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# PALLADIUM-CATALYZED REACTION OF FLUORINATED VINYL IODIDES WITH TERMINAL ALKYNES: A NEW AND GENERAL ROUTE TO FLUORINATED ENYNES

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Dedicated to Professor Dr. Alois Haas on the occasion of his 60th birthday.

## SUMMARY

In the presence of cuprous iodide, the palladium-catalyzed coupling reaction of fluorinated vinyl iodides with terminal alkyl and phenyl substituted alkynes gives the corresponding enynes in good yields under mild conditions. The reaction works well with perfluorovinyl, phenyl and phosphoryl substituted iodides, and the stereochemistry in the vinyl iodide was preserved in the enyne products. With a terminal dialkyne the dienyne is formed when two equivalents of the vinyl iodide are used as substrate. However, upon reaction of Z-iodopentafluoropropene with alkynes containing electron-withdrawing groups such as ethoxycarbonyl or perfluoroalkyl, no desired enynes were observed under similar reaction conditions. The coupling reaction can be carried out in a variety of solvents, including DMF, DMSO, HMPA, acetonitrile, dioxane, chloroform, benzene and hexane as well as in excess triethylamine as solvent.

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## INTRODUCTION

Enynes are important intermediates in organic synthesis [1]. Conjugated enynes react selectively with electrophiles at the double bond to provide an efficient method for the assembly of multifunctional molecules [2]. Alternatively, the triple bond may be partially hydrogenated to the conjugated diene [3]. Compounds of this class have been utilized as essential components in the synthesis of natural products [4], especially biologically active compounds such as enzyme inhibitors [5] and antitumor agents [6]. Thus, one would anticipate that fluorine-containing enynes would also be useful as building blocks to partially fluorinated multifunctional compounds or partially fluorinated biologically active products. Since substitution of a fluorine atom for a hydrogen atom in a biologically active molecule often leads to pronounced activity enhancement [7], preparation of fluorinated building blocks has attracted much attention. However, the lack of general synthetic methodology for the preparation of fluorinated enynes has hampered development along these lines.

Preparation of enynes has been extensively investigated with vinyl halides and terminal alkynes. It was reported that the coupling reaction of vinyl halides with a 1-alkyne could be catalyzed by cuprous iodide [8] or palladium [9] at elevated temperature. However, in the

$$RC{\equiv}CH \quad + \quad R'CH{=}CHX \xrightarrow[CuI \quad Et_3N]{Pd(PPh_3)_2Cl_2} RC{\equiv}C\text{-}CH{=}CHR'$$

presence of cuprous iodide, the palladium catalyzed reaction proceeded under very mild conditions and gave enynes in excellent yields [10]. This method has been widely utilized in the synthesis of natural products [4,5,6]. In contrast, there has been only one publication describing the preparation of fluorinated enynes. Tellier et al. [11] recently reported that fluorinated enynes could be prepared by the palladium-catalyzed coupling reaction of either fluorine-containing vinyl iodides

with terminal alkynylzinc reagents, or 1-haloalkynes with fluorinated vinyl zinc reagents. Although this procedure provided the enynes in reasonable yields, this approach necessitated either the prior generation of the requisite alkynylzinc reagents, fluorinated vinyl zinc reagents or the 1-haloalkynes.

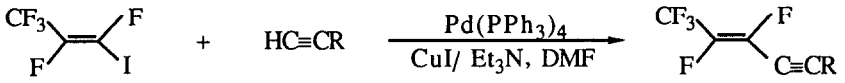
$$RCF{=}CFI \quad + \quad ClZnC{\equiv}CR' \xrightarrow{Pd(PPh_3)_4} RCF{=}CF\text{-}C{\equiv}CR'$$

Recently, we [12] and others [13] have shown that the fluorinated vinyl iodides are capable of participation in a palladium-catalyzed coupling reaction with fluorinated or non-fluorinated vinyl zinc reagents and alkynyl zinc reagents. In the coupling reaction, a key step in the catalytic cycle is the rapid oxidative addition of a fluorinated vinyl iodide to a palladium(0) complex to generate a fluorinated vinylpalladium(II) species. This previous work suggested that the fluorinated vinyl iodide could be utilized in other palladium-catalyzed reactions requiring the vinylpalladium(II) intermediate *via* an oxidative addition. Consequently, it is apparent that a fluorinated vinyl iodide could also undergo a coupling reaction with a terminal alkyne in the presence of palladium and cuprous iodide. In a preliminary communication [14] we briefly described the facile coupling reaction of fluorinated vinyl iodides with terminal alkynes catalyzed by palladium in the presence of cuprous iodide. This methodology avoids the prior preparation of alkynylzinc reagents. We now wish to report in detail the results of the synthesis of various fluorinated enynes.

## RESULTS AND DISCUSSION

**Z**-iodopentafluoropropene **1** [15] reacted with terminal alkynes in the presence of tetrakis(triphenylphosphine)palladium, cuprous iodide

and triethylamine using DMF as the solvent to afford the corresponding enynes in good yields. This reaction proved to be quite general for




**1** **2**

**2a:** $R = C_6H_5$

**2b-2f:** $R = C_nH_{2n+1}$, $n = 3,4,5,6,7$

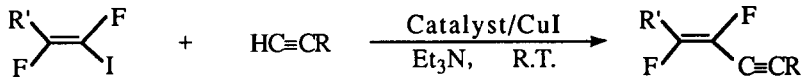
**2g:** $R = Me_3Si$

aryl and alkyl substituted acetylenes. For example, upon reaction of **1** with phenyl acetylene and triethylamine in the presence of $Pd(PPh_3)_4$/CuI in DMF at 70°C for 3 hours, 53% of **2a** was isolated. When alkyl substituted alkynes were used as substrates, the corresponding enynes were formed in 53-86% yields. These results are summarized in Table I. With shorter chain alkynes, such as pentyne, the reaction was conducted in a sealed tube to avoid loss of the lower boiling point alkyne. On the other hand, upon treatment of **1** with trimethysilylacetylene in DMF at 70°C overnight, $^{19}F$ NMR analysis of the reaction mixture indicated the absence of the desired product. The only characterizable fluorinated material was trimethylsilyl fluoride (-157 ppm). However, when the reaction was carried out in excess triethylamine at 70°C for 6 hours, the desired enyne **2g** was formed in 90% yield by $^{19}F$ NMR spectroscopic analysis (integration *vs.* $C_6H_5CF_3$). Despite careful work-up of the reaction mixture, the isolated yield of **2g** was only 44%, due to instability of the product to acid during work-up.

As illustrated in Table I, entry 17, the terminal dialkyne gave the dienyne when two equivalents of **1** were employed. In the case of the reaction of **1** with 1,7-octadiyne in DMF at 50°C, **E,E**-dienyne **3** was obtained in 36% yield. However, when the reaction was carried out in triethylamine as solvent, the yield of **3** increased to 49%.

**TABLE I**

Palladium-Catalyzed Reaction of 1-Alkynes with Fluorinated Vinyl Iodides




| Entry | R | R' | Catalyst | Product No. | Yield % [a] |
|---|---|---|---|---|---|
| 1 | $C_6H_5$ | $CF_3$ | $Pd(PPh_3)_4$ | **2 a** | 53[b] |
| 2 | n-$C_3H_7$ | $CF_3$ | $Pd(PPh_3)_4$ | **2 b** | 61[b] |
| 3 | n-$C_4H_9$ | $CF_3$ | $Pd(PPh_3)_4$ | **2 c** | 86[b] |
| 4 | n-$C_5H_{11}$ | $CF_3$ | $Pd(PPh_3)_2Cl_2$ | **2 d** | 62 |
| 5 | n-$C_6H_{13}$ | $CF_3$ | $Pd(PPh_3)_4$ | **2 e** | 54[b] |
| 6 | n-$C_7H_{15}$ | $CF_3$ | $Pd(PPh_3)_2Cl_2$ | **2 f** | 67 |
| 7 | $Me_3Si$ | $CF_3$ | $Pd(PPh_3)_2Cl_2$ | **2 g** | 44[c] |
| 8 | n-$C_3H_7$ | F | $Pd(PPh_3)_2Cl_2$ | **5 b** | 50[d] |
| 9 | n-$C_4H_9$ | F | $Pd(PPh_3)_2(OAc)_2$ | **5 c** | 69[d] |
| 10 | n-$C_5H_{11}$ | F | $Pd(PPh_3)_2Cl_2$ | **5 d** | 59 |
| 11 | n-$C_6H_{13}$ | F | $Pd(PPh_3)_2Cl_2$ | **5 e** | 66 |
| 12 | n-$C_7H_{15}$ | F | $Pd(PPh_3)_2Cl_2$ | **5 f** | 59 |
| 13 | Ph | F | $Pd(PPh_3)_2Cl_2$ | **5a** | 53 |
| 14 | Ph | Ph | $Pd(PPh_3)_2Cl_2$ | **7** | 73 |
| 15 | Ph | $(^iPrO)_2P(O)$ | $Pd(PPh_3)_2Cl_2$ | **9 a** | 87 |
| 16 | n-$C_6H_{13}$ | $(^iPrO)_2P(O)$ | $Pd(PPh_3)_2Cl_2$ | **9 b** | 77 |
| 17 | $HC{\equiv}C(CH_2)_4$ | $CF_3$ | $Pd(PPh_3)_2Cl_2$ | **3** | 49[e] |

a Isolated yields.

b Reaction was carried out in DMF at 60-70°C.

c Reaction proceeded at 70°C.

d Reaction was conducted in acetonitrile.

e Two equivalents of **Z**-$CF_3CF{=}CFI$ were used at 55°C; product is **E, E**-$CF_3CF{=}CFC{\equiv}C(CH_2)_4C{\equiv}CCF{=}CFCF_3$.

$$2\ \text{Z-CF}_3\text{CF=CFI} + \text{HC}\equiv\text{C(CH}_2)_4\text{C}\equiv\text{CH} \xrightarrow[\text{CuI},\ \text{Et}_3\text{N}]{\text{Pd(PPh}_3)_2\text{Cl}_2} [\text{E-CF}_3\text{CF=CFC}\equiv\text{C(CH}_2)_2]_2$$

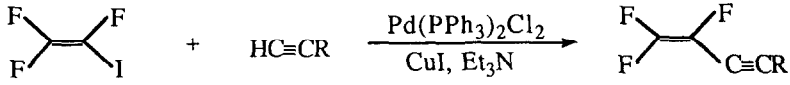
**1** **3**

49%

The reaction of **1** with a terminal alkyne containing an electron-withdrawing group failed. For example, reaction of **1** with ethyl propiolate in the presence of tetrakis(triphenyphosphine)palladium(0), cuprous iodide and triethylamine in DMF at 70°C gave rise to an uncharacterizable mixture. Substitution of bis(triphenylphosphine) palladium(II) dichloride for tetrakis(triphenylphosphine)palladium in triethylamine as the solvent at 50°C was also unsuccessful. Likewise, with nonafluoro-1-hexyne under the similar conditions, no enyne was detected.

The reaction of **1** with phenylacetylene could also be catalyzed by bis(triphenylphosphine)palladium dichloride or acetate and cuprous iodide. The reaction also proceeded readily in a variety of solvents. As illustrated in Table II, in most common solvents, such as DMF, DMSO, HMPA, dioxane and benzene, the reaction was completed within 4 hours at 55°C to 75°C and **2a** was formed in 75-85% yields. In acetonitrile, the reaction required prolonged heating at 70°C, affording **2a** in 56% yield. The best yield (92%) of **2a** was observed in triethylamine.

Trifluoroethenyl iodide, **4**, could also be used as a substrate. As illustrated in Table I, when the reaction was conducted either in acetonitrile or in triethylamine at room temperature, the enynes **5** were obtained in good yields from phenylacetylene and terminal alkyl substituted acetylenes. However, only unidentifiable materials were observed in the case of the reaction of **4** with phenylacetylene in DMF at 70°C.

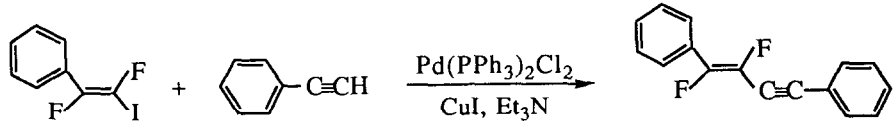



**4** **5**

**5a**: $R = C_6H_5$

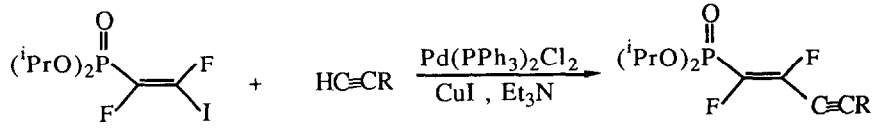
**5b-5f**: $R = C_nH_{2n+1}$, n = 3,4,5,6,7

The phenyl and phosphoryl-substituted fluorinated vinyl iodides worked well with terminal alkynes in the presence of bis(triphenylphosphine)palladium(II) dichloride and cuprous iodide in triethylamine at room temperature. Upon treatment of **Z**-2-phenyl-1,2-difluoroethenyl iodide with phenylacetylene, **E**-1,4-diphenyl-1,2-difluoro-1-buten-3-yne **7** was isolated in 73% yield. Reaction of **E**-2-diisopropoxyphosphinyl-1,2-difluoroethenyl iodide with phenylacetylene or 1-octyne gave the corresponding **9a** and **9b**




**6** **7**

73%




**8** **9**

**9a**: $R = C_6H_5$ 87%

**9b**: $R = C_6H_{13}$ 77%

**TABLE II**

Reaction of 1 with Phenylacetylene and Pd(II)/CuI in Solvent[a]

| Entry | Solvent | T°C | t (hour) | Yield[b] |
|---|---|---|---|---|
| 1 | HMPA | 75 | 4 | 77 |
| 2 | DMSO | 75 | 3 | 75 |
| 3 | DMF | 70 | 3 | 80 |
| 4 | Dioxane | 75 | 4 | 81 |
| 5 | $CH_3CN$ | 70 | 19 | 56[c] |
| 7 | $CHCl_3$ | 55 | 16 | 82 |
| 8 | Benzene | 65 | 4.5 | 83 |
| 9 | Hexane | 65 | 4.5 | 85[d] |
| 10 | $Et_3N$ | 55 | 16 | 92 |

a Reaction of 5 mmol of **1** with 6 mmol of phenylacetylene in a mixture of 5 mol% of CuI, 5 mol% of $PdCl_2$ and 10 mol% of $PPh_3$ and 1 mL of $Et_3N$ in 10 mL of solvent.

b Yield of **2a** was determined by $^{19}F$ NMR integration of the $CF_3$ signal in the enyne *vs* . $C_6H_5CF_3$.

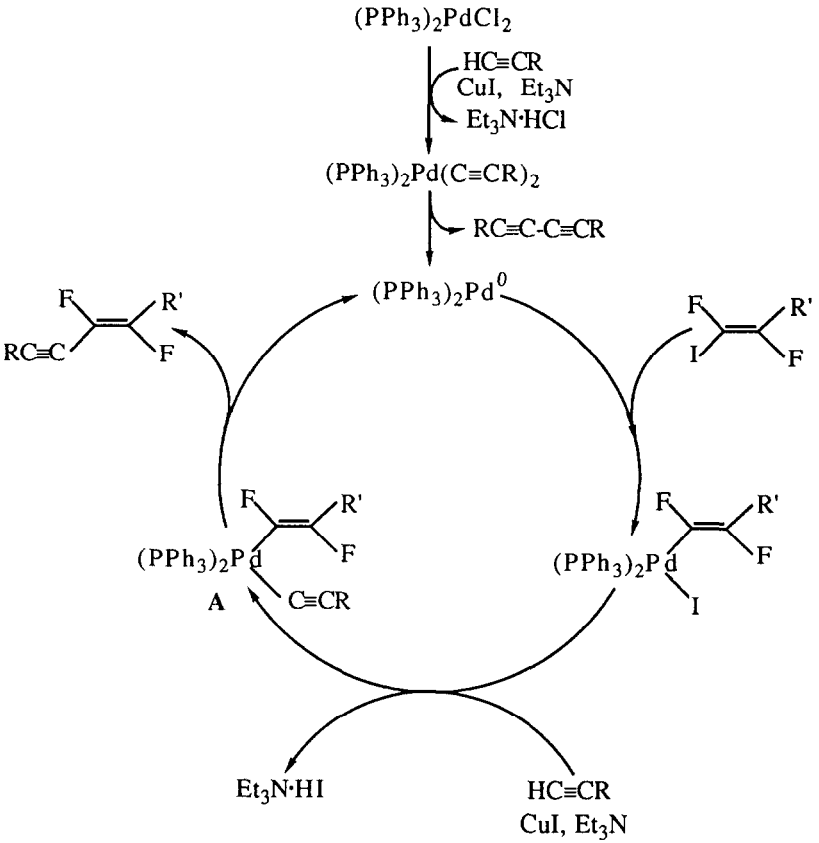
c After 3 hours, conversion of **1** was 62%.

d Conversion of **1** was 86%.

stereospecifically in 87% and 77% yields, respectively. However, attempts to couple perfluoro-2-iodo-3-methyl-2-butene with phenylacetylene under these conditions failed.

The coupling reaction proceeds through a palladium(0) species. When palladium(II) is utilized as a catalyst, the first step is reduction of palladium(II) to palladium(0), presumably by the terminal alkyne in the presence of cuprous iodide and triethylamine [10]. In fact, a small amount of the dialkyne from oxidative coupling of the 1-alkyne was isolated in the reaction of *para*-methoxy-tetrafluorophenyl iodide with

phenylacetylene under similar conditions [16]. The resulting palladium(0) species is then capable of entering the catalytic cycle




**Scheme I.**

(Scheme I) by oxidative addition of the fluorinated vinyl iodide, followed by alkynylation to generate the palladium(II) species, **A**. When the alkynes containing an electron withdrawing group or perfluoro-2-iodo-3-methyl-2-butene were used as substrates, the intermediate **A** may be too stable to undergo reductive elimination to form the enynes, due to the relative higher ionic resonance energy of the palladium carbon bond in **A** [17]; this may account in part for the fact that no enynes were formed with these alkynes and vinyl iodide. Such a situation was also observed in the palladium(II)-catalyzed coupling reaction of the Reformatsky reagent with acid chlorides [18].

It is well-known that palladium catalyzed coupling reactions very often afford products in which the stereochemistry of the vinyl halide is retained in the products [19]. In the palladium-catalyzed reaction of fluorinated vinyl iodides with terminal alkynes, the stereochemistry in the vinyl iodides was preserved in the enyne products as characterized by $^{19}F$ NMR analysis. *Trans*- and *cis*-vinyl fluorines in the enynes are readily distinguished by the large coupling between the *trans*-vinyl fluorines (typically, 114-147 Hz *vs* 0-32 Hz for *cis*-vinyl fluorines). The characteristic 19.5 Hz coupling between the vinyl-$CF_3$ and *cis*-vinyl fluorine atom was also observed for compounds **2**. As expected, the coupling constant between the vinyl-$CF_3$ and *trans*-vinyl fluorine atom was less than 10 Hz [19b].

In conclusion, we have presented a new and useful preparation of fluorinated enynes *via* the palladium-catalyzed coupling reaction of fluorinated vinyl iodides with terminal alkynes in the presence of cuprous iodide. The ready availability of suitable catalysts and alkyne precursors, the simplicity of experimental procedure, and the mild reaction conditions make this direct approach to fluorinated enynes an attractive general entry into this class of partially fluorinated building blocks.

# EXPERIMENTAL

## General

All reactions were performed in an oven-dried apparatus that consisted of a two or three-necked flask equipped with an addition funnel, a Teflon coated magnetic stir bar and a reflux condenser connected to a nitrogen source and mineral oil bubbler. All boiling points were determined during fractional distillation using a partial immersion thermometer and are uncorrected. $^{19}F$ NMR and $^{1}H$ NMR spectra were recorded on a JEOL FX90Q spectrometer. All chemical shifts are reported in parts per million downfield (positive) of the standard. $^{19}F$ NMR (83.81 MHz) spectra are referenced against internal $CFCl_3$, $^{1}H$ NMR (89.09 MHz) spectra against internal tetramethylsilane. FT-IR spectra and IR spectra were recorded as $CCl_4$ solutions using a solution cell with 0.1 cm path length. GC-MS spectra were performed at 70 eV, in the electron impact mode. GLPC analyses were performed on a 5%OV-101 column with a thermal conductivity detector.

## Materials

**Z**-pentafluoropropenyl iodide [15], trifluoroethenyl iodide, **Z**-2-phenyl-1,2-difluoroethenyl iodide [20] and **E**-2-diisopropoxy-phosphinyl-1,2-difluoroethenyl iodide [21] were prepared according to literature methods. All terminal alkynes, palladium dichoride, and cuprous iodide were obtained from Aldrich Chemical Co., and used without further purification. Tetrakis(triphenylphosphine) palladium was prepared acoording to Coulson's procedure [22]. Triethylamine was purified by distillation from potassium hydroxide. HMPA, acetonitrile, chloroform, benzene, hexane, diglyme and dioxane were used without purification, while DMF and DMSO were purified by distillation from calcium hydride.

General procedure for the alkynylation of fluorinated vinyl iodides

Preparation of E-1,1,1,2,3-pentafluoro-2-decen-4-yne (**2d**)

A mixture of 2.0 g (21 mmol) of 1-heptyne, 5.2 g (20 mmol) of **1**, 0.70 g (1 mmol) of bis(triphenylphosphine)palladium dichloride and 0.19 g (1 mmol) of cuprous iodide in 30 mL of triethylamine was stirred at room temperature for 6 hours. The volatile components of the reaction mixture were removed *via* distillation at reduced pressure. The resulting mixture of triethylamine and enyne was slowly poured into 200 mL of 10% aqueous HCl. The organic layer was separated and the aqueous layer was extracted with ether (2×100 mL). The combined organic layers were washed with water and dried over anhydrous $MgSO_4$. After evaporation of the ether, the residue was distilled to give 2.8 g (62%) of **2d**, 100% GLPC purity, b.p. 116-118/80 mmHg. $^{19}F$ NMR($CDCl_3$): -68.2 (dd, J=19.5 Hz, J=12.2 Hz, 3F), -137.4 (dqt, J=139.2 Hz, J=19.5 Hz, J=4.9 Hz, 1F), -164.7 (dq, J=139.2 Hz, J=12.2 Hz, 1F); $^1H$ NMR($CDCl_3$): 2.46 (m, 2H), 1.58-1.32 (m, 6H), 0.93 (t, J=6.1 Hz, 3H); IR($CCl_4$): 2920 (s), 2225 (m), 1680 (m), 1270 (s), 1060 (s); MS: 226 ($M^+$, 0.6), 197 (53.2), 127 (44.0), 119 (59.1), 115 (53.2), 55 (100), 41 (75.9).

Preparation of E-3,4,5,5,5-pentafluoro-1-phenyl-3-penten-1-yne (**2a**)

Similarly, **2a** was prepared from 1.0 g (10 mmol) of $C_6H_5C{\equiv}CH$, 2.6 g (10 mmol) of **1**, 0.7 g (0.6 mmol) of $Pd(PPh_3)_4$, 0.2 g (1.1 mmol) of CuI and 2 mL of $Et_3N$ in 5 mL of DMF at 70°C for 20 hours. Usual work-up gave 1.2 g (53%) of **2a**, b. p. 72-73°C/6 mmHg, 99.6% GLPC purity. $^{19}F$ NMR($CDCl_3$): -68.1(dd, J = 19.5 Hz, J = 12.2 Hz, 3F), -139.0(dq, J = 141.6 Hz, J = 19.5 Hz, 1F), -161.6(dq, J = 141.6 Hz, J = 12.2 Hz, 1F), $^1H$ NMR($CDCl_3$): 7.43-7.45(m); IR($CDCl_3$): 3040(w), 2210(m), 1690(m), 1550(s), 1210(s), 1180(s), 1150(s); MS: 233($M^+$+1, 10.3), 232($M^+$, 100), 182(55.3), 143(15.5), 123(11.2), 69(16.9).

Preparation of E-1,1,1,2,3-pentafluoro-2-nonen-4-yne (**2c**)

Similarly, **2c** was prepared from 0.82 g (10 mmol) of 1-hexyne, 2.6 g (10 mmol) of **1**, 0.3 g (0.26 mmol) of $Pd(PPh_3)_4$, 0.2 g (1.1 mmol) of CuI and 2 mL of $Et_3N$ in 5 mL of DMF at 60°C for 48 hours. Usual work-up gave 1.8 g (86%) of **2c**. $^{19}F$ NMR($CDCl_3$): -68.3(dd, J=22.0 Hz, J=12.2 Hz, 3F), -137.4(dq, J=141.6 Hz, J=22.0 Hz, 1F), -164.8 (dq, J=141.6 Hz, J=12.2 Hz, 1F); $^1H$ NMR($CDCl_3$): 2.49 (m, 2H), 1.77-1.25 (m, 4H), 0.95 (m , 3H); IR($CCl_4$): 2985 (w), 2220 (m), 1685 (w), 1270 (s), 1175 (s), 1150 (s); MS: 212 ($M^{+\cdot}$ 43.2), 197 (77.1), 177 (52.8), 143 (90.2), 127 (77.9), 119 (100), 69 (85.9).

Preparation of E-1,1,1,2,3-pentafluoro-2-undecen-4-yne (**2e**)

Similarly, **2e** was prepared from 1.7 g (15.4 mmol) of 1-octyne, 3.9 g (15 mmol) of **1**, 1.1 g (1 mmol) of $Pd(PPh_3)_4$, 0.2 g (1.1 mmol) of CuI and 3 mL of $Et_3N$ in 8 mL of DMF at 70°C for 20 hours. Usual work-up gave 1.9 g (54%) of **2e**, b.p. 101-103°C/40 mmHg. $^{19}F$ NMR($CDCl_3$): -68.2 (dd, J=19.5 Hz, J=12.2 Hz, 3F), -137.2 (dq, J=141.6 Hz, J=19.5 Hz, 1F), -164.8 (dq, J=141.6 Hz, J=12.2 Hz, 1F); $^1H$ NMR($CDCl_3$): 2.46 (m, 2H), 1.32(m, 8H), 0.90(m, 3H); IR($CCl_4$): 2920(s), 2210(m), 1685(m), 1200-1150(vs), 1050(s); MS: 225($M^+$-$CH_3$, 3.9), 197(66.3), 177(50.7), 127(91.7), 119(100), 115(70.9), 69(79.9), 41(66.1).

Preparation of E-1,1,1,2,3-pentafluoro-2-dodecen-4-yne (**2f**)

Similarly, **2f** was prepared from 1.4 g (11 mol) of 1-nonyne, 2.6 g (10 mmol) of **1**, 0.35 g (0.5 mmol) of $Pd(PPh_3)_2Cl_2$, 0.11 (0.6 mmol) of CuI and 2 mL of $Et_3N$ in 8 mL of DMF at 50°C for 12 hours. Usual work-up gave 1.7 g (67%) of **2f**. $^{19}F$ NMR($CDCl_3$): -68.2(dd, J = 19.5 Hz, J = 12.2 Hz, 3F), -137.1(dqt, J =139.2 Hz, J = 19.5 Hz, J = 4.9 Hz, 1F), -164.7(dq, J 139.2 Hz, J = 12.2 Hz, 1F), $^1H$ NMR($CDCl_3$): 2.43(m, 2H), 1.53-1.30(m, 10H), 0.89(m, 3H), IR(CCl4): 2920(s), 2230(m), 1680(m), 1270(s), 1150(s), 1060(m); MS: 225($M^+$-$C_2H_5$, 1.2), 197(20.4), 115(25.2), 83(26.2), 69(18.7), 55(97.6), 43(84.1), 41(100).

Preparation of 3,4,4-trifluoro-1-phenyl-3-buten-1-yne (**5a**)

Similarly, **5a** was prepared from 1.1 g (11 mmol) of $C_6H_5C{\equiv}CH$, 2.1 g (10 mmol) of **4**, 0.35 g (0.5 mmol) of $Pd(PPh_3)_2Cl_2$, 0.11 g (0.6 mmol) of CuI, and 2 mL of $Et_3N$ in 5 mL of $CH_3CN$ at room temperature for 32 hours. Usual work-up gave 1.5 g (83%) of **5a**. $^{19}F$ NMR($CDCl_3$): -90.7(dd, J = 46.4 Hz, J = 26.9 Hz, 1F), -110.8(dd, J = 114.8 Hz, J = 46.4 Hz, 1F), -172.1(dd, J = 114.8 Hz, J = 26.9 Hz, 1F); $^1H$ NMR($CDCl_3$): 7.52-7.32(m); IR($CCl_4$): 3060(w), 2220(m), 1750(s), 1540(m), 1175(s), 1095(s); MS: 182($M^+$, 100), 132(42.6), 105(15.9), 69(14.4).

Preparation of 1,1,2-trifluoro-1-octen-3-yne (**5c**)

Similarly, **5c** was prepared from 0.9 g (11 mmol) of 1-hexyne, 2.1 g (10 mmol) of **4**, 0.045 g (0.2 mmol) of $Pd(OAc)_2$, 0.105 g (0.4 mmol) of $PPh_3$, 0.057 g (0.3 mmol) of CuI and 10 mL of $Et_3N$ at room temperature for 12 hours. Usual work-up gave 1.1 g (69%) of **5c**[11], b.p. 61-62°C/15 mmHg. $^{19}F$ NMR($CDCl_3$): -93.1(dd, J = 51.3 Hz, J = 26.9 Hz, 1F), -113.9(dd, J = 114.8 Hz, J = 51.3 Hz, 1F), -171.2(ddt, J = 114.8 Hz, J = 26.9 Hz, J = 4.9 Hz, 1F); $^1H$ NMR($CDCl_3$): 2.40(m, 2H), 1.54-1.48(m, 4H), 0.93(t, J = 6.6 Hz, 3H); IR($CCl_4$): 2930(s), 2230(m), 1760(s), 1290(s), 1140(s), 1010(m); MS: 162($M^+$, 23.7), 127(41.4), 119(33.3), 69(79.2), 43(72.0), 41(100).

Preparation of 1,1,2-trifluoro-1-nonen-3-yne (**5d**)

Similarly, **5d** was prepared from 7.2 g (75 mmol) of 1-heptyne, 14.6 g (70 mmol) of **4**, 1.4 g (2 mmol) of $Pd(PPh_3)_2Cl_2$, 0.67 g (3.5 mmol) of CuI, and 50 mL of $Et_3N$ at room temperature for 24 hours. Usual work-up gave 7.2 g (59%) of **5d**, b.p. 67-68°C/33 mmHg. $^{19}F$ NMR($CDCl_3$): -93.0(dd, J = 53.7 Hz, J = 26.9 Hz, 1F), -113.7 (dd, J = 114.7 Hz, J = 53.7 Hz, 1F), -170.9 (ddt, J = 114.7 Hz, J = 26.9 Hz, J = 4.9 Hz, 1F); $^1H$ NMR($CDCl_3$): 2.45(m, 2H), 1.51-1.38(m, 6H), 0.93(m, 3H); IR($CCl_4$):

2930(s), 2230(m), 1750(s), 1285(s), 1130(s); MS: 176($M^+$, 27.8), 127(54.4), 119(53.4), 69(100), 55(65.2).

Preparation of 1,1,2-trifluoro-1-decen-3-yne (**5e**)

Similarly, **5e** was prepared from 4.6 g (42 mmol) of 1-octyne, 8.3 g (40 mmol) of **4**, 0.56 g (0.8 mmol) of $Pd(PPh_3)_2Cl_2$, 0.2 g (1.1 mmol) of CuI and 30 mL of $Et_3N$ at room temperature for 12 hours. Usual work-up gave 5.1 g (66%) of **5e**, b.p. 54-55°C/5.8 mmHg, 100% GLPC purity. $^{19}F$ NMR($CDCl_3$): -93.0(dd, J = 51.3 Hz, J = 26.9 Hz, 1F), 114.0(dd, J = 114.8 Hz, J = 51.3 Hz, 1F), -171.2(ddt, J = 114.8 Hz, J = 26.9 Hz, J = 4.9 Hz, 1F); $^1H$ NMR($CDCl_3$): 2.44(m, 2H), 1.30(m, 8H), 0.91(m, 3H); IR($CCl_4$): 2930(s), 2220(m), 1755(s), 1285(s), 1130(s); MS: 190($M^+$, 2.0), 119(7.7), 97(6.8), 69(25.3), 43(100), 41(65.10).

Preparation of 1,1,2-trifluoro-1-undecen-3-yne (**5f**)

Similarly, **5f** was prepared from 2.7 g (22 mol) of 1-nonyne, 4.2 g (20 mmol) of **4**, 0.28 g (0.4 mmol) of $Pd(PPh_3)_2Cl_2$, 0.1 g (0.5 mmol) of CuI and 30 mL of $Et_3N$ at room temperature for 24 hours. Usual work-up gave 2.4 g (59%) of **5f**, b.p. 68-70°C/10 mmHg. $^{19}F$ NMR($CDCl_3$): -93.1(dd, J = 51.7 Hz, J = 26.9 Hz, 1F), -114.0(dd, J = 114.8 Hz, J = 51.7 Hz, 1F), -171.1(ddt, J = 114.8 Hz, J = 26.9 Hz, J = 4.9 Hz, 1F); $^1H$ NMR($CDCl_3$): 2.46(m, 2H), 1.47-1.3(m, 10H), 0.93(t, J = 5.9 Hz, 3H); IR($CCl_4$): 2920(s), 2230(m), 1755(s), 1280(s), 1135(s); MS: 204($M^+$, 7.6), 127(41.2), 119(42.6), 69(63.1), 55(95.8), 41(100).

Preparation of E-1,1,1,2,3-pentafluoro-2-octen-4-yne (**2b**)

A 50 mL ROTAFLO tube with a cap fitted with a stir bar was charged with 0.1 g (0.5 mmol) of CuI, 0.35 g (0.5 mmol) of $Pd(PPh_3)_4$, 0.70 g (10.3 mmol) of pentyne, 2.6 g (10 mmol) of **1**, 2 mL of $Et_3N$ and 10 mL of DMF. The tube was cooled in liquid nitrogen, degassed and

sealed. The reaction mixture was stirred at 75°C for 4 hours. Usual work-up gave 1.2 g (61%) of **2b**., b. p. 112-113°C, 96% GLPC purity. $^{19}F$ NMR($CDCl_3$): -68.2 (dd, J=19.5 Hz, J=12.2 Hz, 3F), -137.9 (dqt, J=139.2 Hz, J=19.5 Hz, J=4.9 Hz, 1F), -164.7 (dq, J=139.2 Hz, J=12.2 Hz, 1F); $^1H$ NMR($CDCl_3$): 2.46 (m, 2H), 1.64 (m, 2H), 1.05 (t, J=6.8 Hz, 3H); IR($CCl_4$): 2950 (m), 2220 (m), 1685 (s), 1200-1150 (s), 1020 (m); MS: 198 ($M^+$,31.4), 129 ($M^+$-$CF_3$, 73.0), 127 (93.2), 119 (69.0), 109 (100), 99 (60.6), 81 (59.0), 69 (84.3).

Preparation of 1,1,2-trifluoro-1-hepten-3-yne (**5b**)

Similarly, **5b** was prepared from 1.1 g (16 mmol) of 1-pentyne, 3.1 g (15 mmol) of **4**, 0.5 g (0. 75 mmol) of $Pd(PPh_3)_2Cl_2$, 0.14 g (7 mmol) of CuI and 3 mL of $Et_3N$ and 10 mL of $CH_3CN$ at room temperature for 3 days. Usual work-up gave 1.1 g (51%) of **5b**. $^{19}F$ NMR($CDCl_3$): -93.1(dd, J = 53.7 Hz, J = 26.8 Hz, 1F), -113.9 (dd, J = 114.7 Hz, J = 53.7 Hz, 1F), -171.2 (dd, J = 114.7 Hz, J = 26.8 Hz, 1F); $^1H$($CDCl_3$): 2.41(m, 2H), 1.59(m, 2H), 1.02(m, 3H); IR($CCl_4$); 2985(s), 2220(m), 1685(s), 1270(s), 1150(s), 1065(m); MS: 148($M^+$, 73.2), 127(31.9), 119(100), 97(40.4), 69(89.5).

Preparation of E-3,4,5,5,5-pentafluoro-1-trimethylsilyl-3-penten-1-yne (**2g**)

A 50 mL ROTAFLO tube fitted with a stir bar was charged with 0.35 g (0.5 mmol) of $Pd(PPh_3)_2Cl_2$, 0.085 g (0.5 mmol) of CuI, 12 mL of $Et_3N$, 1.2 g (12 mmol) of trimethylsilylacetylene and 3.1 g (10 mmol) of **1**. The tube was cooled in liquid nitrogen, evacuated and sealed. After being stirred at 70°C for 6 hours, the reaction mixture was poured into 200 mL of ether and 100 mL of water. The ether layer was separated and washed with water (3×100 mL), 1% hydrochloric acid (2×100 mL), water (100 mL) and dried over $MgSO_4$. After evaporation of the ether, the residue was distilled to give 1.0 g (43%) of **2g**, b.p. 105-107°C. $^{19}F$ NMR($CDCl_3$): -68.4(dd, J = 22.0 Hz, J = 12.2 Hz, 3H), -139.9(dq, J = 141.6 Hz, J = 22.0 Hz, 1F), -161.8(dq, J = 141.6 Hz, J = 12.2 Hz, 1F); $^1H$

NMR($CDCl_3$): 0.28(s); IR($CCl_4$): 2966(m), 2069(w), 1692(m), 1367(s), 1205(s), 1157(s), 980(s); MS: 228($M^+$, 2.7), 213(27.7), 132(14.0), 81(33.2), 74(74.7), 69(4.2), 63(29.6), 59(100), 45(85.4).

Preparation of E-3,4-difluoro-1,4-diphenyl-3-buten-1-yne (7)

A mixture of 0.71 g (7 mmol) of phenylacetylene, 1.3 g (5 mmol) of **6**, 0.07 g (0.1 mmol) of $Pd(PPh_3)_2Cl_2$, 0.02 g (0.1 mmol) of CuI and 10 mL of $Et_3N$ was stirred at room temperature for 4 hours. $Et_3N$ was removed by distillation at reduced pressure and a mixture of hexane and ether was added. The mixture was washed with 5% of hydrochloric acid and water, and dried over $MgSO_4$. After evaporation of the solvents, the residue was purified by flash chromatography on silica gel (eluent: hexane) to give 0.88 g (73%) of **7**. $^{19}F$ NMR($CDCl_3$): -145.2(d, J = 134.3 Hz, 1F), -148.4(d, J = 134.2 Hz, 1F); $^1H$ NMR($CDCl_3$): 7.76-7.33(m); IR($CCl_4$): 3063(w), 2202(m), 1490(s), 1160(s), 818(s), 787(s); MS: 241($M^+$+1, 15.3), 240($M^+$, 100), 238(61.1), 202(25), 119(13.7), 85(51.6).

Preparation of Z-4-diisopropoxyphosphinyl-3,4-difluoro-1-phenyl-3-buten-1-yne (**9a**)

A mixture of 0.61 g (6 mmol) of phenylacetylene, 1.7 g (5 mmol) of **8**, 0.07 g (0.1 mmol) of $Pd(PPh_3)_2Cl_2$, and 0.02 g (0.1 mmol) of CuI in 10 mL of $Et_3N$ was stirred at room temperature for 3 hours. The $Et_3N$ was evaporated in vacuo and ether was added. Solids were filtered and washed with ether. The ether layer was washed with 5% hydrochloric acid, water, and dried over $MgSO_4$. After evaporation of the ether, the residue (1.6 g) was purified by flash chromatography on silica gel (eluent: hexane:ethyl acetate = 8:2) to give 1.4 g (87%) of **9a**. $^{19}F$ NMR($CDCl_3$): -133.7(dd, J = 146.5 Hz. J = 14.6 Hz, 1F), -156.0(dd, J = 146. 5 Hz, J = 83.0 Hz, 1F); $^1H$ NMR($CDCl_3$): 7.43(m, 5H), 4.79(m, 2H), 1.39(m, 12H); IR($CCl_4$): 3050(w), 2980(s), 2210(m), 1645(m), 1555(m), 1230(s), 1160(s), 1010(s); MS: 328($M^+$, 7.7), 244(100), 180(14.6), 151(27.7), 132(24.1), 43(7.9).

Preparation of Z-1-diisopropoxyphosphinyl-1,2-difluoro-1-decen-3-yne (**9b**)

Similarly, **9b** was prepared from 0.66 g (6 mmol) of 1-octyne, 1.77 g (5 mmol) of **8**, 0.07 g (0.1 mmol) of $Pd(PPh_3)_2Cl_2$, 0.02 g (0.1 mmol) of CuI and 10 mL of $Et_3N$ at room temperature. Usual work-up gave 1.1 g (77%) of **9b**. $^{19}F$ NMR($CDCl_3$): -131.6(dd, J = 146.5 Hz, J = 14.7 Hz, 1F), -159.5(dd, J = 146.5 Hz, J = 83.0 Hz, 1F); $^1H$ NMR($CDCl_3$): 4.73-4.66(m, 2H), 2.42(m, 2H), 1.42-1.32(m, 20H), 0.90(m, 3H); IR($CCl_4$): 2930(s), 2220(m), 1640(m), 1270(s), 1165(s), 1090(s), 1000(s); MS: 336($M^+$, 3.9), 279(14.6), 182(46.7), 107(100), 69(18.3), 65(57.2), 43(91.5), 41(58.7).

Preparation of E,E-1,1,1,2,3,12,13,14,14,14-decafluoro-2,12-tetradecadien-4,10-diyne (**3**)

A mixture of 3.5 g (33 mmol) of 1,7-octadiyne, 15.5 g (60 mmol) of **1**, 1.1 g (1.6 mmol) of $Pd(PPh_3)_2Cl_2$ and 0.4 g (2 mmol) of CuI in 40 mL of $Et_3N$ was stirred at 55°C for 4 hours. Usual work-up gave the residue, which was distilled to give 5.4 g (49%) of **3**, b.p. 88-89°C/2 mmHg. $^{19}F$ NMR($CDCl_3$): -68.3(dd, J = 22.0 Hz, J = 12.2 Hz, 3F), -138.0(dq, J = 141.6 Hz, J = 22.0 Hz, 1F), -164.1 (dq, J = 141.6 Hz, J = 12.2 Hz, 1F); $^1H$ NMR($CDCl_3$): 2.52(m, 4H), 1.77(m, 4H); IR($CCl_4$): 2940(m), 2225(m), 1680(m), 1265(s), 1150(s), 1060(s); MS: 366($M^+$, 0.3), 228(31.9), 169(27.0), 1279(45.7), 119(100), 81(30.9), 69(61.8).

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