



TITLE:

An Enantioselective Synthesis of 2-Imidazolidinones through Bifunctional Thiourea-Catalyzed Tandem Mannich/Cyclization of Isocyanatomalonate Diester

AUTHOR(S):

Kobayashi, Yusuke; Yoshida, Takuma; Uno, Takuya; Tsukano, Chihiro; Takemoto, Yoshiji

CITATION:

Kobayashi, Yusuke ...[et al]. An Enantioselective Synthesis of 2-Imidazolidinones through Bifunctional Thiourea-Catalyzed Tandem Mannich/Cyclization of Isocyanatomalonate Diester. *Heterocycles* 2017, 95(2): 980-993

ISSUE DATE:

2017

URL:

<http://hdl.handle.net/2433/284119>

RIGHT:

© 2017 The Japan Institute of Heterocyclic Chemistry; This article is deposited under the publisher's permission.

HETEROCYCLES, Vol. 95, No. , 2017, pp. -. © 2017 The Japan Institute of Heterocyclic Chemistry
 Received, 2nd September, 2016, Accepted, 14th October, 2016, Published online, .
 DOI: 10.3987/COM-16-S(S)68

AN ENANTIOSELECTIVE SYNTHESIS OF 2-IMIDAZOLIDINONES THROUGH BIFUNCTIONAL THIOUREA-CATALYZED TANDEM MANNICH/CYCLIZATION OF ISOCYANATOMALONATE DIESTER

Yusuke Kobayashi, Takuma Yoshida, Takuya Uno, Chihiro Tsukano, and Yoshiji Takemoto*

Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan; E-mail: takemoto@pharm.kyoto-u.ac.jp

Abstract – A chiral bifunctional thiourea-catalyzed Mannich reaction of diethyl 2-isocyanatomalonate with *N*-sulfonylimines was described. The tandem cyclization proceeded smoothly after Mannich reaction, directly furnishing chiral 2-imidazolidinones in 72–99% yields with 83–98% ees. Sterically demanding sulfonyl group was crucial for aliphatic imines to afford the corresponding product in high enantioselectivity.

INTRODUCTION

Chiral 2-imidazolidinones are found in various natural product and biologically active compounds¹ (Figure 1). In addition, they can be considered to be 1,2-diamine or α,β -diamino acid equivalents, and utilized as useful chiral building blocks.² Furthermore, several 2-imidazolidinones have been used as chiral auxiliaries for stereoselective alkylation and aldol reactions.³ Therefore, continuous effort has been devoted to synthesis of this important scaffold in optically active form.⁴

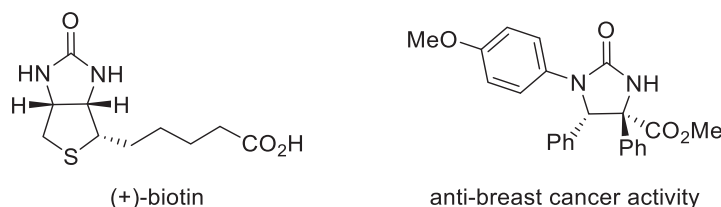
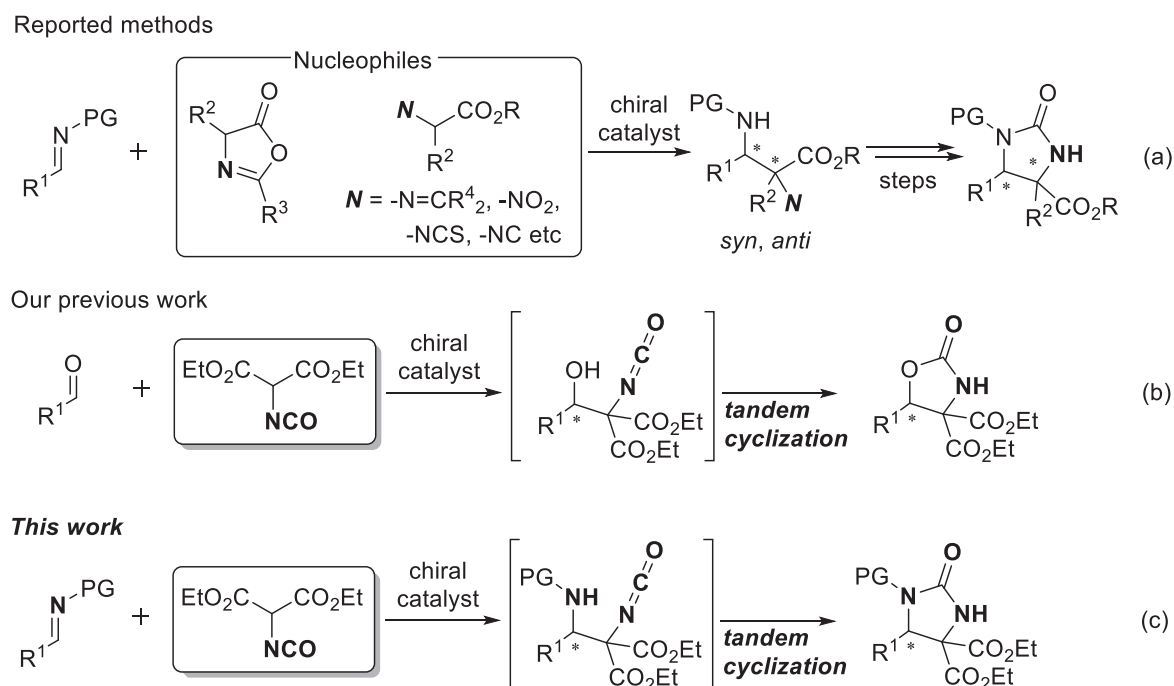


Figure 1. Examples of bioactive compounds bearing chiral 2-imidazolidinone scaffold

Among them, catalytic asymmetric Mannich reactions of azlactones,⁵ glycine Schiff base derivatives,⁶ α -nitro esters,⁷ α -isothiocyano carboxylic acid derivatives,⁸ α -isocyano esters,⁹ and α -azidoamide¹⁰ are one of the most efficient approaches for the construction of two continuous stereocenters (Scheme 1a).

However, these methods require the additional steps, such as deprotection, reduction, and cyclization, for the construction of imidazolidinones.² We envisioned that the utilization of isocyanatomalonate diester would enable a straightforward synthesis of 2-imidazolidinone, since the cyclization would be expected to occur after Mannich reaction (Scheme 1c), according to our previously reported tandem aldol/cyclization reaction¹¹ (Scheme 1b).

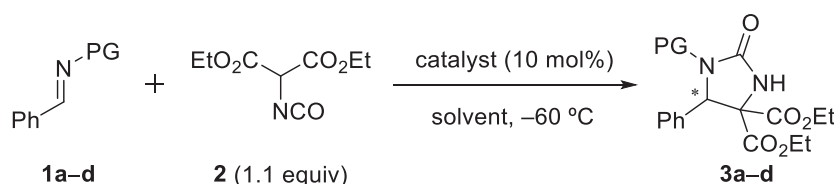


Scheme 1. Synthesis of chiral 2-imidazolidinones through Mannich reaction

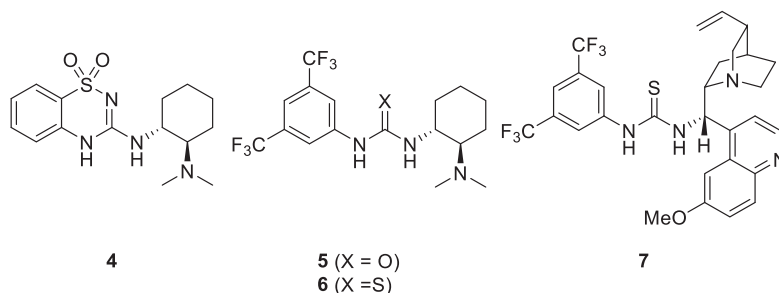
RESULTS AND DISCUSSION

We first investigated the reaction of *N*-tosylimine **1a** with diethyl 2-isocyanatomalonate **2** in the presence of various bifunctional hydrogen bond (HB)-donor catalysts, including benzothiadiazine,¹² urea, and thiourea¹³ (Table 1). As expected, when the catalysts **4–6**, bearing different HB-donating abilities,¹³ were employed at $-60\text{ }^{\circ}\text{C}$,¹¹ the tandem reaction proceeded efficiently within three hours to furnish the desired imidazolidinone **3a** in high yields (89–97%) with similar enantioselectivities (60–64% ees) (entries 1–3), indicating that the HB-donating abilities of the catalysts had little influence on the present tandem reaction. We next screened the solvent of this tandem Mannich/cyclization using thiourea catalyst **6** (entries 4–7). It was found that toluene slightly improved the enantiomeric excess (84% ee), albeit in somewhat lower reaction rate (76% yield in 60 hours), presumably due to the poor solubility of the imine **1a** in toluene (entry 6). The addition of CH_2Cl_2 as co-solvent (toluene/ CH_2Cl_2 = 9/1) improved the solubility and reaction rate (97% yield in 12 hours) while maintaining the selectivity (entry 7). Utilizing this co-solvent system, we next screened several chiral thiourea catalysts, and found that the cinchona

alkaloid-derived thiourea¹³ **7** gave the best result (96% yield, 94% ee) in terms of the chemical yield and selectivity (entry 8). In contrast to our previous work on the direct Mannich reaction,¹⁴ *N*-Boc-imine **1d** resulted in worse selectivity (entry 11, 42% ee) than the results of *N*-sulfonylimines **1a–c** (entries 8–10, 88–97% ees). The decreased selectivity of **3d** might be explained by the inefficient cyclization of the *N*-Boc-amine intermediate due to its relatively poor nucleophilicity to cause retro-Mannich reaction. On the other hand, the *N*-sulfonyl groups played important roles for the efficient Mannich reaction as well as the subsequent cyclization. The absolute configuration of **3a** and **3b** could be determined in analogy to the reported data.¹⁵

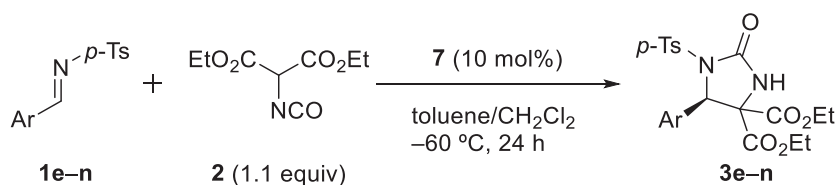
 Table 1. Optimization of the reaction conditions^a


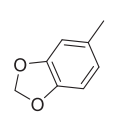
Entry	1 (PG)	catalyst	solvent	time (h)	yield (%) ^b	ee (%) ^c
1	1a (<i>p</i> -Ts)	4	CH ₂ Cl ₂	3	89	60 (<i>S</i>)
2	1a	5	CH ₂ Cl ₂	3	91	62 (<i>S</i>)
3	1a	6	CH ₂ Cl ₂	3	97	64 (<i>S</i>)
4	1a	6	CHCl ₃	3	97	67 (<i>S</i>)
5	1a	6	THF	15	77	67 (<i>S</i>)
6	1a	6	toluene	60	76	84 (<i>S</i>)
7	1a	6	toluene/CH ₂ Cl ₂ ^d	12	97	82 (<i>S</i>)
8	1a	7	toluene/CH ₂ Cl ₂ ^d	21	96	94 (<i>R</i>)
9	1b (<i>p</i> -Ns)	7	toluene/CH ₂ Cl ₂ ^d	21	90	88 (<i>R</i>)
10	1c (Ms)	7	toluene/CH ₂ Cl ₂ ^d	69	92	97
11	1d (Boc)	7	toluene/CH ₂ Cl ₂ ^d	117	60	42



^a 0.1 mmol of **1** was used for each reaction in 1.0 mL of solvent (0.1 M). ^b Isolated yield. ^c Determined by chiral HPLC analyses. ^d The ratio was 9/1.

With optimized conditions in hand, we next examined the substrate scope of aromatic imines **1e–n** (Table 2). Various functional groups, including methoxy, chloro, ester, cyano, and nitro groups, were tolerated under the reaction conditions (entries 1–5). The substrates **1e,f** bearing methoxy and chloro substituents on the aromatic ring reacted efficiently to furnish the corresponding imidazolidinones **3e,f** in high yields with excellent enantioselectivities (entries 1,2). On the other hand, the imines having strong electron-withdrawing groups on the aromatic rings **3g–i** resulted in somewhat lower yields (72–98%) and selectivities (83–90% ees), presumably due to the lower solubility and the enhanced electrophilicity of the imines, even after the minor optimization on the temperature and solvent (entries 3–5). The positions of the substituents on the aromatic ring have little effect on the reaction, and the imidazolidinones **3j** and **3k** were obtained in 85% and 91% yields with 94% ee and 96% ee, respectively (entries 6 and 7). In addition, this tandem asymmetric Mannich/cyclization could be applicable to heteroaromatic imines **1l–n** to afford the corresponding imidazolidinones **3l–n** in good yields with excellent enantioselectivities¹⁵ (entries 8–10).

 Table 2. Substrate Scope of aromatic imines^a


entry	1 (Ar)	yield (%) ^b	ee (%) ^c
1	1e (4-OMe-C ₆ H ₄)	97	97
2	1f (4-Cl-C ₆ H ₄)	86	92
3 ^d	1g (4-CO ₂ Me-C ₆ H ₄)	98	90
4 ^{d,e}	1h (4-CN-C ₆ H ₄)	72	86
5 ^{d,e}	1i (4-NO ₂ -C ₆ H ₄)	81	83
6	1j (3-OMe-C ₆ H ₄)	85	94
7	1k 	91	96
8	1l (3-furyl)	95	98
9	1m (3-thienyl)	97	93
10	1n (3-pyridyl)	78	92

^a 0.1 mmol of **1** was used for each reaction in toluene/CH₂Cl₂ (9/1, 0.1 M). ^b Isolated yield. ^c Determined by chiral HPLC analyses. ^d The reaction was performed at –78 °C. ^e The ratio of toluene/CH₂Cl₂ was 1/1.

It is worth noting that the present tandem asymmetric Mannich/cyclization could be successfully applied to aliphatic *N*-sulfonylimines (Figure 2). For example, when α -branched aliphatic *N*-tosylimines were reacted under the optimized condition (1.1 equiv of **2** and 10 mol% of **7** in toluene/CH₂Cl₂ at -60 °C for 24 hours), the corresponding imidazolidinone **3o** was obtained in 96% yield with 96% ee. However, α,α,α -trisubstituted aliphatic *N*-tosylimine afforded no desired adduct **3p** because of the steric hindrance. On the other hand, a linear aliphatic *N*-tosylimine gave the product **3q** in 90% yield with 55% ee,¹¹ which allowed us to improve the stereoselectivity. Gratifyingly, the replacement of tosyl group to more sterically demanding sulfonyl group (2,4,6-*i*-Pr)₃C₆H₂SO₂-¹⁶ was found to be effective, and the corresponding imidazolidinone **8q** was obtained in 99% yield with 96% ee. Utilizing this protecting group, different aliphatic imines also provided the corresponding heterocycles **8r** and **8s** in 79–97% yields with excellent enantioselectivities (96–97% ees).

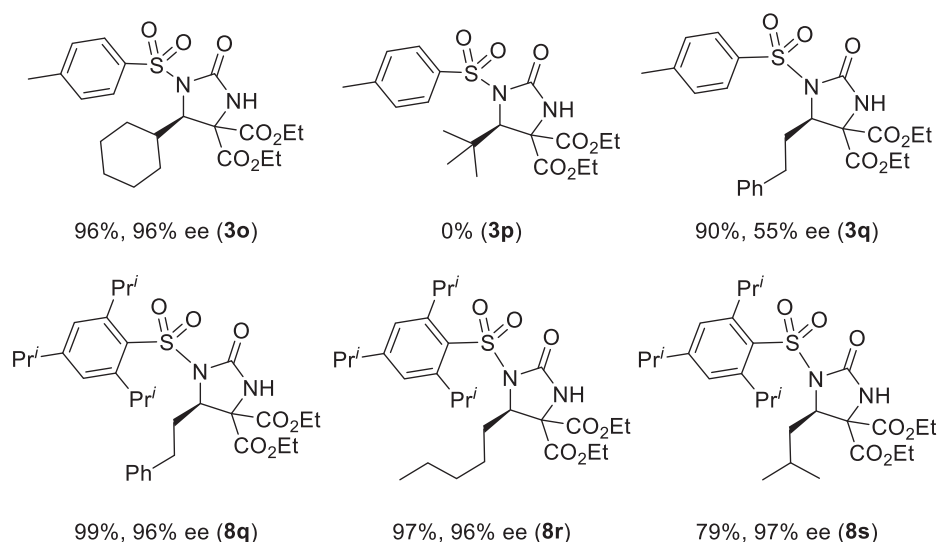


Figure 2. Substrate Scope of aliphatic imines with optimized condition

In conclusion, we have developed a straightforward asymmetric synthesis of 2-imidazolidinones from readily available *N*-sulfonylimines and diethyl 2-isocyanatomalonate. It was found that cinchona-alkaloid derived thiourea catalyst was most effective for both aromatic and aliphatic imines, affording the corresponding imidazolidinones in good yields with high enantioselectivities. In the case of aliphatic imines, the utilization of 2,4,6-triisopropylbenzenesulfonyl group successfully improved the selectivities of the products. The application of the products is now under investigation in our laboratory, and will be reported in due course.

EXPERIMENTAL

Unless otherwise noted, all chemicals and solvents were obtained from commercial suppliers and used without further purification. Analytical thin-layer chromatography was performed with Merck Silica gel 60. Column chromatography was performed on Cica silica gel 60 (particle size, 63–210 μm) and flash column chromatography was performed on Cica silica gel 60 (spherical/40–100 μm). All melting points were measured on BÜCHI M-565 melting point apparatus and are uncorrected. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded with a JEOL JNM-LA 500 at 500 MHz. Chemical shifts are reported relative to CDCl_3 (δ 7.26). Multiplicity is indicated by one or more of the following: s (singlet) d (doublet) dd (doublet of doublets) t (triplet) q (quartet) quin (quintet) sex (sextet) sep (septet) non (nonet) m (multiplet) br (broad). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a JEOL JNM-LA 500 at 126 MHz. Chemical shifts are reported relative to CDCl_3 (δ 77.0). Infrared spectra were recorded on a JASCO FT/IR-4100. High resolution mass spectra were obtained on a Shimadzu LCMS-IT-TOF for ESI-MS. All imines **1** were prepared according to the known procedures.¹⁷ The preparation of isocyanatomalonate diester **2** was reported previously.¹¹

General Procedure of the Tandem Mannich/Cyclization Reaction. To a solution of isocyanate **2** (22.1 mg, 0.11 mmol) in toluene/ CH_2Cl_2 (1.0 mL, 9:1), imine **1** (0.1 mmol) and catalyst **7** (5.9 mg, 0.01 mmol, 10 mol%) were added at -60 °C. The reaction mixture was stirred at the same temperature until the reaction completed (monitored by TLC). The reaction was quenched by the addition of MeOH (10 μL), and the mixture was filtered through a short pad of silica gel. The resulting filtrate was then concentrated *in vacuo*, and purified by preparative thin layer chromatography on silica gel to give the desired product **3**.

Diethyl (*R*)-2-oxo-5-phenyl-1-tosylimidazolidine-4,4-dicarboxylate (3a**):** colorless amorphous; $[\alpha]_{\text{D}}^{30} +62.3$ (*c* 0.68, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 7.47 (d, 2H, $J = 8.0$ Hz), 7.32–7.27 (m, 1H), 7.22 (brm, 4H), 7.10 (d, 2H, $J = 8.0$ Hz), 6.12 (s, 1H), 5.79 (s, 1H), 4.37–4.25 (m, 2H), 3.77–3.70 (m, 1H), 3.64–3.57 (m, 1H), 2.36 (s, 3H), 1.29 (t, 3H, $J = 7.0$ Hz), 0.77 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 166.5, 164.8, 152.7, 144.5, 135.6, 134.3, 129.2, 129.0, 128.3, 128.2, 69.3, 67.0, 63.8, 63.5, 62.7, 21.5, 13.8, 13.2; IR (ATR) 3337, 2984, 2360, 2341, 1737, 1169 cm^{-1} ; HPLC [CHIRALPAK IB, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda = 254$ nm, retention times: (major) 24.4 min, (minor) 32.3 min]; HRMS (ESI): Calcd. for $\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}_7\text{S}$ $[\text{M}+\text{H}]^+$ 461.1377, found 461.1360.

Diethyl (*R*)-2-oxo-5-phenyl-1-nosylimidazolidine-4,4-dicarboxylate (3b**):** colorless oil; $[\alpha]_{\text{D}}^{30} +125.5$ (*c* 0.18, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 8.09 (d, 2H, $J = 9.0$ Hz), 7.71 (d, 2H, $J = 9.0$ Hz), 7.33 (t, 1H, $J = 6.5$ Hz), 7.19 (m, 4H), 6.20 (s, 1H), 6.13 (s, 1H), 4.41–4.29 (m, 2H), 3.79–3.72 (m, 1H), 3.68–3.61 (m, 1H), 1.32 (t, 3H, $J = 7.0$ Hz), 0.75 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 166.23,

166.21, 164.4, 152.4, 150.2, 143.9, 133.7, 129.7, 129.4, 128.5, 123.5, 69.2, 63.8, 63.7, 62.9, 13.8, 13.1; IR (ATR) 3337, 2361, 2340, 1741, 1532, 1178 cm^{-1} ; HPLC [CHIRALPAK IB, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (major) 45.6 min, (minor) 61.0 min] HRMS (ESI): Calcd. for $\text{C}_{21}\text{H}_{22}\text{N}_3\text{O}_9\text{S}$ $[\text{M}+\text{H}]^+$ 492.1071, found 492.1067.

Diethyl (R)-2-oxo-5-phenyl-1-mesyylimidazolidine-4,4-dicarboxylate (3c): colorless oil; $[\alpha]_D^{30} +39.0$ (*c* 2.05, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 7.43–7.36 (m, 5H), 6.21 (s, 1H), 6.04 (s, 1H), 4.40–4.29 (m, 2H), 3.82–3.75 (m, 1H), 3.67–3.61 (m, 1H), 3.01 (s, 3H), 1.32 (t, 3H, $J = 7.0$ Hz), 0.81 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 166.4, 164.8, 153.4, 134.6, 129.7, 128.7, 127.8, 69.5, 63.6, 63.2, 62.9, 41.8, 13.9, 13.3; IR (ATR) 3330, 2985, 2360, 2341, 1734, 1165 cm^{-1} ; HPLC [CHIRALPAK IB, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (major) 31.6 min, (minor) 40.8 min]: HRMS (ESI): Calcd. for $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}_7\text{S}$ $[\text{M}+\text{H}]^+$ 385.1064, found 385.1061.

1-(tert-Butyl) 4,4-diethyl (R)-2-oxo-5-phenylimidazolidine-1,4,4-tricarboxylate (3d): colorless amorphous; $[\alpha]_D^{30} -27.4$ (*c* 0.65, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 7.32 (brs, 5H), 5.88 (s, 1H), 5.73 (s, 1H), 4.37–4.26 (m, 2H), 3.79–3.72 (m, 1H), 3.62–3.56 (m, 1H), 1.30 (t, 3H, $J = 7.0$ Hz), 1.24 (s, 9H), 0.83 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 167.1, 165.5, 153.5, 148.7, 136.2, 128.9, 128.3, 127.3, 83.1, 68.0, 63.3, 62.6, 62.4, 27.6, 13.9, 13.3; IR (ATR) 3309, 2981, 2360, 2341, 1792, 1745, 1158 cm^{-1} ; HPLC [CHIRALPAK AD, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (major) 22.9 min, (minor) 30.9 min]: HRMS (ESI): Calcd. for $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_7\text{Na}$ $[\text{M}+\text{Na}]^+$ 429.1632, found 429.1621.

Diethyl (R)-5-(4-methoxyphenyl)-2-oxo-1-tosylimidazolidine-4,4-dicarboxylate (3e): colorless oil; $[\alpha]_D^{29} +37.2$ (*c* 3.33, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 7.50 (d, 2H, $J = 7.5$ Hz), 7.14–7.11 (m, 4H), 6.72 (d, 2H, $J = 8.5$ Hz), 6.07 (s, 1H), 5.74 (s, 1H), 4.36–4.24 (m, 2H), 3.82–3.73 (m, 4H), 3.70–3.63 (m, 1H), 2.37 (s, 3H), 1.29 (t, 3H, $J = 7.0$ Hz), 0.83 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 166.6, 164.8, 160.2, 152.6, 144.5, 135.8, 129.4, 129.0, 128.2, 126.3, 113.6, 69.3, 63.5, 63.4, 62.7, 55.3, 21.6, 13.9, 13.4; IR (ATR) 3333, 2983, 2359, 2342, 1736, 1168 cm^{-1} ; HPLC [CHIRALPAK IB, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (major) 31.6 min, (minor) 44.0 min]: HRMS (ESI): Calcd. for $\text{C}_{23}\text{H}_{27}\text{N}_2\text{O}_8\text{S}$ $[\text{M}+\text{H}]^+$ 491.1483, found 491.1466.

Diethyl (R)-5-(4-chlorophenyl)-2-oxo-1-tosylimidazolidine-4,4-dicarboxylate (3f): colorless solid; mp 164.9–167.7 $^\circ\text{C}$; $[\alpha]_D^{30} +58.1$ (*c* 0.78, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 7.53 (d, 2H, $J = 8.5$ Hz), 7.21–7.15 (m, 6H), 6.08 (s, 1H), 5.91 (s, 1H), 4.36–4.24 (m, 2H), 3.83–3.77 (m, 1H), 3.70–3.64 (m, 1H), 2.39 (s, 3H), 1.29 (t, 3H, $J = 7.0$ Hz), 0.84 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 166.4, 164.7, 152.5, 144.9, 135.5, 135.3, 133.2, 129.2, 128.5, 128.1, 69.1, 63.6, 63.0, 62.9, 25.3, 21.6, 13.8, 13.3; IR (ATR) 3334, 2984, 2360, 2342, 1737, 1170 cm^{-1} ; HPLC [CHIRALPAK IB, hexane/2-propanol

= 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (major) 23.0 min, (minor) 29.1 min]: HRMS (ESI): Calcd. for $C_{22}H_{24}N_2O_7S$ $[M+H]^+$ 495.0987, found 495.0997.

Diethyl (R)-5-(4-(methoxycarbonyl)phenyl)-2-oxo-1-tosylimidazolidine-4,4-dicarboxylate (3g): colorless oil; $[\alpha]_D^{29} +41.3$ (*c* 1.03, $CHCl_3$); 1H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, 2H, $J = 8.0$ Hz), 7.53 (d, 2H, $J = 9.0$ Hz), 7.33 (d, 2H, $J = 7.5$ Hz), 7.14 (d, 2H, $J = 8.0$ Hz), 6.17 (s, 1H), 5.94 (s, 1H), 4.37–4.24 (m, 2H), 3.94 (s, 3H), 3.79–3.72 (m, 1H), 3.61–3.55 (m, 1H), 2.38 (s, 3H), 1.29 (t, 3H, $J = 7.0$ Hz), 0.80 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.31, 166.29, 164.6, 152.5, 144.9, 139.3, 135.4, 130.9, 129.5, 129.2, 128.1, 69.0, 63.6, 63.2, 62.9, 52.3, 21.6, 13.8, 13.3 (one carbon peak is missing due to overlapping); IR (ATR) 3328, 2984, 2363, 2343, 1742, 1170 cm^{-1} ; HPLC [CHIRALPAK IB, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (major) 28.7 min, (major) 39.0 min]: HRMS (ESI): Calcd. for $C_{24}H_{27}N_2O_9S$ $[M+H]^+$ 519.1432, found 519.1429.

Diethyl (R)-5-(4-cyanophenyl)-2-oxo-1-tosylimidazolidine-4,4-dicarboxylate (3h): brown solid; mp 190.3–191.7 °C; $[\alpha]_D^{29} +52.9$ (*c* 0.49, $CHCl_3$); 1H NMR (500 MHz, $CDCl_3$): δ 7.58 (t, 4H, $J = 8.5$ Hz), 7.41 (d, 2H, $J = 7.5$ Hz), 7.21 (d, 2H, $J = 8.5$ Hz), 6.15 (s, 1H), 5.79 (s, 1H), 4.37–4.24 (m, 2H), 3.83–3.76 (m, 1H), 3.66–3.60 (m, 1H), 2.41 (s, 3H), 1.28 (t, 3H, $J = 7.5$ Hz), 0.84 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 166.1, 164.5, 152.4, 145.3, 139.9, 135.2, 132.1, 129.4, 128.8, 128.1, 118.0, 113.1, 68.9, 63.8, 63.1, 62.9, 21.6, 13.8, 13.4; IR (ATR) 3335, 2984, 2362, 2342, 2230, 1743, 1170 cm^{-1} ; HPLC [CHIRALPAK ADH, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (major) 63.2 min, (minor) 79.1 min]: HRMS (ESI): Calcd. for $C_{23}H_{24}N_3O_7S$ $[M+H]^+$ 486.1329, found 486.1335.

Diethyl (R)-5-(4-nitrophenyl)-2-oxo-1-tosylimidazolidine-4,4-dicarboxylate (3i): yellow solid; mp 188.5–192.5 °C; $[\alpha]_D^{29} +44.0$ (*c* 0.45, $CHCl_3$); 1H NMR (500 MHz, $CDCl_3$): δ 8.13 (d, 2H, $J = 8.0$ Hz), 7.62 (d, 2H, $J = 8.5$ Hz), 7.49 (d, 2H, $J = 8.0$ Hz), 7.20 (d, 2H, $J = 8.0$ Hz), 6.20 (s, 1H), 5.91 (s, 1H), 4.38–4.24 (m, 2H), 3.84–3.78 (m, 1H), 3.66–3.59 (m, 1H), 2.41 (s, 3H), 1.29 (t, 3H, $J = 7.0$ Hz), 0.85 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 166.1, 164.5, 152.4, 148.3, 145.4, 141.7, 135.2, 129.4, 129.1, 128.2, 123.5, 68.9, 63.9, 63.1, 62.7, 21.6, 13.8, 13.4; IR (ATR) 3335, 2361, 2343, 1742, 1524, 1350, 1169 cm^{-1} ; HPLC [CHIRALPAK IB, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (major) 35.4 min, (minor) 40.7 min]: HRMS (ESI): Calcd. for $C_{22}H_{24}N_3O_9S$ $[M+H]^+$ 506.1228, found 506.1233.

Diethyl (R)-5-(3-methoxyphenyl)-2-oxo-1-tosylimidazolidine-4,4-dicarboxylate (3j): colorless oil; $[\alpha]_D^{29} +54.3$ (*c* 0.45, $CHCl_3$); 1H NMR (500 MHz, $CDCl_3$): δ 7.49 (d, $J = 8.5$ Hz, 2H), 7.15–7.11 (m, 3H), 6.84–6.81 (m, 2H), 6.61 (brs, 1H), 6.09 (s, 1H), 5.86 (s, 1H), 4.37–4.25 (m, 2H), 3.80–3.74 (m, 1H), 3.69–3.61 (m, 4H), 2.37 (s, 3H), 1.30 (t, $J = 7.0$, 3H), 0.80 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 166.5, 164.7, 159.4, 152.6, 144.5, 135.6, 135.3, 129.6, 129.3, 129.0, 128.2, 126.4, 115.5, 69.1,

63.8, 63.5, 62.8, 55.0, 21.5, 13.8, 13.2; IR (ATR) 3334, 2365, 2342, 1748 cm^{-1} ; HPLC [CHIRALPAK ADH, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (minor) 68.3 min, (major) 93.5 min]; HRMS (ESI): Calcd. for $\text{C}_{23}\text{H}_{27}\text{N}_2\text{O}_8\text{S}$ $[\text{M}+\text{H}]^+$ 491.1483, found 491.1504.

Diethyl (*R*)-5-(benzo[*d*][1,3]dioxol-5-yl)-2-oxo-1-tosylimidazolidine-4,4-dicarboxylate (3k): white solid; mp 168.9–170.3 $^{\circ}\text{C}$; $[\alpha]_D^{29} +45.6$ (*c* 0.90, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 7.57 (d, 2H, $J = 8.0$ Hz), 7.16 (d, 2H, $J = 8.0$ Hz), 6.75 (brs, 1H), 6.67 (d, 1H, $J = 8.0$ Hz), 6.61 (brs, 1H), 6.02 (s, 1H), 5.94 (d, 1H, $J = 1.5$ Hz), 5.91 (d, 1H, $J = 1.0$ Hz), 5.68 (s, 1H), 4.36–4.23 (m, 2H), 3.88–3.82 (m, 1H), 3.80–3.70 (m, 1H), 2.38 (s, 3H), 1.29 (t, 3H, $J = 7.0$ Hz), 0.89 (t, 3H, $J = 7.5$ Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 166.5, 164.7, 152.5, 148.3, 147.6, 144.6, 135.7, 129.4, 129.1, 128.2, 127.8, 107.9, 101.3, 69.2, 63.7, 63.5, 62.8, 21.6, 13.8, 13.4 (one carbon peak is missing due to overlapping); IR (ATR) 3335, 2985, 2361, 2342, 1741, 1171 cm^{-1} ; HPLC [CHIRALPAK ADH, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (minor) 64.4 min, (major) 95.3 min]; HRMS (ESI): Calcd. for $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_9\text{S}$ $[\text{M}+\text{H}]^+$ 505.1275, found 505.1276.

Diethyl (*R*)-2-oxo-5-(furan-3-yl)-1-tosylimidazolidine-4,4-dicarboxylate (3l): colorless oil; $[\alpha]_D^{29} +54.7$ (*c* 0.94, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 7.62 (d, 2H, $J = 8.5$ Hz), 7.50 (s, 1H), 7.27 (s, 1H), 7.21–7.17 (m, 3H), 6.11 (d, 1H, $J = 5.5$ Hz), 5.85 (s, 1H), 4.36–4.24 (m, 2H), 3.94 (q, 2H, $J = 7.0$ Hz), 2.38 (s, 3H), 1.29 (t, 3H, $J = 7.0$ Hz), 0.97 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 166.3, 164.5, 152.2, 144.6, 143.3, 142.4, 135.6, 129.1, 128.1, 119.2, 108.8, 68.9, 63.5, 62.9, 56.4, 21.6, 13.8, 13.3; IR (ATR) 3336, 2984, 2360, 2342, 1738, 1170 cm^{-1} ; HPLC [CHIRALPAK IB, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (major) 25.6 min, (minor) 29.9 min]; HRMS (ESI): Calcd. for $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_8\text{S}$ $[\text{M}+\text{H}]^+$ 451.1170, found 451.1174.

Diethyl (*R*)-2-oxo-5-(thiophen-3-yl)-1-tosylimidazolidine-4,4-dicarboxylate (3m): colorless amorphous; $[\alpha]_D^{29} +83.9$ (*c* 0.62, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 7.47 (d, 2H, $J = 8.5$ Hz), 7.29–7.28 (m, 1H), 7.13–7.10 (m, 3H), 6.82 (d, 1H, $J = 5.0$ Hz), 6.23 (s, 1H), 5.79 (s, 1H), 4.37–4.26 (m, 2H), 3.87–3.75 (m, 2H), 2.37 (s, 3H), 1.30 (t, 3H, $J = 7.0$ Hz), 0.87 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 166.4, 164.6, 152.3, 144.5, 135.6, 134.9, 129.1, 128.0, 126.4, 126.1, 125.9, 69.0, 63.5, 62.9, 59.4, 21.6, 13.8, 13.3; IR (ATR) 3335, 2983, 2360, 2341, 1740, 1171 cm^{-1} ; HPLC [CHIRALPAK IB, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (major) 26.6 min, (minor) 33.5 min]; HRMS (ESI): Calcd. for $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_7\text{S}_2$ $[\text{M}+\text{H}]^+$ 467.0941, found 467.0952.

Diethyl (*R*)-2-oxo-5-(pyridin-3-yl)-1-tosylimidazolidine-4,4-dicarboxylate (3n): white solid; mp 115.5–116.4 $^{\circ}\text{C}$; $[\alpha]_D^{23} +75.4$ (*c* 1.00, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 8.58–8.57 (m, 2H), 7.57 (d, 2H, $J = 8.0$ Hz), 7.52 (d, 1H, $J = 8.0$ Hz), 7.19–7.14 (m, 3H), 6.15 (s, 1H), 5.89 (s, 1H), 4.40–4.25 (m, 2H), 3.83–3.76 (m, 1H), 3.71–3.64 (m, 1H), 2.39 (s, 3H), 1.29 (t, 3H, $J = 7.0$ Hz), 0.82 (t, 3H, $J = 7.0$

Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 166.2, 164.5, 152.4, 150.5, 149.7, 145.1, 135.4, 130.5, 129.4, 128.1, 123.2, 69.0, 63.8, 63.1, 61.4, 30.9, 21.6, 143.9, 13.3; IR (ATR) 2360, 2342, 1541, 1235, 1195 cm^{-1} ; HPLC [CHIRALPAK IC, hexane/2-propanol = 80/20, 1.5 mL/min, $\lambda=254$ nm, retention times: (minor) 94.2 min, (major) 165.9 min]; HRMS (ESI): Calcd. for $\text{C}_{21}\text{H}_{24}\text{N}_3\text{O}_7\text{S}$ $[\text{M}+\text{H}]^+$ 462.1329, found 462.1345.

Diethyl (*R*)-5-cyclohexyl-2-oxo-1-tosylimidazolidine-4,4-dicarboxylate (3o): Colorless oil; $[\alpha]_D^{24} +19.5$ (*c* 2.54, CHCl_3); ^1H NMR (500 MHz, CDCl_3): 7.91 (d, 2H, $J = 8.0$ Hz), 7.28 (d, 2H, $J = 8.5$ Hz), 5.61 (s, 1H), 5.07 (s, 1H), 4.36–4.28 (m, 2H), 4.19–4.05 (m, 2H), 2.41 (s, 3H), 1.82–1.67 (m, 5H), 1.62–1.61 (d, 1H), 1.53–1.46 (m, 1H), 1.33–1.08 (m, 10H); ^{13}C NMR (126 MHz, CDCl_3): δ 167.1, 165.2, 153.2, 144.7, 135.7, 129.1, 128.7, 69.8, 65.8, 63.2, 63.1, 41.1, 31.1, 26.6, 26.2, 26.0, 25.7, 21.6, 13.9, 13.7; IR (ATR) 3362, 2970, 2933, 2856, 1743, 1170, 1091 cm^{-1} ; HPLC [CHIRALPAK AS, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (minor) 34.1 min, (major) 63.2 min]; HRMS (ESI): Calcd. for $\text{C}_{22}\text{H}_{31}\text{N}_2\text{O}_7\text{S}$ $[\text{M}+\text{H}]^+$ 467.1846, found 467.1852.

(*E*)-2,4,6-Triisopropyl-*N*-(3-phenylpropylidene)benzenesulfonamide (1q): white solid; mp 56.0–59.8 °C; ^1H NMR (500 MHz, CDCl_3): δ 8.64 (t, 1H, $J = 3.5$ Hz), 7.26–7.13 (m, 7H), 4.21–4.15 (m, 2H), 2.98–2.83 (m, 5H), 1.27–1.24 (m, 18H); ^{13}C NMR (126 MHz, CDCl_3): δ 175.4, 153.8, 151.3, 139.8, 130.2, 128.6, 128.3, 126.4, 123.8, 37.6, 34.2, 30.6, 29.7, 24.7, 23.6; IR (ATR) 2954, 1625, 1313, 1153 cm^{-1} ; HRMS (ESI): Calcd. for $\text{C}_{24}\text{H}_{34}\text{NO}_2\text{S}$ $[\text{M}+\text{H}]^+$ 400.2305, found 400.2288.

Diethyl (*R*)-2-oxo-5-phenethyl-1-[(2,4,6-triisopropylphenyl)sulfonyl]imidazolidine-4,4-dicarboxylate (8q): colorless amorphous; $[\alpha]_D^{24} -8.8$ (*c* 0.84, CHCl_3); ^1H NMR (500 MHz, CDCl_3): δ 7.29–7.26 (m, 2H), 7.20–7.16 (m, 5H), 5.73 (s, 1H), 5.38–5.37 (m, 1H), 4.40–4.07 (m, 6H), 3.05 (dt, 1H, $J = 13.0, 4.5$ Hz), 2.89 (quin, 1H, $J = 7.0$ Hz), 2.72 (dt, 1H, $J = 13.5, 4.5$ Hz), 2.57–2.49 (m, 1H), 2.23–2.16 (m, 1H), 1.32–1.19 (m, 24H); ^{13}C NMR (126 MHz, CDCl_3): δ 166.8, 165.4, 154.0, 153.2, 152.6, 141.0, 131.6, 128.41, 128.38, 126.0, 124.0, 68.4, 63.4, 63.2, 61.0, 34.2, 33.7, 31.6, 29.8, 29.5, 25.2, 24.4, 23.47, 23.45, 13.9, 13.8; IR (ATR) 2961, 1733, 1166, 1068, 769 cm^{-1} ; HPLC [CHIRALPAK AD, hexane/2-propanol = 90/10, 0.5 mL/min, $\lambda=254$ nm, retention times: (minor) 12.6 min, (major) 17.6 min]; HRMS (ESI): Calcd. for $\text{C}_{32}\text{H}_{45}\text{N}_2\text{O}_7\text{S}$ $[\text{M}+\text{H}]^+$ 601.2942, found 601.2940.

(*E*)-*n*-Hexylidene-2,4,6-triisopropylbenzenesulfonamide (1r): white solid; mp 93.0–94.8 °C; ^1H NMR (500 MHz, CDCl_3): δ 8.58 (t, 1H, $J = 4.0$ Hz), 7.18 (s, 2H), 4.21–4.13 (m, 2H), 2.95–2.86 (m, 1H), 2.53–2.49 (td, 2H, $J = 7.5, 4.5$ Hz), 1.66–1.60 (m, 2H), 1.33–1.28 (m, 4H), 1.26–1.24 (m, 18H), 0.87 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (126 MHz, CDCl_3): δ 176.6, 153.7, 151.2, 130.3, 123.8, 35.9, 34.2, 31.2, 29.7, 24.7, 24.2, 23.5, 22.3, 13.8; IR (ATR) 2953, 1625, 1313, 1154 cm^{-1} ; HRMS (ESI): Calcd. for $\text{C}_{21}\text{H}_{36}\text{NO}_2\text{S}$ $[\text{M}+\text{H}]^+$ 366.2461, found 366.2474.

Diethyl (R)-2-oxo-5-pentyl-1-((2,4,6-triisopropylphenyl)sulfonyl)imidazolidine-4,4-dicarboxylate (8r): white amorphous; $[\alpha]_D^{24}$ -39.9 (*c* 0.85, CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ 7.16–7.15 (m, 2H), 5.63 (s, 1H), 5.29–5.28 (m, 1H), 4.36–4.04 (m, 6H), 2.88 (sep, 1H, *J* = 7.0 Hz), 2.21–2.13 (m, 1H), 2.01–1.94 (m, 1H), 1.67–1.62 (m, 2H), 1.46–1.16 (m, 28H), 0.89 (t, 3H, *J* = 7.5 Hz); ¹³C NMR (126 MHz, CDCl₃): δ 166.9, 165.4, 153.9, 153.2, 152.4, 131.8, 123.9, 68.3, 63.2, 63.1, 61.5, 34.1, 31.9, 31.4, 29.8, 25.2, 24.3, 23.44, 23.42, 23.0, 22.3, 14.0, 13.9, 13.8; IR (ATR) 2960, 1733, 1167, 1071 cm⁻¹; HPLC [CHIRALPAK IC, hexane/2-propanol = 95/5, 1.0 mL/min, λ=254 nm, retention times: (minor) 13.0 min, (major) 14.5 min]; HRMS (ESI): Calcd. for C₂₉H₄₇N₂O₇S [M+H]⁺ 567.3098, found 567.3122.

(E)-2,4,6-Triisopropyl-N-(3-methylbutylidene)benzenesulfonamide (1s): white solid; mp 78.1–79.8 °C; ¹H NMR (500 MHz, CDCl₃): δ 8.57 (t, 1H, *J* = 5.0 Hz), 7.18 (s, 2H), 4.20–4.12 (m, 2H), 2.95–2.86 (m, 1H), 2.40 (dd, 2H, *J* = 6.5, 4.5 Hz), 2.14–2.03 (m, 1H), 1.26–1.24 (m, 18H), 0.97 (d, 6H, *J* = 7.0 Hz); ¹³C NMR (126 MHz, CDCl₃): δ 176.1, 153.7, 151.3, 130.3, 123.8, 44.5, 34.2, 29.7, 25.8, 24.7, 23.5, 22.5; IR (ATR) 2953, 1624, 1314, 1155, 672 cm⁻¹; HRMS (ESI): Calcd. for C₂₀H₃₄NO₂S [M+H]⁺ 352.2305, found 352.2308.

Diethyl (R)-5-isobutyl-2-oxo-1-((2,4,6-triisopropylphenyl)sulfonyl)imidazolidine-4,4-dicarboxylate (8r): colorless amorphous; $[\alpha]_D^{24}$ -56.1 (*c* 1.11, CHCl₃); ¹H NMR (500 MHz, CDCl₃): δ 7.15 (s, 2H), 5.53 (s, 1H), 5.24 (dd, 1H, *J* = 8.5, 3.5 Hz), 4.37–4.14 (m, 4H), 4.05 (sep, 2H, *J* = 6.5 Hz), 2.88 (sep, 1H, *J* = 6.5 Hz), 2.09–2.03 (m, 1H), 1.78–1.71 (m, 2H), 1.60 (s, 1H), 1.32–1.17 (m, 23H), 1.08 (d, 3H, *J* = 6.0 Hz), 0.94 (d, 3H, *J* = 6.5 Hz); ¹³C NMR (126 MHz, CDCl₃) δ 167.1, 165.9, 153.8, 153.2, 152.4, 131.8, 123.9, 69.0, 63.2, 62.9, 60.0, 40.5, 34.1, 29.7, 25.1, 24.8, 24.3, 23.5, 23.4, 23.2, 21.6, 13.83, 13.80; IR (ATR) 2962, 1735, 1169, 1073, 786, 752 cm⁻¹; HPLC [CHIRALPAK IC, hexane/2-propanol = 90/10, 1.0 mL/min, λ=254 nm, retention times: (minor) 13.0 min, (major) 14.5 min]; HRMS (ESI): Calcd. for C₂₈H₄₅N₂O₇S [M+H]⁺ 553.2942, found 553.2964.

ACKNOWLEDGEMENTS

This work was supported in part by a Grant-in-Aid for Scientific Research on Innovative Areas “Advanced Molecular Transformations by Organocatalysts” and Platform for Drug Discovery, Informatics, and Structural Life Science (Y.T.) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

REFERENCES AND NOTES

1. T.-L. Liu, W. Li, H. Geng, C.-J. Wang, and X. Zhang, *Org. Lett.*, 2013, **15**, 1740; W. Hu, J. Jiang, T. Jia, T. Shi, J. Xi, T. He, S. Wei, Z. Zhao, and W. Wang, *Faming Zhuanli Shenqing* (2011), CN

- 102295582 A 20111228; M, D'Ambrosio, A. Guerriero, M. Ripamonti, C. Debitus, J. Waikedre, and F. Pietra, *Helv. Chim. Acta*, 1996, **79**, 727.
2. A. Viso, R. Fernández de la Pradilla, M. Tortosa, A. García, and A. Flores, *Chem. Rev.*, 2011, **111**, PR1; R. G. Arrayás and J. C. Carretero, *Chem. Soc. Rev.*, 2009, **38**, 1940; A. Viso, R. Fernández de la Pradilla, A. García, and A. Flores, *Chem. Rev.*, 2005, **105**, 3167.
 3. A. A.-M. Abdel-Aziz, J. Okuno, S. Tanaka, T. Ishizuka, H. Matsunaga, and T. Kunieda, *Tetrahedron Lett.*, 2000, **41**, 8533.
 4. R. Fu, B. Zhao, and Y. Shi, *J. Org. Chem.*, 2009, **74**, 7577; T. Oshitari, R. Akagi, and T. Mandai, *Synthesis*, 2004, 1325.
 5. S.-H. Shi, F.-P. Huang, P. Zhu, Z.-W. Dong, and X.-P. Hui, *Org. Lett.*, 2012, **14**, 2010; W.-Q. Zhang, L.-F. Chang, C. J. Yu, and L.-Z. Gong, *Angew. Chem. Int. Ed.*, 2012, **51**, 4085; X. Liu, L. Deng, X. Jiang, W. Yan, C. Liu, and R. Wang, *Org. Lett.*, 2010, **12**, 876; D. Uruguchi, K. Koshimoto, and T. Ooi, *Chem. Commun.*, 2010, **46**, 300; D. Uruguchi, Y. Ueki, and T. Ooi, *J. Am. Chem. Soc.*, 2008, **130**, 14088.
 6. For α -tetrasubstituted- α,β -diamino acids, see: J. Hernández-Toribio, R. G. Arrayás, and J. C. Carretero, *J. Am. Chem. Soc.*, 2008, **130**, 16150; For α -trisubstituted- α,β -diamino acids, see: M. Kondo, T. Nishi, T. Hatanaka, Y. Funahashi, and S. Nakamura, *Angew. Chem. Int. Ed.*, 2015, **54**, 8198; S. Lin, Y. Kawato, N. Kumagai, and M. Shibasaki, *Angew. Chem. Int. Ed.*, 2015, **54**, 5183; Z. Tao, A. Adele, X. Wu, and L. Gong, *Chin. J. Chem.*, 2014, **32**, 969; J. S. Bandar and T. H. Lambert, *J. Am. Chem. Soc.*, 2013, **135**, 11799; Y. Yamashita, S. Yoshimoto, K. Matsuda, and S. Kobayashi, *Asian J. Org. Chem.*, 2012, **1**, 327; T. Arai, A. Mishiro, E. Matsumura, A. Awata, and M. Shirasugi, *Chem. Eur. J.*, 2012, **18**, 11219; E. Hernando, R. G. Arrayás, and J. C. Carretero, *Chem. Commun.*, 2012, **48**, 9622; K. Imae, K. Shimizu, K. Ogata, and S. Fukuzawa, *J. Org. Chem.*, 2011, **76**, 3604; G. Liang, M.-C. Tong, H. Tao, and C.-J. Wang, *Adv. Synth. Catal.*, 2010, **352**, 1851; H. Zhang, S. Syed, and C. F. Barbas III, *Org. Lett.*, 2010, **12**, 708; D. Shang, Y. Liu, X. Zhou, X. Liu, and X. Feng, *Chem. Eur. J.*, 2009, **15**, 3678; J. Hernández-Toribio, R. G. Arrayás, and J. C. Carretero, *Chem. Eur. J.*, 2010, **16**, 1153; X.-X. Yan, Q. Peng, Q. Li, K. Zhang, J. Yao, X.-L. Hou, and Y.-D. Wu, *J. Am. Chem. Soc.*, 2008, **130**, 14362; S. Kobayashi, R. Yazaki, K. Seki, and Y. Yamashita, *Angew. Chem. Int. Ed.*, 2008, **47**, 5613.
 7. For α -tetrasubstituted- α,β -diamino acids, see: M.-X. Zhao, L. Jing, H. Zhou, and M. Shi, *RSC Adv.*, 2015, **5**, 75648; M.-X. Zhao, H.-L. Bi, R.-H. Jiang, X.-W. Xu, and M. Shi, *Org. Lett.*, 2014, **16**, 4566; M. Hayashi, M. Iwanaga, N. Shiomi, D. Nakane, H. Masuda, and S. Nakamura, *Angew. Chem. Int. Ed.*, 2014, **53**, 8411; W. Fan, S. Kong, Y. Cai, G. Wu, and Z. Miao, *Org. Biomol. Chem.*, 2013,

- 11, 3223; D. Uraguchi, K. Koshimoto, C. Sanada, and T. Ooi, *Tetrahedron: Asymmetry*, 2010, **21**, 1189; A. Puglisi, L. Raimondi, M. Benaglia, M. Bonsignore, and S. Rossi, *Tetrahedron Lett.*, 2009, **50**, 4340; B. Han, Q.-P. Liu, R. Li, X. Tian, X.-F. Xiong, J.-G. Deng, and Y.-C. Chen, *Chem. Eur. J.*, 2008, **14**, 8094; D. Uraguchi, K. Koshimoto, and T. Ooi, *J. Am. Chem. Soc.*, 2008, **130**, 10878; A. Singh and J. N. Johnston, *J. Am. Chem. Soc.*, 2008, **130**, 5866; Z. Chen, H. Morimoto, S. Matsunaga, and M. Shibasaki, *J. Am. Chem. Soc.*, 2008, **130**, 2170; K. R. Knudsen and K. A. Jørgensen, *Org. Biomol. Chem.*, 2005, **3**, 1262; For α -trisubstituted- α,β -diamino acids, see: A. Singh, R. A. Yoder, B. Shen, and J. N. Johnston, *J. Am. Chem. Soc.*, 2007, **129**, 3466.
8. For α -tetrasubstituted- α,β -diamino acids, see: S. Kato, T. Yoshino, M. Shibasaki, M. Kanai, and S. Matsunaga, *Angew. Chem. Int. Ed.*, 2012, **51**, 7007; G. Lu, T. Yoshino, H. Morimoto, S. Matsunaga, and M. Shibasaki, *Angew. Chem. Int. Ed.*, 2011, **50**, 4382; For α -trisubstituted- α,β -diamino acids, see: X. Chen, S. Dong, Z. Qiao, Y. Zhu, M. Xie, L. Lin, X. Liu, and X. Feng, *Chem. Eur. J.*, 2011, **17**, 2583; G. A. Cutting, N. E. Stainforth, M. P. John, G. Kociok-Köhn, and M. C. Willis, *J. Am. Chem. Soc.*, 2007, **129**, 10632; Z. Shi, P. Yu, P. J. Chua, and G. Zhou, *Adv. Synth. Catal.*, 2009, **351**, 2797; L. Li, M. Ganesh, and D. Seidel, *J. Am. Chem. Soc.*, 2009, **131**, 11648.
9. For α -tetrasubstituted- α,β -diamino acids, see: S. Nakamura, Y. Maeno, M. Ohara, A. Yamamura, Y. Funahashi, and N. Shibata, *Org. Lett.*, 2012, **14**, 2960; For α -trisubstituted- α,β -diamino acids, see: I. Ortín and D. J. Dixon, *Angew. Chem. Int. Ed.*, 2014, **53**, 3462; Z.-W. Zhang, G. Lu, M.-M. Chen, N. Lin, Y.-B. Li, T. Hayashi, and A. S. C. Chan, *Tetrahedron: Asymmetry*, 2010, **21**, 1715; J. Aydin, A. Rydén, and K. J. Szabó, *Tetrahedron: Asymmetry*, 2008, **19**, 1867; X.-T. Zhou, Y.-R. Lin, L.-X. Dai, J. Sun, L.-J. Xia, and M.-H. Tang, *J. Org. Chem.*, 1999, **64**, 1331.
10. Z. Sun, K. Weidner, N. Kumagai, and M. Shibasaki, *Chem. Eur. J.*, 2015, **21**, 17574.
11. S. Sakamoto, N. Kazumi, Y. Kobayashi, C. Tsukano, and Y. Takemoto, *Org. Lett.*, 2014, **16**, 4758; H. Nakamura, C. Tsukano, M. Yasui, S. Yokouchi, M. Igarashi, and Y. Takemoto, *Angew. Chem. Int. Ed.*, 2015, **54**, 3136.
12. Y. Kobayashi, R. Kuramoto, and Y. Takamoto, *Beilstein J. Org. Chem.*, 2015, **11**, 2654; Y. Kobayashi, S. Li, and Y. Takamoto, *Asian J. Org. Chem.*, 2014, **3**, 403; T. Inokuma, M. Furukawa, Y. Suzuki, T. Kimachi, Y. Kobayashi, and Y. Takamoto, *ChemCatChem*, 2012, **4**, 983; T. Inokuma, M. Furukawa, T. Uno, Y. Suzuki, K. Yoshida, Y. Yano, K. Matsuzaki, and Y. Takamoto, *Chem. Eur. J.*, 2011, **17**, 10470.
13. For recent reviews on thiourea catalysts, see: S. J. Connon, *Chem. Eur. J.*, 2006, **12**, 5418; A. G. Doyle and E. N. Jacobsen, *Chem. Rev.*, 2007, **107**, 5713; S. J. Connon, *Chem. Commun.*, 2008, 2499; Z. Zhang and P. R. Schreiner, *Chem. Soc. Rev.*, 2009, **38**, 1187; Y. Takemoto, *Chem. Pharm.*

- Bull.*, 2010, **58**, 593; T. J. Auvil, A. G. Schafer, and A. E. Mattson, *Eur. J. Org. Chem.*, 2014, 2633.
14. Y. Yamaoka, H. Miyabe, Y. Yasui, and Y. Takemoto, *Synthesis*, 2007, **16**, 2571.
15. See the Supporting Information for details. See also, L. Li, M. Ganesh, and D. Seidel, *J. Am. Chem. Soc.*, 2009, **131**, 11648.
16. Z. Han, W. Yang, C.-H. Tan, and Z. Jiang, *Adv. Synth. Catal.*, 2013, **355**, 1505; T. Hayashi, M. Kawai, and N. Tokunaga, *Angew. Chem. Int. Ed.*, 2004, **43**, 6125.
17. X.-S. Zhang, Y. Li, H. Li, K. Chen, Z.-Q. Lei, and Z.-J. Shi, *Chem. Eur. J.*, 2012, **18**, 16214; S. Morales, F. G. Guijjarro, J. L. G. Ruano, and M. B. Cid, *J. Am. Chem. Soc.*, 2014, **136**, 1082; T. Ooi, Y. Umematsu, and K. Maruoka, *J. Am. Chem. Soc.*, 2006, **128**, 2548.