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Conversion between Difluorocarbene and Difluoromethylene Ylide

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Dedicated to Professor Jean'ne M. Shreeve on the occasion of her 80th birthday

Abstract: The interconversion between difluoromethylene ylide and difluorocarbene is described. The difluoromethylene ylide precursor, $Ph_3P^+CF_2CO_2^-$, could be turned into an efficient difluorocarbene reagent, whereas the classical difluorocarbene reagents, HCF_2Cl and $FSO_2CF_2CO_2TMS$, could generate highly reactive difluoromethylene ylide. Thus the Wittig difluoro-olefination and difluorocyclopropanation could be selectively realized by using the same reagent. In addition, the ylides obtained from different carbene sources showed different reactivity in Wittig reactions.

Keywords: carbenes · difluorocyclopropanation · difluoro-olefination · fluorine · ylides

Introduction

Difluorocarbene and difluoromethylene phosphonium ylide are highly reactive intermediates in the construction of fluorine-containing organic molecules.[1] As a singlet carbene,[2] difluorocarbene ($:CF_2$) is stabilized by two fluorine atoms and reacts readily with electron-rich substrates.[3] Triphenylphosphine can trap difluorocarbene to form phophonium ylide ($Ph_3P^+CF_2^-$) in situ.[4] It seems that $Ph_3P^+CF_2^-$ might be more stable than difluorocarbene. However, computational examination of the binding and structure of difluoromethylene phosphonium ylide showed some discrepancy.[5] Using ab initio molecular orbital energy at the SCF level, Dixon and Smart found that the bond length between carbon and phosphorus in $H_3P^+CF_2^-$ was 3.54 Å, which means that $:CF_2$ and PH_3 could be regarded as two separate species with little interaction.[5a] However, a later calculation of $H_3P^+CF_2^-$ at the HF/3-21G* level by Francl et al. showed that the C–P bond length was 1.635 Å, which could be interpreted as a double bond between carbon and phosphrous.[5b] Recently, Dolbier found that the calculated C–P bond length in $Ph_3P^+CF_2^-$ at the M06-2X/6-311+G (2df, 2p) level is 1.815 Å.[4b] The dissociation of $Ph_3P^+CF_2^-$ to difluorocarbene and PPh_3 in this case would only have to cross a 9.27 kcal mol^{-1} energy barrier, which suggested the possibility of interconversion between the ylide ($Ph_3P^+CF_2^-$) and carbene ($:CF_2$).

The capture of difluorocarbene from HCF_2Cl by triphenylphosphine to form the difluoromethylene phosphonium ylide ($Ph_3P^+CF_2^-$) was first described by Franzen,[6] but a later study claimed that the reaction could not be repeated.[7] Other attempts to trap the difluorocarbene from CF_2Br_2 or $(CF_3)_2Cd$ with PPh_3 were not successful.[7,8] The generation of the ylide from difluorocarbene was also proposed by Fuqua et al. in the Wittig reaction of aldehyde with $ClCF_2CO_2Na/PPh_3$.[9] However, Burton et al. proposed that $Ph_3P^+CF_2^-$ was generated from $Ph_3P^+CF_2CO_2^-$, not from the combination of difluorocarbene and PPh_3.[10] Recently, we successfully synthesized the intermediate $Ph_3P^+CF_2CO_2^-$ and confirmed the conjecture made by Burton et al.[11] The association of difluorocarbene with PPh_3 and the successful application in subsequent Wittig reaction was reported by Robins and Nowak, but a toxic reagent, $(CF_3)_2Hg$, was employed as the difluorocarbene precursor.[4a] Dolbier et al. employed $FSO_2CF_2CO_2CH_3$ as the difluorocarbene source to generate the ylide ($Ph_3P^+CF_2^-$) and successfully realized the Wittig difluoro-olefination.[4b] However, starting from common and easily available difluorocarbene reagents such as HCF_2Cl, attempts to form $Ph_3P^+CF_2^-$ were not successful.[7] Therefore, to make this ylide formation procedure widely applicable for difluoro-olefination, it would be worthwhile to investigate the conversion from difluorocarbene to difluoromethylene ylide.

As for the reverse process, Burton and co-workers observed the dissociation of the difluoromethylene ylide into difluorocarbene in the reaction of (bromodifluoromethyl)triphenylphosphonium bromide with tertiary phosphine and trialkyl phosphite.[12] A similar process was proposed by Jaiswal et al. during the preparation of hydrofluorocarbons.[13] However, this procedure was not applied in typical reactions involving difluorocarbene. Thus the conversion from the difluoromethylene ylide to difluorocarbene remains to be further investigated.

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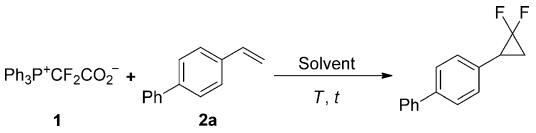
Results and Discussion

We have previously demonstrated that the phosphobetaine intermediate ($Ph_3P^+CF_2CO_2^-$, **1**) is an efficient and reliable precursor of difluoromethylene ylide.[11] The simple decarboxylation of $Ph_3P^+CF_2CO_2^-$ at temperatures below 80 °C can give the difluoromethylene ylide, which would make it feasible and convenient to explore the conversion from difluoromethylene ylide to difluorocarbene. 4-Vinyl-1,1′-biphenyl (**2a**) was chosen as a model substrate to detect the generation of difluorocarbene. It was found that the desired reaction did not happen in polar solvents (Table 1, entries 1 and 2). To our delight, the difluorocyclopropanation did occur in less-polar solvents (Table 1, entries 3–5). Better yields were obtained in cyclohexane or *para*-xylene (Table 1, entries 6 and 7). These results suggest that polar solvents could help to stabilize the charge-separation ylide $Ph_3P^+CF_2^-$, whereas less-polar or non-polar solvents would favor the dissociation of the ylide into difluorocarbene. Further screening of the reaction temperature and molar ratio showed that a 2:1 ratio of **1** to **2a** at 90 °C for 8 h were the optimal reaction conditions (Table 1, entry 11). Due to the volatility of the product, less solvent (0.1 mmol of **2a** in 1 mL of *para*-xylene) was used so that the reaction mixture could be directly subject to column chromatography after the completion of the reaction, thus reducing the inevitable loss of the product during work-up. The reaction proceeded equally well for a scaled-up reaction in a small amount of *para*-xylene (Table 1, entry 12), indicating the high efficiency of this reaction.

Table 1. Conditions for the difluorocyclopropanation with $Ph_3P^+CF_2CO_2^-$.[a]

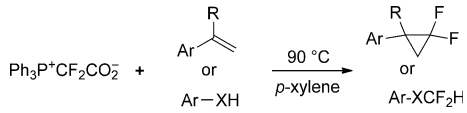


1 2a

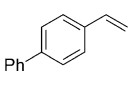
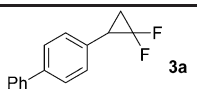
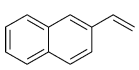
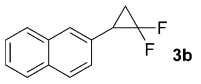
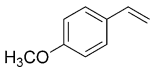
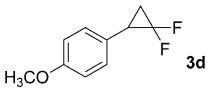
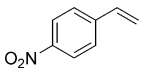
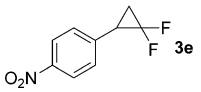
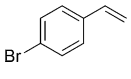
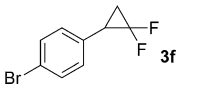
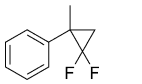
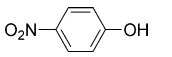
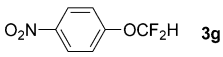
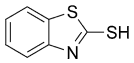
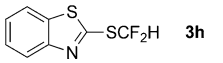
Entry	Solvent	T [°C]	**1**:**2a**[b]	t [h]	Yield [%][c]
1	DMF	80	2:1	8	ND[d]
2	DG	80	2:1	8	ND[d]
3	methyl benzoate	90	2:1	2	24
4	1,4-dioxane	80	2:1	8	45
5	THF	80	2:1	8	30
6	*p*-xylene	80	2:1	8	77
7	cyclohexane	80	2:1	8	73
8	*p*-xylene	80	2:1	4	75
9	*p*-xylene	80	1.5:1	4	54
10	*p*-xylene	60	2:1	8	22
11	*p*-xylene	90	2:1	8	80
12[e]	*p*-xylene	90	2:1	8	80

[a] 0.1 mmol of **2a** in 1 mL of solvent. [b] Molar ratio. [c] Determined by ^{19}F NMR spectroscopy with the quantitative addition of trifluoromethylbenzene as the internal standard. [d] Not detected by ^{19}F NMR spectroscopy. [e] 0.8 mmol of **2a** in 1.2 mL of *p*-xylene. DG = diglyme.

Table 2. Reactions of difluorocarbene generated from the ylide ($Ph_3P^+CF_2^-$).[a]



1 2 3

Entry	Reactant	Product	Yield [%][b]
1		 **3a**	80
2		 **3b**	73
3		 **3d**	92
4		 **3e**	50
5		 **3f**	77
6		 **3c**	62
7[c]		 **3g**	70
8[c]		 **3h**	87
9[c]		 **3i**	81

[a] Reaction conditions: **1** (1.6 mmol) and **2** (0.8 mmol) in *p*-xylene (1.2 mL) for 8 h at 90 °C. [b] Yield of isolated product. [c] Performed for 1 h.

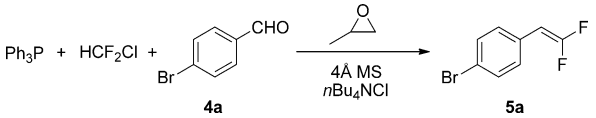
We then investigated the scope of the reaction under the optimal reaction conditions. In most cases, the reaction proceeded very well to give the difluorocyclopropanation product in moderate to good yields (Table 2, entries 1–6). An electron-rich alkene reacted better than an electron-poor alkene (Table 2, entry 3 vs. 4). Moderate yield could be obtained in the case of the disubstituted alkene (Table 2, entry 6), indicating that the steric hindrance did not significantly influence the reaction. Besides the difluorocyclopropanation reaction, heteroatom–hydrogen bond insertion (X–H, X = O, S, N) is another typical reaction of difluorocarbene.[14] However, due to the poor electrophilicity of difluorocarbene, excess base was usually required to produce the heteroatom anion, thereby promoting its reaction with difluorocarbene.[14b–d,15] It was found that the difluorocarbene derived from $Ph_3P^+CF_2CO_2^-$ inserted smoothly into the X–H bond without the addition of any base, giving good yields of the difluoromethylation product (Table 2, entries 7–9). The above difluorocyclopropanation and difluoromethylation reactions demonstrated the successful conversion from difluoromethylene ylide to difluorocarbene. The difluorocarbene can be generated at a relatively low reaction temperature without any external additive or catalyst, which might make the difluoromethylene ylide precursor

($Ph_3P^+CF_2CO_2^-$, **1**) a simple and convenient difluorocarbene reagent.

The successful conversion from difluoromethylene ylide to difluorocarbene prompted us to investigate its reverse process, from difluorocarbene to difluoromethylene ylide. Although many difluorocarbene reagents have been developed, most are inefficient or difficult to obtain: difluorodiazirine, Me_3SnCF_3, and $(CF_3)_2Hg$, for instance, require several steps to prepare and involve expensive or toxic materials.[16] The generation of difluorocarbene from hexafluoropropylene oxide (HFPO) must be carried out in an autoclave at high temperature.[17] Chlorodifluoromethane (HCF_2Cl) is a classical difluorocarbene reagent from which difluorocarbene can be easily generated in the presence of base, such as potassium *tert*-butoxide or hydroxide.[14a,18] Speziale and Ratts once tried to capture the difluorocarbene from HCF_2Cl by PPh_3 to form the difluoromethylene ylide $Ph_3P^+CF_2^-$; however, their attempts failed.[7] It was suggested that difluorocarbene preferentially reacted with the strong base rather than PPh_3. We thought that reducing the concentration of base might help the capture of difluorocarbene with PPh_3. It was reported that the low concentration of alkoxy anion produced from the ring-opening reaction of ethylene epoxide could be used as the base for the generation of $:CF_2$ from HCF_2Cl.[19] Therefore, this procedure was adopted for the trapping of difluorocarbene with PPh_3.

In the presence of propylene oxide and tetra-*n*-butylammonium chloride, the reaction of 4-bromobenzaldehyde with HCF_2Cl and PPh_3 gave the difluoro-olefination product, indicating the formation of difluoromethylene ylide $Ph_3P^+CF_2^-$ in the reaction (Table 3, entry 1). Among the solvents tested, DMF was shown to be the most suitable for the difluoro-olefination (Table 3, entries 1–4). This indicated that polar solvents favored the ylide formation, which is consistent with the previous observation.[4b] Further optimization of the temperature, the amount of propylene epoxide and the reaction time revealed that a moderate yield of the desired product could be obtained after being heated at 110 °C for 6 h in the presence of 2 equivalents of propylene oxide (Table 3, entry 8). Water was known to be detrimental to the reaction of $:CF_2$ or $Ph_3P^+CF_2^-$.[4b,14d] Therefore, 4 Å MS were employed to remove trace amounts of water in the reaction. It was found that the yield was significantly increased with the addition of 4 Å MS (Table 3, entry 9). Under these conditions, we tried to reduce the amount of nBu$_4$NCl. The reaction proceeded smoothly, even when only a catalytic amount of nBu$_4$NCl was used (Table 3, entries 10 and 11). To our surprise, the difluoro-olefination reaction took place even without the presence of nBu$_4$NCl (Table 3, entry 12), suggesting that 4 Å MS acted both as a drying agent and as a Lewis acid to promote the ring opening of propylene epoxide. In the absence of propylene oxide, no desired product was detected (Table 3, entry 13), which means that the alkoxy anion from propylene epoxide initiated the reaction of HCF_2Cl.

Table 3. Optimization of reaction conditions for difluoro-olefination with HCF_2Cl.[a]



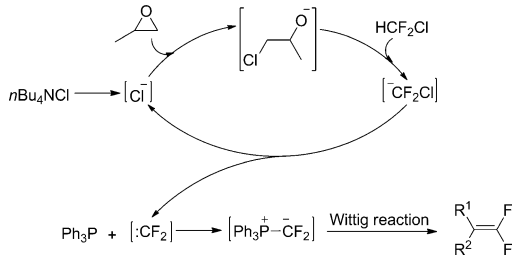
4a **5a**

Entry	Solvent	nBu$_4$NCl [equiv]	T [°C]	PO[b] [equiv]	t [h]	Yield[c] [%]
1	DMF	0.4	80	1.0	4	15
2	DG	0.4	80	1.0	4	<1
3	MB[d]	0.4	80	1.0	4	6
4	*p*-xylene	0.4	80	1.0	4	3
5	DMF	0.4	90	1.0	4	24
6	DMF	0.4	110	1.0	4	42
7	DMF	0.4	110	1.0	6	51
8	DMF	0.4	110	2.0	6	56
9[e]	DMF	0.4	110	2.0	6	80
10[e]	DMF	0.2	110	2.0	6	83
11[e]	DMF	0.1	110	2.0	6	75
12[e]	DMF	–	110	2.0	6	42
13[e]	DMF	–	110	–	6	ND[f]

[a] Performed on a 0.1 mmol scale based on **4a**. [b] Propylene oxide. [c] Determined by ^{19}F NMR spectroscopy with the quantitative addition of trifluoromethylbenzene as the internal standard. [d] Methylbenzoate. [e] 50 mg 4 Å MS was added. [f] Not detected by ^{19}F NMR spectroscopy.

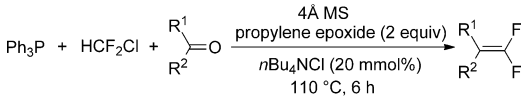
The difluoromethylene ylide derived from HCF_2Cl could be applied to the difluoro-olefination of a variety of aryl aldehydes, giving the corresponding *gem*-difluoroalkenes in good to excellent yields (Table 4, entries 1–5). The relatively lower yield of *meta*-trifluoromethyl benzaldehyde obtained is due to the high volatility of the product; the yield determined by ^{19}F NMR analysis was 81 % (Table 4, entry 2). Heteroaryl aldehydes are also suitable substrates for this reaction (Table 4, entries 6 and 7). The reaction proceeded quite well for the α,β-unsaturated aldehyde or enolizable aldehyde (Table 4, entries 8 and 9). However, even in the case of an activated ketone, only a moderate yield of difluoro-olefinated product could be obtained (Table 4, entry 10).

This reaction occurred through the following process (Scheme 1). The ring-opening reaction of propylene oxide by chloride afforded the alkoxy anion. This then abstracted a proton from HCF_2Cl to form the chlorodifluoromethyl anion, which underwent decomposition to give difluorocarbene and a chloride anion. The chloride anion entered into the next reaction cycle. Therefore, only a catalytic amount of nBu$_4$NCl was needed for the reaction. If water was present in the reaction system, the alkoxy anion would be con-

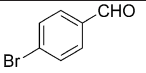
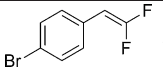
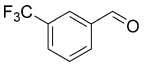
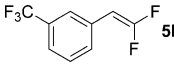
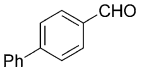
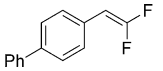
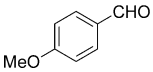
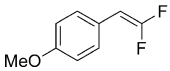
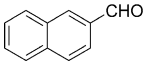
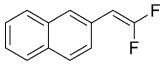
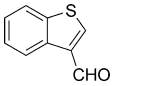
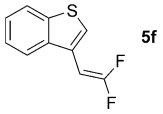
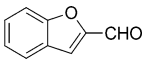
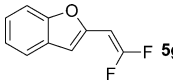
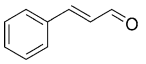
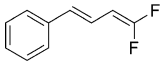
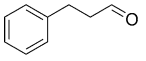
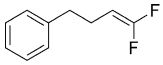
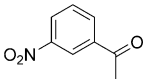
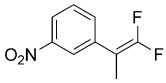


Scheme 1. Formation of difluorocarbene and difluoromethylene ylide from HCF_2Cl.

Table 4. Wittig difluoro-olefination with HCF_2Cl.[a]



4 5

Entry	Reactant	Product	Yield [%][b]
1		 **5a**	77
2		 **5b**	49, 81[c]
3		 **5c**	92
4		 **5d**	78
5		 **5e**	94
6		 **5f**	89
7		 **5g**	74
8		 **5h**	90
9		 **5i**	61
10		 **5j**	43

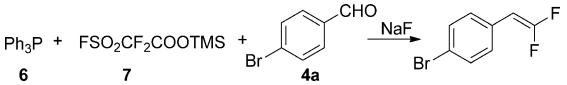
[a] Reaction conditions: Ph_3P (1.6 mmol), HCF_2Cl (3.5 mmol), 4 Å MS (75 mg), nBu_4NCl (0.16 mmol), propylene epoxide (1.6 mmol), and 4 (0.8 mmol) in DMF (1.5 mL) for 6 h at 110 °C. [b] Yield of isolated product. [c] Determined by ^{19}F NMR spectroscopy with trifluoroacetic acid as the internal standard.

sumed. Thus molecular sieves were used to remove it. Because the alkoxy anion was generated by ring-opening of the epoxide, it might always exist in very low concentrations and not impede the capture of difluorocarbene with PPh_3, which would help the formation of difluoromethylene ylide.

It should be noted that the difluoromethylene ylide derived from HCF_2Cl did not react well with electron-deficient aldehydes, such as 4-nitrobenzaldehyde. This was also reported by Fuqua and Dolbier and co-workers.[4b,9c] As we know, the reactivity of difluorocarbene from different precursors varied greatly. This prompted us to consider that different difluorocarbene sources might make some difference in the reactivity of the corresponding difluoromethylene ylides. Recently, trimethylsilyl fluorosulfonyldifluoroacetate ($FSO_2CF_2CO_2TMS$; TFDA) has been found to be an efficient difluorocarbene reagent that can react smoothly with electron-deficient alkenes.[20] To explore the applicability of this ylide formation method and the reactivity of the ylide from different carbene sources, we investigated the generation and reaction of difluoromethylene ylide from TFDA.

It has been reported that $FSO_2CF_2CO_2TMS$ (TFDA) could smoothly generate difluorocarbene in methylbenzoate.[20a,c] The first attempt at Wittig difluoro-olefination of 4-bromobenzaldehyde with TFDA in the presence of PPh_3 was made in this solvent. Indeed, the reaction gave the desired product, indicating the successful conversion from difluorocarbene to difluoromethylene ylide $Ph_3P^+CF_2^-$, but only a low yield was obtained (Table 5, entry 1). Some other

Table 5. Optimization of reaction conditions for Wittig difluoro-olefination of $FSO_2CF_2CO_2TMS$.



6 7 4a

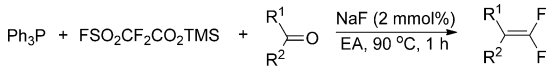
Entry	Solvent	T [°C]	t [h]	Molar ratio **6**:**7**:**4a**	Yield [%][a]
1	MB[b]	120	2	2:2:1	26
2	DMF	120	2	2:2:1	12
3	*p*-xylene	120	2	2:2:1	27
4	benzonitrile	120	2	2:2:1	19
5	CH_3CN	120	2	2:2:1	53
6	EA	120	2	2:2:1	76
7	EA	70	2	2:2:1	72
8	EA	80	2	2:2:1	83
9	EA	90	2	2:2:1	86
10	EA	100	2	2:2:1	85
11	EA	90	2	1:1:1	46
12	EA	90	2	1.5:1.5:1	80
13	EA	90	2	2.5:2.5:1	94
14	EA	90	2	3:3:1	91
15	EA	90	0.5	2.5:2.5:1	70
16	EA	90	1	2.5:2.5:1	95

[a] Determined by ^{19}F NMR spectroscopy with the quantitative addition of trifluoromethylbenzene as the internal standard. [b] Methylbenzoate.

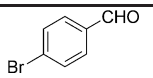
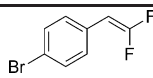
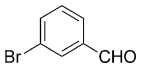
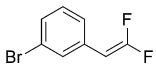
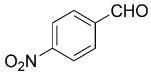
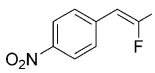
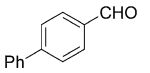
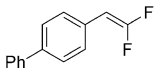
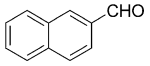
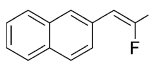
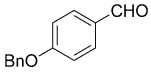
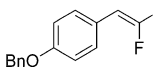
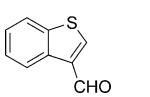
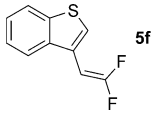
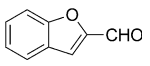
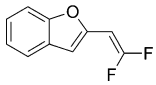
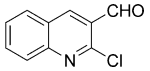
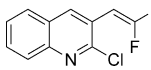
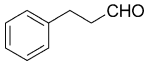
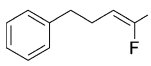
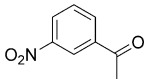
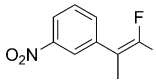
solvents were then investigated (Table 5, entries 2–6) and it was found that solvent had significant impact on the reaction. In ethyl acetate (EA), the result was much better than that in other solvents (Table 5, entry 6). After further screening of the reaction temperature, reaction time, and the molar ratio of $Ph_3P/FSO_2CF_2CO_2TMS$/substrate (Table 5, entries 7–16), we decided that EA as solvent, a reaction temperature of 90 °C, and a molar ratio of 2.5:2.5:1 were the optimal conditions (Table 5, entry 16).

The reaction could be applied to a variety of carbonyl compounds including aromatic, heteroaromatic, and aliphatic aldehydes and activated ketones (Table 6). More importantly, the reaction worked very well in the case of electron-deficient aldehydes (Table 6, entries 3 and 9), demonstrating a higher reactivity of the difluoromethylene ylide obtained from TFDA in comparison with other reported methods.[4b,9c] In the case of 4-nitrobenzaldehyde (Table 6, entry 3), difluoro-olefination with difluoromethylene ylide usually gave very low yields of the expected difluoro-olefinated product; only 2.1% yield was obtained by Fuqua's method,[9c] and only 15% yield by Dolbier's method.[4b] This indicated that ylides obtained from different carbene sources have different reactivity.

Table 6. Wittig difluoro-olefination of $FSO_2CF_2CO_2TMS$.[a]



4 5

Entry	Reactant	Product	Yield [%][b]
1		 **5a**	87
2		 **5b**	91
3		 **5d**	70
4		 **5c**	84
5		 **5e**	86
6		 **5h**	81
7		 **5f**	87
8		 **5g**	93
9		 **5k**	96
10		 **5i**	54
11		 **5j**	65

[a] Reaction conditions: Ph_3P (2.0 mmol), $FSO_2CF_2CO_2TMS$ (2.0 mmol), NaF (0.016 mmol), and **4** (0.8 mmol) in EA (1.5 mL) for 1 h at 90 °C. [b] Yield of isolated product.

Conclusion

The interconversion between difluoromethylene ylide and difluorocarbene has been successfully achieved. By changing the reaction conditions, the difluoromethylene ylide precursor, $Ph_3P^+CF_2CO_2^-$, was converted into an efficient difluorocarbene reagent, whereas the classical difluorocarbene reagents, HCF_2Cl and $FSO_2CF_2CO_2TMS$, generated the highly reactive difluoromethylene ylide. The difluoromethylene ylides obtained from different difluorocarbene reagents showed different reactivity in Wittig reactions. Therefore, the difluoro-olefination and difluorocyclopropanation could be selectively conducted by using the same reagent. Further research on the conversion between other fluorinated ylide and carbene is currently underway.

Experimental Section

General methods: Solvents and reagents were purchased from commercial sources and used as received, unless otherwise noted. The solvents *para*-xylene, DMF, and EA were distilled over CaH_2. ^1H, ^{13}C and ^{19}F NMR spectra were detected on a 500, 400or 300 MHz NMR spectrometer. Data for ^1H, ^{13}C and ^{19}F NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet), coupling constant/s in Hz. Mass spectra were obtained on a GC-MS. High-resolution mass data were recorded on a high resolution mass spectrometer in the EI or ESI mode.

Dissociation of difluoromethylene ylide to carbene: $Ph_3P^+CF_2CO_2^-$ (**1**, 570 mg, 1.6 mmol) and 4-vinyl-1,1′-biphenyl (**2a**, 144 mg, 0.8 mmol) were added to a 5 mL sealed tube. The mixture was degassed and then *para*-xylene (1.2 mL) was added under N_2. The reaction mixture was stirred at 90 °C for 8 h. After being cooled to room temperature, the solution was subjected to flash column chromatography to give the pure product **3a**.

Wittig difluoro-olefination of HCF_2Cl: Ph_3P (420 mg, 1.6 mmol), 4-bromobenzaldehyde (**4a**, 148 mg, 0.8 mmol), and 4 Å MS (75 mg) were added to a 5 mL sealed tube. The mixture was degassed and then a solution of HCF_2Cl in DMF (2.3 M, 1.5 mL) was added under N_2. The reaction mixture was stirred at 110 °C for 6 h. After being cooled to room temperature, the solution was subjected to flash column chromatography to give the pure product **5a**.

Wittig difluoro-olefination of $FSO_2CF_2CO_2TMS$: Ph_3P (525 mg, 2.0 mmol), 4-bromobenzaldehyde (**4a**, 148 mg, 0.8 mmol), and NaF (1.6 mg, 0.038 mmol) were added to a 25 mL Schlenk tube. The mixture was degassed and then EA (1.2 mL) was added under N_2. The reaction mixture was stirred at 90 °C for 1 min. $FSO_2CF_2CO_2TMS$ (501 mg, 2.0 mmol) was added dropwise over 10 min. The resulting mixture was stirred at the same temperature for another 1 h. After being cooled to room temperature, it was subjected to flash column chromatography directly to give the pure product **5a**.

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