# Synthesis of α,α-Difluoro-Functionalized Ketones

Zai-Ming Qiu and Donald J. Burton*

*Department of Chemistry, The University of Iowa, Iowa City, Iowa 52242*

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In the presence of a catalytic amount of tetrakis(triphenylphosphine) palladium [$Pd(PPh_3)_4$], iododifluoromethyl alkyl and phenyl ketones **1** react with alkenes to give the corresponding α,α-difluoro-γ-iodo ketones in high yields at room temperature either neat or in hexane at 60 °C. A variety of functional groups, such as alkyl, trimethylsilyl, hydroxy, epoxy, ketone, and ester, are tolerated under the reaction conditions. The reaction can be completely suppressed by a radical inhibitor, di-*tert*-butyl nitroxide or hydroquinone. A ring closure reaction occurs when **1** reacts with diethyl diallylmalonate in the presence of a catalytic amount of $Pd(PPh_3)_4$. Under UV irradiation, the reaction of **1** with diallyl ether gives a tetrahydrofuran derivative. All these results are consistent with a radical chain mechanism initiated by single electron transfer from $Pd(PPh_3)_4$ to **1**. In the presence of a catalytic amount of nickel dichloride hexahydrate, the iodine in the 1:1 addition adducts is readily reduced by zinc in moist THF under mild conditions to give the corresponding α,α-difluoro ketones in high yields. A one-pot addition–reduction reaction has been developed for the synthesis of α,α-difluoro ketones without the isolation of the 1:1 addition adducts, which provides a new, efficient, and practical method for the preparation of a variety of α,α-difluoro-functionalized ketones.

## Introduction

The presence of a carbon–fluorine bond in a specific position of an organic molecule can result in many unique physical and chemical properties because of the high electronegativity of fluorine, the close van der Waals radius to hydrogen, and the strong carbon–fluorine bond.[1] Many dramatic enhancements of biological activity have been reported for selectively fluorinated biologically important compounds.[2-4] Therefore, selective fluorination has been used as one of the most useful, important, and efficient approaches to change, improve, and modify biological activity. For example, fluoro ketones have been widely employed as enzyme inhibitors in recent years and greatly increased biological activity has been observed compared with their nonfluorinated analogs because the α-fluorinated ketone forms a stable tetrahedral intermediate with the weak nucleophilic serine residue of enzymes.[3] Therefore, the synthesis of α,α-difluoro ketones has attracted much attention.

Although many efforts have been made for the synthesis of carbonyl compounds containing an adjacent difluoromethylene group,[2,4] most work has focused on α,α-difluoro esters presumably because of the available Reformatsky reaction.[4] Only limited work has been directed to the synthesis of α,α-difluoro ketones. Some fluorinating agents, such as elemental fluorine, perchloryl fluoride, xenon difluoride, acetyl hypofluorite, and cesium fluoroxysulfate have been utilized to directly introduce fluorine into the α-position of carbonyl molecules.[5] However, the explosive, hazardous nature or expense of these agents, the low yield or poor selectivity of the reactions, or the extremely severe reaction conditions have strictly limited their practical application. Recently, NF compounds have also been successfully used as fluorinating agents for the preparation of α-fluorinated ketones.[6a-c] Although both mono- and difluoro ketones can be obtained in good yields using NF agents, this reaction is only suitable for the fluorination of enolate anions or compounds with a highly acidic methylene group, such as β-dicarbonyl substituted substrates. The conversion of acetylenes with F-TEDA-$BF_4$ to α,α-difluoro ketones works only for 1-phenyl-substituted alkynes.[6d]

Recently, the Reformasky reaction has also been utilized for the synthesis of α,α-difluoro ketones using

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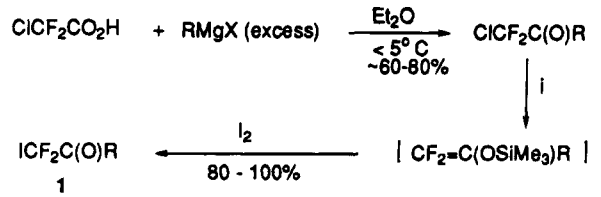
**Scheme 1**[a]




[a] Key: (i) $Me_3SiCl/Zn/CH_3CN$, rt or 60 °C, 80–100%. R: Ph(**a**, 74%), *n*-$C_4H_9$ (**b**, 57%), *n*-$C_6H_{13}$ (**c**, 66%).

chlorodifluoromethyl ketones and carbonyl substrates.[7] However, the reaction is limited to the preparation of β-hydroxy-substituted α,α-difluoro ketones. Similarly, the reaction of the *gem*-difluoroallyl anion with esters can give reasonable yields of α,α-difluoroallyl ketones.[8] However, a low reaction temperature was required, and many functionalities could not be tolerated under the reaction conditions.

In a preliminary paper,[9] we have briefly reported a new, practical, and general method for the preparation of α,α-difluoro ketones *via* the addition of iododifluoromethyl ketones with alkenes in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium, followed by selective reduction of the iodine with Zn/$NiCl_2 \cdot 6H_2O$ under mild conditions. Herein, we wish to report our detailed experimental results.

## Results and Discussion

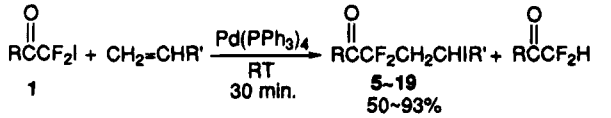
It is well-known that the addition reaction of perfluoroalkyl iodides with carbon–carbon multiple bonds is one of the most important methods for the introduction of $R_f$ groups into organic molecules.[10,11] Recently, many functionalized iododifluoromethyl derivatives [FG$CF_2I$, e.g. FG = ROC(O)–, $(RO)_2P(O)$– , and $RS(O)_2$–] were reported to react with alkenes in the presence of an electron donor to produce the corresponding 1:1 addition adducts *via* a similar radical mechanism.[12–14] Consequently, iododifluoromethyl ketones might also be reacted with alkenes to give the corresponding α,α-difluoro-γ-iodo ketones by a similar reaction. The iododifluoromethyl ketones (**1a–c**) were prepared from the commercially available chlorodifluoroacetic acid by the sequence outlined in Scheme 1.

The reaction of chlorodifluoroacetic acid with Grignard reagents has been reported.[15] By utilization of excess RMgX ($ClCF_2CO_2H$:RMgX = 1:3.3) and careful control of the reaction temperature (<5 °C), a 56–79% yield of chlorodifluoromethyl ketones was obtained.

Treatment of the chlorodifluoromethyl ketones with zinc and trimethylsilyl chloride in acetonitrile gave high yields of the corresponding 1-substituted 2,2-difluorovinyl trimethylsilyl ethers.[16] The reaction of phenyl chlorodifluoromethyl ketone with trimethylsilyl chloride and zinc was exothermic and occurred at room temperature without purification of the commercially available reagent and solvent. In the case of the alkyl chlorodifluoromethyl ketones, however, it was necessary to reflux the reaction mixture and employ dry acetonitrile to minimize the formation of 1,1-difluoromethyl ketones [$HCF_2C(O)R$, **2**]. Small amounts of $RCH(OH)CF_2Cl$ (**3**) were occasionally formed in the reaction as a byproduct. The solution of 1-phenyl-2,2-difluorovinyl trimethylsilyl ether in acetonitrile was stable at room temperature for weeks, although the isolated 1-phenyl-2,2-difluorovinyl trimethylsilyl ether was unstable.[16]

The reaction of 1,1-difluorovinyl trimethylsilyl enol ethers with iodine in triglyme (TG) at room temperature gave high yields of the corresponding iodides. Similar results were obtained when acetonitrile was used as solvent instead of TG, which made it possible to prepare the iododifluoromethyl ketones (**1**) from chlorodifluoromethyl ketones *via* a one-pot reaction without isolation of the enol ethers. By this method, reasonable yields of **1** were obtained. However, the iododifluoromethyl ketones (**1**) are not very stable. Partial decomposition occurred during distillation, and isolated **1** contained a small amount of **2** (2–9%) and iodine. Usually, the iododifluoromethyl ketones do not exhibit a molecular ion signal in GC–MS spectroscopic analysis, and mainly the $M^+ - I$ and $RCO^+$ ($M^+ - CF_2I$, R = alkyl, Ph; base peak) signals were observed. Only **1a** showed a very weak $M^+$, which was further confirmed by high-resolution MS analysis. However, the structure of **1** was supported by $^1H$, $^{19}F$, $^{13}C$ NMR and FTIR spectroscopic analysis data.

In the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium, both the aryl (**1a**) and alkyl (**1b**, **1c**) iododifluoromethyl ketones reacted with alkenes (**4**) in the absence of solvent under a nitrogen atmosphere at room temperature. High yields of the corresponding 1:1 addition products, **5–19**, were produced in 30 min. Similar results were obtained when the reaction was conducted in hexane at 60 °C. These results are summarized in Table 1.




The amount of $Pd(PPh_3)_4$ required in the reaction depended upon the amount of iodine present in the ketones (**1**). The iodine in the ketones could be readily removed by simply shaking the ketones with excess mercury at room temperature. Using the iodine-free ketones, the reaction could be initiated in 10 s in the presence of 1.1–3 mol % of $Pd(PPh_3)_4$. Small amounts of $RC(O)CF_2H$, **2**, were sometimes formed as a byproduct

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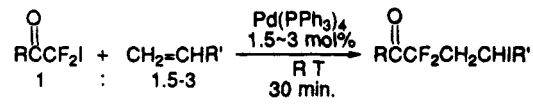
**Table 1. $Pd(PPh_3)_4$-Initiated Addition of 1 to Alkenes**




| no. | R | R' | conversion[a] (%) | product[a,b] (%) |
|---|---|---|---|---|
| **5** | Ph | $n$-$C_5H_{11}$ | 98[c] | 86 |
| **5** | Ph | $n$-$C_5H_{11}$ | 100 | 97 (71) |
| **6** | Ph | $n$-$C_6H_{13}$ | 100[c] | 85 |
| **6** | Ph | $n$-$C_6H_{13}$ | 100 | 94 (81) |
| **7** | Ph | $CH_3CO(CH_2)_2$ | 100 | 100 (84) |
| **8** | Ph | $CH_2CHO(CH_2)_2$ | 100 | 100 (68) |
| **9** | Ph | $Me_3CCH_2$ | 100 | 100 (88) |
| **10** | Ph | $Me_3Si$ | 100 | 100 (92) |
| **11** | Ph | $HO(CH_2)_8$ | 92 | 86 |
| **12** | $n$-$C_4H_9$ | $n$-$C_3H_7$ | 86 | 78 (58) |
| **13** | $n$-$C_4H_9$ | $n$-$C_4H_9$ | 95 | 85 (62) |
| **14** | $n$-$C_4H_9$ | $Me_3Si$ | 100 | 100 (93) |
| **15** | $n$-$C_6H_{13}$ | $CH_3CO(CH_2)_2$ | 100 | 93 (84) |
| **16** | $n$-$C_6H_{13}$ | $HOCH_2CH_2$ | 71 | 76 (50) |
| **17** | $n$-$C_6H_{13}$ | $n$-$C_4H_9$ | 100 | 90 (77) |
| **18** | $n$-$C_6H_{13}$ | $CH_3CO_2CH_2$ | 100 | 93 (87) |
| **19** | $n$-$C_6H_{13}$ | $Me_3Si$ | 100 | 98 (90) |

[a] Determined by $^{19}F$ NMR analysis; small amount of $RC(O)CF_2H$ was sometimes observed. [b] NMR yield based on consumed **1**; isolated yields in parentheses based on **1**. [c] Reaction in hexane at 60 °C.

and easily removed from the products by either distillation or column chromatography. For example, addition of one portion of **1a** to a mixture of 1-heptene and 1.6 mol % of $Pd(Ph_3)_4$ at room temperature under $N_2$, while vigorously stirring, resulted in an exothermic reaction in 5–10 s. The reaction was complete in 30 min and gave the corresponding α,α-difluoro-γ-iodooctyl phenyl ketone, **5**, in 71% isolated yield.

Interestingly, a variety of functionalities substituted on the alkenes are tolerated under the reaction conditions. For example, treatment of **1a** with trimethylvinylsilane under the usual conditions gave the adduct, **10**, in 92% isolated yield. This product should be a useful intermediate for the further preparation of selectively fluorinated compounds. Many interesting reactions and applications of 1-iodo-1-trimethylsilyl substituted compounds have been reported.[17] Similarly, alkenes with functional groups including alkyl, hydroxy, epoxy, ketone and ester have been successfully used in the reaction as shown in Table 1. Therefore, this method conveniently provides the precursors for the preparation of a variety of α,α-difluoro-functionalized ketones under mild conditions. (Table 1).

All the products exhibit a typical AB pattern signal in the $^{19}F$ NMR spectrum, similar to the adducts of iododifluoroacetate[12] and (iododifluoromethyl)phosphonate[13] with alkenes, indicating that the two fluorines in the adducts are not equivalent. For example, in the typical $^{19}F$ NMR spectrum of α,α-difluoro-γ-iodononyl phenyl ketone (**6**, Figure 1.), each fluorine gave a doublet of doublet of doublets at −98.0 ($^2J_{FF}$ = 291.5 Hz, $^3J_{FH}$ = 22.9 and 12.9 Hz) and −100.0 ($^2J_{FF}$ = 291.5 Hz, $^3J_{FH}$ = 21.0 and 12.9 Hz) ppm, respectively. The largest coupling constant was contributed by the F–F coupling. Each fluorine was further split by the two vicinal hydrogens to give another

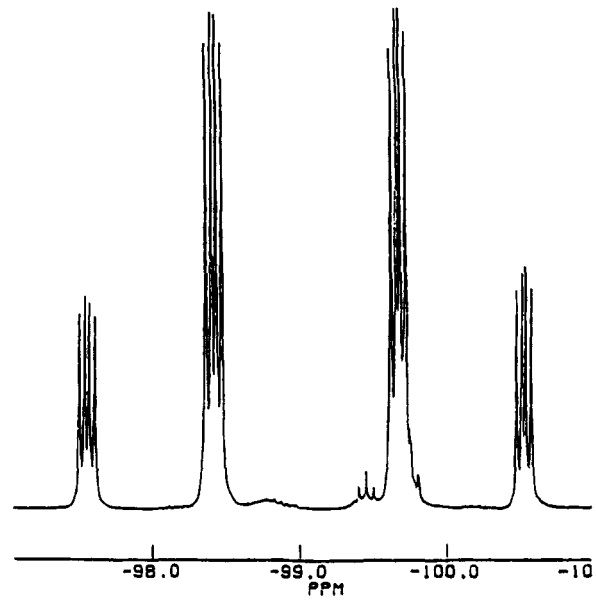



**Figure 1.** Observed $^{19}F$ NMR spectrum of $PhC(O)CF_2CH_2CHIC_6H_{13}$-$n$ (**6**).

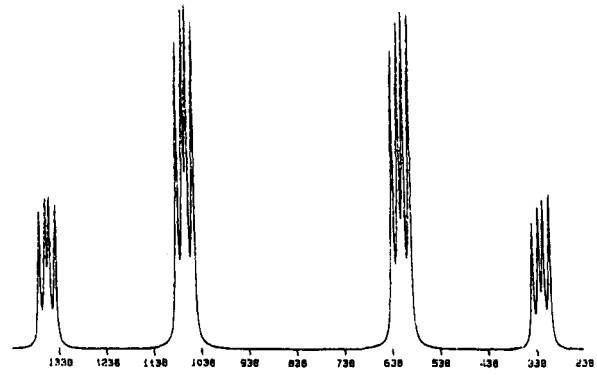


**Figure 2.** Computer simulated $^{19}F$ NMR spectrum of $PhC(O)CF_2CH_2CHIC_6H_{13}$-$n$ (**6**).

doublet of doublets due to the adjacent chiral center in the γ-position. However, one more doublet was observed (dddd) in the $^{19}F$ NMR spectrum of 2,2-difluoro-4-iodo-7,8-epoxy-1-octanone (**8**), due to the presence of a second chiral center in the adduct. The computer simulation of both $^{19}F$ NMR spectra (Figure 2 for **6**) showed excellent coincidence with the experimental ones.[18] The structure of all new products were further assigned *via* $^1H$, $^{13}C$ NMR and FTIR spectra. In the GC–MS spectrum, typical $M^+ - I$ and $I^+$ signals were observed.

It has been well-documented that $Pd(PPh_3)_4$ is a good electron donor and can initiate the radical reaction of perfluoroalkyl iodides[19] and (iododifluoromethyl)phosphonates.[13] Accordingly, a radical chain mechanism involving single electron transfer between $Pd(PPh_3)_4$ and **1** is proposed for the addition reaction of iododifluoromethyl ketones with alkenes (Scheme 2).

Owing to the partial positive charge on the iodide, iododifluoromethyl ketone, as an electron acceptor, could form an electron donor–acceptor complex with $Pd(PPh_3)_4$ by partial charge transfer, similar to the reaction of

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(18) The spectral simulation program was written by Dr. W. E. Bennett of the University of Iowa.

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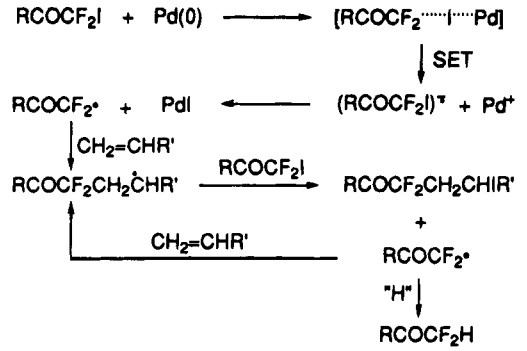
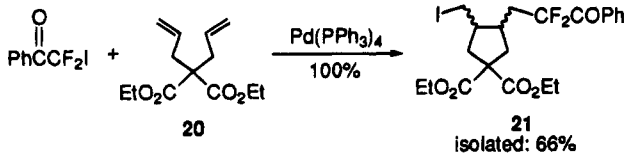
**Scheme 2**



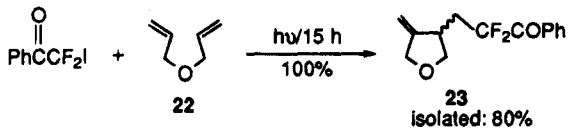

perfluoroalkyl iodides with electron–donors.[20] The formation of this complex should decrease the energy barrier for the SET process and facilitate the single electron transfer between the donor and acceptor in the initiation step, in which the iodine atom acts as a bridge. The formed radical anion is unstable and readily decomposes to generate the corresponding carboalkyldifluoromethyl radical, which adds to the alkene and forms the 1:1 addition adduct by subsequent abstraction of an iodine atom from **1**. The propagating radical, carboalkyldifluoromethyl radical, is regenerated to continue the chain process.

Some experimental evidence has been obtained which is consistent with the proposed mechanism. First, it has been found that the reaction could be completely suppressed in the presence of a radical inhibitor. For example, in the presence of 16% of di-*tert*-butyl nitroxide, the reaction of **1c** and allyl acetate was completely inhibited, and no addition product was observed after reaction overnight. In contrast, the uninhibited reaction was completed in 30 min and gave the addition adduct, **18**, in 87% isolated yield under similar conditions (Table 1). Similarly, only starting material was detected when **1c** reacted with allyl acetate in the presence of 15% of hydroquinone.

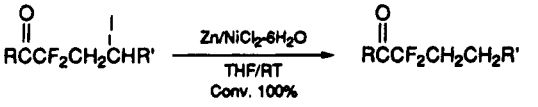
Another well-known method for probing a radical mechanism is the ring closure reaction in the exo-mode from the 5-hexenyl radical system.[13,19,21] In order to further confirm the proposed mechanism, we examined the reaction of **1a** with diethyl diallylmalonate (**20**) under the usual conditions. A cyclopentane derivative, **21**, was formed in 95% yield based on the analysis of the $^{19}F$ NMR spectrum after reaction (isolated yield: 66%), which further supported the proposed radical mechanism.




Photolysis is a classic initiation method for a radical reaction. In fluorine chemistry, the photoreaction of perfluoroalkyl iodides with carbon–carbon multiple bonds has been used as an important method to introduce perfluoroalkyl groups into organic substrates.[10] In order to further comfirm the proposed radical mechanism, we also tried the UV-initiated reaction of iododifluoromethyl phenyl ketones (**1a**) with diallyl ether (**22**). A tetrahydrofuran derivative (**23**) was formed in 90% $^{19}F$ NMR yield (isolated: 80%) after reaction for 10 h, which provides additional evidence for the proposed mechanism.




Usually, the 1:1 addition adduct, α,α-difluoro-γ-iodo ketone, is not very stable, and partial decomposition was always observed during isolation either *via* chromatography or by distillation. It has also been demonstrated that α,α-difluoro-γ-iodo ketones can easily undergo cyclization when reacted with weak nucleophiles, such as ammonium hydroxide.[22] To function as an enzyme inhibitor, it is necessary to remove the iodine from the α,α-difluoro-γ-iodo ketones. Although a number of methods are available for the reduction of carbon–halogen bonds, most of the commonly used reducing reagents are effective for a relatively constrained range of substrates, since they are capable of reducing many other functionalities. The addition reaction of iododifluoromethyl ketones with alkenes afforded a variety of functional group substituted α,α-difluoro-γ-iodo ketones. Consequently, a highly specific reducing reagent was required to reduce the iodine atom from the 1:1 adducts under mild conditions without affecting the other functional groups. Recently, zinc with a catalytic amount of nickel chloride hexahydrate has been found to be a selective reduction system with α,α-difluoro-γ-iodo esters[12a] and phosphonates.[13] A variety of functional groups were tolerated under these reaction conditions. Thus, we employed this system to remove the iodine from the α,α-difluoro-γ-iodo ketones.



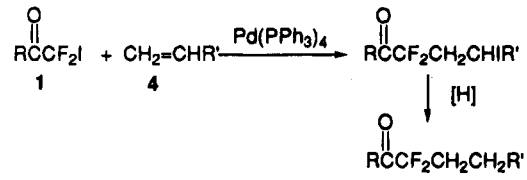

In the presence of zinc and a catalytic amount of nickel chloride hexahydrate, the iodine atom in α,α-difluoro-γ-iodo ketones was smoothly reduced in moist THF at room temperature to give the corresponding α,α-difluoro ketones in excellent yields. A simple triplet signal was observed after reduction when the reaction mixture was monitored by $^{19}F$ NMR. For example, after the mixture of zinc and 10 mol % of nickel chloride hexahydrate in moist THF was stirred for 10 min, α,α-difluoro-γ-iodo-ω-acetylpentyl phenyl ketone (**7**) was added. The mixture was stirred at room temperature overnight, and the typical AB pattern signal of the 1:1 adduct disappeared and a new triplet signal was observed (−100.2 ppm, t, $^3J_{FH}$ = 17.1 Hz) in quantitative yield in the reaction mixture based on $^{19}F$ NMR analysis. The product, α,α-difluoro-ω-acetylpentyl phenyl ketone (**7h**), was isolated in 79% yield by distillation (Table 2). Compared with the γ-iodo ketones, the α,α-difluoro ketones sometimes

(20) (a) Chen, Q. Y.; Qiu, Z. M. *J. Fluorine Chem.* **1987**, *35*, 79. (b) International Symposium on Centenary of Discovery of Fluorine, Paris, 1986; Abstract p 75. (c) Qiu, Z. M. Ph. D. Thesis, Shanghai Institute of Organic Chemistry, Academia Sinica, Shanghai, 1987.

(21) (a) Beckwith, A. L. J.; Easton, C. J.; Lawrence, T.; Serelis, A. K. *Aust J. Chem.* **1983**, *36*, 545. (b) Chen, Q. Y.; Qiu, Z. M. *J. Fluorine Chem.* **1986**, *31*, 301; **1986**, *35*, 343. (c) Chen, Q. Y.; Qiu, Z. M.; Yang, Z. Y. *J. Fluorine Chem.* **1987**, *36*, 149. (d) Chen, Q. Y.; Yang, Z. Y.; Qiu, Z. M. *Kexue Tongbao* **1987**, *183*, 593.

(22) (a) Qiu, Z. M.; Burton, D. J. *Tetrahedron Lett.* **1994**, *35*, 4319. (b) Qiu, Z. M.; Burton, D. J. *A New Precursor for the Synthesis of β-Fluoropyrroles, α,α-Difluoro-γ-iodo-trimethylketones*; Presented at 12th Winter Fluorine Conference, Jan 1995, St. Petersburg, FL, Abst. No. 35; p 26.

**Table 2. Synthesis of α,α-Difluoro Ketones by Reduction with Zn/$NiCl_2$·6$H_2O$/THF[a]**

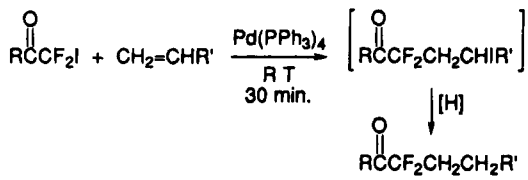



| no. | Pd(0) | [H] Zn/ $NiCl_2$·6$H_2O$ | product | isolated yield (%) |
|---|---|---|---|---|
| **5h** | *b* | 1.2/10% | $PhCOCF_2CH_2CH_2C_5H_{11}$-*n* | 79 |
| **5h** | 1.3% | 1.6/10% | $PhCOCF_2CH_2CH_2C_5H_{11}$-*n* | 74 |
| **7h** | *b* | 2.0/10% | $PhCOCF_2(CH_2)_4COCH_3$ | 79 |
| **11h** | 3.0% | 1.5/20% | $PhCOCF_2(CH_2)_{10}OH$ | 76 |
| **13h** | *b* | 1.3/13% | *n*-$C_4H_9COCF_2C_6H_{13}$-*n* | 82 |
| **13h** | 3.0% | 1.2/8% | *n*-$C_4H_9COCF_2C_6H_{13}$-*n* | 68 |
| **15h** | *b* | 1.3/6% | *n*-$C_6H_{13}COCF_2(CH_2)_4COCH_3$ | 76 |
| **15h** | 1.9% | 1.3/15% | *n*-$C_6H_{13}COCF_2(CH_2)_4COCH_3$ | 82 |

[a] One-pot addition–reduction except where otherwise noted; **1**:**4** = 1:1.3–2.3. [b] Isolated adducts were used for the reduction reaction.

showed a weak $M^+$ signal in the GC–MS spectrum, which was further confirmed by high-resolution MS analysis.

The two-step reaction, $Pd(PPh_3)_4$-initiated addition followed by reduction with a Zn/$NiCl_2$·6$H_2O$ system provided a general, efficient, and practical route to α,α-difluoro ketones from iododifluoromethyl ketones. However, due to the mild conditions of both the addition and reduction reactions, it seemed possible to synthesize α,α-difluoro ketones by a more convenient one-pot reaction without isolation of the 1:1 addition adducts.




Indeed, when the reaction mixture of α,α-difluoro-γ-iodo ketone formed by $Pd(PPh_3)_4$-initiated addition of iododifluoromethyl ketones with alkenes was directly transferred to another flask charged with zinc and a catalytic amount of nickel chloride hexahydrate in moist THF, the corresponding α,α-difluoro ketone was formed in high yield after reaction overnight at room temperature. The addition-reduction products were isolated by simple distillation or column chromatography. Both the addition and the reduction can be simply monitored by $^{19}F$ NMR analysis. For example, coupling of **1c** with 5-hexen-2-one followed by reduction afforded **15h** in 82% overall yield. Representative examples are summarized in Table 2.

## Conclusion

Similar to perfluoroalkyl iodide and other functionalized difluoromethyl iodides, iododifluoromethyl ketones reacted with a series of functionalized alkenes in the presence of a catalytic amount of $Pd(PPh_3)_4$. High yields of the corresponding α,α-difluoro-γ-iodo functionalized ketones were synthesized under mild conditions. A radical chain mechanism initiated by single electron transfer reaction is proposed. The iodine in the adducts was readily reduced by zinc in the presence of a catalytic amount of nickel chloride hexahydrate in moist THF with high selectivity. The development of a one-pot addition–reduction protocol provided a more convenient, practical, and efficient method for the preparation of α,α-difluoro-functionalized ketones, which should stimulate further study of α,α-difluoro ketone chemistry.

## Experimental Section

**General.** Alkyl and aryl bromides, alkenes, chlorotrimethylsilane, Mg, Zn, $I_2$, and $NiCl_2$·6$H_2O$ were obtained from Aldrich Chemical Co. and used without purification. Chlorodifluoromethyl ketones,[15] 2,2-difluoro enol trimethylsilyl ether,[16] and $Pd(PPh_3)_4$[23] were prepared according to literature procedures. Acetonitrile and triglyme were dried by distillation from calcium hydride. All reactions were performed in an oven-dried apparatus that consisted of a two, or three-necked flask equipped with a $H_2O$-cooled reflux condenser connected to a nitrogen source and a mineral oil bubbler, a Teflon-coated magnetic stirring bar, and a septum. All boiling points were recorded during fractional distillation using a partial immersion thermometer and are uncorrected. Chromatography was conducted on a 40 × 400 mm column packed with 60–200 mesh silica gel. $^{19}F$, $^1H$ and $^{13}C$ NMR spectra were recorded in $CDCl_3$ solvent. All chemical shifts are reported in parts per million downfield (positive) of the standard. $^{19}F$ NMR spectra are referenced against internal $CFCl_3$ and $^1H$ and $^{13}C$ NMR spectra against internal tetramethylsilane (TMS). FTIR spectra were recorded in $CCl_4$ solution in a cell with 0.1 cm path length. GC–MS spectra were operated at 70 eV, in the electron impact mode with a DB-1 column. GLPC analysis were performed on a 5% OV-101 column with a thermal conductivity detector. High resolution mass spectra were measured by the University of Iowa high resolution mass spectrometry facility.

**General Procedure for the Preparation of Iododifluoromethyl Ketones from 2,2-Difluoro Trimethylsilyl Enol Ethers. Iododifluoromethyl Phenyl Ketone [PhC(O)$CF_2I$, 1a].** To a solution of 3.8 g (15 mmol) of iodine in 20 mL of TG was added 2.3 g (10 mmol) of 1-phenyl-2,2-difluorovinyl trimethylsilyl ether[11] *via* syringe under 1 atm of nitrogen. The reaction mixture was stirred at room temperature for 5 h, and the 1-phenyl-2,2-difluorovinyl trimethylsilyl ether was completely converted to the corresponding iododifluoromethyl ketone in >95% yield and a small amount of difluoromethyl phenyl ketone (**2a**). The reaction mixture was poured into 100 mL of water and extracted with dichloromethane (3 × 20 mL). The combined organic fractions were washed with 5% aqueous sodium bisulfite to remove excess $I_2$ and then water (2 × 10 mL). After the organic layer was dried over magnesium sulfate for 24 h, the solid was removed by filtration. Distillation at atmospheric pressure to remove the solvent, followed by distillation in vacuum, gave 2.0 g (7 mmol, 71% yield: GLPC purity: 100%) of **1a**. Bp: 95–98 °C/0.05 mmHg. $^{19}F$ NMR: δ -54.7 (s). $^1H$ NMR: δ 8.17 (d, $J$ = 7.7 Hz, 2H), 7.67 (t, $J$ = 7.4 Hz, 1H), 7.52 (t, $J$ = 7.8 Hz, 2H). $^{13}C$ NMR: δ 182.3 (t, $J$ = 23.2 Hz), 135.0, 130.9, 128.9, 128.5, 95.7 (t, $J$ = 326.0 Hz). GC–MS: 282 ($M^+$, 0.02), 177 ($ICF_2^+$, 0.27), 155 ($M^+ - I$, 0.14), 127 ($I^+$, 3.55), 105 ($PhCO^+$, 100), 77 ($Ph^+$, 51.97), 51 ($HCF_2^+$, 23.58); HRMS: obsd 281.9345, $C_8H_5F_2OI$, calcd 281.9354. FTIR: 3067, 3032, 1711, 1599, 1588, 1450, 1343, 1323, 1307, 1290, 1268, 1242, 1190, 1151, 1130, 963, 846, 706 $cm^{-1}$.

Difluoromethyl Phenyl Ketone [$PhC(O)CF_2H$, <5%, GLPC purity: 100%]. $^{19}F$ NMR: δ −122.7 (d, $J$ = 53.5 Hz). $^1H$ NMR: δ 8.05 (dd, $J$ = 8.3, 0.95 Hz, 2H), 7.64 (tt, $J$ = 7.4, 1.5 Hz, 1H), 7.50 (dt, $J$ = 7.0, 1.5 Hz, 2H), 6.30 (t, $J$ = 53.5 Hz, 1H). $^{13}C$ NMR: δ 187.63 (t, $J$ = 25.3 Hz), 135.0, 131.7, 129.7, 129.1, 111.26 (t, $J$ = 253.3 Hz). GC–MS: 156 ($M^+$, 2.78), 105 ($PhCO^+$, 100), 77 ($Ph^+$, 79.49), 51 ($HCF_2^+$, 26.07).

**General Procedure for the One-Pot Synthesis of Iododifluoromethyl Ketones from Chlorodifluoromethyl Ketones in Acetonitrile. Iododifluoromethyl Phenyl**

(23) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121.

**Ketone (1a).** A 250 mL three-neck round-bottom flask fitted with a Teflon-coated magnetic stir bar, an addition funnel, a Teflon thermometer adaptor with a thermometer, and a reflux condenser with a glass tee connected to a source of nitrogen was charged with 13.1 g (0.2 mol) of zinc, 21.7 g (0.2 mol) of chlorotrimethylsilane, and 120 mL of commercial-grade acetonitrile. Then, 30.5 g (0.16 mol) of chlorodifluoromethyl phenyl ketone was added in one portion at room temperature with vigorous stirring. An exothermic reaction occurred in minutes. The mixture was stirred at room temperature for 3 h, and 98% of 1-phenyl-2,2-difluorovinyl trimethylsilyl ether was formed as determined by $^{19}F$ NMR analysis. Then, to the reaction mixture was added iodine (55.9 g, 0.22 mol) at room temperature. The reaction mixture was stirred at room temperature for an additional 5 h and gave 33.6 g (74% yield, GLPC purity: 96%) of **1a** after workup and distillation.

By a similar procedure, iododifluoromethyl *n*-butyl and *n*-hexyl ketones were prepared, except that dry acetonitrile was utilized and the reaction mixture was refluxed for 20 h.

**Iododifluoromethyl *n*-Butyl Ketone [*n*-$C_4H_9C(O)CF_2I$, 1b].** Bp: 76−77 °C/23 mmHg. Yield: 57%. GLPC: 97%. $^{19}F$ NMR: δ -61.2 (s). $^1H$ NMR: δ 2.84 (t, $J$ = 6.3 Hz, 2H), 1.6 (m, 2H), 1.32−1.40 (m, 2H), 0.95 (t, $J$ = 6.8 Hz, 3H). $^{13}C$ NMR: δ 193.4 (t, $J$ = 23.8 Hz), 99.2 (t, $J$ = 327.6 Hz), 33.2, 25.2, 22.0, 13.7. GC−MS: 177 ($ICF_2^+$, 2.04), 135, 127 ($I^+$), 105 ($PhCO^+$, 100), 119 (2.55), 93 (1.81), 85 ($C_4H_9CO^+$, 100), 74 (6.42), 67 (3.41), 57 ($C_4H_9^+$, 76.69), 43 (12.61), 41 (48.17). FT-IR: 2964, 2936, 2876, 1753, 1616, 1466, 1405, 1393, 1381, 1246, 1201, 1143, 1108, 1030, 849, 815, 809, 798, 747 $cm^{-1}$.

**Iododifluoromethyl *n*-Hexyl Ketone [*n*-$C_6H_{13}C(O)CF_2I$, 1c].** Bp: 73−76 °C/3 mmHg. Yield: 66%. GLPC: 91%. $^{19}F$ NMR: δ −61.2 (s). $^1H$ NMR: δ 2.83 (t, $J$ = 7.2 Hz, 2H), 1.75−1.65 (m, 2H), 1.40−1.27 (m, 6H), 0.90 (t, $J$ = 6.7 Hz, 3H). $^{13}C$ NMR: δ 193.4 (t, $J$ = 23.7 Hz), 97.6 (t, $J$ = 327.8 Hz), 33.4, 31.4, 28.5, 23.1, 22.5, 14.0. GC−MS: 177 ($ICF_2^+$, 3.09), 127 ($I^+$, 2.71), 113 ($C_6H_{13}CO^+$, 79.12), 85 ($C_6H_{13}^+$, 22.25), 57 ($C_4H_9^+$, 16.96), 55 (15.35), 43 (100), 41 (30.49). FT-IR: 2959, 2930, 2874, 2860, 1753, 1459, 1405, 1365, 1199, 1141, 1112, 1039, 997, 805, 786, 773, 767, 750 $cm^{-1}$.

**1-Chloro-1,1-difluoro-2-octanol [*n*-$C_6H_{13}CH(OH)CF_2Cl$, 3c].** 1-Chloro-1,1-difluoro-2-octanol was formed in <5% NMR yield during the preparation of **1c** and isolated by column chromatography from the distillation residue. $^{19}F$ NMR: δ −63.9 (dd, $J$ = 165.0, 7.4 Hz, 1F), −66.0 (dd, $J$ = 165.0, 7.4 Hz, 1F). $^1H$ NMR: δ 3.93 (m, 1H), 2.35 (s, 1H, OH), 1.76 (m, 2H), 1.57 (m, 2H), 1.31 (m, 6H), 0.90 (t, $J$ = 6.8 Hz, 3H). $^{13}C$ NMR: δ 130.2 (t, $J$ = 296.7 Hz), 75.39 (t, $J$ = 26.3 Hz), 31.63, 30.39, 28.95, 25.20, 22.59, 14.04. GC−MS: 182/184 ($M^+ - H_2O$, 0.11/0.03), 157 ($M^+ - C_3H_7$, 1.05), 70 (51.06), 55 ($C_4H_7^+$, 100), 43 (64.54). FT-IR: 3615, 2959, 2930, 2873, 2861, 1467, 1458, 1208, 1123, 1086 $cm^{-1}$.

**Preparation of Iodine-Free Difluoroiodomethyl Ketones by Reaction with Hg.** An excess of mercury metal was added to the isolated difluoroiodomethyl ketones, and the mixture was stirred or shaken for several minutes at room temperature. The red iodine color in the ketones faded and gave a colorless or light yellow liquid due to the formation of $HgI_2$. After standing, the top clear iodine-free iododifluoromethyl ketones were ready for use and stored in a refrigerator without filtration.

**Representative General Procedure for the Preparation of α,α-Difluoro-γ-iodoketones. 1,1-Difluoro-3-iododononyl Phenyl Ketone [$PhC(O)CF_2CH_2CHIC_6H_{13}$-*n*, 6].** A 50 mL two-neck flask fitted with a magnetic stirring bar, nitrogen inlet, and septum was charged with 0.36 g (0.32 mmol, 2.3 mol %) of $Pd(PPh_3)_4$ and 3.0 g (26.7 mmol) of 1-octene. Then, 3.78 g (13.4 mmol) of **1a** was syringed into the mixture with stirring at room temperature under nitrogen. An exothermic reaction occurred in 5−10 s. After being stirred for 30 min, the reaction mixture was cooled to room temperature. $^{19}F$ NMR analysis showed that 94% of 1,1-difluoro-3-iodononyl phenyl ketone, **6**, and 5% of $PhCOCF_2H$, **2a**, were formed. To the reaction mixture were added 10 mL of hexane and 5 mL of diethyl ether. The solids were removed by filtration, and the solvents were removed by rotary evaporation. Chromatography (silica gel column 40 × 400 mm) of the residue with hexane−dichloromethane (8:2) eluant gave 4.27 g of **6** in 81% yield (NMR purity: 100%). $^{19}F$ NMR: δ −98.0 (ddd, $J$ = 291.6, 22.97, 12.84 Hz, 1F), −100.0 (ddd, $J$ = 291.6, 21.0, 12.9 Hz, 1F). $^1H$ NMR: δ 8.04 (d, $J$ = 7.7 Hz, 2H), 7.53 (t, $J$ = 7.4 Hz, 1H), 7.39 (t, $J$ = 7.7 Hz, 2H), 4.35 (m, 1H), 3.12−2.79 (m, 2H), 1.82−1.73 (m, 2H), 1.30−1.22 (m, 8H), 0.87 (t, $J$ = 6.8 Hz, 3H). $^{13}C$ NMR: δ 188.0 (t, $J$ = 30.9 Hz), 134.32, 131.45, 130.04, 128.61, 118.74 (t, $J$ = 258.9 Hz), 44.44 (t, $J$ = 25.1 Hz), 40.6, 31.6, 29.5, 28.2, 22.6, 22.6, 14.1. GC−MS: 267 (15.86, $M^+ - I$), 175 (2.46), 161 (4.60), 127 ($I^+$, 3.63), 115 (2.62), 105 ($PhCO^+$, 100), 91 (7.39), 77 ($Ph^+$, 41.55), 55 (8.54), 43 (10.65). FTIR: 2958, 2931, 2859, 1704, 1637, 1467, 1457, 1451, 1437, 1379, 1307, 1271, 1248, 1177, 1163, 1095, 1053, 1027 $cm^{-1}$.

Similarly, $Pd(PPh_3)_4$-initiated reaction of **1a** with 1-octene in hexane at 60 °C was completed in 30 min and gave 85% $^{19}F$ NMR yield of 1:1 adduct (**6**) and 8% of **2a** (Table 1).

**1,1-Difluoro-3-iodooctyl Phenyl Ketone [$PhC(O)CF_2CH_2CHIC_5H_{11}$-*n*, 5].** Similarly, **5** was prepared from 2.82 g (10 mmol) of **1a**, 1.47 g (15 mmol) of 1-heptene, and 0.18 g (0.16 mmol, 1.6 mol %) of $Pd(PPh_3)_4$. $^{19}F$ NMR analysis showed that the conversion was 100%, and 97% of **5** and 3% of **2a** were formed. Chromatography (silica gel column 40 × 400 mm) of the residue with hexane−dichloromethane (8:2) eluant gave 2.7 g (71% yield; NMR purity: >97%) of **5**. $^{19}F$ NMR: δ -98.0 (ddd, $J$ = 290.0, 23.24, 13.0 Hz, 1F), −100.3 (ddd, $J$ = 290.0, 21.2, 13.1 Hz, 1F). $^1H$ NMR: δ 8.07 (d, $J$ = 7.4 Hz, 2H), 7.56 (t, $J$ = 7.4 Hz, 1H), 7.41 (t, $J$ = 7.7 Hz, 2H), 4.35 (m, 1H), 3.15−2.78 (m, 2H), 1.85−1.65 (m, 2H), 1.38−1.25 (m, 6H), 0.88 (t, $J$ = 6.6 Hz, 3H). $^{13}C$ NMR: δ 181.2 (t, $J$ = 30.7 Hz), 134.41, 130.11, 130.07, 128.66, 118.75 (t, $J$ = 256.2 Hz), 44.44 (t, $J$ = 22.0 Hz), 40.5, 30.7, 29.5, 29.2, 24.0, 22.4, 14.0. GC−MS: 323 ($M^+ - C_4H_9$, 0.01), 253 ($M^+ - I$, 39.61), 233 ($M^+ - I - HF$, 3.87), 195 (11.08), 175 (7.75), 161 (22.25), 127 ($I^+$, 7.06), 105 ($PhCO^+$, 100), 91 (25.39), 77 ($Ph^+$, 94.51), 71 (6.86), 57 (9.61), 55 (43.14), 43 (17.06). FTIR: 2959, 2933, 2874, 2861, 1704, 1450, 1193, 1186, 1178, 1128, 1092, 1052, 1027, 821, 819 $cm^{-1}$.

Similarly, $Pd(PPh_3)_4$ initiated reaction of **1a** with 1-heptene in hexane at 60 °C gave 98% conversion of **1a**, in which 86% of **5** and 8% of **2a** were formed based on $^{19}F$ NMR analysis (Table 1).

**2,2-Difluoro-4-iodo-1-phenyl-1,7-octanedione [$PhC(O)CF_2CH_2CHI(CH_2)_2C(O)CH_3$, 7].** Similarly, **7** was prepared from 1.7 g (6.0 mmol) of **1a**, 1.18 g (12.1 mmol) of 5-hexen-2-one, and 0.14 g (0.13 mmol, 2.1 mol %) of $Pd(PPh_3)_4$. After workup, 1.92 g (84% yield; GLPC purity: 95%) of **7** was isolated by chromatography. $^{19}F$ NMR: δ −96.9 (ddd, $J$ = 294.2, 19.53, 14.65 Hz, 1F), −101.0 (ddd, $J$ = 293.0, 19.1, 14.7 Hz, 1F). $^1H$ NMR: δ 8.08 (d, $J$ = 7.3 Hz, 2H), 7.6−7.4 (m, 3H), 4.72 (m, 1H), 3.3−2.8 (m, 2H), 2.7 (t, $J$ = 6.6 Hz, 2H), 2.1 (s, 3H), 2.0 (m, 2H). $^{13}C$ NMR: δ 211.0, 171.8, 137.7, 128.2, 128.1, 126.8, 119.2 (t, $J$ = 251.9 Hz), 54.0, 42.5 (t, $J$ = 24.5 Hz), 36.2, 31.4, 14.5. GC−MS: 380 ($M^+$, 6.57), 253 ($M^+ - I$, 20.48), 127 ($I^+$, 17.05), 105 ($PhCO^+$, 100), 77 ($Ph^+$, 43.51), 43 ($CH_3CO^+$, 88.96). FTIR: 1722, 1704, 1599, 1450, 1360, 1278, 1195, 1186, 1171, 1122, 1082, 821 $cm^{-1}$.

**2,2−Difluoro-4-iodo-7,8-epoxy-1-phenyl-1-octanone [$PhC(O)CF_2CH_2CHI(CH_2)_2\overline{CH_2CH_2O}$, 8].** Similarly, **8** (2.69 g, 68% yield; NMR purity: 100%) was prepared from 2.93 g (10.4 mmol) of **1a**, and 2.15 g (21.9 mmol) of 1,2-epoxy-5-hexene in the presence of 0.21 g (0.18 mmol, 1.8 mol %) of $Pd(PPh_3)_4$ and isolated by chromatography. $^{19}F$ NMR: δ −97.2 (dddd, $J$ = 283.5, 50.8, 18.86, 18.61 Hz, 1F), −101.8 (dddd, $J$ = 283.5, 32.4, 18.6, 13.8 Hz, 1F). $^1H$ NMR: δ 8.09 (d, $J$ = 7.5 Hz, 2H), 7.60 (t, $J$ = 7.4 Hz, 1H), 7.47 (t, $J$ = 7.9 Hz, 2H), 4.88−4.82 (m, 1H), 3.26 (ddd, $J$ = 17.6, 10.2, 7.9 Hz, 1H), 3.18−3.03 (m, 2H), 2.30−2.73 (m, 4H), 2.21−2.02 (m, 2H). $^{13}C$ NMR: δ 189.5 (t, $J$ = 30.0 Hz), 130.0, 128.7, 128.6, 127.7, 118.7 (t, $J$ = 253.3 Hz), 78.6, 78.0, 32.2 (t, $J$ = 37.9 Hz), 31.3, 30.7, 10.5. GC−MS: 380 ($M^+$, 2.25), 360 ($M^+ - HF$, 7.10), 253 ($M^+ - I$, 1.01), 211 (1.24), 175 (2.33), 127 ($I^+$, 3.08), 105 ($PhCO^+$, 100), 77 ($Ph^+$, 40.40). FTIR: 3072, 3068, 3065, 2972, 2958, 2948, 1705, 1450, 1310, 1272, 1214, 1187, 1179, 1161, 1044, 1029 $cm^{-1}$.

**1,1-Difluoro-3-iodo-4,4-dimethylpentyl Phenyl Ketone**

**[PhC(O)$CF_2CH_2CHICMe_3$, 9].** Similarly, **9** (4.51 g, 88% yield: GLPC purity: 100%) was prepared from 3.9 g (14 mmol) of **1a** and 1.68 g (20 mmol) of 3,3-dimethyl-1-butene in the presence of 0.29 g (0.25 mmol, 1.8 mol %) of $Pd(PPh_3)_4$ and isolated by chromatography with hexane–dichloromethane (8:2) eluant. $^{19}F$ NMR: $\delta$ -100.2 (ddd, $J$ = 285.9, 20.7, 15.1 Hz, 1F), −101.7 (ddd, $J$ = 285.9, 19.7, 13.9 Hz, 1F). $^1H$ NMR: $\delta$ 8.11 (d, $J$ = 7.3 Hz, 2H), 7.62 (t, $J$ = 7.4 Hz, 1H), 7.48 (t, $J$ = 7.6 Hz, 2H), 4.24 (m, 1H), 3.09–2.92 (m, 2H), 1.11 (s, 9H). $^{13}C$ NMR: $\delta$ 188.4 (t, $J$ = 30.6 Hz), 134.35, 130.21, 130.16, 128.67, 118.79 (t, $J$ = 255.1 Hz), 41.02 (t, $J$ = 22.6 Hz), 27.87. GC–MS: 239 ($M^+$ − I, 1.10), 221 (1.51), 201 (4.11), 191 (0.34), 181 (2.66), 171 (2.08), 127 (7.77, $I^+$), 105 ($PhCO^+$, 100), 83 (0.27), 77 ($Ph^+$, 57.66), 71 ($Me_3CCH_2^+$, 1.04), 70 (4.73), 57 ($Me_3C^+$, 4.84), 55 (10.36), 51 ($HCF_2^+$, 12.27), 43 (9.35), 41 (11.26). FTIR: 2968, 2940, 2910, 2873, 1704, 1560, 1450, 1369, 1275, 1194, 1186, 1177, 1047, 909, 814 $cm^{-1}$.

**1,1-Difluoro-3-iodo-3-(trimethylsilyl)propyl Phenyl Ketone [PhC(O)$CF_2CH_2CHISiMe_3$, 10].** Similarly, 2.1 g (7.4 m mol) of **1a** was reacted with 1.12 g (11.2 mmol) of vinyltrimethylsilane initiated by 0.11 g (0.10 mmol, 1.3%) of $Pd(PPh_3)_4$. Distillation gave 2.6 g (92% yield; NMR purity: 100%) of **10**. Bp: 114–115 °C/0.5 mmHg. $^1H$ NMR: $\delta$ 8.10 (d, $J$ = 7.43 Hz, 2H), 7.59 (tt, $J$ = 7.38 Hz, 1H), 7.45 (t, $J$ = 7.65 Hz, 2H), 3.26 (dxd, $J$ = 10.2 Hz, 2.99 Hz, 1H), 2.97–2.65 (m, 2H), 0.19 (s, 9H); $^{19}F$ NMR: $\delta$ -100.26 (q, $J$ = 17.15 Hz). $^{13}C$ NMR: $\delta$ 188.82 (t, 31.15 Hz), 131.94, 134.29, 130.13 (t, $J$ = 3.43 Hz), 128.64, 119.05 (t, $J$ = 255.74 Hz), 38.07, 4.19 (t, $J$ = 5.87 Hz), −2.41. GC–MS: 382 ($M^+$, 0.03), 367 ($M^+ - CH_3$, 3.75), 255 ($M^+$ − I, 26.67), 228 (6.86), 185 (11.27), 177 (14.31), 163 (24.12), 144 (23.26), 135 (56.86), 115 (46.67), 105 ($PhCO^+$, 100). 77 ($Ph^+$, 92.55), 73 ($Me_3SI^+$, 81.18), 51 (25.10), 43 (13.92), 45 (16.27). HRMS: obsd 366.9812, $C_{12}H_{14}F_2OISi$ ($M^+$ − Me), calcd: 366.9827. FTIR: 2958, 1703, 1600, 1450, 1286, 1253, 1185, 1177, 1068, 1030, 873, 852, 844, 713 $cm^{-1}$.

**6,6-Difluoro-8-iodo-5-undecanone [$n$-$C_4H_9C(O)CF_2CH_2CHIC_3H_7$-$n$, 12].** Similarly, **12** was prepared from 2.62 g (10 mmol) of **1b**, 1.05 g (15 mmol) of 1-pentene, and 0.27 g (0.24 mmol, 2.4 mol %) of $Pd(PPh_3)_4$. The conversion was 86%; **12** and **2b** were formed in 78% and 16% yield, respectively, based on $^{19}F$ NMR analysis. After workup, 1.92 g (58% yield; NMR purity: 95%) of **12** was isolated by chromatography with hexane–dichloromethane (8:2) eluant. $^{19}F$ NMR ($CFCl_3$): $\delta$ −103.1 (ddd, $J$ = 283.2, 19.5, 14.7 Hz, 1F), −108.9 (ddd, $J$ = 283.2, 19.5, 14.7 Hz, 1F). $^1H$ NMR: $\delta$ 4.0 (m, 1H), 2.6–3.0 (m, 4H), 1.7–1.4 (m, 8H), 1.0 (t, 3H), 0.9 (t, 3H). $^{13}C$ NMR: $\delta$ 200.5, 117.3 (t, $J$ = 254.6 Hz), 43.5 (t, $J$ = 22.5 Hz), 42.8, 36.1, 24.8, 22.9, 22.1, 14.0, 13.8, 13.0. GC–MS: 205 ($M^+$ − I, 21.23), 127 ($I^+$, 13.96), 85 ($C_4H_9CO^+$, 100), 77 (18.75), 69 (14.12), 57 ($C_4H_9^+$, 75.86), 55 (56.03), 43 (29.74). FTIR: 2962, 2934, 2875, 1744, 1466, 1459, 1456, 1381, 1222, 1212, 1209, 1204, 1187, 1167, 1163, 1152, 1148, 1135, 1131, 1119, 1088, 1039 $cm^{-1}$.

**6,6-Difluoro-8-iodo-5-dodecanone [$n$-$C_4H_9C(O)CF_2CH_2CHIC_4H_9$-$n$, 13].** Similarly, 6,6-difluoro-8-iodo-5-dodecanone (**13**) was prepared from 2.62 g (10 mmol) of **1b**, 2.8 g (33 mmol) of 1-hexene and 0.36 g (0.32 mmol, 3.2 mol %) of $Pd(PPh_3)_4$. The conversion of **1b** was 95% after reaction for 30 min at room temperature, in which 85% of 6,6-difluoro-8-iodo-5-dodecanone and 10% of **2b** ($C_4H_9COCF_2H$) were formed (NMR yield). $^{19}F$ NMR ($CFCl_3$): $\delta$ -100.8 (dt, $J$ = 285.1, 15.9 Hz, 1F), −109.4 (dt, $J$ = 285.1, 15.9 Hz, 1F). **13** was directly reduced with $Zn/NiCl_2{\cdot}6H_2O$ in moist THF without isolation, and the structure was further confirmed by the reduced product, 6,6-difluoro-5-dodecanone (**13h**).

**3,3-Difluoro-1-iodo-1-(trimethylsilyl)-4-octanone. [$n$-$C_4H_9C(O)CF_2CH_2CHISiMe_3$, 14].** Similarly, **14** was prepared from 2.20 g (8.4 mmol) of **1b**, 1.34 g (13.4 mmol) of vinyltrimethylsilane in the presence of 0.13 g of $Pd(PPh_3)_4$ (0.11 mmol, 1.3 mol %). Distillation gave 2.83 g (93% yield; GLPC purity: 99%) of **14**. Bp: 85–87 °C/1.4 mmHg. $^1H$ NMR ($CDCl_3$, TMS): $\delta$ 3.11 (dd, $J$ = 9.97 Hz, 3.87 Hz, 1H), 2.78–2.72 (m,2H), 2.62 (m, 2H), 1.63 (m, 2H), 1.36 (m, 2H), 0.93 (t, $J$ = 7.28 Hz, 3H), 0.18 (s, 9H). $^{19}F$ NMR: $\delta$ −103.80 (dt, $J$ = 277.72 Hz, 15.52 Hz, 1F), 109.09 (dt, $J$ = 277.72 Hz, 15.79 Hz, 1F). $^{13}C$ NMR: $\delta$ 200.96 (t, $J$ = 31.07 Hz), 117.54 (t, $J$ = 254.50 Hz), 37.00 (t, $J$ = 23.57 Hz), 36.50, 24.69, 22.03, 13.73, 4.78 (t, $J$ = 2.95 Hz), −2.49 (s). GC–MS: 362 ($M^+$, 1.57), 363, ($M^+$ + 1, 0.28), 347 ($M - CH_3^+$, 1.45), 333 ($M^+$ − Et, 1.83), 235 ($M^+$ − I, 10.30), 208 (8.69), 185(16.90), 167 (8.07), 157 (12.64), 151 (15.38), 143 (21.57), 85 ($C_4H_9CO^+$, 59.89), 73 ($Me_3SI^+$, 100), 57 (81.87), 55 (32.14), 43 (13.60), 41 (24.18). FTIR: 2962, 2944, 2936, 1743, 1254, 1209, 1068, 1038, 854, 843 $cm^{-1}$.

**7,7-Difluoro-5-iodo-2,8-tetradecanedione [$n$-$C_6H_{13}C(O)CF_2CH_2CHI(CH_2)_2C(O)Me$, 15].** Similarly, **15** was prepared from 3.43 g (11.8 mmol) of **1c**, 1.79 g (18 mmol) of 5-hexen-2-one, and 0.29 g (0.25 mmol, 2.1 mol %) of $Pd(PPh_3)_4$. The conversion was 100% and gave 93% (NMR yield) of adduct and 5% of **2c** ($C_6H_{13}COCF_2H$). After workup, 3.87 g (83.7% yield; NMR purity: 98%) of **15** was isolated by chromatography with hexane–ethyl acetate (8:2) eluant, which was directly reduced with $Zn/NiCl_2{\cdot}6H_2O$. $^{19}F$ NMR (90 MHz, $CFCl_3$): $\delta$ −102.1 (dt, $J$ = 277.4, 16.7 Hz, 1F), −107.6 (dt, $J$ = 281.1, 16.7Hz, 1F). The structure of **15** was further confirmed by the reduced product, 7,7-difluoro-2,8-tetradecanedione (**15h**).

**5,5-Difluoro-1-hydroxy-3-iodo-6-dodecanone [$n$-$C_6H_{13}C(O)CF_2CH_2CHI(CH_2)_2OH$, 16].** Similarly, **16** was recated with 1.8 g (6.2 mmol) of **1c** and 0.62 g (8.7 mmol) of 3-buten-1-ol in the presence of 0.19 g (0.17 mmol, 2.67 mol %) of $Pd(PPh_3)_4$. The reaction gave 76% of **16** and 24% of reduced **2c** with the conversion of 71% in $^{19}F$ NMR spectrum. After workup, 1.1 g (50% yield; NMR purity: 92%) of **16** was isolated by chromatography with hexane–ethyl acetate (7:3) as eluant. $^{19}F$ NMR ($CFCl_3$): $\delta$ −103.3 (ddd, $J$ = 283.1, 23.8, 13.2 Hz, 1F), −107.9 (ddd, $J$ = 283.1, 18.8, 14.1 Hz, 1F). $^1H$ NMR: $\delta$ 4.5 (m, 1H), 3.9–3.7 (m, 2H), 3.1 (s, broad, 1H), 2.2 (t, 2H), 2.0 (m, 2H), 1.6 (m, 4H), 1.3 (m, 6H), 0.9 (t, $J$ = 6.9 Hz, 3H). $^{13}C$ NMR: $\delta$ 200.6, 117.3 (t, $J$ = 254.4 Hz), 62.64, 43.7 (t, $J$ = 22.5 Hz), 42.8, 36.4, 31.8, 28.7, 22.7, 22.6, 21.8, 19.4, 14.0. GC–MS: 345 ($M^+$ − OH, 0.03), 321 (0.03), 277 ($M^+ - C_6H_{13}$, 0.05), 235 ($M^+$ − I, 5.0), 215 ($M^+$ − I − HF, 12.12), 197 (10.0), 127 ($I^+$, 4.05), 113 ($C_6H_{13}CO^+$, 45.06), 107 (4.39), 85 ($C_6H_{13}^+$, 23.64), 57 (21.36), 55 (28.94), 43 (100), 41 (40.0). FTIR: 3639–3604 (broad), 2959, 2930, 2874, 2860, 1744, 1046, 1078, 909 $cm^{-1}$.

**8,8-Difluoro-10-iodo-7-tetradecanone [$n$-$C_6H_{13}C(O)CF_2CH_2CHIC_4H_9$-$n$, 17].** Similarly, **17** was prepared from 1.45 g (5 mmol) of **1c**, 0.55 g (6.5 mmol) of 1-hexene, and 0.11 g (0.1 mmol, 1.9 mol %) of $Pd(PPh_3)_4$. The ratio of adduct and **2c** was 9:1. After workup, chromatography with hexane–$CH_2Cl_2$ (8:2) eluant yielded 1.44 g (77% yield; NMR purity: 100%) of **17**. $^{19}F$ NMR ($CFCl_3$): $\delta$ −103.6 (ddd, $J$ = 282.7, 20.7, 13.6 Hz, 1F), −108.4 (ddd, $J$ = 282.7, 16.8, 14.2 Hz, 1F). $^1H$ NMR: $\delta$ 4.2 (m, 1H), 2.9–2.6 (m, 4H), 1.9–1.7 (m, 2H), 1.7–1.6 (m 2H), 1.5–1.3 (m, 10H), 0.9 (t, $J$ = 7.2 Hz, 3H), 0.9 (t, $J$ = 6.9 Hz, 3H). $^{13}C$ NMR: $\delta$ 200.3 (t, $J$ = 31.0 Hz), 117.3 (t, $J$ = 254.3 Hz), 43.5 (t, $J$ = 22.3 Hz), 40.5, 36.4, 31.7, 31.6, 28.7, 23.6 (t, $J$ = 4.3 Hz), 22.7, 22.6, 21.8, 14.0, 13.9. GC–MS: 247 ($M^+$ − I, 5.50), 209 (2.56), 189 (4.92), 155 (3.58), 139 (2.98), 133 (3.46), 127 ($I^+$, 6.17), 113 ($C_6H_{13}CO^+$, 33.33), 85 ($C_6H_{13}^+$, 13.0), 57 (14.25), 55 (35.33), 43 (100), 41 (79.33). FTIR: 2960, 2933, 2874, 2861, 1744, 1467, 1461, 1093, 980 $cm^{-1}$.

**1-Acetoxy-4,4-difluoro-2-iodo-5-undecanone [$n$-$C_6H_{13}C(O)CF_2CH_2CHICH_2OC(O)Me$, 18].** Similarly, **18** was prepared from 2.0 g (6.9 mmol) of **1c** and 1.2 g (12 mmol) of allyl acetate in the presence of $Pd(PPh_3)_4$ (0.16 g, 0.14 mmol). The reaction gave 93% of the 1:1 addition adduct and 7% of **2c** as shown in the $^{19}F$ NMR spectrum. After workup, chromatography with hexane–ethyl acetate (8:2) eluant gave 2.34 g (87%, GLPC purity: 97%) of **18**. $^{19}F$ NMR ($CFCl_3$): $\delta$ −104.59 (ddd, $J$ = 284.8, 34.5, 15.0 Hz, 1F), −107.58 (ddd, $J$ = 284.8, 33.0, 14.2 Hz, 1F). $^1H$ NMR: $\delta$ 4.38–4.24 (m, 3H), 2.87–2.71 (m, 4H), 2.12 (s, 3H), 1.64 (m, 2H), 1.30 (m, 6H), 0.89 (t, $J$ = 6.5 Hz, 3H). $^{13}C$ NMR: $\delta$ 200.0 (t, $J$ = 30.8 Hz), 169.95, 116.9 (t, $J$ = 254.4 Hz), 68.82, 39.68 (t, $J$ = 22.9 Hz), 36.20, 31.49, 28.61, 22.61, 22.47, 20.76, 14.99 (t, $J$ = 3.6 Hz). GC–MS: 331 ($M^+ - CH_3CO_2$, 0.34), 273 (0.36), 217 (1.70), 203 (2.21), 183 (13.89), 119 (1.27), 113 ($C_6H_{13}CO^+$, 93.42), 85 ($C_6H_{13}^+$, 40.33), 69 (8.23), 57 (15.53), 55 (10.19), 43 (100), 41 (19.44). FTIR: 2959, 2932, 2874, 2861, 1751, 1462, 1380, 1367, 1226, 1114, 1039 $cm^{-1}$.

**3,3-Difluoro-1-iodo-1-(trimethylsilyl)-4-decanone [$n$-$C_6H_{13}C(O)CF_2CH_2CHISiMe_3$, 19].** Similarly, **19** was prepared from 2.1 g (7.24 mmol) of **1c** and 1.12 g (11.2 mmol) of vinyltrimethylsilane in the presence of 0.13 g of $Pd(PPh_3)_4$

(0.11 mmol, 1.5 mol%). After reaction, the solids were removed from the reaction mixture by filtration. Then, rotary evaporation followed by full vacuum to remove the solvent and excess vinyltrimethylsilane gave 2.54 g (90% yield; NMR purity: 98%) of **19**. $^1$H NMR: δ 3.11 (dd, $J$ = 10.03 Hz, 3.84 Hz, 1H), 2.73 (m, 2H), 2.61 (m, 2H), 1.64 (m, 2H), 1.31 (m, 6H), 0.89 (t, $J$ = 6.74 Hz, 3H), 0.18 (s, 9H). $^{19}$F NMR: δ −103.75 (dt, $J$ = 277.75 Hz, 15.32 Hz, 1F), −108.99 (dt, $J$ = 277.73 Hz, 15.61 Hz, 1F). $^{13}$C NMR: δ 200.82 (t, $J$ = 30.93 Hz), 117.61 (t, $J$ = 254.62 Hz), 37.10 (t, $J$ = 23.45 Hz), 36.83, 31.66, 28.66, 22.66, 22.53, 14.04, 4.79 (t, $J$ = 3.07 Hz), −2.46. GC−MS: 390 ($M^+$, 0.03), 375 ($M - CH_3^+$, 0.95), 333 ($M - C_4H_9^+$, 0.54), 263 ($M - I^+$, 7.27), 185 ($ICH_2CH{=}CF^+$, 49.55), 171 (11.25), 167 (7.61), 151 (13.75), 113 ($C_6H_{13}CO^+$, 39.09), 85 ($C_6H_{13}^+$, 23.52), 73 ($Me_3SI^+$, 86.36), 69 (23.52), 57 (21.25), 55 (58.64), 43 (100). FTIR: 2959, 2931, 2860, 1758, 1404, 1263, 1254, 1207, 1069, 854, 844, 821, 816, 806, 786.2, 775 cm$^{-1}$.

**The Reaction of 1a with Diethyl Diallylmalonate in the Presence of Pd(PPh$_3$)$_4$.** Similarly, 1.96 g (6.95 mmol) of **1a** was reacted with 2.15 g (8.95 mmol) of diethyl diallylmalonate (**20**) in the presence of 0.13 g (0.11 mmol, 1.5 mol %) of Pd(PPh$_3$)$_4$. After 30 min, $^{19}$F NMR analysis of the reaction mixture showed that **1a** was completely converted and gave 95% of the corresponding cyclized product, **21**. After workup, 2.41 g (66%, GLPC purity: 100%) of **21** was isolated by column chromatography (hexane:ethyl acetate = 8:2). $^{19}$F NMR ($CFCl_3$): δ −98.47 (ddd, $J$ = 286.1, 23.7, 10.7 Hz, 1F), −100.59 (ddd, $J$ = 286.1, 23.9, 13.1 Hz, 1F). $^1$H NMR: δ 8.09-(d, $J$ = 7.7 Hz, 2H), 7.63 (t, $J$ = 7.4 Hz, 1H), 7.49 (t, $J$ = 7.7 Hz, 2H), 4.24−4.16 (m, 4H), 3.27 (dd, $J$ = 9.7, 5.2 Hz, 1H), 3.06 (t, $J$ = 9.9 Hz, 1H), 2.65−2.51 (m, 4H), 2.41−2.04 (m, 4H), 1.27−1.22(m, 6H). $^{13}$C NMR: δ 188.8 (t, $J$ = 31.2 Hz), 172.2, 171.9, 134.4, 131.6, 130.1, 128.7, 119.5(t, $J$ = 253.9 Hz), 61.6, 58.19, 45.6, 39.8, 38.4, 36.25, 32.67(t, $J$ = 22.5 Hz), 14.02, 6.88. GC−MS: 477 ($M^+$ − OEt, 1.89), 395 ($M^+$ − I, 11.57), 349 (3.77), 275 (20.59), 247 (5.27), 227 (3.65), 127 ($I^+$, 2.97), 105 ($PhCO^+$, 100), 77 (24.12). FTIR: 2982, 2939, 2907, 1731, 1704, 1599, 1477, 1450, 1298, 1260, 1238, 1192, 1178, 1131, 1098, 1029 cm$^{-1}$.

**Pd(PPh$_3$)$_4$-Initiated Reaction of 1c with Allyl Acetate in the Presence of Inhibitors. Di-*tert*-butyl Nitroxide-Inhibited Reaction.** **1c** (0.87 g, 3 mmol) was reacted with 0.58 g (5.9 mmol) of allyl acetate in the presence of 0.1 g (0.087 mmol, 2.9 mol %) of Pd(PPh$_3$)$_4$ and 0.07 g (0.5 mmol) of di-*tert*-butyl nitroxide. The mixture was stirred at room temperature overnight under $N_2$. $^{19}$F NMR analysis indicated that no reaction occurred; only **1c** was detected in the reaction mixture.

**Hydroquinone-Inhibited Reaction.** Similarly, 1.67 g (5.76 mmol) of **1c** was reacted with 1.05 g (10.5 mmol) of allyl acetate in the presence of 0.09 g (0.078 mmol, 1.35 mol %) of Pd(PPh$_3$)$_4$ and 0.10 g (0.91 mmol) of hydroquinone. After reaction for 20 h, only **1c** was observed from the reaction mixture as determined by $^{19}$F NMR analysis.

**Photoreaction of 1a with Diallyl Ether.** Into a 50 mL quartz tube were charged 1.78 g (6.3 mmol) of iododifluoromethyl phenyl ketone (**1a**) and 1.23 g (12.6 mmol) of diallyl ether (**22**). After the tube was sealed and the reactants were mixed by shaking, the reaction mixture was irradiated with 254 nm UV light in Rayonet photochemical reactor for 10 h. $^{19}$F NMR analysis of the reaction mixture showed the complete conversion of **1a**, and 90% of the cyclized product was formed. After workup, 1.27 g (80% yield; NMR purity: 96%) of product, **23**, was isolated by column chromatography on silica gel with hexane−ethyl acetate as eluant (2:8). $^{19}$F NMR ($CFCl_3$): δ −98.49 (dt, $J$ = 290.0, 16.8 Hz, 1F), −99.81 (dt, $J$ = 290.4, 17.5 Hz, 1F). $^1$H NMR: δ 8.08 (d, $J$ = 7.6 Hz, 2H), 7.61 (t, $J$ = 7.4 Hz, 1H), 7.47 (t, $J$ = 7.7 Hz, 2H), 5.83 (m, 1H), 5.20 (m, 2H), 4.41 (m, 1H), 3.98 (d, $J$ = 5.6 Hz, 1H), 3.68 (m, 2H), 317 (m, 1H), 2.89 (m, 1H). $^{13}$C NMR: δ 188.22 (t, $J$ = 30.7 Hz), 134.33, 134.03, 131.63, 130.12 (t, $J$ = 3.3 Hz), 128.65, 117.43, 118.66 (t, $J$ = 255.7 Hz), 75.04, 71.62, 40.91 (t, $J$ = 22.7 Hz), 17.65. GC−MS: 253 ($M^+$ + 1, 33.18), 254 (4.65), 211 (4.85), 207 (10.99), 197 (9.98), 183 (12.11), 176 (15.70), 145 (12.11), 107 (9.19), 105 ($PhCO^+$, 100), 77 (42.60), 51 (10.99), 44 (34.99), 41 (25.78). FTIR: 3066, 2940, 2904, 2863, 1704, 1599,1450, 1201, 1186, 1178, 1118, 1070, 1053, 744, 714 cm$^{-1}$.

**Representative General Procedure for the Reduction of α,α-Difluoro-γ-iodo Ketones. 2,2-Difluoro-1-phenyl-1,7-octanedione [PhC(O)CF$_2$(CH$_2$)$_4$C(O)CH$_3$, 7h].** A 25 mL two-neck flask fitted with a magnetic stirring bar and a condenser topped with a $N_2$ inlet was charged with 1.10 g (16.8 mmol) of zinc dust, 0.20 g (0.84 mmol) of $NiCl_2{\cdot}6H_2O$, one drop of water, and 10 mL of commercial THF. The mixture was stirred at room temperature for 10 min, when the green color of $NiCl_2{\cdot}6H_2O$ faded and gave a black solution. Then, 3.2 g (8.4 mmol) of **7** was added and the reaction mixture was stirred at room temperature overnight. $^{19}$F NMR analysis of the mixture showed that the typical AB pattern signal of **7** had disappeared and a new triplet (100%) appeared. The reaction mixture was poured into 20 mL of $NH_4Cl$ aqueous solution and extracted with diethyl ether (3 × 20 mL). The combined ether extracts were washed with water (2 × 10 mL) and dried over $MgSO_4$. After rotary evaporation to remove the solvent, the residue was distilled in vacuum to give 1.69 g (79% yield; GLPC purity: 99%) of **7h**. Bp: 128−132 °C/0.5 mmHg. $^{19}$F NMR ($CFCl_3$): δ −100.2 (t, $J$ = 17.1 Hz). $^1$H NMR: δ 8.1 (d, $J$ = 7.5 Hz, 2H), 7.6 (t, $J$ = 7.4 Hz, 1H), 7.4 (t, $J$ = 7.7 Hz, 2H), 2.4 (t, $J$ = 7.0 Hz, 2H), 2.2−2.1 (m, 2H), 2.0 (s, 3H), 1.6−1.45 (m, 4H). $^{13}$C NMR: δ 207.6, 189.2 (t, $J$ = 31.1 Hz), 134.4, 132.2, 130.1, 128.9, 120.0 (t, $J$ = 252.3 Hz), 42.9, 33.9 (t, $J$ = 23.0 Hz), 29.6, 23.4, 21.1. GC−MS: 254 ($M^+$, 6.02), 253 (1.35), 235 ($M^+$ − F, 2.14), 133 (4.68), 115 (5.46), 105 ($PhCO^+$, 100), 106 (7.04), 77 ($Ph^+$, 31.28), 43 (35.18). HRMS: obsd 254.1115, $C_{11}H_{10}OF_2$, calcd: 254.1118. FTIR: 2949, 2891, 2888, 2877, 1721, 1704, 1669, 1599, 1581, 1464, 1450, 1363, 1275, 1266, 1194, 1178, 1166, 1107, 1103, 1101, 1093, 1047 cm$^{-1}$.

Similarly, **5h**, **13h**, and **15h** were prepared by this method. The results are summarized in Table 2.

**1,1-Difluorooctyl Phenyl Ketone [PhC(O)CF$_2$CH$_2$-CH$_2$C$_5$H$_{11}$-*n*, 5h].** Yield: 79% (GLPC purity: 99%). Bp: 117−119 °C/0.4 mmHg. $^{19}$F NMR: δ −100.2 (t, $J$ = 17.8 Hz). $^1$H NMR: δ 8.08 (d, $J$ = 7.5 Hz, 2H), 7.49 (t, $J$ = 7.4 Hz, 1H), 7.37 (t, $J$ = 7.7 Hz, 2H), 4.35 (m, 1H), 2.14 (m, 2H), 1.52 (m, 2H), 1.27−1.24 (m, 8H), 0.86 (t, $J$ = 6.8 Hz, 3H). $^{13}$C NMR: δ 189.2 (t, $J$ = 31.7 Hz), 134.1, 132.4, 130.3, 128.7, 120.1 (t, $J$ = 252.6 Hz), 34.15 (t, $J$ = 22.7 Hz), 32.0, 29.6, 29.3, 22.9, 21.7, 14.2. GC−MS: 254 ($M^+$, 1.64), 156 (1.52), 233 ($M^+$ − I − HF, 3.87), 105 ($PhCO^+$, 100), 78 (1.46), 77 ($Ph^+$, 17.94), 51 (2.36), 43 (1.4), 41 (2.28). High resolution GC−MS: obsd 254.1474, $C_{11}H_{10}OF_2$, calcd: 254.1482. FTIR: 2958, 2931, 2929, 2873, 2858, 1705, 1599, 1468, 1456, 1450, 1197, 1192, 1178, 1161, 1056 cm$^{-1}$.

**6,6-Difluoro-5-dodecanone [*n*-C$_4$H$_9$C(O)CF$_2$CH$_2$CH$_2$C$_4$H$_9$-*n*, 13h].** Yield: 82% (GLPC purity: 96%). Bp: 40 °C/0.25 mmHg. $^{19}$F NMR ($CFCl_3$): δ −107.7 (t, $J$ = 17.1 Hz). $^1$H NMR: δ 2.7 (t, $J$ = 7.3 Hz, 2H), 2.0 (m, 2H), 1.6 (m, 2H), 1.4−1.3 (m, 10H), 0.9−0.8 (m, 6H). $^{13}$C NMR: δ 201.2 (t, $J$ = 32.0 Hz), 118.5 (t, $J$ = 251.4 Hz), 36.1, 32.8 (t, $J$ = 22.6 Hz), 31.7, 29.2, 25.0, 22.7, 22.3, 21.5, 14.0, 13.8. GC−MS: 86 (5.34), 85 ($C_6H_{13}^+$/ $C_4H_9CO^+$, 100), 77 (2.29), 58 (2.34), 57 ($C_4H_9^+$, 35.42), 55 (5.73), 44 (18.75), 43 (9.57), 42 (3.91), 41 (18.75). FTIR: 2961, 2933, 2963, 2875, 1744, 1467, 1458, 1208, 1045 cm$^{-1}$.

**7,7-Difluoro-2,8-tetradecanedione [*n*-C$_6$H$_{13}$C(O)CF$_2$-CH$_2$CH$_2$(CH$_2$)$_2$C(O)Me, 15h].** Yield: 76% (GLPC purity: 98%). $^{19}$F NMR: δ −107.7 (t, $J$ = 17.1 Hz). $^1$H NMR: δ 2.7 (t, $J$ = 7.2 Hz, 2H), 2.5 (t, $J$ = 7.2 Hz, 2H), 2.1 (s, 3H), 2.0 (m, 2H), 1.6−1.7 (m, 4H), 1.5−1.4 (m, 2H), 1.3 (m, 6H), 0.9 (t, $J$ = 6.8 Hz, 3H). $^{13}$C NMR: δ 208.1, 201.3 (t, $J$ = 31.3 Hz), 118.0 (t, $J$ = 251.6 Hz), 43.0, 36.2, 32.3 (t, $J$ = 23.1 Hz), 31.4, 29.8, 28.5, 23.1, 22.5, 22.4, 20.8 (t, $J$ = 4.3 Hz), 13.9. GC−MS: 262 ($M^+$, 0.02), 263 (0.04), 247 ($M^+$ − Me, 0.02), 243 ($M^+$ − F, 0.19), 223 (0.14), 219 ($M^+$ − $CH_3CO$, 0.06), 204 (0.30), 192 (1.69), 150 (2.43), 113 ($C_6H_{13}CO^+$, 100), 95 (5.74), 85 ($C_6H_{13}^+$, 34.51), 71 (6.76), 57 ($C_4H_9^+$, 15.59), 55 (16.37), 43 (77.25). High resolution GC−MS: obsd 263.1808, $C_{14}H_{24}O_2F_2$, calcd: 253.1822. FTIR: 2958, 2933, 2884, 2873, 2860, 1743, 1722, 1465, 1457, 1364, 1195, 1163 cm$^{-1}$.

**Representative General Procedure for the Synthesis of α,α-Difluoro Ketones by One-Pot Addition−Reduction Reaction. 1,1-Difluorooctyl Phenyl Ketone [PhC(O)-**

**$CF_2CH_2CH_2C_5H_{11}$-*n*, 5h].** In a 50 mL three-neck round-bottom flask was added 2.1 g (7.4 mmol) of **1a** to a mixture of 0.11 g (0.10 mmol, 1.3 mol%) of $Pd(PPh_3)_4$ and 1.1 g (11.2 mmol) of 1-heptene at room temperature in $N_2$. The reaction mixture was stirred for 0.5 h, and the $^{19}F$ NMR analysis showed that the conversion of **1a** was 99%, and **5** was formed in 97% NMR yield. After addition of 10 mL of hexane, the solid was removed from the reaction mixture by filtration. Then, the solvent was removed by rotary evaporation, and the residue was transferred into another flask charged with 0.75 g (11.5 mmol) of zinc and 0.18 g (0.75 mmol) of $NiCl_2{\cdot}6H_2O$ in 10 mL of moist THF. The reaction mixture was stirred for 30 min at room temperature and then poured into a beaker containing 50 mL of aqueous $NH_4Cl$ solution and 40 mL of ether. The solids were removed by filtration and washed with ether. The combined organic layers were washed with water and then dried over $MgSO_4$. After evaporation of the ether, distillation of the residue gave 1.4 g (74% yield; GLPC purity: 96%) of **5h**, which was identified by comparison to an authentic sample.

**1,1-Difluoro-11-hydroxyundecyl Phenyl Ketone [PhC(O)$CF_2(CH_2)_{10}OH$, 11h].** **1a** (2.82 g, 10 mmol) was added into a flask charged with 0.34 g (0.3 mmol, 3 mol %) of $Pd(PPh_3)_4$ and 2.11 g (21 mmol) of 9-decen-1-ol. The reaction mixture was stirred for 0.5 h, and the $^{19}F$ NMR analysis showed that the conversion of **1a** was 92% and **11** was formed in 86% NMR yield. After removal of the solids, the residue was reduced with 1.0 g (15 mmol) of zinc and 0.48 g (2 mmol) of $NiCl_2{\cdot}6H_2O$ in 10 mL of THF. After workup, chromatography with hexane and ethyl acetate (7:3) eluant gave 2.3 g (76%, GLPC purity: 94%) of **11h**. $^{19}F$ NMR: $\delta$ −100.53 (t, $J$ = 17.9 Hz). $^1H$ NMR: $\delta$ 8.08 (d, $J$ = 7.5 Hz, 2H), 7.57 (t, $J$ = 7.4 Hz, 1H), 7.44 (t, $J$ = 7.6 Hz, 2H), 3.57 (t, $J$ = 6.7 Hz, 2H), 3.21 (s, broad, 1H), 2.24−1.99 (m, 2H), 1.58−1.48 (m, 4H), 1.40−1.22 (m, 12H). $^{13}C$ NMR: $\delta$ 198.6, (t, $J$ = 31.1 Hz), 139.07, 134.22, 130.18, 128.69, 119.94 (t, $J$ = 252.2 Hz), 62.64, 34.09 (t, $J$ = 23.0 Hz), 32.75, 29.66, 29.60, 29.55, 29.48, 29.42, 29.03, 25.90. GC−MS: 312 ($M^+$, 0.71), 211 (0.64), 207 ($M^+$ − PhCO, 1.06), 183 (0.59), 105 ($PhCO^+$, 100), 85 (0.62), 77 (21.46), 55 (6.06), 43 (8.30). FTIR: 3638−3629 (broad), 2929, 2856, 1705, 1450, 1360, 1218, 1192, 1177, 1051, 1028, 909 $cm^{-1}$.

**6,6-Difluoro-5-dodecanone [*n*-$C_4H_9C(O)CF_2CH_2CH_2C_4H_9$-*n*, 13h].** Similarly, **13** was prepared from 2.62 g (10 mmol) of **1b**, 1.93 g (23 mmol) of 1-hexene, and 0.35 g (0.30 mmol, 3.0 mol %) of $Pd(PPh_3)_4$. The obtained adduct was reduced with 0.78 g (12 mmol) of zinc and 0.19 g (0.8 mmol) of $NiCl_2{\cdot}6H_2O$ in THF. After workup, 1.5 g (68% yield) of **13h** was isolated by distillation and identified by comparison to an authentic sample.

**7,7-Difluoro-2,8-tetradecanedione. [*n*-$C_6H_{13}C(O)CF_2CH_2CH_2(CH_2)_2C(O)Me$, 15h].** Similarly, **15** was prepared from 2.0 g (6.9 mmol) of **1c**, 0.91 g (9.4 mmol) of 5-hexen-2-one, and 0.14 g (0.13 mmol, 1.9 mol %) of $Pd(PPh_3)_4$. The reaction mixture was directly treated with 0.58 g (8.85 mmol) of zinc and 0.26 g (1.04 mmol) of $NiCl_2{\cdot}6H_2O$ in 10 mL of THF. After workup, chromatography with hexane and ethyl acetate (8:2) eluant gave 1.48 g (82%) of **15h**, which was identified by comparison to an authentic sample.

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**Supporting Information Available:** $^{13}C$ NMR spectra for **1a−c**, **3c**, **5−10**, **12**, **14**, **16−19**, **21**, **23**, **7h**, **5h**, **13h**, **15h**, and **11h** and observed and simulated $^{19}F$ NMR spectra of **8** (26 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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