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# Transition-metal-free, room-temperature radical azidofluorination of unactivated alkenes in aqueous solution†‡

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We report herein the transition-metal-free azidofluorination of unactivated alkenes. Thus, the condensation of various alkenes with $TMSN_3$ and Selectfluor in aqueous $CH_3CN$ at RT led to the efficient and regioselective synthesis of β-fluorinated alkyl azides with excellent functional group compatibility and good stereoselectivity. A single electron transfer mechanism involving the oxidative generation of azidyl radicals is proposed.

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The growing importance of fluorine in agrochemicals and pharmaceuticals[1] as well as the use of $^{18}$F-labeled organic compounds as contrast agents for positron emission tomography (PET)[2] has spurred vigorous research for the development of new methods for C–F bond formation under mild conditions.[3] In this context, the synthesis of β-fluorinated amines has received considerable attention in the past few years. Vicinal aminofluorine moieties are key building blocks of anticancer, anticholinergic and anti-inflammatory drugs[4] as well as therapeutic β-peptides[5] because fluorine can improve the bioavailability of amine drugs by decreasing the basicity of neighboring amine groups. Among various methods developed,[6] the aminofluorination[7,8] of alkenes provides rapid access to this type of molecule. For example, palladium-catalyzed intramolecular aminofluorination of *N*-tosyl-4-pentenyl amines with AgF led to the synthesis of 3-fluoropiperidines.[7a] This fluorocyclization could be carried out enantioselectively using chiral [$ArIF_2$] reagents.[8f] Enantioselective intramolecular aminofluorination of indoles and conjugated dienes with Selectfluor[9] under organocatalysis[7b] or chiral-anion phase-transfer catalysis[7g] was also achieved. However, only limited examples of intermolecular aminofluorination were reported[8] and they were restricted to the use of glycals,[8a] stilbenes,[8b] styrenes[8c,d,f] and other activated alkenes such as α,β-unsaturated aldehydes.[8e] A general and efficient intermolecular aminofluorination of unactivated alkenes is certainly highly desirable in view of the important role of β-fluorinated amines in medicinal chemistry. Herein we report a variant of intermolecular aminofluorination, the unprecedented azidofluorination of unactivated alkenes under transition metal-free conditions.

Our idea originated from our recent finding that, under the catalysis of $AgNO_3$, the reactions of aliphatic carboxylic acids with Selectfluor resulted in oxidative fluorodecarboxylation.[10a] This was then successfully extended to the intramolecular radical[11,12] aminofluorination of *N*-aryl-4-pentenamides in aqueous media.[10b] We envisioned that an intermolecular version of the above aminofluorination might be achieved under similar conditions. To test this idea, we chose *N*-(pent-4-en-1-yl)phthalimide (**A-1**) as the model alkene to screen a suitable nitrogen partner. Thus a number of amides or sulfonamides, including AcNHPh, BzNHPh, BzNHMe, TsNHMe and TfNHPh, were subjected to treatment with **A-1**, Selectfluor and a catalytic amount of $AgNO_3$ (20 mol%) in aqueous $CH_3CN$ or $CH_2Cl_2$ solution at ambient temperature. To our disappointment, no reaction occurred in all cases. However, when $TMSN_3$ was used as the nitrogen source, we were delighted to see that the corresponding azidofluorination product **1** was observed. We then went on to optimize the reaction conditions (Table 1). We found that $AgNO_3$ was not required at all for the azidofluorination, and the direct treatment of **A-1** with Selectfluor (2 equiv.) and $TMSN_3$ (2 equiv.) in $CH_3CN$–$H_2O$ (1 : 1) at room temperature for 5 h afforded β-fluoroalkyl azide **1** in 59% yield along with the bis-azidation product **1D** in 29% yield (entry 2). Switching the mixed solvent to acetone–$H_2O$ or AcOH–$H_2O$ did not modulate yield or selectivity (entries 3 and 4). On the other hand, no azidofluorination could be observed in biphasic systems or in anhydrous organic solvents such as DMSO or acetonitrile (entries 5 and 6). Increasing the ratio of $H_2O$–$CH_3CN$ from 1 : 1 to 2 : 1 slightly improved the yield of **1** (entry 7). Changing the reaction temperature did not help (not shown). In order to inhibit bis-azidation, various additives

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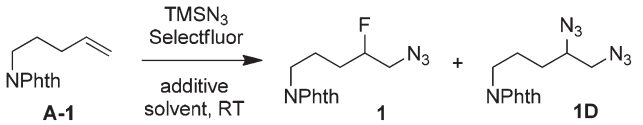
**Table 1** Optimization of reaction conditions

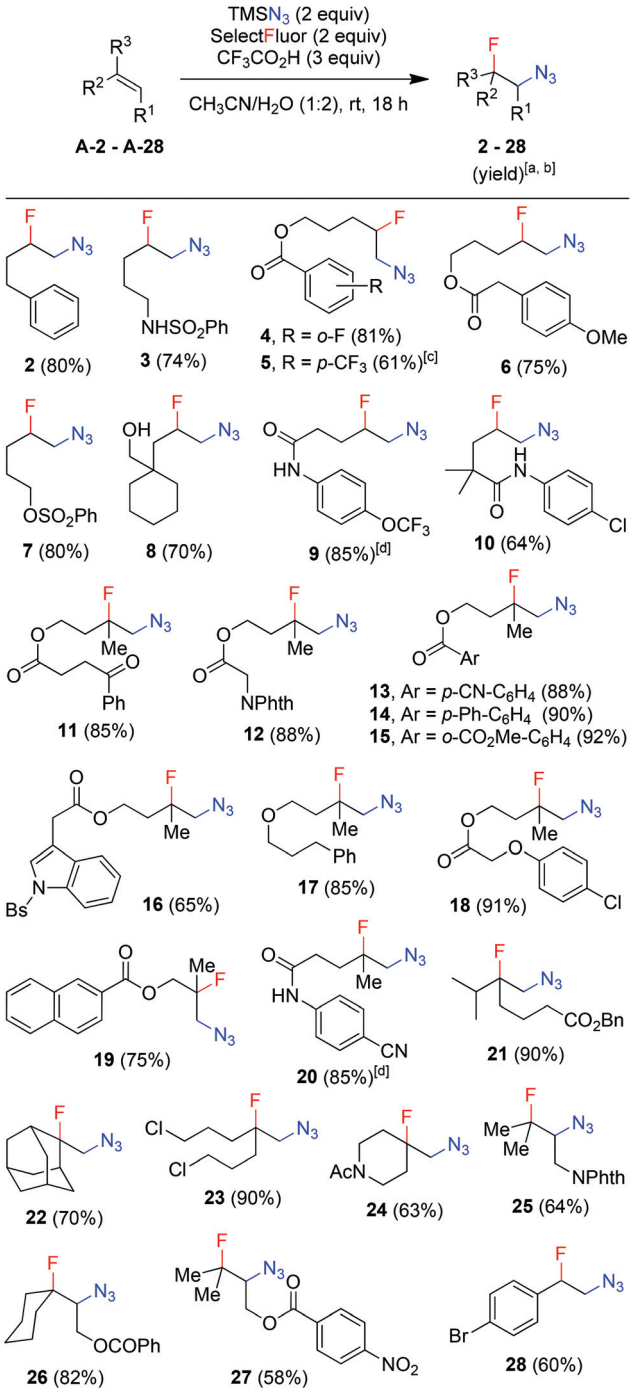



| Entry[a] | Solvent | Additive (equiv.) | Yield[b] (%) 1 | 1D |
|---|---|---|---|---|
| 1 | $CH_3CN–H_2O$ (1 : 1) | $AgNO_3$ (0.2) | 50 | 30 |
| 2 | $CH_3CN–H_2O$ (1 : 1) | None | 59 | 29 |
| 3 | $Me_2CO–H_2O$ (1 : 1) | None | 52 | 32 |
| 4 | $AcOH–H_2O$ (1 : 1) | None | 58 | 29 |
| 5 | $CH_2Cl_2–H_2O$ (1 : 1) | None | 0 | 0 |
| 6 | DMSO, $CH_2Cl_2$, $CH_3CN$, or AcOH | None | 0 | 0 |
| 7 | $CH_3CN–H_2O$ (1 : 2) | None | 64 | 25 |
| 8 | $CH_3CN–H_2O$ (1 : 2) | NaOAc (2) | 40 | 20 |
| 9[c] | $CH_3CN–H_2O$ (1 : 2) | $HNO_3$ (2) | 84 | 7 |
| 10[c] | $CH_3CN–H_2O$ (1 : 2) | TFA (2) | 80 | 8 |
| **11**[c] | **$CH_3CN–H_2O$ (1 : 2)** | **TFA (3)** | **85** | **<5** |
| 12[c] | $CH_3CN–H_2O$ (1 : 2) | TfOH (3) | 68 | 7 |
| 13[c] | $CH_3CN–H_2O$ (1 : 2) | TsOH (3) | 76 | 5 |

[a] Reaction conditions: **A-1** (0.3 mmol), $TMSN_3$ (0.6 mmol), Selectfluor (0.6 mmol), solvent (3 mL), RT, 5 h. [b] $^1H$ NMR yield based on **A-1** with *p*-nitroacetophenone as the internal standard. [c] Reaction time: 18 h.

were screened. The use of NaOAc or $K_2CO_3$ as a base decreased the yield of **1** (entry 8). These phenomena urged us to test the effect of acids other than AcOH. Indeed, with an acid such as TsOH, TfOH, $CF_3CO_2H$ (TFA) or even $HNO_3$ as the additive, the yield of **1D** was decreased. The use of these additives requires a longer reaction time (18 h) for complete conversion (entries 9–13). In the case of TFA (3 equiv.) as the additive, the reaction furnished the desired product **1** in 85% NMR yield (83% isolated yield) while only a small amount of byproduct **1D** could be observed by $^1H$ NMR (entry 11). To the best of our knowledge, this is the first example of azidofluorination of unsaturated carbon–carbon bonds. It is worth mentioning that no azidofluorination could be detected when the fluorine source was changed from Selectfluor to *N*-fluorobis(benzenesulfonyl)-imide (NFSI). Note that the azidofluorination also proceeded with $NaN_3$ as the substitute for $TMSN_3$, but in lower (63%) efficiency.

With the optimized conditions in hand (entry 11, Table 1), we set out to explore the scope and limitations of the above azidofluorination (Scheme 1). The alkene substrate scope proved quite general as not only various unactivated mono- and di-substituted alkenes but also tri-substituted alkenes participated in the azidofluorination reactions effectively. In addition, styrenes could also be used as substrates, as exemplified by the synthesis of azide **28**. Nevertheless, electron-deficient alkenes such as methyl acrylate failed to give the desired product. A wide range of functional groups were well tolerated, including unprotected and protected alcohol, protected amine, alkyl chloride, ether, ketone, ester, sulfonate, amide, sulfonamide, nitrile and N-protected indole. Excellent regioselectivity was observed as the azido group reliably added




**Scheme 1** Azidofluorination of alkenes. [a] Reaction conditions: alkene (0.3 mmol), $TMSN_3$ (0.6 mmol), Selectfluor (0.6 mmol), $CF_3CO_2H$ (0.9 mmol), $CH_3CN$ (1 mL), $H_2O$ (2 mL), RT, 18 h. [b] Isolated yield based on the substrate alkene. [c] The substrate alkene was recovered in 26% yield. [d] AcOH (1 mL) and $H_2O$ (2 mL) were used as the solvent.

to the less sterically hindered carbon of the C=C bond. Moreover, stereoselective azidofluorination could also be achieved. For example, the reaction of norbornene **A-29** gave the *cis*-addition product **29** as the only stereoisomer isolated (eqn (1)). A high diastereoselectivity (>10 : 1) was also obtained in the

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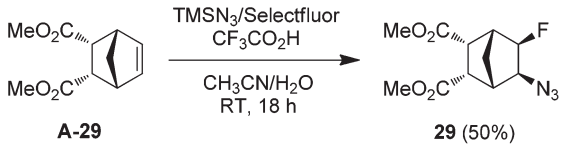
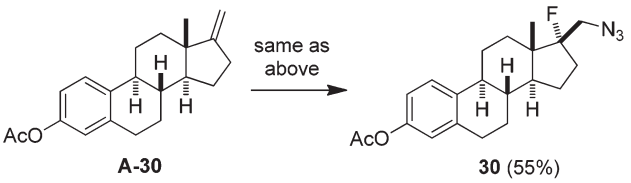
reaction of 17-methylene steroid **A-30** (eqn (2)). Thus, the above azidofluorination provides a convenient and efficient entry to β-fluorinated alkyl azides,[13] which can be readily converted to the corresponding β-fluorinated amines by reduction (see also ESI‡).[13] More importantly, by taking advantage of the versatility of alkyl azides in organic synthesis,[14] β-fluoroalkyl azides can be elaborated into a variety of fluorinated molecules *via* cycloaddition, rearrangement, nitrene chemistry, *etc.*, thus expanding the application of the above azidofluorination reactions (see also ESI‡).

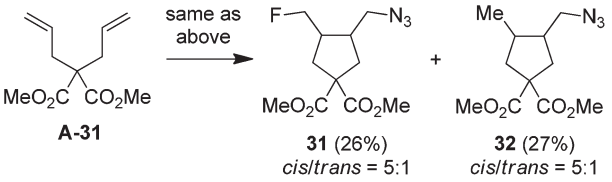
It should be noted that, while a small amount (~5%) of bis-azidation products similar to **1D** could be observed in the cases of monosubstituted alkenes, such byproducts were further suppressed using di- and tri-substituted alkenes and the yields of β-fluoroalkyl azides were generally higher in the reactions of di-substituted terminal alkenes. Presumably the second-step azidation (to give bis-azidation products) is more sensitive to steric hindrance than the fluorination (to give azido-fluorination products). Moreover, a number of substrates capable of electrophilic fluorocyclization[15] with Selectfluor failed to display this competitive behaviour, yielding only the azidofluorination products (**3**, **8–10**, **20**) in high yields. These results also shed light on the mechanism, indicating that the fluorination does not proceed through a carbocationic intermediate. To gain more insight into the mechanism, the reaction of 1,6-diene **A-31** was carried out. Under the above optimized conditions, the cyclized products **31** (26%) and **32** (27%) were isolated, both in preference for the *cis*-configuration (eqn (3)). This result strongly suggests the azidyl radical-mediated free radical mechanism for azidofluorination.[16] Furthermore, vinyl cyclopropane **A-33** was employed as a radical probe.[16] The reaction of **A-33** under the above optimized conditions was slow probably because of its poor solubility in aqueous $CH_3CN$. When a small amount of $CH_2Cl_2$ was added to improve the solubility of **A-33**, the reaction cleanly afforded the ring-opening product, **33**, in 49% yield along with 23% recovered **A-33** (eqn (4)). This experiment provides evidence for the involvement of carbon-centered radicals in the above azidofluorination.



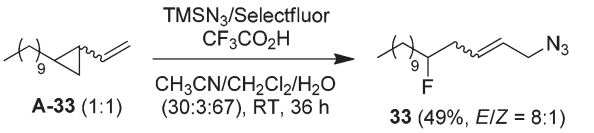

(1)




(2)




(3)




(4)

Although the detailed mechanism remains unclear, a tentative mechanism was proposed based on the above results, as shown in Fig. 1. In aqueous acidic solution $TMSN_3$ is quickly decomposed to hydrazoic acid,[14b,17] which then undergoes single electron transfer (SET) with Selectfluor to generate an azidyl radical[18–21] and a Selectfluor radical anion.[22] The electrophilic[23] azidyl radical adds to an alkene to give the nucleophilic β-azidoalkyl radical. The subsequent fluorine atom transfer from the Selectfluor radical anion to the β-azidoalkyl radical affords the azidofluorination product.[24] The formation of bis-azidation products[18] such as **1D** might result from the coupling between the β-azidoalkyl radical and another azidyl radical. The addition of TFA slows down the SET process and thus the concentration of azidyl radical is kept in a low concentration range. As a result, the bis-azidation byproduct is significantly inhibited.

In conclusion, we have successfully developed a transition-metal-free regioselective azidofluorination reaction of unactivated alkenes with $TMSN_3$ and Selectfluor, providing rapid and efficient access to β-fluorinated alkyl azides. The reaction proceeds in aqueous media at room temperature and exhibits broad substrate scope, wide functional group compatibility as well as good stereoselectivity. The above results further expand the scope of radical fluorination,[10–12] which is emerging as a versatile and powerful tool for $C(sp^3)$–F bond formation. In view of the importance of fluorine and the rich chemistry of alkyl azides, the azidofluorination should find broad applications in organic synthesis.

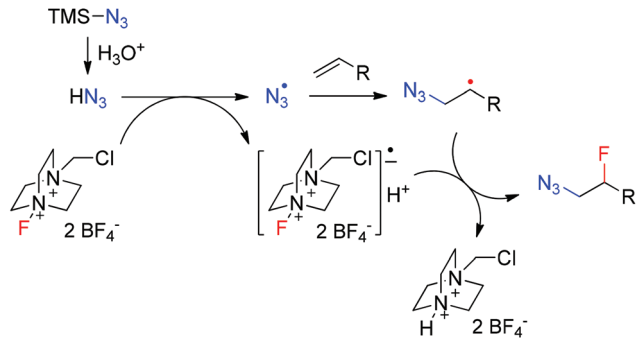



**Fig. 1** Proposed mechanism of azidofluorination.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## Experimental section

### Typical procedure for the azidofluorination of unactivated alkenes

2-(Pent-4-en-1-yl)-isoindoline-1,3-dione (**A-1**, 64.5 mg, 0.3 mmol) and Selectfluor (212 mg, 0.6 mmol) were placed in a Schlenk tube under a nitrogen atmosphere. $CF_3CO_2H$ (69 μL, 0.9 mmol), $TMSN_3$ (78 μL, 0.6 mmol), $CH_3CN$ (1 mL) and water (2 mL) were then added successively at RT. The reaction mixture was stirred at RT for 18 h. The resulting mixture was extracted with $CH_2Cl_2$ (15 mL × 3). The combined organic phase was dried over anhydrous $Na_2SO_4$. After the removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane–ethyl acetate (7 : 1, v/v) as the eluent to give the pure product 2-(5-azido-4-fluoropentyl)isoindoline-1,3-dione (**1**) as a yellow oil. Yield: 68 mg (83%).

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## References

1 (*a*) K. Müller, C. Faeh and F. Diederich, *Science*, 2007, **317**, 1881–1886; (*b*) D. O'Hagan, *Chem. Soc. Rev.*, 2008, **37**, 308–319; (*c*) S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, *Chem. Soc. Rev.*, 2008, **37**, 320–330; (*d*) K. L. Kirk, *Org. Process Res. Dev.*, 2008, **12**, 305–321.

2 (*a*) P. W. Miller, N. J. Long, R. Vilar and A. D. Gee, *Angew. Chem.*, 2008, **120**, 9136–9172, (*Angew. Chem. Int. Ed.*, 2008, **47**, 8998–9033); (*b*) S. M. Ametamey, M. Horner and P. A. Schubiger, *Chem. Rev.*, 2008, **108**, 1501–1516.

3 For the latest selected reviews, see: (*a*) V. V. Grushin, *Acc. Chem. Res.*, 2010, **43**, 160–171; (*b*) T. Furuya, J. E. M. N. Klein and T. Ritter, *Synthesis*, 2010, 1804–1821; (*c*) T. Furuya, A. S. Kamlet and T. Ritter, *Nature*, 2011, **473**, 470–477; (*d*) T. Liang, C. N. Neumann and T. Ritter, *Angew. Chem.*, 2013, **125**, 8372–8423, (*Angew. Chem. Int. Ed.*, 2013, **52**, 8214–8264).

4 (*a*) C. D. Cox, *et al.*, *J. Med. Chem.*, 2008, **51**, 4239–4252; (*b*) J. T. Welch and S. Eswarakrishman, *Fluorine in Bio-organic Chemistry*, Wiley, New York, 1991.

5 D. Seebach, *et al.*, *Helv. Chim. Acta*, 2008, **91**, 1736–1786.

6 For a review, see: J. M. Percy, *Sci. Synth.*, 2005, **34**, 379–416. For the latest example of the synthesis of β-fluorinated amines via ring opening of aziridines, see: J. A. Kalow and A. G. Doyle, *Tetrahedron*, 2013, **69**, 5702–5709.

7 (*a*) T. Wu, G. Yin and G. Liu, *J. Am. Chem. Soc.*, 2009, **131**, 16354–16355; (*b*) O. Lozano, G. Blessley, T. M. del Campo, A. L. Thompson, G. T. Giuffredi, M. Bettati, M. Walker, R. Borman and V. Gouverneur, *Angew. Chem.*, 2011, **123**, 8255–8259, (*Angew. Chem. Int. Ed.*, 2011, **50**, 8105–8109); (*c*) T. Xu, X. Mu, H. Peng and G. Liu, *Angew. Chem.*, 2011, **123**, 8326–8329, (*Angew. Chem. Int. Ed.*, 2011, **50**, 8176–8179); (*d*) Q. Wang, W. Zhong, X. Wei, M. Ning, X. Meng and Z. Li, *Org. Biomol. Chem.*, 2012, **10**, 8566–8569; (*e*) T. Xu and G. Liu, *Org. Lett.*, 2012, **14**, 5416–5419; (*f*) H.-T. Huang, T. C. Lacy, B. Blachut, G. X. Ortiz Jr. and Q. Wang, *Org. Lett.*, 2013, **15**, 1818–1821; (*g*) H. P. Shunatona, N. Früh, Y.-M. Wang, V. Rauniyar and F. D. Toste, *Angew. Chem.*, 2013, **125**, 7878–7881, (*Angew. Chem. Int. Ed.*, 2013, **52**, 7724–7727).

8 (*a*) S. P. Vincent, M. D. Burkart, C.-Y. Tsai, Z. Zhang and C.-H. Wong, *J. Org. Chem.*, 1999, **64**, 5264–5279; (*b*) S. Manandhar, R. P. Singh, G. V. Eggers and J. M. Shreeve, *J. Org. Chem.*, 2002, **67**, 6415–6420; (*c*) J. S. Yadav, B. V. S. Reddy, D. N. Chary and D. Chandrakanth, *Tetrahedron Lett.*, 2009, **50**, 1136–1138; (*d*) S. Qiu, T. Xu, J. Zhou, Y. Guo and G. Liu, *J. Am. Chem. Soc.*, 2010, **132**, 2856–2857; (*e*) C. Appayee and S. E. Brenner-Moyer, *Org. Lett.*, 2010, **12**, 3356–3359; (*f*) W. Kong, P. Feige, T. de Haro and C. Nevado, *Angew. Chem.*, 2013, **125**, 2529–2533, (*Angew. Chem. Int. Ed.*, 2013, **52**, 2469–2473).

9 (*a*) R. P. Singh and J. M. Shreeve, *Acc. Chem. Res.*, 2004, **37**, 31–44; (*b*) P. T. Nyffeler, S. G. Durón, M. D. Burkart, S. P. Vincent and C.-H. Wong, *Angew. Chem.*, 2005, **117**, 196–217, (*Angew. Chem. Int. Ed.*, 2005, **44**, 192–212).

10 (*a*) F. Yin, Z. Wang, Z. Li and C. Li, *J. Am. Chem. Soc.*, 2012, **134**, 10401–10404; (*b*) Z. Li, L. Song and C. Li, *J. Am. Chem. Soc.*, 2013, **135**, 4640–4643; (*c*) C. Zhang, Z. Li, L. Zhu, L. Yu, Z. Wang and C. Li, *J. Am. Chem. Soc.*, 2013, **135**, 14082–14085.

11 For a highlight on radical fluorination, see: M. P. Sibi and Y. Landais, *Angew. Chem.*, 2013, **125**, 3654–3656, (*Angew. Chem. Int. Ed.*, 2013, **52**, 3570–3572).

12 (*a*) M. Rueda-Becerril, C. C. Sazepin, J. C. T. Leung, T. Okbinoglu, P. Kennepohl, J.-F. Paquin and G. M. Sammis, *J. Am. Chem. Soc.*, 2012, **134**, 4026–4029; (*b*) J. C. T. Leung, C. Chatalova-Sazepin, J. G. West, M. Rueda-Becerril, J.-F. Paquin and G. M. Sammis, *Angew. Chem.*, 2012, **124**, 10962–10965, (*Angew. Chem. Int. Ed.*, 2012, **51**, 10804–10807); (*c*) S. Bloom, C. R. Pitts, D. C. Miller, N. Haselton, M. G. Holl, E. Urheim and T. Lectka, *Angew. Chem.*, 2012, **124**, 10732–10735, (*Angew. Chem. Int. Ed.*, 2012, **51**, 10580–10583); (*d*) W. Liu, X. Huang, M.-J. Cheng, R. J. Nielsen, W. A. Goddard III and J. T. Groves, *Science*, 2012, **337**, 1322–1325; (*e*) T. J. Barker and D. L. Boger, *J. Am. Chem. Soc.*, 2012, **134**, 13588–13591; (*f*) S. Mizuta, *et al.*, *Org. Lett.*, 2013, **15**, 2648–2651.

13 β-Fluorinated alkyl azides were typically synthesized from classical nucleophilic substitution reactions of $NaN_3$ or the conversion of alcohols to fluorides by DAST. For examples, see: (*a*) J. A. D. Good, F. Wang, O. Rath, H. Y. K. Kaan, S. K. Talapatra, D. Podgorski, S. P. MacKay and F. Kozielski, *J. Med. Chem.*, 2013, **56**, 1878–1893; (*b*) V. Mascitti, *et al.*,

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*Bioorg. Med. Chem. Lett.*, 2011, **21**, 1306–1309; (*c*) F. Xue, J. Fang, W. W. Lewis, P. Martasek, L. J. Roman and R. B. Silverman, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 554–557; (*d*) R. Sasson and S. Rozen, *J. Fluorine Chem.*, 2006, **127**, 962–965; (*e*) S. C. Annedi, W. Li, S. Samson and L. P. Kotra, *J. Org. Chem.*, 2003, **68**, 1043–1049; (*f*) S. M. Andersen, M. Ebner, C. W. Ekhart, G. Gradnig, G. Legler, I. Lundt, A. E. Stutz, S. G. Withers and T. Wrodnigg, *Carbohydr. Res.*, 1997, **301**, 155–166; (*g*) T. Kajimoto, K. K.-C. Liu, R. L. Pederson, Z. Zhong, Y. Ichikawa, J. A. Proco Jr. and C.-H. Wong, *J. Am. Chem. Soc.*, 1991, **113**, 6187–6196.

14 For selected reviews on organic azides, see: (*a*) S. Bräse, C. Gil, K. Knepper and V. Zimmermann, *Angew. Chem.*, 2005, **117**, 5320–5374, (*Angew. Chem. Int. Ed.*, 2005, **44**, 5188–5240); (*b*) *Organic Azides: Syntheses and Applications*, ed. S. Bräse and K. Banert, Wiley, Chichester, UK, 2010.

15 For selected examples of electrophilic fluorocyclization, see: (*a*) V. Rauniyar, A. D. Lackner, G. L. Hamilton and F. D. Toste, *Science*, 2011, **334**, 1681–1684; (*b*) Y. A. Serguchev, L. F. Lourie, M. V. Ponomarenko, E. B. Rusanov and N. V. Ignat'ev, *Tetrahedron Lett.*, 2011, **52**, 5166–5169; (*c*) S. C. Wilkinson, O. Lozano, M. Schuler, M. C. Pacheco, R. Salmon and V. Gouverneur, *Angew. Chem.*, 2009, **121**, 7217–7220, (*Angew. Chem. Int. Ed.*, 2009, **48**, 7083–7086); (*d*) L. F. Lourie, Y. A. Serguchev, G. V. Shevchenko, M. V. Ponomarenko, A. N. Chernega, E. B. Rusanov and J. A. K. Howard, *J. Fluorine Chem.*, 2006, **127**, 377–385.

16 M. Newcomb, in *Radicals in Organic Synthesis*, ed. P. Renaud and M. P. Sibi, Wiley-VCH, Weinheim, Germany, 2001, vol. 1, pp. 317–336.

17 M. Jafarzadeh, *Synlett*, 2007, 2144–2145.

18 For reviews on the oxidative generation of azidyl radicals, see: (*a*) S. D. Jong, D. G. Nosal and D. J. Wardrop, *Tetrahedron*, 2012, **68**, 4067–4105; (*b*) F. Minisci, *Acc. Chem. Res.*, 1975, **8**, 165–171.

19 For selected examples of oxidative generation of azidyl radicals from $TMSN_3$, see: (*a*) P. Magnus, M. B. Roe and C. Hulme, *J. Chem. Soc., Chem. Commun.*, 1995, 263–265; (*b*) P. Magnus, J. Lacour, P. A. Evans, M. B. Roe and C. Hulme, *J. Am. Chem. Soc.*, 1996, **118**, 3406–3418; (*c*) C. Tang and N. Jiao, *J. Am. Chem. Soc.*, 2012, **134**, 18924–18927; (*d*) K. Matcha and A. P. Antonchick, *Angew. Chem.*, 2013, **125**, 2136–2140, (*Angew. Chem. Int. Ed.*, 2013, **52**, 2082–2086); (*e*) K. Matcha, R. Narayan and A. P. Antonchick, *Angew. Chem.*, 2013, **125**, 8143–8147, (*Angew. Chem. Int. Ed.*, 2013, **52**, 7985–7989).

20 For a review on radical azidation reactions, see: C. Jimeno and P. Renaud, in *Organic Azides: Syntheses and Applications*, ed. S. Bräse and K. Banert, Wiley, Chichester, UK, 2010, pp. 239–267.

21 For the latest example of the generation of azidyl radicals *via* single electron transfer, see: B. Zhang and A. Studer, *Org. Lett.*, 2013, **15**, 4548–4551.

22 X. Zhang, Y. Liao, R. Qian, H. Wang and Y. Guo, *Org. Lett.*, 2005, **7**, 3877–3880.

23 M. S. Workentin, B. D. Wagner, J. Lusztyk and D. D. M. Wayner, *J. Am. Chem. Soc.*, 1995, **117**, 119–126.

24 The F-abstraction of β-azidoalkyl radicals from Selectfluor reagent is unlikely in aqueous solution based on our previous mechanistic study. For details, see ref. 10*a*.

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