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Practical Synthesis of 1,1-Difluoro- or 1-Fluoroalkenes from 2,2,2-Trifluoroacetophenone Derivatives†

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Since the discovery of the fact that compounds bearing a vinylic fluoride moiety often exhibit remarkable biological activities such as enzyme inhibitors, many synthetic methods for fluorine-substituted vinylic compounds have been developed. The synthesis of selectively fluorinated building blocks, such as aryl-substituted fluoro-alkenes, also has become an area of interest in recent years. Herein we describe a novel and practical method for the synthesis of 1,1-difluoro- and 1-fluoroalkenes starting from easily accessible trifluoroacetophenone derivatives. Various 1,1-difluoro- and 1-fluoroalkenes were prepared by the reaction of the corresponding tosyl hydrazones that were derived from trifluoroacetophenone derivatives by treating with alkyl or aryllithium reagents via addition-elimination and single electron transfer (SET) mechanism.

Key Words : 1,1-Difluoroalkenes, 1-Fluoroalkenes, Trifluoroacetophenone, *p*-Toluene sulfonyl hydrazones

Introduction

Many attempts have been made to develop novel methods for the synthesis of fluorinated compounds,[1] because the property of a bioactive molecule can often be modulated by adding fluorine atoms leading changes in solubility, metabolic stability, conformation, hydrogen-bonding ability, or chemical reactivity.[2] Moreover, fluoroalkenes are of special interests since they have potential applications in material science,[3] medicinal chemistry,[4] and organic synthesis.[5] Various synthetic methods for fluoroalkenes have been reported and they include the Wittig-Hornor-Emmons type reaction,[6] addition-elimination of polyfluoroethenes,[7] fluorination of vinylstannane,[8] dehydrocarboxylation of 2-fluoromethylmalonate derivatives,[9] desulfenylation of fluorosulfoxide,[10] and reduction of difluoro-olefins.[11] However, many of the reported methods employ complicated multi-step reactions under drastic reaction conditions, or require expensive reagents. Herein we wish to report a novel and very practical synthetic protocol for 1,1-difluoro- or 1-fluoroalkenes starting from α-trifluoromethyl-*N*-(*p*-toluenesulfonyl)hydrazones which are readily available from trifluoroacetophenone derivatives. This protocol employs relatively cheap starting materials and mild reaction conditions, yet giving the desired products in high yields within short reaction time (ca. 30 min).

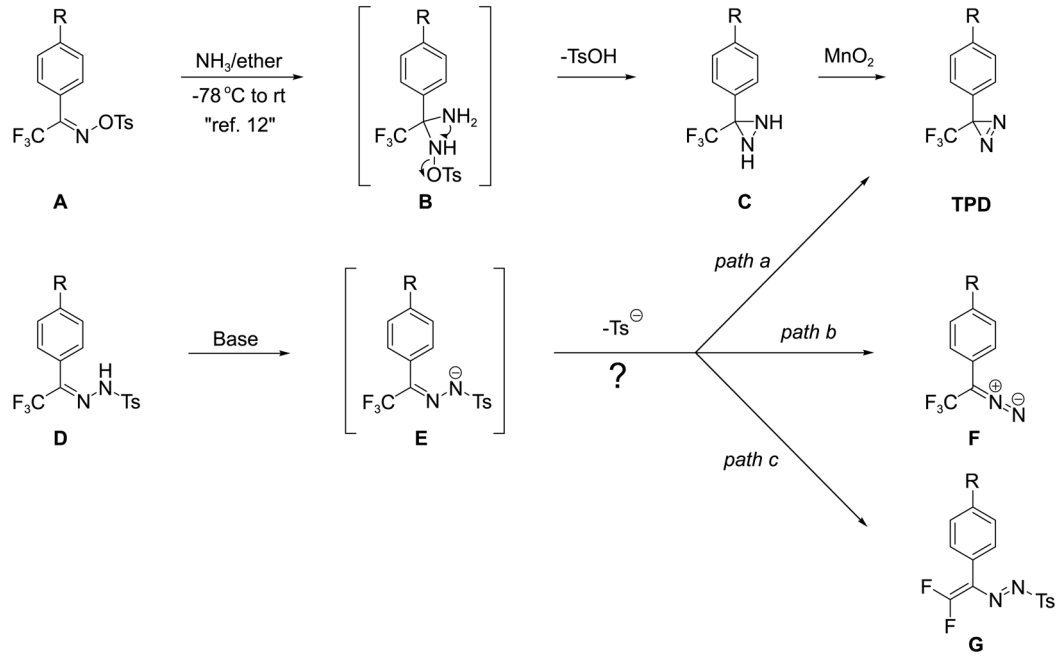
Results and Discussion

Initially we attempted to develop a more efficient synthetic protocol for 3-trifluoromethyl-3-phenyldiazirine (**TPD**)[12] which is a well-known and widely used photo-labeling reagent for bioactive molecules. Although more synthetic routes to diazirines[13] have been developed by several research groups, the original Brunners protocol[12] is still being used due to its practicality and the route is summarized in Scheme 1. The key step of the synthesis is comprised of the reaction of *p*-toluenesulfonyl oxime **A** with excess ammonia to yield diaziridine **C** and the subsequent oxidation of the resulting diaziridine with MnO_2 to afford **TPD**. Although this synthetic sequence is efficient and gives **TPD** in a reasonable yield, the synthesis is still a multistep sequence and requires drastic reaction conditions (ammonia gas). Therefore we desired to develop a more efficient and practical process and envisioned that treatment of *p*-toluenesulfonyl hydrazone **D** with a base might provide the desired **TPD** (*path a*) or its structural isomer **F** (*path b*) by the Bamford-Stevens type skeletal rearrangement[14] of the anion E as depicted in Scheme 1. In addition to these two possible pathways, formation of 1,1-difluoroalkenyl diazo compound **G** might be also feasible (*path c*).

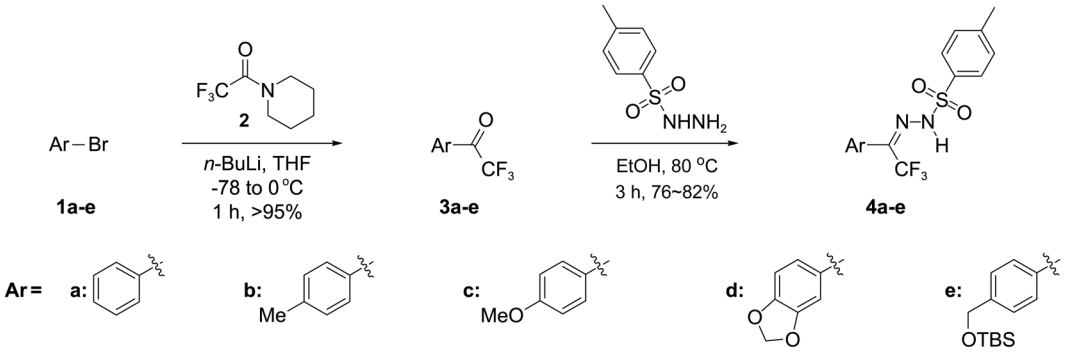
In order to test the hypothesis, *p*-toluenesulfonyl hydrazones **4a-e** were prepared according to the literature procedure as shown in Scheme 2.[15] The readily available aryl bromides **1a-e** were treated with *n*-BuLi and the resulting aryllithium species were trapped with *N*-trifluoroacetylpiperidine (**2**) to afford the corresponding trifluoroacetyl arenes **3a-e** in high yields (> 95%). Condensation of trifluoroacetyl benzenes **3a-e** with *p*-toluenesulfonylhydrazide in ethanol at 80 °C provided the corresponding *p*-toluenesulfonyl hydrazones **4a-e**[16] in 76-82% isolated yields.

Having these substrates in our hands, we then investigated the feasibility of the intramolecular cyclization through hydrazoyl anion (*path a*) by treating with various bases such as pyridine, sodium hydride, and Grignard reagent (MeMgBr or *i*-PrMgCl). Unfortunately, no desired diazirine **TPD** was obtained under these reaction conditions but only α-diazotrifluoroethyl benzene derivatives **F** were produced

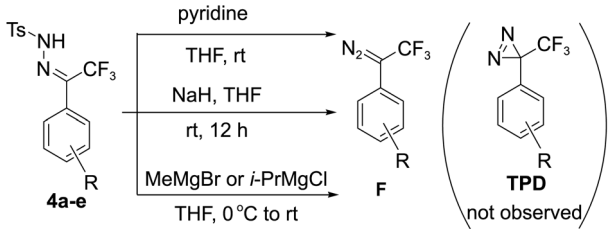
†This paper is dedicated to Professor Eun Lee on the occasion of his honourable retirement.



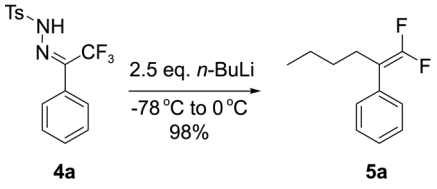
Scheme 1. A general procedure for preparation of 3-trifluoromethyl-3-phenyldiazirine (TPD) from tosyloxime **A**[12] and a newly proposed pathway from tosyl hydrazone **D** (*path a*) along with two other possible pathways to form **F** or **G** (*path b* and *c*).



Scheme 2. Synthesis of various α-trifluoromethyl *N*-tosylhydrazones **4a-e**.



Scheme 3. The reactions of tosylhydrazones **4a-e** with various bases.



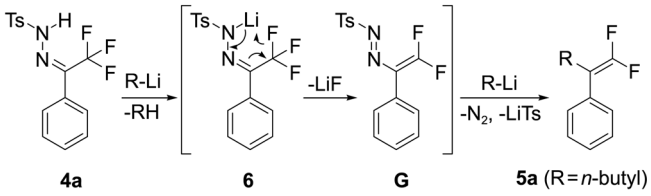
Scheme 4. Reaction of tosylhydrazone **4a** with *n*-butyllithium.

(Scheme 3, checked by ^{1}H-NMR and FT-IR). In contrast, when substrate **4a** was treated with excess *n*-butyllithium at low temperature (−78 °C to 0 °C), diazo-compound **F** was not obtained but only 1,1-difluoroalkene **5a** was isolated in high yield (98%) as the sole product (Scheme 4). The structure of **5a** was verified by ^{1}H- and ^{19}F-NMR spectroscopy and GC-MS.

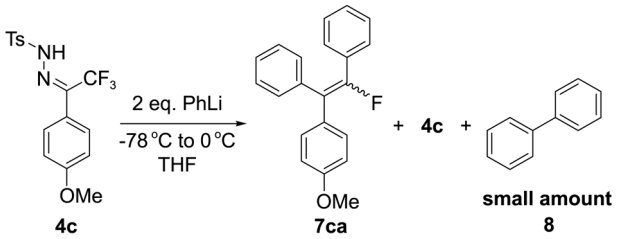
A plausible mechanism of this reaction is proposed in Scheme 5. Initial abstraction of the proton in tosylhydrazone **4a** by 1 equiv of alkyllithium would provide the corresponding hydrazoyl anion **6**. The subsequent release of lithium fluoride from these intermediate would form the intermediate **G**.[17] Another equiv of alkyllithium and the concomitant elimination of nitrogen and lithium tosylate would provide 1,1-difluoro-2-butyl-2-phenylethylene (**5a**). In contrast to the prior cases where softer counter cations (pyridinium, sodium and magnesium cations) were

employed, the use of hard counter cation such as lithium cation seems to be critical to promote the formation of intermediate **G**, which is attributed to the thermodynamically more favorable formation of LiF. This protocol turned out to be quite general as far as the R group is an aliphatic group (Table 1).

However, when the reaction was performed with 2.5 equiv of PhLi instead of alkyllithium under the similar conditions (THF, −78 to 0 °C), the aspect of the reaction was quite different (Scheme 6). In contrast to the previous cases, the expected 1,1-difluoroalkene was not obtained even when 2.0

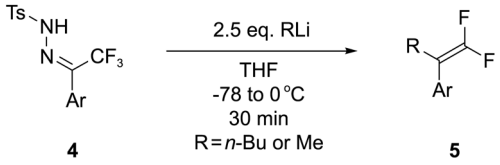


Scheme 5. A proposed mechanism for the formation of **5a** *via* addition-elimination reaction.



Scheme 6. Reaction of α-trifluoromethyl-*N*-tosylhydrazone **4c** with phenyllithium.

Table 1. Preparation of 1,1-difluoro-2-alkylalkenes **5** from -trifluoromethyl-*N*-tosylhydrazone **4**.



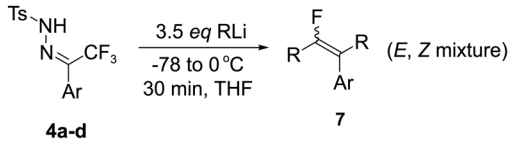
Entry	Reactant (**4**)	Ar	RLi	Product (**5**)	Yield (%)[a]
1	**4a**	**a**	*n*-Bu	**5a**	98
2	**4c**	**c**	*n*-Bu	**5c**	98
3	**4c**	**c**	Me	**5c'**	99
4	**4e**	**e**	*n*-Bu	**5e**	99
5	**4e**	**e**	Me	**5e'**	99

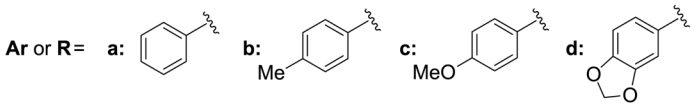
[a]Isolated yields after flash column chromatography

equiv of aryllithium reagent or less was used. Instead, triaryl substituted monofluoroalkene **7ca** and a small amount of biphenyl **8** were obtained along with some unreacted hydrazone 4c. In order to achieve the complete consumption of the hydrazone **4c**, at least 3 equiv of phenyllithium (~3.5 equiv) was required. Under these optimized conditions, triaryl substituted monofluoroalkene **7ca** was obtained in 98% yield as an inseparable 1:1 mixture of *E,Z* isomers. Although the *E,Z*-isomer ratio could be determined by H-NMR, ^{19}F-NMR, and GC-MS analyses, assignment of the absolute stereochemistry of each isomer could not be achieved due to their indistinguishable behavior in flash column chromatography.

After screening of the reaction with various substrates, it was concluded that the feature of the reactions is consistent as far as aryllithium reagents are used as a base. When *p*-toluenesulfonylhydrazones **4a-d** were treated with various aryllithium reagents (PhLi, 4-methylphenyllithium, 4-methoxyphenyllithium),[18] the reactions afforded monofluorotriarylalkenes **7** in high yields (Table 2). All the reactions smoothly proceeded at 0 °C in THF and were completed in 30 min. In contrast to the alkyllithium addition reaction shown in Table 1, the aryllithium addition reactions in Table 2 required more than 3 equiv of aryllithium reagents to warrant high yields. At the initial stage of the reaction, the color of the solution changed from orange to dark blue,

Table 2. Synthesis of various 1-fluoro-1,2,2-triarylalkenes **7** from α-trifluoromethyl-*N*-tosylhydrazone **4**.





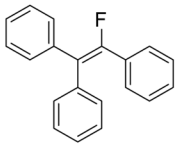
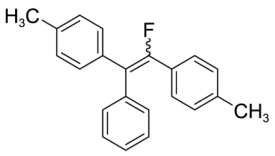
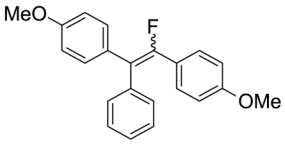
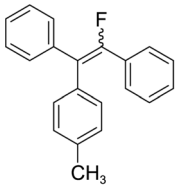
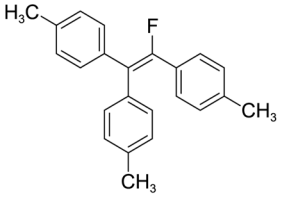
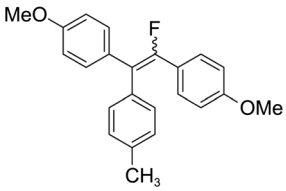
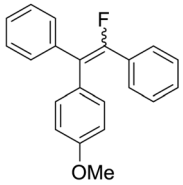
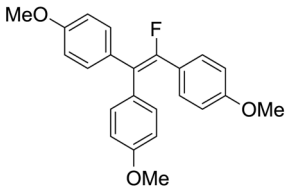
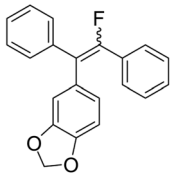
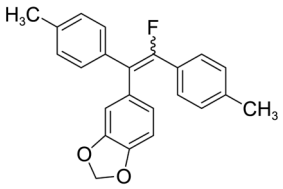
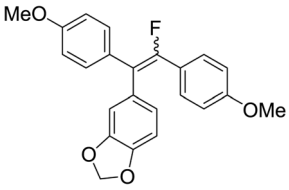
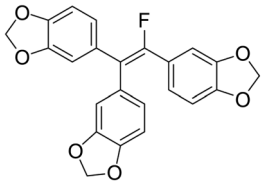
Entry	Reactant (**4**)	RLi	Product (**7**)	*E,Z* mixture ratio[a]	Yield (%)[b]
1	**4a**	C_6H_5Li	 **7aa**	–	95
2	**4a**	4-MeC_6H_4Li	 **7ab**	45 : 55	94
3	**4a**	4-$MeOC_6H_4Li$	 **7ac**	42 : 58	95
4	**4b**	C_6H_5Li	 **7ba**	44 : 56	97
5	**4b**	4-MeC_6H_4Li	 **7bb**	–	83

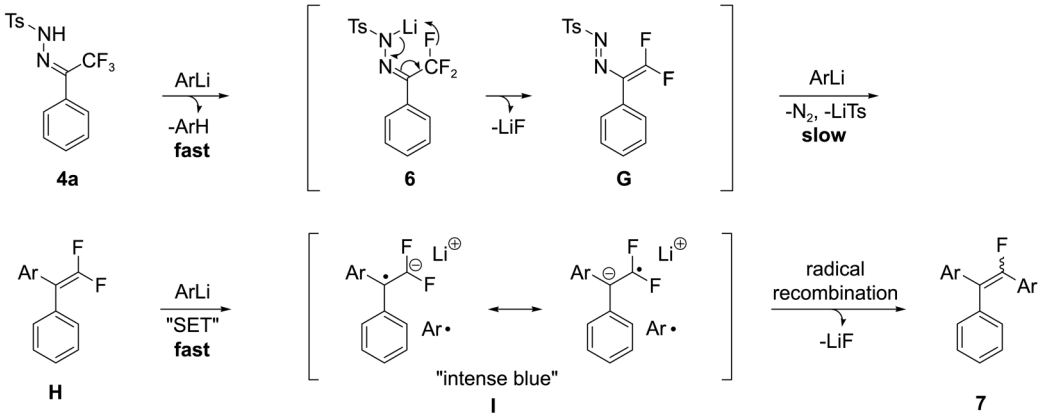
Table 2. continued

Entry	Reactant (**4**)	RLi	Product (**7**)	*E,Z* mixture ratio[a]	Yield (%)[b]
6	**4b**	4-$MeOC_6H_4Li$	 **7bc**	38 : 62	86
7	**4c**	C_6H_5Li	 **7ca**	48 : 52	98
8	**4c**	4-$MeOC_6H_4Li$	 **7cc**	–	71
9	**4d**	C_6H_5Li	 **7da**	48 : 52	96
10	**4d**	4-MeC_6H_4Li	 **7db**	44 : 56	97
11	**4d**	4-$MeOC_6H_4Li$	 **7dc**	40 : 60	91
12	**4d**	3,4-$(CH_2O)C_6H_3Li$	 **7dd**	–	75

[a] *E, Z* mixture ratios were determined by integration of vinyl fluorine signals in ^{19}F-NMR spectra and GC-MS analyses. But the assignment of the absolute *E, Z* stereochemistry could not be achieved due to poor separation of the *E, Z* isomers in chromatography.
[b] *E, Z* combined isolated yields after flash column chromatography

which implies the presence of radical anion-radical cation charge-separated complex. After about 30 min, the color of the solution turned back to orange color. Again, the employment of lithium reagents was critical to induce the formation of triaryl substituted fluoro-olefins **7**. Other organometallic nucleophile such as Grignard reagent did not provide any fluoroolefin product. In cases where two different aryl groups were employed (entries 2~4, 6~7, and 9~11), the reactions provided *E* and *Z* isomers as an inseparable mixture. The mixture ratios could be determined by GC-MS analyses, and they were consistent with the ^{1}H- and ^{19}F-NMR spectra analyses of the mixtures. In most cases, the reactions were not stereoselective providing the *E, Z* mixtures in ~1:1 ratios as shown in Table 2.

All of the above mentioned observations indicate that the aryllithium addition reaction with trifluoroacetyl arenes may



Scheme 7. Proposed mechanism for the formation of triaryl-substituted monofluoroalkene **7** involving a single electron transfer (SET) step.

involve a single electron transfer (SET) step and a plausible mechanism is provided in Scheme 7. The first one equivalent of aryllithium should simply act as a base and it will make the common hydrazoyl anion species **6** as in the case of alkyllithium species. The subsequent LiF elimination step would also release the common intermediate **G**.[19] Then, the second equivalent of aryllithium will start to react with intermediate **G** via addition-elimination reaction to form 1,1-difluoro-2,2-diarylethylene **H**. In contrast to the previous case, because the resulting alkene **H** is a very good electron acceptor especially with a high energy anionic species such as organolithium reagent, very fast SET process might occur between **H** and aryllithium providing the charge transfer complex **I**. The intense blue color of the reaction mixture at the early stage of the reaction was attributed to this intermediate. Once this charge transfer complex **I** is formed, the subsequent radical recombination and LiF elimination reaction should take place at a comparable rate to yield the final product **7**. This proposed mechanism can now explain why the use of less than 3 equiv of aryllithium leaves the starting material **4a** while providing the final product **7**. Formation of biphenyl **8** in trace amount also supports the SET mechanism.

In summary, we have developed a practical and efficient way to prepare highly substituted 1,1-difluoro- or 1-fluoroalkenes starting from readily available trifluoroacetophenone derivatives. The protocol involves conversion of trifluorophenyl acetophenones to the corresponding tosyl hydrazones and treatment with excess alkyl or aryl lithium reagents. When the alkyllithium reagents were used, the reaction yielded 1,1-difluoro-2-alkyl-2-arylethylene as the major product consuming two equivalent of alkyllithium. On the other hand, the use of aryllithium provided 1-fluoro-1,2,2-triarylethylenes in high yields after consumption of three equiv of aryllithium. In the case of aryllithium addition reactions, the reaction seems to proceed *via* single electron transfer (SET) mechanism since the reaction forms a good electron acceptor, 1,1-difluoro-2,2-diarylethylene, as an intermediate. We believe that this strategy will provide an alternative tool for accessing various fluoroalkenes in a practical sense.

Experimental Section

All commercially obtained solvents and reagents were used without further purification except as noted below. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. ^{1}H-NMR and ^{13}C-NMR spectra were obtained using a Varian Gemini-300 (300 MHz for ^{1}H and 75 MHz for ^{13}C) or a Varian Inova-500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) spectrometer. Chemical shifts are reported relative to tetramethylsilane peak (δ 0.00) or solvent peak (δ 7.26 for $CDCl_3$ in ^{1}H NMR, δ 77.2 for $CDCl_3$ in ^{13}C NMR). For determining *E,Z* isomer ratios of fluoroalkenes, ^{19}F-NMR (Varian Gemini-200, 188 MHz for ^{19}F) was employed by integrating fluorine signals from two isomers and hexafluorobenzene was used as an external reference (δ-164.9). IR spectra were obtained using a Thermo-Nicholet Avartar-330 IR spectrometer with a single-bounce ATR (Ge crystal) accessory (Smart MIRacle). Elemental analyses were performed by the Organic Chemistry Research Center at Sogang University using a Carlo Erba EA 1180 elemental analyzer. Tandem gas chromatography/low resolution mass spectroscopy (GC/LRMS) using electron impact (EI) ionization were obtained with a Agilent 6890 series gas chromatography and a 5973N mass selective detector at 70 eV.

General Procedure for *p*-Toluenesulfonylhydrazone 4. 2,2,2-Trifluoroacetophenone **3a** (1.6 g, 7.8 mmol) and *p*-toluenesulfonylhydrazide (2.2 g, 11.7 mmol) were dissolved in EtOH (10 mL) and stirred at 80 °C for 12 h. After 12 h, the reaction mixture was poured into water to yield a precipitate of 2.3 g of crude 2,2,2-trifluoroacetophenone *p*-toluenesulfonylhydrazone **4a**. The crude product was then purified by flash column chromatography (Hex:EtOAc = 1:1). The product was obtained as a white solid (2.3 g, 79%).

Hydrazone 4a: yield = 76%; white solid; R_f = 0.4 (Hex: EtOAc = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.82 (d, J = 8.7 Hz, 2H), 7.55-7.52 (m, 3H), 7.35 (d, J = 8.1 Hz, 2H), 7.26-7.22 (m, 2H), 2.46 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 145.2, 141.7 (q, J = 21 Hz), 134.7, 131.8, 130.2, 130.0, 128.3, 128.2, 125.4, 120.1 (q, J = 164 Hz), 21.9; ESI-HRMS Anal. Calcd for $C_{15}H_{13}F_3N_2O_2SNa$ *m/z*: Acc. Mass $(M + Na)^+$, 365.0547. Obs. Mass $(M + Na)^+$,

365.0546.

Hydrazone 4b: yield = 80%; white solid; R_f = 0.7 (Hex: EtOAc = 6:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.81 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 7.8 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 2.46 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 142.3, 142.0 (q, J = 21 Hz), 134.8, 130.9, 130.0, 128.2, 128.1, 122.3, 121.3, 120.2 (d, J = 164 Hz), 21.9, 21.7; ESI-HRMS Anal. Calcd for $C_{16}H_{15}F_3N_2O_2SNa$ *m/z*: Acc. Mass $(M + Na)^+$, 379.0704. Obs. Mass $(M + Na)^+$, 379.0702.

Hydrazone 4c: yield = 79%; white solid; R_f = 0.3 (Hex: EtOAc = 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.80 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.19 (d, J = 9.0 Hz, 2H), 7.0 (d, J = 8.4 Hz, 2H), 3.86 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.0, 145.1, 141.8 (q, J = 35 Hz), 134.8, 130.0, 128.2, 120.1 (q, J = 273 Hz), 117.0, 115.6, 55.7, 21.9; ESI-HRMS Anal. Calcd for $C_{16}H_{15}F_3N_2O_3SNa$ *m/z*: Acc. Mass $(M + Na)^+$, 395.0653. Obs. Mass $(M + Na)^+$, 395.0655.

Hydrazone 4d: yield = 82%; white solid; R_f = 0.3 (Hex: EtOAc = 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.81 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 7.8 Hz, 2H), 6.92 (d, J = 8.1 Hz, 1H), 6.73 (d, J = 7.8 Hz, 1H), 6.68 (s, 1H), 6.02 (s, 2H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 149.2, 145.1, 141.2 (q, J = 21 Hz), 134.7, 130.0, 128.2, 122.9, 120.1 (q, J = 164 Hz), 118.2, 109.9, 108.4, 102.2, 21.9; ESI-HRMS Anal. Calcd for $C_{16}H_{13}F_3N_2O_2SNa$ *m/z*: Acc. Mass $(M + Na)^+$, 409.0446. Obs. Mass $(M + Na)^+$, 409.0443.

Hydrazone 4e: yield = 80%; white solid; R_f = 0.33 (Hex: EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (br s, 1H), 7.82 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 4.79 (s, 2H), 2.46 (s, 3H), 0.97 (s, 9H), 0.14 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.7, 145.1, 141.9 (q, J_{CF} = 36 Hz), 134.7, 130.0, 128.24, 128.18, 127.4, 123.7, 120.1 (q, J_{CF} = 137 Hz), 64.3, 26.1, 21.9, 18.6, -5.2 ; ESI-LRMS Anal. Calcd for $C_{22}H_{29}F_3N_2O_3SSiNa$ *m/z*: Acc. Mass $(M + Na)^+$, 509.15. Obs. Mass $(M + Na)^+$, 509.37.

General Procedure for 1,1-Difluoro-2-alkylalkenes 5. In a Schlenk flask under an argon atmosphere, *p*-toluenesulfonylhydrazone **4c** (200 mg, 0.54 mmol) was dissolved in dry tetrahydrofuran (5 mL). The solution was cooled to −78 °C. A solution of *n*-butyllithium (1.6 M in hexanes, 0.8 mL, 1.21 mmol) was dropwise added to the reaction mixture in 5 min. Dry ice bath was replaced with an ice bath and the reaction was allowed to warm to 0 °C while stirring. After 30 min, the reaction was quenched by adding a saturated aqueous solution of ammonium chloride (1 mL) and the mixture was extracted with ethyl acetate (X3). The combined extracts were dried over $MgSO_4$, filtered, and the filtrate was concentrated in vacuo. The resulting crude product was purified by flash column chromatography on silica gel (Hex:EtOAc = 30:1) to give **5c** (122 mg, 98% yield).

5a: yield = 94%; R_f = 0.34 (Hexanes:EtOAc = 50:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.25 (m, 5H), 2.38 (br m, 2H), 1.32 (m, 4H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.8 (t, J_{CF} = 288 Hz), 134.1, 128.6, 128.4 (t, J_{CF} = 3.3 Hz), 127.3, 92.6 (t, J_{CF} = 17.0 Hz), 30.1 (t, J_{CF} = 7.8 Hz), 27.5, 22.3, 14.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ −92.5; IR (neat): 3082 (w), 3060 (w), 3025 (w), 2958 (m), 2923 (m), 2863 (w), 1727 (m), 1444 (m), 1233 (s), 1131 (m), 964 (m), 764 (m), 698 (s) cm^{-1}; EI-LRMS *m/e* [%]: 196 (55, M^+), 154 (100), 133 (40), 103 (49), 77 (13).

5c: yield = 98%; R_f = 0.4 (Hexanes:EtOAc = 30:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H), 2.36 (t, J = 6.9 Hz, 2H), 1.31 (m, 4H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 153.6 (t, J_{CF} = 286 Hz), 129.5, 126.2, 114, 92 (t, J_{CF} = 16 Hz), 55.0, 30.0, 27.6, 22.3, 13.9; IR (neat): 3026 (s), 2958 (w), 1727 (m), 1559 (m), 1514 (m), 1291 (m), 1232 (m) cm^{-1}; EI-LRMS *m/e* [%]: 226 (30, M^+), 184 (100), 133(64), 115 (10).

5c': yield = 99%; R_f = 0.4 (Hexanes:EtOAc = 30:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H), 1.94 (t, J = 3.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 153.5 (t, J_{CF} = 283 Hz), 128.8, 127.3, 113.9, 87.1 (t, J_{CF} = 14.6 Hz), 55.5, 13.5; IR (neat): 2930 (w), 1727(w), 1607(w), 1512(m), 1464(w), 1248(s), 1177(m), 1034(m), 831 (s) cm^{-1}; EI-LRMS *m/e* [%]: 184 (100, M^+), 169 (62), 141 (25), 121 (47), 101 (86), 91 (66), 63 (46).

5e: yield = 99%; R_f = 0.8 (Hexanes:EtOAc = 50:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 4.76 (s, 2H), 2.40 (br m, 2H), 1.34 (m, 4H), 0.97 (s, 9H), 0.89 (t, J = 7.3 Hz, 3H), 0.13 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.1 (t, J_{CF} = 285 Hz), 140.6, 128.3, 127.4, 126.3, 92.5, 64.9, 30.1, 27.6, 22.3, 18.7, 14.0, -5.0; EI-LRMS *m/e* [%]: 340 (18), 283 (81), 209 (100), 187 (55), 167 (54), 117 (20).

General Procedure for Triarylmonofluoroethylene 7. In a Schlenk flask under an argon atmosphere, 4-bromotoluene (207 mg, 1.21 mmol) was dissolved in dry tetrahydrofuran (5 mL). The solution was cooled to −78 °C. A solution of *n*-butyllithium (1.6 M in hexanes, 0.8 mL, 1.21 mmol) was added dropwise in 5 min. The resulting yellow solution was further stirred for 10 min and a solution of *p*-toluenesulfonylhydrazone **4c** (150 mg, 0.40 mmol) in dry tetrahydrofuran (2 mL) was added dropwise in 1 min *via* cannula. Dry ice bath was replaced with an ice bath and the reaction was allowed to warm to 0 °C while stirring. After 30 min, the reaction was quenched by adding a saturated aqueous solution of ammonium chloride (1 mL) and the mixture was extracted with ethyl acetate (X3). The combined extracts were dried over $MgSO_4$, filtered, and the filtrate was concentrated in vacuo. The resulting crude product was purified by flash column chromatography on silica gel (Hex:EtOAc = 50:1).

7aa: yield = 95%; R_f = 0.5 (Hexanes:EtOAc = 50:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48-7.02 (m, 15 H); IR (neat): 3058 (w), 1696 (w), 1648 (w), 1496 (m), 1444 (w), 1261 (m), 1183 (w), 9148 (w) cm^{-1}; EI-LRMS *m/e* [%]: 274 (100, M^+), 253 (37), 196 (40), 165 (8), 126 (10), 77 (5).

7ab: yield = 94%; R_f = 0.5 (Hexanes:EtOAc = 50:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 6.94 (m, 13H), 2.32 (s, 3H), 2.33 (s, 3H), 2.63 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1 (d, J = 250 Hz), 139.5 (d, J = 6.8 Hz), 138.9, 138.7, 137.1 (d, J = 2.6 Hz), 136.4 (d, J = 7.1 Hz), 135.8, 131.2 (d, J = 2.9 Hz), 131.0 (d, J = 2.9 Hz), 130.0 (d, J = 4.6 Hz), 129.9 (d, J = 4.8 Hz), 129.4, 128.9, 128.7, 128.6, 128.5, 128.4, 128.1, 127.3, 127.2, 121.6 (d, J = 20.2 Hz), 21.4, 21.3; ^{19}F NMR (188 MHz, $CDCl_3$) δ −106.07, −106.11 (*E,Z* isomer ratio 45 : 55); IR (neat): 3026(w), 2920 (w), 1635 (w), 1513 (m), 1260 (w), 1179 (m), 1054 (m), 819 (s) cm^{-1}; EI-LRMS *m/e* [%]: (E,Z isomer) 302 (100, M^+), 287 (30), 267 (42), 252 (62), 210 (27), 135 (23), 109 (10) and 302 (100, M^+), 287 (33), 267 (50), 252 (72), 210 (31), 135 (26), 109 (11).

7ac: yield = 95%; R_f = 0.3 (Hexanes:EtOAc = 15:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.03 (m, 8H), 6.86-6.67 (m, 5H), 3.79 (s, 3H), 3.77 (s, 3H), 3.75 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 158.9, 158.7, 153.8 (d, J = 249 Hz), 153.6 (d, J = 249 Hz), 139.7 (d, J = 6.8 Hz), 139.1, 132.3 (d, J = 3.1 Hz), 131.7 (d, J = 7.1 Hz), 131.3, 131.2, 131.1, 130.0, 129.98, 129.96, 129.91, 128.6, 128.1, 127.3, 127.1, 125.8 (d, J = 27 Hz), 120.5 (d, J = 18.8 Hz), 114.1, 113.6, 113.5, 113.4, 55.3, 55.2; ^{19}F NMR (188 MHz, $CDCl_3$) δ −106.18, −106.64 (*E,Z* isomer ratio 42 : 58); IR (neat): 2935 (w), 2836 (w), 1607 (m), 1511 (s), 1297 (m), 1248 (s), 1032 (m), 832 (m) cm^{-1}; EI-LRMS *m/e* [%]: (*E,Z* isomer) 334 (100, M^+) , 319 (37), 208 (16), 183 (14), 167 (7) and 334 (100, M^+), 319 (50), 208 (31), 183 (29), 167 (18).

7ba: yield = 97%; R_f = 0.5 (Hexanes:EtOAc = 50:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.00 (m, 14H), 2.35 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8 (d, J = 250 Hz), 139.3 (d, J = 6.8 Hz), 138.8, 137.2, 136.1 (d, J = 6.8 Hz), 135.7, 133.5 (d, J = 1.7 Hz), 133.1 (d, J = 1.7 Hz), 131.2 (d, J = 3.2 Hz), 131.0 (d, J = 3.2 Hz), 130.1 (d, J = 4.6 Hz), 129.9 (d, J = 4.5 Hz), 129.4, 129.2, 128.6, 128.6, 128.1, 127.9, 127.5, 127.4, 122.5, 122.2, 21.4; IR (neat): 3026 (w), 1636 (w), 1599 (w), 1511 (m), 1493 (m), 1445 (m), 1259 (m), 1179 (m), 1056 (m), 756 (s) cm^{-1}; EI-LRMS *m/e* [%]: (*E,Z* isomer) 288 (100, M^+), 273 (28), 252 (60), 196 (41), 135 (15), 109 (9) and 288 (100, M^+), 273 (28), 252 (60), 196 (41), 135 (15), 109 (9).

7bb: yield = 83%; R_f = 0.5 (Hexanes:EtOAc = 50:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24-6.97 (m, 12H), 2.35 (s, 3H), 2.32 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8 (d, J = 249 Hz), 138.5, 137.0 (d, J = 3.5 Hz), 136.5 (d, J = 6.8 Hz), 136.0, 131.0 (d, J = 3.1 Hz), 130.8, 130.4, 129.9 (d, J = 4.6 Hz), 129.3, 128.8 (d, J = 11.9 Hz), 128.4 (d, J = 6 Hz), 121.5 (d, J = 19 Hz), 21.4, 21.3; IR (neat): 3026 (w), 2919 (w), 1639 (w), 1513 (m), 1260 (w), 1176 (m), 1112 (w), 1054 (m), 818 (s) cm^{-1}; EI-LRMS *m/e* [%]: 316 (100, M^+), 281 (10), 266 (19), 224 (7), 210 (7), 135 (7), 109 (5).

7bc: yield = 86%; R_f = 0.4 (Hexanes:EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-6.67 (m, 13H), 3.79 (s, 3H), 3.77 (s, 3H), 3.74 (s, 6H), 2.33 (s, 3H), 2.31 (s, 3H); ^{19}F NMR (188 MHz, $CDCl_3$) δ −106.67, −107.11 (*E,Z* isomer ratio 38:62); IR (neat): 2931 (w), 2836 (w), 1607 (m), 1512 (m), 1297 (m), 1248 (m), 1176 (m), 1032 (m), 832 (m) cm^{-1}; EI-LRMS *m/e* [%]: (*E,Z* isomer) 348 (100, M^+), 333 (13), 257 (14), 213 (18), 170 (14), 109 (8) and 348 (100, M^+), 333 (12), 257 (6), 213 (8), 174 (5), 129 (4).

7ca: yield = 100%; R_f = 0.2 (Hexanes:EtOAc = 50:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.12 (m, 16H), 7.05 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 6.77 (d, J = 8.7 Hz, 2H), 3.81 (s, 3H), 3.78 (s, 3H); IR (neat): 3057 (w), 1633 (w), 1605 (m), 1540 (m), 1511 (s), 1289 (m), 1247 (s), 1055 (m), 828 (m) cm^{-1}; EI-LRMS *m/e* [%]: (*E,Z* isomer) 304 (100, M^+), 239 (13), 183 (12) and 304 (100, M^+), 239 (9), 183 (18); ESI-HRMS Anal. Calcd for $C_{21}H_{17}FONa$ *m/z*: Acc. Mass $(M + Na)^+$, 327.1161. Obs. Mass $(M + Na)^+$, 327.1164.

7cc: yield = 71%; R_f = 0.2 (Hexanes:EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 8.1 Hz, 2H), 7.16 (d, J = 8.7 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 9 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.7 Hz, 2H), 3.79 (d, 3H), 3.78 (d, 3H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 158.9, 158.7, 153.2 (d, J = 248 Hz), 132.3, 131.9, 131.8, 131.4, 131.2 (d, J = 5 Hz), 126.0 (d, J = 29.6 Hz), 120.0 (d, J = 18.5 Hz), 114.1, 113.5, 113.4, 55.3, 55.27; IR (neat): 2932 (w), 2836 (w), 1607 (m), 1511 (s), 1297 (m), 1247 (s), 1032 (m), 831 (m) cm^{-1}; EI-LRMS *m/e* [%]: 364 (100, M^+), 349 (14), 238 (6), 213 (11), 182 (7), 170 (6); ESI-HRMS Anal. Calcd for $C_{23}H_{21}FO_3Na$ *m/z*: Acc. Mass $(M + Na)^+$, 387.1372. Obs. Mass $(M + Na)^+$, 387.1375.

7da: yield = 96%; R_f = 0.6 (Hexanes:EtOAc = 15:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.13 (m), 6.89-6.60 (m), 5.93 (s, 2H), 5.91 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9 (d, J = 251 Hz), 153.8 (d, J = 250 Hz), 148.3, 147.8, 147.1, 146.9, 139.2 (d, J = 7 Hz), 138.5, 133.2 (d, J = 28 Hz), 132.8 (d, J = 7 Hz), 129.9 (d, J = 4.5 Hz), 128.5–128.7, 128.2, 128.0, 127.9, 127.6, 127.5, 124.9 (d, J = 3 Hz), 124.0 (d, J = 4.3 Hz), 111.4, 110.5, 108.6, 108.1, 101.2, 101.1; ^{19}F NMR (188 MHz, $CDCl_3$) δ −106.24, −106.31 (*E,Z* isomer ratio 48 : 52); IR (neat): 3061 (w), 2894 (w), 1487 (s), 1443 (m), 1232 (s), 1101 (w), 1039 (s), 936 (m), 810 (m), 761 (s), 696 (s) cm^{-1}; EI-LRMS *m/e* [%]: (*E,Z* isomer) 318 (100, M^+), 287 (7), 257 (18), 239 (19), 183 (14), 129 (9) and 318 (100, M^+), 287 (7), 257 (18), 239 (19), 183 (14), 129 (9).

7db: yield = 97%; R_f = 0.4 (Hexanes:EtOAc = 15:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24-6.60 (m), 5.95 (s, 2H), 5.93 (s, 2H), 2.35 (s, 3H), 2.32 (s, 3H), 2.30 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 153.9 (d, J = 249 Hz), 153.7 (d, J = 249 Hz), 147.9, 147.5, 147.0, 146.8, 138.6 (d, J = 7 Hz), 137.2, 136.4 (d, J = 13 Hz), 135.9, 133.2 (d, J = 7 Hz), 132.8, 131.0 (d, J = 3 Hz), 129.8 (d, J = 5 Hz), 129.4, 128.9, 128.7 (d, J = 5 Hz), 128.4 (d, J = 3 Hz), 128.3 (d, J = 3 Hz), 111.4, 110.5, 108.6, 108.1, 101.2, 101.1, 21.5, 21.4; ^{19}F NMR (188 MHz, $CDCl_3$) δ −106.57, −106.69 (*E,Z* isomer ratio 44:56); IR (neat): 3024 (w), 2921 (w), 1737 (m), 1506 (m), 1487 (m), 1231 (s), 1041 (s), 937 (m), 817 (s) cm^{-1}; EI-LRMS *m/e* [%]: (*E,Z* isomer) 346 (100, M^+), 301 (18), 257 (16), 170 (9), 91 (25) and 346 (100, M^+), 301 (14), 257 (24), 196 (19), 91 (29).

7dc: yield = 91%; R_f = 0.3 (Hexanes:EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, J = 8.7 Hz, 2H), 7.18 (t,

J = 9 Hz, 3H), 7.04 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 9 Hz, 2H), 6.79-6.61 (m), 5.95 (s, 2H), 5.94 (s, 2H), 3.81 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 158.9, 158.7, 153.5 (d, J = 248 Hz), 147.6, 147.4, 147.2, 146.9, 133.1, 132.9, 132.3 (d, J = 3 Hz), 131.2 (d, J = 5 Hz), 129.9, 125.9 (d, J = 29 Hz), 124.9, 123.9, 119.9, 114.1, 113.6, 113.5, 113.4, 111.5 (d, J = 3 Hz), 110.5 (d, J = 5 Hz), 108.6, 108.0, 101.2, 101.1, 55.4, 55.3; ^{19}F NMR (188 MHz, $CDCl_3$) δ −106.52, −107.14 (*E,Z* isomer ratio 40 : 60); IR (neat): 2903 (w), 2837 (w), 1607 (m), 1511 (s), 1438 (w), 1296 (w), 1248 (s), 1177 (m), 1036 (s), 833 (s), 811 (s) cm^{-1}; EI-LRMS *m/e* [%]: (E,Z isomer) 378 (100, M^+), 277 (15), 233 (49), 207 (38), 170 (32) and 378 (100, M^+), 277 (15), 233 (41), 207 (32), 170 (18).

7dd: yield = 75%; R_f = 0.5 (Hexanes:EtOAc = 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.84 (d, J = 8.1 Hz, 2H), 6.78 (s, 4H), 6.69 (d, J = 7.5 Hz, 2H), 6.61 (d, J = 11.1 Hz, 2H), 5.95 (s, 4H), 5.93 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.4 (d, J = 250 Hz), 147.9, 147.8, 147.5, 147.3, 147.1, 146.8, 132.9 (d, J = 7 Hz), 132.5, 127.1 (d, J = 30 Hz), 124.8 (d, J = 3 Hz), 123.8 (d, J = 4 Hz), 123.0 (d, J = 7 Hz), 120.6 (d, J = 19 Hz), 111.3 (d, J = 3 Hz), 110.4 (d, J = 5 Hz), 108.8 (d, J = 6 Hz), 108.6, 108.0, 101.3, 101.2, 101.1; ^{19}F NMR (188 MHz, $CDCl_3$) δ −104.8; IR (neat): 2894 (w), 1713 (w), 1503 (m), 1487 (s), 1341 (w), 1250 (s), 1225 (s), 1038 (s), 933 (m), 867 (w), 813 (m) cm^{-1}; EI-LRMS *m/e* [%]: 406 (100, M^+), 231 (59), 130 (19).

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