

Photoredox-Induced Three-Component Oxy-, Amino-, and Carbotrifluoromethylation of Enecarbamates

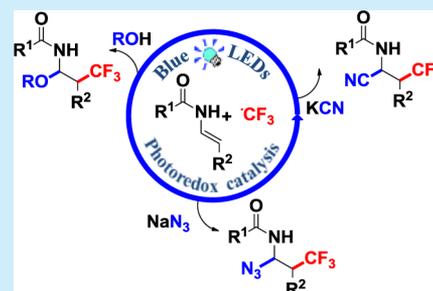
Aude Carboni,[†] Guillaume Dagousset,[†] Emmanuel Magnier,^{*,‡} and Géraldine Masson^{*,†}

[†]Centre de Recherche de Gif, Institut de Chimie des Substances Naturelles, CNRS, 91198 Gif-sur-Yvette Cedex, France

[‡]Institut Lavoisier de Versailles, UMR 8180, Université de Versailles-Saint-Quentin, 78035 Versailles Cedex, France

S Supporting Information

ABSTRACT: A photoredox-catalyzed trifluoromethylation of enecarbamates process is reported. This pathway uses Togni's reagent as the CF₃ source and follows a radical/cationic pathway. Under the optimized conditions using [Ru(bpy)₃(PF₆)₂] as the photocatalyst, a wide range of substituted enecarbamates can readily be difunctionalized by means of various O, N, and C nucleophiles.

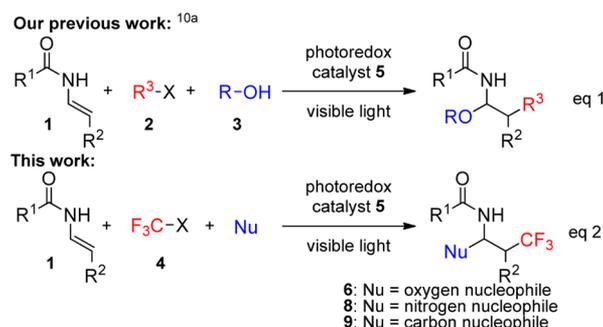


β -Trifluoromethyl amines have been recognized as important structural motifs in many bioactive compounds.¹ The presence of CF₃ enhances the hydrophobicity, metabolic stability, and bioavailability of the amines, making them useful intermediates in the synthesis of fluorinated amino acids and peptidomimetics.² In spite of the prime importance of β -trifluoromethyl amines in the identification of novel drugs, there are few direct syntheses of these amines.³ Indeed, in most synthetic works, the reagents already bear a trifluoromethyl group, such as trifluoromethylated alkenes,^{1d,e,2a,b,d,e,4} ketones,⁵ or epoxides.^{1c} Recently, Loh et al. reported an elegant Cu-catalyzed oxytrifluoromethylation of α -substituted enamides.^{3b} Although this process is effective, the method is restricted to terminal enamides, leading to the formation of quaternary carbon-containing β -trifluoromethylated α -amidoether products. For this reason, establishing methods that can directly incorporate the CF₃ group⁶ at the β -position of a variety of amines continues to be actively pursued.

Photoredox⁷ trifluoromethylation of alkenes has attracted considerable attention over the past few years.^{3b,8} Various substrates such as standard alkynes,^{8e} alkenes,^{8c,j,m,q} styrenes,^{8g,h} allylic alcohols and amines,^{8k} enolates,^{8g} or acryl amides^{8o} are generally involved. Specifically, enecarbamates have never been used as substrates for this type of process, although they are a promising starting material for the synthesis of β -trifluoromethyl amines.⁹

Recently, our group became interested in the C–H functionalization of enamides and enecarbamates.¹⁰ Notably, we could efficiently perform a photocatalyzed α,β -difunctionalization of enecarbamates through a three-component radical/cationic reaction^{11,12} between enecarbamate **1**, alkyl halide **2**, and alcohol **3** (Scheme 1, eq 1).^{10a} Based on this experience as well as on our knowledge of electrophilic trifluoromethylating reagents,^{13,14} we envisioned the direct trifluoromethylation of

Scheme 1. Photocatalyzed Three-Component Reaction of Enecarbamates¹⁰ and Rational Design for Trifluoromethylation of Enecarbamates by Photoredox Catalysis



enecarbamates in the presence of photoredox catalysts **5** (Scheme 1, eq 2). Herein, we wish to report an efficient process giving rise to key and original trifluoromethyl amines. Direct intermolecular oxy-, amino-, and carbotrifluoromethylation of a wide range of substituted enecarbamates is described in this paper.

Our initial investigations focused on the Ru-photocatalyzed trifluoromethylation of benzyl *N*-vinylcarbamate **1a** with Umemoto's reagent **4a** in the presence of methanol **3a** irradiated by blue LEDs. As described in Table 1, we were able to obtain the expected three-component trifluoromethylated adduct **6a** in 19% yield. Replacing **4a** with a more reactive nitro-substituted derivative **4b** resulted only in the degradation of **4b** and enecarbamate **1a**. Various sources of CF₃ radical were then tested. While no reaction took place with potassium or

Received: January 21, 2014

Published: February 12, 2014

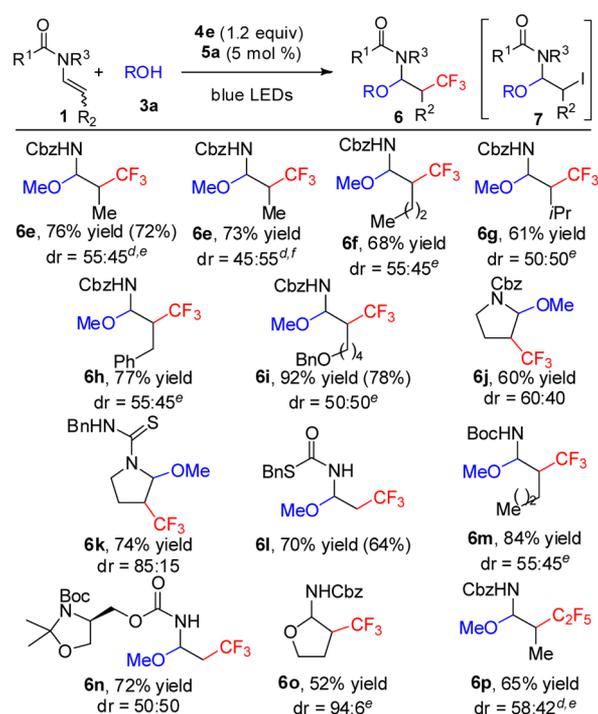
Table 1. Survey of Reaction Conditions for the Photocatalyzed Oxytrifluoromethylation of 1a^a

entry	4	R	photoredox cat.	6	yield ^b (%)
1	4a	Me	Ru(bpy) ₃ (PF ₆) ₂ (5a)	6a	19
2	4b	Me	5a	6a	c
3	4c	Me	5a	6a	
4	4d	Me	5a	6a	
5	4e	Me	5a	6a	83
6	4f	Me	5a	6a	86 ^d
7	4e	Me	Ru(bpy) ₃ Cl ₂ (5b)	6a	70
8	4e	Me	Ir(ppy) ₂ (dtbbpy)(PF ₆) (5c)	6a	77
9	4e	Me	5a	6a	77 ^e
10	4e	Me		6a	f
11	4e	Me		6a	f,g
12	4e	Me	5a	6a	f,g
13	4e	Me	5a	6a	36 ^h
14	4e	Me	5a	6a	c,i
15	4e	Et	5a	6b	71
16	4e	iPr	5a	6c	50
17	4e	H	5a	6d	69 ^j

^aGeneral conditions: 1a (0.10 mmol), CF₃ source (0.12 mmol), 5 (0.05 equiv) in MeOH (2.0 mL) irradiated at rt for 3 h. ^bYields referred to chromatographically pure product. ^cTrace of product 6a and degradation of 1a were observed. ^dYield determined by NMR spectroscopy. ^eWith 1 mol % of 5a, 1a was recovered. ^fWithout any irradiation. ^gWith 2 equiv of Et₃N. ^hWith 2 equiv of 1,3-dinitrobenzene. ⁱWith a 1:1 mixture of THF/H₂O as solvent. dtbbpy = di-tert-butyl-2,2'-bipyridine.

sodium trifluoromethanesulfonate 4c,d (Langlois reagent), Togni's reagents 4e and 4f¹⁵ reacted very smoothly and afforded 6a in 83% and 86% yield (entries 5 and 6), respectively.¹⁶ After screening different Ru and Ir photocatalysts, [Ru(bpy)₃(PF₆)₂] 5a was found to be the most efficient catalyst, since we could decrease its loading to 1 mol % without any significant loss of reactivity (entries 9 vs 5). The stoichiometry of the reaction and the solvents were also optimized (see the Supporting Information). Other alcohols (EtOH (3b), iPrOH (3c)) and water were also found to be suitable reaction partners, affording the corresponding trifluoromethylated aminals or hemiaminals in slightly lower yields (entries 15–17).

With the optimized reaction conditions in hand, the scope of this Ru(bpy)₃(PF₆)₂-catalyzed three-component oxytrifluoromethylation of enecarbamates was investigated (Scheme 2). To our delight, a wide range of β-substituted enecarbamates bearing either a linear or branched alkyl group reacted efficiently to afford the expected trifluoromethylated adducts 6e–j in good to excellent yields (60–92%). However, in some cases it was found that the trifluoromethylated products 6 were contaminated with impurities (<10%) that were attributable to the iodinated products 7. This side product 7 resulted from the iodination of 1 with iodine generated during the reaction,

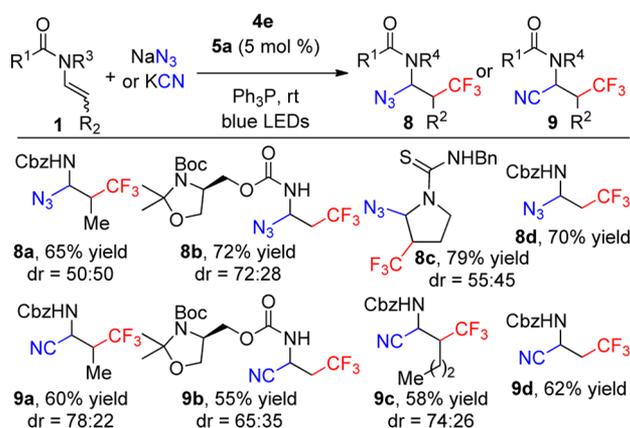
Scheme 2. Substrate Scope of the Oxytrifluoromethylation of Enecarbamates 1^{a–c}


which has not previously been reported.¹⁷ Pleasingly, the side reaction was suppressed by the addition of a catalytic amount of Ph₃P as an iodine trap,¹⁸ and the desired β-trifluoromethyl amines were produced with similar yields. Unexpectedly, both diastereomers (*Z*)-1e and (*E*)-1e of benzyl prop-1-en-1-ylcarbamate led to the corresponding product 6e in similar yield, albeit with a reverse diastereoselectivity. A variety of protecting and functional groups bonded to the nitrogen of 1, including benzylthiourea, benzylthiocarbamate, and Boc, were well tolerated, as well as the functionalized enecarbamate 1n derived from Garner's alcohol. The cyclic enecarbamate 1j and enethiourea 1k also reacted successfully to afford compounds 6j and 6k. They are a direct intermediate, after reduction of the aminal function, to the very rare but promising, in terms of bioactivity, 3-(trifluoromethyl)pyrrolidine.¹⁹ Interestingly, the enecarbamate 1o bearing a free hydroxy group reacted successfully to afford the intramolecular oxytrifluoromethylated product 6o. Finally, we showed that this method can also be applied to the synthesis of β-perfluoroalkylated amino derivatives. Thus, the hypervalent iodine reagent 4g bearing a C₂F₅ substituent was prepared according to the literature procedure²⁰ and gave the expected adduct 6p in 65% yield by using the optimized conditions.

Encouraged by this result, we turned our efforts toward extending this radical/cationic multicomponent protocol to the challenging intermolecular amino- and carbotrifluoromethylation of enecarbamates 1. In contrast to the oxytrifluoromethy-

lation, there have been only few reports of the amino- and carbotrifluoromethylation of alkenes.²¹ The first example of photocatalyzed aminotrifluoromethylation was reported recently by Koike and Akita et al.,^{8h} and photocatalyzed carbotrifluoromethylation of alkenes has been limited to intramolecular aryltrifluoromethylation.^{8o} While the development of such reactions is difficult because of possible competition between the nitrogen or carbon nucleophile with MeOH, we reasoned that under appropriate conditions amino- and carbotrifluoromethylation may also proceed. In our initial experiment, we were pleased to find that irradiation of a THF/H₂O solution of enecarbamate **1e**, Togni's reagent **4e** (1.2 equiv) and NaN₃ (5 equiv) with **5a** as photocatalyst afforded the aminotrifluoromethylated product **8a** in 45% isolated yield, without the formation of the corresponding hemiaminal **6** (R = H). However, a partial decomposition of **4e** and traces of the corresponding β -iodo compound were observed during the reaction. Fortunately, the yield was improved to 65% with 2 equiv of **4e** and 10 mol % of Ph₃P. A variety of functionalized and β -substituted enecarbamates were subjected to these conditions, furnishing the corresponding α -azido- β -CF₃ compounds **8a–d** in good yields (65–79%, Scheme 3), which are

Scheme 3. Substrate Scope of the Intermolecular Amino- and Carbotrifluoromethylation of Enecarbamates 1^{a–c}



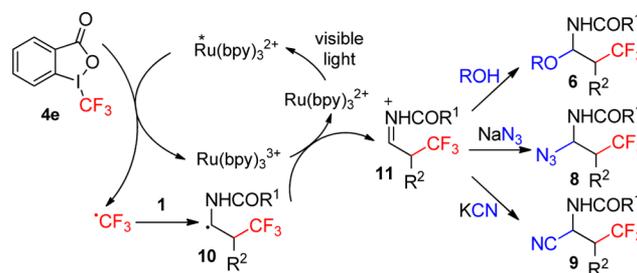
^aGeneral conditions: **1** (0.10 mmol), **4e** (2–2.5 equiv), NaN₃ or KCN (5 equiv), **5a** (0.05 equiv), and Ph₃P (0.1 equiv) in a 1:1 mixture of THF/H₂O (2.0 mL) irradiated at rt for 12 h. ^bYields referred to chromatographically pure product. ^cdr determined by ¹⁹F NMR analysis of crude mixtures. Because of the presence of rotamers, it was impossible to assign the *syn/anti* assignments.

direct precursors of the corresponding α -amino- β -CF₃ compounds. Similarly, KCN could be efficiently used instead of NaN₃, leading to cyanotrifluoromethylated precursors of amino acids.²² This analogous photoinduced intermolecular carbotrifluoromethylation of double bonds remains unexplored. Fortunately, as shown in Scheme 3, all the reactions were also found to proceed smoothly under similar conditions to afford the corresponding α -cyano- β -CF₃ compounds **9a–d** in acceptable yields.

The following control experiments were carried out to gain some mechanistic insight. No reaction took place in the absence of irradiation and/or [Ru(bpy)₃(PF₆)₂] **5a**. Moreover, the formation of **6** was inhibited in the presence of radical scavengers such as TEMPO, suggesting that a radical/cationic process is involved in this reaction. Although the mechanism of this transformation is not yet completely clear, a possible

mechanism can be proposed on the basis of the above results (Scheme 4). First, irradiation with visible light excites

Scheme 4. Proposed Mechanism for the Radical/Cationic Trifluoromethylation of Enecarbamates



Ru(bpy)₃²⁺ into a strong reductant species *Ru(bpy)₃²⁺, which performs a single electron transfer (SET) to generate *CF₃ from Togni's reagent **4e**.^{8i,o} Subsequent regioselective addition of electrophilic *CF₃ to enecarbamate **1** leads to the α -amido radical **10**, which can be rapidly oxidized into *N*-acyliminium cation **11** by SET from Ru(bpy)₃³⁺.^{10a,23} Final nucleophilic trapping by alcohol **3**, NaN₃, or KCN affords the corresponding trifluoromethylated adducts **6**, **8**, or **9**. It is also worth noting that in the case of amino- and carbotrifluoromethylation the desired product **8** or **9** was not observed on addition of NaN₃ or KCN sequentially,²⁴ thus suggesting that the equilibrium between hemiaminal **6** (R = H) and *N*-acyliminium cation **11** does not take place during the reaction and that **11** is directly trapped by NaN₃ or KCN.

In conclusion, a photoredox-induced three-component synthesis of β -trifluoromethyl amines has been developed. The procedure is suitable for the completely regioselective synthesis of a wide variety of functionalized oxytrifluoromethylated carbamates. Importantly, this radical/ionic process has also been adapted and broadened to new N and C nucleophiles. To the best of our knowledge, this method represents the first intermolecular photoinduced carbotrifluoromethylation of carbon–carbon double bonds. Extension of this method, to more elaborated substrates for the preparation of potentially bioactive molecules, is currently underway in our laboratory and will be reported in due course.

■ ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures and spectral data for all new compounds are provided. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: geraldine.masson@cnrs.fr.

*E-mail: emmanuel.magnier@uvsq.fr.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank ICSN and CNRS for financial support and doctoral fellowships to A.C. G.D. thanks Labex Chammmat for a postdoctoral fellowship. Lucy Cooper is acknowledged for improvement of the English usage in the manuscript.

REFERENCES

- (1) (a) Mita, T.; Kudo, Y.; Mizukoshi, T.; Hotta, H.; Maeda, K.; Takii, S. *WO2004018410*, 2004. (b) Mita, T.; Kudo, Y.; Mizukoshi, T.; Hotta, H.; Maeda, K.; Takii, S. *JP2005272452*, 2005. (c) Rano, T. A.; Kuo, G.-H. *Org. Lett.* **2009**, *11*, 2812. (d) Kawai, H.; Okusu, S.; Tokunaga, E.; Sato, H.; Shiro, M.; Shibata, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 4959. (e) Kawai, H.; Yuan, Z.; Kitayama, T.; Tokunaga, E.; Shibata, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 5575.
- (2) (a) Sani, M.; Bruché, L.; Chiva, G.; Fustero, S.; Piera, J.; Volonterio, A.; Zanda, M. *Angew. Chem. Int. Ed.* **2003**, *42*, 2060. (b) Ogu, K.; Matsumoto, S.; Akazome, M.; Ogura, K. *Org. Lett.* **2005**, *7*, 589. (c) Jakowiecki, J.; Loska, R.; Makosza, M. *J. Org. Chem.* **2008**, *73*, 5436. (d) Fustero, S.; Chiva, G.; Piera, J.; Sanz-Cervera, J. F.; Volonterio, A.; Zanda, M.; Ramirez de Arellano, C. *J. Org. Chem.* **2009**, *74*, 3122. (e) Benhaim, C.; Bouchard, L.; Pelletier, G.; Sellstedt, J.; Kristofova, L.; Daigneault, S. *Org. Lett.* **2010**, *12*, 2008.
- (3) (a) Fustero, S.; Albert, L.; Acena, J. L.; Sanz-Cervera, J. F.; Asensio, A. *Org. Lett.* **2008**, *10*, 605. (b) Feng, C.; Loh, T.-P. *Chem. Sci.* **2012**, *3*, 3458.
- (4) Yarmolchuk, V. S.; Shishkin, O. V.; Starova, V. S.; Zaporozhets, O. A.; Kravchuk, O.; Zozulya, S.; Komarov, I. V.; Mykhailiuk, P. K. *Eur. J. Org. Chem.* **2013**, *15*, 3086.
- (5) (a) Tur, F.; Saá, J. M. *Org. Lett.* **2007**, *9*, 5079. (b) Alimardanov, A.; Nikitenko, A.; Connolly, T. J.; Feigelson, G.; Chan, A. W.; Ding, Z.; Ghosh, M.; Shi, X.; Ren, J.; Hansen, E.; Farr, R.; MacEwan, M.; Tadayon, S.; Springer, D. M.; Kreft, A. F.; Ho, D. M.; Potoski, J. R. *Org. Process Res. Dev.* **2009**, *13*, 1161.
- (6) (a) Parsons, A. T.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2011**, *50*, 9120. (b) Xu, J.; Fu, Y.; Luo, D.-F.; Jiang, Y.-Y.; Xiao, B.; Liu, Z.-J.; Gong, T.-J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 15300. (c) Wang, X.; Ye, Y.; Zhang, S.; Feng, J.; Xu, Y.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2011**, *133*, 16410. (d) Ji, Y.; Brueckl, T.; Baxter, R. D.; Fujiwara, Y.; Seiple, I. B.; Su, S.; Blackmond, D. G.; Baran, P. S. *Proc. Natl. Acad. Sci. U.S.A.* **2011**, *108*, 14411. (e) Nagib, D. A.; MacMillan, D. W. C. *Nature* **2011**, *480*, 224. (f) Deb, A.; Manna, S.; Modak, A.; Patra, T.; Maity, S.; Maiti, D. *Angew. Chem., Int. Ed.* **2013**, *52*, 9747. (g) Jiang, X.-Y.; Qing, F.-L. *Angew. Chem., Int. Ed.* **2013**, *52*, 14177. (h) Ilchenko, N. O.; Janson, P. G.; Szabo, K. J. *J. Org. Chem.* **2013**, *78*, 11087.
- (7) For recent reviews on photoredox catalysis, see: (a) Zeitler, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9785. (b) Yoon, T. P.; Ischay, M. A.; Du, J. *Nat. Chem.* **2010**, *2*, 527. (c) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102. (d) Teplý, F. *Collect. Czech. Chem. Commun.* **2011**, *76*, 859. (e) Maity, S.; Zheng, N. *Synlett* **2012**, 1851. (f) Xuan, J.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828. (g) Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 1617. (h) Shi, L.; Xia, W. *Chem. Soc. Rev.* **2012**, *41*, 7687. (i) Xi, H. Y. Y.; Lei, A. *Org. Biomol. Chem.* **2013**, *11*, 2387. (j) Yoon, T. P. *ACS Catal.* **2013**, *3*, 895. (k) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322.
- (8) (a) Nagib, D. A.; Scott, M. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 10875. (b) Pham, P. V.; Nagib, D. A.; MacMillan, D. W. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 6119. (c) Nguyen, J. D.; Tucker, J. W.; Konieczynska, M. D.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2011**, *133*, 4160. (d) Studer, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 8950. (e) Wallentin, C.; Nguyen, J. D.; Finkbeiner, P.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2012**, *134*, 8875. (f) Iqbal, N.; Choi, S.; Kim, E.; Cho, E. J. *J. Org. Chem.* **2012**, *77*, 11383. (g) Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9567. (h) Yasu, Y.; Koike, T.; Akita, M. *Org. Lett.* **2013**, *15*, 2136. (i) Yasu, Y.; Koike, T.; Akita, M. *Chem. Commun.* **2013**, *49*, 2037. (j) Mizuta, S.; Verhoog, S.; Engle, K. M.; Khotavivattana, T.; O'Duill, M.; Wheelhouse, K.; Rassias, G.; Médebielle, M.; Gouverneur, V. *J. Am. Chem. Soc.* **2013**, *135*, 2505. (k) Kim, E.; Choi, S.; Kim, H.; Cho, E. J. *Chem.—Eur. J.* **2013**, *19*, 6209. (l) Mizuta, S.; Engle, K. M.; Verhoog, S.; Galicia-López, O.; O'Duill, M.; Médebielle, M.; Wheelhouse, K.; Rassias, G.; Thompson, A. L.; Gouverneur, V. *Org. Lett.* **2013**, *15*, 1250. (m) Jiang, H.; Cheng, Y.; Zhang, Y.; Yu, S. *Eur. J. Org. Chem.* **2013**, 5485. (n) Wilger, D. J.; Gesmundo, N. J.; Nicewicz, D. A. *Chem. Sci.* **2013**, *4*, 3160. (o) Xu, P.; Xie, J.; Xue, Q.; Pan, C.; Cheng, Y.; Zhu, C. *Chem.—Eur. J.* **2013**, *19*, 14039. (p) Iqbal, N.; Jung, J.; Park, S.; Cho, E. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 539. (q) Mizuta, S.; Verhoog, S.; Wang, X.; Shibata, N.; Gouverneur, V.; Médebielle, M. *J. Fluorine Chem.* **2013**, *155*, 124.
- (9) We found only one example of photocatalyzed oxytrifluoromethylation of non- β -substituted enamine derivatives; see Jiang, H.; Huang, C.; Guo, J.; Zeng, C.; Zhang, Y.; Yu, S. *Chem.—Eur. J.* **2012**, *18*, 15158.
- (10) (a) Courant, T.; Masson, G. *Chem.—Eur. J.* **2012**, *18*, 423. (b) Drouet, F.; Zhu, J.; Masson, G. *Adv. Synth. Catal.* **2013**, *355*, 3563.
- (11) For representative references on radical and radical-ionic multicomponent reactions, see: (a) Godineau, E.; Landais, Y. *Chem.—Eur. J.* **2009**, *15*, 3044. (b) Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177.
- (12) Examples of difunctionalization of enecarbamates: (a) Dagousset, G.; Zhu, J.; Masson, G. *J. Am. Chem. Soc.* **2011**, *133*, 14804. (b) Alix, A.; Lalli, C.; Retailleau, P.; Masson, G. *J. Am. Chem. Soc.* **2012**, *134*, 10389. (c) He, L.; Laurent, G.; Retailleau, P.; Folléas, B.; Brayer, J.-L.; Masson, G. *Angew. Chem., Int. Ed.* **2013**, *52*, 11088. (d) Bekkaye, M.; Su, Y.; Masson, G. *Eur. J. Org. Chem.* **2013**, 3978.
- (13) For reviews on trifluoromethylating reagents, see: (a) Umamoto, T. *Chem. Rev.* **1996**, *96*, 1757. (b) Shibata, N.; Matsnev, A.; Cahard, D. *Beilstein J. Org. Chem.* **2010**, *6*, 65. (c) Macé, Y.; Magnier, E. *Eur. J. Org. Chem.* **2012**, 2479.
- (14) (a) Magnier, E.; Blazejewski, J.-C.; Tordeux, M.; Wakselman, C. *Ang. Chem. Int. Ed.* **2006**, *45*, 1279. (b) Macé, Y.; Raymondeau, B.; Pradet, C.; Blazejewski, J.-C.; Magnier, E. *Eur. J. Org. Chem.* **2009**, 1390.
- (15) Matoušek, V.; Pietrasiak, E.; Schwenk, R.; Togni, A. *J. Org. Chem.* **2013**, *78*, 6763–6768 and references cited therein.
- (16) Compound **4e** was used instead of **4f** for purification reasons.
- (17) We first thought that traces of iodine were present in the commercially available Togni's reagent **4e**. However, after washing **4e** with a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$, the side product **7** was still isolated in similar yield, suggesting that iodine is forming in situ during the reaction process. This generation of iodine from **4e** remains unclear, and further experiments are currently underway to account for this observation.
- (18) Appel, R. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 801.
- (19) Yarmolchuk, V. S.; Shishkin, O. V.; Starova, V. S.; Zaporozhets, O. A.; Kravchuk, O.; Zozulya, S.; Komarov, I. V.; Mykhailiuk, P. K. *Eur. J. Org. Chem.* **2013**, 3086.
- (20) Li, Y.; Studer, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 8221.
- (21) (a) Mu, X.; Wang, H.-Y.; Guo, Y.-L.; Liu, G. *J. Am. Chem. Soc.* **2012**, *134*, 878. (b) Egami, H.; Shimizu, R.; Kawamura, S.; Sodeoka, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 4000. (c) Egami, H.; Shimizu, R.; Sodeoka, M. *J. Fluorine Chem.* **2013**, *152*, 51. (d) Kong, W.; Casimiro, M.; Fuentes, N.; Merino, E.; Nevado, C. *Angew. Chem., Int. Ed.* **2013**, *52*, 13086. (e) Ilchenko, N. O.; Janson, P. G.; Szabó, K. J. *J. Org. Chem.* **2013**, *78*, 11087. (f) Lin, J.-S.; Xiong, Y.-P.; Ma, C.-L.; Zhao, L.-J.; Tan, B.; Liu, X.-Y. *Chem.—Eur. J.* **2014**, *20*, 1332. (g) He, Y.-T.; Li, L.-H.; Yang, Y.-F.; Zhou, Z.-Z.; Hua, H.-L.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2014**, *16*, 270. (h) Wang, F.; Qi, X.; Liang, Z.; Chen, P.; Liu, G. *Angew. Chem., Int. Ed.* **2014**, *53*, 1881.
- (22) Gröger, H. *Chem. Rev.* **2003**, *103*, 2795.
- (23) Oxidation of **10** by Togni's reagent **4e** to regenerate CF_3 (radical chain propagation) was excluded, as the reaction requires continuous irradiation.
- (24) In this case, the reaction leads only to the corresponding hemiaminal **6** (R = H).