Supporting Information for the Paper

Novel N1–C4 β -lactam bond breakage. Synthesis of enantiopure α -alkoxy- γ -keto acid derivatives

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General. General experimental data and procedures have been previously reported.⁵ ^1H NMR and ^{13}C NMR spectra were recorded at 300 MHz or 75 MHz, respectively. NMR spectra were recorded in CDCl_3 solutions, except otherwise stated. Chemical shifts are given in ppm relative to TMS (^1H , 0.0 ppm), or CDCl_3 (^{13}C , 76.9 ppm). Specific rotation $[\alpha]_D$ is given in deg per dm at 20 °C, and the concentration (*c*) is expressed in g per 100 mL. All commercially available compounds were used without further purification.

General Procedure for the Preparation of *cis*-4-formyl- β -lactams **1.** The corresponding alkoxyacetylchloride (38 mmol) in anhydrous dichloromethane (25 mL) was added dropwise via syringe to a solution of the corresponding 2,3-*O*-(isopropylidene)-D-glyceraldehyde imine (25 mmol) and Et_3N (75 mmol) in dichloromethane (160 mL), at 0 °C under argon. The resulting mixture was allowed to warm to room temperature, and was stirred for 16h. The crude mixture was diluted with CH_2Cl_2 (100 mL) and washed with saturated NaHCO_3 (2 x 20 mL) and brine (40 mL). The organic layer was dried (MgSO_4) and concentrated under reduced pressure. Chromatography of the residue eluting with EtOAc/hexanes gave analytically pure (3*R*,4*S*)-4-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-3-alkoxy-1-(aryl)-2-azetidinones.

To a solution of the corresponding acetamide β -lactam (10 mmol) in THF/water (1:1, 200 mL) was added solid *p*-TsOH·H₂O (12 mmol) in a single portion. The resulting clear solution was heated under reflux for 2h. The reaction mixture was allowed to cool to room temperature, and then was neutralized with solid NaHCO₃. The mixture was extracted with ethyl acetate (3 x 40 mL), the organic layer was dried (MgSO₄) and the solvent was removed under reduced pressure to give (3*R*,4*S*)-4-[(*S*)-1,2-dihydroxyethylen]-3-alkoxy-1-(aryl)-2-azetidinones. Further purification was not necessary.

Saturated aqueous sodium hydrogen carbonate (243 μ L) was added to a solution of the corresponding diol (2.43 mmol) in dichloromethane (15 mL), maintaining the temperature below 25 °C. Solid sodium periodate (4.86 mmol) was added over a 10 min period with vigorous stirring and the reaction was allowed to proceed for 2h, while the temperature was maintained below 25 °C. The solid was removed by filtration, the filtrate was dried (MgSO₄) and the solvent was removed under reduced pressure. The crude product was used for next step without any further purification. Spectroscopic and analytical data for some representative forms of *cis*-4-formyl- β -lactams **1** follow.

(+)-(3*R*, 4*R*)-4-Formyl-3-methoxy-1-(*p*-methoxyphenyl)-2-azetidinone, (+)-1a. From 3.50g (14.9 mmol) of the corresponding imine, 2.80g (80%) of compound **(+)-1a** was obtained as a colorless oil. $[\alpha]_D = +104.4$ (*c* 1.2, CH₂Cl₂). ¹H-NMR: δ 3.49 (s, 3H), 3.72 (s, 3H), 4.47 (dd, 1H, *J* = 5.1, 3.9 Hz), 4.82 (d, 1H, *J* = 5.1 Hz), 6.81 and 7.19 (dd, each 2H, *J* = 7.0, 2.2 Hz), 9.70 (d, 1H, *J* = 3.8 Hz). ¹³C-NMR: δ 199.1, 162.8, 157.0, 130.5, 118.1, 114.6, 85.1, 63.2, 59.4, 55.5. IR (CHCl₃, cm⁻¹): ν 1742, 1725. MS (EI), *m/z* : 236 (*M*⁺ + 1, 7), 235 (*M*⁺, 19), 91 (100). (Anal. Calcd for C₁₂H₁₃NO₄: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.29; H, 5.50; N, 5.98).

(+)-(3*R*, 4*R*)-4-Formyl-3-methoxy-1-(*p*-tolyl)-2-azetidinone, (+)-1b. From 5.64g (24.0 mmol) of the corresponding imine, 4.14g (79%) of compound **(+)-1b** was obtained as a colorless oil. $[\alpha]_D = +126.3$ (*c* 0.7, CHCl₃). ¹H-NMR: δ 2.20 (s, 3H), 3.48 (s, 3H), 4.42 (dd, 1H, *J* = 5.2, 3.9 Hz), 4.80 (d, 1H, *J* = 5.2 Hz), 7.09 (m, 4H). ¹³C-NMR: δ 199.1, 163.2, 135.2, 134.7, 130.0, 116.7, 85.1, 63.1, 59.5, 21.0. IR (CHCl₃, cm⁻¹): ν 1747, 1730. MS (EI), *m/z* : 220 (*M*⁺ + 1, 1), 219 (*M*⁺, 100). (Anal. Calcd for C₁₂H₁₃NO₃: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.83; H, 5.94; N, 6.43).

(+)-(3*R*, 4*R*)-4-Formyl-3-methoxy-1-[*p*-(*N,N*-dimethylamino)phenyl]-2-azetidinone, (+)-1c. From 1.64g (5.1 mmol) of the corresponding imine, 0.62g (49%) of compound **(+)-1c** was obtained as a colorless solid. Mp: 135–136 °C (hexanes/ethyl acetate). $[\alpha]_D = +136.6$ (*c* 0.6, CHCl₃). ¹H-NMR: δ 2.92 (s, 6H), 3.53 (s, 3H), 4.48 (dd, 1H, *J* = 4.8, 3.9 Hz), 4.85 (d, 1H, *J* = 5.1 Hz), 6.68 and 7.21 (d, each 2H, *J* = 9.1 Hz), 9.75 (d, 1H, *J* = 3.9 Hz). ¹³C-NMR: δ 199.5, 162.5, 148.1, 127.3, 118.2, 113.0, 85.0, 63.1, 59.3, 40.7. IR (CHCl₃, cm⁻¹): ν 1744, 1724. MS (CI), *m/z* : 249 (*M*⁺ + 1, 100), 248 (*M*⁺, 11). (Anal. Calcd for C₁₃H₁₆N₂O₃: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.79; H, 6.54; N, 11.23).

(+)-(3*R*, 4*R*)-4-Formyl-3-methoxy-1-(*p*-bromophenyl)-2-azetidinone, (+)-1d. From 0.40g (1.59 mmol) of the corresponding imine, 0.24g (59%) of compound **(+)-1d** was obtained as a colorless solid. Mp: 115–116 °C (hexanes/ethyl acetate). $[\alpha]_D = +138.3$ (*c* 0.6, CHCl₃). ¹H-NMR: δ 3.51 (s, 3H), 4.51 (dd, 1H, *J* = 5.4, 3.4 Hz), 4.84 (d, 1H, *J* = 5.4 Hz), 7.12 and 7.40 (d, each 2H, *J* = 8.9 Hz), 9.68 (d, 1H, *J* = 3.4 Hz). ¹³C-NMR: δ 197.8, 135.9, 132.5, 132.1, 118.3, 85.2, 63.1, 59.5. IR (CHCl₃, cm⁻¹): ν 1741, 1723. MS (EI), *m/z* : 286 (*M*⁺ + 2, 100), 284 (*M*⁺, 98). (Anal. Calcd for C₁₁H₁₀BrNO₃: C, 46.50; H, 3.55; N, 4.93. Found: C, 46.42; H, 3.52; N, 4.96).

(+)-(3*R*, 4*R*)-4-Formyl-3-methoxy-1-(2,4-dimethoxyphenyl)-2-azetidinone, (+)-1e. From 2.0g (7.7 mmol) of the corresponding imine, 0.86g (42%) of compound **(+)-1e** was obtained as a colorless oil. $[\alpha]_D = +63.8$ (*c* 1.3, CHCl₃). ¹H-NMR: δ 3.53 (s, 3H), 3.70 and 3.79 (s, each 3H), 4.57 (t, 1H, *J* = 3.9 Hz), 4.83 (d, 1H, *J* = 3.4 Hz), 6.47 (m, 2H), 7.90 (d, 1H, *J* = 8.5 Hz), 9.72 (d, 1H, *J* = 4.2 Hz). ¹³C-NMR: δ 191.2, 164.3, 158.3, 149.7, 126.3, 117.6, 107.1, 98.2, 84.3, 64.3, 59.3, 55.7, 55.4. IR (CHCl₃, cm⁻¹): ν 1742, 1728. MS (EI), *m/z* : 266 (*M*⁺ + 1, 5), 265 (*M*⁺, 100). (Anal. Calcd for C₁₃H₁₅NO₅: C, 58.86; H, 5.70; N, 5.28. Found: C, 58.96; H, 5.73; N, 5.25).

(+)-(3*R*, 4*R*)-4-Formyl-3-benzyloxy-1-(2,4-dimethoxyphenyl)-2-azetidinone, (+)-1f. From 1.35g (7.7 mmol) of the corresponding imine, 0.885g (51%) of compound **(+)-1f** was obtained as a colorless solid. Mp: 98–99 °C (hexanes/ethyl acetate). $[\alpha]_D = +96.2$ (*c* 0.7, CHCl₃). ¹H-NMR: δ 3.62 and 3.72 (s, each 3H), 4.48 (t, 1H, *J* = 4.8 Hz), 4.62 and 4.70 (d, each 1H, *J* = 11.6 Hz), 4.92 (d, 1H, *J* = 5.3 Hz), 6.38 (m, 2H), 7.28 (m, 5H), 7.82 (d, 1H, *J* = 8.6 Hz), 9.66 (d, 1H, *J* = 4.3 Hz). ¹³C-NMR: δ 198.7, 164.9, 158.1, 154.9, 137.4, 128.4, 128.2, 128.1, 122.8, 104.6, 99.3, 83.7, 73.0,

66.5, 55.5, 54.7. IR (CHCl₃, cm⁻¹): ν 1740, 1726. MS (EI), m/z : 342 (M⁺ + 1, 9), 341 (M⁺, 100). (Anal. Calcd for C₁₉H₁₉NO₅: C, 66.85; H, 5.61; N, 4.10. Found: C, 66.94; H, 5.58; N, 4.13).

General Procedure for the synthesis of α -hydroxy carboxamides 2. A solution of 2-(trimethylsilyl)thiazole (TMST) (94 mg, 0.60 mmol) in anhydrous dichloromethane (0.35 mL), was added dropwise to a solution cooled at 0 °C of the corresponding 4-formyl- β -lactam **1** (0.50 mmol) in the same solvent (0.5 mL). The reaction was placed in a 0 °C freezer overnight. The mixture was extracted with EtOAc, washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. Chromatography of the residue eluting with EtOAc/hexanes gave analytically pure compounds **2**, **3**, or **5**.

Reaction between aldehyde (+)-1a and TMST. Preparation of α -alkoxy carboxamide (+)-2a and β -lactam (+)-3a. From 100 mg (0.42 mmol) of 4-formyl- β -lactam (+)-**1a**, and after chromatography of the residue eluting with EtOAc/hexanes (1:3) gave two fractions. The less polar fraction contained β -lactam (+)-**3a** (51 mg, 31%) as a colorless oil. $[\alpha]_D = +54.2$ (c 1.9, CHCl₃). ¹H-NMR: δ 0.00 (9H, s), 3.45 (3H, s), 3.77 (3H, s), 4.59 (1H, d, J = 5.2 Hz), 4.87 (1H, t, J = 5.6 Hz), 5.34 (1H, d, J = 5.9 Hz), 6.76 (1H, d, J = 9.1 Hz), 7.29 (3H, m), 7.83 (1H, d, J = 3.2 Hz). ¹³C NMR: δ 173.8, 165.2, 156.4, 142.9, 131.5, 119.8, 119.5, 113.8, 82.7, 70.9, 62.2, 59.8, 55.5, 0.0. IR (CHCl₃, cm⁻¹): ν 1740. MS (CI), m/z : 393 (M⁺+1, 100), 392 (M⁺, 11). (Anal. Calcd for C₁₈H₂₄N₂O₄SSi: C, 54.96; H, 6.19; N, 7.11. Found: C, 55.07; H, 6.16; N, 7.14). The more polar fraction contained α -alkoxy carboxamide (+)-**2a** (78 mg, 58%) as a colorless oil. $[\alpha]_D = +48.3$ (c 1.0, CHCl₃). ¹H-NMR: δ 3.47 (3H, s), 3.51 (2H, m), 3.72 (3H, s), 4.41 (1H, t, J = 5.8 Hz), 6.80 and 7.42 (each 2H, d, J = 9.0 Hz), 7.63 (1H, d, J = 3.1 Hz), 7.93 (1H, d, J = 3.0 Hz), 8.31 (1H, br s). ¹³C NMR: δ 190.2, 169.1, 165.4, 156.4, 144.7, 130.2, 130.1, 121.4, 114.1, 78.2, 59.1, 55.3, 41.4. IR (CHCl₃, cm⁻¹): ν 3450, 1660. MS (EI), m/z : 321 (M⁺+1, 17), 320 (M⁺, 100). (Anal. Calcd for C₁₅H₁₆N₂O₄S: C, 56.35; H, 5.00; N, 8.70. Found: C, 56.24; H, 5.03; N, 8.74).

Reaction between aldehyde (+)-1b and TMST. Preparation of α -alkoxy carboxamide (+)-2b and β -lactam (+)-3b. From 100 mg (0.45 mmol) of 4-formyl- β -lactam (+)-**1b**, and after chromatography of the residue eluting with EtOAc/hexanes (1:4) gave two fractions. The less polar fraction contained β -lactam (+)-**3b** (52 mg, 31%) as a colorless oil. $[\alpha]_D = +68.1$ (c 1.0,

CHCl₃). ¹H-NMR: δ 0.00 (9H, s), 2.28 (3H, s), 3.45 (3H, s), 4.59 (1H, d, *J* = 5.3 Hz), 4.90 (1H, t, *J* = 5.5 Hz), 5.36 (1H, d, *J* = 5.8 Hz), 7.02 and 7.22 (each 2H, d, *J* = 8.8 Hz), 7.32 (1H, d, *J* = 3.3 Hz), 7.84 (1H, d, *J* = 3.2 Hz). ¹³C NMR: δ 173.2, 165.6, 142.6, 135.5, 133.8, 129.1, 119.6, 118.3, 82.6, 70.8, 62.0, 59.8, 20.9, 0.0. IR (CHCl₃, cm⁻¹): ν 1741. MS (CI), *m/z*: 377 (*M*⁺+1, 100), 376 (*M*⁺, 7). (Anal. Calcd for C₁₈H₂₄N₂O₃SSi: C, 57.41; H, 6.42; N, 7.44. Found: C, 57.51; H, 6.39; N, 7.47). The more polar fraction contained α-alkoxy carboxamide (+)-**2b** (45 mg, 33%) as a pale yellow oil. [α]_D = +56.6 (*c* 1.0, CHCl₃). ¹H-NMR: δ 2.35 (3H, s), 3.55 (3H, s), 3.65 (2H, m), 4.48 (1H, t, *J* = 6.4 Hz), 7.15 and 7.45 (each 2H, d, *J* = 8.8 Hz), 7.71 (1H, d, *J* = 3.0 Hz), 8.02 (1H, d, *J* = 3.0 Hz), 8.40 (1H, br s). ¹³C NMR: δ 190.3, 169.4, 166.5, 144.8, 134.5, 134.2, 129.5, 120.5, 119.8, 78.2, 59.2, 41.5, 20.8. IR (CHCl₃, cm⁻¹): ν 3452, 1655. MS (EI), *m/z*: 305 (*M*⁺+1, 15), 304 (*M*⁺, 100). (Anal. Calcd for C₁₅H₁₆N₂O₃S: C, 59.19; H, 5.30; N, 9.20. Found: C, 59.10; H, 5.34; N, 9.15).

Reaction between aldehyde (+)-1c and TMST. Preparation of α-alkoxy carboxamide (+)-2c and β-lactam (+)-3c. From 40 mg (0.16 mmol) of 4-formyl-β-lactam (+)-**1c**, and after chromatography of the residue eluting with EtOAc/hexanes (1:3) gave two fractions. The less polar fraction contained β-lactam (+)-**3c** (11 mg, 20%) as a colorless oil. [α]_D = +26.7 (*c* 1.7, CHCl₃). ¹H-NMR: δ 0.00 (9H, s), 2.89 (6H, s), 3.43 (3H, s), 4.55 (1H, d, *J* = 5.1 Hz), 4.84 (1H, t, *J* = 5.1 Hz), 5.33 (1H, d, *J* = 5.8 Hz), 6.59 and 7.23 (each 2H, d, *J* = 9.0 Hz), 7.29 (1H, d, *J* = 3.4 Hz), 7.81 (1H, d, *J* = 3.2 Hz). ¹³C NMR: δ 172.5, 165.1, 148.2, 142.8, 126.3, 119.7, 119.4, 112.7, 82.6, 71.0, 62.1, 59.6, 41.0, 0.0. IR (CHCl₃, cm⁻¹): ν 1742. MS (CI), *m/z*: 406 (*M*⁺+1, 100), 405 (*M*⁺, 35). (Anal. Calcd for C₁₉H₂₇N₃O₃SSi: C, 56.26; H, 6.71; N, 10.36. Found: C, 56.38; H, 6.68; N, 10.42). The more polar fraction contained α-alkoxy carboxamide (+)-**2c** (23 mg, 38%) as a pale yellow oil. [α]_D = +51.6 (*c* 1.4, CHCl₃). ¹H-NMR: δ 2.92 (6H, s), 3.53 (3H, s), 3.68 (2H, m), 4.49 (1H, dd, *J* = 6.8, 5.1 Hz), 6.73 and 7.43 (each 2H, d, *J* = 9.1 Hz), 7.69 (1H, d, *J* = 3.2 Hz), 7.99 (1H, d, *J* = 3.2 Hz), 8.28 (1H, br s). ¹³C NMR: δ 190.5, 169.0, 166.7, 148.2, 144.9, 127.0, 126.5, 121.5, 113.1, 78.4, 59.2, 41.8, 40.8. IR (CHCl₃, cm⁻¹): ν 3454, 1658. MS (EI), *m/z*: 334 (*M*⁺+1, 26), 333 (*M*⁺, 100). (Anal. Calcd for C₁₆H₁₉N₃O₃S: C, 57.64; H, 5.74; N, 12.60. Found: C, 57.72; H, 5.70; N, 12.53).

Reaction between aldehyde (+)-1d and TMST. Preparation of α -alkoxy carboxamide (+)-2d and β -lactam (+)-3d. From 50 mg (0.17 mmol) of 4-formyl- β -lactam (+)-1d, and after chromatography of the residue eluting with EtOAc/hexanes (1:3) gave two fractions. The less polar fraction contained β -lactam (+)-3d (17 mg, 23%) as a pale yellow oil. $[\alpha]_D^{25} = +31.0$ (*c* 2.1, CHCl₃). ¹H-NMR: δ 0.00 (9H, s), 3.45 (3H, s), 4.59 (1H, d, *J* = 5.3 Hz), 4.88 (1H, t, *J* = 5.4 Hz), 5.33 (1H, d, *J* = 5.6 Hz), 7.49 (5H, m), 7.82 (1H, d, *J* = 3.4 Hz). ¹³C NMR: δ 172.7, 165.8, 143.0, 136.9, 131.5, 119.9, 118.9, 116.8, 82.7, 70.7, 62.2, 59.8, 0.0. IR (CHCl₃, cm⁻¹): ν 1744. MS (CI), *m/z*: 443 (*M*⁺+2, 100), 441 (*M*⁺, 98). (Anal. Calcd for C₁₇H₂₁N₂O₃SSiBr: C, 46.26; H, 4.80; N, 6.35. Found: C, 46.12; H, 4.84; N, 6.29). The more polar fraction contained α -alkoxy carboxamide (+)-2d (29 mg, 46%) as a pale yellow solid. Mp: 80–82 °C (hexanes/ethyl acetate). $[\alpha]_D^{25} = +33.9$ (*c* 2.1, CHCl₃). ¹H-NMR: δ 3.52 (3H, s), 3.67 (2H, dd, *J* = 6.3, 5.4 Hz), 4.46 (1H, dd, *J* = 6.2, 5.4 Hz), 7.45 (4H, m), 7.69 (1H, d, *J* = 3.2 Hz), 7.98 (1H, d, *J* = 3.4 Hz), 8.51 (1H, br s). ¹³C NMR: δ 190.2, 166.7, 166.5, 144.9, 136.3, 132.4, 126.7, 121.4, 117.2, 78.2, 59.1, 41.2, 40.8. IR (CHCl₃, cm⁻¹): ν 3451, 1656. MS (EI), *m/z*: 371 (*M*⁺+2, 100), 369 (*M*⁺, 98). (Anal. Calcd for C₁₄H₁₃N₂O₃SBr: C, 45.54; H, 3.55; N, 7.59. Found: C, 45.64; H, 3.52; N, 7.64).

Reaction between aldehyde (+)-1e and TMST. Preparation of α -alkoxy carboxamide (+)-2e and β -lactam (+)-3e. From 132 mg (0.50 mmol) of 4-formyl- β -lactam (+)-1e, and after chromatography of the residue eluting with EtOAc/hexanes (1:1) gave two fractions. The less polar fraction contained β -lactam (+)-3e (21 mg, 10%) as a colorless oil. $[\alpha]_D^{25} = +28.8$ (*c* 2.2, CHCl₃). ¹H-NMR: δ 0.00 (9H, s), 3.47 (3H, s), 3.49 (3H, s), 3.74 (3H, s), 4.61 (1H, d, *J* = 5.0 Hz), 4.89 (1H, dd, *J* = 5.0, 3.5 Hz), 5.30 (1H, d, *J* = 3.5 Hz), 6.18 (1H, d, *J* = 2.5 Hz), 6.41 (1H, dd, *J* = 8.6, 2.8 Hz), 7.12 (1H, d, *J* = 3.2 Hz), 7.50 (1H, d, *J* = 8.6 Hz), 7.69 (1H, d, *J* = 3.2 Hz). ¹³C NMR: δ 174.0, 167.0, 158.7, 153.2, 142.2, 126.1, 118.9, 118.6, 103.7, 98.7, 83.4, 70.8, 64.0, 59.3, 55.4, 55.1, 0.0. IR (CHCl₃, cm⁻¹): ν 1742. MS (EI), *m/z*: 423 (*M*⁺+1, 15), 422 (*M*⁺, 100). (Found: C, 54.10; H, 6.25; N, 6.59. Calcd for C₁₉H₂₆N₂O₅SSi: C, 54.00; H, 6.20; N, 6.63). The more polar fraction contained α -alkoxy carboxamide (+)-2e (89 mg, 51%) as a colorless oil. $[\alpha]_D^{25} = +28.4$ (*c* 2.6, CHCl₃). ¹H-NMR: δ 3.55 (3H, s), 3.68 (2H, m), 3.79 (3H, s), 3.86 (3H, s), 4.49 (1H, dd, *J* = 7.8, 4.3 Hz), 6.41 (2H, m), 7.63 (1H, d, *J* = 3.0 Hz), 7.93 (1H, d, *J* = 3.0 Hz), 8.18 (1H, d, *J* = 9.3 Hz), 8.78 (1H, br s). ¹³C NMR: δ 190.4, 169.0, 166.2, 156.7, 149.7, 144.8, 126.4, 120.7, 120.5,

103.7, 98.7, 78.5, 59.2, 55.8, 55.5, 41.9. IR (CHCl₃, cm⁻¹): ν 3450, 1660. MS (EI), m/z 351 ($M^+ + 1$, 20), 350 (M^+ , 100). (Found: C, 54.73; H, 5.14; N, 8.05. Calcd for C₁₆H₁₈N₂O₅S: C, 54.84; H, 5.18; N, 7.99).

Reaction between aldehyde (+)-1f and TMST. Preparation of α -alkoxy carboxamide (+)-2f and β -lactam (+)-3f. From 74 mg (0.21 mmol) of 4-formyl- β -lactam (+)-1f, and after chromatography of the residue eluting with EtOAc/hexanes (1:3) gave two fractions. The less polar fraction contained β -lactam (+)-3f (22 mg, 24%) as a pale yellow solid. Mp: 133–134 °C (hexanes/ethyl acetate). $[\alpha]_D = +45.5$ (c 1.0, CHCl₃). ¹H-NMR: δ 3.53 and 3.72 (each 3H, s), 4.81 (1H, d, J = 11.4 Hz), 4.81 (1H, dd, J = 11.4 Hz), 5.04 (3H, m), 5.33 (1H, m), 6.10 (1H, d, J = 2.7 Hz), 6.36 (1H, dd, J = 8.5, 4.5 Hz), 7.07 (1H, d, J = 3.2 Hz), 7.39 (6H, m), 7.62 (1H, d, J = 3.2 Hz). ¹³C NMR: δ 170.9, 166.3, 159.1, 153.3, 141.2, 136.3, 128.7, 128.5, 128.2, 126.8, 119.4, 117.5, 103.8, 98.6, 81.8, 73.9, 70.6, 63.1, 55.4, 55.1. IR (CHCl₃, cm⁻¹): ν 3320, 1745. MS (EI), m/z : 427 ($M^+ + 1$, 11), 426 (M^+ , 100). (Found: C, 61.96; H, 5.20; N, 6.57. Calcd for C₂₂H₂₂N₂O₅S: C, 62.07; H, 5.24; N, 6.53). The more polar fraction contained α -alkoxy carboxamide (+)-2f (49 mg, 55%) as a colorless oil. $[\alpha]_D = +50.9$ (c 1.4, CHCl₃). ¹H-NMR: δ 3.75 (2H, m), 3.81 (6H, s), 4.75 (3H, m), 6.48 (2H, m), 7.36 (5H, m), 7.69 (1H, d, J = 3.0 Hz), 7.99 (1H, d, J = 2.7 Hz), 8.29 (1H, d, J = 9.5 Hz), 9.07 (1H, br s). ¹³C NMR: δ 190.2, 169.2, 166.2, 156.5, 151.2, 144.6, 137.1, 128.2, 128.1, 127.9, 126.1, 120.1, 103.5, 98.4, 76.1, 73.6, 55.3, 42.2. IR (CHCl₃, cm⁻¹): ν 3454, 1655. MS (EI), m/z 427 ($M^+ + 1$, 24), 426 (M^+ , 100). (Found: C, 61.96; H, 5.20; N, 6.57. Calcd for C₁₆H₁₈N₂O₅S: C, 61.85; H, 5.16; N, 6.61).

Reaction between aldehyde (-)-4a and TMST. Preparation of α -alkoxy carboxamide (+)-2a and β -lactam (+)-5a. From 40 mg (0.16 mmol) of 4-formyl- β -lactam (-)-4a, and after chromatography of the residue eluting with EtOAc/hexanes (1:2) gave two fractions. The less polar fraction contained β -lactam (+)-5a (8 mg, 15%) as a colorless oil. $[\alpha]_D = +4.5$ (c 0.6, CHCl₃). ¹H-NMR: δ 3.06 (3H, s), 3.73 (3H, s), 4.39 (1H, t, J = 1.5 Hz), 4.67 (1H, d, J = 1.4 Hz), 5.54 (1H, dd, J = 4.6, 2.0 Hz), 6.82 (1H, d, J = 8.5 Hz), 7.33 (3H, m), 7.72 (1H, d, J = 3.2 Hz). ¹³C NMR: δ 172.8, 164.6, 156.8, 143.1, 121.6, 119.6, 119.4, 114.7, 82.6, 67.4, 63.6, 58.0, 55.6. IR (CHCl₃, cm⁻¹): ν 3314, 1742. MS (CI), m/z : 321 ($M^+ + 1$, 100), 320 (M^+ , 15). (Anal. Calcd for C₁₅H₁₆N₂O₄S: C, 56.24; H, 5.03; N, 8.74. Found: C, 56.36; H, 5.00; N, 8.78). The more polar fraction contained

α -alkoxy carboxamide (+)-**2a** (27 mg, 52%) as a colorless oil. (Anal. Calcd for $C_{15}H_{16}N_2O_4S$: C, 56.35; H, 5.00; N, 8.70. Found: C, 56.44; H, 5.04; N, 8.65).

Reaction between aldehyde (+)-4a and TMST. Preparation of α -alkoxy carboxamide (–)-2a and β -lactam (+)-5b. From 20 mg (0.085 mmol) of 4-formyl- β -lactam (+)-**4a**, and after chromatography of the residue eluting with EtOAc/hexanes (1:3) gave two fractions. The less polar fraction contained β -lactam (+)-**5b** (5 mg, 15%) as a colorless oil. $[\alpha]_D = +10.4$ (*c* 0.3, $CHCl_3$). 1H -NMR: δ 0.00 (9H, s), 3.26 (3H, s), 3.79 (3H, s), 4.32 (1H, dd, *J* = 6.8, 1.7 Hz), 4.62 (1H, d, *J* = 1.7 Hz), 5.23 (1H, d, *J* = 6.6 Hz), 6.82 (2H, d, *J* = 9.0 Hz), 7.32 (1H, d, *J* = 3.6 Hz), 7.35 (2H, d, *J* = 9.0 Hz), 7.78 (1H, d, *J* = 3.6 Hz). IR ($CHCl_3$, cm^{-1}): ν 1744. MS (CI), *m/z*: 321 ($M^+ + 1$, 100), 320 (M^+ , 15). (Anal. Calcd for $C_{18}H_{24}N_2O_4SSi$: C, 54.96; H, 6.19; N, 7.11. Found: C, 54.82; H, 6.14; N, 7.16). The more polar fraction contained α -alkoxy carboxamide (–)-**2a** (14 mg, 50%) as a pale yellow solid. Mp: 89–90 °C (hexanes/ethyl acetate). $[\alpha]_D = -52.1$ (*c* 0.4, $CHCl_3$). (Anal. Calcd for $C_{15}H_{16}N_2O_4S$: C, 56.35; H, 5.00; N, 8.70. Found: C, 56.45; H, 5.04; N, 8.65).

Reaction between aldehyde (+)-4b and TMST. Preparation of α -alkoxy carboxamide (–)-2e and β -lactam (+)-5c. From 42 mg (0.16 mmol) of 4-formyl- β -lactam (+)-**4b**, and after chromatography of the residue eluting with EtOAc/hexanes (1:1) gave two fractions. The less polar fraction contained β -lactam (+)-**5c** (6 mg, 10%) as a colorless oil. $[\alpha]_D = +27.5$ (*c* 0.4, $CHCl_3$). δ 3.13 (3H, s), 3.82 (3H, s), 3.91 (3H, s), 4.51 (1H, t, *J* = 1.9 Hz), 4.79 (1H, d, *J* = 1.6 Hz), 5.26 (1H, d, *J* = 2.0 Hz), 6.54 (2H, m), 7.38 (1H, d, *J* = 3.2 Hz), 7.42 (2H, d, *J* = 9.0 Hz), 7.81 (1H, d, *J* = 3.2 Hz). ^{13}C NMR: δ 170.2, 166.2, 155.0, 143.4, 128.5, 119.6, 116.7, 105.7, 100.1, 82.8, 69.1, 67.8, 58.3. IR ($CHCl_3$, cm^{-1}): ν 3312, 1746. MS (CI), *m/z*: 351 ($M^+ + 1$, 100), 350 (M^+ , 11). (Anal. Calcd for $C_{16}H_{18}N_2O_5S$: C, 54.84; H, 5.18; N, 7.99. Found: C, 54.94; H, 5.22; N, 7.94). The more polar fraction contained α -alkoxy carboxamide (–)-**2e** (28 mg, 50%) as a pale yellow oil. $[\alpha]_D = -27.1$ (*c* 0.7, $CHCl_3$). (Found: C, 54.73; H, 5.14; N, 8.05. Calcd for $C_{16}H_{18}N_2O_5S$: C, 54.63; H, 5.10; N, 8.10).