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Insertion of *N*-Tosylacetimidates/Acetimidamides onto Arynes via [2 + 2] Cycloaddition

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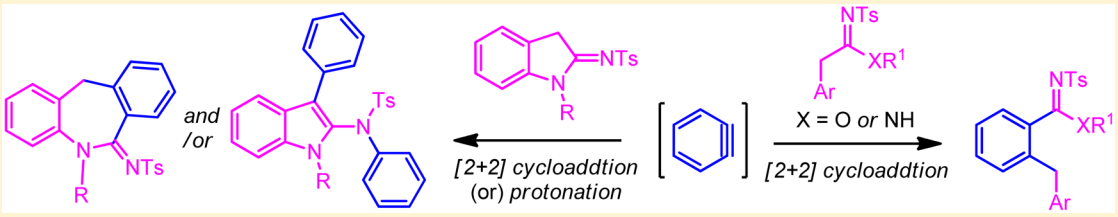
Supporting Information



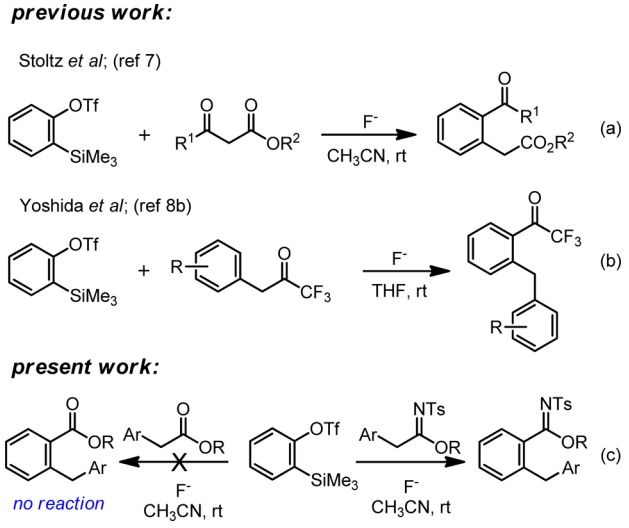
ABSTRACT: A novel insertion reaction of *N*-tosylacetimidates and *N*-tosylacetimidamides onto arynes via a benzocyclobutene intermediate followed by ring cleavage is developed to afford *o*-benzylbenzoic acid derivatives in good yields. Interestingly, the use of cyclic 2-sulfonyliminoindolines provided two distinct products such as azepanimines via [2 + 2] cycloaddition and indolamines via protonation based on solvent medium.

INTRODUCTION

The alkyne functionality is one of the perfect backbones in organic chemistry.[1] The diverse behavior of this functionality is well utilized in both symmetrical and unsymmetrical environments in aliphatic chemistry. The transient and highly reactive alkyne present in "arynes" has provided a new avenue to this linear group. The highly strained acetylenic unit in arynes provides enormous opportunities for further derivatization.[2] These arynes act as excellent dienophiles in the Diels−Alder reaction,[3] [2 + 2] and [3 + 2] cycloadditions,[2f] insertion reactions,[4] multicomponent coupling reactions (MCRs),[5] and many more.[2]

A direct insertion of aryne (in situ preparation under mild conditions using fluoride-induced 1,2-elimination of *o*-silyl aryltriflates)[6] into a C−C σ-bond generated a variety of aromatic compounds. The Stoltz research group has successfully achieved insertion of β-ketoesters into benzyne to form acyl-alkyl arenes (Scheme 1a).[7] In their protocol, the products are generally classified as *o*-acyl phenylacetic acid derivatives. Yoshida and co-workers succeeded in the acylfluorenylation of arynes.[8a] This group was also prudent in the addition of trifluoromethyl ketones to benzynes to furnish *o*-benzyl trifluoroacylarenes (Scheme 1b).[8b] Inspired by these results, we aimed at the synthesis of benzoic acid derivatives through the C−C bond insertion onto aryne. However, initial attempts using 2-arylacetates as the C−C insertion partner to aryne were unfruitful (Scheme 1c). Many unsuccessful attempts using 2-arylacetates finally culminated in identifying the *N*-tosylacetamidate of arylacetic acid as an ideal partner (Scheme 1c) probably due to its lower pK_a value of α-protons compared to 2-arylacetates (ethyl 2-phenylacetate pK_a 23).[9] The results are documented herein.

Scheme 1. Insertion of Arynes into the C−C σ-Bond



RESULTS AND DISCUSSION

Initially, direct installation of imidate and benzyl functionalities on in situ-generated benzyne from **1a** using *N*-tosylacetamidate **2a** (prepared by an easy three-component coupling of terminal alkynes, sulfonyl azide, and alcohol or amine in the presence of a copper catalyst and an amine base)[10] was attempted under mild conditions. To our utmost satisfaction, the insertion reaction was perfect with CsF and MeCN in less than 5 h to generate the desired *o*-benzyl benzimidate **3a** in 81% yield

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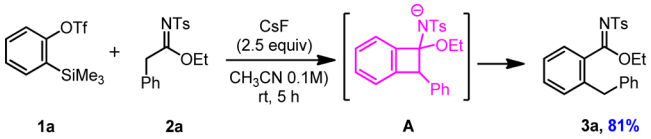
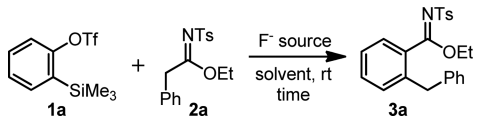
Scheme 2. Initial Result



(Scheme 2). We believe this transformation operates through the cyclobutane intermediate **A** as postulated by earlier workers.[7,8]

Among the tested reaction conditions of varying fluoride sources and solvents (Table 1), the reaction in the presence of

Table 1. Screening Optimal Conditions



entry	F⁻ source	solvent	time (h)	yield (%)[b]
1	CsF	CH_3CN	12	83
2	TBAF	CH_3CN	1	65
3	KF	CH_3CN	12	10
4[c]	KF/18-C-6	CH_3CN	12	61
5	NaF	CH_3CN	12	n.r.
6	CsF	THF	12	64
7	CsF	CH_2CI_2	12	47
8	CsF	OEt_2	12	65
9	CsF	1,4-dioxane	12	<10
10	CsF	CH_3CN	5	81

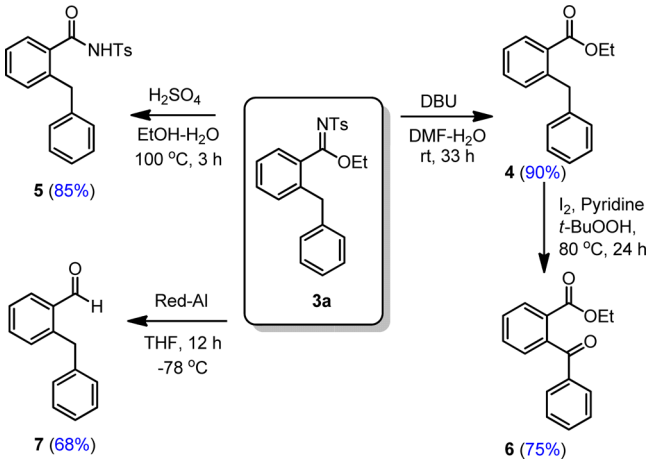
[a]Standard reaction conditions: The reaction was carried out with **1a** (0.15 mmol), **2a** (0.1 mmol), and fluride source (0.25 mmol) in solvent (0.2 M) at room temperature. [b]Yield of the isolated product. [c]A 0.25 mmol amount of 18-crown-6 was used as an addition.

CsF in CH_3CN at room temperature provided the best result. Other fluoride sources such as TBAF and KF/18-C-6 also gave 65% and 61% yields, respectively (Table 1, entries 2 and 4). Further screening of other solvents revealed that the insertion reaction gave moderate to good yields in the presence of THF, CH_2Cl_2, and diethyl ether (Table 1, entries 6−8). In the case of CsF, decreasing the reaction time did not show any significant variation on yields (Table 1, entries 1 and 10).

Synthetic utility of benzimidate **3a** is shown in Scheme 3. The products thus obtained in the insertion reaction are distinctly unique with the imidate group and are sensitive to DBU in DMF−water to provide ethyl ester **4** in 90% yield, whereas exposure to harsh acid provided *N*-tosylbenzamide **5** in 85% yield.[9a] The benzylic methylene group in ester **4** (not accessible with other insertion protocols) is functionalized to ketone using I_2/*t*-BuOOH oxidation which gave benzophenone **6** in 75% yield.[11] Controlled reduction of **3a** with Red-Al at −78 °C furnished aldehyde **7** in 68% yield.[9a]

Next, we surveyed various substrates to determine the scope of the reaction under the aforementioned optimal conditions. We began our studies on the insertion reaction using simple benzyne precursor **1a** with various *N*-tosylacetamidates and *N*-tosylacetimidamides **2** (Table 2). Substrates with both electron-donating and electron-withdrawing groups on aryl groups of imidates participated in this reaction; electron-rich substrates **2b**,**c** as well as electron-deficient **2d**−**f** including ortho-substituted *N*-tosylacetamidates gave products **3b**−**f** in

Scheme 3. Further Transformations of *o*-Benzyl Benzimidate 3a



comparable yields in the range of 72−80% (Table 2, entries 2−6). Similarly, *N*-tosylacetimidamides substituted with natural amino acids **2g**−**j** efficiently underwent the insertion reaction to furnish the corresponding ortho-benzylation products **3g**−**j** in good yields (Table 2, entries 7−10).

After investigation of the scope of acetamidates and acetimidamides, different symmetrical and unsymmetrical substituents on the benzyne precursors **1b**−**d** were tested in the insertion reaction with a variety of *N*-tosylacetamidates **2** (Table 3). The electron-rich methylenedioxy aryne precursor **1b** inserted smoothly into imidates **2d** and **2e** to furnish ortho-benzylated products **3k** and **3l**, respectively, in good yields (Table 3, entries 1 and 2). Next, we observed the coupling of unsymmetrical aryne precursor **1c** with imidates **2a**−**e** to produce the benzimidates **3m**−**q** in 65−75% yields (Table 3, entries 3−7). This reaction furnished all insertion adducts **3m**−**q** as single regioisomers as claimed by earlier workers.[12] Single-crystal X-ray analysis of compound **3q** unambiguously established its regioselective structure (see the Supporting Information).[13] Another symmetrical aryne precursor **1d** also afforded *o*-benzyl benzimidates **3r** and **3s** in excellent yields (Table 3, entries 8 and 9). Disappointingly, aliphatic imidate failed to participate in the insertion reaction under the present conditions (see Experimental Section).

Enticed by these results, we investigated the reactivity of cyclic imidamides[14] in the insertion reaction (Table 4). At first, we performed the reaction of simple benzyne precursor **1a** (2 equiv) with 2-sulfonyliminoindoline **8a** (1 equiv) under standard reaction conditions in CH_3CN using CsF and TBAF independently as fluoride sources (entry 1 and 2). Surprisingly, we observed diphenyl-substituted indolamine **9a** as the major product along with a trace amount of ring expansion product **10a** (≤5%). We hypothesized that the reaction proceeded through α-arylation and subsequent protonation with CH_3CN followed by N-arylation with benzyne to give **9a** as major product. Formation of the minor product **10a** was due to the expected benzocyclobutene intermediate. The structure of **9a** was fully characterized by NMR spectroscopy, IR, and HRMS data. Single-crystal X-ray analysis of compound **9a** has also established the indole structure (Scheme 4).[13] Interestingly, the same reaction with both CsF and TBAF in THF as solvent at room temperature gave major ring expansion product **10a** and a minor amount of diarylation product **9a** (Table 4, entries 3

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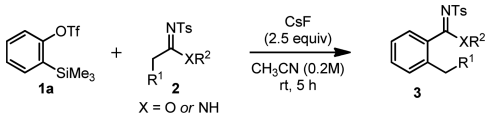
Table 2. Scope for Imidates[a]



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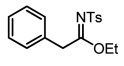
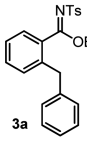
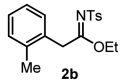
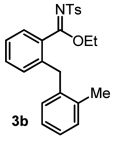
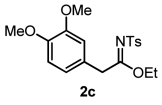
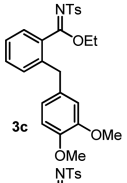
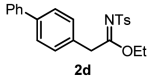
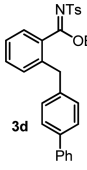
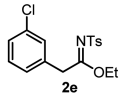
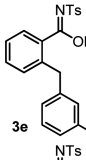
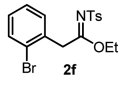
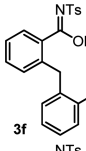
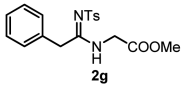
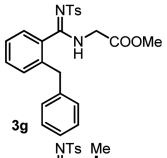
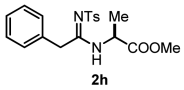
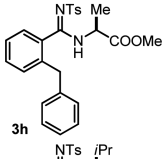
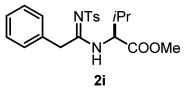
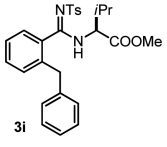
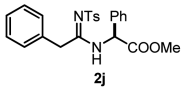
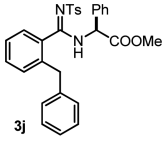
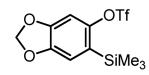
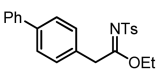
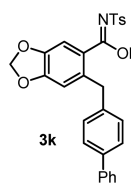
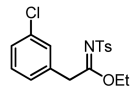
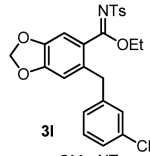
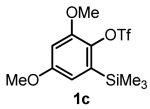
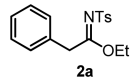
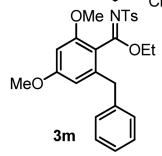
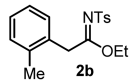
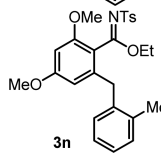
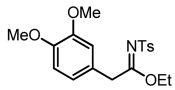
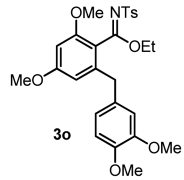
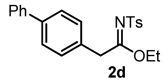
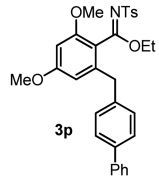
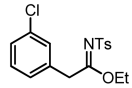
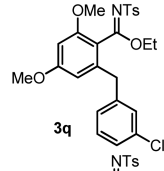
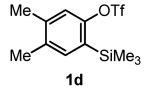
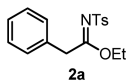
1	 2a	 3a	81%
2	 2b	 3b	75%
3	 2c	 3c	72%
4	 2d	 3d	80%
5	 2e	 3e	72%
6	 2f	 3f	75%
7	 2g	 3g	83%
8	 2h	 3h	80%
9	 2i	 3i	78%
10	 2j	 3j	79%

[a]Standard reaction conditions: The reaction was carried out with **1a** (0.15 mmol), **2** (0.1 mmol), and CsF (0.25 mmol) in CH_3CN (0.2 M) at room temperature. [b]Yield of the isolated product.

Table 3. Scope for Arynes[a]

entry	benzyne precursor	imidate	product	yield[b]
1	 1b	 2d	 3k	63%
2		 2e	 3l	68%
3	 1c	 2a	 3m	75%
4		 2b	 3n	70%
5		 2c	 3o	65%
6		 2d	 3p	74%
7		 2e	 3q	72%
8	 1d	 2a	3r	75%
9		2e	3s	78%

[a]Standard reaction conditions: The reaction was carried out with **1** (0.15 mmol), **2** (0.1 mmol), and CsF (0.25 mmol) in CH_3CN (0.2 M) at room temperature. [b]Yield of the isolated product.

and 4). The starting material **8b** also gave corresponding products **9b** and **10b** with similar ratios in two different solvents. To probe the reaction mechanism in acetonitrile solvent, the reaction was conducted with **1a** and **8a** in the

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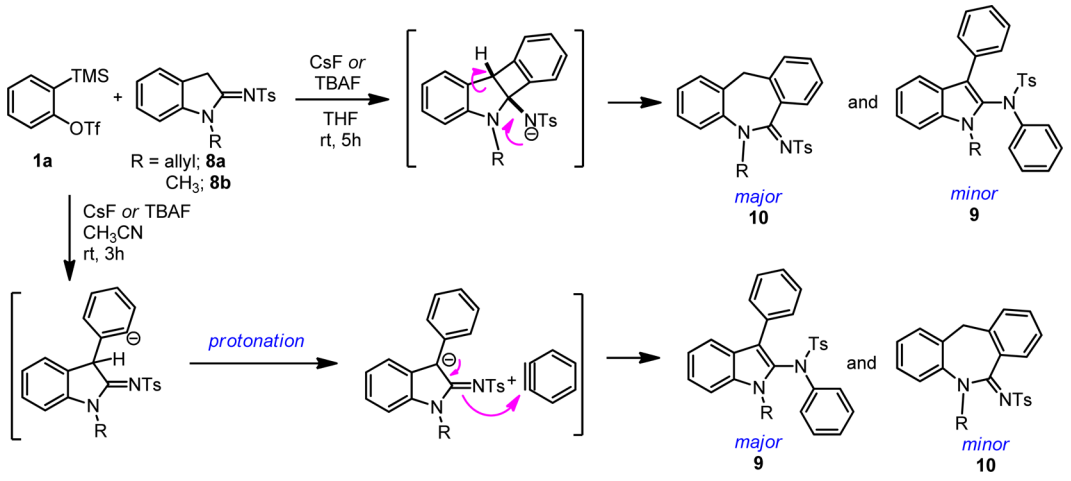
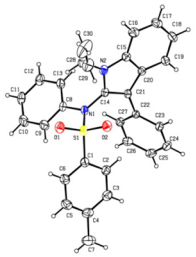
Table 4. Tunable Reactivity of 2-Sulfonyliminoindolines[a]



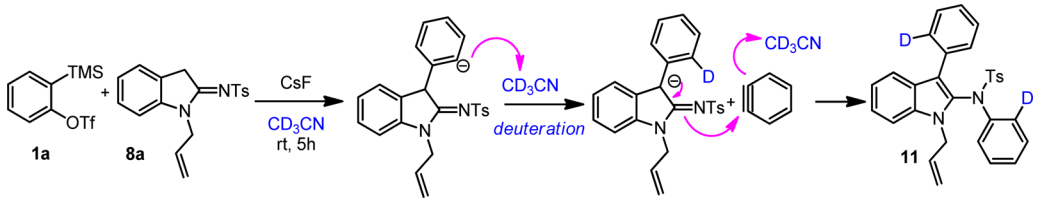


ORTEP diagram of compound **9a**

entry	starting meterials	solvent	F^- source	**9**, yield[b]	**10**, yield[b]
1	**1a, 8a**	CH_3CN	CsF	**9a**, 85%	**10a**, 5%
2	**1a, 8a**	CH_3CN	TBAF	**9a**, 87%	**10a**, <5%
3	**1a, 8a**	THF	CsF	**9a**, <5%	**10a**, 46%
4	**1a, 8a**	THF	TBAF	**9a**, 15%	**10a**, 61%
5	**1a, 8b**	CH_3CN	CsF	**9b**, 82%	**10b**, 7%
6	**1a, 8b**	THF	TBAF	**9b**, 12%	**10b**, 66%

[a]Standard reaction conditions: The reaction was carried out with **1a** (0.2 mmol), **8** (0.1 mmol), and fluoride source (0.25 mmol) in solvent (0.2 M) at room temperature. [b]Yield of the isolated product.

Scheme 4. Mechanistic Study



presence of CsF in CD_3CN to produce compound **11** with deuterium incorporation at the ortho-position of two phenyl rings (Scheme 4). This clearly indicates the formation of **11** proceeded via protonation with solvent. We also observed the reaction with an equimolar ratio of starting materials **1a** and **8a** in the presence of CsF/CH_3CN as well as TBAF/THF conditions. In this case, the insertion reaction produced similar product ratios with lower yields and starting material recovery.[10]

In summary, insertion of *N*-tosylacetimidates and *N*-tosylacetimidamides onto various substituted benzynes is demonstrated. The products thus obtained could be diversified to building blocks with various functionalities. The cyclic 2-sulfonyliminoindolines also were inserted onto benzyne to provide ring expansion products via the benzocyclobutene intermediate and diphenyl-substituted indolamines via protonation based on solvent medium.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all reagents were used as received from commercial suppliers without further purification. All reactions were performed under nitrogen atmosphere and in flame-dried or oven-dried glassware with magnetic stirring. Acetonitrile was dried in the presence of calcium chloride and distilled prior to use. THF was dried in the presence of sodium metal using benzophenone as indicator and distilled prior to use. Reactions were monitored using thin-layer chromatography (SiO_2). TLC plates were visualized with UV light (254 nm), with iodine treatment, or using *p*-anisaldehyde stain. Column chromatography was carried out using silica gel (60−120 mesh and 100−200 mesh) packed in glass columns. NMR spectra were recorded at 300, 400, 500 MHz (H) and at 75, 101, 126 MHz (C), respectively. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (H: δ = 7.26 and C: δ = 77.1 ppm) as internal standard, and coupling constants (J) are given in hertz. HRMS were recorded using ESI-TOF techniques.

a. Representative Procedure for the Preparation of Imidates and Acetimidamides. *General Procedure.* To a vigorously stirred solution alkyne (1 equiv), *p*-toluenesulfonylazide (1.2 equiv), alcohol or amine (1.2 equiv), and CuI (0.1 equiv) in CH_2Cl_2 (0.5 M) was slowly added Et_3N (2.5 equiv, 0.084 mL, 0.6 mmol) at room temperature under nitrogen atmosphere and stirred for 12 h. Later, the reaction mixture was diluted with CH_2Cl_2 and then extracted with aqueous NH_4Cl solution. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue

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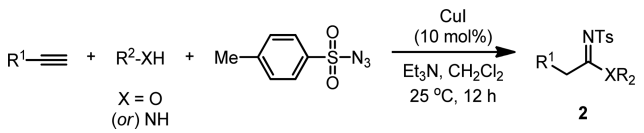

was purified by silica gel column chromatography (EtOAc/hexanes) to give the desired imidate or imidamide **2** in good yields.

*Ethyl (Z)-2-Phenyl-N-tosylacetimidate (**2a**).*[10] Prepared according to the general procedure as described above in 85% yield (2.0 g). It was purified by flash chromatography (6% EtOAc/hexanes) to afford a yellow semisolid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J = 8.2 Hz, 2H), 7.35−7.13 (m, 7H), 4.18 (s, 2H), 4.08 (q, J = 7.1 Hz, 2H), 2.36 (s, 3H), 1.14 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 143.2, 139.1, 133.7, 129.6, 129.4, 128.6, 127.2, 126.7, 64.9, 39.7, 21.6, 13.6; IR (neat) υ_{max} 3230, 3040, 2921, 1718, 1540, 1460, 1380, 1168, 1086, 760; HRMS (ESI) calcd for $C_{17}H_{20}NO_3S$ $[M + H]^+$: 318.1158; found: 318.1149.

*Ethyl (Z)-2-(o-Tolyl)-N-tosylacetimidate (**2b**).* Prepared according to the general procedure as described above in 82% yield (2.3 g). It was purified by flash chromatography (6% EtOAc/hexanes) to afford an yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 7.19−7.09 (m, 4H), 4.26 (s, 2H), 4.14 (q, J = 7.1 Hz, 2H), 2.42 (s, 3H), 2.29 (s, 3H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 143.2, 139.1, 136.8, 132.5, 130.2, 129.8, 129.4, 127.3, 126.7, 126.0, 64.9, 37.6, 21.6, 19.7, 13.5; IR (neat) υ_{max} 3244, 3068, 2923, 2853, 1919, 1715, 1597, 1444, 1344, 1086, 881, 815, 750, 664; HRMS (ESI) calcd for $C_{18}H_{21}NNaO_3S$ $[M + Na]^+$: 354.1134; found: 354.1155

*Ethyl (Z)-2-(3,4-Dimethoxyphenyl)-N-tosylacetimidate (**2c**).* Prepared according to the general procedure as described above in 76% yield (1.7 g). It was purified by flash chromatography (10% EtOAc/hexanes) to afford a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 2.0 Hz, 1H), 6.91 (dd, J = 8.2, 2.0 Hz, 1H), 6.81 (dd, J = 8.2, 4.1 Hz, 1H), 4.16 (s, 2H), 4.13 (q, J = 7.08 Hz, 2H), 3.87(s, 3H), 3.86 (s, 3H), 2.42 (s, 3H), 1.21 (t, J = 8.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 148.8, 148.2, 143.2, 139.2, 129.4, 126.6, 126.0, 121.9, 112.8, 111.1, 64.8, 55.9, 39.8, 21.5, 13.6; IR (neat) υ_{max}3250, 2924, 2851, 1725, 1594, 1515, 1457, 1306, 1264, 1156, 1090, 1027, 854, 769, 688; HRMS (ESI) calcd for $C_{19}H_{23}NNaO_5S$ $[M + Na]^+$: 400.1189; found: 400.1207.

*Ethyl (Z)-2-([1,1′-Biphenyl]-4-yl)-N-tosylacetimidate (**2d**).* Prepared according to the general procedure as described above in 85% yield (1.9 g). It was purified by flash chromatography (6% EtOAc/hexanes) to afford a pale yellow solid; mp = 180 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.4 Hz, 2H), 7.43 (ddd, J = 4.1, 3.3, 1.8 Hz, 2H), 7.41−7.36 (m, 2H), 7.31−7.25 (m, 4H), 7.22−7.16 (m, 1H), 7.16−7.10 (m, 2H), 4.12 (s, 2H), 4.01 (q, J = 7.12 Hz, 2H), 2.26 (s, 3H), 1.07 (q, J = 7.02 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 143.4, 140.9, 140.2, 139.2, 132.8, 130.1, 129.5, 128.9, 127.4, 127.2, 126.8, 65.0, 39.5, 21.7, 13.7; IR (neat) υ_{max}3249, 3031, 2923, 1718, 1598, 1446, 1342, 1168, 1086, 815, 755, 699; HRMS (ESI) calcd for $C_{23}H_{24}NO_3S$ $[M + H]^+$: 394.1471; found: 394.1502.

*Ethyl (E)-2-(3-Chlorophenyl)-N-tosylacetimidate (**2e**).* Prepared according to the general procedure as described above in 80% yield (2.0 g). It was purified by flash chromatography (8% EtOAc/hexanes) to afford a pale yellow semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.3 Hz, 2H), 7.34−7.20 (m, 6H), 4.22 (s, 2H), 4.17 (q, J = 7.1 Hz, 2H), 2.44 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 143.4, 138.9, 135.5, 134.3, 129.8, 129.6, 129.4, 127.9, 127.5, 126.7, 65.0, 39.2, 21.6, 13.5; IR (neat) υ_{max} 3240, 2924, 2855, 1718, 1597, 1575, 1441, 1347, 1170, 1121, 1086, 840, 792, 683; HRMS (ESI) calcd for $C_{17}H_{18}ClNNaO_3S$ $[M + Na]^+$: 374.0588; found: 374.0593.

*Ethyl (E)-2-(2-Bromophenyl)-N-tosylacetimidate (**2f**).* Prepared according to the general procedure as described above in 80% yield (1.7 g). It was purified by flash chromatography (7% EtOAc/hexanes) to afford a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.36 Hz, 2H), 7.54 (dd, J = 6.2, 2.2 Hz, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.28−7.20 (m, 2H), 7.16−7.10 (m, 1H), 4.40 (s, 2H), 4.16 (q, J = 7.13 Hz, 2H), 2.43 (s, 3H), 1.13 (t, J = 7.09 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 143.3, 138.9, 134.1, 132.7, 131.2, 129.4, 128.9, 127.5, 126.8, 125.1, 65.1, 40.6, 21.6, 13.4; IR (neat) υ_{max} 3062, 2985, 1919, 1598, 1472, 1371, 1306, 1157, 1093, 1026, 893, 749, 689; HRMS (ESI) calcd for $C_{17}H_{19}BrNO_3S$ $[M + H]^+$: 396.0264; found: 396.0297.

*Methyl (Z)-4-Phenyl-3-(tosylimino)butanoate (**2g**).* Prepared according to the general procedure as described above in 82% yield (2.8 g). It was purified by flash chromatography (15% EtOAc/hexanes) to afford a pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 8.3 Hz, 2H), 7.43−7.35 (m, 3H), 7.28 (d, J = 8.0 Hz, 2H), 7.26−7.23 (m, 2H), 5.86 (s, 1H), 4.31 (s, 2H), 3.98 (d, J = 4.7 Hz, 2H), 3.66 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 166.5, 142.5, 140.4, 132.6, 130.2, 129.5, 129.2, 128.3, 126.5, 52.6, 43.4, 39.5, 21.5; IR (neat) υ_{max}, 3354, 2955, 2925, 1749, 1560, 1275, 1145, 1091, 813, 759, 694; HRMS (ESI) calcd for $C_{18}H_{21}N_2O_4S$ $[M + H]^+$: 361.1217; found: 361.1239.

*Methyl (Z)-(2-Phenyl-1-(tosylimino)ethyl)-L-alaninate (**2h**).* Prepared according to the general procedure as described above in 85% yield (3.1 g). It was purified by flash chromatography (15% EtOAc/hexanes) to afford a pale yellow oil; $[\alpha]_D$ −7.64 (c 1.5, $CHCl_3$), ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 2H), 7.46−7.34 (m, 3H), 7.32−7.20 (m, 4H), 5.98 (d, J = 6.0 Hz, 1H), 4.53 (p, J = 7.0 Hz, 1H), 4.30 (s, 2H), 3.64 (s, 3H), 2.43 (s, 3H), 1.31 (d, J = 7.08 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 165.7, 142.3, 140.5, 132.8, 130.0, 129.4, 129.2, 128.2, 126.4, 52.6, 50.1, 39.5, 21.5, 17.3; IR (neat) υ_{max} 3306, 3065, 2926, 2855, 2423, 1914, 1744, 1558, 1453, 1360, 1277, 1147, 1023, 814, 763, 700; HRMS (ESI) calcd for $C_{19}H_{23}N_2O_4S$ $[M + H]^+$: 375.1373; found: 375.1404.

*Methyl (Z)-(2-Phenyl-1-(tosylimino)ethyl)valinate (**2i**).* Prepared according to the general procedure as described above in 82% yield (3.2 g). It was purified by flash chromatography (12% EtOAc/hexanes) to afford a yellow oil; $[\alpha]_D$ −22.30 (c 0.9, $CHCl_3$), ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 2H), 7.41 (t, J = 7.3 Hz, 2H), 7.36 (t, J = 7.3 Hz, 1H), 7.30−7.24 (m, 4H), 5.71 (d, J = 7.0 Hz, 1H), 4.47 (dd, J = 7.8, 4.7 Hz, 1H), 4.40 (d, J = 17.5 Hz, 1H), 4.25 (d, J = 17.5 Hz, 1H), 3.61 (s, 3H), 2.42 (s, 3H), 2.13−1.98 (m, 1H), 0.75 (d, J = 6.9 Hz, 3H), 0.67 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 166.4, 142.3, 140.5, 132.8, 130.1, 129.5, 129.2, 128.3, 126.3, 59.0, 52.2, 39.8, 30.7, 21.5, 18.7, 17.7; IR (neat) υ_{max} 3230, 2960, 2926, 2855, 1743, 1551, 1455, 1369, 1274, 1211, 1146, 1090, 1032, 812, 759, 697; HRMS (ESI) calcd for $C_{21}H_{26}N_2NaO_4S$ $[M + Na]^+$: 425.1505; found: 425.1536.

*Methyl (R,Z)-2-Phenyl-2-(2-phenyl-N′-tosylacetimidamido)-acetate (**2j**).* Prepared according to the general procedure as described above in 86% yield (3.2 g). It was purified by flash chromatography (12% EtOAc/hexanes) to afford a pale yellow semisolid; $[\alpha]_D$ +26.82 (c 0.3, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.3 Hz, 2H), 7.45−7.36 (m, 3H), 7.33−7.26 (m, 4H), 7.25 (dd, J = 3.3, 1.7 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.09 (dt, J = 3.7, 2.2 Hz, 2H), 6.35 (d, J = 5.7 Hz, 1H), 5.40 (d, J = 6.1 Hz, 1H), 4.31 (q, J = 17.5 Hz, 2H), 3.58 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 165.3, 142.2, 140.3, 135.2, 132.7, 130.0, 129.5, 129.0, 128.9, 128.8, 128.3, 127.3, 126.3, 58.3, 53.0, 39.6, 21.5; IR (neat) υ_{max} 3320, 2925, 2855, 1746, 1547, 1273, 1219, 1147, 1092, 773, 698; HRMS (ESI) calcd for $C_{24}H_{24}N_2NaO_4S$ $[M + Na]^+$: 459.1349; found: 459.1372.

*Ethyl (Z)-N-Tosylhexanimidate (**S1**).* Prepared according to the general procedure as described above in 88% yield (3.0 g). It was purified by flash chromatography (5% EtOAc/hexanes) to afford a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8.8 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 4.14 (q, J = 7.0 Hz, 2H), 2.86 (t, J = 7.64 Hz, 2H), 2.43 (s, 3H), 1.69 (ddd, J = 15.2, 8.9, 6.6 Hz, 2H), 1.42−1.30 (m, 4H), 1.26 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.4, 143.1, 139.4, 129.4, 126.6, 64.5, 34.0, 31.5, 25.7, 22.3, 21.5, 13.9, 13.7; IR (neat) υ_{max} 2958, 2933, 1601, 1463, 1374, 1311, 1158, 1094, 1022, 889, 815, 690; HRMS (ESI) calcd for $C_{15}H_{23}NNaO_3S$ $[M + Na]^+$: 320.1291; found: 320.1303.

b. General Optimal Reaction Procedure for the Insertion Reaction. A oven-dried round-bottom flask equipped with a magnetic

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stirring bar was charged with aryne precursor **1** (0.3 mmol), imidate or imidamide **2** (0.2 mmol), and CsF (0.5 mmol) in CH_3CN (0.2 M) under nitrogen atmosphere. The resulting mixture was stirred at room temperature for 4 h. After the reaction was finished, the solvent was evaporated and the residue was purified by flash column chromatography (hexanes/ethyl acetate) to give the corresponding product.

*Ethyl (Z)-2-Benzyl-N-tosylbenzimidate (**3a**).* Prepared according to the general procedure as described above in 81% yield (100 mg). It was purified by flash chromatography (7% EtOAc/hexanes) to afford a pale yellow semisolid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.3 Hz, 2H), 7.40−7.32 (m, 2H), 7.27 (d, J = 3.2 Hz, 1H), 7.25−7.16 (m, 5H), 7.14−7.07 (m, 3H), 4.24 (q, J = 7.1 Hz, 2H), 3.89 (s, 2H), 2.41 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 143.3, 139.9, 138.9, 138.3, 132.5, 130.7, 130.2, 129.4, 128.5, 128.0, 127.2, 126.4, 125.9, 65.5, 39.3, 21.7, 13.7; IR (neat) υ_{max} 2925, 2854, 1608, 1592, 1304, 1155, 1091, 940, 736; HRMS (ESI) calcd for $C_{23}H_{24}NO_3S$ $[M + H]^+$: 394.1471; found: 394.1474.

*Ethyl (Z)-2-(2-Methylbenzyl)-N-tosylbenzimidate (**3b**).* Prepared according to the general procedure as described above in 75% yield (91 mg). It was purified by flash chromatography (7% EtOAc/hexanes) to afford a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 8.3 Hz, 2H), 7.38−7.29 (m, 2H), 7.24 (dd, J = 11.5, 4.4 Hz, 3H), 7.18−7.08 (m, 3H), 7.00 (d, J = 6.9 Hz, 1H), 6.89 (d, J = 7.7 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 3.84 (s, 2H), 2.42 (s, 3H), 2.18 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 143.3, 138.9, 137.8, 137.6, 136.9, 132.5, 130.7, 130.5, 130.3, 129.4, 129.2, 127.9, 127.2, 126.8, 126.1, 125.8, 65.5, 36.7, 21.7, 19.8, 13.7; IR (neat) υ_{max} 2981, 2925, 1608, 1450, 1303, 1156, 1091, 1014, 939, 814, 745, 686; HRMS (ESI) calcd for $C_{24}H_{26}NO_3S$ $[M + H]^+$: 408.1628; found: 408.1646.

*Ethyl (Z)-2-(3,4-Dimethoxybenzyl)-N-tosylbenzimidate (**3c**).* Prepared according to the general procedure as described above in 72% yield (86 mg). It was purified by flash chromatography (6% EtOAc/hexanes) to afford a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J = 8.3 Hz, 2H), 7.33−7.27 (m, 2H), 7.20 (d, J = 3.7 Hz, 1H), 7.16 (d, J = 8.1 Hz, 2H), 7.04 (d, J = 7.6 Hz, 1H), 6.69 (d, J = 8.1 Hz, 1H), 6.65−6.59 (m, 2H), 4.19 (q, J = 7.1 Hz, 2H), 3.80 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 2.34 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 147.8, 146.4, 142.1, 137.5, 131.3, 129.6, 128.9, 128.2, 126.8, 125.9, 124.8, 120.2, 111.5, 109.8, 64.3, 54.8, 54.7, 37.7, 20.5, 12.6; IR (neat) υ_{max} 2925, 2854, 1785, 1744, 1593, 1514, 1464, 1304, 1261, 1155, 1090, 1027, 940, 771, 686; HRMS (ESI) calcd for $C_{25}H_{28}NO_5S$ $[M + H]^+$: 454.1683; found: 454.1705.

*Ethyl (Z)-2-([1,1′-Biphenyl]-4-ylmethyl)-N-tosylbenzimidate (**3d**).* Prepared according to the general procedure as described above in 80% yield (95 mg). It was purified by flash chromatography (8% EtOAc/hexanes) to afford a pale yellow solid (80%); mp = 220 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, J = 8.3 Hz, 2H), 7.51−7.45 (m, 2H), 7.42 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 7.6 Hz, 3H), 7.26−7.16 (m, 3H), 7.15−7.07 (m, 5H), 4.16 (q, J = 7.1 Hz, 2H), 3.88 (s, 2H), 2.31 (s, 3H), 1.14 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.6, 143.2, 141.0, 139.3, 139.0, 138.9, 138.3, 132.6, 130.8, 130.3, 129.8, 129.3, 128.9, 128.5, 128.2, 127.3, 127.2, 127.1, 126.1, 65.5, 39.1, 21.7, 13.7; IR (neat) υ_{max} 3027, 2923, 2405, 1593, 1487, 1304, 1155, 1091, 1010, 940, 761, 686; HRMS (ESI) calcd for $C_{29}H_{28}NO_3S$ $[M + H]^+$: 470.1784; found: 470.1794.

*Ethyl (Z)-2-(3-Chlorobenzyl)-N-tosylbenzimidate (**3e**).* Prepared according to the general procedure as described above in 72% yield (87 mg). It was purified by flash chromatography (6% EtOAc/hexanes) to afford a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 8.3 Hz, 2H), 7.42−7.33 (m, 2H), 7.28 (t, J = 6.5 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.19−7.15 (m, 2H), 7.13−7.07 (m, 2H), 7.02 (d, J = 6.6 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.87 (s, 2H), 2.42 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 143.4, 142.0, 138.8, 137.4, 134.3, 132.6, 130.9, 130.1, 129.8, 129.4, 128.2, 127.6, 127.1, 126.6, 126.3, 65.5, 39.0, 21.7, 13.6; IR (neat) υ_{max} 2925, 2854, 1738, 1592, 1448, 1304, 1155, 1091, 1014, 1014, 941, 708, 685; HRMS (ESI) calcd for $C_{23}H_{23}ClNO_3S$ $[M + H]^+$: 428.1082; found: 428.1084.

*Ethyl (Z)-2-(2-Bromobenzyl)-N-tosylbenzimidate (**3f**).* Prepared according to the general procedure as described above in 75% yield (89 mg). It was purified by flash chromatography (5% EtOAc/hexanes) to afford a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.3 Hz, 2H), 7.54 (dt, J = 7.8, 3.9 Hz, 1H), 7.47−7.35 (m, 2H), 7.34−7.28 (m, 1H), 7.24−7.16 (m, 3H), 7.10−7.00 (m, 3H), 4.26 (q, J = 7.1 Hz, 2H), 3.93 (s, 2H), 2.40 (s, 3H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 143.2, 139.2, 138.6, 136.6, 132.5, 132.5, 131.4, 130.8, 129.9, 129.2, 128.3, 128.0, 127.5, 127.0, 126.1, 124.7, 65.4, 39.1, 21.6, 13.5; IR (neat) υ_{max} 2984, 1591, 1469, 1444, 1370, 1307, 1219, 1156, 1091, 1022, 939, 814, 769, 708, 686; HRMS (ESI) calcd for $C_{23}H_{23}BrNO_3S$ $[M + H]^+$: 472.0577; found: 472.0597.

*Methyl (Z)-((2-Benzylphenyl)(tosylimino)methyl)glycinate (**3g**).* Prepared according to the general procedure as described above in 83% yield (100 mg). It was purified by flash chromatography (16% EtOAc/hexanes) to afford a brown oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 8.3 Hz, 2H), 7.29 (dt, J = 4.2, 1.7 Hz, 1H), 7.24 (d, J = 8.7 Hz, 2H), 7.22−7.19 (m, 1H), 7.13−7.08 (m, 3H), 7.03−6.98 (m, 2H), 6.86 (dd, J = 7.1, 2.2 Hz, 2H), 4.35 (s, 2H), 4.27 (s, 2H), 3.60 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.6, 166.5, 142.2, 141.8, 140.5, 134.2, 129.6, 129.1, 128.9, 128.5, 128.2, 127.9, 126.5, 54.5, 52.2, 37.1, 21.5; IR (neat) υ_{max} 3320, 2925, 2850, 1750, 1543, 1495, 1283, 1216, 1147, 1090, 773, 701; HRMS (ESI) calcd for $C_{24}H_{25}N_2O_4S$ $[M + H]^+$: 437.1530; found: 437.1510.

*Methyl (Z)-((2-Benzylphenyl)(tosylimino)methyl)-D-alaninate (**3h**).* Prepared according to the general procedure as described above in 80% yield (96 mg). It was purified by flash chromatography (15% EtOAc/hexanes) to afford a brown oil; $[\alpha]_D$ −49.92 (c 0.4, $CHCl_3$), ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 2H), 7.38−7.27 (m, 3H), 7.25−7.17 (m, 2H), 7.15−7.08 (m, 3H), 6.93−6.79 (m, 3H), 4.73 (q, J = 7.3 Hz, 1H), 4.22 (q, J = 15.3 Hz, 2H), 3.57 (s, 3H), 2.41 (s, 3H), 1.20 (d, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 165.6, 142.2, 140.6, 139.0, 134.4, 129.4, 129.3, 129.1, 129.1, 128.9, 128.5, 128.4, 128.2, 126.5, 126.5, 59.0, 52.2, 38.0, 21.5, 15.2; IR (neat) υ_{max} 3320, 2925, 2856, 2881, 1746, 1541, 1495, 1455, 1377, 1283, 1208, 1149, 1090, 1016, 809, 760, 703; HRMS (ESI) calcd for $C_{25}H_{26}N_2NaO_4S$ $[M + Na]^+$: 473.1505; found: 473.1531.

*Methyl (Z)-((2-Benzylphenyl)(tosylimino)methyl)valinate (**3i**).* Prepared according to the general procedure as described above in 78% yield (92 mg). It was purified by flash chromatography (16% EtOAc/hexanes) to afford a colorless oil; $[\alpha]_D$ −113.28 (c 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 7.8 Hz, 3H), 7.19 (t, J = 7.2 Hz, 2H), 7.13−7.03 (m, 4H), 6.98 (s, 1H), 6.81−6.76 (m, 2H), 4.33 (d, J = 8.6 Hz, 1H), 4.30 (d, J = 15.3 Hz, 1H), 4.18 (d, J = 15.2 Hz, 1H), 3.56 (s, 3H), 2.43 (s, 3H), 2.19−2.28 (m, 1H), 0.94 (d, J = 6.8 Hz, 3H), 0.81 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.3, 166.0, 142.2, 140.5, 134.3, 129.1, 128.7, 128.6, 128.1, 126.5, 126.5, 70.3, 51.8, 38.1, 28.1, 21.5, 20.7; IR (neat) υ_{max} 3306, 2966, 1744, 1540, 1494, 1284, 1205, 1149, 1091, 1013, 771, 704; HRMS (ESI) calcd for $C_{27}H_{31}N_2O_4S$ $[M + H]^+$: 479.1999; found: 479.1999.

*Methyl (S,Z)-2-(2-Benzyl-N′-tosylbenzimidamido)-2-phenylacetate (**3j**).* Prepared according to the general procedure as described above in 79% yield (92 mg). It was purified by flash chromatography (16% EtOAc/hexanes) to afford an orange oil; $[\alpha]_D$ +2.16 (c 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.3 Hz, 2H), 7.25−7.21 (m, 1H), 7.13−7.09 (m, 4H), 7.04 (t, J = 7.3 Hz, 4H), 6.92−6.88 (m, 2H), 6.86 (dd, J = 6.5, 2.9 Hz, 2H), 6.79 (dd, J = 10.8, 5.9 Hz, 1H), 6.16 (d, J = 7.6 Hz, 1H), 6.14 (s, 1H), 4.31−4.19 (m, 2H), 3.55 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.3, 166.2, 142.3, 137.7, 134.5, 132.3, 130.7, 130.5, 130.4, 129.1, 128.6, 128.5, 128.4, 128.3, 128.2, 126.6, 126.4, 66.7, 52.3, 38.2, 21.5; IR (neat) υ_{max} 3306, 2923, 1747, 1536, 1283, 1216, 1148, 1091, 772, 701; HRMS (ESI) calcd for $C_{30}H_{29}N_2O_4S$ $[M + H]^+$: 513.1843; found: 513.1821.

*Ethyl (Z)-6-([1,1′-Biphenyl]-4-ylmethyl)-N-tosylbenzo[d][1,3]-dioxole-5-carbimidate (**3k**).* Prepared according to the general procedure as described above in 68% yield (88 mg). It was purified by flash chromatography (8% EtOAc/hexanes) to afford a brown

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semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 2H), 7.57−7.53 (m, 2H), 7.49 (d, J = 8.2 Hz, 2H), 7.42 (t, J = 7.7 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 7.21 (dd, J = 8.2, 3.3 Hz, 4H), 6.84 (s, 1H), 6.60 (s, 1H), 5.98 (s, 2H), 4.23 (q, J = 7.1 Hz, 2H), 3.85 (s, 2H), 2.40 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 149.6, 145.7, 143.1, 140.9, 139.0, 138.9, 133.2, 129.5, 129.2, 128.7, 128.3, 127.1, 127.0, 125.2,110.3, 108.3, 101.7, 65.4, 38.7, 21.5, 13.6; IR (neat) υ_{max} 3027, 2958, 2923, 1594, 1485, 1374, 1305, 1158, 1091, 1038, 924, 759, 694; HRMS (ESI) calcd for $C_{30}H_{28}NO_5S$ $[M + H]^+$: 514.1683; found: 514.1681.

*Ethyl (Z)-6-(3-Chlorobenzyl)-N-tosylbenzo[d][1,3]dioxole-5-carbimidate (**3l**).* Prepared according to the general procedure as described above in 68% yield (91 mg). It was purified by flash chromatography (10% EtOAc/hexanes) to afford a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71−7.66 (m, 2H), 7.26−7.23 (m, 2H), 7.20−7.16 (m, 2H), 7.11 (t, J = 3.6 Hz, 1H), 7.06−7.00 (m, 1H), 6.81 (s, 1H), 6.52 (s, 1H), 5.98 (s, 2H), 4.23 (q, J = 7.2 Hz, 2H), 3.77 (s, 2H), 2.42 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 149.7, 145.8, 143.3, 142.0, 138.8, 134.2, 132.2, 129.7, 129.3, 129.2, 127.3, 127.0, 126.5, 125.3, 110.1, 108.3, 101.7, 65.5, 38.7, 21.6, 13.5; IR (neat) υ_{max} 2925, 2854, 1606, 1462, 1321, 1204, 1159, 1089, 933, 754, 686; HRMS (ESI) calcd for $C_{24}H_{23}ClNO_5S$ $[M + H]^+$: 472.0980; found: 472.1014.

*Ethyl (Z)-2-Benzyl-4,6-dimethoxy-N-tosylbenzimidate (**3m**).* Prepared according to the general procedure as described above in 75% yield (107 mg). It was purified by flash chromatography (8% EtOAc/hexanes) to afford a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 7.56 Hz, 2H), 7.22−7.13 (m, 5H), 6.23 f− 6.20 (m, 2H), 4.36−4.13 (m, 2H), 3.86 (s, 2H), 3.72 (s, 3H), 3.62 (s, 3H), 2.40 (s, 3H), 1.17 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 162.2, 157.4, 142.9, 141.0, 139.8, 138.8, 129.3, 129.1, 128.5, 127.4, 126.3, 115.2, 106.6, 96.1, 65.3, 55.6, 55.4, 39.5, 21.7, 13.7; IR (neat) υ_{max} 2929, 1606, 1460, 1322, 1159, 1089, 936, 772, 686; HRMS (ESI) calcd for $C_{25}H_{28}NO_5S$ $[M + H]^+$: 454.1683; found: 454.1673.

*Ethyl (Z)-2,4-Dimethoxy-6-(2-methylbenzyl)-N-tosylbenzimidate (**3n**).* Prepared according to the general procedure as described above in 70% yield (98 mg). It was purified by flash chromatography (10% EtOAc/hexanes) to afford a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J = 8.2 Hz, 2H), 7.14 (d, J = 8.1 Hz, 2H), 7.09−6.94 (m, 4H), 6.15 (d, J = 2.0 Hz, 1H), 5.96 (d, J = 2.0 Hz, 1H), 4.21 (q, J = 6.9 Hz, 2H), 3.75 (s, 2H), 3.61 (s, 3H), 3.57 (s, 3H), 2.34 (s, 3H), 2.13 (s, 3H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 162.1, 157.3, 142.9, 140.5, 138.7, 137.4, 136.8, 130.3, 130.1, 129.0, 127.2, 126.6, 125.9, 106.0, 95.7, 65.2, 55.5, 55.2, 36.7, 21.5, 19.7, 13.6; IR (neat) υ_{max} 2924, 2852, 1606, 1462, 1322, 1204, 1159, 1089, 933, 753, 685; HRMS (ESI) calcd for $C_{26}H_{29}NNaO_5S$ $[M + Na]^+$: 490.1659; found: 490.1659.

*Ethyl (Z)-2-(3,4-Dimethoxybenzyl)-4,6-dimethoxy-N-tosylbenzimidate (**3o**).* Prepared according to the general procedure as described above in 65% yield (88 mg). It was purified by flash chromatography (10% EtOAc/hexanes) to afford a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 6.79−6.67 (m, 3H), 6.21 (t, J = 1.9 Hz, 2H), 4.35−4.20 (br.m, 2H), 3.85 (s, 3H), 3.81 (s, 3H), 3.80 (d, J = 3.9 Hz, 1H), 3.77 (d, J = 3.9 Hz, 1H), 3.72 (s, 3H), 3.62 (s, 3H), 2.40 (s, 3H), 1.23 (t, J = 5.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 162.2, 157.4, 149.0, 147.6, 142.9, 141.4, 138.8, 132.3, 129.1, 127.3, 121.4, 112.8, 111.1, 106.4, 96.1, 65.7, 56.0, 55.6, 55.4, 39.0, 21.7, 13.8; IR (neat) υ_{max} 3010, 2933, 2847, 2278, 1735, 1606, 1513, 1463, 1320, 1303, 1206, 1158, 1089, 1027, 936, 814, 758, 684; HRMS (ESI) calcd for $C_{27}H_{31}NNaO_7S$ $[M + Na]^+$: 536.1713; found: 536.1744.

*Ethyl (Z)-2-([1,1′-Biphenyl]-4-ylmethyl)-4,6-dimethoxy-N-tosylbenzimidate (**3p**).* Prepared according to the general procedure as described above in 74% yield (99 mg). It was purified by flash chromatography (8% EtOAc/hexanes) to afford a brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 8.2 Hz, 2H), 7.51−7.45 (m, 2H), 7.44−7.30 (m, 4H), 7.26 (dd, J = 13.2, 5.9 Hz, 1H), 7.14 (dd, J = 12.3, 8.1 Hz, 4H), 6.18 (dd, J = 15.6, 2.0 Hz, 2H), 4.30−4.05 (br.m, 2H), 3.85 (s, 2H), 3.68 (s, 3H), 3.55 (s, 3H), 2.31 (s, 3H), 1.10 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 162.2, 157.6, 142.9, 141.1, 140.9, 139.3, 138.9, 138.8, 129.7, 129.1, 128.8, 127.3, 127.2, 127.2, 127.1, 115.3, 106.8, 96.2, 65.4, 55.7, 55.5, 39.2, 21.6, 13.7; IR (neat) υ_{max} 3024, 2937, 1735, 1605, 1462, 1303, 1205, 1158, 1089, 1049, 936, 757, 686; HRMS (ESI) calcd for $C_{31}H_{32}NO_5S$ $[M + H]^+$: 530.1996; found: 530.1995

*Ethyl (Z)-2-(3-Chlorobenzyl)-4,6-dimethoxy-N-tosylbenzimidate (**3q**).* Prepared according to the general procedure as described above in 68% yield (94 mg). It was purified by flash chromatography (10% EtOAc/hexanes) to afford a yellow solid (72%); mp = 138 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 7.11−7.05 (m, 3H), 6.98 (d, J = 6.8 Hz, 1H), 6.15 (dd, J = 9.8, 2.1 Hz, 2H), 4.28−4.08 (m, 2H), 3.77 (s, 2H), 3.68 (s, 3H), 3.55 (s, 3H), 2.33 (s, 3H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 162.3, 157.6, 143.0, 141.9, 140.0, 138.7, 134.3, 129.7, 129.3, 129.1, 127.5, 127.3, 126.6, 106.7, 96.3, 65.4, 55.7, 55.5, 39.2, 21.7, 13.7; IR (neat) υ_{max} 2926, 2850, 1606, 1465, 1320, 1206, 1158, 1089, 937, 758, 685; HRMS (ESI) calcd for $C_{25}H_{27}ClNO_5S$ $[M + H]^+$: 488.1293; found: 488.1293.

*Ethyl (Z)-2-Benzyl-4,5-dimethyl-N-tosylbenzimidate (**3r**).* Prepared according to the general procedure as described above in 75% yield (99 mg). It was purified by flash chromatography (6% EtOAc/hexanes) to afford a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.3 Hz, 2H), 7.25−7.16 (m, 5H), 7.13 (d, J = 7.4 Hz, 2H), 7.01 (s, 1H), 6.88 (s, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.86 (s, 2H), 2.41 (s, 3H), 2.19 (s, 6H), 1.17 (t, J = 7.1 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.0, 143.0, 140.3, 139.5, 138.9, 135.6, 134.2, 131.4, 129.2, 129.1, 128.8, 128.3, 127.3, 127.1, 126.1, 65.2, 38.9, 21.6, 19.9, 19.3, 13.6; IR (neat) υ_{max} 2924, 1736, 1596, 1473, 1322, 1302, 1158, 1092, 1017, 921, 773, 686; HRMS (ESI) calcd for $C_{25}H_{28}NO_3S$ $[M + H]^+$: 422.1784; found: 422.1781.

*Ethyl (Z)-2-(3-Chlorobenzyl)-4,5-dimethyl-N-tosylbenzimidate (**3s**).* Prepared according to the general procedure as described above in 78% yield (101 mg). It was purified by flash chromatography (7% EtOAc/hexanes) to afford a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.59 (m, 2H), 7.24−7.19 (m, 2H), 7.18−7.09 (m, 3H), 7.04 (dd, J = 7.6, 5.8 Hz, 2H), 6.90−6.83 (m, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.84 (d, J = 3.6 Hz, 2H), 2.41 (s, 3H), 2.23 (s, 3H), 2.21 (s, 3H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 143.0, 142.4, 139.6, 134.6, 134.1, 131.4, 129.6, 129.16, 129.0, 127.4, 127.3, 127.1, 127.0, 126.3, 65.3, 38.6, 21.6, 19.9, 19.3, 13.5; IR (neat) υ_{max} 2924, 1596, 1473, 1322, 1220, 1156, 1092, 921, 773; HRMS (ESI) calcd for $C_{25}H_{27}ClNO_3S$ $[M + H]^+$: 456.1395; found: 456.1399.

*Ethyl 2-Benzylbenzoate (**4**).*[15] To a solution of imidate **3a** (100 mg, 0.254 mmol) in DMF and H_2O (95/5, 1 mL) was added DBU (10 mol %, 6.2 μL). The reaction mixture was stirred at room temperature for 30 h, diluted with water, and then extracted with cold Et_2O (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (EtOAc/hexanes = 2:98) to give the desired ester **4** in 90% yield (55 mg) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92−7.85 (m, 1H), 7.41 (dt, J = 7.5, 3.8 Hz, 1H), 7.33−7.26 (m, 2H), 7.25−7.11 (m, 5H), 4.38 (s, 2H), 4.28 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 141.9, 141.0, 131.8, 131.5, 130.5, 128.9, 128.3, 126.2, 125.9, 60.9, 39.6, 14.2; IR (neat) υ_{max} 2926, 2854, 1720, 1451, 1260, 1130, 1079, 773, 741; HRMS (ESI) calcd for $C_{16}H_{16}NaO_2$ $[M + Na]^+$: 263.1043; found: 263.1045.

*2-Benzyl-N-tosylbenzamide (**5**).* To a solution of sulfonylimidate **3a** (100 mg, 0.254 mmol) in EtOH/H_2O (95/5, 1 mL) was added concd H_2SO_4 (95 μL, 7.0 equiv). The reaction mixture was stirred at 100 °C for 3 h. After cooling to room temperature, the mixture was diluted by addition of CH_2Cl_2. A saturated aqueous solution of $NaHCO_3$ was added, and the reaction mixture was extracted with CH_2Cl_2 (3 × 10 mL).The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (EtOAc/hexanes = 20:80) to give the desired amide **5** in 85% yield (79 mg) as a yellow solid; mp = 140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (bs, 1H),

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7.96 (d, J = 8.4 Hz, 2H), 7.45−7.38 (m, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 11.9 Hz, 1H), 7.23 (d, J = 7.8 Hz, 1H), 7.17−7.12 (m, 3H), 6.96 (dd, J = 7.0, 2.5 Hz, 2H), 4.07 (s, 2H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0, 131.9, 131.6, 129.6, 128.7, 128.6, 128.5, 127.6, 126.6, 126.3, 38.4, 21.7;IR (neat) υ_{max} 3239, 3063, 2924, 1700, 1598, 1493, 1432, 1344, 1241, 1168, 1091, 1060, 890, 813, 745, 701; HRMS (ESI) calcd for $C_{21}H_{19}NNaO_3S$ $[M + Na]^+$: 388.0978; found: 388.0998.

*Ethyl 2-Benzoylbenzoate (**6**).*[16] A mixture of ester **4** (100 mg, 0.416 mmol), iodine (10.5 mg, 0.0416 mmol), pyridine (4.2 μL, 0.0416 mmol), aqueous *tert*-butyl hydroperoxide (70% in H_2O, 1.0 mL) was placed into a 15 mL sealed tube and heated at 80 °C with vigorous stirring for 24 h. The reaction mixture was cooled to room temperature and directly subjected to purification by flash column chromatography (EtOAc/hexanes = 5:95) to afford the desired benzophenone **6** in 75% yield (78 mg) as a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (dd, J = 1.2, 7.8 Hz, 1H), 7.78−7.75 (m, 2H), 7.66−7.62 (m, 1H), 7.59−7.53 (m, 2H), 7.45−7.39 (m, 3H), 4.07 (q, J = 7.1 Hz, 2H), 1.05 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.1, 152.6, 137.4, 133.2, 132.5, 130.3, 129.7, 129.6, 129.5, 128.6, 128.5, 127.8, 61.6, 13.8; IR (neat) υ_{max} 2940, 2863, 1760, 1680, 1520, 1352, 1195, 980, 720, 699; HRMS (ESI) calcd for $C_{16}H_{14}NaO_3$ $[M + Na]^+$: 277.0835; found: 277.0856.

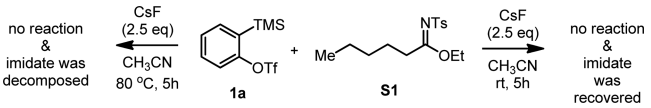
*2-Benzylbenzaldehyde (**7**).*[17] To a stirred solution of imidate **3a** (100 mg, 0.254 mmol) in THF (0.1 M) was added slowly Red-Al (65% w/w toluene solution, 554 μL, 7.0 equiv) at −78 °C. The reaction was continued at −78 °C for 18 h and then quenched by addition of MeOH (0.1 mL) at the same temperature. The mixture was stirred for 5 min at that temperature, and H_2O (5 mL) was added. The temperature was allowed to increase to room temperature, and the mixture was extracted with ethyl acetate (2 × 10 mL) and a saturated aqueous solution of NH_4Cl (10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by flash column chromatography (EtOAc/hexanes = 2:98) to afford the desired aldehyde **7** in 68% yield (30 mg) as a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.24 (s, 1H), 7.85 (dd, J = 7.6, 1.1 Hz, 1H), 7.51 (td, J = 7.5, 1.3 Hz, 1H), 7.40 (t, J = 7.3 Hz, 1H), 7.28 (dd, J = 11.6, 4.8 Hz, 1H), 7.24 (s, 2H), 7.18 (t, J = 7.4 Hz, 1H), 7.13 (d, J = 7.3 Hz, 2H), 4.44 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.4, 143.0, 140.3, 133.9, 132.1, 131.7, 128.8, 128.6, 127.0, 126.3, 38.1; IR (neat) υ_{max} 2923, 2820, 1698, 1599, 1452, 1203, 756, 699; HRMS (ESI) calcd for $C_{14}H_{13}O$ $[M + Na]^+$: 197.0961; found: 197.0957.

c. Reactivity of 2-Sulfonyliminoindolines in the Insertion Reaction with CsF in CH_3CN or THF. *General Procedure.* An oven-dried round-bottom flask equipped with a magnetic stirring bar was charged with aryne precursor **1a** (2equiv), 2-sulfonyliminoindolines **8**[14] (1 equiv), and CsF (2.5 equiv) in CH_3CN or THF (0.2 M) under nitrogen atmosphere. The resulting mixture was stirred at room temperature for 5 h. After the reaction was finished, the solvent was evaporated and the residue was purified by flash column chromatography (hexanes/ethyl acetate) to give the corresponding major and minor products.

d. Reactivity of 2-Sulfonyliminoindolines in the Insertion Reaction with TBAF in CH_3CN or THF. *General Procedure.* An oven-dried round-bottom flask equipped with a magnetic stirring bar was charged with aryne precursor **1a** (2 equiv) and 2-sulfonyliminoindolines **8** (1 equiv) in THF or CH_3CN (0.2 M) under nitrogen atmosphere. The resulting reaction mixture was added TBAF (1.0 M in THF solution, 2.5 equiv) and stirred at room temperature for 3 h. After the reaction was finished, the solvent was evaporated and the residue was purified by flash column chromatography (hexanes/ethyl acetate) to give the corresponding major and minor products.

*N-(1-Allyl-3-phenyl-1H-indol-2-yl)-4-methyl-N-phenylbenzenesulfonamide (**9a**).* Prepared according to the general procedure as described above in 85% yield (124 mg) as the major isomer. It was purified by flash chromatography (2% EtOAc/hexanes) to afford a white solid; mp = 152 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.3 Hz, 1H), 7.37−7.33 (m, 2H), 7.32−7.26 (m, 3H), 7.25−7.20 (m, 5H), 7.20−7.15 (m, 3H), 7.09 (ddd, J = 8.4, 2.6, 1.3 Hz, 1H), 6.96 (d, J = 8.0 Hz, 2H), 5.93 (ddt, J = 17.1, 10.4, 5.7 Hz, 1H), 5.22 (ddd, J = 13.7, 11.6, 1.3 Hz, 2H), 4.88 (qdt, J = 16.6, 5.3, 1.6 Hz, 2H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 142.1, 136.3, 134.9, 133.6, 133.2, 129.6, 129.2, 129.2, 128.4, 128.0, 126.6, 126.2, 124.9, 123.4, 121.4, 120.4, 120.4, 117.8, 115.5, 111.1, 46.4, 21.5; IR (neat) υ_{max} 3060, 2330, 1598, 1492, 1461, 1357, 1217, 1165, 1090, 927, 814, 771, 700; HRMS (ESI) calcd for $C_{30}H_{26}N_2NaO_2S$ $[M + Na]^+$: 501.1607; found: 501.1610.

*4-Methyl-N-(1-methyl-3-phenyl-1H-indol-2-yl)-N-phenylbenzenesulfonamide (**9b**).* Prepared according to the general procedure as described above in 82% yield (123 mg) as the major isomer. It was purified by flash chromatography (2% EtOAc/hexanes) to afford a white solid; mp = 191 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 8.0 Hz, 1H), 7.27−7.38 (m, 4H), 7.25−7.23 (m, 2H), 7.22−7.17 (m, 6H), 7.14−7.08 (m, 3H), 6.96 (d, J = 8.1 Hz, 2H), 3.85 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9, 142.5, 136.7, 135.3, 133.6, 129.9, 129.4, 129.3, 129.3, 128.4, 127.8, 126.4, 125.7, 124.8, 123.5, 120.9, 120.5, 120.4, 114.9, 110.0, 30.0, 21.5; IR (neat) υ_{max}3060, 2926, 2854, 1596, 1491, 1470, 1358, 1166, 1091, 964, 928, 814, 752, 697; HRMS (ESI) calcd for $C_{28}H_{25}N_2O_2S$ $[M + H]^+$: 453.1631; found: 453.1640.



*(Z)-N-(5-Allyl-5,11-dihydro-6H-dibenzo[b,e]azepin-6-ylidene)-4-methylbenzenesulfonamide (**10a**).* Prepared according to the general procedure as described above in 61% yield (78 mg). It was purified by flash chromatography (8% EtOAc/hexanes) to afford as a red colored oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, J = 7.7, 1.2 Hz, 1H), 7.78−7.72 (m, 2H), 7.39−7.27 (m, 3H), 7.23−7.10 (m, 6H), 5.99 (ddt, J = 16.5, 10.3, 5.9 Hz, 1H), 5.19−5.10 (m, 2H), 4.79−4.62 (m, 2H), 3.90 (d, J = 13.2 Hz, 1H), 3.48 (d, J = 13.2 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.6, 142.8, 141.7, 141.5, 140.3, 139.4, 132.4, 132.33, 132.29, 129.0, 127.6, 127.3, 126.9, 126.3, 126.2, 125.4, 124.2, 118.5, 56.5, 38.5, 21.5; IR (neat) υ_{max}3018, 2924, 2854, 1733, 1582, 1519, 1478, 1402, 1286, 1146, 1089, 1023, 909, 821, 766; HRMS (ESI) calcd for $C_{24}H_{22}N_2NaO_2S$ $[M + Na]^+$: 425.1294; found: 425.1295.

*(Z)-4-Methyl-N-(5-methyl-5,11-dihydro-6H-dibenzo[b,e]azepin-6-ylidene)benzenesulfonamide (**10b**).* Prepared according to the general procedure as described above in 66% yield (82 mg). It was purified by flash chromatography (8% EtOAc/hexanes) to afford a brown semisolid, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, J = 7.8, 1.2 Hz, 1H), 7.81−7.78 (m, 2H), 7.38 (tt, J = 5.3, 2.6 Hz, 1H), 7.33−7.27 (m, 2H), 7.24−7.20 (m, 4H), 7.19−7.13 (m, 2H), 3.92 (d, J = 13.1 Hz, 1H), 3.65 (s, 3H), 3.52 (d, J = 13.2 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 142.8, 142.0, 141.8, 140.4, 139.7, 132.8, 132.6, 129.8, 129.2, 128.9, 127.7, 127.3, 127.1, 126.6, 126.4, 126.3, 125.6, 124.2, 41.7, 38.6, 21.6; IR (neat) υ_{max} 2950, 1730, 1517, 1388, 1281, 1145, 1089, 772; HRMS (ESI) calcd for $C_{22}H_{20}N_2NaO_2S$ $[M + Na]^+$: 399.1138; found: 399.1118.

*N-(1-Allyl-3-(phenyl-2-d)-1H-indol-2-yl)-4-methyl-N-(phenyl-2-d)-benzenesulfonamide (**11**).* Prepared according to the general procedure as described above in 78% yield (51 mg). It was purified by flash chromatography (2% EtOAc/hexanes) to afford a white semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.35 (d, J = 8.3 Hz, 2H), 7.29 (ddd, J = 7.5, 6.4, 4.5 Hz, 2H), 7.25−7.15 (m, 7H), 7.10 (dd, J = 10.9, 3.7 Hz, 1H), 6.96 (d, J = 8.2 Hz, 2H), 5.93 (ddd, J = 22.8, 10.7, 5.6 Hz, 1H), 5.23 (ddd, J = 13.7, 11.4, 1.2 Hz, 2H), 4.89 (qd, J = 16.6, 5.6 Hz, 2H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0, 142.2, 136.4, 135.0, 133.6, 133.3, 129.7, 129.3, 129.3, 129.2, 128.5, 128.4, 128.1, 126.7, 126.3, 125.0, 123.5, 121.5, 120.5, 117.9, 115.6, 111.3, 46.5, 21.6; HRMS (ESI) calcd for $C_{30}H_{24}D_2N_2NaO_2S$ $[M + Na]^+$: 503.1733; found: 503.171.

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E. ASSOCIATED CONTENT

Supporting Information

Reactivity of Aliphatic Imidate S1 in the Insertion ReactionThe Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02907.

Copies of ^{1}H and ^{13}C spectra for all new compounds; ORTEPs of **3q** and **9a** (PDF)
X-ray crystallographic data of compound **3q** (CIF)
X-ray crystallographic data of compound **9a** (CIF)

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Notes

The authors declare no competing financial interest.

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