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Efficient Synthesis of Diarylmethylamines via Lewis Acid Catalyzed Friedel–Crafts Reactions of Donor–Acceptor Aziridines with *N*,*N*-Dialkylanilines

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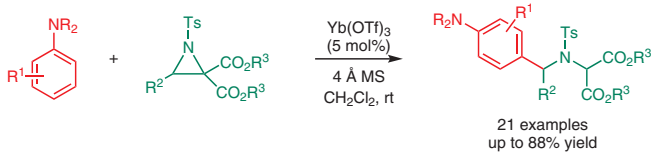

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Abstract A method for efficient and mild synthesis of diarylmethylamine scaffold, via Lewis acid catalyzed Friedel–Crafts reaction of donor–acceptor aziridines with N,N-dialkylanilines to afford a biologically important diarylmethylamine derivatives in high yields (up to 88%), is presented. This reaction is suitable for the synthesis of various diarylmethylamine derivatives and has a broad scope for electron-rich arenes, including dimethoxybenzene.

Key words diarylmethylamine, Friedel–Crafts reaction, donor–acceptor aziridine, *N*,*N*-dialkylaniline, Lewis acid

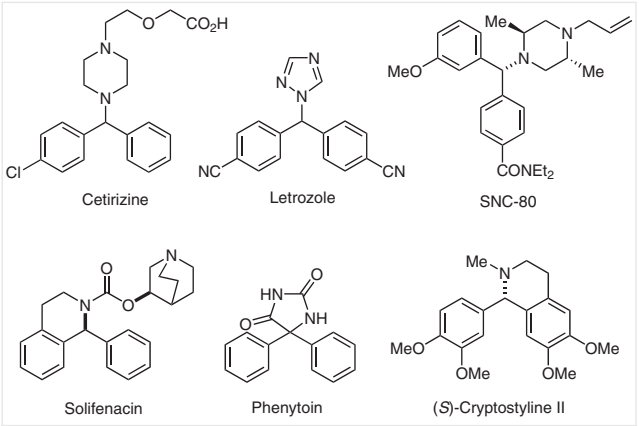

Figure 1 Representative examples of biologically active diarylmethylamine compounds

The diarylmethylamine motif is the structural basis for the distinctive and desirable biological properties of a large number of small molecule natural products and biologically active compounds (Figure 1).[1] This privileged structure is used extensively in the syntheses of drug targets for the treatment of various diseases, such as allergy (Cetirizine),[1c] breast cancer (Letrozole),[1a] and overactive bladder (Solifenacin).[1e] Owing to their unique structural features and potent biological activities, substantial efforts have been devoted in the past decade for establishing a novel and efficient approach for the synthesis of diarylmethylamines.[2] Consequently, various synthetic routes have been developed, in which the transition-metal-catalyzed arylation to aldimine with arylboronic acid was dominant.[3] Although several useful reactions have been reported, developing a simpler and more practical approach for the synthesis of diarylmethylamines remains highly desirable.

The ring-opening reaction of 2-arylazirines with aryl nucleophiles is an effective route for the synthesis of β-diarylamines, although diarylmethylamines cannot be synthesized via this route.[4] In particular, the Lewis acid catalyzed Friedel–Crafts reaction of electron-rich arenes with aziridine has been reported by several research groups (Scheme 1a).[5] In 2001, Yadav et al. reported the ring-opening reaction of *N*-tosylaziridine with arenes in the presence of a catalytic amount of $In(OTf)_3$, affording the corresponding β-diarylamine derivatives.[5a] Subsequently, Wu et al. presented a gold(III) chloride/silver triflate-catalyzed Friedel–Crafts type ring-opening reaction of *N*-tosylaziridine with electron-rich arenes,[5b] while Roy et al. developed a Friedel–Crafts type ring-opening reaction of *N*-tosylaziridine with arenes using $AgPF_6$ as the catalyst.[5c] Ghorai et al. employed $Zn(OTf)_2/Sc(OTf)_3$ as the catalyst for the ring-opening reaction of N-activated aziridines with electron-rich arenes.[5f]

In all these cases, the resulting products are β-diarylamines, which were obtained from the Lewis acid catalyzed C–N bond cleavage of *N*-tosylaziridine owing to the high reactivity of the C–N bond of aziridine (Scheme 1a). As part of our ongoing program on exploring the utility of donor-

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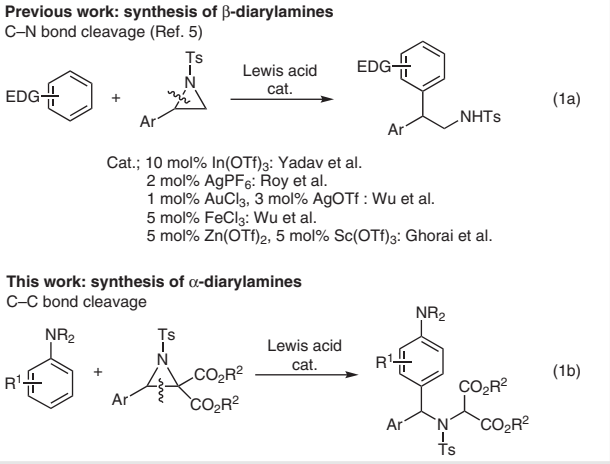
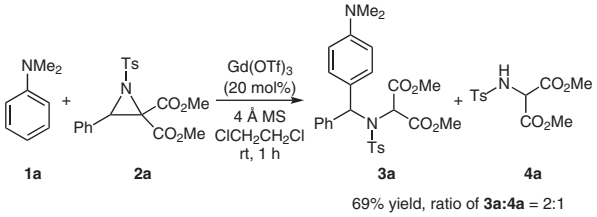


Scheme 1 Friedel–Crafts type ring-opening reactions of *N*-tosylaziridine

acceptor (D–A) 3-membered cyclic compounds,[6] we envisaged that electron-rich benzenes, such as *N*,*N*-dialkylanilines, might undergo Lewis acid catalyzed Friedel–Crafts reaction with D–A aziridines, affording diarylmethylamine derivatives having dialkyl malonate group. D–A aziridines undergo Lewis acid catalyzed C–C bond cleavage to generate $1_C,3_C$-ylides (azomethine ylides),[7,8] which could react with electron-rich arenes to provide diarylmethylamine derivatives rather than β-diarylamine derivatives (Scheme 1b).

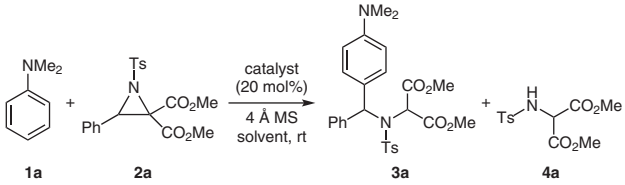
Based on the results of our previous work,[6] we initiated our investigation on the Friedel–Crafts type ring-opening reaction of *N*,*N*-dimethylaniline (**1a**) with 3-phenyl-*N*-tosylaziridinedicatcarboxyate (**2a**),[9] which was selected as the model reaction (Scheme 2). When the reaction of **1a** with **2a** was carried out in the presence of 20 mol% $Gd(OTf)_3$ as the catalyst using 4 Å molecular sieves in $ClCH_2CH_2Cl$ at room temperature, the reaction reached completion within 1 hour, and the desired diarylmethylamine product **3a** was obtained in good yield. However, a significant amount of side product **4a** was also isolated. The two compounds, **3a** and **4a**, had similar R_f values, rendering their separation in columns difficult. It was assumed that **4a** was produced from starting material **2a**, or from product **3a** (vide infra).



Scheme 2 Friedel–Crafts reactions of *N*,*N*-dimethylaniline (**1a**) with *N*-tosylaziridine **2a**

In order to obtain the optimum conditions for the reaction of **1a** with **2a**, various Lewis acids were first screened, and the results are shown in Table 1. While the yield of **3a** was lower and amount of **4a** was higher in the presence of $Sc(OTf)_3$ as compared $Gd(OTf)_3$, the outcomes were similar in the presence of $Sm(OTf)_3$ and $Gd(OTf)_3$ (Table 1, entries 2 and 3). $Yb(OTf)_3$ was found to be a better catalyst and resulted in higher yields, with a good ratio of **3a**:**4a** (entry 4). Other Lewis acids, such as $Cu(OTf)_2$, $Zn(OTf)_2$, $Mg(OTf)_2$, $FeCl_3$, and $Ni(ClO)_4$ were found to be less efficient than $Gd(OTf)_3$ (entries 5–9). To further improve the reaction efficiency, various solvents such as CH_2Cl_2, toluene, trifluorotoluene, and THF were examined in the $Yb(OTf)_3$ catalyzed

Table 1 Screening of Catalysts and Solvents for Optimization[a]



Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]	**3a**:**4a**[c]
1	$Gd(OTf)_3$	$ClCH_2CH_2Cl$	1	69	2:1
2	$Sc(OTf)_3$	$ClCH_2CH_2Cl$	5	18	1:3
3	$Sm(OTf)_3$	$ClCH_2CH_2Cl$	1	67	3:2
4	$Yb(OTf)_3$	$ClCH_2CH_2Cl$	1	86	4:1
5	$Cu(OTf)_2$	$ClCH_2CH_2Cl$	1	12	ND
6	$Zn(OTf)_2$	$ClCH_2CH_2Cl$	12	no reaction	ND
7	$Mg(OTf)_2$	$ClCH_2CH_2Cl$	12	no reaction	ND
8	$FeCl_3$	$ClCH_2CH_2Cl$	1	8	1:2
9	$Ni(ClO_4)_2$	$ClCH_2CH_2Cl$	12	no reaction	ND
10	$Yb(OTf)_3$	CH_2Cl_2	1	86	5:1
11	$Yb(OTf)_3$	toluene	24	58	2:1
12	$Yb(OTf)_3$	$PhCF_3$	1	54	2:1
13	$Yb(OTf)_3$	THF	12	no reaction	ND
14[d]	$Yb(OTf)_3$	CH_2Cl_2	1	66	2:1
15[e]	$Yb(OTf)_3$	CH_2Cl_2	1	57	2:1
16[f]	$Yb(OTf)_3$	CH_2Cl_2	2	52	4:1
17[g]	$Yb(OTf)_3$	CH_2Cl_2	1	72	5:1
18[h]	$Yb(OTf)_3$	CH_2Cl_2	2	78	7:1

[a] The reactions were carried out in solvent (0.1 M) with **1a** (0.10 mmol) and **2a** (0.15 mmol) in the presence of 4 Å molecular sieves and 20 mol% catalyst at rt, unless otherwise noted.
[b] Isolated yield of the mixture **3a** and **4a** after chromatographic purification.
[c] Determined by ^1H NMR analysis of the crude product. ND: Not determined.
[d] Molecular sieves 3 Å were used instead of 4 Å.
[e] Molecular sieves 5 Å were used instead of 4 Å.
[f] The reaction was carried out at 10 °C.
[g] $Yb(OTf)_3$: 10 mol%.
[h] $Yb(OTf)_3$: 5 mol%.

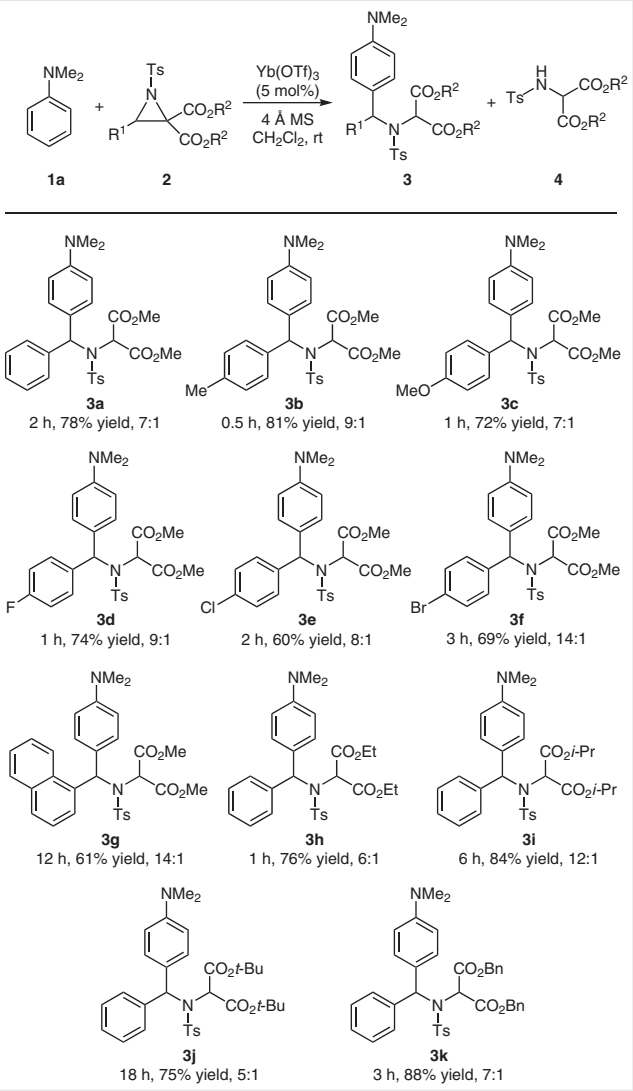
reaction (entries 10–13). The reaction medium was found to have a substantial impact on the conversion efficiency and chemoselectivity of the reaction; among the solvents tested, CH_2Cl_2 emerged as the best choice. To further optimize the reaction conditions, different types of molecular sieves and reaction temperature were tested (entries 14–16). No additional efficiency was rendered using 20 mol% $Yb(OTf)_3$ in CH_2Cl_2, and the best results were still obtained using 4 Å molecular sieves at room temperature. In addition, decreasing the catalyst loading to 5 mol% enhanced the chemoselectivity (ratio of **3a** and **4a** increased to 7:1), without significantly affecting the reaction yield (entry 18).

With the optimized reaction conditions in hand (1 equiv of **1**, 1.5 equiv of **2**, 5 mol% $Yb(OTf)_3$, 4 Å molecular sieves, CH_2Cl_2 solvent, and rt), we explored the scope and functional group tolerance for this novel Friedel–Crafts type ring-opening reaction for the synthesis of diarylmethylamines. As shown in Scheme 3, various D–A *N*-tosylaziridines **2** were reacted with electron-rich *N*,*N*-dimethylaniline (**1a**) to generate the desired products in moderate to good yields. The electronic effect of the substituents showed no obvious influence on the reaction. For example, *N*-tosylaziridines **2** substituted by electron-donating groups Me, OMe (**2b**, **2c**) or electron-withdrawing groups F, Cl, Br (**2d–f**) on the vicinal phenyl ring led to the desired diarylmethylamine derivatives **3b–f** in good yields. Moreover, substrate **2g** with the naphthyl substituent was successfully converted to the desired product **3g** in 61% yield. Furthermore, *N*-tosylaziridines with different ester groups (Et, *i*-Pr, *t*-Bu, Bn) were examined. Substrates **2h–k** were compatible with this reaction, affording the expected products **3h–k** in moderate to good yields (61–88%).

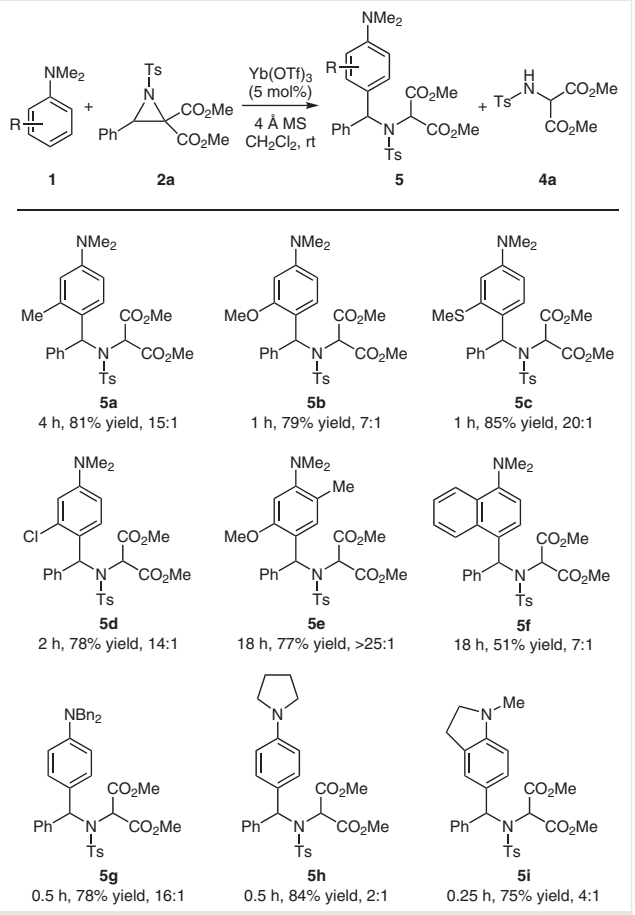
Inspired by these results, we next explored the scope for aniline-derived electron-rich arenes **1** (Scheme 4). It is evident that this Friedel–Crafts type ring-opening reaction was compatible with a wide range of *N*,*N*-dimethylanilines **1** with different substituents (electron-donating and electron-withdrawing group) on the phenyl ring, affording the corresponding *N*-tosyldiarylmethylamino malonates **5a–e** in overall good yields. The electronic effect and the position of the substituents seem to have little influence on the reaction. When *N*,*N*-dimethylnaphthalen-1-amine (**1f**) was used for this ring-opening reaction, the expected product **5f** was obtained in 51% yield. *N*,*N*-Dibenzylaniline (**1g**) was found to be a good substrate and was more reactive than *N*,*N*-dimethylaniline in this reaction, affording the desired product **5h** in 78% yield. We also found that pyrrolidinobenzene **1h** and indoline derivative **1i** were more reactive than *N*,*N*-dimethylaniline (**1a**). However, the chemoselectivities were low for these reactions.

Encouraged by the above results, we next examined the scope of the strategy for the synthesis of diarylmethylamines, employing 1,3-dimethoxybenzene (**6**) as the substrate corresponding to the electron-rich arene. When **6** was treated with **2a** in the presence of 10 mol% $Yb(OTf)_3$ using 4 Å molecular sieves in CH_2Cl_2 at room temperature, the desired diarylmethylamine **7** was obtained in 72% yield, along with the side product **4a** (Scheme 5). However, the reaction of **2a** with *N*-methylindole, another type of electron-rich arene, under the optimized reaction conditions provided complex products.

To test the practicality of our synthetic method, a one mmol scale reaction was performed under the optimized reaction conditions (Scheme 6). The reaction smoothly afforded **3a** in good yield (82%), without any loss in the reaction efficiency (ratio of **3a**:**4a** = 8:1). Finally, when **3a** was



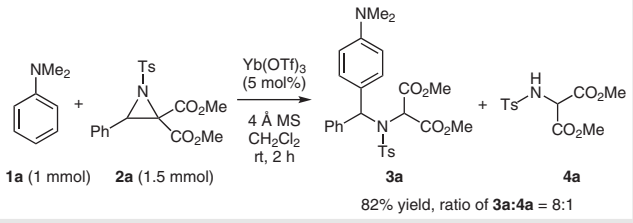
Scheme 3 Substrate scope of *N*-tosylaziridines. *Reagents and conditions*: The reactions were carried out in CH_2Cl_2 (0.1 M) with **1a** (0.10 mmol) and **2** (0.15 mmol) in the presence of 4 Å molecular sieves and 5 mol% $Yb(OTf)_3$ at rt. Isolated yields of a mixture of **3** and **4** are given. The ratio of **3**:**4** was determined by ^1H NMR analysis of the crude product.



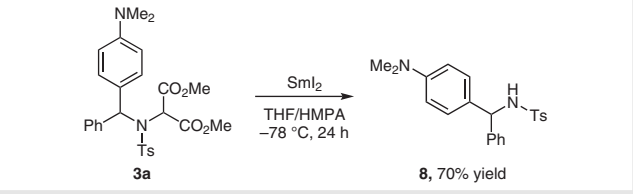
Scheme 4 Substrate scope of aniline-derived electron-rich arenes. *Reagents and conditions*: The reactions were carried out in CH_2Cl_2 (0.1 M) with **1** (0.10 mmol) and **2a** (0.15 mmol) in the presence of 4 Å molecular sieves and 5 mol% $Yb(OTf)_3$ at rt. Isolated yields of a mixture of **5** and **4a** are given. The ratio of **5**:**4a** was determined by ^1H NMR analysis of the crude product.

treated with samarium(II) iodide in THF/HMPA at –78 °C, the dimethylmalonate group was removed, and diarylmethylamine **8** was formed in 70% yield (Scheme 7). However, detosylation could not be accomplished under these reaction conditions.[10]

Based on our experimental results and previous literature,[6,7] we propose a plausible reaction pathway to account for the Lewis acid catalyzed Friedel–Crafts reaction of D–A aziridines with *N*,*N*-dialkylanilines (Scheme 8). The coordination of $Yb(OTf)_3$ to the carbonyl oxygen atoms of the dicarboxylate group of **2a** generates the activated aziridine intermediate **Ia**, which subsequently undergoes selective C–C bond cleavage to generate the metal coordinated azomethine ylide **Ib**. The decomposition of **Ib** in the presence of a trace amount of water produces $TsNHCH(CO_2Me)_2$ (**4a**).[7c,e] The nucleophilic attack of *N*,*N*-dimethylaniline (**1a**) via the Friedel–Crafts type reaction affords a zwitterionic intermediate **Ic**, which undergoes rearomatization to produce intermediate **Id**. The subsequent steps yield the product **3a** predominantly and regenerate the catalytic cycle. Incidentally, conjugative assisted C–N bond cleavage of intermediate **Id** would also generate **4a**.

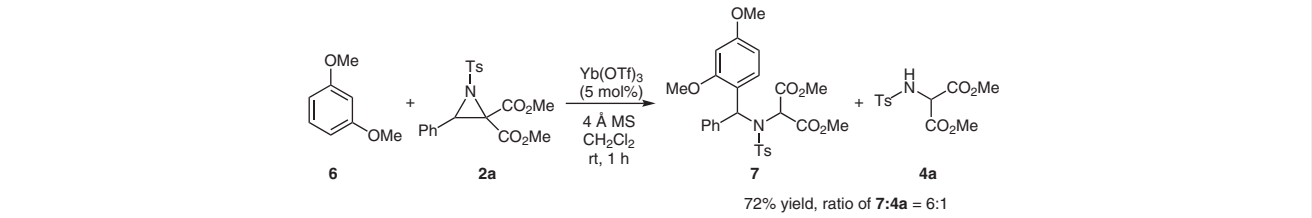


Scheme 6 One mmol scale synthesis

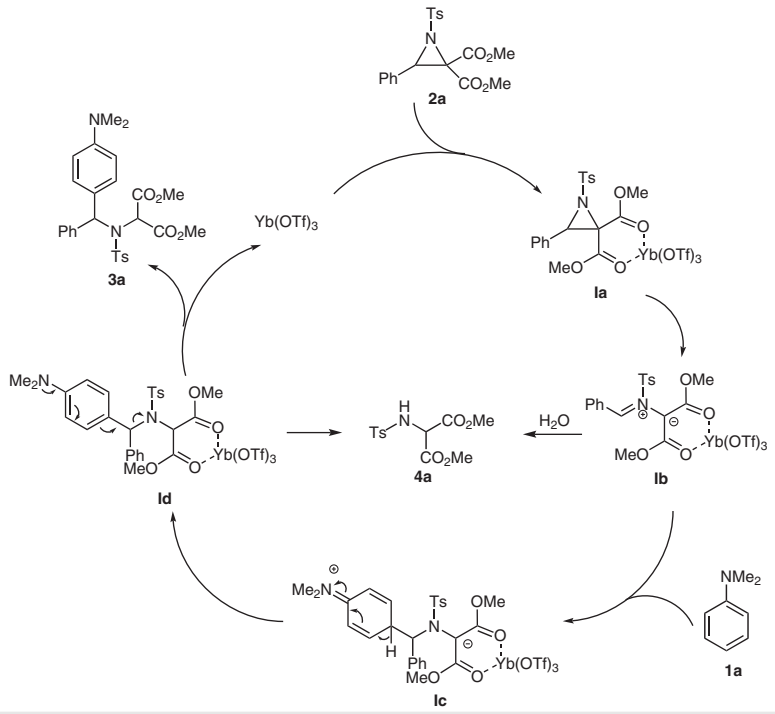


Scheme 7 Removal of dimethylmalonate group

In summary, we have reported an efficient and mild synthesis of diarylmethylamine derivatives via $Yb(OTf)_3$-catalyzed Friedel–Crafts reaction of D–A aziridines with *N*,*N*-dialkylanilines, to afford biologically important diarylmethylamine derivatives in high yields (up to 88%). This reaction is suitable for the synthesis of various diarylmethylamine derivatives and has a broad scope for electron-rich arenes, including dimethoxybenzene. Studies on the asymmetric version of this catalytic reaction are currently underway, and the results will be reported in due course.



Scheme 5 Friedel–Crafts reaction of 1,3-dimethoxybenzene (**6**) with *N*-tosylaziridine (**2a**)



Scheme 8 Proposed mechanism

All reactions were performed using flame- or oven-dried glassware under an atmosphere of dry N_2. Organic solvents were distilled prior to use. Organic solutions were concentrated under reduced pressure using a rotary evaporator. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63. TLC was performed on EM Reagents 0.25 mm silica gel 60-F plates. Developed chromatograms were visualized by fluorescence quenching and with anisaldehyde stain. ^{1}H and ^{13}C NMR spectra were recorded (400 MHz for ^{1}H and 100 MHz for ^{13}C), and were internally referenced to residual protic solvent signals. Data for ^{1}H NMR are reported as follows: chemical shift (δ), multiplicity (standard abbreviations), coupling constant (Hz), and integration. Data for ^{13}C NMR are reported in terms of chemical shift. IR spectra were recorded on an FT IR spectrometer and are reported in wave numbers. High-resolution mass spectroscopy (HRMS) was performed by electron impact (EI).

Friedel–Crafts Reaction of *N*,*N*-Dialkylanilines 1 with *N*-Tosylaziridines 2; General Procedure

To a solution of *N*,*N*-dialkylaniline **1** (0.30 mmol, 1.0 equiv), Yb(OTf)$_3$ (9.3 mg, 0.015 mmol, 5 mol%), and 4 Å molecular sieves (60 mg) in CH_2Cl_2 (3 mL) were added *N*-tosylaziridine **2** (0.45 mmol, 1.5 equiv). The resulting mixture was stirred at rt until complete consumption of *N*,*N*-dialkylaniline **1** was observed as determined by TLC. The resulting mixture was concentrated in vacuo and purified by flash column chromatography with EtOAc/hexanes as the eluent to afford the desired product **3** or **5**.

Dimethyl 2-(*N*-{[4-(Dimethylamino)phenyl](phenyl)methyl}-*N*-tosylamino)malonate (3a)

Yield: 119 mg (78%); white solid; mp 60–62 °C.

IR (neat): 3029, 2952, 2852, 1766, 1743, 1611, 1522, 1447, 1434, 1337, 1246, 1195, 1147, 1088, 1041, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 7.8 Hz, 2 H), 7.32–7.25 (m, 2 H), 7.22–7.10 (m, 5 H), 7.02 (d, *J* = 8.2 Hz, 2 H), 6.54 (d, *J* = 8.3 Hz, 2 H), 6.10 (s, 1 H), 4.80 (s, 1 H), 3.66 (d, *J* = 5.0 Hz, 3 H), 3.56 (s, 3 H), 2.89 (s, 6 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.28, 167.16, 150.12, 143.36, 138.28, 137.04, 130.64, 129.05, 128.67, 128.51, 128.03, 127.37, 124.73, 111.82, 64.28, 62.54, 53.09, 52.79, 40.42, 21.51.

HRMS (EI): *m*/*z* calcd for [M]$^+$: $C_{27}H_{30}N_2O_6S$: 510.1825; found: 510.1804.

Dimethyl 2-(*N*-{[4-(Dimethylamino)phenyl](*p*-tolyl)methyl}-*N*-tosylamino)malonate (3b)

Yield: 127 mg (81%); white solid; mp 127–129 °C.

IR (neat): 2954, 2904, 1732, 1613, 1523, 1443, 1341, 1297, 1246, 1159, 1143, 1087, 1003, 1016 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.2 Hz, 2 H), 7.15 (dd, *J* = 8.2, 2.4 Hz, 4 H), 7.02 (dd, *J* = 11.1, 8.5 Hz, 4 H), 6.54 (d, *J* = 8.7 Hz, 2 H), 6.04 (s, 1 H), 4.78 (s, 1 H), 3.65 (s, 3 H), 3.58 (s, 3 H), 2.90 (s, 6 H), 2.34 (s, 3 H), 2.28 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.32, 167.25, 150.10, 143.37, 137.12, 135.21, 130.48, 129.80, 129.10, 128.76, 128.65, 127.36, 124.95, 111.86, 64.11, 62.44, 53.05, 52.86, 40.48, 21.57, 21.08.

HRMS (EI): *m*/*z* calcd for [M]$^+$: $C_{28}H_{32}N_2O_6S$: 524.1966; found: 524.1981.

Dimethyl 2-(*N*-{[4-(Dimethylamino)phenyl](4-methoxyphenyl)methyl}-*N*-tosylamino)malonate (3c)

Yield: 117 mg (72%); white solid; mp 65–67 °C.

IR (neat): 2951, 2839, 1743, 1610, 1511, 1434, 1366, 1302, 1290, 1244, 1146, 1087, 1029 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.2 Hz, 2 H), 7.17 (t, *J* = 8.8 Hz, 4 H), 7.04 (d, *J* = 8.7 Hz, 2 H), 6.73 (d, *J* = 8.7 Hz, 2 H), 6.55 (d, *J* = 8.7 Hz, 2 H), 6.03 (s, 1 H), 4.78 (s, 1 H), 3.75 (s, 3 H), 3.66 (s, 3 H), 3.59 (s, 3 H), 2.90 (s, 6 H), 2.34 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.38, 167.25, 158.95, 150.10, 143.38, 137.15, 130.33, 130.23, 130.08, 129.12, 128.74, 125.05, 113.40, 111.90, 63.85, 62.39, 55.30, 53.10, 52.91, 40.51, 21.59.

HRMS (EI): *m*/*z* calcd for $[M]^+$: $C_{28}H_{32}N_2O_7S$: 540.1902; found: 540.1930.

Dimethyl 2-(*N*-{[4-(Dimethylamino)phenyl](4-fluorophenyl)methyl}-*N*-tosylamino)malonate (3d)

Yield: 117 mg (74%); white solid; mp 62–64 °C.

IR (neat): 2952, 2839, 1767, 1742, 1610, 1522, 1508, 1434, 1337, 1291, 1247, 1224, 1146, 1087, 1039 cm^{-1}.

^1H NMR (400 MHz, acetone-d_6): δ = 7.81 (d, *J* = 8.2 Hz, 2 H), 7.35 (dd, *J* = 8.3, 5.6 Hz, 2 H), 7.25 (d, *J* = 8.1 Hz, 2 H), 6.97 (dd, *J* = 8.6, 6.8 Hz, 4 H), 6.58 (d, *J* = 8.7 Hz, 2 H), 6.15 (s, 1 H), 4.87 (s, 1 H), 3.67 (s, 3 H), 3.47 (s, 3 H), 2.91 (s, 6 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.29, 167.03, 161.99 (d, J^1 = 246.3 Hz), 150.18, 143.51, 136.96, 134.11 (d, J^4 = 3.1 Hz), 130.56, 130.26 (d, J^3 = 8.0 Hz), 129.09, 128.59, 124.44, 114.81 (d, J^2 = 21.3 Hz), 111.83, 63.67, 62.44, 53.18, 52.79, 40.39, 21.51.

HRMS (EI): *m*/*z* calcd for $[M]^+$: $C_{27}H_{29}FN_2O_6S$: 528.1730; found: 528.1701.

Dimethyl 2-(*N*-{[4-(Dimethylamino)phenyl](4-chlorophenyl)methyl}-*N*-tosylamino)malonate (3e)

Yield: 98 mg (60%); white solid; mp 61–63 °C.

IR (neat): 2951, 2839, 1767, 1742, 1611, 1522, 1490, 1434, 1338, 1289, 1247, 1195, 1148, 1087, 1040, 1013 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.1 Hz, 2 H), 7.25 (d, *J* = 9.1 Hz, 2 H), 7.15 (d, *J* = 7.7 Hz, 4 H), 6.98 (d, *J* = 8.5 Hz, 2 H), 6.55 (d, *J* = 8.5 Hz, 2 H), 6.07 (s, 1 H), 4.76 (s, 1 H), 3.72 (s, 3 H), 3.53 (s, 3 H), 2.91 (s, 6 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.26, 166.99, 150.22, 143.58, 137.00, 136.90, 133.14, 130.72, 129.83, 129.11, 128.58, 128.13, 124.17, 111.84, 63.73, 62.48, 53.24, 52.77, 40.40, 21.54.

HRMS (EI): *m*/*z* calcd for $[M]^+$: $C_{27}H_{29}ClN_2O_6S$: 544. 1435; found: 544.1464.

Dimethyl 2-(*N*-{[4-(Dimethylamino)phenyl](4-bromophenyl)methyl}-*N*-tosylamino)malonate (3f)

Yield: 122 mg (69%); white solid; mp 68–70 °C.

IR (neat): 2950, 2838, 1767, 1743, 1611, 1521, 1486, 1434, 1338, 1290, 1248, 1195, 1150, 1087, 1041, 1009 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 7.9 Hz, 2 H), 7.30 (d, *J* = 8.1 Hz, 2 H), 7.17 (dd, *J* = 14.8, 8.1 Hz, 4 H), 6.98 (d, *J* = 8.2 Hz, 2 H), 6.54 (d, *J* = 8.2 Hz, 2 H), 6.05 (s, 1 H), 4.75 (s, 1 H), 3.72 (s, 3 H), 3.52 (s, 3 H), 2.91 (s, 6 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.25, 166.97, 150.23, 143.60, 137.56, 136.89, 131.09, 130.74, 130.18, 129.12, 128.58, 124.04, 121.33, 111.83, 63.80, 62.48, 53.26, 52.77, 40.40, 21.55.

HRMS (EI): *m*/*z* calcd for $[M]^+$: $C_{27}H_{29}BrN_2O_6S$: 588.0930; found: 588.0912.

Dimethyl 2-(*N*-{[4-(Dimethylamino)phenyl](naphthalen-1-yl)methyl}-*N*-tosylamino)malonate (3g)

Yield: 102 mg (61%); white solid; mp 95–97 °C.

IR (neat): 2950, 2837, 1766, 1742, 1610, 1521, 1434, 1337, 1290, 1248, 1151, 1088, 1049, 1018 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 6.9 Hz, 1 H), 7.73 (d, *J* = 7.9 Hz, 1 H), 7.68–7.55 (m, 4 H), 7.36–7.27 (m, 2 H), 6.96 (d, *J* = 7.8 Hz, 2 H), 6.88 (d, *J* = 7.8 Hz, 2 H), 6.83 (s, 1 H), 6.48 (d, *J* = 7.8 Hz, 2 H), 4.91 (s, 1 H), 3.73 (s, 3 H), 3.52 (s, 3 H), 2.86 (s, 6 H), 2.17 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.51, 167.38, 150.20, 143.00, 136.88, 133.86, 133.64, 131.17, 130.36, 128.65, 128.50, 128.35, 127.86, 125.98, 125.21, 125.02, 124.89 (two peaks overlapped), 123.87, 112.02, 63.62, 62.20, 53.32, 52.51, 40.37, 21.34.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{31}H_{32}N_2O_6S$: 560.1981; found: 560.2011.

Diethyl 2-(*N*-{[4-(Dimethylamino)phenyl](phenyl)methyl}-*N*-tosylamino)malonate (3h)

Yield: 123 mg (76%); colorless gum.

IR (neat): 2982, 2928, 1761, 1741, 1611, 1522, 1447, 1337, 1289, 1241, 1148, 1089, 1040, 1025 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.1 Hz, 2 H), 7.29 (d, *J* = 4.5 Hz, 2 H), 7.17 (d, *J* = 4.0 Hz, 3 H), 7.13 (d, *J* = 8.1 Hz, 2 H), 7.02 (d, *J* = 8.6 Hz, 2 H), 6.54 (d, *J* = 8.7 Hz, 2 H), 6.10 (s, 1 H), 4.76 (s, 1 H), 4.23–4.02 (m, 4 H), 2.89 (s, 6 H), 2.32 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H), 1.16 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.84, 166.68, 150.08, 143.25, 138.43, 137.15, 130.73, 128.99, 128.76, 128.50, 127.95, 127.28, 124.92, 111.78, 64.25, 62.76, 62.24, 61.82, 40.40, 21.50, 13.85, 13.83.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{29}H_{34}N_2O_6S$: 538.2138; found: 538.2153.

Diisopropyl 2-(*N*-{[4-(Dimethylamino)phenyl](phenyl)methyl}-*N*-tosylamino)malonate (3i)

Yield: 142 mg (84%); colorless gum.

IR (neat): 2981, 2933, 1761, 1735, 1612, 1522, 1495, 1449, 1373, 1338, 1276, 1247, 1151, 1103, 1041, 1029 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 8.3 Hz, 2 H), 7.32–7.27 (m, 2 H), 7.20–7.09 (m, 5 H), 7.01 (d, *J* = 8.7 Hz, 2 H), 6.53 (d, *J* = 8.7 Hz, 2 H), 6.07 (s, 1 H), 5.00 (dt, *J* = 12.4, 6.2 Hz, 1 H), 4.83 (dt, *J* = 12.5, 6.3 Hz, 1 H), 4.67 (s, 1 H), 2.89 (s, 6 H), 2.31 (s, 3 H), 1.29 (d, *J* = 6.2 Hz, 3 H), 1.22 (dd, *J* = 6.2, 3.4 Hz, 6 H), 1.07 (d, *J* = 6.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.52, 166.22, 150.04, 143.18, 138.59, 137.19, 130.77, 128.99, 128.94, 128.45, 127.95, 127.21, 125.07, 111.81, 70.28, 69.63, 64.07, 63.00, 40.38, 21.63, 21.57, 21.52, 21.45, 21.38.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{31}H_{38}N_2O_6S$: 566.2451; found: 566.2468.

Di-*tert*-butyl 2-(*N*-{[4-(Dimethylamino)phenyl](phenyl)methyl}-*N*-tosylamino)malonate (3j)

Yield: 133 mg (75%); white solid; mp 59–61 °C.

IR (neat): 2979, 2932, 1757, 1732, 1613, 1522, 1449, 1368, 1338, 1281, 1251, 1136, 1088, 1039, 1028 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 6.8 Hz, 2 H), 7.26–6.94 (m, 9 H), 6.45 (d, *J* = 7.2 Hz, 2 H), 5.97 (s, 1 H), 4.53 (s, 1 H), 2.80 (s, 6 H), 2.20 (s, 3 H), 1.37 (s, 9 H), 1.27 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.96, 165.66, 150.02, 142.92, 138.98, 137.45, 130.82, 128.92, 128.73, 128.58, 127.93, 127.08, 125.50, 112.01, 82.97, 82.31, 64.11, 64.06, 40.43, 27.92, 21.49.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{33}H_{42}N_2O_6S$: 594.2764; found: 594.2748.

Dibenzyl 2-(*N*-{[4-(Dimethylamino)phenyl](phenyl)methyl}-*N*-tosylamino)malonate (3k)

Yield: 175 mg (88%); white solid; mp 114–116 °C.

IR (neat): 3025, 2923, 1747, 1611, 1598, 1522, 1496, 1453, 1377, 1340, 1275, 1228, 1143, 1089, 1041, 1029 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.0 Hz, 2 H), 7.12–7.20 (m, 10 H), 7.10–7.04 (m,, 3 H), 7.02–6.96 (m, 2 H), 6.93 (d, *J* = 8.0 Hz, 2 H), 6.89 (d, *J* = 8.4 Hz, 2 H), 6.35 (d, *J* = 8.4 Hz, 2 H), 6.03 (s, 1 H), 4.99 (s, 2 H), 44.88 (d, *J* = 11.7 Hz, 1 H), 4.74 (s, 1 H), 4.70 (d, *J* = 12.2 Hz, 1 H), 2.73 (s, 6 H), 2.17 (d, *J* = 13.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.67, 166.57, 150.09, 143.41, 138.33, 137.02, 135.04, 135.00, 130.89, 129.83, 129.09, 128.89, 128.75, 128.71, 128.61, 128.51, 128.47, 128.39, 128.34, 128.32, 128.08, 127.39, 124.72, 111.79, 68.09, 67.80, 64.34, 62.90, 40.37, 21.58.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{39}H_{38}N_2O_6S$: 662.2451; found: 662.2429.

Dimethyl 2-(*N*-{[4-(Dimethylamino)-2-methylphenyl](phenyl)methyl}-*N*-tosylamino)malonate (5a)

Yield: 127 mg (81%); white solid; mp 64–66 °C.

IR (neat): 2951, 1765, 1741, 1608, 1564, 1510, 1495, 1448, 1434, 1337, 1289, 1246, 1196, 1147, 1088, 1038, 1017 cm^{--1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 7.6 Hz, 2 H), 7.21–7.05 (m, 6 H), 7.00 (d, *J* = 7.5 Hz, 2 H), 6.41 (d, *J* = 11.8 Hz, 2 H), 6.29 (s, 1 H), 4.88 (s, 1 H), 3.66 (s, 3 H), 3.59 (s, 3 H), 2.87 (s, 6 H), 2.26 (s, 3 H), 2.12 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.42, 167.13, 150.03, 143.02, 138.84, 137.70, 136.93, 129.75, 128.87, 128.66, 128.38, 128.07, 127.21, 124.39, 114.26, 110.01, 63.36, 61.92, 52.92, 52.87, 40.46, 21.42, 20.15.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{28}H_{32}N_2O_6S$: 524.1981; found: 524.1956.

Dimethyl 2-(*N*-{[4-(Dimethylamino)-2-methoxyphenyl](phenyl)methyl}-*N*-tosylamino)malonate (5b)

Yield: 128 mg (79%); white solid; mp 43–45 °C.

IR (neat): 2952, 1766, 1744, 1612, 1567, 1516, 1451, 1435, 1338, 1238, 1150, 1111, 1087, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.2 Hz, 2 H), 7.32–7.26 (m, 2 H), 7.21–7.14 (m, 3 H), 7.10 (d, *J* = 8.1 Hz, 2 H), 7.04 (d, *J* = 8.5 Hz, 1 H), 6.32 (s, 1 H), 6.22–6.12 (m, 1 H), 6.01 (d, *J* = 1.7 Hz, 1 H), 4.90 (s, 1 H), 3.69 (s, 3 H), 3.57 (s, 3 H), 3.45 (s, 3 H), 2.90 (s, 6 H), 2.31 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.56, 167.36, 157.83, 151.76, 142.93, 139.23, 137.14, 130.84, 128.89, 128.69, 128.37, 127.90, 127.05, 114.20, 104.36, 95.41, 63.04, 59.91, 54.94, 52.94, 52.71, 40.54, 21.49.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{28}H_{32}N_2O_7S$: 540.1930; found: 540.1909.

Dimethyl 2-(*N*-{[4-(Dimethylamino)-2-(methylthio)phenyl](phenyl)methyl}-*N*-tosylamino)malonate (5c)

Yield: 142 mg (85%); white solid; mp 64–66 °C.

IR (neat): 2951, 1766, 1742, 1598, 1557, 1494, 1434, 1336, 1284, 1245, 1147, 1087, 1036, 1028 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 7.9 Hz, 2 H), 7.59 (d, *J* = 9.1 Hz, 1 H), 7.22–7.08 (m, 5 H), 7.04 (d, *J* = 7.8 Hz, 2 H), 6.54 (s, 1 H), 6.51–6.45 (m, 2 H), 4.86 (s, 1 H), 3.74 (s, 3 H), 3.50 (s, 3 H), 2.90 (s, 6 H), 2.27 (s, 3 H), 2.15 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.32, 167.29, 150.12, 143.02, 137.98, 136.89, 136.73, 130.30, 128.69, 128.57, 128.42, 128.23, 127.96, 125.31, 112.16, 110.13, 63.55, 61.96, 53.31, 52.58, 40.53, 21.47, 17.43.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{28}H_{32}N_2O_6S_2$: 556.1702; found: 556.1698.

Dimethyl 2-(*N*-{[4-(Dimethylamino)-2-chlorophenyl](phenyl)methyl}-*N*-tosylamino)malonate (5d)

Yield: 127 mg (78%); white solid; mp 63–65 °C.

IR (neat): 2951, 1766, 1743, 1607, 1555, 1509, 1494, 1434, 1337, 1282, 1246, 1150, 1087, 1046, 1026 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.3 Hz, 2 H), 7.59 (d, *J* = 9.4 Hz, 1 H), 7.25–7.17 (m, 3 H), 7.14–7.09 (m, 2 H), 7.07 (d, *J* = 8.1 Hz, 2 H), 6.53–6.46 (m, 2 H), 6.41 (s, 1 H), 4.81 (s, 1 H), 3.75 (s, 3 H), 3.53 (s, 3 H), 2.89 (s, 6 H), 2.29 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.33, 167.28, 150.59, 143.25, 137.48, 136.68, 133.64, 130.02, 129.30, 128.91, 128.60, 128.34, 128.11, 122.92, 112.87, 110.68, 63.58, 61.94, 53.43, 52.73, 40.38, 21.53.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{27}H_{29}ClN_2O_6S$: 544.1426; found: 544.1435.

Dimethyl 2-(*N*-{[4-(Dimethylamino)-2-methoxy-5-methylphenyl](phenyl)methyl}-*N*-tosylamino)malonate (5e)

Yield: 128 mg (77%); white solid; mp 62–64 °C.

IR (neat): 2949, 2780, 1769, 1743, 1611, 1574, 1504, 1451, 1434, 1336, 1289, 1240, 1194, 1143, 1085, 1042, 1009 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.2 Hz, 2 H), 7.25–7.15 (m, 5 H), 7.06 (d, *J* = 8.1 Hz, 2 H), 7.03 (s, 1 H), 6.34 (s, 2 H), 4.85 (s, 1 H), 3.65 (s, 3 H), 3.63 (s, 3 H), 3.46 (s, 3 H), 2.65 (s, 6 H), 2.29 (s, 3 H), 2.12 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.47, 167.35, 155.25, 153.14, 142.94, 138.40, 136.96, 132.06, 128.89, 128.81, 128.56, 128.01, 127.45, 122.91, 119.60, 101.41, 63.17, 59.89, 55.29, 52.82, 43.99, 21.44, 17.64.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{29}H_{34}N_2O_7S$: 554.2087; found: 554.2111.

Dimethyl 2-(*N*-{[1-(Dimethylamino)naphthalen-4-yl](phenyl)methyl}-*N*-tosylamino)malonate (5f)

Yield: 86 mg (51%); white solid; mp 66–68 °C.

IR (neat): 2949, 2782, 1767, 1742, 1581, 1514, 1453, 1434, 1391, 1338, 1289, 1246, 1188, 1151, 1087, 1041, 1016 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.3 Hz, 1 H), 7.73 (d, *J* = 8.3 Hz, 1 H), 7.64 (d, *J* = 8.2 Hz, 2 H), 7.59 (d, *J* = 7.8 Hz, 1 H), 7.40 (t, *J* = 7.4 Hz, 1 H), 7.33 (t, *J* = 7.2 Hz, 1 H), 7.24–7.10 (m, 5 H), 6.97–6.84 (m, 4 H), 4.88 (s, 1 H), 3.57 (s, 3 H), 3.49 (s, 3 H), 2.84 (s, 6 H), 2.21 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.29, 167.09, 151.17, 143.06, 138.33, 136.70, 131.92, 129.61, 128.78, 128.66, 128.46, 128.38, 127.86, 127.71, 126.69, 126.08, 124.78, 124.55, 124.25, 112.97, 63.64, 62.06, 53.03, 52.79, 45.23, 21.37.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{31}H_{32}N_2O_6S$: 560.1981; found: 560.1997.

Dimethyl 2-(*N*-{[4-(Dibenzylamino)-2-methoxy-5-methylphenyl](phenyl)methyl}-*N*-tosylamino)malonate (5g)

Yield: 155 mg (78%); white solid; mp 64–66 °C.

IR (neat): 3028, 2950, 1768, 1741, 1610, 1519, 1494, 1450, 1434, 1395, 1337, 1292, 1176, 1147, 1087, 1041, 1028 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 7.6 Hz, 2 H), 7.24–7.02 (m, 15 H), 6.99 (d, *J* = 7.7 Hz, 2 H), 6.84 (d, *J* = 8.1 Hz, 2 H), 6.45 (d, *J* = 8.2 Hz, 2 H), 5.97 (s, 1 H), 4.69 (s, 1 H), 4.51 (s, 4 H), 3.56 (s, 3 H), 3.38 (s, 3 H), 2.19 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.33, 167.19, 148.66, 143.38, 138.42, 138.26, 137.06, 130.92, 129.08, 128.75, 128.72, 128.46, 128.08, 127.38, 127.11, 126.66, 125.13, 111.84, 64.32, 62.66, 54.38, 53.19, 52.83, 21.58.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{39}H_{38}N_2O_6S$: 662.2451; found: 662.2477.

Dimethyl 2-(*N*-{Phenyl[4-(pyrrolidin-1-yl)phenyl]methyl}-*N*-tosylamino)malonate (5h)

Yield: 135 mg (84%); white solid; mp 56–59 °C.

IR (neat): 2950, 2838, 1767, 1743, 1611, 1521, 1488, 1433, 1372, 1337, 1290, 1245, 1176, 1148, 1087, 1041, 1029 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 7.5 Hz, 2 H), 7.23–7.18 (m, 2 H), 7.13–6.99 (m, 5 H), 6.75 (s, 2 H), 6.19 (d, *J* = 7.9 Hz, 1 H), 6.00 (s, 1 H), 4.73 (s, 1 H), 3.60 (s, 3 H), 3.48 (s, 3 H), 3.17 (t, *J* = 7.9 Hz, 2 H), 2.72 (t, *J* = 7.8 Hz, 2 H), 2.62 (s, 3 H), 2.23 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.29, 167.16, 153.19, 143.27, 138.43, 137.10, 130.13, 129.46, 128.96, 128.65, 128.38, 128.00, 127.26, 126.35, 125.93, 106.16, 64.66, 62.60, 56.11, 53.09, 52.70, 35.98, 28.47, 21.48.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{29}H_{32}N_2O_6S$: 536.1981; found: 536.2009.

Dimethyl 2-{*N*-[(1-Methylindolin-5-yl)(phenyl)methyl]-*N*-tosylamino}malonate (5i)

Yield: 117 mg (75%); white solid; mp 56–58 °C.

IR (neat): 3026, 2952, 2810, 1743, 1615, 1598, 1496, 1450, 1434, 1337, 1275, 1245, 1185, 1149, 1084, 1041, 1029 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.23 (m, 5 H), 7.16–7.08 (m, 1 H), 6.97 (d, *J* = 7.5 Hz, 1 H), 6.82 (td, *J* = 7.5, 0.9 Hz, 1 H), 6.50–6.33 (m, 1 H), 6.20–5.96 (m, 1 H), 5.52–5.47 (m, 1 H), 5.38 (d, *J* = 7.9 Hz, 1 H), 5.16 (d, *J* = 10.7 Hz, 1 H), 5.01 (d, *J* = 10.6 Hz, 1 H), 4.15 (s, 1 H), 1.53 (s, 3 H), 1.47 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.06, 138.68, 134.96, 133.86, 130.26, 129.11, 128.57, 128.54, 124.29, 122.09, 120.49, 119.69, 114.01, 109.42, 78.50, 77.54, 74.22, 25.52, 25.00.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{28}H_{30}N_2O_6S$: 522.1825; found: 522.1848.

Friedel–Crafts Reaction of 1,3-Dimethoxybenzene (6) with *N*-Tosylaziridine 2a; Dimethyl 2-{*N*-[(1-Methylindolin-5-yl)(phenyl)methyl]-*N*-tosylamino}malonate (7)

To a solution of 1,3-dimethoxybenzene (**6**; 41 mg, 0.30 mmol, 1.0 equiv), $Yb(OTf)_3$ (9.3 mg, 0.015 mmol, 5 mol%), and 4 Å molecular sieves (60 mg) in CH_2Cl_2 (3 mL) were added *N*-tosylaziridine (**2a**; 175 mg, 0.45 mmol, 1.5 equiv). The resulting mixture was stirred at rt for 1 h and concentrated in vacuo. The residue was purified by flash column chromatography with EtOAc/hexanes as eluent to afford the desired product **7**; yield: 114 mg (72%); white solid; mp 60–62 °C.

IR (neat): 3028, 2952, 2841, 1766, 1743, 1611, 1587, 1505, 1453, 1435, 1337, 1291, 1247, 1208, 1149, 1118, 1088, 1028 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 7.9 Hz, 2 H), 7.34–7.28 (m, 1 H), 7.24–7.16 (m, 4 H), 7.09 (d, *J* = 7.9 Hz, 2 H), 6.34 (s, 2 H), 6.26 (s, 1 H), 4.86 (s, 1 H), 3.75 (s, 3 H), 3.64 (s, 3 H), 3.62 (s, 3 H), 3.45 (s, 3 H), 2.31 (s, 3 H).

^{13}C NMR (100 MHz, acetone-d_6): δ = 166.93, 166.83, 160.87, 157.72, 143.15, 138.78, 137.66, 130.31, 129.00, 128.70, 128.64, 127.85, 127.34, 118.77, 104.33, 97.96, 63.02, 59.44, 54.80, 54.78, 52.07, 51.91, 20.51.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{27}H_{29}N_2O_8S$: 527.1614; found: 527.1603.

***N*,*N*-Dimethyl-4-[phenyl(tosylamino)methyl]benzenamine (8)**

To a solution of **3a** (61 mg, 0.12 mmol, 1.0 equiv) in THF (2.5 mL) at –78 °C were added HMPA (0.25 mL) and SmI_2 (0.07–0.12 M solution in THF, 5 mL, 4 equiv). The resulting mixture was stirred at –78 °C for 24 h. Then, the mixture was quenched with aq $NaHCO_3$ and extracted with EtOAc. The combined organic layers were washed with brine, dried (anhyd $MgSO_4$), and concentrated in vacuo. The crude residue was purified by flash column chromatography with EtOAc/hexanes as eluent to afford the desired product **8**; yield: 32 mg (70%); white solid; mp 124–126 °C.

IR (neat): 3269, 2919, 2852, 1613, 1519, 1495, 1454, 1439, 1346, 1316, 1286, 1223, 1155, 1093, 1084, 1048, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.3 Hz, 2 H), 7.22–7.06 (m, 7 H), 6.89 (d, *J* = 8.7 Hz, 2 H), 6.53 (d, *J* = 8.8 Hz, 2 H), 5.47 (d, *J* = 6.8 Hz, 1 H), 5.06 (d, *J* = 6.8 Hz, 1 H), 2.88 (s, 6 H), 2.37 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.06, 143.03, 141.15, 137.63, 129.41, 128.44 (two peaks overlapped), 128.40, 127.40, 127.36, 127.31, 112.46, 61.07, 40.59, 21.60.

HRMS (EI): *m*/*z* calcd for $[M]^+$ $C_{22}H_{24}N_2O_2S$: 380.1558; found: 380.1574.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690731.

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