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Electrophilic *N*-Trifluoromethylation of N−H Ketimines

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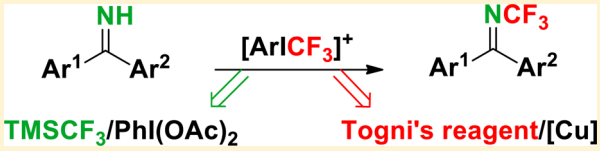
Supporting Information

ABSTRACT: A direct *N*-trifluoromethylation method has been developed by the use of the *in situ* generated $[ArICF_3]^+$ species as the electrophilic trifluoromethyl source. Upon treatment of N−H ketimines with Ruppert−Prakash reagent in the presence of $PhI(OAc)_2$ and KF, or with Togni's reagent II catalyzed by copper salt, *N*-trifluoromethylated imine products were obtained in moderate to good yields.



Recent years have witnessed a rapid development of strategies for the incorporation of CF_3 into various organic structures[1] due to the remarkably increased chemical, physical, or biological activities of trifluoromethylated organic compounds than their nonfluorinated analogues.[2] In this context, numerous methods,[1] diverse CF_3 sources,[3] and efficient catalysts have been well developed for the direct introduction of CF_3 onto both carbon and heteroatoms (including P, S, and O). In contrast, the direct *N*-trifluoromethylation of hard *N*-centered nucleophiles with electrophilic trifluoromethylating reagent remains challenging.[7b,c] On the other hand, *N*-containing compounds are broadly found in naturally occurring and biological molecules and also typically used in materials science and organic synthesis. Accordingly, the NCF_3 derivatives were also reported to exhibit enhanced biological activity compared to those of *N*-alkylated ones.[4] However, few *N*-trifluoromethylated compounds are known at the present date, and limited approaches for their synthesis exist. It may have seriously hampered the wider exploitation of their synthetic potential and the search for new drugs using organofluorine compounds. Thus, efficient and new access to the NCF_3 compounds would be highly desirable.

Among the limited methods accessible to *N*-trifluoromethylated compounds, the antiquated ones rely on functional group interconversions, for example, by the desulfurization−fluorination of dithiocarbamates[5a,b] or by exchange of halide for fluorine from the corresponding *N*-trihalomethyl-substituted derivatives.[5c] In 2007, Umemoto and his co-workers first reported a direct route toward NCF_3 compounds by the *N*-trifluoromethylation reactions of readily available amines or pyridines with CF_3 oxonium salts, a real electrophilic CF_3 species, at −100 °C under the irradiation of a high pressure Hg lamp.[6] Recently, a milder *N*-trifluoromethylation method has been developed by using Togni's reagent as the electrophilic CF_3 species. Guanidines and azoles proved to be suitable substrates in those CF_3 transformations.[7] Obviously, *N*-trifluoromethylation is an ideal strategy for NCF_3 derivative synthesis by taking advantage of providing a direct route with broad scope of the starting materials.

Recently, we have been interested in developing new trifluoromethylating reagents and trifluoromethylation reactions.[8] The unstable CF_3-based hypervalent iodine species ($[PhICF_3]^+$) was first detected by us[8] and successfully used as an electrophilic CF_3 source for the trifluoromethylation of nucleophiles, including ketene dithioacetals and indoles. Taking into consideration the unique reactivity of $[PhICF_3]^+$ as the electrophilic CF_3 source and the importance of NCF_3 compounds, we turned to investigating the application of $[PhICF_3]^+$ in *N*-trifluoromethylation. Herein, we wish to report a direct *N*-trifluoromethylation of N−H ketimines. A general and efficient method to access *N*-trifluoromethylated imines has thus been developed. Both the Ruppert−Prakash reagent and the Togni's reagent proves to be a suitable trifluoromethylating reagent in these processes. During our preparation for this manuscript, a silver-mediated *N*-trifluoromethylation of sulfoximines with $TMSCF_3$ by a radical pathway was reported.[10]

Inspired by both Umemoto's and Togni's pioneering work,[6,7] we initially tested the direct *N*-trifluoromethylation of various *N*-containing compounds, including *N*-methylaniline, *N*-methyl-1-phenylmethanamine, *o*-phthalimide, and pyridine under the reaction conditions developed in our previous work[8] ($TMSCF_3$−KF−$PhI(OAc)_2$ system). However, complex results were often obtained but no desired *N*-trifluoromethylated products were isolated. Delightfully, when we treated benzophenone imine **1a**, a kind of unprotected N−H ketimines bearing relative low steric hindrance and sp^2 hybridized nitrogen,[11] which have been investigated in asymmetric synthesis[11c,e] and also used in directed C−H activation,[11f,g] with $TMSCF_3$, KF, and $PhI(OAc)_2$ in MeCN under N_2, the *N*-trifluoromethylated product **2a** was isolated after reacting for 24 h at room temperature. By short screening of the reaction conditions regarding the amount of each reagent and reaction

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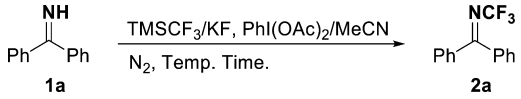
temperature as presented in Table 1, the best yield of product **2a** was obtained with $TMSCF_3$ (4.0 equiv), KF (4.0 equiv), and

Table 1. Screening the Reaction Conditions for the $TMSCF_3$–KF-$PhI(OAc)_2$ System[a]



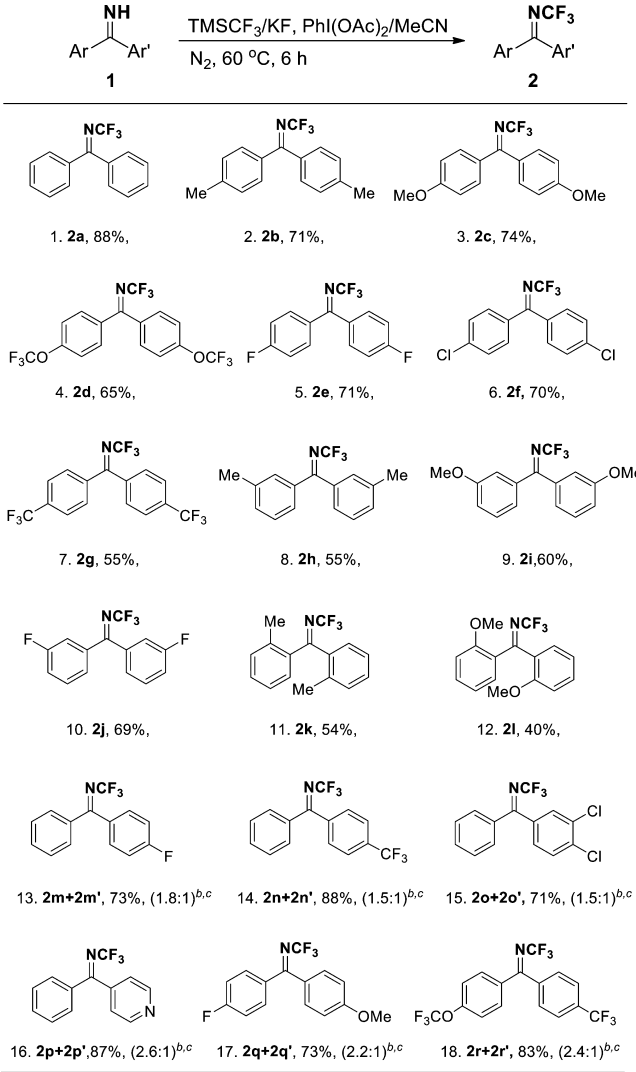
entry	$TMSCF_3$ (equiv)	KF (equiv)	$PhI(OAc)_2$ (equiv)	temp. (°C)	time (h)	yield (%)
1	2.0	2.0	2.0	100	6	23
2	2.0	2.0	2.0	80	6	40
3	4.0	2.0	2.0	80	6	45
4	4.0	4.0	2.0	60	6	88
5	4.0	4.0	2.0	60	4	75
6	4.0	4.0	2.0	60	2	69
7	4.0	4.0	2.0	25	24	47

[a]Conditions: **1a** (0.3 mmol), MeCN (3.0 mL) in a 15 mL sealed glass vial.

$PhI(OAc)_2$ (2.0 equiv) in MeCN (3.0 mL) at 60 °C under N_2. Thus, we extended the scope of the reactions under the optimized conditions. As described in Table 2, the direct *N*-trifluoromethylation of N–H ketimines tolerates various substituents on the benzene. All diaryl N–H ketimines with both electron-donating and electron-withdrawing groups at the 4-position of aromatic ring afforded NCF_3 products in 55–88% yields (Table 2, entries 1–7). The reaction also worked well with different substituents on different positions on the benzene ring (Table 2, entries 8–12). In the case of asymmetric diaryl N–H ketimines as substrates, inseparable isomeric mixtures **2** and **2′** were obtained with good to high yields (Table 2, entries 13–18). In addition, when we synthesized aliphatic N–H imine hydrochlorides, including 1-(4-fluorophenyl)pentan-1-imine hydrochloride and 1-(4-methoxyphenyl)ethanimine hydrochloride toward the optimized conditions, a complex mixture were obtained, while diphenylmethanimine hydrochloride could afford **2a** in 58% yield under the identical conditions. The imine–enamine tautomerization of alkyl ketimines may make the N-CF_3 reaction sluggish.

In Cheng and Bolm's latest work,[10] they used the $TMSCF_3$–Ag_2CO_3–O_2 system to produce CF_3 radical for the direct N–H trifluoromethylation of sulfoximines. However, the N–H trifluoromethylation of diphenylmethanimine gave an inferior experimental result under this condition.[10] By comparison, the efficiency of the present N–H trifluoromethylation of ketimines by the use of the $TMSCF_3$–$PhI(OAc)_2$ system may involve an alternative pathway.[8] In fact, the mechanism of trifluoromethylation reactions by the use of hypervalent iodine reagents is complicated.[9] There is still little evidence to accurately support a real trifluoromethylation process though many possibilities are proposed.[9] Although the mechanism involving a CF_3 radical intermediate cannot be ruled out at the present stage, based on the results on the unique electrophilic reactivity of $[PhICF_3]^+$ species[8] and the knowledge of the nucleophilicity of the nitrogen of N–H ketimines,[11] we prefer an electrophilic *N*-trifluoromethylation process as described in Scheme 1. Intermediate **I** was formed from the reaction of **1** with $[PhICF_3]^+$ which is generated *in situ* from $TMSCF_3$, KF, and $PhI(OAc)_2$ (Scheme 1A).[8] Then, deprotonation of **I**

Table 2. *N*-Trifluoromethylation of N–H Ketimines with $TMSCF_3$.[a]



[a]**1** (0.3 mmol), $TMSCF_3$ (1.2 mmol), KF (1.2 mmol), $PhI(OAc)_2$ (0.6 mmol), MeCN (3.0 mL), 60 °C, under N_2, in sealed tube. [b]The ratio of two isomers was determined by ^{19}F NMR. [c]The configurations of isomers were not determined.

afforded intermediate **II** followed by reductive elimination of PhI to give *N*-trifluoromethylated imine products **2**.

Compared with $[PhICF_3]^+[OAc]^-$ species, its equivalent (**3**, Scheme 1B) derived from Togni's reagent II activated by a Lewis acid has recently been speculated[12a–g] and further proven to act as an active "CF_3^+" species in the electrophilic aminotrifluoromethylations of alkenes.[12g] Encouraged by these results, we envisioned that *N*-trifluoromethylation of N–H ketimines may also occur if we use the electrophilic $[ArICF_3]^+$ derived from Togni's reagent II under the copper catalysis.[12g] This was indeed the case. After we briefly screened copper salts for the activation of Togni' reagent with diphenylmethanimine **1a** as substrate, 5% of $Cu(OAc)_2$ was selected as the best catalyst. In this case, the reaction performed in MeCN at 60 °C could give the desired NCF_3 product **2a** in 89% yield. Thus, the scope of the reaction was investigated. As presented in Scheme 2, all tested substrates **1** are suitable for the CF_3 transformation and *N*-trifluoromethylated products **2** were obtained in good yield.

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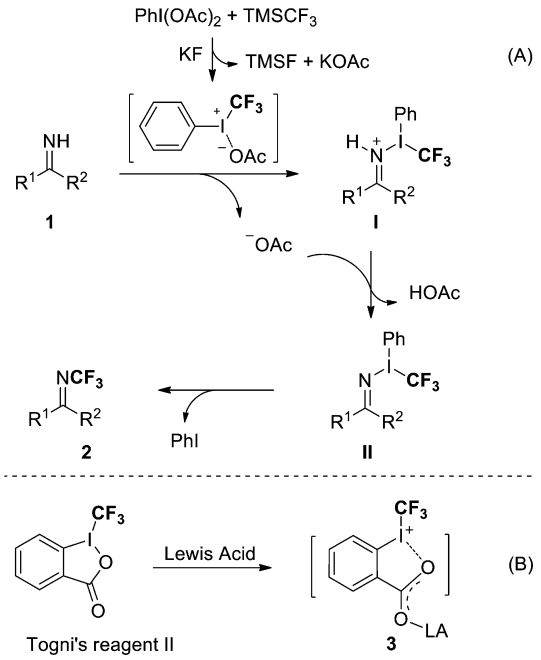
Scheme 1. Proposed Mechanism for Electrophilic *N*-Trifluoromethylation



In conclusion, we have successfully developed a novel and efficient protocol for the synthesis of NCF_3 derivatives by the *N*-trifluoromethylation reaction of N−H ketimines. Either the Ruppert−Prakash reagent in the presence of $PhI(OAc)_2$ or Togni's reagent II catalyzed by copper salt was used for the *in situ* generated electrophilic CF_3-based hypervalent iodonium. The simple execution, mild conditions, and good yields make the protocol very attractive for practical applications in the connection of nitrogen atom and CF_3 directly.

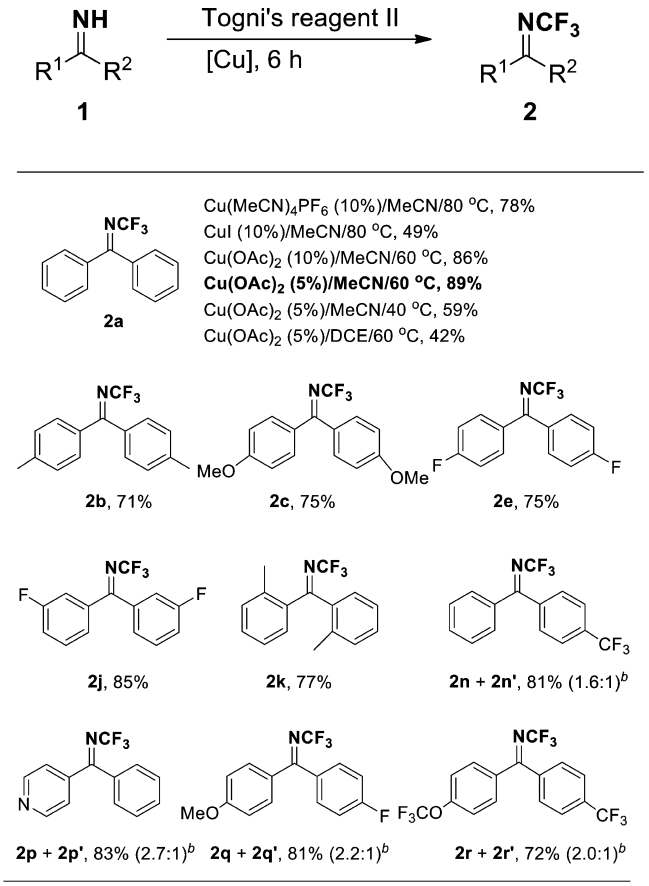
EXPERIMENTAL SECTION

General. All commercially available compounds were used as received unless otherwise noted. $PhI(OAc)_2$, Me_3SiCF_3 ($TMSCF_3$), KF, and MeCN were used directly as received from the manufacturers. Togni's trifluoromethylating reagent II was prepared following the procedure developed by A. Togni. All reactions were performed under nitrogen atmosphere in a sealed reaction vial. Reactions were monitored through thin layer chromatography [TLC, silica gel 60 F254]. Subsequent to elution, spots were visualized using UV radiation (254 nm). Flash column chromatography was performed on silica gel 60 (particle size 200−400 mesh). ^1H NMR and ^{13}C NMR were recorded at 25 °C on 500 and 125 MHz spectrometer, respectively, by using TMS as an internal standard. ^{19}F NMR were recorded at 25 °C on 470 MHz spectrometer by using (trifluoromethyl)benzene (δ −63.2) as external standard. Data for ^1H, ^{13}C, and ^{19}F were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets). High-resolution mass spectra (HRMS) were obtained using a microTOF II focus spectrometer (SI).

Substrates **1** were prepared by the known method reported in the literature.[13] N−H ketimines **1d**, **1i**, **1l**, and **1q** are new compounds.

General Procedures for the Preparation of N−H Ketimines. To a 20 mL scintillation vial equipped with a magnetic stir bar was added the aryl Grignard reagent (6.0 mmol) and 2.0 mL THF. The corresponding arylnitrile (5.4 mmol) was dissolved in 2.0 mL THF and added dropwise with vigorous stirring. The mixture was then transferred to an oil bath (85 °C) and stirred for 12 h. The reaction mixture was cooled to room temperature and quenched by slow, dropwise addition of dry MeOH at 0 °C. The resulting mixture was stirred at room temperature for 30 min, and after this time the volatile materials were evaporated under reduced pressure. The residue was redissolved into ethyl acetate. Further purification was achieved by flash-column chromatography (silica gel; petroleum ether/ethyl acetate/triethylamine: 90/10/1.5, v/v/v).

Scheme 2. *N*-Trifluoromethylation of N−H Ketimines with Togni's Reagent II.[a]



[a]**1** (0.3 mmol), Togni's reagent (0.45 mmol), $Cu(OAc)_2$ (0.015 mmol), MeCN (3.0 mL), 60 °C, under N_2, in sealed tube. [b]The ratio of two isomers was determined by ^{19}F NMR. The configurations of isomers were not determined.

General Procedures for the *N*-Trifluoromethylation of N−H Ketimines 1a−1r by Using $TMSCF_3$−KF−$PhI(OAc)_2$ System (with the Reaction of 1a as an Example). To a 15 mL dried polytetrafluoroethene (PTFE) sealed glass vial was added N−H ketimine **1a** (54 mg, 0.3 mmol), anhydrous MeCN (3.0 mL), $PhI(OAc)_2$ (193 mg, 0.6 mmol), KF (70 mg, 1.2 mmol), and $TMSCF_3$ (178 μL, 1.2 mmol) in sequence in glovebox. Then the glass vial was closed tightly. After taking the glass vial out of the glovebox, the resulting mixture was then stirred at 60 °C and monitored by thin layer chromatography. After complete consumption of **1a** in 6 h, the resulting mixture was poured into water, and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to yield the crude product, which was purified by silica gel chromatography (eluent, 100% petroleum ether) to give **2a** (66 mg, 88%) as light yellow oil.

General Procedures for the *N*-Trifluoromethylation of N−H Ketimines 1a−1c, 1e, 1j−1k, 1n, and 1p-1r by Using Togni'S Reagent II-Lewis Acid System (with the Reaction of 1a as an Example). To a 15 mL dried polytetrafluoroethene (PTFE) sealed glass vial was added N−H ketamine **1a** (54 mg, 0.3 mmol), anhydrous MeCN (3.0 mL), Togni's reagent II (142 mg, 0.45 mmol), and $Cu(OAc)_2$ (2.7 mg, 0.015 mmol) in sequence in glovebox. Then the glass vial was closed tightly. After taking the glass vial out of the

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glovebox, the resulting mixture was then stirred at 60 °C and monitored by thin layer chromatography. After complete consumption of substrates in 6 h, the resulting mixture was poured into water, and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to yield the crude product, which was purified by silica gel chromatography (eluent, 100% petroleum ether) to give **2a** (67 mg, 89%) as light yellow oil.

*Bis(4-(trifluoromethoxy)phenyl)methanimine (**1d**).* Yellow oil (1.2 g, 62%). ^{1}H NMR (500 MHz, DMSO) δ 10.85 (s, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO) δ 173.5, 150.6, 150.0, 138.5, 137.6, 131.1 (2C), 130.2 (2C), 121.2 (2C), 120.9 (2C), 120.7 (q, J = 255.0 Hz, 2C). HRMS (ESI): Calcd for $[M+H]^+$ $C_{15}H_{10}F_6NO_2$ 350.0610, found 350.0613.

*Bis(3-methoxyphenyl)methanimine (**1i**).* Yellow oil (0.53 g, 41%). ^{1}H NMR (400 MHz, DMSO) δ 10.55 (s, 1H), 7.34 (t, J = 8.0 Hz, 3H), 7.14 (s, 1H), 7.06 (d, J = 7.5 Hz, 3H), 6.95 (s, 1H), 3.77 (s, 6H). ^{13}C NMR (125 MHz, DMSO) δ 175.1, 159.1, 140.3 (d, J = 126.3 Hz), 129.3, 122.1, 121.4, 119.8, 118.5, 115.9, 115.3, 114.1, 113.6, 113.0, 55.0 (2C). HRMS (ESI): Calcd for $[M+H]^+$ $C_{15}H_{16}NO_2$ 242.1176, found 242.1175.

*Bis(2-methoxyphenyl)methanimine (**1l**).* Yellow solid. mp (85−86 °C) (0.95 g, 73%). ^{1}H NMR (500 MHz, DMSO) δ 10.74 (s, 1H), 7.37 (t, J = 7.5 Hz, 2H), 7.25 (s, 2H), 7.05 (d, J = 8.5 Hz, 2H), 6.97 (t, J = 7.5 Hz, 2H), 3.64 (s, 6H). ^{13}C NMR (125 MHz, DMSO) δ 173.4, 157.5 (2C), 130.9 (2C), 130.0 (2C), 120.7 (4C), 112.3 (2C), 56.0 (2C). HRMS (ESI): Calcd for $[M+H]^+$ $C_{15}H_{16}NO_2$ 242.1176, found 242.1179.

*(4-Fluorophenyl)(4-methoxyphenyl)methanimine (**1q**).* Yellow solid. mp (78−79 °C) (1.0 g, 81%). ^{1}H NMR (500 MHz, DMSO) δ 10.26 (s, 1H), 7.56 (s, 2H), 7.49 (s, 2H), 7.23 (t, J = 9.0 Hz, 2H), 6.97 (d, J = 9.0 Hz, 2H), 3.79 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ 174.4, 163.5 (d, J = 247.2 Hz), 161.3, 136.3, 131.5, 130.9, 130.2 115.6, 115.4, 114.1 (4C), 55.6. HRMS (ESI): Calcd for $[M+H]^+$ $C_{14}H_{13}FNO$ 230.0976, found 230.0973.

*1,1-Diphenyl-N-(trifluoromethyl)methanimine (**2a**).* Light yellow oil (66 mg, 88% in Table 2; 67 mg, 89%, in Scheme 2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 7.5 Hz, 2H), 7.54−7.43 (m, 4 H), 7.38 (t, J = 7.5 Hz, 2H), 7.26 (d, J = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.0 (q, J = 8.0 Hz, 1C), 137.7, 135.8, 133.0, 130.3 (2C), 129.6, 128.3 (2C), 127.9 (2C), 127.3 (d, J = 1.4 Hz, 2C), 123.7 (q, J = 261.9 Hz, 1C). ^{19}F NMR (470 MHz, $CDCl_3$) δ −56.0 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{14}H_{11}F_3N$ 250.0838, found 250.0847.

*1,1-Di-p-tolyl-N-(trifluoromethyl)methanimine (**2b**).* Light yellow oil (59 mg, 71% in Table 2; 59 mg, 71% in Scheme 2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 7.5 Hz, 2H), 7.18 (dd, J = 12.2, 8.1 Hz, 4H), 2.45 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.1 (q, J = 8.0 Hz, 1C), 143.8, 139.7, 135.4, 133.1, 130.4 (2C), 129.0 (2C), 128.5 (2C), 127.5 (2C), 123.9 (q, J = 261.6 Hz, 1C), 21.6, 21.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ −53.4 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{16}H_{15}F_3N$ 278.1151, found 278.1160.

*1,1-Bis(4-methoxyphenyl)-N-(trifluoromethyl)methanimine (**2c**).* Light yellow oil (69 mg, 74% in Table 2; 70 mg, 75% in Scheme 2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.5 Hz, 2H), 7.22 (d, J = 8.5 Hz, 2H), 6.96 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 3.87 (s, 3H), 3.85 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.1 (q, J = 8.0 Hz, 1C), 163.5, 160.5, 132.6 (2C), 132.2, 130.8, 129.3, 128.3, 123.9 (q, J = 259.5 Hz, 1C), 113.6 (2C), 113.3 (2C), 55.5, 55.3. ^{19}F NMR (470 MHz, $CDCl_3$) − 57.4 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{16}H_{15}F_3NO_2$ 310.1049, found 310.1045.

*1,1-Bis(4-(trifluoromethoxy)phenyl)-N-(trifluoromethyl)-methanimine (**2d**).* Colorless oil (81 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 9.0 Hz, 2H), 7.34 (s, 4H), 7.25 (d, J = 9.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9 (q, J = 7.8 Hz, 1C), 152.8, 150.2, 135.4, 133.5, 132.1 (2C), 129.1 (2C), 123.3 (q, J = 262.4 Hz, 1C), 121.3 (d, J = 13.1 Hz, 1C), 120.4 (2C), 120.2 (2C), 119.2 (d, J = 13.6 Hz, 1C). ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.4 (s, 3F), −59.7 (s, 3F), −59.8 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{16}H_9F_9NO_2$ 418.0484, found 418.0488.

*1,1-Bis(4-fluorophenyl)-N-(trifluoromethyl)methanimine (**2e**).* Colorless oil (61 mg, 71% in Table 2; 64 mg, 75% in Scheme 2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, J = 8.8, 5.4 Hz, 2H), 7.27 (dd, J = 8.5, 4.9 Hz, 2H), 7.17 (t, J = 8.5 Hz, 2H), 7.08 (t, J = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.6 (q, J = 8.0 Hz, 1C), 165.9 (d, J = 256.0 Hz, 1C), 163.4 (d, J = 250.7 Hz, 1C), 133.8 (d, J = 2.8 Hz, 1C), 132.8 (d, J = 9.3 Hz, 2C), 131.4 (d, J = 3.7 Hz, 1C), 129.5 (d, J = 8.4 Hz, 2C), 123.5 (q, J = 262.1 Hz, 1C), 115.7 (d, J = 22.0 Hz, 2C), 115.4 (d, J = 22.0 Hz, 2C). ^{19}F NMR (470 MHz, $CDCl_3$) δ −53.9 (s, 3F), −107.0 to −107.1 (m, 1F), −111.8 to −111.9 (m, 1F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{14}H_9F_5N$ 286.0650, found 286.0654.

*1,1-Bis(4-chlorophenyl)-N-(trifluoromethyl)methanimine (**2f**).* Light yellow oil (67 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 8.5 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.6 (q, J = 7.9 Hz, 1C), 139.9, 136.2, 135.7, 133.6, 131.5 (2C), 128.8 (2C), 128.7 (2C), 128.5 (2C), 123.4 (q, J = 260.8 Hz, 1C). ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.1 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{14}H_9C_{l2}F_3N$ 318.0059, found 318.0059.

*N-(Trifluoromethyl)-1,1-bis(4-(trifluoromethyl)phenyl)me-thanimine (**2g**).* Colorless oil (64 mg, 55%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.5 Hz, 2H), 7.78 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.5 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0 (q, J = 7.8 Hz, 1C), 139.9, 138.6, 134.7 (q, J = 32.8 Hz, 1C), 132.2 (q, J = 33.0 Hz, 1C), 130.5 (2C), 127.7 (2C), 125.6 (d, J = 3.7 Hz, 2C), 125.6 (q, J = 259.0 Hz, 1C), 125.4 (d, J = 3.7 Hz, 2C), 124.0 (q, J = 260.5 Hz, 1C), 122.7 (q, J = 260.5 Hz, 1C). ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.7 (s, 3F), −65.0 (s, 3F), −65.2 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{16}H_9F_9N$ 386.0586, found 386.0578.

*1,1-Di-m-tolyl-N-(trifluoromethyl)methanimine (**2h**).* Colorless oil (46 mg, 55%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.40 (d, J = 7.5 Hz, 1H), 7.35 (t, J = 7.0 Hz, 2H), 7.31−7.25 (m, 2H), 7.07 (d, J = 7.0 Hz, 2H), 2.41 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.4 (q, J = 7.9 Hz, 1C), 138.2, 137.8, 137.6, 135.9, 133.8, 130.3, 130.3, 128.1, 128.0, 127.8, 127.7, 124.8, 124.5, 21.3, 21.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ −53.8 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{16}H_{15}F_3N$ 278.1151, found 278.1150.

*1,1-Bis(3-methoxyphenyl)-N-(trifluoromethyl)methanimine (**2i**).* Colorless oil (56 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.28 (t, J = 8.5 Hz, 1H), 7.16 (d, J = 8.0 Hz, 1H), 7.09 (d, J = 8.0 Hz, 1H), 7.02 (d, J = 8.5 Hz, 1H), 6.85 (d, J = 7.5 Hz, 1H), 6.79 (s, 1H), 3.84 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3 (q, J = 7.9 Hz, 1C), 159.5, 158.9, 138.8, 136.9, 129.2, 129.1, 123.6, 123.5 (q, J = 260.6 Hz, 1C), 119.7, 119.4, 115.1, 114.1, 112.9, 55.4, 55.3. ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.1 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{16}H_{15}F_3NO_2$ 310.1049, found 310.1041.

*1,1-Bis(3-fluorophenyl)-N-(trifluoromethyl)methanimine (**2j**).* Colorless oil (59 mg, 69% in Table 2; 73 mg, 85% in Scheme 2). ^{1}H NMR (400 MHz, DMSO) δ 7.61−7.50 (m, 3H), 7.48−7.40 (m, 2H), 7.36 (dd, J = 15.0, 8.5 Hz, 2H), 7.21 (d, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9, 163.3 (d, J = 246.4 Hz, 1C), 161.3 (d, J = 246.4 Hz, 1C), 139.2 (d, J = 7.2 Hz, 1C), 136.9 (d, J = 7.1 Hz, 1C), 130.2 (m, 1C), 128.3 (d, J = 48.7 Hz, 1C), 127.2, 126.3 (d, J = 2.8 Hz, 1C), 123.2 (q, J = 267.1 Hz, 1C), 120.3 (d, J = 21.5 Hz, 1C), 117.0 (d, J = 18.6 Hz, 1C), 116.6 (d, J = 23.3 Hz, 1C), 114.7 (d, J = 13.0 Hz, 1C). ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.1 (s, 1F), −54.4 (s, 1F), −54.6 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{14}H_9F_5N$ 286.0650, found 286.0651.

*1,1-Di-o-tolyl-N-(trifluoromethyl)methanimine (**2k**).* Colorless oil (45 mg, 54% in Table 2; 64 mg, 77% in Scheme 2). ^{1}H NMR (400 MHz, DMSO) δ 7.39 (t, J = 9.5 Hz, 3H), 7.32 (t, J = 7.5 Hz, 1H), 7.27 (d, J = 6.0 Hz, 2H), 7.18 (t, J = 7.5 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 2.60 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.3 (q, J = 8.4 Hz, 1C), 139.5, 137.3, 136.3, 134.5, 132.4, 132.0, 131.4, 130.2, 129.3, 127.2, 125.7, 125.1, 123.5 (q, J = 262.5 Hz, 1C), 22.6, 19.3. ^{19}F

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NMR (470 MHz, $CDCl_3$) δ −55.9 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{16}H_{15}F_3N$ 278.1151, found 278.1161.

*1,1-Bis(2-methoxyphenyl)-N-(trifluoromethyl)methanimine (**2l**).* Colorless oil (37 mg, 40%). ^1H NMR (400 MHz, DMSO) δ 7.50 (dd, J = 16.5, 8.0 Hz, 2H), 7.40 (t, J = 7.5 Hz, 1H), 7.13 (d, J = 7.0 Hz, 1H), 7.06 (d, J = 8.5 Hz, 2H), 6.99 (dd, J = 16.7, 8.4 Hz, 2H), 3.68 (s, 3H), 3.54 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.8 (q, J = 12.6 Hz, 1C), 158.4, 155.7, 132.6, 130.9, 130.4, 128.8, 128.0, 127.7, 123.2 (q, J = 261.3 Hz, 1C), 120.4, 119.6, 112.2, 110.5, 55.7, 55.6. ^{19}F NMR (470 MHz, $CDCl_3$) δ −56.8 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{16}H_{15}F_3NO_2$ 310.1049, found 310.1055.

*(Z)- and (E)-1-(4-Fluorophenyl)-1-phenyl-N-(trifluorome-thyl)-methanimine (**2m** and **2m′**).* Two isomers could not be completely isolated from each other. The Z- and E- configurations of **2m** and **2m′** are not identified. Yellow oil (58 mg, 73%). For one of two isomers, ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (dd, J = 8.6, 5.5 Hz, 2H), 7.48 (t, J = 7.5 Hz, 2H), 7.26−7.27 (m, 3H), 7.08 (t, J = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6 (q, J = 7.9 Hz, 1C), 165.6 (d, J = 254.1 Hz, 1C), 135.5, 133.2, 132.7, 130.3, 129.7, 128.0 (4C), 123.5 (q, J = 261.4 Hz, 1C), 115.6, 115.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ −53.9 (s, 3F), −107.3 to −107.4 (m, 1F). For the other, ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 8.0 Hz, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.51 (d, J = 7.5 Hz, 2H), 7.42 (t, J = 7.5 Hz, 2H), 7.17 (t, J = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0 (q, J = 7.9 Hz, 1C), 163.3 (d, J = 250.4 Hz, 1C), 137.5, 133.9 (d, J = 2.9 Hz, 1C), 132.8, 129.6, 129.5 (d, J = 1.4 Hz, 1C), 128.4 (2C), 127.2 (d, J = 1.4 Hz, 2C), 123.0, 115.3, 115.2. ^{19}F NMR (470 MHz, $CDCl_3$) δ −53. 8(s, 3F), −112.1 to −112.2 (m, 1F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{14}H_{10}F_4N$ 268.0744, found 268.0744.

*(Z)- and (E)-1-Phenyl-N-(trifluoromethyl)-1-(4-(trifluoromethyl) phenyl) methanimine (**2n** and **2n′**).* Two isomers could not be completely isolated from each other. The Z- and E-configurations of **2n** and **2n′** are not identified. Yellow oil (84 mg, 88% in Table 2; 77 mg, 81% in Scheme 2). For one of two isomers, ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 8.0 Hz, 2H), 7.42−7.40 (m, 4H), 7.28−7.26 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1 (d, J = 8.0 Hz, 1C), 139.2, 136.7, 130.1 (2C), 130.0, 128.5 (2C), 128.1 (2C), 127.7 (2C), 127.1, 125.0, 123.0. ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.0 (s, 3F), −64.9 (s, 3F). For the other, ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 7.57 (t, J = 7.5 Hz, 2H), 7.54 (d, J = 7.0 Hz, 1H), 7.49 (t, J = 7.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.5 (d, J = 8.0 Hz, 1C), 140.7, 135.0, 133.4 (2C), 130.5 (2C), 130.4, 127.6 (2C), 127.1 (2C), 125.2, 125.0, 123.0. ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.6 (s, 3F), −65.1 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{15}H_{10}F_6N$ 318.0712, found 318.0716.

*(Z)- and (E)-1-(3,4-Dichlorophenyl)-1-phenyl-N-(trifluoromethyl)-methanimine (**2o** and **2o′**).* Two isomers could not be completely isolated from each other. The Z- and E-configurations of **2o** and **2o′** are not identified. Yellow oil (68 mg, 71%). For one of two isomers, ^1H NMR (500 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.51−7.41 (m, 5H), 7.26 (d, J = 7.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7 (q, J = 8.1 Hz, 1C), 137.5, 136.7, 134.7, 133.8, 131.1, 130.4, 129.4, 128.6 (2C), 128.3 (2C), 127.2, 123.0. ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.4 (s, 3F). For the other, ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 7.5 Hz, 2H), 7.59−7.53 (m, 4H), 7.38 (s, 1H), 7.14 (d, J = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0 (q, J = 8.0 Hz, 1C), 137.6, 135.4, 134.3, 133.6 (2C), 132.8, 130.3 (2C), 130.1 (2C), 129.2, 126.8, 123.0. ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.0 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{14}H_9C_{l2}F_3N$ 318.0059, found 318.0060.

*(Z)- and (E)-1-Phenyl-1-(pyridin-4-yl)-N-(trifluoromethyl)-methanimine (**2p** and **2p′**).* Two isomers could not be completely isolated from each other. The Z- and E-configurations of **2p** and **2p′** are not identified. Light yellow oil (65 mg, 87% in Table2; 62 mg, 83% in Scheme 2). For one of two isomers, ^1H NMR (500 MHz, $CDCl_3$) δ 8.75 (d, J = 5.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.41 (t, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 1H), 7.20 (d, J = 5.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6 (q, J = 7.6 Hz, 1C), 150.3, 149.6 (2C), 143.5, 133.7, 130.0 (2C), 128.6 (2C), 128.3, 123.2, 121.6. ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.1 (s, 3F). For the other, ^1H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, J = 5.0 Hz, 1H), 8.71 (d, J = 5.0 Hz, 1H), 7.81 (d, J = 7.5 Hz, 1H), 7.57 (m, 2H), 7.50 (dt, J = 14.4, 6.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.5, 150.6, 150.4, 149.9, 144.5, 135.9, 134.3, 133.5, 127.2, 124.3, 122.8, 122.2, 121.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ −55.1 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{13}H_{10}F_3N_2$ 251.0791, found 251.0798.

*(Z)- and (E)-1-(4-Fluorophenyl)-1-(4-methoxyphenyl)-N-(trifluor-omethyl) methanimine (**2q** and **2q′**).* Two isomers could not be completely isolated from each other. The Z- and E-configurations of **2q** and **2q′** are not identified. Light yellow oil (65 mg, 73% in Table 2; 72 mg, 81% in Scheme 2). For one of two isomers, ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 9.0 Hz, 2H), 7.26 (t, J = 7.0 Hz, 2H), 7.15 (t, J = 8.5 Hz, 2H), 6.89 (d, J = 9.0 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1 (q, J = 7.8 Hz, 1C), 164.2, 163.8, 162.2, 132.9, 132.8, 132.5 (2C), 129.6, 129.5, 129.4, 115.3, 113.8 (2C), 55.5. ^{19}F NMR (470 MHz, $CDCl_3$) δ −53.1 (s, 3F), −112.7(m, 1F). For the other, ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (dd, J = 8.8, 5.5 Hz, 2H), 7.23 (d, J = 8.5 Hz, 2H), 7.07 (t, J = 8.5 Hz, 2H), 6.98 (d, J = 8.5 Hz, 2H), 3.88 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7 (q, J = 8.3 Hz, 1C), 166.7, 164.5, 160.8, 134.5, 132.0, 131.9, 130.1, 127.7, 124.8, 122.8, 115.5, 113.4 (2C), 55.3. ^{19}F NMR (470 MHz, $CDCl_3$) δ −53.7 (s, 3F), −107.9 (m, 1F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{15}H_{12}F_4NO$ 298.0850, found 298.0844.

*(Z)- and (E)-1-(4-Methoxyphenyl)-1-(4-(trifluoromethoxy)-phenyl)-N-(trifluoromethyl) methanimine (**2r** and **2r′**).* Two isomers could not be completely isolated from each other. The Z- and E-configurations of **2r** and **2r′** are not identified. Light yellow oil (100 mg, 83% in Table 2; 87 mg, 72% in Scheme 2). For one of two isomers, ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.0 Hz, 2H), 7.75 (d, J = 8.5 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6 (q, J = 8.0 Hz, 1C), 152.8, 138.6, 134.9, 132.0 (2C), 127.6 (2C), 127.5, 125.2 (2C), 125.2, 125.1, 122.3, 120.1 (2C). ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.4 (s, 3F), −59.6 (s, 3F), −65.0 (s, 3F). For the other, ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.5 Hz, 2H), 7.69 (d, J = 8.5 Hz, 2H), 7.39−7.32 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.1 (q, J = 7.9 Hz, 1C), 150.2, 140.2, 133.2, 130.4 (2C), 129.0 (2C), 127.5 (2C), 125.3 (2C), 124.5, 124.2, 122.2, 121.2. ^{19}F NMR (470 MHz, $CDCl_3$) δ −54.7 (s, 3F), −59.7 (s, 3F), −65.2 (s, 3F). HRMS (ESI): Calcd for $[M+H]^+$ $C_{16}H_9F_9NO$ 402.0535, found 402.0539.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01468.

Experimental procedures and analytical data for all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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