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Catalytic Mannich-Type Reactions of Sulfonylimidates

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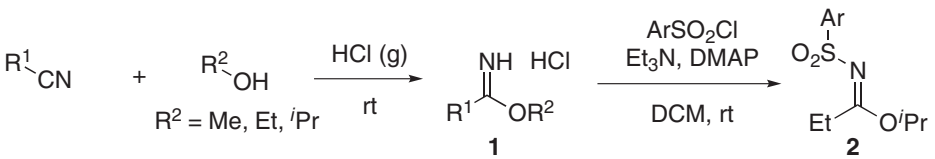
A novel nucleophile, sulfonylimidate, has been successfully employed in Mannich-type reactions. Due to electron-withdrawing property of sulfonyl group of sulfonylimidate, the acidity of α-proton is enhanced so that sulfonylimidate bearing no activating functional group at α-position is deprotonated by relatively weak base. DBU-catalyzed reactions of sulfonylimidates with protected imines in DMF provided the adducts in high yields with high anti selectivity. This reaction represents a wide substrate scope and a high catalytic turnover. A thorough kinetic study revealed that rate-determining step is most likely deprotonation step in case of Ts-imidate. Alkali earth metal alkoxide and its HMDS salt also catalyze Mannich-type reactions of sulfonylimidates. The reactions catalyzed by $Mg(O^tBu)_2$ in DMF provided the adducts with high anti selectivity, while those catalyzed by $[Sr(HMDS)_2]_2$ gave syn selectivity. The asymmetric variant of Mannich-type reaction of sulfonylimidate was also achieved. Several transformations of sulfonylimidates to other functional groups were also demonstrated. Finally, direct-type catalytic formation of β-amino acid ester from aldehyde and sulfonylimidate was achieved via in situ formation of sulfonylimine and DBU-assisted hydrolysis of sulfonylimidate.

Recently much attention has been paid to direct-type reactions, in which no pre-activation of carbonyl compound is necessary.[1] Because the desired adduct through direct-type reaction is formed formally only via CC bond formation and proton transfer, no co-product is formed, which makes these types of reactions attractive. While there have been so many reports on direct reactions so far, the use of ester or ester equivalents bearing no activating functional group at α position such as NO_2, $N{=}CR_2$, COR, OH, CN, and aryl, is still a challenging topic.[2–4] Here we focus on the reactions of sulfonylimidate, which has been recently found to be an effective nucleophile in direct-type reactions by our group.[5]

Results and Discussion

Synthesis of Sulfonylimidates. All the sulfonylimidates used in this report were synthesized according to the reported method (Scheme 1).[6] To a mixture of alcohol and nitrile was bubbled HCl gas at room temperature, and exothermic formation of imidate salt took place. Evaporation of volatiles afforded pure imidate salts in a range of 40–80% yield.[7] Subsequent sulfonylation under the standard conditions (sulfonyl chloride, Et_3N, DMAP, and DCM) led to sulfonylimidate. Most of all the sulfonylimidates used so far are stable in the air, tolerant to SiO_2 chromatography purification, and can be kept for at least several months in the refrigerator without change in purity.

DBU-Catalyzed Direct Mannich-Type Reaction of Sulfonylimidate. The difficulty in direct-type reactions of ester or ester derivatives bearing no activating functional groups at α-position lies in relatively high pK_a value.[8] Two strategies to address this issue have been taken; one is the use of appropriate Lewis acids to lower the α-proton pK_a[2], and the other is an introduction of electron-withdrawing groups into the substituents located across the carbonyl from the α-carbon.[4] Our strategy to be demonstrated in this report is the employment of C=N double bond compounds instead of carbonyl compounds. That the nitrogen of C=N double bond accommodates another bonding enables us to put an electron-withdrawing group on this nitrogen, leading to the increase of acidity at α-position.



Scheme 1. Synthetic method of sulfonylimidate.

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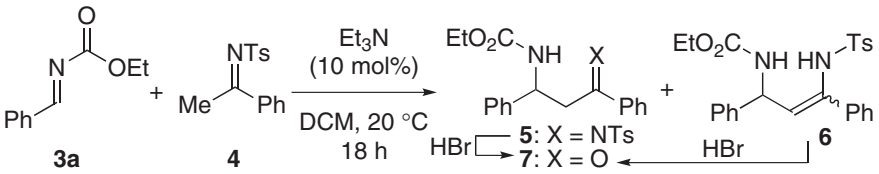
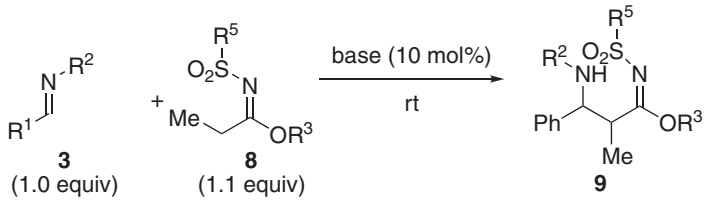


Scheme 2. Direct-type reaction of sulfonylimine **4** with imine **3a**.

Table 1. Base-Catalyzed Direct-Type Reactions of Sulfonylimidates (R^1 = Ph)



Entry	R^2	R^3	R^5	Base	Solvent	Yield/%	anti/syn[a)]	Product
1	CO_2Et	Me	Ph	—	DCM	0	—	—
2	CO_2Et	Me	Ph	Et_3N	DCM	0	—	—
3	CO_2Et	Me	Ph	DBU	DCM	90	69/31	**9aa**
4	CO_2Et	Me	Ph	DBU	DMF	Quant	62/38	**9aa**
5	CO_2Et	*i*-Pr	Ph	DBU	DMF	80	79/21	**9ab**
6	Boc	*i*-Pr	Ph	DBU	DMF	72	93/7	**9bb**
7	Boc	*i*-Pr	2,5-Xylyl	DBU	DMF	65	95/5	**9bc**
8[b)]	Boc	*i*-Pr	2,5-Xylyl	DBU	DMF	75	96/4	**9bc**
9[b),c)]	Boc	*i*-Pr	2,5-Xylyl	DBU	DMF	95	96/4	**9bc**

a) Determined by ^{1}H NMR spectroscopy of crude products. b) 0 °C. c) 1.5 equiv of **3** and 1.0 equiv of **8** were used. Catalyst loading was 5 mol %.

We chose arenesulfonyl group as an electron-withdrawing group on the nitrogen of C=N double bond, because the commercial availability of a range of arenesulfonyl chloride makes it easy to fine-tune the electronic as well as steric property of the molecule. Although the initial object of this research was the use of the C=N compound bearing ester oxidation stage, the acetophenone-derived sulfonylimine was first employed. As shown in Scheme 2, the sulfonylimine **4** reacted with imine **3a** in the presence of a catalytic amount of Et_3N; however, the product was a mixture of sulfonylimine **5** and its tautomerized compound, enesulfonamide **6**. For the purpose of transforming both products to identical product **7**, hydrolysis of a mixture of both products was conducted. However, a significant amount (ca. 20%) of by-product, chalcone, was observed.

Since tautomerization is problematic in case of sulfonylimine, we turned our attention to the use of sulfonylimidate with the expectation that imine-form is more favored than its tautomerized one due to the stabilization by alkoxy group (Figure 1). Sulfonylimidate was examined as a nucleophile in the reaction of Boc imine in the presence of a catalytic amount of base (Table 1). Although no reaction occurred when no base or triethylamine was employed (Entries 1 and 2), DBU turned out to be basic enough to promote the reaction (Entry 3). Gratifyingly, the adduct, sulfonylimidate, proved to be stable, no corresponding enamine-form was detected. Optimization of the protecting group of the electrophile, the sulfonyl group of the nucleophile, solvent, and temperature revealed that the conditions shown in Entry 9 were the best, providing the

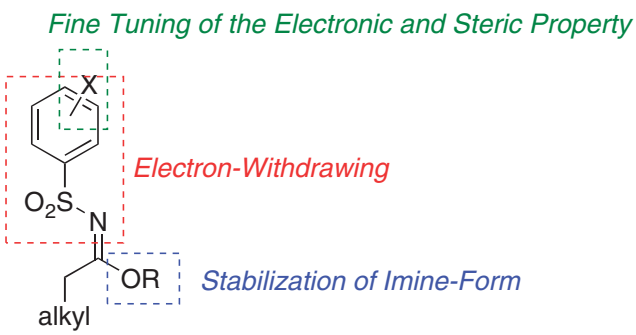
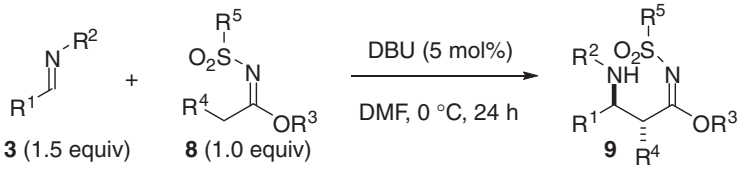


Figure 1. Sulfonylimidate as a nucleophile.

desired product in high yield with high anti selectivity (The origin of high anti selectivity will be discussed later with the results using metal alkoxide catalysts).

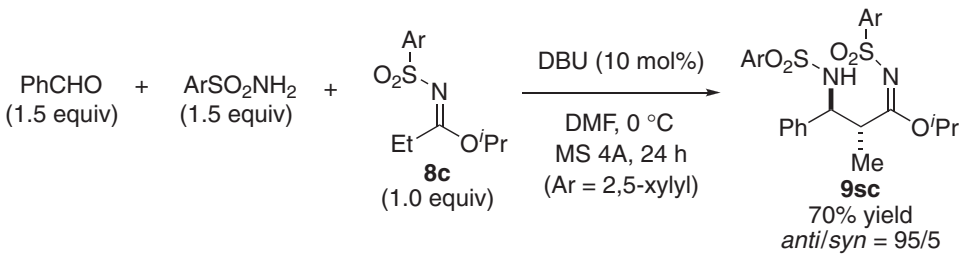
The scope of DBU-catalyzed (5 mol %) direct Mannich-type reactions of sulfonylimidates are shown in Table 2. Substituents at α-position of sulfonylimidates accommodates methyl as well as ethyl groups (Entry 2). The reaction of sulfonylimidate **8e** (R^3 = Et, R^4 = H, R^5 = Ph) was problematic because the mono-adduct further reacted with another molecule of imine, leading to the bis-adduct. Surprisingly, the mono-adduct was not detected under the identical conditions as those of Entry 1, only a complex diastereomer mixture of bis-adducts were obtained (not shown). The use of an excess amount (5 equiv) of sulfonylimidate **8e** was essential to obtain a good yield of the mono-adduct (Entry 3), and the leftover sulfonylimidate

Table 2. DBU-Catalyzed Direct-Type Reactions of Sulfonylimidates



Entry	R^1	R^2	R^3	R^4	R^5	Yield/%	anti/syn[a)]	9
1	Ph	Boc	*i*-Pr	Me	2,5-Xylyl	95	96/4	**9bc**
2	Ph	Boc	*i*-Pr	Et	2,5-Xylyl	94	97/3	**9bd**
3[b),c),d)]	Ph	EtO_2C	Et	H	Ph	79	—	**9ae**
4[c)]	Ph	Ts	*i*-Pr	Me	2,5-Xylyl	91	96/4	**9cc**
5[e)]	*p*-$MeOC_6H_4$	Boc	*i*-Pr	Me	2,5-Xylyl	91	95/5	**9dc**
6	*p*-FC_6H_4	Boc	*i*-Pr	Me	2,5-Xylyl	87	97/3	**9ec**
7	*m*-MeC_6H_4	Boc	*i*-Pr	Me	2,5-Xylyl	Quant	97/3	**9fc**
8[e)]	*o*-MeC_6H_4	Boc	*i*-Pr	Me	2,5-Xylyl	64	93/7	**9gc**
9	*m*-$VinylC_6H_4$	Boc	*i*-Pr	Me	2,5-Xylyl	97	97/3	**9hc**
10	2-Furyl	Boc	*i*-Pr	Me	2,5-Xylyl	92	95/5	**9ic**
11	2-Thienyl	Boc	*i*-Pr	Me	2,5-Xylyl	90	98/2	**9jc**
12	2-Pyridyl	Boc	*i*-Pr	Me	2,5-Xylyl	91	98/2	**9kc**
13[c)]	PhCH=CH	Ts	*i*-Pr	Me	2,5-Xylyl	80	98/2	**9lc**
14[c)]	Cyclopropyl	Ts	*i*-Pr	Me	2,5-Xylyl	84	87/13	**9mc**
15[c),d)]	Cyclopropyl	Boc[h)]	*i*-Pr	Me	2,5-Xylyl	Quant	88/12	**9nc**
16[c),d),g)]	*c*-C_6H_{11}	Ts[h)]	Me	Me	*p*-MeC_6H_4	51	83/17	**9of**
17[c),d),g)]	*c*-C_6H_{11}	Ts[h)]	*i*-Pr	Me	*p*-MeC_6H_4	59	84/16	**9og**
18[c),d),g)]	*i*-Pr	Ts[h)]	Me	Me	*p*-MeC_6H_4	56	69/31	**9pf**
19[c),d),g)]	*i*-Pr	Ts[h)]	*i*-Pr	Me	*p*-MeC_6H_4	54	87/13	**9pg**
20[c),f)]	*t*-Bu	Ts	Me	Me	*p*-MeC_6H_4	51	14/86	**9qf**
21[c),d)]	EtO_2C	*p*-$MeOC_6H_4$	Me	Me	Ph	80	55/45[i)]	**9rc**

a) Determined by ^{1}H NMR spectroscopy of the crude product or isolated product. b) 5 equiv of **8e** and 1 equiv of **3** were used. c) MS 4A (167 g mol^{-1}) were added. d) 10 mol % of DBU was used. e) 38 h. f) 40 °C, 36 h. g) rt. h) 3 equiv of **3** were used. i) Major/minor.



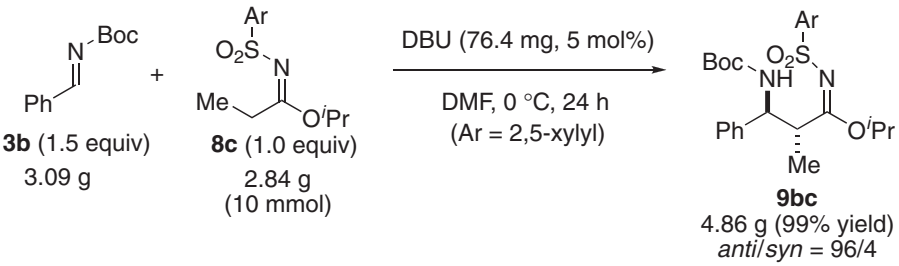
Scheme 3. 3-component reaction.

8e could be recovered after the reaction (403%). Tosylimine (Ts imine) as well as Boc imine were useful in this Mannich-type reaction of sulfonylimidates (Entry 4). Boc imines derived from aromatic aldehydes bearing electron-donating and -withdrawing substituents, ortho-, meta-, and para-substituted benzaldehydes as well as heteroaromatic aldehydes, provided the desired products in high yields with high anti selectivity (Entries 5–12). It is noted that aliphatic aldehyde-derived Boc and Ts imines were also good substrates in the Mannich-type reaction of sulfonylimidates (Entries 13–20). Ethyl glyoxylate-derived *N*-methoxyphenylimine (Entry 21) gave the desired product in good yield albeit the diastereoselectivity was low.

Although Boc and Ts imine can be readily synthesized from the corresponding aldehyde and amide in one or two steps, in situ formation of those imines are desirable. Thus, 3-component reaction using benzaldehyde, sulfonylamide, and sulfonylimidate was conducted with a double amount of MS 4A (Scheme 3). As a result, the desired adduct **9sc** was obtained in good yield with high selectivity.

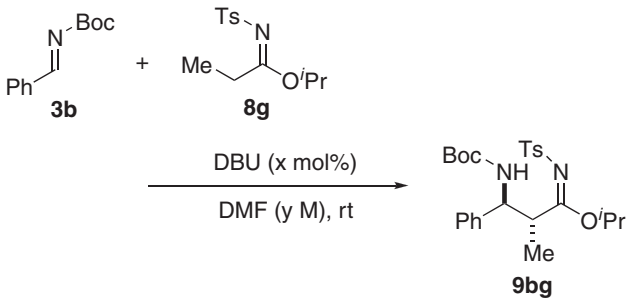
It is noteworthy that the optimized condition was applicable to a large scale reaction (Scheme 4).[5c] Starting from 10 mmol of sulfonylimidate (2.84 g), 76.4 mg of DBU (5 mol %) catalyzed Mannich-type reaction under the same conditions as small scale reaction, affording 4.86 g of the desired adduct with high anti selectivity (96/4).

We then investigated the decrease of catalyst loading in DBU-catalyzed anti selective Mannich-type reaction of sulfonylimidate with Boc imine (Table 3). With 1 mol % of DBU, the reaction proceeded well, giving the desired product in 87% yield in 6 h (Entry 1). The reaction with 0.3 mol % of DBU required longer reaction time (52 h) at higher concentration (1 M) to obtain high yield of the desired product (Entry 2). It is



Scheme 4. Large scale synthesis.

Table 3. Decrease of the Catalyst Loading



Entry	*x*	*y*	Time/h	Yield/%	anti/syn
1	1	0.5	6	87	95/5
2	0.3	1	52	95	95/5
3	0.3	—	52	42	77/23
4	0.1	1	66	89	95/5
5	**0.1**	1	166	**97**	**95/5**
6	0.05	1	166	66	95/5

noted that neat conditions gave lower yield and diastereoselectivity (Entry 3), which suggests that DMF is involved in the stabilization of the transition state (vide infra). The reaction with 0.1 mol % of DBU proceeded smoothly at 1 M concentration, providing the desired adduct in 89% yield in 66 h (Entry 4), and in 97% yield in 166 h (Entry 5). Entry 6 represents that as little as 0.05 mol % of DBU still has catalytic activity to afford moderate yield of the desired product (TON = 1320).

To get insight into the mechanism of the present catalysis, initial rate kinetics on the Boc imine, sulfonylimidate, and DBU was carried out using benzaldehyde-derived Boc imine and Ts imidate as model substrates. The product yield was determined at each specified period by ^{1}H NMR spectroscopy using durene as an internal standard (Figure 2). A series of investigation varying concentration of each component revealed the rate dependency on the Boc imine, the sulfonylimidate, and DBU to be 0.23, 0.79, and 1.43, respectively (Figure 3).

Assumed catalytic cycle is depicted in Figure 4. The reaction is initiated by deprotonation of sulfonylimidate α-proton by DBU, leading to the formation of DBUH$^+$ and enamide anion **10** (step a). DBUH$^+$ is presumably stabilized by solvation, and accordingly **10** behaves as an independent naked anion. Anion **10** reacts with Boc imine **3b** to form N-anion species **11** (step b), which is subsequently protonated (step c) by DBUH$^+$ generated in the preceding deprotonation step a, leading to the desired product **9bg** along with regeneration of DBU for the next catalytic cycle.

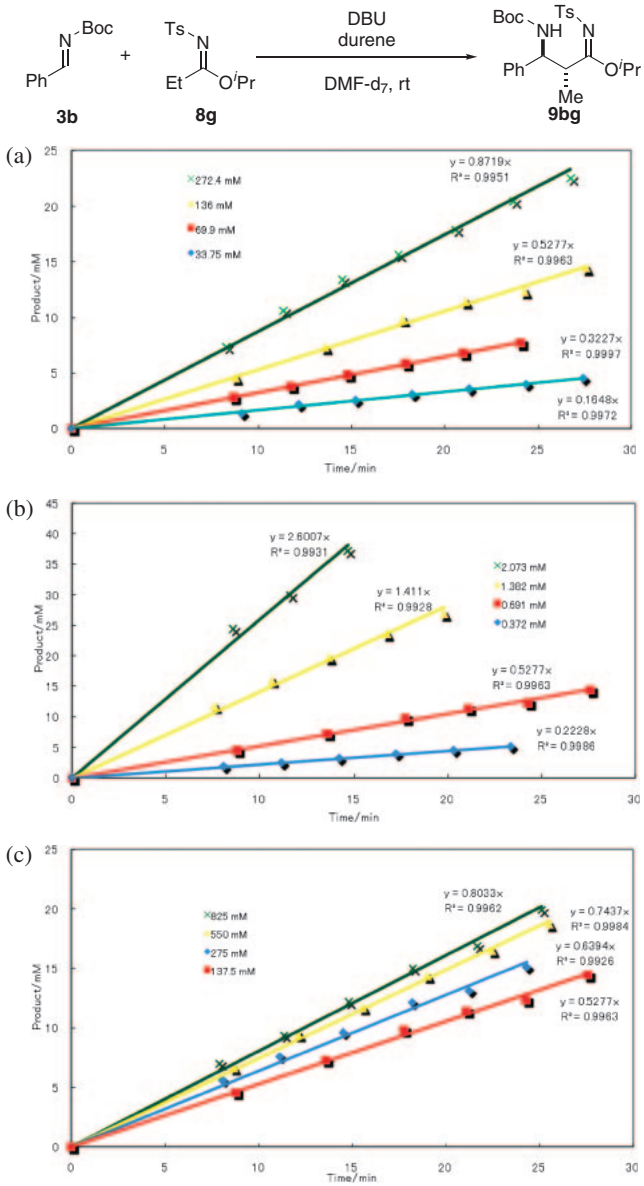


Figure 2. Initial reaction profile varying the concentration of (a) sulfonylimidate **8g**, (b) DBU, and (c) Boc imine **3b**.

On the basis of the obtained kinetic parameters, deprotonation of α-proton of sulfonylimidate (step a) appears to be one of the rate-determining step. Considering low rate dependency on Boc imine (0.23 order), C–C bond-forming reaction between Boc imine and sulfonylimidate anion **10** (step b) takes place relatively fast, and is little involved in rate-

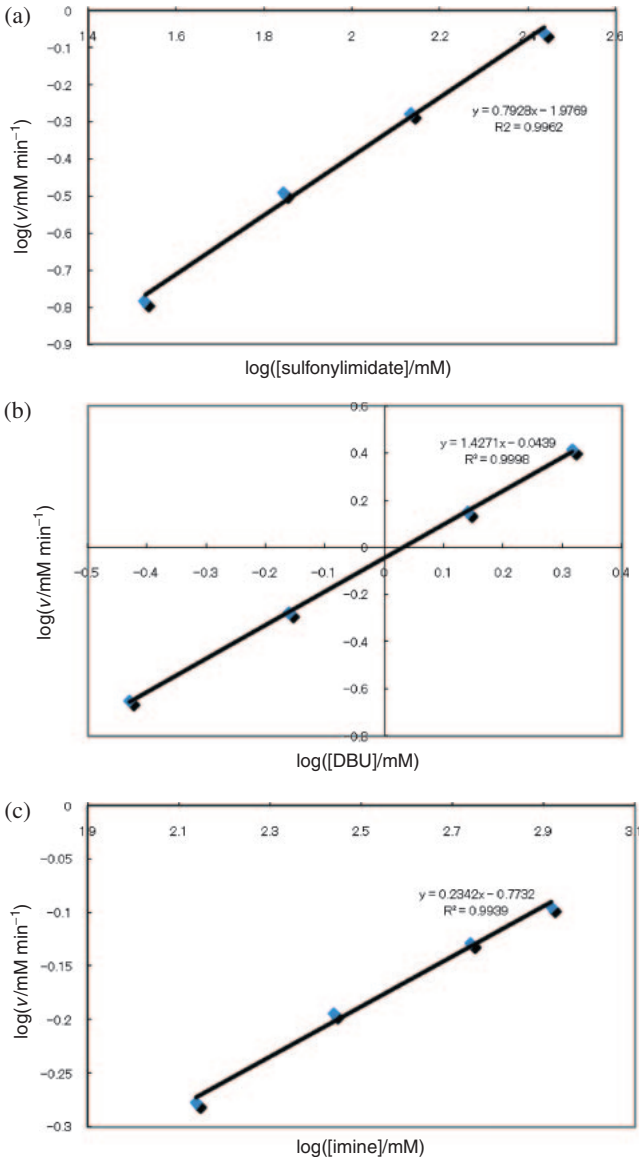


Figure 3. Determination of reaction depencence on (a) sulfonylimidate **8g**, (b) DBU, and (c) Boc imine **3b**.

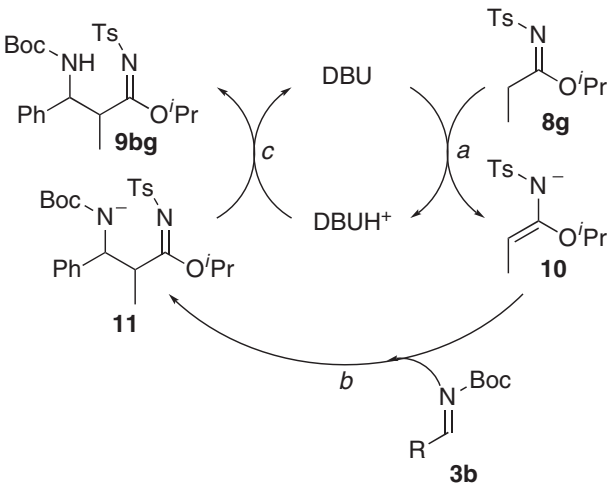
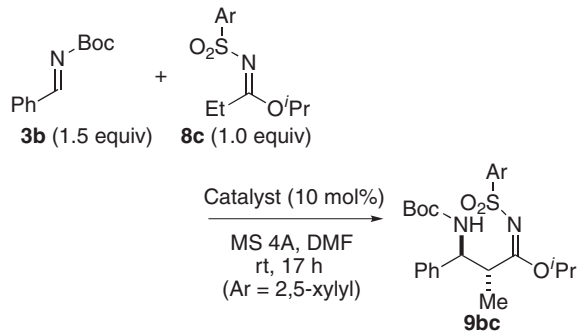


Figure 4. Catalytic cycle.

Table 4. Screening of Metal Bases for Anti Selective Addition Reactions



Entry	Catalyst	Yield/%	anti/syn[a)]
1	$Ca(O^iPr)_2$	72	93/7
2	$Sr(O^iPr)_2$	75	93/7
3	$Ba(O^iPr)_2$	68	90/10
4	$Mg(O^tBu)_2$	**94**	**96/4**
5	$Ca(O^tBu)_2$	78	87/13
6	$Sr(O^tBu)_2$	61	80/20
7	$Ba(O^tBu)_2$	80	90/10
8[b)]	$Mg(O^tBu)_2$	>99	94/6

a) Determined by ^{1}H NMR of the crude product. b) Ar = *p*-NO_2–C_6H_4.

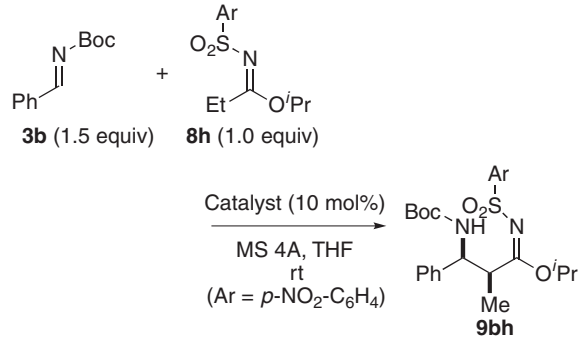
determination. Regeneration of DBU (step c) might be another rate-determining step since the involvement of more than 1 molecule of DBU catalyst in the rate-determining step is suggested by the value of 1.43 observed as the rate dependency on DBU, although more precise mathematic calculation is required for thorough interpretation of the obtained results. It is most likely that the reaction kinetics varies depending on reaction conditions and substrates employed.

Alkali Earth Metal-Catalyzed Reaction. The role of alkali earth metals as catalysts in organic chemistry has received relatively little interest from the academic community in recent years. Despite the attractive features of these metals which are vastly abundant, inexpensive, commercially available, and have no obvious toxicity associated with them, only sporadic reports have appeared in the literature.[9] Alkali earth metal alkoxides display dual properties with both Lewis acidic and Brønsted basic characters, which makes them very attractive in the direct-type addition reactions of enolates to electrophiles. Ongoing research within our group seeks to utilize these properties for the promotion of efficient organic transformations. We have demonstrated the abilities of calcium and strontium alkoxides in the catalytic asymmetric Michael reactions[10] and 1,4-additions of glycine derivatives.[11]

We set out alkali earth metal-catalyzed reaction of sulfonylimidate **8c** with screening of catalysts, and the results are shown in Table 4. Alkali earth metal alkoxides catalyzed the Mannich-type reactions to afford the desired adducts were obtained in good yields with high anti selectivity. The best result was obtained when $Mg(O^tBu)_2$ was employed (Entry 4).

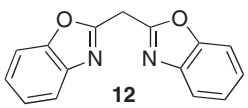
Further optimization revealed that syn selectivity was obtained when the reaction was conducted in THF using *p*-nitrobenzenesulfonylimidate (*p*-Ns-imidate) **8h** (Table 5). The reaction did not proceed when 2,5-dimethylbenzene-

Table 5. Optimization for Syn Selective Addition Reactions



Entry	Catalyst	Time/h	Yield/%	anti/syn[a)]
1	$Ca(O^iPr)_2$	48	56	11/89
2	$Sr(O^iPr)_2$	48	34	32/68
3	$Ba(O^iPr)_2$	48	55	15/85
4	$1/2[Sr(HMDS)_2]_2$	18	>99	14/86
5[b)]	$Ca(O^iPr)_2$	48	68	11/89
6[b)]	$Sr(O^iPr)_2$	48	45	7/93
7[b)]	$Ba(O^iPr)_2$	48	65	9/91
8[b)]	$1/2[Sr(HMDS)_2]_2$	24	**92**	**7/93**
9[b),c)]	$1/2[Sr(HMDS)_2]_2$	48	76	6/94
10[b),d)]	$1/2[Sr(HMDS)_2]_2$	72	65	6/94
11	DBU	24	77	74/26

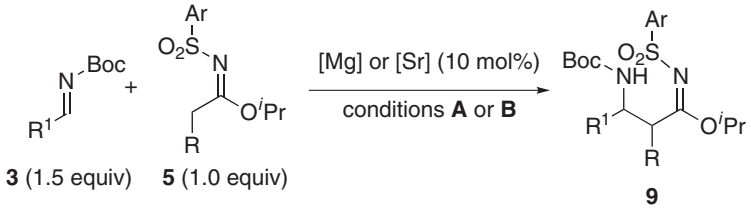
a) Determined by ^{1}H NMR of the crude product. b) Ligand **12** was used. c) At 0 °C. d) At −20 °C.



suflonylimidate **8c** was used in THF instead of *p*-Ns-imidate **8h** (not shown), due to the lower acidity of α-proton of **8c**. While moderate syn selectivities were observed when alkali earth alkoxide was solely used (Entries 1–4), the combination of alkali earth metal alkoxide with ligand **12** led to high syn selectivity (Entries 5–10). The use of $[Sr(HMDS)_2]_2$[12] and ligand **12** gave the best result as shown in Entry 8 (92% yield, syn/anti = 93/7). Interestingly, the $Mg(O^tBu)_2$-catalyzed reaction of *p*-Ns-imidate in DMF (Table 4, Entry 8) and the DBU-catalyzed reaction of *p*-Ns-imidate in THF gave anti selectivity, which indicates the use of both alkali earth metal alkoxide as a catalyst and THF as a solvent is essential for high syn selectivity.

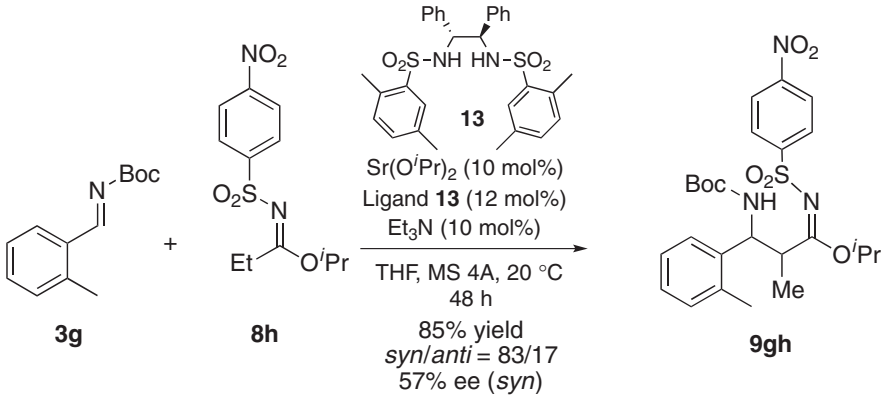
The scope of the present reaction conditions was then surveyed (Table 6). In general, condition A ($Mg(O^tBu)_2$ as a catalyst, 2,5-xylylsulfonylimidate as a substrate in DMF) gave high anti selectivity, while condition B ($[Sr(HMDS)_2]_2$ and ligand **12** as a catalyst, *p*-Ns-imidate as a substrate in THF) afforded the desired adduct with high syn selectivity. Aromatic aldehyde-derived Boc imines (Entries 1–9) including ones with electron-withdrawing or -donating aromatic rings, sterically demanding aromatic ring, and heteroaromatic rings, afforded the desired adducts in good yields under both conditions A and B. It is noteworthy that the reaction of Ts imine instead of Boc imine gave anti adduct as a major product regardless of reaction conditions (this result will be discussed later in the discussion about diastereoselectivity). Imines derived from cyclopropanecarboxaldehyde and cyclohexanecarboxaldehyde were also good substrates (Entries 11 and 13), and α-Et-substituted sulfonylimidate gave the same level of yield and selectivity as α-Me-substituted one (Entry 12).

Table 6. Substrate Scope of Addition Reactions of Sulfonylimidates (R = Me)



Entry	R^1	$Mg(O^tBu)_2$ Condition A[a)]		$[Sr(HMDS)_2]_2$ Condition B[a)]	
		Yield/%	anti/syn[b)]	Yield/%	anti/syn[b)]
1	Ph	94 (**9bc**)	96/4	98 (**9bh**)	7/93
2	*p*-$MeOC_6H_4$	92 (**9dc**)	95/5	99 (**9dh**)	5/95
3	*p*-FC_6H_4	>99 (**9ec**)	98/2	87 (**9eh**)	8/92
4	*m*-MeC_6H_4	>99 (**9fc**)	96/4	99 (**9fh**)	6/94
5	*o*-MeC_6H_4	93 (**9gc**)	93/7	99 (**9gh**)	11/89
6	*m*-Vinyl C_6H_4	>99 (**9hc**)	96/4	90 (**9hh**)	7/93
7	2-Furyl	90 (**9ic**)	96/4	95 (**9ih**)	6/94
8	2-Thienyl	96 (**9jc**)	98/2	99 (**9jh**)	7/93
9	2-Pyridyl	95 (**9kc**)	97/3	70 (**9kh**)	6/94
10[c)]	Ph	98 (**9cc**)	67/33	94 (**9ch**)	93/7
11	Cyclopropyl	94 (**9nc**)	85/15	99 (**9nh**)	15/85
12[d)]	Ph	80 (**9bd**)	95/5	85 (**9bi**)	5/95
13[e)]	Cyclohexyl	99[c)] (**9oc**)	80/20[c)]	82 (**9th**)	16/84

a) Condition A: DMF, rt, 17 h, Ar = 2,5-xylyl. Condition B: Ligand **12** (11 mol %), THF, rt, 24 h, Ar = *p*-NO_2–C_6H_4. b) Determined by ^{1}H NMR spectroscopy of the crude product. c) Ts imine instead of Boc imine was used. d) R = Et. e) 2 equiv of imine were used.



Scheme 5. Catalytic asymmetric addition reaction of sulfonylimidate with *N*-Boc imine.

Preliminary investigation for the asymmetric variant of the present Mannich-type reaction revealed moderate enantioselectivity to be induced with a combination of $Sr(O^iPr)_2$ and bis(sulfonamide) chiral ligand **13**[9c] bearing diphenylethanediamine backbone (Scheme 5).[12b] The addition of a catalytic amount of triethylamine dramatically accelerated the reaction, this is presumably because the complex of $Sr(O^iPr)_2$ and ligand **13** is less basic than $[Sr(HMDS)_2]_2$ and additional Et_3N helps the deprotonation of the α-proton of sulfonylimidate. Et_3N is not basic enough to deprotonate the α-proton of sulfonylimidate, which leads to the assumption that Sr–ligand complex works as a Lewis acid coordinating nitrogen of sulfonylimidate to augment the acidity of the sulfonylimidate α-proton.

Rationalization for High Diastereoselectivity. Single-crystal X-ray diffraction analysis of sulfonylimidate **8a** (R^3 = Me, R^5 = Ph, in Table 1) and the obtained Mannich adducts provided not only information about the relative configuration of the products, but also the general distinctive structure of sulfonylimidate (Figure 5). Without exception, the imine adopts an E configuration. The oxygen at the carbon of the C=N bond is sp^2 hybridized, and displays an s-cis geometry about the N–C–O–C bonds. This phenomena can be rationalized by considering n–σ^* interaction between oxygen lone pair and σ^* anti-bonding orbital of C=N group. Predominant E configuration of the imine stems from the steric repulsion of the alkyl group on oxygen and the sulfonyl group. It is notable that C^1–C^2 and C^2–C^3 bonds rotate so that bulkiest groups are located in anti-periplanar conformation. As a result, only in the anti product, the proton of BocN–H and the oxygen of the sulfonyl group are placed so close to each other that an intramolecular hydrogen-bonding interaction between them is suggested. This observation does not contradict the fact that ^{1}H NMR chemical shifts of N–H of anti products are more deshielded than those of syn products by a range of 0.2–0.5 ppm without exception.

It was confirmed that epimerization of the product sulfonylimidate does not take place under the reaction conditions, which suggests the observed high diastereoselectivity is determined kinetically at the stage of C–C bond formation. On the basis of the experimental information that the imine adopts an E configuration, the geometry of the generated azaenolate is expected to be Z (Scheme 6) under kinetically controlled conditions. The proposed mechanism for anti selectivity in DBU-catalyzed Mannich-type reaction of sulfonylimidate in DMF is demonstrated in Figure 6. Considering the steric repulsion between the methyl substituent and the Boc group (repulsion c), and one between the SO_2Ar group and the R group (repulsion b) in TS-2 led us to the conclusion that TS-1 giving anti product is favored. The syn selectivity observed when pivalaldehyde-derived Ts imine was used (Table 2, Entry 20) may be rationalized by considering that the repulsion between the *t*-Bu group and the Me substituent (repulsion a in TS-1) is large in TS-1. The formation of s-trans configuration about the S–N–C–C bonds of the sulfonylimidate anion as shown in **14** is assumed to be suppressed by steric repulsion between the *i*-Pr group and the methyl substituent (repulsion d). On the contrary to sulfonylimidates bearing *i*-Pr group, ones bearing Me group (Table 1, Entries 3 and 4) may take the s-trans formation as well as s-cis formation, which is the reason for the observed low anti selectivity.

Figure 7 shows plausible transition state models for alkali earth metal-catalyzed Mannich-type reactions in DMF and THF, respectively. In the DMF solvent system, due to the stabilization of counter cation metal by the aprotic polar solvent, DMF, enamide anion is thought to be dissociated from the metal. The naked anion thus formed reacts with imine in TS-3 rather than TS-4 with minimum steric repulsion in analogy to DBU-catalyzed reaction, giving anti adduct as a major product. On the other hand, the use of less polar solvent enables the formation of metal enamide in which metal and nitrogen of sulfonylimidate are covalently bonded. Considering the fact that Ts imine instead of Boc imine showed high anti selectivity even in THF (Entry 10 in Table 6, Condition B), syn selectivity can be ascribed to coordination of Boc group to electron positive metal (TS-6). DBU-catalysis provides anti selectivity regardless of the choice of solvents (Entry 11 in Table 5), probably because $DBUH^+$ is dissociated from sulfonylimidate by solvent molecules via hydrogen bonding.

Kinetic Acidity of the α-Proton of Sulfonylimidate. Recently, Barbas, III and co-workers have evaluated kinetic acidity of the α-proton of several active methylene compounds using proton/deuterium NMR exchange technique, and found that α-phenyl tosylimidate represents a very rapid exchange rate comparable to that of α-nitrophenyl trifluoroethyl thioester.[13] To get information about the effect of N-protecting group of imidate compounds, proton/deuterium exchange

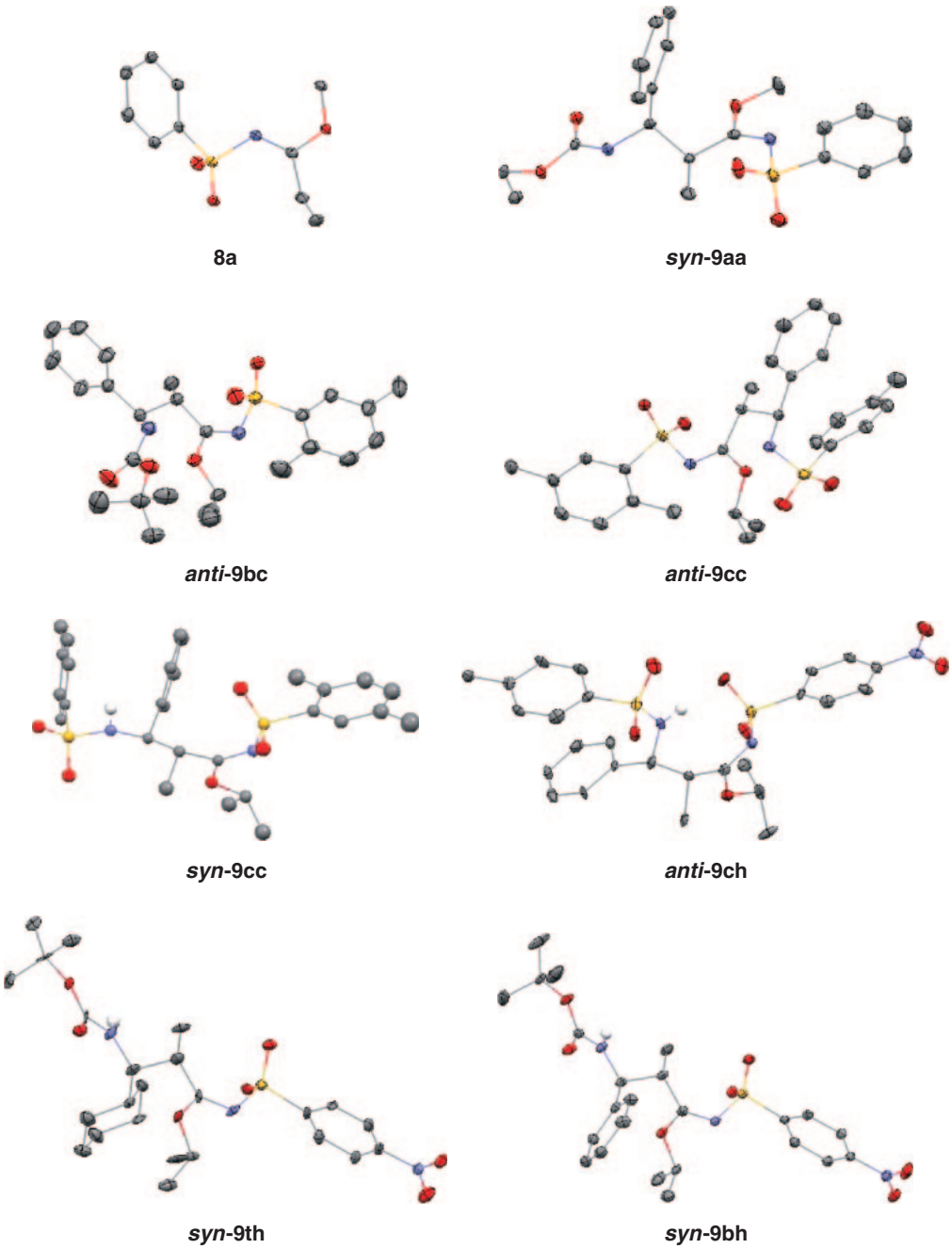
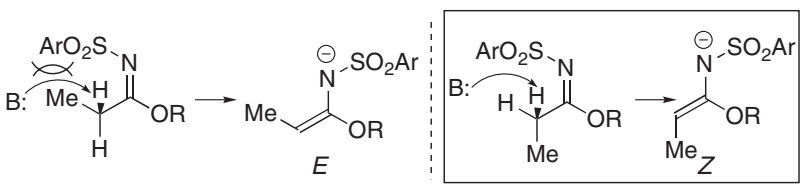


Figure 5. X-ray crystal structures of the products.



Scheme 6. Proposed geometry of aza-enolate derived from sulfonylimidate.

experiments were carried out for various α-methyl imidates bearing different protecting groups, and diethyl malonate was also used as a standard substrate. The results (Figure 8) revealed that an exchange rate determined for *p*-Ns-imidate **8h** is much higher with a $t_{1/2}$ of less than 25 min, than Ts-imidate **8g** (3 h), *p*-methoxybenzenesulfonylimidate **8j** (4 h), and *o*-Ns-imidate **8k** (1.3 h), although diethyl malonate showed much faster exchange rate (<10 min). *N*-Ethoxycarbonylimidate **15** and *N*-phosphonylimidate **16** showed no detectable exchange. Lower exchange rate determined for *o*-Ns-imidate **8k** than that

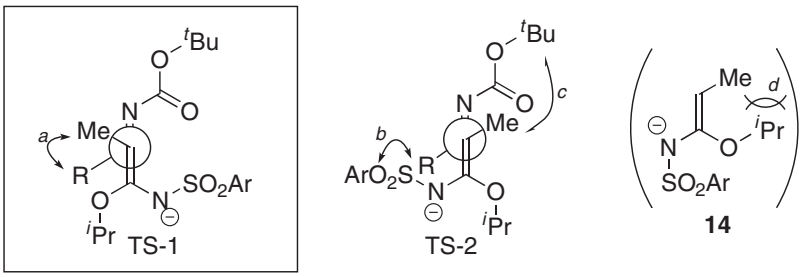


Figure 6. Proposed transition state model.

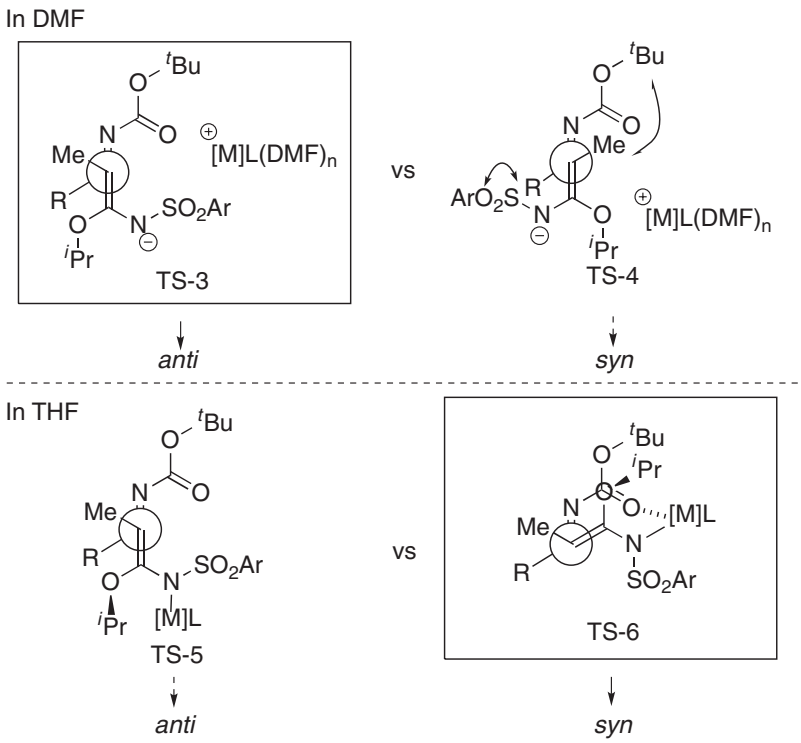
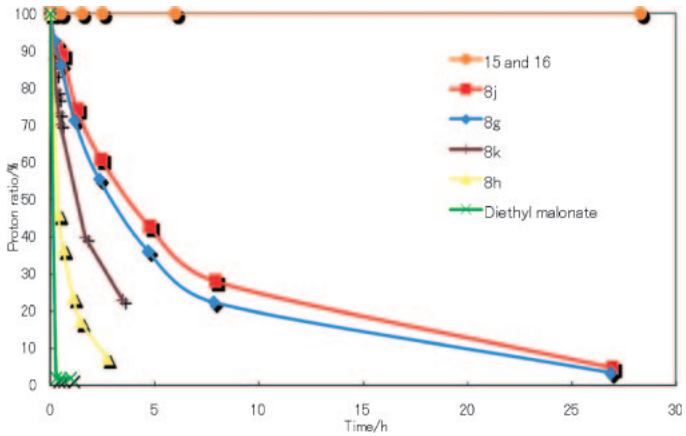


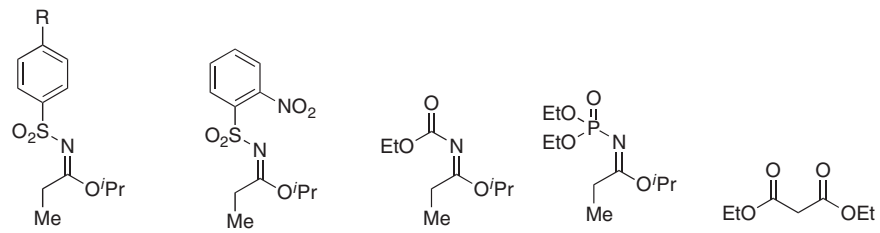
Figure 7. Proposed transition state models (L = ligand).

of *p*-Ns-imidate **8h** is noteworthy, and this results suggest that kinetic acidity of α-protons of sulfonylimidates is subject to not only electronic but also steric factors of sulfonyl groups.

Conversion of the Products. While sulfonylimidate is practically used as a prodrug candidate,[14] the usefulness of sulfonylimidate resides also on its versatility for further transformation into various functional groups by taking advantage of its ester oxidation stage. A trial for the conversion of sulfonylimidate into the corresponding ester was first carried out under acidic conditions. It was revealed that sulfonylimidate was relatively tolerant to acidic conditions, and harsh acidic conditions (100 °C, H_2SO_4) was necessary to hydrolyze sulfonylimidate **9cc**. Under these conditions, *N*-sulfonylamide **17** was obtained instead of the expected corresponding ester (Scheme 7). Conversion of sulfonylimidate **9ba** into the corresponding ester **18** was achieved in 90% yield under basic conditions at room temperature without epimerization (Scheme 8).[15] Treatments of sulfonylimidate **9bc** (R = Boc) and **9cc** (R = Ts) with an excess amount of Red-Al provided the corresponding aldehyde, **19a** and **19b**, respectively (Scheme 9). No corresponding aldimine-type product **20** was observed in contrast to *N*-sulfinylamidate reported by Ellman and co-workers.[16]

Direct Formation of Amino Acid Ester. The experimental results that 3-componet reaction using aldehyde, sulfonamide, and sulfonylimidate provided the desired product through in situ formation of electrophilic sulfonylimine, and that DBU can catalyze hydrolysis of sulfonylimidate into the corresponding ester in the presence of water, prompted us to design a novel catalytic system for facile formation of biologically important compounds, β-amino acid derivatives.[17] Sulfonylimidate **8l** was treated with benzaldehyde in the presence of catalytic amounts of 2,5-dimethylbenzenesulfonamide and DBU, affording β-sulfonylamino acid ester **21** in high yield (Scheme 10). The structure of **21** was unambiguously determined by single-crystal X-ray diffraction analysis. A plausible mechanism on the formation of β-amino acid ester is displayed in Figure 9. Sulfonamide **22** and benzaldehyde first react to form an electrophile, sulfonylimine **23**, and H_2O. The sulfonylimine **23** thus formed readily reacts with sulfonylimidate **8l** in the presence of DBU, providing the adduct, sulfonylimidate **24**, which is subsequently hydrolyzed by H_2O with the assist of

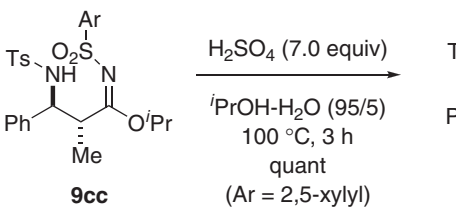




8g: R = Me
8h: R = NO_2
8j: R = OMe

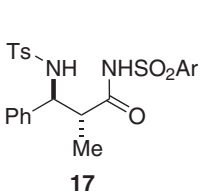
8k **15** **16** diethyl malonate

Figure 8. Deuterium exchange experiment of active methylene compounds.



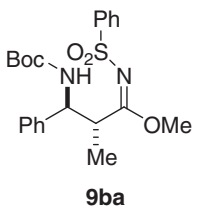
9cc

H_2SO_4 (7.0 equiv)
^{i}PrOH-H_2O (95/5)
100 °C, 3 h
quant
(Ar = 2,5-xylyl)



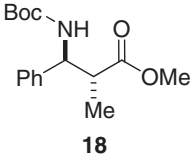
17

Scheme 7. Conversion of the products (1).



9ba

DBU (10 mol%)
DMF-H_2O (95/5)
rt, 33 h
90% yield



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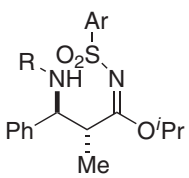
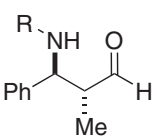
Scheme 8. Conversion of the products (2).

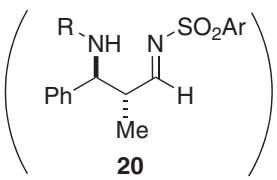


9bc: R = Boc
9cc: R = Ts

Red-Al (7.0 equiv)
THF, -70 °C, 18h
(Ar = 2,5-xylyl)



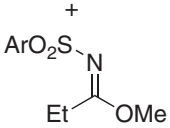
From **9bc**; **19a** (R = Boc): 87% yield
From **9cc**; **19b** (R = Ts): 83% yield



20

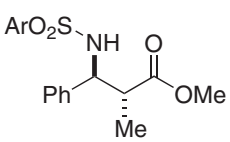
Scheme 9. Conversion of the products (3).

PhCHO
(1.0 equiv)
+



8l
(1.2 equiv)

H_2NSO_2Ar (10 mol%)
DBU (20 mol%)
DMF, rt, 78 h
Slow addition of **8l** over 32 h
(Ar = 2,5-xylyl)



21 (X-ray)
90% yield
anti/*syn* = 87/13

Scheme 10. Direct formation of β-amino acid ester from aldehyde and sulfonylimidate.

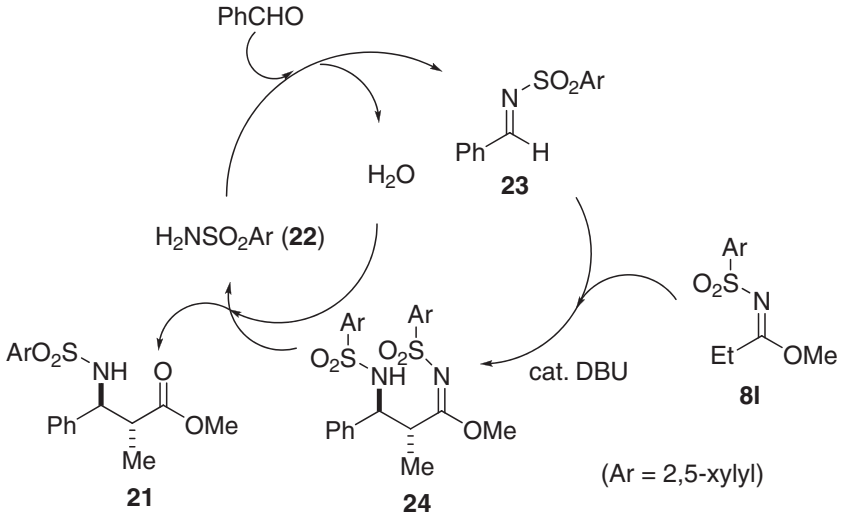


Figure 9. Formation of β-amino acid ester.

DBU to generate the ester product **21** and sulfonamide **22**. The hydrolysis of sulfonylimidate **24** competes with that of starting material sulfonylimidate **8l**, leading to decrease of the yield. To address this issue, sulfonylimidate **8l** was slowly added over 32 h to delay the hydrolysis of **8l**.

Conclusion

A novel nucleophile, sulfonylimidate, has been successfully employed in Mannich-type reactions. Due to electron-withdrawing property of sulfonyl group of sulfonylimidate, the acidity of α-proton is enhanced so that sulfonylimidates bearing no activating functional group at α-position are deprotonated by relatively weaker base. DBU-catalyzed reactions of sulfonylimidates with protected imines in DMF provided the adducts in high yield with high anti selectivity. This reaction represents a wide substrate scope and a high catalytic turnover. A thorough kinetic study for this reaction revealed the rate dependency of this reaction on Boc imine, sulfonylimidate, and DBU to be 0.23, 0.79, and 1.43, respectively. This result suggests that deprotonation of sulfonylimidate by DBU is a rate-determining step and that C–C bond forming step is not involved in rate-determining step, although which step is a rate-determining step may depend on the substrate.

Alkali earth metal alkoxide and its HMDS salt also catalyzed Mannich-type reactions of sulfonylimidates. The reactions of 2,5-dimethylbenzenesulfonylimidate catalyzed by $Mg(O^tBu)_2$ in DMF provided the adducts with high anti selectivity, while those of *p*-Ns-imidate catalyzed by $[Sr(HMDS)_2]_2$ gave syn selectivity. The application of syn selective Mannich-type reaction of sulfonylimidate to asymmetric variant was realized by the use of chiral ligand **13**. High diastereoselectivities in each condition are rationalized on the basis of the experimental results including X-ray diffraction analyses of various sulfonylimidates. Conversions of sulfonylimidates into the corresponding *N*-sulfonylamide, ester, and aldehyde derivatives were performed in acidic, basic, and reductive conditions, respectively, displaying a versatility of sulfonylimidate functional group. Finally a direct catalytic formation of β-amino acid ester from aldehyde and sulfonylimidate was achieved via in situ formation of sulfonylimine and DBU-assisted hydrolysis of sulfonylimidate. Further elaboration of sulfonylimidate would lead to catalysis which otherwise cannot be achieved, and is currently underway in our laboratory.

Experimental

General. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-ECX-400, JNM-ECX-500, and JNM-ECX-600 spectrometer in $CDCl_3$ or C_6D_6 unless otherwise noted. Tetramethylsilane (TMS) served as internal standard (δ 0) for ^{1}H NMR, and $CDCl_3$ (δ 77.0) and C_6D_6 (δ 128.0) were used as internal standard for ^{13}C NMR. IR spectra were measured on a JASCO FT/IR-610 spectrometer. Column chromatography was conducted on Silica gel 60 (Merck) and preparative thin-layer chromatography was carried out using Wakogel B-5F. X-ray diffraction analysis was performed on a Rigaku-RAXIS-RAPID diffractometer. All reactions were carried out under argon atmosphere in dried glassware. All solvents were dried and distilled by standard procedures. All N-protected imines employed in this report were synthesized according to the reported method.[5a] All the metal salts used in this work except $[Sr(HMDS)_2]_2$[12a] were purchased and used without any purification.

Preparation of Sulfonylimidates. Sulfonylimidates **6a–6h** were synthesized by using the similar method to the reported one.[6a] General procedure is as follows.

Imidate HCl Salt Formation. HCl gas was bubbled into a mixture of nitrile (400 mmol) and alcohol (400 mmol) for 10–20 min (exothermic). In some cases (especially when *i*-PrOH was used as an alcohol), temperature higher than room temperature was necessary for the reaction, that is why the reaction was not cooled during the exothermic reaction. After completion of bubbling of HCl, the mixture was left for 3–10 h under Ar atmosphere. Removal of all the volatiles by evaporation gave us almost pure imidate HCl salt in 40–80% yield (moderate yield may be caused by evaporation of the volatile starting materials during the course of the exothermic reactions), which can be used in the next reaction without further purification. Further purification is possible by washing the solid with dry Et_2O. Imidate HCl salts are hygroscopic, but can be kept under inert gas atmosphere in the refrigerator for at least 1 year.

Representative Procedure for the Syntheses of Sulfonylimidates. To a solution of imidate HCl salt **1** (R^1 = Et, R^2 = *i*-Pr, 3.01 g, 19.85 mmol) in dichloromethane (DCM, 50 mL) was added Et_3N (8.3 mL, 59.55 mmol) dropwise at rt. To the resultant suspension was added TsCl (3.785 g, 19.85 mmol) and DMAP (242.5 mg, 1.985 mmol). The reaction mixture was stirred until TsCl was consumed (40 h). The mixture was poured into water, and extracted with DCM. The organics were dried over anhydrous Na_2SO_4. Filtration and evaporation of the solvents afforded the crude product, which was purified by column chromatography on SiO_2 to give us a pure sulfonylimidate **8g** (4.565 g, 85% yield).

Methyl *N*-Benzenesulfonylpropionimidate (8a): ^{1}H NMR ($CDCl_3$): δ 7.98–7.94 (m, 2H), 7.60–7.48 (m, 3H), 3.75 (s, 3H), 2.95 (q, 2H, J = 7.6 Hz), 1.24 (t, 3H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$): δ 177.6, 142.0, 132.4, 128.7, 126.5, 55.4, 27.5, 10.0; IR (neat): 3063, 2985, 2950, 2887, 1602, 1541, 1507, 1446, 1377, 1305, 1235, 1155, 1091, 1023, 945, 798, 758, 733, 690, 621, 585, 536 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{10}H_{14}NO_3S$ $[M + H]^+$, 228.0694. Found 228.0697.

Isopropyl *N*-Benzenesulfonylpropionimidate (8b): ^{1}H NMR ($CDCl_3$): δ 8.09–8.06 (m, 2H), 7.64–7.60 (m, 3H), 4.70 (sept, 1H, J = 6.3 Hz), 2.88 (qd, 2H, J = 7.3, 1.7 Hz), 1.05 (td, 3H, J = 7.3, 1.2 Hz), 0.83 (d, 6H, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$): δ 176.0, 143.6, 132.0, 128.8, 126.9, 71.6, 28.2, 20.9, 10.4; IR (neat): 3055, 2988, 1506, 1448, 1308, 1265, 1157, 1093, 896, 740, 705, 634, 459, 445, 413 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{12}H_{18}NO_3S$ $[M + H]^+$, 256.1007. Found 256.1010.

Isopropyl *N*-(2,5-Xylylsulfonyl)propionimidate (8c): Mp 32–33 °C; ^{1}H NMR ($CDCl_3$): δ 8.20 (s, 1H), 6.90 (d, 1H, J = 7.4 Hz), 6.84 (dd, 1H, J = 7.4, 1.4 Hz), 4.74 (sept, 1H, J = 6.3 Hz), 2.91 (q, 2H, J = 7.4 Hz), 2.77 (s, 3H), 1.94 (s, 3H), 1.07 (t, 3H, J = 7.4 Hz), 0.83 (d, 6H, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$): δ 176.2, 141.2, 135.9, 134.4, 133.0, 132.2, 128.9, 71.2, 28.4, 21.1, 20.6, 20.2, 10.4; IR (neat): 3055, 2988, 1590, 1458, 1308, 1265, 1154, 1092, 1066, 896, 740, 705, 642, 459, 413 cm^{-1}; HRMS (ESI): Exact mass calcd for $C_{14}H_{22}NO_3S$ $[M + H]^+$, 284.1320. Found 284.1323.

Isopropyl *N*-(2,5-Xylylsulfonyl)butyrimidate (8d): Mp 35–36 °C; ^{1}H NMR ($CDCl_3$): δ 8.18 (s, 1H), 6.92 (d, 1H, J = 8.0 Hz), 6.84 (d, 1H, J = 8.0 Hz), 4.77 (sept, 1H, J = 6.2 Hz), 2.93–2.87 (m, 2H), 2.77 (s, 3H), 1.95 (s, 3H), 1.65 (sext, 2H, J = 7.4 Hz), 0.87 (d, 6H, J = 6.2 Hz), 0.82 (t, 3H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$): δ 175.3, 141.2, 135.9, 134.4, 133.0, 132.2, 128.3, 71.2, 36.5, 21.1, 20.6, 20.2, 20.0, 13.8; IR (neat): 3055, 2987, 2933, 2878, 1590, 1457, 1373, 1303, 1219, 1154, 1102, 1067, 918, 896, 739, 706, 641, 459, 412 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{15}H_{24}NO_3S$ $[M + H]^+$, 298.1477. Found 298.1465.

Ethyl *N*-Benzenesulfonylacetimidate (8e): ^{1}H NMR ($CDCl_3$): δ 7.94 (d, 2H, J = 7.9 Hz), 7.60–7.46 (m, 3H), 4.16 (q, 2H, J = 7.2 Hz), 2.49 (s, 3H), 1.27 (t, 3H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$): δ 173.7, 141.7, 132.3, 128.6, 126.5, 64.6, 20.5, 13.5; IR (neat): 3066, 2986, 2940, 2904, 1748, 1606, 1474, 1447, 1396, 1376, 1306, 1158, 1118, 1093, 1046, 1121, 998, 869, 803, 735, 689, 633, 588, 567, 525 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{10}H_{14}NO_3S$ $[M + H]^+$, 228.0694. Found 228.0695.

Methyl *N*-(*p*-Toluenesulfonyl)propionimidate (8f): Mp 46–46.5 °C; ^{1}H NMR ($CDCl_3$): δ 7.82 (d, 2H, J = 8.2 Hz), 7.28 (d, 2H, J = 8.2 Hz), 3.72 (s, 3H), 2.92 (q, 2H, J = 7.6 Hz), 2.40 (s, 3H), 1.22 (t, 3H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$): δ 177.4, 143.1, 139.1, 129.3, 126.6, 55.4, 27.4, 21.5, 10.0; IR (neat): 2983, 2949, 1605, 1496, 1464, 1442, 1378, 1314, 1235, 1190, 1155, 1092, 1030, 1018, 945, 815, 709, 687, 593, 555 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{11}H_{16}NO_3S$ $[M + H]^+$, 242.0851. Found 242.0856.

Isopropyl *N*-(*p*-Toluenesulfonyl)propionimidate (8g): Mp 38–39 °C; ^{1}H NMR ($CDCl_3$): δ 7.82 (d, 2H, J = 8.5 Hz), 7.29 (d, 2H, J = 7.9 Hz), 5.10–4.97 (m, 1H), 2.88 (q, 2H, J = 7.6 Hz), 2.42 (s, 3H), 1.23 (d, 6H, J = 6.2 Hz), 1.21 (t, 3H, J = 6.2 Hz); ^{13}C NMR ($CDCl_3$): δ 176.3, 142.9, 139.4, 129.3, 126.4, 71.9, 27.8, 21.5, 21.1, 10.1; IR (neat): 2983, 2942, 1597, 1496, 1465, 1383, 1356, 1312, 1235, 1183, 1157, 1093, 1032, 1017, 955, 909, 838, 814, 799, 692, 600, 555, 529 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{13}H_{20}NO_3S$ $[M + H]^+$, 270.1164. Found 270.1167.

Isopropyl *N*-(4-Nitrobenzenesulfonyl)propionimidate (8h): Mp 70–71 °C; ^{1}H NMR ($CDCl_3$): δ 8.35 (br d, 2H, J = 9.2 Hz), 8.12 (br d, 2H, J = 9.2 Hz), 5.00 (septet, 1H, J = 6.3 Hz), 2.98 (q, 2H, J = 8.0 Hz), 1.27 (t, 3H, J = 8.0 Hz), 1.26 (d, 6H, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$): δ 177.5, 149.8, 147.6, 127.8, 124.1, 72.9, 28.6, 21.1, 10.2; IR (neat): 3021, 2987, 1579, 1532, 1350, 1308, 1216, 1158, 1094 cm^{-1}; HRMS (APCI): Exact mass calcd for $C_{12}H_{17}N_2O_5S$ $[M + H]^+$, 301.0858. Found 301.0871.

Isopropyl *N*-(4-Nitrobenzenesulfonyl)butyrimidate (8i): Mp 49–50 °C; ^{1}H NMR ($CDCl_3$): δ 8.35 (br d, 2H, J = 8.6 Hz), 8.12 (br d, 2H, J = 8.6 Hz), 5.00 (septet, 1H, J = 6.3 Hz), 2.88 (t, 2H, J = 7.5 Hz), 1.77 (tq, 2H, J = 8.0, 8.0 Hz), 1.26 (d, 6H, J = 6.3 Hz), 1.02 (t, 3H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$): δ 176.7, 149.8, 147.7, 127.8, 124.0, 72.8, 36.6, 21.2, 19.6, 13.7; IR (neat): 2972, 2938, 1582, 1530, 1349, 1311, 1160, 1093 cm^{-1}; HRMS (APCI): Exact mass calcd for $C_{13}H_{19}N_2O_5S$ $[M + H]^+$, 315.1015. Found 315.1028.

Methyl *N*-(2,5-Xylylsulfonyl)propionimidate (8l): Mp 71–72 °C; ^{1}H NMR (C_6D_6): δ 8.17–8.15 (m, 1H), 6.94–6.85 (m, 2H), 3.10 (s, 3H), 2.87 (q, 2H, J = 7.6 Hz), 2.72 (s, 3H), 1.95 (s, 3H), 1.02 (t, 3H, J = 7.4 Hz); ^{13}C NMR (C_6D_6): δ 177.1, 140.9, 135.9, 134.5, 133.1, 132.3, 128.9, 54.6, 27.9, 20.5, 20.2, 10.0; IR (neat): 2982, 2949, 2884, 1602, 1491, 1461, 1442, 1378, 1307, 1234, 1191, 1154, 1142, 1094, 1065, 1028, 944, 884, 821, 798, 747, 705, 630, 579, 548, 503 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{12}H_{18}NO_3S$ $[M + H]^+$, 256.1007. Found 256.1000.

General Procedure of DBU-Catalyzed Addition Reactions of Sulfonylimidates to Imines. To MS 4A (50 mg) was added a solution of imine (0.45 mmol) in DMF (0.5 mL) and sulfonylimidate (0.3 mmol). The mixture was cooled to 0 °C and a solution of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene, 5 mol %) in DMF (100 μL) was added. The mixture was stirred for 24 h and then diluted by addition of Et_2O. The mixture obtained after filtration (for removal of MS 4A) was washed with water 3 times, then dried over anhydrous Na_2SO_4. Filtration and removal of solvents afforded the crude product. Diastereo ratio was determined by ^{1}H NMR spectroscopy analysis of the crude product. Purification of the crude product was conducted by chromatography on SiO_2, to afford the desired product **9**. When it was difficult to determine the diastereomer ratio at the crude product stage, the ratio was determined by the weight of the separated diastereomers after purification.

Procedure of Addition Reaction of Sulfonylimidate 8e to *N*-Boc Imine 3a (Table 2, Entry 3). To MS 4A (50 mg) was added a solution of imine **3a** (53.2 mg, 0.3 mmol) in DMF (0.5 mL). The mixture was cooled to 0 °C, then sulfonylimidate **8e** (340.9 mg, 1.5 mmol) and a solution of DBU in DMF (10 mol %, 100 μL) were added successively. The mixture was stirred for 30 min at 0 °C, and then diluted by addition of Et_2O. The mixture obtained after filtration (for removal of MS 4A) was washed with water 3

times, then dried over anhydrous Na_2SO_4. Filtration and removal of solvents afforded the crude product. Purification of the crude product was conducted by chromatography on SiO_2, to afford the desired product **9ae** (95.8 mg, 79%) and the recovered sulfonylimidate **8e** (275 mg, 1.21 mmol).

Procedure of 3-Component Reaction between Benzaldehyde, Sulfonamide, and Sulfonylimidate 8c. To a suspension of MS 4A (100 mg) in DMF (0.5 mL) were added benzaldehyde (45.7 μL, 0.45 mmol) and 2,5-xylylsulfonylamide (83.4 mg, 0.45 mmol). The mixture was stirred at rt for 20 min, and then cooled to 0 °C. To the suspension were added sulfonylimidate **8c** (85.0 mg, 0.3 mmol) and a solution of DBU in DMF (10 mol %, 100 μL) successively. The mixture was stirred for 23 h at 0 °C, and then diluted by addition of Et_2O. The mixture obtained after filtration (for removal of MS 4A) was washed with water 3 times, then dried over anhydrous Na_2SO_4. Filtration and removal of solvents afforded the crude product. Diastereo ratio was determined by ^{1}H NMR spectroscopy analysis of the crude product (anti/syn = 95/5). Purification of the crude product was conducted by chromatography on SiO_2, to afford the desired product **9sc** (116.8 mg, 70% yield).

General Procedure of Alkali Earth Metal-Catalyzed Addition Reactions of Sulfonylimidates to N-Protected Imines. Condition A: To a flask containing MS 4A (50 mg) and $Mg(O^tBu)_2$ (10 mol %) was added DMF (0.3 mL), followed by sulfonylimidate (0.3 mmol) and finally a solution of imine (0.45 mmol) in DMF (0.3 mL). The mixture was stirred for 17 h at rt and then diluted by addition of Et_2O. The mixture obtained after filtration (for removal of MS 4A) was washed with water 3 times, then dried over anhydrous Na_2SO_4. Filtration and removal of solvents afforded the crude product. Diastereomeric ratio was determined by ^{1}H NMR spectroscopy analysis of the crude product. Purification of the crude product was conducted by chromatography on SiO_2, to afford the desired product **9**. When it was difficult to determine the diastereomeric ratio at the crude product stage, the ratio was determined by the weight of the separated diastereomers after purification.

Condition B: To a flask containing MS 4A (50 mg), $[Sr(HMDS)_2]_2$ (10 mol % of Sr), and ligand **12** (11 mol %) was added THF (0.3 mL), the mixture was stirred at rt for 1 h. Afterwhich sulfonylimidate (0.3 mmol) and finally a solution of imine (0.45 mmol) in THF (0.3 mL) was added. The mixture was stirred for 24 h at rt, then diluted with EtOAc and quenched with aq NH_4Cl. The mixture obtained were separated and then dried over anhydrous Na_2SO_4. Filtration and removal of solvents afforded the crude product. Diastereomeric ratio was determined by ^{1}H NMR spectroscopy analysis of the crude product. Purification of the crude product was conducted by chromatography on SiO_2, to afford the desired product **9**. When it was difficult to determine the diastereomeric ratio at the crude product stage, the ratio was determined by the weight of the separated diastereomers after purification.

Experimental Procedure for the Catalytic Asymmetric Reaction. To a flask containing MS 4A (50 mg), $Sr(O^iPr)_2$ (6.2 mg, 10 mol %), and ligand **13** (19.8 mg, 12 mol %) was added THF (0.8 mL), the mixture was stirred at rt for 1 h. Afterwhich *p*-nitrobenzenesulfonylimidate **8h** (90.1 mg, 0.3 mmol), *o*-tolaldehyde-derived Boc imine **3g** (98.7 mg, 0.45 mmol), THF (0.2 mmol) and a solution of Et_3N (3.03 mg, 10 mol %) in THF (0.05 mL) were successively added in this order. The mixture was stirred for 48 h at 20 °C, then diluted with EtOAc and quenched with aq NH_4Cl. The mixture obtained were separated and then dried over anhydrous Na_2SO_4. Filtration and removal of solvents afforded the crude product. Diastereomeric ratio was determined by ^{1}H NMR spectroscopy analysis of the crude product. Purification of the crude product was conducted by chromatography on SiO_2, to afford the desired product **9gh** (85% yield, syn/anti = 83/17). The enantiomeric excess of the syn product was determined by HPLC (57% ee).

Methyl *anti*-*N*-(Benzenesulfonyl)-3-(ethoxycarbonylamino)-2-methyl-3-phenylpropionimidate (*anti*-9aa): ^{1}H NMR (C_6D_6): δ 8.10–8.07 (m, 2H), 7.38 (d, 2H, J = 7.6 Hz), 7.08–7.04 (m, 2H), 7.03–6.95 (m, 4H), 6.74 (d, 1H, J = 9.6 Hz), 5.08 (t, 1H, J = 10.3 Hz), 4.45–4.38 (m, 1H), 3.98–3.88 (m, 2H), 3.20 (s, 3H), 0.92 (t, 3H, J = 6.9 Hz), 0.88 (t, 3H, J = 7.2 Hz); ^{13}C NMR (C_6D_6): δ 177.9, 155.8, 142.6, 140.9, 132.4, 129.1, 128.8, 127.6, 127.0, 60.8, 59.4, 55.2, 45.6, 14.9, 14.6; IR (neat): 3375, 3064, 3030, 2982, 2951, 1722, 1602, 1518, 1447, 1369, 1303, 1245, 1222, 1152, 1090, 1059, 1025, 999, 950, 907, 842, 772, 758, 734, 701, 689, 623, 525, 426 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{20}H_{25}N_2O_5S$ $[M + H]^+$, 405.1484. Found 405.1494.

Methyl *syn*-*N*-(Benzenesulfonyl)-3-(ethoxycarbonylamino)-2-methyl-3-phenylpropionimidate (*syn*-9aa): Mp 130–131 °C; ^{1}H NMR (C_6D_6): δ 7.96–7.93 (m, 2H), 7.48 (d, 2H, J = 6.9 Hz), 7.18–7.13 (m, 3H), 7.02 (t, 1H, J = 7.2 Hz), 6.95–6.90 (m, 2H), 5.38 (t, 1H, J = 10 Hz), 4.76 (d, 1H, J = 9.6 Hz), 4.39–4.30 (m, 1H), 4.06–3.88 (m, 2H), 2.88 (s, 3H), 1.47 (d, 3H, J = 6.9 Hz), 0.94 (t, 3H, J = 6.9 Hz); ^{13}C NMR (C_6D_6): δ 176.4, 156.3, 143.0, 141.2, 132.1, 128.8, 128.7, 126.9, 60.8, 60.1, 57.3, 54.6, 44.5, 20.5, 15.5, 14.6, 14.2; IR (neat): 3343, 3063, 2924, 2853, 1715, 1697, 1607, 1532, 1448, 1375, 1305, 1287, 1261, 1237, 1155, 1084, 1035, 951, 927, 905, 733, 701, 689, 622, 586 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{20}H_{25}N_2O_5S$ $[M + H]^+$, 405.1484. Found 405.1502.

Isopropyl *anti*-*N*-(Benzenesulfonyl)-3-(ethoxycarbonylamino)-2-methyl-3-phenylpropionimidate (*anti*-9ab): Mp 78 °C; ^{1}H NMR ($CDCl_3$): δ 8.13–8.07 (m, 2H), 7.40 (d, 2H, J = 6.9 Hz), 7.07 (t, 2H, J = 6.9 Hz), 7.04–6.98 (m, 4H), 6.77 (d, 1H, J = 9.6 Hz), 5.09 (t, 1H, J = 11.0 Hz), 4.83 (quint, 1H, J = 6.2 Hz), 4.41 (qd, 1H, J = 11.0, 6.9 Hz), 4.02–3.85 (m, 2H), 1.08 (d, 3H, J = 6.2 Hz), 0.98 (d, 3H, J = 6.2 Hz), 0.94–0.88 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 176.8, 155.7, 143.0, 141.1, 132.4, 129.0, 128.9, 128.2, 127.7, 126.9, 72.5, 60.7, 59.2, 45.7, 20.8, 20.4, 14.9, 14.6; IR (neat): 3063, 3033, 2983, 2938, 2880, 1724, 1593, 1520, 1481, 1456, 1448, 1385, 1374, 1361, 1302, 1245, 1222, 1154, 1091, 1056, 1026, 1000, 974, 929, 909, 852, 829, 769, 758, 738, 702, 689, 671, 636, 597, 566, 537, 504, 470, 418 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{22}H_{29}N_2O_5S$ $[M + H]^+$, 433.1797. Found 433.1803.

Isopropyl *syn*-*N*-(Benzenesulfonyl)-3-(ethoxycarbonylamino)-2-methyl-3-phenylpropionimidate (*syn*-9ab): Mp 145–147 °C; ^{1}H NMR ($CDCl_3$): δ 8.02–7.97 (m, 2H), 7.54 (d, 2H, J = 6.9 Hz), 7.18–7.13 (m, 3H), 7.01 (t, 1H, J = 7.5 Hz), 6.98–6.93 (m, 2H), 5.29 (t, 1H, J = 9.7 Hz), 4.52 (d, 1H, J = 9.7 Hz), 4.46 (quint, 1H, J = 6.2 Hz), 4.34 (dq, 1H, J = 9.7, 7.7 Hz), 4.04–3.86 (m, 2H), 1.54 (d, 3H, J = 6.9 Hz), 0.95 (t, 3H, J = 6.9 Hz), 0.71 (d, 3H, J = 6.2 Hz), 0.45 (d, 3H, J = 5.5 Hz); ^{13}C NMR ($CDCl_3$): δ 175.2, 156.3, 143.4, 141.4, 132.0, 128.8, 128.7, 128.3, 126.8, 71.8, 60.8, 57.5, 44.2, 20.6, 20.0, 16.0, 14.5; IR (neat): 3063, 3033, 2982, 2936, 2876, 1698, 1596, 1532, 1481, 1447, 1382, 1355, 1305, 1286, 1262, 1236, 1157, 1093, 1082, 1034, 1001, 980, 929, 908, 844, 766, 737, 702, 689, 638, 587, 540, 418 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{22}H_{29}N_2O_5S$ $[M + H]^+$, 433.1797. Found 433.1779.

Isopropyl *anti*-*N*-(Benzenesulfonyl)-3-(*tert*-butoxycarbonylamino)-2-methyl-3-phenylpropionimidate (*anti*-9bb): ^{1}H NMR (C_6D_6): δ 8.14 (d, 2H, $J = 6.8$ Hz), 7.38 (d, 2H, $J = 7.4$ Hz), 7.07–6.95 (m, 6H), 6.66 (d, 1H, $J = 9.6$ Hz), 5.06 (t, 1H, $J = 10.5$ Hz), 4.86–4.80 (m, 1H), 4.43–4.32 (m, 1H), 1.34 (s, 9H), 1.12 (d, 3H, $J = 6.2$ Hz), 0.95 (d, 3H, $J = 6.8$ Hz), 0.91 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR (C_6D_6): δ 176.7, 154.9, 143.2, 132.3, 129.0, 128.8, 127.6, 126.9, 78.7, 72.5, 58.8, 45.8, 28.4, 20.8, 20.6, 14.9; IR (neat): 3387, 2979, 2938, 1717, 1592, 1508, 1455, 1386, 1364, 1302, 1247, 1155, 1090, 1054, 1002, 973, 909, 851, 757, 737, 700, 688, 635, 590, 538 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{24}H_{33}N_2O_5S$ $[M + H]^+$, 461.2110. Found 461.2099.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-2-methyl-3-phenyl-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9bc): Mp 122–123 °C; ^{1}H NMR ($CDCl_3$): δ 8.19 (s, 1H), 7.36 (d, 2H, $J = 6.8$ Hz), 7.05–6.93 (m, 4H), 6.89 (d, 1H, $J = 7.3$ Hz), 6.62 (d, 1H, $J = 9.6$ Hz), 5.03 (t, 1H, $J = 10.5$ Hz), 4.87 (quint, 1H, $J = 6.2$ Hz), 4.48 (sext, 1H, $J = 5.9$ Hz), 2.86 (s, 3H), 1.96 (s, 3H), 1.34 (s, 9H), 1.15 (d, 3H, $J = 5.7$ Hz), 0.98 (d, 3H, $J = 6.2$ Hz), 0.91 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 177.5, 154.7, 141.4, 140.5, 136.1, 134.5, 133.4, 132.4, 128.9, 128.3, 127.9, 127.7, 78.6, 72.1, 58.9, 46.0, 28.4, 21.0, 21.0, 20.6, 20.6, 14.9; IR (neat): 3060, 3032, 2941, 2936, 2881, 1715, 1588, 1513, 1495, 1456, 1389, 1365, 1299, 1267, 1248, 1225, 1155, 1102, 1066, 1053, 1004, 973, 930, 910, 884, 851, 824, 738, 707, 644, 599, 553, 499, 465 cm^{-1}; HRMS (ESI): Exact mass calcd for $C_{26}H_{37}N_2O_5S$ $[M + H]^+$, 489.2423. Found 489.2417.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-2-ethyl-3-phenyl-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9bd): Mp 95–96 °C; ^{1}H NMR ($CDCl_3$): δ 8.18 (s, 1H), 7.44 (d, 2H, $J = 7.4$ Hz), 7.08–6.93 (m, 4H), 6.92–6.80 (m, 2H), 5.08 (t, 1H, $J = 10.5$ Hz), 4.93 (quint, 1H, $J = 6.2$ Hz), 4.32 (td, 1H, $J = 11.4$, 4.0 Hz), 2.87 (s, 3H), 1.95 (s, 3H), 1.65–1.59 (m, 1H), 1.34 (s, 9H), 1.40–1.20 (m, 1H), 1.16 (d, 3H, $J = 6.2$ Hz), 0.95–0.88 (m, 6H); ^{13}C NMR ($CDCl_3$): δ 176.9, 153.8, 141.9, 140.6, 136.1, 134.5, 133.4, 132.4, 129.0, 128.9, 128.3, 127.7, 78.6, 72.0, 58.4, 53.7, 28.4, 23.9, 21.1, 21.0, 20.7, 20.6, 11.8; IR (neat): 3062, 3031, 2978, 2934, 2878, 2717, 1717, 1586, 1509, 1496, 1458, 1390, 1365, 1297, 1251, 1202, 1154, 1100, 1065, 1011, 991, 915, 885, 865, 837, 822, 774, 747, 707, 642, 599, 553, 532, 499, 464, 437, 419 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{27}H_{39}N_2O_5S$ $[M + H]^+$, 503.2580. Found 503.2554.

Ethyl *N*-(Benzenesulfonyl)-3-(ethoxycarbonylamino)-3-phenylpropionimidate (9ae): Mp 80–81 °C; ^{1}H NMR (C_6D_6): δ 8.10–8.05 (m, 2H), 7.30–7.26 (m, 2H), 7.10–7.00 (m, 6H), 6.26 (d, 1H, $J = 9.1$ Hz), 5.57–5.47 (m, 1H), 4.03–3.92 (m, 2H), 3.81–3.59 (m, 3H), 2.95 (dd, 1H, $J = 5.1$, 14.2 Hz), 0.95 (t, 3H, $J = 7.1$ Hz), 0.82 (t, 3H, $J = 7.1$ Hz); ^{13}C NMR (C_6D_6): δ 172.8, 155.9, 142.7, 142.0, 132.4, 129.0, 128.8, 127.0, 126.6, 64.8, 60.8, 53.3, 41.1, 14.6, 13.2; IR (neat): 3360, 3065, 2982, 1719, 1599, 1523, 1473, 1446, 1397, 1374, 1305, 1243, 1155, 1091, 1041, 888, 755, 734, 700, 689, 631 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{20}H_{25}N_2O_5S$ $[M + H]^+$, 405.1484. Found 405.1487.

Isopropyl *anti*-2-Methyl-3-phenyl-3-(*p*-toluenesulfonylamino)-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9cc): Mp 140–142 °C; ^{1}H NMR ($CDCl_3$): δ 8.21 (s, 1H), 7.34 (d, 2H, $J = 7.9$ Hz), 6.98 (d, 1H, $J = 7.9$ Hz), 6.95–6.86 (m, 3H), 6.86–6.70 (m, 4H), 6.48 (d, 2H, $J = 8.5$ Hz), 5.02 (quint, 1H, $J = 6.2$ Hz), 4.69 (t, 1H, $J = 10.2$ Hz), 4.30 (qd, 1H, $J = 10.7$, 6.8 Hz), 3.11 (s, 3H), 1.97 (s, 3H), 1.81 (s, 3H), 1.40 (d, 3H, $J = 5.2$ Hz), 1.00 (d, 3H, $J = 6.2$ Hz), 0.93 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR ($CDCl_3$): δ 176.9, 141.8, 140.2, 139.3, 138.6, 136.1, 135.0, 133.6, 132.6, 128.9, 128.8, 128.6, 127.6, 127.0, 73.0, 62.1, 46.7, 21.4, 21.1, 20.9, 20.6, 20.5, 14.6; IR (neat): 3056, 2986, 2938, 2880, 1589, 1494, 1457, 1438, 1423, 1386, 1355, 1333, 1305, 1291, 1266, 1162, 1101, 1092, 1063, 975, 910, 896, 856, 822, 814, 738, 706, 668, 645, 581, 565, 549, 500, 463, 418 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{28}H_{35}N_2O_5S_2$ $[M + H]^+$, 543.1987. Found 543.1990.

Isopropyl *syn*-2-Methyl-3-phenyl-3-(*p*-toluenesulfonylamino)-*N*-(2,5-xylylsulfonyl)propionimidate (*syn*-9cc): Mp 160–161 °C; ^{1}H NMR ($CDCl_3$): δ 7.80 (s, 1H), 7.46 (d, 2H, $J = 8.5$ Hz), 7.21 (d, 1H, $J = 7.4$ Hz), 7.11 (d, 1H, $J = 7.9$ Hz), 7.07–7.00 (m, 7H), 5.17 (d, 1H, $J = 9.6$ Hz), 4.77–4.68 (m, 1H), 4.52 (t, 1H, $J = 9.4$ Hz), 4.17–4.10 (m, 1H), 2.39 (s, 3H), 2.35 (s, 3H), 2.31 (s, 3H), 1.44 (d, 3H, $J = 6.8$ Hz), 1.14 (d, 3H, $J = 6.2$ Hz), 0.78 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 174.6, 142.9, 139.5, 138.5, 137.8, 135.6, 134.2, 133.1, 132.0, 129.2, 128.1, 128.0, 127.6, 127.4, 127.0, 72.1, 60.3, 44.6, 21.4, 21.1, 20.8, 20.5, 19.6, 15.6; IR (neat): 3276, 3032, 2983, 2877, 1592, 1492, 1455, 1381, 1331, 1303, 1184, 1159, 1096, 1062, 981, 909, 813, 764, 733, 704, 669, 646, 607, 562, 511 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{28}H_{35}N_2O_5S_2$ $[M + H]^+$, 543.1987. Found 543.1971.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-3-(*p*-methoxyphenyl)-2-methyl-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9dc): Mp 142–145 °C; ^{1}H NMR ($CDCl_3$): δ 8.20 (s, 1H), 7.29 (d, 2H, $J = 9.1$ Hz), 6.98 (d, 1H, $J = 7.4$ Hz), 6.89 (d, 1H, $J = 7.4$ Hz), 6.65–6.55 (m, 3H), 5.02 (t, 1H, $J = 9.5$ Hz), 4.91 (quint, 1H, $J = 6.2$ Hz), 4.38 (qd, 1H, $J = 11.3$, 6.2 Hz), 3.27 (s, 3H), 2.87 (s, 3H), 1.97 (s, 3H), 1.36 (s, 9H), 1.16 (d, 3H, $J = 6.2$ Hz), 1.04 (d, 3H, $J = 6.8$ Hz), 0.93 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 177.7, 159.6, 154.7, 140.6, 136.1, 134.6, 133.4, 132.4, 131.8, 128.9, 128.7, 114.5, 78.6, 72.1, 58.4, 54.7, 46.2, 28.4, 21.0, 21.0, 20.6, 20.6, 15.0; IR (neat): 3055, 2984, 2937, 1713, 1586, 1513, 1457, 1422, 1386, 1365, 1299, 1265, 1155, 1101, 1054, 1036, 910, 832, 740, 706, 644, 609, 419 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{27}H_{39}N_2O_6S$ $[M + H]^+$, 519.2529. Found 519.2512.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-3-(*p*-fluorophenyl)-2-methyl-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9ec): Mp 131–133 °C; ^{1}H NMR ($CDCl_3$): δ 8.19 (s, 1H), 7.21–7.12 (m, 2H), 6.96 (d, 1H, $J = 7.4$ Hz), 6.88 (d, 1H, $J = 7.4$ Hz), 6.69–6.59 (m, 3H), 4.95 (t, 1H, $J = 10.2$ Hz), 4.87 (quint, 1H, $J = 6.0$ Hz), 4.29 (sext, 1H, $J = 6.4$ Hz), 2.85 (s, 3H), 1.95 (s, 3H), 1.35 (s, 9H), 1.14 (d, 3H, $J = 5.6$ Hz), 0.95 (d, 3H, $J = 6.2$ Hz), 0.91 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 177.2, 160.6 (d, $J_{C-F} = 244.3$ Hz), 154.7, 140.4, 137.1, 136.2, 134.5, 133.5, 132.4, 129.3 (d, $^3J_{C-F} = 8.4$ Hz), 128.9, 115.7 (d, $^2J_{C-F} = 21.5$ Hz), 78.8, 72.1, 58.2, 46.0, 28.4, 21.0, 21.0, 20.6, 14.8; IR (neat): 3056, 2984, 2933, 1714, 1588, 1542, 1457, 1366, 1298, 1266, 1226, 1156, 1096, 1055, 837, 741, 706, 644, 507, 527, 499 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{26}H_{36}N_2O_5SF$ $[M + H]^+$, 507.2329. Found 507.2326.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-2-methyl-*m*-tolyl-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9fc): Mp 110–112 °C; ^{1}H NMR ($CDCl_3$): δ 8.18 (s, 1H), 7.27–7.20 (m, 2H), 6.98 (dd, 2H, $J = 16.1$, 8.2 Hz), 6.90 (d, 1H, $J = 6.8$ Hz), 6.85 (d, 1H, $J = 7.4$ Hz), 6.62 (d, 1H, $J = 9.6$ Hz), 5.04 (t, 1H, $J = 10.5$ Hz), 4.90 (quint, 1H, $J = 6.2$ Hz), 4.40 (qd, 1H, $J = 11.1$, 6.2 Hz), 2.86 (s, 3H), 2.02 (s, 3H), 1.98 (s, 3H), 1.34 (s, 9H), 1.17 (d, 3H, $J = 6.2$ Hz), 1.02 (d, 3H, $J = 6.2$ Hz), 0.93 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 177.6, 154.7, 141.4, 138.6, 136.1, 133.4, 132.4, 129.0, 128.4, 128.3, 124.7, 78.6, 72.1, 58.9, 46.1, 28.4, 28.3, 21.3, 21.1, 21.0, 20.6, 15.0; IR (neat): 3056, 2982, 2936, 2880, 1714, 1588, 1508, 1495, 1457, 1386, 1366, 1298, 1266,

1155, 1102, 1054, 1007, 974, 942, 908, 885, 846, 822, 791, 740, 708, 644, 606, 554, 499, 445, 419 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{27}H_{39}N_2O_5S$ $[M + H]^+$, 503.2580. Found 503.2554.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-3-(*o*-methylphenyl)-2-methyl-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9gc): ^1H NMR ($CDCl_3$): δ 8.20 (s, 1H), 7.58 (d, 1H, $J = 7.3$ Hz), 7.07–6.82 (m, 5H), 6.64 (d, 1H, $J = 9.1$ Hz), 5.44 (t, 1H, $J = 10.5$ Hz), 4.90 (quint, 1H, $J = 6.2$ Hz), 4.46 (qd, 1H, $J = 11.3$, 6.8 Hz), 2.87 (s, 3H), 2.52 (s, 3H), 1.97 (s, 3H), 1.32 (s, 9H), 1.15 (d, 3H, $J = 6.2$ Hz), 1.00 (d, 3H, $J = 6.8$ Hz), 0.90 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 177.5, 154.9, 140.6, 140.3, 136.5, 136.1, 134.5, 133.4, 132.4, 130.6, 128.9, 127.6, 127.4, 126.5, 78.6, 72.1, 46.9, 26.4, 21.1, 21.0, 20.6, 20.6, 19.9, 14.1; IR (neat): 3063, 2980, 2933, 2880, 1715, 1591, 1509, 1494, 1458, 1385, 1364, 1299, 1248, 1233, 1155, 1102, 1056, 1003, 971, 955, 910, 884, 850, 822, 793, 760, 748, 734, 708, 643, 601, 583, 556, 518, 500, 459, 412 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{27}H_{39}N_2O_5S$ $[M + H]^+$, 503.2580. Found 503.2554.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-3-(*m*-vinylphenyl)-2-methyl-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9hc): Mp 87–91 °C; ^1H NMR ($CDCl_3$): δ 8.19 (s, 1H), 7.52 (s, 1H), 7.28 (d, 1H, $J = 7.9$ Hz), 7.10 (d, 1H, $J = 7.4$ Hz), 6.98 (t, 1H, $J = 7.9$ Hz), 6.96 (d, 1H, $J = 7.4$ Hz), 6.88 (d, 1H, $J = 7.9$ Hz), 6.67 (d, 1H, $J = 9.6$ Hz), 6.46 (dd, 1H, $J = 17.6$, 10.7 Hz), 5.57 (d, 1H, $J = 17.6$ Hz), 5.07 (t, 1H, $J = 10.2$ Hz), 5.00 (d, 1H, $J = 10.7$ Hz), 4.88 (quint, 1H, $J = 6.2$ Hz), 4.41 (qd, 1H, $J = 11.3$, 6.8 Hz), 2.86 (s, 3H), 1.96 (s, 3H), 1.34 (s, 9H), 1.16 (d, 3H, $J = 6.2$ Hz), 0.98 (d, 3H, $J = 6.8$ Hz), 0.92 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 177.4, 154.7, 141.8, 140.5, 138.4, 136.9, 136.2, 134.5, 133.4, 132.4, 129.4, 128.9, 126.8, 126.1, 125.7, 114.1, 78.7, 72.1, 58.9, 46.1, 28.4, 21.0, 20.6, 20.6, 14.9; IR (neat): 3087, 3048, 2981, 2933, 2879, 1718, 1602, 1507, 1457, 1389, 1363, 1309, 1250, 1140, 1092, 1055, 1004, 973, 908, 857, 844, 804, 784, 748, 708, 682, 643, 600, 552, 503, 460, 412 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{28}H_{39}N_2O_5S$ $[M + H]^+$, 515.2580. Found 515.2570.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-3-(2-furyl)-2-methyl-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9ic): Mp 84 °C; ^1H NMR ($CDCl_3$): δ 8.17 (s, 1H), 6.97–6.90 (m, 2H), 6.87 (d, 1H, $J = 7.4$ Hz), 6.18 (d, 1H, $J = 9.6$ Hz), 6.09 (d, 1H, $J = 2.7$ Hz), 5.94–5.90 (m, 1H), 5.21 (t, 1H, $J = 10.2$ Hz), 4.87 (quint, 1H, $J = 6.2$ Hz), 4.59 (qd, 1H, $J = 11.3$, 6.8 Hz), 2.82 (s, 3H), 1.95 (s, 3H), 1.34 (s, 9H), 1.13 (d, 3H, $J = 6.2$ Hz), 1.06 (d, 3H, $J = 6.7$ Hz), 0.89 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 176.6, 154.6, 153.1, 140.6, 136.1, 134.6, 133.3, 132.4, 128.9, 110.3, 108.1, 78.8, 72.1, 52.1, 43.7, 28.3, 21.0, 21.0, 20.6, 20.5, 14.8; IR (neat): 3139, 3121, 3056, 2980, 2936, 2879, 1715, 1583, 1509, 1456, 1390, 1367, 1299, 1256, 1200, 1155, 1137, 1103, 1064, 1051, 1010, 971, 910, 884, 860, 848, 822, 798, 754, 731, 709, 680, 644, 592, 556, 498, 424 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{24}H_{35}N_2O_6S$ $[M + H]^+$, 479.2216. Found 479.2225.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-2-methyl-3-(2-thienyl)-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9jc): Mp 104–107 °C; ^1H NMR ($CDCl_3$): δ 8.17 (s, 1H), 7.00–6.85 (m, 3H), 6.76 (d, 1H, $J = 4.6$ Hz), 6.61 (dd, 1H, $J = 5.1$, 3.4 Hz), 6.32 (d, 1H, $J = 9.1$ Hz), 5.35 (t, 1H, $J = 10.5$ Hz), 4.87 (quint, 1H, $J = 6.2$ Hz), 4.59 (qd, 1H, $J = 10.8$, 6.8 Hz), 2.81 (s, 3H), 1.96 (s, 3H), 1.33 (s, 9H), 1.10 (d, 6H, $J = 6.8$ Hz), 0.88 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 176.7, 154.6, 144.7, 140.5, 136.1, 134.5, 133.4, 132.4, 128.9, 127.1, 125.6, 124.8, 78.9, 72.1, 54.0, 46.3, 26.4, 21.0, 20.6, 20.5, 15.2; IR (neat): 3056, 2983, 2934, 2880, 1714, 1588, 1507, 1494, 1456, 1420, 1387, 1366, 1299, 1265, 1233, 1155, 1101, 1054, 1003, 973, 909, 850, 822, 739, 707, 644, 607, 553, 503, 412 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{24}H_{35}N_2O_5S_2$ $[M + H]^+$, 495.1987. Found 495.1980.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-2-methyl-3-(2-pyridyl)-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9kc): Mp 113–115 °C; ^1H NMR ($CDCl_3$): δ 8.79 (s, 1H), 8.45–8.35 (m, 1H), 8.17 (s, 1H), 7.46 (d, 1H, $J = 7.9$ Hz), 6.96 (d, 1H, $J = 7.4$ Hz), 6.87 (d, 1H, $J = 7.4$ Hz), 6.73–6.60 (m, 2H), 5.00 (t, 1H, $J = 9.9$ Hz), 4.84 (quint, 1H, $J = 6.2$ Hz), 4.27 (qd, 1H, $J = 11.3$, 6.8 Hz), 2.83 (s, 3H), 1.96 (s, 3H), 1.33 (s, 9H), 1.11 (d, 3H, $J = 6.2$ Hz), 0.88 (d, 3H, $J = 6.2$ Hz), 0.87 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 176.9, 154.7, 150.0, 149.7, 140.3, 136.4, 136.2, 134.5, 133.8, 133.6, 132.4, 128.9, 123.9, 79.0, 72.3, 56.6, 45.6, 28.4, 21.0, 20.9, 20.6, 14.7; IR (neat): 3059, 2980, 2934, 2880, 1715, 1591, 1507, 1495, 1456, 1429, 1390, 1366, 1298, 1255, 1154, 1101, 1054, 1027, 1005, 973, 910, 883, 852, 820, 779, 735, 708, 643, 602, 554, 499, 460, 412 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{25}H_{36}N_3O_5S$ $[M + H]^+$, 490.2376. Found 490.2356.

Isopropyl *anti*-2-Methyl-5-phenyl-3-(*p*-toluenesulfonylamino)-*N*-(2,5-xylylsulfonyl)pent-4-enimidate (*anti*-9lc): Mp 125–128 °C; ^1H NMR ($CDCl_3$): δ 8.22 (s, 1H), 7.67 (d, 2H, $J = 7.9$ Hz), 7.04–6.98 (m, 3H), 6.95 (d, 1H, $J = 7.9$ Hz), 6.88 (dd, 1H, $J = 7.4$, 1.1 Hz), 6.73 (dd, 2H, $J = 7.6$, 2.0 Hz), 6.58 (d, 2H, $J = 7.9$ Hz), 6.37 (d, 1H, $J = 9.1$ Hz), 5.84 (d, 1H, $J = 15.9$ Hz), 5.24 (dd, 1H, $J = 15.9$, 9.1 Hz), 5.00 (quint, 1H, $J = 6.2$ Hz), 4.32 (q, 1H, $J = 9.8$ Hz), 4.10 (qd, 1H, $J = 10.8$, 6.8 Hz), 2.97 (s, 3H), 1.97 (s, 3H), 1.70 (s, 3H), 1.37 (d, 3H, $J = 6.2$ Hz), 1.12 (d, 3H, $J = 6.2$ Hz), 0.98 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 176.7, 142.4, 140.3, 139.8, 136.2, 136.0, 134.9, 134.3, 133.5, 132.5, 129.6, 129.3, 128.8, 128.3, 127.6, 126.8, 126.2, 72.9, 60.7, 44.7, 21.4, 21.1, 20.9, 20.6, 20.6, 14.8; IR (neat): 3060, 3029, 2982, 2935, 2877, 1595, 1493, 1457, 1385, 1338, 1303, 1212, 1183, 1153, 1104, 1050, 971, 909, 887, 815, 752, 708, 668, 646, 625, 599, 573, 545, 517, 501, 465, 437, 419 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{30}H_{37}N_2O_5S_2$ $[M + H]^+$, 569.2144. Found 569.2150.

Isopropyl *anti*-3-Cyclopropyl-2-methyl-3-(*p*-toluenesulfonylamino)-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9mc): Mp 97–100 °C; ^1H NMR ($CDCl_3$): δ 8.14 (s, 1H), 7.76 (d, 2H, $J = 8.5$ Hz), 6.85 (d, 1H, $J = 8.0$ Hz), 6.79 (d, 1H, $J = 7.4$ Hz), 6.73 (d, 2H, $J = 8.5$ Hz), 6.18 (d, 1H, $J = 8.5$ Hz), 4.84 (quint, 1H, $J = 6.2$ Hz), 4.16 (qd, 1H, $J = 9.6$, 6.8 Hz), 3.25 (q, 1H, $J = 9.0$ Hz), 2.84 (s, 3H), 1.97 (s, 3H), 1.89 (s, 3H), 1.18 (d, 3H, $J = 6.2$ Hz), 1.16 (d, 3H, $J = 6.2$ Hz), 0.88 (d, 3H, $J = 6.2$ Hz), 0.37–0.27 (m, 1H), 0.10–−0.10 (m, 3H), −0.13–−0.25 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 176.8, 142.1, 141.4, 140.4, 136.0, 134.9, 133.4, 132.4, 129.3, 128.9, 127.1, 72.8, 61.4, 46.7, 21.4, 21.1, 21.0, 20.6, 15.9, 15.5, 4.8, 2.7; IR (neat): 3063, 2982, 2936, 2881, 1594, 1493, 1456, 1385, 1357, 1332, 1302, 1239, 1158, 1101, 1052, 1027, 981, 962, 909, 887, 816, 748, 709, 665, 645, 627, 601, 569, 548, 501, 464, 442, 419 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{25}H_{35}N_2O_5S_2$ $[M + H]^+$, 507.1987. Found 507.2003.

Isopropyl *anti*-3-(*tert*-Butoxycarbonylamino)-3-cyclopropyl-2-methyl-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9nc): ^1H NMR ($CDCl_3$): δ 7.86 (s, 1H), 7.27 (d, 1H, $J = 9.2$ Hz), 7.20 (d, 1H, $J = 7.8$ Hz), 5.28 (d, 1H, $J = 10.1$ Hz), 5.09–4.93 (m, 1H), 3.74 (dq, 1H, $J = 6.9$, 10.6 Hz), 3.44 (dt, 1H, $J = 10.1$, 10.1 Hz), 2.64 (s, 3H), 2.38 (s, 3H), 1.38 (s, 9H), 1.34 (d, 3H, $J = 6.9$ Hz), 1.22 (d, 3H, $J = 6.0$ Hz), 1.19 (d, 3H, $J = 6.4$ Hz), 0.90–0.76 (m, 1H), 0.66–0.52 (m, 1H), 0.45–0.30 (m, 3H); ^{13}C NMR ($CDCl_3$): δ

177.6, 155.2, 139.5, 135.6, 134.1, 133.2, 132.1, 128.1, 76.8, 71.9, 56.3, 45.5, 28.2, 21.1, 20.8, 20.8, 20.0, 15.1, 15.0, 4.4, 0.0; IR (neat): 3386, 3082, 2979, 2935, 2882, 1715, 1590, 1513, 1457, 1390, 1365, 1299, 1252, 1229, 1156, 1103, 1057, 1023, 1001, 957, 747, 723, 707, 644, 600, 559, 533, 499 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{23}H_{37}N_2O_5S$ $[M + H]^+$, 453.2423. Found 453.2434.

Isopropyl *syn*-3-(*tert*-Butoxycarbonylamino)-3-cyclopropyl-2-methyl-*N*-(2,5-xylylsulfonyl)propionimidate (*syn*-9nc): ^1H NMR ($CDCl_3$): δ 7.85 (s, 1H), 7.24 (d, 1H, $J = 7.8$ Hz), 7.18 (d, 1H, $J = 7.8$ Hz), 5.10–4.98 (m, 1H), 4.54 (d, 1H, $J = 9.6$ Hz), 3.80–3.66 (m, 1H), 3.29 (q, 1H, $J = 9.5$ Hz), 2.62 (s, 3H), 2.37 (s, 3H), 1.45 (s, 9H), 1.26 (d, 3H, $J = 6.0$ Hz), 1.25 (d, 3H, $J = 6.8$ Hz), 1.21 (d, 3H, $J = 6.4$ Hz), 1.02–0.91 (m, 1H), 0.56–0.26 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 176.4, 155.9, 139.8, 135.6, 134.1, 133.1, 132.0, 128.1, 79.3, 71.9, 56.8, 45.8, 28.3, 21.3, 21.2, 20.8, 19.8, 15.6, 15.3, 5.7, 2.2; IR (neat): 3366, 2979, 2933, 1698, 1591, 1519, 1455, 1365, 1286, 1155, 1103, 1060, 1018, 956, 910, 824, 748, 706, 644, 500 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{23}H_{37}N_2O_5S$ $[M + H]^+$, 453.2423. Found 453.2400.

Methyl *anti*-3-Cyclohexyl-2-methyl-*N*-(*p*-toluenesulfonyl)-3-(*p*-toluenesulfonylamino)propionimidate (*anti*-9of): ^1H NMR ($CDCl_3$): δ 7.86 (apparent d, 2H, $J = 8.5$ Hz), 7.70 (d, 2H, $J = 7.9$ Hz), 7.32 (d, 2H, $J = 7.9$ Hz), 7.19 (d, 2H, $J = 7.9$ Hz), 5.60 (d, 1H, $J = 9.6$ Hz), 3.87 (dq, 1H, $J = 6.2$, 10.2 Hz), 3.56 (dt, 1H, $J = 2.3$, 9.6 Hz), 3.50 (s, 3H), 2.44 (s, 3H), 2.37 (s, 3H), 1.80–1.72 (m, 1H), 1.68–1.54 (m, 3H), 1.52–1.36 (m, 2H), 1.20 (d, 3H, $J = 6.8$ Hz), 1.18–1.08 (m, 2H), 0.84 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 177.5, 143.3, 142.6, 139.6, 129.3, 129.2, 126.6, 61.9, 55.5, 41.7, 39.8, 30.9, 26.3, 26.1, 25.4, 21.5, 21.4, 15.5; IR (neat): 3306, 2928, 2854, 1600, 1495, 1447, 1380, 1329, 1303, 1289, 1182, 1158, 1091, 1039, 1011, 951, 913, 887, 862, 814, 735, 706, 689, 596, 567, 547 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{25}H_{35}N_2O_5S_2$ $[M + H]^+$, 507.1987. Found 507.1970.

Methyl *syn*-3-Cyclohexyl-2-methyl-*N*-(*p*-toluenesulfonyl)-3-(*p*-toluenesulfonylamino)propionimidate (*syn*-9of): ^1H NMR ($CDCl_3$): δ 7.85 (d, 2H, $J = 8.2$ Hz), 7.73 (d, 2H, $J = 8.2$ Hz), 7.30 (d, 2H, $J = 8.2$ Hz), 7.27 (d, 2H, $J = 8.2$ Hz), 4.43 (d, 1H, $J = 9.6$ Hz), 3.85–3.79 (m, 1H), 3.73–3.67 (m, 4H), 2.43 (s, 3H), 2.41 (s, 3H), 1.70–1.46 (m, 5H), 1.20–0.93 (m, 8H), 0.65–0.55 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 176.6, 143.1, 143.1, 139.2, 138.7, 129.4, 129.3, 127.0, 126.6, 60.3, 55.7, 41.2, 40.9, 30.3, 27.6, 26.2, 26.0, 25.9, 21.5, 21.5, 14.2, 13.5; IR (neat): 3293, 2928, 2854, 1599, 1496, 1448, 1319, 1300, 1185, 1157, 862, 814, 737, 687, 606, 570, 553 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{25}H_{35}N_2O_5S_2$ $[M + H]^+$, 507.1987. Found 507.1970.

Isopropyl *anti*-3-Cyclohexyl-2-methyl-*N*-(*p*-toluenesulfonyl)-3-(*p*-toluenesulfonylamino)propionimidate (*anti*-9og): ^1H NMR ($CDCl_3$): δ 7.85 (d, 2H, $J = 8.2$ Hz), 7.71 (d, 2H, $J = 8.2$ Hz), 7.30 (d, 2H, $J = 8.2$ Hz), 7.20 (d, 2H, $J = 7.8$ Hz), 5.68 (d, 1H, $J = 9.6$ Hz), 4.88–4.76 (m, 1H), 3.84 (dq, 1H, $J = 6.9$, 10.0 Hz), 3.59 (dt, 1H, $J = 2.7$, 9.2 Hz), 2.43 (s, 3H), 2.37 (s, 3H), 1.75–0.75 (m, 11H), 1.30 (d, 3H, $J = 6.4$ Hz), 1.22 (d, 3H, $J = 6.0$ Hz), 1.17 (d, 3H, $J = 6.4$ Hz); ^{13}C NMR ($CDCl_3$): δ 176.4, 143.1, 142.5, 139.8, 129.3, 129.1, 126.5, 126.5, 73.1, 61.9, 41.8, 39.8, 30.8, 26.3, 26.1, 25.8, 21.5, 21.4, 21.2, 20.8, 15.7; IR (neat): 3277, 2982, 2929, 2854, 2308, 1593, 1495, 1449, 1385, 1374, 1331, 1302, 1182, 1158, 1091, 1020, 968, 909, 887, 862, 840, 814, 735, 694, 671, 605, 582, 547 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{27}H_{39}N_2O_5S_2$ $[M + H]^+$, 535.2300. Found 535.2297.

Isopropyl *syn*-3-Cyclohexyl-2-methyl-*N*-(*p*-toluenesulfonyl)-3-(*p*-toluenesulfonylamino)propionimidate (*syn*-9og): ^1H NMR ($CDCl_3$): δ 7.81 (d, 2H, $J = 8.2$ Hz), 7.75 (d, 2H, $J = 8.2$ Hz), 7.33–7.25 (m, 4H), 5.08–4.97 (m, 1H), 4.39 (d, 1H, $J = 8.7$ Hz), 3.71 (dq, 1H, $J = 6.4$, 9.2 Hz), 3.62 (dt, 1H, $J = 3.2$, 9.2 Hz), 2.42 (s, 6H), 1.71–0.65 (m, 11H), 1.25 (d, 3H, $J = 6.4$ Hz), 1.22 (d, 3H, $J = 6.4$ Hz), 1.06 (d, 3H, $J = 6.9$ Hz); ^{13}C NMR ($CDCl_3$): δ 175.5, 143.1, 143.0, 139.3, 138.9, 129.4, 129.3, 127.0, 126.5, 72.3, 60.8, 41.6, 41.4, 31.0, 26.6, 26.4, 26.1, 26.0, 21.5, 21.5, 21.0, 20.9, 15.1; IR (neat): 3295, 2981, 2928, 2854, 1596, 1496, 1449, 1381, 1300, 1184, 1159, 1093, 1053, 1019, 982, 960, 909, 839, 814, 718, 693, 609, 569, 547 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{27}H_{39}N_2O_5S_2$ $[M + H]^+$, 535.2300. Found 535.2297.

Methyl *anti*-3-Isopropyl-2-methyl-*N*-(*p*-toluenesulfonyl)-3-(*p*-toluenesulfonylamino)propionimidate (*anti*-9pf): Mp 147–148 °C; ^1H NMR ($CDCl_3$): δ 7.88 (d, 2H, $J = 8.5$ Hz), 7.71 (d, 2H, $J = 8.5$ Hz), 7.32 (d, 2H, $J = 7.9$ Hz), 7.19 (d, 2H, $J = 7.9$ Hz), 5.63 (d, 1H, $J = 9.6$ Hz), 3.82 (dq, 1H, $J = 6.8$, 10.2 Hz), 3.62 (dt, 1H, $J = 2.8$, 10.2 Hz), 3.57 (s, 3H), 2.44 (s, 3H), 2.37 (s, 3H), 1.93–1.83 (m, 1H), 1.21 (d, 3H, $J = 6.2$ Hz), 0.83 (d, 3H, $J = 6.8$ Hz), 0.71 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR ($CDCl_3$): δ 177.4, 143.3, 142.6, 139.6, 138.7, 129.3, 129.2, 126.7, 126.6, 62.2, 55.6, 42.5, 28.9, 21.5, 21.4, 20.6, 15.3, 14.8; IR (neat): 3307, 2965, 1601, 1540, 1496, 1455, 1329, 1304, 1287, 1157, 1090, 1044, 950, 814, 734, 688, 666, 596, 584, 547 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{22}H_{31}N_2O_5S_2$ $[M + H]^+$, 467.1674. Found 467.1673.

Methyl *syn*-3-Isopropyl-2-methyl-*N*-(*p*-toluenesulfonyl)-3-(*p*-toluenesulfonylamino)propionimidate (*syn*-9pf): ^1H NMR ($CDCl_3$): δ 7.83 (d, 2H, $J = 8.2$ Hz), 7.73 (d, 2H, $J = 8.2$ Hz), 7.29 (d, 2H, $J = 8.2$ Hz), 7.25 (d, 2H, $J = 8.2$ Hz), 4.51 (d, 1H, $J = 10.1$ Hz), 3.80–3.66 (m, 2H), 3.71 (s, 3H), 2.41 (s, 3H), 2.39 (s, 3H), 1.63–1.49 (m, 1H), 1.13 (d, 3H, $J = 6.9$ Hz), 0.76 (d, 3H, $J = 6.9$ Hz), 0.71 (d, 3H, $J = 6.9$ Hz); ^{13}C NMR ($CDCl_3$): δ 176.6, 143.2, 143.1, 139.1, 138.8, 129.5, 129.4, 126.9, 126.5, 60.9, 55.6, 41.8, 31.2, 21.5, 21.5, 20.4, 16.7, 14.2; IR (neat): 3295, 2965, 2882, 1599, 1495, 1455, 1436, 1325, 1290, 1157, 1092, 1039, 952, 909, 814, 688, 666, 603, 573, 548 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{22}H_{31}N_2O_5S_2$ $[M + H]^+$, 467.1674. Found 467.1682.

Isopropyl *anti*-3-Isopropyl-2-methyl-*N*-(*p*-toluenesulfonyl)-3-(*p*-toluenesulfonylamino)propionimidate (*anti*-9pg): ^1H NMR ($CDCl_3$): δ 7.87 (d, 2H, $J = 8.2$ Hz), 7.72 (d, 2H, $J = 8.2$ Hz), 7.31 (d, 2H, $J = 7.7$ Hz), 7.20 (d, 2H, $J = 8.2$ Hz), 5.74 (d, 1H, $J = 9.1$ Hz), 4.91–4.83 (m, 1H), 3.79 (dq, 1H, $J = 6.3$, 10.0 Hz), 3.67 (dt, 1H, $J = 2.3$, 9.0 Hz), 2.43 (s, 3H), 2.38 (s, 3H), 1.90–1.80 (m, 1H), 1.33 (d, 3H, $J = 6.3$ Hz), 1.23 (d, 3H, $J = 6.3$ Hz), 1.19 (d, 3H, $J = 6.8$ Hz), 0.80 (d, 3H, $J = 6.8$ Hz), 0.69 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR ($CDCl_3$): δ 176.4, 143.1, 142.5, 139.9, 139.0, 129.3, 129.2, 126.5, 126.5, 73.2, 62.3, 42.6, 29.2, 21.5, 21.4, 21.2, 20.9, 20.6, 15.6, 14.9; IR (neat): 3647, 3273, 2968, 2936, 2877, 1918, 1736, 1592, 1496, 1455, 1387, 1373, 1331, 1286, 1241, 1184, 1155, 1089, 1042, 968, 909, 883, 849, 814, 727, 694, 666, 609, 579, 547 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{24}H_{35}N_2O_5S_2$ $[M + H]^+$, 495.1987. Found 495.1969.

Isopropyl *syn*-3-Isopropyl-2-methyl-*N*-(*p*-toluenesulfonyl)-3-(*p*-toluenesulfonylamino)propionimidate (*syn*-9pg): ^1H NMR ($CDCl_3$): δ 7.80 (d, 2H, $J = 8.5$ Hz), 7.75 (d, 2H, $J = 7.9$ Hz), 7.31–7.26 (m, 4H), 5.06–4.96 (m, 1H), 4.42–4.35 (m, 1H), 3.71–3.62 (m, 2H), 2.42 (s, 3H), 2.41 (s, 3H), 1.65–1.55 (m, 1H), 1.25 (d, 3H, $J = 6.2$ Hz), 1.22 (d, 3H, $J = 6.2$ Hz), 1.11 (d, 3H, $J = 6.2$ Hz), 0.79 (d, 3H, $J = 6.8$ Hz), 0.73 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR ($CDCl_3$): δ 175.4, 143.1, 143.1, 139.3, 139.0,

129.5, 129.3, 126.9, 126.5, 72.3, 61.1, 42.4, 31.0, 21.5, 21.5, 21.0, 20.9, 20.8, 15.9, 15.5; IR (neat): 3295, 2977, 2933, 2878, 1594, 1456, 1374, 1317, 1290, 1159, 1092, 1040, 909, 839, 814, 718, 693, 666, 608, 572, 548, 458 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{24}H_{35}N_2O_5S_2$ $[M + H]^+$, 495.1987. Found 495.1969.

Methyl *anti*-*N*-(*p*-Toluenesulfonyl)-3-(*p*-toluenesulfonylamino)-2,4,4-trimethylpentanimidate (*anti*-9qf): ^1H NMR ($CDCl_3$): δ 7.83 (d, 2H, $J = 8.2$ Hz), 7.73 (d, 2H, $J = 8.2$ Hz), 7.31 (d, 2H, $J = 8.2$ Hz), 7.25 (d, 2H, $J = 8.2$ Hz), 5.47 (d, 1H, $J = 9.6$ Hz), 4.03 (dq, 1H, $J = 6.8$, 6.9 Hz), 3.68 (s, 3H), 3.43 (dd, 1H, $J = 5.5$, 10.4 Hz), 2.43 (s, 3H), 2.40 (s, 3H), 1.25 (d, 3H, $J = 6.9$ Hz), 0.87 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 177.4, 143.4, 142.8, 139.6, 138.8, 129.4, 126.6, 66.6, 55.5, 39.4, 36.4, 27.5, 21.5, 21.5, 18.4; IR (neat): 3325, 2954, 1601, 1540, 1455, 1315, 1259, 1185, 1157, 1091, 1025, 927, 814, 675, 594, 572, 547 cm^{-1}; HRMS (FAB); Exact mass calcd for $C_{23}H_{33}N_2O_5S_2$ $[M + H]^+$, 481.1831. Found 481.1832.

Methyl *syn*-*N*-(*p*-Toluenesulfonyl)-3-(*p*-toluenesulfonylamino)-2,4,4-trimethylpentanimidate (*syn*-9qf): Mp 189–190 °C; ^1H NMR ($CDCl_3$): δ 7.84 (d, 2H, $J = 8.2$ Hz), 7.74 (d, 2H, $J = 8.2$ Hz), 7.30 (d, 2H, $J = 8.2$ Hz), 7.26 (d, 2H, $J = 8.2$ Hz), 4.72–4.65 (m, 1H), 3.88–3.80 (m, 2H), 3.71 (s, 3H), 2.42 (s, 3H), 2.40 (s, 3H), 1.18 (d, 3H, $J = 6.2$ Hz), 0.82 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 177.7, 143.1, 142.9, 139.2, 139.1, 129.4, 129.3, 126.8, 126.5, 63.1, 55.4, 40.0, 36.4, 26.8, 21.5, 21.4, 16.4; IR (neat): 3303, 2952, 1600, 1540, 1456, 1436, 1315, 1301, 1286, 1155, 1093, 1071, 953, 916, 814, 688, 605, 574 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{23}H_{33}N_2O_5S_2$ $[M + H]^+$, 481.1831. Found 481.1832.

Methyl *N*-(Benzenesulfonyl)-3-(ethoxycarbonyl)-3-(*p*-methoxyphenylamino)-2-methylpropionimidate (Major-9rc): Mp 99–100 °C; ^1H NMR ($CDCl_3$): δ 8.09–8.04 (m, 2H), 7.02–6.95 (m, 3H), 6.74–6.67 (m, 4H), 4.90 (d, 1H, $J = 11.9$ Hz), 4.56 (qd, 1H, $J = 10.2$, 6.8 Hz), 4.37 (t, 1H, $J = 10.8$ Hz), 3.93–3.78 (m, 2H), 3.29 (s, 3H), 3.08 (s, 3H), 1.29 (d, 3H, $J = 6.2$ Hz), 0.82 (t, 3H, $J = 7.1$ Hz); ^{13}C NMR ($CDCl_3$): δ 176.5, 171.8, 153.9, 142.8, 141.0, 132.4, 128.8, 127.0, 116.2, 115.1, 62.1, 61.1, 55.1, 42.6, 14.4, 14.1; IR (neat): 3055, 2986, 2953, 2836, 1735, 1607, 1514, 1457, 1447, 1421, 1305, 1265, 1242, 1191, 1156, 1092, 1034, 953, 896, 825, 737, 705, 624, 603, 527, 451, 419 cm^{-1}.

Methyl *N*-(Benzenesulfonyl)-3-(ethoxycarbonyl)-3-(*p*-methoxyphenylamino)-2-methylpropionimidate (Minor-9rc): ^1H NMR ($CDCl_3$): δ 8.14–8.05 (m, 2H), 7.05–6.95 (m, 3H), 6.74 (d, 2H, $J = 9.1$ Hz), 6.62 (d, 2H, $J = 9.1$ Hz), 4.50 (t, 1H, $J = 9.4$ Hz), 4.40 (qd, 1H, $J = 9.0$, 6.8 Hz), 4.07–3.92 (m, 2H), 3.84 (d, 1H, $J = 10.2$ Hz), 3.35 (s, 3H), 3.21 (s, 3H), 1.35 (d, 3H, $J = 8.0$ Hz), 0.94 (t, 3H, $J = 7.1$ Hz); ^{13}C NMR ($CDCl_3$): δ 176.3, 171.7, 143.1, 141.6, 132.3, 128.8, 127.2, 115.9, 115.1, 61.5, 60.7, 55.2, 55.0, 42.9, 14.8, 14.1; IR (neat): 3063, 3033, 2984, 2951, 2907, 2834, 1735, 1608, 1511, 1446, 1369, 1306, 1241, 1198, 1156, 1092, 1077, 1060, 1027, 953, 852, 824, 758, 734, 690, 624, 587, 519, 446, 418 cm^{-1}.

Isopropyl *anti*-2-Methyl-3-phenyl-*N*-(2,5-xylylsulfonyl)-3-(2,5-xylylsulfonylamino)propionimidate (*anti*-9sc): Mp 99–100 °C; ^1H NMR ($CDCl_3$): δ 8.23 (s, 1H), 7.39 (s, 1H), 7.12 (d, 1H, $J = 9.1$ Hz), 6.97–6.90 (m, 3H), 6.87 (dd, 1H, $J = 7.6$, 1.4 Hz), 6.73–6.65 (m, 3H), 6.53 (qd, 2H, $J = 7.6$, 1.4 Hz), 5.03 (quint, 1H, $J = 6.2$ Hz), 4.68 (dd, 1H, $J = 11.0$, 9.3 Hz), 4.48 (qd, 1H, $J = 11.0$, 6.5 Hz), 3.00 (s, 3H), 2.62 (s, 3H), 1.95 (s, 3H), 1.78 (s, 3H), 1.40 (d, 3H, $J = 6.2$ Hz), 0.96 (d, 3H, $J = 6.2$ Hz), 0.91 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 177.0, 140.1, 140.0, 138.0, 136.1, 135.2, 135.0, 133.6, 133.2, 132.6, 132.2, 131.9, 129.7, 128.8, 128.3, 127.3, 73.1, 62.5, 46.4, 21.4, 21.1, 20.8, 20.5, 20.4, 20.0, 14.5; IR (neat): 3060, 3029, 2982, 2936, 2878, 1592, 1578, 1493, 1458, 1386, 1359, 1331, 1292, 1226, 1208, 1162, 1102, 1065, 1030, 973, 910, 855, 824, 768, 747, 725, 707, 645, 607, 580, 548, 516, 501, 464, 436, 419 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{29}H_{37}N_2O_5S_2$ $[M + H]^+$, 557.2144. Found 557.2151.

Isopropyl 3-Cyclohexyl-2-methyl-3-(*p*-toluenesulfonylamino)-*N*-(2,5-xylylsulfonyl)propionimidate (*anti*-9oc): ^1H NMR (C_6D_6): δ 8.25–8.22 (s, 1H), 7.83 (d, 2H, $J = 7.9$ Hz), 6.93 (d, 1H, $J = 7.4$ Hz), 6.87 (d, 1H, $J = 7.9$ Hz), 6.78 (d, 2H, $J = 7.9$ Hz), 6.15 (d, 1H, $J = 9.1$ Hz), 4.98 (quintet, 1H, $J = 6.2$ Hz), 4.32–4.22 (m, 1H), 3.90–3.84 (m, 1H), 2.94 (s, 3H), 1.99–1.96 (m, 1H), 1.97 (s, 3H), 1.88 (s, 3H), 1.64 (d, 1H, $J = 11.9$ Hz), 1.54 (d, 1H, $J = 11.9$ Hz), 1.47 (d, 1H, $J = 13.0$ Hz), 1.42 (d, 2H, $J = 12.5$ Hz), 1.33 (d, 3H, $J = 6.2$ Hz), 1.33–1.30 (m, 1H), 1.13 (d, 3H, $J = 6.8$ Hz), 0.98 (d, 3H, $J = 6.2$ Hz), 1.11–0.70 (m, 4H); ^{13}C NMR (C_6D_6): δ 177.3, 142.3, 141.1, 140.4, 136.0, 134.9, 133.4, 132.4, 129.3, 129.0, 127.0, 73.0, 62.1, 42.7, 40.2, 31.2, 26.7, 26.5, 26.1, 21.4, 21.0, 21.0, 20.6, 20.5, 15.7; IR (neat): 3273, 2977, 2926, 2847, 1589, 1449, 1334, 1303, 1159, 1092, 1066, 909, 814, 708, 643, 547, 508 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{28}H_{41}N_2O_5S_2$ $[M + H]^+$, 549.2457. Found 549.2438.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-2-methyl-*N*-(4-nitrophenylsulfonyl)-3-phenylpropionimidate (*syn*-9bh): Mp 156–157 °C; ^1H NMR (C_6D_6): δ 7.65–7.63 (d, 2H, $J = 9.2$ Hz), 7.55–7.53 (d, 2H, $J = 9.2$ Hz), 7.42–7.41 (d, 2H, $J = 7.2$ Hz), 7.15–7.11 (m, 2H), 7.00–6.98 (t, 1H, $J = 7.2$ Hz), 5.27–5.22 (t, 1H, $J = 10.3$ Hz), 4.46–4.42 (m, 1H), 4.22–4.17 (d, 1H, $J = 10.3$ Hz), 4.16–4.11 (m, 1H), 1.51–1.50 (d, 3H, $J = 6.3$ Hz), 1.39 (s, 9H), 0.73–0.72 (d, 3H, $J = 6.3$ Hz), 0.49–0.47 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (C_6D_6): δ 176.5, 155.3, 149.8, 147.7, 141.4, 128.9, 128.5, 128.3, 127.6, 123.9, 79.3, 72.6, 56.9, 45.1, 28.4, 20.6, 20.0, 16.2; IR (neat): 3367, 2982, 2942, 1715, 1698, 1582, 1531, 1455, 1349, 1305, 1160, 1081, 1010, 907, 855, 746, 701, 657, 607 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{24}H_{32}N_3O_7S$ $[M + H]^+$, 506.1960. Found 506.1959.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-3-(4-methoxyphenyl)-2-methyl-*N*-(4-nitrophenylsulfonyl)propionimidate (*syn*-9dh): Mp 164–165 °C; ^1H NMR (C_6D_6): δ 7.68–7.66 (d, 2H, $J = 9.2$ Hz), 7.57–7.56 (d, 2H, $J = 9.2$ Hz), 7.37–7.35 (d, 2H, $J = 8.9$ Hz), 6.76–6.74 (d, 2H, $J = 8.9$ Hz), 5.23–5.18 (t, 1H, $J = 10.3$ Hz), 4.50–4.45 (m, 1H), 4.30–4.28 (d, 1H, $J = 10.3$ Hz), 4.18–4.12 (m, 1H), 3.23 (s, 3H), 1.55–1.53 (d, 3H, $J = 6.9$ Hz), 1.41 (s, 9H), 0.76–0.75 (d, 3H, $J = 6.3$ Hz), 0.56–0.55 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (C_6D_6): δ 176.8, 159.9, 155.6, 150.0, 148.0, 133.6, 129.3, 128.5, 128.4, 128.2, 127.9, 124.1, 114.4, 79.3, 72.6, 56.5, 54.9, 45.4, 28.6, 20.8, 20.4, 16.3; IR (neat): 3370, 3104, 2980, 2936, 2837, 1712, 1698, 1583, 1531, 1513, 1456, 1349, 1304, 1246, 1160, 1092, 1036, 1010, 983, 907, 879, 855, 833, 746 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{25}H_{34}N_3O_8S$ $[M + H]^+$, 536.2066. Found 536.2042.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-3-(4-fluorophenyl)-2-methyl-*N*-(4-nitrophenylsulfonyl)propionimidate (*syn*-9eh): Mp 189–190 °C; ^1H NMR (C_6D_6): δ 7.65–7.63 (d, 2H, $J = 8.9$ Hz), 7.56–7.53 (d, 2H, $J = 8.9$ Hz), 7.27–7.24 (m, 2H), 6.81–6.78 (t, 2H, $J = 8.6$ Hz), 5.17–5.13 (t, 1H, $J = 9.8$ Hz), 4.43–4.39 (m, 1H), 4.15–4.13 (d, 1H, $J = 9.8$ Hz), 4.05–3.99 (m, 1H), 1.47–1.46 (d, 3H, $J = 6.3$ Hz), 1.40 (s, 9H), 0.72–0.71 (d, 3H, $J = 6.3$ Hz), 0.47–0.45 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (C_6D_6): δ 176.7, 164.3, 162.3, 155.9, 150.5, 148.2, 137.6, 130.3, 129.1, 128.7, 128.5, 128.2, 124.5, 116.3, 116.1, 80.0, 73.2, 56.7, 45.7, 29.0, 21.1,

20.7, 16.4; IR (neat): 3366, 2981, 2834, 1698, 1599, 1583, 1532, 1510, 1456, 1349, 1302, 1225, 1159, 1091, 1011, 907, 838, 746 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{24}H_{31}N_3O_7SF$ $[M + H]^+$, 524.1867. Found 524.1867.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-2-methyl-*N*-(4-nitrophenylsulfonyl)-3-*m*-tolylpropionimidate (*syn*-9fh): Mp 143–144 °C; ^1H NMR (C_6D_6): δ 7.66–7.63 (d, 2H, $J = 8.9$ Hz), 7.57–7.55 (d, 2H, $J = 8.9$ Hz), 7.27–7.23 (m, 2H), 7.09–7.06 (t, 1H, $J = 7.6$ Hz), 6.86–6.85 (d, 1H, $J = 7.6$ Hz), 5.24–5.20 (t, 1H, $J = 10.3$ Hz), 4.47–4.42 (m, 1H), 4.31–4.24 (m, 1H), 4.16–4.12 (m, 1H), 2.16 (s, 3H), 1.54–1.53 (d, 3H, $J = 6.3$ Hz), 1.40 (s, 9H), 0.74–0.73 (d, 3H, $J = 6.3$ Hz), 0.52–0.51 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (C_6D_6): δ 176.8, 155.7, 150.1, 148.2, 141.4, 138.7, 129.1, 128.7, 125.0, 125.5, 124.2, 79.5, 72.8, 52.2, 45.6, 28.8, 21.7, 20.9, 20.4, 16.4; IR (neat): 3367, 2980, 2935, 1698, 1594, 1583, 1531, 1455, 1349, 1305, 1242, 1159, 1090, 1010, 938, 907, 855, 745, 705, 685 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{25}H_{34}N_3O_7S$ $[M + H]^+$, 520.2117. Found 520.2093.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-2-methyl-*N*-(4-nitrophenylsulfonyl)-3-*o*-tolylpropionimidate (*syn*-9gh): $[\alpha]_D^{23}$ +72.6 (57% ee, *c* 0.975, $CHCl_3$); Mp 120–121 °C; ^1H NMR (C_6D_6): δ 7.69–7.68 (d, 2H, $J = 8.6$ Hz), 7.61–7.60 (d, 1H, $J = 7.8$ Hz), 7.56–7.55 (d, 2H, $J = 8.6$ Hz), 7.23–7.20 (m, 1H), 6.98–6.95 (t, 1H, $J = 7.8$ Hz), 6.91–6.90 (d, 1H, $J = 7.8$ Hz), 5.45–5.41 (t, 1H, $J = 10.3$ Hz), 4.40–4.35 (m, 1H), 4.25–4.19 (m, 1H), 4.04–4.01 (d, 1H, $J = 10.3$ Hz), 2.47 (s, 3H), 1.67–1.66 (d, 3H, $J = 6.9$ Hz), 1.40 (s, 9H), 0.69–0.68 (d, 3H, $J = 6.3$ Hz), 0.33–0.31 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (C_6D_6): δ 176.8, 155.7, 150.0, 148.0, 140.0, 137.1, 131.0, 127.8, 127.1, 126.5, 124.1, 79.3, 72.5, 52.4, 45.3, 28.5, 20.8, 20.1, 19.8, 16.9; IR (neat): 3369, 2979, 2933, 1714, 1699, 1594, 1583, 1531, 1456, 1349, 1304, 1159, 1089, 1011, 907, 855, 745, 657 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{25}H_{34}N_3O_7S$ $[M + H]^+$, 520.2117. Found 520.2099. Chiral HPLC; Daicel Chiralcel OD-H; hexane/*i*PrOH = 9/1, flow rate = 0.3 mL min^{-1}: $t_R = 24.6$ min (Minor enantiomer obtained from R,R ligand), $t_R = 33.9$ min (Major enantiomer obtained from R,R ligand). The absolute configuration of the major product has not been determined.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-2-methyl-*N*-(4-nitrophenylsulfonyl)-3-(3-vinylphenyl)propionimidate (*syn*-9hh): Mp 117–118 °C; ^1H NMR (C_6D_6): δ 7.66–7.60 (m, 3H), 7.57–7.52 (m, 2H), 7.32–7.27 (m, 1H), 7.10–7.05 (m, 2H), 6.65 (dd, 1H, $J = 10.8$, 17.6 Hz), 5.84 (d, 1H, $J = 17.6$ Hz), 5.23 (t, 1H, $J = 10.2$ Hz), 5.16 (d, 1H, $J = 10.2$ Hz), 4.40 (quintet, 1H, $J = 6.2$ Hz), 4.25–4.10 (m, 2H), 1.55 (d, 3H, $J = 6.2$ Hz), 1.39 (s, 9H), 0.71 (d, 3H, $J = 6.2$ Hz), 0.50–0.42 (m, 3H); ^{13}C NMR (C_6D_6): δ 176.6, 155.6, 150.0, 147.9, 141.8, 138.6, 137.2, 129.3, 128.7, 128.5, 127.8, 126.4, 125.8, 124.1, 114.7, 79.4, 72.7, 57.1, 28.6, 20.8, 20.2, 16.4; IR (neat): 3734, 3367, 2980, 2938, 1717, 1698, 1594, 1582, 1531, 1455, 1349, 1304, 1159, 1090, 1010, 907, 855, 745, 684 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{26}H_{34}N_3O_7S$ $[M + H]^+$, 532.2117. Found 532.2093.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-3-(2-furyl)-2-methyl-*N*-(4-nitrophenylsulfonyl)propionimidate (*syn*-9ih): Mp 110–111 °C; ^1H NMR (C_6D_6): δ 7.75–7.72 (d, 2H, $J = 9.2$ Hz), 7.62–7.60 (d, 1H, $J = 9.2$ Hz), 6.99–6.98 (d, 1H, $J = 2.9$ Hz), 6.53–6.52 (d, 1H, $J = 2.9$ Hz), 6.02–6.01 (d, 1H, $J = 2.9$ Hz), 5.48–5.44 (t, 1H, $J = 10.3$ Hz), 4.61–4.56 (m, 1H), 4.23–4.21 (d, 2H, $J = 10.3$ Hz), 4.11–4.05 (m, 1H), 1.49–1.47 (d, 3H, $J = 6.9$ Hz), 1.40 (s, 9H), 0.76–0.74 (d, 3H, $J = 6.3$ Hz), 0.65–0.64 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (C_6D_6): δ 176.6, 155.6, 154.3, 150.1, 148.0, 142.3, 128.5, 127.9, 124.2, 110.7, 107.3, 100.5, 79.6, 72.9, 50.5, 44.4, 28.6, 20.7, 20.5, 15.7; IR (neat): 3368, 3107, 2981, 1716, 1597, 1583, 1532, 1455, 1350, 1306, 1238, 1160, 1093, 1011, 945, 908, 884, 856, 746, 685 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{22}H_{30}N_3O_8S$ $[M + H]^+$, 496.1754. Found 496.1776.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-2-methyl-*N*-(4-nitrophenylsulfonyl)-3-(2-thienyl)propionimidate (*syn*-9jh): Mp 126–128 °C; ^1H NMR (C_6D_6): δ 7.71–7.69 (d, 2H, $J = 8.6$ Hz), 7.58–7.55 (d, 2H, $J = 8.6$ Hz), 7.32–7.31 (d, 1H, $J = 2.3$ Hz), 6.73–6.70 (m, 2H), 5.53–5.49 (t, 1H, $J = 10.3$ Hz), 4.54–4.49 (m, 1H), 4.17–4.08 (m, 2H), 1.50–1.49 (d, 3H, $J = 6.9$ Hz), 1.39 (s, 9H), 0.74–0.73 (d, 3H, $J = 6.3$ Hz), 0.58–0.57 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (C_6D_6): δ 176.5, 155.4, 150.1, 147.9, 144.7, 127.9, 127.3, 125.1, 124.1, 79.6, 72.9, 51.6, 45.9, 28.6, 20.7, 20.2, 16.3; IR (neat): 3373, 2981, 1714, 1697, 1594, 1582, 1531, 1349, 1306, 1159, 1092, 1010, 908, 855, 745, 657 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{22}H_{30}N_3O_7S_2$ $[M + H]^+$, 512.1525. Found 512.1509.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-2-methyl-*N*-(4-nitrophenylsulfonyl)-3-(3-pyridyl)propionimidate (*syn*-9kh): Mp 175–177 °C; ^1H NMR (C_6D_6): δ 8.91 (s, 1H), 8.42–8.41 (d, 1H, $J = 4.0$ Hz), 7.64–7.54 (m, 5H), 6.80 (brs, 1H), 5.19–5.15 (t, 1H, $J = 10.3$ Hz), 4.41–4.36 (m, 2H), 4.12–4.08 (m, 1H), 1.46–1.44 (d, 3H, $J = 6.9$ Hz), 1.37 (s, 9H), 0.70–0.68 (d, 3H, $J = 6.3$ Hz), 0.49–0.48 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR ($CDCl_3$): δ 175.5, 155.0, 149.8, 149.2, 147.1, 135.8, 134.5, 127.9, 127.7, 127.5, 124.0, 123.5, 80.2, 73.3, 54.4, 44.6, 28.2, 20.8, 15.4; IR (neat): 3364, 3213, 2981, 2928, 1712, 1597, 1583, 1531, 1349, 1305, 1160, 1091, 1010, 906, 855, 746, 715, 684 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{23}H_{31}N_4O_7S$ $[M + H]^+$, 507.1913. Found 507.1932.

Isopropyl 2-Methyl-*N*-(4-nitrophenylsulfonyl)-3-phenyl-3-(*p*-toluenesulfonylamino)propionimidate (*syn*-9ch): Mp 159–160 °C; ^1H NMR (C_6D_6): δ 7.99–7.97 (d, 2H, $J = 9.2$ Hz), 7.63–7.61 (d, 2H, $J = 9.2$ Hz), 7.38–7.36 (d, 2H, $J = 8.0$ Hz), 6.88–6.86 (d, 2H, $J = 8.6$ Hz), 6.79–6.71 (m, 4H), 6.44–6.42 (d, 2H, $J = 8.6$ Hz), 5.02–4.96 (m, 1H), 4.71–4.67 (t, 1H, $J = 10.6$ Hz), 4.21–4.15 (m, 1H), 1.74 (s, 3H), 1.46–1.45 (d, 3H, $J = 6.3$ Hz), 1.02–1.01 (d, 3H, $J = 6.3$ Hz), 0.89–0.86 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR ($CDCl_3$): δ 177.1, 150.0, 147.0, 142.5, 137.7, 137.4, 128.9, 128.5, 128.0, 127.8, 127.1, 126.6, 124.2, 74.3, 61.7, 46.6, 29.7, 21.3, 21.1, 21.0, 14.7; IR (neat): 3289, 2983, 2922, 2853, 1594, 1583, 1531, 1456, 1349, 1301, 1160, 1090, 1057, 977, 909, 855, 812, 747, 701 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{26}H_{30}N_3O_7S_2$ $[M + H]^+$, 560.1525. Found 560.1550.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-3-cyclopropyl-2-methyl-*N*-(4-nitrophenylsulfonyl)propionimidate (*syn*-9nh): Mp 112–113 °C; ^1H NMR (C_6D_6): δ 7.82–7.80 (d, 2H, $J = 8.6$ Hz), 7.65–7.62 (d, 2H, $J = 8.6$ Hz), 4.74–4.66 (m, 1H), 4.05–4.03 (d, 1H, $J = 9.8$ Hz), 3.84–3.80 (m, 1H), 3.62–3.57 (m, 1H), 1.43 (s, 9H), 1.25–1.24 (d, 3H, $J = 6.9$ Hz), 1.00–0.90 (m, 1H), 0.90–0.89 (d, 3H, $J = 6.3$ Hz), 0.84–0.82 (d, 3H, $J = 6.3$ Hz), 0.51–0.44 (m, 1H), 0.44–0.37 (m, 2H), 0.36–0.32 (m, 1H); ^{13}C NMR (C_6D_6): δ 177.7, 156.3, 150.2, 148.4, 128.8, 128.1, 124.3, 79.1, 73.0, 57.2, 46.6, 28.8, 21.1, 16.5, 15.1, 6.1, 3.2; IR (neat): 3382, 2981, 2933, 1715, 1698, 1582, 1531, 1456, 1349, 1302, 1251, 1159, 1093, 1013, 908, 855, 746, 685 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{21}H_{32}N_3O_7S$ $[M + H]^+$, 470.1961. Found 470.1960.

Isopropyl 2-[(*tert*-Butoxycarbonylamino)phenylmethyl]-*N*-(4-nitrophenylsulfonyl)butanimidate (*syn*-9bi): Mp 156–157 °C; ^1H NMR (C_6D_6): δ 7.60–7.54 (m, 4H), 7.40–7.38 (d, 2H, $J = 7.7$ Hz), 7.11–7.08 (t, 2H, $J = 7.7$ Hz), 6.99–6.96 (t, 1H, $J = 7.7$ Hz), 5.34–5.30 (t, 1H, $J = 9.7$ Hz), 4.52–4.48 (m, 2H), 4.20–

4.16 (m, 1H), 1.98 (brs, 1H), 1.78 (brs, 1H), 1.39 (s, 9H), 1.10–1.07 (t, 3H, $J = 7.2$ Hz), 0.79–0.78 (d, 3H, $J = 6.3$ Hz), 0.57–0.55 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (C_6D_6): δ 174.9, 155.3, 149.8, 147.8, 141.2, 128.8, 128.3, 127.6, 123.9, 79.4, 72.5, 56.2, 51.0, 28.4, 23.6, 20.9, 20.4, 11.4; IR (neat): 3373, 2977, 2938, 1712, 1698, 1597, 1583, 1531, 1456, 1364, 1349, 1305, 1254, 1160, 1088, 1013, 911, 855, 745, 701 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{25}H_{34}N_3O_7S$ $[M + H]^+$, 520.2117. Found 520.2139.

Isopropyl 3-(*tert*-Butoxycarbonylamino)-3-cyclohexyl-2-methyl-*N*-(4-nitrophenylsulfonyl)propionimidate (*syn*-9th): Mp 191–192 °C; ^{1}H NMR (C_6D_6): δ 7.78 (d, 2H, $J = 8.2$ Hz), 7.59 (d, 2H, $J = 8.9$ Hz), 4.71 (quintet, 1H, $J = 6.2$ Hz), 4.27–4.20 (m, 1H), 3.94 (d, 1H, $J = 11.0$ Hz), 3.80–3.75 (m, 1H), 1.95 (d, 1H, $J = 12.4$ Hz), 1.78 (d, 1H, $J = 13.7$ Hz), 1.75–1.65 (m, 2H), 1.55 (d, 1H, $J = 13.7$ Hz), 1.45 (s, 9H), 1.40–1.32 (m, 1H), 1.26 (d, 3H, $J = 6.9$ Hz), 1.30–1.20 (m, 1H), 1.20–1.10 (m, 1H), 1.05–0.95 (m, 1H), 0.91 (d, 3H, $J = 6.2$ Hz), 0.90–0.87 (m, 1H), 0.82 (d, 3H, $J = 6.2$ Hz), 0.79–0.71 (m, 1H); ^{13}C NMR (C_6D_6): δ 178.2, 156.7, 150.4, 148.4, 129.2, 128.5, 128.3, 124.5, 79.3, 73.0, 59.0, 57.4, 43.2, 42.1, 31.9, 29.1, 27.6, 27.4, 27.2, 27.0, 21.2, 15.1; IR (neat): 3389, 2977, 2928, 2847, 1715, 1698, 1578, 1531, 1455, 1349, 1301, 1159, 1093, 992, 908, 855, 746, 684, 658 cm^{-1}; HRMS (DART): Exact mass calcd for $C_{24}H_{38}N_3O_7S$ $[M + H]^+$, 512.2430. Found 512.2422.

Procedure for the Conversion of Sulfonylimidate 9cc to Compound 17. To sulfonylimidate **9cc** (50 mg, 0.092 mmol) were added a mixture of isopropanol and H_2O (95/5, 0.5 mL) and concentrated H_2SO_4 (66 mg, ca. 7.0 equiv). The reaction mixture was stirred at 80 °C for 40 min. TLC analysis revealed that no reaction had occurred, then the mixture was heated to 100 °C and stirred for 3 h. After cooling to rt, the mixture was diluted by addition of CH_2Cl_2. A saturated aqueous solution of $NaHCO_3$ was added, and the mixture was extracted with CH_2Cl_2 three times. The organics were dried over anhydrous $MgSO_4$. Filtration and removal of solvents afforded compound **17** (46.1 mg, quant). The obtained compound **17** was found to be pure by ^{1}H NMR spectroscopy analysis in DMSO-d_6 (**17** was very hard to dissolve in any usual organic solvents except polar solvents such as DMSO).

***anti*-2-Methyl-3-phenyl-3-(*p*-toluenesulfonylamino)-*N*-(2,5-xylylsulfonyl)propionamide (17):** Mp 218–219 °C; ^{1}H NMR (DMSO-d_6): δ 12.08 (s, 1H), 8.67 (d, 1H, $J = 9.6$ Hz), 7.76 (s, 1H), 7.37–7.33 (m, 1H), 7.25–7.20 (m, 3H), 7.03–6.87 (m, 7H), 4.41 (t, 1H, $J = 9.9$ Hz), 2.72–2.60 (m, 1H), 2.50 (s, 3H), 2.34 (s, 3H), 2.18 (s, 3H), 0.59 (d, 3H, $J = 7.4$ Hz); ^{13}C NMR (DMSO-d_6): δ 172.2, 141.5, 138.3, 137.0, 135.4, 134.0, 133.9, 132.2, 130.3, 128.6, 127.8, 126.8, 126.3, 58.9, 46.6, 20.8, 20.3, 19.1, 14.7; IR (neat): 3251, 3063, 3032, 2979, 2926, 2878, 1693, 1655, 1647, 1638, 1617, 1599, 1560, 1542, 1493, 1457, 1382, 1341, 1288, 1223, 1201, 1163, 1123, 1087, 1062, 898, 849, 815, 766, 702, 667 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{25}H_{29}N_2O_5S_2$ $[M + H]^+$, 501.1518. Found 501.1538.

Procedure for the Conversion of Sulfonylimidate 9ba to Ester 18. To sulfonylimidate **9ba** (82.3 mg, 0190 mmol) were added a mixture of DMF and H_2O (95/5, 0.38 mL), and a solution of DBU in DMF (10 mol %, 30 µL). The mixture was stirred at rt for 33 h, and then diluted by addition of Et_2O. The mixture was washed with water 3 times, then dried over anhydrous Na_2SO_4. Filtration and removal of solvents afforded the crude product. Purification of the crude product was conducted by chromatography on SiO_2, to afford the desired ester **18** (50.4 mg, 90% yield).

Methyl *anti*-*N*-(Benzenesulfonyl)-3-(*tert*-butoxycarbonylamino)-2-methyl-3-phenylpropionimidate (9ba): Mp 99–100 °C; ^{1}H NMR ($CDCl_3$): δ 8.01 (d, 2H, $J = 7.4$ Hz), 7.59 (t, 1H, $J = 7.4$ Hz), 7.53 (t, 2H, $J = 7.7$ Hz), 7.35–7.25 (m, 5H), 6.01 (d, 1H, $J = 9.6$ Hz), 4.75 (t, 1H, $J = 10.2$ Hz), 4.07–3.96 (m, 1H), 3.75 (s, 3H), 1.35 (s, 9H), 1.03 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR ($CDCl_3$): δ 177.6, 154.6, 141.8, 140.2, 132.6, 128.7, 128.7, 127.8, 127.1, 126.5, 79.2, 58.2, 55.5, 45.1, 28.2, 14.8; IR (neat): 3381, 2977, 1716, 1602, 1508, 1455, 1392, 1365, 1304, 1246, 1154, 1090, 1057, 1002, 950, 881, 757, 734, 700, 688, 623 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{22}H_{29}N_2O_5S$ $[M + H]^+$, 433.1797. Found 433.1811.

***tert*-Butyl *anti*-2-(Methoxycarbonyl)-1-phenylpropylcarbamate (18):** Mp 89–90 °C; ^{1}H NMR ($CDCl_3$): δ 7.34–7.28 (m, 2H), 7.27–7.20 (m, 3H), 5.78 (s, 1H), 4.83 (s, 1H), 3.58 (s, 3H), 2.92 (s, 1H), 1.42 (s, 9H), 1.23 (d, 3H, $J = 6.2$ Hz); ^{13}C NMR ($CDCl_3$): δ 175.3, 155.4, 127.3, 126.6, 126.2, 79.4, 51.6, 45.2, 28.3, 15.3; IR (neat): 3428, 3360, 2977, 2356, 1716, 1497, 1455, 1434, 1365, 1289, 1245, 1168, 1085, 1051, 1005, 879, 756, 701, 585 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{16}H_{24}NO_4$ $[M + H]^+$, 294.1705. Found 294.1696.

Procedure for Red-Al Reduction of Sulfonylimidates 9bc and 9cc to Aldehydes 19a and 19b. The procedure for the conversion of **9bc** to **19a** is as follows. A solution of **9bc** (100 mg, 0.205 mmol) in 2 mL of THF was cooled to −70 °C, and then Red-Al (65% w/w toluene solution, 385 µL, 7.0 equiv) was added slowly lest the temperature should increase. The mixture was stirred at −70 °C for 18 h, and the reaction was quenched by addition of MeOH (0.1 mL) at −70 °C. The mixture was stirred for 5 min at that temperature, and H_2O was added. The temperature was allowed to increase to rt, and AcOEt and a saturated aqueous solution of NH_4Cl were added. After filtration, the obtained filtrate was extracted with AcOEt three times, and the organics were dried over anhydrous Na_2SO_4. Filtration and removal of solvents afforded the crude product. Purification of the crude product was conducted by chromatography on neutral SiO_2, to afford the aldehyde **19a** (46.9 mg, 87% yield). Aldehyde **19b** was obtained by following the same procedure mentioned above (83% yield).

***tert*-Butyl *anti*-2-Formyl-1-phenylpropylcarbamate (19a):** Mp 82–83 °C; ^{1}H NMR ($CDCl_3$): δ 9.66 (d, 1H, $J = 2.3$ Hz), 7.37–7.22 (m, 5H), 5.28 (s, 1H), 4.78 (s, 1H), 2.81 (s, 1H), 1.39 (s, 9H), 1.02 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR ($CDCl_3$): δ 203.3, 155.2, 139.9, 128.7, 127.7, 126.8, 79.9, 52.1, 28.2, 11.8; IR (neat): 3343, 2978, 2933, 2817, 2723, 1716, 1699, 1519, 1507, 1455, 1392, 1366, 1288, 1249, 1169, 1086, 1002, 755, 701 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{15}H_{22}NO_3$ $[M + H]^+$, 264.1599. Found 264.1606.

***anti*-2-Methyl-3-phenyl-3-(*p*-toluenesulfonylamino)propanal (19b):** Mp 137–138 °C; ^{1}H NMR ($CDCl_3$): δ 9.64 (d, 1H, $J = 2.8$ Hz), 7.47 (d, 2H, $J = 7.9$ Hz), 7.15–6.96 (m, 7H), 5.90 (d, 1H, $J = 8.5$ Hz), 4.54 (t, 1H, $J = 8.5$ Hz), 2.84–2.75 (m, 1H), 2.30 (s, 3H), 0.96 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR ($CDCl_3$): δ 203.2, 143.0, 137.8, 137.2, 129.2, 128.4, 127.6, 127.0, 127.0, 59.1, 51.9, 21.3, 11.8; IR (neat): 3268, 3068, 3030, 2972, 2926, 2872, 2727, 1724, 1598, 1495, 1456, 1325, 1185, 1160, 1090, 1045, 914, 812, 761, 702, 670, 566, 547 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{17}H_{20}NSO_3$ $[M + H]^+$, 318.1184. Found 318.1169.

Procedure for Direct Formation of Ester 21 from Benzaldehyde and Sulfonylimidate 8l. To a solution of benzaldehyde (60.9 µL, 0.6 mmol) and DBU (18.3 mg, 0.12 mmol) in 0.2 mL of DMF was added 2,5-xylylsulfonylamide (11.1 mg, 0.06 mmol). To

the mixture was slowly added over 32 h a solution of sulfonylimidate **8l** (183.8 mg, 0.72 mmol) in 1 mL of DMF. After completion of slow addition, the mixture was stirred at rt for further 46 h (total 78 h), and then diluted by addition of Et_2O. The mixture was washed with water 3 times, then dried over anhydrous Na_2SO_4. Filtration and removal of solvents afforded the crude product. Purification of the crude product was conducted by chromatography on SiO_2, to afford the desired ester **21** (diastereomers mixture, 196.2 mg, 90% yield, anti/syn = 87/13).

Methyl *anti*-2-Methyl-3-phenyl-3-(2,5-xylylsulfonylamino)-propionate (21): Mp 116–117 °C; ^{1}H NMR ($CDCl_3$): δ 7.49 (s, 1H), 7.13–7.09 (m, 3H), 7.06 (d, 1H, $J = 7.4$ Hz), 7.02–6.93 (m, 3H), 6.03 (d, 1H, $J = 8.5$ Hz), 4.44 (t, 1H, $J = 7.7$ Hz), 3.60 (s, 3H), 2.90–2.80 (m, 1H), 2.47 (s, 3H), 2.20 (s, 3H), 1.09 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR ($CDCl_3$): δ 175.0, 138.7, 138.3, 135.6, 133.4, 132.8, 132.0, 129.5, 128.2, 127.6, 126.5, 60.4, 51.9, 45.8, 20.5, 19.7, 15.3; IR (neat): 3292, 2983, 2953, 2878, 1734, 1717, 1540, 1507, 1489, 1456, 1436, 1322, 1278, 1206, 1158, 1063, 916, 818, 766, 751, 701, 616, 594 cm^{-1}; HRMS (FAB): Exact mass calcd for $C_{19}H_{24}NSO_4$ $[M + H]^+$, 362.1426. Found 362.1419.

Crystallographic data reported in this manuscript have been deposited with Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-660388 (**8a**), -660391 (*syn*-**9aa**), -660389 (*anti*-**9bc**), -660390 (*anti*-**9cc**), -660392 (*syn*-**9cc**), -716446 (*anti*-**9ch**), -716444 (*syn*-**9th**), -716445 (*syn*-**9bh**), and -660393 (**21**). Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, U.K.; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

Supporting Information

Kinetic study. This material is available free of charge on the web at http://www.csj.jp/journals/bcsj/.

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