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Grant J. Dixon

Michael R. Rodriguez

Tyler G. Chong

Kevin Y. Kim

C. Wade Downey
University of Richmond, wdowney@richmond.edu

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Synthesis of β,β-Disubstituted Styrenes via Trimethylsilyl Trifluoromethanesulfonate-Promoted Aldehyde-Aldehyde Aldol Coupling-Elimination

Grant J. Dixon, Michael R. Rodriguez, Tyler G. Chong, Kevin Y. Kim, and C. Wade Downey*

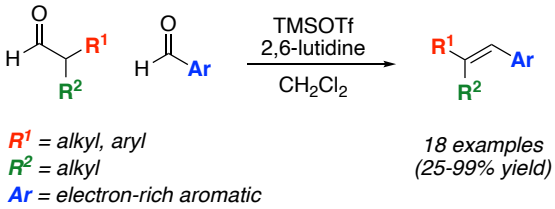
Department of Chemistry, University of Richmond, 138 UR Drive, Richmond, VA, USA 23173, United States

*corresponding author

email: wdowney@richmond.edu (C. W. Downey)

ABSTRACT

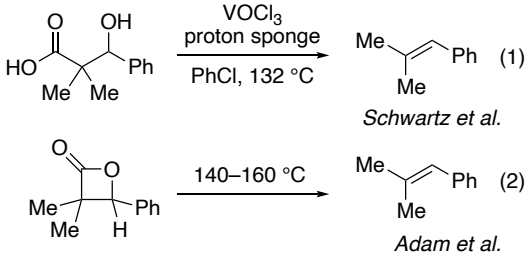
In the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) and 2,6-lutidine, α,α-disubstituted aldehydes condense with electron-rich aromatic aldehydes to yield β,β-disubstituted styrenes. More electron-rich aromatic aldehydes react more rapidly and in higher yield. Preliminary results suggest that the reaction may proceed via the ionization and formal deformylation of an aldol intermediate.



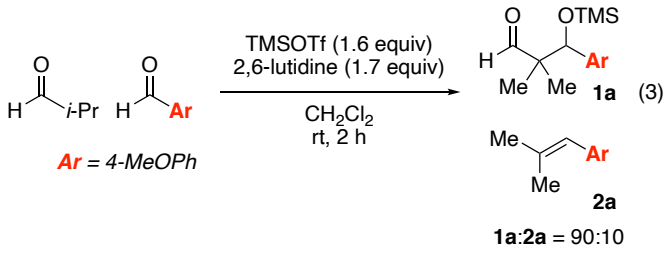
The production of styrenes remains a subject of intense scrutiny owing to the prevalence of styrene building blocks in the electronics,[1] automotive,[2] and chemical synthesis industries.[3] Outside the polymer industry, β,β-disubstituted styrenes specifically are valuable substrates in epoxidation, [4] cyclopropanation, [5] aziridination, [6] dihydroxylation,[7] and olefin-carbonyl cross metathesis reactions.[8] The synthesis of β,β-dialkylstyrenes, including electron-rich styrenes, has been accomplished through a Grignard reaction-dehydration sequence,[9] Wittig-type reactions,[10] and metal-catalyzed cross coupling,[11] but a robust, one-pot synthesis dependent only upon aldehyde reaction partners, which are readily available in wide variety, would be an attractive alternative. Below, we describe the synthesis of β,β-disubstituted styrenes from α,α-disubstituted aliphatic aldehydes and electron-rich aryl aldehydes in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) and 2,6-lutidine, a process that appears to proceed via an aldol intermediate.[12]

The conversion of α,α-dimethylated-β-oxygenated carbonyl compounds to styrenes via decarboxylation is precedented in the literature. In 1989, Schwartz and Meier reported the

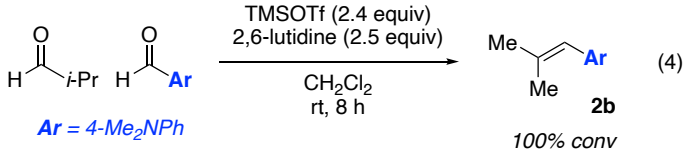
conversion of an α,α-disubstituted-β-hydroxycarboxylic acid to β,β-dimethylstyrene in the presence of vanadium(V) compounds, a decarboxylative process believed to occur via a radical pathway (eq 1). [13] Similarly, Adam and coworkers showed that thermal decarboxylation of β-lactones can provide β,β-dialkylstyrene products (eq 2),[14] and related oxetanes have also been reported to yield styrenes through net [2+2] cycloreversion.[15] The conversion of β-oxygenated aldehydes to styrenes, however, appears to be unknown.



In the course of our development of TMSOTf-promoted aldehyde-aldehyde aldol coupling reactions,[16] trace amounts of a styrene byproduct were observed when isobutyraldehyde was treated with *p*-anisaldehyde (eq 3). Because at prolonged reaction times the styrene came to dominate the product mixture, a series of experiments was conducted to optimize the formation of the styrene, delineate the scope of the reaction, and investigate its mechanism.

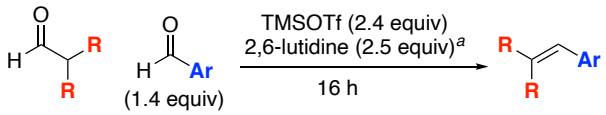


Examination of a number of possible solvents (CH_2Cl_2, THF, Et_2O, toluene) and trialkylamines (*i*-Pr_2NEt, Et_3N, 2,6-lutidine) showed that the combination of CH_2Cl_2 and 2,6-lutidine was superior for the production of styrene, and that the electron-rich aldehyde 4-dimethylaminobenzaldehyde generated styrene more efficiently than did *p*-anisaldehyde. With higher loadings of TMSOTf (2.5 equiv) and base (2.4 eqiv), 70% conv of isobutyraldehyde to styrene **2b** was observed in just 1 h, and the reaction reached completion after 8 h (eq 4). When TMSOTf was replaced by other Lewis acids ($LiClO_4$, $MgBr_2$•OEt_2, $ZnBr_2$, $Zn(OTf)_2$, $In(OTf)_3$, BF_3•OEt_2, $TiCl_4$), however, no conversion to the aldol product or the styrene was observed.[17]



Expansion of the reaction scope to some other aromatic aldehydes required modifications to the reaction conditions (Table 1). Reaction of isobutyraldehyde with a series of electron-rich aryl aldehydes proceeded smoothly at room temperature (entries 1, 2, 4, and 10), but more electronically or sterically challenging aryl aldehydes required heat to achieve optimal conversion to the styrene. In contrast to the electronically similar *p*-anisaldehyde, the more hindered *o*-anisaldehyde provided a product mixture consisting mostly of the aldol adduct when the reaction was conducted at ambient temperature. Even under vigorous reaction conditions (110 °C in toluene), low yield of the styrene was observed (entry 3). When the less electron-rich *p*-tolualdehyde was employed, efficient transformation to the styrene required a temperature of 150 °C (entry 5). Electron-poor aromatic aldehydes yielded no significant styrene formation (entries 7 and 8), but an increase in the steric bulk of the enolizable aldehyde was well tolerated (entries 11 and 12). Most of the reaction products were somewhat volatile, and significant product loss was observed when samples were subjected to high vacuum after chromatography. For example, the styrene derived from benzaldehyde, β,β-dimethylstyrene itself, proved so volatile that removal of even low-boiling solvents (ether, pentane) could not be accomplished in our hands without significant loss of product (entry 6).

Table 1. Reaction of acyclic aliphatic aldehydes

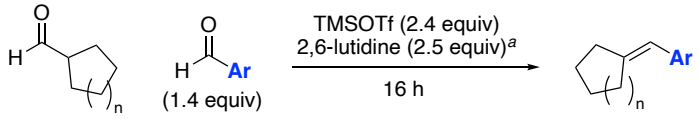


entry	R	Ar	solvent	T (°C)	product	yield (%)[b]
1	Me	4-(MeO)Ph	CH_2Cl_2	23	**2a**	91
2	Me	4-(Me_2N)Ph	CH_2Cl_2	23	**2b**	67
3	Me	2-(MeO)Ph	PhMe	110	**2c**	47
4	Me	3,4-$(MeO)_2$Ph	CH_2Cl_2	23	**2d**	55
5	Me	4-MePh	PhCN	150	**2e**	84
6	Me	Ph	CH_2Cl_2	100[c]	**2f**	33 (57)[d,e]
7	Me	4-FPh	CH_2Cl_2	100[c]	-	trace
8	Me	4-(F_3C)Ph	PhCN	150	-	0
9	Me	3-(1-methyl)indolyl	CH_2Cl_2	40	**2g**	52
10	Me	2-thienyl	CH_2Cl_2	23	**2h**	78[d]
11	Et	4-(MeO)Ph	CH_2Cl_2	40	**2i**	99
12	Et	4-(Me_2N)Ph	CH_2Cl_2	23	**2j**	74

[a]Reaction conditions: 1.0 mmol enolizable aldehyde, 1.4 mmol aromatic aldehyde, 2.5 mmol 2,6-lutidine, 2.4 mmol TMSOTf; solvent and temperature as indicated in Table 1; 16 h.
[b]Isolated yield after chromatography.
[c]Reaction performed in a sealed, thick-walled reaction vessel.
[d]Yield suppressed by product volatility.
[e]Value in parentheses is NMR yield vs. internal standard (hexamethylbenzene)

Cycloalkanecarboxaldehydes also proved to be worthy substrates, as illustrated by Table 2, with reactivity trends similar to those of acyclic aliphatic aldehydes. More electron-poor aryl aldehydes were unsatisfactory reaction partners in general, yielding aldol addition products but often failing to undergo the net deformylative elimination necessary to form the styrene. A very modest yield of the *p*-bromobenzaldehyde derivative could be isolated under forcing conditions, however (entry 6). In contrast, neither the effectively electron-poor *m*-anisaldehyde nor the sterically challenging 2,6-dimethylbenzaldehyde produced styrene under similar conditions (entries 4 and 8).

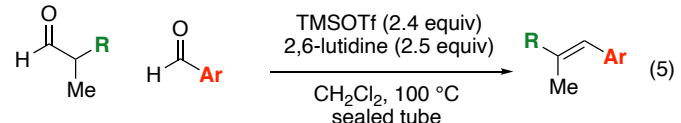
Table 2. Reaction of cyclic aliphatic aldehydes



entry	n	Ar	solvent	T (°C)	product	yield (%)[b]
1	1	4-(MeO)Ph	CH_2Cl_2	23	**2k**	88
2	2	4-(MeO)Ph	CH_2Cl_2	23	**2l**	99
3	2	4-(Me_2N)Ph	CH_2Cl_2	23	**2m**	79
4	2	3-(MeO)Ph	PhCN	150	-	0
5	2	2-(MeO)Ph	CH_2Cl_2	100[c]	**2n**	61
6	2	4-BrPh	PhCN	150	**2o**	25
7	2	2-naphthyl	PhCN	150	**2p**	63
8	2	2,6-Me_2Ph	CH_2Cl_2	100[c]	-	0

[a]Reaction conditions: 1.0 mmol enolizable aldehyde, 1.4 mmol aromatic aldehyde, 2.5 mmol 2,6-lutidine, 2.4 mmol TMSOTf; solvent and temperature as indicated in Table 2; 16 h.
[b]Isolated yield after chromatography.
[c]Reaction performed in a sealed, thick-walled reaction vessel.

Two unsymmetrical enolizable aldehydes were also examined (eq 5). Whereas α-phenylpropionaldehyde reacted with high selectivity (14:1 *E*:*Z*) but required long reaction times to achieve even a modest yield, the benzyl analog reacted more quickly and with higher yield but with lower selectivity.[18]

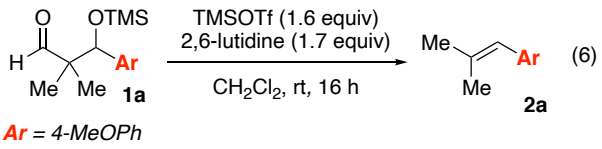


R = Ph, Bn *Ar* = 4-MeOPh

2q: *R* = Ph, 16 h
48% yield, 14:1 E:Z
2r: *R* = Bn, 3 h
79% yield, 4:1 E:Z

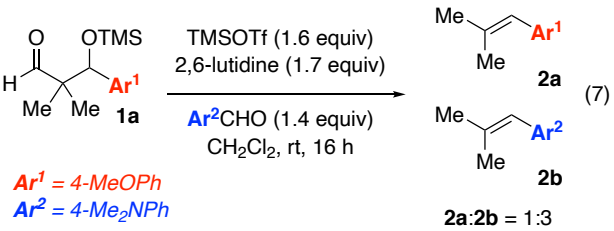
In order to test the importance of the aldol intermediate in the styrene-production pathway, purified aldol product **1a** was subjected to various reaction conditions. Resubjection of aldol **1a** to TMSOTf and 2,6-lutidine produced a significant amount of styrene (16% conv) after 1 h and reached full conversion overnight (eq 6). None of the other Lewis acids examined under these conditions ($LiClO_4$, BF_3•OEt_2, $TiCl_4$, $MgBr_2$•OEt_2) provided styrene

when they were used in place of TMSOTf, and removal of TMSOTf, 2,6-lutidine, or both from the standard reaction conditions resulted in a failure to produce styrene.



(6)

The aldol adduct is not necessarily an intermediate on the styrene generation pathway, however. Retroaldol products of aldol adduct **1a** were sometimes observed, and a crossover experiment further demonstrated the reversibility of aldol formation under the reaction conditions. When aldol product **1a** was mixed with 4-dimethylaminobenzaldehyde and treated with TMSOTf and 2,6-lutidine in CH_2Cl_2 overnight, spectral analysis showed that expected styrene **2a** and crossover styrene **2b** formed in a 1:3 ratio (**2a**:**2b**) (eq 7). Because no isobutyraldehyde was added to the reaction mixture, the isopropyl residue necessary for the formation of product **2b** likely was produced by retroaldol reaction of aldol adduct **1a** to form isobutyraldehyde. Based on this result, and the observation of retroaldol products during other trials, the possibility of a non-aldol route to the styrene cannot be ruled out.

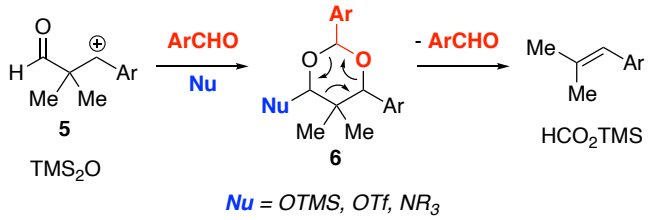


(7)

A series of failed reactions provided further circumstantial evidence for the importance of an aldol intermediate, however. When cyclohexanecarboxaldehyde was treated with the highly hindered 2,6-dimethylbenzaldehyde, no aldol reaction was observed,[19] nor was any styrene formation evident. Similarly, replacement of isobutyraldehyde with a series of analogs (*S*-phenyl thioisobutyrate, isobutyronitrile, isobutyric acid, isobutyryl chloride) provided neither aldol addition nor styrene formation, even when the highly reactive 4-dimethylaminobenzaldehyde was employed as the reaction partner.

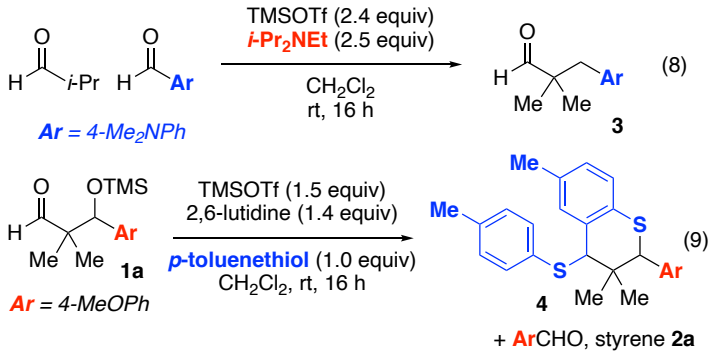
A working model of our proposed mechanism appears in Scheme 1. Assuming the intervention of an aldol intermediate, ionization to form β-carbocation **5** is a reasonable first step and is supported by evidence from several experiments (vide infra). Intervention of an additional equivalent of aldehyde to complete a six-membered transition state is speculative, as is the incorporation of a nucleophile to access a tetrahedral geometry at the formyl position; an analogous mechanism that proceeds via a four-membered transition state may be operative. Formation of the styrene is accompanied by the generation of trimethylsilyl formate, which has been observed by in situ by NMR spectroscopy when the reaction was performed in $CDCl_3$ and a singlet peak consistent with a formate species was observed at 8.05 ppm. A mixture of formic acid, 2,6-lutidine, and TMSOTf in $CDCl_3$ showed a very similar peak at 8.07 ppm, [20] and when the two mixtures were combined into a single NMR sample, only a single formate peak was observed, at 8.05 ppm. These results

suggest that trimethylsilyl formate is a byproduct of the styrene-generation process, although the mechanism of its genesis under the reaction conditions has not been fully elucidated.

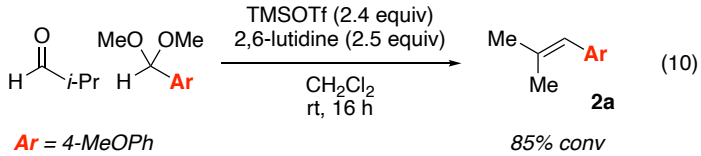


Scheme 1. Working Model of Proposed Mechanism

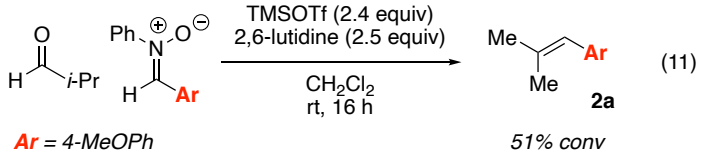
Evidence of carbocation formation was observed when 2,6-lutidine was replaced with *i*-Pr$_2$NEt in the reaction of isobutyraldehyde with 4-dimethylaminobenzaldehyde (eq 8). The major product observed was aldehyde **3**, which likely forms through the donation of a hydride from the amine to the putative carbocation.[21] Similarly, when aldol adduct **1a** was mixed with *p*-toluenethiol in the presence of TMSOTf and 2,6-lutidine, a single diastereomer of thiochroman **4** was observed as a major component of the product mixture, presumably arising from coordination of the thiol to the putative carbocation followed by net intramolecular Friedel–Crafts attack upon the formyl group (eq 9).[22,23] In addition, the incorporation of a second equivalent of thiol at the location of the former carbonyl provides evidence for nucleophilic attack upon the formyl group during or prior to the styrene-generation step, as suggested in Scheme 1.



Certain aldol analogs also capable of undergoing ionization at the β-position react to form styrenes as well. A test reaction showed that replacement of the aryl aldehyde with its derived dimethyl acetal under standard conditions resulted in 85% conv to the styrene, presumably via a β-methoxyaldehyde intermediate (eq 10). Similarly, when the aryl aldehyde was replaced with an N-phenylnitrone, these Mukaiyama–Mannich conditions[21b] produced a 51% conv to the styrene (eq 11).

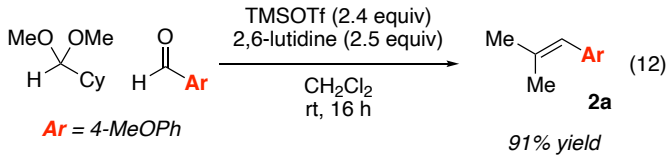


(10)



(11)

Another factor that may influence styrene generation is the electrophilicity of the formyl carbon. When the formyl group in aldol adduct **1a** was replaced with an acyl or carbomethoxy group, no styrene formation was observed upon treatment with TMSOTf and 2,6-lutidine, even under forcing conditions. In contrast, replacement of cyclohexanecarboxaldehyde with its dimethyl acetal derivative resulted in excellent reactivity, as evidenced by the 91% yield observed after its reaction with *p*-anisaldehyde (eq 12). These results, combined with the excellent results with aliphatic aldehydes presented above, suggest that some attack upon the relatively unencumbered formyl residue may be necessary to induce transformation of the aldol adduct to the styrene, perhaps via a six-membered transition state that may only be possible after the coordination of an exogenous nucleophile (e.g., silyl ether, triflate ion, trialkylamine) to the presumed carbocationic intermediate.[24]



(12)

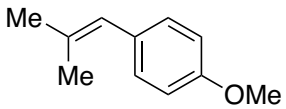
In conclusion, a one-pot synthesis of β,β-disubstituted styrenes via aldehyde-aldehyde coupling has been developed. The reaction requires one α,α-disubstituted enolizable aldehyde and one electron-rich aromatic aldehyde, and likely proceeds through a Mukaiyama aldol reaction followed by ionization of the aldol product and net deformylative elimination. The exact mechanism of the deformylation step remains unclear, and may involve the intervention of other species. Silyl triflates were unique among Lewis acids tested in their ability to generate styrenyl products.

EXPERIMENTAL SECTION

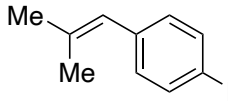
General. Reactions were carried out under an atmosphere of nitrogen with a septum cap in oven-dried glassware with magnetic stirring. Methylene chloride and toluene were purified by passage through a bed of activated alumina. [25] Trimethylsilyl trifluoromethanesulfonate (TMSOTf) was stored in a Schlenk flask under inert atmosphere. Isobutyraldehyde and cyclohexanecarboxaldehyde were distilled from calcium hydride and used within one week of distillation. Certain other aldehydes were

distilled prior to use and stored in a refrigerator (o-anisaldehyde, p-anisaldehyde, p-tolualdehyde, 2-thiophenecarboxaldehyde). Cyclohexanecarboxaldehyde dimethyl acetal was synthesized via literature precedent.[26] All other chemicals were used as received. Purification of reaction products was carried out by flash chromatography using silica gel (230-400 mesh). Analytical thin layer chromatography was performed on silica gel plates. Visualization was accomplished with UV light and/or phosphomolybdic acid stain, followed by heating. Infrared spectra were recorded on an FT-IR spectrometer. ^{1}H NMR spectra were recorded on a 500 MHz spectrometer, 400 MHz spectrometer, or 300 MHz spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.28 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, sx = sextet, sp=septet, m = multiplet, b = broad; coupling constant(s) in Hz; integration). Proton-decoupled ^{13}C NMR spectra were recorded on a 125 MHz spectrometer or 100 MHz spectrometer, and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.0 ppm). High-resolution mass spectra were obtained by electrospray ionization unless otherwise indicated. Melting points were determined using a capillary melting point apparatus. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

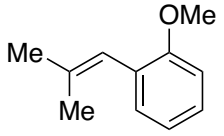
Preparation of β,β-Disubstituted Styrenes



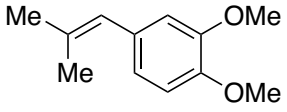
***p*-Methoxy(2-methyl-1-propenyl)benzene (2a)** To an oven-dried round-bottomed flask under N_2 atmosphere were added CH_2Cl_2 (5 mL), isobutyraldehyde (95 μL, 75 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 10 min, and then *p*-anisaldehyde (171 μL, 190 mg, 1.40 mmol) was added. The mixture was stirred for 16 h, then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The crude reaction mixture was dissolved in tetrahydrofuran (THF, 5 mL) and treated with 1.0 N HCl (1.5 mL) in order to desilylate residual aldol adducts. The mixture was stirred for 30 min, then partitioned between Et_2O (25 mL) and water (25 mL). The layers were separated and the organic layer was washed sequentially with saturated $NaHCO_3$ (25 mL) and brine (25 mL). The combined aqueous layers were back-extracted with Et_2O (20 mL). The organic layers were combined and one volume-equivalent of hexane was added. The organic layers were dried over $MgSO_4$, then the desiccant was removed by filtration. The solvent was removed in vacuo, and the residue purified by column chromatography (1-3% EtOAc/hexanes) to yield the title compound[11d] as a colorless oil (201 mg, 91% yield): IR (neat) 2963, 2910, 2833, 1608, 1510, 1440, 1375, 1298, 1245, 1173, 1108, 1037, 847, 799, 768 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.7 Hz, 2H), 6.8 (d, 8.7 Hz, 2H), 6.24 (s, 1H), 3.83 (s, 3H), 1.91 (s, 3H), 1.87 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.7, 134.0, 131.4, 129.8, 124.5, 113.5, 55.2, 26.8, 19.3; HRMS (CI, TOF): Exact mass calcd for $C_{11}H_{14}O$ $[M]^+$, 162.1039; found, 162.1037.



***N*,*N*-Dimethyl[*p*-(2-methyl-1-propenyl)phenyl]amine (2b)** To an oven-dried round-bottomed flask under N_2 atmosphere were added 4-dimethylaminobenzaldehyde (209 mg, 1.40 mmol), CH_2Cl_2 (5 mL), isobutyraldehyde (95 μL, 75 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 16 h, then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (1-3% EtOAc/hexanes) to yield the title compound[27] as a pale yellow oil (121 mg, 67% yield): IR (neat) 1977, 2937, 2856, 2810, 1609, 1517, 1344, 1192, 1178, 1164, 1129, 1059, 947, 842, 818, 795 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 8.8, 2H), 6.80 – 6.69 (d, J = 8.8 Hz, 2H), 6.25 – 6.17 (s, 1H), 2.97 (s, J = 1.8 Hz, 6H), 1.92 – 1.86 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.8, 132.4, 129.6, 127.5, 125.0, 112.4, 40.7, 27.1, 19.5; HRMS (ESI, TOF): Exact mass calcd for $C_{12}H_{18}N$ $[M+H]^+$, 176.1434; found, 176.1426.

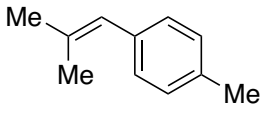


***o*-Methoxy(2-methyl-1-propenyl)benzene (2c)** To an oven-dried round-bottomed flask under N_2 atmosphere were added toluene (1 mL), isobutyraldehyde (95 μL, 75 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 10 min, and then *o*-anisaldehyde (169 μL, 191 mg, 1.40 mmol) was added and the reaction was heated to reflux. After the mixture was stirred for 16 h, the reaction mixture was allowed to cool and then purified directly by column chromatography (0-1% EtOAc/hexanes) to yield the title compound[11e] as a pale yellow oil (76 mg, 47% yield): IR (neat) 2963, 2910, 2834, 1597, 1488, 1463, 1375, 1241, 1185, 1160, 1047, 749 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26 – 7.18 (m, 2H), 6.99 – 6.85 (m, 2H), 6.33 (s, 1H), 3.85 (s, 3H), 1.96 (s, 3H), 1.83 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.0, 135.5, 130.5, 127.5, 127.4, 120.6, 120.1, 110.3, 55.4, 26.7, 19.6; HRMS (CI, TOF): Exact mass calcd for $C_{11}H_{14}O$ $[M]^+$, 162.1039; found, 162.1036.

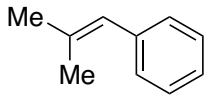


1,2-Dimethoxy-4-(2-methyl-1-propenyl)benzene (2d) To an oven-dried round-bottomed flask under N_2 atmosphere were added CH_2Cl_2 (5 mL), isobutyraldehyde (95 μL, 75 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 10 min, and then 3,4-dimethoxybenzaldehyde (233 mg, 1.40 mmol) was added. The mixture was stirred for 16 h, then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-1% EtOAc/hexanes) to yield the title compound[28] as a colorless oil

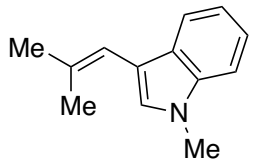
(106 mg, 55% yield): IR (neat) 2965, 2908, 2829, 1605, 1512, 1468, 1255, 1241, 1166, 1139, 1028, 870, 797, 765 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.86 (d, *J* = 8.2 Hz, 1H), 6.81 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.78 (d, *J* = 1.9 Hz, 1H), 6.24 (s, 1H), 3.90 (s, 3H), 3.90 (s, 3H), 1.91 (d, *J* = 1.4 Hz, 3H), 1.89 (d, *J* = 1.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.5, 147.3, 134.2, 131.8, 124.8, 121.1, 112.3, 111.1, 55.9, 55.8, 26.8, 19.4.



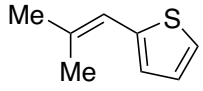
***p*-(2-Methyl-1-propenyl)toluene (2e)** To an oven-dried round-bottomed flask under N_2 atmosphere were added benzonitrile (1.0 mL), isobutyraldehyde (95 μL, 75 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. After 5 min, *p*-tolualdehyde (165 μL, 168 mg, 1.40 mmol) was added and the reaction mixture was heated to 150 °C. The mixture was stirred for 16 h, then allowed to cool to room temperature, after which passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL), and the column was rinsed with CH_2Cl_2 (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-1% EtOAc/hexanes) to yield the title compound[11f] as a pale yellow oil (123 mg, 84% yield, yield depressed by volatility of the product): IR (neat) 3018, 2969, 2920, 2855, 1661, 1516, 1451, 1374, 1177, 1051, 854, 802 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.16 (s, 4H), 6.28 (s, 1H), 2.37 (s, 3H), 1.93 (s, 3H), 1.90 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 135.8, 135.3, 134.8, 128.8, 128.6, 125.0, 26.9, 21.1, 19.4; HRMS (CI, TOF): Exact mass calcd for $C_{11}H_{14}$ $[M]^+$, 146.1090; found, 146.1090.



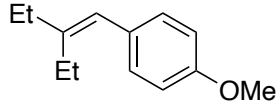
2-Methyl-1-propenyl)benzene 10 (2f) To an oven-dried thick-walled reaction vessel under N_2 atmosphere were added isobutyraldehyde (91 mL, 72 mg, 1.00 mmol), CH_2Cl_2 (2 mL), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 5 min, and then benzaldehyde (143 μL, 149 mg, 1.40 mmol) was added. The reaction vessel was sealed and the mixture was heated to 100 °C. After the mixture was stirred for 16 h, the reaction mixture was allowed to cool and then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (100% pentane) to yield the title compound[29] as a colorless oil (43 mg, 33% yield): IR (neat) 3060, 3028, 2967, 2914, 2855, 1599, 1482, 1443, 1237, 973, 740, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.7 Hz, 2H), 7.27 – 7.23 (m, 2H), 7.23 – 7.17 (m, 1H), 6.30 (s, 1H), 1.93 (s, 3H), 1.89 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 138.7, 135.5, 128.7, 128.0, 125.8, 125.1, 26.9, 19.4.



1-Methyl-3-(2-methyl-1-propenyl)indole (2g) To an oven-dried round-bottomed flask under N_2 atmosphere were added CH_2Cl_2 (5 mL), isobutyraldehyde (95 μL, 75 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 10 min, and then 3-(1-methyl)indolecarboxaldehyde (160 mg, 1.40 mmol) was added. The mixture was stirred for 16 h, at 40 °C, then cooled to room temperature and passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-2% EtOAc/hexanes) to yield the title compound[30] as a green oil (96 mg, 52% yield): IR (neat) 3052, 2961, 2912, 2859, 1618, 1539, 1474, 1381, 1340, 1245, 1152, 1083, 1012, 906, 846, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.26 (d, *J* = 7.9 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.05 (s, 1H), 6.44 (s, 1H), 3.82 (s, 3H), 2.01 (d, *J* = 1.5 Hz, 3H), 1.96 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 135.3, 131.1, 127.0, 125.5, 120.7, 118.2, 118.0, 114.7, 112.2, 107.9, 31.6, 25.7, 19.3.

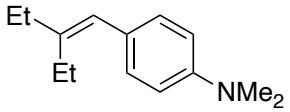


2-(2-Methyl-1-propenyl)thiophene (2h) To an oven-dried round-bottomed flask under N_2 atmosphere were added CH_2Cl_2 (5 mL), isobutyraldehyde (95 μL, 75 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. After 10 min, 2-thiophenecarboxaldehyde (131 μL, 157 mg, 1.40 mmol) was added and the mixture was stirred for 16 h, then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-5% EtOAc/hexanes) to yield the title compound[31] as a colorless oil (107 mg, 78% yield, yield depressed by volatility of product): IR (neat) 2969, 2910, 2855, 1648, 1445, 1380, 1236, 1051, 854, 688 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 5.1, 1H), 7.01 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.92 (d, *J* = 3.6 Hz, 1H), 6.42 (s, 1H), 2.01 (s, 3H), 1.95 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 141.7, 134.7, 126.7, 125.6, 123.7, 118.4, 27.2, 20.1; HRMS (CI, TOF): Exact mass calcd for $C_8H_{10}S$ $[M]^+$, 138.0498; found, 138.0497.

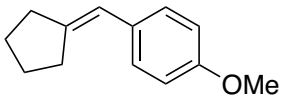


2-Ethyl-1-(*p*-methoxyphenyl)-1-butene (2i) To an oven-dried round-bottomed flask under N_2 atmosphere were added CH_2Cl_2 (5 mL), 2-ethylbutanal (123 μL, 100 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. After

5 min, *p*-anisaldehyde (171 μL, 191 mg, 1.40 mmol) was added. The reaction mixture was heated to reflux and stirred for 16 h. After the mixture was cooled to ambient temperature, it was passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-1% EtOAc/hexanes) to yield the title compound[11c] as a pale yellow oil (188 mg, 99% yield): IR (neat) 2963, 2934, 2875, 2834, 1607, 1508, 1463, 1291, 1244, 1175, 1036, 867, 826, 802 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.1 Hz, 2H), 6.89 (=d, *J* = 8.9 Hz, 2H), 6.20 (s, 1H), 3.83 (d, *J* = 0.8 Hz, 3H), 2.29 (q, *J* = 7.5 Hz, 2H), 2.21 (qd, *J* = 7.5, 1.5 Hz, 2H), 1.13 (t, *J* = 7.5 Hz, 3H), 1.10 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 157.8, 145.2, 131.3, 129.7, 122.8, 113.6, 55.2, 29.6, 23.8, 13.1, 12.9; HRMS (CI, TOF): Exact mass calcd for $C_{13}H_{18}O$ $[M]^+$, 190.1352; found, 190.1351.

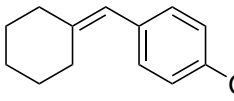


***N*,*N*-Dimethyl[*p*-(2-ethyl-1-butenyl)phenyl]amine (2j)** To an oven-dried round-bottomed flask under N_2 atmosphere were added 4-dimethylaminobenzaldehyde (209 mg, 1.40 mmol), CH_2Cl_2 (5 mL), 2-ethylbutanal (123 μL, 100 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 16 h, then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-3% EtOAc/hexanes) to yield the title compound[32] as a pale yellow oil (151 mg, 74% yield): IR (neat) 1962, 2933, 2874, 2798, 1610, 1517, 1460, 1347, 1190, 1164, 1060, 947, 867, 817, 799 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, 8.7 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.34 (s, 1H), 3.07 (s, 6H), 2.48 (q, *J* = 7.5 Hz, 2H), 2.36 (qd, *J* = 7.5, 1.4 Hz, 2H), 1.29 (t, *J* = 7.5 Hz, 3H), 1.26 (t, *J* = 7.5 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 149.0, 143.8, 129.5, 127.5, 123.4, 112.6, 40.7, 29.9, 24.0, 13.2, 13.1; HRMS (ESI, TOF): Exact mass calcd for $C_{14}H_{21}O$ $[M+H]^+$, 204.1747; found, 204.1737.



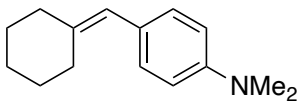
***p*-(Cyclopentylidenemethyl)methoxybenzene (2k)** To an oven-dried round-bottomed flask under N_2 atmosphere were added CH_2Cl_2 (5 mL), cyclopentanecarboxaldehyde (107 μL, 98 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. After 5 min, *p*-anisaldehyde (171 μL, 191 mg, 1.40 mmol) was added and the reaction mixture was stirred for 16 h, then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-1% EtOAc/hexanes) to yield the title compound[11g] as a yellow oil (165 mg, 88% yield): IR (neat) 2951, 2867, 2833, 1607, 1508, 1463, 1301, 1244, 1175, 1035, 868, 821 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.6 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.41 (s, 1H), 3.87 (s, 3H), 2.61 (*J* = 7.4 Hz, 2H), 2.57 (t, *J* = 7.1 Hz, 2H), 1.87 (p, *J* = 6.9 Hz, 2H), 1.80 – 1.70 (p, *J* = 6.9 Hz, 2H); $^{13}C\{^1H\}$ NMR

(125 MHz, $CDCl_3$) δ 157.6, 144.8, 131.9, 129.1, 120.3, 113.7, 55.2, 36.0, 31.1, 27.4, 25.8; HRMS (CI, TOF): Exact mass calcd for $C_{13}H_{16}O$ $[M]^+$, 188.1196; found, 188.1194.



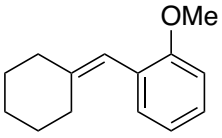
***p*-(Cyclohexylidenemethyl)methoxybenzene (2l)** To an oven-dried round-bottomed flask under N_2 atmosphere were added CH_2Cl_2 (5 mL), cyclohexanecarboxaldehyde (121 μL, 112 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. After 10 min, *p*-anisaldehyde (171 μL, 191 mg, 1.40 mmol) was added and the reaction mixture was stirred for 16 h, then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-3% EtOAc/hexanes) to yield the title compound[11g] as a colorless oil (201 mg, 99% yield): IR (neat) 2931, 2852, 2832, 1616, 1513, 1453, 1299, 1243, 1171, 1040, 909, 846, 738 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, J = 8.2 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 6.19 (s, 1H), 3.83 (s, 3H), 2.42 – 2.36 (m, 2H), 2.29 – 2.24 (m, 2H), 1.70 – 1.59 (m, 4H), 1.59 – 1.53 (m, 2H).; $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 157.7, 142.2, 131.0, 130.0, 121.4, 113.5, 55.2, 37.7, 29.5, 28.7, 27.9, 26.8; HRMS (CI, TOF): Exact mass calcd for $C_{14}H_{18}O$ $[M]^+$, 202.1352; found, 202.1350.

Styrene **2l** was also generated by a different procedure: To an oven-dried round-bottomed flask under N_2 atmosphere were added CH_2Cl_2 (5 mL), cyclohexanecarboxaldehyde dimethyl acetal (160 μL, 157 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. After 10 min, *p*-anisaldehyde (171 μL, 191 mg, 1.40 mmol) was added and the reaction mixture was stirred for 16 h, then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-3% EtOAc/hexanes) to yield the title compound[11g] as a colorless oil (185 mg, 91% yield). Spectral data (^1H NMR and $^{13}C\{^1H\}$ NMR) confirmed the identity and purity of the product.

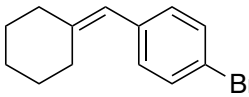


***N*,*N*-Dimethyl[*p*-(cyclohexylidenemethyl)phenyl]amine (2m)** To an oven-dried round-bottomed flask under N_2 atmosphere were added 4-dimethylaminobenzaldehyde (209 mg, 1.40 mmol), CH_2Cl_2 (5 mL), cyclohexanecarboxaldehyde (121 μL, 112 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 16 h, then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-3% EtOAc/hexanes) to yield the title compound[11a] as a pale yellow oil (170 mg, 79% yield): IR (neat) 2923, 2848, 1608,

1521, 1449, 1163, 1060, 949, 850, 814 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.4 Hz, 2H), 6.73 (d, *J* = 8.7 Hz, 2H), 6.17 (s, 1H), 2.96 (s, 6H), 2.42 (t, *J* = 6.1 2H), 2.26 (t, *J* = 5.9 Hz, 2H), 1.70 – 1.59 (m, 4H), 1.59 – 1.53 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 148.7, 141.0, 129.7, 127.0, 121.8, 112.4, 40.8, 37.7, 29.5, 28.7, 27.9, 26.8; HRMS (ESI, TOF): Exact mass calcd for $C_{16}H_{24}N$ $[M+H]^+$, 216.1747; found, 216.1737.

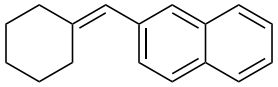


1-(Cyclohexylidenemethyl)-2-methoxybenzene (2n) To an oven-dried thick-walled reaction vessel under N_2 atmosphere were added CH_2Cl_2 (5 mL), cyclohexanecarboxaldehyde (121 μL, 112 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 5 min, and then *o*-anisaldehyde (169 μL, 191 mg, 1.40 mmol) was added. The reaction vessel was sealed and the mixture was heated to 100 °C. After the mixture was stirred for 16 h, the reaction mixture was allowed to cool and then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation. The crude reaction mixture was dissolved in tetrahydrofuran (THF, 5 mL) and treated with 1.0 N HCl (1.5 mL) in order to desilylate residual aldol adducts. The mixture was stirred for 30 min, then partitioned between Et_2O (25 mL) and water (25 mL). The layers were separated and the organic layer was washed sequentially with saturated $NaHCO_3$ (25 mL) and brine (25 mL). The combined aqueous layers were back-extracted with Et_2O (20 mL). The organic layers were combined and one volume-equivalent of hexane was added. The organic layers were dried over $MgSO_4$, then the desiccant was removed by filtration. The solvent was removed in vacuo, and the residue purified by column chromatography (0-1% EtOAc/hexanes) to yield the title compound[11b] as a pale yellow oil (132 mg, 61% yield): IR (neat) 2924, 2852, 2833, 1596, 1578, 1487, 1462, 1288, 1241, 1160, 1096, 788 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.22 (td, *J* = 7.8, 1.8 Hz, 1H), 7.18 (dd, *J* = 7.6, 1.8 Hz, 1H), 6.93 (td, *J* = 7.4, 1.1 Hz, 1H), 6.89 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.25 (s, 1H), 3.85 (s, 3H), 2.35 – 2.31 (m, 4H), 1.68 (td, *J* = 7.7, 7.0, 4.1 Hz, 2H), 1.66 – 1.56 (m, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 157.2, 143.4, 130.6, 127.4, 127.2, 120.0, 117.3, 110.4, 55.4, 37.7, 29.9, 28.7, 27.9, 26.8; HRMS (CI, TOF): Exact mass calcd for $C_{14}H_{18}O$ $[M]^+$, 202.1352; found, 202.1350.

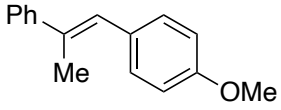


***p*-Bromo(cyclohexylidenemethyl)benzene (2o)** To an oven-dried round-bottomed flask under N_2 atmosphere were added 4-bromobenzaldehyde (259 mg, 1.40 mmol), benzonitrile (1.0 mL), cyclohexanecarboxaldehyde (121 μL, 112 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The reaction mixture was heated to 150 °C. The mixture was stirred for 16 h, then allowed to cool to room temperature, after which passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL), and the column was rinsed with CH_2Cl_2 (20 mL). The solvent was removed by rotary

evaporation and the residue was purified by column chromatography (0-1% EtOAc/hexanes) to yield the title compound[10b] as a yellow oil (69 mg, ~25% yield, yield contaminated trace unidentified impurities): IR (neat) 2929, 2852, 2664, 1651, 1488, 1446, 1397, 1342, 1100, 990, 802 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.40 (m, 2H), 7.13 – 7.03 (m, 2H), 6.16 (s, 1H), 2.35 (t, *J* = 6.0 Hz, 2H), 2.26 (t, *J* = 6.6 Hz, 2H), 1.71 – 1.59 (m, 4H), 1.59 – 1.53 (m, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 144.4, 137.3, 131.1, 130.6, 120.9, 119.6, 37.7, 29.5, 28.6, 27.9, 26.6; HRMS (CI, TOF): Exact mass calcd for $C_{13}H_{15}Br$ $[M]^+$, 250.0352; found, 250.0351.

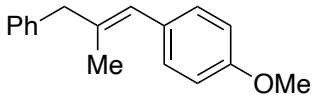


2-(Cyclohexylidenemethyl)naphthalene (2p) To an oven-dried round-bottomed flask under N_2 atmosphere were added 2-naphthaldehyde (219 mg, 1.40 mmol), benzonitrile (1.0 mL), cyclohexanecarboxaldehyde (121 μL, 112 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The reaction mixture was heated to 150 °C. The mixture was stirred for 16 h, then allowed to cool to room temperature, after which passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL), and the column was rinsed with CH_2Cl_2 (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-1% EtOAc/hexanes) to yield the title compound[33] as a pale yellow oil (139 mg, 63% yield, yield contaminated 5-10 mol% of unidentified impurity): IR (neat) 3053, 2924, 2852, 2836, 1647, 1628, 1598, 1504, 1446, 1270, 1125, 934, 947, 856, 834, 814, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.89 (m, 3H), 7.82 (s, 1H), 7.64 – 7.51 (m, 3H), 6.57 (s, 1H), 2.67 – 2.59 (m, 2H), 2.53 – 2.46 (m, 2H), 1.90 – 1.82 (m, 2H), 1.82 – 1.71 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 144.1, 136.1, 133.6, 132.1, 128.0, 127.9, 127.7, 127.6, 127.4, 126.0, 125.5, 122.3, 37.9, 29.8, 28.9, 28.1, 26.9; HRMS (CI, TOF): Exact mass calcd for $C_{17}H_{18}$ $[M]^+$, 222.1403; found, 222.1402.



(*E*)-14-Methyl-4-methoxystilbene (2q) To an oven-dried thick-walled reaction vessel under N_2 atmosphere were added CH_2Cl_2 (1 mL), 2-phenylpropanal (134 μL, 134 mg, 1.00 mmol), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 10 min, and then *p*-anisaldehyde (172 μL, 191 mg, 1.40 mmol) was added. The reaction vessel was sealed and the mixture was heated to 100 °C. After the mixture was stirred for 16 h, the reaction mixture was allowed to cool and then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-1% EtOAc/hexanes) to yield the title compound[11c] as a white solid (108 mg, 48% yield, *E*:*Z* = 14:1). The *E*:*Z* ratio was determined by ^1H NMR spectroscopy: IR (film) 2953, 2920, 2847, 1602, 1573, 1508, 1462, 1294, 1241, 1178, 1081, 1026, 829, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) major isomer: δ 7.60 (d, *J* = 8.7 Hz, 2H), 7.51 – 7.32 (m, 5H), 7.01 (d, *J* = 8.7 Hz, 2H), 6.88 (s, 1H), 3.90 (s, 3H), 2.37 (s, 3H); selected minor isomer peaks: δ 6.73 (d, *J* =

8.6 Hz, 2H), 6.50 (s, 1H), 3.79 (s, 3H), 2.27 (s, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) major isomer: δ 158.3, 144.3, 136.0, 131.0, 130.5, 128.4, 127.4, 127.1, 126.0, 113.7, 55.3, 17.6; HRMS (CI, TOF): Exact mass calcd for $C_{16}H_{16}O$ $[M]^+$, 224.1196; found, 224.1195.



(*E*)-2-Methyl-1-(*p*-methoxyphenyl)-3-phenylpropene (2r) To an oven-dried thick-walled reaction vessel under N_2 atmosphere were added 2-methyl-3-phenylpropionaldehyde (148 mg, 1.00 mmol), CH_2Cl_2 (2 mL), and 2,6-lutidine (291 μL, 268 mg, 2.50 mmol). Immediately afterward, TMSOTf (434 μL, 533 mg, 2.40 mmol) was added dropwise by syringe. The mixture was stirred for 5 min, and then *p*-anisaldehyde (172 μL, 191 mg, 1.40 mmol) was added. The reaction vessel was sealed and the mixture was heated to 100 °C. After the mixture was stirred for 3 h, the reaction mixture was allowed to cool and then passed through a column of silica (4 cm x 1 cm) with Et_2O (20 mL). The solvent was removed by rotary evaporation and the residue was purified by column chromatography (0-1% EtOAc/hexanes) to yield the title compound[32] as a colorless oil (187 mg, 79% yield, *E*:*Z* = 4:1). The *E*:*Z* ratio was determined by ^{1}H NMR spectroscopy: IR (neat) 3026, 2955, 2907, 2834, 1606, 1508, 1452, 1297, 1246, 1175, 1035, 834, 808, 741, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) major isomer: δ 7.55 – 7.36 (m, 7H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.55 (s, 1H), 3.95 (s, 3H), 3.66 (s, 2H), 2.01 (d, *J* = 1.5 Hz, 3H); minor isomer: δ 7.55 – 7.36 (m, 7H), 7.04 (d, *J* = 8.7 Hz, 2H), 6.69 (s, 1H), 3.93 (s, 1H), 3.82 (s, 2H), 2.02 – 2.00 (m, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) major isomer: δ 158.1, 140.2, 136.6, 131.1, 130.2, 129.2, 128.6, 126.5, 126.4, 113.7, 55.3, 47.4, 17.8; minor isomer: δ 158.3, 140.0, 135.8, 130.9, 129.7, 128.8, 128.7, 127.2, 126.2, 113.9, 55.3, 38.7, 24.3; HRMS (CI, TOF): Exact mass calcd for $C_{17}H_{18}O$ $[M]^+$, 238.1352; found, 238.1353.

SUPPORTING INFORMATION

^{1}H and ^{13}C NMR spectra for compounds **2a-2r** and additional experimental methods

ACKNOWLEDGMENTS

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(18) Attempts to isolate or spectroscopically identify the aldol intermediates that correspond to styrenes **2q** and **2r,** and thus track the relationship of diastereoselectivity to the final *E*/*Z* ratio, were unsuccessful due to the complexity of the reaction mixture.
(19) This electrophile is potentially active in aldol reactions, undergoing aldol reaction with acetophenone in the presence of TMSOTf and 2,6-lutidine and providing 50% conv to the β-silyloxyketone overnight.
(20) A mixture of 2,6-lutidine and formic acid provided a singlet peak at 8.35 ppm in $CDCl_3$ in the absence of TMSOTf.
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