The stereospecific Barbier reaction between (Z)- and (E)-1-iodopentafluoropropenes, zinc and aldehydes Mechanistic aspects and scope of the preparation of (Z)- and (E)-partially fluorinated allylic alcohols

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Abstract

The Zn/Barbier reaction of acid-washed zinc or zinc/silver couple with (Z)- or (E)-$CF_3CF=CFI$ and aromatic aldehydes in DMF stereospecifically gives the (Z)- or (E)-allylic alcohol, $CF_3CF=CFCH(OH)C_6H_5$. Substituted aromatic aldehydes, which contain an electron-withdrawing group, undergo Barbier addition reaction. Substituted aromatic aldehydes, which contain an electron-releasing group, fail to undergo Barbier addition reaction. Aliphatic aldehydes, such as butanal, which contain an α-H, fail to undergo Barbier addition and significant amounts of $CF_3CF=CFH$ are formed. When the addition reaction is carried out in the presence of 1,4-dinitrobenzene, no reaction is observed. Mechanistically, the Zn/Barbier addition of $CF_3CF=CFI$ to aromatic aldehydes is best explained by formation of the $[CF_3CF=CF]^\ominus$ anion which adds to the aldehyde and is not adequately explained by formation and addition of an unsolvated zinc reagent, $CF_3CF=CFZnI$ (unsolvated). © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Barbier reaction; Vinylzinc reagents; Fluorinated allylic alcohols; Stereospecific reactions

1. Introduction

Barbier reaction is a powerful tool in the arsenal of the synthetic organic chemist for the construction of carbon–carbon bonds. This reaction was first discovered by Philippe Barbier in 1899. The advantage of this one-step reaction was that the synthetic chemist could by-pass the preparation and storage of unstable organometallic reagents [1–4].

Previous reports of Zn/Barbier reactions involved the reaction of iodoperfluoroalkanes with carbon dioxide or sulfur dioxide in the presence of Zn/Cu couple to give either perfluoroalkyl carboxylic acids or sulfonic acids [5]. Mechanistically, the proposed pathway was suggested to involve insertion of CO_2 or SO_2 into the carbon–zinc bond of the perfluoroalkylzinc reagent. Under these conditions, the stable perfluoropropyl zinc reagent failed to react [5]. Wakselman accomplished a similar reaction with SO_2 and a variety of metals with the cheaper and readily available CF_3Br under pressure [6]. Kitazume and Ishikawa demonstrated that the Zn/Barbier reaction of CF_3I with carbonyl compounds could be accomplished with ultrasound activation [7]. No reaction was observed in the absence of ultrasound activation. Kitazume and Ikeya have shown that zinc and methyl viologen function efficiently as an electron mediator in Barbier-type conversion of perfluoroalkyl iodides to perfluoroalkyl carbinols [8] and Fujita and Hiyama have more recently shown that Zn/Barbier reactions with fluorinated organohalides are effective even without sonication [9]. Perfluoroiodoalkanes and perfluorobromoalkanes also have been demonstrated to react with carbonyl compounds in the presence of zinc and a catalytic amount of palladium or nickel reagents [10]. Wakselman and co-workers extended their earlier work on perfluorinated sulfonic acids to carboxylic acid derivatives [11,12]. Recent reports included the Zn/Barbier reaction of iodoperfluoroalkanes and CFCs with aldehydes [13] and extension of this methodology to the perfluoroalkylation of dideoxy sugar aldehydes [14].

Although many Barbier reactions of carbonyl compounds with bromo- or iodoperfluoroalkanes have been reported, to

the best of our knowledge, only one example has been reported for a partially fluorinated vinyl halide [15], and there are no reports with a haloperfluoroolefin.
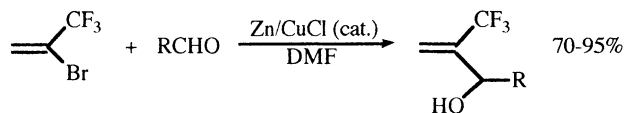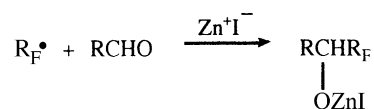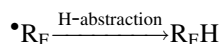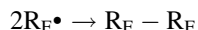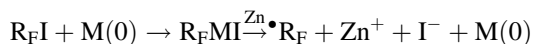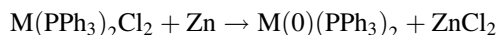

2. Results and discussion

Mechanistically, Barbier reaction is an interesting reaction and several different mechanisms have been proposed to account for the observed results. Blomberg has provided some fascinating insights into the mechanism of magnesium-promoted Barbier reactions [16,17].

In the zinc-promoted reaction of CF_3Br with SO_2, Wakselman has proposed radical anion intermediates [6], as outlined below.

$$R_FI \xrightarrow{M} M^+ + [R_FX]^- \rightarrow {}^\bullet R_F + X^- + M^+$$

$${}^\bullet R_F + SO_2^- \rightarrow R_FSO_2^- \rightarrow products$$
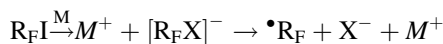
In the Zn/Barbier reactions catalyzed by Pd(II) or Ni(II), Ishikawa and co-workers proposed that the role of zinc is two-fold: (1) the zinc assists the scavenging of chloride from the catalyst to provide the zero valent metal; (2) zinc promotes the single electron transfer reaction which provides the perfluoroalkyl radical, which can behave in three ways: (a) it can abstract a hydrogen atom to give R_FH; (b) it can self-couple to give R_F-R_F; and (c) it can react with the aldehyde to give the zinc alkoxide. These processes are outlined below.

$$M(PPh_3)_2Cl_2 + Zn \rightarrow M(0)(PPh_3)_2 + ZnCl_2$$

$$R_FI + M(0) \rightarrow R_FMI \xrightarrow{Zn} {}^\bullet R_F + Zn^+ + I^- + M(0)$$

$$2R_F{}^\bullet \rightarrow R_F - R_F$$

$${}^\bullet R_F \xrightarrow{H\text{-abstraction}} R_FH$$

In the reaction of R_FI with aldehydes in DMF in the presence of zinc, Shen and Qi proposed that the first step of this Zn/Barbier reaction is a single electron transfer from zinc to R_FI [13]. Loss of Zn^+I^- results in the formation of the perfluoroalkyl radical, which reacts with Zn^+I^- to form an "unsolvated perfluoroalkylzinc reagent", which can react with the aldehyde to form the alcohol (after hydrolysis),

as outlined below.
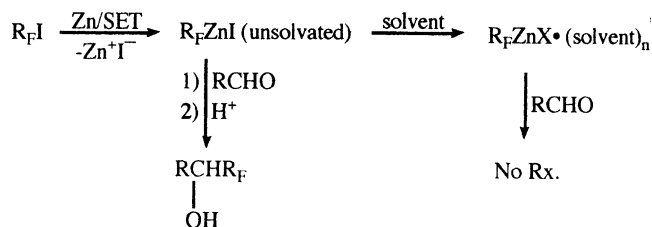
These authors demonstrated that the preformed zinc reagent (solvated) did not add to the aldehyde. Consequently, to account for the observed alcohol product, they suggested that the zinc reagent (unsolvated) was more reactive than the solvated zinc reagent and hence added to the aldehyde. The unsolvated zinc reagent was not observed or generated; consequently it is difficult to know the validity of this intermediate in this reaction. When Klabunde et al. generated the unsolvated trifluoromethylzinc reagent, he showed that it reacted with acetone or pivalaldehyde to produce fluoroform [18], suggesting that the ${}^\bullet CF_3$ radical is involved in the reaction.

$$CF_3ZnI \underset{unsolvated}{\xrightarrow{(CH_3)_3CCHO}} CF_3H$$
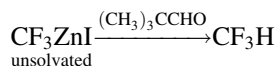
Pivalaldehyde is a poor proton donor, but an excellent source of a hydrogen atom. On the other hand, when bromoform, which is an excellent proton donor but a poor hydrogen atom source, was reacted with the unsolvated trifluoromethylzinc reagent, little CF_3H was formed.

In the one case involving a fluorine-containing vinyl halide, namely, $CF_3CBr=CH_2$, Hu et al. also proposed an "unsolvated" zinc reagent to account for the zinc-promoted addition of this reagent to aldehydes [15], and suggested that the "solvated" zinc reagent (pregenerated) did not add to aldehydes. However, Cu(I)Cl was proposed as a co-catalyst in this reaction but does not appear in any of the mechanistic proposals.

Since our discovery of the facile formation of perfluorovinylzinc reagents via the direct reaction of Zn(0) with perfluorovinyliodides or bromides [19], we have had a continuous interest in the mechanism of the zinc reagent formation. When "wet" solvents are employed in the generation of the perfluorovinylzinc reagents, the amount of the 1-hydroperfluoroolefin increases with the amount of water present. The formation of the reduced alkene suggested the involvement of a perfluorovinyl anion intermediate, which captures a proton to form the 1-hydroperfluoroolefin. Consequently, our "working" mechanism for the formation of the perfluorovinylzinc is outlined below (using (Z)-1-iodoperfluoropropene as a model substrate).
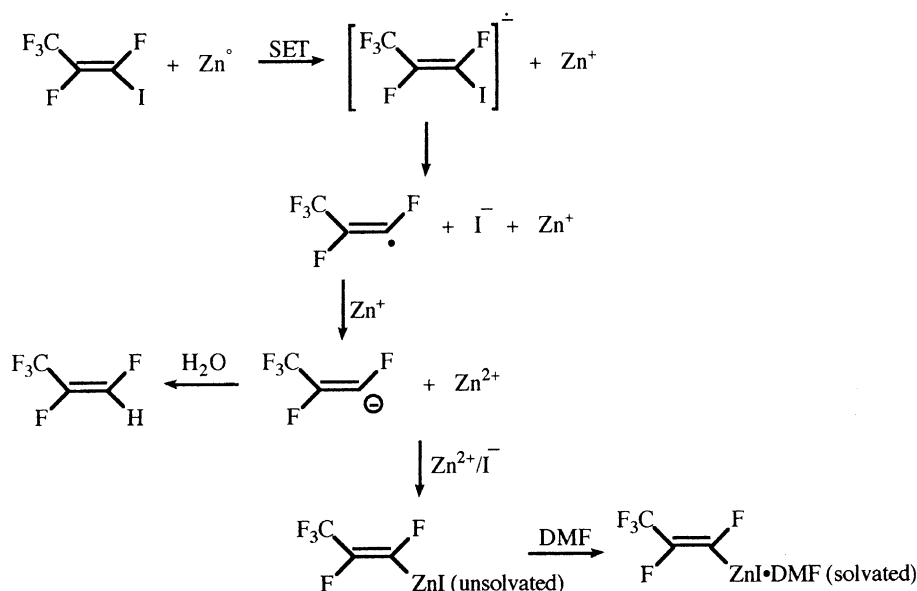
Since the perfluorovinylzinc reagents did not react with aldehydes [20], we decided to explore the Zn/Barbier reaction with these zinc reagents in the presence of aldehydes to: (1) ascertain if fluorinated allylic alcohols could be stereospecifically prepared by this route; and (2) probe the mechanism of the Zn/Barbier reaction, if alcohols were produced. Our emphasis in this investigation has focused on the mechanistic aspects; consequently we have not attempted to maximize the yields of the allylic alcohols or try to remove all unreacted aldehyde from the allylic alcohol product. Our purpose has been to demonstrate stereospecificity and to examine the scope of aldehydes that would participate in the reaction.

When (Z)-CF$_3$CF=CFI was reacted in dry DMF with benzaldehyde and Zn/Ag couple or acid-washed zinc, an exothermic reaction ensued after a short indication period. After hydrolysis with dilute HCl, extraction and chromatography, the corresponding (E)-allylic alcohol (**1**) was isolated in 54% yield. The spectroscopic data for this compound is in agreement with previous reports of this compound [21,22]. No (Z)-isomer was detected by ^{19}F NMR.
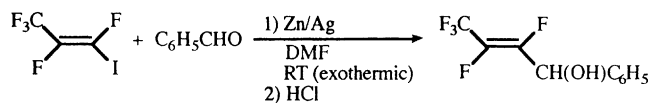
Thus, the (Z)-vinyliodide stereospecifically adds to the aromatic aldehyde. We then examined a series of aromatic aldehydes in this Zn/Barbier reaction and Table 1 summarizes these results. When the aromatic aldehyde contained an electron-withdrawing group on the aryl ring, such as 2-F, 3-F, 4-F, 4-CF$_3$, 2-CF$_3$, 4-Cl, the Zn/Barbier addition gives modest yields of the corresponding (E)-allylic alcohols. When (E)-CF$_3$CF=CFI was reacted with

2-fluorobenzaldehyde and zinc in dry DMF under similar conditions, ~50% yield of the (Z)-allylic alcohol was isolated. No (E)-allylic alcohol was detected by ^{19}F NMR. All new allylic alcohols were completely characterized by ^{1}H, ^{19}F and ^{13}C NMR and HRMS. The (E)- or (Z)-assignment was made based on $^3J_{FF(trans)} \gg {}^3J_{FF(cis)}$. Thus, the (Z)- or (E)-stereochemistry is preserved in the addition to the aldehyde. When the aryl ring contains an electron-releasing group, such as 4-OMe and 4-Me, the Zn/Barbier addition of (Z)-CF$_3$CF=CFI to the aldehyde failed. No alcohol product was detected and only (Z)-CF$_3$CF=CFZnI was formed. The above reactions are consistent with the formation of the (Z)-CF$_3$CF=CF$^\ominus$ anion. When the electrophilicity of the aldehyde is high (electron-withdrawing group on the aryl ring), addition to the aldehyde is favored over trapping of the anion with [ZnI]$^+$. When the electrophilicity of the aldehyde is decreased (electron-releasing group on the aryl ring), the trapping of the anion by [ZnI]$^+$ is favored and only (Z)-zinc reagent is observed. Of course, these results could also be rationalized by invoking an "unsolvated" zinc reagent which is sufficiently nucleophilic to react with aryl aldehydes of high electrophilicity, but not sufficiently nucleophilic to react with aryl aldehydes of low electrophilicity.
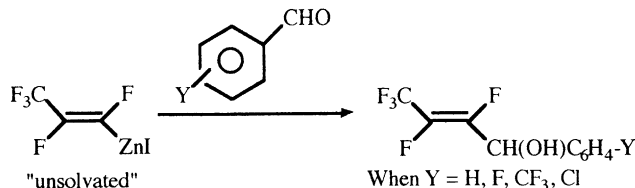
However, when (Z)-CF$_3$CF=CFI, Zn/Ag couple, and butanal are reacted in dry DMF, no (Z)-allylic alcohol is detected, and (E)-CF$_3$CF=CFH and (Z)-CF$_3$CF=CFZnI are the only

Table 1
Stereospecific preparation of (Z)- and (E)-fluorinated allylic alcohols[a]

Compound no.	Z/E (olefin)	X	(%) Yield (alcohol)	Z/E (alcohol)
1	Z	H	54	E
2	Z	2-F	51	E
3	Z	4-F	51[b]	E
4	Z	4-CF$_3$	55	E
5	Z	2-CF$_3$	52[c]	E
6	Z	3-F	48[d]	E
7	Z	4-Cl	53[e]	E
8	Z	4-OMe	0	–
9	Z	4-Me	0	–
10	Z	–[f]	0	–
11	E	2-F	50[g]	Z
12	Z	–[h]	0[i]	–
1	Z	2-F	0[j]	–
1	Z	4-NO$_2$	0	–

[a] (Z)- or (E)-CF$_3$C=CFI + X-C$_6$H$_4$CHO $\xrightarrow[\text{(2) HCl}]{\text{(1) Zn/DMF}}$ (Z)- or (E)-CF$_3$CF=CFCH(OH)C$_6$H$_4$-X
[b] 54:46 mixture with aldehyde.
[c] 60:40 mixture with aldehyde.
[d] 70:30 mixture with aldehyde.
[e] 74:26 mixture with aldehyde.
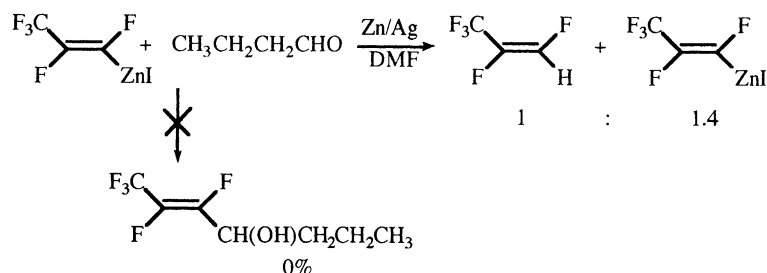[f] (CH$_3$)$_3$CCHO used as the aldehyde.
[g] 80:20 mixture with the aldehyde.
[h] CH$_3$CH$_2$CH$_2$CHO used as aldehyde.
[i] (E)-CF$_3$CF=CFH and (Z)-CF$_3$CF=CFZnI only products.
[j] 1,4-Dinitrobenzene additive.

products detected by NMR.

This observation is consistent only with the vinyl anion intermediate. Shen and Qi have demonstrated that aliphatic aldehydes give high yields of alcohols in a Zn/Barbier reaction with R$_F$I [13]. Consequently, we would expect allylic alcohol formation when (Z)-CF$_3$CF=CFZnI is reacted with butanal under Zn/Barbier conditions. The formation of large amounts of (E)-CF$_3$CF=CFH is best explained by trapping of the vinyl anion by the enol form of butanal.
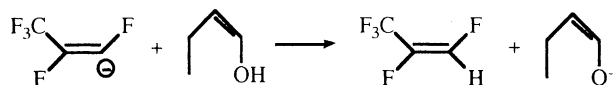
With a highly hindered aldehyde, such as pivalaldehyde, no allylic alcohol was observed; only (Z)-CF$_3$CF=CFZnI was detected, suggesting that the anion reacts significantly faster with [ZnI]$^+$ than with the hindered pivalaldehyde.

In order to gain some information for the formation of the initial vinyl radical in our mechanistic scheme, we carried out the reaction of (Z)-CF$_3$CF=CFI, Zn, 2-fluorobenzaldehyde, and 1,4-dinitrobenzene in dry DMF. No reaction occurred either at RT or elevated temperatures. No allylic alcohol was formed (in contrast to ∼50% allylic alcohol in the absence of 1,4-dinitrobenzene) and no (Z)-CF$_3$CF=CFZnI was formed, consistent with the known ability of 1,4-dinitrobenzene to quench SET reactions. This inhibition of the SET process also explains why 4-nitrobenzaldehyde failed to react with (Z)CF$_3$CF=CFI and Zn in dry DMF (cf. Table 1).

3. Conclusions

The Zn/Barbier reaction of acid-washed zinc or zinc–silver couple with (Z)- or (E)-1-iodoperfluoropropenes and aromatic aldehydes to stereospecifically form (Z)- or (E)-fluorinated allylic alcohols is best explained by the formation of the (Z)- or (E)-CF$_3$CF=CF$^\ominus$ anion which adds to the aldehyde. Electron-withdrawing groups on the aryl

ring promote the addition reaction, whereas electron-releasing groups lower the electrophilicity of the aldehyde and inhibit the addition reaction relative to the formation of the vinylzinc reagent. Aliphatic aldehydes, which contain an α-H, cause reduction of the vinyl halide. The involvement of an ''unsolvated'' vinylzinc reagent intermediate in this reaction is less attractive and does not adequately explain the formation of the reduction product in reactions with aliphatic aldehydes.

4. Experimental

4.1. General

All reactions were monitored by ^{19}F NMR analysis of the reaction mixture on a Bruker AC-300 MHz spectrometer. The ^{1}H NMR spectra of final products were obtained on a Bruker AC-300 MHz (300.17 MHz), a Bruker WM-360 MHz (360.14 MHz) or a Bruker DRX-400 MHz (400.13 MHz) spectrometer. Chemical shifts are reported in ppm with respect to either internal TMS or the lock solvent, CDCl$_3$. ^{19}F NMR spectra were obtained on a Bruker AC-300 MHz (282.41 MHz) spectrometer. Chemical shifts are reported in ppm relative to internal CFCl$_3$ or C$_6$H$_5$CF$_3$. In some cases, the ^{19}F NMR spectra were broadband decoupled from protons. All ^{13}C NMR spectra were obtained on either a Bruker AC-300 MHz (75.49 MHz), a Bruker WM-360 MHz (90.57 MHz), or a Bruker DRX-400 MHz (100.62 MHz) spectrometer with CDCl$_3$ as the lock solvent. All ^{13}C spectra were broadband decoupled from hydrogen, but not from fluorine. Chemical shifts are reported relative to internal TMS or CDCl$_3$ (lock solvent). Low resolution mass spectral analyses were performed at 70 eV in the electron impact mode on a single quadruple instrument interfaced to a gas chromatograph fitted with a DB-1 column (0.25 mm i.d. × 15 m). High resolution mass spectral analyses were performed on a VG-ZAB instrument by the University of Iowa High Resolution Mass Spectroscopy Facility or the Washington University (St. Louis, MO) High Resolution Mass Spectroscopy Laboratory in the electron impact mode. All isolations utilizing column chromatography were carried out on columns >12 in. in length packed with silica gel (325 mesh). All fractions were monitored by TLC using UV light for visualization.

4.2. Materials

DMF was distilled under reduced pressure from CaH$_2$. Zinc was activated as described in previous work [23]. Zinc–silver couple was prepared by the method of Conia and Rousseau [24]. Bromotrifluoroethylene and hexafluoropropene were obtained from commercial sources and used directly. (Z)- and (E)-CF$_3$CF=CFI were prepared by the published procedures [25,26]. The zinc reagent of (Z)-CF$_3$CF=CFI were prepared by the published procedure [23].

4.3. A representative procedure for Barbier preparation of allylic alcohols from (Z)-CF$_3$CF=CFI

4.3.1. 1-Phenyl-(2E)-2,3,4,4,4-pentafluorobuten-1-ol (1), (E)-CF$_3$CF=CFCH(OH)C$_6$H$_5$

A dry 25 ml flask equipped with a side arm, stir bar and a condenser attached to a N$_2$ tee was charged with 1.1 g (17 mmol) of Zn/Ag couple, 5.0 ml of dry DMF and 0.53 g (5.0 mmol) of benzaldehyde. The reaction mixture was stirred at room temperature for 5 min. To this slurry was added 2.59 g (10.0 mmol) of (Z)-CF$_3$CF=CFI. An exotherm (after a short induction period) indicated initiation of the reaction. The reaction mixture was allowed to cool to room temperature and then stirred at RT for 2 h. The reaction mixture was poured into dilute HCl and extracted with ether (3 × 10 ml). The ether extracts were combined and washed with a saturated solution of aqueous NaHSO$_3$ (3 × 10 ml) to remove any unreacted benzaldehyde. The organic layer was then washed with brine (3 × 10 ml), dried over anhydrous MgSO$_4$, concentrated by rotary evaporation, and purified by silica gel chromatography (ethyl acetate:hexane = 5:1) to give 0.65 g (54%) of (E)-CF$_3$CF=CFCH(OH)C$_6$H$_5$ (95% purity). ^{1}H NMR (CDCl$_3$): 7.0–7.3 (m, 5H), 5.7 (dd, $^{4}J_{FH}$ = 4.3, $^{3}J_{FH}$ = 24.5 Hz, 1H), 2.5 (bs, 1H) ppm. ^{19}F NMR (CDCl$_3$): −68.4 (dd, $^{4}J_{FF}$ = 21.8, $^{3}J_{FF}$ = 10.8 Hz, 3F), −155.5 (ddq, $^{3}J_{FF}$ = 135.2, $^{3}J_{FH}$ = 24.2, $^{4}J_{FF}$ = 21.6 Hz, 1F), −172.3 (dqd, $^{3}J_{FF}$ = 133.6, $^{3}J_{FF}$ = 10.7, $^{4}J_{FH}$ = 4.4 Hz, 1F) ppm. {1H} ^{19}F NMR (CDCl$_3$): −68.8 (dd, $^{4}J_{FF}$ = 21.8, $^{3}J_{FF}$ = 10.7 Hz, 3F) −155.5 (dq, $^{3}J_{FF}$ = 134.1, $^{4}J_{FF}$ = 21.6 Hz, 1F) −172.5 (dq, $^{3}J_{FF}$ = 133.8, $^{3}J_{FF}$ = 11.1 Hz, 1F) ppm. ^{13}C NMR (CDCl$_3$): 140.7–127.7 (m), 125.5–130.1 (m), 63.2 (d, $^{2}J_{CF}$ = 21.6 Hz) ppm. GC–MS: 238 (M^+, 31). The ^{19}F NMR data are consistent with literature data [21,22].

A similar Barbier reaction using acid-washed zinc gave 54% (1).

4.3.2. 1-(2-Fluorophenyl)-(2E)-2,3,4,4,4-pentfluorobuten-1-ol (2) (E)-CF$_3$CF=CFCH(OH)-2-FC$_6$H$_4$

Similarly, the reaction of 0.97 g (15.0 mmol) of Zn/Ag couple, 5.0 ml dry DMF, 0.62 g (5.0 mmol) 2-fluorobenzaldehyde and 2.64 g (10.2 mmol) of (Z)-CF$_3$CF=CFI gave 0.65 g, 51% of (E)-CF$_3$CF=CFCH(OH)-2-FC$_6$H$_4$ (2) (95% purity). ^{1}H NMR (CDCl$_3$): 3.9 (bs, 1H), 6.1 (dd, $^{3}J_{FH}$ = 24.9, $^{4}J_{FH}$ = 3.9 Hz, 1H), 7.1–7.7 (m, 4H) ppm. ^{19}F NMR (CDCl$_3$): −75.1 (dd, $^{4}J_{FF}$ = 21.6, $^{3}J_{FF}$ = 12.4 Hz, 3F), −125.2 (d, $^{5}J_{FF}$ = 4.2 Hz, 1F), −162.2 (dm, $^{3}J_{FF}$ = 133.2 Hz, 1F), −177.7 (dm, $^{3}J_{FF}$ = 133.3 Hz, 1F) ppm. ^{13}C NMR (CDCl$_3$): 62.0 (dd, $^{2}J_{CF}$ = 21.6, $^{3}J_{CF}$ = 4.5 Hz), 115.6–130.8 (m), 110.1–154.7 (m). GC–MS: 256 (M^+, 13), 239 (10), 236 (46), 125 (76), 123 (65), 97 (100), 91 (17). HRMS: calcd. for C$_{10}$H$_6$F$_6$O: 256.0323; found: 256.0324.

4.3.3. 1-(4-Fluorophenyl)-(2E)-2,3,4,4,4-pentafluorobuten-1-ol (3), (E)-CF₃CF=CFCH(OH)-4-FC₆H₄

Similarly, 0.97 g (15 mmol) of acid-washed zinc, 5.0 ml dry DMF, 0.63 g (5.1 mmol) 4-fluorobenzaldehyde, and 2.54 g (9.84 mmol) of (Z)-CF₃CF=CFI gave 0.67 g (51%) of a 54:46 mixture of (**3**) and 4-fluorobenzaldehyde. ^{1}H NMR (CDCl₃): 4.6 brs, 1H, 5.8 (dd, $^3J_{FH} = 24.8$, $^4J_{FH} = 4.4$ Hz, 1H), 7.4–8.0 (m, 4H) ppm. ^{19}F NMR (CDCl₃): −68.6 (dd, $^4J_{FF} = 21.4$, $^3J_{FF} = 11.0$ Hz, 3F), −102.7 (m, 1F), −155.8 (ddq, $^3J_{FF} = 133.8$, $^3J_{FH} = 24.4$, $^4J_{FF} = 21.6$ Hz, 1F), −172.7 (dqd, $^3J_{FF} = 133.2$, $^3J_{FF} = 10.7$, $^4J_{FH} = 4.4$ Hz, 1F) ppm. {1H} ^{19}F NMR (CDCl₃): −68.6 (dd, $^4J_{FF} = 21.4$, $^3J_{FF} = 11.0$ Hz, 3F), −102.9 (s, 1F), 155.9 (dq, $^3J_{FF} = 133.9$, $^4J_{FF} = 21.6$ Hz, 1F), −172.8 (dq, $^3J_{FF} = 133.2$, $^3J_{FF} = 10.7$ Hz, 1F) ppm. ^{13}C NMR (CDCl₃): 66.4 (d, $^2J_{CF} = 21.0$ Hz), 127.5–130.9 (m), 130.3–155.6 (m) ppm. GC–MS: 256 (M^+, 11), 239 (21), 236 (10), 125 (100), 123 (49), 97 (60). HRMS: calcd. for C₁₀H₆F₆O: 256.0323; found: 256.0324.

A similar Barbier reaction using Zn/Ag couple gave 51% (**3**) as a 52:48 mixture of (**3**) and 4-fluorobenzaldehyde.

4.3.4. 1-(4-Trifluoromethylphenyl)-(2E)-2,3,4,4,4-pentafluorobut-en-ol (4), (E)-CF₃CF=CFCH(OH)-4-CF₃C₆H₄

Similarly, 0.97 g (15 mmol) Zn/Ag couple, 5.0 ml dry DMF, 0.88 g (5.1 mmol) 4-trifluoromethylbenzaldehyde and 2.63 g (10.2 mmol) of (Z)-CF₃CF=CFI gave 0.86 g (55%) of (**4**) (90% purity). ^{1}H NMR (CDCl₃): 3.2 (bs, 1H), 6.0 (dd, $^3J_{FH} = 23.8$, $^4J_{FH} = 3.3$ Hz, 1H), 7.2–7.9 (m, 4H) ppm. ^{19}F NMR (CDCl₃): −63.4 (s, 3F), −68.7 (dd, $^4J_{FF} = 21.4$, $^3J_{FF} = 10.8$ Hz, 3F), −155.9 (ddq, $^3J_{FF} = 134.2$, $^3J_{FH} = 24.4$, $^4J_{FF} = 21.2$ Hz, 1F), −171.9 (dqd, $^3J_{FF} = 134.3$, $^3J_{FF} = 10.7$, $^4J_{FH} = 4.3$ Hz, 1F) ppm. {1H} ^{19}F NMR (CDCl₃): −63.4 (s, 3F), −68.7 (dd, $^4J_{FF} = 21.4$, $^3J_{FF} = 10.8$ Hz, 3F), −156.1 (dq, $^3J_{FF} = 134.2$, $^4J_{FF} = 21.2$ Hz, 1F), −171.9 (dq, $^3J_{FF} = 134.3$, $^3J_{FF} = 10.7$ Hz, 1F) ppm. ^{13}C NMR (CDCl₃): 66.5 (d, $^2J_{CF} = 21.7$ Hz), 120–125.9 (m), 130.3–175.6 (m) ppm. GC–MS: 306 (M^+, 35), 287 (46), 286 (10), 237 (83), 217 (100), 173 (64), 159 (65), 145 (66). HRMS: calcd. for C₁₁H₆F₈O: 306.0291; found: 306.0291.

4.3.5. 1-(2-Trifluoromethylphenyl)-(2E)-2,3,4,4,4-pentafluorobut-en-1-ol (5), (E)-CF₃CF=CFCH(OH)-2-CF₃C₆H₄

Similarly, 0.99 g (15 mmol) Zn/Ag couple, 5.0 ml dry DMF, 0.85 g (4.2 mmol) 2-trifluoromethylbenzaldehyde and 2.54 g (9.85 mmol) of (Z)-CF₃CF=CFI gave 0.67 g (52%) of a 60:40 mixture of (**5**) and 2-trifluoromethylbenzaldehyde. ^{1}H NMR (CDCl₃): 4.1 (brs, 1H), 6.0 (dd, $^3J_{FH} = 22.4$, $^4J_{FH} = 3.8$ Hz, 1H), 7.2–7.8 (m, 4H) ppm. ^{19}F NMR (CDCl₃): −59.7 (d, $^4J_{FH} = 6.9$ Hz, 3F), −68.9 (dd, $^4J_{FF} = 21.6$, $^3J_{FF} = 10.7$ Hz, 3F), −155.0 (ddq, $^3J_{FF} = 133.3$, $^3J_{FH} = 22.4$, $^4J_{FF} = 21.7$ Hz, 1F), −169.3 (dqdq, $^3J_{FF} = 133.3$, $^3J_{FF} = 10.6$, $^4J_{FH} = 3.8$,

$^6J_{FF} = 3.4$ Hz, 1F) ppm. {1H} ^{19}F NMR (CDCl₃): −59.7 (s, 3F), −68.9 (dd, $^4J_{FF} = 21.6$, $^3J_{FF} = 10.7$ Hz, 3F), −155.1 (dq, $^3J_{FF} = 133.8$, $^4J_{FF} = 22.2$ Hz, 1F), −171.9 (dqq, $^3J_{FF} = 134.0$, $^3J_{FF} = 11.0$, $^6J_{FF} = 3.6$ Hz, 1F) ppm. ^{13}C NMR (CDCl₃): 63.0 (dd, $^2J_{CF} = 22.4$, $^3J_{CF} = 2.2$ Hz), 124.0–134.0 (m), 110.0–160.0 (m). GC–MS: 306 (M^+, 29), 288 (10), 286 (40), 161 (60), 145 (50), 77 (27), 69 (52). HRMS: calcd. for C₁₁H₆F₈O: 306.0291; found: 306.0290.

A similar Barbier reaction using acid-washed zinc gave 52% of a similar product mixture.

4.3.6. 1-(3-Fluorophenyl)-(2E)-2,3,4,4-but-en-1-ol (6), (E)-CF₃CF=CFCH(OH)-3-FC₆H₄

Similarly, 1.07 g (16.5 mmol) Zn/Ag couple, 5.0 ml dry DMF, 0.66 g (5.3 mmol) of 3-fluorobenzaldehyde and 2.71 g (10.5 mmol) of (Z)-CF₃CF=CFI gave 0.65 g (48%) of a 70:30 mixture of (**6**) and 3-fluorobenzaldehyde. ^{1}H NMR (CDCl₃): 2.9 (brs, 1H), 5.7 (dd, $^3J_{FH} = 24.3$, $^4J_{FH} = 4.3$ Hz, 1H), 6.9–7.6 (m, 4H) ppm. ^{19}F NMR (CDCl₃): −68.6 (dd, $^4J_{FF} = 21.8$, $^3J_{FF} = 10.8$ Hz, 3F), −112.1 (m, 1F), −155.9 (ddq, $^3J_{FF} = 134.0$, $^3J_{FH} = 23.5$, $^4J_{FF} = 21.4$ Hz, 1F), −171.8 (dqd, $^3J_{FF} = 134.0$, $^3J_{FF} = 10.9$, $^4J_{FH} = 4.6$ Hz, 1F) ppm. {1H} ^{19}F NMR (CDCl₃): −68.6 (dd, $^4J_{FF} = 21.9$, $^3J_{FF} = 10.8$ Hz, 3F), −112.1 (s, 1F), −155.9 (dq, $^3J_{FF} = 134.2$, $^4J_{FF} = 21.3$ Hz, 1F), −171.8 (dq, $^3J_{FF} = 134.3$, $^3J_{FF} = 10.8$ Hz, 1F) ppm. ^{13}C NMR (CDCl₃): 66.7 (dd, $^2J_{CF} = 21.9$, $^3J_{CF} = 1.2$ Hz), 113.4 (d, $^3J_{CF} = 23.4$ Hz), 116.0 (d, $^2J_{CF} = 23.4$ Hz), 121.7 (d, $^4J_{CF} = 2.9$ Hz), 126.1 (d, $^3J_{CF} = 2.8$ Hz), 130.5 (d, $^3J_{CF} = 8.1$ Hz), 163.0 (d, $^1J_{CF} = 247.7$ Hz), 115–155 (m) ppm. GC–MS: 256, (M^+, 28), 239 (37), 125 (95), 97 (100). HRMS: calcd. for C₁₀H₆F₆O: 256.0323; found: 256.0326.

4.3.7. 1-(4-Chlorophenyl)-(2E)-2,3,4,4,4-pentafluorobut-en-1-ol (7), (E)-CF₃CF=CFCH(OH)-4-ClC₆H₄

Similarly, 0.97 g (15 mmol) Zn/Ag couple, 5.0 ml dry DMF, 0.71 g (5.1 mmol) of 4-chlorobenzaldehyde and 2.61 g (10.1 mmol) of (Z)-CF₃CF=CFI gave 0.73 g (53%) of a 74:26 mixture of (**7**) and 4-chlorobenzaldehyde. ^{1}H NMR (CDCl₃): 4.1 (bs, 1H), 5.6 (dd, $^3J_{FH} = 24.7$, $^4J_{FH} = 4.5$ Hz, 1H), 6.8–7.2 (m, 4H) ppm. ^{19}F NMR (CDCl3): −68.6 (dd, $^4J_{FF} = 21.9$, $^3J_{FF} = 10.8$ Hz, 3F), −155.8 (ddq, $^3J_{FF} = 134.3$, $^3J_{FH} = 24.2$, $^4J_{FF} = 21.8$ Hz, 1F), −172.3 (dqd, $^3J_{FF} = 134.3$, $^3J_{FF} = 10.7$, $^4J_{FH} = 4.4$ Hz, 1F) ppm. {1H} ^{19}F NMR (CDCl₃): −68.6 (dd, $^4J_{FF} = 21.9$, $^3J_{FF} = 10.9$, 3F), −155.8 (dq, $^3J_{FF} = 134.0$, $^4J_{FF} = 21.2$ Hz, 1F), −172.3 (dq, $^3J_{FF} = 134.3$, $^3J_{FF} = 10.7$ Hz, 1F) ppm. ^{13}C NMR (CDCl₃): 66.4 (d, $^2J_{CF} = 21.4$ Hz), 111–116 (m), 127–132 (m), 161–171 (m), ppm. GC–MS: 272 (M^+, 34), 237 (60) 217 (50), 139 (100), 131 (10), 111 (75). HRMS: calcd. for C₁₀H₆F₅O³⁵Cl: 272.0027; found: 272.0021.

A similar reaction with acid-washed zinc gave 51% of a similar product mixture.

4.3.8. Attempted preparation of 1-(4-methyoxyphenyl)-(2E)-2,3,4,4,4-but-en-1-ol (8), (E)-CF₃CF=CFCH(OH)-4-MeOC₆H₄

Similarly 0.65 (10 mmol) of acid-washed zinc, 5 ml dry DMF, 0.27 g (2.0 mmol) of 4-anisaldehyde and 1.0 g (4.0 mmol) of (Z)-CF₃CF=CFI gave 0% (**8**). ¹⁹F NMR analysis of the reaction mixture indicated only (Z)-CF₃CF=CFZnI (spectroscopic data in agreement with the zinc reagent generated from (Z)-CF₃CF=CFI and Zn). There was no trace of (**8**) detected in the reaction mixture by ¹⁹F NMR analysis.

4.3.9. Attempted preparation of 1-(4-methylphenyl)-(2E)-2,3,4,4,4-pentafluorobut-en-1-ol (9)

Similarly, 0.66 g (10.0 mmol) Zn/Ag couple, 5 ml dry DMF, 0.24 g (2.0 mmol) of 4-toluladehyde and 1.2 g (4.7 mmol) of (Z)-CF₃CF=CFI gave 0% (**9**). ¹⁹F NMR analysis of the reaction mixture indicated only (Z)-CF₃CF=CFZnI (spectroscopic data in agreement with the zinc reagent generated from (Z)-CF₃CF=CFI and Zn) and showed no trace of (**9**).

4.3.10. Attempted preparation of 2,2-dimethyl-(4E)-4,5,6,6,6-pentafluorohexen-3-ol (10), (E)-CF₃CF=CFCH(OH)C(CH₃)₃

Similarly, 0.65 g (10 mmol) of acid-washed zinc, 5.0 ml dry DMF, 0.18 g (2.1 mmol) of pivaladehyde and 1.0 g (4.0 mmol) of (Z)-CF₃CF=CFI gave 0% of (**10**). ¹⁹F NMR analysis of the reaction mixture indicated only (Z)-CF₃CF=CFZnI (spectroscopic data in agreement with the zinc reagent generated from (Z)-CF₃CF=CFI and Zn) and showed no trace of (**10**).

4.3.11. 1-(2-Fluorophenyl)-(2Z)-2,3,4,4,4-pentafluorobut-1-ol (11), (Z)-CF₃CF=CFCH(OH)-2-F C₆H₄

Similarly, 0.88 g (14 mmol) Zn/Ag couple, 5.0 ml dry DMF, 0.5 g (4 mmol) of 2-fluorobenzaldehyde and 2.1 g (8.0 mmol) of (E)-CF₃CF=CFI gave 0.51 g (50%) of a 80:20 mixture of (**11**) and 2-fluorobenzaldehyde. ¹H NMR (CDCl₃): 4.2 (brs, 1H), 6.0 (d, ³J_{FH} = 27.8 Hz), 6.7–7.7 (m, 4H) ppm. ¹⁹F NMR (CDCl₃): −73.6 (m, 3F), −125.1 (d, ³J_{FF} = 4.6 Hz, 1F), −145.6 (m, 1F), −162.7 (q, ³J_{FF} = 12.2 Hz, 1F) ppm. ¹³C NMR (CDCl₃): 62.0 (dd, ²J_{CF} = 21.6, ³J_{CF} = 4.5 Hz), 115.6–130.8 (m), 110.1–154.7 (m) ppm. GC–MS: 256 (M^+, 60), 236 (40), 208 (32), 169 (65), 123 (100). HRMS: calcd. for C₁₀H₆F₆O: 256.0323; found: 256.0329.

4.3.12. (2E)-1,1,1,2,3-pentafluorohepten-4-ol (12), (E)-CF₃CF=CFCH(OH)CH₂CH₂CH₃

Similarly, 0.71 g (11 mmol) Zn/Ag couple, 5.0 ml dry DMF, 0.31 g (4.3 mmol) of butanal and 2.2 g (8.4 mmol) of (Z)-CF₃CF=CFI gave 0% (**12**). ¹⁹F NMR analysis of the reaction mixture indicated only (E)-CF₃CF=CFH and (Z)-CF₃CF=CFZnI in a 1:1.4 ratio.

4.3.13. 1-Phenyl-(2E)-2,3,4,4,4-pentafluorobut-en-1-ol (1) via reaction of benzaldehyde with pregenerated (Z)-CF₃CF=CFZnI

Similarly, 0.38 g (3.6 mmol) of benzaldehyde was reacted with 2.8 mmol of pregenerated (Z)-CF₃CF=CFZnI. After 3 h at room temperature, ¹⁹F NMR analysis of the reaction mixture indicated only the zinc reagent and 0% (**1**). The reaction mixture was then heated to 50°C (3 h), 60°C (overnight) and 80°C (3 h); ¹⁹F NMR analysis indicated 0% (**1**) at any of these temperatures.

4.3.14. Effect of 1,4-dinitrobenzene on the reaction of (Z)-CF₃CF=CFI with 2-fluorobenzaldehyde and Zn/Ag couple

Similarly, to 0.36 g (5.5 mmol) acid-washed zinc, 0.51 g (3.0 mmol) of 1,4-dinitrobenzene, 3.6 ml dry DMF, and 0.24 g (1.9 mmol) of 2-fluorobenzaldehyde were added 0.96 g (3.7 mmol) of (Z)-CF₃CF=CFI. No reaction ensued after 1.5 h at RT or heating at elevated temperature. No zinc reagent was formed and no (**2**) was formed.

4.3.15. Pregeneration of (Z)-CF₃CF=CFZnI

A 25 ml flask equipped with a side arm, stir bar, cold water condenser and attached to a N₂ tee was charged with 0.66 g (10 mmol) of acid-washed zinc and 5.0 ml dry DMF. To this slurry was added 1.30 g (5.03 mmol) of (Z)-CF₃CF=CFI. Reaction initiated after a short induction period as indicated by a exotherm. After cooling to room temperature and stirring for 2 h, the solids were allowed to settle and an ¹⁹F NMR spectrum was taken of the supernatant liquid. ¹⁹F NMR (CDCl₃): −67.6 (dd, ⁴J_{FF} = 22.6, ³J_{FF} = 13.1 Hz, 3F), −148.5 (dq, ³J_{FF} = 108.1, ⁴J_{FF} = 21.6 Hz, 1F), −179.8 (dq, ³J_{FF} = 111.3, ³J_{FF} = 12.1 Hz, 1F) ppm; consistent with the literature data [23]. The yield of the zinc reagent varied from 69 to 76% in several trials.

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