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Selective Ene-Yne Coupling-Functionalization: A New Strategy in Constructing Heterocycles

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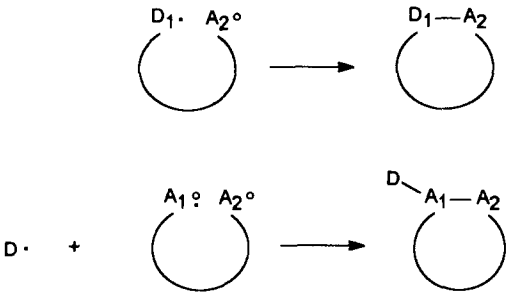
Abstract: Fluorinated derivatives of 3-alkylidene-2(3H)-dihydrofuranone have been synthesized by sodium dithionite initiated tandem perfluoroalkylation-cyclization of allylic 2-alkynoates in fair to good yield and high stereoselectivity. Fluorinated 3-alkylidene-2(3H)-pyrrolidone derivatives were prepared similarly. A mechanistic rationale concerning the different radical steps and the differences between esters and amides was given.

INTRODUCTION

Heterocyclic compounds play important roles in diverse living processes.[1,2] They make up a large class of biologically active species, either natural or artificial. Among them fluoroheterocyclic compounds are especially important because of the significant effect conferred upon molecules by introduction of fluorine atoms.[3-5] For example, the synthetic fluoroanalogs of adenine nucleosides have promising potential as clinical agents,[5a] while 2-fluorourocanic acid shows obvious changes in its inhibitory behavior toward protoenzymes.[5b]

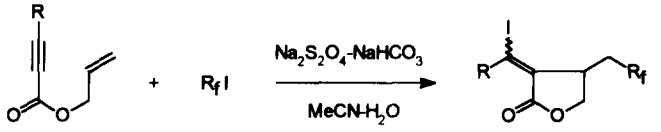
3-Alkylidene-2(3H)-dihydrofuranone (also known as α-alkylidene-γ-butyrolactone) is an integral building block of many biologically active natural products in which the exocyclic double bond is considered to be responsible for their interesting properties.[6] The aza-analog, 3-alkylidene-2(3H)-pyrrolidone, is another important structural unit occurring in nature.[7] Cytotoxic and antitumor activities were frequently reported for compounds of these two classes[6,7] and much interest has been aroused in the synthetic and biological study of these structures. Considering the special properties of many fluorine-containing compounds, synthesizing fluorinated or polyfluoroalkylated derivatives of 3-alkylidene-2(3H)-dihydrofuranone and 3-alkylidene-2(3H)-pyrrolidone might be very promising in these studies.

Radical cyclization is now a well-established method for ring construction, as confirmed by many successful syntheses.[8,9] However, most cases required that the radical precursor and acceptor to which the radical cyclizes be precedently assembled in the substrate, which may cause circumstantial route during synthesis.[10] As effectiveness is concerned, we may prefer to another strategy, in which a radical donor D from outside of the substrate promotes the cyclization (Scheme I, second equation). To accomplish this, the



Scheme I

radical donor D should add to one of the radical acceptors selectively. Lee et al.[11] reported a radical cyclization of allylic 2-alkynoates in which a tin radical selectively added to the electron-deficient triple bond and promoted the cyclization. In a preliminary communication,[12] we reported a facile synthesis of polyfluoroalkylated 3-iodoalkylidene-2(3H)-dihydrofuranone making use of the preferential addition of perfluoroalkyl radicals generated from ET reaction of R_fI with $Na_2S_2O_4$ to electron-rich π bond (Equation 1). In this paper, we further discuss the application of this method in preparing polyfluoroalkylated derivatives of



(Equation 1)

1 **2** **3**

1A: R=H
1B: R=CH_3
1C: R=n-C_8H_{17}

2a: R_f=CF_3
2b: R_f=$Cl(CF_2)_2$
2c: R_f=$Cl(CF_2)_4$
2d: R_f=$Cl(CF_2)_8$

	Yield	E : Z
3Aa	44	32 : 68
3Ab	47	60 : 40
3Ac	50	52 : 48
3Ba	80	95 : 5
3Bb	83	>97 : 3
3Bc	82	>97 : 3
3Bd	92	>97 : 3
3Cb	60	>97 : 3
3Cc	62	>97 : 3

other heterocycles, such as 3-alkylidene-2(3H)-pyrrolidone. The detailed mechanism and the scope of this reaction will also be discussed.

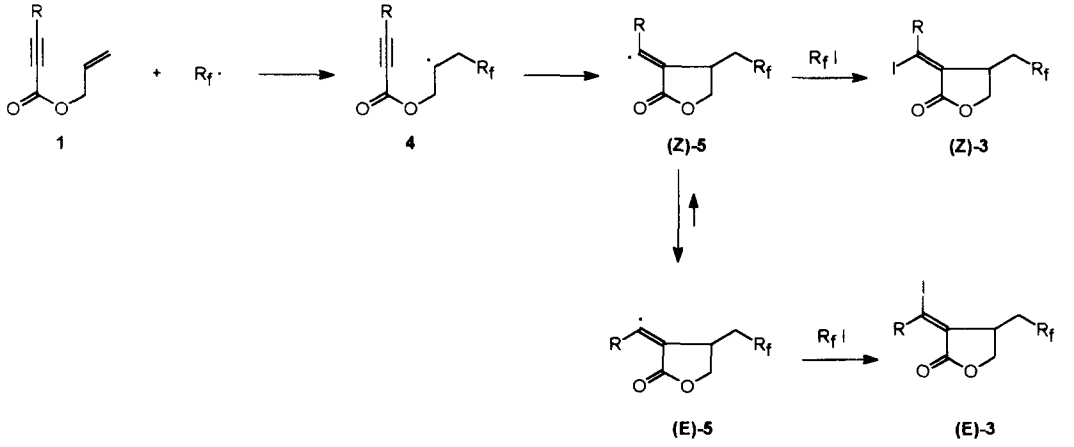
RESULTS AND DISCUSSION

The perfluoroalkylation-cyclization reaction proceeds well for different allyl 2-alkynoates. When allyl 2-alkynoates were subjected to a normal $Na_2S_2O_4$-$NaHCO_3$ initiated perfluoroalkylation[13] (e.g., equimolar R_fI **2** (R_f =CF_3, $Cl(CF_2)_2$, $Cl(CF_2)_4$, $Cl(CF_2)_8$), slightly excess sodium dithionite and sodium bicarbonate were reacted with allyl 2-alkynoate **1** at 10-15°C in aqueous acetonitrile), complete consumption of **1** was achieved within a few minutes giving 3-iodoalkylidene-4-polyfluoroalkyl-2(3H)-dihydrofuranone **3**.

For substrates with a non-terminal triple bond, such as allyl 2-butynoate **1B** and allyl 2-undecynoate **1C**, fair to good yields of products were obtained. For allyl propynoate (**1A**) in which a terminal triple bond was present, yield was somewhat lower probably due to radical induced side reactions.[14]

The stereochemistry of the exocyclic double bond in **3** was established by comparing the chemical shifts of allylic protons (R=CH_3 or n-C_8H_{17}) or the vinylic proton (R=H).[15] **1B** and **1C** gave single isomer except in the case where **1B** was reacted with CF_3I **2a,** two isomers were isolated in 95:5 ratio. In the ^1H NMR spectra of the major products, the allylic protons showed signals at δ 3.10 and δ 3.3 for **3Ba** and **3Cb** respectively, indicating an (E)-configuration for the exocyclic double bond. **1A** gave comparable amounts of two isomers when reacted with **2a**, **2b** or **2c**. The δ 8.00 and δ 7.48 chemical shifts on ^1H NMR spectra of **3Aa** were assigned to E and Z isomer respectively.

The mechanism was briefly discussed in the previous paper as follows (Scheme II). Unlike the tin radical

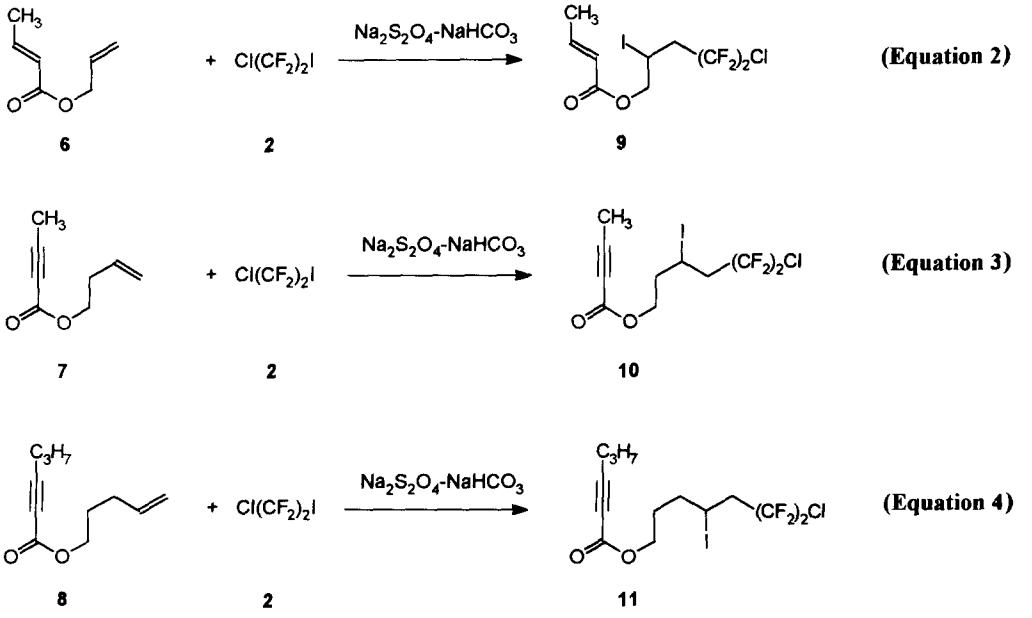


Scheme II

in Lee's report[11], a perfluoroalkyl radical preferentially adds to the relatively electron-rich double bond due to its nucleophilicity to form **4**, and then the sequential radical cyclization, iodione-atom abstraction gave the

product **3**. Here, the preliminary equilibrium of **5** which favored (E)-**5** accounted for the high stereoselectivity obtained for **1B** and **1C**. To better understand the mechanism of this radical process, further studies were carried out in our laboratory.

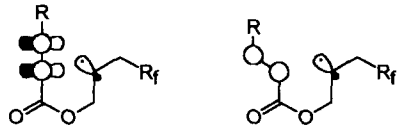
The Radical Cyclization Step. Cyclization of **4** to **5** was the key step to construct the furanone ring. Several model experiments were tested using other substrates. But when molecules of similar structures such as allyl 2-butenoate **6**, homoallyl 2-butynoate 7 and bishomoallyl 2-hexynoate **8** were applied, they all gave simple addition products, and no cyclization products were detected (Equations 2-4).



The unease to form six- and seven-membered ring could be similarly understood as the fact that 6-heptenyl and 7-octenyl radicals cyclize at rather low rate compared to a 5-hexenyl radical.[16] When this applies, the competing iodine abstraction pathway would take control and give acyclic products. While the failure of perfluoroalkylation-cyclization of allyl 2-butenoate could be rationalized by the higher activation energy for a 3-oxa-4-oxo-5-enyl radical to cyclize.[17]

It is the difference between allyl 2-alkynoates and allyl 2-alkenoates that is especially noteworthy in this cyclization. The special property of an electron-deficient alkyne might account for its success in the cyclization step. Unlike an electron-deficient alkene analog, the triple bond in the alkyne could provide two orthogonal π-bonds for the possible cyclization. While **12** must adopt an unfavorable conformation to accomplish the overlap of the radical SOMO and the π-orbital of the double bond, **4** could easily achieve the steric arrangement for

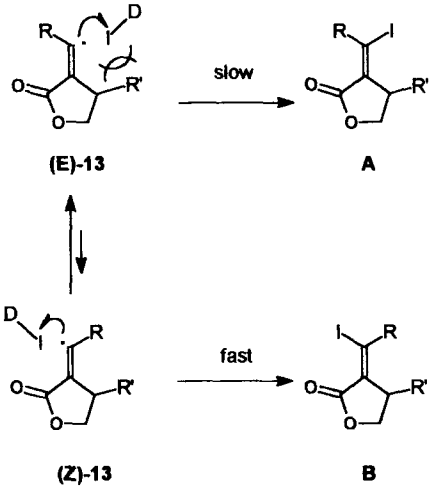
cyclization without disturbing the stabilizing conjugation between the triple bond and the carbonyl group (Figure 1).



4 12

Figure 1

The Iodine-Atom Transfer Step. Iodine-atom transfer from the per(poly)fluoroalkyl iodide to the vinyl radical **5** (Scheme II) completed the chain transfer step and this step is responsible for the stereoselectivity in the product. In a chain transfer step outlined as follows (Scheme III), two conflicting factors are responsible for the stereochemical control: 1) The relative stability of (E)-**13** and (Z)-**13** (thermodynamic control favoring A);[18a] 2) The relative rate of iodine abstraction by (E)-**13** and (Z)-**13** (kinetic control favoring B).[18b] In Curran's

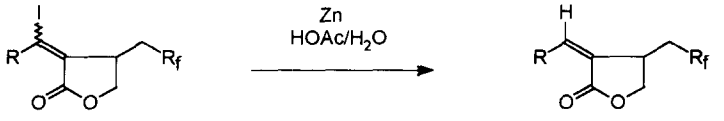


Scheme III

work, the kinetic factors predominated and mainly gave B type products which was ascribed to a diffusion-controlled fast iodine transfer step, or sometimes gave rise to low selectivity when the difference of thermostability became more important.[19] In our case, the stereoselectivity was reversed and high selectivity was obtained for A type products when R^1 (see Scheme III) is CH_3 or n-C_8H_{17}, while comparable amounts of A and B type products were formed when R^1=H. This suggests that the stereoselectivity was governed by the

preliminary equilibrium between (E)-**13** and (Z)-**13** which might result from the slow iodine atom transfer from per(poly)fluoroalkyl iodides.[12] The electrostatic repulsion between the iodine-donor and the carbonyl oxygen in (Z)-**13** may also be responsible for preferential formation of A isomer.

Reduction of the fluorinated 3-iodoalkylidene-2(3H)-dihydrofuranones **3** was achieved by acidic reduction with zinc according to literature method[20] and 3-alkylidene-2(3H)-dihydrofuranone derivatives **14** were obtained in fair yield (Equation 5). When (E)-**3Bc** was reduced, the product had (Z)-configuration implying retention of stereochemistry during zinc reduction. The determination of the double bond configuration was again based on the comparison of the chemical shift of CH_3 in **14Bc** with known compounds[21]. The biological study of this novel type of fluorine-containing furanone compounds is now underway due to the potential biological activity they might possess.



3 **14**

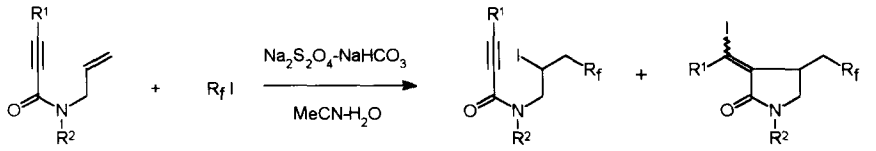
(Equation 5)

(E, Z)-3Aa: R=H, R_f =CF_3 **14Aa:** 67%
(E)-3Bc: R=CH_3, R_f =$Cl(CF_2)_4$ **(Z)-14Bc:** 70%

Perfluoroalkylation of N-allyl 2-alkynamides was carried out using N-allyl 2-propynamide and N-allyl 2-butynamide as substrates. Different from allyl alkynoates, these substrates gave only simple addition products and no cyclization products were formed. This prompted us to examine N-substituted N-allyl 2-alkynamides. When the substituent on N was an alkyl group, the reaction gave both acyclic and cyclic fluoroalkylation products, and when N was blocked by an electron-withdrawing group, only cyclic products were obtained. By this way, we succeeded in synthesizing polyfluoroalkylated 3-alkylidene-2(3H)-pyrrolidone. The results are listed in Table 1.

The mechanism of perfluoroalkylation of N-allyl 2-alkynamide is given below resembling the allyl alkynoate protocol (Scheme IV). It is reasonable for us to assume**18** to be the common intermediate leading to both acyclic product **16** and cyclic product **17**. Since both iodine abstraction and cyclization steps are irreversible,[19a] this cyclization versus non-cyclization selectivity is governed by the relative rate of the two radical processes. From our results, the following conclusion could be drawn: the intermediates from amides with an electron- withdrawing group cyclize faster than they abstract iodine atom, while those from amides with an alkyl group cyclize and abstract iodine at comparable rates. We deduced that the substituent on N affected the cyclization of intermediate **18** through conformational control.

Table 1 Sodium Dithionite-Sodium Bicarbonate Initiated Perfluoroalkylation of N-Allyl 2-alkynamides 15. [a]



15 2 16 17

entry	15		2	16[b]	17[b]	
	R^1	R^2	R_f	Yield (%)[c]	Yield (%)[c]	E : Z[d]
1	H	H(**15A**)	$Cl(CF_2)_4$(**2c**)	41	0	-
2	CH_3	H(**15B**)	$Cl(CF_2)_4$(**2c**)	67	0	-
3	CH_3	CH_3(**15C**)	$Cl(CF_2)_2$(**2b**)	19	53	>97 : 3
4	CH_3	Bn(**15D**)	$Cl(CF_2)_2$(**2b**)	35	50	>97 : 3
5	CH_3	Bn(**15D**)	$Cl(CF_2)_4$(**2c**)	29	49	>97 : 3
6	n-C_3H_7	Bn(**15E**)	$Cl(CF_2)_2$(**2b**)	23	41	>97 : 3
7	n-C_3H_7	Bn(**15E**)	$Cl(CF_2)_4$(**2c**)	27	43	>97 : 3
8	H	CH_3CO(**15F**)	$Cl(CF_2)_2$(**2b**)	0	46	52 : 48
9	CH_3	PhCO(**15G**)	$Cl(CF_2)_2$(**2b**)	0	70	>97 : 3
10	CH_3	PhCO(**15G**)	$Cl(CF_2)_4$(**2c**)	0	60	>97 : 3
11	CH_3	Tosyl(**15H**)	CF_3 (**2a**)[e]	0	72	>97 : 3
12	CH_3	Tosyl(**15H**)	$Cl(CF_2)_4$(**2b**)	0	83	>97 : 3

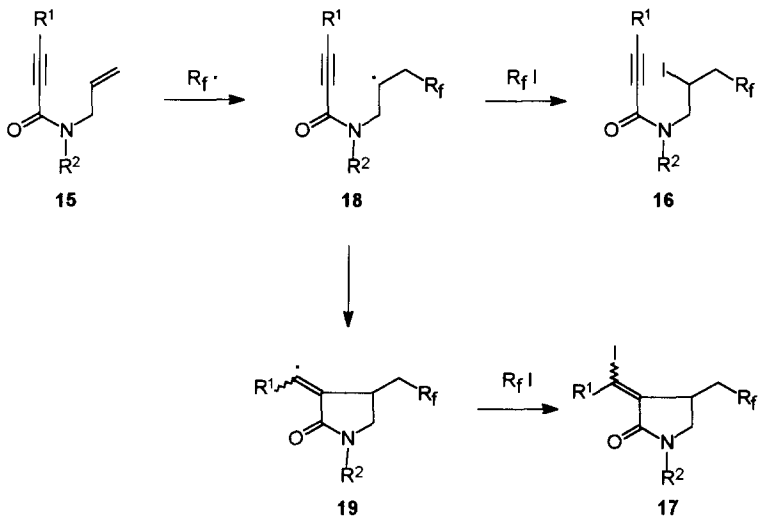
a. Reaction condition. A mixture of **15** (1.0mmol), **2** (1.0mmol), $Na_2S_2O_4$ (208mg, 1.2mmol), $NaHCO_3$ (100mg, 1.2mmol), MeCN (3mL) and water (2mL) was stirred at 10-15°C.

b. The structures of the products were determined by ^1H NMR, ^{19}F NMR, IR, MS data and microanalysis.

c. Isolated yield.

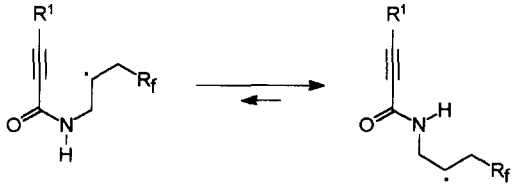
d. The E/Z ratios were determined by ^1H NMR spectra.

e. The gaseous CF_3I was passed into the mixture of **15**, $Na_2S_2O_4$ and $NaHCO_3$ in aqueous acetonitrile.



Scheme IV

Conformational Study of N-Substituted 2-Alkynamides. In N-monosubstituted amides, the C-N bond conformation has been extensively studied and a strong preference for trans-conformer over cis was established by different groups using various methods.[22] For this reason, the trans-conformer of intermediate **18A** or **18B** is the only existing form in the reaction (Scheme V). This rotamer, with a radical centre far apart from the triple bond, is incapable of cyclizing, so **15A** and **15B** with N-unblocked gave only acyclic perfluoroalkylation products.

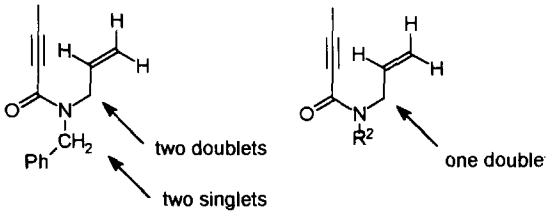


18A: R^1=H
18B: R^1=CH_3

Scheme V

Although the conformational study of N-monosubstituted amides was conclusive, conclusions regarding N,N-disubstituted amides are somewhat controversial,[23] and the study on amides with two substituents of different electronic properties is rare.

In the ^{1}H NMR spectra of a series of N-allyl 2-alkynamides, we found two types of resonance patterns at room temperature: in **15D**, two singlets (δ 4.75 and 4.60 in 1.08: 1 ratio) and two doublets (δ 3.90, J=5Hz and 3.73, J=6Hz, 1 : 1.08) appeared for the benzylic methylene and allylic methylene corresponding to two rotational isomers of the amide. While in **15G** and **15H**, only one doublet appeared for the allylic CH_2 (δ 4.26, J= 6Hz for **15G** and 4.50, J=5Hz for **15H**), indicating a freely rotating conformation (Figure 2) (see also the experimental section). Based on this obversation and literature data,[23] we concluded that the rotational barrier for **15D** was greater than that for **15G** and **15H**.[24]



15D

15G: R^2=PhCO
15H: R^2=Tosyl

Figure 2

Wiberg[25] studied the substituent effect on the conformation of an amide C-N bond using MO calculations and in his opinion, the rotational barrier was stemmed in the electron donation from the nitrogen to the carbonyl carbon atom. In our observation, tertiary amides with two electron-donating substituents on nitrogen (like **15D**) have a higher barrier to rotate than those with one electron-withdrawing group such as **15G** and **15H**, and this is consistent with Wiberg's theory.

Since an N-alkyl substituted N-allyl 2-alkynamide exists as cis- and trans-conformers which can not interconvert at ambient temperature, the radical intermediate generated from it will also be in such two forms. The cis-radical cyclizes leaving the trans-radical abstracting iodine directly. Thus the N-alkyl substituted N-allyl 2-alkynamides **15C**, **15D** and **15E** gave both cyclic and acyclic products.

An N-acyl subsituted or N-tosyl substituted amide intermiate, on the other hand, was able to rotate freely around the amide C-N bond under our experiment conditions. When the iodine transfer pathway was not very competitive, the trans-radical preferentially converted to cis-conformation and cyclized to give polyfluoroalkylated 3-iodoalkylidene-2(3H)-pyrrolidone product, as was in our case.

In summary, we have developed a facile route to polyfluoroalkylated 3-alkylidene-2(3H)-dihydrofuranone and polyfluoroalkylated 3-alkylidene-2(3H)-pyrrolidone derivatives starting from readily available materials and reagents. We found that a quick 5-exo-dig radical cyclization to triple bond and a slow iodine-atom transfer to vinyl radical were responsible for the success in this selective cyclization. In addition, the mechanism through which the substituent on N in an N-allyl 2-alkynamide controlled the radical cyclization was also studied.

Further study including the scope of this ene-yne coupling-functionalization strategy and the application of the perfluoroalkylation-cyclization reaction in the synthesis of natural product analogs is underway.

EXPERIMENTAL SECTION

General Methods. Melting points are uncorrected. IR spectra were run on a Shimadzu IR440 instrument. ^{1}H NMR were recorded with TMS as internal standard on a Varian EM360 or an Bruker XL300 spectrometer. ^{19}F NMR spectra were recorded on an Varian EM356 spectrometer using $CFCl_3$ as external standard. MS data (EI) were obtained on a Finnigan 4201 spectrometer and HRMS data were obtained on an Finnigan MAT 8430 spectrometer. The analytical samples were further purified by recrystalization or column chromatography. The liquid samples were further purified by Kugelrohr distillation at the specified oven temperature (ot).

Materials. Allyl 2-propynoate (**1A**),[26a] allyl 2-butynoate (**1B**)[26a], allyl 2-undecynoate (**1C**),[26b] allyl (E)-2-butenoate(**6**),[26b] homoallyl 2-butynoate(**7**)[26b] and bishomoallyl 2-hexynoate(**8**)[26b] were prepared as reported. Trifluoromethyl iodide[27] was generated from silver trifluoroacetate and iodine using literature method.

General Procedure for the Reaction of Allylic 2-Alkynoates (1) with Per(poly)fluoroalkyl Iodides (2). To a stirred solution of per(poly)fluoroalkyl iodide **2** (1.0mmol) and allyl 2-alkynoate **1** (1.0mmol) in a mixed solvent of acetonitrile (3mL) and water (2mL), was added sodium bicarbonate (100mg, 1.2mmol) and sodium dithionite (208mg, 1.2mmol). Stirring was continued at 10-15°C until TLC monitoring showed complete conversion of the allyl 2-alkynoate. The resulting mixture was diluted with water (4mL) and extracted with ethyl ether (5mL × 3). The combined organic layer was washed with brine (5mL × 2), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography (eluent: petroleum ether / ethyl acetate = 9 / 1) on silica gel to give 4-polyfluoroalkyl-3-iodoalkylidene-2(3H)-dihydrofuranone **3**.

(Z)-3-Iodomethylene-4-(2',2',2'-trifluoroethyl)-2(3H)-dihydrofuranone (Z-3Aa) mp 83-84°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 7.48(d, J=1.9Hz, 1H), 4.49(dd, J=9.4, 8.8Hz, 1H), 4.06(dd, J=9.4, 6.0Hz, 1H), 3.5-3,35(m, 1H), 2.60-2.45(m, 1H), 2.45-2.30(m, 1H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -63.7(m, 3F) ppm; IR

(KBr): 3050, 2920, 1760, 1620, 1280, 620 cm^{-1} ; MS m/e(%): 306(M^+)(100), 276(11), 248(16), 149(8.4), 127(12). HRMS Calcd for $C_7H_6F_3IO_2$: 305.9364. Found: 305.9345.

(E)-3-Iodomethylene-4-(2',2',2'-trifluoroethyl)-2(3H)-dihydrofuranone (E-3Aa) mp 45-47°C. ^1H NMR(300MHz/$CDCl_3$) δ 8.00(d, J=1.9Hz, 1H), 4.49(dd, J=9.9, 6.8Hz, 1H), 4.42(dd, J=9.9, 2.4Hz, 1H), 3.45-3.35(m, 1H), 2.82-2.62(m, 1H), 2.44-2.25(m, 1H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -64.0(m, 3F) ppm; IR (KBr): 3050, 2920, 1765, 1640, 1280, 715cm^{-1} ; MS m/e(%): 306(M^+)(100), 276(19), 248(21), 179(4.1), 149(19), 127(10); HRMS Calcd for $C_7H_6F_3IO_2$: 305.9364. Found: 305.9332.

(Z)-3-Iodomethylene-4-(2'-chlorotetrafluoroethylmethyl)-2(3H)-dihydrofuranone (Z-3Ab) mp 81-83°C. ^1H NMR(300MHz/$CDCl_3$) δ 7.53(d, J=2.2Hz, 1H), 4.56(dd, J=9.4, 8.6Hz, 1H), 4.08(dd, J=9.4, 6.1Hz, 1H), 3.65-3.45(m, 1H), 2.6-2.2(m, 2H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -71.0(m, 2F), -112.5(m, 2F) ppm; IR (KBr): 3030, 2900, 1765, 1640, 1210, 750, 600cm^{-1} ; MS m/e(%): 374[$M^+(^{37}Cl)$] (38), 372[$M^+(^{35}Cl)$](100), 342(9.5), 314(20), 187(35), 151(32), 127(9.5); HRMS Calcd for $C_8H_6ClF_4IO_2$: 371.9036. Found: 371.9003.

(E)-3-Iodomethylene-4-(2'-chlorotetrafluoroethylmethyl)-2(3H)-dihydrofuranone (E-3Ab) mp 60-62°C. ^1H NMR(300MHz/$CDCl_3$) δ 8.01(d, J=2.1Hz, 1H), 4.52(dd, J=9.8, 7.3Hz, 1H), 4.44(dd, J=9.8, 2.1Hz, 1H), 3.60-3.45(m, 1H), 2.86-2.60(m, 1H), 2.47-2.23(m, 1H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -71.0(m, 2F), -112.6(m, 2F) ppm; IR (KBr): 3050, 1760, 1630, 1270, 740, 530cm^{-1} ; MS m/e(%): 374[$M^+(^{37}Cl)$](36), 372[$M^+(^{35}Cl)$](100), 342(7.8), 328(4.3), 314(23), 187(30), 127(8.0); HRMS Calcd for $C_8H_6ClF_4IO_2$: 371.9036. Found: 371.9085.

3-Iodomethylene-4-(4'-chlorooctafluorobutylmethyl)-2(3H)-dihydrofuranone (3Ac) mp 38-39°C. ^1H NMR(300MHz/$CDCl_3$) δ 8.03{d, J=1.9Hz, 0.52H[(E)-isomer]}, 7.50{d, J=2.4Hz, 0.48H[(Z)-isomer]}, 4.54{dd, J=9.4, 7.8Hz, 0.48H[(Z)-isomer]}, 4.52{dd, J=9.9, 5.5Hz, 0.52H[(E)-isomer]}, 4.40{dd, J=9.9, 2.3Hz, 0.52H[(E)-isomer]}, 4.07{dd, J=9.4, 6.2Hz, 0.48H[(Z)-isomer]}, 3.60-3.45(m, 1H), 2.8-2.2(m, 2H)ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.3(m, 2F), -112.4(m, 2F), -119.0(m, 2F), -121.0(m, 2F) ppm; IR (nujol): 3050, 2900, 1740, 1630, 1270, 1180, 730cm^{-1} ; MS m/e(%): 474[$M^+(^{37}Cl)$](41), 472[$M^+(^{35}Cl)$](100), 442(6.0), 428(6.6), 414(15), 287(39), 195(28), 127(4.8); HRMS Calcd for $C_{10}H_6ClF_8IO_2$: 471.8972. Found: 471.8970.

(Z)-3-(1'-Iodoethylidene)-4-(2',2',2'-trifluoroethyl)-2(3H)-dihydrofuranone (Z-3Ba) mp 98-99°C. ^1H NMR(300MHz/$CDCl_3$) δ 4.27(dd, J=10.3, 3.7Hz, 1H), 4.18(d, J=10.3Hz, 1H), 3.68-3.56(m, 1H), 2.84(s, 3H), 2.50-2.20(m, 2H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -64.3(m, 3F) ppm; IR (KBr): 2950, 1750, 1630, 1380, 1280, 1140, 760, 640cm^{-1} ; MS m/e(%): 320(M^+)(100), 193(36), 149(16), 127(7.4), 85(25), 65(20); HRMS Calcd for $C_8H_8F_3IO_2$: 319.9520. Found: 319.9556.

(E)-3-(1'-Iodoethylidene)-4-(2',2',2'-trifluoroethyl)-2(3H)-dihydrofuranone (E-3Ba) mp 45-46°C. ^1H NMR(300MHz/$CDCl_3$) δ 4.30(d, J=5.7Hz, 2H), 3.40-3.28(m, 1H), 3.10(s, 3H), 2.60-2.40(m, 1H), 2.38-2.18(m, 1H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -64.1(m, 3F) ppm; IR (KBr): 2900, 1750, 1640, 1380, 1275,

1130, 760, 640cm^{-1} ; MS m/e(%): 320(M^+)(9.8), 193(100), 149(10), 127(19), 109(19), 85(37), 65(35); Anal. Calcd for $C_8H_8F_3IO_2$: C, 30.01; H, 2.52. Found: C, 29.96; H, 2.32.

(E)-3-(1'-Iodoethylidene)-4-(2'-chlorotetrafluoroethylmethyl)-2(3H)-dihydrofuran-one (E-3Bb) mp 64-65°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 4.40(d, J=3.9Hz, 2H), 3.55-3.45(m, 1H), 3.18(s, 3H), 2.65-2.22(m, 2H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -71.0(m, 2F), -112.7(m, 2F) ppm; IR (KBr): 2900, 1740, 1635, 1380, 1090, 750, 640cm^{-1} ; MS m/e(%): 388[M^+(^{37}Cl)](0.4), 386[M^+(^{35}Cl)](1.2), 261(41), 259(100), 215(15), 159(15), 127(9.0), 85(30), 65(31); Anal. Calcd for $C_9H_8ClF_4IO_2$:C, 27.97; H, 2.09. Found: C, 27.63; H, 1.86.

(E)-3-(1'-Iodoethylidene)-4-(4'-chlorooctafluorobutylmethyl)-2(3H)-dihydrofuran-one (E-3Bc) mp 53-55°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 4.38(d, J=5.8Hz, 2H), 3.58-3.48(m, 1H), 3.13(s, 3H), 2.7-2.2(m, 2H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.5(m, 2F), -113.0(m, 2F), -119.5(m, 2F), -122.6(m, 2F) ppm; IR (KBr): 2930, 1760, 1640, 1360, 1180, 1080, 770, 530cm^{-1} ; MS m/e(%): 486[M^+(^{35}Cl)] (1.0), 361(34), 359(100), 315(12), 237(19), 149(14), 85(51), 65(64); HRMS Calcd for $C_{11}H_8ClF_8O_2$: 359.0084. Found: 359.0069.

(E)-3-(1'-Iodoethylidene)-4-(8'-chlorohexadecafluorooctylmethyl)-2(3H)-dihydrofur-anone (E-3Bd) mp 90-92°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 4.37(d, J=6.1Hz, 2H), 3.60-3.42(m, 1H), 3.16(s, 3H), 2.67-2.22(m, 2H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.5(m, 2F), -112.8(m, 2F), -119.6(m, 2F), -121.0(m, 8F), -122.8(m, 2F) ppm; IR (KBr): 2950, 1740, 1640, 1360, 1300, 1100, 740, 540cm^{-1} ; MS m/e(%): 688[M^+(^{37}Cl)](0.5), 686[M^+(^{35}Cl)](1.5), 561(43), 559(100), 515(23), 237(14), 127(10), 85(83), 65(81); Anal. Calcd for $C_{15}H_8ClF_{16}IO_2$: C, 26.24; H, 1.17. Found: C, 26.04; H, 1.14.

(E)-3-(1'-Iodononylidene)-4-(2'-chlorotetrafluoroethylmethyl)-2(3H)-dihydrofuran-one (E-3Cb) ot 62-64°C(20mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 4.40(d, J=3.9Hz, 2H), 3.58-3.45(m, 1H), 3.40-3.22(m, 2H), 2.63-2.20(m, 2H), 1.70-1.50(m, 2H), 1.50-1.30(m, 10H), 0.90(t, J=5.6Hz, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -70.8(m, 2F), -113.6(m, 2F) ppm; IR (neat): 2920, 2850, 1760, 1630, 1380, 1090, 750, 640cm^{-1} ; MS m/e(%): 487[M^+ (^{37}Cl)+1](3.2), 485[M^+(^{35}Cl)+1](7.3), 359(40), 357(100), 273(41), 127(5.8), 85(7.6), 54(39); Anal. Calcd for $C_{16}H_{22}ClF_4IO_2$: C, 39.65; H, 4.58. Found: C, 40.04; H, 4.53.

(E)-3-(1'-Iodononylidene)-4-(4'-chlorooctafluorobutylmethyl)-2(3H)-dihydrofuran-one (E-3Cc) ot 50-52°C(4mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 4.40(d, J=5.1Hz, 2H), 3.60-3.48(m, 1H), 3.40-3.24(m, 2H), 2.65-2.22(m, 2H), 1.70-1.50(m, 2H), 1.50-1.30(m, 10H), 0.90(t, J=6.5Hz, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.2(m, 2F), -112.5(m, 2F), -119.9(m, 2F), -121.8(m, 2F) ppm; IR (neat): 2920, 2850, 1760, 1635, 1380, 1190, 780, 660cm^{-1} ; MS m/e(%): 586[M^+(^{37}Cl)](2.5), 584[M^+(^{35}Cl)](5.9), 459(30), 457(100), 373(32), 127(2.1), 85(5.4), 65(11); Anal. Calcd for $C_{18}H_{22}ClF_8IO_2$: C, 36.98; H, 3.79. Found: C, 37.08; H, 3.63.

The procedure for the polyfluoroalkylation of allyl (E)-2-butenoate (**6**), homoallyl 2-butynoate (**7**) and bishomoallyl 2-hexynoate (**8**) was the same as the general procedure.

5-Chloro-2-iodo-4,4,5,5-tetrafluoropentyl 2-(E)-butenoate (9) Yield 65%. ot 64-66°C(10mmHg). ^{1}H NMR(60MHz/CCl_4) δ 6.96(dq, J=16, 6Hz, 1H), 5.80(d, J=16Hz, 1H), 4.6-4.3(m, 1H), 4.40(d, J=6Hz, 2H), 3.2-2.4(m, 2H), 1.90(d, J=6Hz, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -70.8(m, 2F), -112.5(M, 2F) ppm; IR (neat): 2900, 1720, 1660, 1250, 1090, 770, 680cm^{-1} ; MS m/e(%): 390[M^+(^{37}Cl)](1.5), 388[M^+(^{35}Cl)](5.6), 261(100), 85(62), 69(54), 65(30); Anal. Calcd for $C_9H_{10}ClF_4IO_2$: C, 27.82; H, 2.59. Found: C, 28.01; H, 2.66.

6-Chloro-3-iodo-5,5,6,6-tetrafluorohexyl 2-butynoate (10) Yield 68%. ot 72-75°C(10mmHg). ^{1}H NMR(56MHz/CCl_4) 4.8-4.25(m, 3H), 3.4-2.7(m, 2H), 2.30(q, J=6Hz, 2H), 2.15(s, 3H) ppm; ^{19}F NMR(60MHz/CCl_4) δ -70.6(m, 2F), -110.2(m, 2F) ppm; IR (neat): 2950, 2230, 1720, 1430, 1150, 940, 750cm^{-1} ; MS m/e(%): 402[M^+(^{37}Cl)](2.7), 400[M^+(^{35}Cl)](10), 273(100), 217(21), 127(6.7), 85(30); Anal. Calcd for $C_{10}H_{10}ClF_4IO_2$: C, 29.99; H, 2.52. Found: C, 29.98; H, 2.42.

7-Chloro-4-iodo-6,6,7,7-tetrafluoroheptyl 2-hexynoate (11) Yield 83%. ot 53-56°C(5mmHg). ^{1}H NMR(60MHz/CCl_4) 4.3-3.8(m, 3H), 3.2-2.4(m, 2H), 2.24(t, J=7Hz, 2H), 2.0-1.3(m, 6H), 0.92(t, J=7Hz, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -71.0(m, 2F), -112.3(m, 2F) ppm; IR (neat): 2960, 2220, 1715, 1380, 1150, 750cm^{-1} ; MS m/e(%): 444[M^+(^{37}Cl)](2.3), 442[M^+(^{35}Cl)](7.3), 315(100), 127(34), 85(62); Anal. Calcd for $C_{13}H_{16}ClF_4IO_2$: C, 35.27; H, 3.64. Found: C, 35.65; H, 4.02.

Preparation of 3-Alkylidene-4-polyfluoroalkyl-2(3H)-dihydrofuranone (14). Typical procedure: **3-Methylene-4-(2',2',2'-trifluoroethyl)-2(3H)-dihydrofuranone (14Aa)** A mixture of **3Aa** (306mg, 1.0mmol), AcOH (0.5mL), water (0.5mL) and freshly activated zinc powder (75mg, 1.2mmol) was stirred at room temperature. After completion of the reaction, the mixture was diluted with water (5mL) and extracted with $CHCl_3$ (5mL × 2) and dried ($MgSO_4$). Column chromatography gave **14Aa** (120mg) in 67% yield. mp 42-44°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 6.72(d, J=2.7Hz, 1H), 5.63(d, J=2.7Hz, 1H), 4.50(t, J=9.0Hz, 1H), 4.00(dd, J=9.0, 7.0Hz, 1H), 3.42-3.25(m, 1H), 2.60-2.40(m, 1H), 2.38-2.18(m, 1H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -64.0(m, 3F) ppm; IR (KBr): 2950, 1740, 1630, 1420, 1180, 890, 670cm^{-1} ; MS m/e(%): 181(M^++1)(5.4), 180(M^+)(14), 150(79), 122(100), 100(22), 70(43); Anal. Calcd for $C_7H_7F_3O_2$: C, 46.68; H, 3.92. Found: C, 46.80; H, 4.00.

(Z)-3-Ethylidene-4-(4'-chlorooctafluorobutylmethyl)-2(3H)-dihydrofuranone (Z-14Bc) Yield 70%. mp 48-49°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 6.26(q, J=7.2Hz, 1H), 4.48(t, J=8.8Hz, 1H), 4.00(dd, J=8.8, 6.6Hz, 1H), 3.46-3.30(m, 1H), 2.48-2.10(m, 2H), 2.17(d, J=7.2Hz, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.3(m, 2F), -112.4(m, 2F), -119.0(m, 2F), -122.0(m, 2F) ppm; IR (nujol): 3020, 2950, 1740, 1635, 1140, 795, 640cm^{-1} ; MS m/e(%): 362[M^+(^{37}Cl)](4.2), 360[M^+(^{35}Cl)](8.8), 117(20), 111(100), 97(7.5), 83(40); Anal. Calcd for $C_{11}H_9ClF_8O_2$: C, 36.63; H, 2.51. Found: C, 36.89; H, 2.77.

Preparation of N-Allyl 2-Propynamide (15A). A solution of allyl amine (1.25g, 22mmol) in methanol (2mL) and water (2mL) was cooled to -20 ~ -30°C. Methyl 2-propynoate (1.68g, 20mmol) in methanol (2mL) was added dropwise to this solution with magnetic stirring. After addition of the propynoate, the stirring was continued for 5 minutes. The solvent was evacuated and the residue was subjected to column chromatography (silica gel; eluent: petroleum ether / ethyl acetate = 7 / 3) to give N-allyl 2-propynamide **15A** (1.64g, 75%). ot 77-79°C(10mmHg). ^{1}H NMR(60MHz/CCl_4) δ 6.60(t, J=6Hz, 1H), 6.20-5.50(m, 1H), 5.45-4.95(m, 2H), 3.90(t, J=6Hz, 2H), 2.80(s, 1H)ppm; IR (neat): 3300, 3100, 2120, 1650, 1280cm^{-1} ; MS m/e(%): 110(M^++1)(22), 109(M^+)(0.9), 108(M^+-1)(13), 80(80), 66(17), 56(41), 53(100); Anal. Calcd for C_6H_7NO: C, 66.04; H, 6.47; N, 12.87. Found: C, 66.11; H, 6.68; N, 13.14.

N-Allyl 2-Butynamide (15B). The procedure was similar to the preparation of **15A**. Yield 83%. ot 85-88°C(8mmHg). ^{1}H NMR(60MHz/CCl_4) δ 6.83(t, J=6Hz, 1H), 6.20-5.30(m, 1H), 5.20-4.75(m, 2H), 3.80(t, J=6Hz, 2H), 1.85(s, 3H)ppm; IR (neat): 3300, 2250, 1680, 1640, 1290cm^{-1} ; MS m/e(%): 124(M^++1)(11), 123(M^+)(14), 122(M^+-1)(68), 109(4.0), 95(11), 68(100), 67(82); Anal. Calcd for C_7H_9NO: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.50; H, 7.29; N, 11.40.

Preparation of N-Allyl-N-Methyl 2-Butynamide (15C). To a solution of 2-butynoic acid (0.71g, 8.4mmol) in CH_2Cl_2 (10mL), was added dropwise the solution of DCC (N, N'-dicyclohexylcarbodiimide) (2.06g, 10mmol) and DMAP (4-N,N-dimethylamino-pyridine) (0.052g, 0.2mmol) in CH_2Cl_2 (10mL) at -20°C. Methyl allyl amine (0.60g, 8.4mmol) in CH_2Cl_2 (5mL) was then added and the mixture was stirred for 20 h at room temperature. The solid was filtered off and the filtrate was washed with 0.1N HCl (10mL) and dried ($MgSO_4$). After removal of the solvent, column chromatography (silica gel; eluent: petroleum ether / ethyl acetate = 9 / 1) gave the oily product **15C** (1.00g, 87%). ot 88-90°C(10mmHg). ^{1}H NMR(60MHz/CCl_4) δ 5.75-5.10(m, 1H), 5.00-4.55(m, 2H), 3.82(d, J=5Hz, 1.20H), 3.63(d, J=5Hz, 0.80H), 2.75(s, 1.20H), 2.50(s, 1.80H), 1.62(s, 3H)ppm; IR (neat): 2960, 2200, 1660, 1340, 1105cm^{-1} ; MS m/e(%): 138(M^++1)(17), 137(M^+)(42), 122(4.2), 96(56), 70(59), 67(100); Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 70.17; H, 8.20, N, 9.88.

The following compounds were prepared similarly.

N-Allyl-N-benzyl 2-butynamide (15D). Yield 85%. ot 143-146°C(10mmHg). ^{1}H NMR(60MHz/CCl_4) δ 7.20(m, 5H), 5.80-5.20(m, 1H), 5.10-4.75(m, 2H), 4.75(s, 0.96H), 4.60(s, 1.04H), 3.90(d, J=5Hz, 1.04H), 3.73(d, J=6Hz, 0.96H), 1.85(s, 3H) ppm; IR (neat): 3100, 2220, 1660, 1620, 750, 700cm^{-1} ; MS m/e(%): 214(M^++1)(18), 213(M^+)(34), 212(M^+-1)(25), 185(3.2), 172(73), 91(61), 67(100); Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.07; N, 6.57. Found: C, 78.66; H, 6.90; N, 6.81.

N-Allyl-N-benzyl 2-hexynamide (15E). Yield 86%. ot 134-136°C(5mmHg). ^{1}H NMR(60MHz/CCl_4) δ 7.16(m, 5H), 6.00-4.80(m, 3H), 4.75(s, 0.98H), 4.60(s, 1.02H), 3.90(d, J=5Hz, 1.02H), 3.73(d, J=6Hz, 0.98H), 2.20(t, J=7Hz, 2H), 1.52(m, 2H), 0.90(t, J=6Hz, 3H)ppm; IR (neat): 3050, 2220, 1660, 1620, 750, 700cm^{-1} ; MS m/e(%): 242(M^++1)(22), 241(M^+)(41), 227(17), 199(7.5), 186(66), 95(98), 91(100); Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.78; H, 7.59; N, 5.67.

N-Acetyl-N-allyl-2-propynamide (15F) To a solution of N-allyl propynamide (**15A**) (109mg, 1.0mmol) in THF (5mL), was added NaH (80%, 60mg, 2.0mmol) under nitrogen. Stirring was continued for 0.5h until no more H_2 evolved. The mixture was cooled to 0°C and a solution of acetyl chloride (98mg, 1.1mmol) in THF (5mL) was added dropwise and the stirring was continued for another 2h after addition. The reaction was quenched with saturated aqueous NH_4Cl (10mL) and extracted with ethyl ether (10mL × 4). The combined organic layer was dried ($MgSO_4$) and concentrated. Column chromatography gave **15F** (96mg, 64%). ot 92-94°C(10mmHg). ^{1}H NMR(60MHz/CCl_4) δ 6.2-5.3(m, 1H), 5.2-4.7(m, 2H), 4.30(d, J=5.0Hz, 2H), 3.15(s, 1H), 2.30(s, 3H) ppm; IR (neat): 3320, 2200, 1680, 1360, 980, 750, 610cm^{-1} ; MS m/e(%): 152(M^++1)(6.3), 151(17), 109(26), 80(48), 56(39), 43(100); Anal. Calcd for $C_8H_9NO_2$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.70; H, 6.20; N, 8.98.

N-Allyl-N-benzoyl-2-butynamide (15G) The procedure was similar to **15F**. Yield 95%. ot 120-122°C(5mmHg). ^{1}H NMR(60MHz/CCl_4) δ 7.6-7.1(m, 5H), 6.3-5.5(m, 1H), 5.4-4.8(m, 2H), 4.26(d, J=6Hz, 2H), 1.93(s, 3H) ppm; IR (neat): 3050, 2950, 2200, 1660, 1600, 1320, 960, 740, 700cm^{-1} ; MS m/e(%): 228(M^++1)(9.8), 227(M^+)(24), 185(29), 174(8.5), 122(34), 105(100), 85(28); Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.31; H, 5.69; N, 6.20.

N-Allyl-N-tosyl-2-butynamide (15H) The procedure was similar to **15F**. Yield 89%. mp 122-124°C. ^{1}H NMR(60MHz/CCl_4) δ 7.80(d, J=7Hz, 2H), 7.25(d, J=7Hz, 2H), 6.30-5.65(m, 1H), 5.6-5.0(m, 2H), 4.50(d, J=5Hz, 2H), 2.45(s, 3H), 1.95(s, 3H) ppm; IR (KBr): 3020, 2200, 1660, 1600, 990, 740, 700cm^{-1} ; MS m/e(%): 278(M^++1)(7.4), 277(M^+)(25), 235(29), 155(94), 91(100), 85(33). Anal. Calcd for $C_{14}H_{15}NO_3S$: C, 60.63; H, 5.45; N, 5.05. Found: C, 60.56; H, 5.80; N, 4.89.

Reaction of Per(poly)fluoroalkyl Iodides (2) with N-Allyl 2-Alkynamides (15). To a stirred solution of per(poly)fluoroalkyl iodide **2** (1.0mmol) and N-allyl 2-alkynamide **15** (1.0mmol) in a mixed solvent of acetonitrile (3mL) and water (2mL), was added sodium bicarbonate (100mg, 1.2mmol) and sodium dithionite (208mg, 1.2mmol). Stirring was continued at 10-15°C until TLC monitoring showed complete conversion of the N-allyl 2-alkynamide. The resulting mixture was diluted with water (4mL) and extracted with ethyl ether (5mL × 3). The combined organic layer was washed with brine (5mL × 2), dried ($MgSO_4$) and concentrated.

The residue was purified by flash chromatography on silica gel to give per(poly)fluoroalkylated products **16** and/or **17**.

N-(3-(4'-Chlorooctafluorobutyl)-2-iodopropyl) 2-propynamide (16Ac) mp 87-89°C. ^{1}H NMR(60MHz/CCl_4) δ 7.04(t, J=6Hz, 1H), 5.0-4.7(m, 1H), 3.70(t, J=6Hz, 2H), 3.25-2.45(m, 2H), 3.10(s, 1H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.0(m, 2F), -112.0(m, 2F), -118.8(m, 2F), -121.7(m, 2F) ppm; IR (neat): 3300, 2970, 2200, 1690, 1115, 780cm^{-1} ; MS m/e(%): 473[M^+(^{37}Cl)](0.5), 471[M^+(^{35}Cl)](1.7), 344(100), 189(67), 85(67), 65(48); Anal. Calcd for $C_{10}H_7ClF_8INO$: C, 25.47; H, 1.50; N, 2.97. Found: C, 25.20; H, 1.83; N, 2.89.

N-(3-(4'-Chlorooctafluorobutyl)-2-iodopropyl) 2-butynamide (16Bc) mp 103-105°C. ^{1}H NMR(60MHz/CCl_4) δ 7.04(t, J=6Hz, 1H), 5.0-4.7(m, 1H), 3.70(t, J=6Hz, 2H), 3.25-2.45(m, 2H), 2.00(s, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.0(m, 2F), -112.0(m, 2F), -119.6(m, 2F), -121.7(m, 2F) ppm; IR (KBr): 3250, 2900, 2200, 1690, 1440, 1115, 780cm^{-1} ; MS m/e(%): 487[M^+(^{37}Cl)](0.6), 485[M^+(^{35}Cl)](2.2), 360(34), 358(100), 203(41), 127(5.4), 85(27); Anal. Calcd for $C_{11}H_9ClF_8INO$: C, 27.21; H, 1.87; N, 2.88. Found: C, 27.55; H, 1.85; N, 3.03.

N-(3-(2'-Chlorotetrafluoroethyl)-2-iodopropyl)-N-methyl 2-butynamide (16Cb) ot 70-72°C(10mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 4.45-4.30(m, 1H), 3.80(dd, J=13.7, 7.0Hz, 1H), 3.40(dd, J=13.7, 7.8Hz, 1H), 3.02(s, 3H), 2.7-2.5(m, 2H), 1.90(s, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -70.8(m, 2F), -112.6(m, 2F) ppm; IR (neat): 2940, 2220, 1635, 1420, 1185, 790, 740cm^{-1} ; MS m/e(%): 401[M^+(^{37}Cl)](1.8), 399[M^+(^{35}Cl)](6.2), 364(10), 274(33), 272(100), 159(7.0), 127(8.0), 85(12); Anal. Calcd for $C_{10}H_{11}ClF_4INO$: C, 30.06; H, 2.78; N, 3.51. Found: C, 29.69; H, 3.00; N, 3.60.

N-Benzyl-N-(3-(2'-chlorotetrafluoroethyl)-2-iodopropyl) 2-butynamide (16Db) ot 125-127°C(10mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 7.45-7.15(m, 5H), 4.95(d, J=15.7Hz, 1H), 4.75(d, J=15.7Hz, 1H), 4.42-4.30(m, 1H), 3.80(dd, J=14.0, 7.3Hz, 1H), 3.43(dd, J=14.0, 7.6Hz, 1H), 2.70-2.50(m, 2H), 1.92(s, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -70.8(m, 2F), -112.6(m, 2F) ppm; IR (neat): 2910, 2220, 1635, 1420, 1150, 790, 740cm^{-1} ; MS m/e(%): 477[M^+(^{37}Cl)](10), 475[M^+(^{35}Cl)](41), 348(23), 193(67), 186(19), 127(25), 91(100); Anal. Calcd for $C_{16}H_{15}ClF_4INO$: C, 40.40; H, 3.18; N, 2.94. Found: C, 40.15; H, 3.40; N, 2.68.

N-Benzyl-N-(3-(4'-chlorooctafluorobutyl)-2-iodopropyl) 2-butynamide (16Dc) ot 140-142°C(10mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 7.45-7.15(m, 5H), 4.93(d, J=15.6Hz, 1H), 4.70(d, J=15.6Hz, 1H), 4.42-4.30(m, 1H), 3.80(dd, J=14.0, 7.3Hz, 1H), 3.43(dd, J=14.0, 7.5Hz, 1H), 2.70-2.50(m, 2H), 1.92(s, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.3(m, 2F), -113.0(m, 2F), -119.2(m, 2F), -122.4(m, 2F) ppm, IR (neat): 3030, 2920, 2240, 1640, 1180, 800, 740cm^{-1} ; MS m/e(%): 577[M^+(^{37}Cl)](8.0), 575[M^+(^{35}Cl)](20), 448(16), 198(3.3), 127(2.3), 120(17), 91(100), 67(65); Anal. Calcd for $C_{18}H_{15}ClF_8INO$: C, 37.56; H, 2.63; N, 2.43. Found: C, 37.51; H, 2.78; N, 2.68.

N-Benzyl-N-(3-(2'-chlorotetrafluoroethyl)-2-iodopropyl) 2-hexynamide (16Eb) ot 132-135°C(8mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 7.45-7.15(m, 5H), 4.90(d, J=15.0Hz, 1H), 4.75(d, J=15.0Hz, 1H), 4.42-4.30(m, 1H), 3.80(dd, J=14.6, 7.3Hz, 1H), 3.35(dd, J=14.6, 7.9Hz, 1H), 2.70-2.55(m, 2H), 2.30(t, J=7.5Hz, 2H), 1.65-1.40(m, 2H), 0.90(t, J=7.3Hz, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -70.5(m, 2F), -112.0(m, 2F) ppm; IR (neat): 3020, 2970, 2220, 1635, 1230, 940, 760cm^{-1} ; MS m/e(%): 505[M^+(^{37}Cl)](7.8), 503[M^+(^{35}Cl)](15), 475(53), 376(31), 348(7.5), 214(11), 91(100). Anal. Calcd for $C_{18}H_{19}ClF_4INO$: C, 42.92; H, 3.82; N, 2.78. Found: C, 43.04; H, 3.88; N, 3.02.

N-Benzyl-N-(4'-(ω-chlorooctafluorobutyl)-2-iodopropyl) 2-hexynamide (16Ec) ot 120-122°C(5mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 7.45-7.15(m, 5H), 4.95(d, J=15.7Hz, 1H), 4.75(d, J=15.7Hz, 1H), 4.40-4.30(m, 1H), 3.80(dd, J=14.6, 7.3Hz, 1H), 3.40(dd, J=14.6, 7.0Hz, 1H), 2.70-2.55(m, 2H), 2.30(t, J=7.5Hz, 2Hz), 1.65-1.40(m, 2H), 0.90(t, J=7.3Hz, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.0(m, 2F), -112.4(m, 2F), -119.0(m, 2F), -122.3 (m, 2F) ppm; IR (neat): 3030, 2920, 2240, 1640, 1180, 800, 740cm^{-1} ; MS m/e(%): 605[M^+(^{37}Cl)](6.4), 603[M^+(^{35}Cl)](16), 575(48), 476(30), 448(10), 127(5.6), 91(100); Anal. Calcd for $C_{20}H_{19}ClF_8INO$: C, 39.79; H, 3.17; N, 2.32. Found: C, 39.56; H, 2.96; N, 2.44.

4-(2'-Chlorotatrafluoroethylmethyl)-3-(E)-(1'-iodoethylidene)-1-methyl-2(3H)-dihydropyrrolidone (E-17Cb) mp 57-58°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 3.58(dd, J=10.7, 3.1Hz, 1H), 3.30(d, J=10.7Hz, 1H), 3.34-3.24(m, 1H), 3.20(s, 3H), 2.89(s, 3H), 2.70-2.47(m, 1H), 2.28-2.05(m, 1H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -70.8(m, 2F), -112.0(m, 2F) ppm; IR (neat): 2900, 1680, 1615, 1425, 1280, 940, 780cm^{-1} ; MS m/e(%): 402[M^+(^{37}Cl)+1](1.8), 400[M^+(^{35}Cl)+1](6.0), 364(5.1), 272(100), 201(19), 127(4.0), 85(8.0), 65(7.7) ; Anal. Calcd for $C_{10}H_{11}ClF_4INO$: C, 30.06; H, 2.78; N, 3.51. Found: C, 30.41; H, 3.22; N, 3.44.

1-Benzyl-4-(2'-Chlorotatrafluoroethylmethyl)-3-(E)-(1'-iodoethylidene)-2(3H)-dihydropyrrolidone (E-17Db) ot 120°C(10mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 7.30-7.10(m, 5H), 4.44(d, J=12.8Hz, 1H), 4.38(d, J=12.8Hz, 1H), 3.48(dd, J=10.5, 6.5Hz, 1H), 3.22-3.12(m, 1H), 3.15(s, 3H), 3.07(d, J=10.5Hz, 1H), 2.55-2.35(m, 1H), 2.15-1.90(m, 1H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -71.0(m, 2F), -112.6(m, 2F) ppm; IR (neat): 3010, 2900, 1690, 1640, 1360, 1150, 760, 700cm^{-1} ; MS m/e(%): 477[M^+(^{37}Cl)] (2.2), 475[M^+(^{35}Cl)](4.7), 438(100), 450(47), 127(1.7), 92(11), 91(96), 65(13); Anal. Calcd for $C_{16}H_{15}ClF_4INO$: C, 40.40; H, 3.18; N, 2.94. Found: C, 40.56; H, 3.48; N, 2.88.

1-Benzyl-4-(4'-Chlorooctafluorobutylmethyl)-3-(E)-(1'-iodoethylidene)-2(3H)-dihydropyrrolidone (E-17Dc) ot 140-143°C(10mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 7.42-7.10(m, 5H), 4.45(s, 2H), 3.45(dd, J=10.4, 6.7Hz, 1H), 3.30-3.20(m, 1H), 3.20(s, 3H), 3.15(d, J=10.4Hz, 1H), 2.58-2.36(m, 1H), 2.16-1.94(m, 1H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.4(m, 2F), -112.5(m, 2F), -119.1(m, 2F), -122.4(m, 2F) ppm; IR (neat): 3010, 2900, 1690, 1640, 1280, 775, 700cm^{-1} ; MS m/e(%): 577[M^+(^{37}Cl)](0.6), 575[M^+(^{35}Cl)](2.6),

540(1.5), 448(52), 127(1.7), 92(10), 91(100), 65(13); Anal. Calcd for $C_{18}H_{15}ClF_8INO$: C, 37.56; H, 2.63; N, 2.43. Found: C, 37.40; H, 2.45; N, 2.65.

1-Benzyl-4-(2'-Chlorotetrafluoroethylmethyl)-3-(E)-(1'-iodobutylidene)-2(3H)-dihydropyrrolidone (E-17Eb) ot 102-105°C(5mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 7.30-7.15(m, 5H), 4.40(s, 2H), 3.45-3.25(m, 3H), 3.22-3.12(m, 1H), 3.06(d, J=10.6Hz, 1H), 2.55-2.30(m, 1H), 2.10-1.85(m, 1H), 1.55(q, J=7.3Hz, 2H), 0.88(t, J=7.3Hz, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -71.0(m, 2F), -112.2(m, 2F) ppm; IR (neat): 3020, 2960, 1690, 1640, 1270, 940, 760, 700cm^{-1} ; MS m/e(%): 505[M^+(^{37}Cl)](0.2), 503[M^+(^{35}Cl)](0.5), 468(3.4), 376(100), 92(9.4), 91(79), 65(11); Anal. Calcd for $C_{18}H_{19}ClF_4INO$: C, 42.92; H, 3.80; N, 2.78; Found: C, 42.80; H, 3.45; N, 3.02.

1-Benzyl-4-(4'-Chlorooctafluorobutylmethyl)-3-(E)-(1'-iodobutylidene)-2(3H)-dihydropyrrolidone (E-17Ec) ot 117-120°C(2mmHg). ^{1}H NMR(300MHz/$CDCl_3$) δ 7.40-7.20(m, 5H), 4.50(d, J=14.6Hz, 1H), 4.45(d, J=14.6Hz, 1H), 3.50-3.35(m, 3H), 3.32-3.22(m, 1H), 3.15(d, J=10.6Hz, 1H), 2.60-2.40(m, 1H), 2.15-1.95(m, 1H), 1.61(q, J=7.4Hz, 2H), 0.95(t, J=7.4Hz, 3H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.0(m, 2F), -112.4(m, 2F), -119.0(m, 2F), -122.3(m, 2F) ppm; IR (neat): 3010, 2960, 1690, 1630, 1260, 700cm^{-1} ; MS m/e(%): 605[M^+(^{37}Cl)](0.6), 603[M^+(^{35}Cl)](0.9), 478(43), 476(94), 372(4.6), 91(100), 65(12); Anal. Calcd for $C_{20}H_{19}ClF_8INO$: C, 39.79; H, 3.17; N, 2.32. Found: C, 39.36; H, 2.91; N, 2.26.

1-Acetyl-4-(2'-chlorotetrafluoroethylmethyl)-3-iodomethylene-2(3H)-dihydropyrroli-done (17Fb) E/Z mixture. mp 82-85°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 7.95{d, J=2.1Hz, 0.52[(E)-isomer]}, 7.39{d, J=2.2Hz, 0.48H[(Z)-isomer]}, 4.08-3.83(m, 2H), 3.40-3.25(m, 1H), 2.60{s, 1.44H[(Z)-isomer]}, 2.55{s, 1.56H[(E)-isomer]}, 2.8-2.1(m, 2H)ppm; ^{19}F NMR(56MHz/CCl_4) δ -70.5(m, 2F), -111.9(m, 2F) ppm; IR (KBr): 2920, 1720, 1700, 1620, 1280, 990, 800cm^{-1} ; MS m/e(%): 415[M^+(^{37}Cl)](2.2), 413[M^+(^{35}Cl)] (6.5), 385(4.6), 286(2.6), 244(14), 127(2.0), 43(100); Anal. Calcd for $C_{10}H_9ClF_4INO_2$: C, 29.04; H, 2.19; N, 3.39. Found: C, 28.90; H, 2.30; N, 3.40.

1-Benzoyl-4-(2'-chlorotetrafluoroethylmethyl)-3-(E)-(1'-iodoethylidene)-2(3H)-dihydropyrrolidone (E-17Gb) mp 148-150°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 7.70-7.35(m, 5H), 4.05(dd, J=10.8, 6.0Hz, 1H), 3.97(d, J=10.8Hz, 1H), 3.52-3.40(m, 1H), 3.10(s, 3H), 2.68-2.20(m, 2H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -70.6(m, 2F), -112.2(m, 2F) ppm; IR (KBr): 3020, 2960, 1720, 1680, 1620, 1260, 740cm^{-1} ; MS m/e(%): 492[M^+(^{37}Cl)+1](0.1), 490[M^+(^{35}Cl)+1] (0.2), 462(1.0), 362(30), 127(0.8), 105(100), 77(30), 51(5.4); Anal. Calcd for $C_{16}H_{13}ClF_4INO_2$: C, 39.25; H, 2.68; N, 2.86. Found: C, 38.95; H, 2.46; N, 2.67.

1-Benzoyl-4-(4'-chlorooctafluorobutyl)methyl-3-(E)-(1'-iodoethylidene)-2(3H)-dihydropyrrolidone (E-17Gc) mp 161-163°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 7.60-7.40(m, 5H), 4.05(dd, J=12.0, 6.7Hz, 1H), 3.96(d, J=12.0Hz, 1H), 3.52-3.38(m, 1H), 3.12(s, 3H), 2.65-2.20(m, 2H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -67.4(m, 2F), -112.5 (m, 2F), -119.1(m, 2F), -122.5(m, 2F) ppm; IR (KBr): 3020, 2950, 1730, 1680, 1625, 1260, 890, 700cm^{-1} ; MS m/e(%): 592[M^+(^{37}Cl)+1](0.1), 590[M^+(^{35}Cl)+1](0.4), 464(8.3), 462(25), 127(0.6), 105(100), 77(22), 51(4.2); Anal. Calcd for $C_{18}H_{13}ClF_8INO_2$: C, 36.67; H, 2.22; N, 2.38. Found: C, 36.88; H, 2.19; N, 2.51.

3-(E)-(1'-Iodoethylidene)-4-(2',2',2'-trifluoroethyl)-1-tosyl-2(3H)-dihydropyrroli-done (E-17Ha) mp 177-179°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 7.93(d, J=8.3Hz, 2H), 7.45(d, J=8.3Hz, 2H), 4.00(d, J=10.6Hz, 1H), 3.83(dd, J=10.6, 6.7Hz, 1H), 3.28(m, 1H), 3.07(s, 3H), 2.45(s, 3H), 2.5-2.1(m, 2H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -64.4(m, 3F) ppm; IR (KBr): 3030, 1720, 1630, 1600, 1360, 1170, 740, 700cm^{-1} ; MS m/e(%): 474(M^++1)(2.0), 346(63), 282(27), 155(100), 127(2.0), 91(93), 65(18); Anal. Calcd for $C_{15}H_{15}F_3INO_3S$: C, 38.07; H, 3.19; N, 2.96. Found: C, 38.14; H, 2.99; N, 3.18.

4-(2'-Chlorotetrafluoroethyl)methyl-3-(E)-(1'-iodoethylidene)-1-tosyl-2(3H)-dihydro-pyrrolidone (E-17Hb) mp 188-190°C. ^{1}H NMR(300MHz/$CDCl_3$) δ 7.93(d, J=8.3Hz, 2H), 7.45(d, J=8.3Hz, 2H), 4.03(d, J=10.6Hz, 1H), 3.83(dd, J=10.6, 6.7Hz, 1H), 3.28-3.18(m, 1H), 3.07(s, 3H), 2.45(s, 3H), 2.6-2.2(m, 2H) ppm; ^{19}F NMR(56MHz/CCl_4) δ -70.7(m, 2F), -112.2(m, 2F) ppm; IR (KBr): 3030, 1720, 1630, 1600, 1360, 1100, 890, 660cm^{-1} ; MS m/e(%): 542[M^+(^{37}Cl)+1](0.6), 540[M^+(^{35}Cl)+1](1.6), 520(0.5), 412(63), 155(97), 127(1.3), 91(100), 65(33); Anal. Calcd for $C_{16}H_{15}ClF_4INO_3S$: C, 35.61; H, 2.80; N, 2.60. Found: C, 35.30; H, 2.60; N, 2.71.

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