JOC The Journal of Organic Chemistry

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Difunctionalization of Styrenes with Perfluoroalkyl and *tert*-Butylperoxy Radicals: Room Temperature Synthesis of (1-(*tert*-Butylperoxy)-2-perfluoroalkyl)-ethylbenzene

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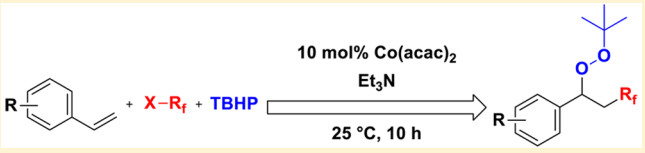
Supporting Information

ABSTRACT: A novel strategy for the difunctionalization of styrenes was developed. This synthesis includes the use of electrophilic perfluoroalkyl and *tert*-butylperoxy radicals and produces (1-(*tert*-butylperoxy)-2-perfluoroalkyl)ethylbenzene at room temperature, which has been traditionally difficult to synthesize. With at least four radical species included in the transformation, its high chemoselectivity was extraordinary; the results were further elucidated using computational studies. The methodology also holds a good potential for application as a result of its mild reaction conditions, ease of further modification, and insensitivity to moisture and air.

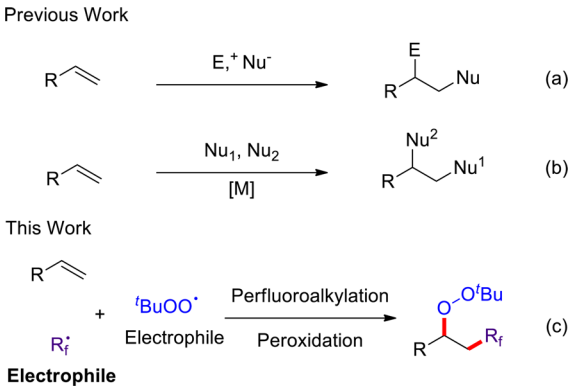


INTRODUCTION

Perfluoroalkyl[1] and peroxy[2] groups have both drawn considerable attention in recent years due to their unique chemical and biological properties. Perfluorinated compounds, which can be prepared via a variety of methods,[3,4] exhibit enhanced stability, lipophilicity, bioavailability, and biopotency over their nonfluorinated counterparts. On the other hand, organic peroxides not only serve as key reactive intermediates in diverse organic synthesis reactions,[5] including oxidation, Kornblum–DeLaMare reactions[6] and epoxidation,[5a−c,f] but also play important roles in cell damage, food safety, and medicine and therapeutic drugs. For example, artemisinin (Qinghaosu), a naturally occurring organic peroxide, is a highly effective treatment against malaria.[7] The simultaneous generation of perfluoroalkyl and peroxide moieties in the same molecule, therefore, may provide easy access to compounds with pharmaceutical potentials. However, to the best of our knowledge, no chemical transformation capable of achieving this feat has been reported in literature.

The vicinal difunctionalization of alkenes, which leads to the simultaneous derivatization of both double bond carbons, is a powerful approach for achieving complex molecular structures.[8,9] In general, this chemical transformation involves a three-component reaction of the alkene either with an electrophile and a nucleophile (Scheme 1a) or with two nucleophiles (Scheme 1b). In contrast, difunctionalization of alkenes with two electrophiles has not been widely explored, which might be due to the difficulty in controlling selectivity. We envision that the development of a new alkene difunctionalization strategy compatible with electrophilic reactants can potentially lead to novel molecular structures that are otherwise inaccessible via conventional synthetic routes. In the current study, the difunctionalization of alkenes was accomplished with electrophilic perfluoroalkyl and *tert*-butylperoxy radicals to afford products that bear a vicinal pair of perfluoroalkyl and peroxide groups (Scheme 1c). However, as both perfluoroalkyl and *tert*-butylperoxy radicals are highly active and electrophilic, chemo- and regioselectivity remain challenges in this study.

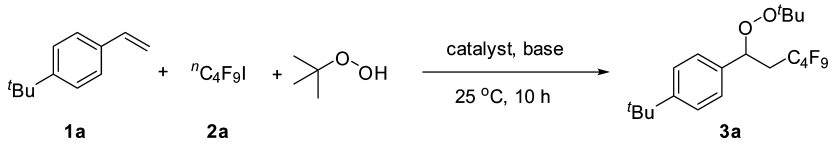
Scheme 1. Strategy for the Difunctionalization of Alkenes



Received: March 16, 2016
Published: June 9, 2016

DOI: 10.1021/acs.joc.6b00575
J. Org. Chem. 2016, 81, 5878−5885

Table 1. Optimization of Reaction Conditions[a]

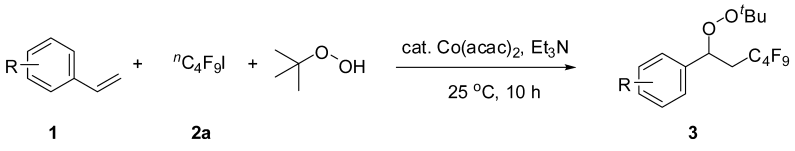


1a 2a 3a

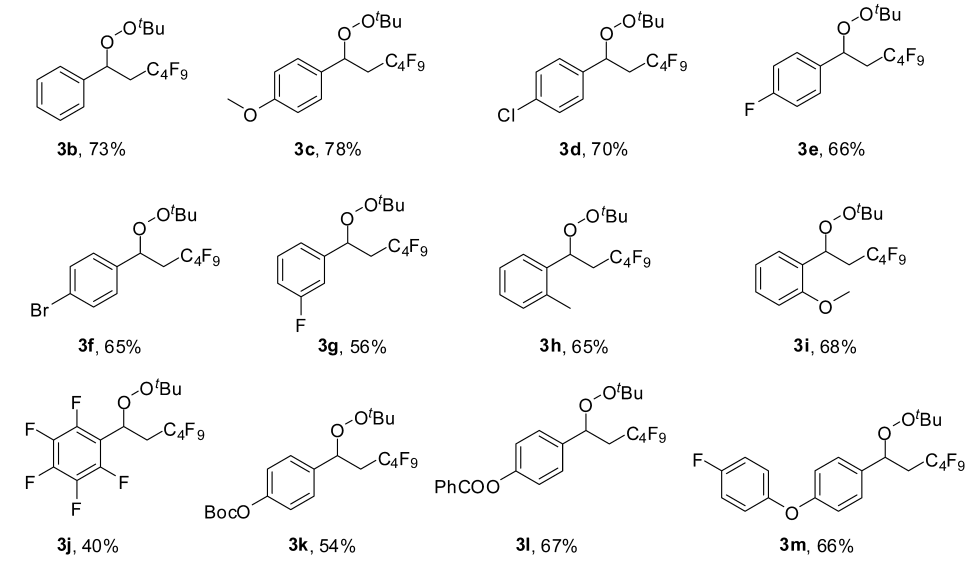
	catalyst	solvent	base	yield (%)[b]
1	$Co(acac)_2$	CCl_3CH_3	Et_3N	77
2		CCl_3CH_3	Et_3N	<5
3	$Co(acac)_2$	CCl_3CH_3		<5
4	$Co(acac)_2$	ethyl acetate	Et_3N	42
5	$Co(acac)_2$	CH_3CN	Et_3N	60
6	$Co(acac)_2$	THF	Et_3N	30
7	$Co(acac)_2$	acetone	Et_3N	51
8	$Co(acac)_2$	CCl_3CH_3	K_2CO_3	<5
9	$Co(acac)_2$	CCl_3CH_3	NaOAc	<5
10	$Co(acac)_2$	CCl_3CH_3	tripropylamine	40
11	$Co(acac)_2$	CCl_3CH_3	Et_2NH	33
12	$Co(acac)_2$	CCl_3CH_3	DABCO	<5
13	I_2	CCl_3CH_3	Et_3N	<5
14	$Cu(acac)_2$	CCl_3CH_3	Et_3N	32
15	$PdCl_2$	CCl_3CH_3	Et_3N	<5
16	$Fe(acac)_2$	CCl_3CH_3	Et_3N	<5
17	CAN	CCl_3CH_3	Et_3N	<5

[a]Reaction conditions: 0.5 mmol of **1a**, 1.0 mmol of **2a**, 0.05 mmol of catalyst, 2.9 mmol of TBHP (70% aqueous solution), and 2.5 mmol of base in 2.0 mL of solvent was stirred at 25 °C for 10 h. [b]Isolated yields.

Table 2. Scope of Styrenes[a]



1 2a 3



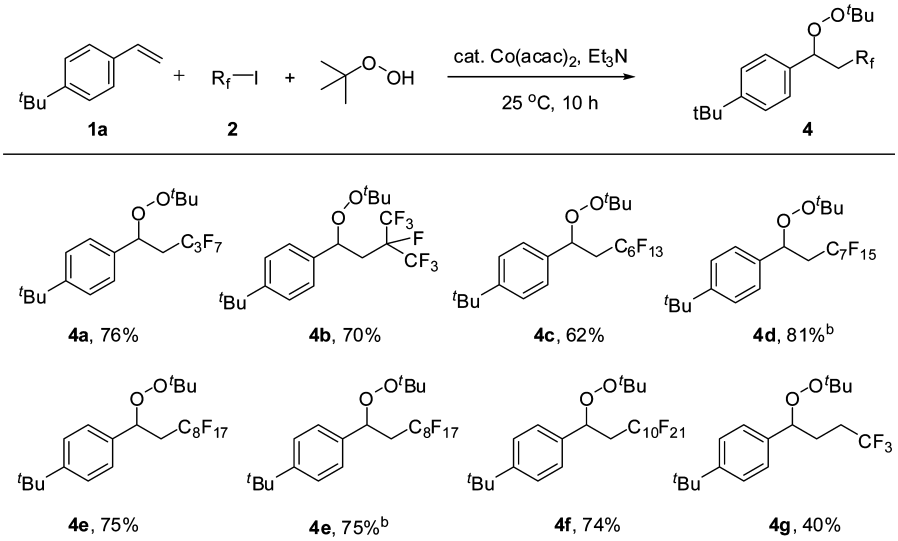
[a]Reaction conditions: 0.5 mmol of **1**, 1.0 mmol of **2a**, 0.05 mmol of $Co(acac)_2$, 2.9 mmol of TBHP (70% aqueous solution), and 2.5 mmol of Et_3N in 2.0 mL of CCl_3CH_3 was stirred at 25 °C for 10 h.

RESULTS AND DISCUSSION

Initial pilot studies indicated that the reaction of 1-(*tert*-butyl)-4-vinylbenzene (**1a**), perfluorobutyl iodide **2a** (perfluoroalkyl radical precursor), and TBHP (*tert*-butylperoxy radical precusor) in CCl_3CH_3 in the presence of $Cu(acac)_2$ at 25 °C for 10 h could afford the desired product **3a** in 32% yield (entry 14, Table 1). Based on the results of a recent study showing that $Co(acac)_2$ could efficiently promote the synthesis of 1,4-dicarbonyl compounds and (*Z*)-*β*-perfluoroalkyl enaminones,[10] $Co(acac)_2$ was subsequently tested as the catalyst, and its use

DOI: 10.1021/acs.joc.6b00575
J. Org. Chem. 2016, 81, 5878−5885

Table 3. Scope of Perfluoroalkyl Halides[a]



[a]Reaction conditions: 0.5 mmol of **1a**, 1.0 mmol of **2**, 0.05 mmol of $Co(acac)_2$, 2.9 mmol of TBHP (70% aqueous solution), and 2.5 mmol of Et_3N in 2.0 mL of CCl_3CH_3 was stirred at 25 °C for 10 h. [b]Perfluoroalkyl bromides were used.

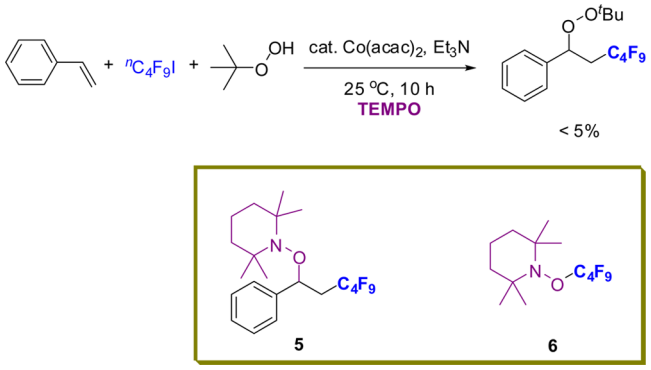
was found to increase the yield of **3a** to 77% (entry 1, Table 1). The one-pot multicomponent free-radical synthesis[11] presented here can be performed in an open flask under air without the need for an inert atmosphere. No product **3a** was detected in the absence of $Co(acac)_2$ or Et_3N (entries 2 and 3, Table 1), In addition, the efficiency of the *tert*-butylperoxy-perfluoroalkyl benzene formation reaction is greatly affected by the choice of solvents and bases (entries 4−12, Table 1).

Screening a variety of substituted styrenes showed that both electron-withdrawing and electron-donating substituents on the benzene ring could be advantageous for product formation (Table 2), while steric hindrance did not produce any significant impact on the reaction efficiency (products **3h** and **3i**). Replacing the benzene ring of the styrene moiety with pentafluorobenzene led to the generation of **3j** in moderate yield. In contrast, no desired products were generated when aliphatic alkenes were used as substrates.

The difunctionalization reaction was next revealed to be compatible with a broad range of perfluoroalkyl iodides (Table 3), including the branched heptafluoroisopropyl iodide (**4b**), all of which afforded the corresponding products in satisfactory yields. The use of perfluoroalkyl bromides was also well-tolerated (**4d** and **4e**). Notably, the oxidative coupling between **1a**, 2,2,2-trifluoroethyl iodide, and TBHP furnished the 1-(*tert*-butyl)-4-(1-(*tert*-butylperoxy)-4,4,4-trifluorobutyl)benzene **4g** in 40% yield.

To probe the mechanism of the reaction, TEMPO (2,2,6,6-tetramethylpiperidine 1-oxyl), a well-known radical inhibitor, was added to the reaction mixture of styrene, perfluorobutyl iodide, and TBHP (Scheme 2). As expected, the formation of the difunctionalized product was suppressed, and product profile analysis detected trace amounts of styrene-derived intermediate **5** and perfluoroalkyl iodide-derived intermediate **6**. These findings offered convincing evidence for the electrophilic addition of the $C_4F_9^\bullet$ radical intermediate generated from the Co-catalyzed C−X (X = Br or I) bond cleavage on the styrene C=C bond. Although $^tBuO^\bullet$ and $^tBuOO^\bullet$ radicals could also be generated in the presence of Co(II) from TBHP, no TEMPO adducts of these species were observed.

Scheme 2. Investigation of Reaction Mechanism

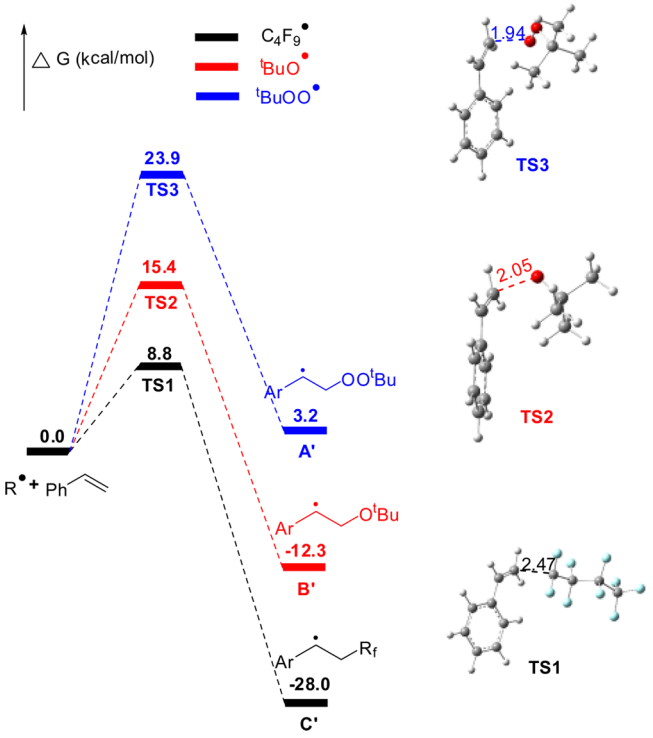


To provide an explanation for the presence of $C_4F_9^\bullet$ radical adduct while the possible $^tBuO^\bullet$ and $^tBuOO^\bullet$ radical adducts are absent, computational studies were carried out to compare the energy profiles of the three radicals attack of styrene. The computational results indicate that the attack of $C_4F_9^\bullet$ to the terminal carbon of styrene has the lowest energy barrier (8.8 kcal/mol), and the formed radical adduct is most exothermic by 28.0 kcal/mol (Scheme 3). In comparison, the energy barriers for the attack of $^tBuO^\bullet$ and $^tBuOO^\bullet$ are substantially higher than that of the $C_4F_9^\bullet$ attack, which are 15.4 and 23.9 kcal/mol, respectively. In addition, the produced radical intermediates B′ is much less exothermic than C′ (the formation of A′ is even endothermic). The natural bond orbital (NBO) charge analysis suggests that the radical center carbon of $C_4F_9^\bullet$ has substantial positive charge (0.78 e) due to the connection with fluorines. In contrast, the terminal oxygens of $^tBuO^\bullet$ and $^tBuOO^\bullet$ have negative charges (−0.30 and −0.18 e, respectively). Therefore, $C_4F_9^\bullet$ is more ready to undergo electrophilic radical addition with styrene, and the formation of a $C_4F_9^\bullet$ attack adduct is more feasible, which is consistent with the experimental observation.

A plausible mechanism for the Co-catalyzed difunctionalization reaction of styrene was proposed based on a combination of our findings and previous literature results[12] (Scheme 4). The Co-based catalyst is responsible for both the reductive

DOI: 10.1021/acs.joc.6b00575
J. Org. Chem. 2016, 81, 5878−5885

Scheme 3. Energy Profile for the Three Radical Attacks of Styrene[a]



[a]In kcal/mol; bond lengths are shown in Å.

cleavage of the C−X (X = Br or I) bond in perfluoroalkyl halide and decomposition of TBHP, which afforded $R_f^•$ **C** and $^tBuOO^•$ **B**, respectively (Schemes 4a and 4b). The electrophilic radical intermediate **C** is then immediately trapped by styrene, leading to the formation of the benzylic radical intermediate **D** (Scheme 4c). Recombination of **D** and **B** results in the perfluoroalkyl-peroxide product. In addition, the benzylic radical may be reversibly tapped by Co^{II} to form an organo-Co(III) intermediate[13] because of the well-established carbophilicity of cobalt. It should be pointed out that **D** could also undergo hydrogen elimination (Scheme 4e) to furnish the perfluoroalkyl-substituted alkene **E**, which would explain its detection as a notable byproduct in this study.

Both the perfluoroalkyl and peroxide groups of **3a** can be subjected to further chemical transformations to generate a wide range of synthetically useful molecules. For instance, the peroxide group of **3a** was hydrogenated using Pd/C or Raney nickel to furnish the β-perfluoroalkyl benzyl alcohol **7** in high yield (Scheme 5a). Under the aid of DABCO, **3a** underwent a Kornblum−DeLaMare reaction and simultaneously eliminated a molecule of HF[14] to generate the α,β-unsaturated aryl ketone **8**[10b] (Scheme 5b), which was then hydrogenated using Pd/C to afford the β-perfluoroalkyl ketone **9** that would otherwise be difficult to synthesize. Notably, (*Z*)-β-perfluoroalkyl enaminone **10** could be prepared in excellent 97% yield (Scheme 5c) by reacting **3a** with Et_2NH in the presence of DABCO, which involved tandem HF elimination, a Kornblum−DeLaMare reaction, and Michael addition.[10b]

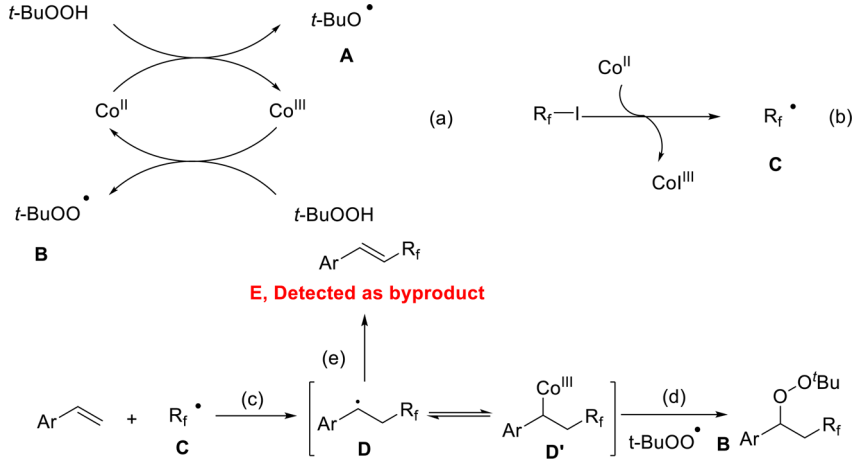
CONCLUSIONS

In conclusion, we have developed an unprecedented difunctionalization reaction that combined styrene, a perfluoroalkyl radical, and a *tert*-butylperoxy radical in a one-pot synthesis to produce (1-(*tert*-butylperoxy)-2-perfluoroalkyl)-ethylbenzene under room temperature, which is a complex compound that is difficult to synthesize through other approaches. With the involvement of multiple radical intermediates, this methodology is distinguished by its high selectivity and mild conditions. Furthermore, both the perfluoroalkyl and peroxide groups of (1-(*tert*-butylperoxy)-2-perfluoroalkyl)ethylbenzene are amenable to further chemical modifications, which allowed the preparation of a variety of synthetically valuable molecules. Investigation into the difunctionalization of alkenes with other electrophiles is currently underway in our laboratory.

EXPERIMENTAL SECTION

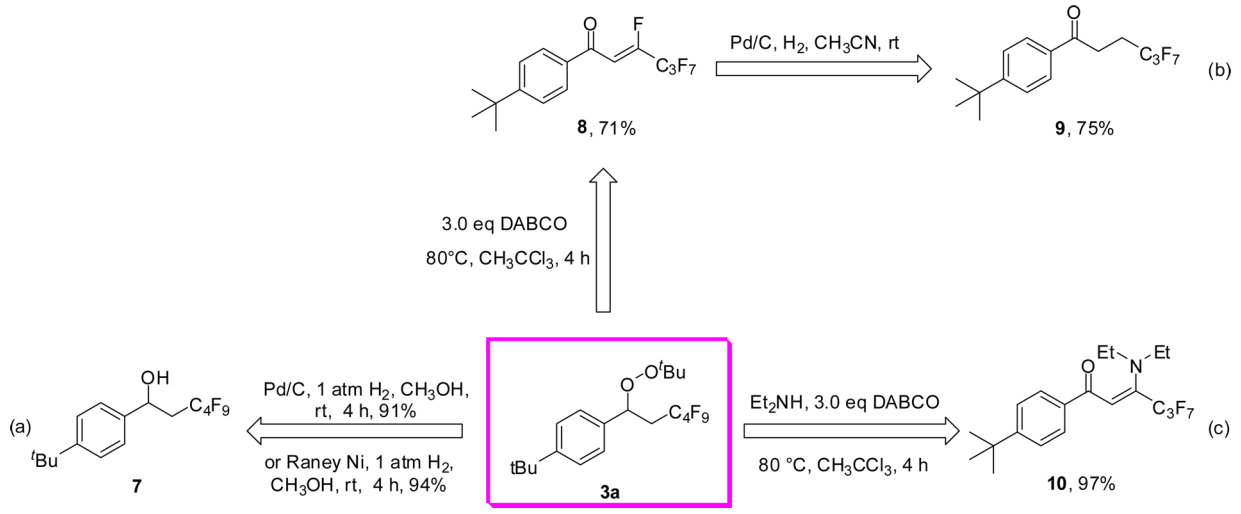
General. All manipulations were carried out under an air atmosphere. Column chromatography was generally performed on silica gel (300−400 mesh), and reactions were monitored by thin-layer chromatography (TLC) using UV light to visualize the course of the reactions. The ^1H (400 MHz), ^{13}C (100 MHz), and ^{19}F NMR (376 MHz) data were recorded on 400 M spectrometers using $CDCl_3$ as the solvent. The chemical shifts (δ) are reported in ppm, and coupling constants (*J*) in Hz. ^1H NMR spectra were recorded with tetramethylsilane (δ = 0.00) as the internal reference; ^{13}C NMR spectra were recorded with $CDCl_3$ (δ = 77.00) as internal reference.

Scheme 4. Proposed Mechanism for *tert*-Butylperoxy-perfluoroalkyl Benzene Formation Reaction



DOI: 10.1021/acs.joc.6b00575
J. Org. Chem. 2016, 81, 5878−5885

Scheme 5. Transformation of *tert*-Butylperoxy-perfluoroalkyl Benzene 3a



IR, MS, and HRMS were performed by the corresponding instruments.

Experimental details: Cobalt(II) acetylacetonate (0.05 mmol) was added to a test tube. 1,1,1-Trichloroethane (2.0 mL), styrenes (0.5 mmol), perfluoroalkyl halides (1.0 mmol), triethylamine (2.5 mmol), and *tert*-butyl hydroperoxide (TBHP, 2.9 mmol, 0.40 mL, 70% solution in water) were added via syringe. The test tube was put on a balloon. The reaction mixture was stirred at 25 °C for 10 h. It was then quenched (consumption of residual TBHP) with a saturated Na_2SO_3 solution and extracted with ethyl acetate. The organic layer was combined and dried with Na_2SO_4. Removal of solvent followed by flash column chromatographic purification afforded products using petroleum.

Computational Methods. The geometries of all stationary points were optimized using the M06-2X density functional method[15] with the 6-31+G(d,p) basis set[16] for all atoms. Vibrational frequency analyses at the same level of theory were performed on all optimized structures to characterize stationary points as local minima or transition states. Transition states were verified to have one imaginary vibrational frequency and were connected to the appropriate reactant and product by optimizations along the reaction coordinate. To consider solvation effects, single-point energy computations using the polarizable continuum model (PCM) model[17] with CCl_3CH_3 as the solvent were performed based on the optimized gas-phase geometries of all species. A larger basis set, 6-311++G(d,p), was utilized for single-point energy calculations on stationary points. The solution-phase Gibbs free energy was determined by adding the solvation single-point energy and the gas-phase thermal correction to the Gibbs free energy obtained from the vibrational frequencies. Unless otherwise specified, the solution-phase Gibbs free energy was used in the present discussions. The Gaussian 09 suite of programs[18] was used for all calculations.

*1-(tert-Butyl)-4-(1-(tert-butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)benzene (**3a**).* Colorless liquid (180 mg, 77% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.29−5.26 (m, 1H), 2.92−2.72 (m, 1H), 2.55−2.37 (m, 1H), 1.32 (s, 9H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 136.3, 126.6, 125.5, 80.8, 78.7, 35.9 (t, J = 21.0 Hz), 34.6, 31.3, 26.3, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.02 to −81.12 (m, 3F), −111.46 to −113.46 (m, 2F), −124.36 to −124.52 (m, 2F), −125.84 to −125.98 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{20}H_{24}F_9O_2$ ($M - H^+$) 467.1633. Found: 467.1620. IR (KBr, cm^{-1}) ν 2968, 1514, 1364, 1219, 1195, 1133.

*(1-(tert-Butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)benzene (**3b**).* Colorless liquid (150 mg, 73% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.29 (m, 5H), 5.31−5.26 (m, 1H), 2.90−2.72 (m, 1H), 2.55−2.37 (m, 1H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 128.6, 128.5, 126.9, 80.8, 78.9, 36.0 (t, J = 21.0 Hz), 26.3, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.22 to −81.31 (m, 3F), −111.54 to −113.43 (m, 2F), −124.46 to −124.60 (m, 2F), −125.96 to −126.10 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{16}H_{17}F_9O_2$: 412.1085. Found: 412.1090. IR (KBr, cm^{-1}) ν 2982, 1497, 1365, 1219, 1195, 1132.

*1-(1-(tert-Butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)-4-methoxybenzene (**3c**).* Colorless liquid (172 mg, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 8.0 Hz, 2H), 5.26−5.19 (m, 1H), 3.79 (s, 3H), 2.96−2.78 (m, 1H), 2.55−2.38 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 131.2, 128.4, 113.9, 80.7, 78.6, 55.1, 35.6 (t, J = 21.0 Hz), 26.3, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.17 to −81.28 (m, 3F), −112.45 to −112.60 (m, 2F), −124.46 to −124.62 (m, 2F), −125.95 to −126.10 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{17}H_{19}F_9O_3$: 442.1190. Found: 442.1179. IR (KBr, cm^{-1}) ν 2981, 1515, 1365, 1218, 1196, 1132.

*1-(1-(tert-Butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)-4-chlorobenzene (**3d**).* Colorless liquid (156 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 5.29−5.23 (m, 1H), 2.85−2.68 (m, 1H), 2.49−2.32 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 134.4, 128.9, 128.2, 80.9, 78.2, 35.9 (t, J = 21.0 Hz), 26.2, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.25 to −81.34 (m, 3H), −111.50 to −113.44 (m, 2H), −124.48 to −124.64 (m, 2H), −125.99 to −126.16 (m, 2H); HRMS (ESI-TOF) Anal. Calcd For $C_{16}H_{17}{}^{35}ClF_9O_2$ ($M + H^+$) 447.0773, $C_{16}H_{17}{}^{37}ClF_9O_2$ ($M + H^+$) 449.0744. Found: 447.0791 (^{35}Cl), 449.0812 (^{37}Cl). IR (KBr, cm^{-1}) ν 2982, 1493, 1365, 1219, 1196, 1133.

*1-(1-(tert-Butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)-4-fluorobenzene (**3e**).* Colorless liquid (142 mg, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36- 7.30 (m, 2H), 7.08−7.01 (m, 2H), 5.29−5.24 (m, 1H), 2.89−2.72 (m, 1H), 2.51−2.34 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 161.6, 135.3, 135.3, 128.7, 128.7, 115.7, 115.4, 80.9, 78.2, 35.9 (t, J = 21.0 Hz), 26.2, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.31 to −81.40 (m, 3F), −111.65 to −113.45 (m, 2F), −113.56 (s, 1F), −124.53 to −124.70 (m, 2F), −126.06 to −126.20 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{16}H_{16}F_{10}O_2$: 430.0991. Found: 430.0987. IR (KBr, cm^{-1}) ν 2982, 1513, 1365, 1220, 1196, 1132.

*1-Bromo-4-(1-(tert-butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)benzene (**3f**).* Colorless liquid (160 mg, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 5.27−5.21 (m, 1H), 2.84−2.67 (m, 1H), 2.49−2.31 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 131.8, 128.5, 122.5, 81.0, 78.2, 35.9 (t, J = 21.0 Hz), 26.2, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.13 to −81.23 (m, 3F), −111.36 to −113.44 (m, 2F), −124.39 to

DOI: 10.1021/acs.joc.6b00575
J. Org. Chem. 2016, 81, 5878−5885

−124.58 (m, 2F), −125.90 to −126.08 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{16}H_{17}{}^{79}BrF_9O_2$ (M + H$^+$) 491.0268, $C_{16}H_{17}{}^{81}BrF_9O_2$ (M + H$^+$) 493.0248. Found: 491.0250 (^{79}Br), 493.0240 (^{81}Br). IR (KBr, cm^{-1}) ν 2981, 1488, 1365, 1219, 1195, 1132.

*1-(1-(tert-Butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)-3-fluorobenzene (**3g**).* Colorless liquid (120 mg, 56% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.29 (m, 1H), 7.15−7.07 (m, 2H), 7.05−6.98 (m, 1H), 5.30−5.25 (m, 1H), 2.83−2.64 (m, 1H), 2.49−2.32 (m, 1H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 161.8, 142.3, 142.3, 130.2, 130.1, 122.4, 122.4, 115.5, 115.3, 113.9, 113.7, 81.0, 78.2, 36.1 (t, J = 21.0 Hz), 26.2, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.23 to −81.32 (m, 3F), −111.43 to −113.60 (m, 2F), −112.65 (s, 1F) −124.46 to −124.62 (m, 2F), −125.99 to −126.15 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{16}H_{16}F_{10}O_2$: 430.0991. Found: 430.1000; IR (KBr, cm^{-1}) ν 2983, 1489, 1365, 1219, 1195, 1132.

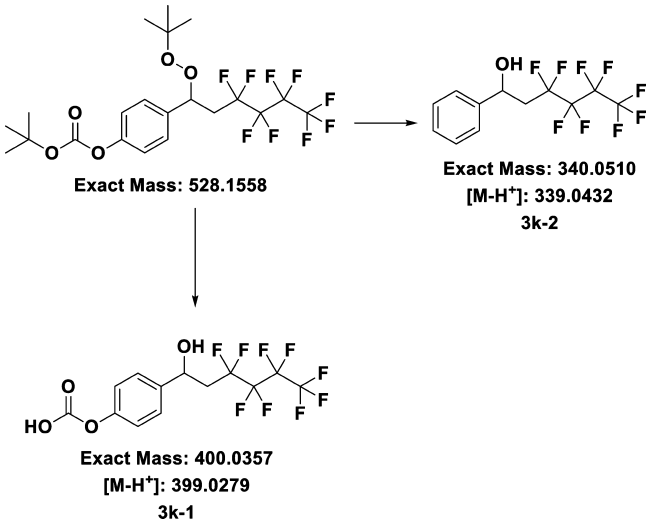
*1-(1-(tert-Butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)-2-methylbenzene (**3h**).* Colorless liquid (139 mg, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.39 (m, 1H), 7.25−7.19 (m, 2H), 7.18−7.13 (m, 1H), 5.62−5.55 (m, 1H), 2.83−2.66 (m, 1H), 2.50−2.39 (m, 1H), 2.37 (s, 3H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 135.1, 130.7, 128.2, 126.5, 126.3, 80.7, 75.1, 35.3 (t, J = 21.0 Hz), 26.3, 18.9, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.04 to −81.14 (m, 3F), −111.56 to −114.00 (m, 2F), −124.43 to −124.58 (m, 2F), −125.86 to −126.02 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{17}H_{20}F_9O_2$ (M + H$^+$) 427.1320. Found: 427.1315; IR (KBr, cm^{-1}) ν 2981, 1493, 1365, 1219, 1195, 1133.

*1-(1-(tert-Butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)-2-methoxybenzene (**3i**).* Colorless liquid (150 mg, 68% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.5 Hz, 1H), 7.30−7.26 (m, 1H), 7.01−6.97 (m, 1H), 6.87 (d, J = 8.2 Hz, 1H), 5.74−5.71 (m, 1H), 3.82 (s, 3H), 2.61−2.57 (m, 1H), 2.55−2.50 (m, 1H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 129.1, 127.9, 127.5, 120.6, 110.6, 83.7, 80.6, 73.6, 55.3, 34.8 (t, J = 21.2 Hz), 26.3, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.18 to −81.24 (m, 3F), −110.74 to −114.75 (m, 2F), −124.64 to −124.67 (m, 2F), −125.91 to −126.04 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{17}H_{20}F_9O_3$ (M + H$^+$) 443.1269. Found: 443.1260. IR (KBr, cm^{-1}) ν 2981, 1493, 1365, 1219, 1196, 1132.

*1-(1-(tert-Butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)-2,3,4,5,6-pentafluorobenzene (**3j**).* Colorless liquid (100 mg, 40% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72−5.65 (m, 1H), 3.08−2.91 (m, 1H), 2.79−2.62 (m, 1H), 1.20 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 81.6, 69.3, 33.0 (t, J = 21.0 Hz), 26.0, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.23 to −81.33 (m, 3F), −113.44 to −113.70 (m, 2F), −124.48 to −124.70 (m, 2F), −126.06 to −126.20 (m, 2F), −142.43 to −142.58 (m, 2F), −152.90 to −153.07 (m, 1F), −161.67 to −161.85 (m, 2F); HRMS (EI) Anal. Calcd For $C_{16}H_{12}F_{14}O_2$: 502.0614. Found: 502.0602. IR (KBr, cm^{-1}) ν 2985, 1506, 1367, 1221, 1196, 1134.

*tert-Butyl-(4-(1-(tert-butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)phenyl) Carbonate (**3k**).* Colorless liquid (143 mg, 54% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 5.31−5.26 (m, 1H), 2.85−2.66 (m, 1H), 2.51−2.32 (m, 1H), 1.56 (s, 9H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 151.1, 137.0, 127.8, 121.4, 83.7, 80.9, 78.2, 36.0 (t, J = 21.0 Hz), 27.6, 26.2, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.09 to −81.19 (m, 3F), −111.45 to −113.52 (m, 2F), −124.43 to −124.58 (m, 2F), −125.90 to −126.07 (m, 2F); HRMS (ESI-TOF) The structure has undergone cleavage in the mass spectrum (see below). Anal. Calcd For (3k-1) $C_{13}H_8F_9O_4$ (M − H$^+$) 399.0279. Found: 399.0275; (3k-2) $C_{12}H_8F_9O$ (M − H$^+$) 339.0432. Found: 339.0417; IR (KBr, cm^{-1}) ν 2983, 1758, 1511, 1366, 1218, 1147, 1132.

*4-(1-(tert-Butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)phenyl Benzoate (**3l**).* Colorless liquid (178 mg, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21−8.19 (m, 2H), 7.64−7.59 (m, 1H), 7.52−7.47 (m, 2H), 7.45−7.41 (m, 2H), 7.26−7.23 (m, 2H), 5.34−5.31 (m, 1H), 2.87−2.72 (m, 1H), 2.54−2.39 (m, 1H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 151.0, 137.1, 133.6, 130.2, 129.4, 128.6, 128.0, 121.9, 80.8, 78.2, 36.0 (t, J = 21.1 Hz), 26.2, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.11 to −81.18 (m, 3F), −111.40 to −113.39 (m, 2F), −124.40 to −124.47 (m, 2F), −125.89 to −126.00 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{23}H_{22}F_9O_4$ (M + H$^+$) 533.1374. Found: 533.1352. IR (KBr, cm^{-1}) ν 2977, 1732, 1510, 1363, 1194, 1130.



*1-(1-(tert-Butylperoxy)-3,3,4,4,5,5,6,6,6-nonafluorohexyl)-4-(4-fluorophenoxy)benzene (**3m**).* Colorless liquid (172 mg, 66% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.6 Hz, 2H), 7.02−6.97 (m, 4H), 6.96−6.93 (m, 2H), 5.29−5.26 (m, 1H), 2.92−2.77 (m, 1H), 2.54−2.39 (m, 1H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 158.2, 157.9, 152.50, 152.48, 133.9, 128.5, 121.03, 120.95, 118.0, 116.5, 116.3, 80.8, 78.5, 35.8 (t, J = 21.10 Hz), 26.2, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.28 to −81.35 (m, 3F), −111.64 to −113.31 (m, 2F), −119.59 (s, 1F), −124.48 to −124.59 (m, 2F), −126.01 to −126.12 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{22}H_{21}F_{10}O_3$ (M + H$^+$) 523.1331. Found: 523.1317. IR (KBr, cm^{-1}) ν 2982, 1498, 1365, 1213, 1193, 1132.

*1-(tert-Butyl)-4-(1-(tert-butylperoxy)-3,3,4,4,5,5,5-heptafluoropentyl)benzene (**4a**).* Colorless liquid (159 mg, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.3 Hz, 2H), 5.29−5.26 (m, 1H), 2.88−2.73 (m, 1H), 2.52−2.37 (m, 1H), 1.32 (s, 9H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 136.4, 126.6, 125.5, 80.8, 78.7, 35.7 (t, J = 21.2 Hz), 34.6, 31.3, 26.3, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.50 (t, J = 9.8 Hz, 3F), −112.32 to −114.22 (m, 2F), −127.86 (t, J = 2.5 Hz, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{19}H_{24}F_7O_2$ (M − H$^+$) 417.1665. Found: 417.1674. IR (KBr, cm^{-1}) ν 2968, 1514, 1364, 1220, 1196, 1114.

*1-(tert-Butyl)-4-(1-(tert-butylperoxy)-3,4,4,4-tetrafluoro-3-(trifluoromethyl)butyl)benzene (**4b**).* Colorless liquid (146 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 5.25−5.20 (m, 1H), 2.94−2.78 (m, 1H), 2.58−2.44 (m, 1H), 1.32 (s, 9H), 1.20 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 136.3, 126.7, 125.5, 80.6, 79.2, 34.6, 33.6, 33.4, 31.3, 26.3, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −76.47 to −76.64 (m, 3F), −76.97 to −77.12 (m, 3F), −184.35 to −184.48 (m, 1F); HRMS (ESI-TOF) Anal. Calcd For $C_{19}H_{24}F_7O_2$ (M − H$^+$) 417.1665. Found: 417.1658. IR (KBr, cm^{-1}) ν 2968, 1515, 1364, 1245, 1220, 1160.

*1-(tert-Butyl)-4-(1-(tert-butylperoxy)-3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)benzene (**4c**).* Colorless liquid (176 mg, 62% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 5.31−5.26 (m, 1H), 2.92−2.73 (m, 1H), 2.56−2.37 (m, 1H), 1.32 (s, 9H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 136.4, 126.6, 125.6, 80.8, 78.8, 36.1 (t, J = 21.0 Hz), 34.6, 31.3, 26.3, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.24 (t, J = 10.0 Hz, 3F),

DOI: 10.1021/acs.joc.6b00575
J. Org. Chem. 2016, 81, 5878−5885

−111.34 to −113.31 (m, 2F), −121.92 (s, 2F), −123.06 (s, 2F), −123.54 to −123.79 (m, 2F), −126.27 to −126.49 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{22}H_{24}F_{13}O_2$ ($M - H^+$) 567.1569. Found: 567.1559. IR (KBr, cm^{-1}) ν 2968, 1514, 1365, 1235, 1192, 1144.

*1-(tert-Butyl)-4-(1-(tert-butylperoxy)-3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-pentadecafluorononyl)benzene (**4d**).* Colorless liquid (250 mg, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 5.31−5.26 (m, 1H), 2.92−2.73 (m, 1H), 2.55−2.38 (m, 1H), 1.32 (s, 9H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 136.5, 126.6, 125.6, 80.8, 78.8, 36.1 (t, J = 21.0 Hz), 34.6, 31.3, 26.3, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.12 (t, J = 10.0 Hz, 3F), −111.35 to −113.30 (m, 2F), −121.75 (s, 2F), −122.25 (s, 2F), −122.93 (s, 2F), −123.63 (s, 2F), −126.25 to −126.49 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{23}H_{24}F_{15}O_2$ ($M - H^+$) 617.1537. Found: 617.1561. IR (KBr, cm^{-1}) ν 2969, 1514, 1365, 1234, 1198, 1147.

*1-(tert-Butyl)-4-(1-(tert-butylperoxy)-3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)benzene (**4e**).* Colorless liquid (251 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 5.31−5.26 (m, 1H), 2.92−2.73 (m, 1H), 2.56−2.37 (m, 1H), 1.32 (s, 9H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 136.5, 126.6, 125.6, 80.8, 78.8, 36.1 (t, J = 21.0 Hz), 34.6, 31.3, 26.3, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.24 (t, J = 10.0 Hz, 3F), −111.39 to −113.38 (m, 2F), −121.61 to −121.91 (m, 2F), −122.16 (s, 4F), −122.99 (s, 2F), −123.68 (s, 2F), −126.33 to −126.58 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{24}H_{24}F_{17}O_2$ ($M - H^+$) 667.1505. Found: 667.1536. IR (KBr, cm^{-1}) ν 2968, 1512, 1364, 1241, 1197, 1146.

*1-(tert-Butyl)-4-(1-(tert-butylperoxy)-3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-henicosafluorododecyl)benzene (**4f**).* Colorless liquid (284 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.29−5.24 (m, 1H), 2.90−2.72 (m, 1H), 2.55−2.37 (m, 1H), 1.32 (s, 9H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 136.5, 126.6, 125.6, 80.8, 78.8, 36.1 (t, J = 21.0 Hz), 34.6, 31.3, 26.3, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.32 to −81.49 (m, 3F), −111.51 to −113.44 (m, 2F), −121.84 (s, 2F), −122.13 (s, 8F), −123.10 (s, 2F), −123.75 (s, 2F), −126.60 (s, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{26}H_{24}F_{21}O_2$ ($M - H^+$) 767.1441. Found: 767.1417. IR (KBr, cm^{-1}) ν 2969, 1364, 1242, 1211, 1150.

*1-(tert-Butyl)-4-(1-(tert-butylperoxy)-4,4,4-trifluorobutyl)benzene (**4g**).* Colorless liquid (66 mg, 40% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H), 4.89−4.86 (m, 1H), 2.22−1.97 (m, 4H), 1.31 (s, 9H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 136.6, 126.5, 125.4, 83.8, 80.4, 34.6, 31.4, 30.33 (q, J = 29.0 Hz), 27.4−27.3 (m), 26.5, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −66.36 (s, 3F); HRMS (ESI-TOF) Anal. Calcd For $C_{18}H_{26}F_3O_2$ ($M - H^+$) 331.1885. Found: 331.1878. IR (KBr, cm^{-1}) ν 2966, 1387, 1363, 1252, 1196, 1141.

*1-(4-(tert-Butyl)phenyl)-3,3,4,4,5,5,6,6,6-nonafluorohexan-1-ol (**7**).* Colorless liquid (180 mg, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 5.12−5.05 (m, 1H), 2.75 (s, 1H), 2.64−2.47 (m, 1H), 2.46−2.27 (m, 1H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 139.8, 125.7, 125.4, 67.6, 39.6 (t, J = 20.5 Hz), 34.5, 31.2, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.16 to −81.26 (m, 3F), −112.19 to −114.77 (m, 2F), −124.53 to −124.77 (m, 2F), −125.93 to −126.09 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{16}H_{17}F_9O$: 396.1136. Found: 396.1129. IR (KBr, cm^{-1}) ν 3388, 2966, 1513, 1356, 1217, 1132.

*(Z)-1-(4-(tert-Butyl)phenyl)-3,4,4,5,5,6,6,6-octafluorohex-2-en-1-one (**8**).*[10b] Colorless liquid (133 mg, 71%yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.0 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 6.74 (d, J = 32.0 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.9, 158.6, 133.6, 128.8, 126.0, 111.0, 110.9, 110.9, 110.9, 35.3, 30.9, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.65 to −80.76 (m, 3F), −113.15 to −113.34 (m, 1F), −119.24 to −119.46 (m, 2F), −126.96 to −127.10 (m, 2F). MS: Anal. Calcd For $C_{16}H_{15}F_8O$ ($M + H^+$) 375. Found: 375; IR (KBr, cm^{-1}) ν 2967, 1701, 1668, 1605, 1226, 1187, 1122.

*1-(4-(tert-Butyl)phenyl)-4,4,5,5,6,6,6-heptafluorohexan-1-one (**9**).* Colorless liquid (134 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.6 Hz, 2H), 7.50 (d, J = 8.6 Hz, 2H), 3.30−3.26 (m, 2H), 2.66−2.52 (m, 2H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 157.5, 133.6, 128.0, 125.7, 35.1, 31.0, 29.3 (t, J = 2.7 Hz), 25.3 (t, J = 21.8 Hz), not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.61 (t, J = 10.0 Hz, 3F), −115.10 to −115.30 (m, 2F), −127.72 to −127.85 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{16}H_{18}F_7O$ ($M + H^+$) 359.1246. Found: 359.1252. IR (KBr, cm^{-1}) ν 2967, 1687, 1607, 1353, 1224, 1175, 1111.

*(Z)-1-(4-(tert-Butyl)phenyl)-3-(diethylamino)-4,4,5,5,6,6,7,7,7-nonafluorohept-2-en-1-one (**10**).* Pale yellow liquid (207 mg, 97% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.5 Hz, 2H), 6.49 (s, 1H), 3.24 (q, J = 7.0 Hz, 4H), 1.35 (s, 9H), 1.10 (t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.8, 156.0, 146.1 (t, J = 22.0 Hz), 136.5, 128.1, 125.5, 106.6 (t, J = 6.5 Hz), 47.2, 35.0, 31.0, 13.1, not all carbons are reported due to extensive ^{19}F splitting; ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.47 (t, J = 10.3 Hz, 3F), −108.33 to −108.42 (m, 2F), −125.40 to −125.48 (m, 2F); HRMS (ESI-TOF) Anal. Calcd For $C_{20}H_{25}F_7NO$ ($M + H^+$) 428.1824. Found: 428.1828. IR (KBr, cm^{-1}) ν 2969, 1650, 1341, 1226, 1209, 1181, 1109.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00575.

Experimental results of radical trappings, copies of ^{1}H NMR and ^{13}C NMR spectra for all products, and the Cartesian coordinates and energies of all structures on which calculations were performed (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD) and the Natural Science Foundation of China NSFC (Grants 21302015, 21302133, 21272165, and 21572148)

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