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Iodine-Catalyzed Synthesis of Chiral 4-Imidazolidinones Using α-Amino Acid Derivatives via Dehydrogenative N-H/C(sp^3)-H Coupling

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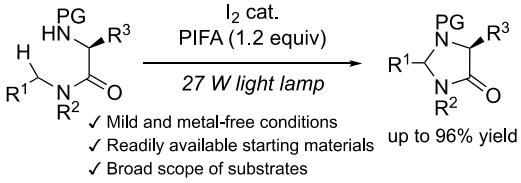
ABSTRACT: An efficient method for the asymmetric synthesis of 4-imidazolidinones via an iodine-catalyzed intramolecular N-H/C(sp^3)-H activation of readily available and abundant feedstocks, amino acids and amines is described. The reaction proceeded under visible light irradiation to afford a variety of 4-imidazolidinone derivatives under mild conditions in moderate to excellent yields. Both benzylic, secondary and tertiary C(sp^3)-H bonds were aminated, and various functional groups were tolerated.



INTRODUCTION

4-Imidazolidinone derivatives are important organic molecules with various interesting biological properties, including antitumor, anticonvulsant, anti-inflammatory and antiviral activities.[1] The 4-imidazolidinone skeleton is also present in drugs such as spiperone, NNC 63-0532 and hetacillin (Figure 1). In addition, 4-imidazolidinones are important organocatalysts, as shown by the pioneering work of MacMillan and coworkers in Diels-Alder reactions and other reactions.[2] The 4-imidazolidinone skeleton is also found in natural products such as oxaline and neoxaline,[3] and it is a useful synthetic intermediate in organic chemistry.

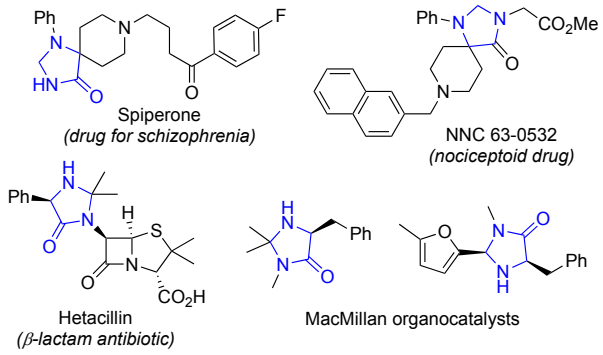
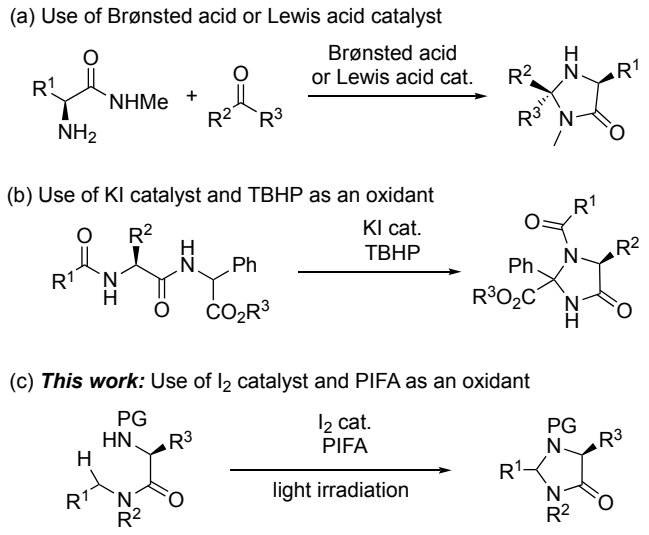


Figure 1. Examples of useful compounds containing 4-imidazolidinone skeleton

Based on this background, various reactions have been developed for the synthesis of 4-imidazolidinones,[4-7] especially achiral derivatives.[4] Considerable effort has been devoted to synthesizing chiral 4-imidazolinones. The most common method is the condensation of a protected amino acid with a carbonyl compound followed by intramolecular cyclization in the presence of a stoichiometric or catalytic amounts of Brønsted acid (Scheme 1(a)).[5] Although this is a powerful method, some substrates undergo racemization, thus limiting

applicability.[5b] The other common strategy is the use of Lewis acid catalysts such as $FeCl_3$, $Sm(OTf)_3$ and $Yb(OTf)_3$.[6] Although excellent enantioselectivities were often obtained, reactions done using this method are sometimes low yielding. Synthesis of chiral 4-imidazolidinones was also reported using *N*-acyl dipeptide esters in presence of *tert*-butyl peroxide as oxidant and KI as catalyst (Scheme 1b).[7] During the enantioselective addition of organozinc reagents to α-aldiminoesters, Kozlowski reported that 4-imidazolidinones were obtained mostly as minor products.[8a] Pattarawarapan and Phakhodee also reported a two-step reaction for the synthesis of 2-imino-4-imidazolidinones.[8b] Recently, a highly enantioselective C(sp^3)-H amination of aliphatic azides using a chiral-Ru catalyst was demonstrated for the synthesis of 4-imidazolidinones by Houk and Meggers groups.[8c] Given the importance of chiral 4-imidazolidinones, the development of new and efficient approaches for their synthesis is highly desired. This paper describes a simple and catalytic metal-free protocol for the preparation of chiral 4-imidazolinones from readily available materials, α-amino acids and amines under mild conditions (Scheme 1(c)).



Scheme 1. Methods for the synthesis of chiral 4-imidazolidinones

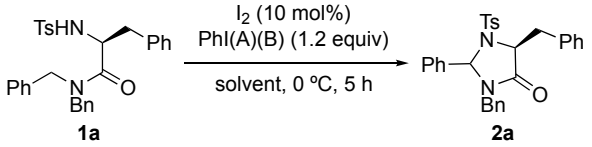
Dehydrogenative N-H/C-H bond coupling is an attractive strategy for the formation of C-N bonds, which are ubiquitous in organic compounds. Although N-H/C(sp^2)-H bond couplings have been well studied,[9] the more challenging N-H/C(sp^3)-H bond formations remain relatively underdeveloped. N-H/C(sp^3)-H bond couplings are mainly realized using stoichiometric or catalytic transition metals, but their toxicity, cost and difficult purification from the target compounds have driven the development of alternative methods. Accordingly, metal-free dehydrogenative N-H/C(sp^3)-H couplings are attractive in terms of greenness and cost-efficiency.[10] The Hofmann-Löffler-Freytag reaction,[11] which allows the synthesis of nitrogen-containing five-membered heterocycles, is a good example that utilizes iodine to form a C-N bond. The original strongly acidic reaction conditions were not compatible with a variety of functional and protecting groups. The modification by Kimura using the photolysis of *N*-chloroamines,[12] followed by those of Suárez[13] and Fan,[14] which use molecular iodine and hypervalent iodine, allowed mild reaction conditions. These modifications made the reaction tolerant to various synthetically important functional groups. Recently, the Muñiz group demonstrated that this transformation can be carried out using catalytic iodine under light irradiation to synthesize pyrrolidine derivatives.[15] Based on this precedent and our ongoing interest in using amino acids as precursors and templates for efficient organic synthesis,[16] we herein demonstrate the iodine-catalyzed synthesis of 4-imidazolidinone derivatives using substrates prepared from readily available α-amino acids and alkylamines.

RESULTS AND DISCUSSION

Our initial studies focused on the intramolecular dehydrogenative N-H/C(sp^3)-H coupling of propanamide **1a**, which was readily prepared from L-phenylalanine and dibenzylamine. When **1a** was treated with a catalytic amount of iodine (10 mol%) and $PhI(OAc)_2$ [(diacetoxyiodo)benzene] (1.2 equiv) as an oxidant in DCE and the mixture was stirred on the benchtop under the overhead fluorescent light on the ceiling for 5 h, only trace amounts of the desired 4-imidazolidinone **2a** were observed (Table 1, entry 1). To our delight, when the oxidant was changed to PIFA [bis(trifluoroacetoxy)iodobenzene], the reaction efficiency improved, and a diastereomeric mixture of **2a** (3.8:1) was obtained in 53% isolated yield. The diastereomers were separated by preparative TLC, and their structures were determined by NOE analyses and ^{1}H-NMR charts in the literature as a reference.[17] Other hypervalent iodine reagents such as Koser's reagent (entry 3) and $PhI(mCBA)_2$ [*m*CBA = *m*-chlorobenzoic acid] (entry 4), which showed the best performance in the synthesis of pyrrolidines by Muñiz and coworkers,[15] gave low yields. A bulkier leaving group on the hypervalent iodine was also ineffective (entry 5). In comparison with THF, MeCN and toluene, DCE gave higher yields possibly due to the higher solubility of the hypervalent iodine (entries 6-8). When the reaction was carried out under 12 W or 27 W fluorescent light irradiation, the yield improved to 83% (entries 9 and 10). Since a small amount of starting material remained in entry 10, we increased the loading of the iodine catalyst to 20 mol% and carried out the reaction for 8 h, which increased the yield of desired product **2a** to 92% (entry 11). A reaction carried out using 1.0 equiv of PIFA resulted in reduced yield (81%, entry 12). The scalability of the reaction was also demonstrated by reactions run for 24 h using 1.0 mmol (0.50 g) or 2.1 mmol (1.05 g) that gave the desired product in 88% and 76% yields, respectively, after purification by flash silica gel chromatography (entry 13

and 14). As a control experiment, a reaction carried out in darkness did not proceed at all (entry 15).

Table 1. Optimization of the reaction conditions[a]

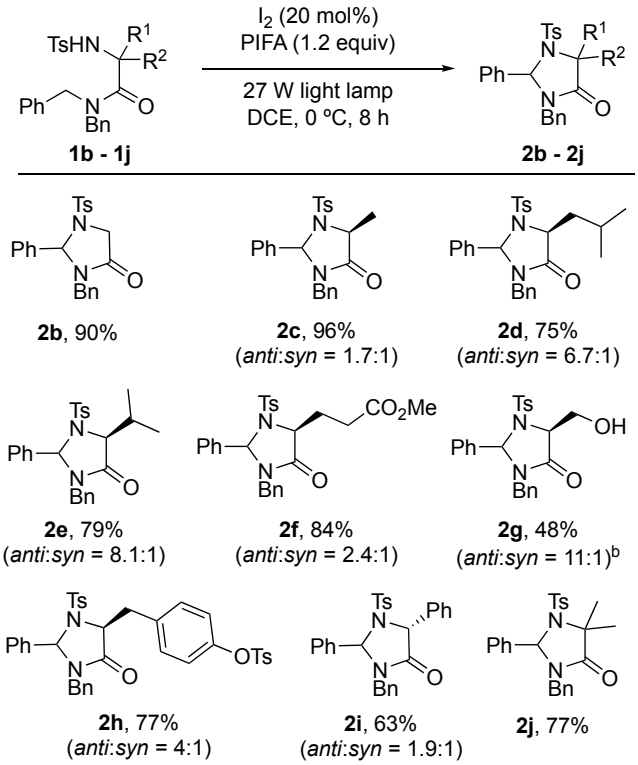


Entry	PhI(A)(B)	Solvent	Yield (%)[b]	*anti*/*syn*[c]
1	$PhI(OAc)_2$	DCE	Traces	N.D.
2	PIFA	DCE	53	3.8:1
3	PhI(OH)(OTs)	DCE	7	3.4:1
4	$PhI(mCBA)_2$	DCE	8	4.0:1
5	$PhI(OPiv)_2$	DCE	18	2.3:1
6	PIFA	THF	16	2.4:1
7	PIFA	MeCN	N.R.	--
8	PIFA	toluene	35	6.1:1
9[d]	PIFA	DCE	83	4.3:1
10[e]	PIFA	DCE	83	4.3:1
11[f]	PIFA	DCE	92	4.3:1
12[f,g]	PIFA	DCE	81	4.3:1
13[f,h]	PIFA	DCE	88	4.3:1
14[f,i]	PIFA	DCE	76	4.3:1
15[j]	PIFA	DCE	N.R.	--

[a] Conditions: **1a** (0.10 mmol), I_2 (10 mol%), PhI(A)(B) (1.2 equiv), solvent (0.70 mL) at 0 °C for 5 h. [b] Isolated yields. [c] Determined by ^{1}H NMR. [d] Using a 12 W fluorescent light. [e] Using a 27 W fluorescent light. [f] Using a 27 W fluorescent light lamp, I_2 (20 mol%), 8 h. [g] Using PIFA (1.0 equiv). [h] Done using 1.0 mmol scale (0.50 g) of **1a** for 24 h. [i] Done using 2.1 mmol scale (1.05 g) of **1a** for 24 h. [j] Conducted under darkness. DCE: 1,2-dichloroethane, MeCN: acetonitrile. N.R.: No reaction, N.D.: Not determined.

With the optimal conditions in hand (Table 1, entry 11), the generality of the reaction was investigated first by using substrates prepared from various α-amino acids and dibenzylamine (Table 2). A reaction carried out using glycine derivative **1b** afforded desired 4-imidazolidinone **2b** in 90% yield under the optimized conditions. Substrates derived from alkyl-containing α-amino acids, such as alanine, leucine and valine, gave corresponding products **2c**-**2e** in 75-96% yields. When protected glutamic acid substrate **1f** was reacted under the iodine-catalyzed irradiation conditions, **2f** was obtained in high yield. The hydroxyl group of serine was tolerated under the oxidative coupling conditions, and **1g** reacted to afford desired product **2g** in moderate yield. On the other hand, the tosyl-protected tyrosine derivative gave 4-imidazolidinone **2h** in a good yield. Two substrates prepared from unnatural amino acids, namely, D-α-phenylglycine (**1i**) and α,α-dimethylglycine (**1j**), also underwent dehydrogenative C-N bond formation to give desired products **2i** and **2j** in 63% and 77% yields, respectively. All these reactions proceeded cleanly, and apart from the desired 4-imidazolidinone product, the unreacted starting materials were easily recovered by preparative TLC.

Table 2. Scope of α-amino acid derivatives [a]

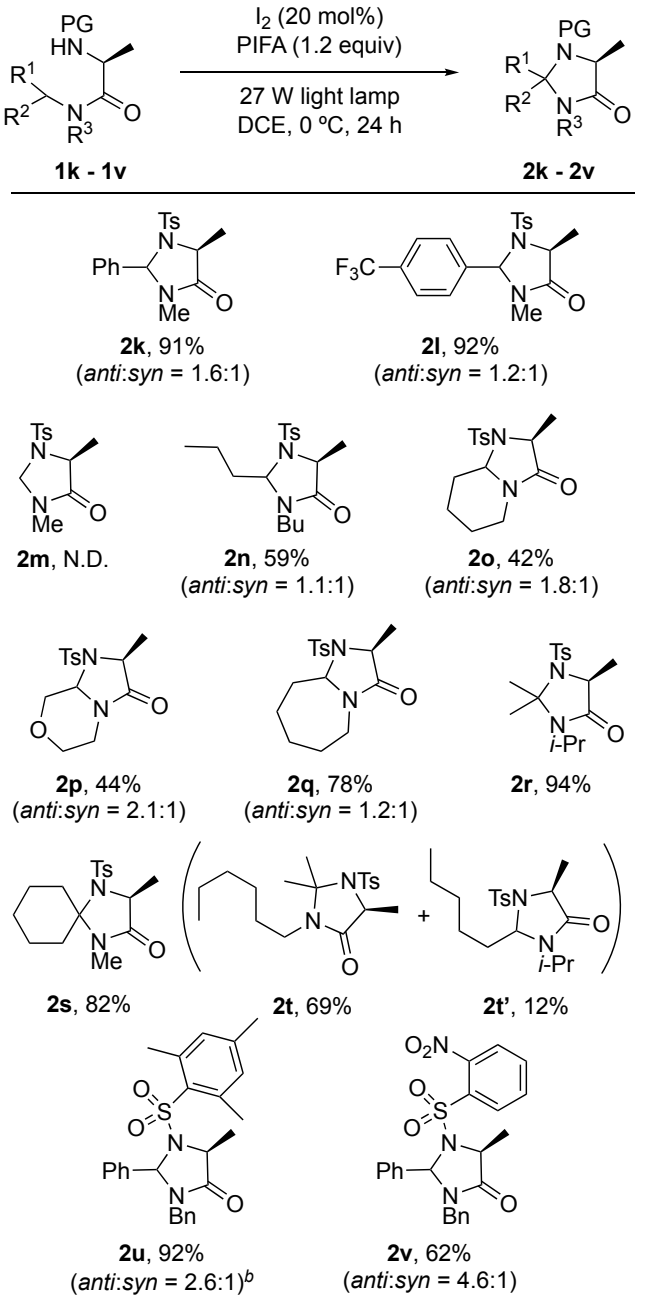


[a] Conditions: **1** (0.10 mmol), I_2 (20 mol%), PIFA (1.2 equiv), DCE (0.70 mL) at 0 °C for 8 h under 27 W fluorescent lamp irradiation. [b] Using 12 W fluorescent lamp irradiation for 5 h.

Next, substrates derived from other types of alkyl amines were examined as well (Table 3). Interestingly,

substrates containing both benzylic and primary C(sp^3)–H bonds reacted regioselectively at the benzylic position. Thus, corresponding products **2k** and **2l** were obtained in excellent yields and the methyl group remained unreacted. Similar observations were recently reported by Muñiz and coworkers.[18] As observed in the reaction of dimethylamide substrate **1m**, the primary C(sp^3)-H bonds were unreactive under the current reaction conditions. A secondary C(sp^3)–H bond of a substrate derived from dibutylamine also participated in the intramolecular C–N bond formation reaction to afford the five-membered heterocycle **2n** as the only product in 59% yield. The secondary C(sp^3)–H bonds of piperidine and morpholine derivatives (**1o** and **1p**) were also aminated to give fused heterocyclic compounds **2o** and **2p** in moderate yields. A seven-membered cyclic amine derivative, which was prepared from azepane, also reacted smoothly to afford **2q** in 78% yield. The dehydrogenative formation of such fused diazabicycles under the metal-free conditions is remarkable owing to their biological and synthetic significance.[19] The congested C(sp^3)–H bonds of the *iso*-propyl group in **1r** and cyclohexylamide **1s** were also selectively aminated to give products **2r** and **2s** in 94% and 82% yields, respectively. To compare the reactivity of secondary C(sp^3)–H bond and tertiary C(sp^3)–H bond in our reaction, we subjected (*S*)-*N*-hexyl-*N*-isopropylpropanamide **1t** to the reaction conditions. Interestingly, the reaction was selective to the tertiary C(sp^3)–H bond activation (**1t**, 69%) compared with the secondary C(sp^3)–H bond activation (**1t'**, 12%). Finally, unlike the tosyl group, the reactions carried out with substrates containing mesitylsulfonyl and 2-nitrophenylsulfonyl (nosyl) groups also proceeded to give corresponding products **2u** and **2v** in 92% and 62% yields.

Table 3. Scope of amines and sulfonyl groups [a]



[a] Conditions: **1** (0.10 mmol), I_2 (20 mol%), PIFA (1.2 equiv), solvent (0.70 mL) at 0 °C for 8 h under 27 W fluorescent lamp irradiation. [b] Done for 8 h.

Based on the reported literatures,[14,15,18,20] a representative mechanism using substrate **1a** is demonstrated in Figure 2. The reaction mechanism is initiated by the reaction of iodine with PIFA to give trifluoroacetyl hypoiodite {$I(OCOCF_3)$}, which serves as the reactive catalytic species. The hypoiodite then reacts with sulfonamide **1a** to give an iodoamide intermediate **A** with concomitant formation of CF_3CO_2H. The nitrogen-iodine bond of **A** undergoes light-induced homolytic cleavage to generate amidyl radical **B**, which is stabilized by the electron-withdrawing tosyl group. Amidyl radical **B** then traps the benzylic hydrogen to

afford benzylic radical **C**, which couples with the iodine radical to give benzyl iodide species **D**. Species **D** is oxidized by the external oxidant (PIFA) to afford **E**. Cyclization to form the desired 4-imidazolidinone **2a** occurs via nucleophilic attack of the benzylic position by the nitrogen and elimination of $I(OCOCF_3)$ and CF_3CO_2H. The fact that a superstoichiometric amount of oxidant was necessary to afford high yields of desired the 4-imidazolidinone means that cyclization of **D** prior to oxidation is not feasible.[15,18] Thus, although a catalytic amount of iodine was sufficient to provide a high yield of **2a**, 1.2 equiv of PIFA was consumed in the catalytic cycle

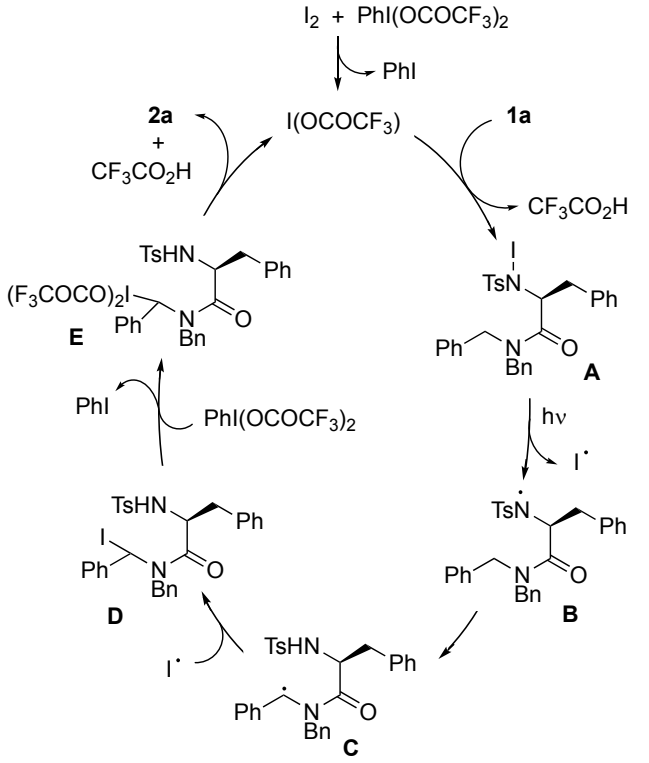
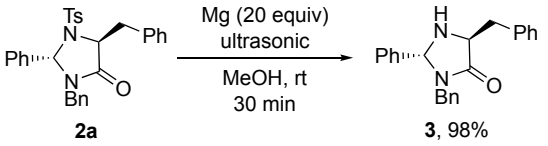


Figure 2. Plausible reaction mechanism

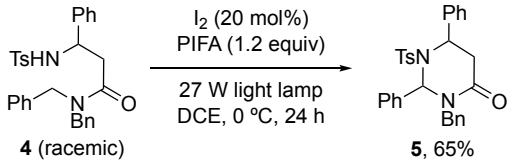
The tosyl group of **2a** was readily removed using magnesium turnings in methanol at rt to give deprotected 4-imidazolidinone **3** in almost quantitative yield (Eq. 1).[21] To underscore the utility of the catalytic reaction, the reaction conditions were applied to synthesize a tetrahydropyrimidin-4-one derivative from a substrate prepared from racemic β-phenyl alanine and dibenzylamine. The reaction of **4** under the dehydrogenative iodine catalysis gave diazaheterocyclic compound **5** in 65% yield (Eq. 2).

Removal of tosyl group



Eq. 1

Synthesis of tetrahydropyrimidin-4-one using β-amino acid derivative



Eq. 2

CONCLUSIONS

We have demonstrated the synthesis of 4-imidazolidiones using an iodine-catalyzed dehydrogenative N-H/C(sp^3)-H coupling under light irradiation in moderate to excellent yields. The reaction is selective for benzylic C-H bonds over primary C-H bonds. Fused heterocyclic compounds, as well as a tetrahydropyrimidinone derivative were accessed from readily available starting materials.

EXPERIMENTAL SECTION

General Information. Unless otherwise mentioned, all reactions were carried out in an argon atmosphere. ^{1}H NMR spectra were recorded on JEOL AL-500 (500 MHz) spectrometers. The chemical shifts were reported in parts per million (δ) relative to internal TMS (0 ppm) for $CDCl_3$. The peak patterns are indicated as follows: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; m, multiplets; q, quartet; br, broad. The coupling constants, *J*, are reported in hertz (Hz). ^{13}C{^{1}H} NMR spectra were obtained by JEOL AL-500 (125 MHz) spectrometer and referenced to the internal solvent signal (central peak is 77.0 ppm in $CDCl_3$ or central peak is 39.5 ppm in DMSO-d_6). $CDCl_3$ or DMSO was use as an NMR solvent. ^{19}F NMR spectra were obtained by JEOL AL-5000 (470 MHz) spectrum, and trifluoroacetic acid was used as an external standard. High-resolution mass spectra (HRMS) were measured on a TOFMS using JMS-T100CS with the ESI (electro spray ionization) method and DART (direct analysis in real time) method.[22] Preparative thin-layer chromatography (PTLC) was performed with silica gel-precoated glass plates (Wakogel B-5F) prepared in our laboratory. Flash column chromatography was performed over silica gel 200-300. Light source was a bulb bought from YAMAZEN (EFD30ED/27PR-E26 27W). All reagents were weighed and handled in air and backfilled with argon at room temperature. All reagents were purchased from Wako, Kanto, Aldrich, TCI, and Strem and used without further purification.

General procedure for the synthesis of starting materials.

*Experimental procedure for the synthesis of (S)-N,N-Dibenzyl-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (**1a**). Step 1.* A 50 mL dry two-necked pear-shaped flask equipped with a magnetic stirred was charged with L-phenylalanine (909 mg, 5.5 mmol) and

H_2O/THF (2/1, 30 mL), then cooled to 0 ºC. *p*-Tosylchloride (953 mg, 1.0 equiv) was added in one portion, and the solution was stirred overnight while warming gradually to rt. The crude solution was evaporated and extracted with diethyl ether. The aqueous layer was acidified with 1N HCl solution to pH 2-3, then extracted with ethyl acetate (× 3). The combined organic layers were dried over Na_2SO_4, and evaporated under reduced pressure. The crude tosyl-L-phenylalanine was dried and used in the next step without further purification.

Step 2. A portion of the crude tosyl-L-phenylalanine (319 mg, 1.0 mmol) obtained above was dissolved in toluene (10 mL) and $SOCl_2$ (0.36 mL, 5.0 equiv) was added, then the solution was heated at 70 ºC (oil bath temperature). The obtained solution was cooled to room temperature, followed by evaporation of toluene under reduced pressure. To the crude acyl chloride was added dichloromethane (7.5 mL) and dibenzylamine (0.22 mL, 2.0 equiv), and stirred at rt for 24 h. 1N HCl was added to the solution, then washed with $NaHCO_3$. The organic layers were dried over Na_2SO_4, evaporated, then the residue was purified by column chromatography on silica gel (toluene/ethyl acetate = 9/1, R_f = 0.4) to afford title compound as a white solid (70%, 347 mg): mp 92 ºC; ^{1}H NMR δ 7.57 (d, J = 7.7 Hz, 2H), 7.20-7.35 (m, 6H), 7.05-7.19 (m, 7H), 6.91 (d, J = 7.5 Hz, 2H), 6.83 (d, J = 7.2 Hz, 2 H), 5.80-5.88 (br, 1H), 4.70 (d, J = 14.5 Hz, 1H), 4.39-4.47 (q, J = 7.2 Hz, 1H), 4.22 (t, J = 7.3 Hz, 2H), 4.04 (d, J = 16.8 Hz, 1H), 2.92-3.00 (m, 1H), 2.81-2.88 (m, 1H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR δ 171.4, 143.4, 137.6, 136.3, 135.7, 135.5, 129.7, 129.7, 129.1, 128.9, 128.7, 128.6, 128.0, 127.8, 127.2, 127.1, 54.5, 49.5, 48.6, 40.7, 21.7 (two aromatic peaks are overlapping); HRMS (ESI, positive) calcd for $C_{30}H_{30}N_2NaO_3S$ $[M+Na]^+$ 521.1875; found 521.1870.

*N,N-Dibenzyl-2-((4-methylphenyl)sulfonamido)acetamide (**1b**).* Isolated by recrystallization from dichloromethane/hexane. The title compound was obtained as a white solid (88%, 1.08 g): mp 136 ºC; ^{1}H NMR δ 7.70 (d, J = 7.8 Hz, 2H), 7.23-7.36 (m, 8H), 7.03-7.09 (m, 2H), 6.93-6.99 (m, 2H), 5.82-5.90 (br, 1H), 4.51 (s, 2H), 4.25 (s, 2H), 3.84 (s, 2H), 2.43 (s, 3 H); ^{13}C{^{1}H} NMR δ 167.7, 143.7, 136.2, 136.1, 135.0, 129.9, 129.3, 128.8, 128.4, 128.1, 127.9, 127.5, 126.5, 49.1, 49.0, 43.9, 21.7; HRMS (ESI, positive) calcd for $C_{23}H_{24}N_2NaO_3S$ $[M+Na]^+$ 431.1400; found 431.1399.

*(S)-N,N-Dibenzyl-2-((4-methylphenyl)sulfonamido)propanamide (**1c**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1, R_f = 0.6). The title compound was obtained as a white solid (78%, 1.64 g): mp 144 ºC; ^{1}H NMR δ 7.70 (d, J = 7.8 Hz, 2H), 7.24-7.29 (m, 8H), 7.01-7.03 (m, 2H), 6.87 (d, J = 7.4 Hz, 2H), 5.97-6.04 (br, 1H), 4.75 (d, J = 14.8 Hz, 1H), 4.36 (d, J = 16.5 Hz, 1H), 4.29 (quint, J = 6.9 Hz, 1H), 4.18 (d, J = 16.5 Hz, 1H), 4.11 (d, J = 14.8 Hz, 1H), 2.44 (s, 3H), 1.37 (d, J = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR δ 172.3, 143.4, 137.5, 136.3, 135.2, 129.8, 129.1, 128.8, 128.2, 128.1, 127.8, 127.2, 126.9, 49.5, 49.2, 48.2, 21.7, 21.2; HRMS (ESI, positive) calcd for $C_{24}H_{26}N_2NaO_3S$ $[M+Na]^+$ 445.1552; found 445.1557.

*(S)-N,N-Dibenzyl-4-methyl-2-((4-methylphenyl)sulfonamido)pentanamide (**1d**).* Isolated by flash column chromatography (hexane/ethyl acetate = 3/1, R_f = 0.4). The title compound was obtained as yellow oil (61%, 564 mg). ^{1}H NMR δ 7.68 (d, J = 7.8 Hz, 2H), 7.21-7.33 (m, 8H), 6.99-7.04 (m, 2H), 6.87-6.92 (m, 2H), 5.80-5.86 (br, 1H), 4.76 (d, J = 14.8 Hz, 1H), 4.32 (d, J = 16.6 Hz, 1H), 4.13-4.21 (m, 2H), 4.08 (d, J = 14.8 Hz, 1H), 2.43 (s, 3H), 1.87-1.98 (m, 1H), 1.51-1.60 (m, 1H), 1.19-1.28 (m, 1H), 0.86 (d, J = 6.7 Hz, 3H), 0.73 (d, J = 6.5 Hz, 3H); ^{13}C{^{1}H} NMR δ 172.5, 143.4, 137.3, 136.5, 135.4, 129.7, 129.1, 128.8, 128.4, 128.1, 127.1, 127.5, 127.0, 51.9, 49.4, 48.5, 43.3, 24.1, 23.5, 21.7, 20.8; HRMS (ESI, positive) calcd for $C_{27}H_{32}N_2NaO_3S$ $[M+Na]^+$ 487.2031; found 487.2025.

*(S)-N,N-Dibenzyl-3-methyl-2-((4-methylphenyl)sulfonamido)butanamide (**1e**).* Isolated by flash column chromatography (hexane/ethyl acetate = 2/1, R_f = 0.5). The title compound was obtained as yellow oil (79%, 710 mg): ^{1}H NMR δ 7.71 (d, J = 7.8 Hz, 2H), 7.22-7.33 (m, 8H), 6.95-7.01 (m, 2H), 6.79 (d, J = 7.4 Hz, 2H), 5.90-6.01 (br, 1H), 4.81 (d, J = 14.8 Hz, 1H), 4.36 (d, J = 16.2 Hz, 1H), 4.06-4.13 (m, 2H), 3.93 (d, J = 14.8 Hz, 1H), 2.45 (s, 3H), 1.87-1.97 (m, 1H), 1.01 (d, J = 6.7 Hz, 3H), 0.88 (d, J = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR δ 171.0, 143.4, 137.3, 136.5, 135.2, 129.8, 129.1, 128.8, 128.4, 128.2, 127.7, 127.5, 127.2, 58.0, 49.6, 47.8, 31.3, 21.8, 20.1, 15.9; HRMS (ESI, positive) calcd for $C_{26}H_{30}N_2NaO_3S$ $[M+Na]^+$ 473.1869; found 473.1868.

*Methyl (S)-5-(dibenzylamino)-4-((4-methylphenyl)sulfonamido)-5-oxopentanoate (**1f**).* Isolated by flash column chromatography (hexane/ethyl acetate = 7/3, R_f = 0.5). The title compound was obtained as a white solid (95%, 705 mg): mp 94 ºC; ^{1}H NMR δ 7.66 (d, J = 7.8 Hz, 2H), 7.20-7.32 (m, 8H), 6.93-7.00 (m, 2H), 6.83 (d, J = 7.3 Hz, 2H), 6.04 (d, J = 7.7 Hz, 1H), 4.79 (d, J = 14.8 Hz, 1H), 4.69 (d, J = 16.2 Hz, 1H), 4.30-4.37 (m, 1H), 4.21 (d, J = 16.2 Hz, 1H), 3.97 (d, J = 14.8 Hz, 1H), 3.63 (s, 3H), 2.74-2.83 (m, 1H), 2.42-2.50 (m, 4H), 1.97-2.06 (m, 1H), 1.62-1.72 (m, 1H); ^{13}C{^{1}H} NMR δ 173.8, 171.5, 143.5, 136.9, 136.3, 135.5, 129.9, 129.0, 128.8, 128.2, 128.0, 127.7, 127.4, 127.3, 52.4, 51.8, 49.3, 47.9, 29.2, 28.7, 21.8; HRMS (ESI, positive) calcd for $C_{27}H_{31}N_2O_5S$ $[M+H]^+$ 495.1948; found 495.1944.

*(S)-N,N-Dibenzyl-3-hydroxy-2-((4-methylphenyl)sulfonamido)propanamide (**1g**).* Isolated by flash column chromatography (toluene/ethyl acetate = 4/1, R_f = 0.3). The title compound was obtained as a white solid (6%, 78 mg): mp 160 ºC; ^{1}H NMR δ 7.72 (d, J = 7.8 Hz, 2H), 7.39 (m, 10H), 7.18-7.00 (m, 2H), 6.95-6.88 (m, 2H), 4.62 (d, J = 15.0 Hz, 1H), 4.45-4.24 (m, 4H), 3.65 (dd, J = 7.2, 4.0 Hz, 1H), 3.61 (dd, J = 7.2, 4.0 Hz, 1H), 2.21 (s, 3H); ^{13}C{^{1}H} NMR using DMSO-d_6 δ 170.7, 143.1, 139.2, 137.4, 136.9, 130.0, 129.1, 128.9, 128.0, 127.9, 127.6, 127.5, 127.0, 62.7, 54.5, 49.9, 48.2, 21.5; HRMS (ESI, positive) calcd for $C_{24}H_{26}N_2NaO_4S$ $[M+Na]^+$ 461.1505; found 461.1506.

*(S)-4-(3-(Dibenzylamino)-2-((4-methylphenyl)sulfonamido)-3-oxopropyl)phenyl 4-methylbenzenesulfonate (**1h**).* Isolated by flash column chromatography (hexane/ethyl acetate = 2/1, R_f = 0.5). The title compound was obtained as yellow oil (64%, 847 mg): ^{1}H NMR δ 7.63 (d, J = 7.3 Hz, 2H), 7.55 (d, J = 7.3 Hz, 2H), 7.38-7.20 (m, 8H), 7.29-7.04 (m, 4H), 6.83 (d, J = 7.2 Hz, 2H), 6.78 (d, J = 7.3 Hz, 2H), 6.64 (d, J = 7.2 Hz, 2H), 6.10-5.96 (br, 1H), 4.63 (d, J = 15.0 Hz, 1H), 4.35 (q, J = 7.2 Hz, 1H), 4.12-4.04 (br, 3H), 2.84 (dd, J = 7.1, 7.1 Hz, 1H), 2.77 (dd, J = 7.1, 7.1 Hz, 1H), 2.42

(s, 3H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR δ 171.2, 148.7, 145.5, 143.6, 137.3, 136.2, 135.5, 134.8, 132.4, 130.9, 129.9, 129.8, 129.2, 128.8, 128.6, 128.1, 127.9, 127.1, 126.9, 122.4, 54.3, 49.7, 49.0, 39.9, 21.8, 21.7 (two aromatic carbon peaks are overlapping); HRMS (ESI, positive) calcd for $C_{37}H_{36}N_2NaO_6S_2$ $[M+Na]^+$ 691.1907; found 691.1901.

*(S)-N,N-Dibenzyl-2-((4-methylphenyl)sulfonamido)-2-phenylacetamide (**1i**).* Isolated by flash column chromatography (hexane/ethyl acetate = 2/1, R_f = 0.5). The title compound was obtained as a white solid (39%, 574 mg): mp 124 ºC; ^1H NMR δ 7.57 (d, J = 7.9 Hz, 2H), 7.08-7.34 (m, 13H), 6.94-7.02 (m, 2H), 6.72 (d, J = 7.4 Hz, 2H), 6.50-6.60 (br, 1H), 5.21 (s, 1H), 4.80 (d, J = 14.8 Hz, 1H), 4.29 (d, J = 16.6 Hz, 1H), 4.11 (d, J = 14.8 Hz, 1H), 4.01 (d, J = 16.6 Hz, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR δ 169.5, 143.2, 137.6, 136.5, 136.2, 135.0, 129.6, 129.3, 129.0, 128.8, 128.7, 128.3, 128.0, 127.9, 127.7, 127.3, 126.9, 58.0, 49.5, 48.6, 21.7; HRMS (ESI, positive) calcd for $C_{29}H_{28}N_2NaO_3S$ $[M+Na]^+$ 507.1713; found 507.1714.

*N,N-Dibenzyl-2-methyl-2-((4-methylphenyl)sulfonamido)propanamide (**1j**).* Isolated by flash column chromatography (hexane/ethyl acetate = 7/3, R_f = 0.3). The title compound was obtained as a brown solid (37%, 122 mg): mp 130 ºC; ^1H NMR δ 7.68 (d, J = 7.8 Hz, 2H), 7.23-7.36 (m, 6H), 7.19 (d, J = 7.8 Hz, 2H), 7.08-7.16 (m, 4H), 5.91-5.98 (m, 1H), 4.40-4.75 (br, 4H), 2.39 (s, 3H), 1.54 (s, 6H); $^{13}C\{^1H\}$ NMR δ 173.3, 143.3, 140.1, 136.5, 129.7, 128.9, 127.6, 127.1, 60.8, 50.0, 26.8, 21.6 (two aromatic carbon peaks are overlapping); HRMS (ESI, positive) calcd for $C_{25}H_{28}N_2NaO_3S$ $[M+Na]^+$ 459.1713; found 459.1712.

*(S)-N-Benzyl-N-methyl-2-((4-methylphenyl)sulfonamido)propanamide (**1k**).* Isolated by flash column chromatography (hexane/ethyl acetate = 3/2, R_f = 0.5). The title compound was obtained as a brown solid (63%, 218 mg): mp 122 ºC; ^1H NMR δ 7.74 (d, J = 7.9 Hz, 0.67×2H), 7.69 (d, J = 7.9 Hz, 0.33×2H), 7.20-7.28 (m, 5H), 6.96-7.03 (m, 0.67×2H), 6.90-6.96 (m, 0.33×2H), 6.25-6.39 (m, 1H), 4.24-4.40 (m, 3H), 2.71-2.78 (m, 3H), 2.36-2.42 (m, 3H), 1.26-1.36 (m, 3H); $^{13}C\{^1H\}$ NMR δ 171.9, 171.8, 143.5, 143.4, 137.5, 137.4, 136.4, 135.7, 129.7, 129.0, 128.7, 127.9, 127.6, 127.2, 126.7, 52.9, 51.2, 49.0, 48.9, 34.3, 34.1, 21.7, 21.6, 20.7, 20.0 (more carbon peaks were observed because the compound exists as a mixture of tautomers). HRMS (ESI, positive) calcd for $C_{18}H_{23}N_2O_3S$ $[M+H]^+$ 347.1424; found 347.1420.

*(S)-N-Methyl-2-((4-methylphenyl)sulfonamido)-N-(4-(trifluoromethyl)benzyl)propanamide (**1l**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1, R_f = 0.5). The title compound was obtained as a white solid (65%, 135 mg): mp 132 ºC; ^1H NMR δ 7.74 (d, J = 7.8 Hz, 0.77×2H), 7.68 (d, J = 7.8 Hz, 0.23×2H), 7.53 (d, J = 7.8 Hz, 2H), 7.28 (d, J = 7.8 Hz, 2H + 0.23×2H), 7.09 (d, J = 8.0 Hz, 0.77×2H), 7.03 (d, J = 8.0 Hz, 0.23×2H), 5.87-5.77 (m, 1H), 4.50 (d, J = 15.0 Hz, 1H), 4.41 (d, J = 15.0 Hz, 0.23×1H), 4.35 (d, J = 15.0 Hz, 0.77×1H), 4.25-4.32 (m, 0.77×1H), 4.18-4.24 (m, 0.23×1H), 2.81 (s, 0.77×3H), 2.77 (s, 0.23×3H), 2.42 (s, 0.77×3H), 2.41 (s, 0.23×3H), 1.35 (s, 0.77×3H), 1.33 (s, 0.23×3H); $^{13}C\{^1H\}$ NMR δ 172.2, 172.0, 143.6, 140.5, 139.7, 137.4, 137.4, 130.2, 130.0, 129.8, 129.7, 128.0, 127.3, 127.2, 126.9, 126.0 (J = 2.5 Hz), 125.125.7 (J = 3.8 Hz), 125.2, 125.1, 123.0, 122.9, 52.5, 51.0, 49.0, 48.9, 34.6, 34.2, 21.7, 21.6, 20.9, 20.1 (the compound exists as tautomer. The coupling of F makes the aromatic carbons difficult to read); ^{19}F NMR δ -62.5; HRMS (ESI, positive) calcd for $C_{19}H_{21}F_3N_2O_3S$ $[M+H]^+$ 415.1298; found 415.1290.

*(S)-N,N-Dimethyl-2-((4-methylphenyl)sulfonamido)propanamide (**1m**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1, R_f = 0.5). The title compound was obtained as yellow solid (65%, 350 mg): mp 94 ºC; ^1H NMR δ 7.70 (d, J = 7.9 Hz, 2H), 7.25 (d, J = 7.9 Hz, 2H), 5.76-5.82 (br, 1H), 4.14-4.23 (m, 1H), 2.82 (s, 3H), 2.71 (s, 3H), 2.41 (s, 3H), 1.24 (d, J = 7.2, 3H); $^{13}C\{^1H\}$ NMR δ 171.4, 143.6, 137.1, 129.5, 127.3, 48.0, 36.8, 35.7, 21.6, 19.9; HRMS (ESI, positive) calcd for $C_{12}H_{19}N_2O_3S$ $[M+H]^+$ 271.1111; found 271.1107.

*(S)-N,N-Dibutyl-2-((4-methylphenyl)sulfonamido)propanamide (**1n**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1, R_f = 0.5). The title compound was obtained as a white solid (80%, 650 mg): mp 54 ºC; ^1H NMR δ 7.70 (d, J = 7.8 Hz, 2H), 7.25 (d, J = 7.8 Hz, 2H), 5.93 (d, J = 7.9 Hz, 1H), 4.04-4.11 (m, 1H), 3.17-3.25 (m, 1H), 2.95-3.09 (m, 3H), 2.40 (s, 3H), 1.11-1.37 (m, 11H), 0.83-0.92 (m, 6H); $^{13}C\{^1H\}$ NMR δ 171.1, 143.4, 137.3, 129.7, 127.3, 48.9, 47.3, 46.0, 31.0, 29.6, 21.6, 21.1, 20.1, 20.0, 13.9, 13.8; HRMS (ESI, positive) calcd for $C_{18}H_{31}N_2O_3S$ $[M+H]^+$ 355.2050; found 355.2047.

*(S)-4-Methyl-N-(1-oxo-1-(piperidin-1-yl)propan-2-yl)benzenesulfonamide (**1o**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1, R_f = 0.4). The title compound was obtained as a light brown solid (75%, 466 mg): mp 93 ºC; ^1H NMR δ 7.71 (d, J = 7.8 Hz, 2H), 7.27 (d, J = 8.3 Hz, 2H), 5.94 (d, J = 7.9 Hz, 1H), 4.08-4.19 (m, 1H), 3.41-3.48 (m, 1H), 3.08-3.26 (m, 3H), 2.40 (s, 3H), 1.38-1.60 (m, 4H), 1.13-1.32 (m, 5H); $^{13}C\{^1H\}$ NMR δ 169.5, 143.5, 137.0, 129.6, 127.5, 48.8, 46.3, 43.4, 26.1, 25.2, 24.3, 21.6, 20.5; HRMS (ESI, positive) calcd for $C_{15}H_{23}N_2O_3S$ $[M+H]^+$ 311.1424; found 311.1420.

*(S)-4-Methyl-N-(1-morpholino-1-oxopropan-2-yl)benzenesulfonamide (**1p**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/3, R_f = 0.6). The title compound was obtained as a white solid (81%, 507 mg): mp 112 ºC; ^1H NMR δ 7.71 (d, J = 7.9 Hz, 2H), 7.29 (d, J = 7.9 Hz, 2H), 5.81 (br, 1H), 4.20-4.12 (m, 1H), 3.54-3.62 (m, 2H), 3.22-3.48 (m, 6H), 2.42 (s, 3H), 1.28 (d, J = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR δ 170.1, 143.7, 137.0, 129.7, 127.5, 66.6, 66.3, 48.6, 45.7, 42.5, 21.6, 20.2; HRMS (ESI, positive) calcd for $C_{14}H_{21}N_2O_4S$ $[M+H]^+$ 313.1217; found 313.1212.

*(S)-N-(1-(Azepan-1-yl)-1-oxopropan-2-yl)-4-methylbenzenesulfonamide (**1q**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1, R_f = 0.4). The title compound was obtained as a yellow solid (88%, 571 mg): mp 94 ºC; ^1H NMR δ 7.72 (d, J = 7.9 Hz, 2H), 7.26 (d, J = 7.9 Hz, 2H), 5.94 (d, J = 9.1 Hz, 1H), 4.06-4.13 (m, 1H), 3.53-3.60 (m, 1H), 3.25-3.32 (m, 1H), 3.11-3.18 (m, 1H), 2.93-3.00 (m, 1H), 2.39 (s, 3H), 1.34-1.66 (m, 6H), 1.32 (d, J = 7.2 Hz, 3H), 1.11-1.28 (m, 2H); $^{13}C\{^1H\}$ NMR δ 171.1, 143.5, 137.1, 129.6, 127.5, 49.0, 47.3, 46.1, 28.9, 27.2, 27.0, 26.3, 21.5, 20.7; HRMS (ESI, positive) calcd for $C_{16}H_{25}N_2O_3S$ $[M+H]^+$ 325.1580; found 325.1574.

*(S)-N,N-Diisopropyl-2-((4-methylphenyl)sulfonamido)propanamide (**1r**).* Isolated by

flash column chromatography (hexane/ethyl acetate = 3/2, R_f = 0.6). The title compound was obtained as a yellow solid (64%, 517 mg): mp 108 ºC; ^{1}H NMR *δ* 7.73 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 6.23 (d, *J* = 7.9 Hz, 1H), 4.02-4.10 (m, 1H), 3.66-3.75 (sept, *J* = 7.3 Hz, 1H), 3.15-3.27 (m, 1H), 2.37 (s, 3H), 1.28 (d, *J* = 7.3 Hz, 3H), 1.22 (d, *J* = 7.3 Hz, 3H), 1.08 (d, *J* = 7.3 Hz, 3H), 0.98 (d, *J* = 7.3 Hz, 3H), 0.91 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR *δ* 169.7, 143.3, 136.9, 129.6, 127.4, 49.7, 48.3, 45.9, 21.4, 20.8, 20.3, 20.3, 20.0, 19.9; HRMS (ESI, positive) calcd for $C_{16}H_{27}N_2O_3S$ $[M+H]^+$ 327.1737; found 327.1733.

*(S)-N-Cyclohexyl-N-methyl-2-((4-methylphenyl)sulfonamido)propanamide (**1s**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1, R_f = 0.5). The title compound was obtained as a white solid (35%, 118 mg): mp 86 ºC; ^{1}H NMR *δ* 7.70 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 7.9 Hz, 2H), 5.92 (d, *J* = 7.6 Hz, 0.40×1H), 5.82 (d, *J* = 8.7 Hz, 0.60×1H), 4.09-4.18 (m, 1H), 3.98-4.06 (m, 0.60×1H), 3.20-3.28 (m, 0.40×1H), 2.64 (s, 0.60×3H), 2.59 (s, 0.40×3H), 2.35-2.41 (m, 3H), 1.55-1.87 (m, 4H), 1.40-1.52 (m, 1H), 1.18-1.35 (m, 1.17 (m, 8H); ^{13}C{^{1}H} NMR *δ* 171.1, 170.9, 143.5, 143.5, 137.1, 136.9, 129.6, 129.6, 127.4, 127.4, 56.4, 53.2, 49.4, 49.1, 30.8, 30.5, 29.7, 29.2, 29.0, 27.7, 25.7, 25.6, 25.5, 25.5, 25.5, 25.2, 21.6, 21.5, 21.2, 20.0 (more carbon peaks were observed because the compound exists as a mixture of tautomers); HRMS (ESI, positive) calcd for $C_{17}H_{27}N_2O_3S$ $[M+H]^+$ 339.1737; found 339.1732 .

*(S)-N-Hexyl-N-isopropyl-2-((4-methylphenyl)sulfonamido)propanamide (**1t**).* Isolated by flash column chromatography (hexane/ethyl acetate = 2/1, R_f = 0.4). The title compound was obtained as brown oil (59%, 523 mg). ^{1}H NMR *δ* 7.74-7.66 (m, 2H), 7.29-7.21 (m, 2H), 6.00 (d, *J* = 7.2 Hz, 0.59×1H); 5.89 (d, *J* = 7.2 Hz, 0.41×1H); 4.20-4.28 (m, 0.41×1H); 4.10-4.19 (m, 0.59×1H); 3.97-4.06 (m, 0.41×1H); 3.71-3.81 (m, 0.59×1H); 2.80-3.01 (m, 2H), 2.36-2.42 (m, 3H), 1.09-1.36 (m, 12.77H), 1.02 (d, J = 7.2 Hz, 0.41×3H), 0.83-.097 (m, 6H); ^{13}C{^{1}H} NMR *δ* 171.3, 170.4, 143.4, 143.3, 137.3, 137.0, 129.6, 129.6, 127.4, 127.4, 49.4, 49.2, 47.9, 47.0, 43.6, 41.5, 31.6, 31.4, 31.1, 29.0, 27.0, 26.8, 22.7, 22.6, 21.5, 21.5, 21.1, 21.1, 21.0, 20.9, 20.1, 14.1, 14.1 (the compound exists as a mixture of tautomers); HRMS (ESI, positive) calcd for $C_{19}H_{33}N_2O_3S$ $[M+H]^+$ 369.2206; found 369.2204

*(S)-N,N-Dibenzyl-2-((2,4,6-trimethylphenyl)sulfonamido)propanamide (**1u**).* Isolated by flash column chromatography (hexane/ethyl acetate = 2/1, R_f = 0.5). The title compound was obtained as yellow oil (72%, 649 mg). ^{1}H NMR *δ* 7.23-7.31 (m, 6H), 7.01-7.05 (m, 2H), 6.91-6.94 (m, 2H), 6.87-6.91 (m, 2H), 6.02 (br, *J* = 7.9 Hz, 1 H), 4.71 (d, *J* = 14.5 Hz, 1H), 4.34 (d, *J* = 16.3 Hz, 1H), 4.22-4.29 (m, 1H), 4.20 (d, *J* = 14.5 Hz, 1H), 4.15 (d, *J* = 16.3 Hz, 1H), 2.61 (s, 6H), 2.31 (s, 3H), 1.33 (d, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR *δ* 172.6, 142.2, 139.1, 136.4, 135.3, 134.5, 132.1, 129.1, 128.8, 128.2, 128.1, 127.8, 126.7, 49.5, 48.8, 48.3, 22.9, 21.2, 21.1; HRMS (ESI, positive) calcd for $C_{26}H_{31}N_2O_3S$ $[M+H]^+$ 451.2050; found 451.2046.

*(S)-N,N-Dimethyl-2-((2-nitrophenyl)sulfonamido)propanamide (**1v**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1, R_f = 0.5). The title compound was obtained as yellow oil (83%, 378 mg): ^{1}H NMR *δ* 7.90 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.71 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.60 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.38-7.22 (m, 6H), 7.04-7.00 (m, 4H), 6.78-7.55 (br, 1H), 4.71 (d, *J* = 14.6 Hz, 1H), 4.60 (q, *J* = 6.9 Hz, 1H), 4.44 (d, *J* = 16.0 Hz, 1H), 4.31 (d, *J* = 16.0 Hz, 1H), 4.12 (d, *J* = 14.6 Hz, 1H), 1.42 (d, *J* = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR *δ* 171.8, 147.9, 136.4, 135.5, 134.8, 133.6, 132.9, 130.2, 129.2, 128.9, 128.2, 127.8, 126.9, 125.8, 50.5, 49.6, 48.4, 20.8 (two aromatic carbon peaks are overlapping); HRMS (ESI, positive) calcd for $C_{23}H_{24}N_3O_5S$ $[M+H]^+$ 454.1431; found 454.1425.

*N,N-Dibenzyl-3-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (**4**).* Isolated by flash column chromatography (dichloromethane/ethyl acetate = 19/1, R_f = 0.6). The title compound was obtained as a white solid (32%, 317 mg). mp 100 ºC; ^{1}H NMR *δ* 7.62 (d, *J* = 8.2 Hz, 2H), 7.22-7.30 (m, 6H), 7.12-7.21 (m, 5H), 7.06-7.11 (m, 2H), 6.98-7.04 (m, 2H), 6.83-6.89 (m, 3H), 4.71-4.77 (m, 1H), 4.52 (d, *J* = 14.7 Hz, 1H), 4.39 (d, *J* = 14.7 Hz, 1H), 4.18 (s, 2H), 2.97 (dd, *J* = 7.0, 3.7 Hz 1H), 2.72 (dd, *J* = 7.0, 3.7 Hz 1H),
2.36 (s, 3H); ^{13}C{^{1}H} NMR *δ* 171.2, 143.1, 140.0, 137.9, 136.7, 135.9, 129.5, 129.1, 128.7, 128.5, 128.3, 127.8, 127.7, 127.6, 127.3, 126.8, 126.3, 55.0, 50.1, 48.5, 38.8, 21.6; HRMS (ESI, positive) calcd for $C_{30}H_{31}N_2O_3S$ $[M+H]^+$ 499.2050; found 499.2039.

General procedure for the synthesis of 4-imidazolidinones: (*S*)-*N*,*N*-Dibenzyl-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (**1a**) (49.9 mg, 0.10 mmol), bis(trifluoroacetoxy)iodobenzene ($PhIOCOCF_3$) (51.6 mg, 0.120 mmol), and iodine (5.1 mg, 0.020 mmol), were placed into a Schlenk tube equipped with a magnetic stirring bar. The Schlenk tube was evacuated and backfilled with argon (×3). To the reaction vessel was added dichloroethane (0.70 mL). The Schlenk was capped and the solution was stirred for 8 h at 0 ºC (ice bath temperature) under 27 W fluorescent light irradiation. The crude material was then purified using preparative TLC to obtain (2*S*,5*S*)-3,5-dibenzyl-2-phenyl-1-tosylimidazolidin-4-one (**2a**) as major diastereomer and (2*R*,5*S*)-3,5-dibenzyl-2-phenyl-1-tosylimidazolidin-4-one (**2a'**) as minor diastereomer.

*(2S,5S)-3,5-Dibenzyl-2-phenyl-1-tosylimidazolidin-4-one (**2a**).* Isolated by PTLC (R_f = 0.5; toluene/ethyl acetate = 9/1) as a white solid (75%, 37.2 mg): mp 157 ºC; ^{1}H NMR *δ* 7.55-7.62 (m, 2H), 7.32-7.40 (m, 3H), 7.20-7.30 (m, 1H), 7.12-7.19 (m, 1H), 7.00-7.10 (m, 4H), 6.83-6.95 (m, 4H), 6.67-6.78 (m, 2H), 6.19 (d, *J* = 7.5 Hz, 2H), 5.21 (d, *J* = 2.6 Hz, 1H), 4.84 (d, *J* = 15.0 Hz, 1H), 4.60 (s, 1H), 3.96 (dd, *J* = 7.7, 3.0 Hz, 1H), 3.36 (dd, *J* = 7.7, 3.0 Hz, 1H), 2.98 (d, *J* = 15.0 Hz, 1H), 2.33 (s, 3H); ^{13}C{^{1}H} NMR *δ* 167.9, 143.1, 136.6, 135.2, 133.7, 133.6, 131.4, 129.7, 129.1, 128.9, 128.6, 128.6, 128.5, 127.9, 127.7, 127.1, 126.6, 76.2, 62.1, 43.4, 37.5, 21.5; HRMS (ESI, positive) calcd for $C_{30}H_{29}N_2O_3S$ $[M+H]^+$ 497.1893; found 497.1887. $[\alpha]^{31}_D$ – 12.0 (c = 0.34, $CHCl_3$).

*(2R,5S)-3,5-Dibenzyl-2-phenyl-1-tosylimidazolidin-4-one (**2a'**).* Isolated by PTLC (R_f = 0.6; toluene/ethyl acetate = 9/1) as colorless oil (17%, 8.4 mg): ^{1}H NMR *δ* 7.46-7.51 (m, 2H), 7.19-7.35 (m, 9H), 7.12-7.19 (m, 2H), 7.03-7.10 (m, 2H), 6.72 (d, *J* = 7.3 Hz, 2H), 6.30 (d, *J* = 7.3 Hz, 2H), 5.34 (s, 1H), 4.86 (d, *J* = 15.0 Hz, 1H), 4.31-4.36 (m, 1H), 3.47 (dd, *J* = 7.7, 3.0 Hz, 1H), 3.34 (dd, *J* = 7.7, 3.0 Hz, 1H), 1H), 3.19 (d, *J* = 15.0 Hz, 1H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR *δ*

168.0, 144.6, 136.1, 135.9, 134.6, 132.8, 131.3, 130.1, 129.4, 128.7, 128.7, 128.6, 128.2, 128.1, 127.9, 127.0, 75.5, 62.6, 43.9, 37.4, 21.7 (two aromatic carbon peaks are overlapping); HRMS (ESI, positive) calcd for $C_{30}H_{29}N_2O_3S$ $[M+H]^+$ 497.1893; found 497.1886.

*3-Benzyl-2-phenyl-1-tosylimidazolidin-4-one (**2b**).* Isolated by PTLC (R_f = 0.2; toluene/ethyl acetate = 9/1) as a white solid (90%, 36.6 mg): mp 102 ºC; ^{1}H NMR *δ* 7.33-7.43 (m, 5H), 7.23-7.33 (m, 3H), 7.17-7.23 (m, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 6.89 (d, *J* = 7.4 Hz, 2H), 5.67 (s, 1H), 4.98 (d, *J* = 15.0 Hz, 1H), 4.06-4.19 (m, 2H), 3.32 (d, *J* = 15.0 Hz, 1H), 2.41 (s, 3H); ^{13}C{^{1}H} NMR *δ* 167.0, 144.3, 136.2, 134.5, 134.0, 130.0, 130.0, 129.2, 129.0, 128.4, 128.2, 127.5, 127.4, 76.0, 49.3, 43.8, 21.7; HRMS (ESI, positive) calcd for $C_{23}H_{22}N_2NaO_3S$ $[M+Na]^+$ 429.1243; found 429.1240.

*(S)-N,N-Dibenzyl-2-((4-methylphenyl)sulfonamido)propanamide (**2c**).* Isolated by PTLC (R_f = 0.4; hexane/ethyl acetate = 7/3) as a yellow diastereomeric mixture in solid form (96%, 40.4 mg). Physical properties of the mixture are shown. ^{1}H NMR *δ* 7.36-7.46 (m, 4H), 7.13-7.35 (m, 6H), 7.01-7.07 (m, 0.38×2H), 6.88-6.97 (m, 2H), 6.82 (d, *J* = 7.6 Hz, 0.62×2H), 5.69 (s, 0.38×1H), 5.58 (s, 0.62×1H), 5.03 (d, *J* = 15.0 Hz, 0.38×1H), 4.99 (d, *J* = 15.0 Hz, 0.62×1H), 4.16-4.22 (m, 1H), 3.33 (d, *J* = 15.0 Hz, 0.62×1H), 3.27 (d, *J* = 15.0 Hz, 0.38×1H), 2.42 (s, 0.62×3H), 2.31 (s, 0.38×3H), 1.80 (d, *J* = 7.2 Hz, 0.38×3H), 1.65 (d, *J* = 7.2 Hz, 0.62×3H); ^{13}C{^{1}H} NMR *δ* 170.1, 169.9, 144.3, 143.2, 136.8, 136.3, 134.7, 134.6, 134.5, 134.0, 130.0, 129.9, 129.8, 129.2, 129.1, 129.1, 128.9, 128.8, 128.7, 128.4, 128.3, 128.2, 128.0, 127.7, 127.7, 126.7, 75.6, 75.3, 57.0, 56.5, 43.9, 43.7, 21.7, 21.5, 20.1, 19.5 (8 pairs of aromatic carbons are overlapping); HRMS (ESI, positive) calcd for $C_{24}H_{25}N_2O_3S$ $[M+H]^+$ 421.1580; found 421.1578.

*(5S)-3-Benzyl-5-isobutyl-2-phenyl-1-tosylimidazolidin-4-one (**2d**).* Isolated by PTLC (R_f = 0.5; hexane/ethyl acetate = 7/3) as a brown diastereomeric mixture in solid form (75%, 34.7 mg). Physical properties of the mixture are shown. ^{1}H NMR *δ* 7.40-7.47 (m, 0.87×1H), 7.27-7.25 (m, 3.91H), 7.10-7.18 (m, 2H), 6.99-7.06 (m, 0.87×2H), 6.87-6.93 (m, 0.87×4H), 6.78-6.86 (m, 2H), 5.68 (s, 0.87×1H), 5.63 (s, 0.13×1H), 5.02 (d, *J* = 14.8 Hz, 0.87×1H), 4.99 (d, *J* = 14.8 Hz, 0.13×1H), 4.11-4.14 (m, 0.87×1H), 4.04-4.07 (m, 0.17×1H), 3.36 (d, *J* = 14.8 Hz, 0.13×1H), 3.22 (d, *J* = 14.8 Hz, 0.87×1H), 2.43 (s, 0.13×3H), 2.31 (s, 0.87×3H), 2.11-2.23 (m, 0.87×3H), 2.03-2.06 (m, 0.13×1H), 1.82-1.91 (m, 0.13×1H), 1.69-1.72 (d, *J* = 7.3 Hz, 0.13×1H), 0.95-1.07 (m, 6H); ^{13}C{^{1}H} NMR *δ* 170.3, 169.7, 144.4, 143.0, 136.8, 136.3, 134.6, 134.5, 134.2, 133.7, 130.2, 129.8, 129.2, 129.1, 129.0, 128.9, 128.7, 128.7, 128.5, 128.3, 128.0, 127.7, 127.6, 127.4, 127.0, 126.7, 75.9, 75.3, 59.6, 59.2, 44.1, 44.0, 43.8, 40.7, 24.4, 24.1, 23.9, 22.8, 22.6, 22.5, 21.7, 21.5; HRMS (ESI, positive) calcd for $C_{27}H_{30}N_2NaO_3S$ $[M+H]^+$ 485.1869; found 485.1871.

*(5S)-3-Benzyl-5-isopropyl-2-phenyl-1-tosylimidazolidin-4-one (**2e**).* Isolated by PTLC (R_f = 0.5; hexane/ethyl acetate = 7/3) as a white diastereomeric mixture in solid form (79%, 35.4 mg). Physical properties of the mixture are shown. ^{1}H NMR *δ* 7.24-7.43 (m, 5H), 7.09-7.21 (m, 2H), 7.00-7.05 (m, 0.89×2H), 6.83-6.96 (m, 5H), , 6.80 (d, *J* = 7.3 Hz, 0.11×2H), 5.68 (s, 0.89×1H), 5.62 (s, 0.11×1H) 5.06 (s, *J* = 15.0 Hz, 0.89×1H), 5.01 (s, *J* = 15.0 Hz, 0.11×1H), 4.17 (s, 0.89×1H), 3.92 (d, *J* = 6.0 Hz, 0.11×1H), 3.42 (d, *J* = 14.7 Hz, 0.11×1H), 3.16 (d, *J* = 14.7 Hz, 0.89×1H), 2.94-3.04 (m, 1H), 2.41 (s, 0.11×3H), 2.32 (s, 0.89×3H), 1.34 (d, *J* = 7.2 Hz, 0.89×3H), 1.15 (d, *J* = 7.2 Hz, 0.11×3H), 1.12 (d, *J* = 7.2 Hz, 0.11×3H), 1.04 (d, *J* = 6.8 Hz, 0.89×3H); ^{13}C{^{1}H} NMR *δ* 168.1, 143.1, 136.6, 134.8, 134.5, 130.1, 129.7, 129.1, 128.9, 128.9, 128.8, 128.7, 128.6, 128.6, 128.2, 128.1, 127.9, 127.7, 126.7, 76.1, 74.8, 66.2, 65.2, 44.2, 43.6, 31.5, 29.8, 21.7, 21.5, 19.7, 18.6, 18.4, 15.5 (some peaks of the minor diastereomer could not be observed); HRMS (ESI, positive) calcd for $C_{26}H_{29}N_2O_3S$ $[M+H]^+$ 449.1893; found 449.1891.

*Methyl 3-((4S)-1-benzyl-5-oxo-2-phenyl-3-tosylimidazolidin-4-yl)propanoate (**2f**).* Isolated by PTLC (R_f = 0.6; dichloromethane/ethyl acetate = 19/1) as a yellow diastereomeric mixture in solid form (84%, 41.4 mg). Physical properties of the mixture are shown. ^{1}H NMR *δ* 7.24-7.48 (m, 5H), 7.12-7.22 (m, 3H), 7.00-7.08 (m, 0.70×2H), 6.81-6.96 (m, 0.70×3H + 0.30×6H), 6.73-6.80 (m, 0.70×1H), 5.68 (br, 0.70×1H), 5.59 (br, 0.30×1H), 5.03 (d, *J* = 14.6 Hz, 0.70×1H), 4.96 (d, *J* = 14.6 Hz, 0.30×1H), 4.20-4.30 (m, 1H), 3.70 (s, 0.70×3H), 3.68 (s, 0.30×3H), 3.35 (d, *J* = 14.6 Hz, 0.30×1H), 3.25 (d, *J* = 14.6 Hz, 0.70×1H), 2.53-2.80 (m, 0.70×3H + 0.30×3H), 2.22-2.45 (m, 0.30×2H + 1H), 2.29 (s, 0.70×3H), 2.14-2.23 (m, 0.30×1H); ^{13}C{^{1}H} NMR *δ* 173.3, 173.2, 169.2, 168.4, 144.5, 143.3, 136.5, 135.5, 134.6, 134.5, 134.2, 133.2, 130.2, 129.9, 129.9, 129.3, 129.2, 129.1, 128.9, 128.8, 128.7, 128.5, 128.4, 128.0, 127.8, 127.6, 126.8, 76.0, 75.3, 59.7, 59.0, 51.8, 51.8, 44.0, 43.9, 29.6, 29.2, 28.1, 27.0, 21.7, 21.5 (two aromatic peaks are overlapping); HRMS (ESI, positive) calcd for $C_{27}H_{29}N_2O_5S$ $[M+H]^+$ 493.1792; found 493.1786.

*(2S,5S)-3-Benzyl-5-(hydroxymethyl)-2-phenyl-1-tosylimidazolidin-4-one (**2g**).* The major diastereomer was isolated by PTLC (R_f = 0.3; hexane/ethyl acetate = 7/3) as a white solid (44%, 19.2 mg): mp 132 ºC; ^{1}H NMR *δ* 7.82 (d, *J* = 7.8 Hz, 2H), 7.42-7.48 (m, 3H), 7.35 (d, *J* = 7.8 Hz, 2H) 7.20-7.30 (m, 5H), 7.02-7.06 (m, 2H), 5.72-5.77 (br, 1H), 5.70 (s, 1H), 5.38 (d, *J* = 15.2 Hz, 1H), 4.15-4.06 (m, 1H), 3.78-3.87 (m, 2H), 3.46 (d, *J* = 15.2 Hz, 1H), 2.44 (s, 3H); ^{13}C{^{1}H} NMR *δ* 166.1, 144.2, 135.3, 135.1, 130.1, 130.0, 129.2, 128.9, 128.1, 128.1, 127.8, 127.6, 87.0, 62.7, 51.4, 47.2, 21.7 (two aromatic peaks are overlapping); HRMS (ESI, positive) calcd for $C_{24}H_{25}N_2O_4S$ $[M+H]^+$ 437.1530; found 437.1522. $[\alpha]^{25}_D$ +118.4 (c = 0.68, $CHCl_3$).

*4-(((4S)-1-Benzyl-5-oxo-2-phenyl-3-tosylimidazolidin-4-yl)methyl)phenyl 4-methylbenzenesulfonate (**2h**).* Isolated by PTLC (R_f = 0.5; toluene/ethyl acetate = 9/1) as a white diastereomeric mixture in solid form (77%, 61.3 mg). Physical properties of the mixture are shown. ^{1}H NMR *δ* 7.69-7.76 (m, 2H), 7.44-7.51 (m, 2H), 7.02-7.35 (m, 9H), 6.80-6.95 (m, 5H), 6.67-6.77 (m, 2H), 6.39 (d, *J* = 7.6 Hz, 0.20×2H), 6.26 (d, *J* = 7.6 Hz, 0.80×2H), 5.33 (br, 0.20×1H), 5.18 (br, 0.80×1H), 4.84 (d, *J* = 15.2 Hz, 0.20×1H), 4.79 (d, *J* = 15.2 Hz, 0.80×1H), 4.51-4.57 (br, 0.80×1H), 4.26-4.30 (br, 0.20×1H), 3.92-3.84 (m, 0.80×1H), 3.35-3.41 (m, 0.20×1H), 3.26-3.34 (m, 0.80×1H + 0.20×1H), 3.18 (d, *J* = 15.2 Hz, 0.20×1H), 2.99 (d, *J* = 15.2 Hz, 0.80×1H), 2.41-2.49 (m, 0.80×3H + 0.20×6H), 2.31 (s, 0.80×3H); ^{13}C{^{1}H} NMR *δ* 167.7, 167.5, 150.9, 149.1, 149.1, 145.5, 144.8, 143.3, 136.2, 135.9, 135.0, 134.4, 134.3, 133.6, 133.5, 132.6, 132.5, 130.2, 129.9, 129.8, 129.7, 129.2, 128.8, 128.7, 128.6, 128.2, 128.1, 128.1, 128.0, 127.9, 126.6, 122.4, 122.3, 76.2, 75.4, 62.4, 61.7, 44.0, 43.5, 36.7, 36.6,

21.8, 21.7, 21.5 (9 aromatic carbons and two aliphatic carbons are overlapping); HRMS (ESI, positive) calcd for $C_{37}H_{35}N_2O_6S_2$ $[M+H]^+$ 667.1931; found 667.1917.

*(2R,5R)-3-Benzyl-2,5-diphenyl-1-tosylimidazolidin-4-one (**2i**).* Isolated by PTLC (R_f = 0.5; toluene/ethyl acetate = 9/1) as a white solid (41%, 19.8 mg): mp 112 ºC; ^{1}H NMR δ 7.30-7.40 (m, 9H), 7.23-7.28 (m, 2H), 7.09 (d, J = 7.3 Hz, 2H), 7.01-7.07 (m, 2H), 6.84-6.93 (m, 4H), 5.90 (s, 1H), 5.20 (s, 1H), 5.07 (d, J = 14.8 Hz, 1H), 3.27 (d, J = 14.8 Hz, 1H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR δ 168.1, 143.2, 137.5, 136.5, 134.9, 134.8, 130.0, 129.1, 129.1, 128.9, 128.8, 128.6, 128.6, 128.4, 127.6, 126.9, 76.3, 65.0, 43.9, 21.5 (two aromatic peaks are overlapping); HRMS (ESI, positive) calcd for $C_{29}H_{27}N_2O_3S$ $[M+H]^+$ 483.1737; found 483.1732. $[\alpha]^{27}_D$ –139.3 (c = 0.68, $CHCl_3$).

*(2S,5S)-3-Benzyl-2,5-diphenyl-1-tosylimidazolidin-4-one (**2i'**).* Isolated by PTLC (R_f = 0.5; dichloromethane = 9/1) as a white solid (22%, 10.6 mg): mp 114 ºC; ^{1}H NMR δ 7.44-7.52 (m, 2H), 7.35-7.45 (m, 3H), 7.20-7.35 (m, 10H), 7.06 (d, J = 7.9 Hz, 2H), 6.90 (d, J = 7.3 Hz, 2H), 5.81 (s, 1H), 5.25 (s, 1H), 5.00 (d, J = 14.8 Hz, 1H), 3.37 (d, J = 14.8 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR δ 167.8, 144.3, 136.1, 135.4, 134.6, 134.3, 130.0, 129.9, 129.0, 129.0, 128.6, 128.5, 128.3, 128.3, 128.2, 127.6, 127.3, 75.3, 63.7, 44.4, 21.7; HRMS (ESI, positive) calcd for $C_{29}H_{27}N_2O_3S$ $[M+H]^+$ 483.1737; found 483.1732.

*3-Benzyl-5,5-dimethyl-2-phenyl-1-tosylimidazolidin-4-one (**2j**).* Isolated by PTLC (R_f = 0.4; hexane/ethyl acetate = 7/3) as a white solid (77%, 33.5 mg): mp 97 ºC; ^{1}H NMR δ 7.22-7.35 (m, 4H), 7.10-7.18 (d, 2H), 7.06 (d, J = 7.8 Hz, 2H), 6.96-7.02 (m, 4H), 6.88 (d, J = 8.2 Hz, 2H), 5.62 (s, 1H), 5.02 (d, J = 14.8 Hz, 1H), 3.21 (d, J = 14.8 Hz, 1H), 2.27 (s, 3H), 1.80 (d, J = 4.2 Hz, 6H); ^{13}C{^{1}H} NMR δ 172.6, 142.9, 138.5, 135.0, 134.6, 129.7, 129.0, 129.0, 128.9, 128.6, 128.3, 128.2, 127.2, 74.3, 65.3, 43.6, 25.9, 25.5, 21.4; HRMS (ESI, positive) calcd for $C_{25}H_{27}N_2O_3S$ $[M+H]^+$ 435.1737; found 435.1731.

*(2S,5S)-3,5-Dimethyl-2-phenyl-1-tosylimidazolidin-4-one (**2k**).* Isolated by PTLC (R_f = 0.6; hexane/ethyl acetate = 3/2) as a yellow solid (56%, 19.3 mg): mp 108 ºC; ^{1}H NMR δ 7.54 (d, J = 7.8 Hz, 2H), 7.35-7.42 (m, 3H), 7.29-7.35 (m, 2H), 7.23 (d, J = 8.2 Hz, 2H), 5.71 (s, 1H), 4.18 (q, J = 7.0 Hz, 1H), 2.56 (s, 3H), 2.40 (s, 3H), 1.58 (d, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR δ 169.8, 144.5, 137.0, 134.7, 130.0, 129.8, 129.1, 127.7, 127.6, 77.6, 56.6, 27.3, 21.6, 19.9; HRMS (ESI, positive) calcd for $C_{18}H_{21}N_2O_3S$ $[M+H]^+$ 345.1267; found 345.1264. $[\alpha]^{25}_D$ –72.5 (c = 0.69, $CHCl_3$).

*(2R,5S)-3,5-Dimethyl-2-phenyl-1-tosylimidazolidin-4-one (**2k'**).* Isolated by PTLC (R_f = 0.7; hexane/ethyl acetate = 3/2) as a white solid (35%, 12.1 mg): mp 134 ºC; ^{1}H NMR δ 7.29-7.35 (m, 1H), 7.19 (dd, J = 7.7 Hz, 7.7 Hz, 2H), 7.03 (d, J = 7.7 Hz, 2H), 6.94-6.99 (m, 4H), 5.85 (s, 1H), 4.12 (q, J = 7.0 Hz, 1H), 2.59 (s, 3H), 2.32 (s, 3H), 1.76 (d, J = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR δ 170.1, 143.2, 136.3, 134.8, 129.8, 129.2, 128.8, 128.4, 126.8, 78.0, 56.3, 27.1, 21.5, 19.3; HRMS (ESI, positive) calcd for $C_{18}H_{21}N_2O_3S$ $[M+H]^+$ 345.1267; found 345.1263.

*(2S,5S)-3,5-Dimethyl-1-tosyl-2-(4-(trifluoromethyl)phenyl)imidazolidin-4-one (**2l**).* Isolated by PTLC (R_f = 0.6; hexane/ethyl acetate = 1/1) as a brown solid (50%, 20.6 mg): mp 152 ºC; ^{1}H NMR δ 7.63 (d, J = 7.6 Hz, 2H), 7.58 (d, J = 7.6 Hz, 2H), 7.43 (d, J = 7.6 Hz, 2H), 7.23 (d, J = 7.6 Hz, 2H), 5.78-5.65 (br, 1H), 4.22-4.05 (m, 1H), 2.60 (s, 3H), 2.41 (s, 3H), 2.60 (s, 3H); ^{13}C{^{1}H} NMR δ 169.8, 144.9, 141.0, 134.2, 132.0 (q, J = 32.5 Hz), 130.0, 128.1, 127.8, 126.1 (q, J = 2.5 Hz), 123.8 (q, J = 2.5 Hz), 56.5, 27.3, 21.6, 19.9 (an aliphatic peak is overlapping with one of $CDCl_3$ peaks); ^{19}F NMR δ -62.7; HRMS (ESI, positive) calcd for $C_{19}H_{20}F_3N_2O_3S$ $[M+H]^+$ 413.1141; found 413.1137. $[\alpha]^{28}_D$ –61.4 (c = 0.78, $CHCl_3$).

*(2R,5S)-3,5-Dimethyl-1-tosyl-2-(4-(trifluoromethyl)phenyl)imidazolidin-4-one (**2l'**).* Isolated by PTLC (R_f = 0.5; hexane/ethyl acetate = 1/1) as yellow oil (41%, 16.9 mg): ^{1}H NMR δ 7.41 (d, J = 7.6 Hz, 2H), 7.08 (d, J = 7.6 Hz, 2H), 7.00-6.92 (m, 4H), 5.88 (s, 1H), 4.22 (q, J = 7.2Hz, 1H), 2.60 (s, 3H), 2.30 (s, 3H), 1.88 (d, J = 7.2Hz, 3H); ^{13}C{^{1}H} NMR δ 170.1, 143.7, 138.7, 136.6, 132.1 (q, J = 32.5 Hz), 129.3, 128.8, 126.5, 125.7 (q, J = 2.5 Hz), 123.7 (q, J = 275 Hz), 56.7, 27.1, 21.4, 19.4 (one of the aliphatic carbons was overlapping with one of $CDCl_3$ peaks); ^{19}F NMR δ -62.7; HRMS (ESI, positive) calcd for $C_{19}H_{20}F_3N_2O_3S$ $[M+H]^+$ 413.1141; found 413.1136.

*(2S,5S)-3-Butyl-5-methyl-2-propyl-1-tosylimidazolidin-4-one (**2n**).* Isolated by PTLC (R_f = 0.5; hexane/ethyl acetate = 7/3) as a brown solid (31%, 14.0 mg): mp 80 ºC; ^{1}H NMR δ 7.80-7.75 (m, 2H), 7.28-7.35 (m, 2H), 5.24 (s, 1H), 3.98 (q, J = 7.0 Hz, 1H), 3.72-3.80 (m, 1H), 2.68-2.78 (m, 1H), 2.42 (s, 3H), 2.10-2.20 (m, 1H), 1.40-1.70 (m, 6H), 1.17-1.30 (m, 3H), 0.68-1.11 (m, 7H); ^{13}C{^{1}H} NMR δ 170.3, 143.9, 138.4, 129.9, 126.9, 73.5, 57.1, 39.6, 34.2, 29.0, 21.6, 20.0, 18.0, 14.7, 13.7, 13.5; HRMS (ESI, positive) calcd for $C_{18}H_{29}N_2O_3S$ $[M+H]^+$ 353.1893; found 353.1889. $[\alpha]^{25}_D$ +31.8 (c = 0.35, $CHCl_3$).

*(2R,5S)-3-Butyl-5-methyl-2-propyl-1-tosylimidazolidin-4-one (**2n'**).* Isolated by PTLC (R_f = 0.6; hexane/ethyl acetate = 7/3) as brown oil (28%, 12.7 mg): ^{1}H NMR δ 7.80-7.63 (m, 2H), 7.28-7.37 (m, 2H), 5.24 (s, 1H), 3.98 (q, J = 7.0 Hz, 1H), 3.58-3.63 (m, 1H), 2.62-2.68 (m, 1H), 2.42 (s, 3H), 1.90-1.98 (m, 1H), 1.42-1.64 (m, 5H), 1.10-1.37 (m, 3H), 1.07-1.20 (m, 1H), 0.68-1.11 (m, 7H); ^{13}C{^{1}H} NMR δ 170.0, 144.7, 133.1, 130.2, 127.9, 73.3, 57.0, 39.6, 36.2, 28.8, 21.7, 19.7, 19.7, 15.9, 13.9, 13.7; HRMS (ESI, positive) calcd for $C_{18}H_{29}N_2O_3S$ $[M+H]^+$ 353.1893; found 353.1889.

*(2S)-2-Methyl-1-tosylhexahydroimidazo[1,2-a]pyridin-3(2H)-one (**2o**).* Isolated by PTLC as a diastereomeric mixture in solid form (R_f = 0.4; hexane/ethyl acetate = 3/2) as yellow oil (42%, 13.0 mg). Physical properties of the diastereomeric mixture are shown. ^{1}H NMR δ 7.67-7.77 (m, 2H), 7.28-7.38 (m, 2H), 4.86-4.94 (m, 0.54×1H), 4.61 (d, J = 3.7 Hz, 10.2 Hz, 0.46×1H), 4.18-4.26 (m, 0.54×1H), 4.07-4.15 (m, 0.46×1H), 4.00-4.07 (m, 0.54×1H), 3.87 (q, J = 6.8 Hz, 0.46×1H), 2.68-2.78 (m, 0.54×1H), 2.50-2.67 (m, 1H), 2.39-2.49 (m, 3H + 0.46×1H), 1.86-1.99 (m, 1H), 1.59-1.72 (m, 1H), 1.20-1.59 (m, 5H + 0.46×1H), 1.07-1.20 (m, 0.54×1H); ^{13}C{^{1}H} NMR δ 168.3, 168.1, 144.8, 144.0, 138.1, 133.3, 130.0, 129.9, 127.8, 127.2, 73.2, 72.9, 56.7, 56.3, 40.5, 40.4, 36.4, 32.8, 24.0, 24.0, 22.5, 22.4, 21.7, 21.6, 20.5, 18.2; HRMS (ESI, positive) calcd for $C_{15}H_{21}N_2O_3S$ $[M+H]^+$ 309.1267; found 309.1260.

*(2S)-2-Methyl-1-tosylhexahydro-3H-imidazo[2,1-c][1,4]oxazin-3-one (**2p**).* Isolated by PLTC as a diastereomeric mixture (R_f = 0.5; hexane/ethyl acetate = 1/1) as a brown solid (44%, 13.7 mg). Physical properties of the mixture are shown. ^{1}H NMR *δ* 7.71-7.77 (m, 2H), 7.32-7.40 (m, 2H), 4.93-4.98 (m, 0.69×1H), 4.69-4.73 (m, 0.31×1H), 4.52-4.58 (m, 0.69×1H), 4.34-4.39 (m, 0.31×1H), 4.14-4.20 (m, 0.69×1H), 4.07-4.13 (m, 0.69×1H), 3.94-3.99 (m, 0.31×1H), 3.82-3.90 (m, 1H + 0.31×1H), 3.25-3.33 (m, 1H), 3.05-3.17 (m, 1H + 0.69×1H), 2.96-3.05 (m, 0.31×1H), 2.46 (s, 0.31×3H), 2.45 (s, 0.69×3H + 0.31×3H), 1.58 (d, *J* = 7.1 Hz, 0.31×3H), 1.45 (d, *J* = 6.8 Hz, 0.69×3H); ^{13}C{^{1}H} NMR *δ* 168.4, 168.2, 145.2, 144.5, 137.4, 132.3, 130.4, 130.1, 128.0, 127.3, 73.9, 72.2, 68.9, 68.7, 65.8, 65.7, 57.0, 56.7, 40.7, 40.7, 21.7, 21.7, 20.3, 17.6; HRMS (ESI, positive) calcd for $C_{14}H_{19}N_2O_4S$ $[M+H]^+$ 311.1060; found 311.1053.

*(2S)-2-Methyl-1-tosyloctahydro-3H-imidazo[1,2-a]azepin-3-one (**2q**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1), R_f = 0.5). The title compound was obtained as a white diastereomeric mixture in solid form (78%, 24.2 mg). Physical properties of the mixture are shown. ^{1}H NMR *δ* 7.68-7.76 (m, 2H), 7.35 (d, *J* = 7.9 Hz, 0.45×2H), 7.31 (d, *J* = 7.9 Hz, 0.55×2H), 5.21-5.16 (m, 0.55×1H), 4.96-4.91 (m, 0.45×1H), 4.15 (q, *J* = 7.2 Hz, 0.55×1H), 3.88-3.78 (m, 1H), 3.70-3.61 (m, 0.45×1H), 2.98-2.94 (m, 0.55×1H), 2.87-2.83 (m, 0.45×1H), 2.43 (s, 0.45×3H), 2.42 (s, 0.55×3H), 2.25-2.08 (m, 2H), 1.84-1.65 (m, 1H), 1.68-1.43 (m, 7H), 1.43-1.31 (m, 1H); ^{13}C{^{1}H} NMR *δ* 170.1, 169.8, 144.8, 143.9, 138.6, 133.0, 130.3, 129.9, 128.0, 127.1, 75.2, 75.0, 57.0, 56.6, 42.1, 41.7, 38.6, 34.5, 29.0, 28.6, 26.7, 26.7, 23.0, 22.7, 21.7, 21.6, 20.3, 17.7; HRMS (ESI, positive) calcd for $C_{16}H_{23}N_2O_3S$ $[M+H]^+$ 323.1424; found 323.1418.

*(S)-3-Isopropyl-2,2,5-trimethyl-1-tosylimidazolidin-4-one (**2r**).* Isolated by PTLC (R_f = 0.3; toluene/ethyl acetate = 9/1) as yellow oil (94%, 34.7 mg). ^{1}H NMR *δ* 7.74 (d, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 3.88 (q, *J* = 7.0 Hz, 1H), 3.29 (sept, *J* = 6.8 Hz, 1H), 2.43 (s, 3H), 1.76 (s, 3H), 1.60 (s, 3H), 1.50 (d, *J* = 7.0 Hz, 3H), 1.43 (d, *J* = 7.0 Hz, 3H), 1.39 (d, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR *δ* 168.7, 143.9, 137.9, 129.8, 127.5, 81.9, 56.2, 45.8, 29.5, 25.3, 21.6, 20.4, 20.1, 20.1; HRMS (ESI, positive) calcd for $C_{16}H_{25}N_2O_3S$ $[M+H]^+$ 325.1580; found 325.1574. $[\alpha]^{26}_D$ +31.8 (c = 0.98, $CHCl_3$).

*(S)-1,3-Dimethyl-4-tosyl-1,4-diazaspiro[4.5]decan-2-one (**2s**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1, R_f = 0.5). The title compound was obtained as a white solid (82%, 27.6 mg): mp 100 ºC; ^{1}H NMR *δ* 7.71 (d, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 4.10 (q, *J* = 6.8 Hz, 1H), 3.11 (s, 3H), 2.86-2.76 (m, 1H), 2.70-2.61 (m, 1H), 2.42 (s, 3H), 2.08-2.01 (m, 1H), 1.98-1.82 (m, 2H), 1.76-1.60 (m, 4H), 1.52 (d, *J* = 6.7 Hz, 3H), 1.43-1.55 (m, 1H); ^{13}C{^{1}H} NMR *δ* 170.1, 143.8, 139.2, 129.8, 127.1, 82.9, 56.8, 39.8, 33.8, 29.7, 23.8, 23.7, 23.6, 21.6, 21.1; HRMS (ESI, positive) calcd for $C_{17}H_{25}N_2O_3S$ $[M+H]^+$ 337.1580; found 337.1575. $[\alpha]^{24}_D$ +38.7 (c = 0.64, $CHCl_3$).

*(S)-3-Hexyl-2,2,5-trimethyl-1-tosylimidazolidin-4-one (**2t**).* Isolated by PTLC as yellow oil (R_f = 0.6; hexane/ethyl acetate = 2/1) of yellow oil (69%, 25.3 mg). ^{1}H NMR *δ* 7.74 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 3.98 (q, *J* = 7.2 Hz, 1H), 3.22-3.12 (m, 1H), 3.10-3.02 (m, 1H), 2.43 (s, 3H), 1.76 (s, 3H), 1.47-1.64 (m, 7H), 1.22-1.35 (m, 6H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR *δ* 169.3, 143.9, 138.0, 129.8, 127.5, 81.4, 56.1, 40.5, 31.4, 29.9, 29.0, 26.9, 25.5, 22.6, 21.6, 20.4, 14.0; HRMS (ESI, positive) calcd for $C_{19}H_{31}N_2O_3S$ $[M+H]^+$ 367.2050; found 367.2047. $[\alpha]^{24}_D$ +27.3 (c = 1.07, $CHCl_3$).

*(5S)-3-Benzyl-1-(mesitylsulfonyl)-5-methyl-2-phenylimidazolidin-4-one (**2u**).* Isolated by PTLC as a diastereomeric mixture (R_f = 0.4; hexane/ethyl acetate = 4/1) of yellow oil (92%, 41.3 mg). Physical properties of the mixture are shown. ^{1}H NMR *δ* 7.25-7.34 (m, 4H), 7.18-7.24 (m, 1H + 0.30×1H), 7.14 (m, 0.30×1H), 6.95-7.09 (m, 3H), 6.91 (d, *J* = 7.2 Hz, 0.70×2H), 6.75 (s, 0.70×2H), 6.60 (s, 0.30×2H), 5.61 (s, 0.70×1H), 5.58 (s, 0.30×1H), 5.07 (d, *J* = 15.0 Hz, 0.70×1H), 5.03 (d, *J* = 15.0 Hz, 0.30×1H), 4.59 (q, *J* = 7.0 Hz, 0.30×1H), 4.47 (q, *J* = 7.0 Hz, 0.70×1H), 3.39 (d, *J* = 15.0 Hz, 0.70×1H), 3.19 (d, *J* = 15.0 Hz, 0.30×1H), 2.38 (s, 0.30×6H), 2.36 (s, 0.70×6H), 2.20 (s, 0.70×3H), 2.14 (s, 0.30×3H), 1.66 (d, *J* = 7.0 Hz, 0.30×3H), 1.40 (d, *J* = 7.0 Hz, 0.70×3H); ^{13}C{^{1}H} NMR *δ* 170.5, 170.5, 144.1, 142.7, 141.2, 139.5, 136.3, 135.1, 134.6, 134.5, 133.5, 132.0, 131.8, 130.6, 129.7, 129.4, 129.0, 128.6, 128.3, 128.2, 128.1, 127.4, 74.8, 74.3, 58.4, 55.4, 44.3, 43.5, 22.6, 22.6, 21.0, 20.8, 19.2, 17.4 (4 pairs of aromatic carbons are overlapping); HRMS (ESI, positive) calcd for $C_{26}H_{29}N_2O_3S$ $[M+H]^+$ 449.1893; found 449.1889.

*(2S,5S)-3-Benzyl-5-methyl-1-((2-nitrophenyl)sulfonyl)-2-phenylimidazolidin-4-one (**2v**).* Isolated by flash column chromatography (hexane/ethyl acetate = 1/1), R_f = 0.5). The title compound was obtained as yellow oil (51%, 22.9 mg) yield). ^{1}H NMR *δ* 7.66 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.46-7.53 (m, 2H), 7.36-7.43 (m, 3H), 7.21-7.32 (m, 5H), 6.97 (d, *J* = 7.8 Hz, 2H), 5.87 (s, 1H), 5.05 (d, *J* = 14.8 Hz, 1H), 4.41 (q, *J* = 6.9 Hz, 1H), 3.43 (d, *J* = 14.8 Hz, 1H), 1.70 (d, *J* = 6.9 Hz, 3H) ^{13}C{^{1}H} NMR δ 169.4, 136.1, 134.6, 134.5, 131.6, 130.5, 130.3, 130.1, 129.3, 129.0, 128.5, 128.2, 127.7, 124.3, 75.2, 57.0, 44.2, 19.9 (two aromatic peaks are overlapping); HRMS (ESI, positive) calcd for $C_{23}H_{22}N_3O_5S$ $[M+H]^+$ 452.1275; found 452.1276. $[\alpha]^{27}_D$ –116.5 (c = 0.88, $CHCl_3$).

*(2R,5S)-3-Benzyl-5-methyl-1-((2-nitrophenyl)sulfonyl)-2-phenylimidazolidin-4-one (**2v'**).* Isolated by flash column chromatography (toluene/ethyl acetate = 9/1, R_f = 0.2). The title compound was obtained as a white solid (11%, 5.0 mg): mp 168 ºC; ^{1}H NMR *δ* 7.50 (d, *J* = 8.0 Hz, 1H), 7.42 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.29-7.35 (m, 3H), 7.17-7.25 (m, 1H), 7.14-7.6.98 (m, 7H), 6.85 (d, *J* = 8.0 Hz, 1H), 5.71 (s, 1H), 5.08 (d, *J* = 14.8 Hz, 1H), 4.86 (q, *J* = 7.0 Hz, 1H), 3.25 (d, *J* = 14.8 Hz, 1H), 1.77 (d, *J* = 7.0 Hz, 3H) ^{13}C{^{1}H} NMR *δ* 169.9, 134.8, 134.1, 133.9, 133.0, 131.1, 131.0, 130.4, 129.1, 129.0, 128.8, 128.4, 128.3, 123.8, 75.3, 58.6, 43.5, 19.9; HRMS (ESI, positive) calcd for $C_{23}H_{22}N_3O_5S$ $[M+H]^+$ 452.1275; found 452.1276.

Gram-scale reaction. (*S*)-*N*,*N*-Dibenzyl-2-((4-methylphenyl)sulfonamido)-3-phenylpropanamide (**1a**) (1.05 g, 2.10 mmol), bis(trifluoroacetoxy)iodobenzene ($PhIOCOCF_3$) (1083 mg, 2.52 mmol, 1.2 equiv), iodine (106.7 mg, 0.42 mmol, 20 mol%), were placed into a Schlenk tube equipped with a magnetic stirring bar. The Schlenk tube was evacuated and backfilled with argon (×3).

To the reaction vessel was added dichloroethane (14.7 mL). The Schlenk was capped and the solution was stirred for 24 h at 0 ºC (ice bath temperature) under 27 W fluorescent light irradiation. The crude material was then purified using silica gel chromatography to obtain a mixture of (2*S*,5*S*)-3,5-dibenzyl-2-phenyl-1-tosylimidazolidin-4-one (**2a**) and (2*R*,5*S*)-3,5-dibenzyl-2-phenyl-1-tosylimidazolidin-4-one (**2a'**) in 76% (790.2 mg) yield.

Deprotection of tosyl group. Magnesium turnings (1.0 mmol, 20 equiv) were added to a solution of (2*S*,5*S*)-3,5-dibenzyl-2-phenyl-1-tosylimidazolidin-4-one (**2a**) (0.05 mmol, 1.0 equiv) in dry methanol (0.25 mL). The reaction mixture was placed in an ultrasound bath and subjected to ultrasonic irradiation for 30 min at rt. The magnesium turnings were then filtered off, and washed with methanol, then concentrated under reduced pressure. The residue was purified by PTLC to give (5*S*)-3,5-dibenzyl-2-phenylimidazolidin-4-one (**3**) as white solid in 98% yield (16.8 mg). The spectra data of compound **3** were matched with those in the literature.[17]

*3-Benzyl-2,6-diphenyl-1-tosyltetrahydropyrimidin-4(1H)-one (**5**).* Isolated by flash column chromatography (dichloromethane/ethyl acetate = 60/1), R_f = 0.5). The title compound was obtained as a white solid (65%, 32.3 mg): mp 174 ºC; ^{1}H NMR δ 7.15-7.40 (m, 12H), 7.03-7.15 (m, 5H), 6.88-6.96 (m, 2H), 6.59 (s, 1H), 4.88-4.99 (m, 2H), 4.06 (d, *J* = 14.6 Hz, 1H), 2.66-2.75 (m, 1H), 2.37-2.47 (m, 4H); ^{13}C{^{1}H} NMR δ 168.5, 144.3, 140.0, 137.7, 135.9, 135.4, 130.1, 129.7, 129.0, 128.7, 128.4, 128.4, 128.3, 127.7, 127.7, 127.0, 126.8, 71.6, 57.4, 49.8, 37.8, 21.7; HRMS (ESI, positive) calcd for $C_{30}H_{29}N_2O_3S$ $[M+H]^+$ 497.1893; found 497.1884.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.
NMR spectra charts of the starting materials and products are provided.

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Notes

The authors declare no competing financial interests.

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