Supporting Information

Lewis Acid-Catalyzed Intermolecular [4+2] Cycloaddition of 3-Alkoxycyclobutanones to Aldehydes and Ketones

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1. General

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Shimadzu FTIR-8100. ^1H NMR spectra were recorded on a JEOL JNM EX270 (270 MHz) or a JEOL JNM GSX500 (500 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. ^{13}C NMR spectra were recorded on a JEOL JNM EX270 (270 MHz) or a JEOL JNM GSX500 (500 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane with the solvent resonance as the internal standard CDCl_3 . High resolution mass spectra (HRMS) were recorded on a JEOL JMS-SX-102A mass spectrometer (EI). Elemental analyses were carried out on a Yanaco CHN Corder MT-5. Analytical TLC was performed on Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Silica-gel column chromatography was carried out on silica gel 60N (Kanto Kagaku Co., Ltd., spherical, neutral, 63–210 μm). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. Dichloromethane was distilled under argon from calcium hydride before use. Diisopropyl ether was distilled under argon from sodium/benzophenone ketyl before use. All cycloaddition reactions were carried out under argon in dried glassware with magnetic stirring. Cyclobutanone **11a** was prepared by the reported procedure.¹

2. Experimental procedures and characterization data

2.1 Preparation of cyclobutanones

2.1.1 Preparation of cyclobutanone **1a**

To a suspension of **26**² (501 mg, 5.1 mmol) and zinc (1.67 g, 25.5 mmol) in dry ether (20 mL) was added dropwise a solution of trichloroacetyl chloride (2.8 mL, 25.1 mmol) in dry ether (15 mL) for 30 min at $15-20\text{ }^\circ\text{C}$ under ultrasound irradiation,³ and the sonication continued for 1 h at the same temperature. After quenching with water, the mixture was filtered through Celite and the filtrate was washed with water, saturated sodium hydrogen carbonate solution, and brine, dried over anhydrous sodium sulfate, filtrated, and concentrated. The crude product was purified by column chromatography on silica gel (25 g, hexane-ethyl acetate = 20/1) to afford **27** (783 mg, 3.75 mmol, 73%) as

¹ Samuel, S. P.; Niu, T.-q.; Erickson, K. L. *J. Am. Chem. Soc.* **1989**, *111*, 1429.

² Weber, G. F.; Hall, S. S. *J. Org. Chem.* **1979**, *44*, 364.

³ Mehta, G.; Rao, H. S. P. *Synth. Commun.* **1985**, *15*, 991.

a yellow oil: ^1H NMR (500 MHz, CDCl_3) δ 1.51 (s, 3H), 1.55-1.71 (m, 3H), 2.11-2.17 (m, 1H), 3.63-3.68 (m, 1H), 4.07-4.11 (m, 1H), 4.31 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 20.1, 23.3, 27.5, 57.8, 63.9, 81.5, 87.1, 200.3; IR (CHCl_3 , cm^{-1}) 1806, 1209; HRMS calcd for $\text{C}_8\text{H}_{10}\text{O}_2\text{Cl}_2$ (m/z) 208.00579, found 208.00614.

To a solution of tributyltin hydride (5.5 mL, 20.4 mmol) in cyclohexane (10 mL) was added at 80 °C a solution of **27** (1.42 g, 6.79 mmol) and AIBN (34.0 mg, 0.21 mmol) in cyclohexane (13 mL) for 2 h.⁴ After concentration, purification by column chromatography on silica gel and potassium fluoride (hexane-ethyl acetate = 10/1) and by Kugelrohr distillation (140 °C/20 mmHg) gave **1a** (514 mg, 3.67 mmol, 54%) as a colorless oil: ^1H NMR (500 MHz, CDCl_3) δ 1.21 (s, 3H), 1.38 (ddd, J = 5.6, 10.5, 13.9 Hz, 1H), 1.49-1.64 (m, 2H), 2.08 (td, J = 4.9, 13.9 Hz, 1H), 2.87 (td, J = 1.5, 17.3 Hz, 1H), 3.33-3.40 (m, 2H), 3.84 (td, J = 3.9, 11.2 Hz, 1H), 4.06 (d, J = 5.6 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 21.6, 21.7, 26.5, 51.4, 60.5, 64.2, 70.2, 211.3; IR (CHCl_3 , cm^{-1}) 1781, 1076; HRMS calcd for $\text{C}_8\text{H}_{12}\text{O}_2$ (m/z) 140.08373, found 140.08378.

2.1.2 Preparation of cyclobutanone **1b**

Compound **29** (8.05 g, 28.2 mmol, 88%) was prepared from **28**⁵ (5.56 g, 31.9 mmol) by the procedure described in the preparation of **27**. Compound **29**: colorless cubic crystals; mp 61.0-61.5 °C; ^1H NMR (500 MHz, CDCl_3) δ 1.48-1.57 (m, 1H), 1.61-1.68 (m, 1H), 1.81 (ddd, J = 4.6, 7.1, 14.0 Hz, 1H), 2.04 (ddd, J = 4.6, 9.3, 14.2 Hz, 1H), 3.08 (d, J = 14.2 Hz, 1H), 3.15 (d, J = 13.9 Hz, 1H), 3.64 (ddd, J = 4.6, 7.1, 11.2 Hz, 1H), 4.11 (ddd, J = 4.6, 6.8, 11.2 Hz, 1H), 4.48 (s, 1H), 7.15-7.17 (m, 2H), 7.25-7.34 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 20.0, 25.9, 41.8, 62.3, 63.8, 79.1, 87.1, 127.4, 128.7, 130.0, 135.3, 199.5; IR (CHCl_3 , cm^{-1}) 1802, 1167; Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{Cl}_2\text{O}_2$: C, 58.97; H, 4.95. Found: C, 58.99, H, 5.02.

⁴ Montaigne, L. G. R.; Roussel, A.; Vanlierde, H.; Mollet, P. *Tetrahedron* **1971**, 27, 615.

⁵ Barrett, A. G.; Betts, M. J.; Fenwick, A. *J. Org. Chem.* **1985**, 50, 169.

To a stirred mixture of **29** (8.04 g, 28.2 mmol) and ammonium chloride (7.55 g, 141 mmol) in methanol (120 mL) was added zinc-copper couple⁶ (5.57 g) at room temperature. Exothermic reaction proceeded and the reaction mixture was stirred for 1 h. The reaction mixture was filtered through Celite pad, and filtrate was concentrated. The residue was diluted with ethyl acetate, and the ethyl acetate solution was washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (100 g, hexane-ethyl acetate = 10/1 then 8/1) to afford **1b** (4.93 g, 22.8 mmol, 81%) as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 1.47-1.61 (m, 3H), 1.92-1.99 (m, 1H), 2.85 (d, J = 14.0 Hz, 1H), 2.89 (d, J = 14.0 Hz, 1H), 2.91 (dd, J = 3.1, 17.7 Hz, 1H), 3.01 (dd, J = 6.1, 17.1 Hz, 1H), 3.34-3.38 (m, 1H), 3.78-3.83 (m, 1H), 4.25 (dd, J = 3.1, 6.7 Hz, 1H), 7.13-7.15 (m, 2H), 7.22-7.30 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 21.3, 24.9, 41.2, 51.3, 63.6, 64.7, 67.9, 126.8, 128.4, 129.8, 136.4, 210.4; IR (CHCl₃, cm⁻¹) 1779, 1073; HRMS calcd for C₁₄H₁₆O₂ (m/z) 216.11503, found 216.11537.

2.1.3 Preparation of cyclobutanone **11b**

To a stirred solution of cyclohexanecarbonyl chloride (10 mL, 73.7 mmol) in acetonitrile (10 mL) was added at room temperature a solution of triethylamine (12.4 mL, 89.0 mmol) and ethyl vinyl ether (12.6 mL, 132 mmol) in acetonitrile (30 mL) for 40 min, and the mixture was refluxed for 3 h. After cooling to room temperature, precipitate was filtered and concentrated. Kugelrohr distillation (150 °C/16 mmHg) of the residue gave **11b** (7.66 g, 42.0 mmol, 57%) as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 1.23 (t, J = 7.1 Hz, 3H), 1.34-1.39 (m, 1H), 1.47-1.61 (m, 5H), 1.66-1.78 (m, 4H), 2.95 (dd, J = 5.4, 17.8 Hz, 1H), 3.15 (dd, J = 6.8, 17.8 Hz, 1H), 3.47-3.57 (m, 2H), 3.82 (dd, J = 5.1, 6.8 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 15.2, 22.5, 22.8, 25.6, 26.4, 32.1, 49.6, 65.3, 67.5, 73.5, 213.3; IR (CHCl₃, cm⁻¹) 1771, 1451, 1188, 1121; HRMS calcd for C₁₁H₁₈O₂ (m/z) 182.13068, found 182.13046.

⁶ Smith, R. D.; Simmons, H. E. *Org. Synth.* **1961**, 41, 72.

2.2 Self-cycloaddition of cyclobutanone **1a** (Scheme 1)

To a stirred solution of **1a** (42.7 mg, 0.30 mmol) in dry dichloromethane (1.5 mL) was added trimethylsilyl triflate (70 μL , 0.39 mmol) at 0 $^\circ\text{C}$. The reaction mixture was stirred at 0 $^\circ\text{C}$ for 30 min and at room temperature for 1 h. The reaction was quenched with saturated sodium hydrogen carbonate solution, and the mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography on silica gel (4.5 g, benzene-ethyl acetate = 25/1 then 15/1) to afford **5** (24.4 mg, 87.0 μmol , 58%, as a mixture of diastereomers (85:15)) and **6** (4.0 mg, 25.3 μmol , 8%).

Compound **5**: ^1H NMR (500 MHz, CDCl_3 , the major diastereomer) δ 1.10 (s, 3H, Me), 1.18 (s, 3H, Me), 1.16-1.65 (m, 5H, 9-2H, 4'-2H, 10-H equatorial, 5'-H equatorial), 1.95 (dd, $J = 7.3, 11.2$ Hz, 8'-H), 2.22-2.32 (m, 2H, 10-H axial, 5'-H axial), 4.64 (d, $J = 15.1$ Hz, 3-H), 2.62 (t, $J = 10.5$ Hz, 8'-H), 2.84 (d, $J = 15.1$ Hz, 3-H), 3.55-3.69 (m, 4H, 1'-H, 8-H equatorial, 3'-2H), 4.00-4.04 (m, 1H, 8-H axial), 4.61 (s, 1H, 6-H); ^{13}C NMR (125 MHz, CDCl_3 , the major diastereomer) δ 19.8, 21.3, 21.6, 26.5, 29.9, 35.6, 44.1, 45.7, 49.0, 61.6, 64.0, 69.4, 73.6, 74.0, 100.4, 210.5; IR (CHCl_3 , cm^{-1}) 1711, 1115, 1034; HRMS calcd for $\text{C}_{16}\text{H}_{24}\text{O}_4$ (m/z) 280.16746, found 280.16717.

Compound **6**: ^1H NMR (500 MHz, CDCl_3) δ 1.12 (d, $J = 7.1$ Hz, 3H), 1.38-1.46 (m, 1H), 1.60-1.69 (m, 2H), 1.71-1.78 (m, 1H), 2.15 (s, 3H), 2.54 (sext, $J = 6.8$ Hz, 1H), 4.16 (dt, $J = 0.5, 6.6$ Hz, 2H), 8.06 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 16.3, 26.2, 28.1, 28.8, 46.6, 63.7, 161.0, 212.0; IR (CHCl_3 , cm^{-1}) 1720, 1716; HRMS calcd for $\text{C}_8\text{H}_{14}\text{O}_3$ (m/z) 158.09430, found 158.09515.

2.3 Cycloaddition of tetrahydropyran-fused cyclobutanone **1b** to aldehydes and ketones (Table 1, entry 4)

To a stirred solution of **1b** (134 mg, 0.62 mmol) and pivalaldehyde (43.4 mg, 0.50 mmol) in diisopropyl ether (2.0 mL) was added boron trifluoride etherate (75 μ L, 0.61 mmol) at room temperature. The reaction mixture was stirred at room temperature for 23 h, and the reaction was quenched with saturated sodium hydrogen carbonate solution. The mixture was extracted with ethyl acetate, and organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by preparative thin-layer chromatography on silica gel (hexane-ether = 3/1) to afford **8** (133.7 mg, 0.44 mmol, 88%).

(1*S,4*S**,6*R**)-1-Benzyl-4-phenyl-5,7-dioxabicyclo[4.4.0]decan-2-one (7)**

The relative configuration was determined by NOE experiments and similarity in ^1H NMR spectrum of **8**.

Compound **7**: colorless oil: ^1H NMR (500 MHz, CDCl_3) δ 1.43-1.53 (m, 2H, 9-H and 10-H equatorial), 1.71-1.80 (m, 1H, 9-H), 2.24-2.30 (m, 1H, 10-H axial), 2.57 (dd, $J = 3.4, 16.4$ Hz, 1H, 3-H equatorial), 2.91 (d, $J = 13.4$ Hz, 1H, benzyl), 2.97 (dd, $J = 12.2, 16.5$ Hz, 1H, 3-H axial), 3.27 (d, $J = 13.4$ Hz, 1H, benzyl), 3.61 (ddd, $J = 4.9, 6.1, 11.0$ Hz, 1H, 8-H equatorial), 4.11 (ddd, $J = 3.7, 7.9, 11.6$ Hz, 1H, 8-H axial), 4.79 (dd, $J = 3.4, 12.5$ Hz, 1H, 4-H), 4.87 (s, 1H, 6-H), 7.22-7.40 (m, 10H, aromatic); ^{13}C NMR (67.5 MHz, CDCl_3) δ 21.4, 28.8, 37.5, 45.5, 52.8, 63.7, 72.8, 99.0, 125.9, 126.6, 127.3, 128.2, 128.7, 130.9, 133.6, 136.2, 139.8, 209.2; IR (CHCl_3 , cm^{-1}) 1713, 1493, 1221, 1142, 1069, 1015; HRMS calcd for $\text{C}_{21}\text{H}_{21}\text{O}_3\text{Cl}$ (m/z) 356.11793, found 356.11838.

(1*S,4*S**,6*R**)-1-Benzyl-4-*tert*-butyl-5,7-dioxabicyclo[4.4.0]decan-2-one (8)**

8

The relative configuration was determined by X-ray crystallography.

Compound **8**: Colorless prisms: mp 95.5-96.0 °C; ^1H NMR (500 MHz, CDCl_3) δ 0.92 (s, 9H, *tert*-butyl), 1.38-1.48 (m, 2H), 1.78-1.88 (m, 1H), 2.07-2.11 (m, 1H), 2.24 (dd, $J = 3.7, 16.5$ Hz, 1H, 3-H equatorial), 2.64 (dd, $J = 12.2, 16.5$ Hz, 1H, 3-H axial), 2.93 (d, $J = 13.4$ Hz, 1H, benzyl), 3.23 (d, $J = 13.4$ Hz, 1H, benzyl), 3.28 (dd, $J = 3.1, 12.2$ Hz, 1H, 4-H axial), 3.62 (dt, $J = 11.6, 4.3$ Hz, 1H, 8-H equatorial), 4.04 (dt, $J = 3.7, 11.0$ Hz, 1H, 8-H axial), 4.65 (s, 1H, 6-H), 7.18-7.28 (m, 5H, aromatic); ^{13}C NMR (125 MHz, CDCl_3) δ 20.9, 25.3, 28.4, 34.2, 36.4, 38.6, 52.9, 62.2, 78.2, 97.9, 126.4, 128.1, 131.0, 136.9, 211.3; IR (CHCl_3 , cm^{-1}) 1705, 1061; HRMS calcd for $\text{C}_{19}\text{H}_{26}\text{O}_3$ (m/z) 302.18820, found 302.18844. Anal. Calcd for $\text{C}_{19}\text{H}_{26}\text{O}_3$: C, 75.46; H, 8.63. Found: C, 75.35, H, 8.81.

(1*S,4*S**,6*R**)-1-Benzyl-4-methyl-4-phenyl-5,7-dioxabicyclo[4.4.0]decan-2-one (9)**

9

Compound **9** was obtained as the major diastereomer, and its relative configuration was determined by NOE experiments.

Compound **9**: colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 1.27 (s, 3H, Me), 1.44-1.56 (m, 2H), 1.83-1.92 (m, 1H), 2.07 (m, 1H, 10-H axial), 2.59 (d, $J = 15.6$ Hz, 1H, 3-H equatorial), 3.03 (d, $J = 14.9$ Hz, 1H, 3-H axial), 3.06 (d, $J = 12.9$ Hz, 1H, benzyl), 3.27 (d, $J = 13.4$ Hz, 1H, benzyl), 3.68 (m, 1H, 8-H equatorial), 4.10 (dt, $J = 2.9, 10.7$ Hz, 1H, 8-H axial), 5.13 (s, 1H, 6-H), 7.20-7.36 (m, 8H, aromatic), 7.45-7.47 (m, 2H, aromatic); ^{13}C NMR (125 MHz, CDCl_3) δ 20.9, 28.3, 28.7, 37.0, 49.5, 52.4, 61.8, 75.4, 94.8, 124.1, 126.6, 127.0, 128.2, 128.3, 131.0, 136.8, 147.3, 210.5; IR (CHCl_3 , cm^{-1}) 1707, 1210; HRMS calcd for $\text{C}_{22}\text{H}_{24}\text{O}_3$ (m/z) 336.17255, found 336.17249.

(1*S,4*R**,6*R**)-1-Benzyl-4-methyl-4-phenyl-5,7-dioxabicyclo[4.4.0]decan-2-one (9')**

Compound **9'** was obtained as the minor diastereomer, and its relative configuration was determined by NOE experiments.

Compound **9'**: colorless plates; mp 112.5-113.5 °C; ^1H NMR (500 MHz, CDCl_3) δ 1.47-1.55 (m, 2H), 1.59 (s, 3H, Me), 1.78-1.87 (m, 1H), 2.11-2.16 (m, 1H, H-10 axial), 2.82 (d, $J = 13.4$ Hz, 1H, benzyl), 2.90 (d, $J = 15.9$ Hz, 1H, 3-H equatorial), 2.97 (d, $J = 15.9$ Hz, 1H, 3-H axial), 2.98 (d, $J = 13.7$ Hz, 1H, benzyl), 3.66 (m, 1H, 8-H equatorial), 4.11 (m, 1H, 8-H axial), 6.96-7.25 (m, 10H, aromatic); ^{13}C NMR (125 MHz, CDCl_3) δ 20.9, 28.4, 33.2, 37.0, 47.6, 52.0, 62.1, 76.0, 95.8, 124.9, 126.3, 127.2, 127.9, 128.5, 130.5, 136.2, 144.4, 210.4; IR (CHCl_3 , cm^{-1}) 1710, 1210; Anal. Calcd for $\text{C}_{22}\text{H}_{24}\text{O}_3$: C, 78.54; H, 7.19. Found: C, 78.55, H, 7.30.

Compound **10**: colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 1.22-1.34 (m, 3H), 1.37-1.54 (m, 6H), 1.58-1.83 (m, 4H), 2.08 (ddd, $J = 4.2, 8.8, 12.9$ Hz, 1H, 10-H axial), 2.30 (d, $J = 15.6$ Hz, 1H, 3-H equatorial), 2.59 (d, $J = 15.6$ Hz, 1H, 3-H axial), 2.98 (d, $J = 13.7$ Hz, 1H, benzyl), 3.07 (d, $J = 13.4$ Hz, 1H, benzyl), 3.05 (ddd, $J = 3.7, 6.3, 11.2$ Hz, 1H, 8-H equatorial), 4.00 (ddd, $J = 3.7, 7.8, 11.1$ Hz, 1H, 8-H axial), 4.90 (s, 1H, 6-H), 7.17-7.26 (m, 5H, aromatic); ^{13}C NMR (125 MHz, CDCl_3) δ 21.4, 21.7, 21.9, 25.2, 28.2, 37.1, 38.9, 39.5, 48.7, 52.4, 63.2, 74.9, 96.9, 126.6, 128.1, 130.6, 136.4, 211.1; IR (CHCl_3 , cm^{-1}) 1707; HRMS calcd for $\text{C}_{20}\text{H}_{26}\text{O}_3$ (m/z) 314.18820, found 314.18781.

2.4 Cycloaddition of 3-ethoxycyclobutanone **11a** to benzaldehyde to afford **12**

To a stirred solution of **11a** (86 mg, 0.60 mmol), benzaldehyde (48.3 mg, 0.455 mmol) in dry dichloromethane (2.5 mL) was added boron trifluoride etherate (63 μL , 0.50 mmol) at $-45\text{ }^\circ\text{C}$, and the reaction mixture was stirred at the same temperature for 1 h. The reaction was quenched with saturated aqueous sodium hydrogencarbonate solution, and the mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by thin layer chromatography on silica gel (benzene/ethyl acetate = 10:1) to afford **12** (105.0 mg, 0.423 mmol, 93%), **13** (2.7 mg, 0.011 mmol, 2.4 %), and **14** (0.5 mg, 2.47 μmol , 0.5%).

Compound **12** was obtained as a mixture of diastereomers (76:24): ^1H NMR (500 MHz, CDCl_3 , the major diastereomer) δ 0.95 (s, 3H), 1.02 (s, 3H), 1.25 (t, $J = 7.1$ Hz, 3H), 2.66 (dd, $J = 2.9, 14.6$ Hz, 1H), 2.88 (dd, $J = 9.5, 14.6$ Hz, 1H), 3.58 (qd, $J = 7.1, 9.5$ Hz, 1H), 3.99 (qd, $J = 7.1, 9.8$ Hz, 1H), 4.32 (s, 1H), 4.77 (dd, $J = 2.9, 9.8$ Hz, 1H), 7.31-7.37 (m, 5H); ^1H NMR (500 MHz, CDCl_3 , the minor diastereomer) δ 0.96 (s, 3H), 1.03 (s, 3H), 1.16 (t, $J = 6.8$ Hz, 3H), 2.50 (dd, $J = 1.2, 14.9$ Hz, 1H), 3.04 (dd, $J = 4.9, 14.6$ Hz, 1H), 3.44 (qd, $J = 6.8, 10.0$ Hz, 1H), 3.64 (qd, $J = 4.2, 7.1$ Hz, 1H), 4.86 (s, 1H), 5.32 (d, $J = 4.9$ Hz, 1H), 7.31-7.37 (m, 5H); ^{13}C NMR (125 MHz, CDCl_3 , the major diastereomer) δ 15.1, 19.3, 19.5, 45.1, 49.6, 64.8, 80.6, 100.2, 127.6, 127.9, 128.1, 136.4, 136.7, 210.0; ^{13}C NMR (125 MHz, CDCl_3 , the minor diastereomer) δ 14.8, 19.3, 19.5, 43.1, 50.1, 62.9, 76.9, 97.8, 127.6, 127.8, 136.7, 209.5; IR (CHCl_3 , cm^{-1}) 1720, 1711, 1383, 1113, 1053; HRMS calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3$ (m/z) 248.14125, found 248.14085.

2.5 One-pot synthesis of dihydro- γ -pyrone derivative **14** from cyclobutanone **11a**

To a stirred solution of **11a** (119.9 mg, 0.843 mmol) and benzaldehyde (71.6 mg, 0.675 mmol) in dichloromethane

(3 mL) was added boron trifluoride etherate (169 μ L, 1.346 mmol) at $-45\text{ }^{\circ}\text{C}$, and the reaction was stirred at $-45\text{ }^{\circ}\text{C}$ for 1 h and then at room temperature for 1 h. The reaction was quenched with saturated aqueous sodium hydrogencarbonate solution, and the mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by preparative thin layer chromatography on silica gel (hexane/ethyl acetate = 3:1) to afford **12** (0.7 mg, 2.82 μ mol, 0.4%) and **14** (126.2 mg, 0.623 mmol, 92%).

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Compound **14**: colorless fine needles; mp $82.2\text{--}83.2\text{ }^{\circ}\text{C}$ (hexane); ^1H NMR (500 MHz, CDCl_3) δ 0.99 (s, 3H), 1.00 (s, 3H), 5.11 (s, 1H), 5.46 (d, $J = 5.9$ Hz, 1H), 7.35–7.41 (m, 5H), 7.47 (d, $J = 5.9$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 18.1, 19.3, 45.1, 88.7, 105.4, 127.8, 128.0, 128.6, 134.9, 162.2, 198.5; IR (CHCl_3 , cm^{-1}) 1669, 1603, 1466, 1406, 1273, 1237, 1159, 1042; HRMS calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$ (m/z) 202.09938, found 202.09957; Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$: C, 77.20; H, 6.98. Found: C, 77.10, H, 7.08.

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Compound **15**: colorless fine needles; mp $46.0\text{--}47.0\text{ }^{\circ}\text{C}$ (hexane); ^1H NMR (500 MHz, CDCl_3) δ 0.91 (s, 3H), 1.08 (s, 3H), 1.74 (s, 3H), 5.44 (d, $J = 6.1$ Hz, 1H), 7.29 (d, $J = 5.9$ Hz, 1H), 7.31–7.40 (m, 3H), 7.47–7.51 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 17.7, 19.1, 22.9, 48.6, 89.9, 104.4, 126.6, 127.5, 127.7, 139.8, 159.0, 198.4; IR (CHCl_3 , cm^{-1}) 1673, 1607, 1275, 1159, 1084; HRMS calcd for $\text{C}_{14}\text{H}_{16}\text{O}_2$ (m/z) 216.11503, found 216.11485.

16

Compound **16**: colorless oil; ^1H NMR (500 MHz, CDCl_3) δ 1.08 (s, 6H), 1.12–1.22 (m, 1H), 1.32–1.38 (m, 2H), 1.55–1.61 (m, 4H), 1.68–1.74 (m, 1H), 2.08 (dd, $J =$, 2H), 5.32 (d, $J =$, 1H), 7.17 (d, $J =$, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 19.4, 21.1, 25.3, 27.5, 47.9, 86.8, 104.9, 158.8, 199.2; IR (CHCl_3 , cm^{-1}) 1665, 1605, 1267, 1153, 1071, 909; HRMS calcd for $\text{C}_{14}\text{H}_{16}\text{O}_2$ (m/z) 216.11503, found 216.11485.

17

Compound **17**: colorless plates; mp 76.2-77.2 °C; ^1H NMR (500 MHz, CDCl_3) δ 1.02-1.09 (m, 1H), 1.21-1.44 (m, 4H), 1.48-1.56 (m, 2H), 1.88-2.04 (m, 2H), 5.21 (s, 1H), 5.37 (d, $J = 5.9$ Hz, 1H), 7.27 (d, $J = 5.9$ Hz, 1H), 7.33-7.38 (m, 5H); ^{13}C NMR (125 MHz, CDCl_3) δ 21.2, 22.2, 25.5, 26.7, 30.8, 46.9, 88.6, 105.4, 128.0, 128.6, 128.7, 135.3, 160.2, 199.4; IR (CHCl_3 , cm^{-1}) 1667, 1607, 1455, 1401, 1254; HRMS calcd for $\text{C}_{16}\text{H}_{18}\text{O}_2$ (m/z) 242.13068, found 242.13103.

18

Compound **18**: colorless needles; mp 96.3-97.3 °C (hexane); ^1H NMR (500 MHz, CDCl_3) δ 1.01-2.10 (m, 20H), 5.22 (d, $J = 5.9$ Hz, 1H), 7.06 (d, $J = 5.6$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 21.1, 22.0, 23.2, 25.4, 25.9, 26.7, 28.9, 51.0, 88.0, 105.1, 157.4, 200.8; IR (CHCl_3 , cm^{-1}) 1663, 1607, 1451, 1402, 1265, 1032; Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_2$: C, 76.88; H, 9.46. Found: C, 76.85, H, 9.65.

The regioisomer **18'** was obtained in 6% isolated yield under the conditions of entry 4 in Table 2.

18'

3. Crystal structure of 8

Figure S1. ORTEP Figure of Compound **8**.

4. ^1H and ^{13}C NMR spectra of new compounds