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Enantioselective Synthesis of Ring-Fused Spiroannulated 1,2,3-Thiadiazole Derivatives

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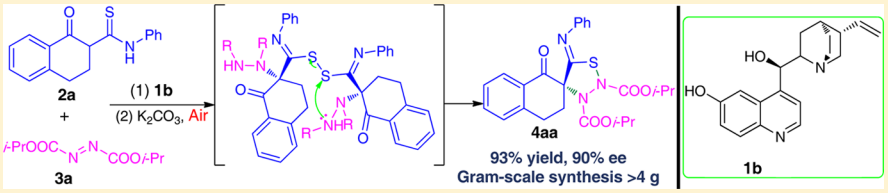
Supporting Information



ABSTRACT: An organocatalytic enantioselective domino α-amination/oxidative coupling/cyclization of thioamides to azodicarboxylates catalyzed by an easily available organic catalyst has been developed. The key step, oxidative coupling, is smoothly fulfilled in air. Optically active spiroannulated 1,2,3-thiadiazole derivatives are obtained with high yields and enantioselectivities for the first time.

INTRODUCTION

Heterocyclic compounds are widespread in nature and have attracted much attention due to their utility as building blocks in the synthesis of natural products, pharmaceutical agents, and materials. Derivatives of 1,2,3-thiadiazole ,which contain three heteroatoms, are known to exhibit broad pharmacological properties, such as anticancer,[1] antimicrobial,[2] anticonvulsant,[3] fungicidal,[4] antihepatitis B virus,[5] and anti-HIV.[6] One of the most significant properties is that systemic acquired resistance (SAR) can be induced by some 1,2,3-thiadiazole derivatives.[7] Figure 1 depicts chemical structures of selected bioactive 1,2,3-thiadiazoles. They are also useful intermediates in the synthesis of various sulfur-containing acyclic, alicyclic, and heterocyclic compounds.[8,9] The Hurd–Mori cyclization of α-diazo (thio)-carbonyl compounds is the most convenient methodology for the synthesis of 1,2,3-thiadiazoles.[10] 1,2,3-Thiadiazoles can also be prepared by thionyl chloride ($SOCl_2$)-induced cyclizations of tosylhydrazones, alkyl 1-hydrazonecarboxylates, or semicarbazones.[11] However, the use of specific substrates and expedited workup has inevitably lowered the overall atomic efficiency. In particular, to the best of our knowledge, there is no report on a direct catalytic asymmetric method for the synthesis of optically active 1,2,3-thiadiazoles. As such, the application of chiral 1,2,3-thiadiazoles in natural products, pharmaceutical agents, and material synthesis has been hampered by the lack of efficient procedures for their synthesis. In this work, we report for the first time an unexpected enantioselective organocatalytic domino α-amination/oxidative coupling/cyclization of thioamides to azodicarboxylates and its direct application in an atom-economic synthesis of chiral spiro 1,2,3-thiadiazole derivatives.

RESULTS AND DISCUSSION

In the past few years, significant effort in our group has been put toward the development of new domino reactions through organocatalyzed 1,3-dicarbonyl compound activation.[12] Recently, we successfully demonstrated an unexpected enantioselective organocatalytic intramolecular oxidative umpolung of thioamides **2** with (*E*)-α-nitrostyrenes to produce spiroannulated dihydrothiophenes (Scheme 1, eq 1).[13] In addition, umpolung is a well-known reversal of expected chemical reactivity and has been proven to be a powerful strategy in chemistry that facilitates the construction of organic molecules in unusual ways.[14] On the basis of these successful results, we envisioned that, under appropriate organocatalytic conditions, a new α-amination would be possible between cyclic thioamide **2a** and diisopropyl azodicarboxylate **3a**, giving a facile protocol to α-amino thioamide **Iaa**. Subsequently, an intramolecular cyclization could proceed by reversal of the thiol polarity (bromide transfer from an oxidant NBS to thiol to yield sulfenyl bromide) to yield the product spiro 1,2,3-thiadiazole derivative **4aa** (Scheme 1, eq 2). Then, the domino reaction of cyclic thioamide **2a** (0.1 mmol) with diisopropyl azodicarboxylate **3a** (0.2 mmol) was first catalyzed by organocatalyst **1a** (Figure 2) using *N*-bromosuccinimide (NBS) as oxidant in DCM at room temperature. To our delight, the expected cyclic product spiro 1,2,3-thiadiazole derivative **4aa** was isolated in 27% yield after 6 h (Scheme 2). The structure of **4aa** was unambiguously confirmed by X-ray crystal structure analysis. Surprisingly, we found that the domino reaction proceeded smoothly in the absence of NBS, i.e., K_2CO_3 is sufficient to promote the reaction to produce racemic compound (Rac-**4aa**,

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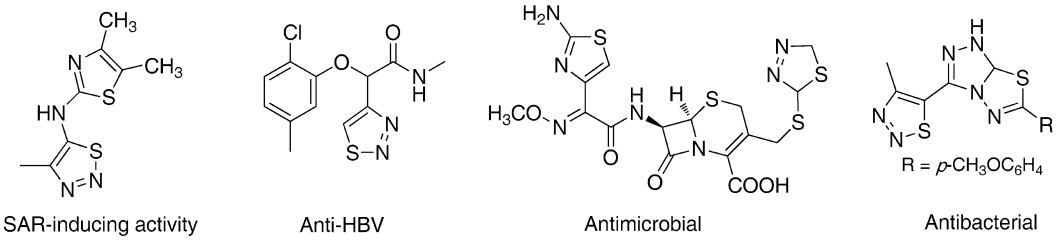
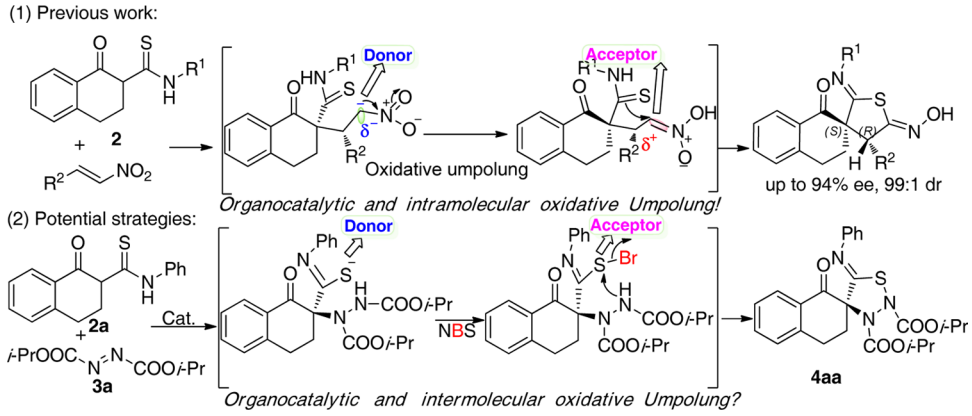


Figure 1. Some representative examples of biologically active compounds.

Scheme 1



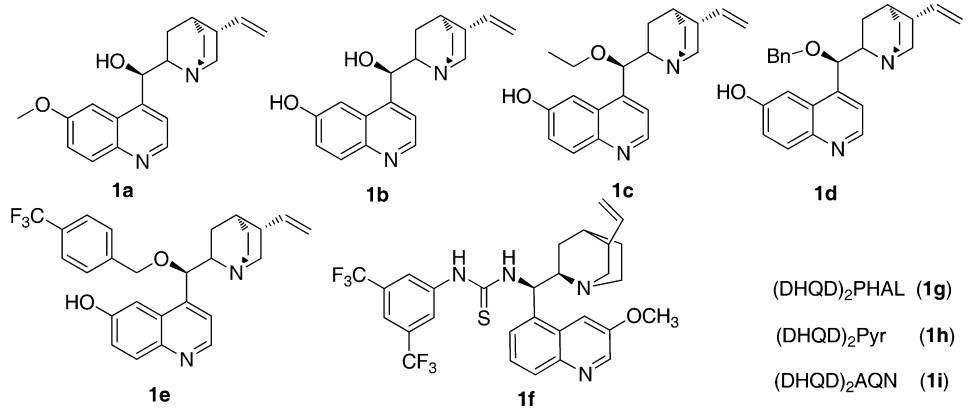
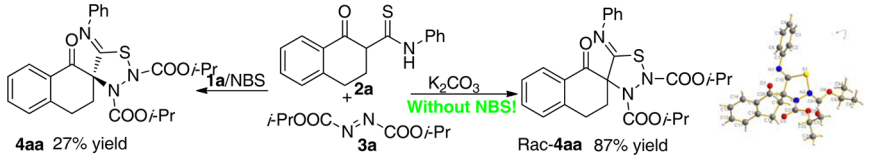


Figure 2. Structure of Organocatalysts **1a**−**i**.

Scheme 2



Scheme 2). As such, K_2CO_3 was selected as additive for further investigation (Table 1).

The results for some of the screening investigations for the enantioselective domino α-amination/cyclization of thioamide **2a** with diisopropyl azodicarboxylate **3a** catalyzed by organocatalysts **1a**−**i** (Figure 2) under various reaction conditions are presented in Table 1. Only trace product **4aa** was observed if only quinine **1a** was used as the catalyst (entry 1). With the addition of 1.0 equiv of K_2CO_3, the spiro 1,2,3-thiadiazole derivative **4aa** was obtained, though the yield and enantioselectivity were poor (entry 2). Cinchona alkaloids bearing a 6′-hydroxyquinoline ring **1b**−**e**, which have been identified recently as effective catalysts for enantioselective conjugate addition,[15] were found to effect the transformation in much higher enantioselectivity and faster rate in comparison to those of catalysts **1f**−**1i** without a 6′-hydroxyquinoline ring (entries 3−6, 82−90% ee vs entries 7−10, 12−30% ee). Screening of catalysts **1** for the domino α-amination/cyclization of thioamide **2a** with diisopropyl azodicarboxylate **3a** in CH_2Cl_2 at room temperature revealed that **1b** afforded excellent enantioselectivities (90% ee) for product **4aa**. In addition, a variety of basic additives (NaOH, KOH, Na_2CO_3) and solvents

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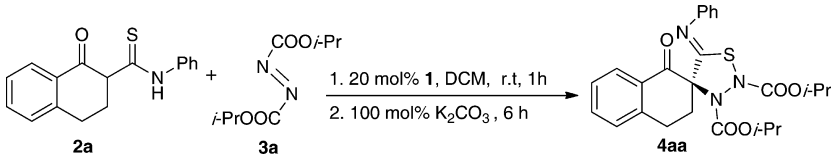
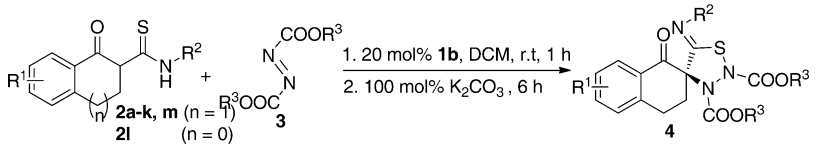
Table 1. Screening Studies of Organocatalytic Domino Reaction of Thioamide 2a to Diisopropyl Azodicarboxylate 3a[a]



entry	cat. 1/additive	yield (%)[b]	ee (%)[c]	entry	cat. 1/additive	yield (%)[b]	ee (%)[c]
1[d]	**1a**/-	trace		8	**1g**/K_2CO_3	55	20
2	**1a**/K_2CO_3	30	4	9	**1h**/K_2CO_3	60	30
3	**1b**/K_2CO_3	93	90	10	**1i**/K_2CO_3	40	12
4	**1c**/K_2CO_3	86	82	11[e]	**1b**/K_2CO_3	93	89
5	**1d**/K_2CO_3	83	82	12[f]	**1b**/K_2CO_3	92	90
6	**1e**/K_2CO_3	94	88	13[g]	**1b**/K_2CO_3	90	90
7	**1f**/K_2CO_3	30	12	14	**1b**/NBS	68	90

[a]All reactions were carried out with **2a** (0.1 mmol) and **3a** (0.20 mmol) in DCM (2.00 mL) with the indicated catalysts for 1 h at room temperature; then, additive (0.1 mmol) was added and stirred for 6 h. [b]Isolated yield. [c]Determined by HPLC analysis. [d]No NBS was added. [e]At 50 °C. [f]At 0 °C. [g]At −10 °C.

Table 2. Substrate Scope for the Synthesis of Products 4[a]



entry	R^1	R^2	2	R^3	3	4[b]	yield (%)	ee (%)[c]
1	H	C_6H_5	**2a**	*i*-Pr	**3a**	**4aa**	93	90
2	H	C_6H_5	**2a**	Et	**3b**	**4ab**	86	90
3	H	C_6H_5	**2a**	*t*-Bu	**3c**	**4ac**	90	91
4	H	*p*-$CH_3C_6H_4$	**2b**	*i*-Pr	**3a**	**4ba**	84	86
5	H	*p*-(*i*-Pr)C_6H_4	**2c**	*i*-Pr	**3a**	**4ca**	93	91
6	H	*m*-$OCH_3C_6H_4$	**2d**	*i*-Pr	**3a**	**4da**	92	89
7	H	*o*-$OCH_3C_6H_4$	**2e**	*i*-Pr	**3a**	**4ea**	80	94
8	*p*-OMe	C_6H_5	**2f**	*i*-Pr	**3a**	**4fa**	82	86
9[d]	H	*p*-ClC_6H_4	**2g**	*i*-Pr	**3a**	**4ga**	90	83
10	H	*m*-ClC_6H_4	**2h**	*i*-Pr	**3a**	**4ha**	83	83
11[e]	H	*o*-ClC_6H_4	**2i**	*i*-Pr	**3a**	**4ia**	84	80
12	H	*p*-FC_6H_4	**2j**	*i*-Pr	**3a**	**4ja**	92	84
13	H	*β*-naphthyl	**2k**	*i*-Pr	**3a**	**4ka**	94	92
14	H	*o*-$OCH_3C_6H_4$	**2e**	Et	**3b**	**4eb**	90	96
15	H	*o*-$OCH_3C_6H_4$	**2e**	*t*-Bu	**3c**	**4ec**	88	98
16	H	C_6H_5	**2l**	*i*-Pr	**3a**	**4la**	85	88
17	H	$CH_3CH_2CH_2$	**2m**	*i*-Pr	**3a**	**4ma**	trace (76)[f]	−(60)[f]

[a]Unless otherwise noted, reactions performed with 0.1 mmol **2**, 0.2 mmol **3**, and 20 mol % **1b** in 2 mL of DCM at room temperature for 1 h; then, K_2CO_3 was added and stirred for 6 h. [b]Isolated yield. [c]Determined by HPLC analysis. [d]At 0 °C. [e]At 20 mol % of **1e**. [f]Catalyzed by 20 mol % of **1b** and 20 mol % of NBS.

(THF, toluene, DMSO, 1,4-dioxane, *n*-hexane) were further screened; unfortunately, inferior results were generally observed. It is worth noting here that the temperature has little effect on the enantioselectivity and yield. Increase the temperature from 25 to 50 °C as well as lowering the temperature to −10 °C resulted in high enantioselectivity and yield (entries 11−13). It is noteworthy that the domino reaction also proceeded smoothly to afford desired product **4aa** with excellent enantioselectivity when the base K_2CO_3 was replaced with the organocatalyst **1b** in the NBS-catalyzed reaction (entry 14).

Encouraged by the promising results described above, a wide range of trisubstituted carbon thioamides **2** were treated with azodicarboxylates **3** in DCM at room temperature in the presence of **1b**/K_2CO_3 (Table 2). The reaction scope proved to be quite broad with respect to both azodicarboxylates and the substitutions on the thioamides. It appeared that substituents' steric nature of azodicarboxylates **3** had minimal impact on efficiency and enantioselectivity of the domino *α*-amination/cyclization (entries 1−3). The electronic nature of a substituent on the aromatic moiety (Ar) of **2** has little effect on enantioselectivity with our organocatalytic protocol (entries 4−7 and 9−12). Maybe the strong p−*π* delocalization of unpaired electrons in the benzene ring leads to a significant decrease in enantioselectivities (entries 9−12). High enantioselectivities were obtained in the domino *α*-amination/cyclization reactions of an electron-donating substituent on the aryl ring (Ar) of thioamides **2**, whereas an electron-withdrawing substituent on the aryl ring of thioamides **2** tended to decrease the enantioselectivities (entries 4−7, 14, and 15 vs

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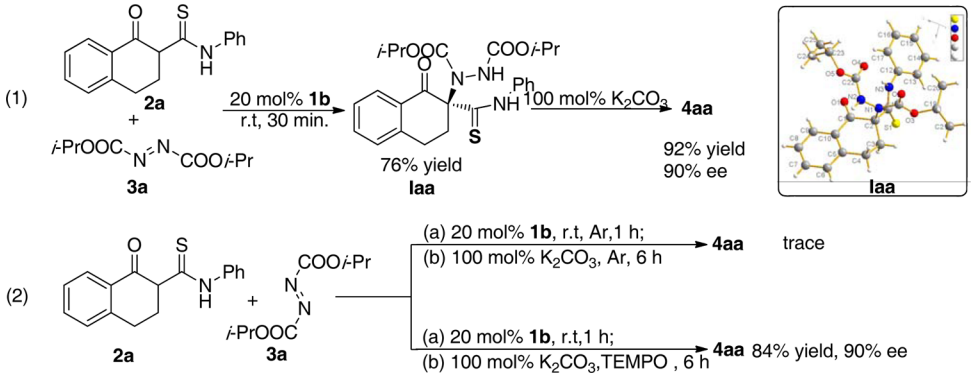
Scheme 3. Control Experiments



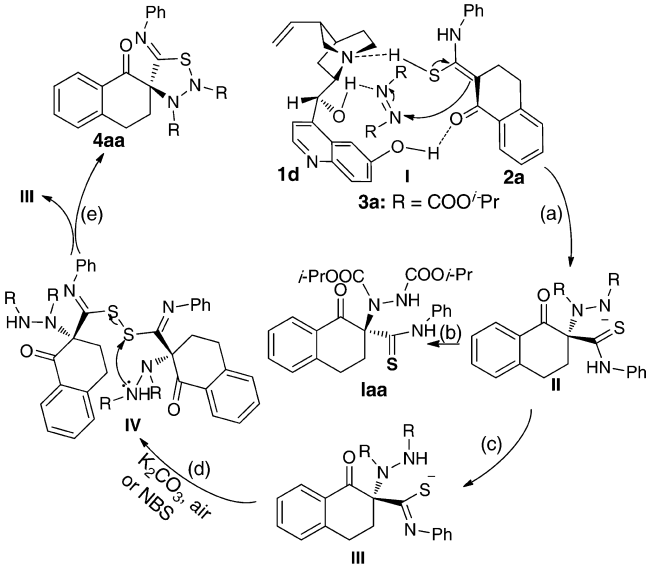
entries 9−12). Obviously, steric hindrance is very important for the reaction, and the best enantioselectivities (94−98%) appear to be observed with the *o*-toluyloxy analogues (entries 7, 14, and 15). In addition, the position of the substituent on the aryl ring of thioamides **2** had a small influence on the enantioselectivity (entries 9−11). Only trace spiroannulated 1,2,3-thiadiazole **4ma** was observed when the aryl ring of thioamides **2** was replaced with *n*-propyl. Interestingly, it is noteworthy that the domino reaction of thioamide **2m** with diisopropyl azodicarboxylate **3a** proceeded smoothly to afford spiroannulated 1,2,3-thiadiazole **4ma** catalyzed by NBS (Table 2, entry 17). The absolute configuration of the polyfunctionalized spiroannulated 1,2,3-thiadiazole derivatives were confirmed by single-crystal X-ray analysis of representative enantiopure **4eb** that bears a sulfur atom. As shown in Figure S1, it composes an (*S*, *Z*) configuration (see Supporting Information, Figure S1).

This new organocatalytic asymmetric domino α-amination/cyclization was also scaled up by 100 times with respect to the reaction shown in Table 2, entry 1. Furthermore, product **4aa** was achieved on a gram scale (>4 g) without any decrease in yield or enantioselectivity. Recycling of the catalyst was also possible, and thus, the reaction provides very easy and inexpensive access to large quantities of enantiopure spiroannulated 1,2,3-thiadiazole derivatives for further biomedical research, natural products, and material synthesis.

For exploring the mechanism of the new organocatalytic asymmetric unexpected domino α-amination/cyclization, more control experiments were conducted (Scheme 3). Intermediate α-amination product **Iaa** was isolated in good yield when the reaction of thioamide **2a** (1 mmo) with diisopropyl azodicarboxylate **3a** (0.1 mmol) was carried out in the presence of **1b**/K_2CO_3 in CH_2Cl_2 at room temperature for 30 min and confirmed by single-crystal X-ray analysis (Scheme 3, eq 1). The reaction in the absence of oxygen was also examined, and only trace product **4aa** was observed when the reaction was performed under argon atmosphere (Scheme 3, eq 2). Subsequently, for trapping free radicals, the nitroxide free-radical trap TEMPO (2,2,6.6-tetramethylpyridinyloxy free radical) is deliberately added to the domino reaction (Scheme 3, eq 2). Interestingly, spiroannulated 1,2,3-thiadiazole **4aa** was also obtained in good yield and excellent enantioselectivity. On the basis of this result, we believe that the reaction did not undergo a radical process.

On the basis of our findings, we proposed the following mechanism for the domino reaction of thioamides **2** with azodicarboxylates **3** (Scheme 4): (a) We hypothesize that both

Scheme 4. Proposed Mechanisms



substrates **2** and **3** can be activated through hydrogen bonding. Then, the α-amination of thioamide **2a** to azodicarboxylate **3a** proceeds via transition-state **I** to generate intermediate **II**. (b) Protonation of intermediate **II** affords α-amination product **Iaa**. (c, d) After the proton transfer, the electron-rich thiol anion **III** might be oxidized to afford disulfide intermediate **IV**;[16] intramolecular attack by N on one of the S atoms in the disulfide intermediate affords final product **4aa** and the release of a molecule of **III**. Nevertheless, the reaction mechanism still remains to be investigated.

CONCLUSION

In summary, we have developed an organocatalytic domino α-amination/oxidative coupling/cyclization of thioamides to azodicarboxylates. The asymmetric reaction is smoothly effected by using simple and green oxygen as the oxidant as well as using NBS. This versatile, atom-economic, and environmentally friendly domino α-amination/oxidation/cyclization affords chiral spiroannulated 1,2,3-thiadiazoles in high yields and enantioselectivities in the presence of an easily available organic catalyst for the first time. Notably, the asymmetric synthesis of chiral spiroannulated 1,2,3-thiadiazoles can be fulfilled on a gram scale (>4 g) without any decrease in yield or enantioselectivity at low cost. Furthermore, it was demonstrated that enantiopure products could be obtained by a

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single recrystallization. A plausible mechanism for this unprecedented domino reaction was given based on the observations. Further development of the related reactions and scopes are being pursued and will be reported in due course.

EXPERIMENTAL SECTION

General Methods. NMR spectra were recorded with tetramethylsilane as the internal standard. TLC was performed on glass-backed silica plates. Column chromatography was performed using silica gel (150−200 mesh) eluting with ethyl acetate and petroleum ether. ^{1}H NMR spectra were recorded at 600 MHz, and ^{13}C NMR spectra were recorded at 150 MHz. Chemical shifts (δ) are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) or DMSO (δ = 2.50 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) or DMSO resonance (δ = 39.5 ppm) for ^{13}C NMR spectroscopy. Coupling constants (J) are given in Hz. ESI-HRMS spectrometer was measured with an ion trap mass spectrometer. Optical rotations were measured at 589 nm at 25 °C in a 1 dm cell, and specific rotations are given in 10^{-1} deg cm^2 g^{-1}. Enantiomeric excess was determined by HPLC analysis using a Chiralpak column (4.6 mm*250 mm, 5 μm).

1. Typical Procedure for the Asymmetric Domino α-Amination/Oxidative Umpolung/Cyclizations. A mixture of thioamide **2a** (28 mg, 0.12 mmol), diisopropyl azodicarboxylate **3a** (40 μL, 0.24 mmol), and **1b** (3.5 mg, 0.024 mmol) was stirred in CH_2Cl_2 (1 mL) at room temperature for 1 h; then, K_2CO_3 (16.5 mmg, 0.12 mmol) was added to the system, and the mixture was stirred for another 4 h. Then, flash chromatography on silica gel (30% DCM/petroleum ether) gave **4aa** (44 mg, 93% yield) as a pale yellow solid.

*(S,Z)-Diisopropyl 1-Oxo-5′-(phenylimino)-3,4-dihydro-1H-spiro-[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4aa**).* Forty-four milligrams, 93% yield, mp 44−46 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, J = 7.7 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.38−7.32 (m, 3H), 7.29 (d, J = 7.6 Hz, 1H), 7.18 (t, J = 7.4 Hz, 1H), 6.90 (d, J = 7.5 Hz, 2H), 5.03−4.97 (m, 1H), 4.96−4.90 (m, 1H), 3.27 (t, J = 6.0 Hz, 2H), 2.77−2.70 (m, 1H), 2.59−2.54 (m, 1H), 1.32−1.12 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.1, 157.8, 150.3, 150.3, 143.7, 133.9, 132.5, 129.6, 128.5, 127.1, 126.4, 119.9, 73.1, 72.8, 71.5, 33.4, 33.3, 25.5, 21.8, 21.8, 21.8, 21.7. ESI-HRMS: calcd for $C_{25}H_{27}N_3O_5S$ + H 482.1744, found 482.1722. $[\alpha]^{25}_D$ +141 (c 0.1, $CHCl_3$); 90% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (10% 2-propanol/hexane, 1 mL/min), t_{major} = 19.896 min, t_{minor} = 14.710 min.

Crystal data for **4aa**. $C_{25}H_{27}N_3O_5S$ (481.56), triclinic, P-1; a = 10.4968(3) Å, alpha = 76.6160(10)°; b = 11.6056(3) Å, beta = 70.0600(10)°; c = 12.3250(3) Å, gamma = 65.5420(10)°. U = 1277.61(6) Å^3, Z = 2, T = 296(2) K, absorption coefficient = 0.166 mm^{-1}, reflections collected = 43556, unique = 5911 [R(int) = 0.0478], refinement by Full-matrix least-squares on F^2, data/restraints/parameters = 5911/0/296, goodness-of-fit on F^2 = 1.266, final R indices [I > 2sigma(I)] R1 = 0.0488, wR2 = 0.1595; R indices (all data) R1 = 0.0721, wR2 = 0.1842, largest diff. peak and hole = 0.421 and −0.289 e Å^{-3}, respectively.

*(S,Z)-Diethyl 1-Oxo-5′-(phenylimino)-3,4-dihydro-1H-spiro-[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4ab**).* Thirty-nine milligrams, 86% yield, mp 45−46 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (d, J = 7.7 Hz, 1H), 7.46 (t, J = 7.3 Hz, 1H), 7.35−7.22 (m, 4H), 7.13 (t, J = 7.3 Hz, 1H), 6.88 (d, J = 7.8 Hz, 2H), 4.31−4.07 (m, 4H), 3.37−3.19 (m, 2H), 2.79−2.70 (m, 1H), 2.68−2.59 (m, 1H), 1.26−1.10 (m, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.1, 172.7, 158.2, 153.0, 150.2, 143.7, 134.0, 132.2, 129.6, 128.6, 128.3, 127.1, 126.6, 119.9, 72.8, 64.8, 63.2, 33.2, 25.4, 14.3, 14.2. ESI-HRMS: calcd for $C_{23}H_{23}N_3O_5S$ + H 454.1431, found 454.1424. $[\alpha]^{25}_D$ +127 (c 0.01, $CHCl_3$); 90% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (10% 2-propanol/hexane, 1 mL/min), t_{major} = 42.537 min, t_{minor} = 29.454 min.

*(S,Z)-Di-tert-butyl 1-Oxo-5′-(phenylimino)-3,4-dihydro-1H-spiro-[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4ac**).* Forty-six milligrams, 90% yield, mp 78−80 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (d, J = 7.5 Hz, 1H), 7.52 (t, J = 7.2 Hz, 1H), 7.39−7.30 (m, 4H), 7.18 (t, J = 7.4 Hz, 1H), 6.91 (d, J = 7.5 Hz, 2H), 3.40−3.32 (m, 1H), 3.29−3.23 (m, 1H), 2.75−2.67 (m, 1H), 2.66−2.60 (m, 1H), 1.52−1.33 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.4, 173.9, 156.8, 150.3, 143.8, 133.8, 132.3, 129.4, 128.7, 128.6, 128.4, 127.1, 127.0, 126.3, 120.0, 100.0, 84.4, 72.5, 33.2, 27.9, 27.9, 27.9, 27.9, 27.9, 25.5. ESI-HRMS: calcd for $C_{27}H_{31}N_3O_5S$ + H 510.2063, found 510.2057. $[\alpha]^{25}_D$ +123 (c 0.03, $CHCl_3$); 91% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (3% 2-propanol/hexane, 1 mL/min), t_{major} = 27.233 min, t_{minor} = 24.825 min.

*(S,Z)-Diisopropyl 1-Oxo-5′-(p-tolylimino)-3,4-dihydro-1H-spiro-[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4ba**).* Forty-two milligrams, 84% yield, mp 46−48 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, J = 7.8 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 6.90−6.84 (m, 4H), 5.04−4.98 (m, 1H), 4.97−4.90 (m, 1H), 3.80 (s, 3H), 3.31−3.26 (m, 2H), 2.79−2.72 (m, 1H), 2.60−2.54 (m, 1H), 1.31−1.14 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.1, 171.2, 158.1, 157.8, 143.7, 143.4, 133.8, 132.4, 128.5, 128.4, 128.4, 127.1, 121.7, 121.7, 114.5, 114.5, 73.1, 72.7, 71.5, 55.5, 33.4, 25.6, 21.8, 21.8, 21.8, 21.7. ESI-HRMS: calcd for $C_{26}H_{29}N_3O_5S$ + H 496.1901, found 496.1903. $[\alpha]^{25}_D$ +183 (c 0.07, $CHCl_3$); 86% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (10% 2-propanol/hexane, 1 mL/min), t_{major} = 41.535 min, t_{minor} = 27.928 min.

*(S,Z)-Diisopropyl 5′-((4-Isopropylphenyl)imino)-1-oxo-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4ca**).* Forty-eight milligrams, 93% yield, pale yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (d, J = 7.6 Hz, 1H), 7.52 (t, J = 7.3 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.22 (d, J = 8.3 Hz, 2H), 6.85 (d, J = 8.3 Hz, 2H), 5.06−5.00 (m, 1H), 4.99−4.91 (m, 1H), 3.33−3.26 (m, 2H), 2.95−2.87 (m, 1H), 2.80−2.73 (m, 1H), 2.63−2.55 (m, 1H), 1.33 (q, J = 10.8, 6.2 Hz, 7H), 1.25−1.15 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.2, 171.9, 157.9, 147.8, 147.3, 143.6, 133.8, 132.4, 128.4, 127.4, 127.4, 127.1, 127.0, 120.1, 73.1, 72.8, 71.5, 33.7, 33.3 25.5, 24.0, 24.0, 23.9, 23.9, 21.8, 21.7 ESI-HRMS: calcd for $C_{28}H_{33}N_3O_5S$ + H 524.2214, found 524.2206. $[\alpha]^{25}_D$ +153 (c 0.035, $CHCl_3$); 91% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (5% 2-propanol/hexane, 1 mL/min), t_{major} = 40.632 min, t_{minor} = 26.471 min.

*(S,Z)-Diisopropyl 5′-((3-Methoxyphenyl)imino)-1-oxo-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3] thiadiazolidine]-2′,3′-dicarboxylate (**4da**).* Forty-eight milligrams, 92% yield, mp 110−113 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, J = 7.7 Hz, 1H), 7.50 (t, J = 7.4 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.23 (t, J = 8.1 Hz, 1H), 6.72 (d, J = 8.3, 2.0 Hz, 1H), 6.48 (d, J = 7.8 Hz, 1H), 6.44 (d, J = 1.9 Hz, 1H), 5.03−4.97 (m, 1H), 4.96−4.89 (m, 1H), 3.76 (s, 3H), 3.26 (t, J = 5.9 Hz, 2H), 2.76−2.69 (m, 1H), 2.59−2.53 (m, 1H), 1.30−1.12 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.1, 173.7, 171.1, 160.6, 157.8, 151.7, 143.6, 133.8, 132.4, 130.4, 128.4, 127.1, 112.7, 111.7, 105.3, 73.1 72.8, 71.5, 55.4, 33.4, 25.5, 25.4, 21.8, 21.7. ESI-HRMS: calcd for $C_{26}H_{29}N_3O_6S$ + H 512.1850, found 512.1847. $[\alpha]^{25}_D$ +128 (c 0.03, $CHCl_3$); 89% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (10% 2-propanol/hexane, 1 mL/min), t_{major} = 27.007 min, t_{minor} = 16.662 min.

*(S,Z)-Diisopropyl 5′-((2-Methoxyphenyl)imino)-1-oxo-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4ea**).* Forty-one milligrams, 80% yield, mp 92−94 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (d, J = 7.4 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.32−7.28 (m, 1H), 7.17 (td, J = 8.0, 1.6 Hz, 1H), 6.95−6.89 (m, 2H), 6.86 (dd, J = 7.7, 1.5 Hz, 1H), 5.04−4.99 (m, 1H), 4.98−4.91 (m, 1H), 3.82 (s, 3H), 3.42−3.36 (m, 1H), 3.30−3.23 (m, 1H), 2.84−2.77 (m, 1H), 2.65−2.58 (m, 1H), 1.32−1.15 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.2, 158.0, 150.2, 143.8, 138.6, 133.7, 132.4, 128.5, 128.4, 127.5, 127.0, 121.1, 121.1, 112.1, 72.9, 71.4, 55.8, 33.3, 25.5, 25.5, 21.8, 21.8, 21.7, 21.7. ESI-HRMS: calcd for $C_{26}H_{29}N_3O_6S$ + H 512.1850, found 512.1841. $[\alpha]^{25}_D$ +182 (c 0.02, $CHCl_3$); 94% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (10% 2-propanol/hexane, 1 mL/min), t_{major} = 48.008 min, t_{minor} = 23.928 min.

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*(S,Z)-Diisopropyl 6-methoxy-1-oxo-5′-(phenylimino)-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4fa**).* Forty-two milligrams, 82% yield, mp 51−53 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (d, J = 8.7 Hz, 1H), 7.35 (t, J = 7.9 Hz, 2H), 7.19 (t, J = 7.4 Hz, 1H), 6.93−6.87 (m, 3H), 6.77 (d, J = 2.3 Hz, 1H), 5.04−4.98 (m, 1H), 4.98−4.92 (m, 1H), 3.88 (s, 3H), 3.32−3.19 (m, 2H), 2.76−2.69 (m, 1H), 2.62−2.54 (m, 1H), 1.31−1.15 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.8, 173.4, 164.0, 157.9, 150.4, 146.1, 131.1, 129.5, 129.4, 126.3, 126.0, 120.0, 119.9, 113.5, 112.5, 73.1, 72.7, 71.3, 55.5, 33.2, 25.9, 21.8, 21.8, 21.7, 21.7. ESI-HRMS: calcd for $C_{26}H_{29}N_3O_6S$ + H 512.1850, found 512.1849. $[\alpha]^{25}_D$ +159 (c 0.025, $CHCl_3$); 86% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (20% 2-propanol/hexane, 1 mL/min), t_{major} = 21.833 min, t_{minor} = 14.705 min.

*(S,Z)-Diisopropyl 5′-((4-Chlorophenyl)imino)-1-oxo-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4ga**).* Forty-seven milligrams, 90% yield, mp 48−50 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, J = 7.8 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.36 (t, J = 16.3, 8.8 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.04 (t, J = 8.5 Hz, 2H), 6.94−6.86 (m, 2H), 5.05−4.98 (m, 1H), 4.97−4.90 (m, 1H), 3.32−3.22 (m, 2H), 2.78−2.70 (m, 1H), 2.59−2.53 (m, 1H), 1.31−1.04 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.1, 173.7, 161.7, 160.1, 157.7, 146.4, 143.6, 133.9, 132.4, 128.4, 127.1, 127.1, 121.7, 121.6, 116.4, 116.2, 73.3, 73.0, 71.6, 33.4, 25.5, 21.8, 21.8, 21.7, 21.7. ESI-HRMS: calcd for $C_{25}H_{26}N_3O_5SCl$ + H 516.1354, found 516.1358. $[\alpha]^{25}_D$ +121 (c 0.05, $CHCl_3$); 83% ee, The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (5% 2-propanol/hexane, 1 mL/min), t_{major} = 29.804 min, t_{minor} = 20.926 min.

*(S,Z)-Diisopropyl 5′-((3-Chlorophenyl)imino)-1-oxo-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4ha**).* Forty-three milligrams, 83% yield, mp 46−48 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, J = 7.6 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.31−7.26 (m, 2H), 6.93 (t, J = 1.9 Hz, 1H), 6.78 (d, J = 7.9 Hz, 1H), 5.04−4.98 (m, 1H), 4.96−4.89 (m, 1H), 3.31−3.20 (m, 2H), 2.74−2.65 (m, 1H), 2.58−2.51 (m, 1H), 1.31−1.13 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.1, 171.2, 157.7, 151.3, 143.5, 135.2, 133.9, 132.3, 130.6, 128.5, 127.2, 126.4, 120.4, 117.7, 73.3, 73.1, 71.7, 33.4, 25.5, 21.8, 21.8, 21.7, 21.7. ESI-HRMS: calcd for $C_{25}H_{26}N_3O_5SCl$ + H 516.1354, found 516.1350. $[\alpha]^{25}_D$ +99 (c 0.02, $CHCl_3$); 83% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (5% 2-propanol/hexane, 1 mL/min), t_{major} = 0.27.048 min, t_{minor} = 16.659 min.

*(S,Z)-Diisopropyl 5′-((2-Chlorophenyl)imino)-1-oxo-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4ia**).* Forty-four milligrams, 84% yield, mp 56−58 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, J = 7.8 Hz, 1H), 7.51 (t, J = 7.3 Hz, 1H), 7.37 (q, J = 18.1, 7.8 Hz, 2H), 7.30 (d, J = 7.6 Hz, 1H), 7.22 (t, J = 7.6 Hz, 1H), 7.10 (t, J = 7.7 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H), 5.05−4.98 (m, 1H), 4.97−4.91 (m, 1H), 3.49−3.41 (m, 1H), 3.26−3.19 (m, 1H), 2.78−2.72 (m, 1H), 2.68−2.62 (m, 1H), 1.31−1.13 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.8, 171.2, 157.9, 147.5, 143.7, 133.9, 132.1, 130.3, 128.5, 127.9, 127.8, 127.1, 125.7, 119.1, 73.4, 72.7, 71.5, 32.9, 25.3, 21.8, 21.8, 21.7, 21.7. ESI-HRMS: calcd for $C_{25}H_{26}N_3O_5SCl$ + H 516.1354, found 516.1343. $[\alpha]^{25}_D$ +90 (c 0.01, $CHCl_3$); 80% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (10% 2-propanol/hexane, 1 mL/min), t_{major} = 21.120 min, t_{minor} = 12.247 min.

*(S,Z)-Diisopropyl 5′-((4-Fluorophenyl)imino)-1-oxo-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4ja**).* Forty-six milligrams, 92% yield, mp 164−165 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, J = 7.6 Hz, 1H), 7.53 (t, J = 6.6 Hz, 1H), 7.38 (t, J = 6.9 Hz, 1H), 7.32 (q, J = 6.4, 2.1 Hz, 3H), 6.86 (d, J = 5.6, 3.0 Hz, 2H), 5.06−4.98 (m, 1H), 4.97−4.90 (m, 1H), 3.33−3.21 (m, 2H), 2.77−2.68 (m, 1H), 2.59−2.53 (m, 1H), 1.33−1.14 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.0, 174.4, 157.7, 148.7, 143.6, 133.9, 132.4, 131.8, 129.6, 128.5, 128.4, 128.4, 127.2, 121.3, 121.3, 73.3, 73.0, 71.6, 33.4, 25.5, 21.8, 21.8, 21.7, 21.7. ESI-HRMS: calcd for $C_{25}H_{26}N_3O_5SF$ + H 500.1650, found 500.1651. $[\alpha]^{25}_D$ +107 (c 0.03, $CHCl_3$); 84% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (5% 2-propanol/hexane, 1 mL/min), t_{major} = 30.562 min, t_{minor} = 23.689 min.

*(S,Z)-Diisopropyl 5′-(Naphthalen-2-ylimino)-1-oxo-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4ka**).* Fifty milligrams, 94% yield, mp 61−63 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (d, J = 7.8 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 8.1 Hz, 1H), 7.68 (d, J = 8.3 Hz, 1H), 7.55−7.44 (m, 3H), 7.42−7.36 (m, 2H), 7.33 (d, J = 7.6 Hz, 1H), 6.90 (d, J = 7.2 Hz, 1H), 5.01−4.91 (m, 2H), 3.40−3.31 (m, 2H), 2.93−2.87 (m, 1H), 2.70−2.64 (m, 1H), 1.27−1.13 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.1, 171.2, 157.8, 147.4, 143.6, 134.1, 133.9, 132.5, 128.5, 127.9, 127.2, 126.9, 126.8, 126.7, 126.6, 126.2, 125.7, 123.4, 113.1, 113.1, 73.1, 71.6, 33.7, 25.7, 21.8, 21.8, 21.7, 21.7. ESI-HRMS: calcd for $C_{29}H_{29}N_3O_5S$ + H 532.1901, found 532.1896. $[\alpha]^{25}_D$ +143 (c 0.09, $CHCl_3$); 92% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (5% 2-propanol/hexane, 1 mL/min), t_{major} = 54.996 min, t_{minor} = 26.189 min.

*(S,Z)-Diethyl 5′-((2-Methoxyphenyl)imino)-1-oxo-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4eb**).* Forty-three milligrams, 90% yield, mp 105−107 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (d, J = 7.8 Hz, 1H), 7.46 (t, J = 7.4 Hz, 1H), 7.33−7.24 (m, 2H), 7.15−7.08 (m, 1H), 6.91−6.84 (m, 2H), 6.82 (d, J = 7.6 Hz, 1H), 4.33−4.14 (m, 4H), 3.76 (s, 3H), 3.43 (d, J = 15.7 Hz, 1H), 3.27−3.20 (m, 1H), 2.81−2.76 (m, 1H), 2.69−2.62 (m, 1H), 1.26 (t, J = 7.1 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.1, 171.8, 167.7, 158.4, 153.0, 150.1, 143.8, 138.2, 133.8, 132.1, 128.5, 127.7, 126.9, 121.3, 121.1, 112.2, 72.9, 64.6, 63.1, 55.8, 33.2, 25.4, 14.3. ESI-HRMS: calcd for $C_{24}H_{25}N_3O_6S$ + H 484.1537, found 484.1538. $[\alpha]^{25}_D$ +105 (c 0.01, $CHCl_3$); 96% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (10% 2-propanol/hexane, 1 mL/min), t_{major} = 28.406 min, t_{minor} = 15.314 min.

Crystal data for **4eb** $C_{24}H_{23}N_3O_6S$ (481.51), orthorhombic, P2(1)2(1)2(1), a = 10.872(4) Å, alpha = 90°; b = 12.354(4) Å, beta = 90°; c = 17.965(6) Å, gamma = 90°. U = 2412.9(14) Å^3, Z = 31, T = 296(2) K, absorption coefficient = 0.178 mm^{-1}, reflections collected = 16849, unique = 5538 [R(int) = 0.0531], refinement by Full-matrix least-squares on F^2, data/restraints/parameters = 5538/0/308, goodness-of-fit on F^2 = 1.004, final R indices [I > 2sigma(I)] R1 = 0.0584, wR2 = 0.1347; R indices (all data) R1 = 0.1172, wR2 = 0.1662, largest diff. peak and hole = 0.286 and −0.214 e Å^{-3}, respectively.

*(S,Z)-Di-tert-butyl 5′-((2-Methoxyphenyl)imino)-1-oxo-3,4-dihydro-1H-spiro[naphthalene-2,4′-[1,2,3]-thiadiazolidine]-2′,3′-dicarboxylate (**4ec**).* Forty-eight milligrams, 88% yield, mp 72−74 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (d, J = 7.7 Hz, 1H), 7.50 (t, J = 7.3 Hz, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.32−7.28 (m, 1H), 7.14 (t, J = 7.3 Hz, 1H), 6.91 (q, J = 17.7, 8.0 Hz, 2H), 6.84 (d, J = 7.5 Hz, 1H), 3.81 (s, 3H), 3.53−3.44 (m, 1H), 3.27−3.18 (m, 1H), 2.77−2.70 (m, 1H), 2.70−2.63 (m, 1H), 1.52−1.33 (m, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.2, 157.0, 150.2, 138.8, 133.7, 132.3, 128.7, 128.5, 127.4, 126.9, 121.0, 120.9, 112.1, 100.0, 84.2, 84.2, 55.8, 33.1, 28.0, 27.9, 27.9, 27.9, 27.9, 27.9, 25.5. ESI-HRMS: calcd for $C_{28}H_{33}N_3O_6S$ + H 540.2163, found 540.2137. $[\alpha]^{25}_D$ +133 (c 0.02, $CHCl_3$); 98% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (10% 2-propanol/hexane, 1 mL/min), t_{major} = 17.741 min, t_{minor} = 12.684 min.

*(S,Z)-Diisopropyl 1-Oxo-5′-(phenylimino)-1,3-dihydrospiro-[indene-2,4′-[1,2,3]thiadiazolidine]-2′,3′-dicarboxylate (**4la**).* Forty milligrams, 85% yield, mp 55−57 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, J = 7.6 Hz, 1H), 7.66 (t, J = 7.4 Hz, 1H), 7.53 (d, J = 7.7 Hz, 1H), 7.42 (t, J = 7.4 Hz, 1H), 7.31 (t, J = 7.8 Hz, 2H), 7.17 (t, J = 7.4 Hz, 1H), 6.79 (d, J = 7.5 Hz, 2H), 5.01−4.89 (m, 2H), 3.78 (s, 2H), 1.29−1.15 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.2, 170.8, 158.8 151.3, 149.7, 135.7, 133.7, 129.5, 128.0, 126.6, 126.6, 126.3, 125.4, 120.2, 120.1, 73.5, 71.4, 29.7, 21.8, 21.7, 21.7. ESI-HRMS: calcd for $C_{24}H_{25}N_3O_5S$ + H 468.1588, found 468.1564. $[\alpha]^{25}_D$ +203 (c 0.03, $CHCl_3$); 88% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (5% 2-propanol/hexane, 1 mL/min), t_{major} = 37.227 min, t_{minor} = 32.796 min.

*(S,Z)-Diisopropyl 1-Oxo-5′-(propylimino)-3,4-dihydro-1H-spiro-[naphthalene-2,4′-[1,2,3]thiadiazolidine]- 2′,3′-dicarboxylate (**4ma**).* Thirty-four milligrams, 76% yield, pale yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (d, J = 7.9 Hz, 1H), 7.61−7.56 (m, 1H), 7.36 (t, J = 7.6 Hz, 1H), 7.32 (d, J = 7.7 Hz, 1H), 5.02−4.93 (m, 2H),

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3.96−3.86 (m, 1H), 3.55−3.46 (m, 2H), 3.04 (d, J = 17.3 Hz, 1H), 2.79−2.55 (m, 2H), 1.68−1.61 (m, 2H), 1.29−1.25 (m, 12H), 0.89 (t, J = 9.2, 5.7 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.1, 167.7, 135.2, 130.1, 129.1, 128.7, 127.1, 72.3, 70.7, 70.1, 40.9, 29.7, 29.0, 24.9, 21.7, 21.8, 21.7, 21.7, 21.2, 11.9. ESI-HRMS: calcd for $C_{22}H_{29}N_3O_5S$ + H 448.1901, found 448.1906. $[\alpha]^{25}_D$ +64 (c 0.02, $CHCl_3$); 60% ee. The enantiomeric ratio was determined by HPLC on a Chiralpak IC column (10% 2-propanol/hexane, 1 mL/min), t_{major} = 13.808 min, t_{minor} = 24.362 min.

*(S)-Diisopropyl 1-(1-Oxo-2-(phenylcarbamothioyl)-1,2,3,4-tetrahydronaphthalen-2-yl)hydrazine-1,2-dicarboxylate (**Iaa**).* Yield of 76%, mp 51−53 °C; ^{1}H NMR (600 MHz, CDCl3) δ 7.95 (d, J = 6.5 Hz, 2H), 7.44−7.35 (m, 4H), 7.30−7.21 (m, 3H), 5.06−4.96 (m, 2H), 3.41 (t, J = 14.5 Hz, 1H), 2.99 (d, J = 15.6 Hz, 2H), 2.39 (d, J = 12.9 Hz, 1H), 1.36 (dd, J = 17.0, 6.1 Hz, 7H), 1.25 (dd, J = 10.1, 6.3 Hz, 5H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.7, 158.1, 154.3, 143.0, 141.4, 139.7, 139.2, 135.0, 133.8, 132.6, 132.1, 128.8, 128.2, 127.5, 127.4, 127.2, 126.8, 126.4, 126.2, 123.6, 122.5, 72.3, 71.5, 33.2, 26.1, 22.0, 21.7, 21.7; $[\alpha]^{25}$D −143 (c 0.01, $CHCl_3$). ESI-HRMS: calcd for $C_{25}H_{29}N_3O_5S$ + H 484.1901, found 484.1921. Anal. Calcd for $C_{25}H_{29}N_3O_5S$: C, 62.09; H, 6.04; N, 8.69; S, 6.63. Found: C, 61.76; H, 6.43; N, 8.38; S, 6.44.

Crystal data for **Iaa** $C_{25}H_{29}N_3O_5S$ (483.57), monclinic, P2(1), a = 8.6809(2) Å, alpha = 90.00°; b = 14.1972(3) Å, beta = 100.5210(10)°; c = 10.4181(3) Å, gamma = 90.00°. U = 1262.39(5) Å^3, Z = 16, T = 296(2) K, absorption coefficient = 0.168 mm^{-1}, reflections collected = 25042, unique = 5806 [R(int) = 0.0381], refinement by Full-matrix least-squares on F^2, data/restraints/parameters = 5806/1/308, goodness-of-fit on F^2 = 1.043, final R indices [I > 2sigma(I)] R1 = 0.0397, wR2 = 0.0810; R indices (all data) R1 = 0.0397, wR2 = 0.0861, largest diff. peak and hole = 0.235 and −0.235 e Å^{-3}, respectively.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications Web site at DOI: XXX. (PDF). (CIF), **Iaa** (CIF) and **4eb** (CIF). The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00127.

^{1}H NMR and ^{13}C NMR spectra for all new compounds- (PDF)

X-ray structural data for **4aa** (CIF)

X-ray structural data for **Iaa** (CIF)

X-ray structural data for **4eb** (CIF)

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Notes

The authors declare no competing financial interest.

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