$Y(OTf)_3$-Catalyzed Diastereoselective [3+2] Cycloaddition of *N*-Tosylaziridines and Imines; Efficient Synthesis of Multisubstituted Imidazolidines

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Abstract: An efficient $Y(OTf)_3$-catalyzed generation of azomethine ylides from donor–acceptor aziridines and their [3+2] cycloaddition with imines was developed. The method provides facile access to multisubstituted imidazolidines, which have been extensively used in organic synthesis. Furthermore, a three-component reaction on a gram scale and an asymmetric variation were also developed in this work.

Key words: bond cleavage, cycloaddition, ylides, Lewis acid, stereoselectivity

Donor–acceptor (DA) cyclopropanes, due to their unique reactivity profile, have received considerable interest and have been extensively studied in the past decades.[1] Many studies have demonstrated that they can be trapped with appropriate dipolarophiles such as aldehydes and imines. However, reports that extend this methodology to DA aziridines are not so common. This is surprising because the strain energy of aziridine (29 kcal/mol) is comparable to that of cyclopropane (27.5 kcal/mol),[2] and it is also a versatile synthetic building-block for convenient access to nitrogen-containing heterocycles, particularly through C–N bond cleavage.[3]

Aziridine-2,3-diesters represent a particular case of DA aziridines in organic synthesis. Since Huisgen's pioneering work,[2a] they have been largely utilized in 1,3-dipolar cycloaddition through azomethine ylide (AMY) intermediates by the thermal or photolytic ring opening of aziridines.[4] A few cases of the generation of AMYs from aziridines promoted by Lewis acids under mild conditions have also been reported.[5] Calculations performed by Carrie, Johnson, as well as Engle[6] have shown that Lewis acids favor C–C bond heterolysis of DA aziridines. Very recently, we and others have expanded this chemistry to the synthesis of highly substituted heterocycles, such as pyrolidines and 1,3-oxazolidines by conducting the reaction with the appropriate dipolarophiles.[7]

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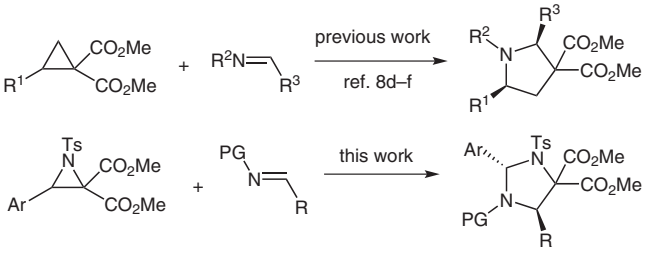
Carriera and co-workers[8a–c] have developed a novel approach to the synthesis of spirotryprostatin and related horsfiline by the MgI_2-catalyzed ring-expansion reaction of 3-spirocyclopropyl-2-oxindoles and imines (Scheme 1). The groups of Kerr,[8d] Tang,[8e] and Johnson[8f] have independently demonstrated that (*E*)-aldimines are also competent dipolarophiles in Lewis acid catalyzed [3+2] annulations with DA cyclopropanes. With this in mind, and due to our interest in the carbon–carbon bond cleavage of DA azirdines, we sought to obtain the imidazolidines through Lewis acid catalyzed diastereoselective [3+2] cycloaddition of imines with AMYs generated from *N*-tosylaziridine dicarboxylates under mild conditions.[9] The products, imidazolidines, are fundamental units of many natural products[10a,b] and biologically active molecules.[10c,d] In particular, imidazolidines can be easily transformed into imidazoles, which are well-known scaffolds in many significant biomolecules,[10e–j] and hydrolyzed to prepare the corresponding 1,2-diamine compounds, which can be used to synthesize organocatalysts and ligands for metal catalysts.[10k,l]

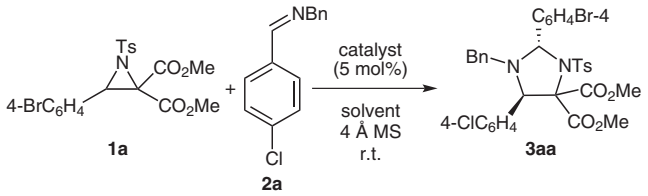


Scheme 1 Previous studies and this work

Our studies in this area began by choosing *N*-tosylaziridine **1a**[11] and imine **2a**[12a] as model substrates, because they are known to be stable and easily prepared and purified; moreover, the benzyl moiety is an easily removable protecting group. A representative selection of Lewis acids including $Sn(OTf)_2$, $Sc(OTf)_3$, $Cu(OTf)_2$, $Fe(OTf)_3$, $In(OTf)_2$, $Mg(OTf)_2$, $Y(OTf)_3$, $Bi(OTf)_3$, $Ni(ClO_4)_2 \cdot 6H_2O$, $Yb(OTf)_3$, and MgI_2 were tested to optimize the reaction conditions. Most of the Lewis acids were found to promote the tandem ring-opening-cyclization reaction of

aziridines with imines. Notably, $Sc(OTf)_3$ and $Yb(OTf)_3$ gave high yields but low diastereoselectivities (Table 1, entries 2 and 10), whereas use of $Sn(OTf)_2$, $Cu(OTf)_2$ and $Mg(OTf)_2$ gave higher diastereoselectivities but lower yields (Table 1, entries 1, 3, and 6). To our delight, both high yield and high diastereoselectivity can be achieved when the reaction was run in 1,2-dichloroethane (DCE) at room temperature with 4 Å molecular sieves as additive under the catalysis of 5 mol% $Y(OTf)_3$ (Table 1, entry 7). Other solvents were then screened and it was found that the use of tetrahydrofuran (THF) failed to improve the result, and the reaction did not take place in toluene (Table 1, entries 12–14). The structure and relative stereochemistry were established by single crystal X-ray crystallography analysis of the *trans* isomer of **3aa** (racemic; see the Supporting Information).[13]

Table 1 Screening Reaction Conditions[a]



Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]	dr (*trans*/*cis*)[c]
1	$Sn(OTf)_2$	DCE	2.5	58	>20:1
2	$Sc(OTf)_3$	DCE	0.5	84	3:1
3	$Cu(OTf)_2$	DCE	3	56	>20:1
4	$Fe(OTf)_3$	DCE	1	64	>20:1
5	$In(OTf)_2$	DCE	3	79	8:1
6	$Mg(OTf)_2$	DCE	10	37	>50:1
7	$Y(OTf)_3$	DCE	3	85	>20:1
8	$Bi(OTf)_3$	DCE	3	75	>20:1
9	$Ni(ClO_4)_2 \cdot 6H_2O$	DCE	3	85	3:1
10	$Yb(OTf)_3$	DCE	3	87	3:1
11	MgI_2	DCE	2	78	>20:1
12	$Y(OTf)_3$	CH_2Cl_2	2	76	14:1
13	$Y(OTf)_3$	THF	3	83	3:1
14	$Y(OTf)_3$	toluene	10	trace	trace

[a] Reaction conditions (0.2 mmol scale): **1a** (0.2 mmol), **2a** (1.5 equiv), catalyst (5 mol%), activated 4 Å MS (100 mg), solvent (2 mL) r.t.
[b] Isolated combined yield of two isomers.
[c] Determined by ^{1}H NMR spectroscopic analysis of the crude product.

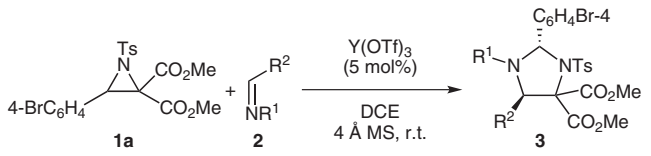
With the optimal conditions in hand, the scope of this $Y(OTf)_3$-promoted [3+2] cycloaddition was explored by submitting a range of imine components **2** to the reaction conditions; the results are presented in Table 2. In general, both electron-deficient and electron-rich *N*-benzyl imines reacted well and gave good to high yields. For instance, 4-bromobenzylaldimine (**2b**) and 2-fluoro-4-bromobenzyl aldimine (**2d**) both give the desired products in 82–86% yields (Table 2, entries 1 and 3). Moreover, electron-rich substrates **2f**–**g** also afforded the corresponding imidazolidines in good to high yields (Table 2, entries 5 and 6). Some observations are particularly noteworthy: (1) the reaction of 4-cyanobenzylaldimine (**2c**) required longer time, which may be due to the coordinating cyano group competing to bind to the Lewis acid with the ester group; (2) when 4-methoxybenzylaldimine was employed as the substrate, the reaction required higher catalyst loading, possibly owing to the strong coordination between the catalyst and the lone pair of the nitrogen atom of aldimine; (3) the products could be generated with excellent diastereoselectivities when the aryl group of aldimines was substituted by a strong electron-withdrawing group, such as cyano or fluoro group, which produced a single isomer almost completely (Table 2, entries 2 and 3); for electron-rich aldehyde derived aldimines, only moderate diastereoselectivities were obtained (Table 1, entries 5 and 6). Gratifyingly, aldimine **2h**, derived from furan-2-carbaldehyde, afforded the desired adduct in nearly quantitative yield but with no selectivity (Table 1, entry 7). Finally, a series of aldimines from aniline were examined; in general, these demonstrated similar properties to those of *N*-benzylaldimines. Both electron-deficient and neutral *N*-phenyl imines provided high yields and excellent diastereoselectivities (Table 2, entries 8 and 9); the electron-rich substituted substrate **2k** afforded the corresponding imidazolidine in 78% yield with moderate diastereoselectivity (Table 2, entry 10).

We then examined the scope of this reaction by variation of the DA aziridines (Scheme 2). The reactions of aziridine **1** bearing either an electron-donating or electron-withdrawing group proceeded smoothly and generated the corresponding cycloadducts **3ba**–**fa** in 66–91% yields, with diastereoisomeric ratios that ranged from 10:1 to more than 20:1. Notably, with **1b** and **1c** the reaction required much longer to reach completion, which may be caused by the strong electron-withdrawing effect of the halogen atoms.

When the acceptor groups were switched to ethyl (**1g**) or isopropyl dicarboxylates (**1h**), the reactions still work very well under the standard conditions. The results obtained from the reactions of **1i** with benzylaldimines **2e**, **2a**, and **2g** further indicate that the electronic effect of the substituents affects the diastereoselectivity rather than the efficiency.

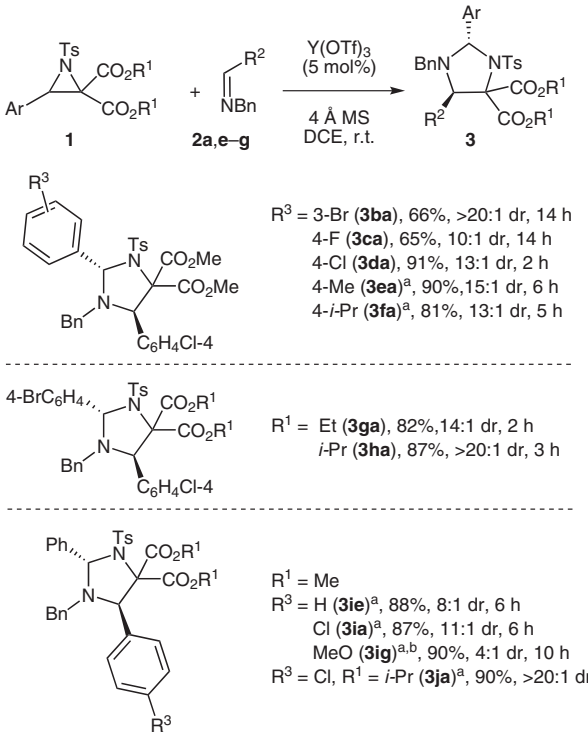
Considering that the aldimine is readily available from aldehyde and amine, the three-component reaction was then tested on a gram scale and found to proceed smoothly, furnishing the product in 83% yield with high diastereoselectivity (Scheme 3, equation 1). Perhaps more importantly, a preliminary experiment showed that an enantioselective variant of this novel reaction can be achieved by the application of *t*-Bu-Pybox[14] as the chiral ligand. The reaction

Table 2 Study of the Reaction Scope by Variation of the Imine Component[a]



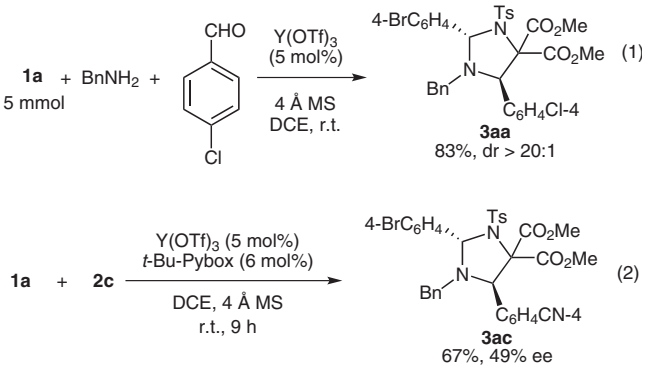
Entry	R^1	R^2	2	Time (h)	3	Yield (%)	*trans*/*cis*
1	Bn	4-BrC_6H_4	**2b**	3	**3ab**	82	18:1
2	Bn	4-CNC_6H_4	**2c**	8	**3ac**	65	>50:1
3	Bn	2-F-4-BrC_6H_4	**2d**	3	**3ad**	86	>50:1
4	Bn	Ph	**2e**	3	**3ae**	86	14:1
5	Bn	4-*i*-PrC_6H_4	**2f**	2	**3af**	87[c]	5:1
6[b]	Bn	4-$MeOC_6H_4$	**2g**	4.5	**3ag**	79[c]	3:1
7	Bn	2-Furyl	**2h**	2	**3ah**	98[c]	1:1
8	Ph	Ph	**2i**	4	**3ai**	86	>20:1
9	Ph	4-ClC_6H_4	**2j**	3	**3aj**	90	>20:1
10[b]	Ph	4-$MeOC_6H_4$	**2k**	8	**3ak**	78[c]	3:1

[a] Reaction conditions: **1a** (0.4 mmol), **2** (1.5 equiv), $Y(OTf)_3$ (5 mol%), activated 4 Å MS (200 mg), DCE (4 mL), r.t.
[b] 10 mol% of $Y(OTf)_3$ was used.
[c] Combined yield of two isomers.



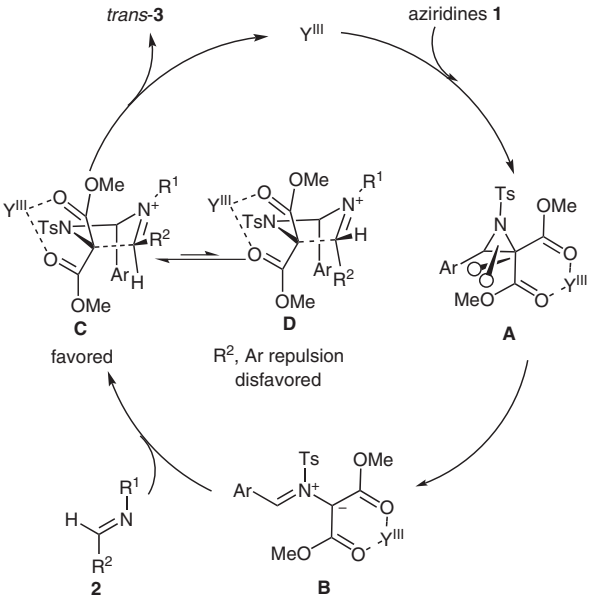
Scheme 2 Study of the reaction scope by variation of the aziridine component. [a] The temperature was 10 °C. [b] Combined yield of two isomers.

of **1a** and **2c** proceeded well at room temperature to give the corresponding product in 49% enantiomeric excess, with a moderate yield (Scheme 3, equation 2). Further exploration and development of this catalytic asymmetric [3+2] cycloaddition is under way in our laboratory.



Scheme 3 Gram-scale reaction (1) and preliminary examination of an enantioselective variant with *t*-Bu-Pybox (2)

A model that accounts for the *trans* selectivity observed in this cycloaddition is proposed in Scheme 4. Based on previous work,[7,15] a possible path is that the azomethine ylide **B** is first produced by C–C bond cleavage of **A**, formed from **1** through the selective coordination of $Y(OTf)_3$ to the dicarboxylate groups. Subsequent diastereoselective addition of the imine would afford two zwitterionic intermediates, **C** and **D**, which can be interconverted through iminium isomerization. Intermediate **D** is less stable than intermediate **C**, owing to the steric hindrance of R and Ar, which are both in pseudo axial orientations within the envelope transition state, thus the *trans* isomer is produced preferentially.



Scheme 4 Proposal mechanism for the formation of *trans*-imidazolidines

In conclusion, we have developed an efficient method for the diastereoselective synthesis of imidazolidines through Lewis acid catalyzed carbon–carbon bond cleavage of DA aziridines. Mild conditions, readily available starting material, as well as the high yield and good selectivity make this protocol potentially useful in organic synthesis. Efforts are under way to develop its application, establish an asymmetric version, and to identify new dipolarophile partners.

All reactions were carried out in flame-dried glassware under an anhydrous N_2 atmosphere with standard vacuum-line techniques. All solvents were purified and dried according to standard methods prior to use. Infrared (IR) spectra were obtained with a Bruker tensor 27 infrared spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker 400 MHz spectrometer in $CDCl_3$. All signals are reported in ppm with TMS (δ = 0 ppm) as an internal standard. Enantiomeric ratios were determined by chiral HPLC analysis and comparison with authentic racemic materials. Aziridines were prepared according to literature procedures.[11] *N*-Benzylimines were synthesized by condensation of the corresponding aldehydes and benzyl amine.[12a] *N*-Phenylimines were synthesized by using the reporting route.[12b]

Y(OTf)$_3$-Catalyzed Diastereoselective [3+2] Cycloaddition of *N*-Tosylaziridines and Imines; Typical Procedure

In an inert atmosphere, a flame-dried vial was charged with a magnetic stir bar, activated 4 Å molecular sieves (200 mg), $Y(OTf)_3$ (10.7 mg, 5 mol%), imine **2** (0.6 mmol, 1.5 equiv), and DCE (3 mL). The mixture was stirred at r.t. for ca. 5 min, then aziridine **1** (0.4 mmol, 1.0 equiv) was added, and washed by DCE (1 mL). The reaction was stirred at r.t. until complete consumption of the aziridine was observed (reaction monitored by TLC analysis). The reaction mixture was then passed over a small plug of silica gel eluted with CH_2Cl_2. After evaporation under reduced pressure, the crude product was subjected to ^{1}H NMR spectroscopic analysis, which gave the diastereomeric ratio. The resulting product was purified by flash chromatography to afford the desired product **3**.

(2*S,5*R**)-Dimethyl 1-Benzyl-2-(4-bromophenyl)-5-(4-chlorophenyl)-3-tosylimidazolidine-4,4-dicarboxylate (3aa)**

Yield: 237.1 mg (85%); white solid; mp 209–212 °C.

IR (neat): 2955, 2840, 1771, 1752, 1594, 1492, 1435, 1419, 1371, 1337, 1307, 1276, 1261, 1227, 1176, 1155, 1139, 1120, 1086, 1071, 1050, 1034, 1007, 949, 906 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 8.0 Hz, 2 H), 7.30 (d, *J* = 8.0 Hz, 4 H), 7.25 (t, *J* = 8.0 Hz, 3 H), 7.10–7.17 (m, 4 H), 6.94 (d, *J* = 8.0 Hz, 2 H), 6.66 (d, *J* = 7.6 Hz, 2 H), 6.00 (s, 1 H), 4.97 (s, 1 H), 3.92 (s, 3 H), 3.69 (s, 3 H), 3.55 (d, *J* = 15.2 Hz, 1 H), 2.72 (d, *J* = 15.2 Hz, 1 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 166.4, 143.4, 137.0, 136.7, 135.0, 134.5, 132.3, 130.84, 130.77, 130.0, 128.61, 128.56, 128.40, 127.9, 127.4, 127.2, 122.7, 78.0, 77.5, 72.2, 53.4, 52.9, 49.4, 21.4.

MS (ESI): *m*/*z* = 697.1 [M + H$^+$].

HRMS: *m*/*z* calcd for $C_{33}H_{31}BrClN_2O_6S^+$: 697.0788; found: 697.0769.

(2*S,5*R**)-Dimethyl 1-Benzyl-2,5-bis(4-bromophenyl)-3-tosylimidazolidine-4,4-dicarboxylate (3ab)**

Yield: 242.4 mg (82%); white solid; mp 97–99 °C.

IR (neat): 2950, 2844, 1752, 1594, 1487, 1453, 1434, 1411, 1348, 1284, 1209, 1161, 1071, 1051, 1010, 977, 940, 906 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 18:1) = 7.46 (d, *J* = 8.0 Hz, 2 H), 7.21–7.36 (m, 7 H), 7.08–7.17 (m, 4 H), 6.94 (d, *J* = 8.0 Hz, 2 H), 6.66 (d, *J* = 8.0 Hz, 2 H), 5.99 (s, 1 H), 4.95 (s, 1 H), 3.92 (s, 3 H), 3.69 (s, 3 H), 3.55 (d, *J* = 15.2 Hz, 1 H), 2.72 (d, *J* = 15.2 Hz, 1 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 166.4, 143.4, 137.1, 136.8, 134.6, 132.9, 131.6, 130.9, 130.8, 130.4, 128.6, 128.4, 127.9, 127.4, 127.2, 123.3, 122.7, 78.1, 77.5, 72.3, 53.4, 52.9, 49.5, 21.4.

MS (ESI): *m*/*z* = 741.0 [M + H$^+$].

HRMS: *m*/*z* calcd for $C_{33}H_{31}Br_2N_2O_6S^+$: 741.0279; found: 741.0264.

(2*S,5*R**)-Dimethyl 1-Benzyl-2-(4-bromophenyl)-5-(4-cyanophenyl)-3-tosylimidazolidine-4,4-dicarboxylate (3ac)**

Yield: 178.3 mg (65%); white solid; mp 220–222 °C.

IR (neat): 2955, 2836, 2229, 1768, 1752, 1595, 1492, 1438, 1373, 1337, 1269, 1228, 1176, 1154, 1110, 1052, 1007, 946, 906 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 50:1) = 7.64 (d, *J* = 8.0 Hz, 2 H), 7.57 (d, *J* = 8.0 Hz, 2 H), 7.20–7.34 (m, 5 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 7.11 (d, *J* = 7.2 Hz, 2 H), 6.95 (d, *J* = 7.6 Hz, 2 H), 6.65 (d, *J* = 7.6 Hz, 2 H), 6.01 (s, 1 H), 5.06 (s, 1 H), 3.93 (s, 3 H), 3.67 (s, 3 H), 3.50 (d, *J* = 15.2 Hz, 1 H), 2.77 (d, *J* = 15.2 Hz, 1 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.0, 166.2, 143.5, 139.5, 136.8, 136.3, 134.2, 132.0, 130.9, 130.7, 129.5, 128.6, 128.4, 127.8, 127.33, 127.26, 122.8, 118.2, 113.0, 78.2, 77.4, 72.1, 53.5, 53.0, 49.6, 21.3.

MS (ESI): *m*/*z* = 688.1 [M + H$^+$].

HRMS: *m*/*z* calcd for $C_{34}H_{31}BrN_3O_6S^+$: 688.1121; found: 688.1112.

(2*S,5*R**)-Dimethyl 1-Benzyl-5-(4-bromo-2-fluorophenyl)-2-(4-bromophenyl)-3-tosylimidazolidine-4,4-dicarboxylate (3ad)**

Yield: 261.7 mg (86%); white solid; mp 97–99 °C.

IR (neat): 3029, 2951, 1756, 1602, 1576, 1484, 1453, 1434, 1410, 1350, 1285, 1211, 1162, 1105, 1089, 1071, 1052, 1010, 997, 941, 906 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = (*trans*/*cis*, 50:1) = 7.45 (t, *J* = 8.0 Hz, 1 H), 7.18–7.32 (m, 7 H), 7.08 (d, *J* = 8.4 Hz, 4 H), 6.91 (d, *J* = 7.6 Hz, 2 H), 6.70 (d, *J* = 8.0 Hz, 2 H), 6.00 (s, 1 H), 5.20 (s, 1 H), 3.94 (s, 3 H), 3.76 (s, 3 H), 3.51 (d, *J* = 15.2 Hz, 1 H), 2.77 (d, *J* = 15.2 Hz, 1 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.5, 166.4, 161.5 (d, $^1J_{C–F}$ = 251.0 Hz), 143.4, 136.9, 136.6, 134.3, 131.2, 130.8, 129.7, 128.6, 128.3, 128.1, 127.7 (d, $J_{C–F}$ = 3.0 Hz), 127.3, 127.2, 123.4 (d, $J_{C–F}$ = 10.0 Hz), 122.8, 120.7 (d, $J_{C–F}$ = 12.0 Hz), 119.5 (d, $^2J_{C–F}$ = 25.0 Hz), 77.6, 76.8, 65.3, 53.6, 53.0, 49.7, 21.4.

MS (ESI): *m*/*z* = 759.0 [M + H$^+$].

HRMS: *m*/*z* calcd for $C_{33}H_{30}Br_2FN_2O_6S^+$:759.0204; found: 759.0170.

(2*S,5*R**)-Dimethyl 1-Benzyl-2-(4-bromophenyl)-5-phenyl-3-tosylimidazolidine-4,4-dicarboxylate (3ae)**

Yield: 227.9 mg (86%); white solid; mp 75–76 °C.

IR (neat): 3062, 3031, 2951, 2842, 1752, 1956, 1492, 1453, 1434, 1415, 1349, 1282, 1208, 1160, 1091, 1072, 1047, 1010, 976, 940, 905 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 14:1) = 7.40 (br, 2 H), 7.21–7.36 (m, 8 H), 7.14 (t, *J* = 7.6 Hz, 4 H), 6.94 (d, *J* = 8.0 Hz, 2 H), 6.69 (d, *J* = 7.6 Hz, 2 H), 6.00 (s, 1 H), 5.00 (s, 1 H), 3.92 (s, 3 H), 3.65 (s, 3 H), 3.63 (d, *J* = 15.2 Hz, 1 H), 2.72 (d, *J* = 15.2 Hz, 1 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 166.5, 143.3, 137.13, 137.09, 134.8, 133.7, 130.9, 130.8, 129.2, 128.6, 128.5, 128.4, 127.9, 127.5, 127.1, 122.6, 78.0, 77.7, 73.0, 53.4, 52.8, 49.5, 21.4.

MS (ESI): *m*/*z* = 663.1 [M + H$^+$].

HRMS: *m*/*z* calcd for $C_{33}H_{32}BrN_2O_6S^+$: 663.1178; found: 663.1159.

Dimethyl 1-Benzyl-2-(4-bromophenyl)-5-(4-isopropylphenyl)-3-tosylimidazolidine-4,4-dicarboxylate (3af)
Yield: 244.8 mg (87%); white solid; dr = 5:1 (*trans*/*cis*).

IR (neat): 2956, 2840, 1751, 1596, 1490, 1433, 1349, 1283, 1209, 1159, 1090, 1072, 1056, 1011, 978, 941, 907 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.88–7.40 (m, 15 H),* 6.69 (d, *J* = 7.6 Hz, 2 H), 6.00 (s, 1 H), 4.97 (s, 1 H), 3.91 (s, 3 H), 3.56–3.66 (m, 4 H), 2.74–2.94 (m, 1 H),* 2.69 (d, *J* = 14.8 Hz, 1 H), 2.30 (s, 3 H), 1.20 (d, *J* = 6.8 Hz, 6 H). δ (*cis* isomer) = 6.88–7.40 (m, 15 H),* 6.81 (d, *J* = 4.0 Hz, 2 H), 5.26 (s, 1 H), 4.60 (s, 1 H), 3.82 (s, 3 H), 3.55 (d, *J* = 14.8 Hz, 1 H), 3.44 (d, *J* = 14.4 Hz, 1 H), 3.23 (s, 3 H), 2.74–2.94 (m, 1 H),* 2.34 (s, 3 H), 1.24 (d, *J* = 6.8 Hz, 6 H). * Peaks overlap with those of the other isomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 168.2, 167.1, 166.4, 149.7, 149.6, 143.1, 142.7, 137.8, 137.2, 134.8, 134.6, 133.2, 132.6, 132.1, 131.3, 130.9, 130.8, 130.72, 130.67, 129.9, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.4, 126.9, 126.3, 123.4, 122.4, 79.2, 77.9, 77.6, 72.7, 72.3, 53.2, 53.1, 52.6, 52.2, 50.5, 49.4, 33.8, 33.6, 23.8, 23.7, 21.31, 21.25.

MS (ESI): *m*/*z* = 705.2 [M + H^+].

HRMS: *m*/*z* calcd for $C_{36}H_{38}BrN_2O_6S^+$: 705.1623; found: 705.1629.

Dimethyl 2-(4-Bromophenyl)-5-(4-methoxyphenyl)-1-phenyl-3-tosylimidazolidine-4,4-dicarboxylate (3ag)
Yield: 218.9 mg (79%); white solid; dr = 3:1 (*trans*/*cis*).

IR (neat): 2952, 2839, 1751, 1611, 1512, 1490, 1453, 1435, 1346, 1282, 1249, 1208, 1158, 1107, 1090, 1072, 1031, 1010, 977, 940, 906.

^1H NMR (400 MHz, $CDCl_3$): δ (*trans* isomer) = 6.75–7.40 (m, 15 H),* 6.68 (d, *J* = 7.6 Hz, 2 H), 5.99 (s, 1 H), 4.93 (s, 1 H), 3.91 (s, 3 H), 3.77 (s, 3 H), 3.71 (s, 3 H), 3.61 (d, *J* = 15.2 Hz, 1 H), 2.69 (d, *J* = 15.2 Hz, 1 H), 2.31 (s, 3 H). δ (*cis* isomer) = 6.75–7.40 (m, 17 H),* 5.25 (s, 1 H), 4.55 (s, 1 H), 3.82 (s, 6 H), 3.52 (d, *J* = 14.8 Hz, 1 H), 3.39 (d, *J* = 14.8 Hz, 1 H), 3.33 (s, 3 H), 2.35 (s, 3 H). * Peaks overlap with those of the other isomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ (*trans*/*cis* mixture) = 168.41, 168.35, 167.1, 166.6, 160.2, 160.0, 143.2, 142.8, 137.9, 137.2, 134.9, 134.6, 133.2, 132.6, 130.84, 130.77, 129.94, 129.87, 128.5, 1228.4, 128.3, 128.09, 128.05, 127.9, 127.5, 127.4, 127.0, 126.6, 125.3, 123.5, 122.5, 113.8, 79.2, 77.9, 77.6, 76.9, 72.5, 72.0, 55.2, 55.1, 53.3, 53.2, 52.8, 52.5, 50.4, 49.3, 21.4, 21.3.

MS (ESI): *m*/*z* = 693.1 [M + H^+].

HRMS: *m*/*z* calcd for $C_{34}H_{34}BrN_2O_7S^+$: 693.1289; found: 693.1265.

Dimethyl 1-Benzyl-2-(4-bromophenyl)-5-(furan-2-yl)-3-tosylimidazolidine-4,4-dicarboxylate (3ah)
Yield: 257.1 mg (98%); white solid; dr = 1:1 (*trans*/*cis*).

IR (neat): 2952, 1750, 1596, 1488, 1453, 1434, 1345, 1277, 1234, 1214, 1158, 1106, 1072, 1057, 982, 943 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.80–7.52 (m, 14 H),* 6.18–6.40 (m, 2 H),* 5.76 (s, 1 H), 5.04 (s, 1 H), 3.93 (s, 3 H), 3.58–3.68 (m, 4 H), 2.99 (d, *J* = 13.6 Hz, 1 H), 2.34 (s, 3 H). δ (*cis* isomer) = 6.80–7.52 (m, 14 H),* 6.18–6.40 (m, 2 H),* 5.21 (s, 1 H), 4.81 (s, 1 H), 3.84 (s, 3 H), 3.55 (s, 3 H), 3.40–3.50 (m, 2 H), 2.37 (s, 3 H). * Peaks overlap with those of the other isomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 168.1, 167.1, 166.1, 149.0, 148.4, 143.3, 143.19, 143.15, 142.9, 137.6, 137.3, 137.0, 135.4, 134.4, 133.6, 132.5, 131.3, 131.1, 130.8, 129.7, 128.5, 128.4, 128.3, 128.19, 128.17, 128.1, 127.9, 127.4, 127.2, 123.6, 123.3, 111.6, 110.8, 110.7, 110.2, 80.2, 79.6, 77.1, 75.5, 66.9, 63.8, 53.5, 53.3, 53.2, 51.4, 49.2, 21.43, 21.41.

MS (ESI): *m*/*z* = 653.1 [M + H^+].

HRMS: *m*/*z* calcd for $C_{31}H_{30}BrN_2O_7S^+$: 653.0971; found: 653.0952.

(2*S,5*R**)-Dimethyl 2-(4-Bromophenyl)-1,5-diphenyl-3-tosylimidazolidine-4,4-dicarboxylate (3ai)**
Yield: 223.2 mg (86%); white solid; mp 183–188 °C.

IR (neat): 3037, 2947, 2841, 1756, 1599, 1499, 1453, 1433, 1413, 1343, 1253, 1233, 1152, 1095, 1057, 1038, 1014, 980, 935, 907 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 20:1) = 7.30 (d, *J* = 7.6 Hz, 2 H), 7.15–7.28 (m, 5 H), 7.10 (d, *J* = 7.2 Hz, 2 H), 7.00 (t, *J* = 9.4 Hz, 4 H), 6.86 (t, *J* = 7.4 Hz, 2 H), 6.68 (s, 1 H), 6.58 (t, *J* = 7.2 Hz, 1 H), 6.44 (d, *J* = 8.0 Hz, 2 H), 5.88 (s, 1 H), 3.92 (s, 3 H), 3.49 (s, 3 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 166.3, 143.5, 141.8, 137.3, 136.6, 134.1, 130.9, 130.7, 128.7, 128.6, 128.2, 127.9, 122.5, 120.6, 120.2, 79.8, 78.0, 70.3, 53.6, 52.7, 21.4.

MS (ESI): *m*/*z* = 649.1 [M + H^+].

HRMS: *m*/*z* calcd for $C_{32}H_{30}BrN_2O_6S^+$: 649.1023; found: 649.1003.

(2*S,5*R**)-Dimethyl 2-(4-Bromophenyl)-5-(4-chlorophenyl)-1-phenyl-3-tosylimidazolidine-4,4-dicarboxylate (3aj)**
Yield: 244.9 mg (90%); white solid; mp 202–206 °C.

IR (neat): 2949, 1754, 1597, 1490, 1434, 1413, 1346, 1256, 1236, 1155, 1089, 1064, 1043, 1013, 975, 931, 910 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 20:1) = 7.29 (d, *J* = 7.6 Hz, 2 H), 7.12–7.26 (m, 4 H), 7.09 (d, *J* = 7.6 Hz, 2 H), 6.98 (d, *J* = 7.6 Hz, 4 H), 6.88 (t, *J* = 7.4 Hz, 2 H), 6.67 (s, 1 H), 6.61 (t, *J* = 7.2 Hz, 1 H), 6.43 (d, *J* = 8.0 Hz, 2 H), 5.84 (s, 1 H), 3.91 (s, 3 H), 3.54 (s, 3 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.0, 166.2, 143.5, 141.5, 137.2, 136.4, 134.4, 132.7, 130.9, 130.6, 129.6, 128.6, 128.4, 128.3, 127.9, 122.6, 121.0, 120.4, 79.9, 77.7, 69.4, 53.6, 52.8, 21.4.

MS (ESI): *m*/*z* = 683.1 [M + H^+].

HRMS: *m*/*z* calcd for $C_{32}H_{29}BrClN_2O_6S^+$: 683.0642; found: 683.0613.

Dimethyl 2-(4-Bromophenyl)-5-(4-methoxyphenyl)-1-phenyl-3-tosylimidazolidine-4,4-dicarboxylate (*trans*/*cis*-3ak)
Diastereomeric ratio 3:1 (*trans*/*cis*).

trans-3ak
Yield: 157.2 mg, (58%); white solid; mp 182–186 °C.

IR (neat): 2950, 2839, 1756, 1599, 1512, 1500, 1485, 1435, 1415, 1346, 1305, 1252, 1211, 1156, 1110, 1090, 1063, 1039, 1010, 972, 939, 929, 910 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 7.6 Hz, 2 H), 7.12–7.23 (m, 2 H), 7.09 (d, *J* = 7.6 Hz, 2 H), 6.99 (t, *J* = 7.4 Hz, 4 H), 6.87 (t, *J* = 7.4 Hz, 2 H), 6.70–6.82 (m, 2 H), 6.68 (s, 1 H), 6.59 (t, *J* = 7.2 Hz, 1 H), 6.45 (d, *J* = 8.0 Hz, 2 H), 5.80 (s, 1 H), 3.92 (s, 3 H), 3.73 (s, 3 H), 3.55 (s, 3 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 166.5, 159.7, 143.4, 141.9, 137.4, 136.8, 130.9, 130.7, 129.4, 128.5, 128.2, 127.9, 125.7, 122.5, 120.6, 120.5, 113.6, 79.9, 77.9, 69.9, 55.0, 53.5, 52.8, 21.4.

MS (ESI): *m*/*z* = 701.1 [M + Na^+].

HRMS: *m*/*z* calcd for $C_{33}H_{31}BrN_2O_7SNa^+$: 701.0932; found: 701.0928.

***cis*-3ak**
Yield: 55.2 mg (20%); white solid; mp 87–89 °C.

IR (neat): 2951, 2839, 1757, 1599, 1511, 1434, 1347, 1248, 1157, 1106, 1092, 1067, 1033, 1011, 971, 942, 905 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.43 (m, 4 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.15 (d, *J* = 7.6 Hz, 2 H), 6.92–7.03 (m, 4 H), 6.87 (d, *J* = 8.0 Hz, 2 H), 6.80 (t, *J* = 7.2 Hz, 1 H), 6.60 (d, *J* = 8.0 Hz, 2 H), 5.90 (s, 1 H), 5.41 (s, 1 H), 4.01 (s, 3 H), 3.80 (s, 3 H), 3.41 (s, 3 H), 2.36 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 166.0, 159.7, 144.7, 143.1, 137.8, 135.4, 132.3, 131.0, 129.3, 129.0, 128.8, 128.5, 128.1, 123.5, 122.0, 118.7, 113.8, 80.0, 78.0, 72.7, 55.2, 53.8, 52.7, 21.4.

MS (ESI): *m*/*z* = 701.1 [M + Na^+].

HRMS: *m*/*z* calcd for $C_{33}H_{31}BrN_2O_7SNa^+$: 701.0945; found: 701.0928.

(2*S,5*R**)-Dimethyl 1-Benzyl-2-(3-bromophenyl)-5-(4-chlorophenyl)-3-tosylimidazolidine-4,4-dicarboxylate (3ba)**
Yield: 184.3 mg (66%); white solid; mp 58–61 °C.

IR (neat): 2952, 2842, 1752, 1596, 1572, 1492, 1475, 1434, 1347, 1285, 1229, 1202, 1161, 1089, 1042, 976, 942, 908 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 20:1) = 7.38 (d, *J* = 8.0 Hz, 2 H), 7.20–7.38 (m, 8 H), 7.14 (d, *J* = 7.2 Hz, 2 H), 6.84–6.96 (m, 4 H), 6.65 (d, *J* = 7.6 Hz, 1 H), 6.00 (s, 1 H), 4.94 (s, 1 H), 3.94 (s, 3 H), 3.69 (s, 3 H), 3.56 (d, *J* = 15.2 Hz, 1 H), 2.71 (d, *J* = 15.2 Hz, 1 H), 2.29 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.0, 166.4, 143.4, 137.7, 136.84, 136.76, 135.1, 132.3, 132.1, 131.4, 130.1, 129.2, 128.6, 128.4, 127.79, 127.76, 127.4, 127.2, 122.2, 78.0, 77.5, 72.2, 53.4, 52.9, 49.6, 21.4.

MS (ESI): *m*/*z* = 697.1 [M + H^+].

HRMS: *m*/*z* calcd for $C_{33}H_{31}BrClN_2O_6S^+$: 697.0801; found: 697.0769.

(2*S,5*R**)-Dimethyl 1-Benzyl-5-(4-chlorophenyl)-2-(4-fluorophenyl)-3-tosylimidazolidine-4,4-dicarboxylate (3ca)**
Yield: 165.1 mg (65%); white solid; mp 83–86 °C.

IR (neat): 2952, 1753, 1602, 1509, 1492, 1453, 1415, 1348, 1284, 1225, 1158, 1089, 1049, 1015, 977, 939, 906 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 10:1) = 7.39 (d, *J* = 7.6 Hz, 2 H), 7.21–7.36 (m, 7 H), 7.13 (d, *J* = 7.2 Hz, 2 H), 6.93 (d, *J* = 7.6 Hz, 2 H), 6.68–6.81 (m, 4 H), 6.06 (s, 1 H), 4.97 (s, 1 H), 3.91 (s, 3 H), 3.70 (s, 3 H), 3.54 (d, *J* = 15.2 Hz, 1 H), 2.70 (d, *J* = 15.2 Hz, 1 H), 2.29 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 166.5, 162.8 (d, $^1J_{C–F}$ = 246.0 Hz), 143.2, 137.3, 136.9, 135.0, 132.5, 131.5, 130.9 (d, $^3J_{C–F}$ = 8.0 Hz), 130.1, 128.6 (d, $^4J_{C–F}$ = 6.0 Hz), 128.4, 127.9, 127.4, 127.2, 114.7 (d, $^2J_{C–F}$ = 21.0 Hz), 78.1, 77.5, 72.1, 53.4, 52.9, 49.5, 21.3.

MS (ESI): *m*/*z* = 637.2 [M + H^+].

HRMS: *m*/*z* calcd for $C_{33}H_{31}ClFN_2O_6S^+$: 637.1579; found: 637.1570.

(2*S,5*R**)-Dimethyl 1-Benzyl-2,5-bis(4-chlorophen-yl)-3-tosylimidazolidine-4,4-dicarboxylate (3da)**
Yield: 236.8 mg (91%); white solid; mp 89–94 °C.

IR (neat): 3052, 2952, 2842, 1753, 1597, 1491, 1453, 1435, 1414, 1285, 1209, 1162, 1089, 1052, 1014, 978, 941, 906 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 13:1) = 7.38 (d, *J* = 7.6 Hz, 2 H), 7.30 (d, *J* = 7.6 Hz, 4 H), 7.25 (d, *J* = 8.0 Hz, 3 H), 7.13 (d, *J* = 6.4 Hz, 2 H), 6.99 (d, *J* = 7.6 Hz, 2 H), 6.94 (d, *J* = 7.2 Hz, 2 H), 6.72 (d, *J* = 7.2 Hz, 2 H), 6.02 (s, 1 H), 4.97 (s, 1 H), 3.92 (s, 3 H), 3.69 (s, 3 H), 3.55 (d, *J* = 15.2 Hz, 1 H), 2.71 (d, *J* = 15.2 Hz, 1 H), 2.31 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 166.4, 143.4, 137.2, 136.8, 135.1, 134.5, 134.2, 132.4, 130.5, 130.1, 128.64, 128.59, 128.4, 128.0, 127.9, 127.4, 127.2, 78.0, 77.5, 72.2, 53.4, 52.9, 49.5, 21.4.

MS (ESI): *m*/*z* = 653.1 [M + H^+].

HRMS: *m*/*z* calcd for $C_{33}H_{31}Cl_2N_2O_6S^+$: 653.1276; found: 653.1274.

(2*S,5*R**)-Dimethyl 1-Benzyl-5-(4-chlorophenyl)-2-(*p*-tolyl)-3-tosylimidazolidine-4,4-dicarboxylate (3ea)**
Yield: 228.4 mg (90%); white solid; mp 90–93 °C.

IR (neat): 2952, 1756, 1598, 1492, 1452, 1434, 1347, 1285, 1211, 1161, 1089, 1049, 1015, 978, 941, 905 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 15:1) = 7.41 (d, *J* = 7.2 Hz, 2 H), 7.21–7.32 (m, 7 H), 7.15 (d, *J* = 6.4 Hz, 2 H), 6.90 (d, *J* = 8.0 Hz, 2 H), 6.86 (d, *J* = 6.8 Hz, 2 H), 6.67 (d, *J* = 6.8 Hz, 2 H), 6.02 (s, 1 H), 5.02 (s, 1 H), 3.89 (s, 3 H), 3.68 (s, 3 H), 3.51 (d, *J* = 15.2 Hz, 1 H), 2.75 (d, *J* = 15.2 Hz, 1 H), 2.28 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 166.7, 142.8, 138.3, 137.4, 137.3, 134.9, 132.7, 132.5, 130.3, 129.0, 128.49, 128.45, 128.2, 128.0, 127.4, 127.0, 78.7, 77.4, 71.9, 53.2, 52.9, 49.3, 21.3, 21.1.

MS (ESI): *m*/*z* = 633.2 [M + H^+].

HRMS: *m*/*z* calcd for $C_{34}H_{34}ClN_2O_6S^+$: 633.1826; found: 633.1821.

(2*S,5*R**)-Dimethyl 1-Benzyl-5-(4-chlorophenyl)-2-(4-isopropylphenyl)-3-tosylimidazolidine-4,4-dicarboxylate (3fa)**
Yield: 212.8 mg (81%); white solid; mp 143–146 °C.

IR (neat): 2961, 2872, 1750, 1724, 1598, 1492, 1451, 1429, 1413, 1350, 1316, 1287, 1217, 1159, 1135, 1090, 1058, 1015, 980, 944, 906 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 13:1) = 7.42 (d, *J* = 8.0 Hz, 2 H), 7.22–7.34 (m, 7 H), 7.15 (d, *J* = 7.2 Hz, 2 H), 6.87 (t, *J* = 9.2 Hz, 4 H), 6.69 (d, *J* = 7.6 Hz, 2 H), 6.06 (s, 1 H), 5.01 (s, 1 H), 3.90 (s, 3 H), 3.70 (s, 3 H), 3.50 (d, *J* = 15.2 Hz, 1 H), 2.72–2.88 (m, 2 H), 2.24 (s, 3 H), 1.18 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 166.7, 149.4, 142.5, 137.4, 137.3, 134.9, 132.8, 132.7, 130.3, 130.0, 129.0, 128.5, 128.4, 128.2, 128.0, 127.9, 127.4, 126.9, 125.9, 125.8, 78.7, 77.4, 72.0, 53.2, 52.9, 49.4, 33.7, 24.0, 23.97, 21.3.

MS (ESI): *m*/*z* = 661.2 [M + H^+].

HRMS: *m*/*z* calcd for $C_{36}H_{38}ClN_2O_6S^+$: 661.2147; found: 661.2134.

(2*S,5*R**)-Diethyl 1-Benzyl-2-(4-bromophenyl)-5-(4-chlorophenyl)-3-tosylimidazolidine-4,4-dicarboxylate (3ga)**
Yield: 237.8 mg (82%); white solid; mp 109–112 °C.

IR (neat): 2978, 2361, 2343, 1756, 1737, 1490, 1597, 1346, 1272, 1299, 1200, 1160, 1090, 1048, 1010, 939, 925 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 14:1) = 7.39 (d, *J* = 7.2 Hz, 2 H), 7.21–7.46 (m, 7 H), 7.08–7.20 (m, 4 H), 6.94 (d, *J* = 7.2 Hz, 2 H), 6.67 (d, *J* = 7.2 Hz, 2 H), 5.97 (s, 1 H), 4.93 (s, 1 H), 4.34–4.48 (m, 2 H), 4.15–4.28 (m, 1 H), 3.96–4.10 (m, 1 H), 3.56 (d, *J* = 15.2 Hz, 1 H), 2.73 (d, *J* = 15.2 Hz, 1 H), 2.32 (s, 3 H), 1.36 (t, *J* = 6.0 Hz, 3 H), 1.23 (t, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.8, 165.8, 143.3, 137.2, 136.9, 135.0, 134.7, 132.6, 130.8, 130.3, 128.6, 128.5, 128.4, 128.1, 127.4, 127.2, 122.6, 78.0, 77.6, 72.1, 62.8, 62.3, 49.4, 21.4, 14.0, 13.7.

MS (ESI): *m*/*z* = 725.1 [M + H^+].

HRMS: *m*/*z* calcd for $C_{35}H_{35}BrClN_2O_6S^+$: 725.1115; found: 725.1082.

(2*S,5*R**)-Diisopropyl 1-Benzyl-2-(4-bromophenyl)-5-(4-chlorophenyl)-3-tosylimidazolidine-4,4-dicarboxylate (3ha)**
Yield: 262.5 mg (87%); white solid; mp 66–69 °C.

IR (neat): 2982, 1760, 1740, 1596, 1490, 1453, 1414, 1374, 1348, 1282, 1229, 1212, 1159, 1103, 1035, 1012, 943, 906 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 20:1) = 7.35–7.48 (m, 4 H), 7.20–7.32 (m, 5 H), 7.13 (t, *J* = 7.8 Hz, 4 H), 6.95 (d, *J* = 7.6 Hz, 2 H), 6.67 (d, *J* = 7.6 Hz, 2 H), 5.89 (s, 1 H), 5.14–5.36 (m, 1 H), 4.89–5.13 (m, 1 H), 4.89 (s, 1 H), 3.54 (d, *J* = 15.2 Hz, 1 H), 2.72 (d, *J* = 15.2 Hz, 1 H), 2.32 (s, 3 H), 1.37 (d, *J* = 6.0 Hz, 6 H), 1.32 (d, *J* = 6.4 Hz, 3 H), 1.05 (d, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.4, 165.3, 143.2, 137.2, 136.9, 134.8, 134.6, 132.6, 130.7, 128.5, 128.4, 128.3, 128.2, 127.4, 127.1, 122.5, 77.8, 71.7, 70.9, 70.6, 49.3, 21.8, 21.64, 21.56, 21.4, 21.2.

MS (ESI): *m*/*z* = 753.1 [M + H$^+$].

HRMS: *m*/*z* calcd for $C_{37}H_{39}BrClN_2O_6S^+$: 753.1407; found: 753.1395.

(2*S,5*R**)-Dimethyl 1-Benzyl-2,5-diphenyl-3-tosyl Imidazolidine-4,4-dicarboxylate (3ie)**
Yield: 204.8 mg (88%); white solid; mp 188–194 °C.

IR (neat): 3028, 2957, 1760, 1737, 1597, 1494, 1291, 1229, 1211, 1091, 1048, 1030, 976, 951, 918 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 8:1) = 7.42–7.50 (m, 2 H), 7.26–7.35 (m, 5 H), 7.18–7.26 (m, 3 H), 7.17 (d, *J* = 6.8 Hz, 3 H), 7.05 (t, *J* = 7.4 Hz, 2 H), 6.88 (d, *J* = 8.0 Hz, 2 H), 6.82 (d, *J* = 7.2 Hz, 2 H), 6.09 (s, 1 H), 5.07 (s, 1 H), 3.89 (s, 3 H), 3.66 (s, 3 H), 3.59 (d, *J* = 15.2 Hz, 1 H), 2.72 (d, *J* = 15.2 Hz, 1 H), 2.26 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 166.7, 142.8, 137.53, 137.47, 135.8, 134.0, 129.1, 128.9, 128.4, 128.34, 128.28, 128.2, 127.9, 127.8, 127.5, 126.9, 78.8, 77.6, 72.7, 53.2, 52.7, 49.4, 21.3.

MS (ESI): *m*/*z* = 585.2 [M + H$^+$].

HRMS: *m*/*z* calcd for $C_{33}H_{33}N_2O_6S^+$: 585.2067; found: 585.2054.

(2*S,5*R**)-Dimethyl 1-Benzyl-5-(4-chlorophenyl)-2-phenyl-3-tosylimidazolidine-4,4-dicarboxylate (3ia)**
Yield: 215.1 mg (87%); white solid; mp 168–171 °C.

IR (neat): 2947, 2926, 2860, 1758, 1597, 1493, 1457, 1437, 1380, 1345, 1291, 1281, 1228, 1205, 1161, 1135, 1088, 1058, 1014, 980, 944, 921 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 11:1) = 7.42 (d, *J* = 8.0 Hz, 2 H), 7.26–7.35 (m, 5 H), 7.13–7.24 (m, 5 H), 7.05 (t, *J* = 7.2 Hz, 2 H), 6.88 (d, *J* = 7.6 Hz, 2 H), 6.79 (d, *J* = 7.6 Hz, 2 H), 6.09 (s, 1 H), 5.03 (s, 1 H), 3.89 (s, 3 H), 3.70 (s, 3 H), 3.52 (d, *J* = 15.2 Hz, 1 H), 2.73 (d, *J* = 15.2 Hz, 1 H), 2.26 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 166.7, 142.9, 137.3, 137.2, 135.5, 134.9, 132.6, 130.3, 129.0, 128.5, 128.4, 128.2, 128.0, 127.84, 127.81, 127.4, 127.0, 78.8, 77.4, 71.9, 53.2, 52.9, 49.4, 21.3.

MS (ESI): *m*/*z* = 619.2 [M + H$^+$].

HRMS: *m*/*z* calcd for $C_{33}H_{32}ClN_2O_6S^+$: 619.1678; found: 619.1664.

Dimethyl 1-Benzyl-5-(4-methoxyphenyl)-2-phenyl-3-tosylimidazolidine-4,4-dicarboxylate (3ig)
Yield: 220.8 mg (90%); white solid; dr = 4:1 (*trans*/*cis*).

IR (neat): 2953, 2933, 2861, 2841, 1781, 1756, 1734, 1613, 1513, 1456, 1440, 1339, 1305, 1285, 1253, 1228, 1212, 1155, 1091, 1059, 1031, 986, 950, 936 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans* isomer) = 6.75–7.55 (m, 18 H),* 6.08 (s, 1 H), 4.99 (s, 1 H), 3.89 (s, 3 H), 3.76 (s, 3 H), 3.71 (s, 3 H), 3.52–3.64 (m, 1 H),* 2.69 (d, *J* = 15.2 Hz, 1 H), 2.46 (s, 3 H). δ (*cis* isomer) = 6.75–7.55 (m, 18 H),* 5.34 (s, 1 H), 4.56 (s, 1 H), 3.81 (s, 6 H), 3.46–3.64 (m, 1 H),* 3.37 (d, *J* = 14.8 Hz, 1 H), 3.31 (s, 3 H), 2.27 (s, 3 H). * Peaks overlap with those of the other isomer.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 168.3, 167.0, 166.8, 160.1, 159.9, 142.7, 142.2, 138.0, 137.6, 137.5, 135.8, 135.5, 133.2, 131.1, 130.0, 129.1, 129.0, 128.4, 128.3, 128.2, 128.1, 128.03, 127.96, 127.9, 127.8, 127.7, 127.44, 127.37, 126.8, 125.6, 113.7, 79.7, 78.7, 77.4, 76.8, 72.3, 71.7, 55.2, 55.1, 53.1, 52.7, 52.3, 50.0, 49.2, 29.6, 21.3.

MS (ESI): *m*/*z* = 615.2 [M + H$^+$].

HRMS: *m*/*z* calcd for $C_{34}H_{35}N_2O_7S^+$: 615.2169; found: 615.2160.

(2*S,5*R**)-Diisopropyl 1-Benzyl-5-(4-chlorophenyl)-2-phenyl-3-tosylimidazolidine-4,4-dicaboxylate (3ja)**
Yield: 243.5 mg (90%); white solid; mp 113–118 °C.

IR (neat): 2983, 2925, 1750, 1730, 1597, 1493, 1455, 1414, 1375, 1338, 1283, 1223, 1207, 1160, 1090, 1038, 944, 905 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (*trans*/*cis*, 20:1) = 7.48 (d, *J* = 8.0 Hz, 2 H), 7.40 (d, *J* = 7.6 Hz, 2 H), 7.18–7.32 (m, 5 H), 7.08–7.20 (m, 3 H), 7.02 (t, *J* = 7.4 Hz, 2 H), 6.89 (d, *J* = 7.6 Hz, 2 H), 6.79 (d, *J* = 7.6 Hz, 2 H), 5.97 (s, 1 H), 5.23–5.35 (m, 1 H), 4.86–4.98 (m, 2 H), 3.50 (d, *J* = 15.2 Hz, 1 H), 2.72 (d, *J* = 15.2 Hz, 1 H), 2.24 (s, 3 H), 1.26–1.40 (m, 9 H), 1.05 (d, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.3, 165.5, 142.6, 137.32, 137.27, 135.5, 134.6, 132.8, 130.9, 128.8, 128.3, 128.22, 128.16, 128.1, 127.6, 127.3, 126.9, 78.4, 77.7, 71.3, 70.6, 70.4, 49.1, 21.7, 21.6, 21.5, 21.2, 21.1.

MS (ESI): *m*/*z* = 675.2 [M + H$^+$].

HRMS: *m*/*z* calcd for $C_{37}H_{40}ClN_2O_6S^+$: 675.2322; found: 675.2290.

Three-Component Reaction Performed on a Gram Scale
In a flame-dried nitrogen-flushed flask, a solution of $BnNH_2$ (0.56 g, 6 mmol), *p*-chlorobenzaldehyde (0.84 g, 6 mmol) and 4 Å MS (1 g) in anhydrous DCE (30 mL) was stirred for 1 h. Aziridine **1a** (2.34 g, 5 mmol) and $Y(OTf)_3$ (134.03 mg, 5 mol%) were added to this mixture, which was stirred at r.t. for 15 h. After filtration to remove the MS, the solution was concentrated under reduced pressure. The crude product was purified by flash chromatography to afford **3aa** (2.89 g, 83%), the identity of which was confirmed by ^{1}H and ^{13}C NMR spectroscopic analysis.

Asymmetric Cycloaddition of 1a with 2c
In an inert atmosphere, a flame-dried vial was charged with a magnetic stir bar, activated 4Å molecular sieves (100 mg), $Y(OTf)_3$ (5.40 mg, 5 mol%), *t*-Bu-Pybox (3.95 mg, 6 mol%) and DCE (2 mL). The mixture was stirred at r.t. for 3 h, then imine **2c** (66.1 mg, 0.3 mmol, 1.5 equiv) was added, followed by aziridine **1a** (93.48 mg, 0.2 mmol, 1.0 equiv). The mixture was stirred at r.t. until complete consumption of the aziridine was observed (reaction monitored by TLC analysis). The reaction mixture was then passed over a small plug of silica gel, eluted with CH_2Cl_2. After evaporation under reduced pressure, the resulting product was purified by flash chromatography to afford the product **3ac** (91.8 mg, 67%). The enantiomeric excess was determined by chiral HPLC analysis [Chiralcel OD-H; hexane–*i*-PrOH, 75:25; 0.8 mL/min; R_t = 16.19 (minor), 13.09 (major) min]: ee = 49%.

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Supporting Information

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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