: δ 3.42 (s, 3H), 3.60 (s, 3H), 3.69 (s, 3H), 3.72 (m, 4H), 3.74 (s, 3H), 3.87 (t, 1H, *J* = 4.5 Hz), 4.04 (dd, 1H, *J* = 6.8, 4.5 Hz), 4.13 (brs , 1H), 4.15 and 4.16 (d, each 1H, *J* = 13.2 Hz), 4.19 (d, 1H,

J = 2.9 Hz), 5.21 (d, 1H, *J* = 6.8 Hz), 6.36 and 6.67 (d, each 2H, *J* = 9.0 Hz), 7.35 (m, 5H). ^{13}C NMR: δ 172.5, 171.3, 169.4, 152.3, 140.3, 136.2, 129.5, 128.3, 127.6, 114.7, 78.6, 68.3, 60.8, 58.7, 58.5, 55.7, 53.9, 52.7, 52.5, 52.0. IR ($CHCl_3$, cm^{-1}): ν 3390, 1739. MS (CI), *m/z* : 517 (M^+ + 1, 100), 516 (M^+, 35). (Anal. Calcd. for $C_{26}H_{32}N_2O_9$: C, 60.46; H, 6.24; N, 5.42. Found: C, 60.32; H, 6.16; N, 5.35).

β-Alkoxycarbonyl γ-lactam (+)-22b. From 24 mg (0.046 mmol) of compound (+)-**21b**, 16 mg (73%) of compound (+)-**22b** was obtained as a yellow oil after purification by flash chromatography (hexanes/ethyl acetate 1/3). $[\alpha]_D$ = +1.6 (*c* 1.0, $CHCl_3$). ^{1}H NMR: δ 3.44 (s, 3H), 3.52 (s, 3H), 3.56 (s, 3H), 3.71 (s, 3H) 3.72 (d, 1H, *J* = 9.0 Hz), 3.81 (s, 1H), 3.88 (brs, 2H), 4.17 and 5.16 (d, each 1H, *J* = 15.0 Hz), 4.64 (d, 1H, *J* = 9.0 Hz), 6.21 and 6.56 (d, each 2H, *J* = 8.8 Hz), 7.31 (m, 5H). ^{13}C NMR: δ 173.8, 172.3, 171.3, 152.4, 139.4, 134.4, 129.5, 128.3, 114.7, 114.6, 77.3, 73.0, 58.6, 56.3, 55.6, 55.5, 52.6, 52.4, 47.0, 45.3. IR ($CHCl_3$, cm^{-1}): ν 3408, 1737, 1723. MS (CI), *m/z* : 487 (M^+ + 1, 100), 486 (M^+, 21). (Anal. Calcd. for $C_{25}H_{30}N_2O_8$: C, 61.72; H, 6.22; N, 5.76. Found: C, 61.73; H, 6.27; N, 5.81).

General Procedure for the Hexacarbonylmolybdenum-Promoted Reductive Ring-Opening/Ring-Closure of Isoxazolidinyl β-Lactams 10 and 11. A mixture of the isoxazolidinyl β-lactams **10c** and **11c** (1 mmol) and $Mo(CO)_6$ (0.7 mmol) in acetonitrile (15 mL) was heated under reflux for 4 h. The reaction mixture was allowed to cool to room temperature, and was concentrated under reduced pressure. After chromatography of the residue eluting with ethyl acetate/hexanes mixtures gave compound **23**.

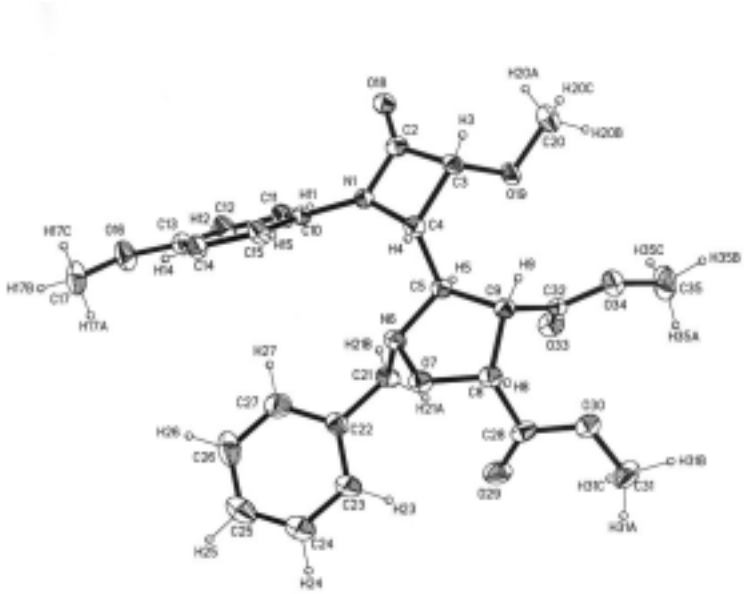
Hydroxy-γ-lactam 23. From 42 mg (0.12 mmol) of cycloadducts **10c** and **11c**, as a mixture (60:40) of epimers, 30 mg (79%) of compound **23**, as a mixture (60:40) of epimers, was obtained as a colorless oil after purification by flash chromatography (ethyl acetate). $[\alpha]_D$ = +48.5 (*c* 1.3, $CHCl_3$). ^{1}H NMR: δ 1.97 (dt, 0.4H, *J* = 14.4, 2.9 Hz), 2.14 (m, 0.6H), 2.46 (m, 1H), 2.61 (s, 1.2H), 2.68 (s, 1.8H), 3.62 (s, 1.8H), 3.63 (s, 1.2H) 3.79 (s, 3H), 3.94 (dd, 0.4H, *J* = 8.3, 2.9 Hz), 4.02 (dd, 0.6H, *J* = 9.0, 1.3 Hz), 4.32 (m, 1H), 4.57 (m, 1H), 4.63 (d, 0.6H, *J* = 5.3 Hz), 4.65 (d, 0.4H, *J* = 5.6 Hz), 6.81 (m, 2H), 7.22 (m, 2H). ^{13}C NMR: δ 175.9 (M), 175.5 (m), 165.2 (m), 165.0 (M), 156.9 (M), 156.8 (m), 130.5 (m), 130.0 (M), 118.9 (m), 118.8 (M), 114.7 (M), 114.6 (m), 83.2 (m), 82.9 (M), 69.6 (m), 68.2 (M), 60.0 (m), 59.8 (M + m), 58.9 (m), 58.8 (M), 57.2 (m), 55.5 (M + m), 31.9

(M), 31.6 (m), 30.6 (m), 30.4 (M). IR ($CHCl_3$, cm^{-1}): ν 3420, 1742, 1725. MS (CI), *m/z*: 321 (M^+ + 1, 100), 320 (M^+, 27).

Conversion of Hydroxy-γ-lactam 23 into Chloro-γ-lactam 24. Methanesulfonyl chloride (1.10 mmol) and triethylamine (1.20 mmol) were sequentially added dropwise to a stirred solution of the hydroxy-γ-lactam **23** (320 mg, 1.0 mmol), in dichloromethane (10 mL) at 0 ºC. The mixture was stirred for 2 h at room temperature, the organic phase was washed with water (2 x 5 mL), dried ($MgSO_4$) and the solvent was removed under reduced pressure. Then, DBU (1.10 mmol) was added dropwise to a solution of the corresponding methanesulfonate in toluene (10 mL), and the resulting solution was heated under reflux for 1 h. The reaction mixture was allowed to cool to room temperature, and was concentrated. Chromatography of the residue eluting with ethyl acetate gave 272 mg of compound **24**.

Chloro-γ-lactam 24. Colorless oil. ^1H NMR: δ 2.26 (m, 0.8H), 2.54 (s, 1.2H), 2.78 (m, 1.2H), 2.87 (s, 1.8H), 3.57 (s, 1.8H), 3.65 (s, 1.2H), 3.78 (s, 1.8H), 3.79 (s, 1.2H), 3.95 (m, 0.4H), 4.26 (ddd, 0.6H, *J* = 9.3, 6.1, 3.1 Hz), 4.37 (dd, 0.6H, *J* = 7.8, 1.4 Hz), 4.46 (t, 0.4H, *J* = 5.6 Hz), 4.57 (dd, 0.6H, *J* = 8.8, 7.1 Hz), 4.71 (m, 1.4H), 6.88 (m, 2H), 7.22 (m, 2H). ^{13}C NMR: δ 171.2 (M), 170.8 (m), 165.2 (m), 164.5 (M), 156.9 (M), 156.8 (m), 130.5 (m), 129.7 (M), 118.8 (m), 118.7 (M), 114.7 (M), 114.6 (m), 83.2 (m), 82.8 (M), 60.1 (M + m), 59.6 (M), 59.2 (m), 56.9 (M), 56.4 (m), 55.5 (M), 55.4 (m), 53.3 (M), 53.0 (m), 33.6 (M), 31.9 (m), 31.2 (m), 30.2 (M). IR ($CHCl_3$, cm^{-1}): ν 1745. MS (CI), *m/z*: 340 (M^+ + 2, 39), 338 (M^+, 100).

X-Ray data for compound (+)-**7**



CRYSTAL DATA

Empirical formula	$C_{25}H_{28}N_2O_8$	
Formula weight	484.49	
Crystal system		monoclini
Space group	P2(1)	
Unit cell dimension		a =
12.4382 (14) Å α =90°		
	b = 5.8976 (7) Å	β = 94.767 (3) °
	c = 16.8160 (19) Å	γ =90°
Volume	1229.3 (2) $Å^3$	
Formula unit per cell, Z	2	
Calculated density	1.309 Mg/m^3	
Absorption coefficient	0.098 mm^{-1}	
F(000)		512
Crystal size		0.14 x 0.2
x 0.28 mm^3		

DATA COLLECTION

Four circle diffractometer		Bruker
AXS.CCD. Area detector.		
		Graphite
oriented monochromator		
Wavelength		Mo Ka
0.71073 Å		
Scan technique	phi and omega	
Temperature	293(2) K	
Theta range for data collection	1.22 to 25.00°.	

Limiting indices		-10 < = h < = 14, -6 < = k <7, -19 < = l < = 19
Reflections collected	6509	
Independent Reflections		3990 [R (int) = 0.0592]

SOLUTION AND REFINAMENT

Solution		Direct methods
Refinement method		Full-matrix least-squares on F^2
Data/restraints/parameters		3990/1/325
Goodness-of-fit on F^2	0.775	
Final R indices [I > 2 sigma (I)]		R1 = 0.0420, wR2 = 0.0868
R indices (all data)		R1 = 0.1223, wR2 = 0.1358
Absolute structure parameter	-1(2)	
Largest diff. peak and hole		0.155 and –0.133 e. A^{-3}
Computers and programs		Shel XTL (Sheldrick, 1997)

Bond distances (Å).

N(1)-C(2)	1.35	C(10)-C(11)	1.38	C(22)-C(23)	1.37
N(1)-C(10)	1.42	C(11)-C(12)	1.38	C(23)-C(24)	1.37
N(1)-C(4)	1.46	C(11)-H(11)	0.93	C(23)-H(23)	0.93
C(2)-O(18)	1.22	C(12)-C(13)	1.36	C(24)-C(25)	1.34
C(2)-C(3)	1.52	C(12)-H(12)	0.93	C(24)-H(24)	0.93
C(3)-O(19)	1.40	C(13)-O(16)	1.37	C(25)-C(26)	1.35
C(3)-C(4)	1.53	C(13)-C(14)	1.37	C(25)-H(25)	0.93
C(3)-H(3)	0.95	C(14)-C(15)	1.38	C(26)-C(27)	1.41
C(4)-C(5)	1.52	C(14)-H(14)	0.93	C(26)-H(26)	0.93
C(4)-H(4)	0.88	C(15)-H(15)	0.93	C(27)-H(27)	0.93
C(5)-N(6)	1.47	O(16)-C(17)	1.41	C(28)-O(29)	1.18
C(5)-C(9)	1.53	C(17)-H(17A)	0.96	C(28)-O(30)	1.33
C(5)-H(5)	0.99	C(17)-H(17B)	0.96	O(30)-C(31)	1.44
N(6)-O(7)	1.45	C(17)-H(17C)	0.96	C(31)-H(31A)	0.96
N(6)-C(21)	1.49	O(19)-C(20)	1.40	C(31)-H(31B)	0.96
O(7)-C(8)	1.43	C(20)-H(20A)	0.96	C(31)-H(31C)	0.96
C(8)-C(28)	1.53	C(20)-H(20B)	0.96	C(32)-O(33)	1.18
C(8)-C(9)	1.52	C(20)-H(20C)	0.96	C(32)-O(34)	1.35
C(8)-H(8)	0.95	C(21)-C(22)	1.50	O(34)-C(35)	1.46

C(9)-C(32)	1.52	C(21)-H(21A	0.97	C(35)-H(35A)	0.96
C(9)-H(9)	0.89	C(21)-H(21B)	0.97	C(35)-H(35B)	0.96
C(10)-C(15)	1.37	C(22)-C(27)	1.37	C(35)-H(35C)	0.96

Bond angles (o).

C(2)-N(1)-C(10)	130.8	O(19)-C(20)-H(20A)	109.5
C(2)-N(1)-C(4)	95.3	O(19)-C(20)-H(20B)	109.5
C(10)-N(1)-C(4	133.6	H(20A)-C(20)-H(20B)	109.5
O(18)-C(2)-N(1)	132.2	O(19)-C(20)-H(20C)	109.5
O(18)-C(2)-C(3)	136.0	H(20A)-C(20)-H(20C)	109.5
N(1)-C(2)-C(3)	91.6	H(20B)-C(20)-H(20C)	109.5
O(19)-C(3)-C(2)	118.8	N(6)-C(21)-C(22)	110.3
O(19)-C(3)-C(4	115.0	N(6)-C(21)-H(21A)	109.6
C(2)-C(3)-C(4)	85.9	C(22)-C(21)-H(21A)	109.6
O(19)-C(3)-H(3)	104.6	N(6)-C(21)-H(21B)	109.6
C(2)-C(3)-H(3)	115.4	C(22)-C(21)-H(21B)	109.6
C(4)-C(3)-H(3)	117.2	H(21A)-C(21)-H(21B)	108.1
N(1)-C(4)-C(5)	115.1	C(27)-C(22)-C(23)	118.4
N(1)-C(4)-C(3)	86.8	C(27)-C(22)-C(21)	120.0
C(5)-C(4)-C(3	117.0	C(23)-C(22)-C(21)	121.5
N(1)-C(4)-H(4)	120.1	C(24)-C(23)-C(22)	119.9
C(5)-C(4)-H(4)	100.8	C(24)-C(23)-H(23)	120.0
C(3)-C(4)-H(4)	118.1	C(9)-C(8)-H(8)	111.4
N(6)-C(5)-C(4)	108.1	C(32)-C(9)-C(8)	114.6
N(6)-C(5)-C(9)	108.0	C(32)-C(9)-C(5)	111.3
C(4)-C(5)-C(9)	111.0	C(8)-C(9)-C(5)	104.1
N(6)-C(5)-H(5)	115.2	C(32)-C(9)-H(9	102.3
C(4)-C(5)-H(5)	108.8	C(8)-C(9)-H(9)	115.0
C(9)-C(5)-H(5)	105.7	C(5)-C(9)-H(9)	109.7
O(7)-N(6)-C(5)	104.5	C(15)-C(10)-C(11)	119.4
O(7)-N(6)-C(21)	109.4	C(15)-C(10)-N(1)	120.4
C(5)-N(6)-C(21)	113.1	C(11)-C(10)-N(1)	120.2
C(8)-O(7)-N(6)	110.1	C(12)-C(11)-C(10	119.9
O(7)-C(8)-C(28)	114.3	C(12)-C(11)-H(11)	120.1
O(7)-C(8)-C(9)	105.6	C(10)-C(11)-H(11)	120.1
C(28)-C(8)-C(9)	115.0	C(13)-C(12)-C(11)	120.0
O(7)-C(8)-H(8)	107.9	C(13)-C(12)-H(12)	120.0

C(28)-C(8)-H(8)	102.6	C(11)-C(12)-H(12)	120.0
C(22)-C(23)-H(23)	120.0	O(16)-C(17)-H(17A)	109.5
C(25)-C(24)-C(23)	122.3	O(16)-C(17)-H(17B)	109.5
C(25)-C(24)-H(24)	118.9	H(17A)-C(17)-H(17B)	109.5
C(23)-C(24)-H(24)	118.9	O(16)-C(17)-H(17C)	109.5
C(24)-C(25)-C(26)	119.2	H(17A)-C(17)-H(17C)	109.5
C(24)-C(25)-H(25)	120.4	H(17B)-C(17)-H(17C)	109.5
C(26)-C(25)-H(25)	120.4	C(3)-O(19)-C(20)	113.9
C(25)-C(26)-C(27)	119.7	C(28)-O(30)-C(31)	116.4
C(25)-C(26)-H(26)	120.2	O(30)-C(31)-H(31A)	109.5
C(27)-C(26)-H(26)	120.2	O(30)-C(31)-H(31B)	109.5
C(22)-C(27)-C(26)	120.4	H(31A)-C(31)-H(31B)	109.5
C(22)-C(27)-H(27)	119.8	O(30)-C(31)-H(31C)	109.5
C(26)-C(27)-H(27)	119.8	H(31A)-C(31)-H(31C)	109.5
O(29)-C(28)-O(30)	125.8	H(31B)-C(31)-H(31C)	109.5
O(29)-C(28)-C(8)	126.1	O(33)-C(32)-O(34)	124.5
O(30)-C(28)-C(8)	108.0	O(33)-C(32)-C(9)	125.1
C(12)-C(13)-O(16)	115.3	O(34)-C(32)-C(9)	110.4
O(16)-C(13)-C(14)	124.0	C(32)-O(34)-C(35)	114.4
C(13)-C(14)-C(15)	119.1	O(34)-C(35)-H(35A)	109.5
C(13)-C(14)-H(14)	120.5	O(34)-C(35)-H(35B)	109.5
C(15)-C(14)-H(14)	120.5	H(35A)-C(35)-H(35B)	109.5
C(10)-C(15)-C(14)	120.8	O(34)-C(35)-H(35C)	109.5
C(10)-C(15)-H(15)	119.6	H(35A)-C(35)-H(35C)	109.5
C(14)-C(15)-H(15)	119.6	H(35B)-C(35)-H(35C)	109.5
C(13)-O(16)-C(17)	117.9		