JOC The Journal of Organic Chemistry

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Enantiospecific Aluminum-Catalyzed (3+2) Cycloaddition of Unactivated Aziridines with Isothiocyanates

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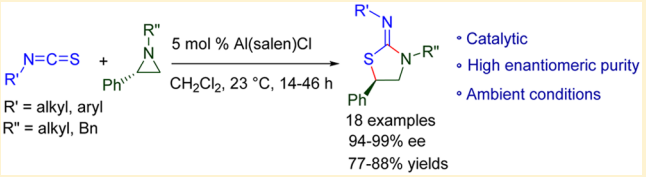
Supporting Information

ABSTRACT: An Al(salen)Cl efficiently catalyzed the enantiospecific (3+2) cycloaddition of unactivated chiral aziridines with isothiocyanates to furnish functionalized iminothiazolidines at room temperature with 94−99% ee. The use of an aluminum Lewis acid as the catalyst, high enantiomeric purities, mild reaction conditions, broad substrate scope, and the high atom economy are the significant practical features.



The (3+2) cycloaddition of aziridines with heterocumulenes affords a powerful synthetic strategy for the construction of five-membered heterocycles.[1−5] Among these, iminothiazolidines are important structural scaffolds of numerous biologically active compounds.[6] For example, compounds with the 2-iminothiazolidine core structure exhibit anti-inflammatory,[6d] antidepressant,[6b] and radioprotective properties[6f] (Figure 1). In addition, they have found wide applications as catalysts for organocatalysis.[7] Considerable efforts are therefore made on the development of (3+2) cycloaddition of aziridines with isothiocayanates using NaI,[4b] PBu_3,[4c] pyrrolidine,[4d] and Fe[5] based systems as catalysts or stoichiometric reagents. However, asymmetric versions of this strategy are rare.[4d,8−10] Recently, Stoltz and co-workers demonstrated the cyclization of activated *N*-sulfonyl aziridines with isothocyanates using 1.25 equiv $ZnCl_2$ as the Lewis acid at room temeprature with 60−95% ee (Scheme 1a, eq 1).[9] During the preparation of the article, Ghorai and co-workers disclosed the same transformation using 20 mol% $BF_3{\cdot}Et_2O$ with a stoichiometric amount of tetrabutylammonium hydrogen sulfate (TBAHS) as an additive at −30 °C in 20−99% ee (Scheme 1a, eq 2).[10] These reactions are generally effective using an excess of isothiocyanates under inert atmosphere.[9,10] In continuation of our studies,[4d,5] we herein report an efficient Al(salen)Cl-catalyzed enantiospecific (3+2) cycloaddition of unactivated chiral aziridines with one equiv of isothocyanates at room temeprature (Scheme 1b).[11,12] This protocol includes the advantages of high atom-economy, ambient reaction conditions, free from additive, catalytic, and excellent enantiomeric purities (94−99% ee).

First, optimization of the reaction condition was performed with phenyl isothiocyanate **1a** and 1-isopropyl-2-phenylaziridine **2a** as the model substrates in the presence of Al(salen)Cl catalysts in CH_2Cl_2 at ambient conditions (Scheme 2, Table S1, see Supporting Information). Gratifyingly, the reaction occurred to give thiazolidin-2-ylidene **3a** in 97% ee and 87% yield, when the substrates **1a** and **2a** were stirred with 5 mol% Al(salen)Cl **C1** for 18 h. The use of Al(salen)Cl **C2** led to the formation of **3a** in 89% ee and 85% yield. Subsequent screening of the solvents, such as CH_3CN, toluene, THF, $CHCl_3$, MeOH, and $(CH_2Cl)_2$, yielded the target heterocycle **3a** in 80−96% ee. Recrystallization of **3a** in hexane provided single crystals whose structure was confirmed by X-ray analysis (see Supporting Information). A control experiment confirmed that without the aluminum catalyst the reaction was not observed.

To reveal the substrate scope, the reaction of a series of alkyl/aryl isothiocyanates **1b−i** was investigated with aziridine **2a** as a standard substrate (Table 1). As above, the reaction efficiently occurred to afford the target iminothiazolidines **3b−i** with excellent enantiomeric purities and yields. For example, isothiocyanates **1b−d** with ethyl, methyl, and nitro groups in the phenyl rings effected the reaction to provide iminothiazolidines **3b−d** in 96−97% ee and 76−87% yields. The reaction of 2,4-, 3,4-, and 3,5-dimethyl substituted isothiocyanates **1e−g** afforded the corresponding iminothiazolidines **3e−g** in 94−98% ee and 75−85% yields. Furthermore, 1-naphthyl-substituted **1h** and (*R*)-(+)-*α*-methyl benzyl isothiocyanates **1i** underwent reaction to give iminothiazolidines **3h** and **3i** in 97% and 94% ee, respectively.

Next, the reaction of a series of aziridines **2b−i** containing *N*-benzyl and *N*-alkyl substituents was investigated with 1-naphthyl-substituted isothiocyanate **1h** as a representative example (Table 1). Aziridines **2b−e** having allyl, isobutyl, benzyl, and cyclohexyl substituents on the nitrogen atom underwent reaction to furnish iminothiazolidines **3j−m** in 99% ee and 69−83% yields. The reaction of aziridines **2f−g** containing 4-bromo and 4-methoxy groups furnished iminothiazolidines **3n** and **3o** in 98 and 99% ee, respectively. In

Received: September 6, 2016
Published: October 12, 2016

DOI: 10.1021/acs.joc.6b02190
J. Org. Chem. 2016, 81, 11508−11513

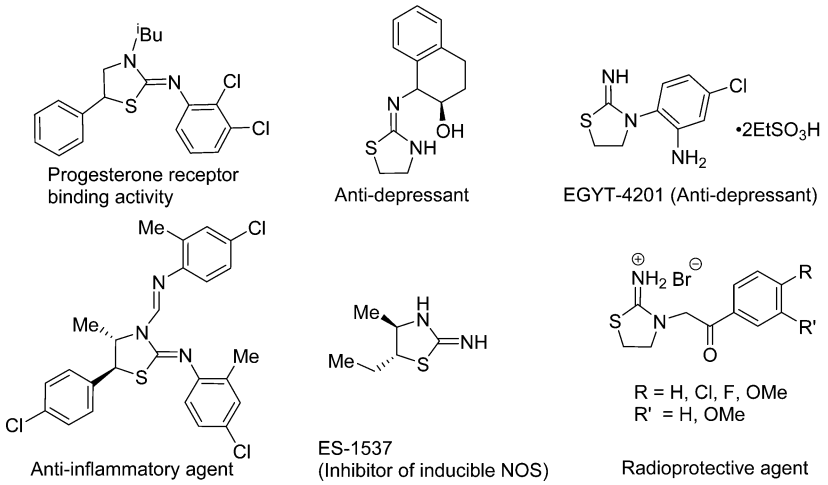
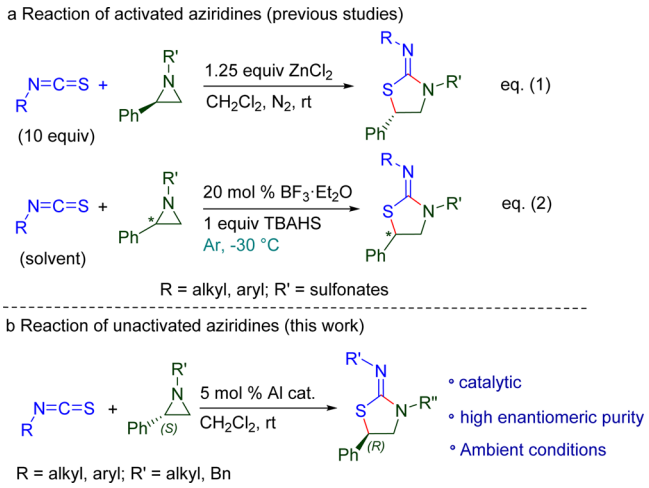


Figure 1. Examples of some biologically active iminothiazolidines.

Scheme 1. Stereospecific (3+2) Cycloaddition of Chiral Aziridines with Isothiocyanates



addition, aziridines **2h** and **2i** with 2-furyl and 1-naphthyl substituents produced iminothiazolidines **3p** and **3q** in 98 and 99% ee, respectively. These results suggest the protocol is general and the substrates bearing both electron withdrawing and donating groups in the aryl ring can be readily reacted with excellent enantiomeric purities and yields.

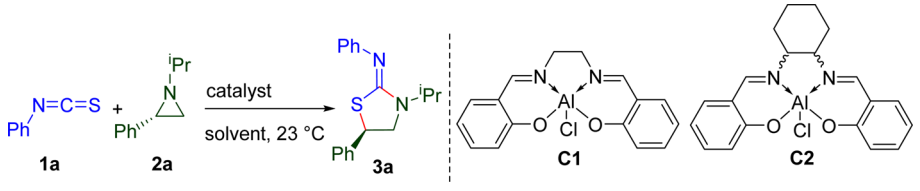
To get insight into the mechanism, isothiocyanate **1a** was reacted with the azirdines **2a** and **ent-2a** with opposite configurations as the representative examples (Scheme 3). The cycloaddition occurred to produce iminothiazolidines **3a** and **ent-3a**, in 97% and 96.5% ee, respectively, with opposite configurations. In addition, the single X-ray analysis of **3a** suggests that the reaction proceeds via stereospecific S_N2 nucleophilic opening followed by intramolecular 5-exo-dig cyclization. Thus, the coordination of the Lewis acid AlL_n to nitrogen lone pair of aziridine may lead to the formation of the complex **a** (Scheme 4).[12] Nucleophilic ring (S_N2) opening at the benzylic position of **b** with isothiocyanates may furnish **c**,[5] which can lead an intramolecular 5-exo-dig cyclization to give the target iminothiazolidines and AlL_n to complete the catalytic cycle.

In summary, we described Al-catalyzed (3+2) cycloaddition of unactivated chiral aziridines with isothiocyanates to furnish 2-iminothiazolidines at room temperature under air. The use of readily accessible and nontoxic Al(salen)Cl as the catalyst, mild reaction conditions, high atom economy, broad substrate scope, and excellent enantiomeric purities and yields are the significant practical advantages.

EXPERIMENTAL SECTION

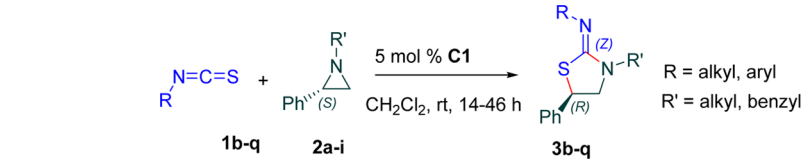
General Information. Amines, alkenes, and amino acids were purchased from commercial suppliers and used as received. Isothiocyanates[5] and aziridines[13,14] were prepared according to the reported procedure. The reactions were monitored by analytical TLC using silica gel G/GF 254 plates. The column chromatography was performed employing 60−120 mesh silica gel. NMR (^{1}H and ^{13}C) spectra were recorded on 400 and 600 MHz spectrometers and the data are accounted as follows: chemical shifts (δ ppm) (multiplicity, coupling constant (Hz), integration). The abbreviations for multiplicity are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets. Chemical shifts (δ) are reported relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^{1}H NMR and 77.23 ppm for ^{13}C NMR). Melting points were determined with a melting point apparatus and are uncorrected. Optical rotation were determined by polarimeter. FT-IR spectra were recorded using IR spectrometer. Mass spectra were recorded on a ESI-MS TOF instrument. HPLC analysis was carried out using Daicel Chiralcel OD and OJ columns. Single crystal X-ray analysis was performed using CCD diffractometer equipped with 1.75 kW sealed-tube Mo Kα irradiation (λ= 0.71073 Å) at 298(2) K, and the structure was solved

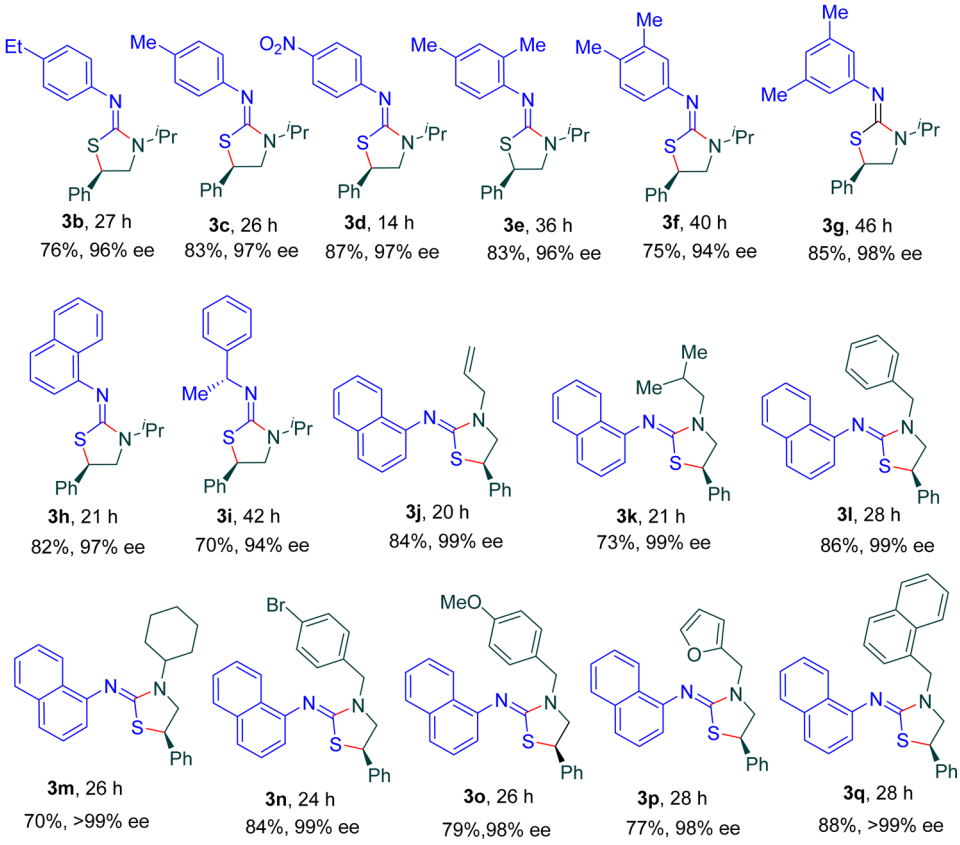
Scheme 2. Optimization of Reaction Conditions



DOI: 10.1021/acs.joc.6b02190
J. Org. Chem. 2016, 81, 11508−11513

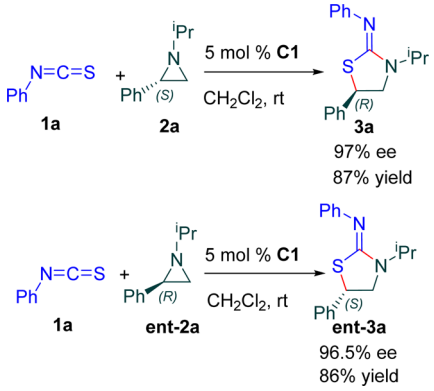
Table 1. Substrate Scope[a,b]



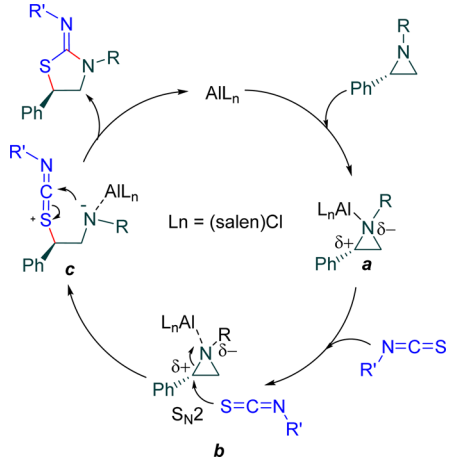


[a]Reaction conditions: **1b–i** (0.25 mmol), **2a–i** (0.25 mmol), **C1** (5 mol %), CH_2Cl_2 (1.0 mL), 23 °C, air. [b]Determined by chiral HPLC analysis.

Scheme 3. Mechanistic Experiments



Scheme 4. Proposed Catalytic Cycle



by direct methods using SHELXS-2014 (Göttingen, Germany) and refined with full-matrix least-squares on F^2 using SHELXL-2014.

General Procedure for the Cycloaddition of Isothiocyanates with Aziridines. Isothiocyanates (0.25 mmol), aziridine (0.25 mmol), and Al-catalyst (5 mol%) were stirred in CH_2Cl_2 (1 mL) at room temperature under air. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as an eluent. The reaction mixture was then evaporated on a rotary evaporator and the residue was purified on a silica gel column chromatography using hexane and ethyl acetate (19:1).

(R,Z)-N-(3-Isopropyl-5-phenylthiazolidin-2-ylidene)aniline ***3a.*** Colorless solid; yield 87% (64.5 mg); mp 109–110 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (d, J = 7.2 Hz, 2H), 7.33 (t, J = 6.6 Hz, 2H), 7.30–7.25 (m, 3H), 7.01 (t, J = 7.2 Hz, 1H), 6.99 (d, J = 7.8 Hz,

DOI: 10.1021/acs.joc.6b02190
J. Org. Chem. 2016, 81, 11508–11513

2H), 4.71−4.66 (m, 2H), 3.88 (dd, J = 9.6, 6.6 Hz, 1H), 3.56 (dd, J = 9.6, 7.8 Hz, 1H), 1.29 (d, J = 6.6 Hz, 3H), 1.25 (d, J = 6.6 Hz, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.3, 152.4, 139.4, 129.0, 128.3, 127.7, 123.1, 122.3, 53.1, 46.9, 46.5, 20.2, 19.2; FT-IR (KBr) 3059, 3029, 2971, 2929, 2869, 1619, 1587, 1490, 1212, 1068, 936, 856 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{18}H_{20}N_2SH$: 297.1420, found: 297.1426; $[\alpha]_D^{20}$ = +70 (c= 0.2, $CHCl_3$); HPLC analysis: 97% ee [Daicel CHIRALCEL OJ column, hexane/^{i}PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 13.53 min (major), 20.66 min (minor)]. **3a′:** $[\alpha]_D^{20}$ = −72 (c= 0.2, $CHCl_3$); HPLC analysis: 96.5% ee [Daicel CHIRALCEL OJ column, hexane/^{i}PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 13.20 min (minor), 19.36 min (major)].

(R,Z)-4-Ethyl-N-(3-isopropyl-5-phenylthiazolidin-2-ylidene)aniline ***3b***. Colorless liquid; yield 76% (61.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (d, J = 7.8 Hz, 2H), 7.32 (t, J = 7.2 Hz, 2H), 7.28 (t, J = 7.2 Hz, 1H), 7.09 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 4.70−4.50 (m, 2H), 3.86 (dd, J = 9.6, 6.6 Hz, 1H), 3.55 (dd, J = 9.6, 7.8 Hz, 1H), 2.60 (q, J = 7.8 Hz, 2H), 1.27 (d, J = 6.6 Hz, 3H), 1.24 (d, J = 6.6 Hz, 2H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.2, 150.0, 139.5, 138.9, 129.0, 128.3, 128.2, 127.7, 122.1, 53.1, 46.9, 46.5, 28.5, 20.2, 19.2, 15.8; FT-IR (neat) 3061, 3025, 2966, 2929, 2870, 1622, 1598, 1504, 1455, 1243, 1212, 1066, 935, 861 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{20}H_{24}N_2SH$: 325.1733, found: 325.1733; $[\alpha]_D^{20}$ = +244 (c= 0.2, $CHCl_3$); HPLC analysis: 96% ee [Daicel CHIRALCEL OJ column, hexane/^{i}PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 8.35 min (major), 12.82 min (minor)].

(R,Z)-N-(3-Isopropyl-5-phenylthiazolidin-2-ylidene)-4-methylaniline ***3c***. Colorless solid; yield 83% (64 mg); mp 88−89 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (d, J = 7.8 Hz, 2H), 7.33 (t, J = 7.2 Hz, 2H), 7.28 (t, J = 7.8 Hz, 1H), 7.08 (d, J = 7.8 Hz, 2H), 6.88 (dd, J = 8.4, 2.4 Hz, 2H), 4.70−4.65 (m, 2H), 3.87 (dd, J = 9.6, 6.6 Hz, 1H), 3.55 (dd, J = 9.6, 7.8 Hz, 1H), 2.30 (s, 3H), 1.28 (d, J = 7.2 Hz, 3H), 1.24 (d, J = 6.6 Hz, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.3, 149.9, 139.4, 132.4, 129.6, 128.9, 128.3, 127.7, 122.0, 53.1, 46.9, 46.4, 21.1, 20.1, 19.2; FT-IR (KBr) 3025, 2970, 2920, 2859, 1618, 1597, 1504, 1403, 1236, 1213, 1178, 1061, 949, 861 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{19}H_{22}N_2SH$: 311.1576, found: 311.1588; $[\alpha]_D^{20}$ = +85 (c= 0.2, $CHCl_3$); HPLC analysis: 97% ee [Daicel CHIRALCEL OJ column, hexane/^{i}PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 12.92 min (major), 18.91 min (minor)].

(R,Z)-N-(3-Isopropyl-5-phenylthiazolidin-2-ylidene)-4-nitroaniline ***3d***. Yellow solid; yield 87% (74 mg); mp 70−71 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (d, J = 9.0 Hz, 2H), 7.41 (d, J = 7.2 Hz, 2H), 7.36 (t, J = 7.2 Hz, 2H), 7.31 (t, J = 7.2 Hz, 1H), 7.06 (d, J = 8.4 Hz, 2H), 4.75 (t, J = 7.2 Hz, 1H), 4.71−4.67 (m, 1H), 3.94 (dd, J = 9.6, 6.6 Hz, 1H), 3.63 (dd, J = 10.2, 7.8 Hz, 1H), 1.29 (d, J = 6.6 Hz, 3H), 1.25 (d, J = 6.6 Hz, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.7, 158.5, 143.1, 138.7, 129.2, 128.6, 127.6, 125.1, 122.7, 53.2, 47.2, 46.8, 20.1, 19.4; FT-IR (KBr) 3061, 3029, 2967, 2925, 2853, 1612, 1571, 1502, 1330, 1271, 1218, 1065, 1018, 941, 856 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{18}H_{19}N_3O_2SH$: 342.1276, found: 342.1284; $[\alpha]_D^{20}$ = +297 (c= 0.2, $CHCl_3$); HPLC analysis: 97% ee [Daicel CHIRALCEL OJ column, hexane/^{i}PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 27.65 min (minor), 30.77 min (major)].

(R,Z)-N-(3-Isopropyl-5-phenylthiazolidin-2-ylidene)-2,4-dimethylaniline ***3e***. Colorless solid; yield 83% (67 mg); mp 69−70 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (d, J = 7.2 Hz, 2H), 7.33 (t, J = 7.2 Hz, 2H), 7.28 (t, J = 7.2 Hz, 1H), 6.97 (s, 1H), 6.92 (d, J = 7.8 Hz, 1H), 6.78 (d, J = 7.8 Hz, 1H), 4.71−4.65 (m, 2H), 3.88 (dd, J = 9.6, 7.2 Hz, 1H), 3.55 (dd, J = 9.6, 7.2 Hz, 1H), 2.27 (s, 3H), 2.20 (s, 3H), 1.30 (d, J = 6.6 Hz, 3H), 1.27 (d, J = 6.6 Hz, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 157.8, 148.6, 139.7, 132.5, 131.1, 130.2, 128.9, 128.2, 127.6, 127.0, 121.2, 53.3, 46.7, 46.6, 21.1, 20.1, 19.2, 18.2; FT-IR (KBr) 3056, 3020, 2969, 2929, 2866, 1622, 1597, 1495, 1453, 1242, 1209, 1067, 1022, 953, 874 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{20}H_{24}N_2SH$: 325.1733, found: 325.1735; $[\alpha]_D^{20}$ = +162 (c= 0.2, $CHCl_3$); HPLC analysis: 94% ee [Daicel CHIRALCEL OJ column, hexane/*i*PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 11.95 min (major), 15.40 min (minor)].

(R,Z)-N-(3-Isopropyl-5-phenylthiazolidin-2-ylidene)-3,4-dimethylaniline ***3f***. Colorless liquid; yield 75% (61 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (d, J = 7.2 Hz, 2H), 7.34 (t, J = 7.2 Hz, 2H), 7.29 (t, J = 7.2 Hz, 1H), 7.03 (d, J = 7.8 Hz, 1H), 6.79 (s, 1H), 6.75 (d, J = 7.8 Hz, 1H), 4.70−4.66 (m, 2H), 3.87 (dd, J = 9.6, 6.6 Hz, 1H), 3.56 (dd, J = 9.6, 7.8 Hz, 1H), 2.23 (s, 3H), 2.21 (s, 3H), 1.29 (d, J = 7.2 Hz, 3H), 1.25 (d, J = 6.6 Hz, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.0, 150.1, 139.4, 137.0, 131.1, 130.1, 128.9, 128.2, 127.7, 123.5, 119.2, 53.0, 46.9, 46.4, 20.2, 20.1, 19.4, 19.2; FT-IR (neat) 3056, 3028, 2970, 2922, 2870, 1629, 1596, 1494, 1455, 1243, 1211, 1122, 1066, 938, 841 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{20}H_{24}N_2SH$: 325.1733, found: 325.1729; $[\alpha]_D^{20}$ = +112 (c= 0.2, $CHCl_3$); HPLC analysis: 96% ee [Daicel CHIRALCEL OJ column, hexane/^{i}PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 9.47 min (major), 12.82 min (minor)].

(R,Z)-N-(3-Isopropyl-5-phenylthiazolidin-2-ylidene)-3,5-dimethylaniline ***3g***. Colorless solid; yield 85% (69 mg); mp 72−73 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (d, J = 7.2 Hz, 2H), 7.34 (t, J = 7.2 Hz, 1H), 7.29 (t, J = 7.2 Hz, 1H), 6.67 (s, 1H), 6.62 (s, 2H), 4.70−4.66 (m, 2H), 3.86 (dd, J = 10.2, 7.2 Hz, 1H), 3.55 (dd, J = 9.6, 7.8 Hz, 1H), 2.30 (s, 6H), 1.28 (d, J = 6.6 Hz, 3H), 1.24 (d, J = 6.6 Hz, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 157.8, 152.2, 139.4, 138.4, 128.9, 128.3, 127.7, 124.9, 119.9, 53.0, 46.9, 46.4, 21.6, 20.2, 19.2; FT-IR (KBr) 3056, 3028, 2970, 2925, 2865, 1622, 1587, 1469, 1401, 1241, 1210, 1069, 1026, 957, 844 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{20}H_{24}N_2SH$: 325.1733, found: 325.1734; $[\alpha]_D^{20}$ = +141 (c= 0.2, $CHCl_3$); HPLC analysis: 98% ee [Daicel CHIRALCEL OJ column, hexane/^{i}PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 6.99 min (major), 10.43 min (minor)].

(R,Z)-N-(3-Isopropyl-5-phenylthiazolidin-2-ylidene)naphthalen-1-amine ***3h***. Colorless liquid; yield 82% (71 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21−8.20 (m, 1H), 7.83−7.82 (m, 1H), 7.57−7.55 (m, 1H), 7.49−7.48 (m, 2H), 7.42−7.40 (m, 3H), 7.34 (t, J = 7.2 Hz, 2H), 7.29 (t, J = 7.2 Hz, 1H), 7.10−7.08 (m, 1H), 4.96−4.91 (m, 1H), 4.69 (t, J = 7.8 Hz, 1H), 3.94 (dd, J = 10.2, 7.2 Hz, 1H), 3.63 (dd, J = 10.2, 7.8 Hz, 1H), 1.40 (d, J = 6.6 Hz, 3H), 1.37 (d, J = 6.6 Hz, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.3, 148.9, 139.4, 134.5, 128.9, 128.2, 127.9, 127.6, 126.1, 126.0, 125.2, 124.1, 123.1, 116.3, 53.2, 46.8, 46.7, 20.3, 19.5; FT-IR (neat) 3058, 2969, 2929, 2869, 1613, 1571, 1501, 1456, 1388, 1245, 1213, 1181, 1065, 1039, 997 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{22}H_{22}N_2SH$: 347.1576, found: 347.1589; $[\alpha]_D^{20}$ = +154 (c= 0.2, $CHCl_3$); HPLC analysis: 97% ee [Daicel CHIRALCEL OD column, hexane/^{i}PrOH = 90:10, flow rate: 1 mL/min, λ = 215 nm, t_R = 12.89 min (major), 22.52 min (minor)].

(R,Z)-3-Isopropyl-5-phenyl-N-((R)-1-phenylethyl)thiazolidin-2-imine ***3i***. Pale yellow liquid; yield 70% (57 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.8 Hz, 2H), 7.14 (d, J = 7.2 Hz, 2H), 7.34 (t, J = 7.2 Hz, 2H), 731−7.29 (m, 3H), 7.20 (t, J = 7.2 Hz, 1H), 4.62−4.59 (m, 2H), 4.29 (q, J = 6.6 Hz, 1H), 3.72 (dd, J = 9.6, 6.6 Hz, 1H), 3.43 (dd, J = 9.6, 8.4 Hz, 1H), 1.49 (d, J = 6.6 Hz, 3H), 1.19 (d, J = 7.2 Hz, 6H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 156.2, 147.4, 140.3, 128.9, 128.3, 128.2, 127.7, 126.7, 126.4, 64.2, 52.9, 46.8, 46.4, 26.0, 19.8, 19.0; FT-IR (neat) 3060, 3027, 2969, 2925, 2865, 1629, 1492, 1396, 1241, 1208, 1178, 1063, 1013, 817 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{20}H_{24}N_2SH$: 325.1733, found: 325.1732; $[\alpha]_D^{20}$ = −20.0 (c= 0.2, $CHCl_3$); HPLC analysis: 94% ee [Daicel CHIRALCEL OJ column, hexane/^{i}PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 9.58 min (major), 20.85 min (minor)].

(R,Z)-N-(3-Allyl-5-phenylthiazolidin-2-ylidene)naphthalen-1-amine ***3j***. Pale yellow liquid; yield 84% (72 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20−8.18 (m, 1H), 7.83−7.81 (m, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.48−7.47 (m, 2H), 7.41−7.38 (m, 3H), 7.33 (t, J = 7.2 Hz, 2H), 7.29 (t, J = 7.2 Hz, 1H), 7.08 (d, J = 7.2 Hz, 1H), 6.10−6.03 (m, 1H), 5.37 (d, J = 16.8 Hz, 1H), 5.32 (d, J = 10.2 Hz, 1H), 4.76 (t, J = 7.8 Hz, 1H), 4.41 (dd, J = 15.0, 6.0 Hz, 1H), 4.32 (dd, J = 15.0, 6.0 Hz, 1H), 3.92 (dd, J = 10.2, 7.2 Hz, 1H), 3.66 (dd, J = 10.2, 8.4 Hz, 1H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.5, 148.7, 139.0, 134.5, 133.1, 129.0, 128.9, 128.3, 127.9, 127.7, 126.1, 126.0, 125.2, 124.1, 123.3, 118.2, 116.1, 58.1, 49.5, 47.0; FT-IR (neat) 3058, 2921, 2854,

DOI: 10.1021/acs.joc.6b02190
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1618, 1571, 1502, 1386, 1347, 1246, 1183, 1158, 1079, 1014, 928 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{22}H_{20}N_2SH$: 345.1420, found: 345.1416; $[\alpha]_D^{20}$ = +35 (c= 0.2, $CHCl_3$); HPLC analysis: 99% ee [Daicel CHIRALCEL OJ column, hexane/*i*PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 16.70 min (major), 25.07 min (minor)].

(R,Z)-N-(3-Benzyl-5-phenylthiazolidin-2-ylidene)naphthalen-1-amine ***3k***. Colorless liquid; yield 86% (85 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.25−8.22 (m, 1H), 7.87−7.84 (m, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.51−7.49 (m, 4H), 7.46−7.42 (m, 3H), 7.37−7.35 (m, 3H), 7.31−7.29 (m, 3H), 7.16 (d, *J* = 7.2 Hz, 1H), 5.09 (d, *J* = 15.2, 1H), 4.88 (d, *J* = 14.8, 1H), 4.76 (t, *J* = 7.2, 1H), 3.87 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.62 (dd, *J* = 10.0, 8.0 Hz, 1H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 158.7, 148.7, 138.8, 137.3, 134.5, 128.9, 128.8, 128.5, 128.3, 127.9, 127.7, 127.6, 126.1, 125.2, 124.2, 123.3, 116.0, 58.0, 50.5, 47.0; FT-IR (neat) 3058, 3022, 2919, 2856, 1615, 1571, 1495, 1453, 1386, 1246, 1158, 1078, 1014, 928, 850 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{26}H_{22}N_2SH$: 395.1576, found: 395.1574; $[\alpha]_D^{20}$ = +86 (c= 0.2, $CHCl_3$); HPLC analysis: 99% ee [Daicel CHIRALCEL OD column, hexane/^{i}PrOH = 90:10, flow rate: 1 mL/min, λ = 215 nm, t_R = 9.32 min (major), 13.16 min (minor)].

(R,Z)-N-(3-Isobutyl-5-phenylthiazolidin-2-ylidene)naphthalen-1-amine ***3l***. Colorless liquid; yield 73% (66 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.21−8.18 (m, 1H), 7.84−7.81 (m, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.50−7.47 (m, 2H), 7.43−7.38 (m, 3H), 7.36−7.32 (m, 3H), 7.08 (dd, *J* = 7.2, 1.2 Hz, 1H), 4.73 (t, *J* = 7.2 Hz, 1H), 3.97 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.71(dd, *J* = 10.0, 7.6 Hz, 1H), 3.64 (dd, *J* = 13.6, 7.6 Hz, 1H), 3.48 (dd, *J* = 13.6, 7.2 Hz, 1H), 2.19−2.14 (m, 1H), 1.11 (d, *J* = 6.8 Hz, 6H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 159.0, 149.1, 139.2, 134.5, 129.0, 128.9, 128.3, 127.9, 127.7, 126.1, 126.0, 125.2, 124.1, 123.1, 116.2, 59.4, 54.3, 47.0, 27.7, 20.6; FT-IR (neat) 3056, 2958, 2926, 2868, 1617, 1571, 1503, 1468, 1387, 1248, 1220, 1118, 1078, 1014, 962 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{23}H_{24}N_2SH$: 361.1733, found: 361.1732; $[\alpha]_D^{20}$ = +73 (c= 0.2, $CHCl_3$); HPLC analysis: 99% ee [Daicel CHIRALCEL OJ column, hexane/^{i}PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 7.59 min (major), 12.48 min (minor)].

(R,Z)-N-(3-Cyclohexyl-5-phenylthiazolidin-2-ylidene)naphthalen-1-amine ***3m***. Pale yellow liquid; yield 70% (67 mg); ^1H NMR (600 MHz, $CDCl_3$) δ 8.22−8.21 (m, 1H), 7.85−7.84 (m, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.51−7.50 (m, 2H), 7.42−7.40 (m, 3H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.12−7.10 (m, 1H), 4.67 (t, *J* = 7.2 Hz, 1H), 4.56−4.54 (m, 1H), 3.98 (dd, *J* = 10.2, 7.2 Hz, 1H), 3.67 (dd, *J* = 10.2, 7.2 Hz, 1H), 2.14−2.13 (m, 2H), 1.92−1.90 (m, 2H), 1.77−1.75 (m, 1H), 1.56−1.50 (m, 3H), 1.33−1.29 (m, 1H), 1.19−1.15 (m, 1H); ^{13}C {^1H} NMR (150 MHz, $CDCl_3$) δ 158.2, 149.0, 139.6, 134.5, 128.9, 128.8, 128.1, 127.9, 127.5, 126.1, 126.0, 125.1, 124.1, 123.0, 116.3, 54.8, 54.3, 46.8, 30.8, 30.1, 26.0, 25.9; FT-IR (neat) 3057, 2930, 2854, 1611, 1571, 1503, 1450, 1387, 1245, 1215, 1176, 1078, 1012, 945 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{25}H_{26}N_2SH$: 387.1889, found: 387.1889; $[\alpha]_D^{20}$ = +123 (c= 0.2, $CHCl_3$); HPLC analysis: 99% ee [Daicel CHIRALCEL OJ column, hexane/^{i}PrOH = 85:15, flow rate: 1 mL/min, λ = 215 nm, t_R = 7.10 min (major), 13.19 min (minor)].

(R,Z)-N-(3-(4-Bromobenzyl)-5-phenylthiazolidin-2-ylidene)-naphthalen-1-amine ***3n***. Colorless liquid; yield 84% (100 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.18−8.15 (m, 1H), 7.86−7.83 (m, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.51−7.49 (m, 2H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.37−7.28 (m, 7H), 7.14 (d, *J* = 7.2 Hz, 1H), 4.97 (d, *J* = 15.2, 1H), 4.82 (d, *J* = 15.2, 1H), 4.74 (t, *J* = 7.2, 1H), 3.83 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.59 (dd, *J* = 10.0, 8.0 Hz, 1H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 158.7, 148.5, 138.6, 136.4, 134.5, 132.0, 130.2, 128.9, 128.8, 128.4, 128.0, 127.6, 126.2, 126.1, 125.3, 124.0, 123.4, 121.6, 116.0, 58.1, 49.8, 47.0; FT-IR (neat) 3057, 3003, 2921, 2856, 1630, 1587, 1488, 1386, 1217, 1174, 1144, 1073, 1012, 949, 797, 776 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{26}H_{21}BrN_2SH$: 475.0664, found: 475.0668; $[\alpha]_D^{20}$ = +268 (c= 0.2, $CHCl_3$); HPLC analysis: 99% ee [Daicel CHIRALCEL OD column, hexane/^{i}PrOH = 90:10, flow rate: 1 mL/min, λ = 215 nm, t_R = 12.96 min (major), 15.63 min (minor)].

(R,Z)-N-(3-(4-Methoxybenzyl)-5-phenylthiazolidin-2-ylidene)-naphthalen-1-amine ***3o***. Colorless liquid; yield 79% (84 mg); ^1H NMR (600 MHz, $CDCl_3$) δ 8.21−8.19 (m, 1H), 7.83−7.81 (m, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.48−7.47 (m, 2H), 7.41−7.39 (m, 3H), 7.35−7.33 (m, 2H), 7.30−7.25 (m, 3H), 7.11 (d, *J* = 7.2 Hz, 1H), 6.94 (d, *J* = 9.0 Hz, 2H), 4.97 (d, *J* = 14.4, 1H), 4.80 (d, *J* = 14.4, 1H), 4.71 (t, *J* = 7.2, 1H), 3.85−3.82 (m, 4H), 3.58 (dd, *J* = 10.2, 8.4 Hz, 1H); ^{13}C {^1H} NMR (150 MHz, $CDCl_3$) δ 159.3, 158.7, 148.8, 139.0, 134.5, 130.0, 129.4, 128.9, 128.3, 128.0, 127.7, 125.2, 124.2, 123.3, 116.1, 114.3, 58.0, 55.5, 50.0, 47.0; FT-IR (neat) 3057, 3006, 2954, 2930, 2835, 1629, 1571, 1510, 1467, 1282, 1245, 1173, 1078, 1035, 908 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{27}H_{24}N_2OSH$: 425.1682, found: 425.1688; $[\alpha]_D^{20}$ = +99 (c= 0.2, $CHCl_3$); HPLC analysis: 98% ee [Daicel CHIRALCEL OD column, hexane/^{i}PrOH = 90:10, flow rate: 1 mL/min, λ = 215 nm, t_R = 11.95 min (major), 17.82 min (minor)].

(R,Z)-N-(3-(Furan-2-ylmethyl)-5-phenylthiazolidin-2-ylidene)-naphthalen-1-amine ***3p***. Pale yellow liquid; yield 77% (74 mg); ^1H NMR (600 MHz, $CDCl_3$) δ 8.25−8.24 (m, 1H), 7.85−7.84 (m, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.51−7.48 (m, 3H), 7.44−7.43 (m, 1H), 7.38−7.36 (m, 2H), 7.33−7.28 (m, 3H), 7.13−7.11 (m, 1H), 6.45−6.44 (m, 2H), 4.97 (d, *J* = 15.6, 1H), 4.92 (d, *J* = 15.6, 1H), 4.74 (t, *J* = 7.8, 1H), 3.95 (dd, *J* = 10.2, 7.2 Hz, 1H), 3.69 (dd, *J* = 9.6, 7.8 Hz, 1H); ^{13}C {^1H} NMR (150 MHz, $CDCl_3$) δ 158.4, 151.0, 148.6, 142.5, 138.9, 134.4, 128.9, 128.8, 128.3, 127.9, 127.6, 126.1, 126.0, 125.2, 124.2, 123.3, 116.0, 110.6, 109.0, 58.1, 47.0, 43.1; FT-IR (neat) 3056, 2922, 2856, 1622, 1571, 1503, 1386, 1350, 1246, 1224, 1183, 1143, 1076, 1013, 933 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{24}H_{20}N_2OSH$: 385.1369, found: 385.1368; $[\alpha]_D^{20}$ = +50 (c= 0.2, $CHCl_3$); HPLC analysis: 98% ee [Daicel CHIRALCEL OD column, hexan^e/*i*PrOH = 90:10, flow rate: 1 mL/min, λ = 215 nm, t_R = 8.84 min (major), 11.63 min (minor)].

(R,Z)-N-(3-(Naphthalen-1-ylmethyl)-5-phenylthiazolidin-2-ylidene)naphthalen-1-amine ***3q***. Colorless liquid; yield 88% (98 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.4 Hz, 1H), 8.43−8.40 (m, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.89−7.85 (m, 2H), 7.70 (t, *J* = 7.2 Hz, 1H), 7.62−7.54 (m, 2H), 7.53−7.44 (m, 5H), 7.23−7.17 (m, 6H), 5.65 (d, *J* = 14.8, 1H), 5.17 (d, *J* = 14.8, 1H), 4.60 (t, *J* = 7.6, 1H), 3.75 (dd, *J* = 10.0, 7.2 Hz, 1H), 3.54 (dd, *J* = 10.0, 8.0 Hz, 1H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 158.7, 148.7, 138.8, 134.6, 134.1, 133.2, 132.1, 129.0, 128.9, 128.85, 128.81, 128.2, 128.1, 127.6, 126.8, 126.4, 126.2, 125.4, 125.37, 125.33, 124.7, 124.2, 123.4, 116.2, 57.7, 49.3, 46.8; FT-IR (neat) 3047, 2998, 2950, 2922, 2856, 1618, 1571, 1506, 1496, 1387, 1246, 1217, 1181, 1078, 1041, 1016, 934 cm^{-1}; HRMS (ESI) *m/z*: $[M+H]^+$ calcd for $C_{30}H_{24}N_2SH$: 445.1733, found: 445.1738; $[\alpha]_D^{20}$ = +134 (c= 0.2, $CHCl_3$); HPLC analysis: 99% ee [Daicel CHIRALCEL OD column, hexane/^{i}PrOH = 90:10, flow rate: 1 mL/min, λ = 215 nm, t_R = 10.79 min (major), 16.42 min (minor)].

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02190.

HPCL chromatograms and NMR spectra (^1H and ^{13}C) of the products (PDF)

X-ray crystallographic data of compound **3a** (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Department of Science and Technology, International Division, (DST/INT/JSPS/P-197/2015) for the finan-

DOI: 10.1021/acs.joc.6b02190
J. Org. Chem. 2016, 81, 11508−11513

cial support. M.S. thanks University Grants Commission for Senior Research Fellowship. We are grateful to Central Instrumentation Facility, Indian Institute of Technology, Guwahati, for NMR and mass facilities. We also thank Department of Chemistry, Indian Institute of Technology, Guwahati, for single crystal X-ray analysis.

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DOI: 10.1021/acs.joc.6b02190
J. Org. Chem. 2016, 81, 11508−11513