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Journal of Fluorine Chemistry 128 (2007) 1198–1215
JOURNAL OF FLUORINE CHEMISTRY
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The preparation of HCF_2CdX and HCF_2ZnX *via* direct insertion into the carbon halogen bond of CF_2HY (Y = Br, I)

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Received 13 March 2007; received in revised form 18 May 2007; accepted 18 May 2007
Available online 25 May 2007

Dedicated to Professor Kenji Uneyama.

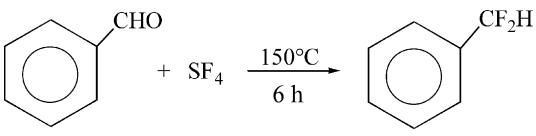
Abstract

The difluoromethylcadmium and zinc reagents have been prepared in DMF *via* direct insertion of Cd^0 into the carbon halogen bond of CF_2HY (Y = Br, I). These reagents are stable at 65–75 °C and exhibit prolonged stability and activity at room temperature. Metathesis of the difluoromethylcadmium reagents with Cu(I)X (X = Br, Cl) at −55 °C rapidly produces difluoromethylcopper. The copper reagent is significantly less stable than the cadmium or zinc reagent and rapidly decomposes at room temperature. The difluoromethylcadmium and copper reagents exhibit good reactivity with allylic halides, propargylic derivatives and 1-iodoalkynes to provide good yields of the corresponding difluoromethylalkenes, difluoromethylallenes and difluoromethyl-2-alkynes. Alkylation is successful only with reactive alkyl halides. Generally, the difluoromethylcopper reagent is more reactive than the difluoromethylcadmium reagent and generally exhibits higher regioselectivity in reactions that can occur by either α- or γ-attack.

Keywords: Difluoromethylcadmium reagent; Difluoromethylzinc reagent; Difluoromethylcopper reagent; Allenes; Alkynes; Difluoromethyl allylic derivatives; Organometallics

1. Introduction

The methods for the incorporation of the difluoromethyl group into organic compounds fall into two main categories. One is the fluorination of aldehydes with fluorinating agents, such as SF_4, DAST and related analogues, or metal fluorides (MoF_6, CoF_3, etc.). For example, SF_4 reacts with aldehydes to afford the corresponding difluoromethyl substituted compounds. A number of reviews have dealt with the properties and reactions of SF_4 with carbonyl compounds [1–3]. A typical example is illustrated in Eq. (1) [4]. In general, aldehydes which do not possess α-hydrogens give good yields of the difluoromethylated product. The yields of



61% (1)

aliphatic aldehydes, which contain α-hydrogens, are significantly lower due to complicating side reactions, which include the formation of 1,2-difluoroalkanes and bis-(1-fluoroalkyl) ethers [5] (Eq. (2)). The formation of these products and their ratio

$$RCH_2CHO + SF_4 \xrightarrow{-20\ \text{to}\ +40\ ^\circ C} RCFHCFH_2 + (RCFH)_2O + RCH_2CF_2H \quad (2)$$

is strongly dependent on the degree of alkyl substitution of the aldehydes and on the reaction conditions. Most straight chain aldehydes produce the corresponding 1,1-difluoroalkanes as the predominant or sole product; however, substituted aldehydes, such as isobutyraldehyde, α-ethylbutyraldehyde and α-methylbutyraldehydes, afford comparable amounts of 1,1-difluoroalkanes and rearranged 1,2-difluoroalkanes [5]. Heterocyclic aldehydes have also been demonstrated to successfully provide the difluoromethylated product with SF_4 [6]. Interest in chemotherapeutic agents similarly led to the preparation of the difluoromethyl heteroaromatic, 5-difluoromethyluracil (Eq. (3)) [7]. Fluorination of α,β-unsaturated aldehydes with SF_4, DAST and Et_2NCF_2CFHCl afforded the corresponding

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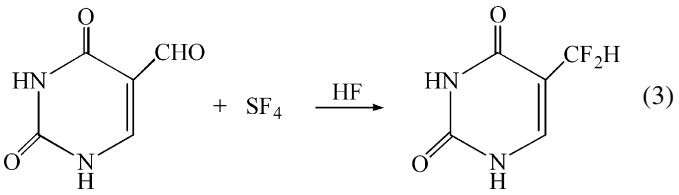
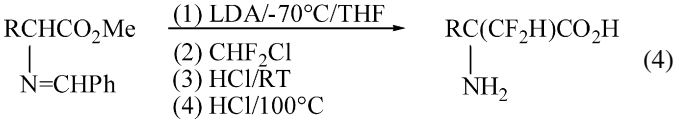
doi:10.1016/j.jfluchem.2007.05.015

difluoromethyl substituted olefins [8]. Middleton reported the fluorination of substituted aldehydes with DAST and indicated that the amount of side-products could be controlled using DAST in the appropriate solvent [9]. The yields reported by Middleton are comparable to those reported with SF_4 and aldehydes without α-hydrogen. The primary use of DAST has been for the introduction of the fluorinated substituent into natural products [10–14]. DAST avoids several of the disadvantages of SF_4: (1) fluorinations are more selective; (2) fewer rearrangements or eliminations result; (3) less elaborate apparatus is required, and (4) DAST or related analogues are commercially available and easier to handle than SF_4.



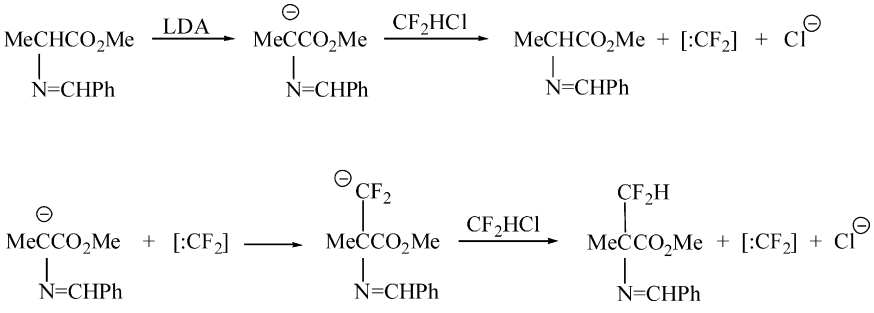
(3)

The second major method utilized for the introduction of the difluoromethyl group into organic compounds is chlorodifluoromethane. This methodology relies on the fact that a stabilized α-carbanion can be formed with an appropriate base and was first introduced by Sarett and co-workers [15]. Bey et al. prepared a number of difluoromethyl amino acids using chlorodifluoromethane as the difluoromethyl precursor (Eq. (4)) [16–19]. Although these reactions with CHF_2Cl can be rationalized



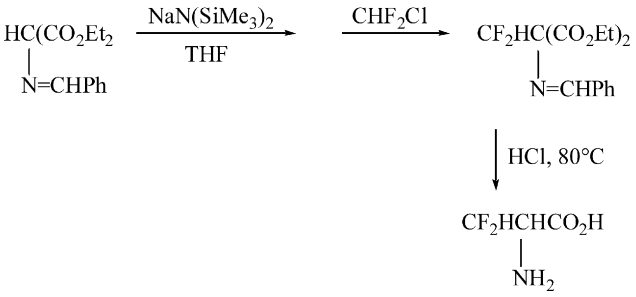
(4)

as an S_N2 process, more likely they involve difluorocarbene as a reaction intermediate (Eq. (5)). Difluoromethylation *via* chlorodifluoromethane has been



(5)

extended to aminomalonates by Tsushima and Kawada for the preparation of β-fluorinated alanines [20] (Eq. (6)). Amino malonates provide methodology for the preparation of amino acids which are only substituted at the α-carbon by the difluoromethyl group. Tsushimi et al. utilized this methodology to prepare an α-difluoromethyl glutamic acid, which was then utilized to prepare a fluorinated analog of methotrexate [21].



(6)

The preparation of *F*-alkyl and *F*-vinyl cadmium reagents has recently received considerable attention [22–26]. The *F*-cadmium, zinc, and copper reagents display excellent thermal stability and have been utilized in a variety of *F*-alkyl and *F*-vinyl transfer reactions. However, partially fluorinated *F*-organometallic reagents have received little attention and hydro-fluoro organometallic reagents have received no attention. Thus, our attention was drawn to the preparation of a difluoromethyl organometallic reagent and its ability to transfer the difluoromethyl group to produce new difluoromethyl building blocks.

The ease of reaction of *F*-alkyl iodides and bromides, *F*-vinylhalides, and bromopentafluorobenzene with cadmium metal prompted us to explore this approach as a route to a partially fluorinated cadmium reagent [27–30]. Our initial interest focused on: (1) the ease of formation of a partially fluorinated cadmium reagent *versus* the *F*-alkyl analog; (2) the stability of this reagent *versus* the *F*-analog; and (3) the reactivity of this reagent *versus* the *F*-analog. A preliminary report documents our preliminary work to prepare an HCF_2CdX reagent [31]. Subsequent to our preliminary report, German workers reported an alternative preparation of this reagent *via* the reaction of R_2Cd (R = Me, Et) with CF_2HI [32]. This work focused on the preparation of the reagent, its spectroscopic properties and the formation of adducts with donors, such as diglyme or TMEDA. Little or no chemistry with organic substrates was reported. In this manuscript, we detail the preparation and thermal stability of HCF_2CdX, its metathesis to prepare HCF_2Cu, and the reaction of the reagent with allyl halides, propargyl halides, haloacetylenes, and alkylating reagents.

2. Results and discussion

2.1. Preparation of the difluoromethylcadmium reagent

Difluoromethylcadmium can be readily prepared from iododifluoromethane or bromodifluoromethane and acid-washed cadmium metal in DMF. The CHF_2I rapidly inserts cadmium at RT to give a 91% ^{19}F NMR yield of a mixture of mono- and bis-difluoromethylcadmium. In contrast, bromodifluoromethane requires 5 days at 55 °C (in DMF) to give a 65–75% ^{19}F NMR yield of the mono- and bis-difluoromethylcadmium reagent (Eq. (7)) with a mono/bis ratio of ~3/1.

$$\begin{array}{l} CF_2HI + 2\,Cd^0 \\ \quad\Big\downarrow \text{RT/1 h, DMF, 91\%} \\ HCF_2CdX + (HCF_2)_2Cd \qquad X = Br, I \\ \quad 75 \qquad\quad 25 \\ \quad\Big\uparrow \text{5 days/55°C, DMF, 65–75\%} \\ HCF_2Br + 2\,Cd^0 \end{array} \tag{7}$$

The mono/bis reagents were identified *via* their characteristic ^{19}F NMR spectrum, which exhibited the expected doublet at −117.7 ppm and −119.2 ppm, respectively, for the difluoromethyl group with the distinctive $^{111}Cd/^{113}Cd$ satellites (cf. Ref. [31] for a detailed picture of this spectrum). The mono and bis reagents were unequivocally identified from the ^{113}Cd NMR spectrum of the mixture, which shows a triplet of doublets at 253.3 ppm for the mono reagent and a pentet of triplets for the bis reagent (see Ref. [31] for a detailed picture of this spectrum). Additional evidence for the assignments of the mono- and bis-difluoromethylcadmium reagents was obtained by addition of CdI_2 to the difluoromethylcadmium reagent. The mono/bis ratio was shifted in favor of the mono-reagent, with a corresponding increase in the signal at −117.7 ppm in agreement with the Schlenk equilibrium shown in the following equation:

$$(HCF_2)_2Cd + CdI_2 \rightleftarrows HCF_2CdI \tag{8}$$

Further identification was obtained chemically by hydrolysis of the reaction mixture with D_2O to give a 65% isolated yield of HCF_2D. Likewise, treatment of the reaction mixture with I_2 gave a 96% isolated yield of HCF_2I (Eq. (9)). By the same procedure,

$$\begin{array}{l} CF_2HD \\ \quad\Big\uparrow D_2O, 65\% \\ HCF_2CdX + (HCF_2)_2Cd \\ \quad\Big\downarrow I_2, 96\% \\ CF_2HI \end{array} \tag{9}$$

DCF_2Br was converted to the corresponding deuterated cadmium reagent. This reagent can be utilized to incorporate the $-CF_2D$ group into organic compounds (Eq. (10)). The thermal stability of the difluoromethylcadmium reagent was evaluated

$$CF_2DBr + 2\,Cd^\circ \xrightarrow[\text{4 days/60°C, 96\% } ^{19}F \text{ NMR yield}]{\text{DMF}} DCF_2CdBr + (DCF_2)_2Cd \tag{10}$$

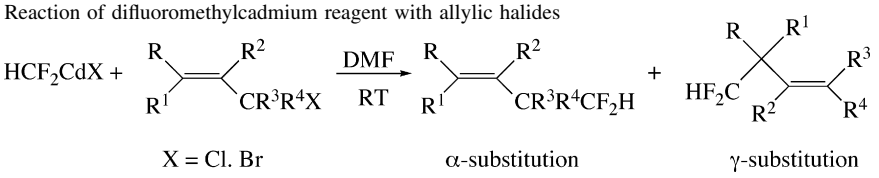
as follows: a 0.5 ml aliquot of the difluoromethylcadmium reagent (in DMF) was charged into a 5 mm NMR tube and 10 μl of $C_6H_5CF_3$ was added as a reference. The NMR tube was placed in the probe of a 90 MHz JEOL FX90Q NMR spectrometer. The ^{19}F NMR spectrum was recorded at 25 °C and then recorded every 10–20 min as the temperature was slowly raised (in 10 °C intervals) to 115 °C. The difluoromethylcadmium reagent exhibits excellent stability at RT—with a loss of only 31% activity of the original reagent after 2 months. Thus, a large solution of the reagent can be prepared, and aliquots utilized over a period of days to weeks. On heating (in DMF) little decomposition occurs until 65–75 °C. At temperatures >75 °C the rate of decomposition slowly increases, and at temperatures above 105 °C decomposition is rapid. The main decomposition product detected is CF_2H_2 [33].

2.2. Preparation of the difluoromethylzinc reagent

Similar to the preparation of the difluoromethylcadmium reagent, the analogous difluoromethylzinc reagent can be prepared *via* the reaction of HCF_2Br at 60 °C/5 days to give 73–85% ^{19}F NMR yield of the zinc reagent, with a mono/bis ratio of 88:12 (Eq. (11)). The mono/bis assignment is based on the decrease in the intensity

$$CF_2HBr + Zn^0 \xrightarrow[\substack{\text{60°C/ 5 days} \\ \text{73–85\%} \\ ^{19}F \text{ NMR yield}}]{\text{DMF}} \underset{88}{HCF_2ZnBr} + \underset{12}{(HCF_2)_2Zn} \tag{11}$$

Table 1
Reaction of difluoromethylcadmium reagent with allylic halides

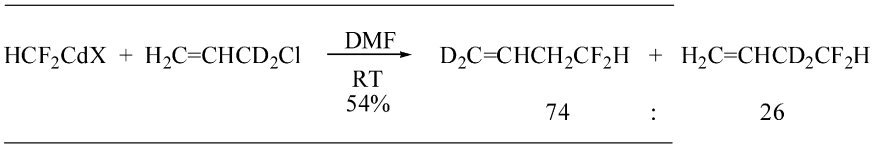


X = Cl. Br α-substitution γ-substitution

Entry	Allylic halides	Isolated yield (%)	α (attack)	γ (attack)
1	$H_2C{=}CHCH_2Br$	85	–	–
2	$H_2C{=}C(CH_3)CH_2Cl$	68	–	–
3	$H_2C{=}CHCD_2Cl$	55	26	74
4	(*E*)-$CH_3CH{=}CHCH_2Cl$	62	37	63
5	$H_2C{=}CHCH(Cl)CH_3$	45	7	93
6	$(CH_3)_2C{=}CHCH_2Cl$	68	89	3[a]
7	$H_2C{=}CHC(CH_3)_2Cl$	63	15	78[b]
8	(*E*)-$PhCH{=}CHCH_2Br$	87	52	48
9	(*E*)-$PhCH{=}CHCH_2Cl$	62	56	44

[a] 8% $H_2C{=}C(CH_3)CH{=}CH_2$.
[b] 5% $H_2C{=}C(CH_3)CH{=}CH_2$.

of the signal at −126.0 ppm (bis reagent) with a corresponding increase in the intensity of the signal at −125.9 ppm upon the addition of $ZnCl_2$ to the reaction mixture.



(13)

gave both 1,1-dideutero-4,4-difluoro-1-butene and 3,3-dideutero-4,4-difluoro-1-butene (Eq. (13)). This result indicates that there is a preference for

2.3. Allylation of the HCF_2CdX reagent

Typically, organocadmium reagents have been used to prepare ketones from acyl halides. A less common reaction of organocadmium reagents is their coupling with allylic halides [34]. Jones and Costanzo have demonstrated that diphenylcadmium reacts with allyl bromide and 3-bromo-1-cyclohexene in refluxing ether to give 39% and 81% GLPC yields of the allylated products [35]. However, di-*n*-octylcadmium failed to react with allyl bromide [36]. Similarly, CF_3CdX gave less than 5% of $CF_3CH_2CH{=}CH_2$ when reacted for 7 days with allyl bromide in DMF. The reactivity of a partially fluorinated organocadmium reagent had not previously been reported. Thus, for HCF_2CdX to provide a convenient method for the introduction of the difluoromethyl moiety into organic substrates *via* allylation, it must exhibit a unique reactivity with these substrates relative to *n*-octyl and trifluoromethylcadmium reagents.

Fortunately, when HCF_2CdX was reacted with allyl bromide, the reaction occurred readily to give an 85% isolated yield of 4,4-difluoro-1-butene (Eq. (12)) [37].

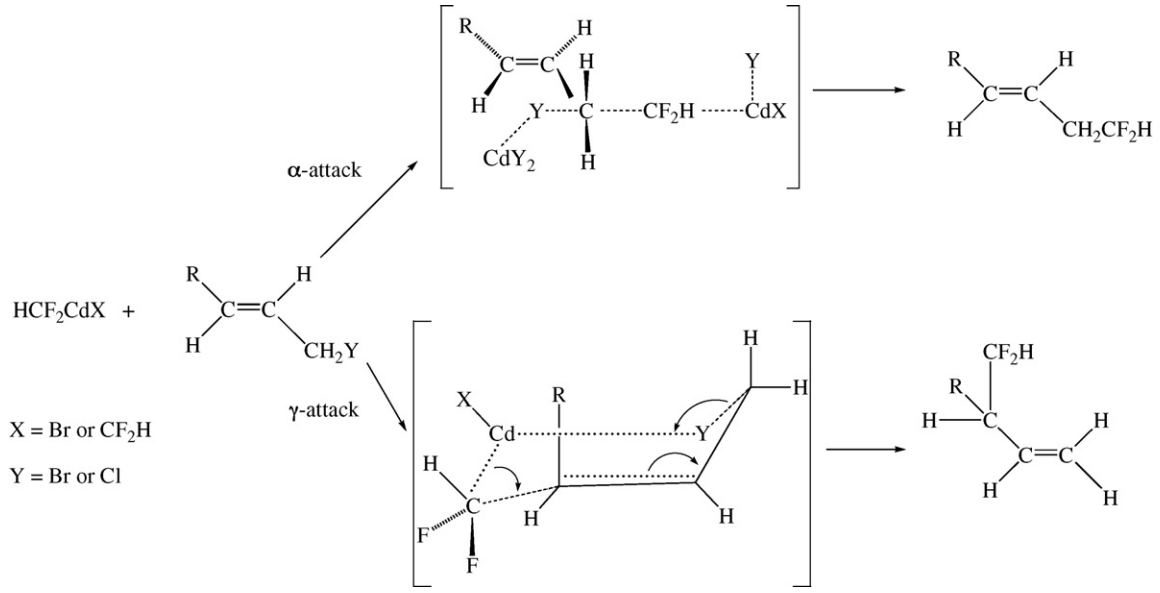
(12)

Since both α- and γ-attack would yield the same product, we investigated the same reaction with the corresponding 3-chloro-3,3-dideutero-1-propene. Reaction of the deuterated analog attack at the γ-carbon in a 3/1 ratio when the α- and γ-carbons do not possess alkyl substituents.

The effect of steric hindrance on the regioselectivity of the HCF_2CdX reagent with allylic halides was examined by the reaction of HCF_2CdX with allylic halides substituted at the α- and γ-carbons. (These results are summarized in Table 1.) The regiospecificity of the reaction of HCF_2CdX is that expected. As the steric hindrance at the α-center increases, the amount of the γ-attack product increases, and as the steric hindrance at the γ-center increases, the yield of the α-product increases.

The HCF_2ZnX reagent was also found to react with allylic halides; however, the reactivity of this reagent is significantly lower than the HCF_2CdX reagent. For example, after heating HCF_2ZnX (in DMF) with cinnamyl bromide for 19 h at 45 °C, followed by 28 h at 55 °C, 18% of HCF_2ZnX still remained. ^{19}F NMR analysis of the reaction mixture indicated a 74% (^{19}F NMR yield) of a mixture containing (*E*)-4,4-difluoro-1-phenyl-1-butene and 4,4-difluoro-3-phenyl-1-butene in a 42:58 ratio. Although the yield was slightly lower due to unreacted zinc reagent and longer reaction times were required, it is noteworthy that the HCF_2ZnX reagent does react with allyl halides (albeit slower) and provides a less toxic alternative to the cadmium analog.

The mechanism for attack at the α-carbon most likely involves a simple S_N2 displacement of the halide to give the corresponding difluoromethyl-substituted olefin (Scheme 1). The preference for γ-substitution in the reaction of HCF_2CdX with $H_2C{=}CHCD_2Cl$ discounts the possibility of a free ionic intermediate, since an ionic intermediate would give ~1/1 ratio of both isomers. An alternative explanation is that a six-



Scheme 1. Mechanism of nucleophilic attack at the α- and γ-carbons.

membered cyclic intermediate is involved (Scheme 1) in which the cadmium reagent is co-ordinated to the halide and the difluoromethyl group is co-ordinated to the γ-carbon. The ability of the HCF_2CdX to act as both the alkylating agent and halogen abstraction agent in the six-membered intermediate is the driving force behind its formation. A similar intermediate can explain the elimination product observed in reaction with 1-chloro-3-methyl-2-butene and 3-chloro-3-methyl-1-butene (Scheme 2). In this case the difluoromethyl group accepts an α-hydrogen to give CF_2H_2, a product observed in the reaction.

2.4. Formation of the HCF_2Cu reagent

In previous work with trifluoromethylcadmium [38], fluorinated vinyl cadmium reagents [39], perfluoroallyl cadmium reagents and fluorinated arylcadmium reagents [40,41,42] we have shown that fluorinated cadmium reagents readily exchange with Cu(I) halides to form (*in situ*) the analogous fluorinated copper reagent. A number of qualities make organocopper reagents attractive; these include (1) easy preparation, (2) good reactivity, (3) low toxicity, and (4) generally good regiospecificity when alternative sites of attack exist. Thus, we were prompted to attempt to prepare HCF_2Cu, study its stability, and to investigate its reactivity and regiospecificity with allylic halides compared to HCF_2CdX.

When the difluoromethylcadmium reagent (in DMF) is reacted with CuBr or CuCl at −50 to −60 °C, a rapid metathesis reaction occurs to form difluoromethylcopper in >90% ^{19}F NMR yield. This HCF_2Cu^a reagent exhibits a doublet at −114.6 ppm (^{19}F NMR). When the temperature of the solution was increased, a second HCF_2Cu^b reagent appeared (^{19}F NMR, −116.4 (d)). At $T > -30$ °C the copper reagent began to decompose rapidly to HCF_2CF_2H and *cis*-CFH=CFH (Eq. (14)) [43,44].

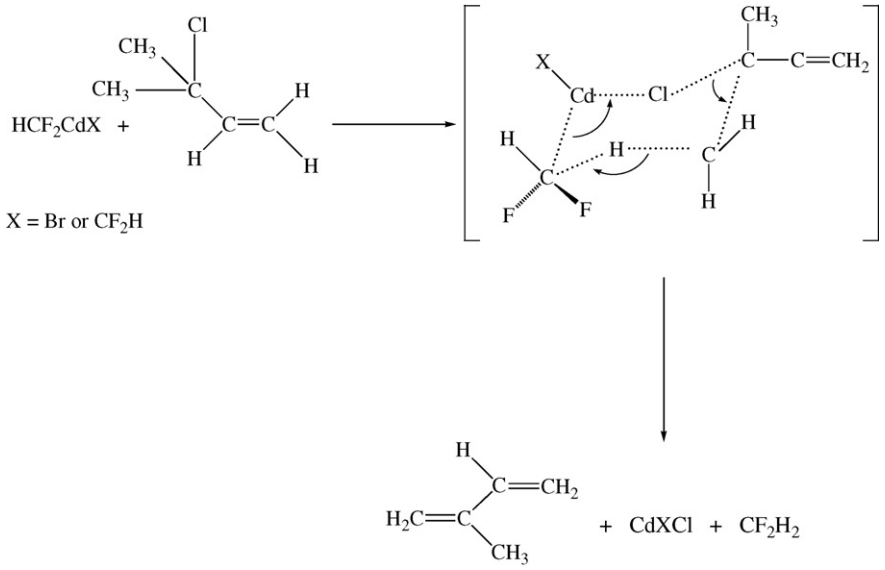
$$HCF_2CdX \xrightarrow[\text{DMF}\ \text{-50 to -60°C}]{\text{CuBr}} HCF_2Cu^a \xrightarrow{\text{warming}} HCF_2Cu^b \xrightarrow{> \text{RT}} HCF_2CF_2H + \textit{cis}\text{-CFH=CFH} \quad (14)$$

2.5. Allylation of the HCF_2Cu reagent

Although HCF_2Cu is relatively unstable, reactions with allyl halides are rapid and the reagent is a useful difluoromethyl transfer reagent. Generally, the HCF_2CdX (in DMF) reagent is cooled to −50 to −60 °C, and an equivalent amount of CuBr or CuCl is added, maintaining the −50 to −60 °C temperature; then the allyl halide is added and the solution slowly warmed to RT (Eq. (15)). Since the HCF_2Cu easily decomposes, a slight excess of HCF_2Cu is utilized in these allylation reactions. These results are summarized in Table 2. Comparison of the results summarized in

$$HCF_2CdX \xrightarrow[\text{2) CuBr}\ \text{3) } H_2C{=}CHCD_2Cl\ \text{4) warm to RT}\ \text{5) 63\% isolated yield}]{\text{1) -50°C}} D_2C{=}CHCH_2CF_2H + H_2C{=}CHCD_2CF_2H \quad (15)$$

90 : 10



Scheme 2. Mechanism for the elimination reaction of dimethyl-substituted allylic halides.

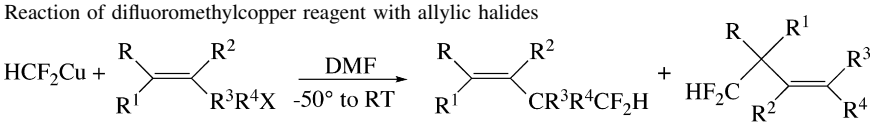
Table 2 shows that the HCF_2Cu is generally a more regiospecific reagent for the introduction of the $–CF_2H$ into allylic halides. The reactions are faster (even at the −50 °C temperature) and the diene (elimination) products noted in Table 1 are not observed with the HCF_2Cu reagent. Also, 3-chlorocyclohexene cleanly gives 3-(difluoromethyl)-1-cyclohexene with HCF_2Cu, whereas HCF_2CdX with 3-chlorocyclohexene gives significant amounts of 1,3-cyclohexadiene and difluoromethane.

Since $H_2C{=}CHCD_2Cl$ does not give approximately equal amounts of product from α- or γ-attack, a free ionic intermediate has been ruled out for the HCF_2Cu reactions with allylic halides. Thus, a concerted S_N2 or S_N2'[1] mechanism is proposed for this reaction with preference for attack at the least hindered site. The HCF_2Cu reagent is presumably aggregated in solution and hence more sterically bulkier than the HCF_2CdX reagent; hence the increased selectivity for preferred attack at the less hindered site.

2.6. Reaction of the HCF_2CdX reagent with propargyl derivatives

The increased nucleophilicity of HCF_2CdX compared to *n*-octylcadmium and trifluoromethylcadmium prompted us to study the reaction of HCF_2H with propargyl halides and tosylates. We had previously demonstrated that perfluoroalkylcopper reagents readily reacted with this class of substrates to afford the corresponding allenes in good yields (Eq. (16)) [45].

Table 2
Reaction of difluoromethylcopper reagent with allylic halides



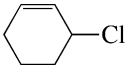
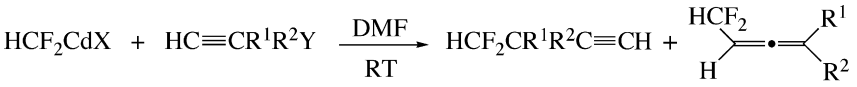
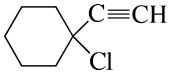
Entry	Allylic halides	Isolated yield (%)	α (attack)	γ (attack)
1	$H_2C{=}CHCD_2Cl$	63	10	90
2	(*E*)-$CH_3CH{=}CHCH_2Cl$	68	54	46
3	$H_2C{=}CHCH(Cl)CH_3$	74	–	100
4	$(CH_3)_2C{=}CHCH_2Cl$	80	100	–
5	$H_2C{=}CHC(CH_3)_2Cl$	76	–	100
6	(*E*)-$PhCH{=}CHCH_2Cl$	86	100	–
7	$H_2C{=}CHCF_2Br$	74	–	100
8		62	–	–

Table 3
Yields and isomeric ratio for the reaction of HCF_2CdX with propargylic halides and tosylates



	α-substitution	γ-substitution	
Propargylic halide/OTs	Yield (%)[a]	α (attack)	γ (attack)
$HC{\equiv}CCH_2Cl$	41	5	95
$HC{\equiv}CCH(CH_3)OTs$	(87)	0	100
$HC{\equiv}CCH(CH_3)Cl$	(84)	0	100
$HC{\equiv}CC(CH_3)_2Br$	64	0	100
$CH_3C{\equiv}CCH_2Br$	69	22	78
	(56)[b]	0	100
$ClCH_2C{\equiv}CCH_2Cl$	(52)	0	100

[a] Yields in parentheses are ^{19}F NMR yields; all other yields are isolated yields.
[b] 30% of 1-ethynyl-1-cyclohexene.

Thus, we were interested to determine if

(16)

X = Cl or OTs

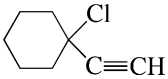
HCF_2CdX was sufficiently nucleophilic to accomplish a similar transformation. When HCF_2CdX reacts with propargyl chloride at RT, a slow reaction (3 days at RT and 7 days at 50 °C) produced a mixture (isolated) of 4,4-difluoro-1,2-butadiene and 4,4-difluoro-1-butyne; some propargyl chloride remained unreacted. A similar reaction with 3-tosyl-1-butyne (7 h at RT) gave an 87% (^{19}F NMR) yield of 1,1-difluoro-2,3-pentadiene. Several other propargyl derivatives were investigated and these results are summarized in Table 3. Only $HC{\equiv}CC(CH_3)_2Cl$ gave a clean, rapid, regiospecific reaction to form the allene. Several other derivatives gave good regioselectivity, but the reactions were sluggish or gave by-products that made isolation of the allene difficult (cf. Section 3).

2.7. Reaction of the HCF_2Cu reagent with propargyl derivatives

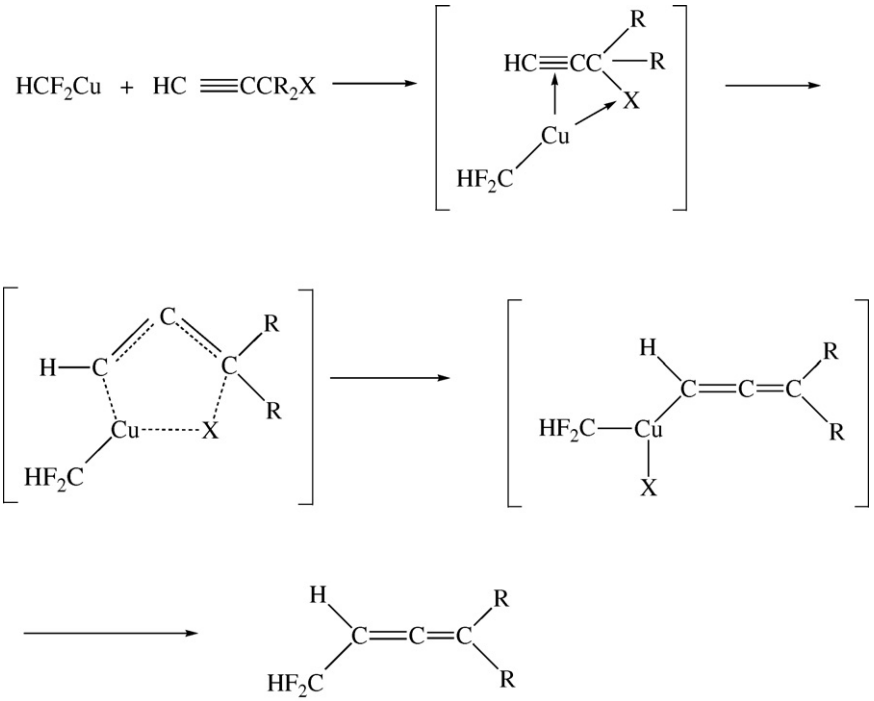
In contrast to the sluggish reaction of HCF_2CdX with propargyl derivatives, the HCF_2Cu reagent reacted readily with most of these derivatives. When HCF_2Cu reacted with propargyl chloride only a 7% (^{19}F NMR) yield of 4,4-difluoro-1,2-butadiene was detected. Similar reaction with the more reactive tosylate derivative was employed; only a 33% (^{19}F NMR) yield was detected; and 3-chloro-1-butyne gave only a 25% (^{19}F NMR) yield of the expected allene. With the more reactive 1-tosyl-2-butyne, a 53% isolated yield was obtained. The low reactivity of HCF_2Cu with simple propargyl derivatives could be explained by complexation of the HCF_2Cu reagent with the triple bond of the alkyne. We had observed similar complexation of fluorinated aryl copper reagents with alkynes in other work in our laboratory [42,46]. Fortunately, with derivatives other than simple propargyl compounds, reasonable isolated yields of the products was obtained. These results are summarized in Table 4. The results

Table 4
Isolated yields for the reaction of the HCF_2Cu reagent with propargylic halides or tosylates

X = Cl, Br, OTs α-substitution γ-substitution

Entry	Propargyl halide/OTs	Yield[a]	α	γ (%)
1	$HC{\equiv}CCH_2Cl$	(7)	0	100
2	$HC{\equiv}CCH_2OTs$	(33)	0	100
3	$HC{\equiv}CCH(Cl)CH_3$	(25)	0	100
4	$HC{\equiv}CCH(OTs)CH_3$	53 (61)	0	100
5	$HC{\equiv}CC(CH_3)_2Cl$	78 (77)	0	100
6	$CH_3C{\equiv}CCH_2Br$	59 (74)	13	87
7		71 (72)	0	100
8	$ClCH_2C{\equiv}CCH_2Cl$	46 (55)	0	100

[a] Yields in parentheses are ^{19}F NMR yields.



Scheme 3. Mechanism of the formation of difluoromethyl allenes from propargyl substrates and difluoromethyl copper reagent.

in Table 4 (compared to Table 3) again demonstrate the enhanced reactivity of the HCF_2Cu reagent and the enhanced regioselectivity of the copper reagent. For entries (4–7, Table 4) good isolated yields of the allenes were obtained. In entry 7 only the allene was obtained, no 1-ethynyl-1-cyclohexene was formed (cf. Table 3). With 1,4-dichloro-2-butyne, the bis-2,3-(difluoromethyl)-1,3-butadiene was formed by two successive γ-attacks of HCF_2Cu. Thus, for the preparation of difluoromethylallenes from a propargyl precursor, HCF_2CdX may be the reagent of choice for simple analogs, such as propargyl halides or tosylates; whereas HCF_2Cu would be the reagent of choice for more reactive analogs.

The mechanism for the reaction of HCF_2Cu with propargylic halides or tosylates is proposed to occur *via* initial complexation of the copper reagent with the triple bond of the alkyne (Scheme 3). A stronger complex would be expected for HCF_2Cu, since the electron-withdrawing effect of the fluoroalkyl group results in a greater electron deficiency for the copper atom. Oxidative addition occurs to afford a copper(III) intermediate which subsequently undergoes a reductive elimination to afford the difluoromethyl substituted allene. The oxidative addition–reduction elimination mechanism has been previously proposed by Posner for coupling reactions of fluoroalkyl copper reagents [46]. The regiospecificity observed in the formation of the allenes is due to the complexation of the copper reagent and the proximity of the copper atom to the γ-carbon as a result of the complexation. In addition, the γ-carbon is always the least hindered site when the propargylic halide is a terminal alkyne. Substitution at the γ-carbon by a difluoromethyl group occurs by oxidative addition at the γ-carbon to form a copper(III) intermediate; reductive elimination of copper halide affords the difluoromethylated allene.

2.8. Preparation of difluoromethylated substituted alkynes

Perfluoroalkylcopper reagents, prepared from the corresponding iodide and copper metal in DMSO, have been coupled with iodoalkynes at temperatures below 5 °C to produce the perfluoroalkyl substituted alkynes in a single step [47]. At higher temperatures self-coupling of the iodoalkynes to form the symmetrical diynes was a significant side reaction (Eq. (17)). With 1-iodoperfluoroalkynes and R_FCu, an

$$R_FI + Cu^\circ \xrightarrow[\substack{RC\equiv CI\\110^\circ C}]{DMSO} [R_FCu] \xrightarrow[\substack{5^\circ C\\30\ min.}]{RC\equiv CI} R_FC\equiv CR$$

$$\Big\downarrow \begin{matrix} RC\equiv CI \\ higher\ temp. \end{matrix} \qquad (17)$$

$$R_FC\equiv CR + RC\equiv C\text{-}C\equiv CR$$

exchange reaction occurs between the iodoperfluoroalkyne and the R_FCu reagent to produce R_FI and the perfluoroalkynyl copper reagent, which then couples with a second equivalent of the iodoperfluoroalkyne to give a perfluoroalkyldiyne [48]. Thus, it was not obvious that HCF_2Cu would couple with both classes of iodoalkynes.

Table 5
Isolated yields from the reaction of HCF_2Cu with 1-iodo-1-alkynes $HCF_2Cu + RC{\equiv}CI \longrightarrow^{DMF}_{-55\,^\circ C \text{ to } RT} RC{\equiv}CCF_2H$

R	Isolated yield of $RC{\equiv}CCF_2H$ (%)
C_4H_9	75
C_5H_{11}	74
C_6H_5	44
C_4F_9	52
C_6F_{13}	55
C_8F_{17}	66

To our delight, HCF_2Cu readily coupled with $RC{\equiv}CI$ to give moderate to good yields of the resultant difluoromethyl alkyne. With 1-iodoperfluoroalkyl alkynes, two different situations were observed. With 1-iodo-trifluoropropyne only traces of the desired difluoromethyl substituted *F*-alkyne was observed. However, with longer chain R_F derivatives, good isolated yields of the difluoromethyl substituted alkyne was obtained (cf. Table 5) (Eq. (18)), Thus, HCF_2Cu exhibits a unique reactivity with 1-iodoperfluoroalkynes.

$$HCF_2C{\equiv}CR \xleftarrow[RC{\equiv}CI,\ -55^\circ C]{DMF} HCF_2Cu \xrightarrow[R_FC{\equiv}CI,\ -55^\circ C]{DMF} R_FC{\equiv}CCF_2H \qquad (18)$$

44-75% 52-66%

2.9. Alkylation with HCF_2Cu

The HCF_2Cu reagent reacts with strong alkylating agents, such as chloromethyl ethyl ether or benzyl bromide to give the corresponding difluoromethylated product (Eq. (19)). The by-products of the reaction were

$$C_6H_5CH_2CF_2H \xleftarrow{C_6H_5CH_2Br} HCF_2Cu \xrightarrow[DMF,\ -55^\circ C]{ClCH_2OCH_2CH_3} HCF_2CH_2OCH_2CH_3 \qquad (19)$$

33% 72%

CF_2HCF_2H and *cis*-CFH=CFH from the decomposition of HCF_2Cu. With less reactive alkylating reagents the difluoromethylalkylated product is either not obtained or only in trace amounts.

3. Experimental

3.1. General experimental procedures

The ^{19}F NMR spectra were recorded on a JEOL FX90Q Spectrometer operated at 83.81 MHz. Chemical shifts have been reported relative to $CFCl_3$ and were generally determined in $CDCl_3$ solvent (unless otherwise noted). Quantitative measurements were carried out by integration relative to internal benzotrifluoride. Routine ^1H NMR spectra were recorded on a JEOL FX90Q Spectrometer operated at 89.09 MHz. High field ^1H NMR spectra were recorded on a Bruker WM 360X Spectrometer operated at 360.14 MHz. Typically $CDCl_3$ was used as the NMR lock solvent and chemical shifts are reported in ppm relative to internal TMS. The ^{13}C NMR spectra were recorded on a Bruker WM 360X Spectrometer operated at 90.56 MHz. The spectra were run unlocked with neat samples and an internal TMS capillary or as 10–20% (v/v) solutions in $CDCl_3$ with TMS as an internal standard. The ^2D NMR spectra were recorded on a JEOL FX90Q Spectrometer operated at 13.63 MHz. Solvent and internal references are reported with the NMR data for any deuterium-containing compound. The ^{113}Cd NMR spectra were recorded on a Bruker WM 360X Spectrometer operated at 19.84 MHz. The samples were reaction mixtures in DMF and chemical shifts are reported relative to external $CdSO_4$. Mass spectra of liquid samples were recorded on a Hewlett-Packard 5985 GC–MS system operated at 30 eV in the electron impact mode. The GC contained an 8 ft × 1/8 in. glass column packed with 5% ov101 on Chromosorb P. Solid samples were recorded by direct inlet into the probe in the electron impact mode. High resolution MS were recorded on a VG Analytical ZAB-HF operated at 70 eV in the electron impact mode. Infrared spectra were recorded on a Mattson Cygnus 25 FTIR Spectrometer as solutions in CCl_4. Spectra of gaseous samples were recorded in a 10 cm evacuated gas cell containing ~10 mm of gas sample. Analytical GLPC were performed on a Hewlett-Packard model 5890 equipped with a TCD. Capillary GLPC was performed using a FID. All bp were determined during fractional distillation and are incorrected. Melting points were determined in a Thomas-Hoover Unimelt apparatus and are incorrected.

Bromodifluoromethane was used as received from the Dow Chemical Company. Bromodeuterodifluoromethane was prepared by hydrolysis of bromodifluoromethyltriphenylphosphornium bromide with D_2O and purified by bulb-to-bulb distillation. ^2D NMR (DMF, d_6-acetone ref.): 6.2 ppm (t); ^{19}F NMR (DMF): −69.3 ppm (t, J_{FD} = 9.8 Hz). Allylic halides, benzyl bromide and ethylchloroethyl ether were purchased commercially and used directly. The 3-chloro-3,3-dideutero-1-propene was prepared by reported procedures [49,50]. Propargyl chloride and 1,4-dichloro-2-butyne were purchased commercially and distilled prior to use. The propargyl tosylates and halo-substituted alkynes were prepared by the procedure reported by Brandsma and Verkuijsse [51] from the corresponding alcohols. The aliphatic alkynyl iodides were prepared by Brandsma's procedure [51]. The perfluoroalkynyl iodides were prepared by the procedure developed by Spawn [52].

3.2. Preparation of the difluoromethylcadmium reagent

3.2.1. From bromodifluoromethane

A three-neck 500 ml flask fitted with a septum, stir bar, and a 400 cm isopropyl alcohol condenser with a nitrogen inlet was charged which 250 ml of dry DMF and 84.3 g (0.75 mol) of acid-washed cadmium metal. A low temperature probe of a Neslab Cryocool 100 was employed to cool the isopropyl alcohol to −78 °C. Bromodifluoromethane (50 g, 0.38 mol) was condensed into the reaction mixture, and the solution was heated for 5–7 days at 50–55 °C. Completion of the reaction was determined *via* ^{19}F NMR analysis of the reaction mixture. Typically 65–75% ^{19}F NMR yields were obtained in 5 days with a mono:bis ratio of 75:25. HCF_2CdBr; ^{19}F NMR: −117.7 ppm, $J(^{113}CdF)$ = 341.9 Hz, $J(^{111}CdF)$ = 327.0 Hz, $^2J_{HF}$ = 43.0 Hz; ^{113}Cd NMR: 253.3 ppm, $J(^{113}CdH)$ = 115.6 Hz. $(HCF_2)_2Cd$; ^{19}F NMR: −119.2 ppm, $J(^{113}CdF)$ = 292.4 Hz, $J(^{111}CdF)$ = 277.8 Hz, $^2J_{HF}$ = 43.2 Hz; ^{113}Cd NMR: 228.6 ppm, $J(^{113}CdH)$ = 75.9 Hz (see Ref. [31] for a detailed picture).

3.2.2. From iododifluoromethane

A 25 ml flask equipped with a septum, stir bar and dry ice/isopropyl alcohol condenser (with nitrogen inlet) was charged with 10 ml of dry DMF and 1.7 g (15 mmol) of acid-washed cadmium metal. Iododifluoromethane (1.6 g, 9.2 mmol) was condensed into the reaction mixture. After an induction period (∼10 min) a slight exotherm was observed. After the reaction mixture was stirred at room temperature for 1 h, ^{19}F NMR analysis indicated a 91% yield of the difluoromethylcadmium reagent. The ^{19}F NMR data was consistent with that obtained with the difluoromethylcadmium reagent prepared from HCF_2Br.

3.2.3. From bromodeuterodifluoromethane

Following the procedure outlined in Section 3.2.1, DCF_2Br (6.6 g, 50 mol), 5.7 (100 mmol) of acid-catalyzed cadmium metal and 50 ml dry DMF gave a 96% (^{19}F NMR) yield of the deuterated difluoromethylcadmium reagent after 4 days at 60 °C; mono:bis ratio ∼3/1. DCF_2CdBr; ^{19}F NMR: −120.0 ppm, $J(^{113}CdF)$ = 341.9 Hz; $J(^{111}CdF)$ = 328.9 Hz, $^2J_{DF}$ = 6.8 Hz; ^{113}Cd NMR: 262.0 ppm. $(DCF_2)_2Cd$: ^{19}F NMR: −121.6 ppm, $J(^{113}CdF)$ = 293.4 Hz, $J(^{111}CdF)$ = 280.3 Hz, $^2J_{DF}$ = 6.8 Hz; ^{113}Cd NMR: 234.7 ppm, $J(^{113}CdD)$ = 11.4 Hz.

3.3. Preparation of the difluoromethylzinc reagent

A 50 ml flask fitted with a septum, stir bar and a 400 cm isopropyl alcohol condenser (with a nitrogen inlet) was charged with 25 ml of dry DMF and 1.6 g (25 mmol) of acid-washed zinc metal. With cooling of the isopropyl alcohol to −78 °C with a Neslab Cryocool 100 3.3 g (25 mmol) of HCF_2Br was condensed into the reaction mixture. The suspension was heated for 5 days at 60 °C to give 73–85% of the difluoromethylzinc reagent, as determined by ^{19}F NMR analysis; mono:bis ratio of 88:12. HCF_2ZnBr: ^{19}F NMR: −125.9 ppm (d, $^2J_{HF}$ = 43.9 Hz); $(HCF_2)_2Zn$: ^{19}F NMR: −126.0 ppm (d, $^2J_{HF}$) = 43.9 Hz.

3.4. Hydrolysis of difluoromethylcadmium with D_2O

A 56 ml aliquot of a 0.88 M HCF_2CdX reagent (49 mmol) in 50 ml DMF was syringed into a three-neck flask equipped with septum, stir bar and a dry ice/isopropyl alcohol condenser (with nitrogen inlet). Then, 1.5 g (75 mmol) of D_2O was added dropwise to the cadmium reagent solution, and the reaction mixture was stirred for 2 h at RT and then heated at 50 °C for an additional 2 h. The dry ice/isopropyl alcohol condenser was replaced by a flash distillation head equipped with a 100 ml receiving flask (cooled in liquid N_2) and the product distilled under full vacuum at 50 °C. Trap-to-trap distillation gave 1.73 g (65%) of CF_2HD. ^{19}F NMR (CCl_4) (ppm): δ −143 (dt, $^2J_{FD}$ = 7.8 Hz, $^2J_{FH}$ = 50.8 Hz); ^{1}H NMR (CCl_4) (ppm) 5.6 (t); ^{2}D NMR (CCl_4. d_6-acetone ref.): 3.6 ppm (t); MW (expt.): 53.1 g/mol, calculated. 53.02 g/mol; GC–MS, *m/z* (relative intensity): 53 (12.1), 52 (100.0), 51 (43.1), 50 (5.4). IR (6 mm Hg): 2988 (w), 2232 (w), 1367 (w), 1113 (s).

3.5. Iodination of difluoromethylcadmium

A 62 ml aliquot of a 0.81 M HCF_2CdX reagent (50 mmol) in DMF was syringed into a three-neck flask equipped with a septum, stir bar and dry/ice isopropyl condenser (with nitrogen inlet). The solution was cooled in an ice bath and 25.4 g (100 mmol) of I_2 was added in small portions from a solids addition tube. Then the reaction mixture was warmed and stirred at RT for 2 h. The condenser was replaced by a flash distillation head, and the product distilled under full vacuum at 50 °C, trap-to-trap distillation gave 8.5 g (96%) of HCF_2I. ^{19}F NMR (d_6-acetone) (ppm): δ −67.5 (d, $^2J_{FH}$ = 56.2 Hz); ^{1}H NMR (d_6-acetone) (ppm): δ 8.16 (t); MW (expt.): 176.4 g/mol, calculated 177.9 g/mol; GC–MS, *m/z* (relative intensity): 178 (60.6), 159 (21.9), 140 (3.0), 127 (100.0), 51 (33.7). IR (6 mm Hg): 3015 (w), 1251 (m), 1090 (s), 503 (m).

3.6. General procedure for the allylation of difluoromethylcadmium

A 67 ml aliquot of a 0.75 M difluoromethylcadmium reagent (50 mmol) in DMF was syringed into a dry three-neck 100 ml flask equipped with a septum, stir bar and a dry ice/isopropyl alcohol condenser (with a nitrogen inlet). The reaction flask was cooled in an ice water bath and then 6.1 g (50 mmol) of allyl bromide was added dropwise *via* a syringe. The reaction mixture was warmed and stirred for 4 h at RT. The condenser was replaced by a flash distillation head equipped with a 100 ml receiving flask (cooled in liquid N_2). The product was flash distilled under full vacuum, then trap-to-trap distilled to give 3.9 g (85%) of 4,4-difluoro-1-butene, GLPC = 100%. ^{19}F NMR ($CDCl_3$) (ppm): δ −115.3 (dt, $^2J_{FH}$ = 56.5 Hz, $^3J_{FH}$ = 18.3 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) = 6.09 (tt, $^2J_{FH}$ = 56.5 Hz, $^3J_{HH}$ = 4.3 Hz) δ (CH_2) 2.61 (tdddd, $^3J_{FH}$ = 18.3 Hz, $^3J_{HH}$ = 4.3 Hz, $^3J_{HH}$ = 6.9 Hz, $^4J_{HH}$ = 1 Hz, $^4J_{HH}$ = 1 Hz), δ (vinyl *H*) = 5.76 (ddt, $^3J_{HH}$ = 17.3 Hz, $^3J_{HH}$ = 10.3 Hz, $^3J_{HH}$ = 6.9 Hz), δ (vinyl *H*) 5.22 = (ddd, $^3J_{HH}$ = 10.3 Hz, $^2J_{HH}$ = 1.2 Hz, $^4J_{HH}$ = 1 Hz), δ (vinyl *H*) = 5.25 (ddd,

$^3J_{HH}$ = 17.3 Hz, $^2J_{HH}$ = 1.2 Hz, $^4J_{HH}$ = 1 Hz); ^{13}C NMR ($CDCl_3$) (ppm): 116.5 (t, $^1J_{CF}$ = 238.0 Hz), 38.0 (t, $^2J_{CF}$ = 21.2 Hz), 128.9 (t, $^3J_{CF}$ = 6.6 Hz) 120.2 (s). GC–MS, *m/z* (relative intensity): 92 (50.3), 77 (28.2), 73 (50.4), 72 (19.7), 64 (14.9), 57 (13.1), 53 (28.0), 51 (100.0), 50 (22.7), 46 (28.2), 45 (13.3), 41 (19.7). IR (6 mm Hg): 3097 (w), 2977 (m), 1654 (w), 1648 (w), 1435 (w), 1400 (w), 1394 (m), 1389 (w), 1123 (s), 1077 (s), 1004 (m), 929 (m), 875 (w).

3.6.1. Reaction of difluoromethylcadmium with 3-chloro-3,3-dideutero-1-propene

Similarly, a 56 ml aliquot of a 0.88 M difluoromethylcadmium reagent (49 mmol) in DMF was reacted with 2.6 g (33.3 mmol) of 3-chloro-3,3-dideutero-1-propene. After trap-to-trap distillation, 1.7 g (55%) of a 74:26 mixture of 1,1-dideutero-4,4-difluoro-1-butene and 3,3-dideutero-4,4-difluoro-1-butene was obtained. The isomeric ratio was determined by integration of the ^{2}D NMR spectrum of the isolated mixture. NMR: $D_2C{=}CHCH_2CF_2H$: ^{19}F NMR ($CDCl_3$) (ppm): δ −116.1 (dt, $^2J_{FH}$ = 56.7 Hz, $^3J_{FH}$ = 17.8 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) = 5.97 (tt, $^2J_{FH}$ = 56.7 Hz, $^3J_{HH}$ = 4.4 Hz), δ (CH_2) = 2.62 (tdd, $^3J_{FH}$ = 17.8 Hz, $^3J_{HH}$ = 4.4 Hz, $^3J_{HH}$ = 7.0 Hz), δ (vinyl *H*) = 5.79 (dm, $^3J_{HH}$ = 7.0 Hz); ^{2}D NMR ($CDCl_3$) (ppm): δ −2.10 (s), δ −1.94 (d, $^3J_{HD}$ = 0.5 Hz). GC–MS, *m/z* (relative intensity): 94 (100.0), 79 (10.0), 78 (20.1), 77 (36.6), 75 (19.2), 55 (14.5), 51 (30.5), 46 (10.4), 43 (92.9), 41 (26.9), 40 (37.4). NMR: $H_2C{=}CHCD_2CF_2H$: ^{19}F NMR ($CDCl_3$) (ppm): δ −116.3 (dp, $^2J_{FH}$ = 56.6 Hz, $^3J_{FD}$ = 2.6 Hz), ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) = 5.97 (tm, $^2J_{FH}$ = 56.6 Hz), δ (vinyl *H*) = 5.79 (m), δ (=CH_2) = 5.21 (dm, $^3J_{HH}$ = 10.4 Hz), δ (=CH_2) = 5.25 (dd, $^3J_{HH}$ = 17.4 Hz, $^2J_{HH}$ = 1.8 Hz); ^{2}D NMR ($CDCl_3$) (ppm): (δ −4.71 CD_2, tdd, $^3J_{FD}$ = 2.6 Hz), $^3J_{HH}$ = 1 Hz, $^3J_{HH}$ = 1). ^{13}C NMR (mixture) ($CDCl_3$) (ppm): δ (CF_2H) = 117.4 (t, $^1J_{CF}$ = 238.3 Hz), δ (CH_2) = 39.1 (t, $^2J_{CF}$ = 19.2 Hz), δ (vinyl *C*) = 129.5 (t, $^3J_{CF}$ = 6.9 Hz), δ (=CD_2) = 120.5 (p). GC–MS, *m/z* (relative intensity): 94 (4.1), 80 (18.5), 78 (55.3), 45 (11.2), 43 (100.0), 41 (38.1), 40 (49.9).

3.6.2. Reaction of difluoromethylcadmium with 3-chloro-2-methyl-1-propene

A 64 ml aliquot of a 0.78 M difluoromethylcadmium reagent (50 mmol) in DMF was reacted with 4.3 g (48 mmol) of 3-chloro-2-methyl-1-butene. After trap-to-trap distillation, 2.9 g (68%) of 4,4-difluoro-2-methyl-1-butene was obtained, GLPC purity = 95%. ^{19}F NMR ($CDCl_3$) (ppm): δ −113.9 (dt, $^2J_{FH}$ = 56.6 Hz, $^3J_{FH}$ = 17.2 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) = 5.86 (tt, $^2J_{FH}$ = 56.6 Hz, $^3J_{HH}$ = 4.7 Hz), δ (CH_2) = 2.54 (td, $^3J_{FH}$ = 17.2 Hz, $^3J_{HH}$ = 4.7 Hz), δ (CH_3) = 1.80 (s), δ (=CH_2), 5.88 (s), 5.95 (s). ^{13}C NMR (neat) (ppm): 117.4 (t, $^1J_{CF}$ = 239.8 Hz), 43.1 (t, $^2J_{CF}$ = 21.4 Hz), 138.4 (t, $^3J_{CF}$ = 5.7 Hz), 23.1 (s), 115.6 (s). GC–MS, *m/z* (relative intensity): 106 (9.3), 91 (4.0), 85 (4.1), 66 (3.5), 64 (11.9), 51 (100.0), 46 (14.4). IR (6 mm Hg): 3094 (w), 2980 (m), 2935 (w), 1659 (w), 1450 (w), 1392 (m), 1214 (w), 1123 (s), 1079 (s), 1047 (w), 903 (m).

3.6.3. Reaction of difluoromethylcadmium with 3-chloro-1-butene

A 86 ml aliquot of a 0.58 M difluoromethylcadmium reagent (50 mmol) in DMF was reacted with 3.6 g (40 mmol) of 3-chloro-1-butene. The reaction mixture was stirred at RT for 48 h, then flash distilled, an equal volume of ice water added to the flash distillate, the organic layer separated and washed with 2× 100 ml of water and dried over 4 Å molecular sieves. The crude product was distilled (bp 45–47 °C) to give 1.9 g (45%) of a mixture that contained 92.4% (*E*)-5,5-difluoro-2-pentene (*E*/*Z* = 87:13) and 6.9% 4,4-difluoro-3-methyl-1-butene (as determined by GLPC analysis). NMR (*E*-$CH_3CH{=}CHCH_2CF_2H$): ^{19}F NMR (neat) (ppm): δ −116.3 (dt, $^2J_{FH}$ = 56.9 Hz, $^3J_{FH}$ = 17.4 Hz), ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) = 5.78 (tt, $^2J_{HH}$ = 56.9 Hz, $^3J_{HH}$ = 4.6 Hz), δ (CH_2) 2.51 (tddd, $^3J_{FH}$ = 17.4 Hz, $^3J_{HH}$ = 7.4 Hz, $^3J_{HH}$ = 4.6 Hz, $^4J_{HH}$ = 1.2 Hz), δ 5.38 (=CH, dtq, $^3J_{HH}$ = 15.9 Hz, $^3J_{HH}$ = 7.4 Hz, $^4J_{HH}$ = 1.7 Hz), δ 5.64 (=CH, dt, $^3J_{HH}$ = 15.9 Hz, $^4J_{HH}$ = 1.2 Hz), δ 1.70 (CH_3, dd, $^3J_{HH}$ = 6.4 Hz, $^4J_{HH}$ = 1.7 Hz); ^{13}C NMR (neat) (ppm): 117.5 (t, $^1J_{CF}$ = 239.1 Hz), 38.5 (t, $^2J_{CF}$ = 21.8 Hz), 121.9 (t, $^3J_{CF}$ = 6.6 Hz), 131.7 (s), 18.1 (s). NMR ($H_2C{=}CHCH(CF_2H)CH_3$): ^{19}F NMR ($CDCl_3$) (ppm): δ^a = −123.9 (ddd), δ −122.2 (ddd (AB), $^2J_{FF}$ = 276.6 Hz, $^2J_{FH}$ = 56.8 Hz, $^3J_{FH}$ = 14.6 Hz), ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): d 5.62 (CF_2H, dt, $^2J_{FH}$ = 56.8 Hz, $^3J_{HH}$ = 14.6 Hz), δ 2.56 (–$CH(CH_3)CF_2H$, m), δ 1.12 (CH_3, d, $^3J_{HH}$ = 7.0 Hz), δ 5.78 (=CH, ddd, $^3J_{HH}$ = 15.5 Hz, $^3J_{HH}$ = 10.2 Hz, $^3J_{HH}$ = 7.3 Hz), δ 5.18 (=CH, dd, $^3J_{HH}$ = 10.2 Hz, $^2J_{HH}$ = 1.1 Hz), δ 5.20 (=CH, dd, $^3J_{HH}$ = 15.5 Hz, $^2J_{HH}$ = 1.1 Hz), ^{13}C NMR (neat) (ppm): 119.0 (t, $^1J_{CF}$ = 242.6 Hz), 42.8 (t, $^2J_{CF}$ = 20.2 Hz), 12.5 (t, $^3J_{CF}$ = 4.5 Hz), 136.0 (t, $^3J_{CF}$ = 5.5 Hz), δ 118.0 (s).

3.6.4. Reaction of difluoromethylcadmium with (E)-1-chloro-2-butene

A 74 ml aliquot of a 0.68 M difluoromethylcadmium reagent (50 mmol) in DMF was reacted with 4.4 g (49 mmol) of (*E*)-1-chloro-2-butene. The reaction mixture was stirred at RT for 24 h and worked-up as described previously. After trap-to-trap distillation 3.2 g (62%) of a 63:37 mixture (determined by GLPC) of 4,4-difluoro-3-methyl-1-butene and (*E*)-5,5-difluoro-2-pentene was obtained, GLPC purity = 92%. Spectroscopic data was identical to the data described in Section 3.6.3 for 3-chloro-1-butene.

3.6.5. Reaction of difluoromethylcadmium with 1-chloro-3-methyl-2-butene

An 82 ml aliquot of a 0.61 M difluoromethylcadmium reagent (50 mmol) in DMF was reacted with 3.7 g (35 mmol) of 1-chloro-3-methyl-2-butene at 0 °C. The reaction mixture was stirred overnight at RT, then flash distilled at 80 °C. The distillate was washed (in a separatory funnel) with an equal volume of ice water; the organic layer separated and washed with water (2× 100 ml), dried over 4 Å molecular sieves, and distilled (by 88–90 °C/atm. press.) to give 2.9 g (68%) of a mixture which contained 8.3% $H_2C{=}C(CH_3)CH{=}CH_2$, 3.1% 4,4-difluoro-3-3-dimethyl-1-butene and 88.6% 5,5-difluoro-2-methyl-2-pentene (as determined by GLPC analysis). NMR

($CF_2HCH_2CH{=}C(CH_3)_2$: ^{19}F NMR ($CDCl_3$) (ppm): δ −115.9 (dt, $^2J_{FH}$ = 57.0 Hz, $^3J_{FH}$ = 17.6 Hz); ^1H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) = 5.72 (tt, $^2J_{FH}$ = 57.0 Hz, $^3J_{HH}$ = 4.6 Hz), δ (CH_2) = 2.53 (tdd, $^3J_{FH}$ = 17.8 Hz, $^3J_{HH}$ = 7.4 Hz, $^3J_{HH}$ = 4.6 Hz), δ (=C*H*) = 5.12 (tqq, $^3J_{HH}$ = 7.4 Hz, $^4J_{HH}$ = 1 Hz, $^4J_{HH}$ = 1 Hz), δ (–CH_3) = 1.74 (d, $^4J_{HH}$ = 1 Hz), δ (–CH_3) = 1.65 (d, $^4J_{HH}$ = 1 Hz); ^{13}C NMR (neat) (ppm): 116.8 (t, $^1J_{CF}$ = 239.9 Hz), 33.6 (t, $^2J_{CF}$ = 21.8 Hz), 113.9 (t, $^3J_{CF}$ = 6.4 Hz), 137.4 (s), 35.8 (s) 18.0 (s). GC–MS [$(CH_3)_2C{=}CHCH_2CF_2H$] *m/z* (relative intensity): 120 (27.1), 69 (100.0), 59 (14.7), 53 (17.6), 51 (31.3), 41 (93.7). GC–MS, *m/z* ($CF_2HC(CH_3)_2CH{=}CH_2$) (relative intensity): 120 (8.9), 84 (11.7), 77 (19.4), 69 (100.0), 67 (13.5), 65 (14.3), 59 (12.5), 53 (23.2), 51 (31.4), 49 (22.4), 41 (69.1). GC–MS ($H_2C{=}C(CH_3)CH{=}CH_2$): *m/z* (relative intensity): 68 (65.4), 67 (100.0).

3.6.6. Reaction of difluoromethylcadmium with 3-chloro-3-methyl-1-butene

A 80 ml aliquot of a 0.57 M difluoromethylcadmium reagent (46 mmol) in DMF was reacted with 4.7 (45 mmol) of 3-chloro-3-methyl-1-butene. The reaction mixture was stirred for several hours at RT, flash distilled, washed with water as described in Section 3.6.3 and the crude product distilled (bp 88–90 °C/atm. press.) to give 3.4 g (63%) of a mixture that contained 4.8% ($CH_2{=}C(CH_3)CH{=}CH_2$), 14.7% 4,4-difluoro-3,3-dimethyl-1-butene and 77.9% 5,5-difluoro-2-methyl-2-pentene. Spectroscopic data were identical to the compounds described in Section 3.6.5.

3.6.7. Reaction of difluoromethylcadmium with (E)-3-bromo-1-phenyl-1-propene

A 72 ml aliquot of a 0.54 difluoromethylcadmium reagent (39 mmol) in DMF was reacted with 7.7 g (38.8 mmol) of (*E*)-3-bromo-1-phenyl-1-propene. The reaction mixture was stirred overnight at RT, steam distilled, the organic layer separated, dried over 4 Å molecular sieves to give 5.7 g (87%) of a 47.6:52.3 mixture of 4,4-difluoro-3-phenyl-1-butene and (*E*)-4,4-difluoro-1-phenyl-1-butene (as determined by GLPC). The regioisomers were separated by spinning band distillation (1 ft column) to give two major fractions with GLPC purity 98%: bp 81–82 °C/0.5 mm (4,4-difluoro-3-phenyl-1-butene) and bp 101–103 °C/0.5 mm [(*E*)-4,4-difluoro-1-phenyl-1-butene]. NMR: (*E*)-4,4-difluoro-1-phenyl-1-butene): ^{19}F ($CDCl_3$) (ppm): δ −116.1 (dt, $^2J_{FH}$ = 56.6 Hz, $^3J_{FH}$ = 17.2 Hz); ^1H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) = 5.84 (tt, $^2J_{FH}$ = 56.6 Hz, $^3J_{HH}$ = 4.5 Hz), δ (CH_2) = 2.73 (tddd, $^3J_{FH}$ = 17.2 Hz, $^3J_{HH}$ = 7.3 Hz, $^3J_{HH}$ = 4.5 Hz, $^4J_{HH}$ = 1.4 Hz), δ 6.13 (=C*H*, dt, $^3J_{HH}$ = 15.9 Hz, $^3J_{HH}$ = 7.3 Hz), δ 6.54 (=C*H*, d, $^3J_{HH}$ = 15.9 Hz), δ 7.29 (m). ^{13}C NMR (neat) (ppm): 116.8 (t, $^1J_{CF}$ = 240.0 Hz), 38.1 (t, $^2J_{CF}$ = 21.9 Hz), 119.8 (t, $^3J_{CF}$ = 6.7 Hz), 135.5 (s), 137.2 (s), 126.7 (s), 128.9 (s), 128.0 (s). GC–MS, *m/z* (relative intensity): 168 (39.3), 117 (100.0), 116 (11.2), 115 (54.5), 91 (17.8). IR (CCl_4): 3085 (w), 3061 (w), 3029 (w), 2917 (m), 1495 (m), 1450 (m), 1427 (m), 1397 (m), 1382 (m), 1215 (m), 1117 (s), 1055 (s), 1025 (s), 968 (s), 926 (w), 887 (m). NMR: (4,4-difluoro-3-phenyl-1-butene): ^{19}F NMR ($CDCl_3$) (ppm): δ^a −121.5 (ddd), δ^b = −119.3 (ddd, $^2J_{FF}$ = 277.8 Hz, $^2J_{FH}$ = 56.3 Hz, $^3J_{FH}$ = 15.5 Hz). (AB), ^1H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) 5.92 (td, $^2J_{FH}$ = 56.3 Hz, $^3J_{HH}$ = 15.5 Hz), δ (C*H*) 3.72 (m), δ (aromatic H) 7.29 (m), δ (=C*H*) 6.08 (ddd, $^3J_{HH}$ = 17.3 Hz, $^3J_{HH}$ = 10.4 Hz, $^3J_{HH}$ = 7.5 Hz), δ (=C*H*) 5.30 (d, $^3J_{HH}$ = 10.4 Hz), δ (=C*H*) 5.20 (d, $^3J_{HH}$ = 17.2 Hz); ^{13}C NMR (neat) (ppm): 117.4 (t, $^1J_{CF}$ = 244.4 Hz), 54.2 (t, $^2J_{CF}$ = 20.5 Hz), 133.4 (t, $^3J_{CF}$ = 5.0 Hz), 119.5 (s), 136.6 (s), 129.0 (s), 129.2 (s), 127.9 (s). GC–MS, *m/z* (relative intensity): 168 (10.8), 117 (100.0), 116 (11.9), 115 (60.6), 91 (24.1). IR (CCl_4): 3089 (m), 3066 (m), 3034 (m), 2972 (m), 1642 (m), 1603 (m), 1495 (m), 1455 (m), 1377 (m), 1126 (s), 1077 (s), 1058 (s), 991 (m), 930 (m).

3.6.8. Reaction of difluoromethylcadmium with (E)-3-chloro-1-phenyl-1-propene

A 75 ml aliquot of a 0.80 M difluoromethylcadmium reagent (60 mmol) in DMF was reacted with 7.6 g (50 mmol) of (*E*)-3-chloro-1-phenyl-1-propene. The reaction mixture was stirred for 53 h at RT, steam distilled and worked up as described for (*E*)-3-bromo-1-phenyl-1-propene to give 5.2 g (62%) of a 56:44 mixture of 4,4-difluoro-3-phenyl-1-butene and (*E*)-4,4-difluoro-1-phenyl-1-butene (as determined by GLPC analysis). Spectroscopic data was identical to the isomers prepared from (*E*)-3-bromo-1-phenyl-1-propene.

3.6.9. Reaction of difluoromethylcadmium with propargyl chloride

Via the general procedure utilized for allyl halides, a 66 ml aliquot of a 0.76 M difluoromethylcadmium reagent (50 mmol) in DMF was reacted with 3.7 g (49 mmol) of propargyl chloride. The reaction mixture was stirred at RT for 3 days and heated at 50 °C for an additional 7 days. After flash distillation and trap-to-trap distillation, 1.8 g (41%) of a mixture, which contained 80% 4,4-difluoro-1,2-butadiene, 4.3% 4,4-difluoro-1-butyne, 11% unreacted propargyl chloride and 5% of two other impurities was obtained. NMR ($CF_2HCH{=}^{\bullet}{=}CH_2$): ^{19}F NMR ($CDCl_3$) (ppm): δ −107.9 (ddt, $^2J_{FH}$ = 56.2 Hz, $^3J_{DH}$ = 7.3 Hz, $^5J_{FH}$ = 7.6 Hz); ^1H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) = 6.14 (tdt, $^2J_{FH}$ = 56.2 Hz, $^3J_{HH}$ = 6.2 Hz, $^5J_{HH}$ = 1 Hz), δ ($CF_2HCH{=}$) = 5.41 (ttd, J_{FH} = 7.3 Hz, $^3J_{HH}$ = 6.2 Hz, $^4J_{HH}$ = 6.8 Hz), δ (=CH_2) 5.11 (tdd, $^5J_{FH}$ = 7.6 Hz, $^4J_{HH}$ = 6.8 Hz, $^3J_{HH}$ = 1 Hz); ^{13}C NMR (neat) (ppm): 115.3 (t, $^1J_{CF}$ = 236.1 Hz), 88.4 (t, $^2J_{CF}$ = 29.0 Hz), 211.1 (t, $^3J_{CF}$ = 12.3 Hz), 79.7 (s). GC–MS, *m/z* (relative intensity): 90 (44.4), 71 (25.9), 70 (15.5), 51 (100.0), 50 (26.9).

3.6.10. Reaction of difluoromethylcadmium with 3-tosyl-1-butyne

A 0.5 ml aliquot of a 0.84 M difluoromethylcadmium reagent (0.42 mmol) was added to a 5 mm NMR tube, followed by addition of 0.094 g (0.42 mmol) of 3-tosyl-1-butyne and 10 μl of $C_6H_5CF_3$. After 7 h at RT, an 87% yield of 1,1-difluoro-2,3-pentadiene was determined by ^{19}F NMR analysis of the reaction mixture. See Section 3.7.9 for NMR data.

3.6.11. Reaction of difluoromethylcadmium with 3-chloro-1-butyne

A 0.5 ml aliquot of a 0.76 M difluoromethylcadmium reagent (0.38 mmol) in DMF was reacted with 0.034 g (0.38 mmol) of 3-chloro-1-butyne in an NMR tube (as described above) for 2 days to give an 84% ^{19}F NMR yield of 1,1-difluoro-2,3-pentadiene. See Section 3.7.9 for NMR data.

3.6.12. Reaction of difluoromethylcadmium with 3-bromo-3-methyl-1-butyne

An 86 ml aliquot of a 0.70 M difluoromethylcadmium reagent (60 mmol) in DMF was reacted with 10.0 g (60 mmol) of 3-bromo-3-methyl-1-butyne at 0 °C in a three-neck flask fitted with a septum, stir bar and a nitrogen tee. The reaction mixture was stirred overnight at RT. After flash distillation the distillate was washed with an equal volume of ice water, the organic layer separated and washed with 2× 100 ml of water and dried over 4 Å molecular sieves. Distillation gave 3.80 g (64%), bp 77–79 °C, of 1,1-difluoro-4-methyl-2,3-pentadiene, GLPC purity = 100%. ^{19}F NMR ($CDCl_3$) (ppm): δ −107.4 (dd, $^2J_{FH}$ = 56.6 Hz, $^3J_{FH}$ = 6.4 Hz); ^{1}H NMR (360 Hz) ($CDCl_3$) (ppm): δ (CF_2H) 6.02 (td, $^2J_{FH}$ = 56.6 Hz, $^3J_{HH}$ = 6.3 Hz), δ (–C*H*=) 5.21 (tdsept, $^3J_{FH}$ = 6.4 Hz, $^3J_{HH}$ = 6.3 Hz, $^3J_{HH}$ = 3.0 Hz), δ (=C(CH_3)$_2$) 1.75 (d, $^5J_{HH}$ = 3.0 Hz); ^{13}C NMR (neat) (ppm): 115.2 (t, $^1J_{CF}$ = 236.2 Hz), 86.6 (t, $^2J_{CF}$ = 28.9 Hz), 204.4 (t, $^3J_{CF}$ = 12.4 Hz), 101.2 (s), 19.3 (s). GC–MS, *m/z* (relative intensity): 118 (51.0), 103 (17.8), 97 (12.1), 83 (18.9), 79 (11.8), 77 (32.4), 67 (100.0), 65 (27.3), 57 (12.0), 51 (47.0), 50 (14.2), 41 (55.9). IR (CCl_4): 2989 (m), 2948 (m), 2916 (m), 2859 (w), 1978 (m), 1449 (m), 1421 (m), 1367 (m), 1329 (m), 1121 (s), 1055 (s), 1021 (s).

3.6.13. Reaction of difluoromethylcadmium with 1-bromo-2-butyne

A 94 ml aliquot of a 0.64 M difluoromethylcadmium reagent (60 mmol) in DMF was reacted with 6.7 g (50 mmol) of 1-bromo-2-butyne as described above for 3-bromo-3-methyl-1-butyne. After stirring overnight at RT, the reaction mixture was worked-up as described in the previous experiment to give 3.6 g (69%, bp 53–56 °C, of an isomeric mixture (77.6:22.4) of 4,4-difluoro-3-methyl-1,2-butadiene and 5,5-difluoro-2-pentyne (as determined by GLPC analysis). NMR: ($CF_2HC(CH_3)$=C=CH_2): ^{19}F NMR ($CDCl_3$) (ppm): δ = −114.3 (dt, $^2J_{FH}$ = 56.5 Hz, $^5J_{FH}$ = 6.8 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) 6.09 (t, $^2J_{FH}$ = 56.5 Hz), δ (–CH_3) 1.77 (td, $^5J_{HH}$ = 3.2 Hz, $^4J_{HH}$ < 1 Hz), δ (=CH_2) 4.97 (qt, $^3J_{HH}$ = 3.2 Hz, $^5J_{FH}$ = 6.8 Hz); ^{13}C NMR (neat) (ppm): 116.1 (t, $^1J_{CF}$ = 239.3 Hz), 95.9 (t, $^2J_{CF}$ = 26.2 Hz), 9.9 (t, $^3J_{CF}$ = 9.8 Hz), 208.4 (s), 77.7 (s). GC–MS, *m/z* (relative intensity): 104 (100.0), 103 (16.8), 83 (14.7), 77 (11.6), 57 (13.7), 53 (57.9), 51 (48.4), 50 (21.0). IR (CCl_4) (mixture of isomers): 2986 (w), 2935 (w), 2865 (w), 1989 (w), 1962 (w), 1685 (w), 1463 (w), 1441 (w), 1385 (m), 1367 (w), 1228 (w), 1079 (s), 1063 (m), 1040 (m), 1026 (vs), 993 (w), 861 (m). NMR: (CF_2HCH_2C≡CCH_3): ^{19}F NMR ($CDCl_3$) (ppm): δ −115.7 (dt, $^2J_{FH}$ = 56.4 Hz, $^3J_{FH}$ = 15.6 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) 5.83 (tt, $^2J_{FH}$ = 56.4 Hz, $^3J_{HH}$ = 4.5 Hz), δ (CH_2) 2.69 (tdq, $^3J_{FH}$ = 15.6 Hz, $^3J_{HH}$ = 4.5 Hz, $^3J_{HH}$ = 2.6 Hz), δ (CH_3) 1.80 (t, $^5J_{HH}$ = 2.6 Hz); ^{13}C NMR (neat) (ppm): 115.1 (t, $^1J_{CF}$ = 241.0 Hz), 25.6 (t, $^2J_{CF}$ = 26.5 Hz), 69.9 (t, $^3J_{CF}$ = 9.7 Hz), 79.3 (s), 14.9 (s). GC–MS, *m/z* (relative intensity): 104 (88.8), 103 (10.6), 84 (14.2), 83 (18.3), 77 (15.7), 65 (11.7), 59 (10.4), 57 (14.3), 53 (100.0), 52 (18.7), 51 (54.3), 50 (23.5), 49 (16.1).

3.6.14. Reaction of difluoromethylcadmium with 1-chloro-1-ethynylcyclohexane

A 70 ml aliquot of a 0.71 M difluoromethylcadmium reagent (50 mmol) in DMF was reacted with 5.7 g (40 mmol) of 1-chloro-1-ethynylcyclohexane as described above for 3-bromo-3-methyl-1-butyne. Distillation (bp 61–73 °C/20 mm) gave three fractions (combined wt. of 3.4 g) which contained 52%, 71% and 94% of 4,4-difluoro-1-pentamethylene-1,2-propadiene and 48%, 29% and 6% of 1-ethynyl-1-cyclohexene, respectively. GC–MS, *m/z* (relative intensity) for (CH_2)$_5$C=C=$CHCF_2H$: 158(100.0)). GC–MS, *m/z* (relative intensity) for c-C_6H_9C≡CH: 106 (62.9), 105 (29.5), 91 (100). See Section 3.7.12 for NMR data of 4,4-difluoro-1-pentamethylene-1,2-propadiene.

3.6.15. Reaction of difluoromethylcadmium with 1,4-dichloro-2-butyne

A 0.5 ml aliquot of a 0.67 M difluoromethylcadmium reagent (0.34 mmol) in DMF was reacted with 0.021 g (0.17 mmol) of 1,4-dichloro-2-butyne in a 5 mm NMR tube. After 70 h at RT, a 52% yield of bis-(2,3-difluoromethyl)-1,3-butadiene was determined by ^{19}F NMR of the reaction mixture. See Section 3.7.13 for NMR data.

3.7. In situ preparation of the difluoromethylcopper reagent

A 50 ml aliquot of the 1.13 M difluoromethylcadmium reagent (56.5 mmol) in DMF was added to a 100 ml three-neck flask equipped with septum, stir bar and dry ice/isopropyl alcohol condenser (with nitrogen inlet). The solution was cooled to −60 °C and then 5.6 g (56.6 mmol) of CuCl was added in one portion. The solution was slowly warmed to RT over 4 h. 1,1,2,2-Tetrafluoroethane and *cis*-difluoroethene were obtained in a 77:23 ratio, as determined by ^{19}F NMR analysis of the reaction mixture. Flash distillation followed by trap-to-trap distillation gave 2.85 g of a mixture which contained CF_2HCF_2H and *cis*-CFH=CFH. GC–MS, *m/z* (relative intensity) of the mixture: 102 (1.5), 101 (4.4), 83 (66.1), 82 (7.4), 64 (36.9), 63 (11.9), 51 (100.0), 45 (39.9), 44 (29.6). The chemical shift and coupling constants reported by Stone for *cis*-CFH=CFH are consistent with those observed in our spectrum [53], and the ^{19}F NMR spectrum reported by Ellerman et al. match our observed spectral data for CF_2HCF_2H [54].

In a separate NMR tube experiment, the difluoromethylcadmium reagent in DMF was reacted with CuBr or CuCl at −55 °C to afford HCF_2Cu^a in >90% yield, δ −114.6 ppm (d, $^2J_{FH}$ = 44.0 Hz). When the temperature of the NMR tube was increased, a second HCF_2Cu^b reagent appeared in the ^{19}F NMR spectrum at δ −116.4 (d, $^2J_{HF}$ = 51.3 Hz). At temperatures

>-30 °C the copper reagents began to decompose rapidly to CF_2HCF_2H and *cis*-CFH=CFH. After 5 h at RT, no CF_2HCu[a] remained and <13% of CF_2HCu[b] remained.

3.7.1. Reaction of difluoromethylcopper with 3-chloro-3,3-dideutero-1-propene

A 42 ml aliquot of a 0.92 M difluoromethylcadmium reagent (39 mmol) in DMF was added into a three-neck 100 ml flask equipped with a septum stir bar and nitrogen tee. The solution was cooled to −50 °C and then 5.6 g (39 mmol) of CuBr added. After 15 min, 2.9 g (33 mmol) of 3-chloro-3,3-dideutero-1-propene was added dropwise from a syringe. The reaction mixture was slowly warmed to RT over 4 h. Flash distillation of the reaction mixture followed by trap-to-trap distillation of the crude distillate gave 1.8 g (63%) of a 90:10 mixture of CD_2=$CHCH_2CF_2H$ and CH_2=$CHCD_2CF_2H$, respectively, as determined by ^{19}F NMR analysis. The ^{19}F, ^{1}H, ^{2}D and ^{13}C NMR data were identical to the data reported for the reaction of HCF_2CdX with CH_2=$CHCD_2Cl$.

3.7.2. Reaction of difluoromethylcopper with 3-chloro-1-butene

Similar to the reaction with CH_2=$CHCD_2Cl$, a 62 ml aliquot of a 0.89 M difluoromethylcadmium reagent (55 mmol) in DMF, 7.9 g (55 mmol) of CuBr, and 4.5 g (50 mmol) of 3-chloro-1-butene were reacted at −50 °C. The reaction mixture was slowly warmed to RT over 5 h. Flash distillation, followed by addition of an equivalent volume of ice water, separation of the organic layer, washing with 2× 100 ml of water and drying over a 4 Å molecular sieves, and fractional distillation (bp 68–70 °C) gave 3.9 g (74%) of (*E*)-5,5-difluoro-2-pentene, GLPC purity = 100%. The ^{19}F, ^{1}H and ^{13}C NMR data were identical to the data obtained from the reaction of HCF_2CdX with $CH_3CH(Cl)CH$=CH_2. GC–MS, *m/z* (relative intensity): 106 (100.0), 85 (8.6), 77 (8.6), 59 (9.5), 55 (39.5), 51 (11.2). IR (CCl_4): 3031 (w), 2972 (m), 2945 (m), 2920 (w), 2887 (w), 2858 (w), 1451 (w), 1437 (w), 1428 (w), 1391 (w), 1364 (w), 1218 (w), 1119 (vs), 1057 (vs), 1031 (m), 1012 (m), 969 (m), 913 (w), 875 (w), 855 (w).

3.7.3. Reaction of difluoromethylcopper with (E)-1-chloro-2-butene

A 58 ml aliquot of a 0.89 M difluoromethylcadmium reagent (52 mmol) in DMF, 7.6 g (50 mmol) CuBr, and 4.5 g (50 mol) of (*E*)-1-chloro-2-butene were reacted at −50 °C. The reaction mixture was warmed to RT over 5 h. Isolation and distillation (as described above) gave 3.5 g (68%) (bp 68–70 °C) of a 46:54 isomeric mixture of 4,4-difluoro-3-methyl-1-butene and (*E*)-5,5-difluoro-2-pentene (as determined by GLPC analysis). The ^{19}F, ^{1}H, and ^{13}C NMR data were identical to the compounds formed from the reaction of HCF_2CdX with 3-chloro-1-butene (as described above).

3.7.4. Reaction of difluoromethylcopper with 3-chloro-3-methyl-1-butene

A 72 ml aliquot of a 0.83 M difluoromethylcadmium reagent (60 mmol) in DMF, 8.6 g (60 mmol) CuBr and 5.2 g (50 mmol) of 3-chloro-3-methyl-1-butene were reacted at −50 °C (as described previously). The reaction mixture was slowly warmed to RT over 5 h. Isolation and distillation (as described above) gave 4.9 g (76%) (bp 88–90 °C) of 5,5-difluoro-2-methyl-2-pentene, GLPC purity = 100%. ^{19}F, ^{1}H and ^{13}C NMR data were identical to the product formed from the reaction of HCF_2CdX with $(CH_3)_2C(Cl)CH$=CH_2.

3.7.5. Reaction of difluoromethylcopper with 1-chloro-3-methyl-2-butene

A 77 ml aliquot of a 0.88 M difluoromethylcadmium reagent (68 mmol) in DMF, 9.9 g (68 mmol) CuBr, and 6.3 g (60 mmol) of 1-chloro-3-methyl-2-butene were reacted at −50 °C (as described previously). The reaction mixture was slowly warmed to RT over 5 h. Isolation and distillation (as described previously) gave 5.7 g (80%) (bp 88–90 °C) of 5,5-difluoro-2-methyl-2-pentene, GLPC purity = 100%. ^{19}F, ^{1}H, ^{13}C NMR data were identical to the product from the reaction of HCF_2CdX with 1-chloro-3-methyl-2-butene.

3.7.6. Reaction of difluoromethylcopper with (E)-3-chloro-1-phenyl-1-propene

A 58 ml aliquot of a 0.89 M difluoromethyl cadmium reagent (52 mmol) in DMF, 7.6 g (52 mmol) CuBr, and 7.6 g (50 mmol) of (*E*)-3-chloro-1-phenyl-1-propene were reacted at −50 °C (as described previously). The reaction mixture was slowly warmed to RT over 5 h, then steam distilled. The organic layer of the steam distillate was separated, dried over 4 Å molecular sieves and distilled to give 7.2 g (86%) (bp 100–103 °C/0.5 mm) of (*E*)-4,4-difluoro-1-phenyl-1-butene, GLPC purity = 100%. The ^{19}F, ^{1}H, ^{13}C NMR data were identical to the product from the reaction of HCF_2CdX with (*E*)-3-bromo-1-phenyl-1-propene.

3.7.7. Reaction of difluoromethylcopper with 3-chloro-1-cyclohexene

A 53 ml aliquot of a 0.84 M difluoromethyl cadmium reagent (45 mmol) in DMF, 6.5 g (45 mmol) CuBr, and 2.8 g (24 mmol) of 3-chloro-1-cyclohexene were reacted at −50 °C. The reaction mixture was slowly warmed to RT over 5 h. Flash distillation, washing of the flash distillate with water (as described previously), drying over 4 Å molecular sieves and distillation gave 2.0 g (62%) (bp 51–53 °C/53 mm) of 3-(difluoromethyl-1-cyclohexene), GLPC purity = 95%. ^{19}F NMR ($CDCl_3$) (ppm): δ −121.4 (ddd, $^{2}J_{FF}$ = 277.5 Hz, $^{2}J_{FH}$ = 57.0 Hz, $^{3}J_{FH}$ = 13.9 Hz), δ −122.9 (AB system); ^{1}H NMR (360 M) ($CDCl_3$) (ppm) δ (CF_2H) 5.55 (td, $^{2}J_{FH}$ = 57.0 Hz, $^{3}J_{HH}$ = 13.9 Hz), 2.55 (m), 5.59 (m), 5.82 (m), 2.03 (m), 1.81 (m), 1.53 (m); ^{13}C NMR (neat) (ppm): 118.6 (t, $^{1}J_{CF}$ = 242.8 Hz), 40.1 (t, $^{2}J_{CF}$ = 19.6 Hz), 122.4 (t, $^{3}J_{CF}$ = 6.0 Hz), 131.4 (s), 24.9 (s), 20.5 (s), 22.3 (t, $^{3}J_{CF}$ = 4.5 Hz). GC–MS, *m/z* (relative intensity): 132 (16.7), 81 (100.0), 79 (42.7), 77 (14.4), 51 (11.6). IR (CCl_4): 3035 (w), 2953 (m), 2944 (m), 2938 (m), 1687 (vs), 1451 (w), 1435 (w), 1388 (w), 1130 (m), 1086 (m) 1076 (s), 1050 (s), 1029 (w), 987 (w), 887 (w).

3.7.8. Reaction of difluoromethylcopper with 3-bromo-3,3-difluoro-1-propene

A 76 ml aliquot of a 0.79 difluoromethylcadmium reagent (60 mmol) in DMF, 8.6 g (60 mmol) CuBr and 8.6 (55 mmol) of 3-bromo-3,3-difluoro-1-propene were reacted at −50 °C (as described previously). The reaction mixture was slowly warmed to RT over 5 h. Flash distillation followed by trap-to-trap distillation gave 6.09 g (87%), GLPC purity = 100%, of 1,1,4,4-tetrafluoro-1-butene. Distillation gave 5.2 g (74%) (bp 38–39 °C). ^{19}F NMR ($CDCl_3$) (ppm): $\delta = -117.3$ (dtdd, $^2J_{FH}$ =56.4 Hz, $^3J_{FH}$ = 17.0 Hz, $^5J_{FF}$ = 1.8 Hz, $^5J_{FF}$ = 1.8 Hz), δ −85.2 (dm, $^3J_{FH}$ = 38.5 Hz), δ −88.5 (ddtt, $^5J_{FF}$ = 1.8 Hz, $^4J_{FH}$ = 1.8 Hz, $^3J_{FH}$ = 24.2 Hz, $^3J_{FH}$ = 38.5 Hz), ^{1}H NMR ($CDCl_3$) (ppm): δ (CF_2H) 5.79 (tt, $^2J_{FH}$ = 56.4 Hz, $^3J_{HH}$ = 4.2 Hz), δ (–C*H*$_2$) 2.53 (tm, $^3J_{FH}$ = 17.0 Hz), δ (–C*H*=) 4.23 (ddt, $^3J_{FH}$ = 38.5 Hz, $^3J_{FH}$ = 24.2 Hz, $^3J_{HH}$ = 8.1 Hz). ^{13}C NMR (neat) (ppm): 115.0 (t, $^1J_{CF}$ = 239.1 Hz), 27.2 (td, $^2J_{CF}$ = 23.7 Hz, $^3J_{CF}$ = 4.6 Hz), 69.1 (ddt, $^2J_{CF}$ = 28.5 Hz, $^2J_{CF}$ = 20.1 Hz, $^3J_{CF}$ = 7.2 Hz), 157.7 (t, $^2J_{CF}$ = 286.8 Hz). GC–MS, *m/z* (relative intensity): 128 (38.5), 89 (13.8), 77 (100.0). 51 (25.5). IR (CCl_4): 2979 (w), 1755 (w), 1398 (w) 1341 (w), 1311 (w), 1291 (m), 1254 (m), 1201 (m), 1128 (m), 1123 (m), 1069 (m), 1049 (m), 1033 (w), 917 (w).

3.7.9. Reaction of difluoromethylcopper with 3-tosyl-1-butyne

A 65 ml aliquot of a 0.85 M difluoromethylcadmium reagent (55 mmol) in DMF was added to a three-neck 100 ml flask equipped with a septum, stir bar and nitrogen tee. The solution was cooled to −50 °C, then 7.9 g (55 mmol) of CuBr was added. After 15 min, 11.2 g (50 mmol) of 3-tosyl-1-butyne was added in one portion. The reaction mixture was slowly warmed to RT over 5 h. Flash distillation, followed by washing of the flash distillate with an equal volume of ice water, separation of the organic layer, followed by washing with 2× 100 ml of water, drying over 4 Å molecular sieves, and distillation gave 2.8 g (53%) of 1,1-difluoro-2,3-pentadiene. ^{19}F NMR ($CDCl_3$) (ppm): δ −107.6 (ddd, $^2J_{FH}$ = 56.5 Hz, $^3J_{FH}$ = 6.4 Hz, $^5J_{FH}$ = 7.2 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) 6.07 (tdd, $^2J_{FH}$ = 56.5 Hz, $^3J_{HH}$ = 6.2 Hz, $^5J_{HH}$ = < 1 Hz), δ (–C*H*=) 5.32 (tddq, $^3J_{FH}$ = 6.4 Hz, $^3J_{HH}$ = 6.2 Hz, $^4J_{HH}$ = 6.8 Hz, $^5J_{HH}$ = 3.2 Hz), δ (=C*H*CH$_3$) (qtdd, $^3J_{HH}$ = 7.3 Hz, $^5J_{FH}$ = 7.2 Hz, $^4J_{HH}$ = 6.8 Hz, $^5J_{HH}$ = < 1), δ (–C*H*$_3$) 1.74 (dd, $^3J_{HH}$ = 7.3 Hz, $^3J_{HH}$ = 3.2 Hz); ^{13}C NMR (neat) (ppm): 115.0 (t, $^1J_{CF}$ = 236.3 Hz), 87.9 (t, $^2J_{CF}$ = 29.0 Hz), 207.2 (t, $^3J_{CF}$ = 12.2 Hz), 90.9 (s), 12.9 (s). HRMS: $C_5F_2H_6$ calculated, 104.0438; found, 104.0433. IR (CCl_4): 2984 (w), 2958 (w), 2930 (w), 2929 (w), 2864 (w), 1973 (w), 1428 (s), 1374 (w), 1344 (m), 1155 (w), 1136 (m), 1108 (vs), 1097 (s), 1072 (s), 1057 (vs), 1029 (vs), 888 (w), 866 (w).

3.7.10. Reaction of difluoromethylcopper with 3-chloro-3-methyl-1-butyne

Similarly, a 35 ml aliquot of a 0.90 M difluoromethylcadmium reagent (31.5 mmol) in DMF, 4.6 g (32 mmol) of CuBr and 2.4 g (23.4 mmol) of 3-chloro-3-methyl-1-butyne were reacted at −50 °C. After distillation, 2.15 g (78%) of 1,1-difluoro-4-methyl-2,3-pentadiene (bp 77–80 °C) was obtained, GLPC purity = 100%. ^{19}F, ^{1}H and ^{13}C NMR data were identical to the data reported previously from the reaction of difluoromethylcadmium with 3-bromo-3-methyl-1-butyne. HRMS: $C_6H_8F_2$ calculated, 118.0594; found, 118.0587.

3.7.11. Reaction of difluoromethylcopper with 1-bromo-2-butyne

Similarly, a 30 ml aliquot of a 0.84 M difluoromethylcadmium reagent (25 mmol) in DMF, 3.6 g (25 mmol) CuBr and 2.6 g (19.2 mmol) of 1-bromo-2-butyne were reacted at −50 °C. After distillation, 1.2 g (59%) (bp 53–56 °C) of a 87:13 isomeric mixture of 4,4-difluoro-3-methyl-1,2-butadiene and 5,5-difluoro-2-pentyne was obtained (as determined by GLPC). ^{19}F, ^{1}H and ^{13}C NMR data were identical to the data reported previously for the reaction of difluoromethylcadmium with 1-bromo-2-butyne.

3.7.12. Reaction of difluoromethylcopper with 1-chloro-1-ethynylcyclohexane

Similarly, a 72 ml aliquot of a 0.83 M difluoromethylcadmium reagent (60 mmol) in DMF, 8.6 g (60 mmol) CuBr and 7.1 g (50 mmol) of 1-chloro-1-ethynylcyclohexane were reacted at −50 °C. After distillation, 5.6 g (71%) (bp 68–72 °C) of 4,4-difluoro-1-pentamethylene-1,2-butadiene was obtained, GLPC purity, 100%. ^{19}F NMR ($CDCl_3$) (ppm): δ −106.8 (dd, $^2J_{FH}$ = 56.7 Hz, $^3J_{FH}$ = 6.3 Hz), ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) 6.02 (td, $^2J_{FH}$ = 56.7 Hz, $^3J_{HH}$ = 6.2 Hz), d (CF_2HCH=) 5.21 (bs), 2.16 (bs), 1.61 (bs), 1.54 (bs), ^{13}C NMR (neat) (ppm): 115.5 (t, $^1J_{CF}$ = 236.8 Hz), 86.7 ($^2J_{CF}$ = 28.8 Hz), 201.4 (t, $^3J_{CF}$ = 12.4 Hz), 108.2 (s), 31.2 (s), 27.6 (s), 26.3 (s). GC–MS, *m/z* (relative intensity): 158 (100.0), 143 (26.0), 130 (17.7), 129 (24.8), 125 (15.5), 123 (26.0), 116(13.2), 115(38.7), 111 (13.8), 109 (27.7), 107 (26.3), 105 (15.7), 103 (16.0), 101 (13.7), 97 (34.7), 93 (15.9), 91 (48.4), 79 (60.8), 77 (33.4), 51 (12.5). IR (CCl_4): 2936 (s), 2895 (m), 2857 (m), 1973 (m), 1685 (w), 1448 (s), 1438 (s), 1369 (w), 1355 (m), 1336 (w), 1120 (vs), 1078 (s), 1055 (vs), 1024 (vs), 973 (w), 932 (w), 896 (w), 853 (w).

3.7.13. Reaction of difluoromethylcopper with 1,4-dichloro-2-butyne

Similarly, a 46 ml aliquot of a 1.2 M difluoromethyl cadmium reagent (55 mmol) in DMF, 5.4 g (55 mmol) CuCl, and 3.1 g (50 mol) of 1,4-dichloro-2-butyne were reacted at −60 °C. After distillation 1.8 g (46%) (bp 53–55 °C/94 mm) of bis-2,3-(difluoromethyl)-1,3-butadiene was obtained, GLPC purity 100%). ^{19}F NMR ($CDCl_3$) (ppm): δ −115.4 (d, $^2J_{CFH}$ = 56.2 Hz), ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) 6.21 (t, $^2J_{FH}$ = 56.2 Hz), δ (=C*H*) 5.72 (m), δ (=C*H*) 5.71 (s); ^{13}C NMR ($CDCl_3$) (ppm): 114.9 (t, $^1J_{CF}$ = 240.1 Hz), 135.9 ($^2J_{CF}$ = 20.3 Hz), 121.3 (t, $^3J_{CF}$ = 10.0 Hz). HRMS: $C_6H_6F_4$ calculated, 154.0406; found, 154.0373. IR (CCl_4): 3745 (w), 2972 (w), 1607 (w), 1405 (m), 1389 (m), 1350 (m), 1261 (w), 1218 (m), 1196 (m), 1185 (m), 1110 (s), 1093 (s), 1058 (s), 1045 (vs), 947 (m), 833 (w).

3.7.14. Reaction of difluoromethylcopper reagent with 1-iodo-1-hexyne

A 66 ml aliquot of a 0.78 M difluoromethylcadmium reagent (52 mmol) in DMF, 7.5 g (52 mmol) CuBr, and 10.0 g (48 mmol) of 1-iodo-1-hexyne were reacted at −50 °C. After distillation 4.8 g (75%) (bp 74–76 °C/127 mm) of 1,1-difluoro-2-heptyne was obtained, GLPC purity 100%. ^{19}F NMR ($CDCl_3$) (ppm): δ −104.4 (dt, $^2J_{FH}$ = 55.7 Hz, $^5J_{FH}$ = 5.9 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) 6.16 (tt, $^2J_{FH}$ = 55.7 Hz, $^5J_{HH}$ = 1.5 Hz), δ (–CH_2–) 2.29 (m), δ (–$CH_2CH_2CH_2$) 1.50 (m), δ (–CH_3) 0.92 (t, $^3J_{HH}$ = 7.0 Hz). ^{13}C NMR (neat) (ppm): 104.3 (t, $^1J_{CF}$ = 229.8 Hz), 72.4 (t, $^2J_{CF}$ = 33.5 Hz), 90.5 (t, $^3J_{CF}$ = 7.1 Hz), 30.0 (s), 22.0 (s), 17.9 (s), 13.1 (s). GC–MS, *m/z* (relative intensity): 117 (44.0), 104 (26.0) 103 (15.7), 101 (19.0), 99 (56.8), 97 (68.7), 91 (20.8), 86 (33.5), 85 (24.9), 83 (34.6), 81 (100.0), 79 (26.9), 77 (56.2), 70 (35.8), 67 (17.5), 51 (24.9), 43 (37.5), 41 (17.9). IR (CCl_4): 2961 (m), 2938 (m), 2876 (w), 2337 (s), 2257 (m), 1687 (s), 1467 (w), 1429 (w), 1374 (vs), 1341 (w), 1168 (vs), 1087 (w), 1046 (vs).

3.7.15. Reaction of difluoromethylcopper with 1-iodo-1-heptyne

A 52 ml aliquot of a 1.16 M difluoromethylcadmium reagent (60 mmol) in DMF, 5.9 g (60 mmol) of CuCl and 12.3 g (55.3 mmol) of 1-iodo-1-heptyne was reacted at −50 °C. After distillation 6.0 g (74%) (bp 71–73 °C/76 mm) of 1,1-difluoro-2-octyne was obtained, GLPC purity 100%. ^{19}F NMR ($CDCl_3$) (ppm): δ −104.4 (dt, $^2J_{FH}$ = 55.7 Hz, $^5J_{FH}$ = 5.8 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): δ (CF_2H) 6.16 (tt, $^2J_{FH}$ = 55.7 Hz, $^5J_{HH}$ = 1.4 Hz), δ (–CH_2) 2.28 (m), δ (–$CH_2CH_2CH_2CH_2$–) 1.40 (m), δ (–CH_3) 0.91 (t, $^3J_{HH}$ = 7.1 Hz). ^{13}C NMR (neat) (ppm): 103.6 (t, $^1J_{CF}$ = 230.3 Hz), 71.9 (t, $^2J_{CF}$ = 33.7 Hz), 89.9 (t, $^3J_{CF}$ = 7.1 Hz), 30.6 (s), 27.2 (s), 21.8 (s), 17.7 (s), 13.01 (s). GC–MS, *m/z* (relative intensity): 145 ($M-1$, 1.4), 117 (18.4), 97 (29.1), 95 (74.2), 81 (24.9), 78 (21.5), 77 (32.4), 70 (31.8), 67 (23.8), 63 (38.6), 57 (75.2), 56 (46.3), 55 (85.5), 51 (57.0), 41 (100.0). IR (CCl_4): 2960 (m), 2934 (m), 2875 (w), 2884 (w), 2337 (w), 2257 (m), 1468 (w), 1461 (w), 1457 (w), 1374 (vs), 1053 (vs), 1049 (vs).

3.7.16. Reaction of difluoromethylcopper with 1-iodo-2-phenylethyne

A 45 ml aliquot of a 0.96 M difluoromethylcadmium reagent (43 mmol) in DMF, 6.4 g (43 mmol) of CuBr and 8.5 g (37 mmol) of 1-iodo-2-phenylethyne was reacted at −50 °C. After flash distillation, the flash distillate was washed with an equal volume of ice water. The organic layer was washed with 2× 25 ml of water, and dried over 4 Å molecular sieves. Then, 15 ml of tetraglyme were added to the reaction pot and the mixture flash distilled, washed with an equal volume of ice water, the organic layer separated, washed with 2× 25 ml and dried over 4 Å molecular sieves. Repetition of the addition of tetraglyme an additional time, followed by combination of the organic layers gave 2.7 g of crude 3,3-difluoro-1-phenylpropyne. Distillation gave 2.5 g (44%) (bp 50–52 °C/4 mm) of 3,3-difluoro-1-phenylpropyne, GLPC purity 100%. ^{19}F NMR ($CDCl_3$) (ppm): δ −105.7 (d, $^2J_{FH}$ = 55.2 Hz); ^{1}H NMR ($CDCl_3$) (ppm): δ (CF_2H) 6.40 (t, $^2J_{FH}$ = 55.2 Hz), 7.4 (aromatics) (m); ^{13}C NMR (neat) (ppm): 104.5 (t, $^1J_{CF}$ = 231.2 Hz), 79.7 (t, $^2J_{CF}$ = 33.7 Hz), 88.3 (t, $^3J_{CF}$ = 7.4 Hz), 119.6 (s), 128.4 (s), 131.9 (s), 130.0 (s). GC–MS, *m/z* (relative intensity): 152 (80.5), 151 (100.0), 133 (48.9), 102 (57.9), 99 (10.7), 76 (10.0), 75 (13.2), 74 (12.1). IR (CCl_4): 3062 (w), 2971 (w), 2956 (w), 2286 (m), 2222 (w), 1687 (m), 1491 (m), 1445 (w), 1372 (vs), 1258 (w), 1049 (s), 973 (m), 918 (w).

3.7.17. Reaction of difluoromethylcopper with 1-iodo-1-perfluorohexyne

A 50 ml aliquot of a 0.87 M difluoromethylcadmium reagent (44 mmol) in DMF, 6.5 g (45 mmol) of CuBr and 13.2 g (35.8 mmol) of 1-iodo-1-perfluorohexyne were reacted at −50 °C. After flash distillation washing with water and drying the organic layer, distillation gave 5.52 g (52%) (bp 68–73 °C) of 1-hydro-2-perfluoroheptyne, was obtained, GLPC purity 100%. ^{19}F NMR ($CDCl_3$) (ppm): δ (CF_2H) −111.8 (dt, $^2J_{FH}$ = 52.7 Hz, $^5J_{FF}$ = 5.5 Hz), −101.4 (m), −121.8 (m), −123.3 (m), −123.1 (m), −126.6 (m), −81.3 (t, $^4J_{FF}$ = 9.8 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): 6.31 (tt, $^2J_{FH}$ = 52.7 Hz, $^5J_{FH}$ = 2.4 Hz); ^{13}C NMR ($CDCl_3$) (ppm): 102.0 (CF_2H) (t, $^1J_{CF}$ = 236.3 Hz), 72.8 (CF_2H–C≡C–CF_2–) (tt, $^2J_{CF}$ = 37.8 Hz, $^3J_{CF}$ = 6.9 Hz), 80.9 ($CF_2HC{\equiv}CCF_2$–) (tt, $^3J_{CF}$ = 5.9 Hz, $^2J_{CF}$ = 36.4 Hz), 105–113 (m, $3CF_2$), 112.4 (CF_3) (qt, $^1J_{CF}$ = 286.4 Hz, $^2J_{CF}$ = 33.1 Hz). GC–MS, *m/z* (relative intensity): 293 ($M-1$, 0.1), 187 (10.8), 137 (14.5), 125 (100.0), 119 (13.1), 106 (18.3), 100 (13.1), 75 (25.2), 69 (20.7). IR (CCl_4): 1372 (w), 1354 (w), 1263 (w), 1240 (vs), 1217 (m), 1212 (m), 1141 (s), 1081 (m), 980 (w), 873 (w).

3.7.18. Reaction of difluoromethylcopper with 1-iodo-1-perfluorooctyne

A 45 ml aliquot of a 0.97 M difluoromethylcadmium reagent (43.7 mmol) in DMF, 6.3 g (44 mmol) of CuBr and 15.9 g (33.7 mmol) of 1-iodo-1-perfluorooctyne were reacted at −50 °C and the reaction mixture was worked-up as described in the previous reaction. After distillation 7.3 g (55%) (bp 115–117 °C) of 1-hydro-2-perfluorononye was obtained, GLPC purity 95%. ^{19}F NMR ($CDCl_3$) (ppm): δ (CF_2H) −111.8 (dt, $^2J_{FH}$ = 52.7 Hz, $^5J_{FF}$ = 5.5 Hz), −101.4 (m), −121.8 (m), −123.3 (m), −123.1 (m), −126.6 (m), −81.3 (t, $^4J_{FF}$ = 9.8 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): d (CF_2H) 6.31 (tt, $^2J_{FH}$ = 52.7 Hz, $^5J_{FH}$ = 2.4 Hz); ^{13}C NMR ($CDCl_3$) (ppm): 102.4 (CF_2H) (t, $^1J_{CF}$ = 236.9 Hz), 73.7 (CF_2H–C≡C) (t, $^2J_{CF}$ = 37.5 Hz), 81.7 (t, $^3J_{CF}$ = 36.3 Hz), 105–118 (m, $(CF_2)_5CF_3$). GC–MS, *m/z* (relative intensity): 393 ($M-1$, 0.1), 125 (100.0), 75 (18.4), 69 (17.4): IR (CCl_4): 1686 (w), 1552 (w), 1372 (m), 1242 (vs), 1208 (s), 1150 (s), 1128 (m), 1080 (m).

3.7.19. Reaction of difluoromethylcopper with 1-iodo-1-perfluorodecyne

An 8 ml aliquot of 1.45 M difluoromethylcadmium reagent (11.6 mmol) in DMF, 1.7 g (11.6 mmol) CuBr and 5.4 g (9.5 mmol) of 1-iodo-1-perfluorodecyne were reacted at

−50 °C, and the reaction mixture worked-up as described previously. The dry organic layer obtained was 3.1 g (66%) of 1-hydro-2-perfluorodecyne, GLPC; purity 100%. ^{19}F NMR ($CDCl_3$) (ppm). δ (CF_2H) −111.9 (dt, $^2J_{FH}$ = 52.7 Hz, $^5J_{FF}$ = 5.5 Hz), −101.5 (bs), −121.7 (bs), −122.6 (4 CF_2) (m), −126.7 (bs), −81.4 (CF_3) (t, $^4J_{FF}$ = 9.2 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): 6.29 (tt, $^2J_{FH}$ = 52.7 Hz, $^5J_{FH}$ = 2.3 Hz); ^{13}C NMR ($CDCl_3$) (ppm): 101.8 (CF_2H) (t, $^1J_{CF}$ = 236.3 Hz), 72.7 ($CF_2HC{\equiv}C–CF_2–$) (tt, $^2J_{CF}$ = 37.7 Hz, $^3J_{CF}$ = 6.8 Hz), 80.9 (tt, $–C{\equiv}CCF_2CF_2–$, $^2J_{CF}$ = 36.4 Hz, $^3J_{CF}$ = 5.9 Hz), −103 to 122 (7 CF_2) (m), 117.0 (CF_3) (qt, $^1J_{CF}$ = 286.9 Hz, $^2J_{CF}$ = 33.0 Hz). GC–MS, *m/z* (relative intensity): 493 ($M-1$, 0.1), 131 (14.4), 125 (100.0), 119 (1.4), 75 (24.4), 69 (45.8). IR (CCl_4): 1685 (w), 1372 (m), 1243 (vs), 1218 (vs), 1156 (s), 1137 (m), 1123 (m), 1081 (m), 1005 (w).

3.7.20. Reaction of difluoromethylcopper with ethylchloromethyl ether

A 65 ml aliquot of 0.85 M difluoromethylcadmium reagent (55 mmol) in DMF, 7.9 g (55 mmol) CuBr and 4.9 g (52 mmol) of ethylchloromethyl ether were reacted at −50 °C, The reaction mixture was slowly warmed to RT over 5 h. Flash distillation was followed by simple distillation of the volatile material to give 4.1 g (72%) (bp 65–67 °C) of 2,2-difluoroethyl ethyl ether, GLPC; purity 100%. ^{19}F NMR ($CDCl_3$) (ppm). δ (CF_2H) −125.5 (dt, $^2J_{FH}$ = 56.2 Hz, $^3J_{FH}$ = 14.2 Hz); ^{1}H NMR (360 MHz) ($CDCl_3$) (ppm): 5.86 (tt, $^2J_{FH}$ = 56.2 Hz, $^3J_{HH}$ = 4.2 Hz), 3.62 (q, $^3J_{HH}$ = 7.1 Hz), 1.22 (t, $^3J_{HH}$ = 7.1 Hz); ^{13}C NMR (neat) (ppm): 115.0 (t, $^1J_{CF}$ = 239.7 Hz), 69.8 (t, $^2J_{CF}$ = 27.2 Hz), 67.3 (s), 14.3 (s). GC–MS, *m/z* (relative intensity): 110 (38.8), 95 (46.4), 85 (95.0), 63 (33.6), 59 (100.0), 51 (37.3), 46 (12.1), 45 (38.3), 43 (35.9). IR (CCl_4): 2983 (s), 2952 (m), 2945 (m), 2875 (w), 1437 (w), 1394 (w), 1317 (w), 1269 (w), 1244 (w), 1179 (w), 1149 (s), 1123 (vs), 1073 (vs), 1034 (w), 914 (w).

3.7.21. Reaction of difluoromethylcopper with benzyl bromide

A 61 ml aliquot of 0.90 M difluoromethylcadmium reagent (55 mmol) in DMF, 8.0 g (56 mmol) CuBr and 8.6 g (50 mmol) of benzyl bromide were reacted at −50 °C. The reaction was slowly warmed to RT over 5 h. Flash distillation; washing of the flash distillate with an equal volume of water, separation of the organic layer, washing of the organic layer with 2× 50 ml water and drying of the organic layer with 4 Å molecular sieves gave the crude product, which on distillation gave 2.5 g (35%) of 1,1-difluoro-2-phenylethane. ^{19}F NMR ($CDCl_3$) (ppm). δ −115.3 (dt, $^2J_{FH}$ = 56.6 Hz, $^3J_{FH}$ = 17.3 Hz); ^{1}H NMR ($CDCl_3$) (ppm): δ (CF_2H) 5.89 (tt, $^2J_{FH}$ = 56.6 Hz, $^3J_{FH}$ = 17.3 Hz), δ ($CF_2HCH_2–$) (td, $^3J_{FH}$ = 17.3 Hz, $^3J_{HH}$ = 4.6 Hz), δ 7.2–7.3 (m, aromatic H's); ^{13}C NMR (neat) (ppm): 116.7 (t, $^1J_{CF}$ = 240.0 Hz), 40.2 (t, $^2J_{CF}$ = 21.8 Hz), 132.4 (t, $^3J_{CF}$ = 5.6 Hz), 129.6 (s), 128.3 (s), 127.1 (s). GC–MS, *m/z* (relative intensity): 142 (17.0), 91 (100.0), 89 (5.6), 65 (9.4), 51 (6.2). IR (CCl_4): 3092 (m), 3069 (m), 3035 (m), 2975 (m), 2934 (w), 2851 (w), 1947 (w), 1876 (w), 1805 (w) 1687 (w), 1605 (w), 1495 (m), 1457 (m), 1434 (m), 1393 (s), 1363 (m), 1336 (w), 1208 (m), 1118 (vs), 1083 (s), 1060 (vs), 1032 (s), 1018 (m), 867 (m).

4. Conclusions

Difluoromethylcadmium is readily prepared by oxidative addition of cadmium with iododifluoromethane and bromodifluoromethane. The difluoromethylcadmium reagent is thermally stable to 65–70 °C; rapid decomposition occurs at temperatures >105 °C. At room temperature the reagent is stable for weeks and only loses 31% of its activity after 2 months at RT. The difluoromethylcadmium reagent reacts readily with allylic halides at RT to give products of both α- and γ-attack in good yields. Metathesis of the difluoromethylcadmium reagent with Cu(I)X (X = Cl, Br) in DMF at −55 °C readily gives the difluoromethylcopper reagent. The copper reagent is stable only at low temperatures (−30 to −55 °C) and rapidly decomposes to HCF_2CF_2H and *cis*-CFH=CFH above these temperatures. However, HCF_2Cu is more nucleophilic than HCF_2CdX, and the copper reagent readily reacts with allylic halides at −55 °C, The regiospecificity of HCF_2Cu is vastly superior to HCF_2CdX and most of the reactions of HCF_2Cu with allylic halides occur regiospecifically. When HCF_2CdX is reacted with propargylic halides or tosylates, the predominant product is the corresponding allene. The HCF_2Cu reagent again is more reactive, completely regiospecific, and in most cases gives good isolated yields of the allenes. The HCF_2Cu reagent also readily couples with 1-iodoalkynes and 1-iodoperfluoroalkynes to give good yields of the corresponding difluoromethylalkynes. The HCF_2Cu reagent only undergoes alkylation with reactive alkylating agents, such as chloromethyl ethyl ether and benzyl bromide.

Acknowledgement

We gratefully appreciate the financial support from the Air Force Office of Scientific Research and the National Science Foundation.

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