Synthesis H. E. Bartrum et al. Paper

Highly Diastereoselective and Irreversible Aldol Reactions of *N*-Sulfonylimidates

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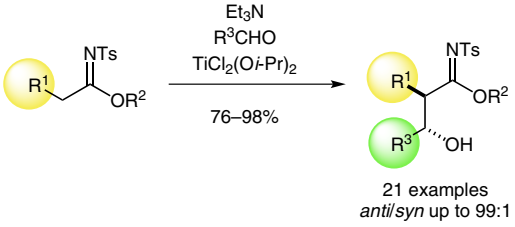
Dedicated to the memory of Prof. Jean Normant, an exceptional and inspiring supervisor



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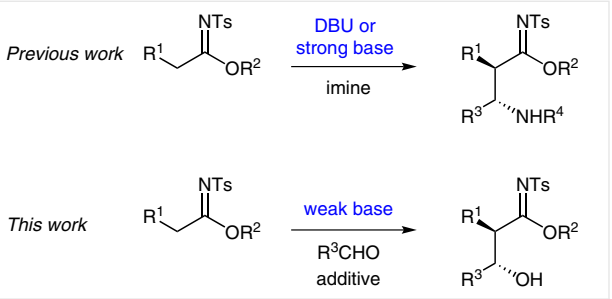
Abstract A mild method for the aldolization of *N*-sulfonylimidates was developed. The reaction proceeds in excellent diastereoselectivity to provide a range of useful β-hydroxyimidates in high yield. The innate reversibility of the reaction is suppressed by the use of a titanium complex as a Lewis acid.

Key words aldolization, imidates, titanium, stereoselectivity, sulfonyl

N-Sulfonylimidates represent an important class of organic derivatives with a large variety of applications: they have received interest as pro-drug candidates and pharmacophores and been employed as precursors to active drug molecules featuring ester or sulfonamide functional groups.[1] They also represent versatile synthetic building blocks and are widely utilized as intermediates for the synthesis of heterocycles.[2]

Despite this synthetic utility and the variety of existing methods for the formation of *N*-sulfonylimidates, limited attention has been devoted to their functionalization, particularly at the α-position. Kobayashi et al. have investigated the catalytic Mannich-type reaction of alkyl *N*-sulfonylimidates with imines to give β-amino imidates in good to excellent yields and with good diastereocontrol.[3] Subsequently, Barbas III et al. developed an organocatalytic enantioselective Michael addition reaction of *N*-sulfonylimidates to α,β-unsaturated aldehydes: the reaction proceeded with low diastereoselectivity and in moderate yield.[4] Strikingly, the more obvious and synthetically useful direct reaction with an aldehyde has not been reported to date (Scheme 1). We have recently studied the aldolization of sulfinylimidates, and found that the high reversibility of the reaction could be overcome by using a titanium Lewis acid.[5] We wondered whether the parent sulfonylimidates would show a similar pattern of reactivity. We report herein the successful aldol reaction of sulfonylimidates under mild basic conditions, with the aid of titanium salts to stabilize the products and prevent retro-aldolization.[5]



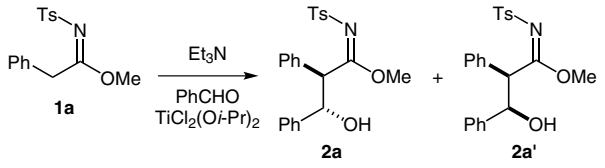
Scheme 1 Context of this work

The required *N*-sulfonylimidates **1a–f** were synthesized from the corresponding imidate hydrochloride salts.[6] In general, synthesis *via* the ortho ester intermediate[6b,7] gave higher yields of the desired sulfonylimidate than direct conversion from the imidate hydrochloride.[3a] However, the direct method was necessary to provide access to the bulkier isopropyl sulfonylimidate **1c**, for which the ortho ester intermediate could not be formed, presumably as a result of steric congestion.

The reaction of methyl 2-phenyl-*N*-tosylacetimidate (**1a**) with benzaldehyde was first studied (Table 1). Treatment of *N*-sulfonylimidate **1a** with various bases including triethylamine (entry 1), followed by addition of benzaldehyde resulted only in recovery of unreacted starting material, even after prolonged reaction times.[8] These results were comparable to those obtained during previous studies of the aldolization of *N*-sulfinylimidates and highlight the inherent reversibility of the reaction.[9] Subsequently, the treatment of *N*-sulfonylimidate **1a** and benzaldehyde with

three equivalents of $TiCl_2(Oi\text{-}Pr)_2$ in combination with triethylamine pleasingly afforded the product **2a** in excellent yield and as a single diastereoisomer (entry 2). Further optimization showed that the amount of base and $TiCl_2(Oi\text{-}Pr)_2$ utilized could be reduced to three and two equivalents, respectively, without any detrimental effect on either the yield or selectivity of the reaction (entry 4). However, attempts to further reduce the amount of $TiCl_2(Oi\text{-}Pr)_2$ resulted in incomplete conversion, lower diastereoselectivity (entry 5), and eventually complete retardation of the reaction (entry 6). In addition, quite disappointingly, attempts to change the isopropoxy group on titanium by various chiral diols failed to produce the desired product.

Table 1 Optimization of Conditions for the Aldolization Reaction[a]



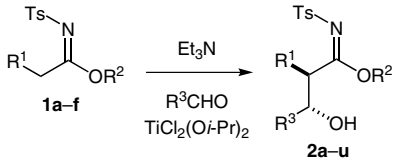
Entry	Et_3N (equiv)	[Ti] (equiv)[b]	Time (h)	Conv. (%)[c,d]	dr (**2a**/**2a′**)
1	4	0	18	0	–
2	4	3	2	100 (95)[d]	>99:1
3	3	2.5	2	100 (95)[d]	>99:1
4	3	2	2	100 (95)[d]	>99:1
5[e]	3	1.5	24	70	96:4
6	3	0.5	48	0	–

[a] Reaction conditions: PhCHO (1.5 equiv), CH_2Cl_2.
[b] [Ti] = $TiCl_2(Oi\text{-}Pr)_2$.
[c] Conversion determined by ^1H NMR analysis of the crude reaction mixture.
[d] Yield given in parentheses.
[e] PhCHO (1.2 equiv) used.

The scope of the reaction was next investigated (Table 2). To determine the influence of the OR^2 group of the imidate on the diastereoselectivity of the reaction, the reactivities of methyl, ethyl, and isopropyl imidates (**1a**, **1b**, and **1c**, respectively) were compared. Reaction with benzaldehyde was highly selective, in all cases yielding a single diastereoisomer in excellent yield (entries 1–3). The reactions utilizing 2-thiophenecarboxaldehyde were slightly less selective and indicated that there was no significant difference in the diastereoselectivity observed for the three imidates (entries 4–6). This suggests that the steric bulk of the OR^2 group is not a determining factor in the stereochemical outcome of the reaction. Variation of the other substituent on the imidate (R^1) was successfully tolerated, and reactions with imidates **1d** (R^1 = *p*-$MeOC_6H_4$) and **1e** (R^1 = *p*-FC_6H_4) proceeded with diastereoselectivities and efficiencies comparable to the reactions with imidate **1a** (R^1 = Ph), to give similar yields of the desired products **2** (entries 13–19). The chloroalkyl-substituted imidate **1f** (R^1 = Cl) also reacted with high diastereoselectivity, although the yields of the aldol products were slightly lower due to the presence of an unidentified byproduct (entries 20 and 21). A range of aromatic, heteroaromatic, unsaturated and tertiary alkyl aldehydes were well tolerated by the reaction conditions. The reaction of aldehydes bearing electron withdrawing or electron donating groups on the aromatic ring were equally efficient providing the corresponding products in high yields (entries 7 and 8).

In addition, more sterically hindered aromatic aldehydes, including those bearing *ortho* substituents on the aromatic ring, reacted well under these conditions (Table 2, entry 14), as did those bearing *meta* or *para* substituents. Aromatic aldehydes containing halide substituents (F, Br) on the ring were also well tolerated and no erosion of the

Table 2 Scope of the Sulfonylimidate Aldolization[a,b]

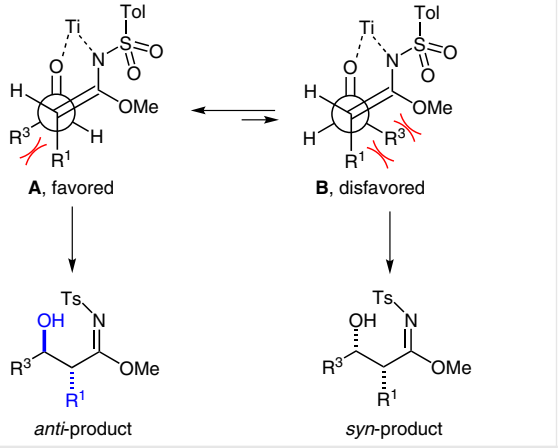


Entry	**2**	R^1	R^2	R^3	dr	Yield (%)[c]
1	**2a**	Ph	Me	Ph	>99:1	95
2	**2b**	Ph	Et	Ph	>99:1	96
3	**2c**	Ph	*i*-Pr	Ph	>99:1	93
4	**2d**	Ph	Me	2-thienyl	93:7	94[d]
5	**2e**	Ph	Et	2-thienyl	96:4	96[d]
6	**2f**	Ph	*i*-Pr	2-thienyl	93:7	94[d]
7	**2g**	Ph	Me	*p*-$NO_2C_6H_4$	99:1	97
8	**2h**	Ph	Me	*m*-$MeOC_6H_4$	99:1	98
9	**2i**	Ph	Me	*m*-FC_6H_4	99:1	95
10	**2j**	Ph	Me	2-furyl	98:2	93
11	**2k**	Ph	Me	PhCH=CH	83:17	76
12	**2l**	Ph	Me	*t*-Bu	>99:1	96
13	**2m**	*p*-$MeOC_6H_4$	Me	Ph	99:1	98
14	**2n**	*p*-$MeOC_6H_4$	Me	*o*-MeC_6H_4	>99:1	97
15	**2o**	*p*-$MeOC_6H_4$	Me	*p*-BrC_6H_4	98:2	95
16	**2p**	*p*-$MeOC_6H_4$	Me	1-naphthyl	96:4	95[d]
17	**2q**	*p*-FC_6H_4	Me	Ph	99:1	97
18	**2r**	*p*-FC_6H_4	Me	*m*-$MeOC_6H_4$	98:2	94
19	**2s**	*p*-FC_6H_4	Me	*t*-Bu	>99:1	96
20	**2t**	Cl	Me	Ph	99:1	81
21	**2u**	Cl	Me	*m*-FC_6H_4	99:1	79

[a] Reaction conditions: **1** (1 equiv), R^3CHO (1.5 equiv), Et_3N (3 equiv), CH_2Cl_2, $TiCl_2(Oi\text{-}Pr)_2$ (2 equiv), r.t., 1–2 h.
[b] Only the major diastereoisomer is depicted.
[c] Yield of a single isolated diastereoisomer (>99:1).
[d] Yield of the mixture of diastereoisomers.

high diastereoselectivity was observed (entries 9, 15 and 21). Heterocyclic aldehydes were compatible with the reaction conditions, as were α,β-unsaturated aldehydes and naphthaldehyde (entries 4–6, 10, 11, and 16). The aldolization was also successful when using pivaldehyde, which gave the corresponding product in excellent yield and excellent diastereoselectivity (entries 12 and 19), but not with enolizable aldehydes.

The relative *anti* configuration of the major diastereoisomer was secured by X-ray crystallographic analysis of crystalline **2a**.[10] This *anti* configuration is in agreement with previous reports on α-functionalization of sulfonylimidates.[3a,4] This structure also confirmed the *E* geometry of the *N*-tosylimidates that we previously observed in the *N*-sulfinylimidate series.[5] A rationalization of this stereochemical outcome is that the deprotonation of the *N*-sulfonylimidate occurs selectively to form the preferred *E*-enolate (with the bulky N–Ts group and the R^1 group on opposite sides of the C–C bond).[3a] Due to the steric repulsions between the R^3 group of the aldehyde and both the R^1 and the OR^2 group of the imidate in transition state **B**, it is envisaged that the reaction occurs *via* transition state **A** to give the *anti* product (Scheme 2). In analogy to work conducted with the *N*-sulfinylimidate,[5] it is likely that titanium plays an important role not only in templating the reaction, but also in remaining coordinated to the final product, thus preventing the retro-aldolization.



Scheme 2 Stereochemical rationalization

In summary, we have successfully developed a mild and efficient method for the previously unreported and challenging aldolization of *N*-sulfonylimidates. The reaction was found to be highly efficient and in most cases proceeded with high levels of stereocontrol to give diastereomerically pure products.

Reactions were carried out under argon in glassware flame-dried under vacuum. Standard inert atmosphere techniques were used in handling all air- and moisture-sensitive reagents. Anhydrous CH_2Cl_2 was obtained by filtration through activated alumina. A 1 M solution of $TiCl_2(Oi\text{-}Pr)_2$ in anhydrous CH_2Cl_2 was made directly prior to use (from freshly distilled $TiCl_4$ and $Ti(Oi\text{-}Pr)_4$).[11] Et_3N was distilled from CaH_2 and stored over KOH. All aldehydes were distilled before use. TLC was performed on (0.2 mm) silica gel aluminum backed plates, which were visualized by exposure to UV light followed by staining with basic $KMnO_4$ solution. Silica gel (0.040–0.063 mm) was employed for flash column chromatography. Melting points are uncorrected. An FT-IR spectrometer was used to record IR spectra. NMR spectra were recorded at 298 K, at the frequency stated; samples were prepared as dilute solutions in $CDCl_3$. Chemical shifts are expressed in ppm; the solvent residual peaks are used as the internal standard ($CDCl_3$: δ_H = 7.26, δ_C = 77.16). Assignments of ^{13}C NMR spectra were made with the aid of DEPT experiments. Mass spectra were recorded by using ESI techniques. HRMS was carried out on an Orbitrap apparatus (ESI).

3-Hydroxy-*N*-tosylimidates 2 by Aldol Reaction of *N*-Tosylimidates 1; General Procedure

Et_3N (49 µL, 0.354 mmol, 3 equiv) was added dropwise to a stirred solution of one of the *N*-sulfonylimidates **1a–f** (0.118 mmol, 1 equiv) in CH_2Cl_2 (1.5 mL) under argon at r.t. A preformed solution of aldehyde R^3CHO (0.177 mmol, 1.5 equiv) and $TiCl_2(Oi\text{-}Pr)_2$ (0.236 mL, 0.236 mmol, 2 equiv, 1 M solution in CH_2Cl_2) was then added dropwise *via* a cannula or syringe over approximately 10 min, and the resulting solution was stirred at r.t. until TLC analysis indicated the absence of starting material (typically 1–2 h). The reaction mixture was poured into a mixture of ice and sat. aq NaCl and the organic layer was separated. The aqueous layer was extracted (3 × CH_2Cl_2) and the combined organic extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography to give the corresponding pure β-hydroxyimidate **2a–u**.

Methyl 3-Hydroxy-2,3-diphenyl-*N*-tosylpropanimidate (2a)

Yield: 46 mg (95%); colorless solid; mp 185–186 °C; R_f = 0.3 (EtOAc–pentane, 3:7).

IR (neat): 3478, 3029, 3010, 2955, 2928, 1611, 1596, 1492, 1451, 1438, 1284, 1248, 1161, 1146, 1086, 1042, 1018 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.4 Hz, 2 H), 7.31–7.17 (m, 12 H), 5.35 (d, *J* = 10.4 Hz, 1 H), 5.23 (d, *J* = 10.4 Hz, 1 H), 3.86 (s, 3 H), 3.07 (br s, 1 H), 2.43 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9 (C=N), 143.5 (C), 141.3 (C), 139.1 (C), 134.2 (C), 129.7 (CH), 129.5 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.1 (CH), 127.0 (CH), 126.8 (CH), 76.9 (CH), 58.4 (CH), 56.2 (CH_3), 21.7 (CH_3).

ESI-MS: *m*/*z* = 409.9 $[M + H]^+$

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{24}NO_4S$: 410.1420; found: 410.1420; *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{22}NNaO_4S$: 432.1240; found: 432.1240.

Ethyl 3-Hydroxy-2,3-diphenyl-*N*-tosylpropanimidate (2b)

Yield: 48 mg (96%); colorless needles; mp 156–157 °C; R_f = 0.3 (EtOAc–pentane, 3:7).

IR (neat): 3501, 3067, 2996, 2939, 1610, 1594, 1572, 1312, 1278, 1248, 1143, 1090, 1020 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.4 Hz, 2 H), 7.22–7.09 (m, 12 H), 5.24 (d, *J* = 10.2 Hz, 1 H), 5.13 (d, *J* = 10.2 Hz, 1 H), 4.27–4.10 (m, 2 H), 3.08 (br s, 1 H), 2.34 (s, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.3 (C=N), 143.4 (C), 141.4 (C), 139.2 (C), 134.4 (C), 129.7 (CH), 129.5 (CH), 128.5 (CH), 128.4 (CH), 128.2 (CH), 127.9 (CH), 126.8 (CH), 126.7 (CH), 77.0 (CH), 65.4 (CH_2), 58.5 (CH), 21.7 (CH_3), 13.7 (CH_3).

ESI-MS: *m*/*z* = 446.2 $[M + Na]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{26}NO_4S$: 424.1577; found: 424.1576; *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{25}NNaO_4S$: 446.1396; found: 446.1395.

Isopropyl 3-Hydroxy-2,3-diphenyl-*N*-tosylpropanimidate (2c)

Yield: 48 mg (93%); colorless needles; mp 113–114 °C; R_f = 0.2 (EtOAc–pentane, 2:8)

IR (neat): 3482, 3031, 2989, 2911, 1589, 1497, 1454, 1295, 1282, 1149, 1090, 1051, 1037 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.0 Hz, 2 H), 7.30–7.24 (m, 4 H), 7.23–7.16 (m, 8 H), 5.30 (d, *J* = 10.4 Hz, 1 H), 5.19 (d, *J* = 10.4 Hz, 1 H), 5.16–5.10 (m, 1 H), 3.10 (br s, 1 H), 2.42 (s, 3 H), 1.39 (d, *J* = 6.0 Hz, 3 H), 1.24 (d, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7 (C=N), 143.3 (C), 141.5 (C), 139.4 (C), 134.5 (C), 129.6 (CH), 129.5 (CH), 128.4 (CH), 128.1 (CH), 127.8 (CH), 126.7 (CH), 77.0 (CH), 73.2 (CH), 58.5 (CH_3), 21.6 (CH_3), 21.3 (CH_3), 21.2 (CH_3).

ESI-MS: *m*/*z* = 437.9 $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{28}NO_4S$: 438.1733; found: 438.1735; *m*/*z* $[M + Na]^+$ calcd for $C_{25}H_{27}NNaO_4S$: 460.1553; found: 460.1555.

Methyl 3-Hydroxy-2-phenyl-3-(2-thienyl)-*N*-tosylpropanimidate (2d)

Yield: 46 mg (94%); colorless needles; R_f = 0.2 (EtOAc–pentane, 3:7).

IR (neat): 3497, 3452, 2954, 2923, 1610, 1436, 1284, 1255, 1148, 1090, 1039, 1016 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.2 Hz, 2 H), 7.56–7.49 (m, 2 H), 7.31–7.20 (m, 5 H), 7.06 (dd, *J* = 4.4, 1.6 Hz, 1 H), 6.74–6.72 (m, 2 H), 5.44 (d, *J* = 10.4 Hz, 1 H), 5.31 (d, *J* = 10.4 Hz, 1 H), 3.75 (s, 3 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.2 (C=N), 145.0 (C), 143.6 (C), 139.0 (C), 134.2 (C), 129.5 (CH), 128.7 (CH), 128.2 (CH), 127.0 (CH), 126.8 (CH), 125.3 (CH), 125.2 (CH), 72.0 (CH), 58.5 (CH), 56.2 (CH_3), 21.7 (CH_3).

ESI-MS: *m*/*z* = 437.8 $[M + Na]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{22}NO_4S_2$: 416.0984; found: 416.0983; *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{21}NNaO_4S_2$: 438.0804; found: 438.0805.

Ethyl 3-Hydroxy-2-phenyl-3-(2-thienyl)-*N*-tosylpropanimidate (2e)

Yield: 48 mg (96%); isolated as a 96:4 mixture of diastereoisomers; colorless needles; R_f = 0.4 (EtOAc–pentane, 3:7).

IR (neat): 3465, 2992, 2953, 2922, 1590, 1285, 1256, 1117, 1090, 1019 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.0 Hz, 2 H), 7.31–7.30 (m, 2 H), 7.29–7.16 (m, 5 H), 7.05 (dd, *J* = 4.4, 1.2 Hz, 1 H), 6.74–6.73 (m, 2 H), 5.43 (d, *J* = 10.6 Hz, 1 H), 5.28 (d, *J* = 10.6 Hz, 1 H), 4.26–4.00 (m, 2 H), 2.34 (s, 3 H), 1.24 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.6 (C=N), 145.2 (C), 143.5 (C), 139.1 (C), 134.4 (C), 129.5 (CH), 128.7 (CH), 128.2 (CH), 126.9 (CH), 126.8 (CH), 125.2 (CH), 125.1 (CH), 72.2 (CH), 65.4 (CH_2), 58.5 (CH), 21.7 (CH_3), 13.6 (CH_3).

ESI-MS: *m*/*z* = 452.2 $[M + Na]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{24}NO_4S_2$: 430.1141; found: 430.1140; *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{23}NNaO_4S_2$: 452.0960; found: 452.0961.

Isopropyl 3-Hydroxy-2-phenyl-3-(2-thienyl)-*N*-tosylpropanimidate (2f)

Yield: 49 mg (94%); isolated as a 93:7 mixture of diastereoisomers; colorless needles; R_f = 0.2 (EtOAc–pentane, 2:8).

IR (neat): 3471, 3067, 3027, 2953, 2928, 1615, 1597, 1508, 1442, 1285, 1248, 1226, 1147, 1089, 1019 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.0 Hz, 2 H), 7.30–7.27 (m, 2 H), 7.22–7.12 (m, 5 H), 7.06–7.04 (m, 1 H), 6.74–6.70 (m, 2 H), 5.39 (d, *J* = 10.2 Hz, 1 H), 5.26 (d, *J* = 10.2 Hz, 1 H), 5.02 (*app* pent., *J* = 6.2 Hz, 1 H), 3.00 (br s, 1 H), 2.34 (s, 3 H), 1.26 (d, *J* = 6.2 Hz, 3 H), 1.20 (d, *J* = 6.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.0 (C=N), 145.3 (C), 143.3 (C), 139.3 (C), 134.5 (C), 129.6 (CH), 129.5 (CH), 128.6 (CH), 128.1 (CH), 126.8 (CH), 126.7 (CH), 125.1 (CH), 125.0 (CH), 73.2 (CH), 72.2 (CH), 58.5 (CH), 21.6 (CH_3), 21.2 (CH_3), 21.1 (CH_3).

ESI-MS: *m*/*z* = 443.8 $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{26}NO_4S_2$: 444.1297; found: 444.1294; *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{25}NNaO_4S_2$: 466.1117; found: 466.1116.

Methyl 3-Hydroxy-3-(4-nitrophenyl)-2-phenyl-*N*-tosylpropanimidate (2g)

Yield: 52 mg (97%); colorless needles; mp 184–185 °C; R_f = 0.15 (EtOAc–pentane, 3:7).

IR (neat): 3483, 2955, 2918, 1594, 1519, 1496, 1436, 1348, 1310, 1288, 1246, 1188, 1091, 1055, 1018 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 8.8 Hz, 2 H), 7.76 (d, *J* = 8.0 Hz, 2 H), 7.29–7.19 (m, 6 H), 7.15–7.14 (m, 3 H), 5.26 (d, *J* = 10.6 Hz, 1 H), 5.18 (d, *J* = 10.6 Hz, 1 H), 3.80 (s, 3 H), 3.47 (br s, 1 H), 2.36 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.0 (C=N), 148.6 (C), 147.7 (C), 143.8 (C), 138.6 (C), 133.3 (C), 129.7 (CH), 129.6 (CH), 128.9 (CH), 128.6 (CH), 127.7 (CH), 126.9 (CH), 123.6 (CH), 76.0 (CH), 58.5 (CH), 56.4 (CH_3), 21.7 (CH_3).

ESI-MS: *m*/*z* =454.8 $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{23}N_2O_6S$: 455.1271; found: 455.1269; *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{22}N_2NaO_6S$: 477.1090; found: 477.1089.

Methyl 3-Hydroxy-3-(3-methoxyphenyl)-2-phenyl-*N*-tosylpropanimidate (2h)

Yield: 51 mg (98%); colorless needles; mp 155–156 °C; R_f = 0.3 (EtOAc–pentane, 3:7).

IR (neat): 3470, 3021, 2958, 2904, 1608, 1594, 1493, 1455, 1437, 1329, 1285, 1266, 1246, 1148, 1087, 1037, 1016 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.4 Hz, 2 H), 7.24–7.22 (m, 4 H), 7.15–7.10 (m, 3 H), 7.05 (t, *J* = 8.0 Hz, 1 H), 6.76 (d, *J* = 7.6 Hz, 1 H), 6.68–6.63 (m, 2 H), 5.26 (d, *J* = 10.4 Hz, 1 H), 5.12 (d, *J* = 10.4 Hz, 1 H), 3.78 (s, 3 H), 3.62 (s, 3 H), 2.93 (br s, 1 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9 (C=N), 159.7 (C), 143.5 (C), 142.9 (C), 139.1 (C), 134.3 (C), 129.8 (CH), 129.6 (CH), 129.5 (CH), 128.6 (CH), 128.0 (CH), 126.9 (CH), 119.0 (CH), 114.0 (CH), 112.2 (CH), 76.8 (CH), 58.3 (CH), 56.2 (CH_3), 55.3 (CH_3), 21.7 (CH_3).

ESI-MS: *m*/*z* = 439.9 $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{26}NO_5S$: 440.1526; found: 440.1527; *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{25}NNaO_5S$: 462.1345; found: 462.1347.

Methyl 3-(3-Fluorophenyl)-3-hydroxy-2-phenyl-*N*-tosylpropanimidate (2i)

Yield: 48 mg (95%); colorless needles; mp 180–181 °C; R_f = 0.3 (EtOAc–pentane, 3:7)

IR (neat): 3467, 2953, 2927, 1595, 1490, 1451, 1438, 1284, 1267, 1256, 1148, 1118, 1045, 1019 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.0 Hz, 2 H), 7.23–7.18 (m, 4 H), 7.15–7.05 (m, 4 H), 6.91–6.80 (m, 2 H), 6.79–6.76 (m, 1 H), 5.21 (d, *J* = 10.4 Hz, 1 H), 5.13 (d, *J* = 10.4 Hz, 1 H), 3.77 (s, 3 H), 3.07 (br s, 1 H), 2.34 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.5 (C=N), 164.0 (C), 150.2 (C, d, *J* = 226), 144.0 (C, d, *J* = 7), 143.6 (C), 133.8 (C), 130.0 (CH, d, *J* = 8), 129.7 (CH), 129.5 (CH), 128.7 (CH), 128.2 (CH), 126.9 (CH), 122.4 (CH, d, *J* = 3), 115.1 (CH, d, *J* = 21), 113.8 (CH, d, *J* = 21.8), 76.2 (CH, d, *J* = 2), 58.3 (CH), 56.2 (CH_3), 21.7 (CH_3)

^{19}F NMR (377 MHz, $CDCl_3$): δ = –112.7.

ESI-MS: *m*/*z* = 427.9 $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{23}FNO_4S$: 428.1326; found: 428.1328; *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{22}FNNaO_4S$: 450.1145; found: 450.1149.

Methyl 3-(2-Furyl)-3-hydroxy-2-phenyl-*N*-tosylpropanimidate (2j)

Yield: 44 mg (93%); colorless needles; mp 189–190 °C; R_f = 0.3 (EtOAc–pentane, 3:7).

IR (neat): 3472, 3033, 2953, 2932, 1610, 1595, 1496, 1439, 1310, 1283, 1254, 1149, 1139, 1087, 1017 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.0 Hz, 2 H), 7.30–7.13 (m, 8 H), 6.09 (dd, *J* = 3.2, 2.0 Hz, 1 H), 6.01 (d, *J* = 3.2 Hz, 1 H), 5.49 (d, *J* = 11.0 Hz, 1 H), 5.21 (d, *J* = 11.0 Hz, 1 H), 3.75 (3 H, s), 2.84 (1 H, br s), 2.35 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.2 (C=N), 153.2 (C), 143.6 (C), 142.6 (CH), 139.0 (C), 134.1 (C), 129.5 (CH), 129.3 (CH), 128.7 (CH), 128.1 (CH), 127.0 (CH), 110.3 (CH), 108.3 (CH), 69.6 (CH), 56.2 (CH), 55.7 (CH_3), 21.7 (CH_3).

ESI-MS: *m*/*z* = 421.8 $[M + Na]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{22}NO_5S$: 400.1213; found: 400.1213; *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{21}NNaO_5S$: 422.1032; found: 422.1033.

Methyl 3-Hydroxy-2,5-diphenyl-*N*-tosylpent-4-enimidate (2k)

Yield: 38 mg (76%); pale yellow oil; R_f = 0.4 (EtOAc–pentane, 3:7).

IR (neat): 3487, 3059, 3029, 2951, 1593, 1495, 1440, 1288, 1265, 1150, 1090, 1017 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.0 Hz, 2 H), 7.38–7.36 (m, 2 H), 7.25–7.10 (m, 10 H), 6.49 (dd, *J* = 16.0, 0.4 Hz, 1 H), 5.98 (dd, *J* = 16.0, 6.0 Hz, 1 H), 5.00 (d, *J* = 10.0 Hz, 1 H), 4.87–4.83 (m, 1 H), 3.72 (s, 3 H), 2.84 (br s, 1 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.6 (C=N), 143.5 (C), 139.0 (C), 136.4 (C), 132.2 (C), 129.6 (CH), 129.5 (CH), 129.1 (CH), 128.9 (CH), 128.6 (CH), 128.2 (CH), 127.9 (CH), 126.9 (CH), 74.3 (CH), 57.6 (CH), 56.1 (CH_3), 21.6 (CH_3).

ESI-MS: *m*/*z* = 458.3 $[M + Na]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{26}NO_4S$: 436.1577; found: 436.1574; *m*/*z* $[M + Na]^+$ calcd for $C_{25}H_{25}NNaO_4S$: 458.1396; found: 458.1395.

Methyl 3-Hydroxy-4,4-dimethyl-2-phenyl-*N*-tosylpentanimidate (2l)

Yield: 44 mg (96%); colorless needles; mp 121–122 °C; R_f = 0.4 (EtOAc–pentane, 3:7).

IR (neat): 3512, 2973, 2955, 2911, 2867, 1609, 1583, 1444, 1362, 1344, 1297, 1285, 1255, 1147, 1092, 1009 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.2 Hz, 2 H), 7.39 (d, *J* = 8.2 Hz, 2 H), 7.23–7.18 (m, 5 H), 5.11 (d, *J* = 10.0 Hz, 1 H), 3.96 (br d, *J* = 10.0 Hz, 1 H), 3.65 (s, 3 H), 2.73 (br s, 1 H), 2.35 (s, 3 H), 0.74 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.0 (C=N), 143.4 (C), 139.2 (C), 136.2 (C), 130.0 (CH), 129.5 (CH), 128.6 (CH), 128.0 (CH), 126.8 (CH), 80.4 (CH), 56.0 (CH), 54.7 (CH_3), 36.8 (C), 26.8 (CH_3), 21.7 (CH_3).

ESI-MS: *m*/*z* = 390.0 $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{28}NO_4S$: 390.1733; found: 390.1736; *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{27}NNaO_4S$: 412.1553; found: 412.1556.

Methyl 3-Hydroxy-2-(4-methoxyphenyl)-3-phenyl-*N*-tosylpropanimidate (2m)

Yield: 51 mg (98%); colorless needles; mp 134–135 °C; R_f = 0.3 (EtOAc–pentane, 3:7).

IR (neat): 3540, 3068, 3028, 3006, 2952, 1581, 1514, 1443, 1260, 1251, 1171, 1091, 1046 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.0 Hz, 2 H), 7.30 (d, *J* = 8.4 Hz, 2 H), 7.26–7.18 (m, 7 H), 6.72 (d, *J* = 8.4 Hz, 2 H), 5.29 (d, *J* = 10.6 Hz, 1 H), 5.18 (d, *J* = 10.6 Hz, 1 H), 3.85 (s, 3 H), 3.72 (s, 3 H), 2.95 (br s, 1 H), 2.43 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3 (C=N), 159.3 (C), 143.5 (C), 141.5 (C), 139.2 (C), 130.8 (CH), 129.5 (CH), 128.6 (CH), 128.2 (CH), 126.9 (CH), 126.8 (CH), 126.2 (C), 114.0 (CH), 76.9 (CH), 57.6 (CH), 56.1 (CH_3), 55.3 (CH_3), 21.7 (CH_3).

ESI-MS: *m*/*z* = 439.9 $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{26}NO_5S$: 440.1526; found: 440.1525; *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{25}NNaO_5S$: 462.1345; found: 462.1346.

Methyl 3-Hydroxy-2-(4-methoxyphenyl)-3-(2-tolyl)-*N*-tosylpropanimidate (2n)

Yield: 52 mg (97%); colorless needles; mp 172–173 °C; R_f = 0.3 (EtOAc–pentane, 3:7).

IR (neat): 3483, 3022, 2949, 2832, 1604, 1511, 1442, 1308, 1296, 1287, 1258, 1244, 1150, 1118 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.4 Hz, 2 H), 7.57 (d, *J* = 7.6 Hz, 1 H), 7.30–7.26 (m, 2 H), 7.23–7.18 (m, 3 H), 7.10 (td, *J* = 7.6, 1.2 Hz, 1 H), 6.97 (d, *J* = 7.6 Hz, 1 H), 6.69 (dd, *J* = 6.4, 2.0 Hz, 2 H), 5.49 (d, *J* = 10.4 Hz, 1 H), 5.44 (d, *J* = 10.4 Hz, 1 H), 3.89 (s, 3 H), 3.71 (s, 3 H), 2.42 (s, 3 H), 2.15 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3 (C=N), 159.3 (C), 143.4 (C), 139.5 (C), 139.2 (C), 136.1 (C), 130.6 (CH), 130.5 (CH), 129.5 (CH), 128.1 (CH), 126.9 (CH), 126.8 (CH), 126.0 (CH), 113.9 (CH), 72.3 (CH), 56.9 (CH), 56.1 (CH_3), 55.2 (CH_3), 21.7 (CH_3), 19.4 (CH_3).

ESI-MS: *m*/*z* = 453.8 $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{28}NO_5S$: 454.1682; found: 454.1682; *m*/*z* $[M + Na]^+$ calcd for $C_{25}H_{27}NNaO_5S$: 476.1502; found: 476.1503.

Methyl 3-(4-Bromophenyl)-3-hydroxy-2-(4-methoxyphenyl)-*N*-tosylpropanimidate (2o)

Yield: 58 mg (95%); colorless needles; mp 158–159 °C; R_f = 0.3 (EtOAc–pentane, 3:7).

IR (neat): 3518, 2990, 2951, 1595, 1511, 1325, 1299, 1287, 1259, 1248, 1148, 1074, 1048, 1030, 1011 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.4 Hz, 2 H), 7.34–7.31 (m, 4 H), 7.19 (d, *J* = 8.8 Hz, 2 H), 7.09 (d, *J* = 8.4 Hz, 2 H), 6.73 (d, *J* = 8.8 Hz, 2 H), 6.70 (d, *J* = 10.8 Hz, 1 H), 5.14 (d, *J* = 10.8 Hz, 1 H), 3.84 (s, 3 H), 3.73 (s, 3 H), 3.10 (br s, 1 H), 2.43 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9 (C=N), 159.4 (C), 143.6 (C), 140.6 (C), 139.0 (C), 131.6 (CH), 130.9 (CH), 129.5 (CH), 128.5 (CH), 126.9 (CH), 125.8 (C), 122.1 (C), 114.1 (CH), 76.2 (CH), 57.6 (CH), 56.2 (CH_3), 55.3 (CH_3), 21.7 (CH_3).

ESI-MS: *m*/*z* = 517.8 and 519.8 (1:1) $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{25}BrNO_5S$: 518.0631; found: 518.0626; *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{24}BrNNaO_5S$: 540.0450; found: 540.0448.

Methyl 3-Hydroxy-2-(4-methoxyphenyl)-3-(1-naphthyl)-*N*-tosylpropanimidate (2p)

Yield: 55 mg (95%); isolated as a 96:4 mixture of diastereoisomers; colorless needles; R_f = 0.4 (EtOAc–pentane, 3:7).

IR (neat): 3527, 3036, 2949, 2835, 1591, 1511, 1438, 1287, 1251, 1183, 1154, 1091, 1031, 1021 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 8.4 Hz, 1 H), 7.87 (d, *J* = 8.4 Hz, 2 H), 7.79 (d, *J* = 7.6 Hz, 1 H), 7.72 (d, *J* = 8.4 Hz, 1 H), 7.56–7.51 (m, 2 H), 7.50–7.43 (m, 1 H), 7.38–7.34 (m, 1 H), 7.30–7.26 (m, 2 H), 7.23–7.19 (m, 2 H), 6.69 (d, *J* = 8.4 Hz, 2 H), 6.05 (d, *J* = 10.6 Hz, 1 H), 5.83 (d, *J* = 10.6 Hz, 1 H), 3.91 (s, 3 H), 3.64 (s, 3 H), 2.43 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.2 (C=N), 159.1 (C), 143.4 (C), 139.2 (C), 136.5 (C), 134.0 (C), 131.5 (C), 130.4 (CH), 129.5 (CH), 129.1 (CH), 128.9 (CH), 126.9 (CH), 126.4 (CH), 126.3 (C), 125.8 (CH), 125.4 (CH), 124.8 (CH), 123.7 (CH), 114.0 (CH), 72.7 (CH), 56.2 (CH), 55.8 (CH_3), 55.2 (CH_3), 21.7 (CH_3).

ESI-MS: *m*/*z* = 511.9 $[M + Na]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{28}H_{28}NO_5S$: 490.1682; found: 490.1680; *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{27}NNaO_5S$: 512.1502; found: 512.1501.

Methyl 2-(4-Fluorophenyl)-3-hydroxy-3-phenyl-*N*-tosylpropanimidate (2q)

Yield: 49 mg (97%); colorless needles; mp 148–149 °C; R_f = 0.3 (EtOAc–pentane, 3:7).

IR (neat): 3470, 3027, 2953, 2927, 1615, 1598, 1508, 1495, 1455, 1442, 1284, 1248, 1225, 1147, 1088, 1019 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.4 Hz, 2 H), 7.23–7.11 (m, 9 H), 6.80 (t, *J* = 8.4 Hz, 2 H), 5.26 (d, *J* = 10.4 Hz, 1 H), 5.09 (d, *J* = 10.4 Hz, 1 H), 3.78 (s, 3 H), 2.99 (br s, 1 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.6 (C=N), 161.2 (C), 152.3 (C, d, *J* = 247), 143.6 (C), 141.1 (C), 131.3 (CH, d, *J* = 8), 130.0 (C, d, *J* = 3), 129.5 (CH), 128.6 (CH), 128.4 (CH), 126.9 (CH), 126.8 (CH), 115.5 (CH, d, *J* = 21), 76.9 (CH), 57.6 (CH), 56.2 (CH_3), 21.7 (CH_3).

^{19}F NMR (377 MHz, $CDCl_3$): δ = –114.1.

ESI-MS: *m*/*z* = 427.8 $[M + Na]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{23}FNO_4S$: 428.1326; found: 428.1326; *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{22}FNNaO_4S$: 450.1145; found: 450.1146.

Methyl 2-(4-Fluorophenyl)-3-hydroxy-3-(3-methoxyphenyl)-*N*-tosylpropanimidate (2r)

Yield: 51 mg (94%); colorless needles; mp 131–132 °C; R_f = 0.2 (EtOAc–pentane, 2:8).

IR (neat): 3484, 3012, 2955, 2897, 1609, 1597, 1507, 1494, 1439, 1321, 1286, 1267, 1247, 1222, 1153, 1118, 1090, 1053, 1017 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.0 Hz, 2 H), 7.31–7.15 (m, 4 H), 7.13 (t, *J* = 8.0 Hz, 1 H), 6.90 (t, *J* = 8.6 Hz, 2 H), 6.81–9.72 (m, 3 H), 5.32 (d, *J* = 10.4 Hz, 1 H), 5.14 (d, *J* = 10.4 Hz, 1 H), 3.85 (s, 3 H), 3.71 (s, 3 H), 2.94 (br s, 1 H), 2.42 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.5 (C=N), 161.2 (C), 159.7 (C), 151.3 (C, d, *J* = 247), 143.6 (C), 142.7 (C), 131.3 (CH, d, *J* = 8), 130.0 (C, d, *J* = 3), 129.7 (CH), 129.5 (CH), 126.9 (CH), 119.0 (CH), 115.5 (CH, d, *J* = 21), 114.0 (CH), 112.3 (CH), 76.8 (CH), 57.5 (CH), 56.2 (CH_3), 55.3 (CH_3), 21.7 (CH_3).

^{19}F NMR (377 MHz, $CDCl_3$): δ = –114.1.

ESI-MS: *m*/*z* = 480.2 $[M + Na]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{25}FNO_5S$: 458.1431; found: 458.1430; *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{24}FNNaO_5S$: 480.1251; found: 480.1251.

Methyl 2-(4-Fluorophenyl)-3-hydroxy-4,4-dimethyl-*N*-tosylpentanimidate (2s)

Yield: 46 mg (96%); colorless needles; mp 116–117 °C; R_f = 0.4 (EtOAc–pentane, 3:7).

IR (neat): 3499, 2956, 2905, 2869, 1610, 1505, 1444, 1296, 1223, 1090, 1036, 1013 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.4 Hz, 2 H), 7.46–7.43 (m, 2 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 7.01–6.97 (m, 2 H), 5.19 (d, *J* = 10.8 Hz, 1 H), 3.98 (t, *J* = 10.8 Hz, 1 H), 3.73 (s, 3 H), 2.761 (d, *J* = 10.8 Hz, 1 H), 2.43 (s, 3 H), 0.82 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.7 (C=N), 163.8 (C), 150.2 (C, d, *J* = 223), 143.6 (C), 132.0 (C, d, *J* = 4), 131.5 (CH, d, *J* = 8), 129.5 (CH), 126.8 (CH), 115.6 (CH, d, *J* = 21), 80.5 (CH), 56.1 (CH_3), 53.8 (CH), 36.8 (C), 26.8 (CH_3), 21.7 (CH_3).

^{19}F NMR (377 MHz, $CDCl_3$): δ = –114.2.

ESI-MS: *m*/*z* = 407.9 $[M + H]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{27}FNO_4S$: 408.1639; found: 408.1643; *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{26}FNNaO_4S$: 430.1458; found: 430.1461.

Methyl 2-Chloro-3-hydroxy-3-phenyl-*N*-tosylpropanimidate (2t)

Yield: 35 mg (81%); colorless needles; mp 153–154 °C; R_f = 0.2 (EtOAc–pentane, 2:8).

IR (neat): 3427, 3033, 2952, 2913, 1610, 1434, 1302, 1289, 1245, 1145, 1084, 1040, 1014 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.4 Hz, 2 H), 7.50–7.32 (m, 7 H), 5.82 (d, *J* = 8.6 Hz, 1 H), 4.90 (t, *J* = 8.6 Hz, 1 H), 3.89 (s, 3 H), 3.08 (d, *J* = 8.6 Hz, 1 H), 2.44 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8 (C=N), 144.1 (C), 139.3 (C), 138.2 (C), 129.7 (CH), 129.3 (CH), 129.0 (CH), 127.2 (CH), 127.1 (CH), 76.6 (CH), 56.6 (CH), 56.5 (CH_3), 21.7 (CH_3).

ESI-MS: *m*/*z* = 390.2 $[M + Na]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{19}ClNO_4S$: 368.0717; found: 368.0719; *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{18}ClNNaO_4S$: 390.0537; found: 390.0540.

Methyl 2-Chloro-3-(3-fluorophenyl)-3-hydroxy-*N*-tosylpropanimidate (2u)

Yield: 36 mg (79%); colorless needles; mp 141–142 °C; R_f = 0.2 (EtOAc–pentane, 2:8).

IR (neat): 3421, 2952, 1613, 1596, 1456, 1433, 1304, 1291, 1268, 1241, 1147, 1085, 1041, 1015 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.0 Hz, 2 H), 7.43–7.28 (m, 4 H), 7.23–7.20 (m, 1 H), 7.11–7.07 (m, 1 H), 5.78 (d, *J* = 9.6 Hz, 1 H), 4.92 (d, *J* = 9.6 Hz, 1 H), 3.90 (s, 3 H), 3.28 (br s, 1 H), 2.47 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4 (C=N), 164.2 (C), 149.9 (C, d, *J* = 237), 144.2 (C), 141.8 (C, d, *J* = 7), 130.5 (CH, d, *J* = 8), 129.7 (CH), 127.1 (CH), 122.8 (CH, d, *J* = 3), 116.2 (CH, d, *J* = 21), 114.4 (CH, d, *J* = 22), 76.0 (CH, d, *J* = 2), 56.7 (CH), 56.4 (CH_3), 21.7 (CH_3).

^{19}F NMR (377 MHz, $CDCl_3$): δ = –112.0.

ESI-MS: *m*/*z* = 408.2 $[M + Na]^+$.

ESI-HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{18}ClFNO_4S$: 386.0623; found: 386.0628; *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{17}ClFNNaO_4S$: 408.0443; found: 408.0446.

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Supporting Information

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(8) Reaction of **1a** under analogous conditions to those utilized by Kobayashi for the Mannich-type reaction[3] resulted in complete recovery of the starting material.
(9) Treatment of product **2a** with triethylamine in dichloromethane at room temperature resulted in complete retro-aldolization yielding the starting material *N*-sulfonylimidate **1a** and benzaldehyde.
(10) CCDC 1481884 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures. The ORTEP representation is included in the Supporting Information.
(11) This procedure is adapted from: Reetz, M. T.; Westermann, J.; Steinbach, R.; Wenderoth, B.; Peter, R.; Ostarek, R.; Maus, S. *Chem. Ber.* **1985**, *118*, 1421.