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Nucleophilic Fluoroalkylation of α,β-Enones, Arynes, and Activated Alkynes with Fluorinated Sulfones: Probing the Hard/Soft Nature of Fluorinated Carbanions

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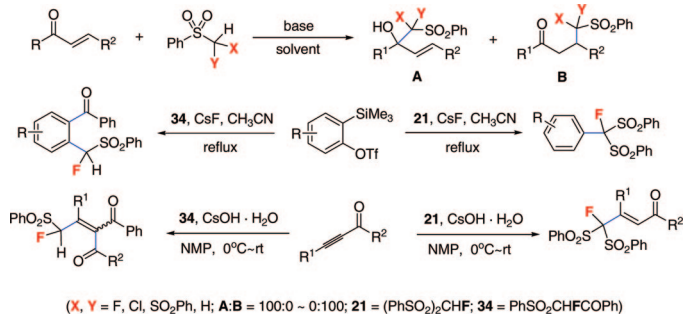

We have successfully accomplished the nucleophilic fluoroalkylation of α,β-enones, arynes, and activated alkynes with fluorinated sulfones. It was found that for acylic α,β-enones, although the reaction medium and the structure of the enones can all influence the regioselectivity of the nucleophilic alkylation reactions, the hard/soft nature of the carbanions played a major role. By using the 1,4- and 1,2-addition product ratio as a probe to determine the hard/soft nature of the above-mentioned four halogenated carbanions, the order of the softness of these carbanions can be given as follows: $[(PhSO_2)_2CF^-]$ (**20**) ≈ $PhSO_2CCl_2^-$ (**32**) > $PhSO_2CHF^-$ (**31**) > $PhSO_2CF_2^-$ (**30**). In the case of fluoroalkylation of aryne (**35** as the precursor) and α,β-acetylenic ketones **46** with fluorobis(phenylsulfonyl)methane (**21**), fluorobis(phenylsulfonyl)methylated arenes **36** and β-fluorobis(phenylsulfonyl)methylated α,β-enones **47** were obtained as the corresponding products in good yields. During the reaction between 2-fluoro-2-(phenylsulfonyl)acetophenone (**34**) and arynes or activated alkynes **46**, an intramolecular tandem reaction process leads to the formation of acyl-fluoroalkylated arenes **43** or α-acyl-β-fluoroalkylated α,β-enones **48**. It turned out that the softness of a fluorine-bearing carbanion (such as **20** or **33** derived from **21** or **34**) plays a crucial role for the success of the nucleophilic fluoroalkylation reactions with arynes and some activated alkynes (α,β-acetylenic ketones).

Introduction

Although organofluorine compounds are the least abundant natural organohalides,[1] many man-made organofluorine compounds have exhibited unique physical, chemical, and biological properties in life science- and material science-related applications.[2] Nucleophilic fluoroalkylation, typically involving the transfer of a fluorinated carbanion (R_f^-, the fluorine substitution is commonly on the carbanionic carbon) to an electrophile, represents one of the major synthetic methods to synthesize organofluorine compounds.[3–11] During the past 3 decades, a number of electrophiles (such as aldehydes, ketones, enones, imines, nitrones, indanones, esters, lactones, cyclic anhydrides, oxazolidinones, amides, imides, azirines, nitroso compounds,

[†] Contributed equally to this work.

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sulfur-based electrophiles, thiocyanates, selenocyanates, alkyl triflates, alkyl halides, aryl halides, epoxides, cyclic sulfates, and sulfamidates, among others) have been successfully fluoroalkylated using various nucleophilic fluoroalkylating agents.[3–11] However, to the best of our knowledge, nucleophilic fluoroalkylation of arynes and alkynes with fluorinated carbanions has never been reported.[12] Another existing challenge in nucleophilic fluoroalkylation reactions is the regioselective introduction of certain fluoroalkyl groups into the β-position of an α,β-enone.[13]

In general, the intrinsic thermal stability and nucleophilicity of a fluorinated carbanion (R_f^-) play a pivotal role in nucleophilic fluoroalkylation reactions. Fluorinated carbanions are commonly recognized as thermodynamically stable but kinetically unstable species.[3–5,14,15] The lifetimes, reactivity, and synthetic utility of fluorinated carbanions are affected by many factors, and as a result, the chemistry of fluorinated carbanions is much different from their nonfluorinated counterparts.[4,5] Previously, in the course of our study on nucleophilic fluoroalkylation of epoxides with fluorinated sulfones, we found there was a "negative fluorine effect (NFE)", i.e., the fluorine substitution on the carbanion center decreases the carbanion's nucleophilicity toward epoxides.[16] α-Functionalization of the fluorinated carbanions with phenylsulfonyl group(s) was found to be a useful approach to alleviate the NFE.[7,16] We envisioned that the electron-withdrawing phenylsulfonyl group *delocalizes* the electron pair on the fluorinated carbanion center, which could result in two important effects on the fluorinated carbanion. First, the *electron delocalization* can significantly reduce the electron repulsion between the electron pairs on the small fluorine atom(s) and the electron lone pair occupying the p-orbital of the carbanion center, and as a result, it increases the thermal stability of a fluorinated carbanion by decreasing its tendency to undergo α-elimination of a fluoride ion (or other groups). Second, the *electron delocalization* increases the polarizability (or softness) of a fluorinated carbanion, which enables its nucleophilic fluoroalkylation reaction with many soft electrophiles (such as many carbon-electrophiles). Both effects imparted by the phenylsulfonyl group(s), i.e., increasing both *thermal stability* and *softness*, are important for the nucleophilicity of a fluorinated carbanion.

We have been particularly interested in the second effect (increasing softness), with the expectation that by tuning the hard/soft nature of a fluorinated carbanion bearing phenylsulfonyl group(s), some previously unkonwn nucleophilic fluoroalkylation reactions might be accomplished. In particular, we assumed that through a detailed study on nucleophilic fluoroalkylation of α,β-enones, the 1,4- and 1,2-addition product ratios can be used as a *probe* to determine the hard/soft nature of the fluorinated carbanions. Furthermore, the "soft" fluorinated carbanions can be apllied in the unprecedent nucleophilic fluoroalkylation of arynes and alkynes, which may give corresponding new fluorine-containing products. In this article, we wish to report our studies toward these goals.

Results and Discussion

1. Nucleophilic Fluoroalkylation of α,β-Enones. 1.1. General Remarks. α,β-Unsaturated compounds (such as α,β-enones) are ambident electrophiles, which have been extensively used in organic synthesis.[17,18] It has been realized that, on the basis of the balance of Coulombic and frontier orbital terms, hard nucleophiles attack the carbonyl group of α,β-enones (called 1,2-addition), whereas soft nucleophiles prefer attacking the β-carbon atom of α,β-enones (called 1,4-addition or Michael addition).[19,20] Because of the high electronegativity of the fluorine atom, many fluorinated carbanions are regarded as hard nucleophiles and thus usually undergo 1,2-addition reactions with α,β-enones.[6,21] In general, the selective nucleophilic introduction of a trifluoromethyl or perfluoroalkyl group into the β-position of an α,β-enone is a challenging task.[13] It was reported that nucleophilic trifluoromethylation and perfluoroalkylation of α,β-enones usually gave 1,2-addition products, and 1,4-addition reactions were only achieved when the carbonyl group of α,β-enone was "protected in situ" or the β-position of α,β-enone was activated with an electron-withdrawing group.[13,22,23] The 1,4-addition between a *gem*-difluorinated carbon-nucleophile and α,β-enones is rare, with the only example that we noticed being the reaction between difluoroenoxysilanes and enones under Lewis acid activation.[24] Kumadaki and co-workers reported a "Michael type reaction" between ethyl bromodifluo-

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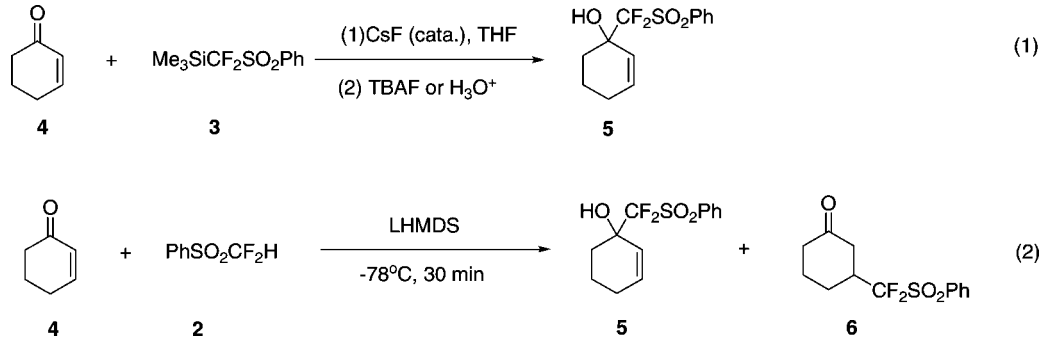
SCHEME 1. (Phenylsulfonyl)difluoromethylation of 2-Cyclohexenone



roacetate and α,β-enones in the presence of copper powder,[25] but it is also possible that the real reaction mechanism involved a free radical process.[26] On the other hand, more examples of 1,4-addition reaction between a monofluorinated carbon-nucleophilie and α,β-enones have been reported.[27] However, little is known about the regioslectivity of the reaction of phenylsulfonyl-substituted fluorocarbanions with the Michael acceptors.[28]

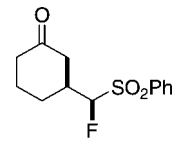
1.2. Addition of Lithiated Di- and Monofluoromethyl Sulfones to Cyclic Enones. Previously, we have reported the nucleophilic difluoromethylation of aldehydes and ketones with two kinds of difluoromethylation agents, $PhSO_2CF_2Li$ (**1**) (generated in situ from the combination of $PhSO_2CF_2H$ (**2**) and LHMDS)[28b] and $Me_3SiCF_2SO_2Ph$ (**3**).[28c] In the case of 2-cyclohexenone (**4**), only the 1,2-addition product **5** was obtained using fluoride-induced (phenylsulfonyl)difluoromethylation with **3** (Scheme 1, reaction 1).[28c] However, when $PhSO_2CF_2Li$ (**1**) was used as a fluoroalkylating agent, we could mainly obtain the 1,4-addition product **6** in the presence of hexamethylphosphoric triamide (HMPA) (Scheme 1, reaction 2 and Table 1, entry 2). Without HMPA, the reaction took place in a 1,2-addition manner, giving allylic alcohol **5** as the major product (Table 1, entry 1). The role of HMPA in controlling the regioselectivity was in accordance with the earlier study of nonfluorinated sulfones.[29] In the absence of HMPA, carbonyl complexation with Li^+ is expected to be pronounced in the transition state of the sulfone reactions, and thus 1,2-addition was favored. Solvation of the lithium counterion by HMPA will prevent the complexation of an enone carbonyl with Li^+, and conjugate addition was favored.[29a,30]

TABLE 1. Addition of Fluorinated Sulfone Anions to 2-Cyclohexenone

entry[a]	fluorinated sulfone	solvent	product	product ratio[b]	overall yield (%)
1	$PhSO_2CF_2H$ (**2**)	THF	**5**, **6**	99:1	98
2	$PhSO_2CF_2H$ (**2**)	THF−HMPA (5:1)	**5**, **6**	7:93	98
3	$PhSO_2CH_2F$ (**8**)	THF	**9**,**10**	99:1	97
4	$PhSO_2CH_2F$ (**8**)	THF−HMPA (5:1)	**9**,**10**	8:92	75[c,d]

[a] Reactant molar ratio **4/2**/LHMDS = 1:1:1.2 (entries 1 and 2) or **4/8**/LHMDS = 2:1:1.2 (entries 3 and 4). [b] Product ratio was determined by ^{19}F NMR analysis of the reaction mixture. [c] Isolated yield of **10**. [d] Diastereomeric ratio of **10** was 4:1.

For lithiated monofluoromethyl phenyl sulfone $PhSO_2CFHLi$ (**7**) (generated in situ from the combination of $PhSO_2CH_2F$ (**8**) and LHMDS), similar results were obtained (Scheme 2). As shown in Table 1, 2-cyclohexenone (**4**) was readily monofluoromethylated with good regioselectivity to give corresponding 1,2- or 1,4-addition product (entries 3 and 4). The two possible diastereomers of the 1,2-adduct **9** were formed in nearly 1:1 ratio, while the 1,4-adduct **10** was formed in 4:1 diastreomeric ratio. The relative configuration of the major diastereomer **10a** was determined to be *syn* configuration by single-crystal X-ray analysis (see Supporting Information).



10a

1.3. Addition of Lithiated Difluoromethyl Phenyl Sulfone to Acyclic Enones. Inspired by the above regioselective fluoromethylation results for the cyclic enone, we continued our efforts in the fluoroalkylation of acyclic enones. First, we examined the reactions of chalcones, which are known to react readily with various organometallics in THF or ether mainly at the C-3 position. This has been observed with a variety of organometallics including α-lithionitrosamines, α-lithiosulfides and α-lithioselenides, α-lithiodithioacetal *S*-oxides, some phosphorus ylides, α-lithiophenylacetonitrile, and α-potassiophosphonates.[31,32]

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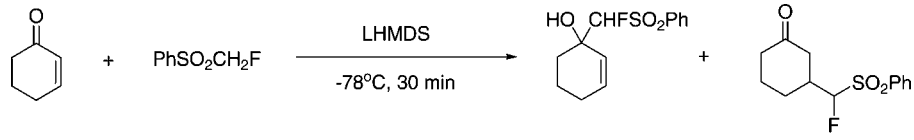
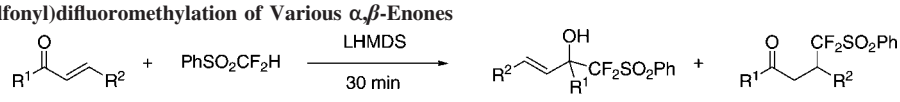
SCHEME 2. (Phenylsulfonyl)monofluoromethylation of 2-Cyclohexenone



4 8 9 10

TABLE 2. (Phenylsulfonyl)difluoromethylation of Various α,β-Enones



11 2 12 13

entry[a]	enone	products	overall yield (THF), %[b,c]	overall yield (THF-HMPA), %[c,d]
1	$R^1 = C_6H_5$, $R^2 = C_6H_5$ (**11a**)	**12a**	97	90
2	$R^1 = C_6H_5$, $R^2 = 4\text{-}ClC_6H_4$ (**11b**)	**12b**	91	95
3	$R^1 = 4\text{-}BrC_6H_4$, $R^2 = C_6H_5$ (**11c**)	**12c**	93	93
4	$R^1 = C_6H_5$, $R^2 = 4\text{-}MeOC_6H_4$ (**11d**)	**12d**, **13d**	97 (68:32)	90 (>99:1)
5	$R^1 = 4\text{-}MeOC_6H_4$, $R^2 = C_6H_5$ (**11e**)	**12e**, **13e**	95 (73:27)	98 (>99:1)
6	$R^1 = 4\text{-}MeOC_6H_4$, $R^2 = 4\text{-}MeOC_6H_4$ (**11f**)	**12f**, **13f**	90 (68:32)	93 (>99:1)
7[e]	$R^1 = CH_3$, $R^2 = C_6H_5$ (**11g**)	**12g**	91	91
8[d,e]	$R^1 = C_6H_5$ $R^2 = CH_3CH_2CH_2$ (**11h**)	**12h**, **13h**	88 (60:40)	60 (85:15)
9[d,f]	$R^1 = CH_3$, $R^2 = H$ (**11i**)	**12i**, **13i**	63 (>99:1)	50 (82:18)

[a] For entries 1−6, **11/2**/LHMDS = 1.0:1.2:1.2. [b] Reaction was performed at −98 °C. [c] Overall yield of the isolated products. The number in parentheses refers to the ratio of **12**:**13**, which was determined by ^{19}F NMR analysis of the isolated product mixture. [d] Reaction was performed at −78 °C. [e] **11/2**/LHMDS = 1.2:1.0:1.2. [f] **11/2**/LHMDS = 1:1:1.

However, when $PhSO_2CF_2Li$ (**1**) was used as a carbon-nucleophile, it was found that 1,2-addition reaction predominated (Table 2). When the aromatic rings are nonsubstituted or substituted with an electron-withdrawing group (such as Cl and Br), only 1,2-addition products **12** were obtained (Table 2, entries 1−3). For the chalcones with an electron-donating substituent such as OMe, although the reactions gave a mixture of 1,2- and 1,4-adducts **12** and **13**, the 1,2-addition products **12** were found to be the major ones (with the ratio **12/13** ranging from 2.3:1 to 2.7:1; see entries 4−6). It should be noted that the reactions were typically carried out at low temperature (−98 °C) in order to suppress the reverse reaction of the 1,2-addition product **12** to the enone **11** and sulfone **2** under the basic reaction condition.[33]

It is interesting that for the chalcones we examined, when the reaction was performed in the presence of HMPA, the 1,2-addition was favored (Table 2, entries 1−6). This indicates that HMPA had different effects in the (phenylsulfonyl)difluoromethylation reactions of 2-cyclohexenone (**4**) (Table 1) and chalcones (**11**) (Table 2). Previously, Krief and co-workers also found that a series of α-thio- and seleno-alkyllithiums added to chalcone exclusively at carbonyl carbon in THF−HMPA.[32] As shown in Table 2 (entries 4−6), the methoxyl chalcones were prone to undergo 1,4-addition while others were not. The 1,4-addition of the methoxy-substituted chalcones may be attributed to the electron-donating property of the methoxy group, which makes the carbonyl carbon less electrophilic and thus increases the tendency to undergo 1,4-addition.

For a better understanding of the influence of the structure of the enones on the regioselectivity, we compared the addition manner of acylic enones with that of different substituents. For the β-aryl-substituted enones **11a** and **11g**, the sole carbonyl addition products **12a** and **12g** were obtained (Table 2, entries 1 and 7). For the β-alkyl-substituted benzalpentanone **11h** (Table 2, entry 8), the regioselectivity was different from that of the β-aryl-substituted ones (Table 2, entries 1 and 7). The difference between **11g** and **11h** may originate from the loss of π-conjugation energy at the transition state when the β-carbon goes from sp^2 hybridization to sp^3 hybridization,[34] which is greater for β-aryl-substituted enones **11g** than for β-alkyl-substituted enone **11h**. Therefore, the β-carbon of the aryl-conjugated enones is less likely to be attacked by nucleophiles. The result with methylvinylketone **11i** (Table 2, entry 9) indicates that in the absence of any aryl substituent, the lithium complexation with the carbonyl promotes a 1,2-addition and the solvation effect of HMPA could somewhat promote the 1,4-addition, which is similar to the case with cyclic enones.

Although the influence of lithium ion−carbonyl complexation on the 1,2- or 1,4-addition manner is not fully understood, our experimental results indicate that for aryl ketones, the 1,4-addition was promoted by the lithium ion−carbonyl complexation (Table 2, entries 4−6 and 8), while for alkyl ketones, the 1,2-addition was promoted by lithium ion−carbonyl complexation (Table 1, entries 1 and 2 and Table 2, entry 9).

To understand the hard/soft nature of different halogenated carbanions, we also studied the reactivity of the chlorinated carbanion $PhSO_2CCl_2Li$ (**14**, generated in situ from the combination of $PhSO_2CCl_2H$ (**15**) and LHMDS). The results are summarized in Table 3. Surprisingly, when THF was used as solvent, $PhSO_2CCl_2Li$ (**14**) readily reacted with a variety of α,β-enones to provide the conjugated addition products **16**. It is remarkable that even in the presence of HMPA, the reaction

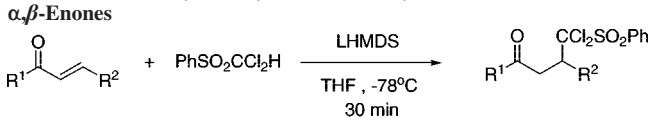
(31) (a) Wartski, L.; El Bouz, M.; Seyden-Penne, J.; Dumont, W.; Krief, A. *Tetrahedron Lett.* **1979**, *20*, 1543–1546. (b) Brown, C. A.; Yamaichi, A. *J. Chem. Soc., Chem. Commun.* **1979**, *100*, 101. (c) Brown, C. A.; Chapa, O.; Yamaichi, A. *Heterocycles* **1982**, *18*, 187–189. (d) Binns, M. R.; R. K. Haynes, R. K. *J. Org. Chem.* **1981**, *46*, 3790–3795. (e) Colombo, L.; Gennari, C.; Resnati, G.; Scolastico, C. *Synthesis* **1981**, *74*, 76.

(32) Dumont, W.; Lucchetti, J.; Krief, A. *J. Chem. Soc., Chem. Commun.* **1983**, 66–68.

(33) *Sulfones in Organic Synthesis, Tetrahedron Organic Chemistry Series, Volume 10*; Baldwin, J. E., Magnus, P. D., Eds.; Pergamon: New York, 1993.

(34) (a) Cossentini, M.; Deschamps, B.; Anh, N. T.; Seyden-Penne, J. *Tetrahedron* **1977**, *33*, 409–412. (b) Deschamps, B.; Seyden-Penne, J. *Tetrahedron* **1977**, *33*, 413–417.

TABLE 3. (Phenylsulfonyl)dichloromethylation of of Various α,β-Enones



4, 11 **15** **16a-g**

entry[a]	enone	product	yield (%)[b]
1	$R^1 = C_6H_5$, $R^2 = C_6H_5$ (**11a**)	**16a**	95(97)
2	$R^1 = C_6H_5$, $R^2 = 4\text{-}MeOC_6H_4$ (**11d**)	**16d**	93
3	$R^1 = 4\text{-}MeOC_6H_4$, $R^2 = C_6H_5$ (**11e**)	**16e**	93
4	$R^1 = 4\text{-}MeOC_6H_4$, $R^2 = 4\text{-}MeOC_6H_4$ (**11f**)	**16f**	97(92)
5	$R^1 = C_6H_5$, $R^2 = CH_3CH_2CH_2$ (**11h**)	**16h**	92
6[c]	$R^1 = CH_3$, $R^2 = H$ (**11i**)	**16i**	40
7	R^1, $R^2 = CH_2CH_2CH_2$ (**4**)	**16j**	95

[a] Reaction was performed using enone/**15**/LHMDS = 1.0:1.0:1.2 molar ratio. [b] Isolated yield of the analytical pure compound. Number in parentheses refers to the isolated yield when the reaction was performed in the presence of HMPA. [c] **11i**/**15**/LHMDS = 1.0:1.2:1.2.

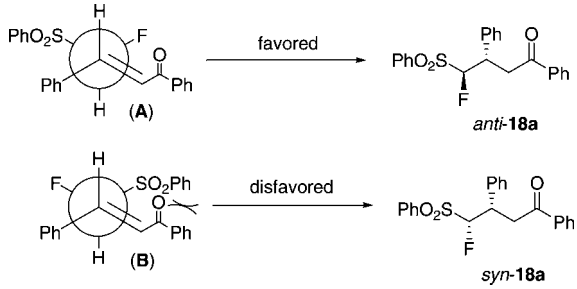


FIGURE 1. Transition state representations for reactions between lithiated monofluoromethyl sulfone **8** and chalcones **11a**.

still occurred in a 1,4-addition manner (Table 3, entries 1 and 4), which is in sharp contrast to the case of $PhSO_2CF_2Li$ (Table 2). This indicates that chlorine- and fluorine-substitution on the carbanion center pose different effects on the hard/soft nature of the carbanion: *a chlorinated carbanion has much softer nature than a fluorinated one*.

1.4. Addition of Lithiated Monofluoromethyl Phenyl Sulfone to Chalcones. On the basis of the above studies, we turned our interest to the nucleophilic monofluoroalkylation of chalcones with lithiated monofluoromethyl sulfone, assuming that the monofluorinated carbanion would be softer than the difluorinated one. According to the general procedure for the difluoromethylation of enones, we performed the reaction with $PhSO_2CH_2F$ (**8**). Treatment of a mixture of the chalcones **11a**−**f** and sulfone **8** with LHMDS in THF at −78 °C resulted in the formation of a mixture of 1,2- and 1,4-adducts **17** and **18** in excellent overall yields, with 1,4-addition products **18** being the major products (Table 4). This indicates that the *monofluorinated carbanion* $PhSO_2CHF^-$ *is a softer nucleophile than the difluorinated carbanion* $PhSO_2CF_2^-$.

In most cases, the 1,2-adducts **17** showed a 1:1−1:1.6 diastereomeric ratio (for details, see Supporting Information), while the 1,4-adducts **18** had better diastereoselectivity (dr = 1:2.2−1:20). The relative configuration of the main diastereomer of **18** was determined to be *anti* by X-ray analysis of the benzoylhydrazone derivate **19** (see Scheme 3 and Supporting Information). It was interesting that the chalcones gave good diastereoselectivity although the fluorine atom is only slightly larger (r_v = 1.35 Å) than the hydrogen atom (r_v = 1.20 Å). The obtained *anti* diastereoselectivity of **18** is depicted in Figure 1. Taking all the possible transition states into account, species (**A**) could be the most sterically favored one, having both two *anti*-positioned hydrogen atoms and *anti*-positioned phenylsulfonyl and carbonyl groups at the two vicinal stereogenic centers. It is important to mention that, in all cases when HMPA was added, mainly 1,2-addition product **17** was obtained. The results are also summarized in Table 4.

1.5. Addition of Bis(benzenesulfonyl)monofluoromethyl Anion to Acyclic Enones. To further understand the hard/soft nature of fluorinated carbanions, we studied fluoroalkylation of α,β-enones with bis(benzenesulfonyl)monofluoromethyl anion [$(PhSO_2)_2CF^-$] (**20**). We envisioned that a better delocalization of the negative charge of the carbanion by two benzenesulfonyl groups could significantly increase the carbanion's softness and therefore favor 1,4-addition with α,β-enones. Fluorobis(benzenesulfonyl)methane $(PhSO_2)_2CFH$ (**21**), as a monofluoromethide equivalent, has been independently reported by the groups led by Shibata,[35] Hu,[16] and Prakash.[36] We applied it in the nucleophilic fluoroalkylation of epoxides and aziridines.[16] With a modified procedure, when an excess amount (1.5 equiv) of the bis(phenylsulfonyl)methane (**22**) reacted with NaH (1.0 equiv), followed by adding SelectFluor (1.0 equiv),[37] product **21** was obtained in 75% isolated yield.

Initially, we studied the nucleophilic addition of $(PhSO_2)_2CF^-$ (**20**) to chalcones using *n*-BuLi or LHMDS as a base; however, the reaction was sluggish. Then we applied a milder phase-transfer-catalysis (PTC) reaction condition using 10 mol % of *N*-(4-trifluoromethylbenzoyl)cinchonine bromide. However, with toluene as solvent, after 12 h of stirring at ambient temperature, we found no expected reaction occurred. The reaction was then attempted using a polar solvent DMF.[38] Much to our delight, we found that the combination of DMF and aqueous NaOH was a most suitable and effective solvent/base pair. The reaction proceeded smoothly at room temperature affording the Michael adduct **23a** in excellent yield (Table 5, entry 1). Even the weaker bases (such as Et_3N) could also be used, but longer reaction time was required to reach a complete conversion of the starting material. It should be mentioned that when $(PhSO_2)_2CH_2$ (**22**) was used instead of $(PhSO_2)_2CFH$ (**21**) under NaOH/H_2O/DMF condition, the reaction became much slower. The higher reactivity of **21** might arise from its increased C−H acidity due to the electron-withdrawing effect of the fluorine substituent.

With the optimized reaction condition established, the scope of the reaction in terms of substrates was investigated. The results are as shown in Table 5. For both chalcones (entries 1−6 and 11) and methyl benzalacetones (entries 7−10), the 1,4-addition products were obtained in good to excellent yield, indicating that $(PhSO_2)_2CF^-$ (**20**) possesses much better nucleophilicity toward the Michael acceptors than $PhSO_2CHF^-$ (**7**) due to the enhanced softness imparted by two phenylsulfonyl groups.

1.6. Addition of Fluorinated and Chlorinated Sulfone to Other Michael Acceptors. For further understanding of the polarizability (softness) of the fluorinated and chlorinated carbanions, we also examined the reactions of the fluorinated and chlorinated sulfones with other Michael acceptors such as

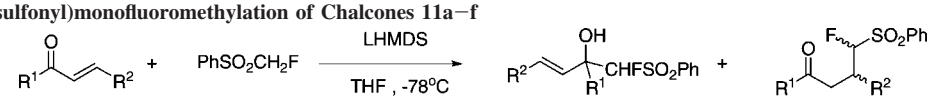
(35) (a) Fukuzumi, T.; Shibata, N.; Sugiura, M.; Yasui, H.; Nakamura, S.; Toru, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4973–4977. (b) Mizuta, S.; Shibata, N.; Goto, Y.; Furukawa, T.; Nakamura, S.; Toru, T. *J. Am. Chem. Soc.* **2007**, *129*, 6394–6395.

(36) Prakash, G. K. S.; Chacko, S.; Alconcel, S.; Stewart, T.; Mathew, T.; Olah, G. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 4933–4936.

(37) SelectFluor is the commercial name of 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate), a electrophilic fluorinating agent manufactured by Air Products.

(38) Liang, Y.; Dong, D.; Lu, Y.; Wang, Y.; Pan, W.; Chai, Y.; Liu, Q. *Synthesis* **2006**, 3301–3304.

TABLE 4. (Phenylsulfonyl)monofluoromethylation of Chalcones 11a−f



11a-f 8 17a-f 18a-f

entry[a]	enone	products	product ratio (**17**:**18**)[b]	dr of **18** (syn:anti)[b]	overall yield (%)[c,d]
1	$R^1 = C_6H_5$, $R^2 = C_6H_5$ (11a)	**17a**,**18a**	42:58	1:15	98(97)
2	$R^1 = C_6H_5$, $R^2 = 4\text{-}ClC_6H_4$ (11b)	**17b**,**18b**	26:74	1:7.5	97(95)
3	$R^1 = 4\text{-}BrC_6H_4$, $R^2 = C_6H_5$ (11c)	**17c**, **18c**	56:44	1:2.2	93(96)
4	$R^1 = C_6H_5$, $R^2 = 4\text{-}MeOC_6H_4$ (11d)	**17d**,**18d**	36:64	1:15	98(96)
5	$R^1 = 4\text{-}MeOC_6H_4$, $R^2 = C_6H_5$ (11e)	**17e**, **18e**	38:62	1:21	97(97)
6	$R^1 = 4\text{-}MeOC_6H_4$, $R^2 = 4\text{-}MeOC_6H_4$ (11f)	**17f**, **18f**	34:66	1:17	93(93)

[a] Reaction was performed using **11**/**8**/LHMDS = 1.0:1.0:1.2 molar ratio. [b] Both the product ratio and the diastereomer ratio were determined by ^{19}F NMR analysis of the isolated products. [c] Overall yield of **17** and **18**. [d] Number in parentheses refers to the isolated yield when the reaction was performed in THF−HMPA (**17**:**18** > 99:1).

SCHEME 3. Separation of 17a and 18a for Determination of the Relative Configuration of 18

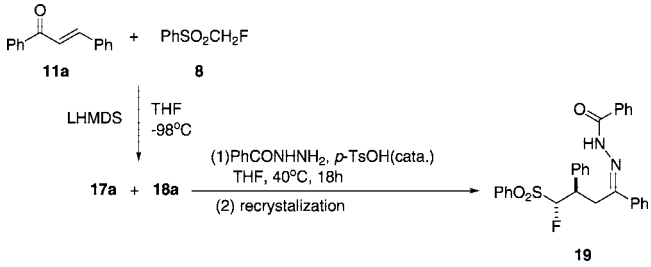
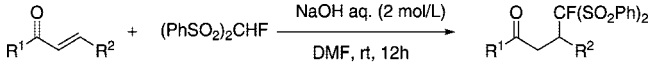


TABLE 5. Bis(benzenesulfonyl)monofluoromethylation of Various α,β-Enones



11 21 23a-k

entry[a]	enone	product	yield (%)[b]
1	$R^1 = C_6H_5$, $R^2 = C_6H_5$ (**11a**)	**23a**	98
2	$R^1 = C_6H_5$, $R^2 = 4\text{-}ClC_6H_4$ (**11b**)	**23b**	75
3	$R^1 = 4\text{-}BrC_6H_4$, $R^2 = C_6H_5$ (**11c**)	**23c**	96
4	$R^1 = C_6H_5$, $R^2 = 4\text{-}MeOC_6H_4$ (**11d**)	**23d**	97
5	$R^1 = 4\text{-}MeOC_6H_4$, $R^2 = C_6H_5$ (**11e**)	**23e**	95
6	$R^1 = 4\text{-}MeOC_6H_4$, $R^2 = 4\text{-}MeOC_6H_4$ (**11f**)	**23f**	83
7	$R^1 = CH_3$, $R^2 = C_6H_5$ (**11g**)	**23g**	90
8	$R^1 = CH_3$, $R^2 = 4\text{-}MeOC_6H_4$ (**11j**)	**23j**	94
9[c]	$R^1 = CH_3$, $R^2 = 4\text{-}Me_2NC_6H_4$ (**11k**)	**23k**	72
10	$R^1 = CH_3$, $R^2 = 4\text{-}FC_6H_4$ (**11l**)	**23l**	73
11	$R^1 = C_6H_5$, $R^2 = 4\text{-}Me_2NC_6H_4$ (**11m**)	**23m**	92

[a] Unless otherwise noted, all the reactions were performed on 0.3 mmol scale with 0.9 mL of DMF and 0.6 mL of aqueous NaOH. [b] Isolated yield. [c] Reaction was performed on 0.2 mmol scale at room temperature for 48 h.

α,β-unsaturated aldehyde **24**, ester **26**, and nitroolefin **28**. The results are summarized in Table 6.

For cinnamaldehyde **24**, only 1,2-addition product was obtained due to the high reactivity of the aldehyde (Table 6, entries 1−3). It should to be mentioned that HMPA plays an important role in promoting the reaction between **24** and $PhSO_2CH_2F$ (**8**). In the absence of HMPA, very low yield of 1,2-addition product **25b** was obtained (Table 6, entry 2). When $(PhSO_2)_2CFH$ (**21**) was used as the fluorinated nucleophile to react with **24**, the reaction turned out to be sluggish in DMF with NaOH as a base or in THF with *n*-BuLi as a base.

In the case of α,β-unsaturated ester **26**, the addition manner is similar to that of α,β-unsaturated enones (Table 6, entries 4−6). We also examined the reaction between **26** and $(PhSO_2)_2CFH$ (**21**) using NaOH as a base, no desired product was obtained and the hydrolysis of **26** was observed. For phenyl nitroolefin **28**, it showed the character as a good Michael acceptor for all the fluorinated and chlorinated sulfone anions that were tested, and β-subsitituted nitroalkanes were obtained in moderate to excellent yields (Table 6, entries 7−10).

1.7. Order of Softness of Some Fluorinated Carbanions. As discussed above, the nucleophilic alkylation of cyclic and acylic α,β-enones was carried out with three fluorinated carbanions, $PhSO_2CF_2^-$ (**30**), $PhSO_2CHF^-$ (**31**), and $(PhSO_2)_2CF^-$ (**20**), and dichlorinated carbanion $PhSO_2CCl_2^-$(**32**). Although the reaction medium and the structure of the enones can all influence the regioselectivity of the nucleophilic alkylation reactions, the hard/soft nature of the carbanions played a major role. By using the 1,4- and 1,2-addition product ratio as a probe to determine the hard/soft nature of the above-mentioned four halogenated carbanions, the order of the softness of these carbanions can be given as follows: $[(PhSO_2)_2CF^-]$ (**20**) ≈ $PhSO_2CCl_2^-$ (**32**) > $PhSO_2CHF^-$ (**31**) > $PhSO_2CF_2^-$ (**30**) (see Table 7).

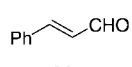
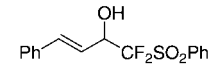
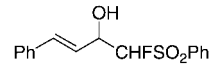
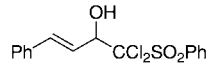
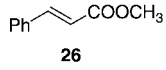
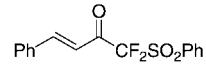
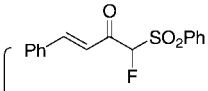
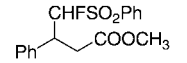
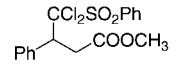
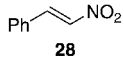
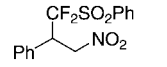
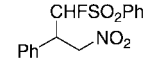
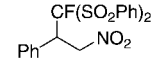
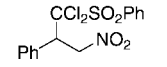
2. Nucleophilic Fluoroalkylation of Arynes and Activated Alkynes. 2.1. General Remarks. Arynes[39] and alkynes[40] are two categories of compounds that are highly useful in organic synthesis. However, the nucleophlic fluoroalkylation of arynes and alkynes with fluorinated carbanions are generally difficult due to their unmatched hard−soft nature.[19] In our previous studies, we found that the substitution of one or two phenylsulfonyl groups on the fluorinated carbanion center could alleviate the "negative fluorine effect (NFE)" and enhance the nucleophilicity of fluorinated carbanions.[7,16] We envisioned that by using the "softened" fluorinated carbanions **20** and **33** that were derived from fluorobis(phenylsulfonyl)methane (**21**)[16,35,36] and 2-fluoro-2-(phenylsulfonyl)acetophenone (**34**),[41] nucleophilic fluoroalkylation of arynes and some activated alkynes might be achieved. As our continuing efforts in trying to understand the hard/soft nature of fluorinated carbanions as well as their nucleophilicity (see above), we carried out the unprecedented nucleophilic fluoroalkylation of arynes (**35** as the

(39) For reviews on the use of arynes in organic synthesis, see:(a) Peña, D.; Pérez, D.; Guitián, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 3579–3581. (b) Pellissier, H.; Santelli, M. *Tetrahedron* **2003**, *59*, 701–730. (c) Wenk, H. H.; Winkler, M.; Sander, W. *Angew. Chem., Int. Ed.* **2003**, *42*, 502–528. (d) Kessar, S. V. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991.

(40) For reviews on the use of alkynes in organic synthesis, see: (a) *Acetylene Chemistry: Chemistry, Biology, and Material Science*; Diederich, F.; Stang, P.; Tykwinski, R. R., Eds.; Wiley-VCH: Weinheim, 2005. (b) *Modern Acetylene Chemistry*; Stang, P. J.; Diederich, F., Eds.; VCH: Weinheim, 1995.

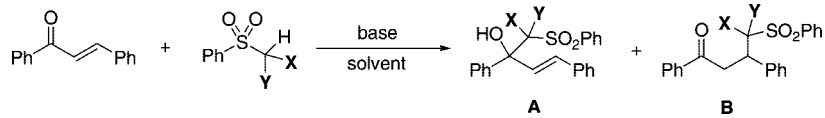
(41) Toyota, A.; Ono, Y.; Chiba, J.; Sugihara, T.; Kaneko, C. *Chem. Pharm. Bull.* **1996**, *44*, 703–708.

TABLE 6. Addition of Fluorinated and Chlorinated Sulfone to Other Michael Acceptors

entry[a]	Michael acceptor	sulfone	product		yield[b], %
1	 **24**	$PhSO_2CF_2H$ (**2**)		(**25a**)	(84)
2		$PhSO_2CH_2F$ (**8**)		(**25b**)	27(92)
3		$PhSO_2CCl_2H$ (**15**)		(**25c**)	94
4	 **26**	$PhSO_2CF_2H$ (**2**)		(**27a**)	(94)
5[c]		$PhSO_2CH_2F$ (**8**)	 	(**27b**) (**27b′**)	63(79) 32[d](15)[e]
6		$PhSO_2CCl_2H$ (**15**)		(**27c**)	(91)
7	 **28**	$PhSO_2CF_2H$ (**2**)		(**29a**)	(77)
8		$PhSO_2CH_2F$ (**8**)		(**29b**)	63[f]
9		$(PhSO_2)_2CFH$ (**21**)		(**29c**)	65
10		$PhSO_2CCl_2H$ (**15**)		(**29d**)	93

[a] All reactions were carried out at −78°C except for entries 3 and 4, which were carried out at −98 °C. [b] Isolated yield. The number in parentheses refers to the isolated yield when the reaction was performed in THF−HMPA. [c] Yields of **27b** and **27b′** were determined by ^{19}F NMR analysis of the products mixture. [d] Only one diastereomer was observed by ^{19}F NMR. [e] Diastereomeric ratio was 1:1 determined by ^{19}F NMR analysis. [f] Diastereomer ratio was 6:1 determined by ^{19}F NMR analysis.

TABLE 7. Summary of Results of the Addition of Fluorinated and Chlorinated Sulfone to Chalcone



A **B**

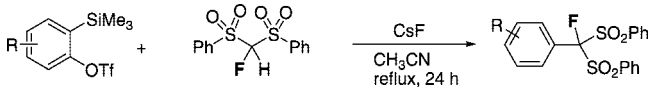
entry	X	Y	yield (**A** + **B**)	**A**:**B**
1	F	F	97	100:0
2	F	H	98	42:58
3	F	SO_2Ph	98	0:100
4	Cl	Cl	95	0:100

precursor) and activated alkynes **46** to give the fluoroalkylated arenes and fluoroalkylated alkenes as the corresponding products.

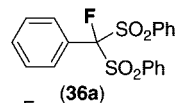
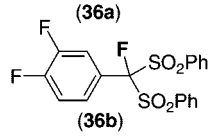
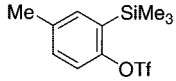
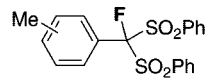
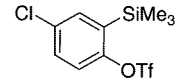
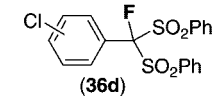
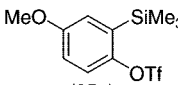
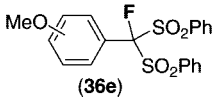
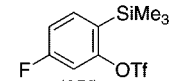
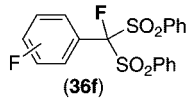
2.2. Nucleophilic Fluoroalkylation of Arynes with Fluorobis(phenylsulfonyl)methane (21). In 1983, Kobayashi and co-workers[42] developed a convenient route to arynes via fluoride-induced 1,2-elimination of *o*-trimethylsilylaryl triflates under mild conditions. Since then, this method has been extensively used in various organic reactions where arynes were needed.[39,43] Initially, we chose *o*-trimethylsilylphenyl triflate (**35a**) as a model compound (as a benzyne precursor) to react with fluorobis(phenylsulfonyl)methane (**21**) in the presence of CsF in THF at varied temperatures, but no expected product was observed. After a quick scanning of different solvents, we found that acetonitrile was the best solvent for the reaction. The optimized reactant molar ratio was **21**:**35a**:CsF = 1.0:1.5:3.0, and the reaction mixture was heated at reflux temperature for 24 h to give product **36a** in 62% yield (Table 8, entry 1). In this reaction, CsF acted both as nucleophile to activate the C−Si bond cleavage of compound **35,** and as a base to deprotonate compound **21** to generate fluorinated carbanion **20** (Scheme 4).

(42) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211–1214.

TABLE 8. Fluorobis(phenylsulfonyl)methylation of Arynes

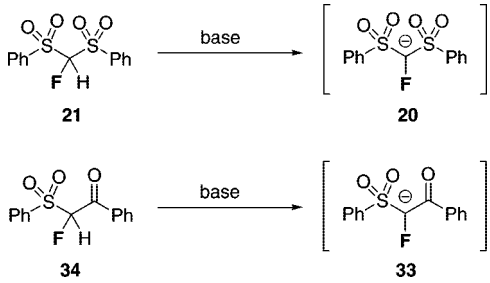


35 21 36

entry[a]	substrate 35	product 36	yield (%)[b]
1	 (35a)	 (36a)	62
2	 (35b)	 (36b)	60
3	 (35c)	 (36c)	70 (ratio = 1:1.3)[c]
4	 (35d)	 (36d)	90 (ratio = 1:1.6)[c]
5	 (35e)	 (36e)	82 (ratio = 1:1.5)[c]
6	 (35f)	 (36f)	88 (ratio = 1:1.5)[c]

[a] Molar ratio of the reactants: **21/35/CsF**=1.0:1.5:3.0. [b] Isolated yield. [c] Isomeric ratio of *meta*- and *para*-fluoroalkylated products, determined by ^{19}F NMR spectroscopy.

SCHEME 4. Generation of Carbanions 20 and 33



The structure of compound **36a** was confirmed by X-ray single crystal structure analysis (see Supporting Information).

We then investigated the scope of this new type of nucleophilic fluoroalkylation of arynes, and the results are shown in Table 8. It turned out that in the presence of CsF, the nucleophilic fluoroalkylating agent **21** (more precisely, the carbanion **20**) smoothly reacted with a variety of aryne precursors **35** to accomplish the Ar-R_f bond formation, giving the fluoroalkylated products **36** in good yields. For unsymmetrical arynes, the products were obtained as a combination of *meta*- and *para*-substituted isomers with the isomeric ratio 1:1.3−1.6 (Table 8, entries 3−6). For the methyl- and methoxy-substituted benzynes, the major products were also *para*-substituted isomers (Table 8, entries 3 and 5), indicating that the steric effect (due to the bulkiness of nucleophile **20**) is the major factor to control the product outcomes.[44]

It is worthwhile to mention that the nonfluorinated compound bis(phenylsulfonyl)methane **22** could also readily react with aryne under slightly modified reaction conditions to give diphenylated product **37** in 55% isolated yield (Scheme 5). It seems obvious that during the reaction between **35a** and **22** in the presence of CsF, the deprotonation−arylation reaction sequence occurred twice (see proposed mechanism in Scheme 5).

2.3. Nucleophilic Fluoroalkylation of Arynes with 2-Fluoro-2-(phenylsulfonyl)acetophenone (34). Encouraged by the above results, we further studied the reaction between arynes and another nucleophilic fluoroalkylating agent **34**. 2-Fluoro-2-(phenylsulfonyl)acetophenone (**34**) was previously prepared by Kaneko and co-workers[41] via direct fluorination of 2-(phenylsulfonyl)acetophenone (**42**) with F_2/N_2 (5% v/v) in low yield (31%). We carried out an improved preparation of 2-fluoro-2-(phenylsulfonyl)acetophenone (**34**) by electrophilic fluorination of 2-(phenylsulfonyl)acetophenone (**42**) with SelectFluor,[37] and product **34** was obtained in 60% isolated yield (Scheme 6). The results of the reaction between arynes and fluoroalkylating agent **34** are shown in Table 9. Under the similar reaction conditions as mentioned above (except the reaction time was reduced to 12 h), compound **34** showed excellent reactivity toward arynes, enabling both Ar-R_F bond and Ar-C(O)Ph bond formations in one pot to give products **43** in 70−98% yields. For unsymmetrical arynes, the products were obtained as the combination of two isomers with the isomeric ratio 1:1.0−1.5 (Table 9, entries 4−7).

Recently, Stoltz and co-workers reported a direct acylalkylation of arynes by using β-ketoesters.[43] Larock and coworkers also demonstarted two interesting trifluoroacetylation-amination and trifluorosulfinylation-amination reactions of arynes by using trifluoroacetamides and trifluoromethanesulfinamides.[43] More recently, Huang and Xue reported a multicomponent reaction of arynes, β-keto sulfones, and Michael-type acceptors.[45] However, none of these reports described a reaction between an aryne and a fluorine-bearing carbon nucleophile. The reaction mechanism for our current acylation-fluoroalkylation of arynes was proposed in Scheme 7. It can be rationalized that, the strong electron-withdrawing effect imposed by fluorine substitution could facilitate both the deprotonation for **34** and the ring-opening step for **45**, which could be in part explain the good to excellent chemical yields for the current reactions (as shown in Table 9).

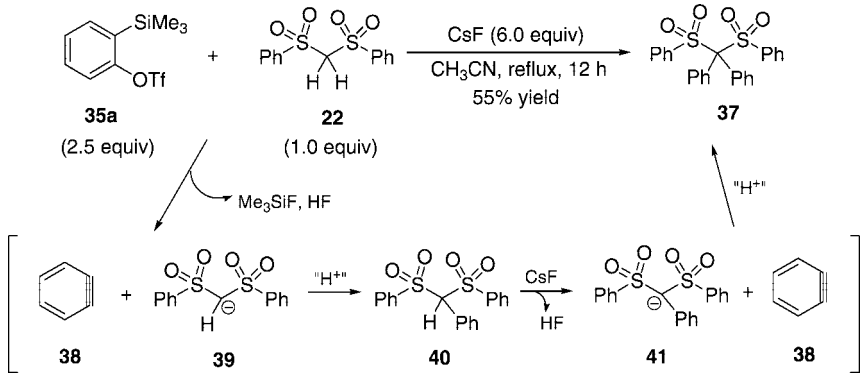
2.4. Nucleophilic Fluoroalkylation of Activated Alkynes (46) with Fluorobis(phenylsulfonyl)methane (21). Based on the above-mentioned results of nucleophilic fluoroalkylation of arynes, we turned our interest to the unprecedented nucleophilic fluoroalkylation of alkynes. First of all, we attempted the

(43) For selected recent examples, see: (a) Gilmore, C. D.; Allan, K. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2008**, *130*, 1558–1559. (b) Liu, Z.; Shi, F.; Martinez, P. D. G.; Raminelli, C.; Larock, R. C. *J. Org. Chem.* **2008**, *73*, 219–226. (c) Ding, H.; Zhang, Y.; Bian, M.; Yao, W.; Ma, C. *J. Org. Chem.* **2008**, *73*, 578–584. (d) Henderson, J. L.; Edwards, A. S.; Greaney, M. F. *Org. Lett.* **2007**, *9*, 5589–5592. (e) Liu, Z.; Larock, R. C. *Angew. Chem., Int. Ed.* **2007**, *46*, 2535–2538. (f) Zhao, J.; Larock, R. C. *J. Org. Chem.* **2007**, *72*, 223–232. (g) Zhao, J.; Larock, R. C. *J. Org. Chem.* **2007**, *72*, 583–588. (h) Xie, C.; Zhang, Y.; Huang, Z.; Xu, P. *J. Org. Chem.* **2007**, *72*, 5431–5434. (i) Yoshida, H.; Morishita, T.; Fukushima, H.; Ohshita, J.; Kunai, A. *Org. Lett.* **2007**, *9*, 3367–3370. (j) Jayanth, T. T.; Cheng, C.-H. *Angew. Chem., Int. Ed.* **2007**, *46*, 5921–5924. (k) Yoshida, H.; Mimura, Y.; Ohshita, J.; Kunai, A. *Chem. Commun.* **2007**, *2405*, 2407. (l) Yoshida, H.; Watanabe, M.; Morishita, T.; Ohshita, J.; Kunai, A. *Chem. Commun.* **2007**, *1505*, 1507.

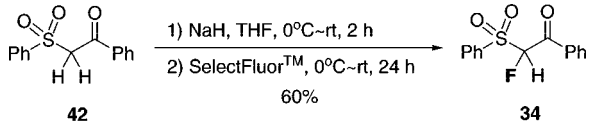
(44) The *para*-substituted isomers of **36c** and **36e** were found to be identical to the authentic samples (see Supporting Information).

(45) During our prepration of this manuscript, we noticed a recently appeared report on the reaction between arynes and β-keto sulfones. See: Huang, X.; Xue, J. *J. Org. Chem.* **2007**, *72*, 3965–3968.

SCHEME 5. Formation of Compound 37 and Its Proposed Mechanism



SCHEME 6. Modified Preparation of 34



(SelectFluor™ = 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate))

reaction between **21** and phenylacetylene in the presence of a base (such as CsOH), but no addition reaction was observed. Thereafter, we used the activated alkyne 1,3-diphenyl-2-propyn-1-one (**46a**) as a model compound to test the reaction with **21** in the presence of CsOH in *N*-methylpyrrolidinone (NMP). The results are shown in Table 10. It was found that a conjugated addition of $(PhSO_2)_2CF^-$ (**20**) to the **46a** occurred and produced the fluoroalkylated **47a** in moderate to good yields. Although the best result was obtained when 2.5 equiv of **46a** was applied in the reaction (Table 10, entry 4), we chose **21**:**46a**:CsOH = 1:1.5:1.2 (entry 2) as the optimized reaction condition for the economical purpose.

By using the established standard reaction conditions, we studied the scope of the nucleophilic fluoroalkylation between soft fluorinated carbanion $(PhSO_2)_2CF^-$ (**20**) and α,β-acetylenic ketones **46**. The results are summarized in Table 11. Fluorobis(phenylsulfonyl)methane **21** was found to be able to fluoroalkylate a variety of structurally diverse α,β-acetylenic ketones **46** to give corresponding β-fluoroalkylated α,β-enones **47** as products. The electron-withdrawing or electron-donating substituents on the aromatic rings of **46** did not show a significant effect on the outcome of the reaction (entries 1−8). It is interesting that β-alkyl-substituted α,β-acetylenic ketone **46i** also worked well, and an excellent yield of product **47i** was obtained. The absolute configuration of **47a** was determined by X-ray single crystal structure analysis (see Supporting Information), and the configurations of **47b**−**47i** were assigned by analogy.

2.5. Nucleophilic Fluoroalkylation of Activated Alkynes (46) with 2-Fluoro-2-(phenylsulfonyl)acetophenone (34). By using the similar reaction conditions as used in Table 11, we studied the nucleophilic fluoroalkylation of **46** using 2-fluoro-2-(phenylsulfonyl)acetophenone (**34**) as the fluoroalkylating agent. The chemistry turned out to be more interesting, and α-acylated-β-fluoroalkylated α,β-enones **48** were obtained as the products in good yields (Table 12). The reaction mechanism was proposed in Scheme 8. A conjugate addition between enolate **33′** and α,β-acetylenic ketone **46** gives an allenolate species **49**, and the latter undergoes an intramolecular addition to the carbonyl groups to give a four-membered alkoxide intermediate **50**.[46] As described in Scheme 8, the highly strained species **50** can readily undergo retro-aldol-type ring-opening reaction to give the final product **48**.

2.6. Other Related Reactions. The nucleophilic fluoroalkylation reaction of arynes was also attempted with other fluoroalkylating agents such as Me_3SiCF_3, $Me_3SiCF_2SO_2Ph$, and $PhSO_2CF_2H$ with no success. The reaction between difluoromethyl phenyl sulfone ($PhSO_2CF_2H$) and 1,3-diphenyl-2-propyn-1-one (**46a**) in the presence of CsOH was also investigated to no avail. These results suggested that the softness of a fluorine-bearing carbanion plays a crucial role for the success of the nucleophilic fluoroalkylation reactions with arynes and some activated alkynes (α,β-acetylenic ketones).

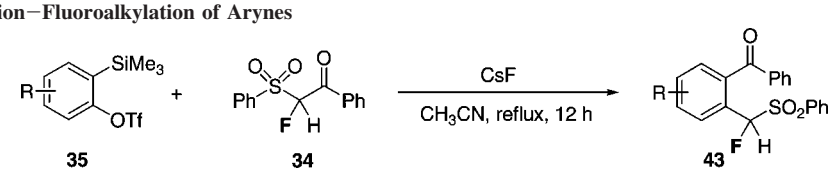
3. Elaboration of the Products. To further demonstrate the synthetic potential of the above-mentioned fluoroalkylated products, the reductive desulfonylation was invested. The α-(phenylsulfonyl)difluoromethyl allylic alcohol **12a** was converted easily into the corresponding α-difluoromethyl allylic alcohol **51** in excellent yield with conventional Na(Hg) amalgam reagent;[28b] however, our previously developed Mg/HOAc/NaOAc reagent[28c] was not effective for this kind of allylic alcohol, probably due to its susceptivity toward acids. Similarly, the α-(phenylsulphonyl)monofluoromethyl allylic alcohol **17a** could also be converted into the monofluoromethyl allylic alcohol **52** in 50% yield with the same reductive desulfonylation procedure. Furthermore, as shown in Scheme 9, fluorobis(phenylsulfonyl)methylbenzene **36a** and 1,2-difluoro-4-[fluorobis(phenylsulfonyl)methyl]benzene **36b** were converted to fluoromethylbenzene **53** and 1,2-difluoro-4-fluoromethylbenzene **54** in good yield, respectively (78% and 82% determined by ^{19}F NMR). Compound **43a** was reduced to **55** by $NaBH_4$, and the latter was treated with a reductive desulfonylation to furnish the monofluoromethyled product **56** in excellent yield (98%). Similarly, compound **43c** was transformed into **58** in 81% overall yield.

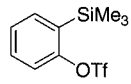
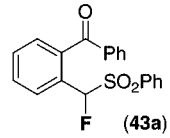
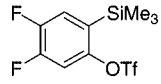
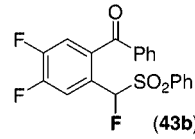
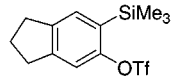
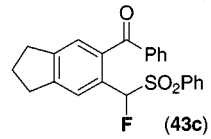
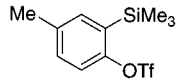
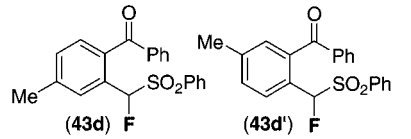
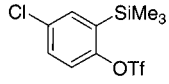
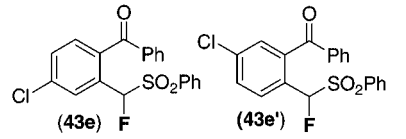
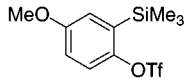
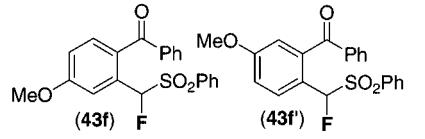
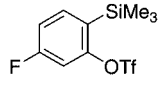
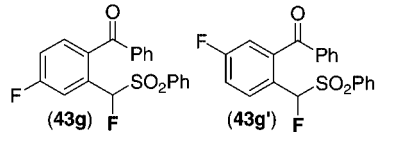
Conclusions

In conclusion, we have shown the nucleophilic fluoroalkylation of α,β-enones, arynes, and activated alkynes. The nucleophilic fluoroalkylation of cyclic and acylic α,β-enones was carried out with the three fluorinated carbanions $PhSO_2CF_2^-$ (**30**), $PhSO_2CHF^-$ (**31**), and $(PhSO_2)_2CF^-$ (**20**) and dichlorinated

(46) For a related report, see: Hachiya, I.; Shibuya, H.; Shimizu, M. *Tetrahedron Lett.* **2003**, *44*, 2061–2063.

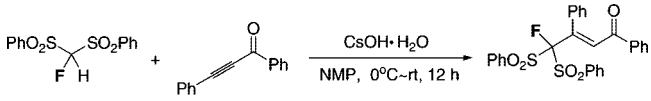
TABLE 9. Direct Acylation−Fluoroalkylation of Arynes



entry[a]	Substrate **35**	product **43**	yield (%)[b]
1		 **(43a)**	95
2		 **(43b)**	90
3		 **(43c)**	80
4		 **(43d) (43d')**	82 (ratio = 1:1)[c]
5		 **(43e) (43e')**	98 (ratio = 1:1.5)[c]
6		 **(43f) (43f')**	75 (ratio = 1:1)[c]
7		 **(43g) (43g')**	70 (ratio = 1:1.5)[c]

[a] Molar ratio of the reactants: **34**:**35**:CsF = 1.0:1.5:3.0. [b] Isolated yield. [c] Isomeric ratio was determined by ^{19}F NMR spectroscopy.

TABLE 10. Survey of Reaction Conditions

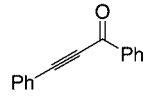
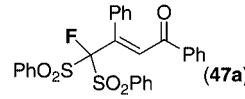
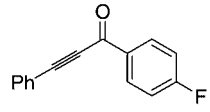
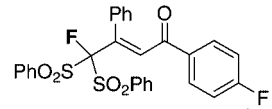
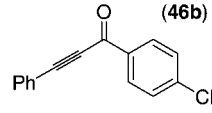
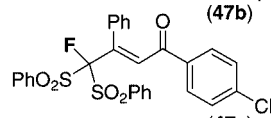
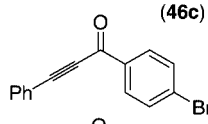
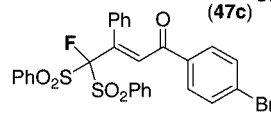
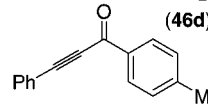
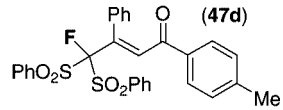
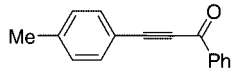
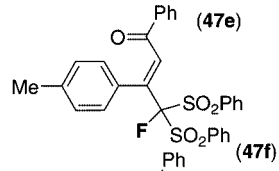
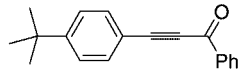
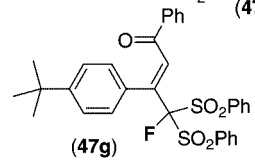
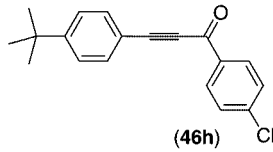
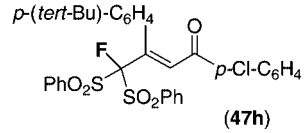
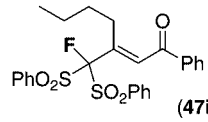


entry	**21**:**46a**:(CsOH·H_2O)[a]	yield (%)[b]
1	1:1.2:1.2	47
2	1:1.5:1.2	67
3	1:2.0:1.2	68
4	1:2.5:1.2	71
5	1:3.0:1.2	32
6	1:1.5:0.2	36[c]
7	1:1.5:0.7	42

[a] Molar ratio. [b] Isolated yield. [c] Determined by ^{19}F NMR.

carbanion $PhSO_2CCl_2^-$ (**32**). It was found that for acylic α,β-enones, although the reaction medium and the structure of the enones can all influence the regioselectivity of the nucleophilic alkylation reactions, the hard/soft nature of the carbanions played a major role. We also looked at these effects by using various other Michael acceptor systems with varying electrophilicity at β-positions. For the difluoromethyl phenyl sulfone anion $PhSO_2CF_2^-$ (**30**), the carbonyl 1,2-addition was favored, although the reaction is reversible and the conjugate addition product would be more thermodynamically stable. The further study of the reaction of $PhSO_2CF_2^-$ (**30**) to various enones revealed that the enone structure could slightly influence the addition manner. For the bis(benzenesulfonyl)monofluoromethyl anion $[(PhSO_2)_2CF^-]$ (**20**) and (phenylsulfonyl)dichloromethyl anion $PhSO_2CCl_2^-$ (**32**), the 1,4-addition maner was preferred. For $PhSO_2CHF^-$ (**31**), a variation in solvent can alter the outcome of the reaction: both 1,4-addition and the 1,2-addition occurred in THF, whereas mainly 1,2-addition occurred in THF−HMPA. By using the 1,4- and 1,2-addition product ratio as a probe to determine the hard/soft nature of the above-

TABLE 11. Fluoroalkylation of 46 with Reagent 21

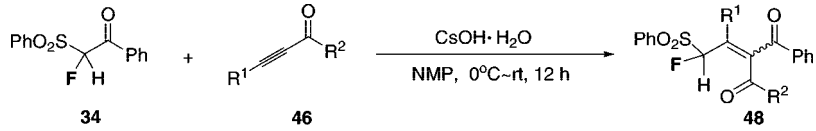
entry[a]	compound **46**	product **47**	yield (%)[b]
1	 (**46a**)	 (**47a**)	67
2	 (**46b**)	 (**47b**)	65
3	 (**46c**)	 (**47c**)	88
4	 (**46d**)	 (**47d**)	70
5	 (**46e**)	 (**47e**)	80
6	 (**46f**)	 (**47f**)	60
7	 (**46g**)	 (**47g**)	63
8	 (**46h**)	 (**47h**)	60
9	 (**46i**)	 (**47i**)	90

[a] In all cases, the reactant ratio **21**/**46**/(CsOH·H_2O) = 1:1.5:1.2. [b] Isolated yield.

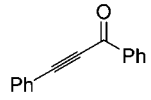
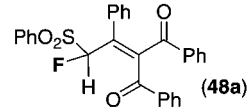
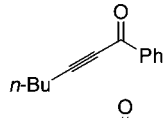
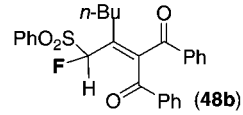
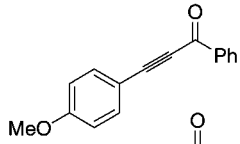
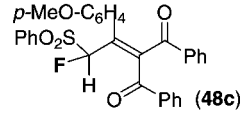
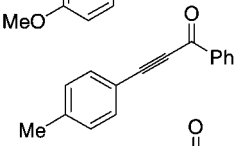
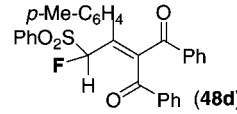
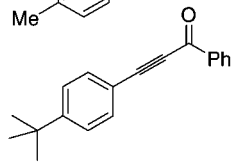
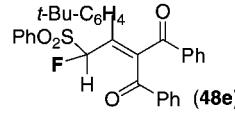
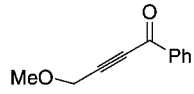
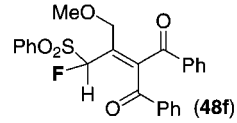
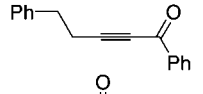
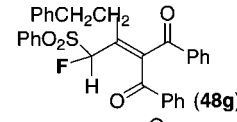
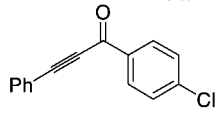
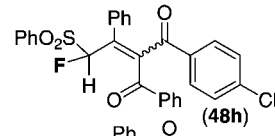
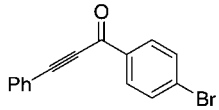
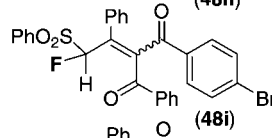
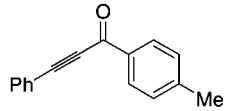
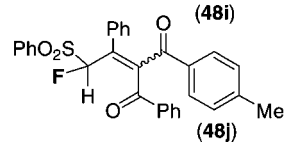
mentioned four halogenated carbanions, the order of the softness of these carbanions can be given as follows: [$(PhSO_2)_2CF^-$] (**20**) ≈ $PhSO_2CCl_2^-$ (**32**) > $PhSO_2CHF^-$ (**31**) > $PhSO_2CF_2^-$ (**30**).

We also achieved the nucleophilic fluoroalkylation of arynes (**35** as the precursor) and activated alkynes (α,β-acetylenic ketones, **46**) by using fluorobis(phenylsulfonyl)methane (**21**) and 2-fluoro-2-(phenylsulfonyl)acetophenone (**34**) as the nucleophilic fluoroalkylating agents. In the case of the fluoroalkylation of aryne (**35** as the precursor) and α,β-acetylenic ketones **46** with **21**, fluorobis(phenylsulfonyl)methylated arenes **36** and β-fluorobis(phenylsulfonyl)methylated α,β-enones **47** were obtained as the corresponding products in good yields. During the reaction between 2-fluoro-2-(phenylsulfonyl) acetophenone (**34**) and arynes (**35** as the precursor) or α,β-acetylenic ketones **46**, an intramolecular tandem reaction process leads to the formation of acyl-fluoroalkylated arenes **43** or α-acyl-β-fluoroalkylated α,β-enones **48**. It turned out that the softness of a fluorine-bearing carbanion (such as **20** or **33** derived from **21** or **34**) plays a crucial role for the success of the nucleophilic fluoroalkylation reactions with arynes and some activated alkynes (α,β-acetylenic ketones). The present synthetic methodology provides new insights into the nucleophilic fluoroalkylation chemistry and may find some useful applications in the synthesis of fluorine-containing materials and biologically interesting molecules.

TABLE 12. Fluoroalkylation of 46 with Reagent 34



34 46 48

entry[a]	compound **46**	product **48**	yield (%)[b]
1		 (**48a**)	66
2		 (**48b**)	85
3		 (**48c**)	65
4		 (**48d**)	45
5		 (**48e**)	88
6		 (**48f**)	86
7		 (**48g**)	82
8		 (**48h**)	82 (ratio = 1.4 :1)[c]
9		 (**48i**)	75 (ratio = 1:1)[c]
10		 (**48j**)	64 (ratio = 1:1)[d]

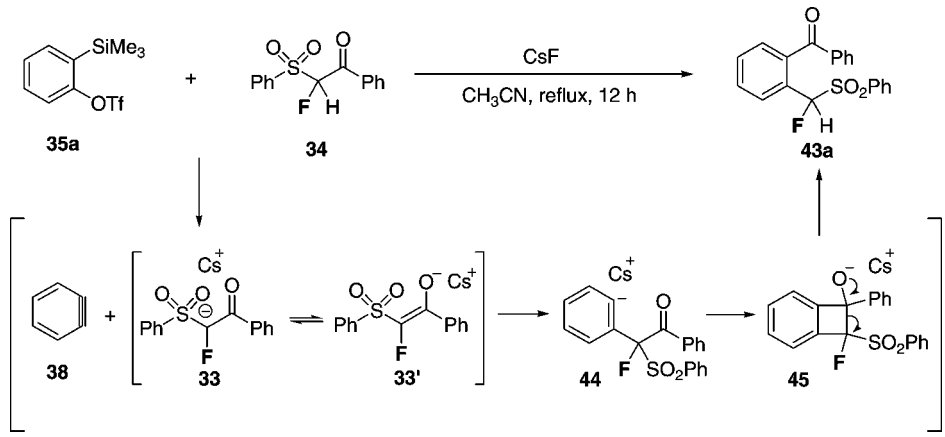
[a] In all cases, the reactant ratio **34/46**/($C_sOH·H_2O$) = 1:1.5:1.2. [b] Isolated yield. [c] Isomeric ratio was determined by ^{19}F NMR spectroscopy. [d] Isomeric ratio was determined by ^1H NMR spectroscopy.

Experimental Section

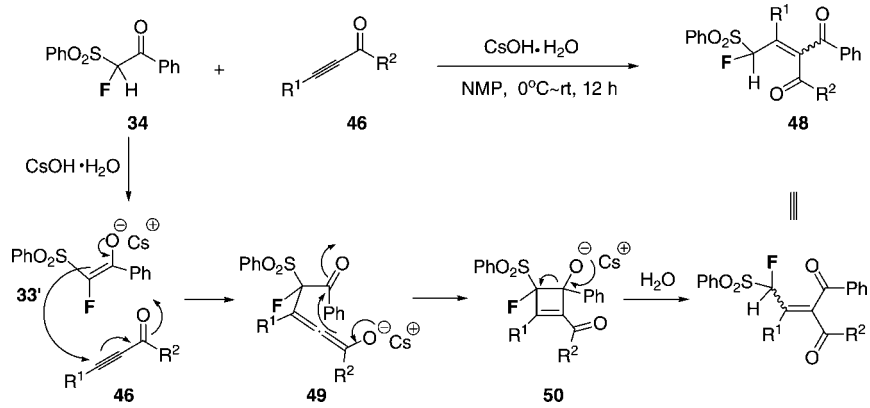
Typical Procedure for the Addition Reaction of Difluoromethyl Phenyl Sulfone 2 to α,β-Enones (Table 2). Under N_2 atmosphere, into a Schlenk tube containing chalcone **11a** (104 mg, 0.5 mmol) and $PhSO_2CF_2H$ (**2**) (115 mg, 0.6 mmol) in THF (2.5 mL) at −98 °C was added dropwise 0.6 mmol of $(TMS)_2NLi$ (LHMDS, 1.0 M in THF, 0.6 mL). The reaction mixture was then stirred vigorously at −98 °C for 30 min, followed by adding a saturated NH_4Cl water solution (2 mL) at this temperature. The solution mixture was extracted with EtOAc (20 mL°3), and the combined organic phase was dried over $MgSO_4$. After the removal of volatile solvents under vacuum, the crude product was further purified by silica gel column chromatography (petroleum ether/EtOAc 4:1 as eluent) give product **12a**.

(*E*)-1,1-Difluoro-2,4-diphenyl-1-(phenylsulfonyl)but-3-en-2-ol (12a) (Table 2, entry 1). White solid, mp 155−156 °C, 97% yield. ^1H NMR ($CDCl_3$, 300 MHz): δ 4.26 (s, 1H), 6.92 (dd, *J* = 16, 1.1 Hz, 1H), 7.02 (d, *J* = 16 Hz, 1H), 7.28−7.38 (m, 6H), 7.45 (d, *J* = 6.7 Hz, 2H), 7.55 (t, *J* = 8.0 Hz, 2H), 7.63 (m, 2H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.92 (d, *J* = 7.5 Hz, 2H). ^{19}F NMR ($CDCl_3$, 282

SCHEME 7. Formation of Compound 43a



SCHEME 8. Formation of Compound 48



MHz): δ −107.4 (d, *J* = 237 Hz, 1F), −104.7 (d, *J* = 237 Hz, 1F). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 78.9 (t, *J* = 21 Hz), 120.2 (t, *J* = 302 Hz), 126.4 (d, *J* = 2.8 Hz), 127.2, 127.3, 128.2, 128.4, 128.7, 128.8, 129.3, 130.6, 132.9, 133.7, 135.4, 136.0, 137.8. MS (ESI, *m*/*z*): 418.0 ($M+NH_4^+$). Anal. Calcd for $C_{22}H_{18}F_2O_3S$: C, 65.99; H, 4.53. Found: C, 65.57; H, 4.46. IR(KBr): 3526, 3515, 3062, 3028, 1450, 1310, 1149, 1130 cm^{-1}.

Addition Reaction of Dichloromethyl Phenyl Sulfone 15 to α,β-Enones (Table 3). Into a Schlenk tube containing the chalcone **11a** (104 mg, 0.5 mmol) and $PhSO_2CCl_2H$ (**15**) (112 mg, 0.5 mmol) in THF (2.5 mL) at −78 °C was added dropwise 0.6 mmol of LHMDS (1.0 M in THF, 0.6 mL). The reaction mixture was then stirred at −78 °C for 30 min. After usual workup as above, the desired product **16a** was obtained (petroleum ether/EtOAc 5:1 as eluent).

4,4-Dichloro-1,3-diphenyl-4-(phenylsulfonyl)butan-1-one (16a) (Table 3, entry 1). White solid, mp 174−175 °C, 95% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.95 (dd, *J* = 17.8, 10.0 Hz, 1H), 4.27 (dd, *J* = 17.8, 2.6 Hz, 1H), 4.83 (dd, *J* = 10.0, 2.6 Hz, 1H), 7.22−7.35 (m, 3H), 7.39−7.66 (m, 7H), 7.74 (t, *J* = 7.5 Hz, 1H), 7.92 (d, *J* = 7.8 Hz, 2H), 8.08 (d, *J* = 7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 42.4, 49.4, 102.7, 128.1, 128.2, 128.3, 128.6, 128.8, 130.2,132.4, 133.2, 133.3, 135.2, 136.6, 137.3. MS (ESI, *m*/*z*): 433.0 ($M + H^+$). Anal. Calcd for $C_{22}H_{18}Cl_2O_3S$: C, 60.98; H, 4.19. Found: C, 60.99; H, 4.22. IR(KBr): 1682, 1449, 1333, 1154, 1082 cm^{-1}.

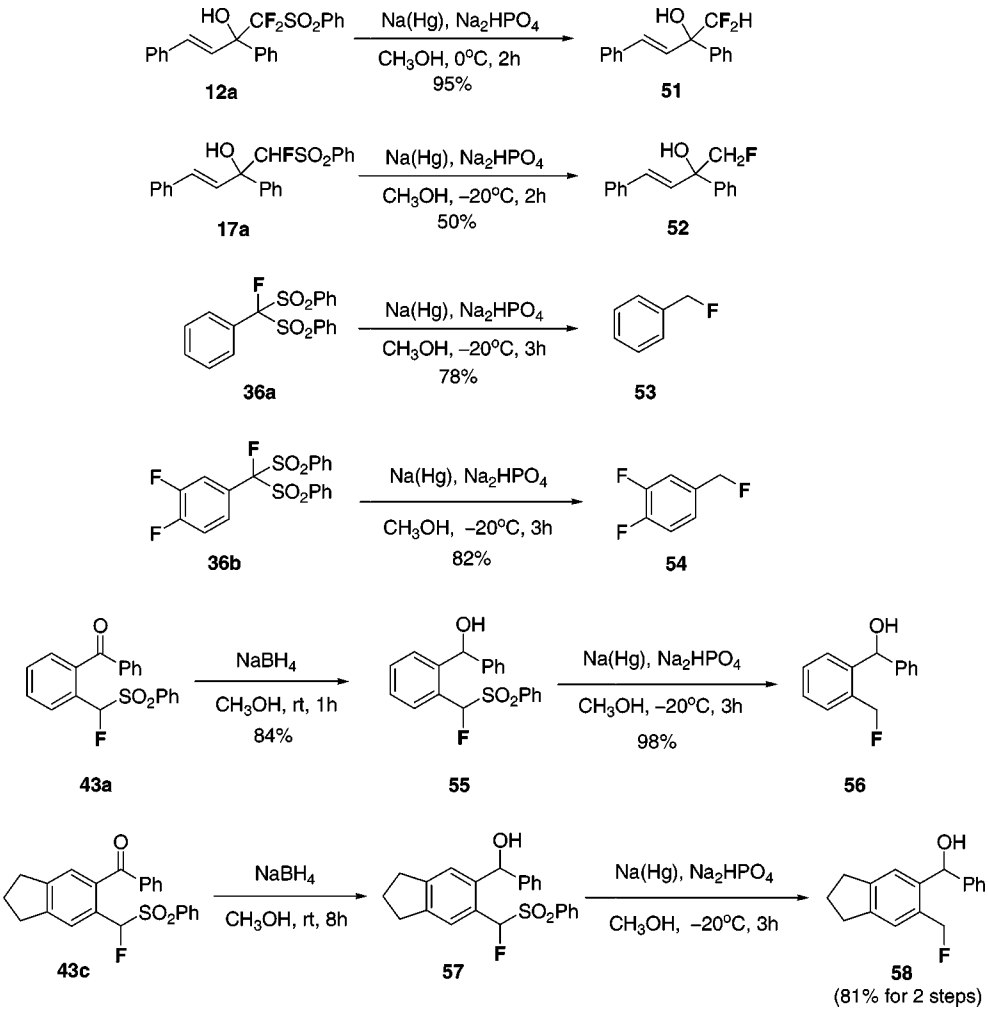
Typical Procedure for the Addition Reaction of Monofluoromethyl Phenyl Sulfone 8 to α,β-Enones (Table 4). Under N_2 atmosphere, into a Schlenk tube containing the enone **11a** (104 mg, 0.5 mmol) and $PhSO_2CH_2F$ (**8**) (87 mg, 0.5 mmol) in THF (2.5 mL) and HMPA (0.5 mL) at −78 °C was added dropwise 0.6 mmol of LHMDS (1.0 M in THF, 0.6 mL). The reaction mixture was then stirred vigorously at −78 °C for 30 min and finally quenched by saturated NH_4Cl water solution. After usual workup and purification as above, the desired product **17a** was obtained as a mixture of 2 stereoisomers in the ratio 3:2 (petroleum ether/EtOAc 4:1 as eluent).

(*E*)-1-Fluoro-2,4-diphenyl-1-(phenylsulfonyl)but-3-en-2-ol (17a) (Table 4, entry 1). White foam, 97% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) for a mixture of isomers: δ 4.38 (s, 1H), 5.20−5.50 (2d, *J* = 45 Hz, 1H), 6.65−6.75 (2d, *J* = 16 Hz, 1H), 6.86−6.99 (2d, *J* = 16 Hz, 1H), 7.20−7.57 (m, 12H), 7.58−7.70 (m, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 7.7 Hz, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz) for a mixture of isomers: δ −178.8 (d, *J* = 45 Hz, 0.6F), −178.5 (d, *J* = 45 Hz, 0.4F). MS (ESI, *m*/*z*): 400.1 ($M + NH_4^+$). Anal. Calcd for $C_{22}H_{19}FO_3S$: C, 69.09; H, 5.01. Found: C, 68.76; H, 5.12. IR(KBr): 3494 (br), 1494, 1448, 1309, 1162, 1073 cm^{-1}.

Preparation of Benzoylhydrazone 19 (Scheme 3). Under N_2 atmosphere, into a Schlenk tube containing the chalcone **11a** (416 mg, 2.0 mmol) and $PhSO_2CH_2F$ (350 mg, 2.0 mmol) in THF (10 mL) at −78 °C was added dropwise 2.4 mmol of LHMDS (1.0 M in THF, 2.4 mL). The reaction mixture was then stirred vigorously at −78 °C for 30 min and quenched by saturated NH_4Cl water solution. After usual workup and purification as above, a mixture of **17a** and **18a** was obtained in the ratio 1:1.4 (760 mg). Into the product mixture (400 mg, containing **18a** 0.6 mmol) in THF (0.5 mL) were added benzhydrazide (95 mg, 0.7 mmol) and *p*-TsOH (5 mg). The reaction mixture was then stirred vigorously at 40 °C for 18 h. After cooling to room temperature, EtOAc (5 mL) was added and then stirred vigorously for 10 min. After filtration, the solid (300 mg) was collected and crystalized from EtOAc/PE 1:2, benzoylhydrazone **19** was obtained as colorless crystals, 250 mg (83%).

(*E*)-*N*′-((3*R,4*R**)-4-Fluoro-1,3-diphenyl-4-(phenylsulfonyl)butylidene)benzohydrazide (19).** Mp 152−154 °C. ^{1}H NMR ($CDCl_3$,

SCHEME 9. Further Elaboration of Fluorinated Products



300 MHz): δ 3.31 (dd, J = 15, 12 Hz, 1H), 3.75−4.05 (m, 2H), 5.40 (d, J = 48 Hz, 1H), 7.07−7.20 (m, 5H), 7.26−7.35 (m, 34H), 7.37−7.55 (m, 3H), 7.56−7.85 (m, 7H), 7.93 (d, J = 7.6 Hz, 2H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −185.5 (dd, J = 48, 29 Hz). MS (ESI, m/z): 501.2 (M + H^+). Anal. Calcd for $C_{29}H_{25}N_2FO_3S$: N, 5.60; C, 69.58; H, 5.03. Found: N, 5.46; C, 69.61; H, 5.24. IR(KBr): 3191, 3063, 1650, 1325, 1151 cm^{-1}.

Typical Procedure for the Addition Reaction of Bis(benzenesulfonyl)monofluoromethane 21 to α,β-Enones (Table 5). NaOH (2.0 M aq, 0.6 mL) was added to a stirred solution of **11a** (62.5 mg, 0.3 mmol) and **21** (94 mg, 0.3 mmol) at room temperature in DMF (0.9 mL), and the resulting mixture was stirred until the reaction was complete (usually 12 h as indicated by TLC), then neutralized with a NH_4Cl water solution (10% w/w, 2 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica gel chromatography (PE/EtOAc, 5:1) to give the desired product **23a**.

4-Fluoro-1,3-diphenyl-4,4-bis(phenylsulfonyl)butan-1-one (23a) (Table 5, entry 1). White solid, mp 195−197 °C, 98% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.36 (d, J = 18.6 Hz, 1H), 4.57 (dd, J = 18.6, 10.5 Hz, 1H), 4.69 (dm, J = 10.5 Hz, 1H), 7.05−7.15 (m, 5H), 7.43−7.50 (m, 4H), 7.55−7.65 (m, 4H), 7.75−7.83 (m, 3H), 7.93 (d, J = 8.4 Hz, 2H), 8.03 (m, 2H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ −128.3 (s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 37.4, 43.2 (d, J = 19 Hz), 114.0 (d, J = 265 Hz), 127.8, 127.9, 128.1, 128.4, 128.6, 129.1, 130.4, 130.9, 131.2, 133.4, 133.6 (d, J = 6 Hz), 134.0, 134.8, 135.4, 136.27, 136.34, 195.5. MS (ESI, m/z): 540.2 (M + NH_4^+). Anal. Calcd for $C_{28}H_{23}FO_5S_2$: C, 64.35; H, 4.44. Found: C, 64.44; H, 4.43. IR(KBr): 1683, 1583, 1449, 1350, 1336, 1148, 1079 cm^{-1}.

Typical Procedure for Nucleophilic Fluoroalkylation of Aryne with Fluorobis(phenylsulfonyl)methane (21) (Table 8). Under N_2 atmosphere, into a 10-mL Schlenk flask containing **35a** (134 mg, 0.45 mmol), **21** (94 mg, 0.3 mmol), and acetonitrile (5 mL) was added CsF (137 mg, 0.9 mmol). The reaction mixture was heated at reflux temperature for 24 h and then cooled to room temperature. After being quenched with brine, the reaction mixture was extracted with Et_2O (25 mL × 3), and the combined organic phase was dried over anhydrous $MgSO_4$. The volatile solvents were removed under vacuum, and the crude product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:7 v/v) to give product **36a** (73 mg, 62% yield) as a white solid.

[Fluorobis(phenylsulfonyl)methyl]benzene (36a) (Table 8, entry 1). Mp: 150−152 °C. ^{1}H NMR: δ 7.66 (d, J = 8.2 Hz, 5H), 7.54 (t, J = 7.3 Hz, 3H), 7.35 (t, J = 7.9 Hz, 7H).^{19}F NMR: δ −147.2 (s, 1F).^{13}C NMR: δ 135.0, 134.9, 131.1, 130.6, 128.6, 128.4, 125.9, 125.8, 113.0 (d, J = 261.4 Hz). MS (ESI, m/z): 408.0 (M + NH_4^+). Anal. Calcd for $C_{19}H_{15}FO_4S_2$: C, 58.45; H, 3.87. Found: C, 58.15; H, 4.05. IR (film): 3093, 1583, 1477, 1446, 1340, 1224, 1168 cm^{-1}.

Typical Procedure for Nucleophilic Fluoroalkylation of Aryne with 2-Fluoro-2-(phenylsulfonyl)acetophenone (34) (Table 9). Under N_2 atmosphere, into a 20-mL Schlenk flask containing **35a** (447 mg, 1.5 mmol), **34** (278 mg, 1.0 mmol), and acetonitrile (10 mL) was added CsF (456 mg, 3.0 mmol). The reaction mixture was heated at reflux temperature for 12 h and then cooled to room temperature. After being quenched with brine, the reaction mixture was extracted with Et_2O (50 mL × 3), and the combined organic

phase was dried over anhydrous $MgSO_4$. The volatile solvents were removed under vacuum, and the crude product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:7 v/v) to give product **43a** (337 mg, 95% yield) as a white solid.

[2-Fluoro(phenylsulfonyl)methyl]phenyl(phenyl)methanone (43a) (Table 9, entry 1). Mp 100−102 °C. ^{1}H NMR: δ 7.77 (d, J = 7.8 Hz, 4H), 7.67 (d, J = 7.2 Hz, 1H), 7.61−7.36 (m, 9H), 7.17 (d, J = 46.5 Hz, 1H). ^{19}F NMR: δ −181.2 (d, J = 46.8 Hz). ^{13}C NMR: δ 197.5, 138.1, 137.5, 135.7, 134.5, 133.1, 131.2, 130.8, 130.5, 129.9, 129.5, 129.2, 128.4, 128.3, 127.8, 98.3 (d, J = 217.0 Hz). MS (ESI, *m*/*z*): 355.0 (M + H$^+$). Anal. Calcd for $C_{20}H_{15}FO_3S$: C, 67.78; H, 4.27. Found: C, 67.70; H, 4.22. IR (film): 3068, 1659, 1596, 1577, 1448, 1329, 1151 cm^{-1}.

Typical Procedure for Nucleophilic Fluoroalkylation of Activated Alkynes (46) with Fluorobis(phenylsulfonyl)methane (21) (Table 11). Into a 10-mL Schlenk flask containing **21** (157 mg, 0. 50 mmol), **46a** (155 mg, 0.75 mmol), and NMP (5 mL) at 0 °C was added $CsOH\cdot H_2O$ (101 mg, 0.60 mmol). The reaction mixture was warmed up to room temperature over 12 h. After being quenched with brine, the reaction mixture was extracted with Et_2O (50 mL × 3), and the combined organic phase was dried over anhydrous $MgSO_4$. The volatile solvents were removed under vacuum, and the crude product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5 v/v) to give product **47a** (175 mg, 67% yield) as a white solid.

(*E*)-4-Fluoro-1,3-diphenyl-4,4-bis(phenylsulfonyl)but-2-en-1-one (47a) (Table 11, entry 1). Mp: 204−206 °C. ^{1}H NMR: δ 8.08 (s, 1H), 8.03 (t, J = 7.3 Hz, 4H), 7.93 (d, J = 7.4 Hz, 2H), 7.78 (t, J = 7.4 Hz, 2H), 7.62 (t, J = 7.5 Hz, 4H), 7.49 (t, J = 7.5 Hz, 1H), 7.38 (t, J = 7.4 Hz, 2H), 7.07 (t, J = 7.4 Hz, 1H), 6.95 (t, J = 7.5 Hz, 2H), 6.44 (d, J = 7.5 Hz, 2H). ^{19}F NMR: δ −141.3 (s). ^{13}C NMR: δ 191.8, 136.2, 135.9, 135.5, 135.2, 133.6, 131.4, 129.5, 129.4, 129.2, 129.1, 128.6, 128.5, 127.4, 112.3 (d, J = 261.4 Hz). MS (ESI, *m*/*z*): 538.2 (M + NH_4^+). Anal. Calcd for $C_{28}H_{21}FO_5S_2$: C, 64.60; H, 4.07. Found: C, 64.48; H, 4.17. IR (film): 3066, 1677, 1600, 1581, 1450, 1347, 1235 cm^{-1}.

Typical Procedure for Nucleophilic Fluoroalkylation of Activated Alkynes (46) with 2-fluoro-2-(phenylsulfonyl)acetophenone (34) (Table 12). Into a 15-mL Schlenk flask containing **34** (139 mg, 0. 50 mmol), **46a** (155 mg, 0.75 mmol), and NMP (8 mL) at 0 °C was added $CsOH\cdot H_2O$ (101 mg, 0.60 mmol). The reaction mixture was warmed up to room temperature over 12 h. After being quenched with brine, the reaction mixture was extracted with Et_2O (50 mL × 3), and the combined organic phase was dried over anhydrous $MgSO_4$. The volatile solvents were removed under vacuum, and the crude product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5 v/v) to give product **48a** (160 mg, 66% yield) as a white solid.

2-[2-Fluoro-1-phenyl-2-(phenylsulfonyl)ethylidene]-1,3-diphenylpropane-1,3-dione (48a) (Table 12, entry 1). Mp: 140−141 °C. ^{1}H NMR: δ 8.00 (d, J = 7.4 Hz, 2H), 7.81 (d, J = 7.4 Hz, 2H), 7.70 (d, J = 7.4 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.49−7.28 (m, 8H), 7.21 (t, J = 7.4 Hz, 2H), 7.07 (m, 3H), 6.56 (d, J = 47.2 Hz, 1H). ^{19}F NMR: δ −175.9 (d, J = 49.4 Hz). ^{13}C NMR: δ 193.05, 193.01, 148.4, 148.3, 138.1, 137.9, 136.4, 135.6, 134.7, 134.0, 133.8, 132.0, 130.3, 130.1, 129.9, 129.4, 129.3, 128.7, 128.5, 128.1, 100.4 (d, J = 220.9 Hz). MS (ESI, *m*/*z*): 485.2 (M + H$^+$). Anal. Calcd for $C_{29}H_{21}FO_4S$: C, 71.89; H, 4.37. Found: C, 71.69; H, 4.59. IR (film): 3062, 1652, 1596, 1580, 1449, 1334, 1234, 1157 cm^{-1}.

Typical Procedure for Reductive Desulfonylation (Scheme 9). Into a 10-mL flask containing **43a** (354 mg, 1.0 mmol) and CH_3OH (8 mL) was added $NaBH_4$ (45.6 mg, 1.2 mmol) at room temperature, and the reaction mixture was stirred for 1 h. The solvent was removed under vacuum, and 20 mL of brine was added, followed by extracting with EtOAc (30 mL × 3). The combined organic phase was dried over $MgSO_4$. The volatile solvents were removed under vacuum, and the crude product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5 v/v) to give product **55** (299 mg, 84% yield).

Under N_2 atmosphere, into a 15-mL flask containing **55** (249 mg, 0.7 mmol) and Na_2HPO_4 (994 mg, 7.0 mmol) in 10 mL of anhydrous methanol at −20 °C was added Na/Hg amalgam (11.5 wt % Na in Hg, net sodium content 7.0 mmol). The reaction mixture was stirred at −20 to −15 °C for 3 h. The liquid phase was decanted, and most of the organic phase was removed under vacuum. Then 20 mL of brine was added, followed by extracting with Et_2O (30 mL × 3). The combined organic phase was dried over anhydrous $MgSO_4$. The volatile solvents were removed under vacuum, and the crude product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:10 v/v) to give product **56** (148 mg, 98% yield) as a white solid.

[2-(Fluoromethyl)phenyl](phenyl)methanol (56). Mp: 58−60 °C. ^{1}H NMR: δ 7.50 (m, 9H), 6.07 (d, J = 3.2 Hz, 1H), 5.40 (d, J = 48.0 Hz, 2H), 2.46 (s, 1H). ^{19}F NMR: δ −206.7 (t, J = 48.5 Hz). ^{13}C NMR: δ 142.5, 133.8, 129.3, 129.2, 128.9, 128.5, 127.9, 127.7, 127.6, 126.8, 82.7 (d, J = 163.7 Hz), 72.9. MS (EI, *m*/*z*, %): 216 (M$^+$, 17.90), 195(100.00). HRMS (EI): calcd for $C_{14}H_{13}FO$ 216.0950. found 216.0955. IR (film): 3190, 1603, 1494, 1451, 1176, 1020, 771, 700 cm^{-1}.

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Supporting Information Available: General experimental information and the characterization data of the isolated compounds including CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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