Organic LETTERS

Letter

pubs.acs.org/OrgLett

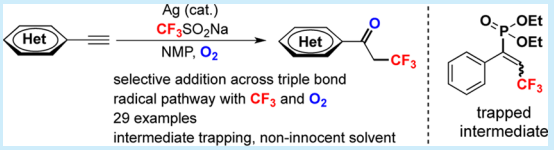
Direct Synthesis of α-Trifluoromethyl Ketone from (Hetero)arylacetylene: Design, Intermediate Trapping, and Mechanistic Investigations

Arun Maji, Avijit Hazra, and Debabrata Maiti*

Department of Chemistry, Indian Institute of Technology Bombay, Powai, Mumbai 400076, India

Supporting Information

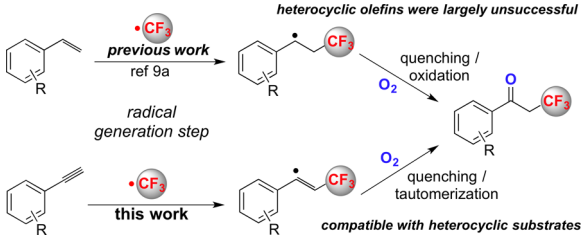
ABSTRACT: Regioselective addition across the alkynes has been achieved in a silver-catalyzed protocol utilizing Langlois reagent (CF_3SO_2Na) and molecular O_2 to access medicinally active α-trifluoromethyl ketone compounds. This method was successful in producing α-trifluoromethyl ketone in heterocyclic scaffolds, which are incompatible with earlier strategies. Experimental findings suggest a mechanism involving α-styrenyl radical intermediate and 1-methyl-2-pyrrolidinone (NMP) solvent, which leads to crystallographically characterized *N*-methylsuccinimide. Isotope labeling, kinetic studies, and intermediate trapping further helped to gain insight into this energy-demanding process.



Trifluoromethyl groups (CF_3) are prevalent in pharmaceuticals,[1] materials,[2] and agrochemicals.[3] The unique advantages conferred by the presence of trifluoromethyl moiety in metabolic stability, lipophilicity, and binding selectivity have led to the extensive utilization of this moiety in industrial and academic sectors.[4] Thus, development of an efficient protocol for the synthesis of the C−CF_3 bond in diverse substrate scaffolds has become an area of intense research effort.[5] Notably, α-trifluoromethyl ketone is one such functionality, which serves as building block for various trifluoromethyl-containing complex moieties.[6] Not surprisingly, significant efforts have been invested to develop novel and diverse synthetic tools for the generation of α-CF_3-substituted carbonyl compounds.[7−10]

In this regard, Carreira and co-workers have developed a synthesis of α-trifluoromethyl ketones through classic homologation of aldehyde by (trifluoromethyl)diazomethane.[8] Recently, olefins have been used as the precursor for the α-trifluoromethyl ketone formation.[9] Various enols and enolates were also employed previously.[10] Despite this significant progress, implementation of an easily accessible and economical alkynic scaffold as the synthon remains elusive.[11]

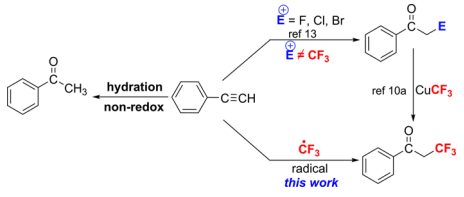
Recently, we have developed the protocol for the synthesis of α-trifluoromethyl ketone compounds from styrenes via a benzylic radical intermediate.[9a] Unfortunately, this method failed for common heterocycles such as quinoline, indole, pyrimidine, thiophene, and benzothiazole.



Owing to the importance of these scaffolds, we thought to design an alternative pathway for their synthesis. The structural correlation between the target molecule and the benzylic radical intermediate,[9a] prompted us to realize that α-styrenyl radical can lead to an alternative method for α-CF_3 substituted carbonyl compounds.[12] Such a strategy would require addition of CF_3 and OH moieties across the alkyne.

In this regard, although aryl acetylenes were extensively used to generate ketomethyl (−$COCH_3$) and α-functionalized keto (−$COCH_2X$) compounds,[13] mostly halo-electrophiles (F, Cl, Br) were introduced at the α-position of the ketomethyl following such approaches (Scheme 1). In contrast, exploring

Scheme 1. Novel Approach to α-Trifluoromethyl Ketone



α-trifluoromethylation reaction using similar strategy is constrained by the economic viability of electrophilic trifluoromethyl source as well as stability of the target molecule under basic condition.

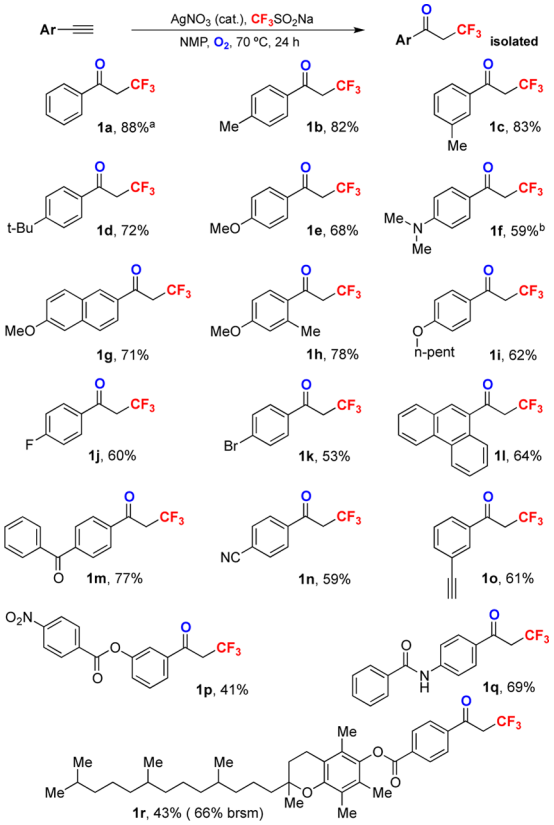
We envisioned that CF_3 radical could attack alkyne to form the α-styrenyl radical, which upon quenching by O-radical will form α-trifluoromethylketone. Hu and co-workers have reported a copper mediated electrophilic decarboxylative trifluoromethylation of propiolic acid derivatives ($RCCCO_2H$).[14] Hereby, we are disclosing an efficient protocol of converting the widely available alkynes to the α-trifluoromethylketone in the presence of oxygen (Scheme 1).

Received: July 15, 2014
Published: August 15, 2014

 © 2014 American Chemical Society dx.doi.org/10.1021/ol502071g | *Org. Lett.* 2014, 16, 4524−4527

Detailed optimization studies revealed that a 88% yield of α-trifluoromethylketone from phenylacetylene can be realized with $AgNO_3$/ CF_3SO_2Na in polar aprotic solvents such as NMP, DMF and DMA under O_2 atmosphere at 70 °C (Table 1).[15]

Table 1. Substrate Scope with Arylalkynes*



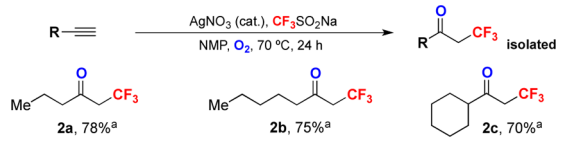
*Average of two runs. All of the reactions were performed on a 0.25 mmol scale. 20 % $AgNO_3$ and CF_3SO_2Na (1.2 equiv) were added twice during the reaction. [a]GC-yield with *n*-decane as reference. [b]^{19}F NMR yield calculated using hexafluorobenzene as reference. brsm: based on recovered starting materials

After extensive experimentations, we found that 1-methyl-2-pyrrolidinone (NMP) was the best solvent for this transformation. Notably, no external oxidant is required for this transformation. Phenylacetylene with functional groups such as halo (**1j** and **1k**), keto (**1m**) and cyano (**1n**) were also employed. Aromatic ring with electron-donating substituent (**1a-1d**) delivered the product in better yield as compared to the electron-withdrawing substituents (**1j**, **1k** and **1n**). Therefore, it is likely that the electron rich substituents stabilize the reactive intermediate efficiently. Substrate in which two alkynes were available, oxidation occurred at only one alkyne (**1o**, 61%). Phenylacetylene with benzanilide (**1q**), 4-nitrobenzoate (**1p**) and tocopherol (vitamin E, **1r**) unit produced trifluoromethylketone in moderate to good yields.

Aliphatic alkynes, both cyclic and acyclic, delivered the desired trifluoromethylated compounds in good yields (Table 2, 2a-c).

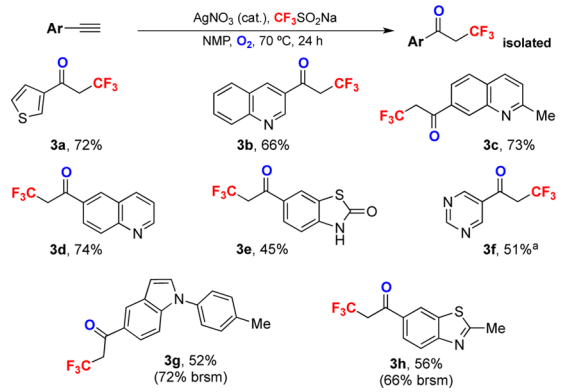
Next we tested heterocyclic alkyne as the precursor for this reaction. Note that previous strategies were not efficient in producing heterocyclic α-trifluoromethyl ketone compounds.[7−10,16] Interestingly, quinoline possessing an ethynyl group either on the phenyl or pyridine ring were suitable (**3b** and **3d**) under the present conditions. Scaffolds like thiophene (**3a**), pyrimidine

Table 2. Scope with Aliphatic Alkynes



[a]^{19}F NMR yield calculated using α,α,α-trifluorotoluene as reference.

Table 3. Generation of Heterocyclic α-Trifluoromethyl Ketones*



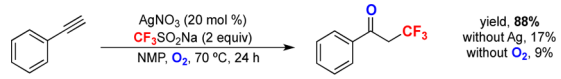
*Average of two runs. 20 mol % $AgNO_3$ and CF_3SO_2Na (1.2 equiv) were added two times in the reaction. [a]^{19}F NMR yield calculated using hexafluorobenzene as reference. brsm: based on recovered starting materials.

(**3f**), indole (**3g**), benothiazole (**3h**), and thiazolone (**3e**) were also found to be compatible. Therefore, Table 3 demonstrated the power of this strategy to form heterocyclic α-trifluoromethyl ketones.

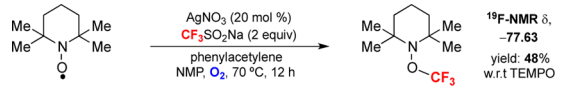
Unfortunately, both aromatic and aliphatic internal alkynes gave only 5−10% (GC) yield of the trifluoromethylated product.

A number of control experiments were carried out to gain insights into the mechanistic pathway. The presence of silver salt and an oxygen environment was found to be essential (Scheme 2). The radical nature of the reaction was studied by trapping CF_3 with TEMPO (Scheme 3) and by carrying out radical scavenger experiments (Scheme 4).

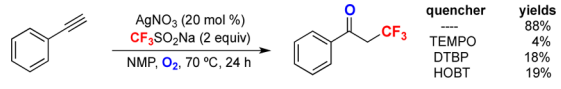
Scheme 2. Control Experiments



Scheme 3. CF_3 Radical Trapping



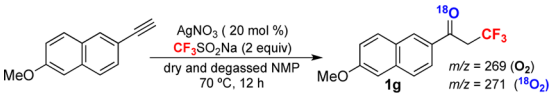
Scheme 4. Radical Scavenger Experiment



Isotope-labeling studies were planned to attain a better understanding of the origin of the newly introduced atoms in phenylacetylene to form the α-trifluoromethyl ketone. Formation of O-18-labeled α-trifluoromethyl ketone under $^{18}O_2$ atmosphere

dx.doi.org/10.1021/ol502071g | Org. Lett. 2014, 16, 4524−4527

Table 4. Isotope Labeling Experiment



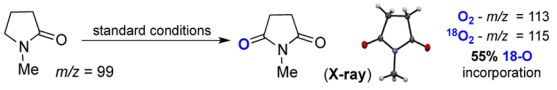
oxygen	solvent	observation
$^{18}O_2$	NMP	^{18}O-incorporated
O_2	NMP + H_2O^{18} (1 equiv)	no isotope labeling
O_2	NMP + D_2O (1 equiv)	no D insertion

indicated that the aerobic oxygen was the likely source of O atom in the target molecule (Table 4).

On the contrary, no isotope-labeled product was obtained when the standard reaction was performed either in the presence of $H_2{}^{18}O$ or D_2O. These observations suggested that adventitious water, which might be present in the commercially available solvents, was not involved in the reaction profile.

Interestingly *N*-methylsuccinimide was formed in all of the reactions (also see X-ray). The $^{18}O_2$-labeling studies showed the shift of mass peak from *m*/*z* 113 to *m*/*z* 115 (Scheme 5).

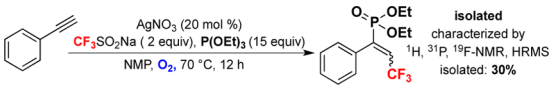
Scheme 5. Role of NMP Solvent



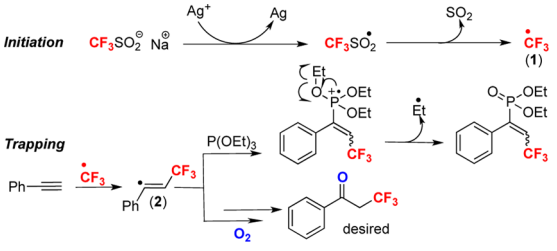
This is indicative of the fact that the oxygen atoms in α-trifluoromethyl ketone and *N*-methylsuccinimide were originated from molecular O_2.

An α-styrenyl radical intermediate was presumed for the synthesis of α-trifluoromethyl ketone from alkyne. Since $P(OEt)_3$ had previously been employed as a selective trapping agent for vinylic radical intermediates,[17] we added it under the standard trifluoromethylation reaction conditions (Scheme 6). Isolation and characterization of the expected trapped intermediate thus further strengthened the initial hypothesis (Scheme 7).

Scheme 6. Trapping of α-Styrenyl Radical by $P(OEt)_3$



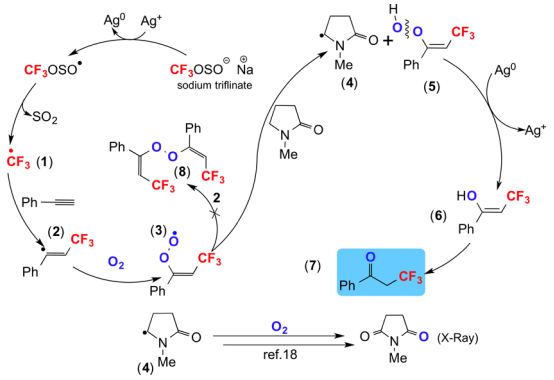
Scheme 7. α-Styrenyl Adduct with $P(OEt)_3$



Next, the kinetic investigation of the reaction suggested a first-order (0.98) rate dependency with respect to the alkyne, which is indicative to the fact that dimeric species **8** (Scheme 8) is less likely to form.[15] On the basis of all these experimental observations, a radical-based pathway involving NMP and molecular O_2 has been proposed (Scheme 8).

The reaction initiated with the formation of CF_3 radical **1** from sodium triflinate (CF_3SO_2Na) and silver catalyst. Subsequently,

Scheme 8. Plausible Mechanistic Cycle



1 attacked the alkyne generating a reactive α-styrenyl radical intermediate **2**, which interacted with molecular oxygen to produce **3**. This active species **3** abstracted one hydrogen atom from NMP solvent generating hydroperoxo species **5** along with **4**, which was further oxidized to *N*-methylsuccinimide.[18] Decomposition of **5** led to the formation of α-trifluoromethylated product **7** via tautomerization of **6** along with the regeneration of cationic silver.

Notably, silver(0) is unlikely to be oxidized by molecular oxygen but can adsorb oxygen, whereas atomic oxygen can easily oxidize silver(0) to silver(I).[19]

Hence, it is likely that the active hydroxy radical, formed upon the decomposition of **5**, can assist in the regeneration of silver(I). During optimization study, Ag_2O was also found to catalyze the transformation. The first-order rate dependency also supported the involvement of one molecule of reactant in the catalytic cycle.

In summary, we have devised an Ag^+/CF_3SO_2Na-based protocol that enabled the rapid installation of the trifluoromethyl moiety utilizing the alkynic feedstock. This strategy was successful in introducing α-trifluoromethylketone in heterocyclic scaffolds known to be incompatible with the earlier strategies. Given the simplicity and broad scope demonstrated in this study, we anticipate that this protocol will find application in the synthesis of biologically active organofluorine-containing medicinal agents.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: dmaiti@chem.iitb.ac.in.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This activity is supported by SERB (SR/S1/IC-24/2011), India. Financial support received from CSIR-India (fellowship to A.M.) is gratefully acknowledged.

dx.doi.org/10.1021/ol502071g | *Org. Lett.* 2014, 16, 4524−4527

REFERENCES

(1) Filler, R.; Yagupolskii, L. M. *Organofluorine Compounds in Medicinal Chemistry & Biomedical Applications*; Elsevier: New York, 1993.

(2) Hiyama, T. *Organofluorine Compounds: Chemistry and Application*; Yamamoto, H., Hiyama, T., Kanie, K., Kusumoto, T., Morizawa, Y., Shimzu, M.; Springer: Berlin, 2000.

(3) Banks, R. E.; Tatlow, C. J. *Organofluorine Chemistry, Principles and Commercial Applications*; Springer: New York, 1994.

(4) (a) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, *473*, 470. (b) Muller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881. (c) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320. (d) Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475. (e) Kirk, K. L. *J. Fluorine Chem.* **2006**, *127*, 1013. (f) Hagmann, W. K. *J. Med. Chem.* **2008**, *51*, 4359. (g) Kirk, K. L. *Org. Process Res. Dev.* **2008**, *12*, 305. (h) Begue, J. P.; Bonnet-Delpon, D.; Crousse, B.; Legros, J. *Chem. Soc. Rev.* **2005**, *34*, 562. (i) Oishi, M.; Kondo, H.; Amii, H. *Chem. Commun.* **2009**, *45*, 1909. (j) Morimoto, H.; Tsubogo, T.; Litvinas, N. D.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2011**, *50*, 3793. (k) Zhang, C. P.; Wang, Z. L.; Chen, Q. Y.; Zhang, C. T.; Gu, Y. C.; Xiao, J. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 1896. (l) Fier, P. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2012**, *134*, 5524. (m) Zhang, C. P.; Chen, Q. Y.; Guo, Y.; Xiao, J. C.; Gu, Y. C. *Chem. Soc. Rev.* **2012**, *41*, 4536. (n) Liu, X.; Xiong, F.; Huang, X.; Xu, L.; Li, P.; Wu, X. *Angew. Chem., Int. Ed.* **2013**, *52*, 6962. (o) Zhu, L.; Liu, S.; Douglas, J. T.; Altman, R. A. *Chem.—Eur. J.* **2013**, *19*, 12800. (p) Ambler, B. R.; Altman, R. A. *Org. Lett.* **2013**, *15*, 5578.

(5) (a) Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9567. (b) Yasu, Y.; Arai, Y.; Tomita, R.; Koike, T.; Akita, M. *Org. Lett.* **2014**, *16*, 780. (c) Yasu, Y.; Koike, T.; Akita, M. *Org. Lett.* **2013**, *15*, 2136. (d) Noritake, S.; Shibata, N.; Nakamura, S.; Toru, T.; Shiro, M. *Eur. J. Org. Chem.* **2008**, *2008*, 3465. (e) Nagib, D. A.; MacMillan, D. W. C. *Nature* **2011**, *480*, 224. (f) Cho, E. J.; Senecal, T. D.; Kinzel, T.; Zhang, Y.; Watson, D. A.; Buchwald, S. L. *Science* **2010**, *328*, 1679. (g) Fujiwara, Y.; Dixon, J. A.; O'Hara, F.; Funder, E. D.; Dixon, D. D.; Rodriguez, R. A.; Baxter, R. D.; Herle, B.; Sach, N.; Collins, M. R.; Ishihara, Y.; Baran, P. S. *Nature* **2012**, *492*, 95. (h) Iqbal, N.; Jung, J.; Park, S.; Cho, E. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 539. (i) Wang, Y.-F.; Lonca, G. H.; Chiba, S. *Angew. Chem., Int. Ed.* **2014**, *53*, 1067. (j) Jiang, X.-Y.; Qing, F.-L. *Angew. Chem., Int. Ed.* **2013**, *52*, 14177. (k) Zhang, B.; Studer, A. *Org. Lett.* **2014**, *16*, 1216. (l) Bao, H.; Bayeh, L.; Tambar, U. K. *Angew. Chem., Int. Ed.* **2014**, *53*, 1664. (m) Ilchenko, N. O.; Janson, P. G.; Szabo, K. J. *J. Org. Chem.* **2013**, *78*, 11087. (n) Ilchenko, N. O.; Janson, P. G.; Szabo, K. J. *Chem. Commun.* **2013**, *49*, 6614. (o) Janson, P. G.; Ghoneim, I.; Ilchenko, N. O.; Szabo, K. J. *Org. Lett.* **2012**, *14*, 2882. (p) Larsson, J. M.; Pathipati, S. R.; Szabo, K. J. *J. Org. Chem.* **2013**, *78*, 7330. (q) Zhao, T. S. N.; Szabo, K. J. *Org. Lett.* **2012**, *14*, 3966. (r) Hamilton, J. Y.; Morandi, B.; Carreira, E. M. *Synthesis* **2013**, *45*, 1857. (s) Kreis, L. M.; Krautwald, S.; Pfeiffer, N.; Martin, R. E.; Carreira, E. M. *Org. Lett.* **2013**, *15*, 1634. (t) Kunzi, S. A.; Morandi, B.; Carreira, E. M. *Org. Lett.* **2012**, *14*, 1900. (u) Morandi, B.; Carreira, E. M. *Org. Lett.* **2011**, *13*, 5984. (v) Morandi, B.; Cheang, J.; Carreira, E. M. *Org. Lett.* **2011**, *13*, 3080. (w) Presset, M.; Oehlrich, D.; Rombouts, F.; Molander, G. A. *J. Org. Chem.* **2013**, *78*, 12837. (x) Argintaru, O. A.; Ryu, D.; Aron, I.; Molander, G. A. *Angew. Chem. Int. Ed* **2013**, *52*, 13656. (y) Merino, E.; Nevado, C. *Chem. Soc. Rev.* **2014**, DOI: 10.1039/C4CS00025K. (z) Straathof, N. J. W.; van Osch, D. J. G. P.; Schouten, A.; Wang, X.; Schouten, J. C.; Hessel, V.; Noël, T. *J. Flow. Chem.* **2014**, *4*, 12. (aa) Straathof, N. J. W.; Gemoets, H. P. L.; Wang, X.; Schouten, J. C.; Hessel, V.; Noël, T. *ChemSusChem* **2014**, *7*, 1612.

(6) (a) Alvernhe, G. R.; Langlois, B.; Laurent, A.; Le Drean, I.; Selmi, A.; Weissenfels, M. *Tetrahedron Lett.* **1991**, *32*, 643. (b) Schenck, H. A.; Lenkowski, P. W.; Choudhury-Mukherjee, I.; Ko, S.-H.; Stables, J. P.; Patel, M. K.; Brown, M. L. *Bioorg. Med. Chem.* **2004**, *12*, 979. (c) Li, Z. J.; Cui, Z. L.; Liu, Z. Q. *Org. Lett.* **2013**, *15*, 406. (d) Ye, Y. D.; Kuenzi, S. A.; Sanford, M. S. *Org. Lett.* **2012**, *14*, 4979. (e) Rudler, H.; Parlier, A. e.; Denneval, C.; Herson, P. *J. Fluorine Chem.* **2010**, *131*, 738. (f) Muzalevskiy, V. M.; Nenajdenko, V. G.; Rulev, A. Y.; Ushakov, I. A.; Romanenko, G. V.; Shastin, A. V.; Balenkova, E. S.; Haufe, G. n. *Tetrahedron* **2009**, *65*, 6991. (g) Ash, A. B.; Montagne, M. P. L.; Markovac, A. US 3,940,404, 1976. (h) Petasis, N. A.; Myslinska, M. US Patent Appl. 20090247766. (i) Wang, P. F.; Li, N.; Liu, W. M; Lee, S. T.; Lee, C. S. US Patent Appl. 20090102356.

(7) (a) Matousek, V.; Togni, A.; Bizet, V.; Cahard, D. *Org. Lett.* **2011**, *13*, 5762. (b) Petrik, V.; Cahard, D. *Tetrahedron Lett.* **2007**, *48*, 3327. (c) Mikami, K.; Tomita, Y.; Ichikawa, Y.; Amikura, K.; Itoh, Y. *Org. Lett.* **2006**, *8*, 4671. (d) Sato, K.; Yuki, T.; Tarui, A.; Omote, M.; Kumadaki, I.; Ando, A. *Tetrahedron Lett.* **2008**, *49*, 3558. (e) Cantillo, D.; de Frutos, O.; Rincon, J. A.; Mateos, C.; Kappe, C. O. *Org. Lett.* **2014**, *16*, 896. (f) Umemoto, T.; Adachi, K. *J. Org. Chem.* **1994**, *59*, 5692. (g) Sato, K.; Yuki, T.; Yamaguchi, R.; Hamano, T.; Tarui, A.; Omote, M.; Kumadaki, I.; Ando, A. *J. Org. Chem.* **2009**, *74*, 3815. (h) Sato, K.; Higashinagata, M.; Yuki, T.; Tarui, A.; Omote, M.; Kumadaki, I.; Ando, A. *J. Fluorine Chem.* **2008**, *129*, 51. (i) Zheng, Y.; Ma, J.-A. *Adv. Synth. Catal.* **2010**, *352*, 2745. (j) Cantillo, D.; de Frutos, O.; Rincon, J. A.; Mateos, C.; Kappe, C. O. *Org. Lett.* **2014**, *16*, 896.

(8) Morandi, B.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 9085.

(9) (a) Deb, A.; Manna, S.; Modak, A.; Patra, T.; Maity, S.; Maiti, D. *Angew. Chem., Int. Ed.* **2013**, *52*, 9747. (b) Zhang, C. P.; Wang, Z. L.; Chen, Q. Y.; Zhang, C. T.; Gu, Y. C.; Xiao, J. C. *Chem. Commun.* **2011**, *47*, 6632. (c) Tomita, R.; Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 7144.

(10) (a) Novak, P.; Lishchynskyi, A.; Grushin, V. V. *J. Am. Chem. Soc.* **2012**, *134*, 16167. (b) Zanardi, A.; Novikov, M. A.; Martin, E.; Benet-Buchholz, J.; Grushin, V. V. *J. Am. Chem. Soc.* **2011**, *133*, 20901. (c) Nagib, D. A.; Scott, M. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 10875. (d) Allen, A. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2010**, *132*, 4986. (e) Pham, P. V.; Nagib, D. A.; MacMillan, D. W. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 6119. (f) Itoh, Y.; Mikami, K. *Org. Lett.* **2005**, *7*, 4883. (g) Itoh, Y.; Houk, K. N.; Mikami, K. *J. Org. Chem.* **2006**, *71*, 8918. (h) Itoh, Y.; Mikami, K. *J. Fluorine Chem.* **2006**, *127*, 539. (i) Itoh, Y.; Mikami, K. *Tetrahedron Lett.* **2006**, *49*, 3819. (j) Tomita, Y.; Ichikawa, Y.; Itoh, Y.; Kawada, K.; Mikami, K. *Tetrahedron Lett.* **2007**, *48*, 8922. (k) Itoh, Y.; Mikami, K. *Org. Lett.* **2005**, *7*, 649.

(11) Umemoto, T.; Ishihara, S. *J. Am. Chem. Soc.* **1993**, *115*, 2156.

(12) Benson, S. W. *Thermochemical Kinetics: Methods for the Estimation of Thermochemical Data and Rate Parameters*, 2nd ed.: John Wiley & Sons: New York, 1976.

(13) (a) Nobuta, T.; Hirashima, S. i.; Tada, N.; Miura, T.; Itoh, A. *Tetrahedron Lett.* **2010**, *51*, 4576. (b) de Haro, T.; Nevado, C. *Adv. Synth. Catal.* **2010**, *352*, 2767. (c) Madabhushi, S.; Jillella, R.; Mallu, K. K. R.; Godala, K. R.; Vangipuram, V. S. *Tetrahedron Lett.* **2013**, *54*, 3993. (d) Kore, R.; Srivastava, R. *Tetrahedron Lett.* **2012**, *53*, 3245. (e) Chen, D. F.; Han, Z. Y.; He, Y. P.; Yu, J.; Gong, L. Z. *Angew. Chem., Int. Ed.* **2012**, *51*, 12307. (f) Xu, X.; Kim, S. H.; Zhang, X.; Das, A. K.; Hirao, H.; Hong, S. H. *Organometallics* **2012**, *32*, 164. (g) Václavík, J.; Servalli, M.; Lothschütz, C.; Szlachetko, J.; Ranocchiari, M.; van Bokhoven, J. A. *ChemCatChem* **2013**, *5*, 692. (h) Zhang, C.; Jiao, N. *J. Am. Chem. Soc.* **2010**, *132*, 28.

(14) He, Z.; Zhang, R.; Hu, M.; Li, L.; Ni, C.; Hu, J. *Chem. Sci.* **2013**, *4*, 3478.

(15) See the Supporting Information for a detailed description.

(16) Heterocyclic alkene (ref 9a) failed completely to incorporate indole, quinolone, thiophene, pyrimidine, and benzothiazole moieties to produce the desired α-trifluoromethylketone compounds.

(17) (a) Jiao, X. Y.; Bentrude, W. G. *J. Am. Chem. Soc.* **1999**, *121*, 6088. (b) Jiao, X. Y.; Bentrude, W. G. *J. Org. Chem.* **2003**, *68*, 3303.

(18) (a) Drago, R. S.; Riley, R. *J. Am. Chem. Soc.* **1990**, *112*, 215. (b) Friesen, D. A.; Headley, J. V.; Langford, C. H. *Environ. Sci. Technol.* **1999**, *33*, 3193.

(19) Moore, W. M.; Codella, P. J. *J. Phys. Chem.* **1988**, *92*, 4421.