Stereocomplementary Synthesis of *cis*- and *trans*-2-(*p*-Bromophenyl)-5-methylthiazolidin-4-ones: Useful Umpolung-type Suzuki–Miyaura Cross-coupling Partner and Donor

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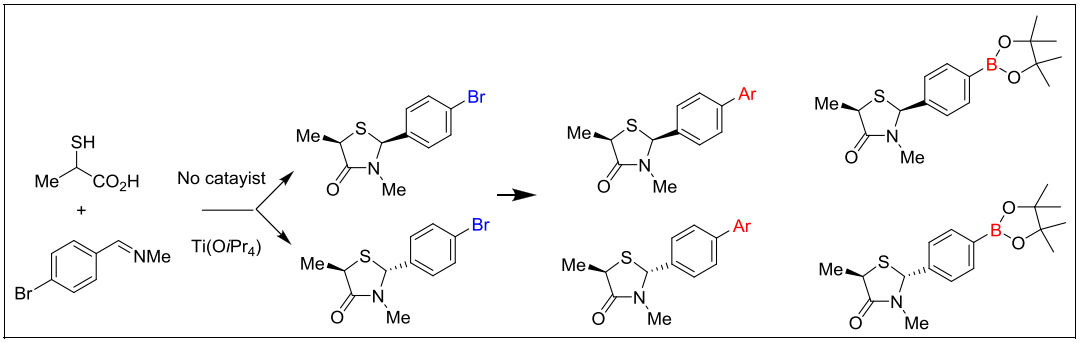

Novel *cis*- and *trans*-2-(*p*-bromophenyl)-5-methylthiazolidin-4-ones, *S*,*N*-containing heterocyclic compounds, were provided in a *cis*-stereocomplementary and *trans*-stereocomplementary synthetic manner. *cis*-Selective cyclo-condensation proceeded between 2-sulfanylpropanoic acid (thiolactic acid) and an imine derived from 4-bromobenzaldehyde and methylamine, whereas Ti(O*i*Pr)$_4$ and Ti(O*i*Bu)$_4$-promoted *trans*-selective cyclo-condensation proceeded between benzyl 2-sulfanylpropanoate and the imine. The obtained *cis*- and *trans*-2-(*p*-bromophenyl)-5-methylthiazolidin-4-ones were successfully converted to 2-(3-furyl)phenyl derivatives and bis(pinacolato)diborane derivatives utilizing Suzuki–Miyaura and Miyaura–Ishiyama cross-coupling reactions, respectively, in an umpolung manner.

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INTRODUCTION

Thiazolidin-4-ones are representative *S*,*N*-containing heterocycles as isosters of oxazoles and thiazoles. These compounds comprise a variety of clinically used pharmaceuticals, such as antimicrobial, antiviral, anti-inflammatory, and antitubercular agents. A recent comprehensive review to index original studies published between 2000 and 2011 revealed the significance of a number of biologically active thiazolidin-4-ones [1]. Synthetic studies of thiazolidin-4-ones, therefore, have been well-investigated to date from the standpoint of both medicinal and process chemistries [2].

Compared with simple 5-unsubstituted thiazolidin-4-ones, the construction of more complex 2,5-disubstituted thiazolidin-4-ones **1** is, however, quite limited due to the *cis/trans* stereoselection issue (Fig. 1). Recent representative studies of **1** include the following: (i) 2-phenyl-5-methyl derivative as mycelial growth inhibitor [3], (ii) 2-aryl-5-(amide methylene) derivatives as C–C chemokine receptor type 4 (CCR4) antagonists [4], (iii) 2-aryl-5-(amide methylene) derivatives as follicle-stimulating hormone receptor antagonists [5], (iv) 2-aryl-5-(carbonyl methylene) derivatives as bacterial and fungal growth inhibitors [6], and (v) 2-aryl-5-carboxymethyl derivatives as nematicidal agents against Bacillus subtilis, Staphlococcus aureus, and *Escherichia coli* [7].

Beside the bioorganic and medicinal chemistries, Sausa's group reported unique photolytic and thermal ring-contractions using sulfone derivatives of 2-phenyl-5-methyl-thiazolidin-4-ones to β-lactams [8]. Feringa's and Kellogg's groups utilized 2-(2-pyridyl)-5-methylthiazolidin-4-ones as chiral ligands for Cu(I)-catalyzed asymmetric1,4-addition to enones [9]. Bazureau and Fraga-Dubreuil reported a task-specific ionic liquid and microwave-assisted method for preparing 2,5-disubstituted thiazolidin-4-ones [10].

This background led us to investigate a *cis/trans* stereocomplementary preparative method and its extension to Suzuki–Miyaura (SM) cross-coupling reactions. Here, we describe a *cis/trans* stereocomplementary synthesis of novel 2-(4-bromopheneyl)-3,5-dimethyl-2-thiazolidin-4-ones (*cis*-**2**) and (*trans*-**2**) (Fig. 2). Moreover, *cis*-**2** and *trans*-**2** served as useful precursors of umpolung-type SM cross-couplings. 2-(3-Furyl)phenyl derivatives *cis*-**3** and *trans*-**3**

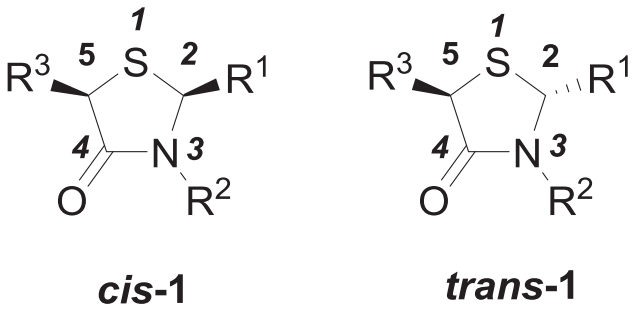


Figure 1. Structure of 2,5-disubstituted thiazolidin-4-ones.

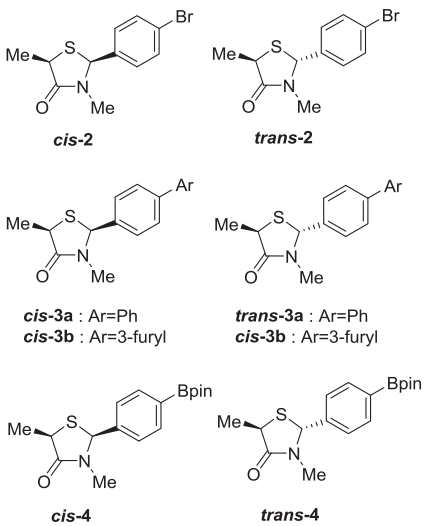


Figure 2. *cis/trans* Stereocomplementary synthesis of novel 2-(4-bromopheneyl)-3,5-dimethyl-2-thiazolidin-4-ones and the derivatives.

were produced from *cis*-**2** and *trans*-**2** as the SM acceptor, and $(pinB)_2$ [bis(pinacolato)diborane] derivatives *cis*-**4** and *trans*-**4** were also provided from *cis*-**2** and *trans*-**2** as SM donors.

RESULTS AND DISCUSSION

The most traditional procedure for the preparation of 2,5-disubstituted thiazolidin-4-ones *cis*-**1** and *trans*-**1** involves a three- (*or* two-) component cyclo-condensation reaction using 2-sulfanyl(*or* mercapto)carboxylic acids, aldehydes, and amines (*or* their imines derived from aldehydes, and amines) [2]. This reaction predominantly yields *cis*-rich products, consistent with the related preparative method for chiral *cis*-2,5-disubstituted 1,3-dioxolan-4-ones (Seebach and Fráter's chiral template) [11,12] and 2,5-oxathiol-4-ones [13]. During our synthetic studies of the antiplatelet factor drug possessing-specific 2-(3-pyridyl)-3,5-dimethylthiazolidin-4-one and 5-(*p*-chloro)phenyl analogues, we performed a *cis/trans* stereocomplementary synthesis of these compounds [14] and revealed the stereostructure–activity relationship between all the four chiral stereoisomers [15]. Utilizing this method, our initial attempt toward the *cis*-selective cyclo-condensation between 2-sulfanylpropanoic acid (thiolactic acid) (**5**) and *N*-(4-bromobenzylidene)methylamine (**6**) afforded novel 2,5-disubstituted thiazolidin-4-ones *cis*-**2** (82%) with small amounts of *trans*-**2** (14%) (Scheme 1).

For metal alkoxide-mediated *trans*-selective cyclo-condensations, benzyl 2-sulfanylpropanoate (**7**) was selected instead of the original methyl ester due to its unpleasant odor. The reaction between ester **7** and imine **6** proceeded smoothly to afford thiazolidin-4-ones *trans*-**2** as a major stereoisomer. The successful results are listed in Table 1. Among boronium, aluminum, and titanium alkoxides, $Ti(OiPr)_4$ and $Ti(OiBu)_4$ produced the best results in terms of both yield and *trans*-selectivity (entries 3 and 4). To the best of our knowledge, this is the first and most reliable method for preparing less accessible *trans*-2,5-disubstituted thiazolidin-4-ones.

To further investigate the *cis*-selectivity and *trans*-selectivity issue, cyclo-condensations using the t-Butyl dimethylsilyl (TBS) ester **8** as an isoster of acid **5** and benzyl ester **7** were examined (Scheme 2). TBS ester **8** was readily prepared from acid **5** using $TBSCl/Et_3N$ in 84% yield (Experimental section). The cyclo-condensation reaction of **8** with imine **6** proceeded smoothly to give *cis*-**2**, mainly with *trans*-**2** (total 94%). In contrast, $Al(OsBu)_3$ and $Ti(OiPr)_4$ catalysts promoted *trans*-selective cyclo-condensation to yield *trans*-**2**. Their effects on these *cis*-selectivities and *trans*-selectivities, however, were in a similar those of intact acid **5** and benzyl ester **7**.

These successful outcomes and along with our recent interest in practical cross-coupling reactions [16] led us to investigate a couple of SM cross-couplings (Scheme 3). The reaction of thiazolidin-4-ones *trans*-**2** with phenylboronic acid under several SM cross-coupling conditions was initially investigated (Table 2). Salient features are as follows. (i) Among various ligands for

Scheme 1. *cis*-Selective cyclo-condensation between thiolactic acid (**5**) and imine **7**.

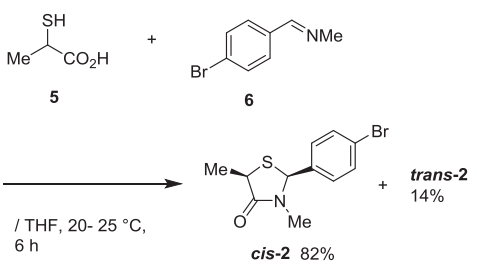


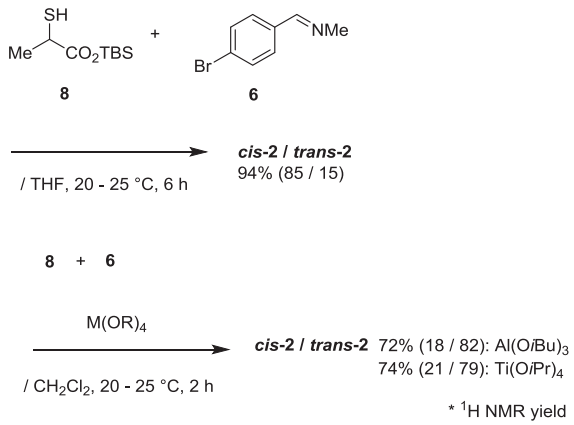
Table 1

$M(OR)_n$-mediated *trans*-selective cyclo-condensation of benzyl ester **7**.

Entry	Lewis acid	Yield/%[a]	*cis*/*trans*[a]
1	$B(OiPr)_3$	20	86:14
2	$Al(OsBu)_3$	52	26:74
3	$Ti(OiPr)_4$	85 (*cis*: 14; *trans*:71)[b]	18:82
4	$Ti(OiBu)_4$	93	18:82

[a]Determined by ^1H nuclear magnetic resonance of the crude products.
[b]Isolated.

Scheme 2. *cis*-Selective and *trans*-selective cyclo-condensation between thiolactic acid TBS ester (**5**) and imine **7**.



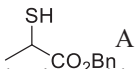
$Pd(OAc)_2$, SPhos gave the best result in yield (entry 7). (ii) K_3PO_4 base was somewhat more effective than K_2CO_3 (entries 10–13). (iii) THF solvent gave the best yield (entry 13).

With this successful result in hands, SM cross-coupling reaction using 3-furylboronic acid in the presence of $Pd(OAc)_2$ (5 mol%)/SPhos ligand (10 mol%)/K_3PO_4 furnished the desired coupling product *cis*-**3** in 66% yield, wherein the thiazolidin-4-one skeleton tolerated during the reaction conditions. The *trans*-**3** isomer was similarly obtained from *trans*-**2** in 99% excellent yield under the identical conditions.

Finally, we focused our interest on the related Miyaura–Ishiyama cross-couplings [17] of *cis*-**2** and *trans*-**2** with $(pinB)_2$ [bis(pinacolato)diborane] to obtain the corresponding (pinB)-products *cis*-**4** and *trans*-**4** as the umpolung-type cross-coupling partners. The desired reaction catalyzed by $Pd(dppf)Cl_2$ (5 mol%)/KOAc proceeded successfully to produce the pinB-substituted derivatives *cis*-**4** and *trans*-**4** products in 76% and in 74% yields, respectively.

In conclusion, we performed *cis*-stereocomplementary and *trans*-stereocomplementary synthesis of novel 2-(*p*-bromophenyl)-5-methylthiazolidin-4-ones. The cyclo-condensation of 2-sulfanylpropanoic acid with *N*-(4-bromobenzylidene)methylamine afforded the desired *cis*-product, whereas use of the $Ti(OiPr)_4$ or $Ti(OiBu)_4$ catalyst afforded the complementary *trans*-product with high diastereoselectivity. As a notable application of the obtained thiazolidin-4-ones, a set of umpolung-type cross-couplings (SM and Miyura–Ishiyama) was performed to afford the corresponding coupling products. This strategy to obtain thiazolidin-4-one core building blocks will contribute to the research for medicinal and process chemistry.

EXPERIMENTAL

Benzyl 2-sulfanylpropanoate (7) [14]. 

A mixture of 2-sulfanylpropanoic acid (thiolactic acid) (1.77 mL, 20.0 mmol), benzyl alcohol (4.33 g, 40.0 mmol), and *p*-toluenesulfonic acid (190 mg, 1.00 mmol) in toluene was refluxed for 5 h using Dean–Stark apparatus with continual removal of water. After cooling to room temperature, water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane/AcOEt = 8:1) to give the desired product **1** (3.61 g, 92%).

Colorless oil; ^1H nuclear magnetic resonance (NMR) (500 MHz, $CDCl_3$): δ = 1.54 (d, J = 6.87 Hz, 3H), 2.17 (d, J = 8.02 Hz, 1H), 3.55 (dq, J = 6.87 Hz, 8.02 Hz, 1H), 5.16 (d, J = 12.03 Hz, 1H), 5.19 (d, J = 12.03 Hz, 1H), 7.31–7.41 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.0, 35.6, 67.0, 128.1 (2C), 128.3, 128.5 (2C), 135.5, 173.4; IR (neat): ν_{max} = 1732, 1454, 1379, 1325, 1163, 1103 cm^{-1}.

Scheme 3. Umpolung-type Suzuki–Miyaura cross-coupling using *cis*-**2** and *trans*-**2**.

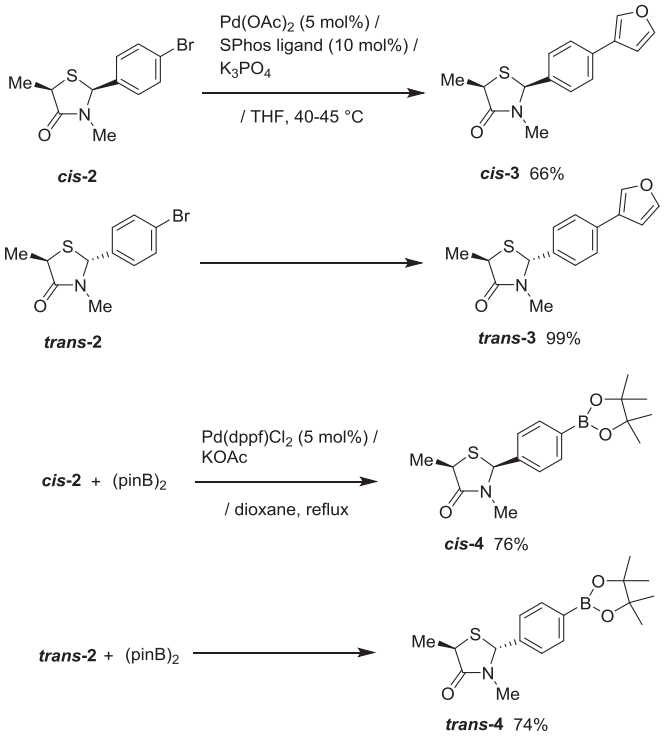
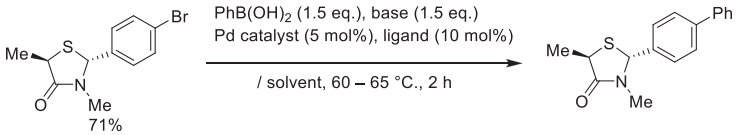


Table 2

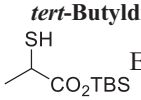
Suzuki–Miyaura cross-coupling using *trans*-**2**.



Entry	Pd catalyst	Ligand	Base	Solvent	Temp./°C	Yield/%[a]
1	$Pd(OAc)_2$	PPh_3	K_2CO_3	Toluene	60–65	37
2		PBu_3				50
3		PCy_3				54
4		*t*BuXPhos				28
5		JhonPhos				65
6		DavePhos				73
7		SPhos				81
8	$Pd(PPh_3)_2$	–				36
9	$Pd(dppe)Cl_2$	–				45
10	$Pd(OAc)_2$	SPhos	K_3PO_4			93
11				MeCN	40–45	39
12				*i*PrOH		90
13				THF		99 (94)[b, c]

[a]Determined by ^1H nuclear magnetic resonance of the crude products.
[b]Isolated.
[c]Reaction time is 4 h.

***tert*-Butyldimethylsilyl 2-sulfanylpropanoate (8).**

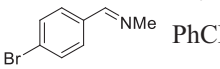


Et_3N (1.52 mL, 11.0 mmol) and a solution of TBSCl (1.51 g, 10.0 mmol) in CH_2Cl_2 (5.0 mL) were successively added to a stirred solution of thiolactic acid (1.17 g, 11.0 mmol) in CH_2Cl_2 (10 mL) at 0–5°C under an Ar atmosphere, and the mixture was stirred at the same temperature for 1 h. Water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with 1 M aqueous

HCl, brine, dried (Na_2SO_4), and concentrated. The obtained product (1.85 g, 84%) was sufficient pure.

Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.290 (s, 3H), 0.294 cm^{-1} (s, 3H), 0.96 (s, 9H), 1.50 (d, *J* = 7.45 Hz, 3H), 2.10 (d, *J* = 7.45 Hz, 1H), 3.50 (quin, *J* = 7.45 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.1, −5.0, 17.7, 21.0, 25.4 (3C), 37.3, 173.5.

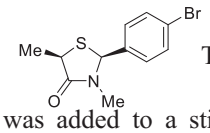
***N*-(4-bromobenzylidene)methylamine (6) [18].**



PhCHO (9.25 g, 50.0 mmol) in EtOH (70 mL) was added to a stirred 40% aqueous $MeNH_2$ solution (100 mL) at 0–5°C, and the mixture was stirred at the same temperature for 2 h. The mixture was extracted twice with AcOEt, and the combined organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was distilled under reduced pressure to give the desired product **2** (8.41 g, 85%).

Pale yellow oil; BP 119–123°C/23 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.51 (d, *J* = 1.72 Hz, 3H), 7.52–7.60 (m, 4H), 8.23 (d, *J* = 1.72 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.1, 124.8, 129.2 (2C), 131.8 (2C), 135.0, 161.1; IR (neat): ν_{max} = 2847, 1651, 1589, 1487, 1400, 1067, 1009 cm^{-1}.

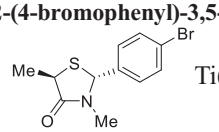
2*S,5*R**)-*cis*-2-(4-bromophenyl)-3,5-dimethylthiazolidin-4-one (*cis*-2).**



Thiolactic acid (318 mg, 3.00 mmol) was added to a stirred solution of imine **2** (713 mg, 3.60 mmol) in THF (6 mL) at room temperature under an Ar atmosphere, and the mixture was stirred at the same temperature for 6 h. The mixture was concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane/AcOEt = 5:1–3:1) to give the desired product ***cis*-3** *(701 mg, 82%) and* **trans-*3*** *(123 mg, 14%).*

Colorless crystals; mp 113–115°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.64 (d, *J* = 6.87 Hz), 2.70 (s, 3H), 3.95 (q, *J* = 6.87, 1H), 5.42 (s, 1H), 7.18–7.22 (m, 2H), 7.51–7.55 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.2, 30.4, 42.3, 63.0, 123.0, 128.9 (2C), 132.1 (2C), 138.0, 173.8; IR (neat): ν_{max} = 1674, 1487, 1448, 1388, 1334, 1263, 1211 cm^{-1}; *Anal*. Calcd for $C_{11}H_{12}BrNOS$ (286.19): C, 46.17; H, 4.23; N, 4.89. Found C, 46.01; H, 4.19; N, 4.80. HRMS (ESI): *m/z* calcd for $C_{11}H_{12}BrNOS$ [*M* + Na]$^+$ 307.9721; found: 307.9742.

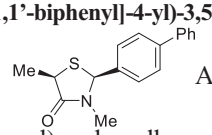
(2*R,5*R**)-*trans*-2-(4-bromophenyl)-3,5-dimethylthiazolidin-4-one (*trans*-2).**



Ti(O*i*Pr)$_4$ (1.58 mL, 6.0 mmol) was added to a stirred solution of ester **7** (981 mg, 5.0 mmol) and imine **6** (1.19 g, 6.0 mmol) in CH_2Cl_2 (10 mL) at room temperature under an Ar atomosphere, and the mixture was stirred at the same temperature for 2 h. Water was added to the mixture, and organic phase was separated by Celite filtration using $CHCl_3$. The separated organic phase was dried (Na_2SO_4) and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane/AcOEt = 5:1–2:1) to give the desired product ***trans*-3** (1.01 g, 71%) and ***cis*-3** (199 mg, 14%).

Colorless crystals; mp 153–155°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.59 (d, *J* = 7.45 Hz, 3H), 2.75 (s, 3H), 4.05 (dq, *J* = 1.72, 7.45 Hz, 1H), 5.42 (d, *J* = 1.72 Hz, 1H), 7.14–7.17 (m, 2H), 7.50–7.54 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.9, 30.3, 41.5, 62.7, 122.8, 128.2 (2C), 132.2 (2C), 138.6, 173.8; IR (neat): ν_{max} = 1672, 1487, 1448, 1390, 1259, 1215, 1070, 1008 cm^{-1}.

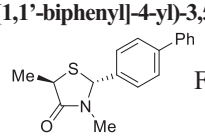
(2*S,5*R**)-cis-2-([1,1'-biphenyl]-4-yl)-3,5-dimethylthiazolidin-4-one (*cis*-3a).**



A mixture of ***cis*-2** (286 mg, 1.0 mmol), phenylboronic acid (183 mg, 1.5 mmol), K_3PO_4 (637 mg, 3.0 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and SPhos (41 mg, 0.1 mmol) in THF (2 mL) was stirred at 40–45°C for 4 h. After cooling down, water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane/AcOEt = 4:1) to give the desired product ***cis*-3a** *(246 mg, 87%).*

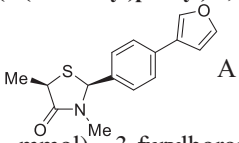
Pale yellow crystals; mp 87–89°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.68 (d, *J* = 7.45 Hz, 3H), 2.76 (s, 3H), 3.98 (q, *J* = 7.45 Hz, 1H), 5.52 (s, 1H), 7.35–7.41 (m, 3H), 7.43–7.48 (m, 2H), 7.57–7.63 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.4, 30.4, 42.4, 63.4, 127.0 (2C), 127.59, 127.65 (2C), 127.7 (2C), 128.8 (2C), 137.8, 140.1, 142.1, 173.9; IR (neat): ν_{max} = 1674, 1485, 1449, 1389, 1341, 1263, 1209, 1120 cm^{-1}; *Anal*. Calcd for $C_{17}H_{17}NOS$ (283.39): C, 72.05; H, 6.05; N, 4.94; O, 5.65; S, 11.31. Found C, 71.91; H, 5.91; N, 4.91. HRMS (ESI): *m/z* calcd for $C_{17}H_{17}NOS$ [*M* + Na]$^+$ 306.0929; found: 306.0918.

(2*R,5*R**)-*trans*-2-([1,1'-biphenyl]-4-yl)-3,5-dimethylthiazolidin-4-one (*trans*-3a).**

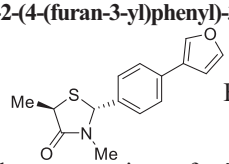


Following a similar procedure for the preparation of ***cis*-2**, the reaction of ***trans*-2** (286 mg, 1.0 mmol), phenylboronic acid (183 mg, 1.5 mmol), K_3PO_4 (637 mg, 3.0 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), and SPhos (41 mg, 0.1 mmol) in THF (2 mL) at 40–45°C for 4 h yielded the crude oil, which was purified by silica-gel column chromatography (hexane/AcOEt = 5:1) to give the desired product ***trans*-3a** (267 mg, 94%).

Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.61 (d, *J* = 6.87 Hz, 3H), 2.79 (s, 3H), 4.09 (dq, *J* = 1.72, 7.45 Hz, 1H), 5.50 (d, *J* = 1.72 Hz, 1H), 7.31–7.38 (m, 3H), 7.41–7.47 (m, 2H), 7.54–7.62 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.5, 31.1, 42.3, 63.7, 127.61 (2C), 127.63 (2C), 128.2, 128.4 (2C), 129.4 (2C), 139.0, 140.8, 142.5, 174.6; IR (neat): ν_{max} = 1672, 1485, 1449, 1391, 1339, 1258, 1213, 1122 cm^{-1}.

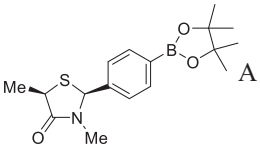
(2*S,5*R**)-*cis*-2-(4-(furan-3-yl)phenyl)-3,5-dimethylthiazolidin-4-one (*cis*-3).**  A mixture of ***cis*-2** (143 mg, 0.50 mmol), 3-furylboronic acid (84 mg, 0.75 mmol), K_3PO_4 (318 mg, 1.50 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), and SPhos (21 mg, 0.05 mmol) in THF (1 mL) was stirred at 40–45°C for 2 h. After cooling down, water was added to the mixture, which was extracted twice with AcOEt. The combined organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane/AcOEt = 3:1) to give the desired product (91 mg, 66%).

Pale yellow crystals; mp 72–76°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.67 (d, *J* = 6.87 Hz, 3H), 2.73 (s, 3H), 3.97 (q, *J* = 6.87 Hz, 1H), 5.48 (s, 1H), 6.68–6.72 (m, 1H), 7.30–7.34 (m, 2H), 7.48–7.52 (m, 3H), 7.74–7.76 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.3, 30.4, 42.4, 63.4, 108.6, 125.7, 126.4 (2C), 127.7 (2C), 133.4, 137.4, 138.8, 143.8, 173.9; IR (neat): ν_{max} = 1668, 1520, 1362, 1263, 1161, 1053, 1015 cm^{-1}; *Anal*. Calcd for $C_{15}H_{15}NO_2S$ (273.35): C, 65.91; H, 5.53; N, 5.12; Found C, 65.87; H, 5.49; N, 5.05. HRMS (ESI): *m/z* calcd for $C_{15}H_{15}NO_2S$ [*M* + Na]$^+$ 296.0721; found: 296.0733.

(2*R,5*R**)-*trans*-2-(4-(furan-3-yl)phenyl)-3,5-dimethylthiazolidin-4-one (*trans*-3).**  Following the similar procedure for the preparation of ***cis*-3**, the reaction of ***trans*-2** (143 mg, 0.50 mmol), 3-furylboronic acid (84 mg, 0.75 mmol), K_3PO_4 (318 mg, 1.50 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), and SPhos (21 mg, 0.05 mmol) in THF (1 mL) at 40–45°C for 2 h gave the crude product, which was purified by silica-gel column chromatography (hexane/AcOEt = 4:1) that gave the desired product (135 mg, 99%).

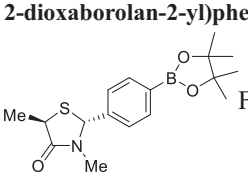
Pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.61 (d, *J* = 6.87 Hz, 3H), 2.77 (s, 3H), 4.08 (dq, *J* = 1.72, 6.87 Hz, 1H), 5.47 (d, *J* = 1.72 Hz, 1H), 6.68–6.71 (m, 1H), 7.25–7.30 (m, 2H), 7.48–7.52 (m, 3H), 7.73–7.77 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$, 59°C): δ = 19.9, 30.4, 41.6, 63.3, 108.7, 125.9, 126.5 (2C), 127.1 (2C), 133.4, 138.3, 138.8, 143.8, 174.0; IR (neat): ν_{max} = 1759, 1668, 1392, 1259, 1161, 1055, 1014 cm^{-1}.

(2*S,5*R**)-*cis*-3,5-dimethyl-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)thiazolidin-4-one (*cis*-4).**

 A mixture of ***cis*-3** (143 mg, 0.50 mmol), bis(pinacolato)diborane (190 mg, 0.75 mmol), KOAc (147 mg, 1.50 mmol), and Pd(dppf)Cl_2 (18 mg, 0.025 mmol) in dioxane (2.5 mL) was stirred at 95–100°C for 16 h. After cooling down, water was added to the mixture, which was filtered. Filtrate was extracted twice with AcOEt. The combined organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane/AcOEt = 3:1) to give the desired product (126 mg, 76%).

Colorless crystals; mp 163–164°C, ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (s, 12H), 1.65 (d, *J* = 6.87 Hz, 3H), 2.71 (s, 3H), 3.95 (q, *J* = 6.87 Hz, 1H), 5.47 (s, 1H), 7.29–7.32 (m, 2H), 7.81–7.85 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.5, 24.9 (2C), 25.0 (2C), 30.6, 42.5, 63.7, 84.1 (2C), 126.5 (2C), 135.6 (2C), 142.0, 174.2; IR (neat): ν_{max} = 2976, 1678, 1611, 1357, 1265, 1142, 1088 cm^{-1}; *Anal*. Calcd for $C_{17}H_{24}BNO_3S$ (333.25): C, 61.27; H, 7.26; N, 4.20. Found C, 61.15; H, 7.21; N, 4.18. HRMS (ESI): *m/z* calcd for $C_{17}H_{24}BNO_3S$ [*M* + Na]$^+$ 356.1471; found: 356.1470.

(R*S,5*R**)-*trans*-3,5-dimethyl-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)thiazolidin-4-one (*trans*-4).**

 Following a similar procedure for the preparation of ***cis*-5**, the reaction of ***trans*-3** (143 mg, 0.50 mmol), bis(pinacolato)diborane (140 mg, 0.55 mmol), KOAc (147 mg, 1.50 mmol), and Pd(dppf)Cl_2 (18 mg, 0.025 mmol) in dioxane (2.5 mL) at 95–100°C for 4 h gave the crude product, which was purified by silica-gel column chromatography (hexane/AcOEt = 3:1) that gave the desired product (122 mg, 74%).

Colorless crystals; mp 115–116°C, ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (s, 12H), 1.60 (d, *J* = 6.87 Hz, 3H), 2.76 (s, 3H), 4.70 (dq, *J* = 1.72, 6.87 Hz, 1H), 5.46 (d, *J* = 1.72 Hz, 1H), 7.24–7.28 (m, 2H), 7.81–7.85 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.8, 24.8 (2C), 24.8 (2C), 30.4, 41.5, 63.2, 83.9 (2C), 125.7 (2C), 135.5 (2C), 142.5, 174.0; IR (neat): ν_{max} = 2976, 1678, 1611, 1358, 1265, 1144, 1088 cm^{-1}.

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