Recent Progress in One-Pot Syntheses of Fluorinated Building Blocks

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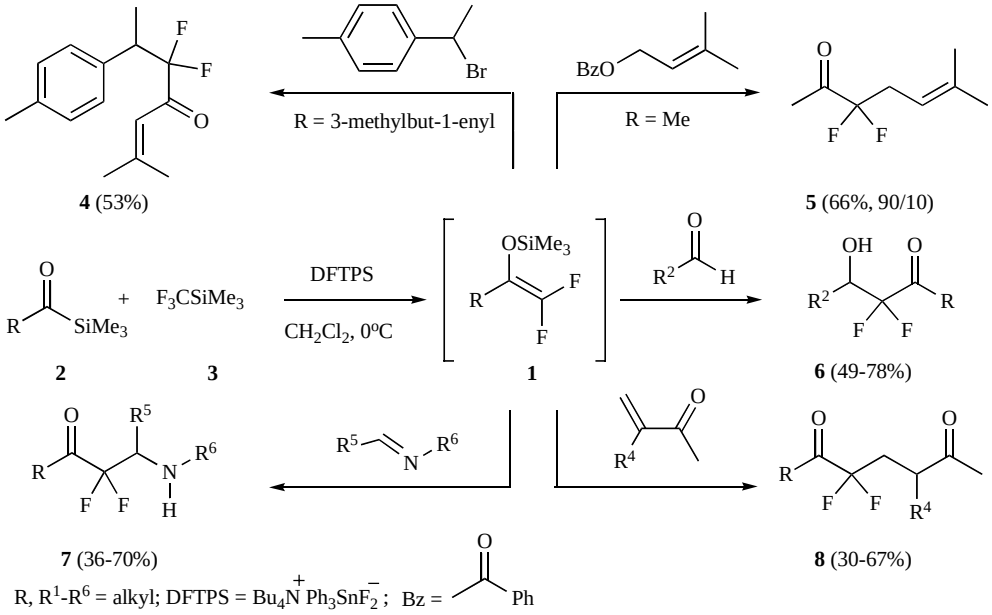
Abstract: Fluorine-containing molecules are now widely selected for both fundamental research and industrial applications in the fields of pharmaceuticals, agrochemicals, and advanced materials. The development of methodologies for the efficient synthesis of fluorine-containing molecules has become one of the most important issues in organic chemistry for long time. This mini-review focuses on the recent development in the one-pot syntheses of some important fluorinated building blocks which are recognized as the versatile tools for the construction of fluorine-containing molecules.

Keywords: One-pot synthesis, multi-component reaction, fluorinated building block, fluorinated heterocycles.

1. INTRODUCTION

Fluorine-containing molecules are found to increase utilities in various fields such as pharmaceuticals, agrochemicals and material sciences. Currently, "as many as 30–40% of agrochemicals and 20% of pharmaceuticals on the market are estimated to contain fluorine" [1]. The research on how to increase efficiency of drug-like molecule synthesis has attracted much attention from both academic and industrial views.

Synthetic methodologies for the synthesis of organofluorine compounds are roughly classified into two basic strategies: the direct fluorination and through the fluorinated building-blocks. Direct fluorination includes C-F bond formation by treatment of substrate with a fluorinating reagent, such as elemental fluorine [2], hydrogen fluoride [3], perchloryl fluoride [4], *N*-fluoro reagent [5-7], diethylaminosulfur trifluoride (DAST) [8], etc. The handling of such fluorinating reagents requires special apparatus and techniques due to their extraordinary corrosion and toxicity. The building-block based methodologies involve appropriate chemical transformations starting from unique and easily prepared fluorine-containing molecules [9]. Since normal experimental procedures are usually applicable to these reactions with lower pollution and toxicity, the building-block based methodologies are more acceptable for synthetic purposes.



Scheme 1.

Recently, one-pot synthesis has drawn great interest for its brevity and efficiency. It can be defined as a simple and efficient route to target molecules by including two or more-step transformations in a single operation starting from relatively simple precursors [10]. It encompasses either a multi-component reaction (MCR) [11], or a domino (sometimes called tandem, cascade or zipper) reaction [12]. It's obviously that this "integrated chemistry process" [13]

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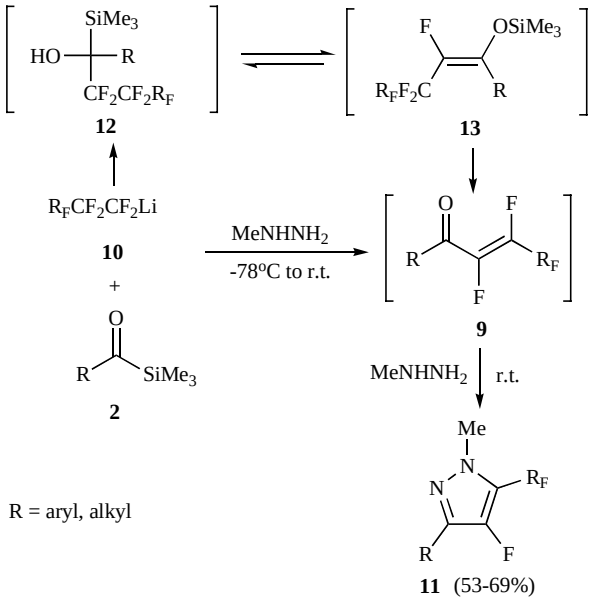
would allow to minimize the consumption of solvents, reagents, energy, and the starting materials are either commercially available or easily prepared. Furthermore, the structure of the reaction product is easily diversified by systematic variation of each input.

Thus, one-pot syntheses of fluorinated building blocks provide some facile and practical methods, which encourage chemists to utilize these readily available and versatile tools for the synthesis of interested fluorine-containing molecules. This mini-review focuses on the recent development in the syntheses of some important fluorinated building blocks according to their different functionalities.

2. ONE-POT SYNTHESIS OF FLUORINATED CARBONYL BUILDING BLOCKS

2.1. One-Pot Synthesis of *gem*-Difluorocarbonyl Building Blocks

Difluoroeneoxysilane **1** can be readily obtained from acylsilane **2** and trifluoromethyltrimethylsilane **3** by using Portella's method [14]. This *in-situ* generated difluoroeneoxysilane **1** could be reacted with different electrophiles in the presence of Lewis acids to afford a variety of corresponding *gem*-difluorocarbonyl derivatives (Scheme **1**) [15-20]. Using similar procedures, difluoro-C-glycosides have been prepared [21]. These compounds with *gem*-difluorocarbonyl structures also have some bioactivities and synthetic utilities. For example, difluoroanalogue **4** [15] of *ar*-turmerone is a sesquiterpene displaying an antitumor activity [22]. Since monoterpene could be employed as pheromones [23], flavors [24], etc., 3,3-difluoro-6-methyl-hept-5-en-2-one **5** was prepared as the difluoroanalogue of a key intermediate towards monoterpene synthesis [16]. Difluoroegomaketone with potential bovine respiratory toxicity [25], which contains the moiety of difluoroaldol **6**, could be also prepared by using this one-pot methodology [17]. The insertion of the β-amino-α,α-difluoroketone **7** [18] unit into a peptide proved to be successful in the design of enzyme inhibitors such as protease inhibitors [26]. It's also reported that the Michael addition and subsequent annulation of **8** led to the formation of multisubstituted difluorocyclohexenones and fluorophenols [19].

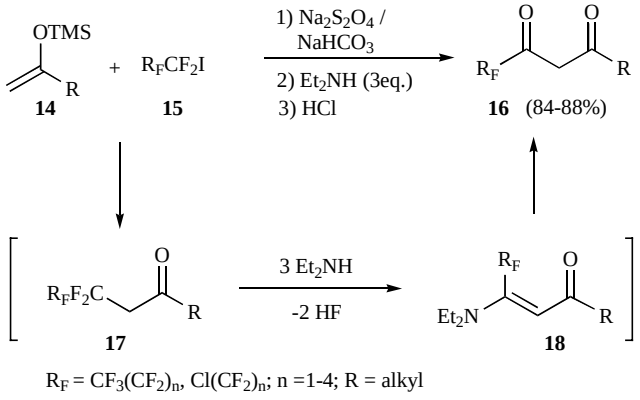


Scheme 2.

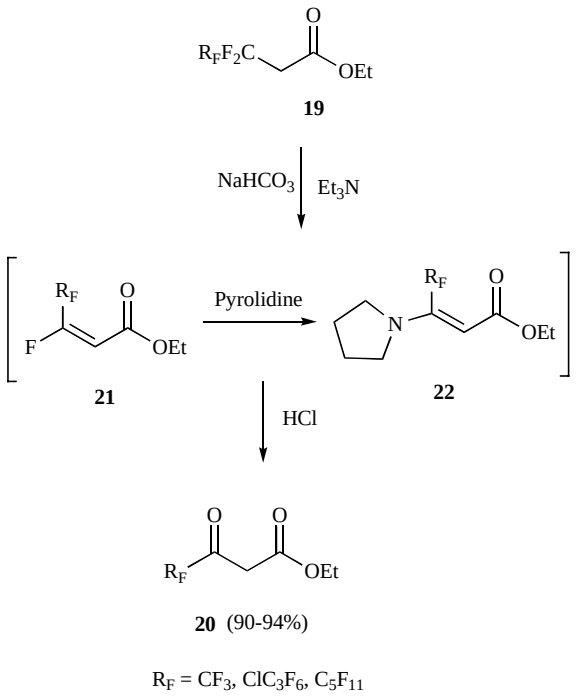
The similar α,β-unsaturated intermediates **9**, which were obtained by the treatment of acylsilanes **2** with perfluoro organolithium reagents **10**, reacted with methylhydrazine to afford a series of 4-fluoro-5-(perfluoroalkyl)pyrazoles **11** in 53-69% yields (Scheme **2**) [27]. The isolated silyl ethers of enols **9** or their synthetic equivalents **12** or **13** were utilized to react with binucleophilic reagents for the construction of various fluorinated heterocycles [28].

2.2. One-Pot Synthesis of Fluorinated 1,3-Dicarbonyl Building Blocks

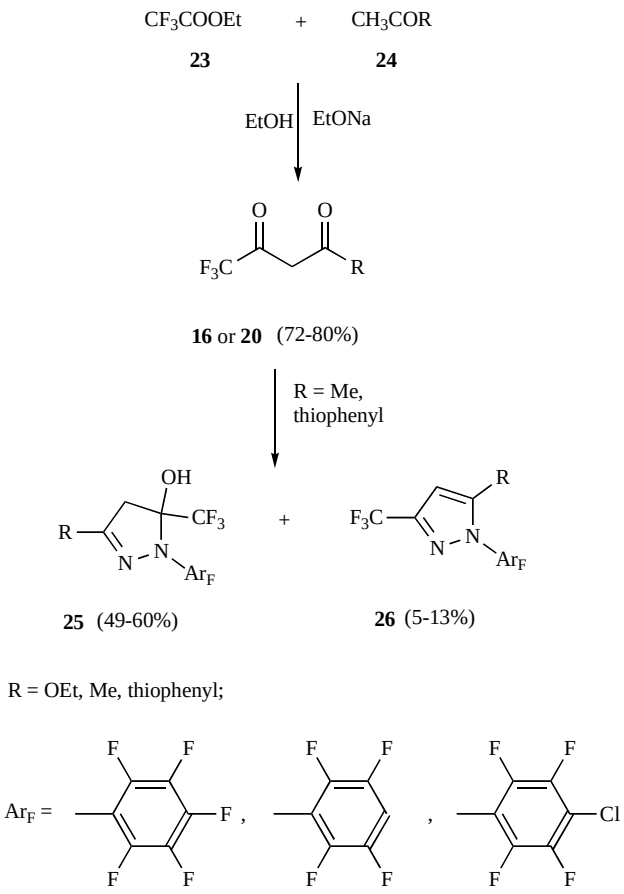
Huang *et al.* [29] described a one-pot preparation of fluorinated β-diketones **16**. silyl enol ethers **14** were reacted with perfluoroalkyl iodides **15** to yield fluorinated ketones **17**. The subsequent double dehydrofluorination and addition-elimination of **17** led to the formation of **18**, which were further hydrolysized to yield the final products **16** (Scheme **3**). Fluoroalkylacetoacetates **20** were obtained from 2,2-dihydropolyfluoroalkanonates **19** through a similar route (Scheme **4**) [30], and both dicarbonyl compounds **16** and **20** could also be prepared by Claisen condensation of trifluoroacetate **23** and ketones or esters **24** (Scheme **5**) [31].



Scheme 3.



Scheme 4.



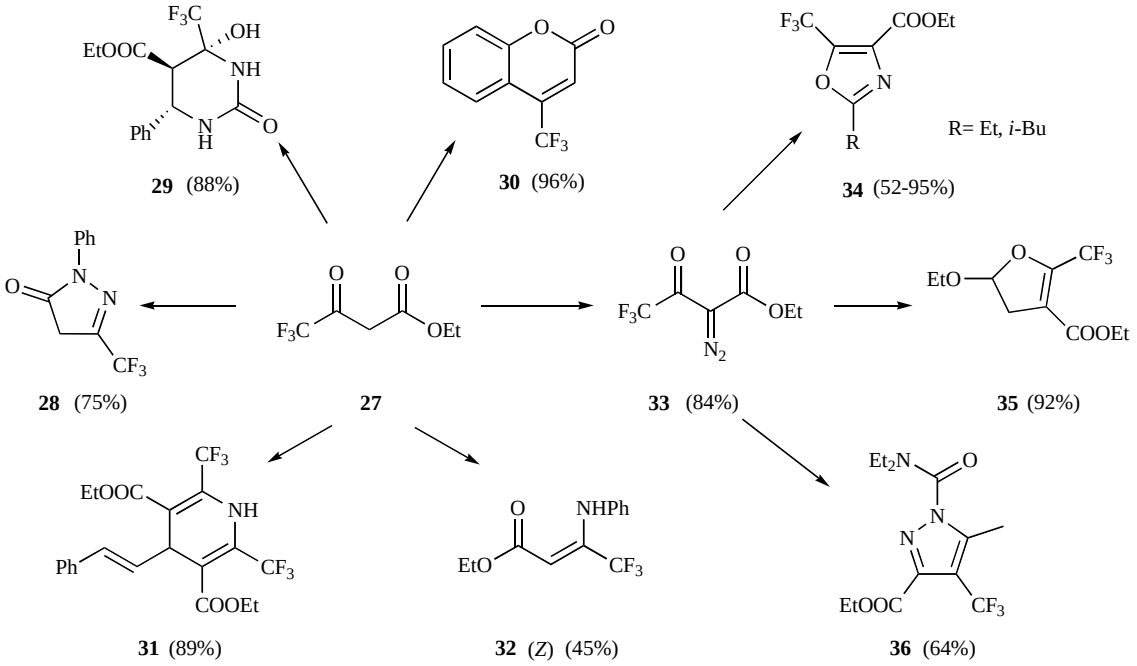
Scheme 5.

Much attention has been paid to the fluorinated β-diketones **16** because they are not only employed as insecticides [32] or used in luminescence analysis [33], but also utilized as fluorinated building blocks to build a variety of fluoroalkylated heterocycles. Fluorinated β-diketones **16** were reacted with hydrazines to afford trifluoromethyl pyrazoles **25** and **26** (Scheme **5**) [31]. Comparing with **16**, fluoroalkylacetoacetates **20** play more important roles in the syntheses of fluorinated heterocycles (Scheme **6**). Ethyl 4,4,4-trifluoroacetoacetate **27** was reacted with dinucleophilic phenylhydrazine to give pyrazolone **28** [34], it could also undergo Biginelli reaction, Pechmann reaction and Hantzsch reaction to afford dihydropyrimidinone **29** [35], substituted coumarin **30** [36] and dihydropyridine **31** [37] respectively. In addition, β-amino acid precursors **32** could be obtained from **27** [38]. Ethyl 2-diazo-4,4,4-trifluoroacetoacetate **33**, which was readily prepared by a diazo transfer reaction from **27** [39], also has been wildly used for synthesis of fluorinated oxazole **34** [30], dihydrofuran **35** [40], and pyrazole **36** [41].

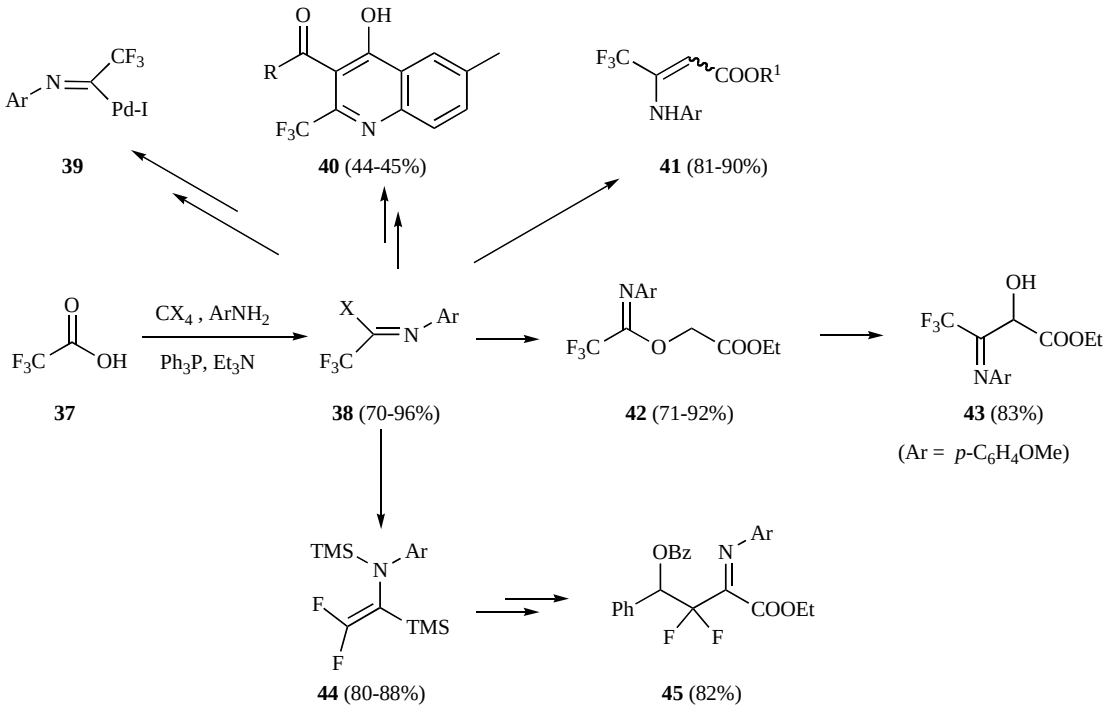
3. ONE-POT SYNTHESIS OF PERFLUOROACETIMIDOYL HALIDES

In 1993, Uneyama *et al*. [42] developed a simple one-pot synthesis of perfluoroimidoyl halides **38**, which were obtained in 80-90% yields when a mixture of fluorinated carboxylic acid **37** and a aryl amine was refluxed in carbon tetrachloride (or carbon tetrabromide) in the presence of triethylamine and triphenylphosphine (Scheme **7**).

As the preparation of perfluoroimidoyl halides **38** could be performed in large scale with good to excellent yields, this method has encouraged chemists to utilize this type of readily available and multifunctional building blocks for the synthesis of various organofluorine compounds (Scheme **7**) [43]. The trifluoroacetimidoyl metals, such as palladium species **39** obtained from imidoyl iodide [44], could be employed in heck reaction or other palladium catalyzed reactions [45]. **38** could also be nucleophilically substituted by ambident reagents such as diethyl malonate and then cyclized to form the fluoroalkyl substituted quinolines **40** [46]. Different kinds of amino acid precursors could be prepared from **38**. γ-Fluorinated-β-enamino ester **41** could be obtained exclusively as *Z* isomers by treatment of **38** with lithium ester enolates [47]. The fluorinated isoserine precursor, γ-Fluorinated-α-hydroxyl ester **43**, was obtained *via* intramolecular wittig-type rearrangement of imino ethers



Scheme 6.

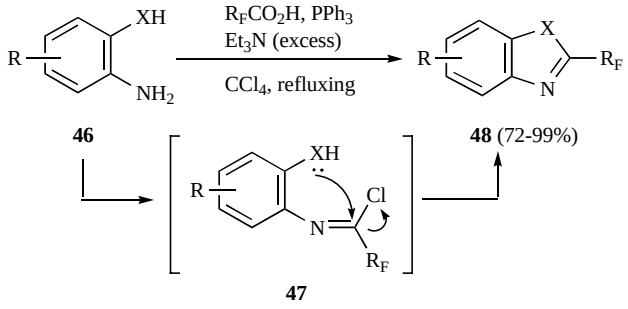


X = Cl, Br; R = Me, OMe; R^1 = $C(CH_3)_3$, $CH(CH_3)_2$, (1*R*)-(-)-menthyl

Scheme 7.

42, which could be simply prepared from the reaction of **38** with ethyl glycolate [48]. Mg(0)-promoted double silylation of **38** gave enamines **44**, which underwent electrophilic addition to benzaldehyde and subsequent transformations lead to the formation of β-hydroxy-α,α-difluoroamino acid precursors **45** [49].

If there is a nucleophilic substituent presented at *ortho* position on benzene ring in *N*-aryl imidoyl chloride **47**, the intramolecular nucleophilic substitution would occur and lead to the ring-cyclized benzo-1,3-diazoles in a single step (Scheme **8**) [50].



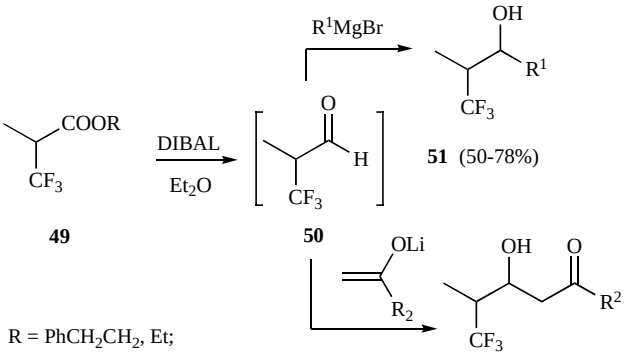
R_F = CF_3, CF_2H; X = NH, S, O; R = alkyl, NO_2, Cl

Scheme 8.

This process was carried out under mild condition and without the participation of any transition metal catalysts. The starting materials are commercially available, thus it is a smart strategy for the preparation of fluorinated benzo-1,3-diazoles even in a large scale.

4. ONE-POT CONSTRUCTION OF TRIFLUORO-METHYLATED ALDOL STRUCTURES

Fluorinated alcohol derivatives could be utilized as inhibitor of amyloid-β, which has long been associated with Alzheimer's disease [51]. Yamazaki *et al.* [52] described a general one-pot preparation of trifluoromethylated aldol structures, R^1-$CH(CF_3)$-CH(OH)-R^2. The reduction of α-trifluoromethyl propionates **49** with DIBAL from -78°C to 0°C afforded corresponding aldehydes **50** as key intermediates, which could be smoothly reacted with appropriate nucleophiles to yield compounds **51** or **52** with trifluoromethylated aldol structures (Scheme **9**). The nucleophiles, such as Grignard reagents and various types of enolates, could be used in this reaction. It's considered to be a novel method for carbon-carbon bond formation which avoids any direct handling with the unstable aldehydes **50**.



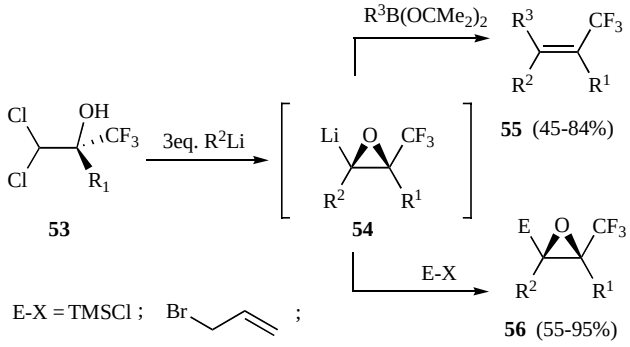
R^1 = alkyl, Ph, PhC≡C; R^2 = Ph, Me, EtO, Me_2N

Scheme 9.

5. ONE-POT SYNTHESIS OF FLUORINATED OLEFINIC BUILDING BLOCKS

Alkenes possessing a fluoroalkyl group are well known as one of the important building blocks because they are often found in the framework of biologically active molecules, such as panomifene, tamoxifen [53], etc. Shimizu *et al.* [54] reported that treatment of 2-substituted 3,3-

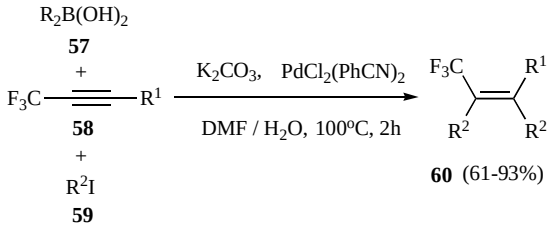
dichloro-1,1,1-trifluoropropan-2-ol **53** with an organolithium reagent R^2Li in THF at -98 °C produced intermediate 2,3-disubstituted 2-lithio-3-trifluoromethyloxirane **54**, which reacted with an organoborane $R^3B(OCMe_2)_2$ to yield tetrasubstituted fluoroolefins **55** with excellent stereoselectivity. The intermediates **54** could also be reacted with electrophiles E-X to afford trifluoromethyl oxiranes **56** (Scheme **10**).



R^1 = $Ph(CH_2)_2$, Ph, (*E*)-PhCH =CH; R^2 = *n*-Bu, Ph; R^3 = *n*-Bu, Ph

Scheme 10.

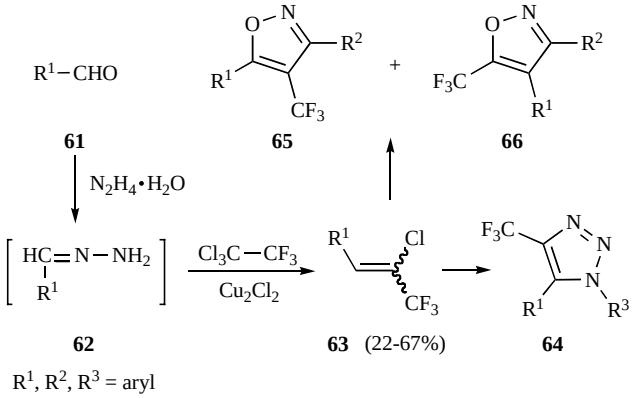
However, this one-pot process suffered from harsh reaction conditions such as low temperature at -98 °C. When R^1 and R^2 of **55** were permitted to be the same, the Suzuki-Miyaura crosscoupling reaction would be more practical one-pot method [55]. The treatment of trifluoromethyl substituted alkynes **58** with aryl boronic acids **57** and aryl iodides **59** in the presence of 5 mol% Pd (0) in DMF/H_2O at 100 °C produced **60** in 69-93% yields (Scheme **11**).



R^1 = aryl; R^2 = *p*-MeC_6H_4, *p*-$MeOC_6H_4$, Ph

Scheme 11.

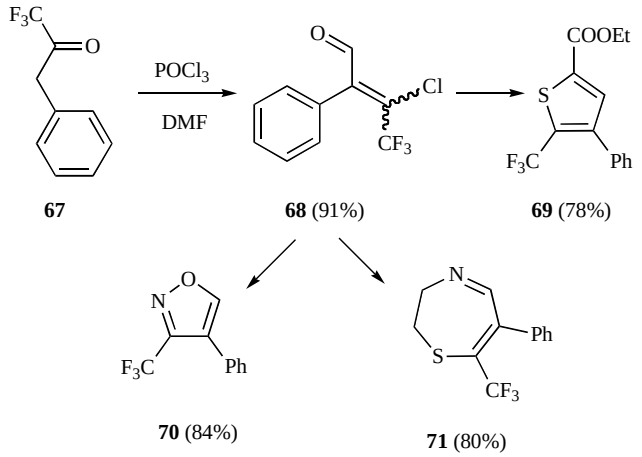
Compounds containing the $CH=C(Cl)CF_3$ moiety are normally used as synthetic precursors of trifluoromethylacetylenes in the synthesis of five-membered heterocycles **64**, **65** and **66** [56]. The classic routes to 2-chloro-3,3,3-trifluoroprop-1-enylbenzenes **63** are based on Wittig reaction [57] or organometallic approach [58]. Nenajdenko *et al.* [59] described a one-pot transformation of aromatic aldehydes **61** to **63** *via* hydrazone intermediate **62**. The reaction proceeded stereoselectively in good yields and the *Z*-isomers of **63** were formed preferentially (Scheme **12**).



R^1, R^2, R^3 = aryl

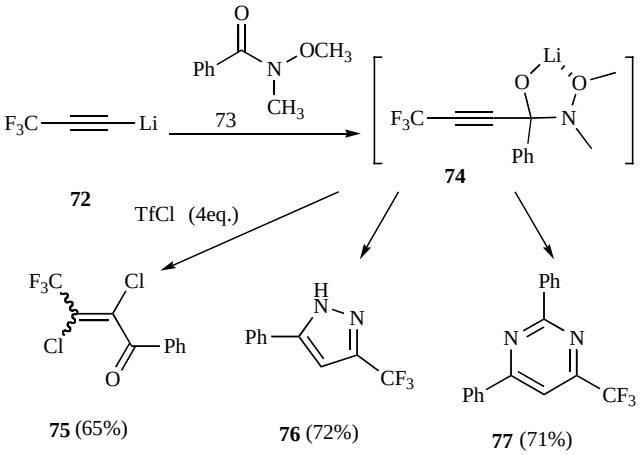
Scheme 12.

Comparing with **63**, compounds, such as aryl substituted **68** with carbonyl group, are more useful for the formation of thiophene **69**, isoxazole **70** and dihydrothiazepine **71** through the dinucleophilic attack [60]. The one–pot synthesis of β-chloro-β-(trifluoromethyl)acrolein **68** was achieved by Vilsmeier-Haack reaction when 1,1,1-trifluoro-3-phenylacetone **67** was treated with DMF and phosphoryl chloride (Scheme **13**) [61].



Scheme 13.

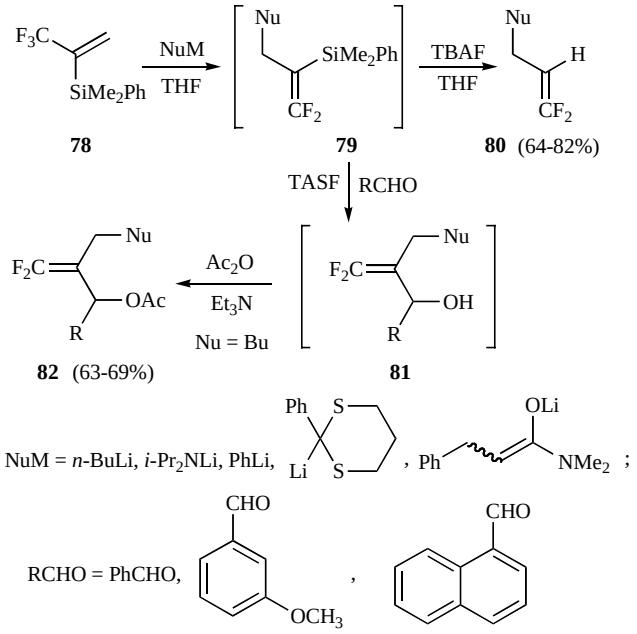
Recently, Jeong *et al.* [62] developed an efficient one-pot synthesis of α,β-dichloro-β-trifluoromethylated enone **75**, which has similar structure of **68**. The enone **75** was obtained in good yield when Trifluoropropynyl lithium **72** reacted with *N*-methoxy-*N*-methylbenzamide **73** in THF from -78 °C to 0 °C to afford lithium coordinated intermediate **74**, followed by treatment with trifluoro-methanesulfonyl chloride. The intermediate **74** could also react with water and dinucleophiles to afford pyrazole **76** and pyrimidine **77** in a one-pot process (Scheme **14**) [63].



Scheme 14.

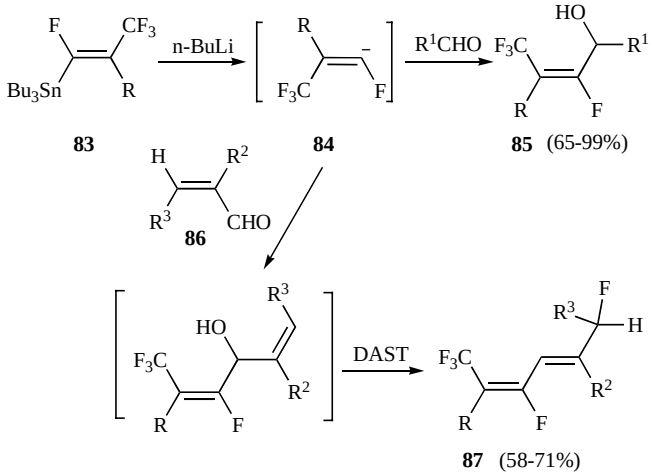
1-Trifluoromethylvinyl compounds are known to be attacked by nucleophiles in S_N2' mechanism to afford 1,1-difluoro-1-alkenes [64]. Junji *et al.* [65] have established a novel one-pot method for functionalized 1,1-difluoro-1-

alkenes such as monosubstituted 1,1-difluoro-1-alkenes **80**, 3,3-difluoroallylic alcohols **81** and their acetates **82**. These compounds are simply synthesized in two steps from 1-trifluoromethylvinylsilane **78**: (i) S_N2' reaction of **78** with nucleophiles to construct 2,2-difluorovinylsilanes **79**, and (ii) the removal of the silyl group followed by the attack of electrophile, such as benzaldehyde. The combination of these two processes allows a one-pot synthesis of the functionalized 1,1-difluoro-1-alkenes bearing two kinds of substituents (Nu, E) starting from 1-trifluoromethylvinylsilane **78**, which functions as a CF_2=C$^-$-CH_2^+ equivalent (Scheme **15**).



Scheme 15.

Fluorinated vinyl stannanes **83** could be used to generate anionic **84** *in situ*, which could be applicable to form a variety of functionalized alkenes by one-pot process. (*E*)-α-fluoro-β-trifluoromethylallylic alcohols **85** were obtained in 65-99% yields when the anionic species **84** reacted with aldehydes [66]. The key intermediates **84** could also react with α, β-unsaturated aldehydes **86** to form 1,4-diene intermediates, which were subsequentially fluorinated by DAST and resulted in the formation of polyfluorinated alka-

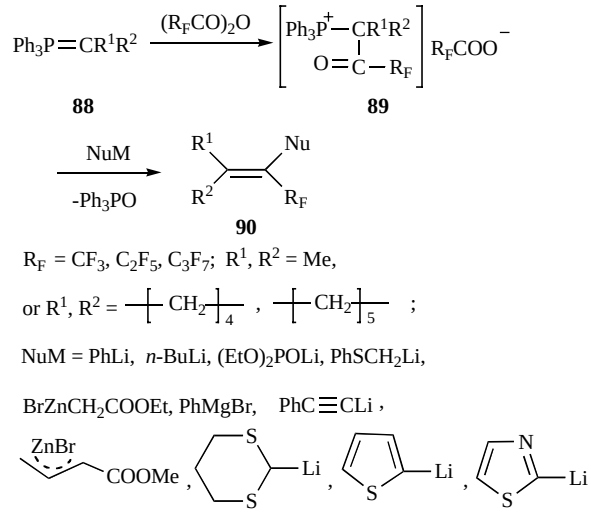


R= aryl, alkyl, (*E*)-PhCH=CH; R^1 = aryl; R^2 = H, Et; R^3 = Me, *n*-Pr

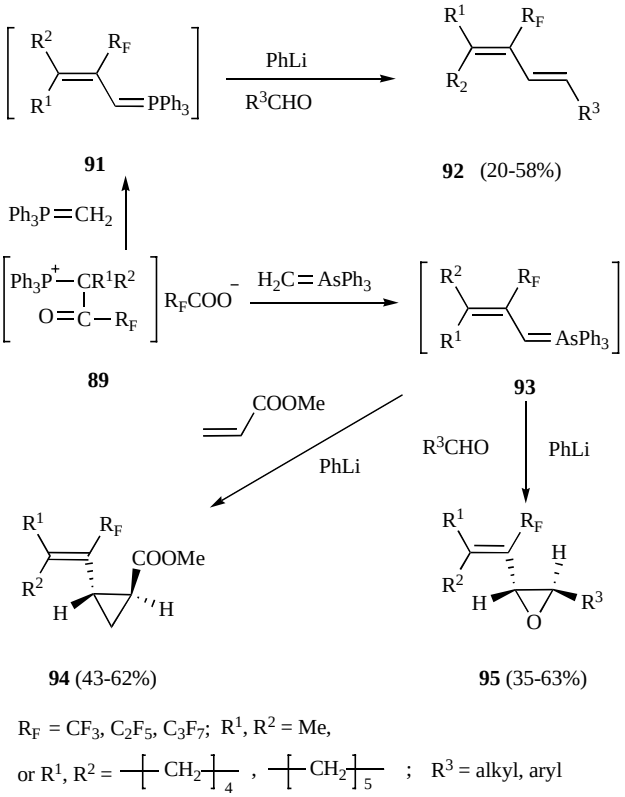
Scheme 16.

(*2E,4E*)dienes **87** in 58-71% yields (Scheme **16**) [67]. It's remarkable that the reaction of DAST with polyfluorinated diallylic alcohols yielded polyfluorinated (*2E, 4E*) isomers specifically. The migration of double bond occurred only at the non-fluorine-containing analogues.

Generally, different kinds of functionalized perfluoroalkyl substituted alkenes **90** could be easily prepared by one-pot reactions from fluorinated β-ketophosphonium salts **89**. The phosphoranes **88** were acylated by the addition of perfluoroalkanoic anhydrides to generate fluorinated β-ketophosphonium salts **89** *in-situ*, which were attacked by nucleophiles, such as organolithium, organozinc or Grignard reagents, and afforded a fluorinated carbon-carbon double bond (Scheme **17**) [68].



Scheme 17.



Scheme 18.

While methylenetriphenylphosphorane **88** ($R^1 = R^2 = H$) was employed as a nucleophile to attack fluorinated β-ketophosphonium salts **89**, **91** was formed after the deprotonation and elimination of triphenylphosphine oxide. Subsequential reaction of **91** with aldehydes enatio-selectively afforded (*E*)-fluorodienes **92** in 20-58% yields [69]. The similar result was observed in the synthesis of intermediate **93**, which could further react with acrylates or aldehydes to yield trifluoromethylated vinylcyclopropanes **94** or fluorovinylic epoxides **95** as *trans*-isomers (Scheme **18**) [70].

6. CONCLUSION

Fluorine-containing molecules attract widespread attention as important components of agrochemicals, pharmaceuticals, and advanced materials. To provide a facile and direct access to these molecules, a number of valuable one-pot syntheses of fluorinated building blocks and their synthetic utilities are described here. Such one-pot process allows easy and efficient formation of some structurally interested and biologically important building blocks which open possibilities to the design of new fluorine-containing molecules. It is expected that new and useful fluorinated building blocks and their novel syntheses will be developed in the future.

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REFERENCES

[1] Thayer, A. M. *Chem. Eng. News*, June 5, **2006**; pp. 15.
[2] a) Rozen, S. *Methods of Organic Chemistry*; Houben-Weyl, Ed.; Thieme: Stuttgart, **2000**; Vol. *E10a*, pp.167-187; b) Pohmer, K.; Bulan, A. *Methods of Organic Chemistry*; Houben-Weyl, Ed.; Thieme: Stuttgart, **2000**; Vol. *E10a*, pp. 305-320.
[3] Mietchen, R.; Peters, D. *Methods of Organic Chemistry*; Houben-Weyl, Ed.; Thieme: Stuttgart, **2000**; Vol. *E10a*, pp. 95-158.
[4] Zupan, M. *Methods of Organic Chemistry*; Houben-Weyl, Ed.; Thieme: Stuttgart, **2000**; Vol. *E10a*, pp. 265-269.
[5] Furin, G. G. *Methods of Organic Chemistry*; Houben-Weyl, Ed.; Thieme: Stuttgart, **2000**; Vol. *E10a*, pp. 432-499.
[6] a) Nyffeler, P. T.; DurMn, S. G.; Burkart, M. D.; Vincent, S. P.; Wong, C. H. *Angew. Chem.*, **2005**, *117*, 196. b) Banks, R. E.; Lawrence, N. J.; Popplewell, A. L. *J. Chem. Soc., Chem. Commun.*, **1994**, 343; c) Lal, S. G. *J. Org. Chem*., **1993**, *58*, 2791; d) Matthews, D. P.; Miller, S. C.; Jarvi, E. T.; Sabol, J. S.; McCarthy, J. R. *Tetrahedron Lett*., **1993**, *34*, 3057.
[7] a) Lee, S. H.; Schwartz, J. *J. Am. Chem. Soc*., **1986**, *108*, 2445. b) Barnette, W. *J. Am. Chem. Soc*., **1984**, *106*, 452.
[8] Rock, M. H. *Methods of Organic Chemistry*; Houben-Weyl, Ed.; Thieme: Stuttgart, **2000**; Vol. *E10a*, pp.167-187.
[9] Percy, J. M. *Top. Curr. Chem.*, **1997**, *193*, 131.
[10] Ho, T. L. *Tandem Reactions in Organic Chemistry*, Wiley – Interscience: New York, **1992**.
[11] a) Dömling, A. *Chem. Rev*., **2006**, *106*, 17; b) Diego, J. R.; Miguel, Y. *Angew. Chem. Int. Ed. Engl.*, **2005**, *44*, 1062; c) Zhu, J. P. *Eur. J. Org. Chem.*, **2003**, *7*, 1133; d) Dömling, A.; Ugi, I. *Angew. Chem. Int. Ed. Engl*., **2000**, *39*, 3168.
[12] a) Nicolaou, K. C.; Tamsyn, M.; Scott, A. S. *Chem. Commun*., **2003**, *5*, 551; b) Jean, R. *Synlett*, **1999**, *5*, 505; c) Tietze. L. F. *Chem. Rev*., **1996**, *96*, 115; d) Philip, J. P.; Clive, S. P.; Adrian, J. S. *Chem. Rev*., **1996**, *96*, 195; e) Richard, A. B. *Tetrahedron*, **1995**, *51*, 131.
[13] David, G. C.; Tohru, S. *Laboratory Automation in the Chemical Industries*; Junzo, O., Ed.; Marcel Dekker, Inc.: New York, **2002**; Vol. *8*, pp. 235-263.
[14] Brigaud, T.; Doussot. P.; Portella, C. *J. Chem. Soc., Chem. Commun.*, **1994**, *18*, 2117.
[15] Lefebvre, O.; Brigaud, T.; Portella, C. *Tetrahedron*, **1999**, *55*, 7233.
[16] Lefebvre, O.; Brigaud, T.; Portella, C. *J. Org. Chem*., **2001**, *66*, 4348.
[17] Lefebvre, O.; Brigaud, T.; Portella, C. *J. Org. Chem*., **2001**, *66*, 1941.
[18] Lefebvre, O.; Brigaud, T.; Portella, C. *Eur. J. Org. Chem.*, **2005**, 4304.
[19] Lefebvre, O.; Brigaud, T.; Portella, C. *Tetrahedron*, **1998**, *54*, 5939.
[20] Portella, C.; Brigaud, T.; Lefebvre, O.; Plantier-Royon, R. *J. Fluor. Chem*., **2000**, *101*, 193.
[21] a) Berber, H.; Brigaud, T.; Lefebvre, O.; Plantier-Royon, R.; Portella, C. *Chem. Eur. J*., **2001**, *7*, 903; b) Brigaud, T.; Lefebvre, O.; Plantier-Royon, R.; Portella, C. *Tetrahedron Lett*., **1996**, *37*, 6115.
[22] Itokawa, H.; Hirayama, F.; Funakoshi, K.; Takeya, K. *Chem. Pharm. Bull*., **1985**, *33*, 3488.
[23] a) Camps, F.; Messeguer, A.; Sanchez, F. J. *Tetrahedron*, **1988**, *44*, 5161; b) Camps, F.; Sanchez, F. J.; Messeguer, A. *Synthesis*, **1988**, 823; c)Camps, F.; Canela, R.; Coll, J.; Messeguer, A.; Rocca, A. *Tetrahedron*, **1978**, *34*, 2179.
[24] .a) Michel, D.; Schlosser, M. *Tetrahedron*, **2000**, *56*, 4253; b) Gotzo, S. P.; Seebach, D.; Sanglier, J. J. *Eur. J. Org. Chem.*, **1999**, 2533. See also the following for the influence of fluorosubstitution on olfactometric properties: c) Schlosser, M.; Michel, D. *Tetrahedron*, **1996**, *52*, 99; d) Watanabe, S.; Fujita, T.; Sakamoto, M.; Mino, Y.; Kitazume, T. *J. Fluor. Chem.*, **1995**, *73*, 21.
[25] Wilson, B. J.; Garst, J. E.; Linnabary, R. D.; Channell, R. B. *Science (Washington, D.C.)*, **1977**, *197*, 573.
[26] Monica, S.; Roberta, S.; Fiorenza, V. *Curr. Top. Med. Chem.*, **2006**, *6*, 1545.
[27] Bouillon, J. P.; Didier, B.; Dondy, B.; Doussot, P.; Plantier-Royon, R.; Portella, C. *Eur. J. Org. Chem*., **2001**, 187.
[28] Dondy, B.; Doussot, P.; Iznaden, M.; Muzard, M.; Portella, C. *Tetrahedron Lett.*, **1994**, *35*, 4357.
[29] Huang, W. Y.; Wu, Y. M. *J. Fluor. Chem.*, **1992**, *59*, 179.
[30] Wang, Y. L.; Zhu, S. Z. *J. Fluor. Chem.*, **2000**, *103*, 139.
[31] Song, L. P.; Chu, Q. L.; Zhu, S. Z. *J. Fluor. Chem.*, **2001**, *107*, 107.
[32] Crouse, G. D.; McGowan, M. J.; Boisvenue, R. J. *J. Med. Chem*., **1989**, *32*, 2148.
[33] Shchegolkov, E. V.; Khudina, O. G.; Anikina, L. V.; Burgart, Ya. V.; Saloutin, V. I. *Pharm. Chem. J*., **2006**, *40*, 373.
[34] Hidehiko, N.; Ryo, O.; Ayako, K.; Takayoshi, S.; Naoki, M. *Bioorg. Med. Chem. Lett.*, **2006**, *16*, 5939.
[35] Gowravaram, S.; Kumar, K. R. G. S.; Srinivas, R. C.; Yadav, J. S. *Synlett*, **2003**, 858.
[36] Bose, D. S.; Rudradas, A. P.; Mereyala, H. B. *Tetrahedron Lett.*, **2002**, *43*, 9195.
[37] Sharma, G. V. M.; Laxmi, R. K.; Sree, L. P.; Radha, K. P. *Synthesis*, **2006**, 55.
[38] Dai, Q.; Yang, W. R.; Zhang, X. M. *Org. Lett.*, **2005**, *7*, 5343.
[39] Doering, W. V. E.; Depuy, C. H. *J. Am. Chem. Soc*., **1953**, *75*, 5955.
[40] Michael, G. H.; Ernest, W. *Tetrahedron*, **1993**, *49*, 1057.
[41] Michael, G.; Zdenek, J.; Heinz, G. V.; Chantal, W.; Jean-Paul, D.; Bernard, T. *J. Fluor. Chem*., **1994**, *69*, 253.
[42] Tamura, K.; Mizukami, H.; Maeda, K.; Watanabe, H.; Uneyama, K. *J. Org. Chem.*, **1993**, *58*, 32.
[43] a) Uneyama, K.; Amii, H.; Katagiri, T.; Kobayashi, T.; Hosokawa, T. *J. Fluor. Chem.*, **2005**, *126*, 165; b) Uneyama, K. *J. Fluor. Chem.*, **1999**, *97*, 11.
[44] Tanaka, K.; Susuki, T.; Maeno, S.; Mitsuhashi, K. *Bull. Chem. Soc. Jpn*., **1987**, *60*, 4480.
[45] Amii, H.; Kohda, M.; Seo, M.; Uneyama, K. *Chem. Commun.*, **2003**, 1752.
[46] Uneyama, K.; Morimoto, O.; Yamashita, F. *Tetrahedron Lett.*, **1989**, *30*, 4821.
[47] Uneyama, K.; Hao, J.; Amii, H. *Tetrahedron Lett*., **1998**, *39*, 3079.
[48] Fustero, S.; Pina, B.; Simon-Fuentes, A. *Tetrahedron Lett.*, **1997**, *38*, 6771.
[49] Kobayashi, T.; Nakagawa, T.; Amii, H.; Uneyama, K. *Org. Lett.*, **2003**, *5*, 4297.

[50] Ge, F. L.; Wang, Z. X.; Wan, W.; Lu, W. C.; Hao, J. *Tetrahedron Lett.*, **2007**, *48*, 3251.
[51] Kondubhotla, S.; Stine, B.; Dahlgren, K.; Manelli, A.; Ladu, M. J.; Krafft, G. A. *Abstracts of Papers, 221st ACS National Meeting*, **2001**. MEDI-091.
[52] Yamazaki, T.; Kobayashi, R.; Kitazume, T.; Kubota, T. *J. Org. Chem.*, **2006**, *71*, 2499.
[53] Nemeth, G.; Kapiller-Dezsofi, R.; Lax, G.; Simig, G. *Tetrahedron*, **1996**, *52*, 12821.
[54] Shimizu, M.; Fujimoto, T.; Minezaki, H.; Takeshi, T. *J. Am. Chem. Soc.*, **2001**, *123*, 6947.
[55] Konno, T.; Taku, K.; Ishihara, T. *J. Fluor. Chem.*, **2006**, *127*, 966.
[56] a) Meazza, G.; Zanardi, G. *J. Fluor. Chem.*, **1991**, *55*, 199; b) Meazza, G.; Capuzzi, L.; Piccardi, P. *Synthesis*, **1989**, 331.
[57] Li, X. Y.; Fu, W. M.; Ma, S. M.; Jiang, X. K. *Huaxue Xuebao*, **1989**, *47*, 360.
[58] a) Fujita, M.; Hiyama, T. *Tetrahedron Lett.*, **1986**, *27*, 2135; b) Fujita, M.; Hiyama, T.; Kondo, K. *Tetrahedron Lett.*, **1986**, *27*, 2139; c) Fujita, M.; Hiyama, T. *Tetrahedron Lett.*, **1986**, *27*, 3655.
[59] Korothchenko, V. N.; Shastin, A. V.; Nenajdenko, V. G.; Balenkova, E. S. *Tetrahedron*, **2001**, *57*, 7519.
[60] a) Hale, J. J.; Lynch, C. L.; Neway, W.; Mills, S. G.; Hajdu, R.; Keohane, C. A.; Rosenbach, M. J.; Milligan, J. A.; Shei, G.-J.; Parent, S. A.; Chrebet, G.; Bergstrom, J.; Card, D.; Ferrer, M.; Hodder, P.; Strulovici, B.; Rosen, H.; Mandala, S. *J. Med. Chem.*, **2004**, *47*, 6662; b) Diab, J.; Laurent, A.; Le Drean, I. *J. Fluor. Chem.*, **1997**, *84*, 145; c) Alvernhe, G.; Laurent, A.; Le Drean, I.; Selmi, A. *Tetrahedron Lett.*, **1993**, *34*, 2483.
[61] Selmi, A.; El Gaied, M. M.; Alvernhe, G. *J. Fluor. Chem.*, **1995**, *72*, 1.
[62] Jeon, S. L.; Kim, J. K.; Son, J. B.; Kim, B. T.; Jeong, I. H. *J. Fluor. Chem.*, **2007**, *128*, 153.
[63] Jeong, I. H.; Jeon, S. L.; Kim, M. S.; Kim, B. T. *J. Fluor. Chem.*, **2004**, *125*, 1629.
[64] For the S_N2' reaction of 1-trifluoromethylvinyl compounds [CH_2=C(Y)CF_3], see: Y = $CO_2R(CO_2H)$: a) Kitazume, T.; Ohnogi, T.; Miyauchi, H.; Yamazaki, T. *J. Org. Chem.*, **1989**, *54*, 5630; b) Fuchikami, T.; Shibata, Y.; Suzuki, Y. *Tetrahedron Lett.*, **1986**, *27*, 3173. Y = SPh, SePh; c) Feiring, A. E. *J. Org. Chem.*, **1980**, *45*, 1962. Y = Ph; d) Begue, J.-P.; Bonnet-Delpon, D.; Rock, M. H. *J. Chem. Soc., Perkin Trans. 1*, **1996**, 1409. Y = H (Me): e) Kendrick, D. A.; Kolb, M. *J. Fluor. Chem.*, **1989**, *45*, 265; f) Bergstrom, D. E.; Ng, M. W.; Wong, J. J. *J. Org. Chem.*, **1983**, *48*, 1902; g) Hiyama T.; Obayashi, M.; Sawahata, M. *Tetrahedron Lett.*, **1983**, *24*, 4113.
[65] Junji, I.; Hiroki, F.; Yuichiro, I. *J. Org. Chem.*, **2003**, *68*, 7802.
[66] Shen, Y. C.; Wang, G. P. *Synthesis*, **2003**, 209.
[67] Shen, Y. C.; Wang, G. P. *Synthesis*, **2004**, 999.
[68] Shen, Y. C. *Acc. Chem. Res.*, **1998**, *31*, 584.
[69] Shen, Y. C.; Qiu, W. M. *Tetrahedron Lett.*, **1987**, *28*, 4283.
[70] Shen, Y. C.; Liao, Q.; Qiu, W. M. *J. Chem. Soc. Chem. Commun.*, **1988**, 130.

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