Organic LETTERS
Cite This: Org. Lett. XXXX, XXX, XXX−XXX
Letter
pubs.acs.org/OrgLett

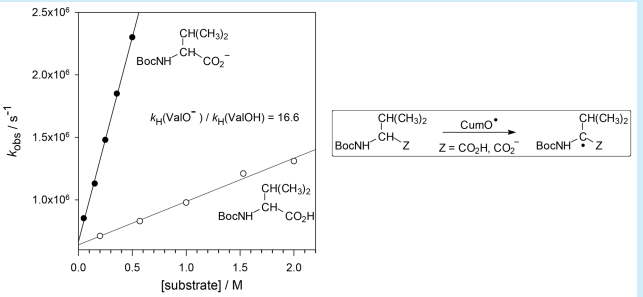
Enhancing Reactivity and Site-Selectivity in Hydrogen Atom Transfer from Amino Acid C−H Bonds via Deprotonation

Luca Maria Pipitone, Giulia Carboni, Daniela Sorrentino, Marco Galeotti, Michela Salamone,* and Massimo Bietti*

Dipartimento di Scienze e Tecnologie Chimiche, Università "Tor Vergata", Via della Ricerca Scientifica, 1 I-00133 Rome, Italy

Supporting Information

ABSTRACT: A kinetic study on the reactions of the cumyloxyl radical (CumO•) with *N*-Boc-protected amino acids in the presence of the strong organic base DBU has been carried out. CO_2H deprotonation increases the electron density at the α-C−H bonds activating these bonds toward HAT to the electrophilic CumO• strongly influencing the intramolecular selectivity. The implications of these results are discussed in the framework of HAT-based aliphatic C−H bond functionalization of amino acids and peptides.

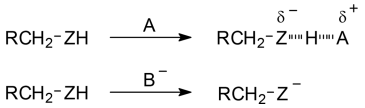


The selective functionalization of aliphatic C−H bonds is currently a mainstream topic of organic chemistry and one of the most investigated approaches to develop new synthetic methodology.[1−3] Among the available procedures, those based on hydrogen atom transfer (HAT) to radical or radical-like species have attracted considerable interest.[4−7] Because the majority of the HAT reagents employed in these procedures display an electrophilic character, the highest reactivities have been generally observed for HAT from electron-rich C−H bonds.[8] Accordingly, in substrates such as amines, ethers and alcohols, functionalization selectively occurs at the most electron rich C−H bonds, i.e., those that are α to the heteroatom.[9−11]

Within this framework, medium effects have also emerged as a powerful tool that has been successfully employed to alter both reactivity and site-selectivity. Time-resolved kinetic studies have provided a quantitative evaluation of the effect of hydrogen bond donor (HBD) solvents and acid−base interactions on HAT from the aliphatic C−H bonds of amine, amide, and ether substrates to the electrophilic radical cumyloxyl ($PhC(CH_3)_2O$•, CumO•).[12] An up to 4 order of magnitude decrease in the second-order rate constant for HAT (k_H) has been measured on going from acetonitrile to a strong HBD solvent such as 2,2,2-trifluoroethanol or following addition of protic acids and alkali and alkaline earth metal ion salts, with the effect being most pronounced for amine and amide substrates. These interactions convert an electron-donating group into a strong electron-withdrawing one, inverting the polarity of the adjacent C−H bonds and decreasing their reactivity toward electrophilic hydrogen atom abstracting species. Following these guidelines, remote non-directed aliphatic C−H bond functionalization of amine, amide, ether, and alcohol substrates has been successfully achieved following deactivation of the proximal C−H bonds via hydrogen bonding, protonation, or Lewis acid complexation at the nitrogen or oxygen center.[13−17]

On the basis of the deactivating effects described above, it can be reasonably expected that in the reactions with an electrophilic HAT reagent an increase in electron density at the C−H bonds that are α to a functional group can produce an opposite effect, namely an activation of these bonds toward HAT, thus enforcing site-selectivity. This increase in electron density can be achieved via hydrogen bonding to a HBD functional group such as the OH group of a primary or secondary alcohol or, more efficiently, by deprotonation of an OH or CO_2H group (Scheme 1, where A represents an hydrogen bond acceptor (HBA) additive and Z = O, CO_2).

Scheme 1. α-C−H Activation via Hydrogen Bonding or Deprotonation



This approach has been successfully exploited by MacMillan for the selective functionalization of alcohol α-C−H bonds[11] and by Studer for the development of a radical based procedure for aromatic hydrodeiodination.[18]

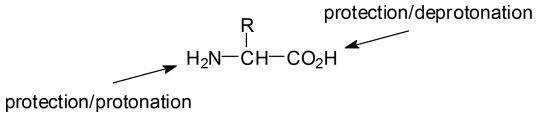
Within this framework, α-amino acids can represent preferential substrates for a detailed understanding of the role of structural and medium effects on HAT from aliphatic C−H bonds. With these substrates the electron density at the α-C−H bond can be strongly influenced by the protonation state of

Received: December 19, 2017

DOI: 10.1021/acs.orglett.7b03948
Org. Lett. XXXX, XXX, XXX−XXX

both the NH_2 and CO_2H groups as well as by introduction of protecting groups (Scheme 2).

Scheme 2. Possible Modifications for α-C−H Activation and Deactivation



Thus, by promoting C−H bond activation or deactivation, structural and medium effects are expected to influence both reactivity and site-selectivity in the reactions of these substrates with electrophilic HAT reagents, allowing discrimination between C−H bonds at the α- and more remote side-chain positions.

Previous studies on the reactions of protonated or *N*-acetylated amino acids with electrophilic Cl$^\bullet$ and HO$^\bullet$ radicals have shown that HAT predominantly occurs from remote side-chain C−H bonds rather than from the weaker α-C−H bond. This behavior has been explained on the basis of an early transition state where polar effects determined by the presence of the electron-withdrawing H_3N^+ or AcNH groups deactivate the proximal C−H bonds toward HAT.[19] Full support of this picture has been provided by computational studies that have probed moreover the matching/mismatching effect of the philicity of both the abstracting radical and C−H bond on HAT.[20] However, although some data on the effect of pH on the reaction of HO$^\bullet$ and *t*BuO$^\bullet$ with amino acids and oligopeptides are available,[21] to the best of our knowledge, no systematic study on the effect of carboxylic group deprotonation on HAT reactivity and site-selectivity is available. This is quite surprising if one considers in particular that the synthesis of modified amino acids and peptides is attracting increasing interest,[22] and that HAT based procedures for aliphatic C−H bond functionalization play an important role in this respect.[23−25]

For this purpose, herein we report on the results of a time-resolved kinetic study in acetonitrile on the effect of CO_2H deprotonation on HAT from the C−H bonds of a series of *N*-*tert*-butoxycarbonyl (*N*-Boc)-protected amino acids to CumO$^\bullet$.[26] The following substrates have been investigated: *N*-Boc-glycine (*N*-BocGlyOH), *N*-Boc-alanine (*N*-BocAlaOH), *N*-Boc-valine (*N*-BocValOH), *N*-Boc-leucine (*N*-BocLeuOH), *N*-Boc-proline (*N*-BocProOH), and *N*-Boc-phenylalanine (*N*-BocPheOH). The study has been also extended to the dipeptide *N*-Boc-glycilglycine (*N*-BocGlyGlyOH). The results have been discussed in comparison with those obtained previously for the corresponding reactions of CumO$^\bullet$ with the neutral form of the amino acids and of the dipeptide.[27]

Efforts have been initially made in order to select a suitable organic base for deprotonation of the amino acid CO_2H group via UV−vis spectrophotometric titration. The base should be soluble in acetonitrile both in the neutral and protonated form, sufficiently strong to promote stoichiometric deprotonation of the *N*-Boc-protected amino acids, and unreactive in its protonated form toward CumO$^\bullet$. 1,8-Diazabicyclo[5.4.0]-undec-7-ene (DBU) has been tested for this purpose (in MeCN pK_a = 24.34 for DBUH$^+$).[28,29] UV−vis titration of MeCN solutions containing *N*-BocAlaOH and *N*-BocPheOH have been carried out employing DBU as the deprotonating base. The spectroscopic analysis displayed in the Supporting Information (Figures S1−S4 and S5−S8 for *N*-BocAlaOH and *N*-BocPheOH, respectively) shows that this base is strong enough to promote stoichiometric deprotonation of both amino acids and has been thus selected for the kinetic studies.

CumO$^\bullet$ has been generated by 355 nm LFP of nitrogen-saturated MeCN or DMSO solutions (T = 25 °C) containing 1.0 M dicumyl peroxide. Under these conditions, CumO$^\bullet$ displays a visible absorption band centered at 485 nm and mainly decays through C−CH_3 β-scission.[30] The k_H for reaction of CumO$^\bullet$ with DBU has been measured employing the laser flash photolysis (LFP) technique, following the decay of the CumO$^\bullet$ visible absorption band as a function of [DBU]. By plotting the observed rate constants (k_{obs}) against [DBU], an excellent linear relationship has been observed and the k_H value has been obtained from the slope of this plot (Figure 1, black circles).

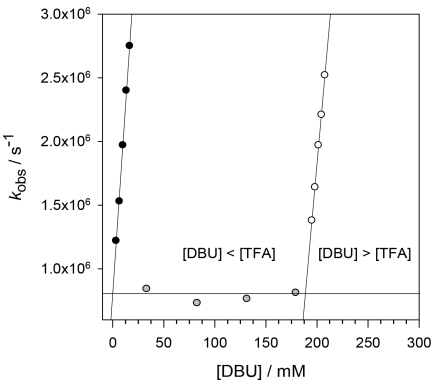
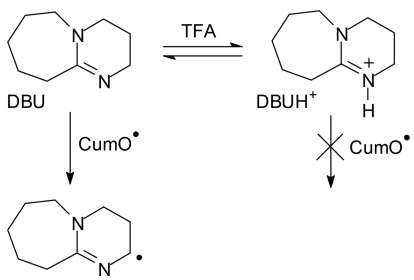


Figure 1. Plots of the observed rate constant (k_{obs}) against [DBU] for the reactions of CumO$^\bullet$ measured in nitrogen-saturated MeCN (black circles) and MeCN containing 0.20 M TFA (gray and white circles) at t = 25 °C following the decay of CumO$^\bullet$ at 490 nm. From the linear regression analysis, MeCN (black circles): $k_H = 1.17 \times 10^8$ M^{-1} s^{-1}, r^2 = 0.9967. MeCN + 0.20 M TFA (white circles, [DBU] > [TFA]): $k_H = 9.00 \times 10^7$ M^{-1} s^{-1}, r^2 = 0.9984.

The k_H value measured in MeCN ($k_H = 1.14 \pm 0.03 \times 10^8$ M^{-1} s^{-1}) is in line with those measured previously under analogous experimental conditions for the reactions of CumO$^\bullet$ with tertiary amines ($k_H = 1-3 \times 10^8$ M^{-1} s^{-1}),[31] where HAT occurs from the α-C−H bonds. This observation strongly supports the hypothesis that HAT from DBU predominantly occurs from the most electron-rich C−H bond (Scheme 3, left).

In the presence of 0.20 M TFA, no increase in k_{obs} has been observed up to [DBU] = [TFA] (Figure 1, gray circles), a behavior that is indicative of stoichiometric DBU protonation

Scheme 3. Effect of TFA on the Reaction of CumO$^\bullet$ with DBU



DOI: 10.1021/acs.orglett.7b03948
Org. Lett. XXXX, XXX, XXX−XXX

by TFA and of strong C−H bond deactivation in $DBUH^+$ toward HAT to $CumO^•$ (Scheme 3, right), as described previously for the effect of TFA on the reactions of $CumO^•$ with other tertiary amines.[12] On the basis of this observation, an upper limit to the rate constant for HAT from $DBUH^+$ to $CumO^•$ could be derived as $k_H < 5 \times 10^4\ M^{-1}\ s^{-1}$. For [DBU] > [TFA], a linear increase in k_{obs} with increasing [DBU] has been observed (Figure 1, white circles), and a k_H value for HAT has been obtained as $k_H = 9.0 \times 10^7\ M^{-1}\ s^{-1}$, a value that is very close to that measured in the absence of TFA indicating that the measured value now reflects HAT from the nonprotonated DBU. By increasing [TFA] to 1.0 M, no increase in k_{obs} has been observed up to [DBU] = [TFA] so that the upper limit to the rate constant for HAT from $DBUH^+$ to $CumO^•$ could be lowered to $k_H < 10^4\ M^{-1}\ s^{-1}$, indicating that protonation determines a greater than 4-order of magnitude decrease in k_H for HAT from the C−H bonds of this substrate to $CumO^•$.

The k_H values for reaction of $CumO^•$ with the *N*-Boc-protected amino acids have been measured analogously by LFP in MeCN containing an equimolar amount of DBU. The pertinent k_{obs} vs [substrate] plots are displayed in the SI (Figures S9−S14). The k_H values thus obtained are collected in Table 1. Also included in Table 1 are the corresponding k_H values measured previously in MeCN,[27] and the rate constant ratios $k_H(DBU)/k_H$.

Table 1. Second-Order Rate Constants (k_H) for Reaction of the Cumyloxyl Radical ($CumO^•$) with *N*-Boc Protected Amino acids, Measured in MeCN at t = 25 °C.[a]

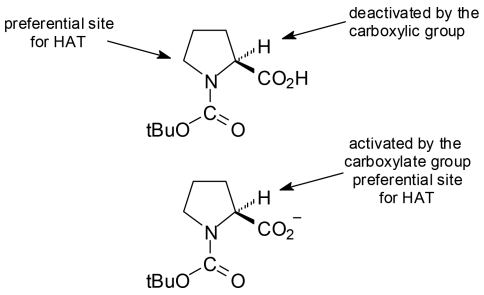
substrate	[DBU][b] (M)	k_H ($M^{-1}\ s^{-1}$)	$k_H(DBU)/k_H$
N-BocGlyOH		$3.96 \pm 0.05 \times 10^5$[c]	
	0.50	$4.4 \pm 0.2 \times 10^6$	11.1
N-BocAlaOH		$2.76 \pm 0.02 \times 10^5$[c]	
	0.50	$2.7 \pm 0.2 \times 10^6$	9.8
N-BocValOH		$1.99 \pm 0.02 \times 10^5$[c]	
	0.50	$3.30 \pm 0.03 \times 10^6$	16.6
N-BocLeuOH		$5.9 \pm 0.2 \times 10^5$[c]	
	0.50	$2.35 \pm 0.03 \times 10^6$	4.0
N-BocProOH		$2.51 \pm 0.08 \times 10^6$[c]	
	0.20	$1.1 \pm 0.1 \times 10^7$	4.4
N-BocPheOH		$3.2 \pm 0.3 \times 10^5$	
	0.40	$2.0 \pm 0.2 \times 10^6$	6.3

[a]Experiments carried out at [substrate] = [DBU]. [b]Initial concentration. [c]Reference 27.

Previous studies have shown that in the reaction of $CumO^•$ with *N*-BocGlyOH, *N*-BocAlaOH, and *N*-BocValOH, HAT occurs exclusively or almost exclusively from the α-C−H bonds.[27] When the reactions of $CumO^•$ with the same substrates were studied in MeCN containing DBU, a ≥10-fold increase in reactivity has been observed, quantified on the basis of the $k_H(DBU)/k_H$ ratios ($k_H(DBU)/k_H$ = 11.1, 9.8 and 16.6 for *N*-BocGlyOH, *N*-BocAlaOH, and *N*-BocValOH, respectively). This behavior can be rationalized on the basis of an increase in electron density at the α-C−H bonds determined by CO_2H deprotonation that leads to a corresponding increase in k_H for HAT from the α-C−H bonds of these amino acids to the electrophilic $CumO^•$.

Smaller activating effects have been instead observed in the reactions of *N*-BocLeuOH, *N*-BocProOH, and *N*-BocPheOH, for which $k_H(DBU)/k_H$ = 4.0, 4.4, and 6.3, respectively. Previous studies have shown that in the reaction of $CumO^•$ with *N*-BocLeuOH, competitive HAT from the α- and γ-C−H bonds occurs.[27] With *N*-BocProOH, HAT predominantly occurs from the δ-C−H bonds,[32] a behavior that has been explained on the basis of the contribution of activating and deactivating polar effects exerted by the carbamate nitrogen and carboxylic group, respectively (Scheme 4, top).[27]

Scheme 4. Effect of CO_2H Deprotonation on HAT from *N*-BocProOH



Comparison between the k_H values measured previously for reaction of $CumO^•$ with *N*-BocGlyOH, *N*-BocAlaOH, and *N*-BocValOH ($k_H = 2.0 \times 10^5$ (statistically corrected for the number of hydrogens at $C_α$), 2.76×10^5, and $1.99 \times 10^5\ M^{-1}\ s^{-1}$, respectively) that, as mentioned above, undergo HAT exclusively or almost exclusively from the α-C−H bonds, with the value measured in this study for the corresponding reaction of *N*-BocPheOH ($k_H = 3.2 \times 10^5\ M^{-1}\ s^{-1}$), indicates that with the latter amino acid competitive HAT from the α-C−H and benzylic β-C−H bonds occurs. Along these line, the lower $k_H(DBU)/k_H$ ratios measured for *N*-BocLeuOH, *N*-BocProOH, and *N*-BocPheOH as compared to *N*-BocGlyOH, *N*-BocAlaOH, and *N*-BocValOH reflect again CO_2H deprotonation promoted by DBU, where, however, the activating effect will now be mainly directed toward the most adjacent hydrogen atom donor site of the former amino acids (Scheme 4, bottom), i.e., the α-C−H bond, influencing to a lesser extent the reactivity of the remote hydrogen atom donor site (namely the γ-C−H bond of *N*-BocLeuOH, δ-C−H bonds of *N*-BocProOH, and β-C−H bonds of *N*-BocPheOH), thus changing the relative reactivity of the two sites and altering the intramolecular selectivity.

In order to probe this mechanistic picture, we have extended the kinetic study to the reaction of $CumO^•$ with the dipeptide *N*-BocGlyGlyOH that in DMSO has been previously shown to undergo competitive HAT from the α-C−H bonds of the two glycine residues with $k_H = 5.8 \times 10^5\ M^{-1}\ s^{-1}$.[27] In the presence of DBU, a 6-fold increase in k_H has been measured ($k_H = 3.5 \times 10^6\ M^{-1}\ s^{-1}$), indicative of a change in the relative reactivity of the two hydrogen atom donor sites, with HAT that now predominantly occurs from the α-C−H bonds of the C-terminal glycine residue, in full agreement with the reactivity and selectivity patterns discussed above for the reactions of *N*-BocLeuOH, *N*-BocProOH, and *N*-BocPheOH.

Taken together, these results clearly show that deprotonation of the carboxylic acid group of amino acids and dipeptides can be successfully employed for α-C−H bond activation toward electrophilic hydrogen atom abstracting species. Kinetic effects that can exceed 1 order of magnitude have been measured, showing moreover that these activating polar effects can strongly influence the intramolecular selectivity. The vast majority of the available HAT-based procedures for aliphatic

DOI: 10.1021/acs.orglett.7b03948
Org. Lett. XXXX, XXX, XXX−XXX

C−H bond functionalization of amino acids and peptides have been carried out on substrates protected at the terminal CO_2H group.[23−25] The results reported herein indicate, however, that, where applicable, deprotonation of this group can represent a powerful tool to implement reactivity and site-selectivity in these processes.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b03948.

UV−vis titrations; plots of k_{obs} vs substrate concentration for the reactions of CumO• (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: michela.salamone@uniroma2.it.
*E-mail: bietti@uniroma2.it.

ORCID

Massimo Bietti: 0000-0001-5880-7614

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Prof. Miquel Costas (University of Girona, Catalonia, Spain) for helpful discussions and Prof. Lorenzo Stella (University of Rome "Tor Vergata", Italy) for the use of the LFP equipment.

■ REFERENCES

(1) (a) Hartwig, J. F.; Larsen, M. A. *ACS Cent. Sci.* **2016**, *2*, 281−292. (b) Hartwig, J. F. *J. Am. Chem. Soc.* **2016**, *138*, 2−24.
(2) Cernak, T.; Dykstra, K. D.; Tyagarajan, S.; Vachal, P.; Krska, S. W. *Chem. Soc. Rev.* **2016**, *45*, 546−576.
(3) (a) Brückl, T.; Baxter, R. D.; Ishihara, Y.; Baran, P. S. *Acc. Chem. Res.* **2012**, *45*, 826−839. (b) Gutekunst, W. R.; Baran, P. S. *Chem. Soc. Rev.* **2011**, *40*, 1976−1991.
(4) Nanjo, T.; de Lucca, E. C., Jr.; White, M. C. *J. Am. Chem. Soc.* **2017**, *139*, 14586−14591.
(5) Kawamata, Y.; Yan, M.; Liu, Z.; Bao, D.-H.; Chen, J.; Starr, J. T.; Baran, P. S. *J. Am. Chem. Soc.* **2017**, *139*, 7448−7451.
(6) (a) Ravelli, D.; Fagnoni, M.; Fukuyama, T.; Nishikawa, T.; Ryu, I. *ACS Catal.* **2018**, *8*, 701−713. (b) Yamada, K.; Fukuyama, T.; Fujii, S.; Ravelli, D.; Fagnoni, M.; Ryu, I. *Chem. - Eur. J.* **2017**, *23*, 8615−8618.
(7) Czaplyski, W. L.; Na, C. G.; Alexanian, E. J. *J. Am. Chem. Soc.* **2016**, *138*, 13854−13857.
(8) Roberts, B. P. *Chem. Soc. Rev.* **1999**, *28*, 25−35.
(9) Boess, E.; Schmitz, C.; Klussmann, M. *J. Am. Chem. Soc.* **2012**, *134*, 5317−5325.
(10) Nielsen, M. K.; Shields, B. J.; Liu, J.; Williams, M. J.; Zacuto, M. J.; Doyle, A. G. *Angew. Chem., Int. Ed.* **2017**, *56*, 7191−7194.
(11) Jeffrey, J. L.; Terrett, J. A.; MacMillan, D. W. C. *Science* **2015**, *349*, 1532−1536.
(12) (a) Salamone, M.; Carboni, G.; Bietti, M. *J. Org. Chem.* **2016**, *81*, 9269−9278. (b) Salamone, M.; Bietti, M. *Acc. Chem. Res.* **2015**, *48*, 2895−2903.
(13) Dantignana, V.; Milan, M.; Cussó, O.; Company, A.; Bietti, M.; Costas, M. *ACS Cent. Sci.* **2017**, *3*, 1350−1358.
(14) Schultz, D. M.; Lévesque, F.; DiRocco, D. A.; Reibarkh, M.; Ji, Y.; Joyce, L. A.; Dropinski, J. F.; Sheng, H.; Sherry, B. D.; Davies, I. W. *Angew. Chem., Int. Ed.* **2017**, *56*, 15274−15278.
(15) Mack, J. B. C.; Gipson, J. D.; Du Bois, J.; Sigman, M. S. *J. Am. Chem. Soc.* **2017**, *139*, 9503−9506.
(16) Lee, M.; Sanford, M. S. *Org. Lett.* **2017**, *19*, 572−575.
(17) Howell, J. M.; Feng, K.; Clark, J. R.; Trzepkowski, L. J.; White, M. C. *J. Am. Chem. Soc.* **2015**, *137*, 14590−14593.
(18) Dewanji, A.; Mück-Lichtenfeld, C.; Studer, A. *Angew. Chem., Int. Ed.* **2016**, *55*, 6749−6752.
(19) Watts, Z. I.; Easton, C. J. *J. Am. Chem. Soc.* **2009**, *131*, 11323−11325.
(20) (a) Chan, B.; Easton, C. J.; Radom, L. *J. Phys. Chem. A* **2015**, *119*, 3843−3847. (b) Amos, R. I. J.; Chan, B.; Easton, C. J.; Radom, L. *J. Phys. Chem. B* **2015**, *119*, 783−788. (c) O'Reilly, R. J.; Chan, B.; Taylor, M. S.; Ivanic, S.; Bacskay, G. B.; Easton, C. J.; Radom, L. *J. Am. Chem. Soc.* **2011**, *133*, 16553−16559.
(21) (a) Easton, C. J.; Kelly, J. B.; Ward, C. M. *J. Chem. Res., Synop.* **1997**, 470−471. (b) Rao, P. S.; Hayon, E. *J. Phys. Chem.* **1975**, *79*, 109−115. (c) Simic, M.; Neta, P.; Hayon, E. *J. Am. Chem. Soc.* **1970**, *92*, 4763−4768.
(22) See, for example: (a) Sengupta, S.; Mehta, G. *Tetrahedron Lett.* **2017**, *58*, 1357−1372. (b) Rémond, E.; Martin, C.; Martinez, J.; Cavelier, F. *Chem. Rev.* **2016**, *116*, 11654−11684. (c) Clerici, F.; Erba, E.; Gelmi, M. L.; Pellegrino, S. *Tetrahedron Lett.* **2016**, *57*, 5540−5550. (d) Salwiczek, M.; Nyakatura, E. K.; Gerling, U. I. M.; Ye, S.; Koksch, B. *Chem. Soc. Rev.* **2012**, *41*, 2135−2171.
(23) Osberger, T. J.; Rogness, D. C.; Kohrt, J. T.; Stepan, A. F.; White, M. C. *Nature* **2016**, *537*, 214−219.
(24) Easton, C. J. *Chem. Rev.* **1997**, *97*, 53−82.
(25) (a) Annese, C.; Fanizza, I.; Calvano, C. D.; D'Accolti, L.; Fusco, C.; Curci, R.; Williard, P. G. *Org. Lett.* **2011**, *13*, 5096−5099. (b) Rella, M. R.; Williard, P. G. *J. Org. Chem.* **2007**, *72*, 525−531. (c) Saladino, R.; Mezzetti, M.; Mincione, E.; Torrini, I.; Paglialunga Paradisi, M.; Mastropietro, G. *J. Org. Chem.* **1999**, *64*, 8468−8474.
(26) Protection of the NH_2 group was required in order to ensure solubility under the experimental conditions employed.
(27) Salamone, M.; Basili, F.; Bietti, M. *J. Org. Chem.* **2015**, *80*, 3643−3650.
(28) Kaljurand, I.; Kütt, A.; Soovälli, L.; Rodima, T.; Mäemets, V.; Leito, I.; Koppel, I. A. *J. Org. Chem.* **2005**, *70*, 1019−1028.
(29) 1,1,3,3-Tetramethylbutylamine (*tert*-octylamine) and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) have been also tested as bases. Full details are given in the Supporting Information.
(30) Salamone, M.; Bietti, M. *Synlett* **2014**, *25*, 1803−1816.
(31) (a) Finn, M.; Friedline, R.; Suleman, N. K.; Wohl, C. J.; Tanko, J. M. *J. Am. Chem. Soc.* **2004**, *126*, 7578−7584. (b) Pischel, U.; Nau, W. M. *J. Am. Chem. Soc.* **2001**, *123*, 9727−9737.
(32) Burgess, V. A.; Easton, C. J.; Hay, M. P. *J. Am. Chem. Soc.* **1989**, *111*, 1047−1052.

DOI: 10.1021/acs.orglett.7b03948
Org. Lett. XXXX, XXX, XXX−XXX