JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

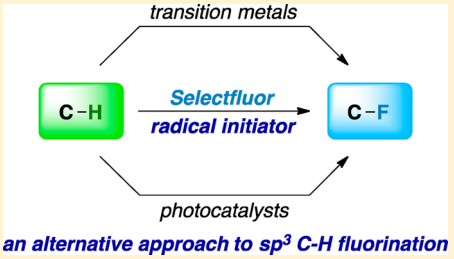
Triethylborane-Initiated Radical Chain Fluorination: A Synthetic Method Derived from Mechanistic Insight

Cody Ross Pitts, Bill Ling, Ryan Woltornist, Ran Liu, and Thomas Lectka*

Department of Chemistry, Johns Hopkins University, 3400 North Charles Street, Baltimore, Maryland 21218, United States

Supporting Information

ABSTRACT: We offer a mild, metal-free sp^3 C−H fluorination alternative using Selectfluor and a substoichiometric amount of triethylborane—an established radical initiator in the presence of O_2. This radical-chain-based synthetic method is particularly noteworthy as an offspring of the insight gained from a mechanistic study of copper-promoted aliphatic fluorination, constructively turning O_2 from an enemy to an ally. Furthermore, BEt_3/O_2 is a preferred initiator in industrial processes, as it is economical, is low in toxicity, and lends way to easier workup.



Though the elucidation of a reaction mechanism can be troublesome, it can provide the insight into developing a new synthetic method that would otherwise remain undiscovered. For example, our laboratory recently investigated the mechanism of the copper(I)/Selectfluor sp^3 C−H fluorination system.[1] We reported a detailed scheme whereby Selectfluor **1** is used to generate the radical dication species **2** (via inner-sphere electron transfer from copper(I), accompanied by loss of fluoride) responsible for H atom abstraction, generating an alkyl radical. This radical, in turn, reacts homolytically with Selectfluor to yield the desired fluorinated product and to regenerate the radical dication, which propagates the chain. Considering that copper(I) proved to be unnecessary during the H atom abstraction and fluorination stages of the mechanism and the radical dication chain propagator is generated by a homolytic cleavage of the N−F bond in Selectfluor, we gathered that a catalytic amount of an established "radical initiator" in the presence of Selectfluor and a substrate should also effect C−H fluorination in a similar fashion (Figure 1). If true, this mechanistic hypothesis permits us to design a new radical chain fluorination method rationally by choosing an appropriate initiator. Beyond proof of concept, alternative manners of initiating the same chain propagation can be envisioned that are advantageous over existing methods.

A number of radical initiators that might be suitable surrogates come to mind, including (but not limited to) halogens, AIBN, organic peroxides, and inorganic peroxides;[2] however, more punishing conditions such as heat or ultraviolet light are typically necessary to generate the radicals, which may also foster issues regarding selectivity. On the other hand, triethylborane famously undergoes a homolytic substitution (S_H2) reaction with triplet O_2 at room temperature (or lower), from which an ethyl radical is liberated.[3] Conceivably, this ethyl radical will behave like any other alkyl radical in our system to create the volatile and easily removed fluoroethane upon reaction with Selectfluor and the desired radical dication **2**, thus initiating the fluorination reaction. Furthermore, in an industrial

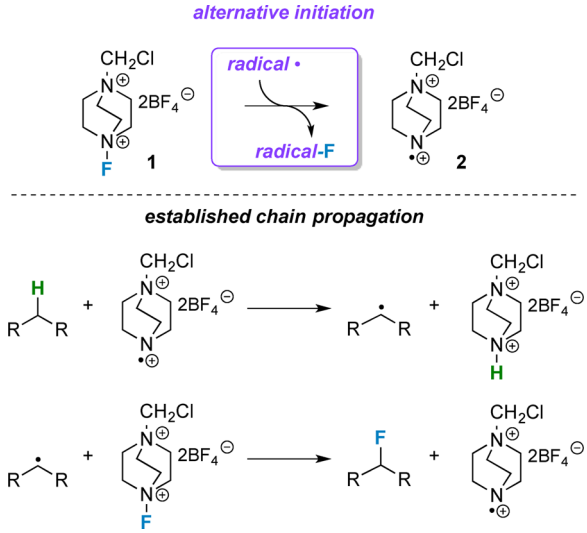


Figure 1. Hypothesized alternative initiation to sp^3 C−H fluorination method.

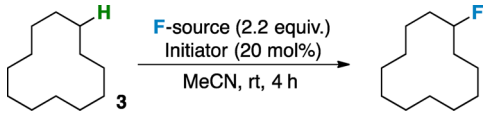
setting, BEt_3/O_2 is the preferred radical initiator wherever possible, as the reagent is atom-economical, is low in toxicity, and lends way to easier workup.[4] Accordingly, we explored the possibility of effecting this reaction by implementing a catalytic amount of triethylborane, Selectfluor, and a substrate.

We examined a variety of conditions with cyclododecane **3** as a test substrate (Table 1) and were satisfied to find that stirring 1.0 equiv of cyclododecane with 20 mol % of triethylborane (administered as a 1.0 M solution in hexanes) and 2.2 equiv of Selectfluor in anhydrous MeCN (with no measures taken to remove dissolved O_2) at room temperature under N_2 will produce 1-fluorocyclodecane in 50% yield after 4 h.[5] The same

Received: July 9, 2014
Published: August 19, 2014

   dx.doi.org/10.1021/jo501520e | J. Org. Chem. 2014, 79, 8895−8899

Table 1. Screening for Reaction Initiation Conditions



entry	initiator	F source	yield (%)
1		Selectfluor	0
2	**BEt_3**	**Selectfluor**	**50**
4	$B(sec\text{-butyl})_3$	Selectfluor	0
5	BEt_3	NFSI	0
6	BEt_3/Ph_3SnH	Selectfluor	4
7	BEt_3/R_3SiH	Selectfluor	8
8	$ZnEt_2$	Selectfluor	4

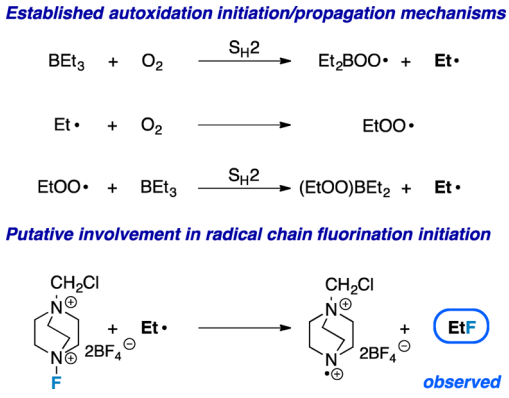
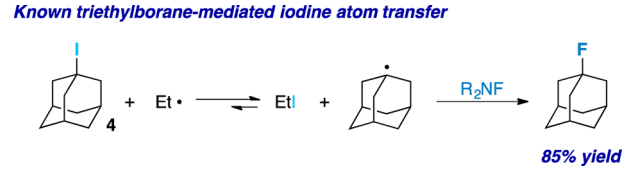


Figure 2. Proposed initiation through formation of ethyl radicals.

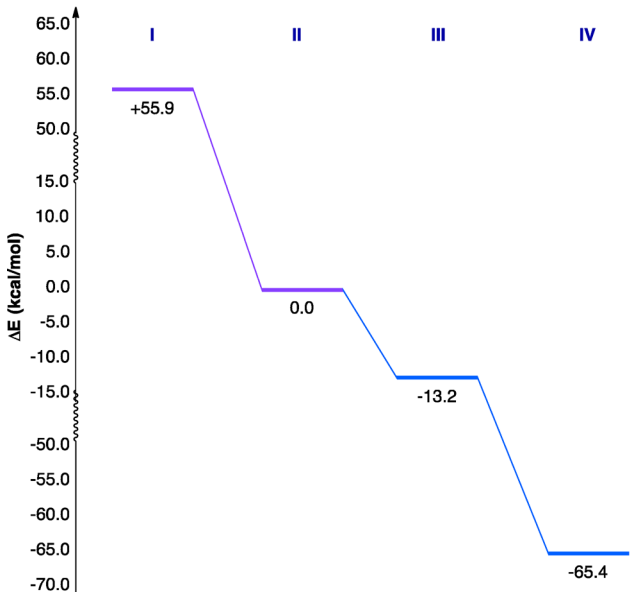
reaction was attempted using *N*-fluorobenzenesulfonimide (NFSI), another precedented source of atomic fluorine by Sammis and co-workers,[6] but no 1-fluorocyclododecane was observed, indicating that Selectfluor is a necessary player for H atom abstraction. The Inoue[7] and Chen[8] laboratories similarly observed this dependence on Selectfluor in their aliphatic fluorination systems (using NDHPI and V_2O_3, respectively), as have others using photochemical approaches.[9] Other trialkylborane reagents such as tri-*sec*-butylborane were also screened

Scheme 1



and afforded no fluorinated products. As triethylborane has also proven effective for the generation of tin and silyl radicals from trialkyltin hydrides and trialkylsilanes, we examined the reaction in the presence of each of these species but found significant depletions in yield. However, evidence of the Si–F bond being formed can be seen in the crude ^{19}F NMR spectra, which may indicate that the silyl radicals were at least formed over the course of each reaction. Finally, diethylzinc was employed as an alternative initiator to triethylborane;[10] the reaction provided 1-fluorocyclododecane in a low yield and is also a less desirable alternative, as dialkylzinc species are notably harsher reagents than trialkylboranes.

The success of the fluorination reaction appeared to rely intimately on (1) the purity of the triethylborane reagent and (2) the amount of O_2 present. Regarding the latter, product yields diminished using acetonitrile that was subjected to rigorous freeze–pump–thaw degasification, and notably, the reaction completely shut down in the presence of air or an O_2 atmosphere. If the fluorination reaction is, in fact, initiated by release of ethyl radicals via autoxidation of triethylborane (Figure 2), this result should be anticipated—O_2 reacts with triethylborane to produce the ethyl radicals responsible for initiation but also inhibits propagation of the H atom abstraction/fluorination steps. Whereas O_2 played a solely deleterious role as a quencher in the copper(I)/Selectfluor system, the BEt_3/O_2 radical chemistry assigns it a productive role in reaction initiation. Moreover, the previously observed induction period due to O_2 quenching in the copper system has virtually disappeared. In turn, overall reaction times have satisfyingly decreased. Fortunately, we found that the amount of dissolved O_2 in the solvent at 1 atm ($[O_2] \approx 8$ mM)[11] was



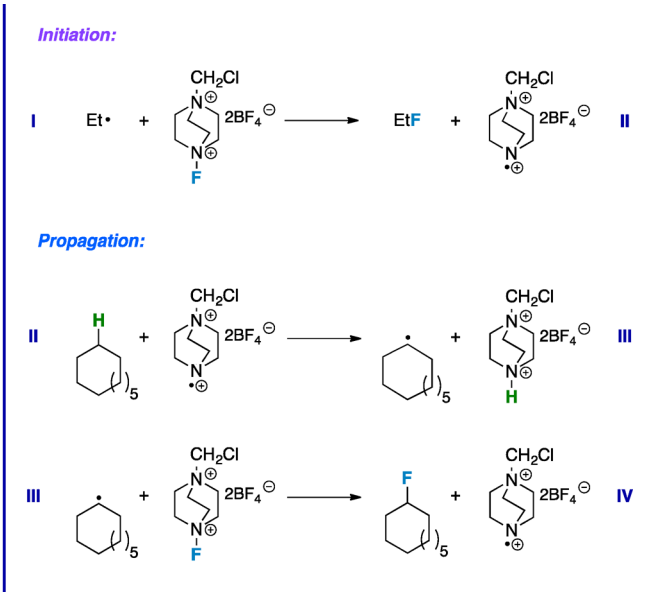


Figure 3. Energetic landscape of ethyl radical initiated fluorination of cyclodecane at the B3PW91/6-311++G**(MeCN) level.

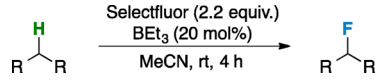
dx.doi.org/10.1021/jo501520e | J. Org. Chem. 2014, 79, 8895–8899

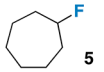
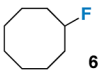
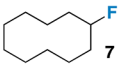
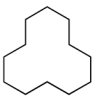
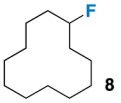
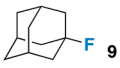
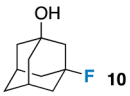
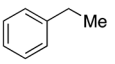
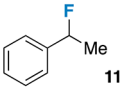
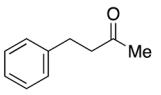
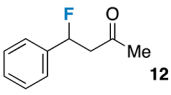
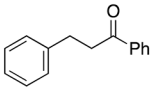
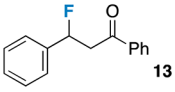
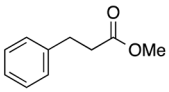
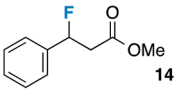
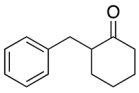
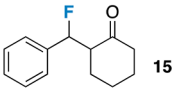
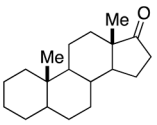
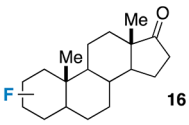
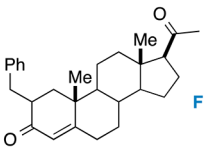
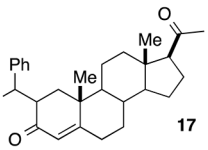
enough to produce satisfactory results in a standard organic laboratory setting, obviating the need for a more sophisticated setup controlling $[O_2]$. While we believe product yields and reaction efficiency could benefit greatly from a detailed kinetic study on the most optimal $[O_2]$ on the basis of our proposed mechanism, such a study is beyond the scope of this work.

In support of our claim for reaction initiation by ethyl radicals, we found two particularly convincing artifacts that signify autoxidation of triethylborane. First, fluoroethane is unambiguously observed as a triplet of quartets (^2J = 47.4 Hz, ^3J = 26.8 Hz) at −212.5 ppm in the crude ^{19}F NMR spectra of all fluorination reactions.[12] Second, monitoring the reaction by ^{11}B NMR in CD_3CN revealed a rapid formation of $B(OEt)(Et)_2$ at +56 ppm, a typical byproduct of the autoxidation reaction.[13] Furthermore, considering the BEt_3/O_2 interplay is utilized in iodine atom abstraction of alkyl iodides,[14] we designed a system to probe the presence of ethyl radicals under our reaction conditions using 1-iodoadamantane (**4**) and NFSI in place of Selectfluor, as NFSI will act only as a source of atomic fluorine and will not propagate a chain reaction. We found that 1-fluoroadamantane was produced in 85% yield based on triethylborane, feasibly as a result of iodine atom transfer to the ethyl radical and subsequent fluorination of the adamantyl radical (Scheme 1). Finally, the reaction of an ethyl radical with Selectfluor to produce fluoroethane and the radical dication was calculated at the B3PW91/6-311++G**(MeCN) level to be a substantial 56 kcal/mol downhill,[15] demonstrating a highly favorable reaction (Figure 3). Thus, this method very likely operates as a radical chain reaction initiated via a well-precedented autoxidation mechanism and propagated in an manner analogous to that for the previously reported copper(I)/Selectfluor system.

Upon evaluating the scope of the reaction, we found trends in selectivity very similar to those of the copper(I)/Selectfluor method. (1) Aliphatic substrates, viz. the cyclic alkanes in Table 2 (**5**−**10**), provided monofluorinated adducts in better yields relative to benzylic substrates (**11**−**15**). This may suggest a minor steric influence of the phenyl ring in the transition state, characteristic of H atom abstraction by *N*-radical cations.[16] (2) In almost every instance, *strictly* monofluorination is observed, which we have previously attributed to a manifestation of "the polar effect."[17] A minor amount of difluorination only materialized in the adamantane-based substrates **9** and **10** in the methine positions (as previously noted in other Selectfluor-based systems[18]). (3) On more complex substrates, i.e. the androsterone **16** and progesterone **17** derivatives (vide infra), a good degree of site selectivity is observed inherent to the parent molecules. Interestingly, fluorination was favored primarily in the C2 and C3 positions on the androsterone derivative[19] and occurred solely in the benzylic position on the progesterone derivative. (4) We noted that the reaction conditions generally endure oxygen-containing substrates well and tend to falter in fluorinating most nitrogen-containing compounds, likely due to N oxidation over desired reactivity.[20] (5) Finally, note that the product yields are mostly comparable to those reported for the copper(I)/Selectfluor system as well as other sp^3 C−H fluorination methods in the literature to date. Beyond mild reaction conditions and short reaction times, the virtue of using BEt_3 and Selectfluor lies in the minimal contamination from byproducts upon workup/isolation—starting materials can be easily recovered and fluorinated products can be obtained in high purity via chromatography.

Table 2. Substrate Scope



Entry	Substrate	Product	% Yield
1		 **5**	47
2		 **6**	41
3		 **7**	40
4		 **8**	50[a]
5		 **9**	42 (50)[b]
6		 **10**	37 (45)[b]
7		 **11**	30
8		 **12**	38[a]
9		 **13**	36[a]
10		 **14**	31[a]
11		 **15**	41[a,c]
12		 **16**	47
13		 **17**	28[a]

Product yields determined by ^{19}F NMR using 3-chlorobenzotrifluoride as an internal standard unless otherwise stated. [a]Isolated yield. [b]Yield including 1,3-difluorinated products. [c]Isolated as a 1.4:1 *cis*:*trans* mixture of diastereomers.

These parallels to the copper(I)/Selectfluor system and the aforementioned experiments maintain the notion that the ethyl radical liberated by BEt_3/O_2 acts as an initiator in what we previously established to be a radical chain fluorination mechanism propagated by a radical dication. Although the reaction inherently has a two-edged sensitivity for $[O_2]$, under optimal conditions it provides a mild, cheap, and easy

dx.doi.org/10.1021/jo501520e | J. Org. Chem. 2014, 79, 8895−8899

alternative to sp^3 C−H fluorination methods requiring transition metals, ultraviolet light, or "catalysts" that are not commercially available.

EXPERIMENTAL SECTION

General Considerations. Unless otherwise stated, all reactions were carried out under strictly anhydrous, air-free conditions under nitrogen. All solvents were dried and distilled by standard methods. ^{1}H NMR spectra were acquired on a 400 MHz NMR spectrometer in $CDCl_3$, ^{13}C spectra were taken on a 300 MHz NMR spectrometer in $CDCl_3$, and ^{19}F spectra were taken on a 300 MHz NMR spectrometer in $CDCl_3$ or CD_3CN. The ^{1}H, ^{13}C, and ^{19}F chemical shifts are given in parts per million (δ) with respect to an internal tetramethylsilane (TMS, δ 0.00 ppm) standard and/or 3-chlorobenzotrifluoride (δ −64.2 ppm relative to $CFCl_3$).[21] NMR data are reported in the following format: chemical shift (multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constants (Hz)). IR data were obtained using an ATR-IR instrument. High-resolution mass spectra (HRMS) were recorded using ESI-TOF (electrospray ionization time of flight) mass spectrometry. All measurements were recorded at 25 °C unless otherwise stated. Characterization data for fluorocycloheptane (**5**),[22] fluorocyclooctane (**6**),[23] fluorocyclodecane (**7**),[9a] fluorocyclododecane (**8**),[7] fluoroadamantane (**9**),[24] 3-fluoroadamantan-1-ol (**10**),[7] (1-fluoroethyl)benzene (**11**),[25] 4-fluoro-4-phenylbutan-2-one (**12**),[20] 3-fluoro-1,3-diphenylpropan-1-one (**13**),[22] methyl 3-fluoro-3-phenylpropanoate (**14**),[22] and 2-(fluoro(phenyl)methyl)cyclohexanone (**15**)[26] were consistent with literature precedent. Compounds **5**−**7** and **11** are reported as crude ^{19}F and ^{1}H NMR spectra due to their volatility. Spectral data were processed with ACD/NMR Processor Academic Edition.[27]

Sample Procedure. Selectfluor (390.0 mg, 1.1 mmol, 2.2 equiv) was placed in a 10 mL flame-dried round-bottom flask equipped with a stir bar under N_2. Acetonitrile (6.0 mL) was added to the reaction flask, and the solution was stirred vigorously at room temperature. 2-Benzylcyclohexanone (94.0 mg, 0.5 mmol, 1.0 equiv) was added, followed by 1.0 M triethylborane solution in hexanes (10.0 mg, 0.1 mmol, 0.2 equiv). The reaction mixture was stirred for 4 h. The product was diluted with Et_2O and filtered through Celite. The solvents were removed by rotary evaporation, and the residue was subjected to preparative TLC on silica with an ethyl acetate/hexanes mixture as eluent to afford 2-(fluoro(phenyl)methyl)cyclohexanone as a clear oil (43 mg, 41%).

Compound Characterization. *Fluorocycloheptane (**5**).* ^{1}H NMR (CD_3CN): 5.26−4.97 (1 H, dm, J = 47.7 Hz), 2.46−1.19 (12 H, m). ^{19}F NMR (CD_3CN): −164.55 (1 F, m). Yield: 47%.[22]

*Fluorocyclooctane (**6**).* ^{1}H NMR (CD_3CN): 5.25−4.92 (1 H, dm, J = 46.3), 2.38−1.19 (14 H, m). ^{19}F NMR (CD_3CN): −164.51 (1 F, m). Yield: 41%.[23]

*Fluorocyclodecane (**7**).* ^{1}H NMR (CD_3CN): 5.36−5.06 (1 H, dm, J = 46.5 Hz), 2.42−1.16 (18 H, m). ^{19}F NMR (CD_3CN): −166.29 (1 F, m). Yield: 40%.[9a]

*Fluorocyclododecane (**8**).* ^{1}H NMR ($CDCl_3$): 4.72 (1 H, dm, J = 47.5 Hz), 1.87−1.51 (4 H, m), 1.48−1.26 (18 H, m). ^{19}F NMR ($CDCl_3$): −176.88 (1 F, m). Yield: 47 mg (50%).[7]

*Fluoroadamantane (**9**).* ^{1}H NMR ($CDCl_3$): 2.27−2.20 (3 H, br s), 1.91−1.86 (6H, m), 1.66−1.60 (6H, m). ^{19}F NMR ($CDCl_3$): −128.5 (1 F, m). Yield: 42%.[24]

*3-Fluoroadamantan-1-ol (**10**).* ^{1}H NMR ($CDCl_3$): 2.41−2.34 (2 H, m), 1.92−1.88 (2 H, d, J = 5.7 Hz), 1.84−1.80 (4 H, dd, J = 5.4 Hz, 3.3 Hz), 1.72−1.61 (4 H, m), 1.52−1.47 (3 H, m). ^{19}F NMR ($CDCl_3$): −132.34 (1 F, m), −138.96 (1 F, m). Yield: 37%.[7]

*(1-Fluoroethyl)benzene (**11**).* ^{19}F NMR (CD_3CN): −167.06 (1 F, dq, J = 47.4 Hz, 23.7 Hz). Yield: 30%.[25]

*4-Fluoro-4-phenylbutan-2-one (**12**).* ^{1}H NMR ($CDCl_3$): 7.46−7.32 (5 H, m), 6.08−5.86 (1 H, ddd, J = 46.9 Hz, 8.7 Hz, 3.8 Hz), 3.31−3.16 (1 H, m), 2.94−2.75 (1H, ddd, J = 32.2 Hz, 16.6 Hz, 4.0 Hz), 2.24 (3 H, s). ^{19}F NMR ($CDCl_3$): −173.59 (1 F, ddd, J = 47.4 Hz, 34.0 Hz, 15.5 Hz). Yield: 32 mg (38%).[20]

*3-Fluoro-1,3-diphenylpropan-1-one (**13**).* ^{1}H NMR ($CDCl_3$): 8.00−7.32 (10 H, m), 6.29−6.08 (1 H, ddd, J = 46.9 Hz, 8.3 Hz, 4.5 Hz), 3.88−3.73 (1 H, ddd, J = 17.1 Hz, 14.8 Hz, 8.2 Hz), 3.42−3.24 (1 H, ddd, J = 29.6 Hz, 17.0 Hz, 4.1 Hz). ^{19}F NMR ($CDCl_3$): −172.97 (1 F, ddd, J = 46.4 Hz, 29.9 Hz, 15.5 Hz). Yield: 41 mg (36%).[22]

*Methyl 3-Fluoro-3-phenylpropanoate (**14**).* ^{1}H NMR ($CDCl_3$): 7.41−7.34 (5 H, m), 6.03−5.82 (1 H, ddd, J = 46.7 Hz, 9.0 Hz, 4.1 Hz), 3.74 (3 H, s), 3.11−2.98 (1 H, ddd, J = 16.0 Hz, 13.6 Hz, 9.0 Hz), 2.89−2.71 (1 H, ddd, J = 32.6 Hz, 16.2 Hz, 4.3 Hz). ^{19}F NMR ($CDCl_3$): −172.92 (1 F, ddd, J = 46.4 Hz, 32.0 Hz, 13.4 Hz). Yield: 28 mg (31%).[22]

*2-(Fluoro(phenyl)methyl)cyclohexanone (**15**).* ^{1}H NMR ($CDCl_3$): 7.67−7.03 (10 H, m), 6.17−5.96 (dd, J = 46.5 Hz, 4.1 Hz), 5.95−5.74 (1 H, dd, J = 45.8 Hz, 7.5 Hz), 3.03−2.80 (1 H, m), 2.77−2.60 (1 H, m), 2.58−2.22 (4 H, m), 2.18−1.49 (11 H, m), 1.35−1.15 (1 H, m). ^{19}F NMR ($CDCl_3$): −191.84 (1 F, dd, J = 46.4 Hz, 21.7 Hz), −172.64 (1 F, dd, J = 45.4 Hz, 14.4 Hz). Yield: 43 mg (41%).[26]

*3β-Fluoro-5α-androstan-17-one and 2α-Fluoro-5α-androstan-17-one (Major Products) (**16**).* ^{19}F NMR (CD_3CN): −170.7 (1 F, dm, J = 49.5 Hz); −174.9 (1 F, dm, J = 47.4 Hz). Yield: 47%.[19]

*2-(Fluoro(phenyl)methyl)progesterone (**17**).* ^{1}H NMR ($CDCl_3$): δ 7.41−7.36 (m, 2 H), 7.34−7.27 (m, 3 H), 6.55−6.42 (dd, 1 H, J = 46.2 Hz, 1.8 Hz), 5.84−5.82 (d, 1 H, J = 1.2 Hz), 2.72−2.58 (dddd, 1 H, J = 30.3 Hz, 13.3 Hz, 5.3 Hz, 2.0 Hz), 2.56−2.50 (t, 1 H, J = 9.2 Hz), 2.42−2.32 (m, 2 H), 2.20−2.15 (m, 1 H), 2.11 (s, 3 H), 2.04−1.99 (dt, 1 H, J = 12.1 Hz, 2.9 Hz), 1.89−1.61 (m, 5 H), 1.53−1.07 (m, 10 H), 1.06−1.03 (s, 3 H), 1.03−1.00 (m, 1 H), 0.61 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ 209.3 (s), 196.4 (s), 170.9 (s), 139.1 (s), 138.9 (s), 129.9 (s), 128.4 (s), 127.7 (s), 124.7 (s), 124.6 (s), 123.9 (s), 90.2 (d, J = 175.6 Hz), 63.5 (s), 55.9 (s), 53.8 (s), 49.4 (s), 48.1 (s), 47.9 (s), 43.8 (s), 38.7 (s), 38.6 (s), 35.4 (s), 33.7 (s), 33.6 (s), 32.5 (s), 31.7 (s), 31.5 (s), 24.3 (s), 22.8 (s), 20.9 (s), 17.6 (s), 13.3 (s). ^{19}F NMR ($CDCl_3$): δ −198.57 (dd, 1 F, J = 46.4 Hz, 30.9 Hz). IR ($CDCl_3$) 1701, 1671 cm^{-1}. HRMS-(ESI+): calcd for $C_{28}H_{35}FO_2Na^+$ 445.2513, found 445.2527. Yield: 59 mg (28%).

ASSOCIATED CONTENT

Supporting Information

Figures and tables giving spectral data for all compounds prepared in the paper and details of the computed structures. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail for T.L.: lectka@jhu.edu.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

T.L. thanks the NSF (CHE 1152996) for support. C.R.P. thanks Johns Hopkins for a Gary H. Posner Fellowship.

REFERENCES

(1) Pitts, C. R.; Bloom, S.; Woltornist, R.; Auvenshine, D.; Ryzhkov, L. R.; Siegler, M. A.; Lectka, T. *J. Am. Chem. Soc.* **2014**, *136*, 9780−9791.

(2) For a fairly comprehensive introduction to radical initiators, see: Denisov, E. T.; Denisova, T. G.; Pokidova, T. S. *Handbook of Free Radical Initiators*; Wiley: Hoboken, NJ, 2003.

(3) Ollivier, C.; Renaud, P. *Chem. Rev.* **2001**, *101*, 3415−3434 and references cited therein.

(4) Brotherton, R. J.; Weber, C. J.; Guibert, C. R.; Little, J. L. Boron Compounds. In *Ullman's Encyclopedia in Industrial Chemistry*; Wiley-VCH: Weinheim, Germany, 2000.

(5) Regarding optimization of our reaction conditions, we found that heating was unnecessary and promoted ionization over time, which was deleterious to product yields. Colder temperatures (e.g., 10 °C) are viable, but there is an increase in reaction times with no increase in yield. Reactions were monitored at room temperature by TLC and/or ^{19}F NMR; we found that 4 h is a reliable, generalized time period to accomplish this reaction across all substrates (in some instances, the reaction may be done in less time). Finally, given the solubility issues with Selectfluor in most organic solvents and its unique reactivity in acetonitrile, this is the solvent de choix for aliphatic fluorination.
(6) Rueda-Becerril, M.; Sazepin, C. C.; Leung, J. C. T.; Okbinoglu, T.; Kennepohl, P.; Paquin, J.-F.; Sammis, G. M. *J. Am. Chem. Soc.* **2012**, *134*, 4026−4029.
(7) Amaoka, Y.; Nagatomo, M.; Inoue, M. *Org. Lett.* **2013**, *15*, 2160−2163.
(8) Xia, J.-B.; Ma, Y.; Chen, C. *Org. Chem. Front.* **2014**, *1*, 468−472.
(9) However, some of these photochemical approaches may be operating very differently mechanistically. For some examples, see: (a) Bloom, S.; Knippel, J. L.; Lectka, T. *Chem. Sci.* **2014**, *5*, 1175−1178. (b) Kee, C. W.; Chin, K. F.; Wong, M. W.; Tan, C.-H. *Chem. Commun.* **2014**, *50*, 8211−8214. (c) Xia, J.-B.; Zhu, C.; Chen, C. *J. Am. Chem. Soc.* **2013**, *135*, 17494−17500.
(10) (a) Bertrand, M. P.; Feray, L.; Nouguier, R.; Perfetti, P. *J. Org. Chem.* **1999**, *64*, 9189−9193. (b) Ryu, I.; Araki, F.; Minakata, S.; Komatsu, M. *Tetrahedron Lett.* **1998**, *39*, 6335−6336.
(11) Achord, J. M.; Hussey, C. L. *Anal. Chem.* **1980**, *52*, 601−602.
(12) Tanuma, T.; Ohnishi, K.; Okamoto, H.; Morikawa, S. *J. Fluorine Chem.* **1996**, *76*, 45−48.
(13) Zhang, Z.-C.; Chung, T. C. M. *Macromolecules* **2006**, *39*, 5187−5189.
(14) (a) Byers, J. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, Germany, 2001; Vol. *1*, p 72. (b) Curran, D. P.; Chen, M.-H.; Spetzler, E.; Seong, C. M.; Chang, C.-T. *J. Am. Chem. Soc.* **1989**, *111*, 8872−8878.
(15) Frisch, M. J., et al. *Gaussian 09, Revision A.1*; Gaussian, Inc., Wallingford, CT, 2009.
(16) Bernardi, R.; Galli, R.; Minisci, F. *J. Chem. Soc. B* **1968**, 324−325.
(17) For a more extensive discussion on the ionic-like selectivity of recent sp C−H fluorination methods, see ref 1 and works cited therein.
(18) For example, see: Xia, J.-B.; Ma, Y.; Chen, C. *Org. Chem. Front.* **2014**, *1*, 468−472.
(19) Similar site selectivity was observed on the same substrate by Groves et al. in a different approach to sp C−H fluorination: Liu, W.; Huang, X.; Cheng, M.-J.; Nielsen, R. J.; Goddard, W. A., III; Groves, J. T. *Science* **2012**, *337*, 1322−1325.
(20) See discussion and references in: Bloom, S.; Pitts, C. R.; Woltornist, R.; Griswold, A.; Holl, M. G.; Lectka, T. *Org. Lett.* **2013**, *15*, 1722−1724.
(21) Naumann, D.; Kischkewitz, J. *J. Fluorine Chem.* **1990**, *47*, 283−299.
(22) Schneider, H.-J.; Gschwendtner, W.; Heiske, D.; Hoppen, V.; Thomas, F. *Tetrahedron* **1977**, *33*, 1769−1773.
(23) Beaulieu, F.; Beauregard, L.; Courchesne, G.; Couturier, M.; LaFlamme, F.; L'Heureux, A. *Org. Lett.* **2009**, *11*, 5050−5053.
(24) Aoyama, M.; Fukuhara, T.; Hara, S. *J. Org. Chem.* **2008**, *73*, 4186−4189.
(25) York, C.; Prakash, G. K. S.; Olah, G. A. *Tetrahedron* **1996**, *52*, 9−14.
(26) Bloom, S.; Sharber, S. A.; Holl, M. G.; Knippel, J. L.; Lectka, T. *J. Org. Chem.* **2013**, *78*, 11082−11086.
(27) *ACD/NMR Processor Academic ed., version 12.0*; Advanced Chemistry Development, Inc., Toronto, ON, Canada, 2012; www.acdlabs.com.