# Fluorinated Ylides and Related Compounds†

Donald J. Burton*

*Department of Chemistry, University of Iowa, Iowa City, Iowa 52242*

Zhen-Yu Yang* and Weiming Qiu*

*E.I. DuPont de Nemours Central Research & Development, Experimental Station, P.O. Box 80328, Wilmington, Delaware 19880-0328*

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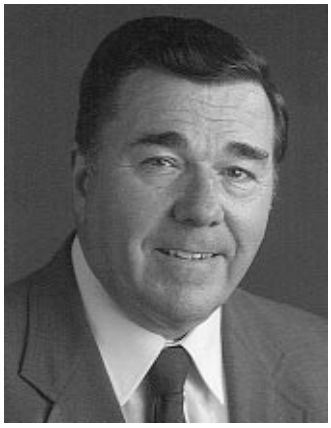
## I. Introduction

Since the initial report by Wittig and Geissler[1] in 1953 of the reaction of methylenetriphenylphosphorane with benzophenone to give 1,1-diphenylethylene, a plethora of applications of this unique olefination reaction have appeared and numerous reviews and books have detailed the progress of the Wittig reaction. In contrast to this explosion of information, only two brief reviews[2,3] detail the preparation and reactions of fluoromethylene ylides. No comprehensive review of fluorinated ylides has been reported, and it is the purpose of this review to remedy this void.



Donald J. Burton, born in Baltimore, MD, received his B.S. (1956) in Chemistry from Loyola College (Baltimore) and his Ph.D. (1961) in Organofluorine Chemistry from Cornell University under Professor W. T. Miller, Jr. Following postdoctoral work with Professor H. C. Brown at Purdue University (1961–62), he joined the faculty of the University of Iowa and is currently Carver/Shriner Professor of Chemistry at the University of Iowa. He has been a Fellow of the Japan Society for the Promotion of Science (1979) and a Visiting Professor in Japan (1985), China (1985), Korea (1986), Russia (1990), and Taiwan (1994). His research interests include fluorine-containing ylides, fluoroolefin chemistry, stable fluorinated organometallics, synthetic methodology in organofluorine chemistry, fluorocarbene chemistry, single electron transfer reactions, and the development of new fluorine-containing synthons. In 1984 he received the American Chemical Society (Fluorine Division) Award for Creative Work in Fluorine Chemistry; in 1988, the Governor's Science Medal for Scientific Achievement, and in 1990 he was the recipient of the American Chemical Society Midwest Award in Chemistry. He is a member of the Editorial Boards of *Fluorine Chemistry Reviews* and the *Journal of Fluorine Chemistry*, and in 1978 served as the Chairman of the Fluorine Division of the American Chemical Society.

Zhen-Yu Yang was born in Zhijiang, China, in 1961. He received his Ph.D. degree from Shanghai Institute of Organic Chemistry, Academia Sinica under the supervision of Professor Qing-Yun Chen in 1986. After postdoctoral research with Professor D. J. Burton at the University of Iowa, he became a research chemist at DuPont Central Research & Development in 1992 and a senior research chemist in 1995. He received the National Chemistry Prize for Young Chemists from the Chinese Chemical Society in 1985–1986 and shared the National Nature Science Prize from the Chinese Science & Technology Commission in 1989. He has authored or coauthored over 50 research papers, book chapters, and review articles and been issued 10 U.S. patents with many more pending. His research interests are organofluorine chemistry and fluoropolymer chemistry.

Weiming Qiu (b. 1954, in Shanghai, China) received his Ph.D. degree from Shanghai Institute of Organic Chemistry, Academia Sinica in China under the supervision of Professor Yangchan Shen in 1987. After spending one year in the same institute as a research associate, he joined Professor Burton's research group at the University of Iowa as a postdoctoral fellow in 1988. He moved to Triangle Park, NC, and worked for Natland International Co. for one year before he joined DuPont Central Research & Development early in 1995. His main research interest is organofluorine chemistry.

For the purpose of this review, the types of fluorinated ylides, both phosphonium, arsonium, and nitrogen ylides and phosphonate carbanions, have been divided into several classes to facilitate the assimilation of a vast amount of material by the reader and to minimize the effort in retrieval of information from either the text or the tables. Each subclass of fluorinated ylides details preparative work on both ylide precursors and ylide preparation; discussion of ylide stabilities (both experimental and calculation studies); and numerous application of these fluorinated ylides in organic synthesis. Detailed tables enumerate applications of these ylides. Phosphorus(III) ylides, such as $R_FP{=}CF_2$, have not been utilized in organic synthesis and are not included in this review.

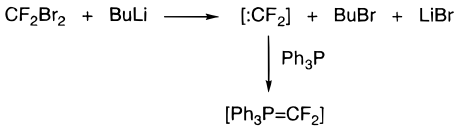
## *II. Fluoromethylene Ylides*

### 1. Preparation of Difluoromethylene Ylides and/or Their Precursors

#### *1.1. Difluoromethylene Ylides (Early Work)*

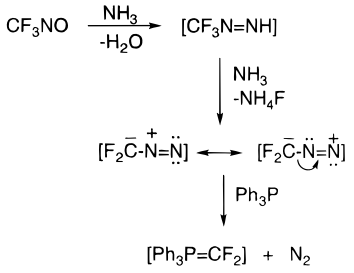
The first report of difluoromethylene ylide preparation (without experimental details) from equimolar amounts of dibromodifluoromethane, triphenylphosphine, and butyllithium was described by Franzen in 1960.[4,5] The formation and capture of difluorocarbene was proposed (Scheme 1). However, in a later study, this result could not be reproduced.[6]

**Scheme 1**

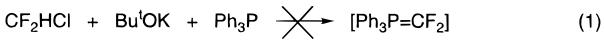



It has also been claimed that difluoromethylene ylide is formed from the reaction of trifluoronitrosomethane with ammonia and triphenylphosphine[7] (Scheme 2). Difluorodiazomethane was proposed as an intermediate in this transformation. However, no evidence has been reported in support of the formation of the ylide and no subsequent reports on the use of this method have appeared.

**Scheme 2**



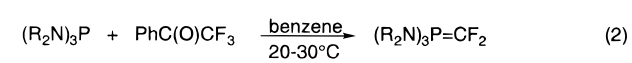

*In situ* generation of difluorocarbene via the reaction of potassium *tert*-butoxide and chlorodifluoromethane, and capture of the carbene by triphenylphosphine, also failed to produce difluoromethylene ylide as evidenced by the quantitative recovery of triphenylphosphine from the reaction mixture (eq 1).




(1)

A high yield of chloride ion (determined by potentiometric titration) indicated that carbene generation had occurred. It was suggested that difluorocarbene had preferentially reacted either with $Bu^tOK$ or $Bu^tOH$.

In 1964 Mark reported the synthesis of stable, isolable liquid difluoromethylene ylides by the reaction of hexaalkylphosphorus triamides with trifluoroacetophenone (eq 2).[8] However, these alleged




(2)

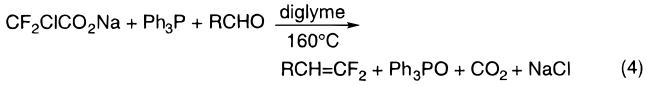
ylides did not react with either benzaldehyde or *o*-chlorobenzaldehyde to give 1,1-difluoromethylene olefins. Subsequent work by Ramirez unequivocally showed that the products of Mark's report were *not* the claimed difluoromethylene ylides but were in fact the tris(dialkylamino)difluorophosphoranes (eq 3).[9]




(3)

#### *1.2. Difluoromethylene Ylides (Halodifluoroacetate Approach)*

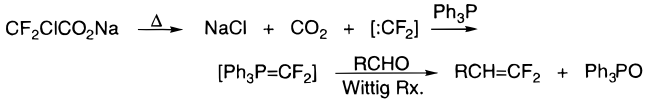
The first successful preparation and capture of a difluoromethylene ylide was reported by Fuqua and co-workers in 1964.[10,11] This method involved a one-step transformation of aldehydes to 1,1-difluoromethylene olefins by heating a solution of an aldehyde, sodium chlorodifluoroacetate, and triphenylphosphine (eq 4). The authors favored a mechanism for




(4)

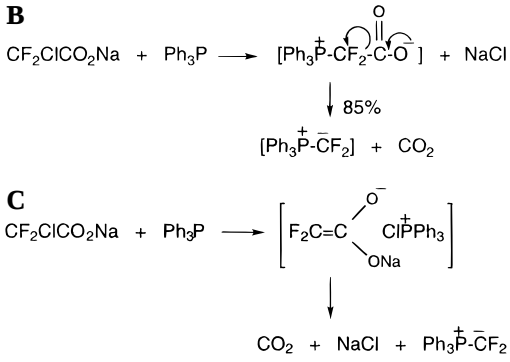
this transformation which proceeded via *in situ* formation of difluorocarbene, which was trapped by triphenylphosphine to form the ylide which undergoes a Wittig reaction with the aldehyde (Scheme 3).

**Scheme 3. Mechanism A**




Two other plausible mechanisms can also explain the proposed ylide intermediate (Scheme 4). In related

**Scheme 4. Mechanisms B and C**




work by Herkes,[12] it was shown that the rate of thermal decomposition of sodium chlorodifluoroacetate was greatly accelerated by triphenylphosphine and required only 4−6 h for 70% of the theoretical amount of $CO_2$ to be evolved. In the absence of triphenylphosphine, the decomposition of $CF_2ClCO_2Na$ required 17 h under similar conditions. This acceleration of salt decomposition and the failure to trap [:$CF_2$] either with tetramethylethylene or isopropyl alcohol suggest that mechanism B best explains ylide formation.[12]

The difluoromethylene ylide generated from chlorodifluoroacetate precursors must be captured *in situ*. When triphenylphosphine and sodium chlorodifluoroacetate was heated in diglyme at 100 °C followed by addition of trifluoroacetophenone, no 1,1-difluoroolefin was detected and 95% of the ketone was recovered (eq 5).[12] Similarly, when the ylide was generated in diglyme at 100 °C, the reaction mixture cooled to room temperature, and benzaldehyde added,

no $PhCH{=}CF_2$ was detected (eq 6).[12] Apparently the

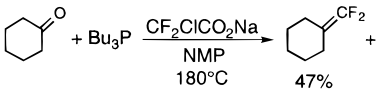
$$Ph_3P + CF_2ClCO_2Na \xrightarrow[100°C]{\text{diglyme}} [Ph_3\overset{+}{P}\text{-}\overset{-}{C}F_2] \xrightarrow{PhC(O)CF_3} PhC(CF_3){=}CF_2,\ 0\% \quad (5)$$

$$Ph_3P + CF_2ClCO_2Na \xrightarrow[2)\ RT]{1)\ \text{diglyme/100°C}} [Ph_3\overset{+}{P}\text{-}\overset{-}{C}F_2] \xrightarrow{PhCHO} PhCH{=}CF_2,\ 0\% \quad (6)$$

difluoromethylene ylide is not stable under these reaction conditions and decomposes rapidly in the absence of a carbonyl trapping agent.

On a small scale (<0.1 mol) a mixture of the tertiary phosphine, chlorodifluoroacetate salt and aldehyde can simply be heated in diglyme at 100 °C. For larger preparative size reactions a saturated solution of sodium chlorodifluoroacetate is added dropwise to a mixture of the carbonyl compound and triphenylphosphine in diglyme at 140−150 °C in order to control the violent, exothermic decomposition of sodium chlorodifluoroacetate.[12] Other solvents utilized were triglyme, 1-methyl-2-pyrrolidone, and dimethylformamide. Dimethyl sulfoxide gives significantly lower yields of 1,1-difluoroolefins and generated copious amounts of dimethyl sulfide.[12]

When the halodifluoroacetate methodology was extended to nonactivated ketones, Fuqua found that replacement of triphenylphosphine and diglyme by tributylphosphine and 1-methyl-2-pyrrolidone (NMP) gave modest yields of 1,1-difluoroolefins (eq 7).[13,14]



(7)

The reaction was more complex with $Bu_3P$ and side products containing the butylidene ($CH_3CH_2CH_2$-CH=) group were occasionally isolated. When trifluoroacetophenone was employed as the substrate, the butylidene product was the only product isolated (eq 8).[14] Although a detailed mechanism involving

$$Bu_3P + PhC(O)CF_3 \xrightarrow[NMP\ 180°C]{CF_2ClCO_2Na} PhC(CF_3){=}CH(CH_2)_2CH_3\ (15\%) \quad (8)$$

rearrangement of $[Bu_3P^+-{}^-CF_2]$ was proposed to explain the butylidene product, later work demonstrated that the butylidene product from trifluoroacetophenone was formed directly via reaction of tributylphosphine and trifluoroacetophenone (eq 9).[15]

$$RC(O)CF_3 + R'_3P \xrightarrow[reflux]{hexane} RC(CF_3){=}CHR'' \quad (9)$$

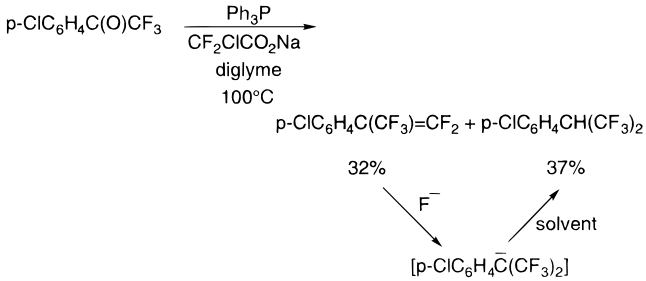
R = Ph, p-$CH_3C_6H_4$ R', = Bu, octyl 43-64%

Although nonactivated ketones did not produce 1,1-difluoroolefins under the initial Fuqua conditions, Herkes found that activated ketones readily reacted under these conditions to give good to excellent yields of the difluoromethylene olefins (eq 10).[12,16]

$$Ph_3P + PhC(O)CF_3 \xrightarrow[CF_2ClCO_2Na\ 150°C]{\text{diglyme}} PhC(CF_3){=}CF_2 + NaCl + CO_2 + Ph_3PO\ (59\%) \quad (10)$$

Cyclohexyl trifluoromethyl and trifluoromethyl benzyl ketones also gave good yields of 1,1-difluoroolefins under these conditions. However, when the aromatic ring contained a good carbanion stabilizing substituent (Cl, Br, or $NO_2$), the initially formed difluoroolefin subsequently added the elements of "HF" to give a saturated product (Scheme 5).[11,12] With Br and $NO_2$ substituents, only the saturated product was formed. The saturated product presumably arises by attack of fluoride ion (formed either by decomposition of the ylide or in decarboxylation of $CF_2ClCO_2Na$) on the difluoromethylene carbon of the initially formed olefin to generate the benzylic fluorinated carbanion which subsequently abstracts a proton from the solvent. As expected, good carbanion stabilizing groups on the aryl ring facilitates carbanion formation. Addition of potassium fluoride and water (or $D_2O$) to a crude ylide reaction mixture gives good yields of the saturated products.[17]

**Scheme 5**




Fluoride ion is also a problem for ketones containing perfluoroalkyl groups of more than one carbon atom. For example, pentafluoroethyl phenyl ketone gave a mixture of 2-phenylheptafluorobut-1-ene and the isomeric internal olefins (eq 11).[12,16] The amount

$$PhC(O)C_2F_5 \xrightarrow[CF_2ClCO_2Na\ diglyme\ 100°C]{Ph_3P} PhC(C_2F_5){=}CF_2 + PhC(CF_3){=}CFCF_3\ (cis/trans) \quad (11)$$

of the internal olefins increased with reaction time and with increased amount of sodium chlorodifluoroacetate.[18,19] This fluoride ion isomerization mechanism has been studied in detail, and the reader is referred to the original work.[20]

Fluoride ion addition to substituted trifluoroacetophenones and ketones containing perfluoroalkyl groups of more than one carbon atom could be avoided by replacement of sodium chlorodifluoroacetate in diglyme with lithium chlorodifluoroacetate in dimethylformamide (DMF) (eqs 12 and 13).[18,19]

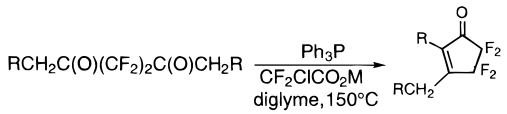
$$p\text{-}ClC_6H_4C(O)CF_3 \xrightarrow[CF_2ClCO_2Li\ DMF\ 90°C]{Ph_3P} p\text{-}ClC_6H_4C(CF_3){=}CF_2\ (67\%) \quad (12)$$

$$PhC(O)C_2F_5 \xrightarrow[CF_2ClCO_2Li\ DMF\ 90°C]{Ph_3P} PhC(C_2F_5){=}CF_2\ (48\%) \quad (13)$$

Lithium fluoride is less dissociated than the other alkali metal fluorides and eliminates the formation of saturated or isomerized products.

Attempts to extend the halodifluoroacetate methodology to the synthesis of dienes has met with little

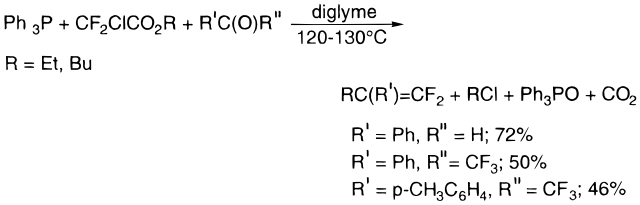
success. Either low yields of dienes were obtained or the diketone cyclized (eq 14).[21]



$$RCH_2C(O)(CF_2)_2C(O)CH_2R \xrightarrow[CF_2ClCO_2M,\ \text{diglyme, 150°C}]{Ph_3P} \text{cyclopentenone}(R, RCH_2, F_2, F_2, O) \qquad (14)$$

The halodifluoroacetate methodology works well for a variety of aldehydes and ketones. One of the tedious experimental problems is the necessity to obtain the anhydrous salt. Herkes minimized the amount of water formed in the neutralization of chlorodifluoroacetic acid by the use of sodium or lithium carbonate in ether.[12] However, the removal of even the stoichiometric amount of water is tedious and time consuming. Zawistowski[22] developed a modification which replaces the halodifluoroacetate salt with an alkylchlorodifluoroacetate, thus avoiding the drying procedure (Scheme 6). This modification

**Scheme 6**



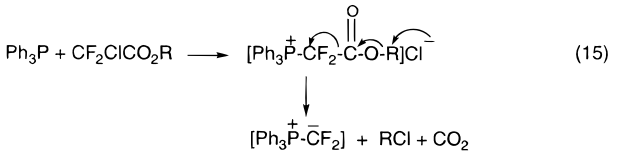
$$Ph_3P + CF_2ClCO_2R + R'C(O)R'' \xrightarrow[120\text{-}130°C]{\text{diglyme}}$$

R = Et, Bu

$$RC(R')=CF_2 + RCl + Ph_3PO + CO_2$$

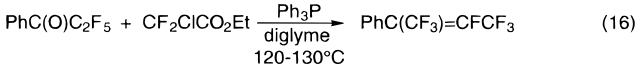
R' = Ph, R'' = H; 72%
R' = Ph, R'' = $CF_3$; 50%
R' = p-$CH_3C_6H_4$, R'' = $CF_3$; 46%

gives comparable yields of 1,1-difluoroolefins with aldehydes and trifluoromethyl ketones. Presumably the mechanism involves *in situ* formation of an ylide intermediate similar to the halodifluoroacetate salt method (eq 15). Of course, this modification does not eliminate the fluoride ion problem (eq 16).



$$Ph_3P + CF_2ClCO_2R \longrightarrow [Ph_3\overset{+}{P}\text{-}CF_2\text{-}C(=O)\text{-}O\text{-}R]Cl^- \qquad (15)$$

$$[Ph_3\overset{+}{P}\text{-}\bar{C}F_2] + RCl + CO_2$$



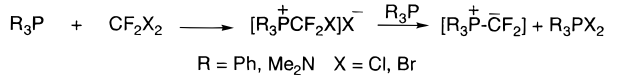
$$PhC(O)C_2F_5 + CF_2ClCO_2Et \xrightarrow[\text{diglyme}]{Ph_3P} PhC(CF_3)=CFCF_3 \qquad (16)$$
$$120\text{-}130°C$$

### *1.3. Difluoromethylene Ylides (Dihalodifluoromethane Approach)*

As noted in the previous section, the reaction of sodium chlorodifluoroacetate and either triphenylphosphine or tributylphosphine with aldehydes and ketones has been demonstrated to be a general method for the preparation of 1,1-difluoroolefins. One shortcoming of this method was the generally low yield from nonactivated ketones. The extension to polyfluorinated ketones showed that many $\beta$-substituted olefins could be synthesized in excellent yield. The formation of fluoride ion caused two problems: (a) isomerization of olefins with perfluoroalkyl groups with more than one carbon atom to internal isomers, and (b) addition of hydrogen fluoride occurred with olefins which contained a good carbanion stabilizing group.

Therefore, an alternative method which avoided the above limitations was developed. This method consists of the reaction of 2 equiv of a tertiary phosphine with 1 equiv of a dihalodifluoromethane. The initially formed (halodifluoromethyl)phosphonium salt is dehalogenated by the second equivalent of tertiary phosphine to give the difluoromethylene ylide (Scheme 7).

**Scheme 7**

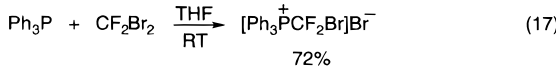


$$R_3P + CF_2X_2 \longrightarrow [R_3\overset{+}{P}CF_2X]X^- \xrightarrow{R_3P} [R_3\overset{+}{P}\text{-}\bar{C}F_2] + R_3PX_2$$

R = Ph, $Me_2N$ X = Cl, Br

The initial report of the reaction of either dibromodifluoromethane or dichlorodifluoromethane with triphenylphosphine and benzaldehyde to form a 1,1-difluoroolefin was described by Rabinowitz.[23,24] The product was not isolated but assigned either on the basis of GLPC retention or mass spectrometry. The detailed work of Naae provided the useful methodology for this approach and provided mechanistic details of the overall process.[25]

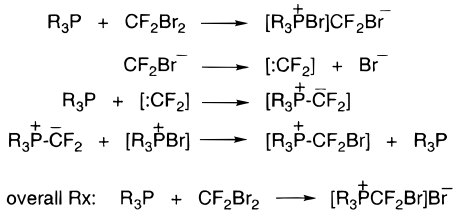
The preparation of the (bromodifluoromethyl)triphenylphosphonium bromide was readily accomplished by reaction of triphenylphosphine and $CF_2Br_2$ in THF.[3,25] The salt precipitated and could be isolated as a pale yellow solid via filtration in a fritted Schlenk funnel (eq 17).[3,25] Similar salts were pre-



$$Ph_3P + CF_2Br_2 \xrightarrow[RT]{THF} [Ph_3\overset{+}{P}CF_2Br]Br^- \qquad (17)$$
$$72\%$$

pared from tris-*p*-tolylphosphine (60%), tris(dimethylamino)phosphine (65%), and tris(diethylamino)phosphine (54%).[25] Mechanistic studies suggest that the phosphonium salts are *not* formed by an $S_N2$ process but involve difluorocarbene as an intermediate (Scheme 8).[3]

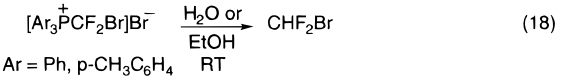
**Scheme 8**



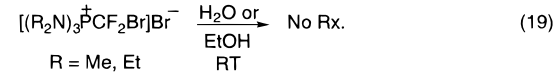
$$R_3P + CF_2Br_2 \longrightarrow [R_3\overset{+}{P}Br]CF_2Br^-$$
$$CF_2Br^- \longrightarrow [:CF_2] + Br^-$$
$$R_3P + [:CF_2] \longrightarrow [R_3\overset{+}{P}\text{-}\bar{C}F_2]$$
$$R_3\overset{+}{P}\text{-}\bar{C}F_2 + [R_3\overset{+}{P}Br] \longrightarrow [R_3\overset{+}{P}\text{-}CF_2Br] + R_3P$$

overall Rx: $R_3P + CF_2Br_2 \longrightarrow [R_3\overset{+}{P}CF_2Br]Br^-$

The triarylphosphonium salts were readily hydrolyzed by water or ethanol, whereas the tris(dialkylamino)phosphonium salts were stable to water and ethanol (eqs 18 and 19).[3,25]



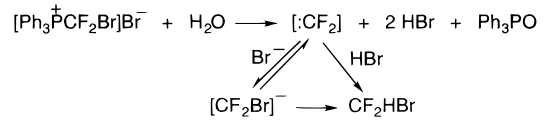
$$[Ar_3\overset{+}{P}CF_2Br]Br^- \xrightarrow[EtOH,\ RT]{H_2O\ or} CHF_2Br \qquad (18)$$
Ar = Ph, p-$CH_3C_6H_4$



$$[(R_2N)_3\overset{+}{P}CF_2Br]Br^- \xrightarrow[EtOH,\ RT]{H_2O\ or} \text{No Rx.} \qquad (19)$$
R = Me, Et

Mechanistic studies have unequivocally established that the hydrolysis of (bromodifluoromethyl)triphenylphosphonium bromide proceeds through a difluorocarbene intermediate (Scheme 9).[26]

**Scheme 9**



$$[Ph_3\overset{+}{P}CF_2Br]Br^- + H_2O \longrightarrow [:CF_2] + 2\,HBr + Ph_3PO$$
$$Br^- \quad HBr$$
$$[CF_2Br]^- \longrightarrow CF_2HBr$$

When tributylphosphine is employed in this transformation, either a (halodifluoromethyl)tributylphosphonium salt or a bis-phosphonium salt could be formed.[3,27] Thus, when $Bu_3P$ is slowly added to a stirred solution of $CF_2BrCl$ in triglyme, a 50:50 mixture of monophosphonium salts is obtained (eq 20).[27]

$$CF_2BrCl \xrightarrow[\text{triglyme}]{Bu_3P} [Bu_3\overset{+}{P}CF_2Br]Cl^- + [Bu_3\overset{+}{P}CF_2Cl]Br^- \quad (20)$$
$$1 : 1$$

However, if the bromochlorodifluoromethane is slowly added to a stirred solution of tributylphosphine in triglyme, so that the phosphine is always in excess, the bis-phosphonium salt is formed (eq 21).[3,27] Similar bis-phosphonium salts are formed

$$Bu_3P \xrightarrow[\text{triglyme}]{CF_2BrCl} [Bu_3\overset{+}{P}CF_2\overset{+}{P}Bu_3]Br^-,Cl^- \quad (21)$$
$$77\%$$

from $CF_2Br_2$ (71%) and $CF_2BrI$ (69%).[27] Triethylphosphine similarly gave a 40% yield of the analogous bis-phosphonium salt.[27] Dichlorodifluoromethane was inert even at elevated temperature. The bis-phosphonium salts could also be prepared via reaction of the monophosphonium salt with a second equivalent of a tertiary phosphine (eq 22).[27] The

$$[Bu_3\overset{+}{P}CF_2Br]Br^- + Bu_3P \longrightarrow [Bu_3\overset{+}{P}CF_2\overset{+}{P}Bu_3]2\,Br^- \quad (22)$$
$$86\%$$

trialkylphosphonium salts are intermediate in reactivity toward hydrolysis; they are hydrolyzed by water but not by alcohol.[27] Recent reports[28,29] replicate and extend the work of Naae,[25] Kesling,[27] Van Hamme,[30] Vander Haar,[31] and Cox.[32]

For the preparation of 1,1-difluoroolefins it is not necessary to prepare and isolate the intermediate (halodifluoromethyl)phosphonium salt. Salt formation and subsequent dehalogenation of the salt can both be accomplished in a one-step sequence, and the intermediate ylide captured *in situ* (eq 23).[33] With

$$2\,Ph_3P + CF_2Br_2 + m\text{-}BrC_6H_4C(O)CF_3 \xrightarrow[70°C]{\text{diglyme}} m\text{-}BrC_6H_4C(CF_3)=CF_2 \quad (23)$$
$$83\%$$

aliphatic and aromatic aldehydes and trifluoromethyl (activated) ketones, good yields of 1,1-difluoroolefins were obtained. Significantly, with ketones, such as *p*-chloro- and *m*-bromotrifluoroacetophenone, *only* the 1,1-difluoroolefins were obtained; *no* HF addition product was detected.[33] Similarly, with pentafluoropropiophenone *only* the 1,1-difluoroolefin was obtained; *no* isomerized (internal) olefins were detected (eq 24).[33] Thus, the problems associated with fluoride

$$PhC(O)C_2F_5 \xrightarrow[\substack{CF_2Br_2\\ \text{triglyme}\\ 70°C}]{Ph_3P} PhC(C_2F_5)=CF_2 \quad (24)$$
$$82\%$$

ion formation in the halodifluoroacetate method were *not* observed in the $Ph_3P/CF_2Br_2$ method, and this route is the clear choice for the preparation of 1,1-difluoroolefins from aliphatic and aromatic aldehydes and activated ketones. The methodology does have a few limitations: (*a*) nonactivated ketones, such as acetophenone, gave low yields (2%); and (*b*) aldehydes or ketones containing the pentafluoroaryl group, such as pentafluorobenzaldehyde (20%), gave low yields of olefin due to reaction of the pentafluoroaryl substrate with triphenylphosphine.[25,27]

Limitation *a* above is easily circumvented by replacement of triphenylphosphine with tris(dimethylamino)phosphine. Thus, when tris(dimethylamino)phosphine, dibromodifluoromethane, and nonactivated ketones are reacted in triglyme at room temperature, good yields of 1,1-difluoroolefins were obtained (eq 25).[34] The more nucleophilic $[(Me_2N)_3P^+-^-$

$$PhC(O)C_2H_5 + (Me_2N)_3P + CF_2Br_2 \xrightarrow[RT]{\text{triglyme}} PhC(C_2H_5)=CF_2 \quad (25)$$
$$82\%$$

$CF_2]$ intermediate reacts with the nonactivated ketones, whereas the less nucleophilic ylide reacts only with aldehydes and activated ketones.[3]

The $R_3P/CF_2Br_2$ reactions are rapid, relatively free of side reactions, and give good to excellent yields of 1,1-difluoroolefins. In addition, reaction of tris(dimethylamino)phosphine and dibromodifluoromethane in triglyme generates a stable olefination solution.[34] When aliquots of this solution were reacted with acetophenone, 68−75% yields of $PhC(CH_3)=CF_2$ were obtained.[25,35] Filtration of the olefination solution gave a 90% yield of $[(Me_2N)_3P^+CF_2Br]Br^-$.[25,35] When the filtrates were treated with methyl iodide, a quantitative yield of $[(Me_2N)_3P^+CH_3]I^-$ was obtained. These results suggest that dehalogenation of the (bromodifluoromethyl)phosphonium salt is reversible and the equilibrium lies far to the left side (eq 26).[25,35] A similar equi-

$$[(Me_2N)_3\overset{+}{P}CF_2Br]Br^- + (Me_2N)_3P \rightleftharpoons [(Me_2N)_3\overset{+}{P}\text{-}\bar{C}F_2] + (Me_2N)_3PBr_2 \quad (26)$$

librium was found in the reaction of triphenylphosphine and (bromodifluoromethyl)triphenylphosphonium bromide (eq 27).[27,35] For example, when 2.5

$$[Ph_3\overset{+}{P}CF_2Br]Br^- + Ph_3P \rightleftharpoons [Ph_3\overset{+}{P}\text{-}\bar{C}F_2] + Ph_3PBr_2 \quad (27)$$

equiv of triphenylphosphine and 1 equiv of $CF_2Br_2$ were reacted in triglyme at 70 °C, the heavy precipitate formed was isolated by filtration and shown to be $[Ph_3P^+CF_2Br]Br^-$ (98%) by $^{19}F$ NMR and melting point. The excess triphenylphosphine in the filtrate was reacted with methyl iodide to give methyltriphenylphosphonium iodide (85%). Where the olefination solution was reacted with trifluoroacetophenone, 74% of $PhC(CF_3)=CF_2$ was formed.[35] These results again are best accommodated via an equilibrium reaction that lies far to the left side. Since $[Ph_3P^+CF_2Br]Br^-$ is not very soluble in triglyme and to rule out a possible solvent effect, the reaction of the phosphonium salt and $Ph_3P$ was carried out in acetonitrile (homogeneous solution). After 6 h at reflux, $^{19}F$ NMR analysis showed only the presence of $[Ph_3P^+CF_2Br]Br^-$. Addition of trifluoroacetophenone gave 53% $PhC(CF_3)=CF_2$ after 6 h at 75−80 °C and 77% after 24 h. Thus, even in a homogeneous solution the equilibrium lies to the left.[35]

The mechanism of this equilibrium reaction has been demonstrated to proceed via dissociation of the

intermediate difluoromethylene ylide. Naae first observed a facile exchange process when the tertiary phosphine utilized for dehalogenation of the phosphonium salt was different than the tertiary phosphine used to prepare the salt (eqs 28 and 29).[25] The

$$[Ph_3\overset{+}{P}CF_2Br]Br^- + (p\text{-}CH_3C_6H_4)_3P \xrightarrow[70°C,\ 48\ h]{\text{triglyme}} Ph_3P + [(p\text{-}CH_3C_6H_4)_3\overset{+}{P}CF_2Br]Br^- \quad (28)$$

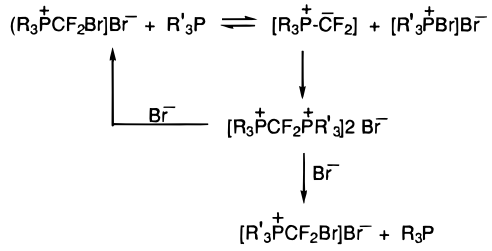
7% 93%

$$[(Me_2N)_3\overset{+}{P}CF_2Br]Br^- + (Et_2N)_3P \xrightarrow[70°C]{\text{triglyme}} [(Et_2N)_3\overset{+}{P}CF_2Br]Br^- + (Me_2N)_3P \quad (29)$$

50% 50%

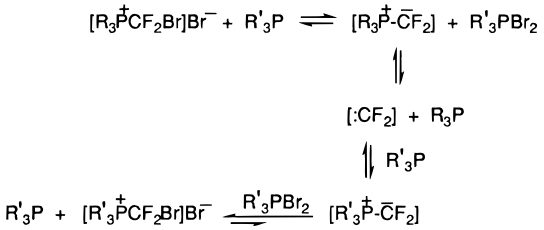
exchange mechanism could be rationalized by two mechanistic pathways: (1) bis-phosphonium salt formation followed by cleavage of the bis-phosphonium salt by halide ion (Scheme 10); alternatively,

**Scheme 10**



(2) dissociation of the intermediate ylide to give difluorocarbene which could scramble between the two available tertiary phosphines (Scheme 11).

**Scheme 11**



When an equimolar amount of $[Ph_3P^+CF_2Br]Br^-$ and $Ph_3P$ is heated (reflux) in an excess of tetramethylethylene (TME), a 35% yield of 1,1-difluoro-2,2,3,3-tetramethylcyclopropane was formed. When $[Ph_3P^+CF_2Br]Br^-$ is heated in TME under the same conditions in the absence of $Ph_3P$, no cyclopropane was detected either by GLPC or NMR. In addition, bis-phosphonium salts, such as $[Et_3P^+CF_2P^+Bu_3]2Br^-$ do *not* undergo exchange with bromide ion to form either (bromodifluoromethyl)phosphonium salts or difluoromethylene ylide.[27] Therefore mechanism 2 best accommodates the exchange reaction.

It is important to consider the equilibrium processes noted above when designing this type of Wittig reaction since some polyfluorinated ketones and olefins react with tertiary phosphines. Thus, the low yield obtained in the reaction of pentafluorobenzaldehyde (20%) with $Ph_3P/CF_2Br_2$ is due to the rapid and destructive reaction of this aldehyde with $Ph_3P$. Similarly, the low yield (25%) of olefin from PhC(O)-$CF_3$ and $(Me_2N)_3P/CF_2Br_2$ is due to the rapid reaction of this ketone with $(Me_2N)_3P$.[9]

### *1.4. Difluoromethylene Ylides (From Bis-phosphonium Salts)*

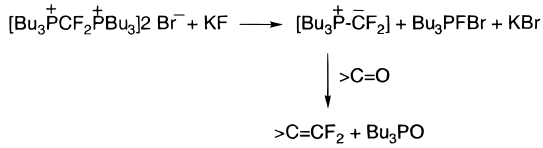
As noted in the previous section, bis-phosphonium salts are readily prepared via reaction of trialkylphosphines with dihalodifluoromethanes (eq 21).[3,27] Kesling utilized such bis-salts to generate $[Bu_3P^+-^-CF_2]$ which was captured *in situ* with aldehydes and activated ketones (eq 30).[27] Benzaldehyde (62%),

$$[Bu_3\overset{+}{P}CF_2\overset{+}{P}Bu_3]2\,Br^- + KF\ (\text{or NaOAc}) + PhC(O)CF_3 \xrightarrow[80°C,\ 24\ h]{\text{triglyme}} PhC(CF_3)=CF_2 \quad (30)$$

96%

trifluoromethyl benzyl ketone (68%), (chlorodifluoromethyl)acetophenone (34%), (pentafluoroethyl)propiophenone (54%) were successfully converted to 1,1-difluoroolefins via this alternative approach.[27] Unactivated ketones, such as acetophenone (5%), gave poor yields of olefins. The reaction presumably occurs as outlined in Scheme 12.[27]

**Scheme 12**



### *1.5. Difluoromethylene Ylides (Metal-Assisted Approach)*

As indicated in section 1.3, perfluorinated ketones, such as hexafluoroacetone, and aldehydes or ketones containing the pentafluoroaryl group reacted with tertiary phosphines and gave low yields in the $R_3P/CF_2Br_2$ reaction. An alternative methodology which resolved this problem was developed by Naae and Kesling,[37] who employed metal dehalogenation of (bromodifluoromethyl)phosphonium salts to generate the intermediate ylide (eq 31). This alternative

$$[R_3\overset{+}{P}CF_2Br]Br^- + M\ (\text{Metal}) \longrightarrow [R_3\overset{+}{P}\text{-}\bar{C}F_2] + MBr_2 \quad (31)$$

methodology avoids competitive or destructive side reactions of the carbonyl substrates or products of the reaction with the second equivalent of the tertiary phosphine. Some typical examples which illustrate the utility of this approach are illustrated below (eqs 32−34).[37]

$$C_6F_5CHO + [Ph_3\overset{+}{P}CF_2Br]Br^- \xrightarrow[\text{triglyme, RT}]{\text{Zn}} C_6F_5CH=CF_2 \quad (32)$$

54%

$$C_6F_5C(O)CF_3 + [Ph_3\overset{+}{P}CF_2Br]Br^- \xrightarrow[\text{triglyme, RT}]{\text{Cd}} C_6F_5C(CF_3)=CF_2 \quad (33)$$

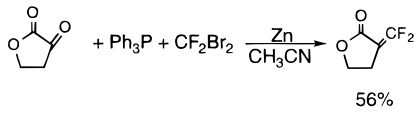
75%

$$PhC(O)CF_2Cl + [Ph_3\overset{+}{P}CF_2Br]Br^- \xrightarrow[\text{triglyme, RT}]{\text{Cd}} PhC(CF_2Cl)=CF_2 \quad (34)$$

76%

A variety of metals can be used in the dehalogenation step; zinc, cadmium, mercury, and aluminum gave the best results.[25,27,37]

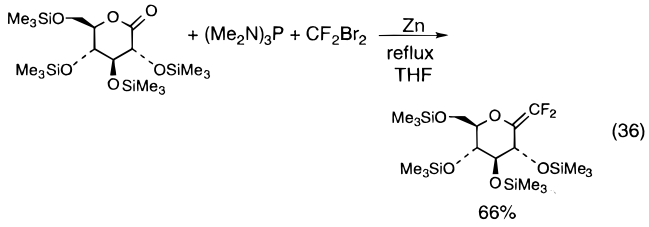
Lactone derivatives were readily converted to 1,1-difluoroolefin derivatives via this alternative methodology. Thus, when 4,4-dimethyloxolane-2,3-dione was reacted with triphenylphosphine, dibromodifluoromethane, and zinc, only the ketone group reacted (eq 35),[38] whereas in the analogous dichloro-




(35)

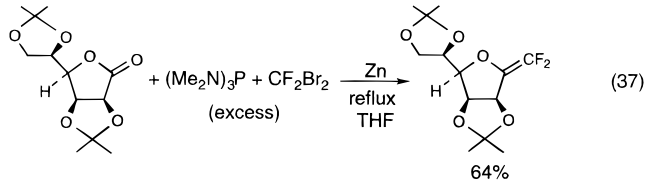
and dibromomethylenation of this compound by triphenylphosphine and $CCl_4$ or $CBr_4$ both carbonyl groups participated and two dihalomethylene lactones were isolated.[39]

Although a recent delusive statement indicated that this approach gave low yields and complications with functionalized carbonyl substrates,[40] Motherwell has demonstrated that carbohydrate lactones gave good yields of the difluoromethylated product (eq 36).[41] This relatively unreactive $\delta$-lactone derivative




(36)

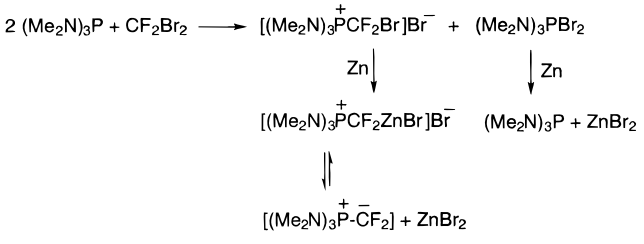
also indicates that the readily removed silyl ether protecting group is tolerated in these reactions. Similarly, isopropylidene groups are readily accommodated in this transformation (eq 37).



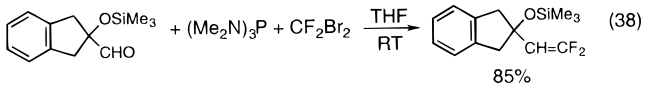

(37)

A recent elegant modification by Motherwell used catalytic (10%) amounts of $(Me_2N)_3P$ for the second step in the reaction.[42] The zinc was employed to reduce the *in situ* formed tris(dimethylamino)phosphine dibromide to tris(dimethylamino)phosphine (Scheme 13). The yields of the reaction were found to be less variable and side products formed from bromide ion in solution were minimized.

**Scheme 13**




The silyl ether protecting group is tolerated even when the dihalophosphorane byproduct is formed in the reaction enabling Ortiz de Montellano to convert trimethylsilylated α-hydroxy aldehydes to protected 1,1-difluoro-1-alken-3-ols (eq 38).[43]

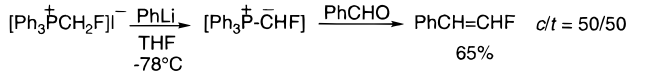



(38)

## 2. Preparation of Fluoromethylene Ylides

### *2.1. Fluoromethylene Ylides (Phosphonium Salt + Base Approach)*

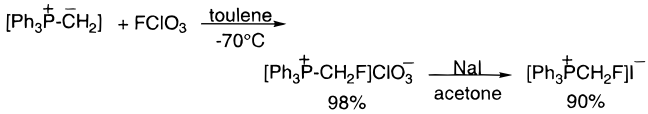
The first successful preparation and capture of a fluoromethylene ylide was reported by Schlosser in 1969 (eq 39).[44] The requisite phosphonium salt was




(39)

prepared via fluorination of the methylenetriphenylphosphonium ylide with perchloryl fluoride followed by an exchange of anions (Scheme 14). The capricious nature of perchloryl fluoride has discouraged the preparation of (fluoromethyl)triphenylphosphonium iodide via this route although the yields are excellent. The yields of the fluoromethylene olefins are modest, and the *cis*/*trans* ratios are approximately 1:1.

**Scheme 14**

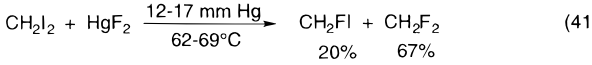



Greenlimb prepared the same salt via reaction of triphenylphosphine with fluoroiodomethane (eq 40).[45]




(40)

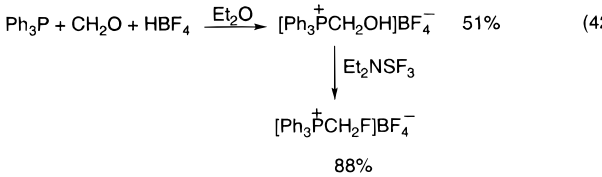
The fluoroiodomethane was prepared by reaction of methylene iodide with mercuric fluoride under reduced pressure (eq 41). The main product of the




(41)

fluorination is methylene fluoride. Thus, the use of perchloryl fluoride is avoided, but the overall two-step yield of the phosphonium salt is low.

Later work by Wiemers[46] provided two routes to a more useful phosphonium salt precursor in high yield from readily available precursors. In route 1 (eq 42)

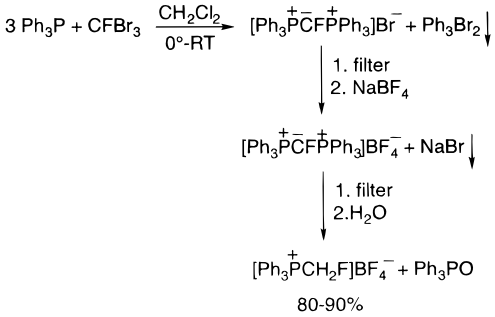



(42)

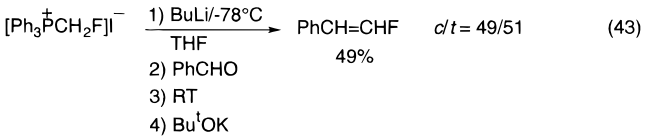
(hydroxymethyl)triphenylphosphonium tetrafluoroborate is prepared from triphenylphosphine, paraformaldehyde, and fluoroboric acid. Subsequent reaction of the tetrafluoroborate salt with DAST gave the (fluoromethyl)phosphonium salt. This work is readily scaled up to give useful preparative amounts of the

phosphonium salt precursor. In route 2 (Scheme 15) hydrolysis of the phosphoranium salt prepared from triphenylphosphine and fluorotribromomethane gives the same salt after anion exchange with sodium tetrafluoroborate.

**Scheme 15**




Greenlimb generated the fluoromethylene ylide from reaction of the fluoromethyl phosphonium salt with either BuLi or lithium diisopropylamide (eq 43).[45] Subsequent addition of the carbonyl substrate




(43)

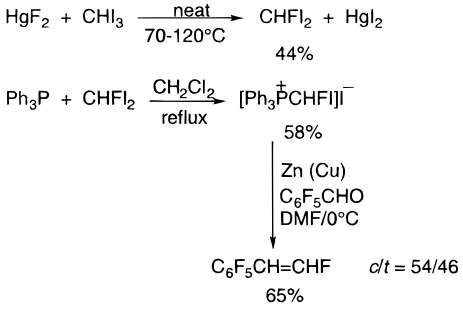
followed by warming to room temperature did not result in complete collapse of the Wittig intermediate (presumably due to a stable complex with lithium salts), and addition of potassium *tert*-butoxide was necessary to provide the fluoromethylene olefins in fair to good yields.[45]

Like the Schlosser report, the *cis*:*trans* ratios are close to unity. In addition to the fluoromethylene olefin product significant formation (14−23%) of *n*-butyl derivatives of the product olefin, such as PhCH=CHBu, were also formed.

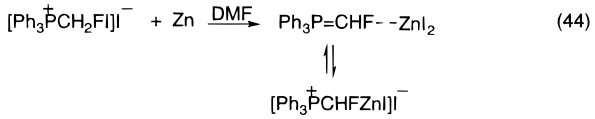
### *2.2. Fluoromethylene Ylides (Metal Dehalogenation Approach)*

To avoid the difficulties associated with the preparation of the phosphonium iodide precursor, the problem of betaine or oxaphosphetane collapse (Wittig intermediate), and the formation of butyl-substituted products, Greenlimb developed an alternative methodology similar to the methodology described in section 1.5 above. This route involved the preparation of (fluoroiodomethyl)triphenylphosphonium iodide (two steps) followed by dehalogenation of this salt with zinc−copper couple (Scheme 16).[47,48] Tris-

**Scheme 16**




(dimethylamino)phosphine was totally ineffective as a dehalogenation agent for this phosphonium salt.[47] This route worked reasonably well with aldehydes and activated ketones. Unactivated ketones, such as acetophenone, gave poor yields (12%) compared to the route from $[Ph_3PCH_2F]I^-$/BuLi (49%) suggesting that the intermediate in the dehalogenation route was less active (presumably due to complexation of the ylide with zinc iodide (eq 44).[47] This route is milder, easier

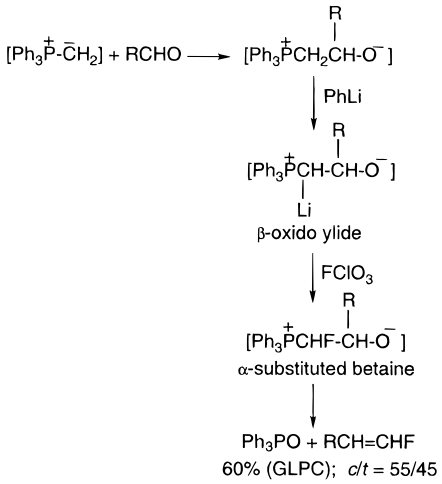



(44)

to carry out experimentally, and gives higher yields for aldehydes and activated ketones relative to the previous routes.

Schlosser has also prepared 1-fluoroolefins via fluorination of $\beta$-oxido ylides with $FClO_3$ (Scheme 17).[49] Similar reaction with PhCH=CHCHO (25%), $PhCH(CH_3)CHO$ (37%, >98% *cis*) gave 1-fluoroolefins or dienes.[49] The modest yields and the use of $FClO_3$ has limited this approach.

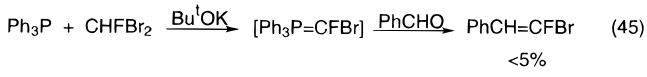
**Scheme 17**




## 3. Preparation of Bromofluoromethylene Ylides

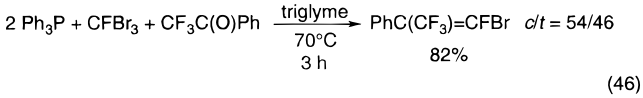
### *3.1. Bromofluoromethylene Ylides (Fluorotribromomethane Approach)*

Initial attempts at generation and capture of fluorobromocarbene with triphenylphosphine followed by Wittig reaction of the resultant ylide (eq 45) gave very




(45)

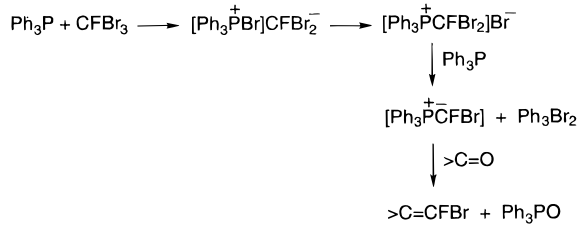
low yields of bromofluoromethylene olefins.[50] A more useful approach was developed by Vander Haar via a one-pot reaction utilizing triphenylphosphine, fluorotribromomethane, and the appropriate carbonyl substrate in glyme solvents at 70 °C (eq 46).[31,51]




(46)

Other activated ketones, $PhC(O)CF_2Cl$ (72%), $PhC(O)C_2F_5$ (65%), and aromatic aldehydes PhCHO (64%),

**Scheme 18**



gave good yields of bromofluoromethylene olefins under these conditions. Unactivated ketones, acetophenone (18%), and aliphatic aldehydes, heptanal (28%), gave lower yields of olefins.[31,51]

The mechanism of this transformation is similar to other tetrahalomethanes (except $CF_2X_2$) (Scheme 18).[3,31] The (fluorodibromomethyl)triphenylphosphonium bromide is readily hydrolyzed by water (eq 47) and ethanol, and mechanistic experiments prove

$$Ph_3P + CFBr_3 \xrightarrow{THF} \underset{85\text{-}95\%}{[Ph_3\overset{+}{P}CFBr_2]Br^-} \quad (47)$$

$$[Ph_3\overset{+}{P}CFBr_2]Br^- \xrightarrow{H_2O} \underset{95\%}{Ph_3PO} + \underset{99\%}{CHFBr_2} + HBr$$

that the hydrolysis proceeds via the fluorodibromomethide ion and not via fluorobromocarbene.[52] The analogous phosphonium salt from tris(dimethylamino)phosphine was similarly prepared but efforts to remove remaining $CFBr_3$ from the salt were unsuccessful (eq 48).[31] Similar to the (bromodifluoromethyl)phosphonium salts, the tris(dimethylamino) derivative is stable to both water and ethanol.[31]

$$(Me_2N)_3P + CFBr_3 \xrightarrow{THF} \underset{>70\%}{[(Me_2N)_3\overset{+}{P}CFBr_2]Br^-} \quad (48)$$

Bromofluoromethylene olefins could also be prepared starting from (fluorodibromomethyl)triphenylphosphonium bromide (eq 49).[31] Benzaldehyde

$$[Ph_3\overset{+}{P}CFBr_2]Br^- + PhC(O)CF_3 \xrightarrow[THF,\ 70°C]{Ph_3P} \underset{85\%}{PhC(CF_3)=CFBr} \quad (49)$$

(70%) and acetophenone (45%) gave slightly higher yields via this route. This route is most useful where solvents other than glymes or THF are necessary (eq 50) or excess tertiary phosphine is to be avoided.

$$[Ph_3\overset{+}{P}CFBr_2]Br^- + (CF_3)_2CO \xrightarrow[CH_3CN,\ RT]{Ph_3P} \underset{80\%}{(CF_3)_2C=CFBr} \quad (50)$$

### *3.2. Bromofluoromethylene Ylides (Metal Dehalogenation Approach)*

Similar to methodology described in sections 1.5 and 2.2 above, (fluorodibromomethyl)triphenylphosphonium salts can be dehalogenated with metals, such as zinc, zinc−copper couple, mercury, and cadmium, in the presence of aldehydes and ketones to give bromofluoromethylene olefins (eq 51).[31] This

$$[Ph_3\overset{+}{P}CFBr_2]Br^- + PhC(O)C_2H_5 \xrightarrow[TG,\ RT]{Zn} \underset{65\%}{PhC(C_2H_5)=CFBr} \quad c/t = 51/49 \quad (51)$$

approach is synthetically preferrable for the preparation of bromofluoromethylene olefins from nonactivated substrates or when glymes or THF are not suitable solvents, $(C_3F_7)_2CO$ in $Et_2O$.

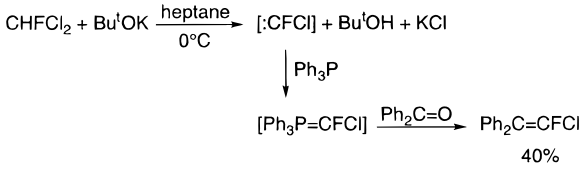
Since bromofluoromethylene olefins are useful precursors for metalation reactions, coupling with organometallic reagents or conversion to organometallic reagents, a stereospecific route to these olefins would be extremely useful. Unfortunately, the described ylide routes give *cis*:*trans* ratios close to unity and future utility of these olefins awaits advances in the stereospecificity of these approaches.

## 4. Preparation of Chlorofluoromethylene Ylides

### *4.1. Chlorofluoromethylene Ylides (Chlorofluorocarbene Approach)*

The first report of the generation and capture of a chlorofluoromethylene ylide was by Speziale and Ratts in 1962.[6] The ylide was produced by capture of chlorofluorocarbene by triphenylphosphine as illustrated in Scheme 19. Substitution of tributylphosphine for triphenylphosphine appeared (yellow color) to give the corresponding ylide; however, addition of benzophenone gave no olefin.[6]

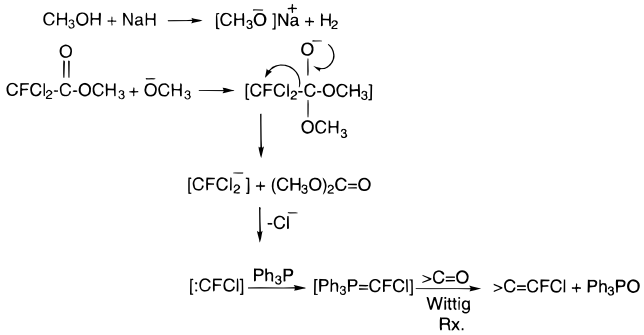
**Scheme 19**



Subsequent work by Ando provided a useful route to chlorofluoromethylene olefins via an ylide route.[53] These workers generated chlorofluorocarbene from methyl dichlorofluoroacetate in the presence of triphenylphosphine as outlined in eq 52. Aromatic aldehydes and activated ketones gave higher yields than nonactivated ketones. The mechanism of this transformation is outlined in Scheme 20. The intermediate ylide (pregenerated) is sufficiently stable to provide modest yields of the chlorofluoromethylene olefins.

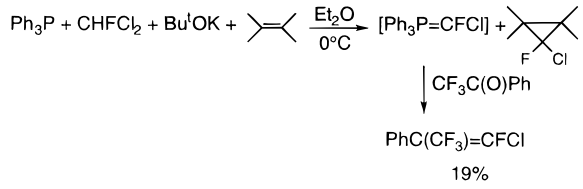
$$CFCl_2CO_2CH_3 + CH_3OH \xrightarrow[Ph_3P,\ Pet.\ Ether,\ 25\text{-}30°C]{NaH} [Ph_3P{=}CFCl] \xrightarrow[60\text{-}80°C]{>C=O} \underset{8\text{-}63\%}{>C=CFCl} \quad (52)$$

**Scheme 20**



In later work, Krutzsch pregenerated the same ylide in the presence of tetramethylethylene via the Speziale method (Scheme 21).[54,55] Subsequent addition of trifluoroacetophenone gave *both* the chloro-

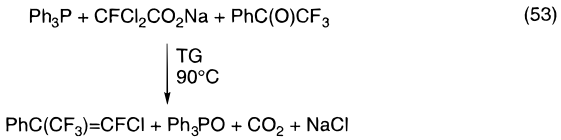
**Scheme 21**




fluoromethylene olefin and the chlorofluorocyclopropane derivative after workup. This experiment indicated that under these conditions the olefin was competitive with triphenylphosphine in trapping the chlorofluorocarbene intermediate.[50,55]

### *4.2. Chlorofluoromethylene Ylides (Dihalofluoroacetate Approach)*

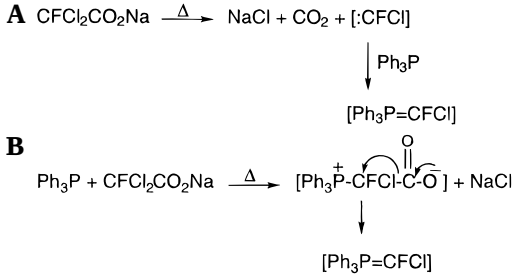
Coincident with the Ando work, Krutzsch reported the preparation of chlorofluoromethylene olefins from sodium dichlorofluoroacetate (eq 53).[54,55] Similar to



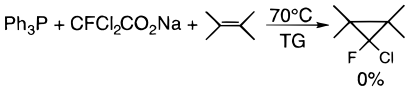

(53)

other mixed fluoromethylene ylides, *cis*:*trans* ratios of the chlorofluoromethylene ylides were close to unity. Yields with a variety of trifluoromethyl ketones and aromatic aldehydes were 29−70%. Benzophenone and cyclopentanone give low yields of olefins. Several mechanisms can be proposed to explain the formation of the chlorofluoromethylene ylide via this approach (Scheme 22). Mechanism A

**Scheme 22. Mechanisms A and B**




involves prior formation of chlorofluorocarbene followed by capture with the tertiary phosphine. In mechanism B, triphenylphosphine reacts with sodium dichlorofluoroacetate to form a phosphobetaine salt, which loses carbon dioxide to form the chlorofluoromethylene ylide. In mechanism B, *no* free carbene is involved. To delineate between these two mechanistic pathways, Krutzsch[50,55] reacted sodium dichlorofluoroacetate, triphenylphosphine, and tetramethylethylene in triglyme at 70 °C (eq 54). *No*

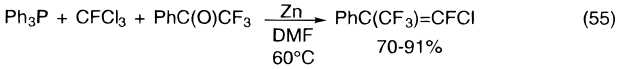



(54)

cyclopropane was detected. Earlier work (cf. section 4.1) had demonstrated that TME and $Ph_3P$ were competitive in trapping chlorofluorocarbene.[50,55] The absence of cyclopropane product (eq 54) suggests that the phosphobetaine salt is the intermediate in the formation of the chlorofluoromethylene ylide via the halodifluoroacetate method.

### *4.3. Chlorofluoromethylene Ylides (Fluorotrichloromethane Approach)*

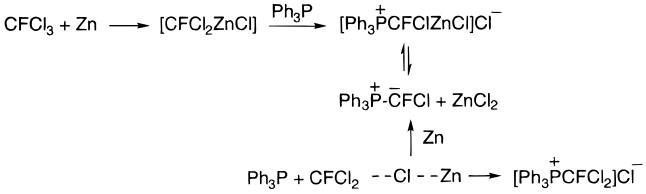
Although triphenylphosphine does not react readily with fluorotrichloromethane, Van Hamme found that a mixture of triphenylphosphine, zinc dust or zinc−copper couple, and fluorotrichloromethane reacted smoothly in DMF in the presence of aldehydes and ketones to give chlorofluoromethylene olefins (eq 55).[56] Aliphatic and aromatic aldehydes and acti-



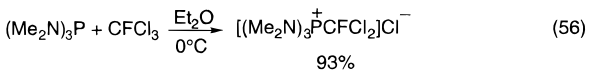

(55)

vated ketones gave modest to good yields of olefins; nonactivated ketones gave low yields. The mechanism of this reaction was suggested to involve a zinc-assisted formation of the ylide intermediate (Scheme 23).[30,56]

**Scheme 23**

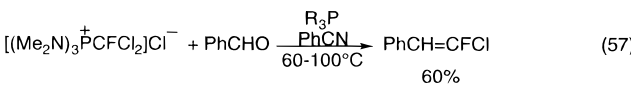



In later work, Van Hamme was able to prepare a (dichlorofluoromethyl)phosphonium salt via the reaction of fluorotrichloromethane with tris(dimethylamino)phosphine (eq 56).[30,57] Dehalogenation of this salt




(56)

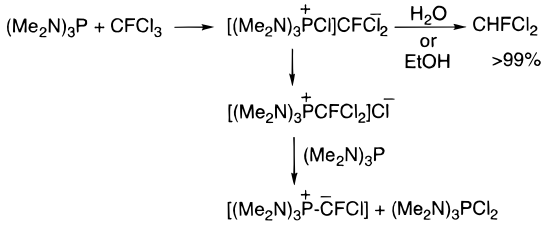
with either $Ph_3P$ or $(Me_2N)_3P$ in the presence of aldehydes, ketones, and activated esters gave good to excellent yields of chlorofluoromethylene olefins (eq 57).[57] The mechanism of salt formation is similar




(57)

to other reactions of tertiary phosphines with carbon tetrahalides (Scheme 24), and mechanistic experiments are consistent with this mechanism.[30] (Dichlorofluoromethyl)tris(dimethylamino)phosphonium chloride is stable to both water and ethanol.[30] The dehalogenation of the (dichlorofluoromethyl)phosphonium salt by tertiary phosphines provides a stable

**Scheme 24**



olefination solution (cf. section 1.3 above) an indication of an equilibrium process that lies to the left (eq 58).[3,57]

$$[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^- + Ph_3P \rightleftharpoons [(Me_2N)_3\overset{+}{P}\text{-}\overset{-}{C}FCl] + Ph_3PCl_2 \quad (58)$$

### *4.4. Chlorofluoromethylene Ylides (Metal Dehalogenation Approach)*

Van Hamme found that a facile dehalogenation occurs between (dichlorofluoromethyl)tris(dimethylamino)phosphonium chloride and group IIB metals to form complexes of the type $[(Me_2N)_3P^+CFCl(MCl)]Cl^-$ where M = Zn, Cd, or Hg. These complexes exhibit surprising stability in ethereal solvents. For example, the zinc complex retains olefination ability for ~1 month (eq 59).[30,58] When

$$[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^- + Zn \longrightarrow \underset{\text{stable}}{[(Me_2N)_3\overset{+}{P}CFClZnCl]Cl^-} \quad (59)$$

these complexed ylides are reacted with aldehydes, ketones, and activated esters, excellent yields of chlorofluoromethylene olefins are obtained (eq 60).

$$[(Me_2N)_3\overset{+}{P}CFClZnCl]Cl^- + PhC(O)CH_3 \xrightarrow[60°C]{THF} \underset{70\%}{PhC(CH_3)=CFCl} \quad (60)$$

Aliphatic and aromatic aldehydes, activated and nonactivated ketones, and activated esters gave good to excellent yields of chlorofluoromethylene ylides.[30,58] The *cis*:*trans* ratios of olefins was identical to *cis*:*trans* ratios obtained from other methods of preparation of the intermediate ylide, suggesting that the metal-complexed ylide was in equilibrium with the "free" ylide which is the reactive intermediate (Scheme 25).[30,58]

**Scheme 25**

$$[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^- + Zn \longrightarrow [(Me_2N)_3\overset{+}{P}CFClZnCl]Cl^- \rightleftharpoons [(Me_2N)_3\overset{+}{P}\text{-}\overset{-}{C}FCl] + ZnCl_2$$

## 5. Preparation of Phosphoranium Salts

When tertiary phosphines react with carbon tetrahalides, such as $CF_2Br_2$, $CFCl_3$, and $CFBr_3$, the reaction can be stopped at the initial monophosphonium salt stage by choice of a solvent in which the phosphonium salt is insoluble and thus precipitates (eq 61).[3,25,27] With $CF_2Br_2$ the reaction could be

$$R_3P + CFX_2Y \longrightarrow [R_3\overset{+}{P}CFX_2]Y^- \downarrow \quad (61)$$

carried further to give the bis-phosphonium salt (eq 22) via the following mechanism (Scheme 26).[3,27] The bis-phosphonium salt from $CF_2Br_2$ stops cleanly at the bis-salt. Further reaction would require abstraction of ($F^+$) by the tertiary phosphine. However, when $CFCl_3$ or $CFBr_3$ are utilized with $Bu_3P$, the third stage of the reaction is possible (abstraction of $Cl^+$ or $Br^+$) and produces the phosphoranium salt (Scheme 27).[32,59] With $CFCl_3$ and $CFBr_3$, excellent yields (85−95%) of phosphoranium salts are obtained. With $CFCl_3$, triphenylphosphine does not react; however, with $CFBr_3$, triphenylphosphine gives the

**Scheme 26**

$$Bu_3P + CF_2Br_2 \longrightarrow [Bu_3\overset{+}{P}Br][CF_2Br^-]$$
$$\downarrow$$
$$Bu_3PBr_2 + [:CF_2]$$
$$\downarrow Bu_3P$$
$$Bu_3P + [Bu_3\overset{+}{P}CF_2Br]Br^- \rightleftharpoons[Bu_3\overset{+}{P}Br] Bu_3\overset{+}{P}\text{-}\overset{-}{C}F_2$$
$$\downarrow [Bu_3\overset{+}{P}Br]$$
$$[Bu_3\overset{+}{P}CF_2\overset{+}{P}Bu_3]\ 2\ Br^-$$

**Scheme 27**

$$Bu_3P + CFX_3 \longrightarrow [Bu_3\overset{+}{P}X][CFX_2]^- \quad (X = Cl, Br)$$
$$\downarrow$$
$$[Bu_3\overset{+}{P}CFX_2]X^-$$
$$\downarrow Bu_3P$$
$$[Bu_3\overset{+}{P}\text{-}\overset{-}{C}FX] + [Bu_3\overset{+}{P}X]X^-$$
$$\downarrow$$
$$[Bu_3\overset{+}{P}CFX\overset{+}{P}Bu_3]\ 2\ X^- \xrightarrow{Bu_3P} \underset{\text{phosphoranium salt}}{[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]X^-} + Bu_3PX_2$$

corresponding phosphoranium salt. If the reaction is initiated with a monosubstituted phosphonium salt, mixed phosphoranium salts can be obtained (eq 62).[32,59] The phosphoranium salts are stable (but

$$[Ph_3\overset{+}{P}CFBr_2]Br^- + Bu_3P \xrightarrow[<5°C]{CH_2Cl_2} \underset{81\%}{[Ph_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Br^-} \quad (62)$$

moisture sensitive) and are readily detected via NMR.[59]

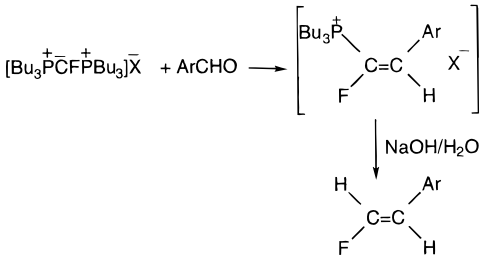
Phosphoranium salts react readily with aldehydes to give vinylphosphonium salts.[60] The stereochemistry of vinylphosphonium salt formation depends upon the type of aldehyde employed. With aliphatic aldehydes, the predominant vinylphosphonium salt isomer formed is the (*E*)-isomer (Scheme 28). Base

**Scheme 28**

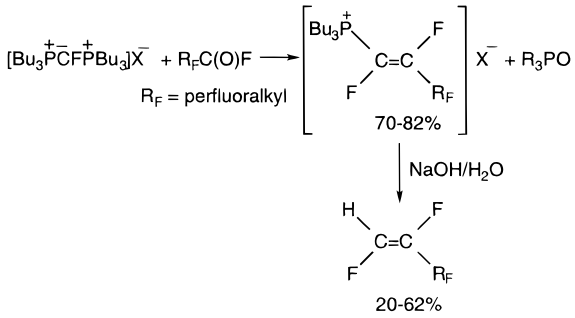
$$[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]X^- + RCHO \longrightarrow \left[Bu_3\overset{+}{P}\text{—}\underset{F}{\overset{H}{C}}\text{=}\underset{R}{C}\right]X^-$$
$$\downarrow NaOH/H_2O$$
$$\underset{F}{\overset{H}{C}}\text{=}\underset{R}{\overset{H}{C}}$$

hydrolysis of this isomer gives the (*Z*)-olefin.[60] In contrast to this stereochemical result, reaction with aromatic aldehydes gives predominantly the (*Z*)-vinylphosphonium salts. Subsequent basic hydrolysis gives the (*E*)-olefin (Scheme 29).[60] To account for this dramatic shift in stereochemistry, an intramolecular, through-space, charge-transfer complex involving one of the tri-*n*-butylphosphonium groups in the phosphoranium salt and the $\pi$-electrons of the aromatic ring of the aldehyde was proposed.[60] The hydrolysis reactions proceed with retention of configuration.

**Scheme 29**



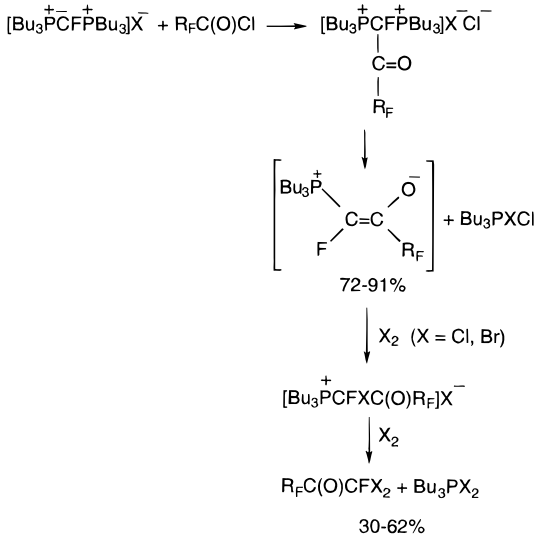
**Scheme 30**



Although phosphonium ylides generally undergo acylation when reacted with acyl halides, the phosphoranium salts undergo a Wittig type of reaction[61] with perfluoroacyl fluorides[62] as outlined in Scheme 30. Only the (*Z*)-isomer of the vinylphosphonium salt is formed.[61] Subsequent base hydrolysis gives *only* the (*E*)-olefin.[61]

Acylation of fluorinated phosphoranium salts with perfluoroacyl chlorides, followed by chlorination or bromination of the resultant betaine intermediate, provided a useful synthesis of α,α-dihalofluoromethyl perfluoralkyl ketones (Scheme 31).[32,63,64,65]

**Scheme 31**

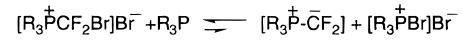


## 6. Stability of Fluoromethylene Ylides

### 6.1. Difluoromethylene Ylides

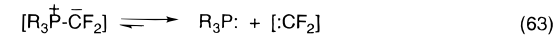
All attempts to pregenerate $[R_3P^+-{}^-CF_2]$ have been unsuccessful. This ylide has not been detected by NMR spectroscopy, and addition of aldehydes or ketones to pregenerated $[R_3P^+-{}^-CF_2]$ did not produce 1,1-difluoroolefins. The only stable olefination solutions, which allow subsequent capture of the ylide by carbonyl substrates, were formed via reaction of

**Scheme 32**



tertiary phosphines with dibromodifluoromethane (cf. section 1.3). In this case, an equilibrium reaction was proposed in which the equilibrium lies far to the left (Scheme 32).[25,35] Recapture of positive halogen by the ylide occurs faster than destructive side reactions. Exchange reactions (eqs 28 and 29) indicate that dissociation of the ylide occurs;[25,36] however, recapture of $[:CF_2]$ by tertiary phosphine re-forms the ylide which can subsequently recapture positive halogen to regenerate the phosphonium salt.

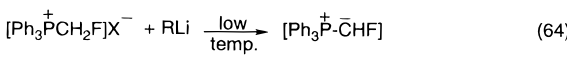
The low stability of $[R_3P^+-{}^-CF_2]$ was initially proposed by Naae, and subsequent calculations by Dixon and Smart confirmed Naae's proposal.[66] When the stability of the model ylide, $[H_3P^+-{}^-CF_2]$, was calculated by *ab initio* molecular orbital theory at the SCF level, it was found that the $P-CF_2$ binding energy was *only* 1.2 kcal/mol.[66] Thus, it is not surprising that the difluoromethylene ylide is unstable and readily decomposes to give tertiary phosphine and difluorocarbene (eq 63).



(63)

### 6.2. Fluoromethylene Ylides

Both Schlosser[44] and Greenlimb[45] pregenerated the fluoromethylene ylide at low temperature via reaction of lithium bases with (fluoromethyl)triphenylphosphonium salts (eq 64). Generally temperatures ≤−50

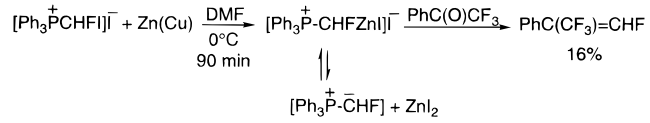


(64)

°C are required to prevent ylide decomposition,[44,45] although Greenlimb found limited stability at 0 °C (detected by reaction with an activated ketone).[45,47] At 28 °C total decomposition had occurred.[47] *Ab initio* molecular orbital calculations at the SCF level with the model ylide, $[H_3P^+-{}^-CHF]$, indicate a binding energy of 16.6 kcal/mol. Thus, $[R_3P^+-{}^-CHF]$ is more stable than the difluoromethylene analog, yet much less stable than the simple methylene analog ($[H_3P^+-{}^-CH_2]$, binding energy of 53.2 kcal/mol).

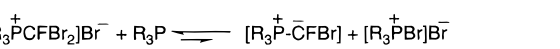
When (fluoroiodomethyl)triphenylphosphonium iodide was dehalogenated with metals, such as zinc, the subsequent metal-complexed ylide exhibited limited stability at 0 °C (Scheme 33).[47] A similar reaction carried out in the presence of $PhC(O)CF_3$ gave 80% olefin.

**Scheme 33**



### 6.3. Bromofluoromethylene Ylide

When (dibromofluoromethyl)phosphonium salts react with tertiary phosphines, a stable olefination solution is formed (eq 65) (similar to $[R_3P^+CF_2Br]Br^-$)



(65)

that lies to the left.[31] In contrast to the (bromodif-

luoromethyl)phosphonium case, exchange reactions do *not* occur[31] (eq 66), indicating that the bromofluo-

$$[Ph_3\overset{+}{P}CFBr_2]Br^- + (tol)_3P \xrightarrow[TG]{0°C} [(tol)_3\overset{+}{P}CFBr_2]Br^- + Ph_3P \quad (66)$$

romethylene ylides do *not* readily dissociate to tertiary phosphine and bromofluorocarbene (eq 67).[31]

$$R_3\overset{+}{P}\text{-}\bar{C}FBr \not\longrightarrow R_3P: + [:CFBr] \quad (67)$$

When (dibromofluoromethyl)triphenylphosphonium bromide was dehalogenated with metals, such as zinc, no stability was found for the resultant metal-complexed ylide (eq 68).[31]

$$[Ph_3\overset{+}{P}CFBr_2]Br^- + Zn \xrightarrow{THF} [\text{intermediate}] \xrightarrow{PhC(O)CF_3} \underset{(0\%)}{PhC(CF_3)=CF_2} \quad (68)$$

### 6.4. Chlorofluoromethylene Ylides

The work of Speziale,[6] Ando,[53] and Krutzsch[55] (section 4.1) demonstrated that chlorofluorocarbene could be captured by triphenylphosphine to give a stable solution of the chlorofluoromethylene ylide (eq 69). Even at higher temperatures the chlorofluorom-

$$CHFCl_2 + Bu^tOK \xrightarrow{Ph_3P} \underset{\text{stable}}{[Ph_3\overset{+}{P}\text{-}\bar{C}FCl]} \xrightarrow{>C=O} >C=CFCl \quad (69)$$

ethylene ylide exhibited some stability. For example, when triphenylphosphine and sodium dichlorofluoroacetate were heated in triglyme at 70 °C until $CO_2$ evolution ceased followed by addition of an activated ketone, a modest yield of the chlorofluoromethylene olefin was obtained (eq 70).[50,55]

$$Ph_3P + CFCl_2CO_2Na \xrightarrow[70°C]{TG} \underset{+ NaCl + CO_2}{[Ph_3\overset{+}{P}\text{-}\bar{C}FCl]} \xrightarrow[\text{after } CO_2 \text{ evolution stopped}]{PhC(O)CF_3,\ 2\text{-}5 \text{ min}} \underset{36\text{-}44\%}{PhC(CF_3)=CFCl} \quad (70)$$

When (dichlorofluoromethyl)tris(dimethylamino)-phosphonium chloride was dehalogenated with a tertiary phosphine, a stable olefination solution was obtained.[57] An equilibrium was proposed similar to stable olefination solutions obtained from (bromodifluoromethyl)phosphonium salts and (dibromofluoromethyl)phosphonium salts (eq 71). In contrast to the stability of the solution outlined in eq 71, when

$$[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^- + Ph_3P \underset{}{\overset{PhCN/60°C}{\rightleftharpoons}} [(Me_2N)_3\overset{+}{P}\text{-}\bar{C}FCl] + [Ph_3\overset{+}{P}Cl]Cl^- \quad (71)$$

tris(dimethylamino)phosphine is used for dehalogenation of the salt, no stable olefination solution was obtained (eq 72).[30,57] Apparently, an equilibrium is

$$[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^- + (Me_2N)_3P \xrightarrow[60°C]{PhCN} (Me_2N)_3\overset{+}{P}\text{-}\bar{C}FCl + [(Me_2N)_3\overset{+}{P}Cl]Cl^- \quad (72)$$
$$\downarrow \text{decomposition}$$

not established in this reaction, and the ease of recapture of halogen from the dihalophosphorane is dependent upon both the nature of the halogen and the substituents attached to phosphorus.

When (dichlorofluoromethyl)tris(dimethylamino)-phosphonium chloride is dehalogenated with zinc−copper couple, a *stable* olefination solution is formed.[58] This solution exhibits olefination ability for ∼1 month. The intermediate chlorofluoromethylene ylide is presumably stabilized as a zinc complex as illustrated in eq 73.

$$[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^- + Zn \longrightarrow [(Me_2N)_3\overset{+}{P}CFClZnCl]Cl^- \quad (73)$$
$$\rightleftharpoons$$
$$(Me_2N)_3\overset{+}{P}\text{-}\bar{C}FCl + ZnCl_2$$

### 6.5. Phosphoranium Salts

The most stable of the fluoromethylene type ylides are the phosphoranium salts, $[R_3P^{+-}CFP^+R_3]X^-$. In this ylide the negative charge is stabilized by two phosphonium centers and these ylides exhibit indefinite stability at room temperature.[59] They are easily detected by NMR spectroscopy ($^{19}F$, $^{31}P$, $^{13}C$).[32,59]

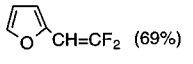
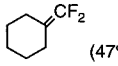
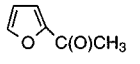
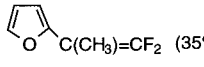
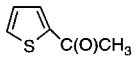
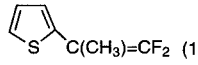
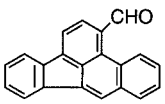
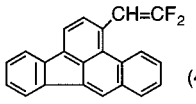
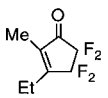
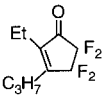
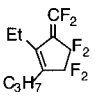
## 7. Application of Fluoromethylene Ylides

### 7.1. Difluoromethylene Ylides (Reaction with Carbonyl Substrates)

Table 1 summarizes the preparation of 1,1-difluoroolefins via the chlorodifluoroacetate method. Good yields are obtained with aromatic aldehydes (entries 1, 2, 3, 5, and 28) and activated ketones (entries 15−18, 20−22, 23, and 26) using triphenylphosphine and sodium chlorodifluoroacetate and scale-up details of this approach have been described in *Organic Synthesis*.[67] Replacement of sodium chlorodifluoroacetate with lithium chlorodifluoroacetate (entries 19, 24, and 25) retards further reaction of the olefin with fluoride ion. Nonactivated ketones (entries 7−10, 12−13, and 27) and α,β-unsaturated cyclic ketones (entries 29 and 30) give lower yields of olefin even when triphenylphosphine is replaced with tributylphosphine. Thus, this method can only be recommended for use with aromatic aldehydes and activated ketones.

Table 2 illustrates the preparation of 1,1-difluoroolefins via the reaction of dihalodifluoromethanes with tertiary phosphines. This method works reasonably well with aromatic (entries 10, 18−20, and 25) aldehydes, aliphatic aldehydes (entry 11), aldehydrosugar derivatives (entries 28−37), activated

**Table 1. Preparation of Difluoromethylene Olefins From Chlorodifluoroacetates ($ClCF_2CO_2M$), Tertiary Phosphines, and Aldehydes and Ketones**

| Entry | Substrate | $R_3P$ | M | Solvent | Temp. | Product (yield) | Ref. |
|---|---|---|---|---|---|---|---|
| 1 | PhCHO | $Ph_3P$ | Na | DG[a] | 160°C | $PhCH=CF_2$ (74%) | 11 |
| 2 | p-$CH_3OC_6H_4CHO$ | $Ph_3P$ | Na | MG[b] | 95°C | p-$CH_3OC_6H_4CH=CF_2$ (60%) | 10,11 |
| 3 | p-$FC_6H_4CHO$ | $Ph_3P$ | Na | DG | 160°C | p-$FC_6H_4CH=CF_2$ (65%) | 11 |
| 4 | $CH_3(CH_2)_5CHO$ | $Ph_3P$ | Na | NMP[c] | 185°C | $CH_3(CH_2)_5CHO$ (52%) | 11 |
| 5 |  | $Ph_3P$ | Na | TG[d] | 160°C |  (69%) | 11 |
| 6 | p-$O_2NC_6H_4CHO$ | $Ph_3P$ | Na | DG | 160°C | p-$O_2NC_6H_4CH=CF_2$ (low) | 11 |
| 7 |  | $Bu_3P$ | Na | NMP | 180°C |  (47%) | 13,14 |
| 8 | $PhC(O)CH_3$ | $Bu_3P$ | Na | NMP | 180°C | $PhC(CH_3)=CF_2$ (35%) | 13,14 |
| 9 |  | $Bu_3P$ | Na | NMP | 180°C |  (35%) | 14 |
| 10 | $Ph_2CO$ | $Bu_3P$ | Na | DMF[e] | 160°C | $Ph_2C=CF_2$ (13%) | 14 |
| 11 | $PhC(O)CF_3$ | $Bu_3P$ | Na | NMP | 180°C | $PhC(CF_3)=CF_2$ (0%) | 14 |
| 12 | $CH_3C(O)(CH_2)_4CH_3$ | $Bu_3P$ | Na | DMF | 150°C | $CH_3(CH_2)_5C(CH_3)=CF_2$ (28%) | 14 |
| 13 |  | $Bu_3P$ | Na | NMP | 180°C |  (13%) | 14 |
| 14 | $CH_3(CH_2)_5CHO$ | $Bu_3P$ | Na | NMP | 180°C | $CH_3(CH_2)_5CH=CF_2$ (7%) | 14 |
| 15 | $PhC(O)CF_3$ | $Ph_3P$ | Na | DG | 145°C | $PhC(CF_3)=CF_2$ (68%)[f] | 12 |
| 16 | $C_6H_{11}C(O)CF_3$ | $Ph_3P$ | Na | DG | 145°C | $C_6H_{11}C(CF_3)=CF_2$ (65%)[f] | 12 |
| 17 | $PhCH_2C(O)CF_3$ | $Ph_3P$ | Na | DG | 145°C | $PhCH_2C(CF_3)=CF_2$ (61%)[f] | 12 |
| 18 | p-$FC_6H_4C(O)CF_3$ | $Ph_3P$ | Na | DG | 145°C | p-$FC_6H_4C(CF_3)=CF_2$ (66%)[f] | 12 |
| 19 | p-$ClC_6H_4C(O)CF_3$ | $Ph_3P$ | Li | DMF | 80°C | p-$ClC_6H_4C(CF_3)=CF_2$ (64%)[f] | 12 |
| 20 | p-$CH_3C_6H_4C(O)CF_3$ | $Ph_3P$ | Na | DG | 145°C | p-$CH_3C_6H_4C(CF_3)=CF_2$ (72%)[f] | 12 |
| 21 | p-$CH_3OC_6H_4C(O)CF_3$ | $Ph_3P$ | Na | DG | 145°C | p-$CH_3OC_6H_4C(CF_3)=CF_2$ (78%)[f] | 12 |
| 22 | p-$(CH_3)_2NC_6H_4C(O)CF_3$ | $Ph_3P$ | Na | DG | 145°C | p-$(CH_3)_2NC_6H_4C(CF_3)=CF_2$ (16%)[f] | 12 |
| 23 | $C_4H_9C(O)CF_3$ | $Ph_3P$ | Na | DG | 145°C | $C_4H_9C(CF_3)=CF_2$ (59%)[f] | 12 |
| 24 | $PhC(O)C_2F_5$ | $Ph_3P$ | Li | DMF | 80-110°C | $PhC(C_2F_5)=CF_2$ (48%)[f] | 12 |
| 25 | $PhC(O)C_3F_7$ | $Ph_3P$ | Li | DMF | 80-110°C | $PhC(C_3F_7)=CF_2$ (40%) | 12 |
| 26 | $PhC(O)CF_3$ | $Ph_3P$ | Na | TG | 170°C | $PhC(CF_3)=CF_2$ (77%) | 77 |
| 27 | $PhC(O)CH_3$ | $Ph_3P$ | Na | TG | 170°C | $PhC(CH_3)=CF_2$ (0%) | 77 |
| 28 |  | $Ph_3P$ | Na | DG | 160°C |  (41%) | 70 |
| 29 |  | $Ph_3P$ | Li | DMF | 90-100°C |  (15%) | 21 |
| 30 |  | $Ph_3P$ | Li | DMF | 90°C |  (27%) | 21 |

[a] DG = diglyme; [b] MG = monoglyme; [c] NMP = 1-methyl-2-pyrrolidone; [d] TG = triglyme; [e] DMF = N,N-dimethylformamide; [f] GLPC yield

ketones (entries 1−5 and 12−17), trimethylsilylated α-hydroxy aldehydes (entries 38−41), nonactivated ketones (entries 21−24), *ribo*- and *xylo*-hexafuranos-3-uloses (entries 26 and 27), and formate (entry 42).

For the less reactive substrates, substitution of tris-(dimethylamino)phosphine for triphenylphosphine achieves successful olefination (entry 9 *vs* 21). This route does not produce fluoride ion and is successful

**Table 2. Preparation of (Difluoromethylene)olefins From Dihalodifluoromethanes ($CF_2X_2$), Tertiary Phosphines, and Carbonyl Substrates**

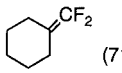
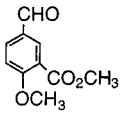
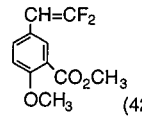
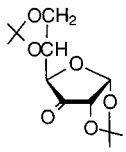
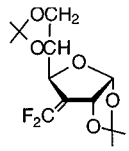
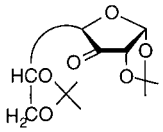
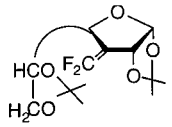
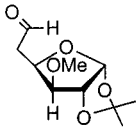
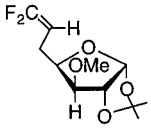
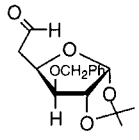
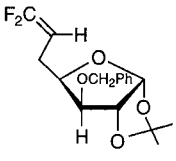
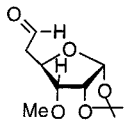
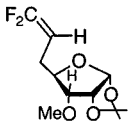
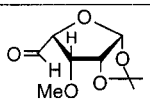
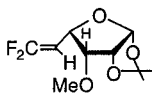
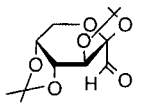
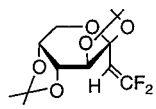
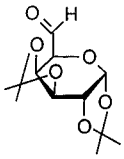
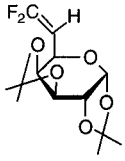
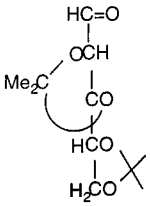
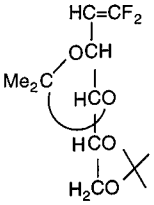
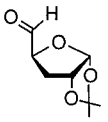
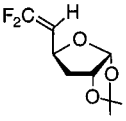
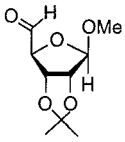
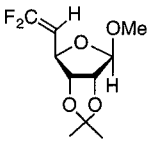
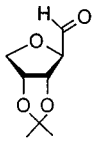
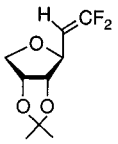
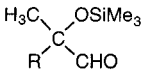
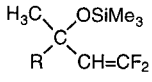
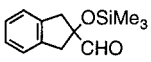
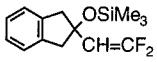
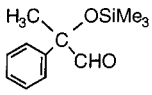
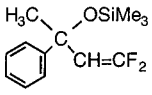
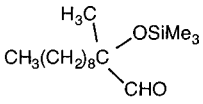
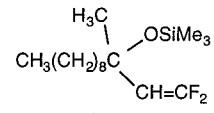
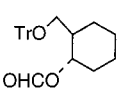
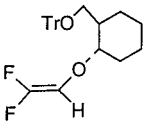
| Entry | Substrate | $R_3P$ | $CF_2X_2$ | Solvent | Temp. | Product (yield) | Ref. |
|---|---|---|---|---|---|---|---|
| 1 | $PhC(O)CF_3$ | $Ph_3P$ | $CF_2Br_2$ | DG[a] | 70°C | $PhC(CF_3)=CF_2$ (85%)[d] | 33 |
| 2 | m-$BrC_6H_4C(O)CF_3$ | $Ph_3P$ | $CF_2Br_2$ | DG | 70°C | m-$BrC_6H_4C(CF_3)=CF_2$ (83%)[d] | 33 |
| 3 | p-$ClC_6H_4C(O)CF_3$ | $Ph_3P$ | $CF_2Br_2$ | DG | 70°C | p-$ClC_6H_4C(CF_3)=CF_2$ (86%)[d] | 33 |
| 4 | $PhC(O)C_2F_5$ | $Ph_3P$ | $CF_2Br_2$ | DG | 70°C | $PhC(C_2F_5)=CF_2$ (82%)[d] | 33 |
| 5 | m-$BrC_6H_4C(O)C_2F_5$ | $Ph_3P$ | $CF_2Br_2$ | DG | 70°C | m-$BrC_6H_4C(C_2F_5)=CF_2$ (87%)[d] | 33 |
| 6 | $C_6F_5CHO$ | $Ph_3P$ | $CF_2Br_2$ | TG[b] | 70°C | $C_6F_5CH=CF_2$ (20%)[d] | 25 |
| 7 | $C_6F_5C(O)CF_2Cl$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | $C_6F_5C(CF_2Cl)=CF_2$ (25%)[d] | 25 |
| 8 | $C_6H_{11}C(O)CF_3$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | $C_6H_{11}C(CF_3)=CF_2$ (90%)[d] | 25 |
| 9 | $PhC(O)CH_3$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | $PhC(CH_3)=CF_2$ (2%)[d] | 25 |
| 10 | PhCHO | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | $PhCH=CF_2$ (65%)[d] | 25 |
| 11 | $CH_3(CH_2)_5CHO$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | $CH_3(CH_2)_5CH=CF_2$ (72%)[d] | 25 |
| 12 | m-$CH_3C_6H_4C(O)C_2F_5$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | m-$CH_3C_6H_4C(C_2F_5)=CF_2$ (40%) | 69 |
| 13 | p-$CH_3C_6H_4C(O)C_2F_5$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | p-$CH_3C_6H_4C(C_2F_5)=CF_2$ (49%) | 69 |
| 14 | p-$FC_6H_4C(O)C_2F_5$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | p-$FC_6H_4C(C_2F_5)=CF_2$ (35%) | 69 |
| 15 | p-$ClC_6H_4C(O)C_2F_5$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | p-$ClC_6H_4C(C_2F_5)=CF_2$ (38%) | 69 |
| 16 | m-$CF_3C_6H_4C(O)C_2F_5$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | m-$CF_3C_6H_4C(C_2F_5)=CF_2$ (33%) | 69 |
| 17 | p-$CF_3C_6H_4C(O)C_2F_5$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | p-$CF_3C_6H_4C(C_2F_5)=CF_2$ (35%) | 69 |
| 18 | m-$CF_3C_6H_4CHO$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | m-$CF_3C_6H_4CH=CF_2$ (30%) | 69 |
| 19 | p-$CF_3C_6H_4CHO$ | $Ph_3P$ | $CF_2Br_2$ | TG | 70°C | p-$CF_3C_6H_4CH=CF_2$ (21%) | 69 |
| 20 | PhCHO | $(Me_2N)_3P$ | $CF_2Br_2$ | TG | RT | $PhCH=CF_2$ (55%) | 25 |
| 21 | $PhC(O)CH_3$ | $(Me_2N)_3P$ | $CF_2Br_2$ | TG | RT | $PhC(CH_3)=CF_2$ (81%)[d] | 34 |
| 22 | $PhC(O)C_2H_5$ | $(Me_2N)_3P$ | $CF_2Br_2$ | TG | RT | $PhC(C_2H_5)=CF_2$ (82%)[d] | 34 |
| 23 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | TG | RT |  (71%)[d] | 34 |
| 24 | $(C_2H_5)_2CO$ | $(Me_2N)_3P$ | $CF_2Br_2$ | TG | RT | $(C_2H_5)_2C=CF_2$ (70%)[d] | 34 |
| 25 |  | $(Et_2N)_3P$ | $CF_2Br_2$ | TG | RT |  (42%) | 71 |
| 26 |  | $Ph_3P$ | $CF_2Cl_2$/KF | DME[c] | 20°C |  (65%) | 72 |
| 27 |  | $Ph_3P$ | $CF_2Cl_2$/KF | DME | 20°C |  (28%) | 72 |
| 28 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | DME | 20°C |  (60-72%) | 73,74 |
| 29 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | DME | 20°C |  (56-74%) | 73,74 |
| 30 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | DME | 20°C |  (60-67%) | 73,74 |

**Table 2 (Continued)**

| Entry | Substrate | $R_3P$ | $CF_2X_2$ | Solvent | Temp. | Product (yield) | Ref. |
|---|---|---|---|---|---|---|---|
| 31 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | DME | 20°C |  (64%) | 74 |
| 32 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | DME | 20°C |  (58-74%) | 73,74 |
| 33 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | DME | 20°C |  (60%) | 74 |
| 34 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | DME | 20°C |  (62%) | 74 |
| 35 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | DME | 20°C |  (71%) | 73 |
| 36 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | DME | 20°C |  (69%) | 73 |
| 37 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | DME | 20°C |  (61%) | 73 |
| 38 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | THF | RT |  (---) | 43 |
| | R = $(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CH(CH_2)_2$- | | | | | | |
| 39 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | THF | RT |  (85%) | 43 |
| 40 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | THF | RT |  (65%) | 43 |
| 41 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | THF | RT |  (---) | 43 |
| 42 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | TG | 85°C |  (95%) | 75 |

[a] DG = diglyme; [b] TG = triglyme; [c] DME = dimethoxyethane; [d] GLPC Yield

for the preparation of olefins that readily add "HF" or undergo fluoride ion-catalyzed isomerization (entries 2, 3, 5, and 12−17). This route is more general than the halodifluoroacetate methodology and is the recommended route for nonactivated ketones and olefinic products prone to further reaction with fluoride ion. Substrates containing pentafluoroaryl groups (entries 6 and 7) do not give good yields of

**Table 3. Metal-Assisted Preparation of (Difluoromethylene)olefins**

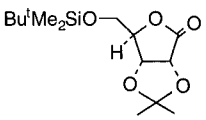
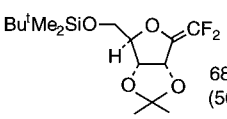
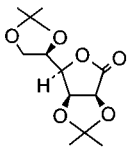
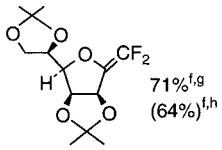
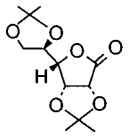
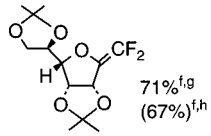
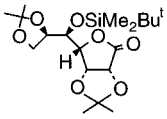
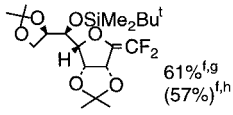
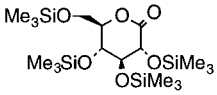
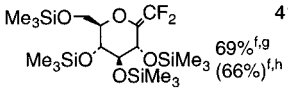
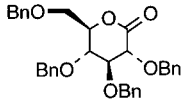
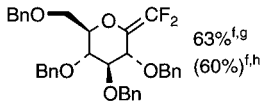
| Entry | Substrate | $R_3P/[R_3\overset{+}{P}CF_2Br]Br^-$ | $CF_2X_2$ | Metal | Solvent | Temp. | Product (yield) | Ref. |
|---|---|---|---|---|---|---|---|---|
| 1 | $PhC(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Zn | TG[a] | 70°C | $PhC(CF_3)=CF_2$ (80%)[e] | 25 |
| 2 | $PhC(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Zn (Cu) | TG | 30°C | $PhC(CF_3)=CF_2$ (48%)[e] | 25 |
| 3 | $PhC(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Hg | TG | 70°C | $PhC(CF_3)=CF_2$ (63%)[e] | 25 |
| 4 | $PhC(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Al | TG | 70°C | $PhC(CF_3)=CF_2$ (45%)[e] | 25 |
| 5 | $C_6F_5CHO$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Cd | TG | RT | $C_6F_5CH=CF_2$ 62%[e] (35%)[f] | 37 |
| 6 | $C_6F_5CHO$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Zn | TG | RT | $C_6F_5CH=CF_2$ (54%)[e] | 37 |
| 7 | $C_6F_5CHO$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Hg | TG | RT | $C_6F_5CH=CF_2$ (41%)[e] | 37 |
| 8 | $PhC(O)CF_2Cl$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Cd | TG | RT | $PhC(CF_2Cl)=CF_2$ 76%[e] (60%)[f] | 37 |
| 9 | $PhC(O)CF_2Cl$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Zn | TG | RT | $PhC(CF_2Cl)=CF_2$ (35%)[e] | 37 |
| 10 | $PhC(O)CF_2Cl$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Hg | TG | RT | $PhC(CF_2Cl)=CF_2$ (21%)[e] | 37 |
| 11 | $C_6F_5C(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Cd | TG | RT | $C_6F_5C(CF_3)=CF_2$ 83%[e] (75%)[f] | 37 |
| 12 | $C_6F_5C(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Zn | TG | RT | $C_6F_5C(CF_3)=CF_2$ (68%)[e] | 37 |
| 13 | $C_6F_5C(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Hg | TG | RT | $C_6F_5C(CF_3)=CF_2$ 71%[e] (56%)[f] | 37 |
| 14 | $C_6F_5C(O)CF_2Cl$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Cd | TG | RT | $C_6F_5C(CF_2Cl)=CF_2$ 72%[e] (67%)[f] | 37 |
| 15 | $C_6F_5C(O)CF_2Cl$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Hg | TG | RT | $C_6F_5C(CF_2Cl)=CF_2$ (64%)[e] | 37 |
| 16 | $p\text{-}CH_3OC_6H_4C(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Cd | TG | RT | $p\text{-}CH_3OC_6H_4C(CF_3)=CF_2$ 68%[e] (54%)[f] | 37 |
| 17 | $p\text{-}CH_3OC_6H_4C(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Hg | TG | RT | $p\text{-}CH_3OC_6H_4C(CF_3)=CF_2$ 61%[e] (54%)[f] | 37 |
| 18 | $m\text{-}CF_3C_6H_4C(O)C_2F_5$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Cd | TG | RT | $m\text{-}CF_3C_6H_4C(C_2F_5)=CF_2$ 87%[e] (69%)[f] | 27 |
| 19 | $m\text{-}CF_3C_6H_4C(O)C_2F_5$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Hg | TG | RT | $m\text{-}CF_3C_6H_4C(C_2F_5)=CF_2$ (69%)[e] | 27 |
| 20 | $PhC(O)CF_2Br$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Cd | TG | RT | $PhC(CF_2Br)=CF_2$ 73%[e] (60%)[f] | 27 |
| 21 | $PhC(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Cd | TG | RT | $PhC(CF_3)=CF_2$ 91%[e] (83%)[f] | 27 |
| 22 | $PhC(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Zn | TG | RT | $PhC(CF_3)=CF_2$ (67%)[e] | 27 |
| 23 | $PhC(O)CF_3$ | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Hg | TG | RT | $PhC(CF_3)=CF_2$ (72%)[e] | 27 |
| 24 | PhCHO | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Cd | TG | RT | $PhCH=CF_2$ (52%)[f] | 27 |
| 25 | PhCHO | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Zn | TG | RT | $PhCH=CF_2$ (31%)[f] | 27 |
| 26 | PhCHO | $[Ph_3\overset{+}{P}CF_2Br]Br^-$ | --- | Hg | TG | RT | $PhCH=CF_2$ (29%)[f] | 27 |
| 27 | $C_6H_{13}CHO$ | $Ph_3P$ | $CF_2Br_2$ | Zn | DMAC[b] | 110°C | $C_6H_{13}CH=CF_2$ 80%[e] (60%)[f] | 76 |
| 28 | $C_{10}H_{21}CHO$ | $Ph_3P$ | $CF_2Br_2$ | Zn | DMAC | 110°C | $C_{10}H_{21}CH=CF_2$ 76%[e] (56%)[f] | 76 |
| 29 | PhCH=CHCHO | $Ph_3P$ | $CF_2Br_2$ | Zn | DMAC | 110°C | $PhCH=CHCH=CF_2$ 33%[e] (30%)[f] | 76 |
| 30 | $PhC(O)CH_3$ | $(Me_2N)_3P$ | $CF_2Br_2$ | Zn | DMAC | 110°C | $PhC(CH_3)=CF_2$ (43%)[e] | 76 |
| 31 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | Zn | THF[c] | reflux |  68%[f,g] (56%)[f,h] | 41,42 |
| 32 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | Zn | THF | reflux |  71%[f,g] (64%)[f,h] | 41,42 |

**Table 3 (Continued)**

| Entry | Substrate | $R_3P/[R_3\overset{+}{P}CF_2Br]Br^-$ | $CF_2X_2$ | Metal | Solvent | Temp. | Product (yield) | Ref. |
|---|---|---|---|---|---|---|---|---|
| 33 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | Zn | THF | reflux |  71%[f,g] (67%)[f,h] | 41,42 |
| 34 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | Zn | THF | reflux |  61%[f,g] (57%)[f,h] | 41,42 |
| 35 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | Zn | THF | reflux |  69%[f,g] (66%)[f,h] | 41,42 |
| 36 |  | $(Me_2N)_3P$ | $CF_2Br_2$ | Zn | THF | reflux |  63%[f,g] (60%)[f,h] | 41,42 |
| 37 |  | $Ph_3P$ | $CF_2Br_2$ | Zn | $CH_3CN$[d] | --- |  (56%) | |
| 38 | | | | | | | | |

[a] TG = triglyme; [b] DMAC = $CH_3C(O)N(CH_3)_2$; [c] THF =  ; [d] $CH_3CN$ = acetonitrile; [e] GLPC yield; [f] isolated yield; [g] catalytic $(Me_2N)_3P$ method; [h] excess $(Me_2N)_3P$.

olefins via this route due to reaction of the substrate with the tertiary phosphine.

Table 3 illustrates the metal-assisted approach for the conversion of aldehydes and ketones to 1,1-difluoroolefins. The effect of various metals with activated aldehydes and ketones (entries 1−23) demonstrates the utility of this approach. This is the only method that achieved success (good yields) with substrates containing the pentafluoroaryl group (entries 6, 7, and 11−15) or substrates that yield substituted perfluoroallyl halides (entries 8, 14, 15, and 20). Aromatic (entries 24 and 25) and aliphatic aldehydes (entries 27 and 28), activated ketones (entries 1−4, 16−19, and 21−23) also give good yields via this route; α,β-unsaturated aldehydes (entry 29) and nonactivated ketones (entry 30) give only modest yields of olefin. Carbohydrate lactones give good yields via *this route* (entries 30−36) and illustrate the variety of functionalities and protecting groups tolerated in this reaction.

### *7.2. Difluoromethylene Ylides (Chain-Extension Reactions)*

Difluoromethylene ylides are nucleophilic and when generated in the presence of a fluoroolefin undergo an addition−elimination reaction with the fluoroolefin to give an allylic phosphonium salt.[68,69] Subsequent hydrolysis of the allylic phosphonium salt gave a chain-extended alkene or diene (Scheme 34). *No* protonation occurred at the difluoromethylene carbon to give $CF_2HCF{=}C(Ph)CF_3$. With 2-phenylperfluoro-1-butene and 2-phenylperfluoro-1-pentene, the diene is the major product (eqs 74 and 75).[68,69] When

$$[Ph_3\overset{+}{P}CF_2Br]Br^- + F_2C{=}C(Ph)CF_2CF_3 \xrightarrow[CH_3CN]{Hg} [Ph_3\overset{+}{P}CF_2CF{=}C(Ph)CF_2CF_3]X^- \xrightarrow{H_2O} F_2C{=}CFC(Ph){=}CFCF_3 \quad (74)$$

(70%) 8:1 E/Z

$$[Ph_3\overset{+}{P}CF_2Br]Br^- + F_2C{=}C(Ph)CF_2CF_2CF_3 \quad (75)$$

$$\downarrow \text{Hg, } CH_3CN$$

$$[Ph_3\overset{+}{P}CF_2CF{=}C(Ph)CF_2CF_2CF_3]X^-$$

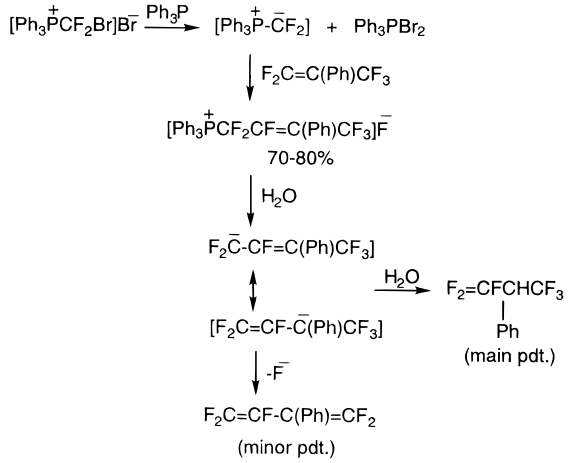
$$\downarrow H_2O$$

$$F_2C{=}CFC(Ph){=}CFCF_2CF_3$$

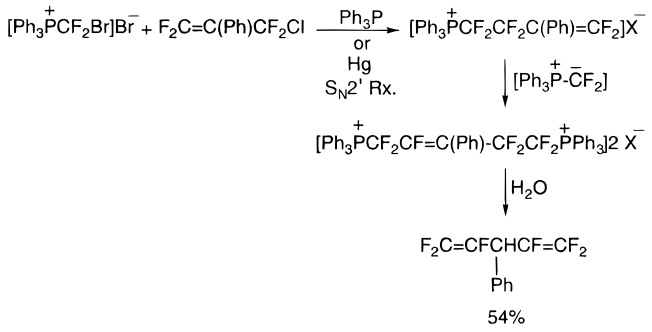
(68%) 9:1 E/Z

2-phenyl-3-chloroperfluoropropene is employed as a reactant with excess ylide, a bis-phosphonium salt is formed (Scheme 35), which on hydrolysis gave 3-phenyl-3-hydroperfluoro-1,4-pentadiene.[68,69]

**Scheme 34**




**Scheme 35**




### 7.3. Fluoromethylene Ylides

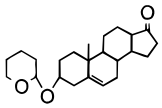
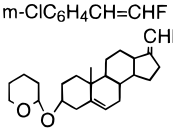
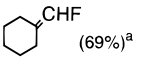
Table 4 summarizes the reaction of fluoromethylene ylide with aldehydes and ketones. The pregenerated ylide (from phosphonium salt + RLi) gives modest yields with aliphatic (entries 1 and 11) and aromatic (entries 2−4 and 10) aldehydes, activated ketones (entries 6 and 12), cyclic ketones (entries 5 and 9), and nonactivated ketones (entries 7 and 8). Metal dehalogenation of $[Ph_3P^+CHFI]I^-$ gives good yields of fluoromethylene olefins with an aliphatic aldehyde (entry 16), aromatic aldehyde (entry 14), and activated aldehydes and ketones (entries 13 and 15). Nonactivated ketones (entry 17) gave poor yields via the metal dehalogenation approach.

### 7.4. Bromofluoromethylene Ylides

The direct reaction of fluorotribromomethane with tertiary phosphines in the presence of aldehydes and ketones (Table 5) gave good yields of bromofluoromethylene olefins (mixture of geometrical isomers) with activated ketones (entries 6, 7, 9−11, 14, and 15) in triglyme, THF, DMF, and $CHCl_3$ and aromatic aldehydes (entry 12). Ether (entry 8) is not a suitable solvent for this reaction. Aliphatic aldehydes and nonactivated ketones gave lower yields (entries 13 and 17).

Dehalogenation of (dibromofluoromethyl)triphenylphosphonium bromide with a tertiary phosphine in the presence of an aldehyde or ketone gave good

**Table 4. Preparation of (Fluoromethylene)olefins**

| Entry | Substrate | Salt | Base | Metal | Product (yield) | Ref. |
|---|---|---|---|---|---|---|
| 1 | $C_5H_{11}CHO$ | $[Ph_3P^+CH_2F]I^-$ | PhLi | --- | $C_5H_{11}CH=CHF$ 55[a] (35%)[b,c] | 44 |
| 2 | PhCHO | $[Ph_3P^+CH_2F]I^-$ | PhLi | --- | PhCH=CHF 65[a] (43%)[b,d] | 44 |
| 3 | m-$CF_3C_6H_4CHO$ | $[Ph_3P^+CH_2F]I^-$ | PhLi | --- | m-$CF_3C_6H_4CH=CHF$ (25%)[a,d] | 44 |
| 4 | m-$ClC_6H_4CHO$ | $[Ph_3P^+CH_2F]I^-$ | PhLi | --- | m-$ClC_6H_4CH=CHF$ 65[a] (45%)[b,d] | 44 |
| 5 |  | $[Ph_3P^+CH_2F]I^-$ | PhLi | --- |  (16%)[b] | 44 |
| 6 | $PhC(O)CF_3$ | $[Ph_3P^+CH_2F]I^-$ | BuLi | --- | $PhC(CF_3)=CHF$ (50%)[a,e] | 45 |
| 7 | $PhC(O)CH_3$ | $[Ph_3P^+CH_2F]I^-$ | BuLi | --- | $PhC(CH_3)=CHF$ (49%)[a,f] | 45 |
| 8 | $Ph_2CO$ | $[Ph_3P^+CH_2F]I^-$ | BuLi | --- | $Ph_2C=CHF$ (47%)[a] | 45 |
| 9 |  | $[Ph_3P^+CH_2F]I^-$ | BuLi | --- |  (69%)[a] | 45 |
| 10 | PhCHO | $[Ph_3P^+CH_2F]I^-$ | BuLi | --- | PhCH=CHF (44%)[a,g] | 45 |
| 11 | $C_6H_{13}CHO$ | $[Ph_3P^+CH_2F]I^-$ | BuLi | --- | $C_6H_{13}CH=CHF$ (26%)[a,h] | 45 |
| 12 | $PhC(O)CF_3$ | $[Ph_3P^+CH_2F]I^-$ | $LiN(Pr^i)_2$ | --- | $PhC(CF_3)=CHF$ (48%)[a,i] | 45 |
| 13 | $PhC(O)CF_3$ | $[Ph_3P^+CHFI]I^-$ | --- | Zn(Cu) | $PhC(CF_3)=CHF$ (80%)[j,h] | 46 |
| 14 | PhCHO | $[Ph_3P^+CHFI]I^-$ | --- | Zn(Cu) | PhCH=CHF (52%)[j,l] | 46 |
| 15 | $C_6F_5CHO$ | $[Ph_3P^+CHFI]I^-$ | --- | Zn(Cu) | $C_6F_5CH=CHF$ (65%)[j,m] | 46 |
| 16 | $C_6H_{13}CHO$ | $[Ph_3P^+CHFI]I^-$ | --- | Zn(Cu) | $C_6H_{13}CH=CHF$ (54%)[j,m] | 46 |
| 17 | $PhC(O)CH_3$ | $[Ph_3P^+CHFI]I^-$ | --- | Zn(Cu) | $PhC(CH_3)=CHF$ (12%)[j,o] | 47 |

[a] GLPC yield; [b] isolated yield; [c] 45:55 *c/t*; [d] 50:50 *c/t*; [e] 46:54 *c/t*; [f] 49:51 *c/t*; [g] 44:55 *c/t*; [h] 48:52 *c/t*; [i] 49:51 *c/t*; [j] NMR yield; [k] 52:48 *c/t*; [l] 41:59 *c/t*; [m] 54:46 *c/t*; [n] 43:57 *c/t*; [o] 57:43 *c/t*..

**Table 5. Preparation of (Bromofluoromethylene)olefins**

| Entry | Substrate | $R_3P$ | Salt[a] | $CFBr_3$ | Metal | Solvent | Temp. | Product (yield) | *d/t* | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | PhCHO | $Ph_3P$ | Yes | --- | --- | THF[b] | 70°C | PhCH=CFBr (70%)[h] | 55/45 | 31 |
| 2 | $PhC(O)CF_3$ | $Ph_3P$ | Yes | --- | --- | THF | 70°C | $PhC(CF_3)$=CFBr (85%)[h] | 53/47 | 31 |
| 3 | $PhC(O)C_2H_5$ | $Ph_3P$ | Yes | --- | --- | THF | 70°C | $PhC(C_2H_5)$=CFBr (20%)[h] | 48/52 | 31 |
| 4 | $PhC(O)CH_3$ | $Ph_3P$ | Yes | --- | --- | THF | 70°C | $PhC(CH_3)$=CFBr (45%)[h] | 46/54 | 31 |
| 5 | $PhCH_2C(O)CF_3$ | $Ph_3P$ | Yes | --- | --- | THF | 70°C | $PhCH_2C(CF_3)$=CFBr (59%)[h] | 57/43 | 51 |
| 6 | $PhC(O)CF_3$ | $Ph_3P$ | --- | Yes | --- | TG[c] | 70°C | $PhC(CF_3)$=CFBr (82%)[h] | 54/46 | 51 |
| 7 | $PhC(O)CF_3$ | $Ph_3P$ | --- | Yes | --- | THF | 70°C | $PhC(CF_3)$=CFBr (92%)[h] | 55/45 | 31 |
| 8 | $PhC(O)CF_3$ | $Ph_3P$ | --- | Yes | --- | $Et_2O$[d] | 33°C | $PhC(CF_3)$=CFBr (9%)[h] | 50/50 | 31 |
| 9 | $PhC(O)CF_3$ | $Ph_3P$ | --- | Yes | --- | DMF[e] | RT | $PhC(CF_3)$=CFBr (50%)[h] | 83/17 | 31 |
| 10 | $PhC(O)CF_3$ | $Ph_3P$ | --- | Yes | --- | $CHCl_3$[f] | RT | $PhC(CF_3)$=CFBr (68%)[h] | 50/50 | 31 |
| 11 | $PhC(O)CF_3$ | $Ph_3P$ | --- | Yes | --- | $CH_3CN$[g] | RT | $PhC(CF_3)$=CFBr (92%)[h] | 42/58 | 31 |
| 12 | PhCHO | $Ph_3P$ | --- | Yes | --- | TG | 70°C | PhCH=CFBr (64%)[h] | 54/45 | 31 |
| 13 | $PhC(O)CH_3$ | $Ph_3P$ | --- | Yes | --- | TG | 70°C | $PhC(CH_3)$=CFBr (18%)[h] | 53/47 | 51 |
| 14 | $PhC(O)CF_2Cl$ | $Ph_3P$ | --- | Yes | --- | TG | 70°C | $PhC(CF_2Cl)$=CFBr (72%)[h] | 57/43 | 31 |
| 15 | $PhC(O)C_2F_5$ | $Ph_3P$ | --- | Yes | --- | TG | 70°C | $PhC(C_2F_5)$=CFBr (65%)[h] | 60/40 | 51 |
| 16 | $(CF_3)_2CO$ | $Ph_3P$ | --- | Yes | --- | TG | 70°C | $(CF_3)_2C$=CFBr (38%)[h] | --- | 51 |
| 17 | $C_6H_{13}CHO$ | $Ph_3P$ | --- | Yes | --- | TG | 70°C | $C_6H_{13}CH$=CFBr (28%)[h] | 50/50 | 31 |
| 18 | $PhC(O)CF_3$ | $Ph_3P$ | Yes | --- | --- | $CH_3CN$ | RT | $PhC(CF_3)$=CFBr (97%)[h] | 44/56 | 31 |
| 19 | $PhC(O)CF_3$ | $Ph_3P$ | Yes | --- | --- | $CHCl_3$ | RT | $PhC(CF_3)$=CFBr (95%)[h] | 48/52 | 31 |
| 20 | PhCHO | $Ph_3P$ | Yes | --- | --- | $CH_3CN$ | RT | PhCH=CFBr (26%)[h] | 61/39 | 31 |
| 21 | $(CF_3)_2CO$ | $Ph_3P$ | Yes | --- | --- | $CHCl_3$ | RT | $(CF_3)_2C$=CFBr (80%)[h] | --- | 31 |
| 22 | $(C_3F_7)_2CO$ | $Ph_3P$ | Yes | --- | --- | $CHCl_3$ | 0°C | $(C_3F_7)_2C$=CFBr (79%)[h] | --- | 31 |
| 23 | $PhC(O)CF_3$ | — | Yes | --- | Zn | TG | RT | $PhC(CF_3)$=CFBr (86%)[h] | 52/48 | 31 |
| 24 | $PhC(O)CF_3$ | — | Yes | --- | Zn(Cu) | THF | RT | $PhC(CF_3)$=CFBr (65%)[h] | 49/51 | 31 |
| 25 | $PhC(O)CF_3$ | — | Yes | --- | Hg | THF | RT | $PhC(CF_3)$=CFBr (83%)[h] | 51/49 | 31 |
| 26 | $PhC(O)CF_3$ | — | Yes | --- | Cd | THF | RT | $PhC(CF_3)$=CFBr (81%)[h] | 52/48 | 31 |
| 27 | $PhC(O)CH_3$ | — | Yes | --- | Zn | TG | RT | $PhC(CH_3)$=CFBr (55%)[h] | 51/49 | 31 |
| 28 | $PhC(O)CF_2Cl$ | --- | Yes | --- | Zn | TG | RT | $PhC(CF_2Cl)$=CFBr (38%)[h] | 55/45 | 31 |
| 29 | $PhC(O)C_2F_5$ | — | Yes | --- | Zn | TG | RT | $PhC(C_2F_5)$=CFBr (65%)[h] | 51/49 | 31 |
| 30 |  | — | Yes | --- | Zn | TG | RT |  (14%)[h] | --- | 31 |
| 31 | $(CF_3)_2CO$ | --- | Yes | --- | Zn | THF | 50°C | $(CF_3)_2C$=CFBr (37%)[h] | --- | 31 |
| 32 | $C_6H_5CHO$ | --- | Yes | --- | Zn | THF | RT | PhCH=CFBr (64%)[h] | 55/45 | 31 |
| 33 | $(C_3F_7)_2CO$ | --- | Yes | --- | Zn | $Et_2O$ | RT | $(C_3F_7)_2C$=CFBr (43%)[h] | --- | 31 |
| 34 | $C_6F_5CHO$ | --- | Yes | --- | Zn | THF | RT | $C_6F_5CH$=CFBr (20%)[h] | 43/57 | 31 |

[a] salt = $[Ph_3\overset{+}{P}CFBr_2]Br^-$; [b] THF =  ; [c] TG = triglyme; [d] $Et_2O$ = ether; [e] DMF = N,N-dimethylformamide; [f] $CHCl_3$ = chloroform; [g] $CH_3CN$ = acetonitrile; [h] GLPC yield.

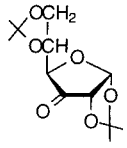
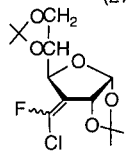
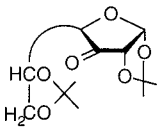
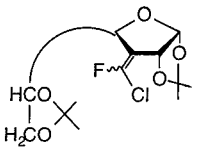
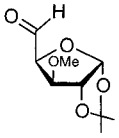
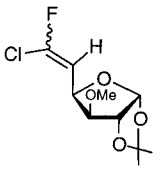
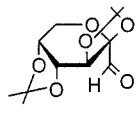
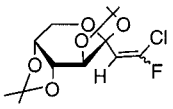
yields of bromofluoromethylene olefins with aromatic aldehyde (entry 1) in THF and activated ketones (entries 2, 5, 18, 19, 21, and 22). Nonactivated ketones (entries 3 and 4) gave lower yields of olefins.

The metal dehalogenation approach gave high yields of bromofluoromethylene olefins with activated ketones (entries 23−26, 29, and 33) and aromatic aldehydes (entries 32 and 34). Modest yields were achieved with nonactivated ketones (entry 27), and cyclic ketones (entry 30) gave low yields of olefin. Metals such as Zn, Zn (Cu), Hg, and Cd gave similar results (entries 23−26).

### *7.5. Chlorofluoromethylene Ylides*

The *in situ* generation of chlorofluorocarbene and capture of the carbene by a tertiary phosphine to produce chlorofluoromethylene ylide is summarized in Table 6. The carbene has been produced from dichlorofluoromethane, methyl dichlorofluoroacetate, and (dichlorofluoromethyl)mercury. The formation of chlorofluoromethylene ylide from triphenylphosphine, dichlorofluoromethane, and potassium *tert*-butoxide gave only low to modest yields of chlorofluoromethylene olefins (entries 1 and 12−15). Com-

**Table 6. Preparation of (Chlorofluoromethylene)olefins From Tertiary Phosphines and Chlorofluorocarbene Precursors**

| Entry | Substrate | $R_3P$ | Chlorofluoro Carbene Precursor | Solvent | Temp. | Product (yield) | Ref. |
|---|---|---|---|---|---|---|---|
| 1 | $Ph_2CO$ | $Ph_3P$ | $CHFCl_2$ | heptane | 0°C | $Ph_2C$=CFCl (40%) | 6 |
| 2 | $PhC(O)CH_3$ | $Ph_3P$ | $CFCl_2CO_2CH_3$ | Pet. Ether | 80°C | $PhC(CH_3)$=CFCl (8%) | 53 |
| 3 | PhCHO | $Ph_3P$ | $CFCl_2CO_2CH_3$ | Pet. Ether | 80°C | PhCH=CFCl (40%) | 53 |
| 4 | p-$ClC_6H_4CHO$ | $Ph_3P$ | $CFCl_2CO_2CH_3$ | Pet. Ether | 80°C | p-$ClC_6H_4CH$=CFCl (63%) | 53 |
| 5 | p-$CH_3OC_6H_4CHO$ | $Ph_3P$ | $CFCl_2CO_2CH_3$ | Pet. Ether | 80°C | p-$CH_3OC_6H_4CH$=CFCl (40%) | 53 |
| 6 | o-$CH_3OC_6H_4CHO$ | $Ph_3P$ | $CFCl_2CO_2CH_3$ | Pet. Ether | 80°C | o-$CH_3OC_6H_4CH$=CFCl (50%) | 53 |
| 7 | $PhC(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2CH_3$ | Pet. Ether | 80°C | $PhC(CF_3)$=CFCl (40%)[c] | 53 |
| 8 | p-$FC_6H_4C(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2CH_3$ | Pet. Ether | 80°C | p-$FC_6H_4C(CF_3)$=CFCl (45%) | 53 |
| 9 | p-$ClC_6H_4C(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2CH_3$ | Pet. Ether | 80°C | p-$ClC_6H_4C(CF_3)$=CFCl (41%) | 53 |
| 10 | p-$CH_3C_6H_4C(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2CH_3$ | Pet. Ether | 80°C | p-$CH_3C_6H_4C(CF_3)$=CFCl (38%) | 53 |
| 11 | p-$CH_3OC_6H_4C(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2CH_3$ | Pet. Ether | 80°C | p-$CH_3OC_6H_4C(CF_3)$=CFCl (36%) | 53 |
| 12 | PhCHO | $Ph_3P$ | $CHFCl_2$ | heptane | 0°C | PhCH=CFCl (39%)[a,d] | 54 |
| 13 | $PhC(O)CF_3$ | $Ph_3P$ | $CHFCl_2$ | heptane | 0°C | $PhC(CF_3)$=CFCl (31%)[a,e] | 54 |
| 14 | $Ph_2CO$ | $Ph_3P$ | $CHFCl_2$ | heptane | 0°C | $Ph_2C$=CFCl (0%)[a] | 54 |
| 15 |  | $Ph_3P$ | $CHFCl_2$ | heptane | 0°C |  (27%)[a] | 54 |
| 16 |  | $Ph_3P$ | $PhHgCFCl_2$ | xylene | 80°C |  (74%)[f] | 72 |
| 17 |  | $Ph_3P$ | $PhHgCFCl_2$ | xylene | 80°C |  (60%) | 72 |
| 18 |  | $Ph_3P$ | $PhHgCFCl_2$ | benzene | 80°C |  (74%)[g] | 73 |
| 19 |  | $Ph_3P$ | $PhHgCFCl_2$ | benzene | 80°C |  (72%)[h] | 73 |

[a] GLPC yield; [b] E/Z 57:43; [c] E/Z 48:52; [d] E/Z 44:56; [e] E/Z 52:48; [f] E/Z 16:31; [g] E/Z 56:44; [h] E/Z 42:58.

petitive capture of chlorofluorocarbene with either $Bu^tOK$ or $Bu^tOH$ presumably accounts for the low yields of olefins and this route is not a viable entry to this class of olefins.

*In situ* capture of chlorofluorocarbene from reaction of triphenylphosphine, methyl dichlorofluoroacetate and methoxide ion is a useful entry to chlorofluoromethylene olefins. Aromatic aldehydes (entries 3−6) and activated ketones (entries 7−11) give reasonable isolated yields of olefins. Nonactivated ketones (entry 2) are not successful via this approach.

The organomercurial methodology for *in situ* chlorofluorocarbene generation and capture by triphenylphosphine gave excellent yields of chlorofluoromethylene olefin derivatives with aldehydrosugar derivatives (entries 18 and 19) and *ribo*- and *xylo*-hexafuranos-3-uloses (entries 16 and 17). The main limitation of this methodology is the necessity to prepare the mercury precursor and the toxicity of organomercury compounds.

Chlorofluoromethylene olefins can also be synthesized via the *in situ* reaction of dichlorofluoroacetate salts, tertiary phosphines and aldehydes or ketones (Table 7). Aromatic aldehydes (entry 1) and activated ketones (entries 2−11) give modest yields of chlorofluoromethylene olefins; cyclic ketones (entries 12 and 14) and nonactivated ketones (entry 13) give low yields of olefins. The yields are comparable to the methyl dichlorofluoroacetate route (Table 6) and significantly lower than the organomercurial route (Table 6).

An alternative route to chlorofluoromethylene olefins is via dehalogenation of (dichlorofluoromethyl)-tris(dimethylamino)phosphonium salts by tertiary

**Table 7. Preparation of (Chlorofluoromethylene)olefins from Sodium Dichlorofluoroacetate, Tertiary Phosphines, Aldehydes, and Ketones**

| Entry | Substrate | $R_3P$ | Salt | Solvent | Temp. | Product (yield) | Ref. |
|---|---|---|---|---|---|---|---|
| 1 | PhCHO | $Ph_3P$ | $CFCl_2CO_2Na$ | TG[a] | 90°C | PhCH=CFCl (49%)[b,c] | 55 |
| 2 | $PhC(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $PhC(CF_3)$=CFCl (56%)[b,d] | 55 |
| 3 | $p\text{-}ClC_6H_4C(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $p\text{-}ClC_6H_4C(CF_3)$=CFCl (53%)[b,e] | 55 |
| 4 | $p\text{-}CH_3OC_6H_4C(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $p\text{-}CH_3OC_6H_4C(CF_3)$=CFCl (67%)[b,f] | 55 |
| 5 | $p\text{-}FC_6H_4C(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $p\text{-}FC_6H_4C(CF_3)$=CFCl (27%)[b,g] | 55 |
| 6 | $p\text{-}CH_3C_6H_4C(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $p\text{-}CH_3C_6H_4C(CF_3)$=CFCl (48%)[b,h] | 55 |
| 7 | $PhCH_2C(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $PhCH_2C(CF_3)$=CFCl (37%)[b,i] | 55 |
| 8 | $C_4H_9C(O)CF_3$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $C_4H_9C(CF_3)$=CFCl (34%)[b,j] | 55 |
| 9 | $PhC(O)CF_2Cl$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $PhC(CF_2Cl)$=CFCl (29%)[b,k] | 55 |
| 10 | $PhC(O)C_2F_5$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $PhC(C_2F_5)$=CFCl (42%)[b,l] | 50 |
| 11 | $PhC(O)C_3F_7$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $PhC(C_3F_7)$=CFCl (41%)[b,m] | 50 |
| 12 |  | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C |  (9%)[b] | 55 |
| 13 | $Ph_2CO$ | $Ph_3P$ | $CFCl_2CO_2Na$ | TG | 90°C | $Ph_2C$=CFCl (0%)[b] | 55 |
| 14 |  | $Bu_3P$ | $CFCl_2CO_2Na$ | TG | 90°C |  (23%)[b] | 55 |

[a] TG = triglyme; [b] GLPC yield; [c] E/Z 44:56; [d] E/Z 53:47; [e] E/Z 55:45; [f] E/Z 52:48; [g] E/Z 55:45; [h] E/Z 53:47; [i] E/Z 50:50; [j] E/Z 48:52; [k] E/Z 52:48; [l] E/Z 59:41; [m] E/Z 60:40.

**Table 8. Preparation of (Chlorofluoromethylene)olefins from Dehalogenation of (Dichlorofluoromethyl)tris(dimethylamino)phosphonium Salts by Tertiary Phosphines**

| Entry | Substrate | $R_3P$ | Salt | Solvent | Temp. | Product (yield) | Ref. |
|---|---|---|---|---|---|---|---|
| 1 | $PhC(O)CF_3$ | $Ph_3P$ | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | PhCN[a] | 60°C | $PhC(CF_3)$=CFCl (83%)[b,c] | 57 |
| 2 | PhCHO | $Ph_3P$ | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | PhCN | 100°C | PhCH=CFCl (60%)[b,d] | 57 |
| 3 | $CF_3CO_2Pr^i$ | $Ph_3P$ | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | PhCN | 60°C | $CF_3C(OPr^i)$=CFCl (40%)[b,e] | 57 |
| 4 | $CF_3CO_2Pr^i$ | $(Me_2N)_3P$ | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | PhCN | RT | $CF_3C(OPr^i)$=CFCl (67%)[b,e] | 57 |
| 5 | $PhC(O)CH_3$ | $(Me_2N)_3P$ | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | PhCN | 55°C | $PhC(CH_3)$=CFCl (56%)[b,f] | 57 |
| 6 | $PhC(O)CF_3$ | $Ph_3P$ | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | THF | 60°C | $PhC(CF_3)$=CFCl (0%) | 57 |
| 7 | $PhC(O)CH_3$ | $Ph_3P$ | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | PhCN | 60°C | $PhC(CH_3)$=CFCl (3%)[a,g] | 57 |

[a] PhCN =benzonitrile; [b] GLPC yield; [c] E/Z 53:47; [d] E/Z 44:56; [e] 100% E; [f] E/Z 48:52; [g] E/Z 50:50.

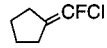
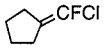
phosphines (Table 8). Although a limited number of examples utilizing this method have been reported, the yields of olefins from aromatic aldehydes, activated and nonactivated ketones, and activated esters were good to excellent. The requisite salt, $[(Me_2N)_3P^+CFCl_2]Cl^-$, is easily prepared from $(Me_2N)_3P$ and $CFCl_3$. This method is comparable or superior to the carbene or acetate salt route.

Table 9 illustrates two metal-assisted approaches to chlorofluoromethylene olefins. The first approach (entries 1−7) utilizes an *in situ* reaction between triphenylphosphine, fluorotrichloromethane, zinc metal, and aldehydes or ketones. Since triphenylphosphine does not react directly with $CFCl_3$ under these conditions, it is presumed that the reactive intermediate is an organozinc. The yields with aromatic (entry 4) and aliphatic (entry 5) aldehydes, activated ketones (entries 1−3) gave modest yields of chlorofluoromethylene olefins; only cyclic ketones (entry 6) and nonactivated ketones (entry 7) gave poor yields of olefins. The availability and cost of $CFCl_3$ as well as the simplicity and ease of this approach make this route attractive for aldehydes and activated ketones.

Also in Table 9 is summarized the metal dehalogenation of (dichlorofluoromethyl)tris(dimethylamino)-phosphonium chloride with zinc−copper couple. A *stable* olefination solution is produced. Subsequent reaction of this stable olefination solution with aromatic aldehydes (entry 9), activated ketone (entries 8 and 12), aliphatic aldehydes (entry 10), nonactivated ketones (entry 11), and some activated esters (entries 16 and 17) gave excellent yields of chlorofluoromethylene olefins; only benzophenone (entry 14) and cyclopentanone (entry 13) gave low yields. The main value of this method is the capability to pregenerate a stable olefination solution, ease of scale-up, ease of salt preparation, and the reactivity of this olefination solution with a wide variety of carbonyl substrates.

Thus, a variety of methods are available for the preparation of chlorofluoromethylene olefins. The methodology described in Tables 8 and 9 provide the best entry to these olefins. For cyclic ketone derivatives the organomercurial route described in Table 6 appears to be the best entry to chlorofluoromethylene olefin derivatives.

**Table 9. Metal-Assisted Preparation of (Chlorofluoromethylene)olefins**

| Entry | Substrate | $R_3P$ | Fluorochloromethylene Precursor | Metal | Solvent | Temp. | Product (yield)[a] | Ref. |
|---|---|---|---|---|---|---|---|---|
| 1 | $PhC(O)CF_3$ | $Ph_3P$ | $CFCl_3$ | Zn | DMF[b] | 60°C | $PhC(CF_3)=CFCl$ (71%)[a,e] | 56 |
| 2 | $PhC(O)CF_3$ | $Ph_3P$ | $CFCl_3$ | Zn(Cu) | DMF | 60°C | $PhC(CF_3)=CFCl$ (48%)[a] | 56 |
| 3 | $PhC(O)CF_3$ | $Ph_3P$ | $CFCl_3$ | Zn(Hg) | DMF | 60°C | $PhC(CF_3)=CFCl$ (53%)[a] | 56 |
| 4 | PhCHO | $Ph_3P$ | $CFCl_3$ | Zn | DMF | 60°C | PhCH=CFCl (64%)[a,f] | 56 |
| 5 | $C_6H_{13}CHO$ | $Ph_3P$ | $CFCl_3$ | Zn | DMF | 60°C | $C_6H_{13}CH=CFCl$ (49%)[a,g] | 56 |
| 6 |  | $Ph_3P$ | $CFCl_3$ | Zn | DMF | 60°C |  (4%)[a] | 56 |
| 7 | $PhC(O)CH_3$ | $Ph_3P$ | $CFCl_3$ | Zn | DMF | 60°C | $PhC(CH_3)=CFCl$ (17%)[a,h] | 30 |
| 8 | $PhC(O)CF_3$ | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | THF[c] | 60°C | $PhC(CF_3)=CFCl$ (100%)[a,i] | 58 |
| 9 | PhCHO | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | THF | 60°C | PhCH=CFCl (100%)[a,j] | 58 |
| 10 | $C_6H_{13}CHO$ | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | THF | 60°C | $C_6H_{13}CH=CFCl$ (100%)[a,k] | 58 |
| 11 | $PhC(O)CH_3$ | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | THF | 60°C | $PhC(CH_3)=CFCl$ (70%)[a,l] | 58 |
| 12 | $(CF_3)_2CO$ | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | TG[d] | 0°C | $(CF_3)_2C=CFCl$ (75%)[a] | 58 |
| 13 |  | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | THF | 60°C |  (18%)[a] | 58 |
| 14 | $Ph_2C=O$ | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | THF | 60°C | $Ph_2C=CFCl$ (0%)[a] | 58 |
| 15 | $CF_3C(O)OPr^i$ | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | TG | 60°C | $CF_3C(OPr^i)=CFCl$ (51%)[a,m] | 58 |
| 16 | $CF_3C(O)OCH_3$ | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | TG | 60°C | $CF_3C(OCH_3)=CFCl$ (90%)[a,m] | 58 |
| 17 | $CF_2ClC(O)OCH_3$ | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | TG | 60°C | $CF_2ClC(OCH_3)=CFCl$ (71%)[a,m] | 58 |
| 18 | $C_2F_5C(O)OC_2H_5$ | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | TG | 60°C | $C_2F_5C(OC_2H_5)=CFCl$ (22%)[a,m] | 58 |
| 19 | $C_3F_7C(O)OCH_3$ | --- | $[(Me_2N)_3\overset{+}{P}CFCl_2]Cl^-$ | Zn(Cu) | TG | 60°C | $C_3F_7C(OCH_3)=CFCl$ (21%)[a,m] | 58 |

[a] GLPC yield; [b] DMF = N,N-dimethylformamide; [c] THF =  ; [d] TG = triglyme; [e] E/Z 53:47; [f] E/Z 47:53; [g] E/Z 59:41; [h] E/Z 57:43; [i] E/Z 44:56; [j] E/Z 47:53; [k] E/Z 59:41; [l] E/Z 52:48; [m] E/Z < 0.1.

**Table 10. Phosphoranium Salts via Reaction of Fluorotrihalomethanes with Tertiary Phosphines**

| Entry | $R_3P$ | $CFX_3$ | Solvent | Temp. | Product (yield)[a] | Ref. |
|---|---|---|---|---|---|---|
| 1 | $Bu_3P$ | $CFCl_3$ | $CH_2Cl_2$ | <5°C | $[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Cl^-$ (95%) | 32 |
| 2 | $Bu_3P$ | $CFCl_3$ | PhCN | <5°C | $[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Cl^-$ (94%) | 32 |
| 3 | $Bu_3P$ | $CFCl_3$ | $CH_3CN$ | <5°C | $[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Cl^-$ (91%) | 32 |
| 4 | $Bu_3P$ | $CFCl_3$ | dioxane | <5°C | $[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Cl^-$ (90%) | 32 |
| 5 | $Bu_3P$ | $CFCl_3$ | $CH_2Cl_2$ | <5°C | $[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Cl^-$ (85%) | 32 |
| 6 | $Bu_3P$ | $CFBr_3$ | o-$ClC_6H_4CH_3$ | <5°C | $[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Br^-$ (91%) | 32 |
| 7 | $Bu_3P$ | $CFBr_3$ | $CH_2Cl_2$ | RT | $[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Br^-$ (92%) | 32 |
| 8 | $Bu_3P$ | $CFBr_3$ | PhCN | <5°C | $[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Br^-$ (91%) | 32 |
| 9 | $Bu_3P$ | $CFBr_3$ | $CH_3CN$ | <5°C | $[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Cl^-$ (93%) | 32 |
| 10 | $Bu_3P$ | $CFBr_3$ | dioxane | <5°C | $[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Br^-$ (89%) | 32 |
| 11 | $Ph_3P$ | $CFBr_3$ | $CH_2Cl_2$ | <5°C | $[Ph_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Ph_3]Br^-$ (95%) | 32 |

[a] Yield determined by $^{19}F$ NMR

### *7.6. Phosphoranium Salts*

Tables 10 and 11 summarize the preparation of symmetrical and unsymmetrical phosphoranium salts. The availability of $CFCl_3$ and $CFBr_3$ and the high yields obtained in phosphoranium salt preparation make these stable intermediates attractive methodology for olefin or ketone preparation.

Phosphoranium salts react readily with aldehydes but sluggishly or not at all with ketones. With aldehydes (Table 12), the resultant phosphonium salt intermediates are hydrolyzed by aqueous base to give good yields of 1-fluoroalkenes. The overall transformation gives a 1-fluoroolefin that is chain extended by one carbon. The stereochemistry of the resultant olefin depends on the type of aldehyde precursor. With aromatic aldehydes (entries 1−9) the phosphobetaine intermediate is predominantly the (*Z*)-isomer, which gives predominately the (*E*)-1-fluoroalkene on hydrolysis. With aliphatic aldehydes (entries 10−12), the (*E*)-phosphobetaine intermediate is the predominate isomer, which leads to the (*E*)-1-fluoroalkene isomer on base hydrolysis. This route

**Table 11. Preparation of Mixed Phosphoranium Salts**

| Entry | Salt | $R_3P$ | Solvent | Temp. | Product (yield)[a] | Ref. |
|---|---|---|---|---|---|---|
| 1 | $[Ph_3\overset{+}{P}CFBr_2]Br^-$ | $Bu_3P$ | $CH_2Cl_2$ | <5°C | $[Ph_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]Br^-$ (81%) | 32 |
| 2 | $[Ph_3\overset{+}{P}CFBr_2]Br^-$ | $Oct_3P$ | $CH_2Cl_2$ | <5°C | $[Ph_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Oct_3]Br^-$ (60%) | 32 |
| 3 | $[Ph_3\overset{+}{P}CFBr_2]Br^-$ | $Et_3P$ | $CH_2Cl_2$ | <5°C | $[Ph_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Et_3]Br^-$ (60%) | 32 |

[a] Yield determined by $^{19}F$ NMR

**Table 12. Preparation of 1-Fluoroalkenes via Phosphoranium Salts[a]**

$$[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]X^- \xrightarrow{RCHO} [Bu_3\overset{+}{P}CF{=}CHR]X^- \xrightarrow{NaOH\ (aq.)} HCF{=}CHR$$

I II III

| Entry | R | II % | II Z/E | III % | III Z/E | Ref. |
|---|---|---|---|---|---|---|
| 1 | $C_6H_5$ | (80) 56 | 87/13 | (76) 61 | 13/87 | 60 |
| 2 | p-$CH_3C_6H_4$ | (83) | 88/12 | (74) 54 | 12/88 | 60 |
| 3 | p-$CH_3OC_6H_4$ | (96) | 83/17 | (78) 51 | 17/83 | 60 |
| 4 | p-$ClC_6H_4$ | (94) | 79/21 | (81) 60 | 25/75 | 60 |
| 5 | p-$NO_2C_6H_4$ | (75) | 57/43 | | | 60 |
| 6 | m-$CF_3C_6H_4$ | (85) | 75/25 | (73) 57 | 25/75 | 60 |
| 7 | o-$CH_3C_6H_4$ | (90) | 100/0 | 50 | 0/100 | 60 |
| 8 | o-$CH_3OC_6H_4$ | (92) | 77/23 | 54 | 20/80 | 60 |
| 9 | o-$ClC_6H_4$ | (89) | 93/7 | (64) | 5/95 | 60 |
| 10 | $CH_3(CH_2)_5$ | (84) | 3/97 | (71) 51 | 100/0 | 60 |
| 11 | $CH_3(CH_2)_6$ | (82) | 6/94 | (73) 57 | 100/0 | 60 |
| 12 | $C_6H_{11}$ | (85) | 0/100 | (77) 50 | 100/0 | 60 |

Parentheses indicate $^{19}F$ NMR yield *vs.* benzotrifluoride. Z/E ratios were calculated by $^{19}F$ NMR.

[a] Reprinted with permission from *J. Am. Chem. Soc.* **1985**, *107*, 2811.

**Table 13. Preparation of 1-Hydroperfluoroalkenes from Phosphoranium Salts**

$$[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]X^- \xrightarrow{R_FC(O)F} (Z)\text{-}[Bu_3\overset{+}{P}CF{=}CFR_F]X^- \xrightarrow[H_2O]{NaOH} (E)\text{-}CHF{=}CFR_F$$

I[a] II[b] III

| Entry | $R_F$ | II % | III[c], % | Ref. |
|---|---|---|---|---|
| 1 | $CF_3$ | 73 | 45 | 61 |
| 2 | $CF_3CF_2$ | 80 | 62 | 61 |
| 3 | $CF_3CF_2CF_2$ | 82 | 52 | 61 |
| 4 | $CF_2Cl$ | 73 | 50 | 61 |
| 5 | $CH_3O_2CCF_2$ | 70 | 20 | 61 |
| 6 | $CF_3(CF_2)_2OCF(CF_3)$ | 75 | 49 | 61 |

[a] The phosphoranium salt was generated in all but the last case from 0.150 mol of $Bu_3P$ and 0.050 mol of $CFCl_3$. In the $CF_3(CF_2)_2OCF(CF_3)COF$ case, $CFBr_3$ was utilized. [b] $^{19}F$ NMR yield *vs.* $C_6F_6$. [c] Isolated yield of pure olefin.

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provides a useful stereoselective approach to 1-fluoroalkenes.

Phosphoranium salts undergo a Wittig reaction with perfluoroacyl fluorides to give a (*Z*)-vinylphosphonium salt intermediate, which on base hydrolysis gives the (*E*)-1-fluoro-2-(perfluoroalkyl)olefin (Table 13). The overall yields are good in most cases and provide a stereospecific route to these (*E*)-olefins. The (*E*)-olefins are readily metalated, and the resultant metalated derivatives are easily functionalized. Thus, this methodology provides a general route for the introduction of the perfluorinated (*E*)-1-olefinic unit into organic compounds.

**Table 14. Preparation of α,α-Dihalofluoromethyl Perfluoroalkyl Ketones from Phosphoranium Salt Precursors**

$$[Bu_3\overset{+}{P}\overset{-}{C}F\overset{+}{P}Bu_3]X^- \xrightarrow{R_FC(O)Cl} [(Z)\text{-}Bu_3\overset{+}{P}CF{=}C(O^-)R_F] \xrightarrow{X_2} R_FC(O)CFX_2$$

I II

| Entry | $R_F$ | X | Product (yield)[a] | Ref. |
|---|---|---|---|---|
| 1 | $CF_3$ | Cl | $CF_3C(O)CFCl_2$ 68 (41%) | 64 |
| 2 | $CF_2Cl$ | Cl | $CF_2ClC(O)CFCl_2$ 56 (40%) | 64 |
| 3 | $CF_3CF_2$ | Cl | $CF_3CF_2C(O)CFCl_2$ 72 (60%) | 64 |
| 4 | $CF_3(CF_2)_2$ | Cl | $CF_3(CF_2)_2C(O)CFCl_2$ 75 (62%) | 64 |
| 5 | $CF_3(CF_2)_6$ | Cl | $CF_3(CF_2)_6C(O)CFCl_2$ (56%)[b] | 64 |
| 6 | $CF_3$ | Br | $CF_3C(O)CFBr_2$ 68 (42%) | 64 |
| 7 | $CF_2Cl$ | Br | $CF_2ClC(O)CFBr_2$ 60 (30%) | 64 |
| 8 | $CF_3CF_2$ | Br | $CF_3CF_2C(O)CFBr_2$ 77 (52%) | 64 |
| 9 | $CF_3(CF_2)_2$ | Br | $CF_3(CF_2)_2C(O)CFBr_2$ 79 (53%) | 64 |

[a] Yield determined by $^{19}F$ NMR analysis relative to $C_6F_6$; yield in parenthesis is the isolated yield based on acyl chloride; [b] product was not entirely soluble in the reaction mixture and $^{19}F$ NMR yield was not determined.

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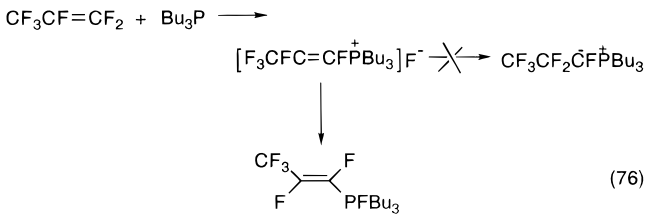
When phosphoranium salts are reacted with perfluoroacyl chlorides, the normal acylation reaction occurs to give the (*Z*)-betaine. Halogenation of the (*Z*)-betaine intermediate with chlorine or bromine gives good yields of the α,α-dihalomethyl perfluoroalkyl ketones (Table 14). For best results, $CFCl_3/Cl_2$ is utilized for the preparation of dichloro ketones and $CFBr_3/Br_2$ is utilized for the corresponding dibromo ketones.

## *III. Fluorinated Alkyl, Alkenyl, and Aryl Ylides*

## 1. Preparation of Fluorinated Alkyl, Alkenyl, and Aryl Ylides

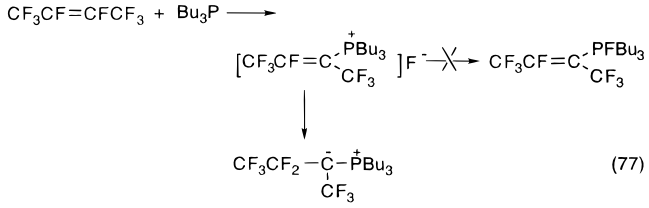
### *1.1. Preparation of Fluorinated Alkyl Ylides*

Phosphines readily reacted with fluorinated olefins due to their strong electrophilic properties. The products formed in these reactions depended upon the structure of the olefins. When tributylphosphine reacted with terminal perfluoroolefins such as hexafluoropropene, 1-perfluoropentene, or 1-perfluoroheptene in ether, fluorinated vinylphosphoranes were obtained in nearly quantitative yields with high or exclusive (*Z*)-stereoselectivity and no F-ylides could be observed (eq 76).[78] However, reaction of 2-perfluorobutene with $Bu_3P$ gave the phosphonium ylide



(76)

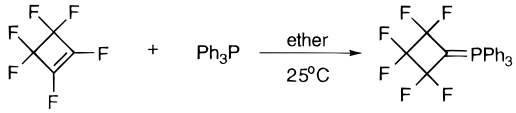
under similar conditions; and no vinylphosphorane was detected (eq 77).[78] Although this ylide has not



(77)

been isolated, the structure of the ylide was determinated by $^{19}F$ NMR spectroscopy and chemical transformations. The different behaviors between terminal and internal perfluoroolefins were ascribed the role of α- and *β*-fluorines. When only *β*-fluorines were present, the initial addition−elimination adduct was converted into the phosphonium ylide. However, when both α- and *β*-fluorines were present, the ylide was either not formed or exhibits a very short lifetime, and the vinylphosphorane became the stable product.

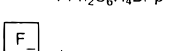
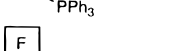
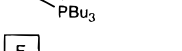
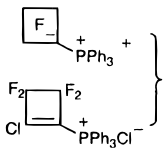
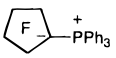
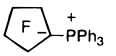
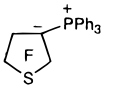
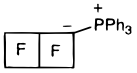
The presence of the perfluoroalkyl group in the α-position was also crucial since a perfluoroalkyl group stabilized an α-carbanion, while fluorine in the α-position destabilized the carbanion. Thus, cyclic perfluoroolefins exhibited behavior similar to that of the internal perfluoroolefins. The reaction of triphenylphosphine with perfluorocyclobutene in ether at 25 °C gave a white powder, which could be isolated as crystals.[79,80] The early report postulated the structure as either a dipolar species which underwent rapid equilibration in solution or a nonclassic structure based on $^{19}F$ NMR data.[79] Later, Burton and co-workers were able to isolate the product and obtained a single crystal by recrystallization from a mixture of THF and ether. X-ray crystallography indicated that the product had an ylide structure in which the phosphorus−ylide carbon bond length was 1.713 Å compared with C═P of 1.665 Å and C−P of 1.828 Å, which indicated a considerable amount of double-bond character formed by the overlap of phosphorus d orbitals with the ylide carbon p orbitals (eq 78 and Table 15).[80]



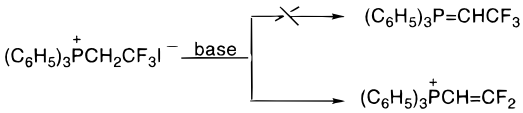
(78)

Unlike hydrocarbon phosphorus ylides, deprotonation of the phosphonium salts is usually unsuitable for the preparation of fluorinated ylides, since phosphines failed to react with fluorinated secondary halides such as $(CF_3)_2CHX$.[81] Although low yields of the phosphonium salt $(Ph_3PCH_2CF_3)X$ were obtained from the photoreaction of triphenylphosphine with $CF_3CH_2X$, no ylide $Ph_3P{=}CHCF_3$ was generated upon

**Table 15. Preparation of Stable Fluorinated Cyclic Ylides**

| Cycloalkane | $R_3P$ | Temp. | Product | Yield(%) | Ref. |
|---|---|---|---|---|---|
|  | p-$CF_3C_6H_4PPh_2$ | RT |  | 83 | 80b |
|  | p-$BrC_6H_4PPh_2$ | 0°C |  | 70 | 80b |
|  | $Ph_3P$ | RT |  | 86 | 80c |
|  | $Bu_3P$ | RT |  | 49 | 80b |
|  | $Bu_3P$ | RT |  | 100 | 80c |
|  | $Ph_3P$ | 0°C |  | 87 | 80c |
|  | $Ph_3P$ | RT |  | 80 | 80b |
|  | $Ph_3P$ | RT |  | 84 | 80c |
|  | $Ph_3P$ | RT |  | 50 | 80c |
|  | $Ph_3P$ | RT |  | 55 | 80c |

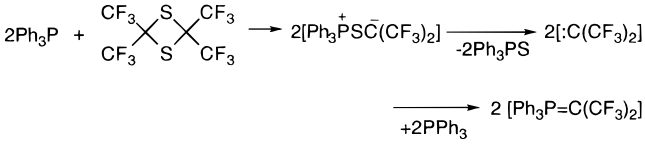
treatment with base. Instead, rapid dehydrofluorination gave a vinylphosphonium salt (eq 79a).[82] *In*



**(79a)**

*situ* generation of ylide $Ph_3P{=}C(CF_3)_2$ could be achieved by reaction of triphenylphosphine with tetrakis(trifluoromethyl)-1,3-dithietane in ether at −78 °C. The mechanism of this reaction may involve bis(trifluoromethyl)carbene intermediate as illustrated in Scheme 36.[83,84]

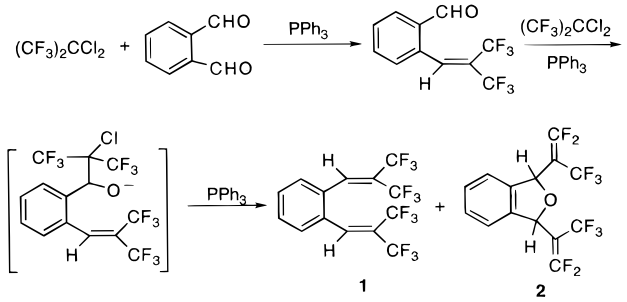
**Scheme 36**



However, the ylide was not prepared by the reaction of triphenylphosphine with bis(trifluoromethyl)-diazirine[85] or bis(trifluoromethyl)diazomethane.[85] Hanack reported that reaction of $(CF_3)_2CCl_2$ with aldehydes in the presence of $Ph_3P$ gave 1,1-bis-(trifluoromethyl)olefins. In the initial paper, he postulated a thermally unstable ylide as an intermediate, although there was no experimental evidence.[87,88] Later, his studies indicated that this conversion occurred not by a Wittig reaction but

rather by a Knoevenagel-type reaction. The anion intermediate, $(CF_3)_2CCl^-$, could be trapped by a carbonyl group to give compounds **1** and **2** (Scheme 37).[89]

**Scheme 37**

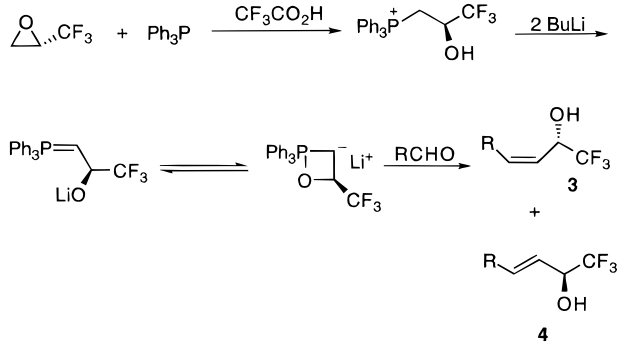


Although $Ph_3P$ failed to react with $R_FCH_2X$, it reacted smoothly with $R_FCH_2CH_2I$. When $Ph_3P$ was heated with $R_FCH_2CH_2I$ at 95 °C in the absence of a solvent, 60−85% of the corresponding salt was obtained. The salt was further treated with BuLi to afford the ylide $Ph_3P{=}CHCH_2R_F$ (eq 79b).[90,91]

$$Ph_3P + R_FCH_2CH_2I \longrightarrow R_FCH_2CH_2PPh_3I \xrightarrow{\text{Base}} R_FCH_2CH{=}PPh_3 \quad \textbf{(79b)}$$

A fluorinated epoxide was also employed as a precursor to prepare an ylide. Triphenylphosphine reacted with 3,3,3-trifluoropropylene oxide in the presence of trifluoroacetic acid in $CH_2Cl_2$ to give the phosphonium salt. When treated with BuLi, the salt gave no trifluoropropene. Instead, oxaphosphetane and ylide were formed, which could subsequently be trapped by aldehydes to give allylic alcohols (Scheme 38).[92]

**Scheme 38**



### *1.2. Preparation of Fluorinated Alkenyl Ylides*

Fluorinated alkenyl ylides were obtained by either reaction of $Ph_3P$ with fluorinated allyl halides or reaction of hydrocarbon ylides with fluorinated olefins. When $Ph_3P$ was treated with $CH_2{=}CHCF_2Br$, the phosphine regiospecifically attacked the $CH_2$ terminus of $CH_2{=}CHCF_2Br$ to give the 3,3-difluoroallylic phosphoniun salt, which on treatment with $K_2CO_3$ formed the alkenyl ylide. Although the ylide could not be isolated or detected, it could be trapped by aryl aldehydes to produce the corresponding dienes in moderate yields (eq 80).[93]

$$Ph_3P + CH_2{=}CHCF_2Br \longrightarrow [Ph_3\overset{+}{P}CH_2CH{=}CF_2]Br^- \xrightarrow[K_2CO_3]{ArCHO} ArCH{=}CHCH{=}CF_2 \quad (80)$$

5-44%

Ylides such as $Ph_3P{=}CMe_2$ also reacted cleanly with chlorotrifluoroethylene to give allylic phosphonium salts (eq 81).[94] The transylidation process is precluded since there is no acidic hydrogen. However, reaction of $Ph_3P{=}CHCH_3$ with 2-phenylperfluoropropene gave fluorinated alkenyl ylide **5** which was formed via a transylidation reaction with the initial ylide reactant. The alkenyl ylide, however, was not stable and further $\beta$-eliminated fluoride ion to give an allenic phosphonium salt **6** (eq 82).[94]

$$Ph_3P{=}CMe_2 + CF_2{=}CFCl \longrightarrow \underset{F}{\overset{Cl}{}}\!\!>\!C{=}C\!<\!\underset{CMe_2\overset{+}{P}Ph_3F^-}{\overset{F}{}} \quad (81)$$

$$Ph_3P{=}CHMe + CF_2{=}C(CF_3)Ph \longrightarrow \left[\, Ph_3P{=}\underset{MeF}{C}{-}C{=}C(CF_3)Ph \,\right] \quad \textbf{5}$$

$$\longrightarrow \left[ Ph_3\overset{+}{P}\!\!>\!\underset{Me}{C}{=}C{=}C(CF_3)Ph \right]F^- \quad \textbf{6} \quad (82)$$

An elegant method for the preparation of fluorinated vinyl ylides was developed by Birum and Matthews, who used hexaphenylcarbodiphosphorane as an ylide synthon.[95] When hexafluoroacetone was added to a solution of $Ph_3P{=}C{=}PPh_3$ in diglyme at 40−50 °C, a stable adduct 4,4-bis(trifluoromethyl)-1,2-oxaphosphetane was isolated and characterized by X-ray diffraction. Heating of the adduct in chlorobenzene at 120−125 °C for 5−10 min gave the (2,2-trifluoromethyl)vinylidene(triphenyl)phosphorane and triphenylphosphine oxide (eq 83).[95] Due to the high

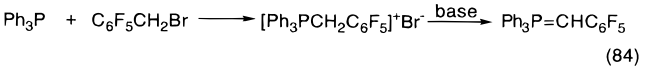
$$Ph_3P{=}C{=}PPh_3 + (CF_3)_2CO \longrightarrow \left[ Ph_3P\!<\!\underset{CF_3}{\overset{O}{}}\!\!>\!\underset{CF_3}{\overset{PPh_3}{}} \right] \longrightarrow Ph_3P{=}C{=}C(CF_3)_2 \quad (83)$$

reactivity of the ylide and the similar solubility with triphenylphosphine oxide, it was very difficult to isolate the pure ylide. However, the mixture could be used for the synthesis of derivatives, since $Ph_3PO$ did not interfere with other reactions.

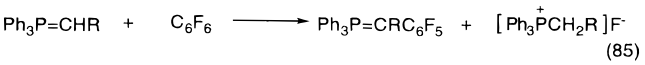
### *1.3. Preparation of Fluorinated Aryl Ylides*

Preparation of fluoroaryl ylides was achieved by two main methods. First, direct reaction of phosphines with pentafluorobenzyl bromide gave the corresponding salts, which were treated with a base to afford the ylide. Secondly, the hydrocarbon phosphorus ylide reagents reacted with fluorinated aromatics to give the fluorinated aryl ylides. In the first method, phosphines such as triphenylphosphine reacted smoothly with pentafluorobenzyl bromide in refluxing benzene to give greater than 95% yields of the corresponding salts, which could be further

purified by recrystallization. Treatment of the salt with BuLi in benzene produced orange-yellow ylide solution, which could be used for functionalization reactions without isolation or purification (eq 84).[96,97] In the latter case, 2 equiv of the phosphorus ylide reacted with hexafluorobenzene or chloropentafluorobenzene to give the fluorinated aryl ylides (eq 85).[98−101] The first equivalent of ylide as a nucleophile attacked the fluorinated benzene to give a phosphonium salt, which underwent a transylidation reaction with additional ylide to afford the fluoroaryl ylide. The transylidation reaction occurred due to greater acidity of the formed fluorinated phosphorus ylide.

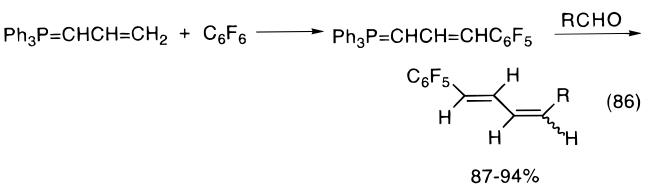


(84)



(85)

When triphenylallylphosphorane was treated with hexafluorobenzene, the $\gamma$-carbon of the allyl group in the ylide attacked the perfluorobenzene exclusively. The resultant ylide could be used to prepare 1-perfluorophenyl-1,3-dienes (eq 86).[102]

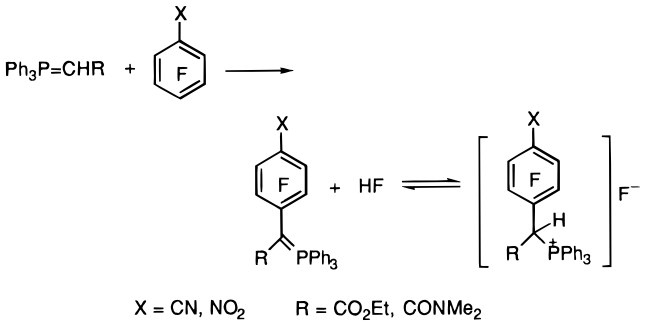


(86)

87-94%

Stabilized ylides such as $Ph_3P{=}CHCOX$ (X = OMe, OEt, $NMe_2$) or $Tol_3P{=}CH(Py\text{-}2)$ readily reacted with activated polyfluorobenzenes $C_6F_5Y$ (Y = $NO_2$, CN) in ether at room temperature.[103,104] Like other nucleophilic displacement reaction of substituted polyfluorobenzenes, the ylides exclusively attacked the *para*-position of the substituted polyfluorobenzenes. Due to connection with two strong electron-withdrawing groups, the phosphonium salts had a strong acidic character and existed in an equilibrium between the ylides and the salts (Scheme 39). When X = $NO_2$, the pure ylide could be isolated from the reaction mixture by removal of HF upon concentration (Scheme 39). Although a mixture was formed when Y = CN, the pure ylide and the phosphonium salt could be obtained by treatment with $Na_2CO_3$ and $HClO_4$, respectively. The X-ray crystal structure of $Ph_3P{=}C(CO_2Et)C_6F_4CN$ indicated that the phosphorus−carbon bond length was 1.722 Å, which is shorter than the standard $C_{sp2}$(Ar−P) bond distance [1.793 Å], but longer than in noncarbonyl ylides such as $Ph_3P{=}CH_2$ [1.697 Å].

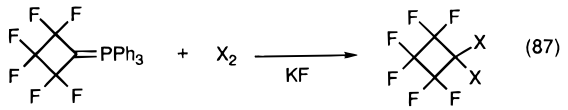
**Scheme 39**



X = CN, $NO_2$ R = $CO_2Et$, $CONMe_2$

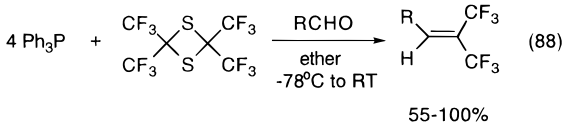
## 2. Application of Fluorinated Alkyl, Alkenyl, and Aryl Ylides

Pregenerated perfluorocyclic ylides were unreactive with carbonyl compounds, but they reacted with halogens such as iodine, bromine, and chlorine to give *gem*-dihalides (eq 87).[105]



(87)

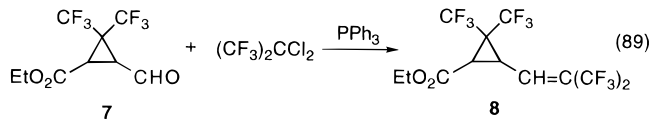
$Ph_3P{=}C(CF_3)_2$, prepared from reaction of $Ph_3P$ with tetrakis(trifluoromethyl)-1,3-dithietane, reacted *in situ* under mild conditions with a variety of aliphatic, aromatic, and heterocyclic aldehydes to form the corresponding olefins as shown in eq 88 and Table 16.[83,84]



(88)

55-100%

The ylide failed to react with ketones due to low reactivity of the ketones and instability of the ylide. Although $(CF_3)_2CCl_2/PPh_3$ did not form a ylide intermediate, the reaction with carbonyl compounds could give fluorinated olefins. When $(CF_3)_2CCl_2/PPh_3$ was treated with aldehydes in $CH_2Cl_2$ at low temperature, the corresponding 1,1-bis(trifluoromethyl)olefins were obtained in modest to good yields (eq 89 and Table 16).[88] Ketones reacted with $(CF_3)_2CCl_2/PPh_3$ to give olefins only when they were activated by a trifluoromethyl group (entries 12−15 in Table 16).[87−89] The byproduct in the reaction was $Ph_3PCl_2$, which could react with carbonyl compounds to give *gem*-dichloro compounds in some cases. However, the side reaction could be suppressed when the olefinations were carried out at low temperatures.



(89)

7 8

The ylides, $R_FCH_2CH{=}PPh_3$, reacted with aliphatic and aromatic adehydes to give olefins in moderate to good yields. The ylides were usually generated by treatment of their salts with a base. The use of BuLi or $K_2CO_3$ does not affect the stereoselectivity and (*Z*)-isomers were the major products (*Z*/*E* = 70/30) (eq

**Table 16. Preparation of 1,1-Bis(trifluoromethyl)-Substituted Olefins**

| Substrate | Trimethylfluoro Source | Solvent | Temp. | Product | Yield(%) | Ref. |
|---|---|---|---|---|---|---|
| EtCHO | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | $EtCH=C(CF_3)_2$ | 31 | 87 |
| PrCHO | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | $PrCH=C(CF_3)_2$ | 22 | 87 |
| p-$ClC_6H_4CHO$ | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | p-$ClC_6H_4CH=C(CF_3)_2$ | 88 | 87 |
| p-$MeOC_6H_4CHO$ | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | p-$MeOC_6H_4CH=C(CF_3)_2$ | 27 | 87 |
| c-$C_6H_{11}CHO$ | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | c-$C_6H_{11}CH=C(CF_3)_2$ | 4 | 87 |
| 2-thiophenecarboxaldehyde | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | 2-thienyl-$CH=C(CF_3)_2$ | 37 | 87 |
| $Cl_2C=CHCHO$ | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | $Cl_2C=CHCH=C(CF_3)_2$ | 83 | 87 |
| $Me_2CHCHClCHO$ | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | $Me_2CHCHClCH=C(CF_3)_2$ | 62 | 87 |
| PhCHO | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | $PhCH=C(CF_3)_2$ | 54 | 87 |
| p-$OHCC_6H_4CHO$ | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | p-$(CF_3)_2C=CHC_6H_4CH=C(CF_3)_2$ | 50 | 87 |
| o-$OHCC_6H_4CHO$ | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | o-$(CF_3)_2C=CHC_6H_4CH=C(CF_3)_2$ | 10 | 87 |
| $PhCOCF_3$ | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | $PhC(CF_3)=C(CF_3)_2$ | 9 | 89 |
| $(CF_3)_2CO$ | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | $(CF_3)_2C=C(CF_3)_2$ | 35 | 89 |
| $CF_3COCH_3$ | $CF_3CCl_2CF_3$ | $CH_2Cl_2$ | ≤50°C | $CF_3CMe=C(CF_3)_2$ | 77 | 89 |
| PhCHO | dithietane | $Et_2O$ | -78°C to RT | $PhCH=C(CF_3)_2$ | 50 | 83 |
| o-$ClC_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | o-$ClC_6H_4CH=C(CF_3)_2$ | 45 | 84 |
| p-$MeC_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | p-$MeC_6H_4CH=C(CF_3)_2$ | 42 | 83 |
| p-$MeOC_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | p-$MeOC_6H_4CH=C(CF_3)_2$ | 40 | 83 |
| m-$CF_3C_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | m-$CF_3C_6H_4CH=C(CF_3)_2$ | 64 | 83 |
| p-$NCC_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | p-$NCC_6H_4CH=C(CF_3)_2$ | 80 | 84 |
| o-$O_2NC_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | o-$O_2NC_6H_4CH=C(CF_3)_2$ | 48 | 83 |
| m-$O_2NC_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | m-$O_2NC_6H_4CH=C(CF_3)_2$ | 46 | 84 |
| p-$O_2NC_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | p-$O_2NC_6H_4CH=C(CF_3)_2$ | 44 | 84 |
| p-$Me_2NC_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | p-$Me_2NC_6H_4CH=C(CF_3)_2$ | 27 | 84 |
| o-$OHCC_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | p-$OHCC_6H_4CH=C(CF_3)_2$ | 41 | 84 |
| $C_6F_5CHO$ | dithietane | $Et_2O$ | -78°C to RT | $C_6F_5CH=C(CF_3)_2$ | 62 | 83 |
| 2-pyridinecarboxaldehyde | dithietane | $Et_2O$ | -78°C to RT | 2-pyridyl$CH=C(CF_3)_2$ | 42 | 83 |
| $PhCHMe_2CHO$ | dithietane | $Et_2O$ | -78°C to RT | $PhCHMeCH=C(CF_3)_2$ | 26 | 84 |
| $C_6H_{13}CHO$ | dithietane | $Et_2O$ | -78°C to RT | $C_6H_{13}CH=C(CF_3)_2$ | 38 | 84 |
| PhCH=CHCHO | dithietane | $Et_2O$ | -78°C to RT | $PhCH=CHCH=C(CF_3)_2$ | 57 | 83 |
| 2-thiophenecarboxaldehyde | dithietane | $Et_2O$ | -78°C to RT | 2-thienyl$CH=C(CF_3)_2$ | 31 | 84 |
| MeCH=CHCHO | dithietane | $Et_2O$ | -78°C to RT | $MeCH=CHCH=C(CF_3)_2$ | 15 | 84 |
| o-$OHCC_6H_4CHO$ | dithietane | $Et_2O$ | -78°C to RT | o-$(CF_3)_2C=CHC_6H_4CH=C(CF_3)_2$ | 33 | 84 |
| $HCO_2Me$ | dithietane | $Et_2O$ | -78°C to RT | $MeOCH=C(CF_3)_2$ | 0 | 84 |

90).[90,91] However, when a mixture of $NaNH_2$ and $Bu^t$-

$$(C_6H_5)_3\overset{+}{P}CH_2CH_2R_F\,I^- + RCHO \xrightarrow{K_2CO_3} R_FCH_2CH{=}CHR \quad (90)$$

Z/E = 70/30

$R_F = C_8F_{17}$, R = $C_4H_9$: 55%
$R_F = C_6F_{13}$, R = $C_4H_9$: 35%
$R_F = C_4F_9$, R = $C_4H_9$: 23%
$R_F = C_4F_9$, R = $C_6H_{13}$: 30%
$R_F = C_4F_9$, R = $C_8H_{17}$: 60%

OK was employed as a base, $[CF_3CH_2CH_2PPh_3]^+I^-$ reacted with aliphatic aldehydes to give the (*Z*)-olefin exclusively.[106]

Fluorinated vinyl ylide $Ph_3P{=}C{=}C(CF_3)_2$ reacted with acids to give the corresponding phosphonium salts. When treated with alcohols, thiophenol, or amines, displacement reactions occurred to give vinyl ethers, vinyl sulfides and enamines, respectively. The dimer of bis(trifluoromethyl)thioketene was obtained from the reaction of the ylide with sulfur. A Wittig reaction with diphenylketene proceeded smoothly to give fluorinated cumulene as illustrated in Scheme 40.[95]

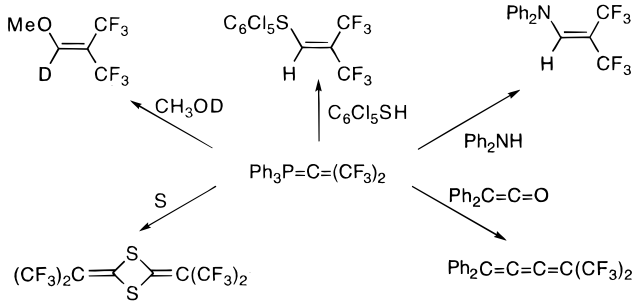
The fluorinated aryl ylides have also proved useful as reagents for the preparation of fluoroaryl-containing compounds. The ylides were ozonolyzed to give fluoroaryl ketones in good yields (eq 91).[101]

$$Ph_3P{=}C(R)C_6F_4X\text{-}p + O_3 \longrightarrow p\text{-}XC_6F_4COR \quad (91)$$

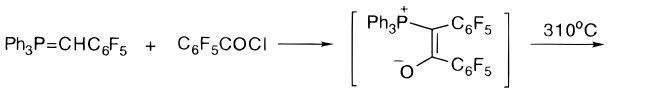
X = F, Cl; R = $C_nH_{2n+1}$ (n = 3,4,5,7) 46-60%

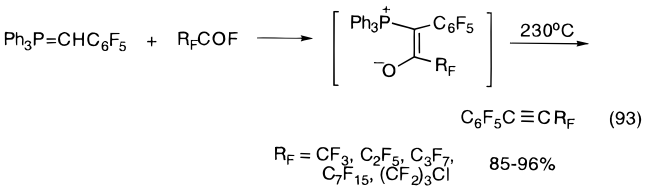
The ylides also underwent nucleophilic attack on the carbonyl group of perfluoroalkyl or perfluoroaryl

**Scheme 40**



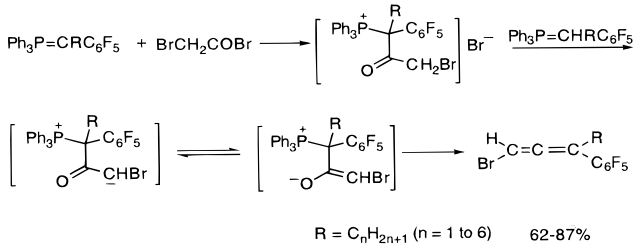

anhydrides and acyl halides in ether at −78 °C to room temperature to produce the corresponding phosphoranes, which could be isolated and pyrolyzed in vacuum at 230−310 °C to give fluorinated acetylenes in good yields (eqs 92 and 93).[98,99] With




α-bromoacetyl bromide, 1-(fluorophenyl)-3-bromoallenes were obtained (Scheme 41).[100]

**Scheme 41**

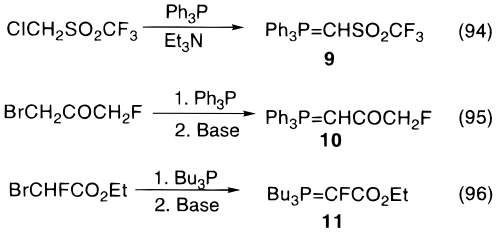



## *IV. Fluorine-Containing Stabilized Phosphonium Ylides*

## 1. Preparation

### *1.1. Preparation via Salt Method*

Deprotonation of phosphonium salts, generated from quaternization of phosphines with fluorine-containing halides, gave rise to the corresponding phosphonium ylides. Thus, ylides **9**,[107] **10**,[108] and **11**[109] have been successfully prepared by this method (eqs 94−96).




### *1.2. Transylidation*

Transylidation is a method in which an existing ylide is treated with an electrophile to form a new ylide. Usually the reactant ylide is easily prepared and the product ylide is more complex. For the preparation of fluorine-containing stabilized phosphonium ylides, the starting ylide could be either fluorinated or nonfluorinated and the electrophiles usually were fluorinated compounds such as fluorinated esters,[110−112] acid halides,[111,113−120] anhydrides,[121−124] aromatics,[122] olefins,[125] epoxides,[126] or ketophosphonium salts.[123,127] This strategy is illustrated in eq 97, and the results are summarized in Table 17. In these reactions, the reactant ylide **12** underwent an addition−elimination process with

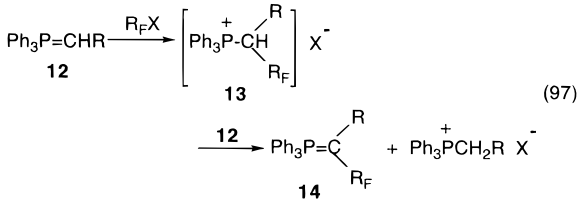


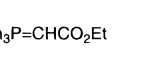
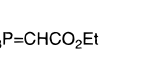
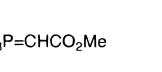
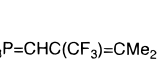
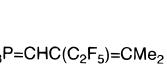

**Table 17. Formation of Fluorinated Ylides vis Transylidation**

| $Ph_3P$=CHR | R'X | Product | Yield | ref. | $Ph_3P$=CHR | R'X | Product | Yield | ref. |
|---|---|---|---|---|---|---|---|---|---|
| $Ph_3P$=$CHC_6F_5$ | $C_6F_5COCl$ | $Ph_3P$=C(COC$_6F_5$)($C_6F_5$) | 74 | 113 | $Ph_3P$=CHOPh | $C_2F_5COCl$ | $Ph_3P$=C(COC$_2F_5$)(OPh) | 74 | 118 |
| | $C_6H_5COCl$ | $Ph_3P$=C(COC$_6H_5$)($C_6F_5$) | 86 | 113 | | $C_3F_7COCl$ | $Ph_3P$=C(COC$_3F_7$)(OPh) | 72 | 118 |
| $Ph_3P$=$CHCO_2CH_3$ | $CF_3COCl$ | $Ph_3P$=C(COCF$_3$)($CO_2CH_3$) | 73 | 114a | | $C_3F_7OCF(CF_3)COCl$ | $Ph_3P$=C(COCF(CF$_3$)OC$_3F_7$)(OPh) | 62 | 118 |
| | $C_3F_7COCl$ | $Ph_3P$=C(COC$_3F_7$)($CO_2CH_3$) | 61 | 114a | $Ph_3P$=$CHOC_6H_4Cl$-4 | $C_2F_5COCl$ | $Ph_3P$=C(COC$_2F_5$)($OC_6H_4Cl$-4) | 72 | 118 |
| $Ph_3P$=$CHCO_2CH(Me)Et$ | $CF_3COCl$ | $Ph_3P$=C(COC$_3F_7$)($CO_2CH(Me)Et$) | 64 | 114b | | $C_3F_7COCl$ | $Ph_3P$=C(COC$_3F_7$)($OC_6H_4Cl$-4) | 78 | 118 |
| $Ph_3P$=CHCOPh | $CF_3COCl$ | $Ph_3P$=C(COCF$_3$)(COPh) | 91 | 116a | | $C_3F_7OCF(CF_3)COCl$ | $Ph_3P$=C(COCF(CF$_3$)OC$_3F_7$)($OC_6H_4Cl$-4) | 65 | 118 |
| | $C_3F_7COCl$ | $Ph_3P$=C(COC$_3F_7$)(COPh) | 95 | 116a | $Ph_3P$=$CHCOSCH_3$ | $C_2F_5COCl$ | $Ph_3P$=C(COC$_2F_5$)($COSCH_3$) | 97 | 119 |
| $Ph_3P$=$CHCOC_6H_4OMe$-4 | $CF_3COCl$ | $Ph_3P$=C(COCF$_3$)($COC_6H_4OMe$-4) | 73 | 116a | | $C_3F_7COCl$ | $Ph_3P$=C(COC$_3F_7$)($COSCH_3$) | 90 | 119 |
| | $C_3F_7COCl$ | $Ph_3P$=C(COC$_3F_7$)($COC_6H_4OMe$-4) | 68 | 116a | | $Cl(CF_2)_3COCl$ | $Ph_3P$=C(CO(CF$_2$)$_3$Cl)($COSCH_3$) | 80 | 119 |

**Table 17 (Continued)**

| $Ph_3P=CHR$ | R'X | Product | Yield | ref. |
|---|---|---|---|---|
| $Ph_3P=CHCN$ | $CF_3COCl$ | $Ph_3P=C(CN)(COCF_3)$ | 85 | 115a |
| | $C_2F_5COCl$ | $Ph_3P=C(CN)(COC_2F_5)$ | 82 | 115a |
| | $C_3F_7COCl$ | $Ph_3P=C(CN)(COC_3F_7)$ | 90 | 115a |
| | $ClCF_2COCl$ | $Ph_3P=C(CN)(COCF_2Cl)$ | 85 | 115b |
| | $Cl(CF_2)_3COCl$ | $Ph_3P=C(CN)(CO(CF_2)_3Cl)$ | 91 | 115b |
| | $Cl(CF_2)_5COCl$ | $Ph_3P=C(CN)(CO(CF_2)_5Cl)$ | 90 | 115b |
| | $C_3F_7OCF(CF_3)COCl$ | $Ph_3P=C(CN)(COCF(CF_3)OC_3F_7)$ | 77 | 115b |
| $Ph_3P=CH_2$ | $CF_3CO_2Et$ | $Ph_3P=CHCOCF_3$ | 75<br>81 | 111<br>112 |
| | $C_2F_5CO_2Et$ | $Ph_3P=CHCOC_2F_5$ | 76<br>84 | 111<br>112 |
| | $C_3F_7CO_2Et$ | $Ph_3P=CHCOC_3F_7$ | 76<br>81 | 111<br>112 |
| | $C_7F_{15}CO_2Et$ | $Ph_3P=CHCOC_7F_{15}$ | 70 | 111 |
| $Ph_3P=CHCOCF_3$ | $CF_3COCl$ | $Ph_3P=C(COCF_3)_2$ | 96 | 111 |
| $Ph_3P=CHCOC_2F_5$ | $C_2F_5COCl$ | $Ph_3P=C(COC_2F_5)_2$ | 93 | 111 |
| $Ph_3P=CHCOC_3F_7$ | $C_3F_7COCl$ | $Ph_3P=C(COC_3F_7)_2$ | 85 | 111 |
| $Ph_3P=CHCOC_7F_{15}$ | $C_7F_{15}COCl$ | $Ph_3P=C(COC_7F_{15})_2$ | 58 | 111 |
| $Ph_3P=CHP(O)(OPh)_2$ | $CF_3COCl$ | $Ph_3P=C(COCF_3)P(O)(OPh)_2$ | 80 | 117 |
| | $C_2F_5COCl$ | $Ph_3P=C(COC_2F_5)P(O)(OPh)_2$ | 60 | 117 |
| | $C_3F_7COCl$ | $Ph_3P=C(COC_3F_7)P(O)(OPh)_2$ | 98 | 117 |
| $Ph_3P=CHCHO$ | $CF_3COCl$ | $Ph_3P=C(COCF_3)CHO$ | 84 | 116b |
| | $C_2F_5COCl$ | $Ph_3P=C(COC_2F_5)CHO$ | 65 | 116b |
| | $C_3F_7COCl$ | $Ph_3P=C(COC_3F_7)CHO$ | 80 | 116b |
| $Ph_3P=CHSePh$ | $CF_3COCl$ | $Ph_3P=C(COCF_3)SePh$ | 46 | 121 |
| $Ph_3P=CHCONEt_2$ | $CF_3COCl$ | $Ph_3P=C(COCF_3)CONEt_2$ | 87 | 124 |
| | $C_3F_7COCl$ | $Ph_3P=C(COC_3F_7)CONEt_2$ | 77 | 124 |
| $Ph_3P=CHCONHBu$ | $CF_3COCl$ | $Ph_3P=C(COCF_3)CONHBu$ | 87 | 124 |
| | $C_3F_7COCl$ | $Ph_3P=C(COC_3F_7)CONHBu$ | 63 | 124 |
| $Ph_3P=CHCON$(cyclohexyl) | $CF_3COCl$ | $Ph_3P=C(COCF_3)CON$(cyclohexyl) | 85 | 124 |
| | $C_3F_7COCl$ | $Ph_3P=C(COC_3F_7)CON$(cyclohexyl) | 80 | 124 |
| $Ph_3P=CHCO_2Me$ | $C_6F_5CN$ | $Ph_3P=C(C_6F_4CN\text{-}4)CO_2Me$ | 61 | 163 |
| $Ph_3P=CHCO_2Me$ | $Cl(CF_2)_5COCl$ | $Ph_3P=C(CO(CF_2)_5Cl)COSCH_3$ | 90 | 119 |
| | $C_7F_{15}COCl$ | $Ph_3P=C(COC_7F_{15})COSCH_3$ | 91 | 119 |
| | $C_3F_7OCF(CF_3)COCl$ | $Ph_3P=C(COCF(CF_3)OC_3F_7)COSCH_3$ | 81 | 119 |
| $Ph_3P=CHC_6F_5$ | $CF_3COCl$ | $Ph_3P=C(COCF_3)C_6F_5$ | 83 | 122 |
| | $C_2F_5COCl$ | $Ph_3P=C(COC_2F_5)C_6F_5$ | 77 | 122 |
| | $C_3F_7COCl$ | $Ph_3P=C(COC_3F_7)C_6F_5$ | 65 | 122 |
| $Ph_3P=CH$-(2-thienyl) | $CF_3COCl$ | $Ph_3P=C(2\text{-thienyl})COCF_3$ | 82 | 120 |
| | $C_2F_5COCl$ | $Ph_3P=C(2\text{-thienyl})COC_2F_5$ | 88 | 120 |
| | $C_3F_7COCl$ | $Ph_3P=C(2\text{-thienyl})COC_3F_7$ | 90 | 120 |
| | $Cl(CF_2)_3COCl$ | $Ph_3P=C(2\text{-thienyl})CO(CF_2)_3Cl$ | 94 | 120 |
| | $C_3F_7OCF(CF_3)COCl$ | $Ph_3P=C(2\text{-thienyl})COCF(CF_3)OC_3F_7$ | 84 | 120 |
| $Ph_3P=CHCO_2Et$ | $C_2F_5CH_2CH_2I$ | $Ph_3P=C(CO_2Et)CH_2CH_2C_2F_5$ | 40 | 166 |
| | $C_4F_9NCS$ | $Ph_3P=C(CO_2Et)C(S)NHC_2H_4C_4F_9$ | 75 | 167 |
| | $C_6F_{13}NCS$ | $Ph_3P=C(CO_2Et)C(S)NHC_2H_4C_6F_{13}$ | 76 | 167 |
| | $C_8F_{17}NCS$ | $Ph_3P=C(CO_2Et)C(S)NHC_2H_4C_8F_{17}$ | 87 | 167 |
| $Ph_3P=CHC_6F_5$ | $C_7F_{15}COCl$ | $Ph_3P=C(COC_7F_{15})C_6F_5$ | 75 | 122 |
| | $Cl(CF_2)_3COCl$ | $Ph_3P=C(CO(CF_2)_3Cl)C_6F_5$ | 51 | 122 |
| | $Cl(CF_2)_5COCl$ | $Ph_3P=C(CO(CF_2)_5Cl)C_6F_5$ | 71 | 122 |
| $Ph_3P=CHC(C_3F_7)=CMe_2$ | $(C_3F_7CO)_2O$ | $Ph_3P=C(COC_3F_7)C(C_3F_7)=CMe_2$ | 48 | 123 |
| $Ph_3P=CHC(CF_3)=C$(cyclopentyl) | $(CF_3CO)_2O$ | $Ph_3P=C(COCF_3)C(CF_3)=C$(cyclopentyl) | 50 | 123 |
| $Ph_3P=CHC(C_2F_5)=C$(cyclopentyl) | $(C_2F_5CO)_2O$ | $Ph_3P=C(COC_2F_5)C(C_2F_5)=C$(cyclopentyl) | 52 | 123 |
| $Ph_3P=CHC(C_2F_5)=C$(cyclopentyl) | $(C_3F_7CO)_2O$ | $Ph_3P=C(COC_3F_7)C(C_3F_7)=C$(cyclopentyl) | 58 | 123 |
| $Ph_3P=CHC(CF_3)=C$(cyclohexyl) | $(CF_3CO)_2O$ | $Ph_3P=C(COCF_3)C(CF_3)=C$(cyclohexyl) | 42 | 123 |
| $Ph_3P=CHCO_2Et$ | $(CF_3CO)_2O$ | $Ph_3P=C(COCF_3)CO_2Et$ | 86[a]<br>89-93[a] | 128a<br>128b |

**Table 17 (Continued)**

| $Ph_3P$=CHR | R'X | Product | Yield | ref. |
|---|---|---|---|---|
| $Ph_3P$=$CHCO_2Et$ | $C_6F_5NO_2$ |  | 74 | 163 |
| $Ph_3P$=$CHCONMe_2$ | $C_6F_5CN$ |  | 72 | 163 |
| | $C_6F_5NO_2$ |  | 78 | 163 |
| $Ph_3P$=$CHCO_2Et$ | $C_6F_5CN$ |  | 88 | 163 |
| $Ph_3P$=$CHCO_2Me$ | $C_6F_5NO_2$ |  | 60 | 163 |
| $Ph_3P$=$CHC(CF_3)$=$CMe_2$ | $(CF_3CO)_2O$ |  | 44 | 123 |
| $Ph_3P$=$CHC(C_2F_5)$=$CMe_2$ | $(C_2F_5CO)_2O$ |  | 52 | 123 |
| $Ph_3P$=$CHC(C_2F_5)$=$CMe_2$ | $(C_2F_5CO)_2O$ |  | 69[a] | 128a |
| | $(HCF_2CO)_2O$ |  | 77[a] | 128a |
| | $(Cl_2CFCO)_2O$ |  | 52[a] | 128a |
| $Ph_3P$=$CHCO_2Me$ | $(ClCF_2CO)_2O$ |  | 93[a] | 128a |
| $Ph_3P$=$CHCOBz$ | $(CF_3CO)_2O$ |  | 98[a] | 128a |
| $Ph_3P$=$CHCO_2Bu$-t | $(CF_3CO)_2O$ |  | 69[a] | 128a |

a. By modified method using $Et_3N$ as an acid scavenger.

**Table 18. Reaction of Ylide with Fluorinated Alkynes**

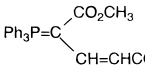
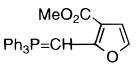
| $Ph_3P$=CHR | Alkyne | Conditions | Product ratio **21:22:23** | Yield (%) | ref. |
|---|---|---|---|---|---|
| $Ph_3P$=$CHCO_2CH_3$ | $CF_3C{\equiv}CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 98 | 130 |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 97 | 130 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 99 | 130 |
| $Ph_3P$=$CHCOCH_3$ | $CF_3C{\equiv}CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 95 | 131 |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 91 | 131 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 90 | 131 |
| $Ph_3P$=$CHCOPh$ | $CF_3C{\equiv}CCO_2CH_3$ | $C_6H_6$/RT | 95:0:5 | 94 | 134 |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | $C_6H_6$/RT | 81:0:19 | 96 | 134 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $C_6H_6$/RT | 78:0:22 | 93 | 134 |
| $Ph_3P$=$CHCOCH_3$ | $CF_3C{\equiv}CCO_2CH_3$ | DMF/RT | 100:0:0 | 98 | 168 |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | DMF/RT | 100:0:0 | 98 | 168 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | DMF/RT | 100:0:0 | 98 | 168 |
| $Ph_3P$=$CHC_6H_4NO_2$-4 | $CF_3C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 41:59:0 | 93 | 170 |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 48:52:0 | 100 | 170 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 42:58:0 | 98 | 170 |
| $Ph_3P$=$CHCOPh$ | $C_2F_5C{\equiv}CCN$ | $CH_2Cl_2$/RT | 100:0:0 | 98 | 135 |
| | $C_3F_7C{\equiv}CCN$ | $CH_2Cl_2$/RT | 100:0:0 | 96 | 135 |
| | $C_2F_5C{\equiv}CCN$ | $CH_2Cl_2$/-78°C | 0:100:0 | 52 | 135 |
| | $C_3F_7C{\equiv}CCN$ | $CH_2Cl_2$/-78°C | 0:100:0 | 55 | 135 |
| $Ph_3P$=$CHCH$=$CHCO_2CH_3$ | $CF_3C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 94 | 132 |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 96 | 132 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 97 | 132 |
| $Ph_3P$=$CHC_6H_4CO_2CH_3$-2 | $CF_3C{\equiv}CCO_2CH_3$ | DME/RT | a | 94 | 133b |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | DME/RT | a | 100 | 133b |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | DME/RT | a | 97 | 133b |
| $Ph_3P$=$CHC_6H_4CO_2Et$-2 | $CF_3C{\equiv}CCO_2CH_3$ | DME/RT | a | 98 | 133a |
|  | $CF_3C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 92 | 140 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 97 | 140 |
| $Ph_3P$=CHCN | $CF_3C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/-78°C | 60:40:0 | 91 | 171 |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/-78°C | 57:43:0 | 90 | 171 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/-78°C | 52:48:0 | 90 | 171 |
|  | $CF_3C{\equiv}CCO_2CH_3$ | DME/RT | a | 93 | 169 |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | DME/RT | a | 92 | 169 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | DME/RT | 21:79:0 | 95 | 169 |
| $Ph_3P$=$CHPh$ | $CF_3C{\equiv}CCO_2CH_3$ | DME/RT | a | 100 | 133b |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | DME/RT | a | 93 | 133b |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | DME/RT | a | 100 | 133b |
| $Ph_3P$=$CHC_6H_4Cl$-4 | $CF_3C{\equiv}CCO_2CH_3$ | DME/RT | a | 100 | 133b |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | DME/RT | a | 97 | 133b |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | DME/RT | a | 93 | 133b |
| $Ph_3P$=$CHC_6H_4Br$-3 | $CF_3C{\equiv}CCO_2CH_3$ | DME/RT | a | 100 | 133b |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | DME/RT | a | 100 | 133b |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | DME/RT | a | 99 | 133b |
| $Ph_3P$=$CHC_6H_4Me$-2 | $CF_3C{\equiv}CCO_2CH_3$ | DME/RT | a | 100 | 133b |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | DME/RT | a | 100 | 133b |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | DME/RT | a | 100 | 133b |
| $Ph_3P$=$CHC_6H_4CO_2Me$-2 | $CF_3C{\equiv}CCO_2CH_3$ | DME/RT | a | 94 | 133b |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | DME/RT | a | 100 | 133b |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | DME/RT | a | 97 | 133b |
| $Ph_3P$=$CHCH$=$CHCOCF_3$ | $CF_3C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 89 | 139b |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 85 | 139b |

**Table 18 (Continued)**

| $Ph_3P$=CHR | Alkyne | Conditions | Product ratio **21**:**22**:**23** | Yield (%) | ref. |
|---|---|---|---|---|---|
| $Ph_3P$=CHCH=CHCOCF$_3$ | $C_3F_7C{\equiv}CCO_2CH_3$ | DME/RT | a | 96 | 133b |
| $Ph_3P$=CHCOCH$_3$ | $CF_3C{\equiv}CCO_2CH_3$ | CH$_3$OH/RT | | 0 | 168 |
| $Ph_3P$=CHCOPh | $CF_3C{\equiv}CCO_2CH_3$ | CH$_3$OH/RT | | 0 | 168 |
| | $CF_3C{\equiv}CCO_2CH_3$ | EtOH/RT | 36:67:0 | 56 | 168 |
| $Ph_3P{=}C(CO_2CH_3)(CH{=}CHCOCH_3)$ | $CF_3C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 58 | 140 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 85 | 140 |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 89 | 139b |
| $Ph_3P$=CHCH=CHCOC$_2$F$_5$ | $CF_3C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 78 | 139b |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 90 | 139b |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 85 | 139b |
| $Ph_3P$=CHCH=CHCOC$_3$F$_7$ | $CF_3C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 94 | 139b |
| | $C_2F_5C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 93 | 139b |
| | $C_3F_7C{\equiv}CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 90 | 139b |

a. Both **21** and **22** were formed and the ratios were not reported. Upon heating the mixture all of **22** could be converted to **21**.

an appropriate electrophile to form a phosphonium salt intermediate **13** which was then deprotonated by a second mole of the ylide to give a new ylide **14**. Thus, 2 equiv of the reactant ylide were required. Only 1 equiv of the reagent ylide was required for the reaction of perfluoroacylmethylene phosphoranes with perfluoroacyl chlorides. In this instance, equimolar $Ph_3P{=}CHCOCF_3$ (**15**) and $CF_3COCl$ were applied to furnish the bis(trifluoroacetyl)-substituted ylide **16** since basicity of **15** was very weak and its conjugated acid was a strong acid. Therefore, no **17** was isolated, and HCl evolution was observed in the reaction (eq 98).[111] This indicates that either **15** as a base is too

$$Ph_3P{=}CHCOCF_3 \xrightarrow{CF_3COCl} Ph_3P{=}C(COCF_3)_2 + HCl\uparrow \quad (98)$$

**15** **16**

$$\left[Ph_3\overset{+}{P}CH_2COCF_3\ \overset{-}{Cl}\right]\ \text{not observed}$$

**17**

weak to trap HCl or α-protons in salt **17** are so acidic that they could be removed by chloride. Hamper published a modified method of equimolar transylidation which utilized 2 equiv of triethylamine as a base. Salt **18**, a precursor to ylide $Ph_3P{=}CHCO_2Et$, was then directly converted into the fluorinated ylide **19** (eq 99).[128] The reactions involving fluoroolefins

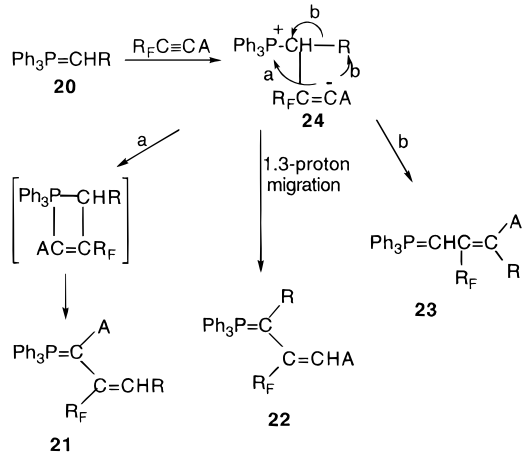
$$[Ph_3PCH_2CO_2Et]^+\ Br^- \xrightarrow[Et_3N]{(CF_3CO)_2O} Ph_3P{=}C(COCF_3)(CO_2Et) \quad (99)$$

**18** **19**

and fluoroepoxides as electrophiles have been reviewed,[129] and the details have not been included here.

A number of fluorinated phosphonium ylides were prepared by the nucleophilic addition of phosphonium ylides to fluorinated alkynes followed by rearrangement (Scheme 42, Table 18). Only 1 equiv of the reactant ylide was required in this preparation since the product ylide was derived by proton or group transfer instead of deprotonation by a second equivalent of the ylide. The products from these reactions were dependent upon the structure of the ylides and reaction conditions. In aprotic solvents at room temperature, the reaction of ylides **20** (R = $CO_2Me$,[130] COMe,[131] and $CH{=}CHCO_2Me$[132]) with $R_FC{\equiv}CCO_2$-Me gave only **21**. Under similar conditions, both **21**

**Scheme 42**




and **22** were formed by the reaction of ylide **20** (R = $C_6H_4X$)[133] with $R_FC{\equiv}CCO_2Me$, whereas **21** was isolated as the major product along with **23** from the reaction of ylide **20** (R = COPh)[134] and $R_FC{\equiv}CCO_2$-Me. Treatment of ylide **20** (R = COPh) with $R_FC{\equiv}CCN$ at room temperature afforded **21** only. However, the same reaction at −78 °C provided **22** exclusively.[135] The mechanism of the reaction can be rationalized as follows: nucleophilic attack of the ylide at the *β*-position of the fluorinated alkyne formed intermediate **24** which underwent a four-membered ring rearrangement (pathway a) to give **21**, 1,3-proton transfer to **22**, or acyl group (when R = COPh or $COCF_3$) migration to **23** (pathway b).

Phosphonium ylides also react with perfluorinated nitriles under mild conditions to form the iminoylides in excellent yields (Table 19, eq 100).[136]

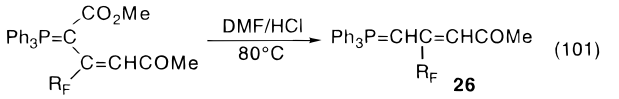
$$Ph_3P{=}C(Me)CO_2Me \xrightarrow{C_3F_7CN} Ph_3P{=}N(C_3F_7)C(Me){=}C(CO_2Me) \quad (100)$$

Decarboxylation of ylide **25** (DMF, concentrated HCl, 80 °C) followed by treatment with sodium carbonate gave ylide **26** in excellent yields (eq 101). The latter ylide **26** also reacted with fluoroalkynes to produce cyclic ylide **27** (eq 102).[137]

Reaction of fluorinated epoxides with triethyl phosphite formed stabilized ylide **28** (eq 103).[138]

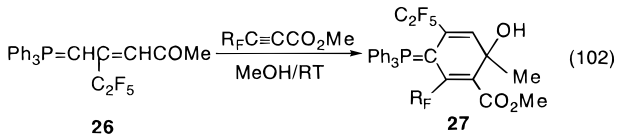
**Table 19. Reaction of Ylide with Fluorinated Nitriles[136]**

| Ylide | $R_FCN$ | Product | Yield(%) |
|---|---|---|---|
| $Ph_3P{=}C(Me)CO_2Me$ | $C_3F_7CN$ | $Ph_3P{=}N{-}C(C_3F_7){=}C(Me)CO_2Me$ | 85 |
| | $C_5F_{11}CN$ | $Ph_3P{=}N{-}C(C_5F_{11}){=}C(Me)CO_2Me$ | 98 |
| | $C_7F_{15}CN$ | $Ph_3P{=}N{-}C(C_7F_{15}){=}C(Me)CO_2Me$ | 94 |
| $Ph_3P{=}C(Me)CO_2Et$ | $C_5F_{11}CN$ | $Ph_3P{=}N{-}C(C_5F_{11}){=}C(Me)CO_2Et$ | 91 |
| | $C_7F_{15}CN$ | $Ph_3P{=}N{-}C(C_7F_{15}){=}C(Me)CO_2Et$ | 97 |
| $Ph_3P{=}C(Et)CO_2Et$ | $C_7F_{15}CN$ | $Ph_3P{=}N{-}C(C_7F_{15}){=}C(Et)CO_2Et$ | 96 |
| $Ph_3P{=}C(Pr)CO_2Et$ | $C_7F_{15}CN$ | $Ph_3P{=}N{-}C(C_7F_{15}){=}C(Pr)CO_2Et$ | 85 |
| $Ph_3P{=}C(Bu)CO_2Et$ | $C_7F_{15}CN$ | $Ph_3P{=}N{-}C(C_7F_{15}){=}C(Bu)CO_2Et$ | 95 |
| $Ph_3P{=}C(CH_2CH{=}CH_2)CO_2Et$ | $C_7F_{15}CN$ | $Ph_3P{=}N{-}C(C_7F_{15}){=}C(CH_2CH{=}CH_2)CO_2Et$ | 90 |
| $Ph_3P{=}C(Me)COCH_3$ | $C_7F_{15}CN$ | $Ph_3P{=}N{-}C(C_7F_{15}){=}C(Me)COMe$ | 87 |



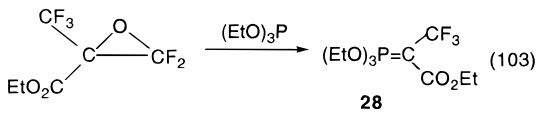
(101)

| $R_F$ | Yield (%) |
|---|---|
| $CF_3$ | 93 |
| $C_2F_5$ | 92 |
| $C_3F_7$ | 98 |



(102)

| $R_F$ | Yield (%) |
|---|---|
| $CF_3$ | 98 |
| $C_2F_5$ | 94 |
| $C_3F_7$ | 97 |



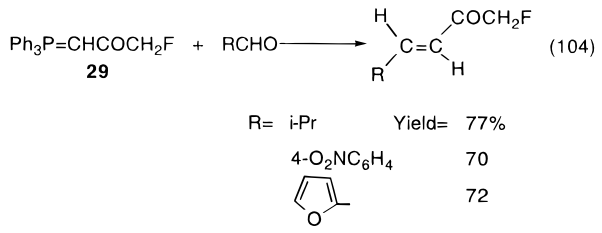
(103)

## 2. Synthetic Applications

### 2.1. Olefin Formation

There are only a few examples of the conventional Wittig reaction of fluorinated stabilized phosphonium ylides with carbonyl compounds. The reaction of ylide **29** with aldehydes gave α,β-unsaturated ketones (eq 104).[108] As expected, the geometry of the newly formed double bond in the reaction was exclusively *trans*.

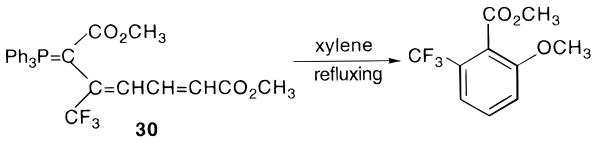
Fluorinated aromatic compounds were obtained by thermolysis of ylides **30**−**32** via intramolecular Wittig



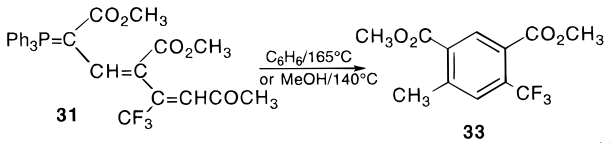
(104)

R= i-Pr Yield= 77%
4-$O_2NC_6H_4$ 70
72

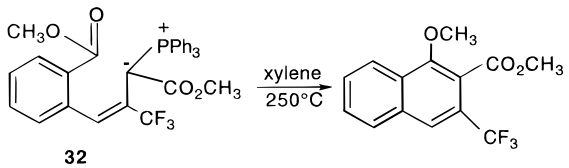
olefination (Table 20). In refluxing xylene, for example, ylides **30** were converted to benzoate derivatives only in moderate yields (eq 105).[132,139] Diester **33** was obtained in high yield by heating ylide **31** in a sealed tube in several different solvent systems at temperatures between 120 and 220 °C (eq 106).[140] Thermolysis of ylides **32** proceeded at 250 °C in xylene in a sealed tube to give excellent yields of substituted naphthalene (eq 107).[133a] In these aromatic ring formation reactions, ylidic nucleophiles attack carbonyl groups intramolecularly via a six-member ring transition state followed by elimination of $Ph_3PO$ to give benzene and naphthalene derivatives. Vigorous reaction conditions were required since the low reactivity of phosphonium ylides bearing electron-withdrawing groups.



(105)



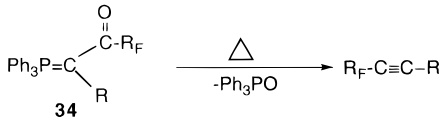
(106)



(107)

### 2.2. Alkyne Formation

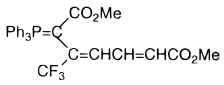
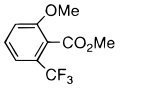
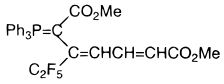
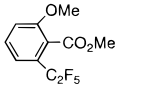
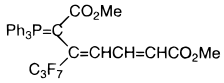
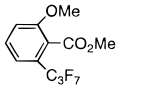
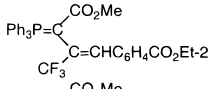
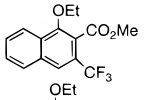
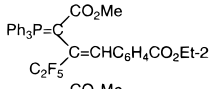
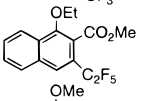
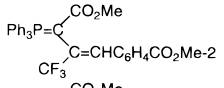
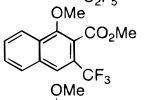
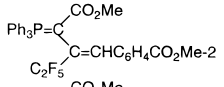
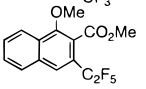
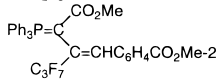
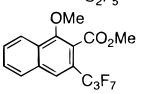
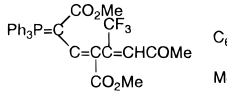
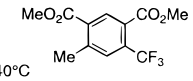
Intramolecular Wittig reaction of β-keto phosphonium ylides is a useful method for the preparation of fluorinated alkynes (Table 21). A variety of functional groups, such as ketone,[111,116a] ester,[114] nitrile,[115] aldehyde,[116b] phosphonate,[117] ether,[118] thioester,[119] thienyl,[120] PhSe,[121] and amide,[124] were tolerated in the reaction. High yields of the alkyne could be achieved from perfluoro or polyfluoro alkyl or aryl substituted ylides **34** (eq 107a). However, pyrolysis of trichloromethyl-substituted ylide afforded no alkyne.[115b] The fluoroalkyne products obtained from this method usually are easily purified. Various fluoroalkynes have been prepared by this convenient method.

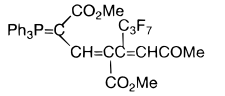
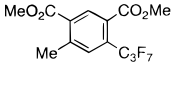
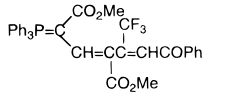
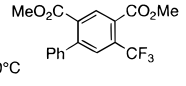
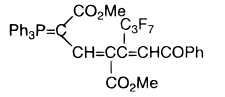
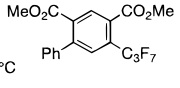
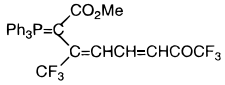
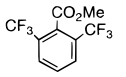
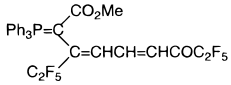
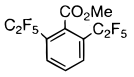
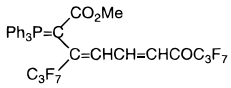
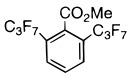
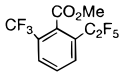
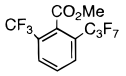
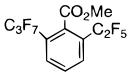


**(107a)**

R: ketone, ester, nitrile, aldehyde, phosphonate, ether, thioester, thienyl, PhSe, and amide.

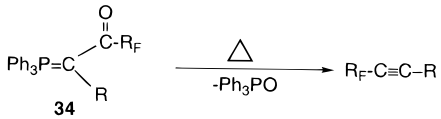
**Table 20. Aromatic Ring Formation vis Intramolecular Wittig Reaction**

| Ylide | conditions | Products | yield(%) | ref. |
|---|---|---|---|---|
|  | Xylene refluxing |  | 57 | 132 |
|  | |  | 45 | 132 |
|  | |  | 45 | 132 |
|  | Xylene 250°C |  | 81 | 133b |
|  | |  | 90 | 133b |
|  | |  | 90 | 133b |
|  | |  | 77 | 133b |
|  | |  | 85 | 133b |
|  | $C_6H_6$/165°C |  | 93 | 140 |
| | $MeOH/H_2O$/140°C | | 90 | 140 |
| | MeOH/140°C | | 95 | 140 |
| | MeOH/120°C | | 86 | 140 |

| Ylide | conditions | Products | yield(%) | ref. |
|---|---|---|---|---|
|  | $C_6H_6$/165°C |  | 98 | 140 |
|  | $C_6H_6$/220°C |  | 91 | 140 |
| | $MeOH/H_2O$/160°C | | 82 | 140 |
|  | $C_6H_6$/220°C |  | 90 | 140 |
| | $MeOH/H_2O$/160°C | | 77 | 140 |
|  | $C_6H_6$/140-50°C |  | 93 | 139b |
|  | $C_6H_6$/140-50°C |  | 82 | 139b |
|  | $C_6H_6$/140-50°C |  | 94 | 139b |
| a | $C_6H_6$/140-50°C |  | 88 | 139b |
| a | $C_6H_6$/140-50°C |  | 89 | 139b |
| a | $C_6H_6$/140-50°C |  | 88 | 139b |

a. the starting ylide was not stated in the original paper.

**Table 21. Alkyne Formation via Intramolecular Wittig Reaction**



**34**

| R | $R_F$ | Conditions | Product | Yield | Ref. |
|---|---|---|---|---|---|
| Ph | $C_6F_5$ | 310 °C/10 Torr | $C_6F_5C{\equiv}CPh$ | 86 | 113 |
| $C_6F_5$ | $C_6F_5$ | 310 °C/10 Torr | $C_6F_5C{\equiv}CC_6F_5$ | 74 | 113 |
| CN | $CF_3$ | 220−260 °C/10−15 Torr | $CF_3C{\equiv}CCN$ | 50 | 115a |
| CN | $C_2F_5$ | 220−260 °C/10−15 Torr | $C_2F_5C{\equiv}CCN$ | 82 | 115a |
| CN | $C_3F_7$ | 220−260 °C/10−15 Torr | $C_3F_7C{\equiv}CCN$ | 80 | 115a |
| $CO_2CH(Me)C_2H_5$ | $CF_3$ | 240 °C/10 Torr | $CF_3C{\equiv}CCO_2CH(Me)C_2H_5$ | 78 | 114b |
| $COCF_3$ | $CF_3$ | 160−200 °C/2 Torr | $CF_3C{\equiv}CCOCF_3$ | 70 | 111 |
| $COC_2F_5$ | $C_2F_5$ | 160−200 °C/2 Torr | $C_2F_5C{\equiv}CCOC_2F_5$ | 88 | 111 |
| $COC_3F_7$ | $C_3F_7$ | 160−200 °C/2 Torr | $C_3F_7C{\equiv}CCOC_3F_7$ | 96 | 111 |
| $COC_7F_{15}$ | $C_7F_{15}$ | 160−200 °C/2 Torr | $C_7F_{15}C{\equiv}CCOC_7F_{15}$ | 90 | 111 |
| COPh | $CF_3$ | 200−220 °C/10 Torr | $CF_3C{\equiv}CCOPh/PhC{\equiv}CCOCF_3$ 1:4 | 84 | 116a |
| $COC_6H_4OCH_3$-*p* | $CF_3$ | 200−220 °C/10 Torr | $CF_3C{\equiv}CCOC_6H_4OCH_3$-*p*/*p*-$CH_3OC_6H_4C{\equiv}CCOCF_3$ 2:3 | 89 | 116a |
| COPh | $C_3F_7$ | 200−220 °C/2 Torr | $C_3F_7C{\equiv}CCOPh/PhC{\equiv}CCOC_3F_7$ 1:1 | 86 | 116a |
| $COC_4H_4OCH_3$-*p* | $C_3F_7$ | 200−220 °C/2 Torr | $C_3F_7C{\equiv}CCOC_4H_4OCH_3$-*p*/*p*-$CH_3OC_6H_4C{\equiv}CCOC_3F_7$ 1:1 | 84 | 116a |
| $(PhO)_2P(O)$ | $CF_3$ | 220 °C/$10^{-5}$ Torr | $CF_3C{\equiv}CP(O)(OPh)_2$ | 84 | 117 |
| $(PhO)_2P(O)$ | $C_2F_5$ | 220 °C/$10^{-5}$ Torr | $C_2F_5C{\equiv}CP(O)(OPh)_2$ | 78 | 117 |
| $(PhO)_2P(O)$ | $C_3F_7$ | 220 °C/$10^{-5}$ Torr | $C_3F_7C{\equiv}CP(O)(OPh)_2$ | 85 | 117 |
| PhSe | $CF_3$ | 210 °C/$10^{-3}$ Torr | $CF_3C{\equiv}C$-SePh | 42 | 121 |
| $C_6F_5$ | $CF_3$ | 230−260 °C/2 Torr | $C_6F_5C{\equiv}CCF_3$ | 94 | 122 |
| $C_6F_5$ | $C_2F_5$ | 230−260 °C/2 Torr | $C_6F_5C{\equiv}CC_2F_5$ | 85 | 122 |
| $C_6F_5$ | $C_3F_7$ | 230−260 °C/2 Torr | $C_6F_5C{\equiv}CC_3F_7$ | 96 | 122 |
| $C_6F_5$ | $C_7F_{15}$-*n* | 230−260 °C/2 Torr | $C_6F_5C{\equiv}CC_7F_{15}$-*n* | 95 | 122 |
| $C_6F_5$ | $(CF_2)_3Cl$ | 230−260 °C/2 Torr | $C_6F_5C{\equiv}C(CF_2)_3Cl$ | 87 | 122 |
| $C_6F_5$ | $(CF_2)_5Cl$ | 230−260 °C/2 Torr | $C_6F_5C{\equiv}C(CF_2)_5Cl$ | 85 | 122 |
| PhO | $CF_3$ | 250−270 °C/10 Torr | $CF_3C{\equiv}COPh$ | 28 | 118 |
| PhO | $C_3F_7$ | 250−270 °C/10 Torr | $C_3F_7C{\equiv}COPh$ | 35 | 118 |
| PhO | $C_3F_7OCF(CF_3)$ | 250−270 °C/10 Torr | $C_3F_7OCF(CF_3)C{\equiv}COPh$ | 38 | 118 |
| 4-$ClC_6H_4$ | $CF_3$ | 250−270 °C/10 Torr | $CF_3C{\equiv}COC_6H_4Cl$-4 | 31 | 118 |
| 4-$ClC_6H_4$ | $C_3F_7$ | 250−270 °C/10 Torr | $CF_3C{\equiv}COC_6H_4Cl$-4 | 36 | 118 |
| 4-$ClC_6H_4$ | $C_3F_7OCF(CF_3)$ | 250−270 °C/10 Torr | $C_3F_7OCF(CF_3)C{\equiv}COC_6H_4Cl$-4 | 40 | 118 |

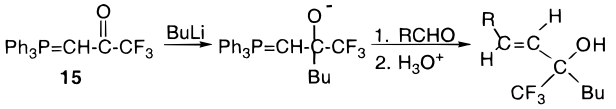
**Table 21 (Continued)**

| R | $R_F$ | Conditions | Product | Yield | Ref. |
|---|---|---|---|---|---|
| CHO | $CF_3$ | 220−260 °C/10 Torr | $CF_3C{\equiv}CCHO/HC{\equiv}CCOCF_3$ 2:3 | 60 | 116b |
| CHO | $C_2F_5$ | 220−260 °C/10 Torr | $C_2F_5C{\equiv}CCHO/HC{\equiv}CCOC_2F_5$ 5:6 | 60 | 116b |
| CHO | $C_3F_7$ | 220−260 °C/10 Torr | $C_3F_7C{\equiv}CCHO/HC{\equiv}CCOC_3F_7$ 3:4 | 85 | 116b |
| CN | $ClCF_2$ | 280 °C/1 Torr | $ClCF_2C{\equiv}CCN$ | 53 | 115b |
| CN | $Cl(CF_2)_3$ | 280 °C/1 Torr | $Cl(CF_2)_3C{\equiv}CCN$ | 83 | 115b |
| CN | $Cl(CF_2)_5$ | 280 °C/1 Torr | $Cl(CF_2)_5C{\equiv}CCN$ | 85 | 115b |
| CN | $C_3F_7OCF(CF_3)$ | 280 °C/1 Torr | $C_3F_7OCF(CF_3)C{\equiv}CCN$ | 77 | 115b |
| $COSCH_3$ | $C_2F_5$ | 190−220 °C/1 Torr | $C_2F_5C{\equiv}CCOSCH_3$ | 92 | 119 |
| $COSCH_3$ | $C_3F_7$ | 190−220 °C/1 Torr | $C_3F_7C{\equiv}CCOSCH_3$ | 95 | 119 |
| $COSCH_3$ | $C_7F_{15}$-*n* | 190−220 °C/1 Torr | *n*-$C_7F_{15}C{\equiv}CCOSCH_3$ | 93 | 119 |
| $COSCH_3$ | $(CF_2)_3Cl$ | 190−220 °C/1 Torr | $Cl(CF_2)_3C{\equiv}CCOSCH_3$ | 95 | 119 |
| $COSCH_3$ | $(CF_2)_5Cl$ | 190−220 °C/1 Torr | $Cl(CF_2)_5C{\equiv}CCOSCH_3$ | 90 | 119 |
| $COSCH_3$ | $C_3F_7OCF(CF_3)$ | 190−220 °C/1 Torr | $C_3F_7OCF(CF_3)C{\equiv}CCOSCH_3$ | 94 | 119 |
| $CONEt_2$ | $CF_3$ | 220−240 °C/2 Torr | $CF_3C{\equiv}CCONEt_2$ | 95 | 124 |
| $CONEt_2$ | $C_3F_7$ | 220−240 °C/2 Torr | $C_3F_7C{\equiv}CCONEt_2$ | 91 | 124 |
| CONHBu-*n* | $CF_3$ | 220−240 °C/2 Torr | $CF_3C{\equiv}CCONHBu$-*n* | 62 | 124 |
| CONHBu-*n* | $C_3F_7$ | 220−240 °C/2 Torr | $C_3F_7C{\equiv}CCONHBu$-*n* | 72 | 124 |
| $CON(CH_2)_4CH_2$ | $CF_3$ | 220−240 °C/2 Torr | $CF_3C{\equiv}CCON(CH_2)_4CH_2$ | 93 | 124 |
| $CON(CH_2)_4CH_2$ | $C_3F_7$ | 220−240 °C/2 Torr | $C_3F_7C{\equiv}CCON(CH_2)_4CH_2$ | 82 | 124 |
|  | $CF_3$ | 220−240 °C/30 Torr | $CF_3C{\equiv}C$-  | 82 | 120 |
|  | $C_2F_5$ | 220−240 °C/30 Torr | $C_2F_5C{\equiv}C$-  | 88 | 120 |
|  | $C_3F_7$ | 220−240 °C/30 Torr | $C_3F_7C{\equiv}C$-  | 90 | 120 |
|  | $Cl(CF_2)_3$ | 220−240 °C/30 Torr | $Cl(CF_2)_3C{\equiv}C$-  | 94 | 120 |
|  | $C_3F_7OCF(CF_3)$ | 220−240 °C/30 Torr | $C_3F_7OCF(CF_3)C{\equiv}C$-  | 84 | 120 |
| $(CH_3)_2C{=}C(CF_3)$- | $CF_3$ | 250−260 °C/10 Torr | $(CH_3)_2C{=}C(CF_3)C{\equiv}CCF_3$ | 94 | 123 |
| $(CH_3)_2C{=}C(C_2F_5)$- | $C_2F_5$ | 250−260 °C/10 Torr | $(CH_3)_2C{=}C(C_2F_5)C{\equiv}CC_2F_5$ | 94 | 123 |
| $(CH_3)_2C{=}C(C_3F_7)$- | $C_3F_7$ | 250−260 °C/10 Torr | $(CH_3)_2C{=}C(C_3F_7)C{\equiv}CC_3F_7$ | 90 | 123 |
| $CH_2(CH_2)_3C{=}C(CF_3)$- | $CF_3$ | 250−260 °C/10 Torr | $CH_2(CH_2)_3C{=}C(CF_3)C{\equiv}CCF_3$ | 99 | 123 |
| $CH_2(CH_2)_3C{=}C(C_2F_5)$- | $C_2F_5$ | 250−260 °C/10 Torr | $CH_2(CH_2)_3C{=}C(C_2F_5)C{\equiv}CC_2F_5$ | 85 | 123 |
| $CH_2(CH_2)_3C{=}C(C_3F_7)$- | $C_3F_7$ | 250−260 °C/10 Torr | $CH_2(CH_2)_3C{=}C(C_3F_7)C{\equiv}CC_3F_7$ | 86 | 123 |
| $CH_2(CH_2)_4C{=}C(CF_3)$- | $CF_3$ | 250−260 °C/10 Torr | $CH_2(CH_2)_4C{=}C(CF_3)C{\equiv}CCF_3$ | 96 | 123 |
| $CH_2(CH_2)_3C{=}C(CF_3)$- | $C_3F_7$ | 250−260 °C/10 Torr | $CH_2(CH_2)_3C{=}C(CF_3)C{\equiv}CC_3F_7$ | 90 | 123 |
| $CO_2CH_3$ | $CF_3$ | 190−230 °C/10 Torr | $CF_3C{\equiv}CCO_2CH_3$ | 58 | 114a |
| $CO_2CH_3$ | $C_3F_7$ | 190−230 °C/10 Torr | $C_3F_7C{\equiv}CCO_2CH_3$ | 90 | 114a |
| $(CH_3)_2C{=}C(CF_3)$- | $CF_3$ | 250−260 °C/10 Torr | $(CH_3)_2C{=}C(CF_3)C{\equiv}CCF_3$ | 94 | 123 |
| $(CH_3)_2C{=}C(C_2F_5)$- | $C_2F_5$ | 250−260 °C/10 Torr | $(CH_3)_2C{=}C(C_2F_5)C{\equiv}CC_2F_5$ | 94 | 123 |
| $(CH_3)_2C{=}C(C_3F_7)$- | $C_3F_7$ | 250−260 °C/10 Torr | $(CH_3)_2C{=}C(C_3F_7)C{\equiv}CC_3F_7$ | 90 | 123 |
| $CH_2(CH_2)_3C{=}C(CF_3)$- | $CF_3$ | 250−260 °C/10 Torr | $CH_2(CH_2)_3C{=}C(CF_3)C{\equiv}CCF_3$ | 99 | 123 |
| $CH_2(CH_2)_3C{=}C(C_2F_5)$- | $C_2F_5$ | 250−260 °C/10 Torr | $CH_2(CH_2)_3C{=}C(C_2F_5)C{\equiv}CC_2F_5$ | 85 | 123 |
| $CH_2(CH_2)_3C{=}C(C_3F_7)$- | $C_3F_7$ | 250−260 °C/10 Torr | $CH_2(CH_2)_3C{=}C(C_3F_7)C{\equiv}CC_3F_7$ | 86 | 123 |
| $CH_2(CH_2)_4C{=}C(CF_3)$- | $CF_3$ | 250−260 °C/10 Torr | $CH_2(CH_2)_4C{=}C(CF_3)C{\equiv}CCF_3$ | 96 | 123 |
| $CH_2(CH_2)_3C{=}C(CF_3)$- | $C_3F_7$ | 250−260 °C/10 Torr | $CH_2(CH_2)_3C{=}C(CF_3)C{\equiv}CC_3F_7$ | 90 | 123 |
| $CO_2CH_3$ | $CF_3$ | 190−230 °C/10 Torr | $CF_3C{\equiv}CCO_2CH_3$ | 58 | 114a |
| $CO_2CH_3$ | $C_3F_7$ | 190−230 °C/10 Torr | $C_3F_7C{\equiv}CCO_2CH_3$ | 90 | 114a |

### *2.3. Reaction of Fluorinated Phosphonium Ylides with Nucleophiles*

Perfluoroacylmethylene phosphoranes are very unreactive as nucleophiles due to the fact that the negative charge is delocalized over the P−C−C−O bonding system. The electron density is further reduced by the strong electron-withdrawing perfluoroalkyl group. Shen and co-workers demonstrated that the carbonyl group in ylide **15** was electrophilic enough to be attacked by a lithium reagent to generate the ylide anion, which further reacted with aromatic aldehydes to afford the corresponding *trans*-olefins stereoselectively (Scheme 43).[141] The ylide anion could also be protonated by AcOH to give trisubstituted *trans*-olefins stereoselectively via betaine intermediates.[142−144] However, when the ylide bearing an amide group was applied as a reactant, the *cis*-isomer was the major product (Scheme 44, Table 22).[145] No explanation is available for the

**Scheme 43**




| R= Ph, | Yield=54% |
|---|---|
| 4-$MeC_6H_4$ | 51 |
| 4-$ClC_6H_4$ | 48 |
| 4-$FC_6H_4$ | 55 |
| 4-$O_2NC_6H_4$ | 46 |
| 4-$MeOC_6H_4$ | 49 |
| 2,4-$Cl_2C_6H_4$ | 49 |
| PhCH=CH | 46 |

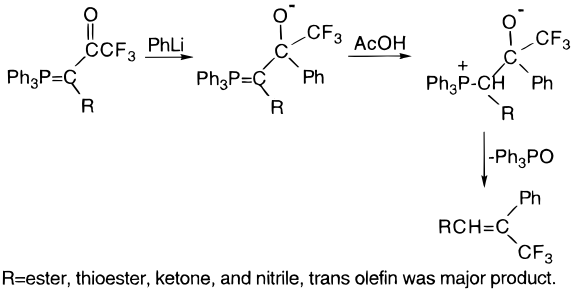
**Table 22. Nucleophilic Attack on Fluorinated Ylides Followed by Protonation**

| | RLi | Temp.(°C) | Product | Z:E | Yield(%) | Ref. |
|---|---|---|---|---|---|---|
| $Ph_3P{=}C(COCF_3)(CO_2Me)$ | n-BuLi | -60 | $Bu(CF_3)C{=}CHCO_2H$ | 15:85 | 92[a] | 144 |
| | PhLi | -60 | $Ph(CF_3)C{=}CHCO_2H$ | 38:62 | 95[a] | 144 |
| $Ph_3P{=}C(COC_2F_5)(CO_2Me)$ | n-BuLi | -60 | $Bu(C_2F_5)C{=}CHCO_2H$ | 9:91 | 94[a] | 144 |
| | PhLi | -60 | $Ph(C_2F_5)C{=}CHCO_2H$ | 42:58 | 90[a] | 144 |
| $Ph_3P{=}C(COC_3F_7)(CO_2Me)$ | MeLi | 0 | $Me(C_3F_7)C{=}CHCO_2H$ | 44:56 | 93[a] | 144 |
| | n-BuLi | -60 | $Bu(C_3F_7)C{=}CHCO_2H$ | 18:81 | 93[a] | 144 |
| | PhLi | -60 | $Ph(C_3F_7)C{=}CHCO_2H$ | 38:62 | 90[a] | 144 |
| $Ph_3P{=}C(COCF_3)(CON)$ | PhLi | -30 | $Ph(CF_3)C{=}CHCO$-N | 100:0 | 80[b] | 145 |
| | MeLi | 0 | $Me(CF_3)C{=}CHCO$-N | 73:27 | 90[b] | 145 |
| | BuC≡CLi | 10 | $BuC{\equiv}C(CF_3)C{=}CHCO$-N | 58:42 | 72[b] | 145 |
| | PhC≡CLi | 10 | $PhC{\equiv}C(CF_3)C{=}CHCO$-N | 53:47 | 78[b] | 145 |
| $Ph_3P{=}C(COCF_3)(CN)$ | BuC≡CLi | 0 | $BuC{\equiv}C(CF_3)C{=}CHCN$ | 14:86 | 90 | 143 |
| | PhC≡CLi | 0 | $PhC{\equiv}C(CF_3)C{=}CHCN$ | 8:92 | 98 | 143 |
| | 2-thienyl-Li | 0 | 2-thienyl$(CF_3)C{=}CHCN$ | 0:100 | 90 | 143 |
| | PhLi | -60 | $Ph(CF_3)C{=}CHCN$ | 12:88 | 91 | 143 |
| $Ph_3P{=}C(COC_3F_7)(CN)$ | BuC≡CLi | 0 | $BuC{\equiv}C(C_3F_7)C{=}CHCN$ | 13:87 | 93 | 143 |
| | PhC≡CLi | 0 | $PhC{\equiv}C(C_3F_7)C{=}CHCN$ | 5:95 | 93 | 143 |
| | 2-thienyl-Li | 0 | 2-thienyl$(C_3F_7)C{=}CHCN$ | 0:100 | 96 | 143 |
| | PhLi | -60 | $Ph(C_3F_7)C{=}CHCN$ | 13:87 | 90 | 143 |
| $Ph_3P{=}C(COCF_3)(CONEt_2)$ | PhLi | -30 | $Ph(CF_3)C{=}CHCONEt_2$ | 100:0 | 85 | 145 |
| | MeLi | 0 | $Me(CF_3)C{=}CHCONEt_2$ | 72:28 | 81 | 145 |
| | BuC≡CLi | 10 | $BuC{\equiv}C(CF_3)C{=}CHCONEt_2$ | 52:48 | 84 | 145 |
| | PhC≡CLi | 10 | $PhC{\equiv}C(CF_3)C{=}CHCONEt_2$ | 51:49 | 74 | 145 |
| $Ph_3P{=}C(COCF_3)(CO_2Et)$ | 2-thienyl-Li | 0 | 2-thienyl$(CF_3)C{=}CHCO_2Et$ | 12:88 | 92 | 146 |
| $Ph_3P{=}C(COCF_3)(CO_2Me)$ | PhLi | -60 | $Ph(CF_3)C{=}CHCO_2Me$ | 14:86 | 93 | 142 |
| $Ph_3P{=}C(COC_3F_7)(CO_2Me)$ | BuLi | -60 | $Bu(C_3F_7)C{=}CHCO_2Me$ | 0:100 | 95 | 142 |
| | PhLi | -60 | $Ph(C_3F_7)C{=}CHCO_2Me$ | 33:67 | 97 | 142 |
| $Ph_3P{=}C(COC_3F_7)(COSMe)$ | BuLi | -60 | $Bu(C_3F_7)C{=}CHCOSMe$ | 10:90 | 94 | 142 |
| $Ph_3P{=}C(COC_2F_5)(COSMe)$ | 2-thienyl-Li | 0 | 2-thienyl$(C_2F_5)C{=}CHCOSMe$ | 15:85 | 95 | 142 |
| | PhLi | -60 | $Ph(C_2F_5)C{=}CHCOSMe$ | 17:83 | 90 | 142 |
| $Ph_3P{=}C(COC_3F_7)(COPh)$ | MeLi | 0 | $Me(CF_3)C{=}CHCOPh$ | 0:100 | 94 | 142 |
| | BuLi | -60 | $Bu(CF_3)C{=}CHCOPh$ | 0:100 | 94 | 142 |
| | PhLi | -60 | $Ph(CF_3)C{=}CHCOPh$ | 24:76 | 93 | 142 |
| $Ph_3P{=}C(COCF_3)(CO_2Et)$ | PhLi | -50 | $Ph(CF_3)C{=}CHCO_2Et$ | 8:92 | 95 | 146 |
| $Ph_3P{=}C(COCF_3)(CO_2Bu\text{-}t)$ | PhLi | -50 | $Ph(CF_3)C{=}CHCO_2Bu\text{-}t$ | 7:93 | 88 | 146 |
| $Ph_3P{=}C(COCF_3)(CO_2Bu\text{-}t)$ | 2-thienyl-Li | 0 | 2-thienyl$(CF_3)C{=}CHCO_2Bu\text{-}t$ | 70:30 | 85 | 146 |

a. Protonated and hydrolyzed by KOH/$H_2O$-MeOH.

b. Protonated by AcOH

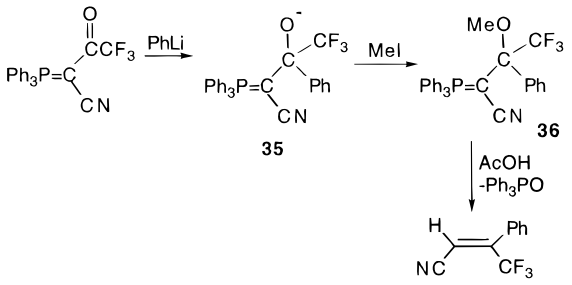
**Scheme 44**




R=ester, thioester, ketone, and nitrile, trans olefin was major product.

R=amide, cis olefin was major product.

**Scheme 45**




unusual *cis* selectivity. The *cis*-olefins are also accessible by a modified procedure. Oxygen methylation of the ylide anions **35** by MeI gave the corresponding ylides **36**, which were hydrolyzed in refluxing AcOH to form the trisubstituted *cis*-olefins stereoselectively (Scheme 45, Table 23).[146]

The methodology has been extended utilizing Grignard reagents as nucleophiles.[147] In this case, both *trans*- and *cis*-olefins could be accessed selectively by using different protonating reagents. (*Z*)-Selectivity was observed when weak acids, AcOH or aqueous methylamine hydrochloride, were applied as protonating reagents. The use of strong acid such as HCl (5%), on the other hand, gave (*E*)-olefins (Table 24). The typical reaction is illustrated in Scheme 46. An exception was the observation that PhMgX gave *trans*-olefins predominately with both strong and weak acids (Table 25). In these reactions, the nu-

**Table 23. Reaction via Methylated Intermediates To Form Olefins[146]**

| Ylide | RLi | temp. (°C) | Product | Z:E | Yield(%) |
|---|---|---|---|---|---|
| $Ph_3P{=}C(COCF_3)(CO_2Bu\text{-}t)$ | PhLI | -50 | $Ph(CF_3)C{=}CHCO_2Bu\text{-}t$ | 84:16 | 92 |
| | 2-Li-thiophene | 0 | 2-thienyl$(CF_3)C{=}CHCO_2Bu\text{-}t$ | 70:30 | 85 |
| $Ph_3P{=}C(COCF_3)(CN)$ | PhLi | -60 | $Ph(CF_3)C{=}CHCN$ | 87:13 | 93 |
| | PhC≡CLi | 0 | $Ph\text{-}{\equiv}(CF_3)C{=}CHCN$ | 92:8 | 93 |
| | 2-Li-thiophene | 0 | 2-thienyl$(CF_3)C{=}CHCN$ | 88:12 | 94 |
| $Ph_3P{=}C(COCF_3)(CO_2Et)$ | PhLi | -50 | $Ph(CF_3)C{=}CHCO_2Et$ | 62:38 | 85 |
| | 2-Li-thiophene | 0 | 2-thienyl$(CF_3)C{=}CHCO_2Et$ | 87:13 | 93 |

**Table 24. Grignard Reagents Attack Ylides Followed by Protonation To Form Olefins[147]**

| Ylide | RMgX | Z:E a | Z:E b | Z:E c | Yield(%) a | Yield(%) b | Yield(%) c |
|---|---|---|---|---|---|---|---|
| $Ph_3P{=}C(COCF_3)(CO_2Bu\text{-}t)$ | n-$C_6H_{13}$MgBr | 0:100 | 71:29 | 94:6 | 94 | 95 | 94 |
| | $PhCH_2MgCl$ | 3:97 | 40:60 | 91:9 | 86 | 84 | 85 |
| | n-BuMgBr | 4:96 | 68:32 | 90:10 | 95 | 92 | 92 |
| | EtMgI | 8:92 | 93:7 | | 84 | 81 | |
| | MeMgI | 10:90 | 92:8 | | 89 | 90 | |
| | PhC≡CMgI | 12:88 | 77:23 | | 88 | 85 | |
| $Ph_3P{=}C(COCF_3)(CO_2Et)$ | MeMgI | 25:75 | 70:30 | | 72 | 75 | |
| | PhC≡CMgI | 25:75 | 73:27 | | 91 | 87 | |

a. Results from HCl(5%) as protonation reagent.
b. Results from AcOH as protonation reagent.
c. Results from $MeNH_2$•HCl as protonation reagent.

**Scheme 46**

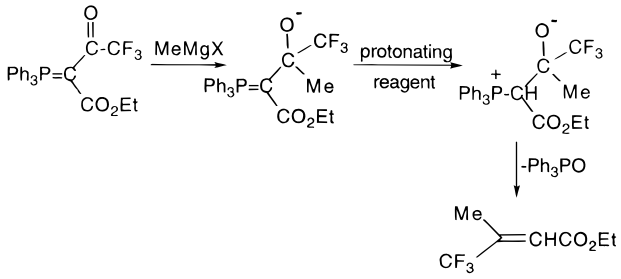


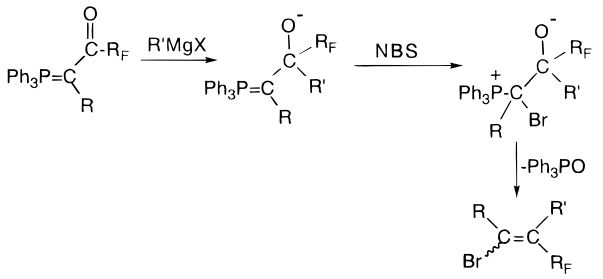

**Table 25. PhMgBr Attack Ylides Followed by Protonation To form Olefins[147]**

| Ylide | Protonating reagent | temp. (°C) | Z:E | Yield(%) |
|---|---|---|---|---|
| $Ph_3P{=}C(COCF_3)(CO_2Bu\text{-}t)$ | HCl | 0 | 8:92 | 86 |
| | HOAc | 0 | 8:92 | 81 |
| | $[MeNH_3]^+ Cl^-$ | 0 | 8:92 | 81 |
| $Ph_3P{=}C(COCF_3)(CO_2Et)$ | HCl | -10 | 8:92 | 85 |
| | HOAc | -10 | 8:92 | 82 |

cleophiles regiospecifically attacked the ylide on the carbonyl group bearing the perfluoroalkyl group when the ylide was substituted by both perfluoroacyl and other functional groups, such as esters, nitriles, and amides. This reaction provided a useful methodology to achieve fluorinated, trisubstituted olefins with desired configurations.

The ylide anion intermediate has also been brominated by NBS. Subsequent elimination of triphenylphosphine oxide led to vinyl bromide derivatives (Scheme 47).[108]

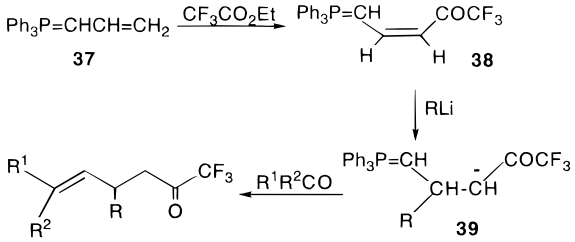
**Scheme 47**




| R= | R'= | $R_F$= | Yield(%)= | Z:E= |
|---|---|---|---|---|
| CN | Ph | $CF_3$ | 90 | 56:44 |
| CN | Ph | $C_3F_7$ | 85 | 60:40 |
| CN | Bu | $C_3F_7$ | 66 | 63:37 |
| $CO_2Et$ | Ph | $CF_3$ | 85 | 71:29 |
| $CO_2Me$ | Ph | $CF_3$ | 83 | 71:29 |
| $CO_2Me$ | Bu | $C_3F_7$ | 65 | 67:33 |
| $CO_2Me$ | 2-thienyl | $CF_3$ | 84 | 67:33 |

Acylation of ylide **37** with fluorinated ester occurred at the $\gamma$-position to give the $\alpha,\beta$-unsaturated ketone substituted ylide **38**. Organolithium reagents could regiospecifically attack the $\beta$-carbon of the ylide **38** to provide ylide anion **39**. Ylide anion **39** further reacted with both aldehydes and ketones to give the corresponding fluorinated $\gamma,\delta$-unsaturated ketones with exclusive *trans* configuration (Scheme 48).[149]

**Scheme 48**




| $R^1$= | $R^2$= | R= | Yield(%)= |
|---|---|---|---|
| Ph | H | n-$C_4H_9$ | 63 |
| Ph | Ph | n-$C_4H_9$ | 46 |
| c-$C_6H_{11}$ | H | Ph | 82 |
| Ph | H | Ph | 92 |
| Ph | Ph | Ph | 66 |
| 4-$ClC_6H_4$ | H | Ph | 85 |
| 4-$MeC_6H_4$ | H | Ph | 90 |
| 2,4-$Cl_2C_6H_4$ | H | Ph | 83 |

## 2.4. Hydrolysis

Hydrolysis of ylides **40** and **41** or their mixture proceeded under rather extreme conditions (150−180 °C), aqueous MeOH) to afford good yields of fluorinated olefins **42** with exclusive (*Z*)-geometry (Scheme 49, Table 26). The double bond in **42** was conjugated with the aryl group. When the hydrolysis of **40** was carried out in $MeOH/D_2O$, the vinyl deuterium analog was obtained, indicating migration of the double bond during the reaction.[133b]

Fluorinated iminophosphoranes were also readily hydrolyzed in acidic media and led to the correspond-

**Table 26. Synthesis of Unsaturated Esters via Hydrolysis of Stabilized Phosphonium Ylides**

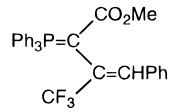
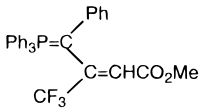
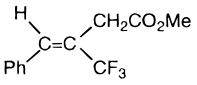
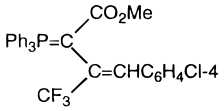
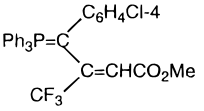
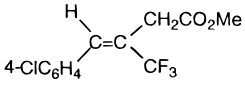
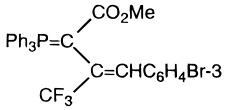
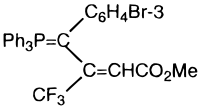
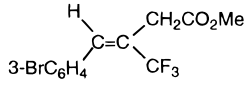
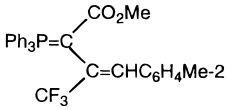
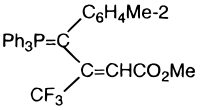
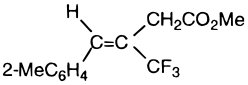
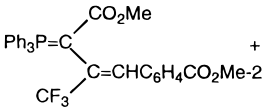
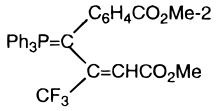
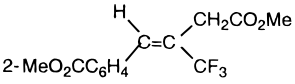
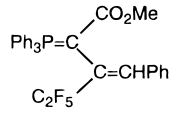
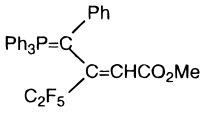
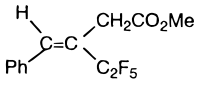
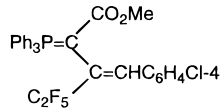
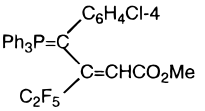
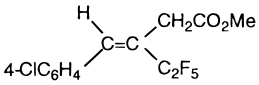
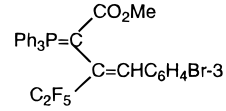
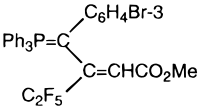
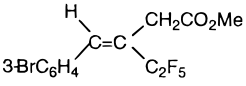
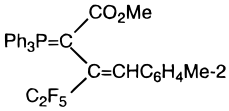
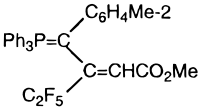
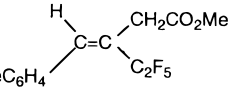
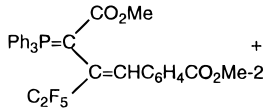
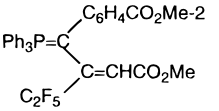
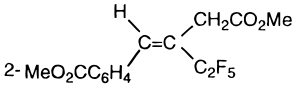
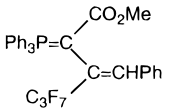
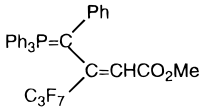
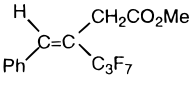
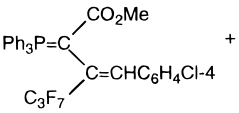
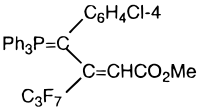
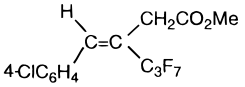
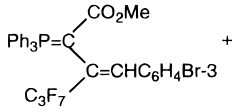
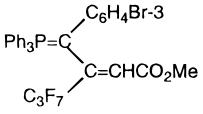
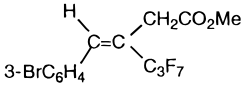
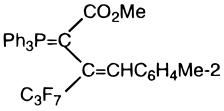
| Ylides | | Products | yield | ref. |
|---|---|---|---|---|
|  |  |  | 92 | 133b |
|  |  |  | 66 | 133b |
|  |  |  | 57 | 133b |
|  |  |  | 78 | 133b |
|  |  |  | 87 | 133b |
|  |  |  | 83 | 133b |
|  |  |  | 67 | 133b |
|  |  |  | 82 | 133b |
|  |  |  | 59 | 133b |
|  |  |  | 90 | 133b |
|  |  |  | 76 | 133b |
|  |  |  | 90 | 133b |
|  |  |  | 94 | 133b |
|  |  |  | 73 | 133b |
|  |  |  | 92 | 133b |
|  | |  | 95 | 170 |

**Table 26 (Continued)**

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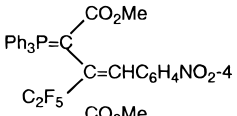
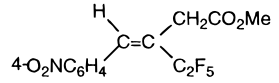
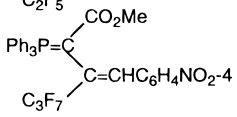
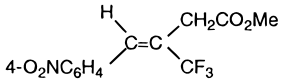
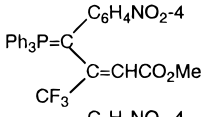
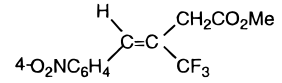
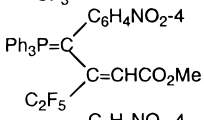
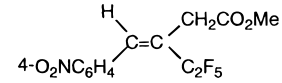
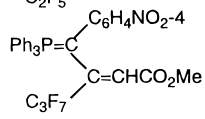
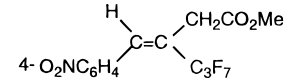
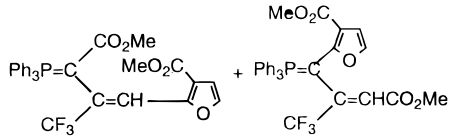
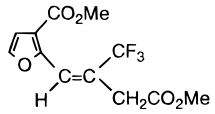
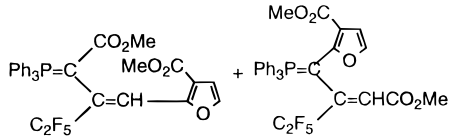
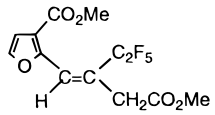
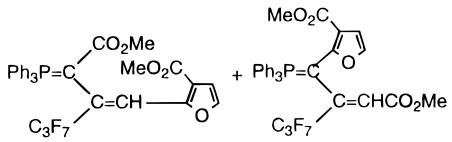
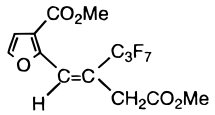
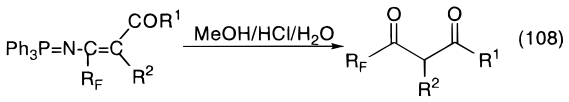
|  |  | 87 | 170 |
|  |  | 98 | 170 |
|  |  | 98 | 170 |
|  |  | 84 | 170 |
|  |  | 83 | 170 |
|  |  | 76 | 169 |
|  |  | 76 | 169 |
|  |  | 76 | 169 |

ing fluorinated $\beta$-diketones in excellent yields (eq 108).[136]

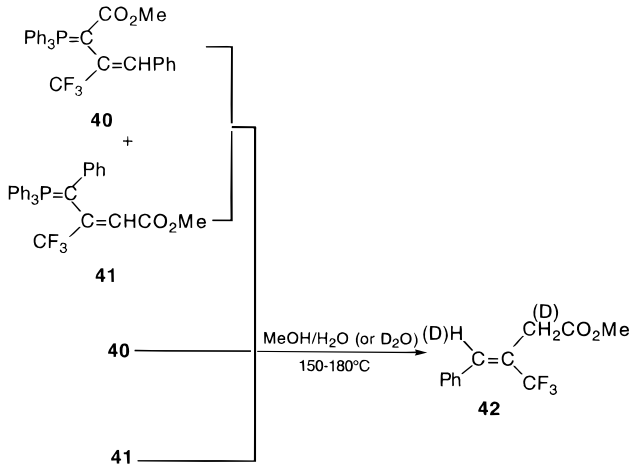


(108)

| $R^1$ | $R^2$ | $R_F$ | Yield(%) | $R^1$ | $R^2$ | $R_F$ | Yield(%) |
|---|---|---|---|---|---|---|---|
| OMe | Me | $C_3F_7$ | 70 | OEt | Bu | $C_7F_{15}$ | 94 |
| OMe | Me | $C_5F_{11}$ | 92 | OEt | allyl | $C_7F_{15}$ | 93 |
| OMe | Me | $C_7F_{15}$ | 92 | Me | Me | $C_7F_{15}$ | 87 |
| OEt | Me | $C_7F_{15}$ | 91 | Ph | H | $C_5F_{11}$ | 92 |
| OEt | Me | $C_7F_{15}$ | 86 | Ph | H | $C_7F_{15}$ | 90 |
| OEt | Et | $C_7F_{15}$ | 95 | Me | H | $C_5F_{11}$ | 81 |
| OEt | Pr | $C_7F_{15}$ | 92 | Me | H | $C_7F_{15}$ | 96 |

Alkylation of ylide **11** with organic halides could be accomplished under mild conditions. The alkylation exclusively occurred on carbon, and no O-alkylated products were observed. Activated bromides such as allylic and benzyl bromides gave alkylated products within 12 h and primary alkyl iodides required 12−120 h, depending on the chain length. Secondary alkyl halides failed to provide the alkylation products. Interestingly, when substituted allyl bromides were utilized as substrates, the ylide exclusively attacked the α-position of the allylic halides due to steric effects. The resulting alkylated

**Scheme 49**



phosphonium intermediates readily underwent hydrolysis [$NaHCO_3$ (5%) or NaOH (5%)] to afford α-fluoroalkanoates **43** as shown in eq 109.[109]

Ylide **11** was also successfully acylated with acid chlorides and anhydrides to form carbon-acylated phosphonium intermediates exclusively. A variety of acid chlorides, such as primary, secondary, tertiary, cyclic, and aromatic acid chlorides, could be employed in the acylation reaction. The phospho-

$$Bu_3P{=}CFCO_2Et \xrightarrow[2.\ NaHCO_3(aq.)]{1.\ RX} RCHFCO_2Et \quad (109)$$
**11** **43**

| R= | Yield(%)= |
|---|---|
| $CH_3$ | 59(75)[a] |
| $CH_3CH_2$ | 42(87) |
| n-$C_3H_7$ | 42(74) |
| n-$C_4H_9$ | 34(61) |
| n-$C_7H_{15}$ | 52(72) |
| n-$C_{10}H_{21}$ | 44(50) |
| $PhCH_2$ | 59(61) |
| $CH_2{=}CHCH_2$ | 52(73) |
| $CH_3CH{=}CHCH_2$ | 38(72) |
| $PhCH{=}CHCH_2$ | 45(76) |
| $CH_3OCOCH{=}CHCH_2$ | 41(45) |

a. The yield in parenthesis is NMR yield.

nium intermediates readily underwent hydrolysis under mild conditions with aqueous $NaHCO_3$ (5%) to give α-fluoro-*β*-ketoalkanoates **44** in good yields (eq 110). When ylide **11** was acylated with chloroformate, diesters were obtained after hydrolysis of the phosphonium intermediates. Acylation of ylide **11** with fluorinated acid chlorides did not proceed cleanly to give good yields of the desired phosphonium intermediates. For example, treatment of **11** with $CF_3COCl$ led to the formation of a mixture of phosphonium intermediate, $[Bu_3P^+CF(COCF_3)CO_2Et]Cl^-$, and $(CF_3CO)_2CFCO_2Et$. This problem has been solved by treatment of $Li[(EtO)_2P(O)CFCO_2Et]$ with fluorinated acid chlorides followed by hydrolysis to afford the corresponding *β*-ketoalkanoates (cf. section VI.2.2.2.2).

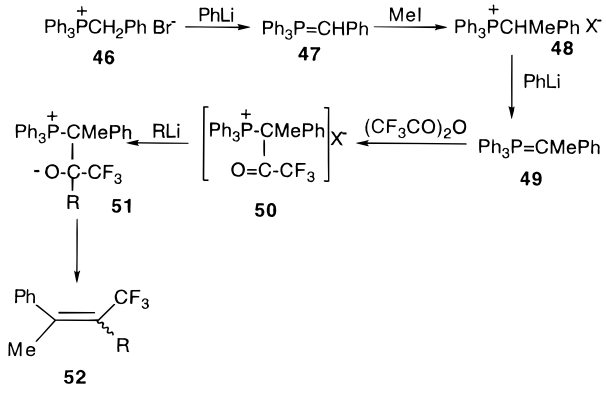
$$Bu_3P{=}CFCO_2Et \xrightarrow[2.\ NaHCO_3(aq.)]{1.\ RC(O)Cl} RC(O)CHFCO_2Et \quad (110)$$
**11** **44**

| R= | Yield(%)= |
|---|---|
| $CH_3$ | 60 |
| $CH_3CH_2$ | 50 |
| $Me_2CH$ | 58 |
| t-$C_4H_9$ | 56 |
| $C_6H_{11}$ | 68 |
| EtO | 50 |
| Ph | 70 |
| $CH_3OCOCH_2CH_2$ | 38 |

### *2.5. Reactions of β-Keto Phosphonium Salts*

Attempts to attack *β*-keto phosphonium salt **45** with BuLi led to only a low yield of the product, presumably due to steric effects.[151] In contrast, Shen and co-workers found that fluorinated *β*-keto phosphonium salts did react with organolithium reagents, which provided a useful method for the preparation of fluorinated olefins. For example, the reaction of ylides **49** and fluorinated anhydrides provided fluorinated *β*-keto phosphonium salts **50**, which were readily attacked by nucleophiles to form betaine **51**. Subsequent elimination of $Ph_3PO$ from **51** gave fluorinated tetrasubstituted olefins **52** (Scheme 50, Table 27).[152−158] The powerful electron-withdrawing perfluoroalkyl group facilitated nucleophilic attack on the carbonyl group. The reactant ylide **49** could be prepared from ylide **47** and alkyl iodides; allyl or benzyl bromides (method A listed in Table 27); or directly generated from salts **48** (method B listed in Table 27). A variety of functional groups, such as alkyl, alkenyl, phenyl, benzyl, ether, and ester groups, could be tolerated in this reaction. In the case of *β*-keto phosphonium salts substituted by both a perfluoroacyl group and an ester group, the nucleophile regiospecifically attacked the ketone.

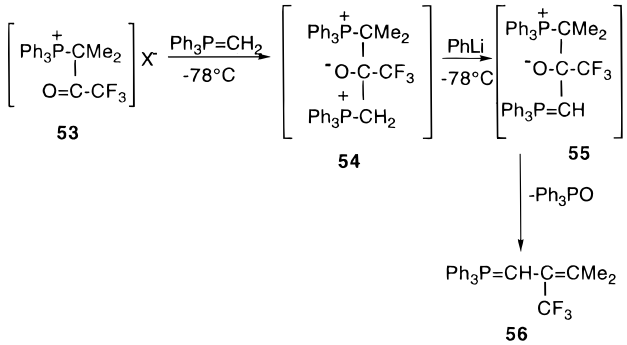
**Scheme 50**



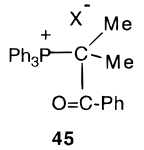

Organolithium reagents, organozinc reagent and ylides have been employed as nucleophiles. When there was a great difference in size between two substituents on the ylide **49**, the reaction gave the olefin products with one isomer predominating. Thus, hydrocarbon lithium reagents produced *trans*-olefins as major products while sulfur-containing lithium reagents (thienyllithium and $PhSCH_2Li$) and $(EtO)_2POLi$ provided *cis*-olefins stereospecifically or stereoselectively. When the two groups have similar size, the two isomers were observed in about 1:1 ratio.

The ylides also readily attacked *β*-keto phosphonium salts **53** to form intermediate **54** which was deprotonated with a lithium reagent to generate betaine **55**. The deprotonation must be carried out at low temperature in order to prevent potentially competitive elimination of $Ph_3PO$ to form the undesired olefin (Scheme 51).[123,127]

**Scheme 51**

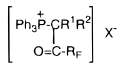



The ylide **56**, generated by this method, has been acylated with anhydrides to give stabilized ylides

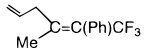
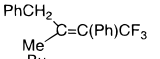
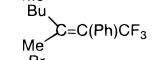
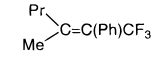
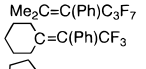
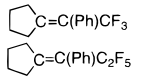
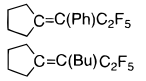
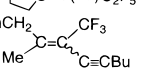
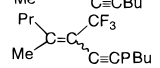
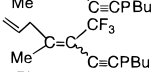
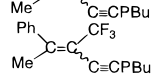
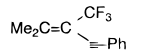
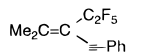
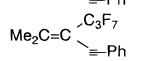
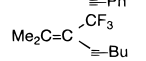
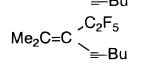
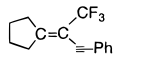
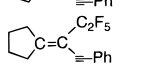
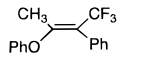
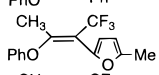
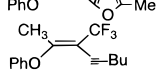
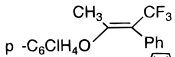
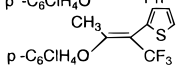
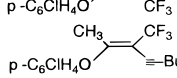
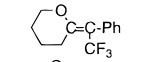
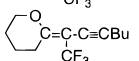
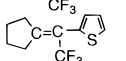
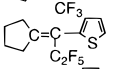
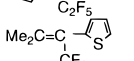
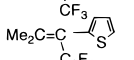
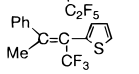


45

**Table 27. Alkene Formation via Nucleophilic Attack on Fluorinated β-Keto Phosphonium Salts**



RLi

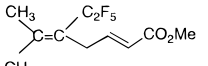
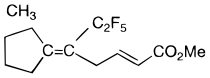
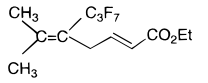
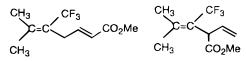
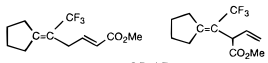
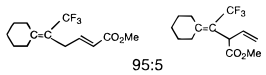
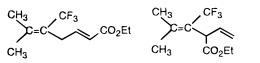
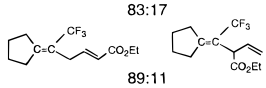
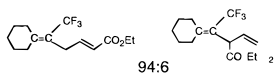
| $R^1$ | $R^2$ | $R_F$ | R | Method | Product | E/Z | Yield | Ref. |
|---|---|---|---|---|---|---|---|---|
| $CH_2=CHCH_2$ | $CH_3$ | $CF_3$ | Ph | A |  | 55:45 | 42 | 152 |
| $PhCH_2$ | $CH_3$ | $CF_3$ | Ph | A |  | 87:13 | 60 | 152 |
| Bu | $CH_3$ | $CF_3$ | Ph | A |  | 45:55 | 61 | 152 |
| Pr | $CH_3$ | $CF_3$ | Ph | A |  | 45:55 | 56 | 152 |
| $CH_3$ | $CH_3$ | $CF_3$ | Ph | B | $Me_2C=C(Ph)CF_3$ | | 62 | 152 |
| $CH_3$ | $CH_3$ | $C_2F_5$ | Ph | B | $Me_2C=C(Ph)C_2F_5$ | | 63 | 152 |
| $CH_3$ | $CH_3$ | $C_3F_7$ | Ph | B | $Me_2C=C(Ph)C_3F_7$ | | 70 | 152 |
| $-(CH_2)_5-$ | | $CF_3$ | Ph | B |  | | 42 | 152 |
| $-(CH_2)_4-$ | | $CF_3$ | Ph | B |  | | 67 | 152 |
| $-(CH_2)_4-$ | | $C_2F_5$ | Ph | B |  | | 71 | 152 |
| $-(CH_2)_4-$ | | $C_2F_5$ | Bu | B |  | | 44 | 152 |
| $PhCH_2$ | $CH_3$ | $CF_3$ | BuC≡C | A |  | 87:13 | 80 | 153 |
| Pr | $CH_3$ | $CF_3$ | BuC≡C | A |  | 60:40 | 72 | 153 |
| $CH_2=CHCH_2$ | $CH_3$ | $CF_3$ | BuC≡C | A |  | 60:40 | 47 | 153 |
| Ph | $CH_3$ | $CF_3$ | BuC≡C | B |  | 98:2 | 44 | 153 |
| $CH_3$ | $CH_3$ | $CF_3$ | PhC≡C | B |  | | 73 | 153 |
| $CH_3$ | $CH_3$ | $C_2F_5$ | PhC≡C | B |  | | 50 | 153 |
| $CH_3$ | $CH_3$ | $C_3F_7$ | PhC≡C | B |  | | 43 | 153 |
| $CH_3$ | $CH_3$ | $CF_3$ | BuC≡C | B |  | | 50 | 153 |
| $CH_3$ | $CH_3$ | $C_2F_5$ | BuC≡C | B |  | | 70 | 153 |
| $-(CH_2)_4-$ | | $CF_3$ | PhC≡C | B |  | | 61 | 153 |
| $-(CH_2)_4-$ | | $C_2F_5$ | PhC≡C | B |  | | 72 | 153 |
| PhO | $CH_3$ | $CF_3$ | Ph | A |  | 100:0 | 62 | 155 |
| PhO | $CH_3$ | $CF_3$ |  | A |  | 100:0 | 66 | 155 |
| PhO | $CH_3$ | $CF_3$ | BuC≡C | A |  | 100:0 | 85 | 155 |
| p-$ClC_6H_4O$ | $CH_3$ | $CF_3$ | Ph | A |  | 100:0 | 62 | 155 |
| p-$ClC_6H_4O$ | $CH_3$ | $CF_3$ |  | A |  | 0:100 | 66 | 155 |
| p-$ClC_6H_4O$ | $CH_3$ | $CF_3$ | BuC≡C | A |  | 100:0 | 85 | 155 |
| $-O(CH_2)_4-$ | | $CF_3$ | Ph | B |  | 100:0 | 40 | 155 |
| $-O(CH_2)_4-$ | | $CF_3$ | BuC≡C | B |  | 61:39 | 57 | 155 |
| $-(CH_2)_4-$ | | $CF_3$ |  | B |  | | 72 | 158a |
| $-(CH_2)_4-$ | | $C_2F_5$ |  | B |  | | 70 | 158a |
| $CH_3$ | $CH_3$ | $CF_3$ |  | B |  | | 56 | 158a |
| $CH_3$ | $CH_3$ | $C_2F_5$ |  | B |  | | 67 | 158a |
| Ph | $CH_3$ | $CF_3$ |  | B |  | 0:100 | 82 | 158a |



RLi

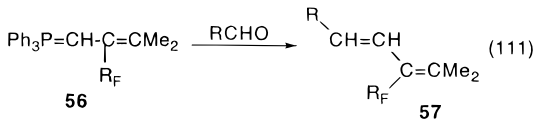
| $R^1$ | $R^2$ | $R_F$ | R | Method | Product | E/Z | Yield | Ref. |
|---|---|---|---|---|---|---|---|---|
| $PhCH_2$ | $CH_3$ | $CF_3$ |  | B |  | 29:71 | 60 | 158a |
| Pr | $CH_3$ | $CF_3$ |  | B |  | 27:73 | 69 | 158a |
| Bu | $CH_3$ | $CF_3$ |  | B |  | 33:67 | 80 | 158a |
| $CH_3$ | $CH_3$ | $CF_3$ | $PhSCH_2$ | B | $Me_2C=C(CH_2SPh)CF_3$ | | 65 | 158b |
| $CH_3$ | $CH_3$ | $C_2F_5$ | $PhSCH_2$ | B | $Me_2C=C(CH_2SPh)C_2F_5$ | | 53 | 158b |
| $-(CH_2)_4-$ | | $CF_3$ | $PhSCH_2$ | B |  | | 57 | 158b |
| $-(CH_2)_4-$ | | $C_2F_5$ | $PhSCH_2$ | B |  | | 51 | 158b |
| Ph | $CH_3$ | $CF_3$ | $PhSCH_2$ | B |  | 0:100 | 60 | 158b |
| Pr | $CH_3$ | $CF_3$ | $PhSCH_2$ | A |  | 45:55 | 69 | 158b |
| Bu | $CH_3$ | $CF_3$ | $PhSCH_2$ | A |  | 44:56 | 80 | 158b |
| $CO_2Et$ | $CH_3$ | $CF_3$ | Ph | B |  | 85:15 | 66 | 154 |
| | | | PhC≡C | B |  | 77:23 | 41 | 154 |
| | | | BuC≡C | B |  | 92:8 | 50 | 154 |
| | | | $C_8H_{17}C≡C$ | B |  | 100:0 | 46 | 154 |
| | | | 4-$MeC_6H_4$ | B |  | 95:5 | 66 | 154 |
| | | | 2-$MeC_6H_4$ | B |  | 86:14 | 59 | 154 |
| | | | 4-$MeOC_6H_4$ | B |  | 100:0 | 47 | 154 |
| | | | 2-$MeOC_6H_4$ | B |  | 100:0 | 40 | 154 |
| Ph | $CH_3$ | $CF_3$ | $(EtO)_2POLi$ | B |  | 0:100 | 68 | 156 |
| Ph | $CH_3$ | $C_2F_5$ | | B |  | 15:85 | 56 | 156 |
| $-(CH_2)_4-$ | | $CF_3$ | | B |  | | 45 | 156 |
| | | $C_2F_5$ | | B |  | | 42 | 156 |
| $-(CH_2)_5-$ | | $CF_3$ | | B |  | | 72 | 156 |
| $CH_3$ | $CH_3$ | $CF_3$ | $(EtO)_2POLi$ [a] | |  | | 52<br>13 | 156<br>156 |
| $CH_3$ | $CH_3$ | $CF_3$ | $(EtO)_2POLi$ [b] | |  | | 2<br>51 | 156<br>156 |
| $CH_3$ | $CH_3$ | $C_2F_5$ | $(EtO)_2POLi$ [b] | |  | | 0<br>42 | 156<br>156 |
| $CH_3$ | $CH_3$ | $C_2F_5$ | Me | |  | | 43 | 159 |

**Table 27 (Continued)**

| $[Ph_3\overset{+}{P}\text{-}CR^1R^2]\ X^-$ / $O{=}C\text{-}R_F$ | | | RLi | | | | | |
|---|---|---|---|---|---|---|---|---|
| $R^1$ | $R^2$ | $R_F$ | R | Method | Product | E/Z | Yield | Ref. |
| $CH_3$ | $CH_3$ | $C_2F_5$ | Me | |  | | 43 | 159 |
| -$(CH_2)_4$- | | $C_2F_5$ | Me | |  | | 42 | 159 |
| $CH_3$ | $CH_3$ | $C_3F_7$ | Et | |  | | 37 | 159 |
| $CH_3$ | $CH_3$ | $CF_3$ | Me | |  | 73:27 | 42 | 159 |
| -$(CH_2)_4$- | | $CF_3$ | Me | |  | 85:15 | 52 | 159 |
| -$(CH_2)_5$- | | $CF_3$ | Me | |  | 95:5 | 42 | 159 |
| $CH_3$ | $CH_3$ | $CF_3$ | Et | |  | 83:17 | 41 | 159 |
| -$(CH_2)_4$- | | $CF_3$ | Et | |  | 89:11 | 55 | 159 |
| -$(CH_2)_5$- | | $CF_3$ | Et | |  | 94:6 | 47 | 159 |

a. $(EtO)_2POLi$ is generated from BuLi. b. $(EtO)_2POLi$ is generated from MeLi.

(Table 17).[123] Also, the ylide **56** underwent Wittig reaction with aldehydes to afford fluorinated dienes (eq 111). The geometry of the newly formed double bond in **57** was exclusively *E*.[127]



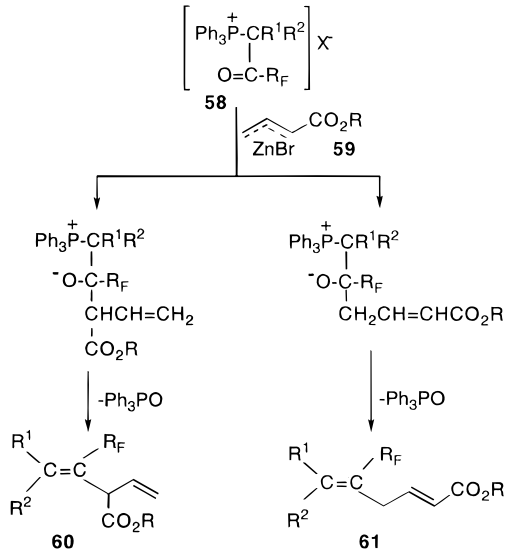
**56** **57** (111)

| R | $R_F$ | Yield(%) |
|---|---|---|
| Ph | $CF_3$ | 55 |
| 4-$ClC_6H_4$ | $CF_3$ | 56 |
| 4-$O_2NC_6H_4$ | $CF_3$ | 51 |
| PhCH=CH | $CF_3$ | 47 |
| Ph | $C_3F_7$ | 46 |
| 4-$ClC_6H_4$ | $C_3F_7$ | 51 |
| 4-$O_2NC_6H_4$ | $C_3F_7$ | 58 |
| n-$C_5H_{11}$ | $C_3F_7$ | 20 |

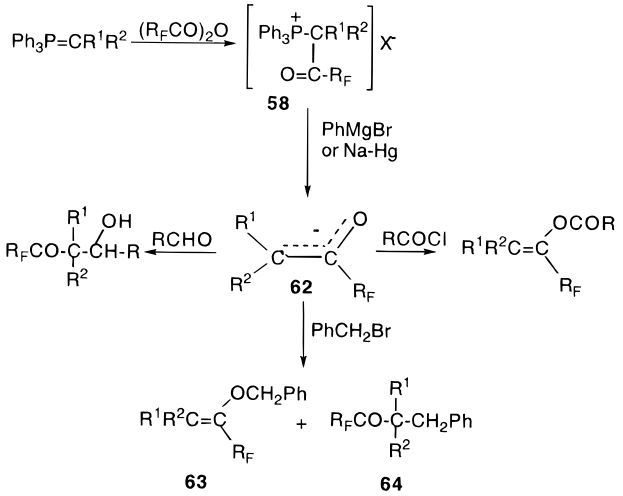
Zinc reagents **59** were also useful nucleophiles to attack the $\beta$-keto phosphonium salts. Upon reaction of **59** with the trifluoromethyl-substituted group salts **58**, two regioisomers **60** and **61** were isolated. However, in the case of salts **58** bearing a longer chain perfluoroalkyl group, only one isomer **61** was obtained (Scheme 52, Table 27).[159] Thus, steric effects played an important role in determining product distribution in this reaction.

The nucleophiles utilized to attack $\beta$-keto phosphonium salts were limited to lithium reagents (BuLi, PhLi, RC≡CLi, etc.), zinc reagents, and ylides (both phosphonium and arsonium ylides). When a Grignard reagent was employed as a nucleophile, reduction of salts **58** instead of nucleophilic addition was observed.[160] The same reduction of **58** also occurred with Na−Hg reagent[161] to provide the corresponding enolate **62**, which has been successfully trapped by suitable electrophiles. The trapped products depended on the nature of the electrophiles used. Both O- and C-alkylation products (**63** and **64**) were obtained when benzyl bromide was employed. With acid chlorides, only O-acylation occurred, whereas

**Scheme 52**



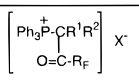
**Scheme 53**

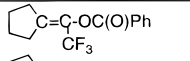
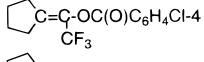
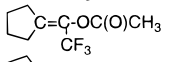
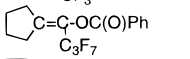
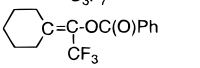
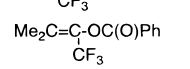
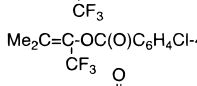
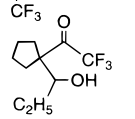
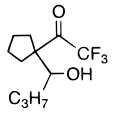
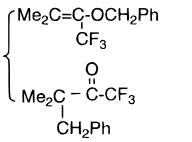


$\beta$-hydroxy ketones were exclusively isolated when the enolate was trapped with aldehydes (Scheme 53, Table 28).

The $\beta$-keto phosphonium salts **58** readily hydrolyzed with aqueous NaOH (5%) to produce perfluo-

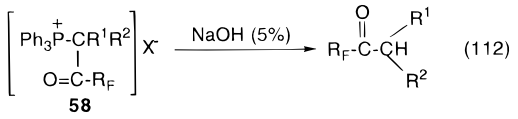
**Table 28. Reduction of β-Keto Phosphonium Salts and Capture of the Enolates by Electrophiles**



| $R^1$ | $R^2$ | $R_F$ | electrophile | Product | Yield(%)[a] |
|---|---|---|---|---|---|
| $-(CH_2)_4-$ | | $CF_3$ | PhCOCl |  | 90(70) |
| $-(CH_2)_4-$ | | $CF_3$ | $4\text{-}ClC_6H_4COCl$ |  | 94(58) |
| $-(CH_2)_4-$ | | $CF_3$ | $CH_3COCl$ |  | 80(58) |
| $-(CH_2)_4-$ | | $C_3F_7$ | PhCOCl |  | 69(41) |
| $-(CH_2)_5-$ | | $CF_3$ | PhCOCl |  | 73(65) |
| $CH_3$ | $CH_3$ | $CF_3$ | PhCOCl |  | 74(64) |
| $CH_3$ | $CH_3$ | $CF_3$ | $4\text{-}ClC_6H_4COCl$ |  | 79(69) |
| $-(CH_2)_4-$ | | $CF_3$ | $C_2H_5CHO$ |  | 51(46) |
| $-(CH_2)_4-$ | | $CF_3$ | $C_3H_7CHO$ |  | 43(43) |
| $CH_3$ | $CH_3$ | $CF_3$ | $PhCH_2Br$ |  | 36(24)<br>29(25) |

a. The yield was from the reaction using $PhMgBr$[160] as reductant and the yield in parentheses was from the reaction using Na-Hg[161] as reductant.

roalkyl-substituted ketones in good yields (eq 112).[162]



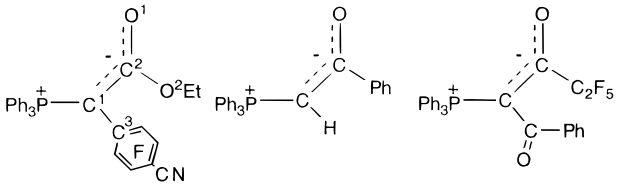
(112)

**58**

| $R^1$ | $R^2$ | $R_F$ | Yield(%) |
|---|---|---|---|
| Me | $PhCH_2$ | $CF_3$ | 78 |
| Me | $PhCH_2$ | $C_2F_5$ | 67 |
| Me | $PhCH_2$ | $C_3F_7$ | 75 |
| Et | $PhCH_2$ | $CF_3$ | 66 |
| Pr | $PhCH_2$ | $CF_3$ | 70 |
| Bu | $PhCH_2$ | $CF_3$ | 70 |
| Me | Ph | $CF_3$ | 40 |
| Me | $Me_2CH(CH_2)_4-$ | $CF_3$ | 54 |
| Me | $PhCH{=}CHCH_2$ | $CF_3$ | 37 |

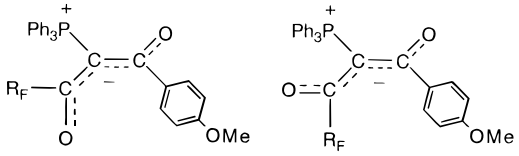
## 3. Structure and Reactivity

The solid-state structure of several stabilized fluorinated phosphonium ylides have been published. X-ray crystallography[163] of **65** showed the coplanarity of atoms P, C(1), C(2), C(3), O(1), and O(2); the rotation of $C_6F_4CN$ ring by 59° out of plane; a shortened C(1)−C(2) bond; and lengthened C(2)═O-(1) bond. These features indicated that the negative charge was delocalized over the O−C−C−P bonding system. In the fluorinated ylide **66**, the charge was delocalized through the O−C−C−P bonding network.[164] In contrast, the crystal structure of **67** indicated that the negative charge was predominantly delocalized through the O−C−C−P bonding system adjacent to the perfluoroethyl group.[165] That is due to the strong inductive effect of the perfluorinated group, which is well-known to stabilize carbanions.

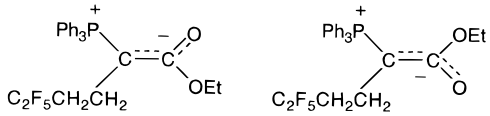


**65** **66** **67**

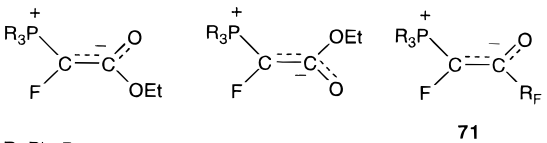
Shen and co-workers observed two different methyl protons of **68** in the $^1H$ NMR and suggested that they corresponded to the (*Z*,*Z*)- and (*E*,*Z*)-isomers.[116a] Cambon and co-workers made a similar observation for the ethyl protons of **69**.[166] They suggested that there was an equilibrium between "*cis*" and "*trans*" isomers due to hindered rotation at room temperature. At higher temperature (100 °C), the signals had coalesced to one set of ethyl protons because the rotation became much easier at higher temperature. Both $Bu_3P{=}CFCO_2Et$ (**11**) and $Ph_3P{=}CFCO_2Et$ (**70**) also exist as mixture of *cis*- and *trans*-isomers based on $^{19}F$ and $^{31}P$ NMR data.[109b] Interestingly, only one isomer of ylide **71** was observed at room temperature



E,Z-isomer **68** Z,Z-isomer



"cis" isomer **69** "trans" isomer



R=Ph, Bu **71**

in the $^{19}F$ and $^{31}P$ NMR spectra, which was assigned as the (*Z*)-form based on the magnitude of the $^4J_{F,CF_2}$ coupling constant ($J = 18-29$ Hz), similar to that for (*Z*)-fluoroolefins ($^4J_{F,CF_2} = 20-27$ Hz) and greater than for (*E*)-fluoroolefins ($^4J_{F,CF_2} = 7-12$ Hz).[64] The NMR observation of geometric isomers in these ylides was consistent with the crystallographic results that depicted the ylidic negative charge as being delocalized through the P−C−C−O bonding system resulting in partial double-bond character for the bond between the ylidic carbon and carbonyl carbon.

Introduction of fluorinated substituents into stabilized ylides generally imparts added stability. The degree of stabilization depends upon the number of fluorine atoms. For example, fluoroacetylidene triphenylphosphorane reacts with aldehydes in a manner similar to its nonfluorinated analog, but the reaction requires longer times and affords lower yields of alkenes. Trifluoroacetylidene triphenylphosphorane

**15**, however, is unreactive with aldehydes. No Wittig olefination product is obtained even with *p*-nitrobenzaldehyde. With stronger electrophiles such as acid halides and anhydrides it can be converted to bis(perfluoroacyl)methylene triphenylphosphorane **16**. Phosphorane **16** is even more stable. To date the only useful application for this ylide is an intramolecular Wittig reaction to prepare fluorinated alkynes.

## *V. Fluorinated As, N, S, and Sb Ylides*

In contrast to the well-documented chemistry of fluorinated phosphonium ylides, relatively little information has been published about fluorinated arsonium, nitrogen, sulfur, and stibine ylides, especially the latter two types.

### 1. Fluorinated Arsonium Ylides

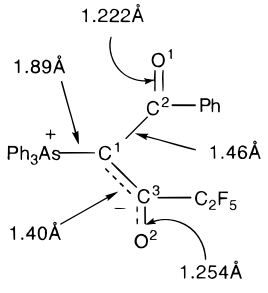
#### *1.1. Structure and Reactivity*

Like phosphonium ylides, arsonium ylides may be classified as stabilized (ylidic carbon bearing at least one electron-withdrawing group, such as nitrile, ester, acyl, etc.); semistabilized (substituted by aryl or vinyl); and nonstabilized (unsubstituted or substituted by alkyl group) ylides. Stabilized ylides are inert to air and water at room temperature and are isolable. Nonstabilized ylides and semistabilized ylides usually are prepared and used *in situ*. Introduction of fluorine atom(s) or fluorinated group(s) into the ylides generally imparted a stabilizing effect with the exception of direct introduction of fluorine on the ylidic carbon. The degree of the stabilization depended upon the structure of the ylide and the number of fluorine and fluorinated groups introduced. For example, (acetylmethylene)triphenylarsorane readily reacted with carbonyl compounds. [(Trifluoroacetyl)methylene]triphenylarsorane, however, failed to react with *p*-nitrobenzaldehyde, even at higher temperatures (75 °C) for a prolonged period of time.[172] In contrast, the monofluoroarsonium ylide, [(fluorobenzoyl)methylene]triphenylarsorane, underwent Wittig olefination similar to its nonfluorinated analog, but with longer reaction times and lower yields.[173] Introduction of fluorine atoms directly onto the ylidic carbon destabilized the ylide due to the well-known ability of fluorine to destabilize α-anions. (Difluoromethylene)triphenylarsorane is unknown and is expected to be less stable than its nonfluorinated analog $Ph_3As{=}CH_2$ based on the observed stability of $Ph_3P{=}CF_2$ and $Ph_3P{=}CH_2$. Both $Ph_3As{=}CH_2$ and $Ph_3P{=}CH_2$ are thermally stable at room temperature. However, $Ph_3P{=}CF_2$ is much less stable than $Ph_3P{=}CH_2$ and has been neither pregenerated nor observed by NMR, only trapped by electrophiles during the reaction (cf. section II.6.1).

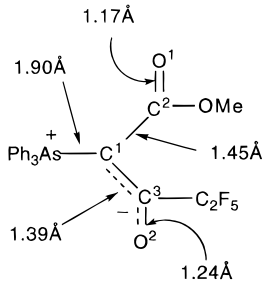
In general, arsonium ylides are more reactive than phosphonium ylides with identical structure due to the less effective $d\pi-p\pi$ overlap between the ylidic carbon $sp^2$ orbitals and the arsenic 4d orbitals.[173] The higher HOMO levels of the arsonium ylides compared to the phosphonium ylides also contributed to the enhanced reactivity.[174] Both of these effects result in a lowering of the As−C bond order and an increase in the negative charge on the ylidic carbons. For example, $Ph_3As{=}CHC_6F_5$ (**72**) reacted with *p*-chlorobenzaldehyde at room temperature for 30 min to form olefin, $p\text{-}ClC_6H_4CH{=}CHC_6F_5$ in 90% yield.[175] $Ph_3P{=}CHC_6F_5$, however, furnished the same olefin at 40 °C for 2 h in 51% yield.[99]

An NMR study suggested that the ylidic carbon in $R_3As{=}CH_2$ has a pseudotetrahedral geometry ($sp^3$),[176,177] whereas X-ray crystallography has demonstrated the ylidic carbon to be planar ($sp^2$) when it bears an acyl group (fluorinated or nonfluorinated).[164,172]

There was no typical ketone carbonyl absorption in the IR spectrum of [(pentafluoropropionyl)benzoylmethylene]triphenylarsorane (**73**). It was suggested that the ylidic charge was delocalized over the neighboring carbonyl groups.[126,129] This delocalization was further confirmed by X-ray crystallography, which revealed that the C(1)−C(2) bond length was in the range of a $C(sp^2)-C(sp^2)$ single bond and the C(2)−O(1) bond length was close to conjugated carbonyl double bond, whereas the C(1)−C(3) bond was significantly shortened and C(3)−O(2) bond was longer than the normal C=O double bond. The atoms As, C(1), C(2), C(3), and O(2) were coplanar, whereas O(1) was out of the plane.[178] Thus the ylidic carbon was $sp^2$-hybridized and the ylidic negative charge predominantly delocalized through the As−C(1)−C(3)−O(2) bonding system. The X-ray crystallography analysis of the arsonium ylide **73** also confirmed its (*Z*,*Z*)-conformation which was suggested by Gosney based on an NMR study.[179] The X-ray crystal structure of ylide **74** gave very similar results.[180]

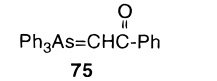



**73**

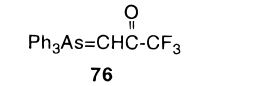



**74**

A comparative study of the crystal structure of (benzoylmethylene)triphenylarsorane (**75**) and [(trifluoroacetyl)methylene]triphenylarsorane (**76**) showed that the ylidic C−As in **75** was less polar than that in **76**. The bond order of As−C (1.855) in **76** was higher than that (1.55) in **75**. This was consistent with their chemical reactivities. Wittig reaction of **75** with carbonyl compounds proceeded smoothly. Compound **76**, however, was unable to convert aldehydes to the corresponding olefins, although it did react with stronger electrophiles, such as fluorinated anhydrides.




**75**

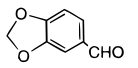
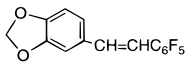
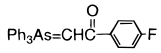
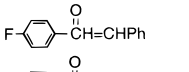
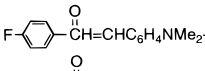
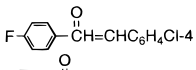
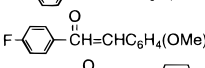
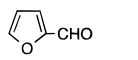
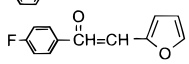
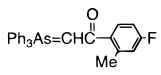
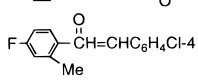
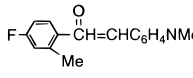
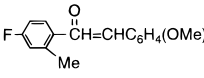
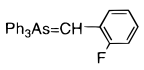
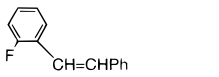
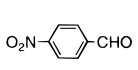
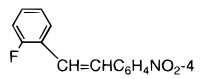
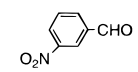
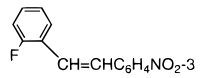
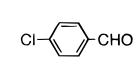
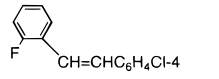
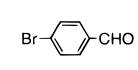
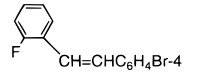
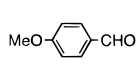
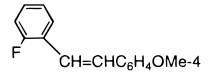
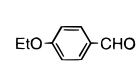
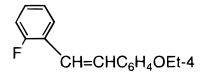



**76**

### *1.2. Preparations and Synthetic Applications of Fluorinated Arsonium Ylides*

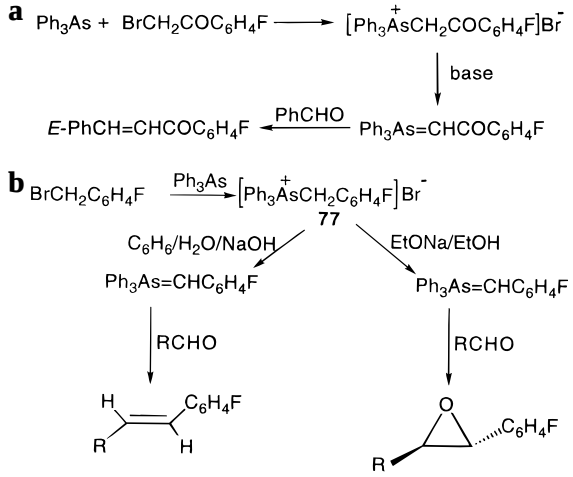
**1.2.1. Salt Method.** Deprotonation of arsonium salts, generated from quaternization of $Ph_3As$ with fluorine-containing halides, gave rise to the corresponding arsonium ylides. Thus, the stabilized ylide, [(fluorobenzoyl)methylene]triphenylarsorane, was prepared, isolated and reacted with aldehydes to form the corresponding *trans*-olefins (Scheme 54a, Table 29).[173] The semistabilized ylide (fluorobenzylidene)-triphenylarsorane, generated from salt **77**, reacted with aldehydes to afford either alkenes or epoxides dependent on reaction conditions. Under benzene/aqueous NaOH phase transfer conditions, *trans*-olefins were obtained exclusively (Table 29)[181] while only *trans*-epoxides were isolated from the EtOH/

**Table 29. Olefin Formation via Conventional Wittig Reaction of Fluorinated Arsonium Ylides**

| Ylide | RCHO | Product[a] | Yield | Ref. |
|---|---|---|---|---|
| $Ph_3As=CHC_6F_5$ | PhCHO | $C_6F_5CH=CHPh$ | 85 | 175 |
| | PhCH=CHCHO | $C_6F_5CH=CHCH=CHPh$ | 93 | 175 |
| | 2-$ClC_6H_4CHO$ | $C_6F_5CH=CHC_6H_4Cl$-2 | 90 | 175 |
| | 4-$ClC_6H_4CHO$ | $C_6F_5CH=CHC_6H_4Cl$-4 | 92 | 175 |
| | 4-$FC_6H_4CHO$ | $C_6F_5CH=CHC_6H_4F$-4 | 89 | 175 |
| | 4-$NO_2C_6H_4CHO$ | $C_6F_5CH=CHC_6H_4NO_2$-4 | 86 | 175 |
| | 2,4-$Cl_2C_6H_4CHO$ | $C_6F_5CH=CHC_6H_4Cl_2$-2,4 | 83 | 175 |
| | 4-$BrC_6H_4CHO$ | $C_6F_5CH=CHC_6H_4Br$-4 | 94 | 175 |
| | 4-$MeOC_6H_4CHO$ | $C_6F_5CH=CHC_6H_4OMe$-4 | 92 | 175 |
| |  |  | 90 | 175 |
|  | PhCHO |  | 62 | 173 |
| | 4-$Me_2NC_6H_4CHO$ |  | 70 | 173 |
| | 4-$ClC_6H_4CHO$ |  | 68 | 173 |
| | 3,4-$(MeO)_2C_6H_3CHO$ |  | 65 | 173 |
| |  |  | 60 | 173 |
|  | 4-$ClC_6H_4CHO$ |  | 67 | 173 |
| | 4-$Me_2NC_6H_4CHO$ |  | 71 | 173 |
| | 3,4-$(MeO)_2C_6H_3CHO$ |  | 64 | 173 |
|  | PhCHO |  | 86 | 181 |
| |  |  | 86 | 181 |
| |  |  | 94 | 181 |
| |  |  | 94 | 181 |
| |  |  | 89 | 181 |
| |  |  | 89 | 181 |
| |  |  | 88 | 181 |

a. Trans isomer only.

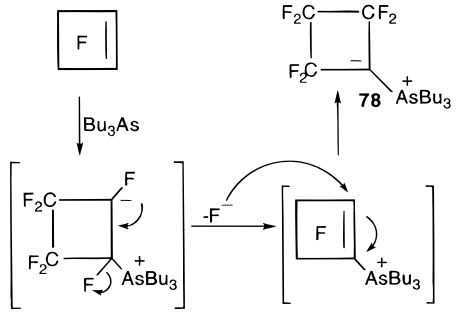
**Scheme 54**



EtONa solvent/base system (Scheme 54b, Table 30).[182,183] These results (solvent system, product, geometry of the product, and yield) were very similar to the corresponding nonfluorinated ylide, $Ph_3As{=}CHPh$.[129]

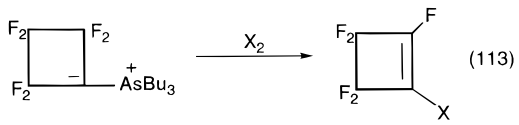
**1.2.2. From Tributylarsine and Perfluorocyclobutene.** Tributylarsine reacted with perfluorocyclobutene in ether at room temperature to form the ylide **78** in quantitative yield (Scheme 55). Presum-

**Scheme 55**



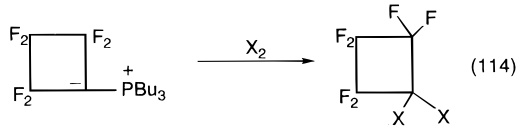
ably, $Bu_3As$ attacked the double bond in cyclobutene followed by fluoride ion elimination. Subsequently, fluoride ion added to the intermediate olefinic carbon $\beta$ to the As atom.[105]

Bromination and iodination of arsonium ylide **78** gave rise to bromo- or iodocyclobutene, respectively (eq 113). Bromination reaction proceeded much faster than iodination. In contrast, halogenation of the corresponding phosphonium ylide formed saturated compounds (eq 114).[183]



(113)

X=Br, I



(114)

X=Br, I

**1.2.3. From Triphenylarsine Oxide and Perfluoroalkyne.** Addition of triphenylarsine oxide to

**Table 30. Epoxidation of Arsonium Ylide and Aldehydes[183]**

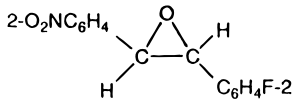
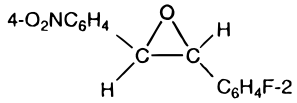
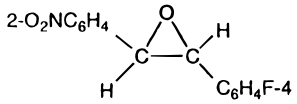
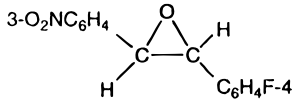
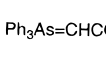
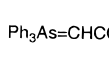
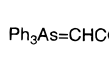
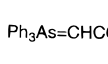
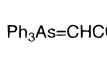
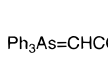
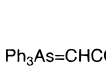
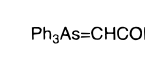
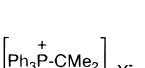
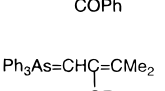
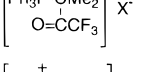
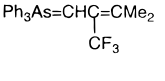
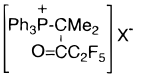
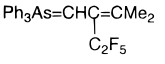
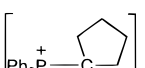
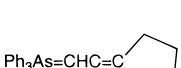
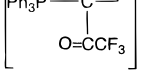
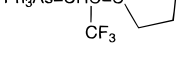
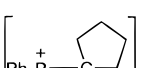
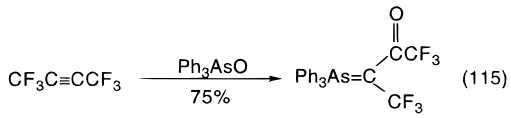
| Ylide | RCHO | Product | Yield (%) |
|---|---|---|---|
| $Ph_3As=CHC_6H_4F$-2 | 2-$O_2NC_6H_4CHO$ |  | 64 |
| | 4-$O_2NC_6H_4CHO$ |  | 64 |
| $Ph_3As=CHC_6H_4F$-4 | 2-$O_2NC_6H_4CHO$ |  | 50 |
| | 3-$O_2NC_6H_4CHO$ |  | 49 |

**Table 31. Synthesis of Fluorinated Arsoranes via Transylidation**

| $Ph_3As=CHR$ | $R_FX$ | Product | Yield[a] | ref. |
|---|---|---|---|---|
| $Ph_3As=CH_2$ | $CF_3CO_2Et$ | $Ph_3As=CHCOCF_3$ | 65 | 172 |
| | $C_2F_5CO_2Et$ | $Ph_3As=CHCOC_2F_5$ | 64 | 185 |
| | $C_3F_7CO_2Et$ | $Ph_3As=CHCOC_3F_7$ | 65 | 185 |
| | $C_7F_{15}CO_2Et$ | $Ph_3As=CHCOC_7F_{15}$ | 66 | 185 |
| | $Cl(CF_2)_3CO_2Et$ | $Ph_3As=CHCO(CF_2)_3Cl$ | 66 | 185 |
| | $Cl(CF_2)_5CO_2Et$ | $Ph_3As=CHCO(CF_2)_5Cl$ | 65 | 185 |
| $Ph_3As=CHCOCF_3$ | $(CF_3CO)_2O$ |  | 79(86) | 185 |
| $Ph_3As=CHCOC_2F_5$ | $(C_2F_5CO)_2O$ |  | 64(80) | 185 |
| $Ph_3As=CHCOC_3F_7$ | $(C_3F_7CO)_2O$ |  | 78(91) | 185 |
| $Ph_3As=CHCOC_7F_{15}$ | $(C_7F_{15}CO)_2O$ |  | 92 | 185 |
| $Ph_3As=CHCO(CF_2)_3Cl$ | $[Cl(CF_2)_3CO]_2O$ |  | 70 | 185 |
| $Ph_3As=CHCO(CF_2)_5Cl$ | $[Cl(CF_2)_5CO]_2O$ |  | 81 | 185 |
| $Ph_3As=CHCOCF_3$ | $(C_2F_5CO)_2O$ |  | 94(90) | 185 |
| | $(C_3F_7CO)_2O$ |  | 90(86) | 185 |
| $Ph_3As=CHCOC_2F_5$ | $(C_3F_7CO)_2O$ |  | 72(72) | 185 |
| $Ph_3As=CH_2$ | $C_6F_6$ | $Ph_3As=CHC_6F_5$ | b | 175,187 |
| | $C_6F_5Cl$ | $Ph_3As=CHC_6F_4Cl$-4 | b | 187 |
| $Ph_3As=CHCOPh$ | $(CF_3CO)_2O$ |  | 73 | 192 |
| | $(C_2F_5CO)_2O$ |  | 70 | 192 |
| | $(C_3F_7CO)_2O$ |  | 83 | 192 |
| $Ph_3As=CH_2$ |  |  | b | 188,189 |
| |  |  | b | 189 |
| |  |  | b | 189 |
| |  |  | b | 189 |
| |  |  | b | 189 |
| |  |  | b | 189 |

a. The yield in parentheses is from the reaction using $Et_3N$ as an acid scavenger.
b. The ylide was prepared and used *in situ.*

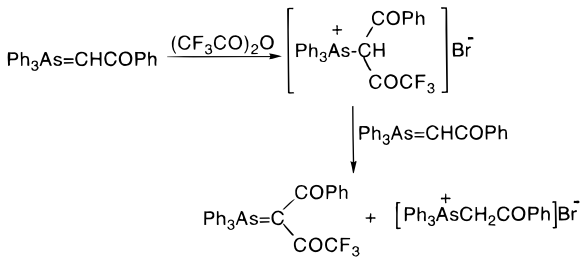
perfluoro-2-butyne led to the corresponding ylide in 75% yield (eq 115).



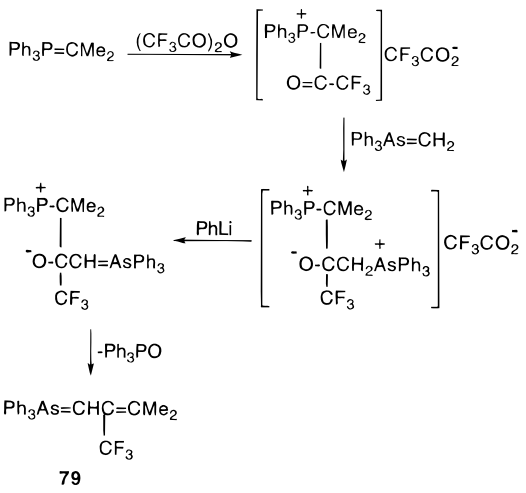
$$CF_3C{\equiv}CCF_3 \xrightarrow[75\%]{Ph_3AsO} Ph_3As{=}C(C(=O)CF_3)CF_3 \quad (115)$$

**1.2.4. Transylidation.** The majority of fluorinated arsonium ylides have been prepared by the transylidation method. Thus, fluorinated arsonium ylides have been prepared from nonfluorinated arsonium ylides with fluorinated compounds, such as esters,[172,185] acid halides,[114a] anhydrides,[172] olefins,[125,186] aromatics,[175,187] epoxides,[126] and fluorinated phosphonium salts[188−190] (Table 31). A typical reaction is illustrated in Scheme 56. In these reactions, 2 equiv of the reagent ylide were required. The first equivalent of the ylide acted as a nucleophile and the

**Scheme 56**



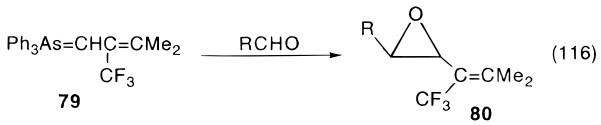
**Scheme 57**



second mole of the ylide was used as a base. Stabilized ylides were isolated, and semistabilized ylides were generated and used *in situ*. Shen and coworkers reported a modified transylidation. When 1 equiv of triethylamine was used as an acid scavenger, only 1 equiv of $Ph_3As{=}CHC(O)CF_3$ was required to react with equimolar $(CF_3CO)_2O$ to give bis(trifluoroacetyl)-substituted ylide in good yield. The basicity of $Ph_3As{=}CHC(O)CF_3$ was weaker than $Et_3N$, so that it could be regenerated by $Et_3N$ from its conjugate acid.

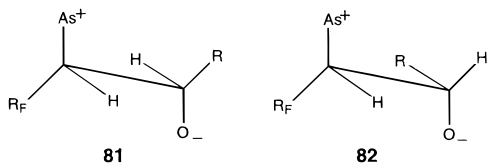
Addition of $Ph_3As{=}CH_2$ to the carbonyl group of fluorinated $\beta$-keto phosphonium salts followed by treatment with PhLi formed ylides **79** as illustrated in Scheme 57, which is similar to the reaction of $Ph_3P{=}CH_2$ and $\beta$-keto phosphonium salts (cf. section IV.2.5).

The resultant fluorinated arsonium ylide **79** was treated *in situ* with aromatic aldehydes to give exclusively fluorinated *trans*-epoxides **80**, which could not be prepared by other means (eq 116). The



(116)

| R: | Yield | R: | Yield |
|---|---|---|---|
| Ph, | 45%; | 4-$BrC_6H_4$ | 35%; |
| 4-$ClC_6H_4$ | 63%; | 4-$MeOC_6H_4$ | 55%; |
| 2-$ClC_6H_4$ | 40%; | 2-$MeOC_6H_4$ | 42%; |
| 4-$FC_6H_4$ | 40%; | 4-$O_2NC_6H_4$ | 55%; |



explanation for the excellent *trans* selectivity was the superior stability of intermediate **81** which led to the *trans*-epoxides.[188]

Fluorinated arsonium ylides **79** were also useful reagents for the synthesis of diene esters or amides by reaction with α-bromoacetates or α-bromoacetamides. Thus, fluorinated 2,4-dienamides or 2,4-dienyl carboxylates were obtained by treatment of acetates or amides with the ylide **79** (Scheme 58,

**Scheme 58**

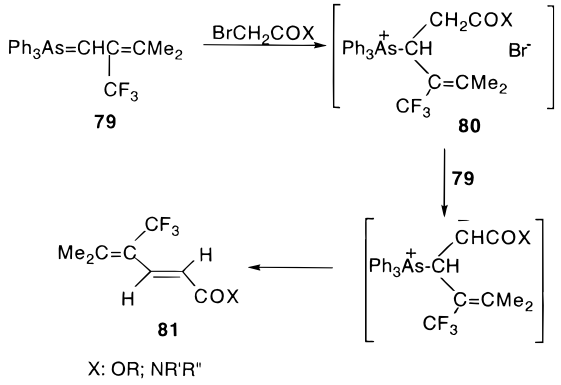
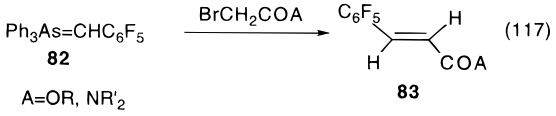
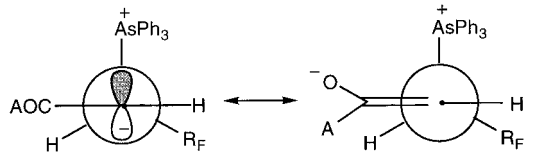


Table 32). Similarly amides and esters were obtained by the reaction of α-bromoacetamides or α-bromoacetates with ylide **82** (eq 117, Table 32).[187] The

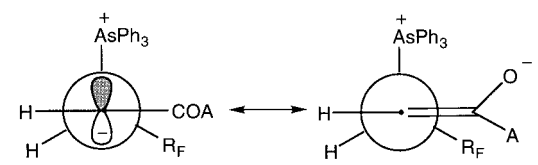


(117)

latter ylide was prepared *in situ* by transylidation of $Ph_3As{=}CH_2$ with fluorobenzenes. The reaction proceeded under mild conditions and gave very good yields of **81** and **83** with excellent (*E*)-selectivity for the newly formed double bond. The mechanism of the reaction may involve nucleophilic attack of the ylide on the α-bromo compounds to form salts **80** which were deprotonated by a second mole of the ylide **79** to produce betaine intermediates. Subsequent elimination of triphenylarsine from the betaine led to the olefins. The excellent (*E*)-selectivity was achieved in these reactions due to the more stable intermediate **84a** (or its enolate form) compared to **84b**.



**84a**



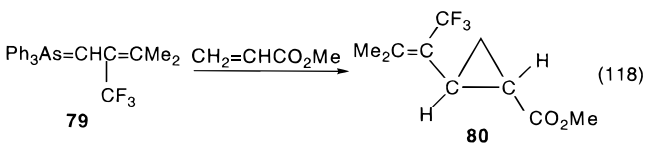
**84b**

Upon treatment of ylide **79** with acrylates, disubstituted cyclopropanes **85** were obtained exclusively

**Table 32. Alkene Formation via the Reaction of Fluorinated Arsonium Ylides and α-Bromo Ester or α-Bromoamide**

| Ylide | $BrCH_2COA$ | Product | Yield | Ref. |
|---|---|---|---|---|
| $Ph_3As=CHC(CF_3)=CMe_2$ | $BrCH_2CO_2Me$ | $Me_2C=C(CF_3)CH=CHCO_2Me$ | 45 | 189a |
| | $BrCH_2CO_2Et$ | $Me_2C=C(CF_3)CH=CHCO_2Et$ | 43 | 189a |
| | $BrCH_2CO_2Bu$-n | $Me_2C=C(CF_3)CH=CHCO_2Bu$-n | 65 | 189a |
| | $BrCH_2CO_2Bu$-i | $Me_2C=C(CF_3)CH=CHCOBu$-i | 59 | 189a |
| $Ph_3As=CHC(CF_3)=C$(cyclopentyl) | $BrCH_2CO_2Me$ | $C$(cyclopentyl)$=C(CF_3)CH=CHCO_2Me$ | 62 | 189a |
| | $BrCH_2CO_2Et$ | $C$(cyclopentyl)$=C(CF_3)CH=CHCO_2Et$ | 68 | 189a |
| | $BrCH_2CO_2Bu$-n | $C$(cyclopentyl)$=C(CF_3)CH=CHCO_2Bu$-n | 69 | 189a |
| | $BrCH_2CO_2Bu$-i | $C$(cyclopentyl)$=C(CF_3)CH=CHCOBu$-i | 69 | 189a |
| $Ph_3As=CHC(CF_3)=CMe_2$ | $BrCH_2CONEt_2$ | $Me_2C=C(CF_3)CH=CHCONEt_2$ | 59 | 189b |
| | $BrCH_2CONPr^i_2$ | $Me_2C=C(CF_3)CH=CHCONPr^i_2$ | 45 | 189b |
| | $BrCH_2CON(Bu$-n$)_2$ | $Me_2C=C(CF_3)CH=CHCON(Bu$-n$)_2$ | 75 | 189b |
| | $BrCH_2CON$(pyrrolidine) | $Me_2C=C(CF_3)CH=CHCON$(pyrrolidine) | 57 | 189b |
| $Ph_3As=CHC(CF_3)=C$(cyclopentyl) | $BrCH_2CONEt_2$ | $C$(cyclopentyl)$=C(CF_3)CH=CHCONEt_2$ | 55 | 189b |
| | $BrCH_2CONPr^i_2$ | $C$(cyclopentyl)$=C(CF_3)CH=CHCONPr^i_2$ | 51 | 189b |
| | $BrCH_2CON(Bu$-n$)_2$ | $C$(cyclopentyl)$=C(CF_3)CH=CHCON(Bu$-n$)_2$ | 85 | 189b |
| | $BrCH_2CON$(pyrrolidine) | $C$(cyclopentyl)$=C(CF_3)CH=CHCON$(pyrrolidine) | 51 | 189b |
| $Ph_3As=CHC_6F_5$ | $BrCH_2CO_2Me$ | $C_6F_5CH=CHCO_2Me$ | 99 | 187b |
| | $BrCH_2CO_2Et$ | $C_6F_5CH=CHCO_2Et$ | 97 | 187b |
| | $BrCH_2CO_2Bu$-n | $C_6F_5CH=CHCO_2Bu$-n | 99 | 187b |
| | $BrCH_2CO_2Bu$-i | $C_6F_5CH=CHCO_2Bu$-i | 95 | 187b |
| | $BrCH_2CONEt_2$ | $C_6F_5CH=CHCONEt_2$ | 65 | 187a |
| | $BrCH_2CONPr_2$ | $C_6F_5CH=CHCONPr_2$ | 75 | 187a |
| | $BrCH_2CON(Bu$-n$)_2$ | $C_6F_5CH=CHCON(Bu$-n$)_2$ | 80 | 187a |
| | $BrCH_2CON$(pyrrolidine) | $C_6F_5CH=CHCON$(pyrrolidine) | 62 | 187a |
| $Ph_3As=CHC_6F_4Cl$-4 | $BrCH_2CO_2Me$ | 4-$ClC_6F_4CH=CHCO_2Me$ | 95 | 187b |
| | $BrCH_2CO_2Et$ | 4-$ClC_6F_4CH=CHCO_2Et$ | 94 | 187b |
| | $BrCH_2CO_2Bu$-n | 4-$ClC_6F_4CH=CHCO_2Bu$-n | 97 | 187b |
| | $BrCH_2CO_2Bu$-i | 4-$ClC_6F_4CH=CHCO_2Bu$-i | 99 | 187b |
| | $BrCH_2CONEt_2$ | 4-$ClC_6F_4CH=CHCONEt_2$ | 52 | 187a |
| | $BrCH_2CONPr_2$ | 4-$ClC_6F_4CH=CHCONPr_2$ | 74 | 187a |
| | $BrCH_2CON(Bu$-n$)_2$ | 4-$ClC_6F_4CH=CHCON(Bu$-n$)_2$ | 79 | 187a |
| | $BrCH_2CON$(pyrrolidine) | 4-$ClC_6F_4CH=CHCO$N(pyrrolidine) | 75 | 187a |

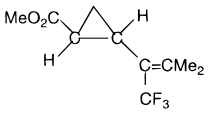
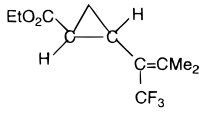
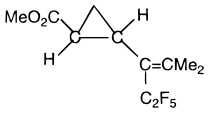
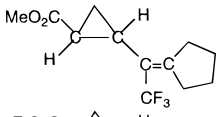
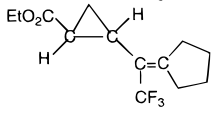
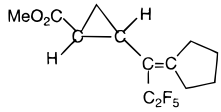
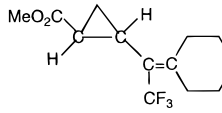
as the *trans*-isomer (eq 118, Table 33).[190] The




79 80 (118)

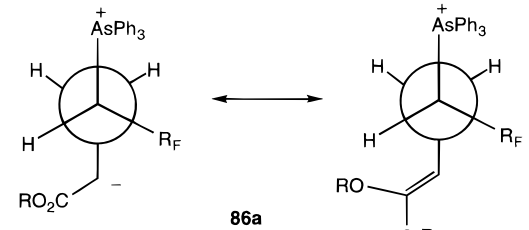
proposed mechanism of the cyclization included

**Table 33. Synthesis of Cyclopropane Derivatives from Arsonium Ylide and Acrylate[190]**

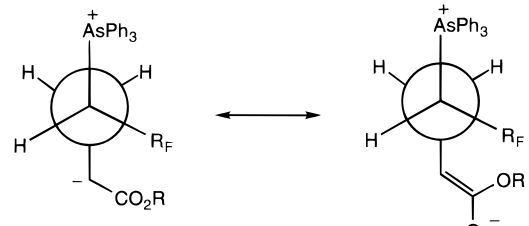
| Ylide | Acrylate | Product[a] | Yield |
|---|---|---|---|
| $Ph_3As=CHC(CF_3)=CMe_2$ | $CH_2=CHCO_2Me$ |  | 51 |
| | $CH_2=CHCO_2Et$ |  | 50 |
| $Ph_3As=CHC(C_2F_5)=CMe_2$ | $CH_2=CHCO_2Me$ |  | 54 |
| $Ph_3As=CHC(CF_3)=C$(cyclopentyl) | $CH_2=CHCO_2Me$ |  | 62 |
| | $CH_2=CHCO_2Et$ |  | 49 |
| $Ph_3As=CHC(CF_3)=C$(cyclopentyl) | $CH_2=CHCO_2Me$ |  | 43 |
| $Ph_3As=CHC(CF_3)=C$(cyclohexyl) | $CH_2=CHCO_2Me$ |  | 46 |

a, Trans isomer only.

initial attack of ylide **79** at the $\beta$-carbon of the acrylate to produce intermediate **86** in which the negative charge was stabilized by the ester group. Subsequently, the anion attacked the carbon α to the arsenic atom intramolecularly, which led to elimination of triphenylarsine and formation of the cyclopropane derivatives **85**. The *trans* selectivity may be explained by the formation of the more stable conformation **86a** (or its enolate form).




**86a**




**86b**

Conventional Wittig reaction of arsonium ylide **82** with carbonyl compounds gave (*E*)-olefins exclusively (eq 119, Table 29).[175] The reaction with arsonium ylide proceeded under milder conditions and gave

**Table 34. Reaction of Arsonium Ylides with Fluorinated Alkynes**

| $Ph_3As=CHR$ | Fluorinated alkynes | Conditions | Product ratio 88:89:90 | Yield | ref. |
|---|---|---|---|---|---|
| $Ph_3As=CHCO_2CH_3$ | $CF_3C\equiv CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 90 | 130 |
| | $C_2F_5C\equiv CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 93 | 130 |
| | $C_3F_7C\equiv CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 95 | 130 |
| $Ph_3As=CHCOCH_3$ | $CF_3C\equiv CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 91 | 131 |
| | $C_2F_5C\equiv CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 94 | 131 |
| | $C_3F_7C\equiv CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 90 | 131 |
| $Ph_3As=CHCOPh$ | $CF_3C\equiv CCO_2CH_3$ | $C_6H_6$/RT | 100:0:0 | 98 | 134 |
| | $C_2F_5C\equiv CCO_2CH_3$ | $C_6H_6$/RT | 88:0:12 | 95 | 134 |
| | $C_3F_7C\equiv CCO_2CH_3$ | $C_6H_6$/RT | 88:0:12 | 98 | 134 |
| $Ph_3As=CHCOCH_3$ | $CF_3C\equiv CCO_2CH_3$ | $CH_3OH$/RT | 42:58:0 | 47 | 168 |
| | $C_2F_5C\equiv CCO_2CH_3$ | $CH_3OH$/RT | 41:59:0 | 48 | 168 |
| | $C_3F_7C\equiv CCO_2CH_3$ | $CH_3OH$/RT | 30:70:0 | 49 | 168 |
| | $CF_3C\equiv CCO_2CH_3$ | DMF/RT | 100:0:0 | 98 | 168 |
| $Ph_3As=CHC_6H_4NO_2$-4 | $CF_3C\equiv CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 89 | 170 |
| | $C_2F_5C\equiv CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 100 | 170 |
| | $C_3F_7C\equiv CCO_2CH_3$ | $CH_2Cl_2$/RT | 100:0:0 | 100 | |
| $Ph_3As=CHCOPh$ | $C_2F_5C\equiv CCN$ | $CH_2Cl_2$/RT | 74:26:0 | 95 | 135 |
| | $C_3F_7C\equiv CCN$ | $CH_2Cl_2$/RT | 73:27:0 | 96 | 135 |
| | $C_2F_5C\equiv CCN$ | $CH_2Cl_2$/-78°C | 0:100:0 | 50 | 135 |
| | $C_3F_7C\equiv CCN$ | $CH_2Cl_2$/-78°C | 0:100:0 | 53 | 135 |
| | $CF_3C\equiv CCO_2CH_3$ | $CH_3OH$/RT | 15:85:0 | 94 | 168 |
| | $C_2F_5C\equiv CCO_2CH_3$ | $CH_3OH$/RT | 19:81:0 | 99 | 168 |
| | $C_3F_7C\equiv CCO_2CH_3$ | $CH_3OH$/RT | 24:76:0 | 100 | 168 |
| $Ph_3As=CHCOCF_3$ | $CF_3C\equiv CCO_2CH_3$ | $CH_2Cl_2$/RT | 56:44:0 | 75 | 191 |
| | $C_2F_5C\equiv CCO_2CH_3$ | $CH_2Cl_2$/RT | 38:62:0 | 71 | 191 |
| | $C_3F_7C\equiv CCO_2CH_3$ | $CH_2Cl_2$/RT | 43:57:0 | 84 | 191 |
| $Ph_3As=CHCOC_2F_5$ | $C_3F_7C\equiv CCO_2CH_3$ | $CH_2Cl_2$/RT | 38:62:0 | 81 | 191 |
| $Ph_3As=CHCOC_3F_7$ | | $CH_2Cl_2$/RT | 49:51:0 | 82 | 191 |

better yields in comparison with the reaction with the corresponding phosphonium ylides.

$$Ph_3As=CHC_6F_5 + RCHO \longrightarrow \underset{R}{\overset{H}{}}\!\!>\!\!=\!\!<\underset{H}{\overset{C_6F_5}{}} \quad (119)$$

A number of fluorinated arsonium ylides were prepared by the nucleophilic addition of arsonium ylides to fluorinated alkynes followed by rearrangement (Scheme 59, Table 34). Like phosphonium ylide chemistry, three types of compounds were observed in the reaction and included a four-membered ring rearrangement product **88** (pathway a), 1,3-proton migration product **89**, and acyl group migration product **90** (pathway b). In aprotic solvents, ylides **87** (R = $CO_2Me$[130] and COMe[131]) reacted with $R_FC\equiv CCO_2Me$ to form ylides **88** only. In protic solvents, reaction of ylide **87** (R = COMe) with $R_FC\equiv CCO_2Me$ formed ylides **88** and **89**, whereas both **88** and **90** were obtained from the reaction of ylide **87** (R = COPh) with $R_FC\equiv CCO_2Me$.[168] Temperature also affected the distribution of the products. At room temperature, reaction of **87** (R = COPh) with $R_FC\equiv CCN$ formed **88** and **89**, whereas only **89** was obtained when the reaction was carried out at −78 °C.[135]

**Scheme 59**

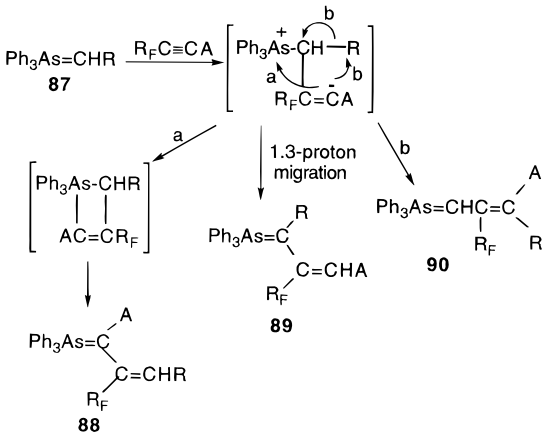
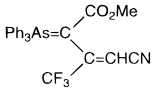
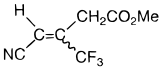
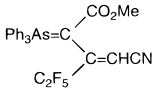
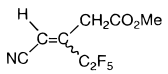
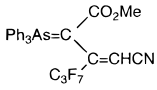
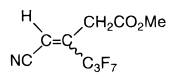
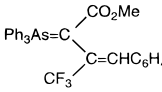
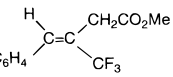
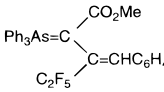
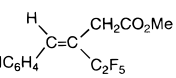
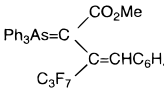
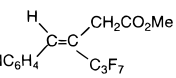
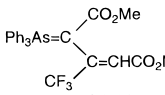
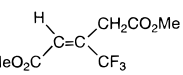
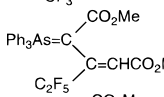
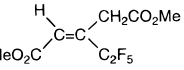
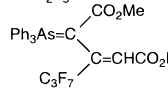
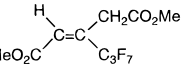


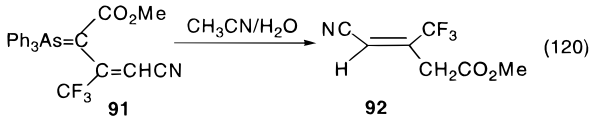

**Table 35. Synthesis of Unsaturated Esters via Hydrolysis of Arsonium Ylides**

| Ylide | Products | Z:E | yield | ref. |
|---|---|---|---|---|
|  |  | 95:5 | 69 | 171 |
|  |  | 95:5 | 73 | 171 |
|  |  | 96:4 | 75 | 171 |
|  |  | 100:0 | 100 | 170 |
|  |  | 100:0 | 99 | 170 |
|  |  | 100:0 | 92 | 170 |
|  |  | a | 88 | 130 |
|  |  | a | 84 | 130 |
|  |  | a | 82 | 130 |

a. only one isomer, but the configuration was not reported.

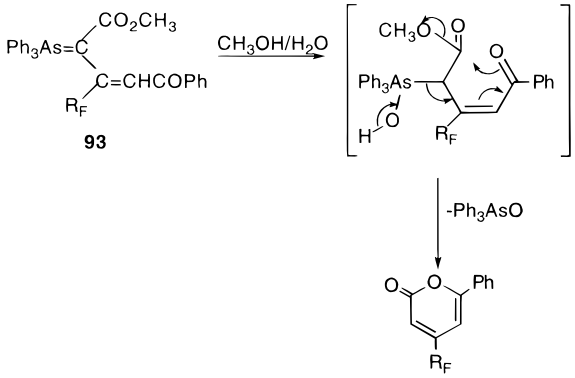
**1.2.5. Hydrolysis.** Hydrolysis of arsonium ylide **91** provided fluorinated olefins **92**. Unsaturated esters were formed quantitatively by hydrolysis of **91** (eq 120, Table 35).[171] The double bond in **92** was conjugated with nitrile group and was predominantly *cis*. The hydrolysis of **91** proceeded smoothly in refluxing aqueous MeCN. In contrast, the corresponding phosphonium ylides **40** were hydrolyzed at 150−180 °C. The mechanism of the hydrolysis for these two types of ylides may be similar. However,

more stable phosphonium ylides required harsher reaction conditions.



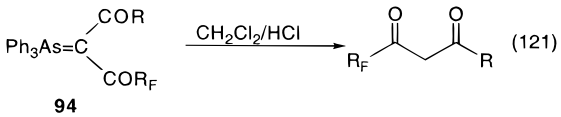

Hydrolysis of arsonium ylide **93** in aqueous MeOH at reflux formed a pyrone as the sole fluorinated product and triphenylarsine oxide (Scheme 60).[134a]

**Scheme 60**




The authors proposed that the reaction may proceed via addition of $H_2O$ to the ylide followed by elimination of $Ph_3AsO$ and MeOH.[134b]

Hydrolysis of arsonium ylides **94** in $CH_2Cl_2$ at room temperature with excess HCl gas afforded the corresponding $\beta$-keto esters (R = OMe) and $\beta$-diketones (R = Ph), respectively (eq 121).[192]



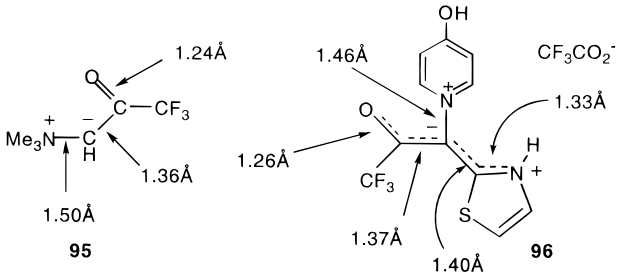

| R | $R_F$ | Yield(%) |
|---|---|---|
| OMe | $CF_3$ | 78 |
| OMe | $C_2F_5$ | 76 |
| OMe | $CF_3CFH$ | 85 |
| Ph | $CF_3$ | 96 |
| Ph | $C_2F_5$ | 77 |
| Ph | $C_3F_7$ | 75 |

In short, monofluoroarsonium ylides exhibit reactivity similar to their nonfluorinated analogs. The semistabilized ylide $Ph_3As{=}CHC_6F_5$ (**82**) converts aldehydes to *trans*-olefins. Fluorinated *trans*-epoxides are also obtained from the reaction of ylide **82** and aldehydes. In all these reactions, only aldehydes (no ketones) have been utilized as carbonyl substrates. Both **79** and **82** can convert α-bromoacetates and α-bromoacetamides into the corresponding α,$\beta$-unsaturated compounds. The stabilized ylide $Ph_3As{=}CHCOCF_3$ is much less reactive than its nonfluorinated counterpart and does not react with aldehydes, but readily reacts with anhydrides. Stabilized fluorinated arsonium ylides have been isolated and characterized and semistabilized fluorinated ylides are generated and used *in situ*. The reaction of arsonium ylides with fluorinated alkynes forms various fluorinated ylides, which are useful for the preparation of functionalized alkenes and heterocycles.

## 2. Fluorinated Nitrogen Ylide

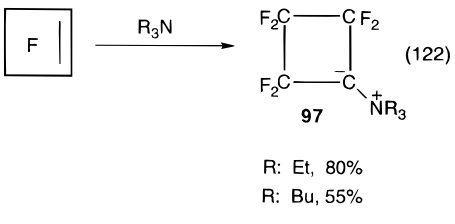
### *2.1. Structure and Property*

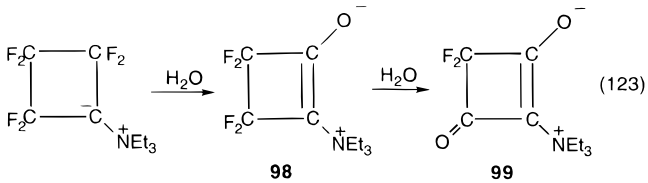
The X-ray diffraction results for **95**[193] and **96**[194] have been reported. In both cases, the ylidic negative charge is significantly delocalized over the neighboring carbonyl group. The ylidic C−N bond in **95** is almost the same in length as the average length of the remaining C−N bonds. Similarly the ylidic C−N bond in **96** is very close to the C−N single bond in length. In contrast, both the ylidic C−P bond in phosphonium ylide **67** and the ylidic C−As bond in arsonium ylide **76** have significant partial double-bond character. The bond order is 1.60 for C═P in **67** and 1.55 for C═As in **76**. The ability of heteroatoms to stabilize an adjacent ylidic anion is in the order P > As > N. We have mentioned the reason why phosphorus is superior to arsenic in stabilizing a neighboring ylidic anion. Nitrogen, however, was the least effective due to the absence of a d$\pi$−p$\pi$ interaction.




### *2.2. Preparations and Synthetic Applications*

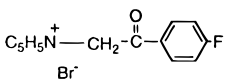
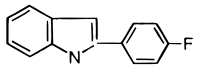
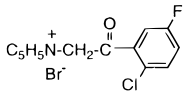
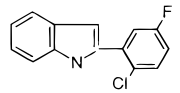
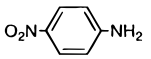
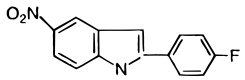
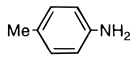
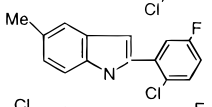
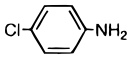
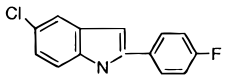
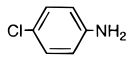
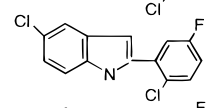
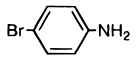
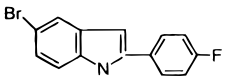
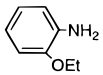
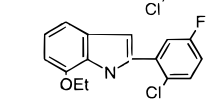
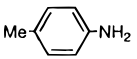
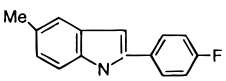
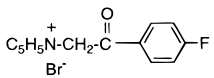
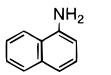
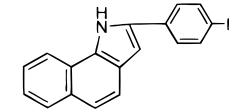
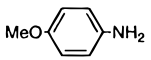
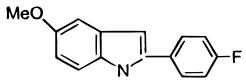
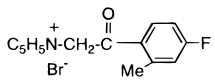
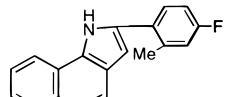
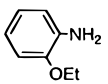
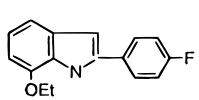
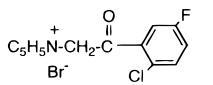
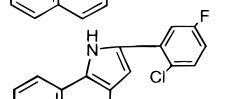
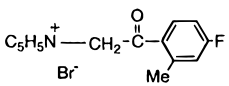
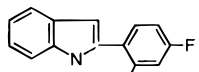
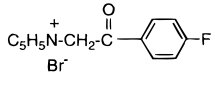
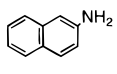
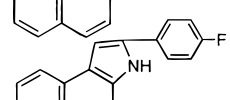
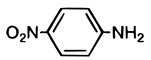
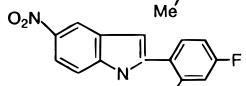
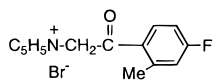
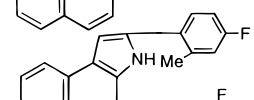
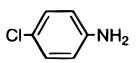
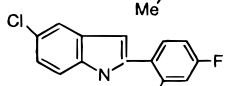
Burton and co-workers[195] reported that the addition of trialkylamine to perfluorocyclobutene gave ylide **97** (eq 122) which was readily hydrolyzed to afford **98** and **99** (eq 123). The preparation and



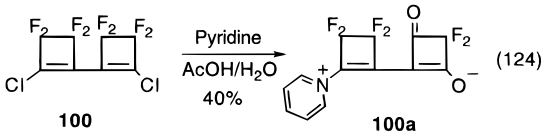




hydrolysis were similar to its phosphorus and arsenic analogs. In aqueous AcOH, pyridine added to flu-

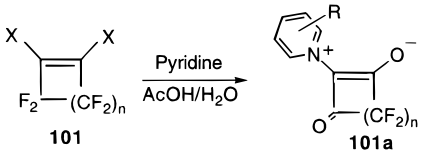
**Table 36. Synthesis of Fluorinated Indole Derivatives[198]**

| Pyridium salts | $ArNH_2$ | Product | Yield (%) | Pyridium Salt | $ArNH_2$ | Product | Yield (%) |
|---|---|---|---|---|---|---|---|
|  | $PhNH_2$ |  | 58 |  | $PhNH_2$ |  | 54 |
| |  |  | 60 | |  |  | 57 |
| |  |  | 62 | |  |  | 55 |
| |  |  | 56 | |  |  | 62 |
| |  |  | 60 |  |  |  | 63 |
| |  |  | 58 |  | |  | 56 |
| |  |  | 65 |  | |  | 59 |
|  | $PhNH_2$ |  | 56 |  |  |  | 61 |
| |  |  | 61 |  | |  | 54 |
| |  |  | 62 |  | |  | 56 |
| |  |  | 58 | | | | |
| |  |  | 60 | | | | |
| |  |  | 55 | | | | |
| |  |  | 63 | | | | |

orinated olefins **100**[196] or **101**[197] to form betaines **100a** and **101a**, respectively (eqs 124 and 125).




(124)

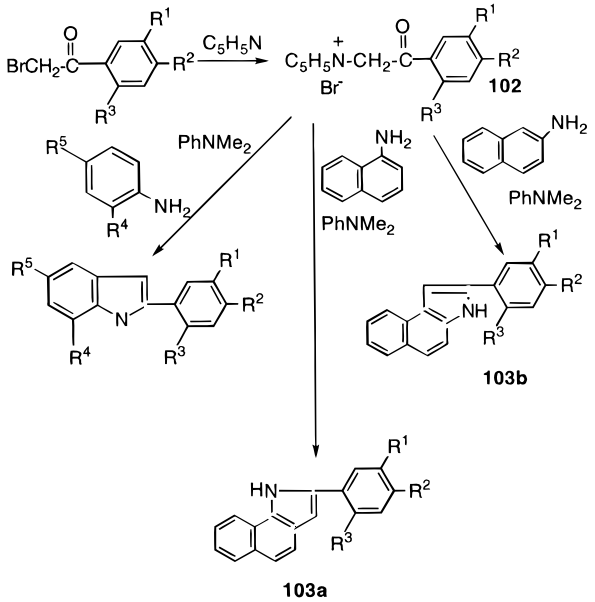



(125)

| X= | F | R= | H | n= | 1 | Yield (%) | 100 |
|---|---|---|---|---|---|---|---|
| | Cl | | H | | 1 | | 97 |
| | Cl | | H | | 2 | | 97 |
| | Cl | | H | | 3 | | 87 |
| | Cl | | 4-$CO_2$Et | | 1 | | 84 |
| | Cl | | 4-$CO_2$Et | | 2 | | 36 |
| | Cl | | Br | | 2 | | 33 |

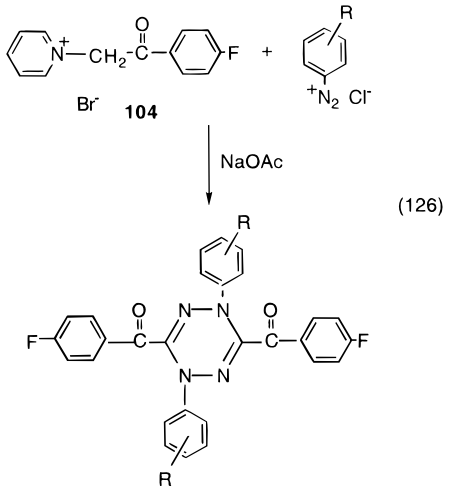
Bansal and co-worker[198] have prepared several fluorinated pyridinium salts by the reaction of pyridine and an α-bromoacetophenone. In refluxing *N*,*N*-dimethylaniline, reaction of salts **102** with substituted anilines furnished the corresponding fluorinated indoles. Similarly, compounds **103a** and **103b** were obtained from the reaction of the pyridinium salts with 1- or 2-naphthylamines, respectively (Scheme 61, Table 36). The reaction was considered to proceed

**Scheme 61**




through a pyridinium ylide. However, no further details or mechanistic information are available.

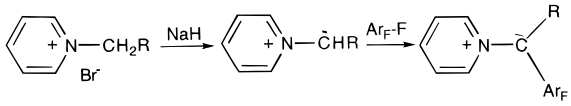
Tetrazines were isolated in 60−70% yields from the reaction of pyridinium salts **104** and aromatic diazonium salts in the presence of sodium acetate (eq 126).[199] The proposed mechanism for this reaction was similar to the reaction of arsonium ylide $Ph_3As{=}CHCOPh$ with aromatic diazonium salts, which also formed tetrazines.[200]




(126)

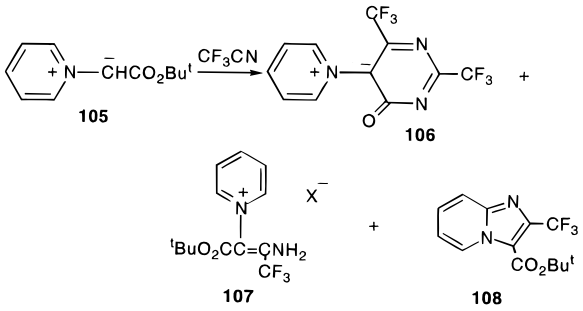
R= 2-$CO_2$H, 4-$CO_2$H, 3-$COCH_3$, 4-$COCH_3$, 4-$SO_3$H

Banks and co-workers[201−203] published the preparation of several fluorinated pyridinium ylides by reaction of nonfluorinated pyridinium ylides with fluorinated aromatics (eqs 127 and 128). Reaction of ylide **105** with trifluoroacetonitrile in 1:2 ratio also gave a fluorinated nitrogen ylide **106** (in 29% yield) along with compounds **107** and **108**.



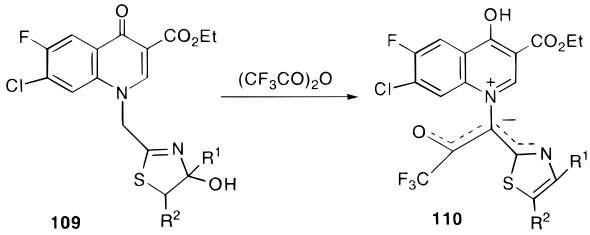

(127)

R= CN, $Ar_F$=4-$C_5F_4N$, Yield=75%
R= $CO_2Bu^t$, $Ar_F$=4-$C_5F_4N$, 85%
$Ar_F$=4-$C_6F_4CF_3$, 85%
$Ar_F$= 80%
$Ar_F$= 81%




(128)

During the dehydration of compound **109** by trifluoroacetic anhydride (TFAA), an unexpected *N*-ylide **110** was obtained (eq 129). Since **110** was difficult

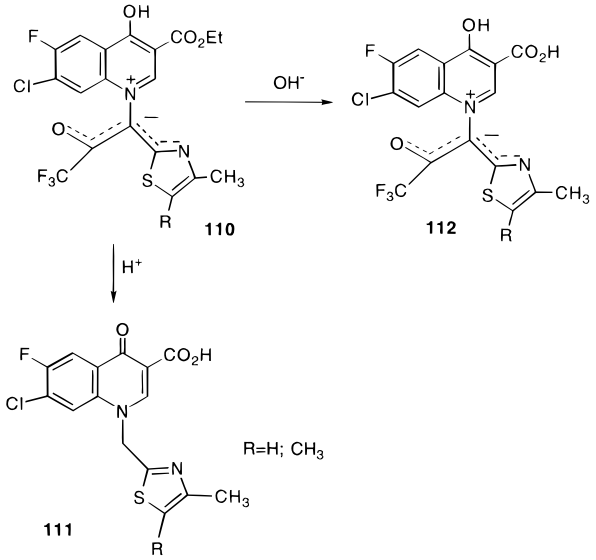



(129)

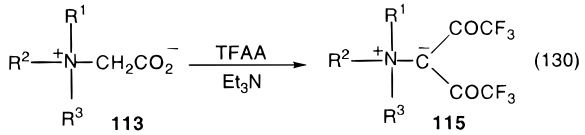
$R^1$=$R^2$=$CH_3$
$R^1$=$CH_3$, $R^2$=H
$R^1$=$CO_2$Et, $R^2$=H

to form crystal, a model *N*-ylide **96** was prepared by a similar method and its crystal structure was investigated. Under acidic conditions (6 N HCl, refluxing in propanol) ylide **110** was hydrolyzed to **111**. Alkaline hydrolysis (2 equiv of NaOH, refluxing in propanol) of **110**, however, gave the ylide **112** in which only the ester group was hydrolyzed and the ylidic bonding had survived (Scheme 62).

**Scheme 62**

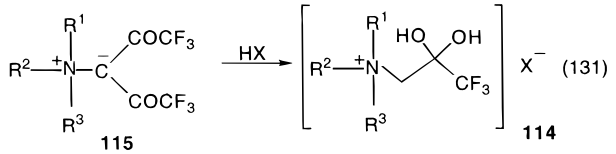



Reaction of betaine $Me_3N^+CH_2CO_2^-$ (**113**) with excess trifluoroacetic anhydride gave the ammonium salt **114** in 37%, whereas equimolar reaction gave very low yields of ylide **115**.[204] In the presence of triethylamine, however, the betaine **113** was converted to bistrifluoroacetyl-substituted ylides **115** (eq 130).[205,206] The ylide **115** was readily hydrolyzed by



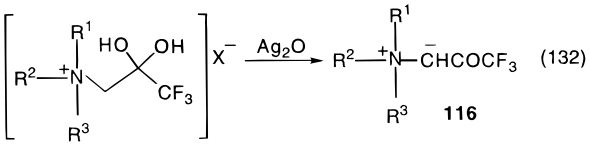

| $R^1$ | $R^2$ | $R^3$ | Yield (%) |
|---|---|---|---|
| Me | Me | Me | 82 |
| Me | Me | Et | 46 |
| Me | Et | Et | 41 |

acid to the corresponding monotrifluoroacetyl-substituted ammonium salt hydrate **114** (eq 131).[205,206]



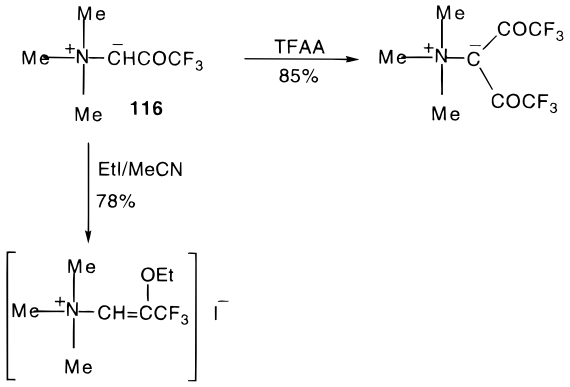

| $R^1$ | $R^2$ | $R^3$ | X | Yield (%) |
|---|---|---|---|---|
| Me | Me | Me | I | 83 |
| Me | Me | Et | Br | 98 |
| Me | Et | Et | Br, $CF_3CO_2$ | 84 |
| Et | Et | Et | I, $CF_3CO_2$ | 80 |

Upon treatment with $Ag_2O$, ylides **116** were obtained in good yields from **114** (eq 132).[206] The monotrifluoroacetyl-substituted ylide **116** reacted with trifluoroacetic anhydride to form the C-acylation product and with ethyl iodide to afford the O-alkylation product (Scheme 63).[207]

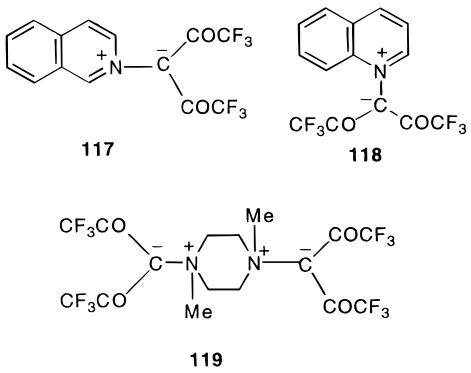



| $R^1$ | $R^2$ | $R^3$ | Yield (%) |
|---|---|---|---|
| Me | Me | Me | 86 |
| Me | Me | Et | 75 |
| Me | Et | Et | 76 |
| Et | Et | Et | 84 |

**Scheme 63**



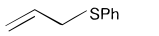
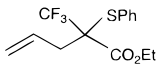
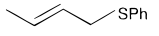
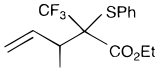
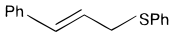
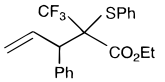
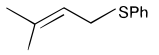
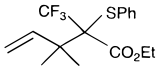
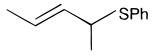
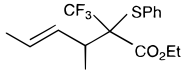
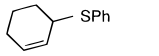
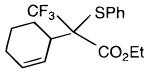
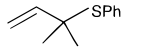
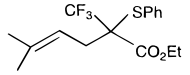
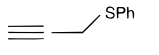
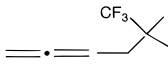
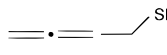
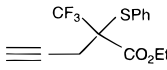
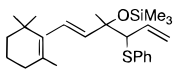
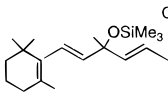

Bis(trifluoroacetyl)-substituted ylides **117** (75%) and **118** (75%) as well as bisylide **119** (50%) were prepared by a similar strategy.[208]



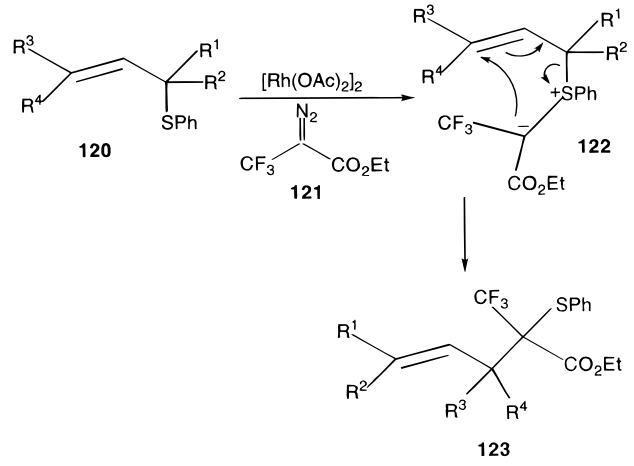

## 3. Fluorinated Sulfur and Stibonium Ylides

There have been few reports of fluorinated sulfur ylides. Xu and co-workers[209] reported that in the presence of a rhodium catalyst, $[Rh(OAc)_2]_2$, ethyl 3,3,3-trifluoro-2-diazopropionate (**121**) reacted with allylic sulfides to produce **123** in excellent yield. They suggested that the reaction proceeded via [2,3]-sigmatropic rearrangement of fluorinated sulfur ylide intermediate **122**. First, **121** was decomposed by the Rh catalyst to form a reactive carbenoid, which was trapped by sulfides **120** to give fluorinated sulfur ylides **122**. Subsequent [2,3]-sigmatropic rearrangement of **122** provided **123** (Scheme 64, Table 37). In the case where the allylic sulfide had an α-alkyl substituent, the rearrangement led to the exclusive formation of a product with the newly formed double bond in a *trans* configuration. This stereospecificity

**Table 37. Reaction of 121 with Allylic Sulfides in the Presence of "Rh" Catalyst**

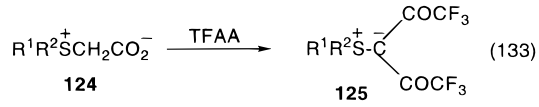
| Sulfide | Reaction conditions T(°C)/t(h) | Product | Yield |
|---|---|---|---|
|  | 68/0.4 |  | 96 |
|  | 65/0.4 |  | 97 |
|  | 70/0.4 |  | 99 |
|  | 65/0.5 |  | 95 |
|  | 45/0.5 |  | 98 |
|  | 55/0.5 |  | 93 |
|  | 35/0.6 |  | 80 |
|  | 60/0.5 |  | 85 |
|  | 35/0.7 |  | 82 |
|  | 40/0.6 |  | 90 |

**Scheme 64**

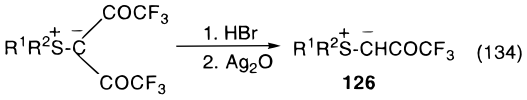


has also been observed in a nonfluorinated allylic sulfur ylide rearrangements.

Double trifluoracetylation of sulfonium betaine **124** with TFAA led to bis(trifluoroacetyl)-substituted sulfonium ylide **125** (eq 133).[210,211] Hydrolysis of ylides **125** with HBr or HCl followed by treatment with $Ag_2O$ or $Na_2CO_3$ provided monosubstituted ylides **126** (eq 134).[210,211] Acylation of ylide **126** with TFAA or TCA (trichloroacetic anhydride) gave excellent yields of the corresponding ylides **125**, whereas a much lower yield resulted when trichloroacetyl chloride was applied as the acylating reagent (eq 135).[212] The reaction of ylide **126a** with diazonium salt solely provided the novel ylide **127** (eq 136). However, in a similar reaction, **126b** formed sulfonium salt **128**

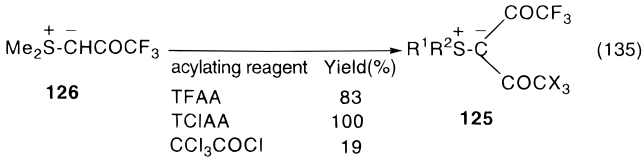


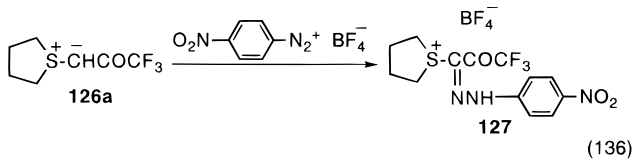
| $R^1$ | $R^2$ | Yield(%) |
|---|---|---|
| Me | Me | 65 |
| Me | Et | 52 |
| Et | Et | 50 |
| -$(CH_2)_4$- | | 60 |
| -$(CH_2)_5$- | | 86 |

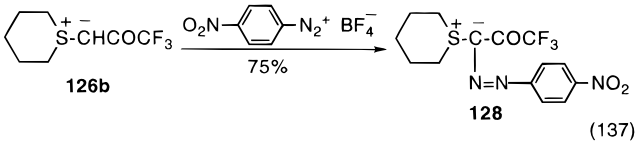


| $R^1$ | $R^2$ | Yield(%) |
|---|---|---|
| Me | Me | 63 |
| Me | Et | 44 |
| -$(CH_2)_4$- | | 29 |
| -$(CH_2)_5$- | | 55 |

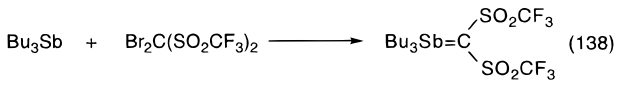
only (eq 137).[213,214] There was no explanation for this observation.







A fluorinated stibonium ylide has also been reported. Pavleuko and co-workers prepared [bis[(trifluoromethyl)sulfonyl]methylene]tributylstibonium ylide in 50% yield by treatment of $Br_2C(SO_2CF_3)_2$ with a 3-fold excess of tributylstibine (eq 138).[215] This stibonium ylide was a stable, colorless crystalline solid and did not react with 2,4-dinitrophenylhydrazine upon prolonged heating (1 month).

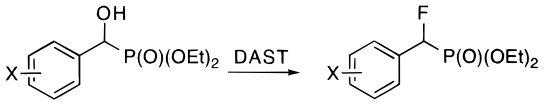


## *VI. α-Fluoro Phosphonates and Their Anions*

### 1. Preparation of α-Fluoro Phosphonates

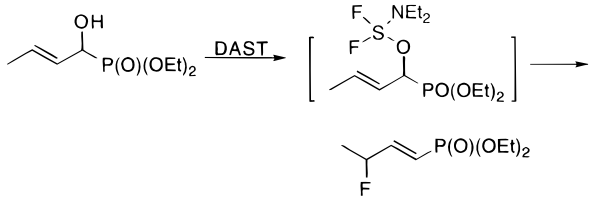
(Diethylamido)sulfur trifluoride (DAST) has been widely used to fluorinate alcohols to give the corresponding alkyl fluorides.[216] α-Fluoro phosphonates have been obtained by fluorination of α-hydroxy phosphonates, which were conveniently prepared by the sodium methoxide-catalyzed condensation of dialkyl phosphites with aldehydes.[217] Blackburn successfully prepared (α-fluorobenzyl)phosphonates by

reaction of α-hydroxy-α-(phenylmethyl)phosphonates with DAST (eq 139).[218,219] The substitution of the

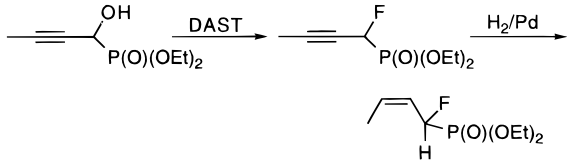



(139)

hydroxy group by fluorine generally proceeded smoothly and efficiently with a small excess of DAST in methylene chloride at 0 °C. Substituents such as chlorine and methyl could be tolerated but the reaction failed with a methoxy substituent. However, with (α-hydroxyallyl)phosphonates, the replacement of the hydroxy group by fluorine proceeded via an SN2′ or a cyclic SNi′ mechanism giving exclusively γ-fluoro-α,β-unsaturated phosphonates with the (*E*)-configuration rather than the α-fluoro phosphonates (eq 140).[219] In contrast to this behavior, regiospecific fluorination of the hydroxy group of (α-hydroxypropargyl)phosphonate occurred to produce (α-fluoropropargyl)phosphonates (eq 141).[220]




(140)




(141)

Electrophilic fluorination of carbanions has provided an alternative means for the introduction of fluorine into organic compounds. Perchloryl fluoride ($FClO_3$) was the first utilized as an electrophilic reagent and reacted with a variety of carbanions to give organo fluorides.[221] The highly stabilized methylene bisphosphonates (eq 142),[222] phosphonoacetates (eq 143),[223] and [α-(phenylsulfonyl)methyl]-phosphonate (eq 144)[224] gave good to excellent yields of the corresponding fluorinated compounds with high selectivities (eqs 142−144), although less stabilized carbanion did not lead to the desired products. However, the toxicity and explosive properties of this reagent hampered large scale applications.

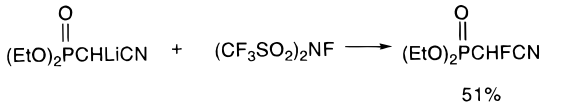
$$[(EtO)_2P(O)]_2CH_2 + FClO_3 \xrightarrow{tBuOK} [EtO)_2P(O)]_2CHF \quad (142)$$

$$(EtO)_2P(O)CH_2CO_2Et + FClO_3 \xrightarrow{NaH} (EtO)_2P(O)CHFCO_2Et \quad (143)$$

$$PhSO_2CH_2P(O)(OEt)_2 + FClO_3 \xrightarrow{KH} PhSO_2CHFP(O)(OEt)_2 \quad (144)$$

Recently, a variety of N−F compounds with different reactivities that are safe and easy to handle have been developed. Diffferding reacted alkylphosphonates with KDA in THF at −78 to −90 °C, followed by treatment with *N*-fluorobenzenesulfonimide to α-fluoro phosphonates.[225] Davis obtained α-phosphono-α-fluoroacetates in 78% yield by reaction of phosphonoacetates with NaHMDS and *N*-fluoro-*o*-benzenedisulfonimide at −78 °C to 0 °C for 2 h (eq 145).[226] Reaction of the anion of diethyl (cyanomethyl)phosphonate with *N*-fluorobis[(trifluoromethyl)-sulfonyl]imide in THF at −78 °C gave 51% of (cyanofluoromethyl)phosphonate (eq 146).[227]


(145)

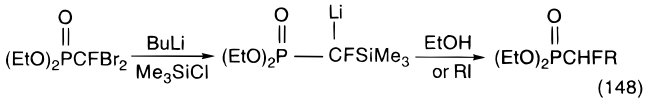



(146)

The Michaelis−Arbuzov reaction is one of the most facile methods for the preparation of (α-fluoromethyl)phosphonates. Reaction of trialkyl phosphites with fluorohalomethane, such as $CFBr_3$, was conveniently carried out in ether or triglyme at 25−50 °C to give good yields of the phosphonates $(RO)_2P(O)CFBr_2$ (eq 147).[228]


(147)

$(EtO)_2P(O)CFBr_2$ reacted with 2 equiv of BuLi in the presence of $Me_3SiCl$ to give [lithio(trimethylsilyl)-fluoromethyl]phosphonate, which was trapped by electrophiles followed by hydrolysis to give a various α-fluoro phosphonates.[229]

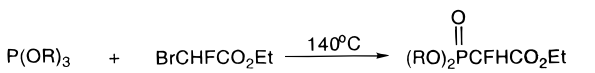



(148)

| | |
|---|---|
| R = H | 93% |
| R = Me | 96% |
| R = Et | 93% |
| R = n-$C_3H_7$ | 96% |
| R = n-$C_4H_9$ | 95% |
| R = $CH_2CH{=}CH_2$ | 91% |
| R = $CH_2CH{=}CHMe$ | 92% |
| R = n-$C_5H_{11}$ | 93% |

[Lithio(trimethylsilyl)fluoromethyl]phosphonate also reacted with $ClCO_2Et$ at −78 °C, followed by hydrolysis with 2 N HCl to give $(EtO)_2P(O)CFHCO_2Et$.[230]

Phosphonofluoroacetates also were prepared by reaction of trialkyl phosphites with ethyl bromofluoroacetate at elevated temperatures (140 to 150 °C) (eq 149).[231−233] The phosphonofluoroacetates could be obtained in higher yields if an air condensor was used for the reaction.




(149)

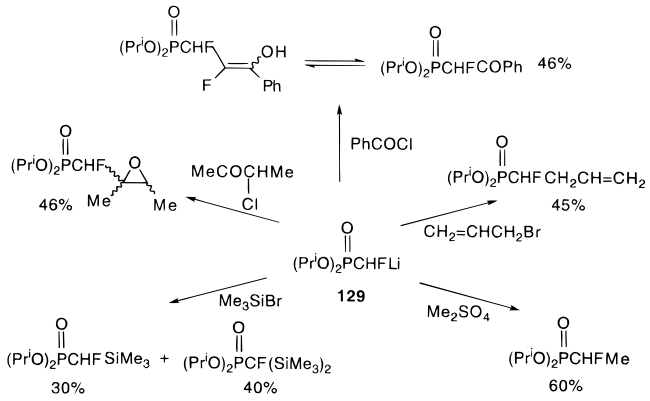
Reduction of α-halo-α-fluoro phosphonates also lead to α-fluoro phosphonates. Treatment of $(EtO)_2POCHCFCl$ with Raney Ni formed $(EtO)_2POCH_2F$, along with the overreduced product methylphosphonate.[234]

## 2. Application of Anions of α-Fluoro Phosphonates

### *2.1. The Anion of (α-Fluoroalkyl)phosphonates*

Treatment of diisopropyl (fluoromethyl)phosphonate with LDA at low temperatures generated the lithiated carbanion ($i$-PrO)$_2$P(O)CFHLi, **129**, which could be used in reactions at temperatures in the range −78 to 0 °C.[235,236] Alkylation of **129** with allyl bromide and dimethyl sulfate occurred smoothly to produce the alkylated products. Upon reaction with trimethylsilyl bromide or chloride, the silylated product was initially formed, which underwent a proton exchange reaction resulting in further silylation to give [α,α- di(trimethylsilyl)methyl]phosphonate. Acylation with benzoyl chloride provided (α-fluoro-$\beta$-oxoalkyl)phosphonate, which existed exclusively as an $E/Z$ mixture of enol form. With an α-halo ketone, a Darzens-type reaction occurred and resulted in the formation of epoxide as described in Scheme 65.[235,236]

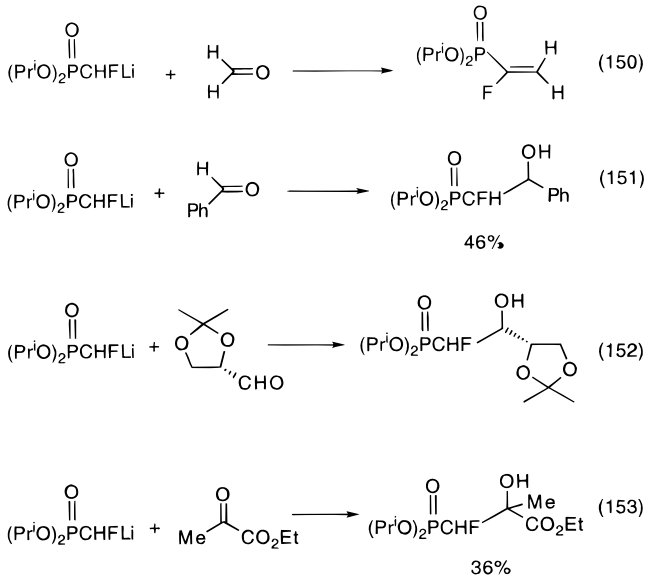
**Scheme 65**



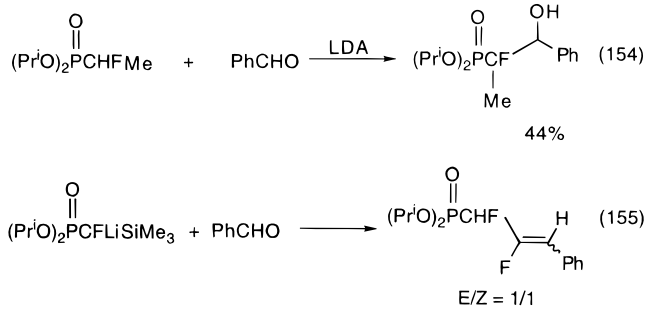

Diethyl (fluoromethyl)phosphonate works equally well with electrophiles under similar conditions.

Compound **129** also added to various aldehydes and ketones to form the corresponding α-fluoro-$\beta$-hydroxy phosphonates. The reaction time and temperature must be carefully controlled, since heating and prolonged stirring at room temperature resulted in the Wadsworth−Emmons reaction to give a fluoroolefin. From the reaction with paraformaldehyde, only fluoroolefin was observed (eq 150).[236] Acetaldehyde gave $\beta$-hydroxy-α-fluoro phosphonate along with a small amount of olefin. However, sterically hindered aldehydes exclusively produced $\beta$-hydroxy-α-fluoro phosphonates and no dehydration reaction occurred under the reaction conditions.[236] A chiral aldehyde produced an adduct with fair (5:2) degree of diastereoselectivity (eq 152) at the $\beta$-carbon center while there appeared to be no size discrimination between hydrogen and fluorine at α-carbon. Therefore, achiral aldehydes showed no diastereoselectivity (eqs 150, 151, and 153).[236]

Longer chain phosphonates such as (α-fluoroethyl)-phosphonate **130** also underwent similar reaction with aldehydes. $\beta$-Hydroxy-α-fluoro phosphonate was exclusively obtained when **130** was treated with




benzaldehyde (eq 154). When [α-lithio-α-(trimethylsilyl)-α-fluoromethyl]phosphonate reacted with benzaldehyde, Peterson reaction occurred resulting in the formation of vinylphosphonate (eq 155).[236]

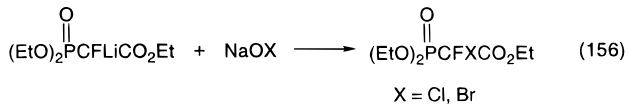



### *2.2. The Anion of Stabilized α-Fluoro Phosphonates*

**2.2.1. The Anion of Phosphorylfluoroacetic Acid Derivatives.** *2.2.1.1. Reactions with Carbonyl Substrates.* Machleidt was first able to prepare the diethyl (fluorocarbethoxymethyl)phosphonate anion by treatment of its precursor phosphonate, (EtO)$_2$P(O)CFHCO$_2$Et **131**, with a slurry of NaH in diethyl ether.[231] Elkik later also reported the utilization of NaH as a base in ether to generate the carbanion.[237] Both procedures required long reaction periods at ether reflux temperature, and low yields of the carbonyl compound condensation products were observed, which was probably due to decomposition of the formed carbanion. Burton and others used organolithium reagents as bases to deprotonate **131** in THF. The yields of the final condensation products with carbonyl compounds were good to excellent when BuLi was empolyed as a base.[238] Unlike NaH in ether, the depronation of **131** with alkyllithium rapidly occurred at −78 °C and was usually completed in 20 min. The $^{19}$F NMR spectrum of a THF solution of the anion exhibited a resonance at −231.1 ppm (d, $J$ = 73 Hz, rel CFCl$_3$), upfield shift compared to the precursor (−211.1 ppm, dd). In contrast, the

proton-decoupled $^{31}P$ NMR signal was shifted downfield, and its resonance occurred at 24.6 ppm (d, $J$ = 73 Hz, rel 85% $H_3PO_4$). These data indicated that the anion in THF had the negative charge localized on carbon exclusively rather than on oxygen. If it localized at oxygen, two sets of doublets were expected as a result of two stereoisomers of the enolate.[238]

Compound **131** could be fluorinated with $FClO_3$ to give the difluoro analog.[239] When **131** reacted with aqueous hypohalides in neutral conditions, the corresponding fluorohaloacetates were obtained in almost quantitative yields (eq 156).[240]

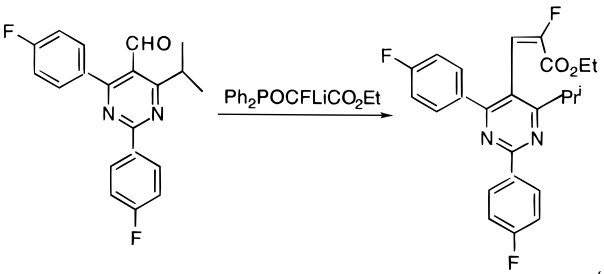


(156)

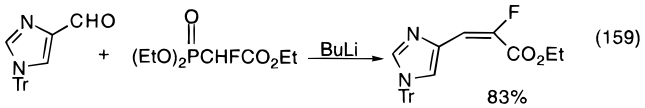
Machleidt and co-workers were the first to use the anion in the synthesis of α-fluoro-α,β-unsaturated esters by the Horner−Wadsworth−Emmons reaction of **131** with carbonyl substrates.[213] However, no stereochemistry of the formed products were reported. Recently, Moghadam and co-workers have examined the stereochemistry of the olefination reaction.[241] Their study indicated that high stereoselectivity could be achieved if the reaction was carried out in THF at low temperatures (−78 °C). A variety of aldehydes, including aryl aldehydes, aliphatic aldehydes, and α,β-unsaturated aldehydes, gave the corresponding olefination products with greater than 98% (*E*)-selectivity (eqs 157−160, Table 38).[242−247]



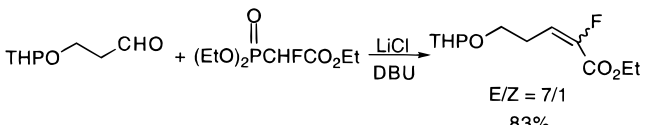
(157)



(158)

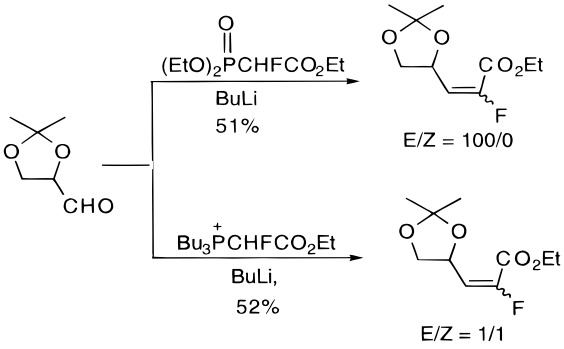


(159)

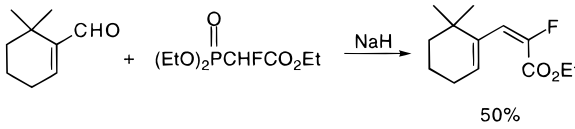


(160)

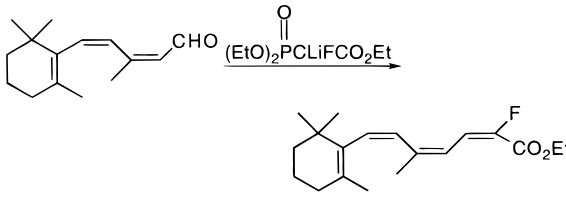
This method has preference over (fluorocarbethoxymethylene)tri-*n*-butylphosphorane which showed no stereoselectivity and provided equal amounts of (*E*)- and (*Z*)-isomers (eq 161).[249] The high stereoselective method was used in the synthesis of intermediates of fluororetinal (eq 162)[235,250,252,253] and fluorinated rhodopsin (eq 163).[252]



((161)



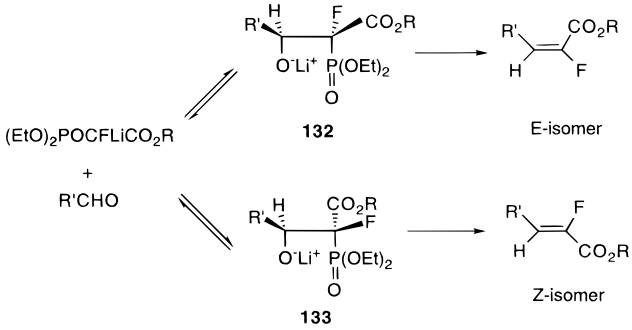
(162)



(163)

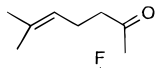
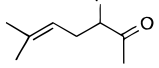
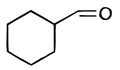
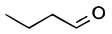
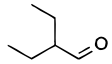
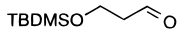
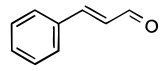
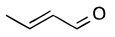
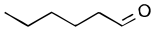
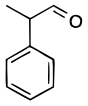
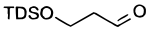
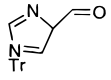
The mechansim for the formation of α-fluoro-α,β-unsaturated esters with high stereoselectivity is illustrated in Scheme 66. The addition of the anion

**Scheme 66**

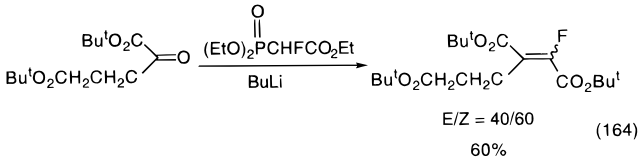



to aldehyde step is reversible and that intermediate can exist in two diastereoisomeric forms, **132** and **133**. Complexation of soluble lithium salts with the intermediate retards its reversibility between kinetic **132** and thermodynamic **133** isomers at low temperature. Consequently, **132** decomposes irreversibly to produce (*E*)-isomer as major product. However, raising the reaction temperature results in the loss of the stereoselectivity since **132** reversibly converts into more stable isomer **133**, which decomposes to (*Z*)-isomeric olefin.[241] Also, the reaction was less stereoselective when the corresponding phosphine oxide was used as a substrate in the olefination reaction.[241]

**Table 38. Reaction of $(EtO)_2POCFLiCO_2Et$ with Carbonyl Compounds**

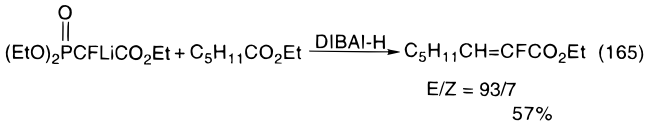
| Carbonyl compound RR'C=O | Yield (%) RR'C=CFCO$_2$Et | E/Z | Ref |
|---|---|---|---|
|  | 58 | | 231 |
|  | 53 | | 231 |
| $(FCH_2)_2C=O$ | 54 | | 231 |
|  | 87 | >98/2 | 245 |
|  | 65 | >98/2 | 245 |
|  | 83 | >98/2 | 245 |
|  | 84 | >98/2 | 245 |
|  | 80 | >98/2 | 245 |
|  | 87 | | 245 |
| PhCHO | 95 | 98/2 | 241 |
|  | 75 | 98/2 | 241 |
|  | 76 | 98/2 | 241 |
|  | 55 | 98/2 | 241 |
|  | 98 | 98/2 | 241 |
|  | 90 | 98/2 | 241 |
|  | 76 | 100/0 | 247 |
|  | 83 | 100/0 | 246 |

Reaction with ketones gave the desired products in good yield but only low stereoselectivity was observed (eq 164).[237,254,255]

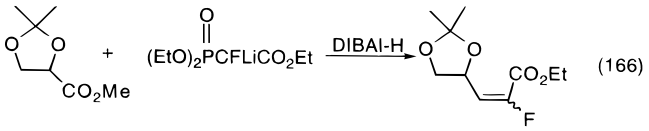



E/Z = 40/60
60% (164)

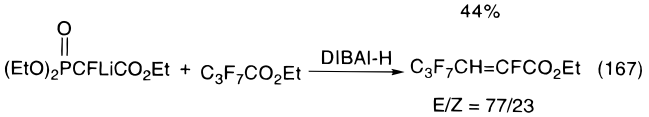
Esters could be converted into α-fluoro-α,β-unsaturated esters by a reduction−olefination sequence with **131**.[256,257] The preformed lithium anion of **131** solution was transferred to the *in situ* pregenerated aldehydes from reduction of the esters with DIBAl-H in THF. The stereoselectivity was fair to high (*E*/*Z* = 77/23 to 100/0). Although hydrocarbon aromatic and aliphitic esters were sucessfully used as substrates (eqs 165 and 166), this process was particularly useful for the synthesis of polyfluoro compounds since easily distillable fluoro esters could be employed as synthons for fluoro aldehydes which are not available (eq 167).[256,257]




E/Z = 93/7
57% (165)

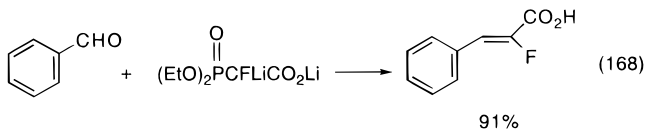



E/Z = 10/1
44% (166)




E/Z = 77/23
66% (167)

α-Fluoro-α,β-unsaturated acids could be prepared from diethoxyphosphorylfluoroacetic acid **134**. The acid **134** was first treated with 2 equiv of BuLi at −78 °C and then reacted with carbonyl compounds to give the desired products.[258] In comparison with the anion of ester **131**, the dianion of **134** only gave modest stereoselectivity with aliphatic aldehydes. Aromatic aldehydes, however, afforded (*Z*)-isomers exclusively in high yields in contrast to the predomination of (*E*)-isomer observed with **131** (eq 168).[258]

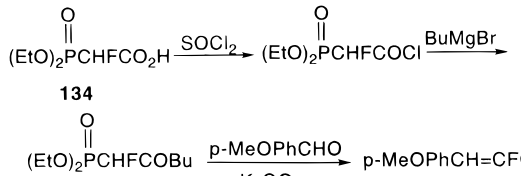



91% (168)

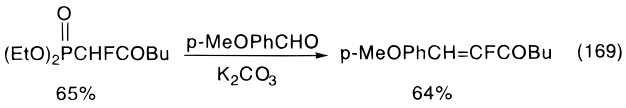
The mechanism for high (*Z*)-stereoselective olefination of the dianion of **134** with aromatic aldehydes is illustrated in Scheme 66 (R = Li$^+$, R′ = Ar). The addition of the anion to aldehyde step is probably reversible and the formed intermediate **133** should be more stable than the intermediate **132**, and **133** leads to the (*Z*)-olefin. The stablization of **133** may be due to the stereoelectronic interactions between a carboxylate group and a phenyl group in **133**.[258]

Compound **134** was also readily converted into the corresponding acyl chloride. Treatment of the acyl chloride with organometallic reagents such as lithium, magnesium, and cuprate reagents produced the α-(diethoxyphosphoryl)-α-fluoro ketones. The resultant ketones reacted with aldehydes in the presence of $K_2CO_3$ to give the α-fluoro-α,β-unsaturated ketones in modest yields (eqs 169 and 170).[259]

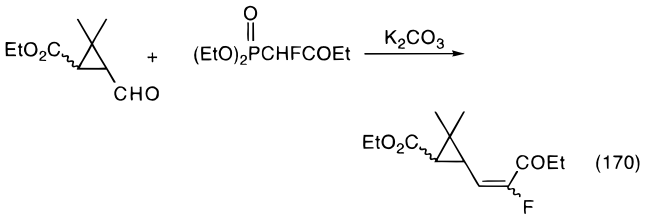
The anion of diethylphosphorylfluoroacetonitrile **135** was prepared by either deprotonation of its precursor with a base[227] or reaction of lithium α-fluoroacetonitrile with diethoxyphosphoryl chloride.[260]



**134**

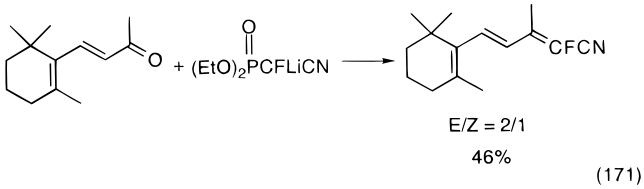


(169)

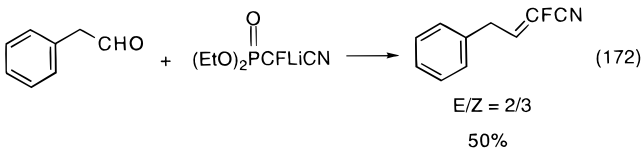


(170)

When **135** was treated with NaH in DME at 20 °C and the resultant anion reacted with an aldehyde **136**, the desired product was obtained in 72% yield with no stereoselectivity. The use of BuLi as a base in THF at −78 °C somewhat improved the stereoselectivity as summarized in eqs 171 and 172 and Table 39.[227,260]



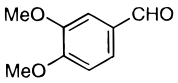
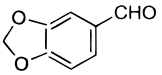
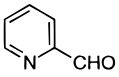
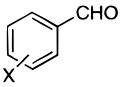
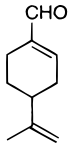
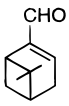
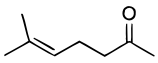
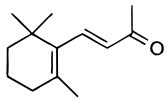
(171)



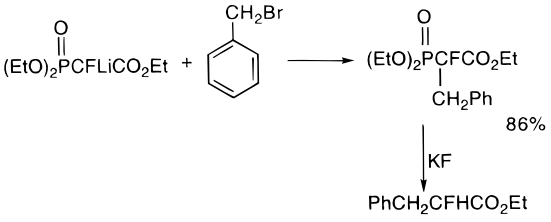
(172)

*2.2.1.2. Reactions with Alkyl Halide or Acyl Halide Substrates.* The anion of **131** underwent carbon alkylation with methyl iodide and allyl and benzyl bromide to give the corresponding alkylated products in 60−85% yields.[261−263] Secondary alkyl halides could be alkylated in THF under refluxing conditions. When the anion of **131** was used, the alkylated phosphonates suffered partial dealkylation by SN2 attack of the halide produced in the reaction. This side reaction could be readily suppressed by employment of the corresponding isopropylphosphonate carbanion, (*i*-PrO)$_2$P(O)CFLiCO$_2$Et, and CH$_3$CH(Ph)Br and (CH$_3$)$_2$CHI gave the C-alkylated products in 60−72% yields. Although treatment of the alkylated phosphonates with aqueous base under reflux conditions did not hydrolyze the phosphorus−carbon bond, the hydrolysis occurred smoothly with KF in triglyme to provide α-fluoro esters, along with toxic (RO)$_2$POF in good yields (eq 173). Unlike alkylation, silylation of the anion with bromotrimethylsilane proceeded predominantly at oxygen to form the corresponding silyl ketene acetal phosphonate as a mixture of two isomers. The driving force for O-silylation might be the formation of strong silicon−oxygen bond in the

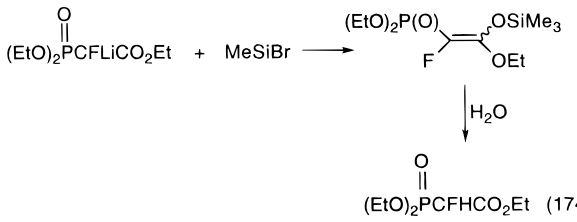
**Table 39. Reactions of (EtO)$_2$P(O)CFLiCN with Carbonyl Compounds RR′C=O**

| Carbonyl Compound RR′C=O | Yield (%) RR′C=CFCN | E/Z | Ref |
|---|---|---|---|
|  | 46 | 1/2 | 260 |
|  | 45 | 1/4 | 260 |
|  | 53 | 3/2 | 227 |
|  | | | |
| X = p-OMe | 52 | 1/1 | 260 |
| X = o-NO$_2$ | 62 | 1/1.6 | 260 |
| X = p-Ph | 82 | 1/3 | 260 |
| X = p-Me | 51 | 1/3 | 260 |
| X = p-NO$_2$ | 45 | 1/2 | 260 |
| X = H | 54 | 2/1 | 260 |
| E-PhCH=CHCHO | 38 | 3/2 | 227 |
| n-C$_6$H$_{13}$CHO | 30 | 3/7 | 227 |
| PhCH$_2$CHO | 50 | 2/3 | 227 |
|  | 42 | 2/1 | 227 |
|  | 54 | 2/1 | 227 |
|  | 40 | 1/1 | 227 |
|  | 46 | 2/1 | 227 |

product, which could be hydrolyzed with water to form phosphonate **131** (eq 174).

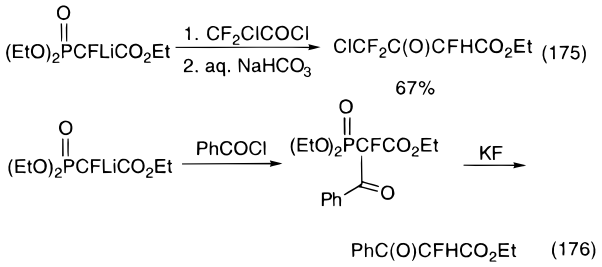


(173)

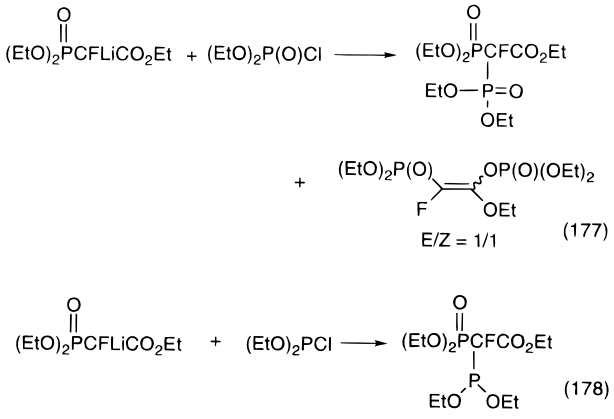


(174)

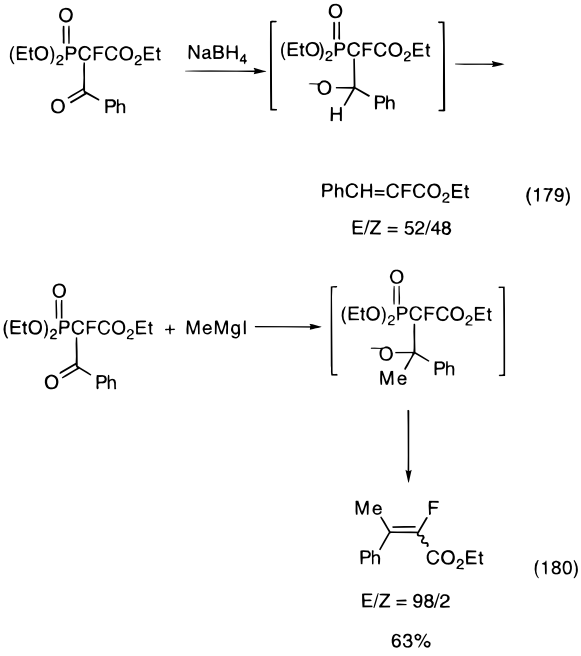
Acylation of the anion **131** with acid chlorides and anhydrides was also facile.[264,265] Unlike the hydrocarbon analog, the transylidation of the acylated ylide did not occur since there was no acidic proton in the product. Benzoyl chloride, acetyl chloride, and ethyl chloroformate gave the carbon-acylated phosphonates in 71−97% yields. With perfluoroacyl chlorides such as $C_3F_7COCl$, $CF_3COCl$, and $ClCF_2COCl$, the acylated products were isolated in 60−77% yields. Interestingly, hydrolytic cleavage of the acylated phosphonates depends on the type of acyl groups. Nonfluorinated acylated phosphonates were treated with 5% NaOH resulting in the formation of **131** along with less than 10% of phosphorus−carbon cleavage products. Fluorinated acylated phosphonates, however, exclusively underwent phosphorus−carbon cleavage to produce $R_FCOCHFCO_2Et$ (eq 175). On the other hand, selective cleavage of the nonofluorinated acylated products could be achieved by the use of fluoride ion. Treatment with KF resulted in the formation of $RCOCFHCO_2Et$ and $(EtO)_2POF$. The regioselectivity of the cleavage reaction might be best explained by the formation of the strong P−F bond (176).[265]



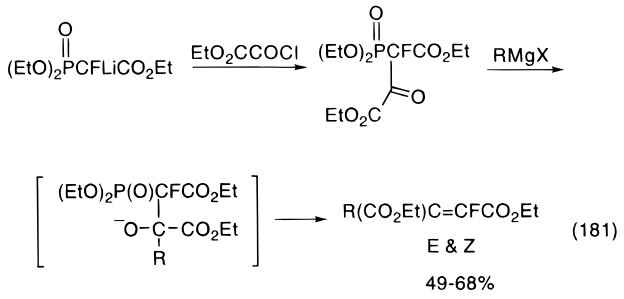

In addition to carboxylic acid halides, phosphoric acid chlorides also acylated the anion. A mixture of carbon- and oxygen-acylated products in a ratio of 25:37 were obtained upon reaction with $(EtO)_2P(O)Cl$ (eq 177). In contrast, the reaction of $(EtO)_2PCl$ with the anion led exclusively to the C-acylated phosphonate product (eq 178).[265]




The carbonyl group of the acylated product derived from the acyl halide was subjected to a nucleophilic attack to form a betaine-type intermediate, which then underwent intramolecular elimination to give an α-fluoro ester. $NaBH_4$[265] and various Grignard reagents such as alkyl-, phenyl-, and fluorinated phenylmagesium halides were used as nucleophiles and usually an *E*/*Z* mixture of α-fluoro-unsaturated esters were obtained in good yields (eqs 179 and 180).[266,267]



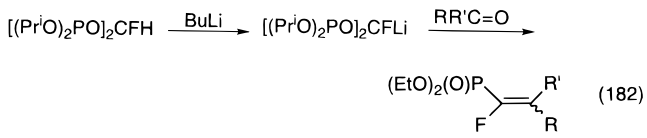

The acylated products with methyl or ethyl oxalyl chloride also underwent nucleophilic attack. Addition of the pregenerated carbanion in THF solution to oxalyl chloride at −78 °C formed $(EtO)_2POCF(COCO_2R)CO_2Et$, which reacted *in situ* with Grignard reagents to afford α-fluoro α,*β*-diesters, $R(CO_2R)C{=}CFCO_2Et$ (eq 181).[267] Alkyl Grignard reagents




gave the diester with 98−100% (*E*)-selectivity, while alkenyl and phenyl Grignard reagents significantly increased the (*Z*)-isomers. Exclusive (*Z*)-isomer was observed upon reaction with (phenylacetylenic)magnesium bromide. The stereoselectivity of the diester also depended on the metal counterions and solvents. In the case of reaction of the vinyl Grignard with $(EtO)_2POCF(COCO_2R)CO_2Et$, the *E*/*Z* ratio changed from 88/12 to 71/29 when the base was changed from LDA to NaH. In the presence of hexamethylphosphoric triamide (HMPT) or *N*,*N*-dimethylpropyleneurea (DMPU) as cosolvents, 98−99% (*E*)-stereoselectivity was observed.[267]

**2.2.2. The Anion of Phosphorylfluoromethyl Phosphonates and Sulfones.** The anion of tetraisopropyl or tetraethyl fluoromethylene bisphosphonates were readily prepared by treatment of the bisphosphonates with BuLi in THF at −78 °C. The anion condensed smoothly with aliphatic, aromatic, and α,*β*-unsaturated aldehydes and methyl ketones

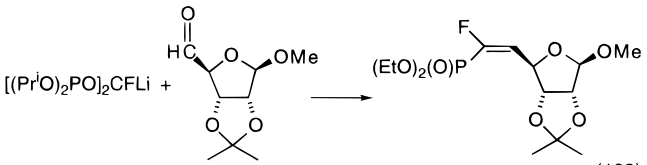
giving the (α-fluorovinyl)phosphonates in good yields as shown in eq 182.[268,269]



| | |
|---|---|
| R' = H, R = H | 69% |
| R' = $Me_2CH$, R = H | 95%, E/Z =5/1 |
| R' = Ph, R = H | 73%, E/Z = 6/1 |
| R' = Me, R = Me | 73% |
| R' = Ph, R = Me | 66%, E/Z = 4/1 |

(182)

However, condensation reaction with more sterically hindered ketones such as D-camphor and 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuran-3-ulose gave only poor yields of the desired products. Attempts to trap hydroxy(bisphosphonates) adduct by rapid quenching of the reaction with acetophenone with diluted acid at 10 °C failed, and only the (α-fluorovinyl)phosphonate was obtained. The stereochemistry of the products was dependent on the carbonyl substrates. With simple aldehydes, (*E*)-selectivity was high and ranged from *E*/*Z* = 5:1 to *E*/*Z* = 20:1, and the (*E*)-isomer was obtained exclusively upon reaction with methyl 2,3-*O*-isopropylidene-β-D-*ribo*-pentodialdehydo-1,4-furanoside (eq 183). However, the stereoselectivity usually decreased with ketones.[269]



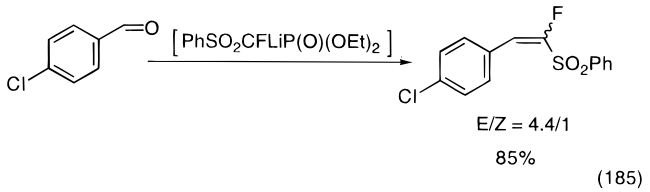
(183)

The [1-lithio-1-fluoro-1-(phenylsulonyl)methyl]phosphonate could be generated by treatment of LDA and [1-fluoro-1-(phenylsulfonyl)methyl]phosphonate, which was prepared by fluorination of [(phenylsulfonyl)-methyl]phosphonate with perchloryl fluoride. It also could be prepared by reaction of fluoromethyl phenyl sulfone, diethyl chlorophosphonate, and 2 equiv of either LDA or LiHMDS at −78 °C (eq 184).[271−273] When the carbonyl compounds were directly added to the pregenerated anion solution and then warmed to room temperature, the desired α-fluoro-α,β-unsaturated sulfones were formed in good to excellent yields but with relatively low stereoselectivity (eqs 185 and 186).

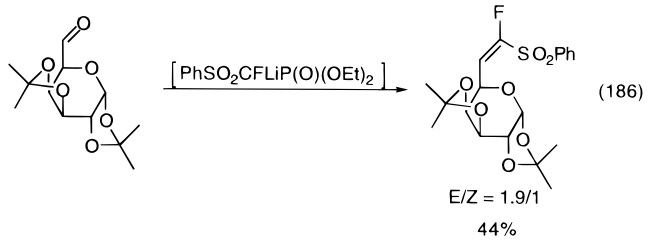
In contrast to the reaction of [(phenylsulfonyl)-fluoromethyl]lithium with carbonyl compounds containing an α-hydrogen, such as acetophenone, to give allylic fluoro sulfones,[273] [1-lithio-1-fluoro-1-(phenylsulfonyl)methyl]phosphonate reacted with various carbonyl compounds to form only α-fluorovinyl sulfones. The α-fluorovinyl sulfones were readily converted into (α-fluorovinyl)tin reagents when treated with $Bu_3SnH$ and AIBN.[274−276] The resultant stannanes underwent either hydrolysis reaction with CsF or Stille-type coupling reactions with aromatic halides and acyl chorides (Scheme 67).[277]



(184)

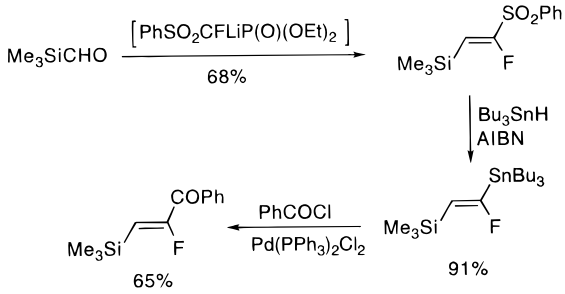


(185)



(186)

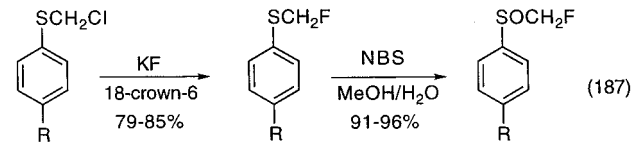
**Scheme 67**



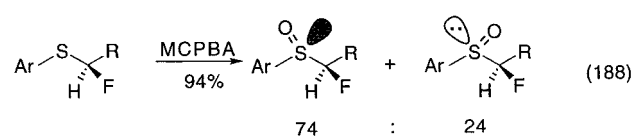
## *VII. α-Fluoralkyl Sulfoxides, Sulfones, and Sulfoximine and Their Anions*

### 1. Preparations of α-Fluoralkyl Sulfoxides, Sulfones, and Sulfoximines

The first aryl fluoromethyl sulfoxide was prepared from the halogen exchange of aryl chloromethyl sulfide and KF in the presence of 18-crown-6 ether followed by oxidation. The exchange reaction was slow and it required 4−5 days in refluxing acetonitrile to give good yields of the desired fluorides. NBS in moist methanol or THF was used to oxidize the fluoro sulfides into the corresponding sulfoxides in high yield at 0 °C, but sodium metaperiodate was not effective (eq 187).[278] Oxidation with MCPBA or $Bu^t$-OOH/$VO(acac)_2$ preferentially proceeded via anti attack of the oxidant to the C−F bond giving the sulfoxides stereoselectively (eq 188).[279]



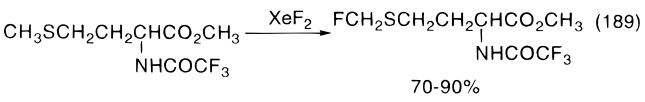
(187)



(188)

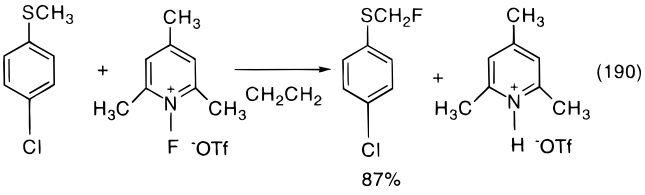
Although direct fluorination of alkyl phenyl sulfides with $XeF_2$ also gave α-fluoro sulfides under mild conditions, the reagent's cost and difficulty in

handling limited its application for large-scale preparations (eq 189).[280,281] An elegant method has been



(189)

developed by Umemoto and Tomizawa, who fluorinated sulfides with *N*-fluoropyridinium salts in $CH_2Cl_2$.[282] Although the fluorinating power of *N*-fluoro-3,5-dichloropyridinium triflate was greater than that of *N*-fluoropyridinium and *N*-fluoro-2,4,6-trimethylpyridinium triflates, *N*-fluoro-2,4,6-trimethylpyridinium triflate was the most reactive in this particular reaction and fluorination proceeded in methylene chloride at room temperature to give high yields of α-fluoro sulfides. However, the use of THF or acetonitrile as a solvent failed to produce the desired products. *N*-Fluoro-2,4,6-trimethylpyridinium tetrafluoroborate salt was also effective in $CH_2Cl_2$ but reaction required refluxing conditions. When methyl alkyl or aromatic sulfides were used as substrates, only fluoromethyl alkyl or aromatic sulfides were obtained. Ethyl (methylthio)- or (phenylthio)acetates gave products resulting from fluorination at the activated hydrogen site while benzyl methyl sulfide afforded a mixture of benzyl fluoromethyl sulfide and α-fluorobenzyl methyl sulfide (eq 190, Table 40).[282] Electrochemical fluorination has also been utlized for conversion of the alkyl sulfides to α-fluoro sulfides. An excellent review has summarized recent developments in this field and the reader is referred to this review.[283]



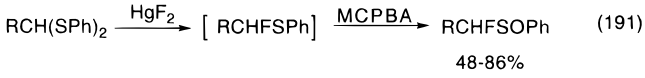
(190)

The thioacetals could be readily converted into α-fluoro thioethers when reacted with $HgF_2$ in acetonitrile due to the stabilization of the carbocation and the affinity of mercury for sulfur. To liberate the formed α-fluoro thioethers required treatment of the reaction mixture with basic $NaBH_4$ since mercuric ion complexed with the thioethers. The crude

**Table 40. Preparation of α-Fluoro Sulfides by Fluorination**

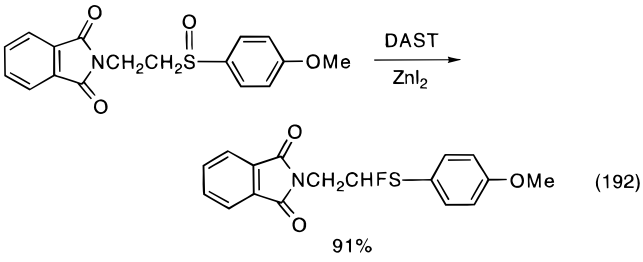
| Sulfide | a-Fluoro sulfides | Yield(%) |
|---|---|---|
| $PhSCH_3$ | $PhSCH_2F$ | 85 |
| $n\text{-}C_{12}H_{25}SCH_3$ | $n\text{-}C_{12}H_{25}SCH_2F$ | 44 |
| $CH_3SCH_2CO_2Et$ | $CH_3SCFHCO_2Et$ | 46 |
| $PhSCH_2CO_2Me$ | $PhSCFHCO_2Me$ | 45 |
| $PhCH_2SCH_3$ | $PhCFHSCH_3$<br>$PhCH_2SCH_2F$ | 77 |
| $CH_3SCH_2CH_2CHCO_2CH_3$<br>$NHCOCF_3$ | $FCH_2SCH_2CH_2CHCO_2CH_3$<br>$NHCOCF_3$ | 39 |

α-fluoro thioethers were oxidized to give the corresponding sulfoxides (eq 191).[284]

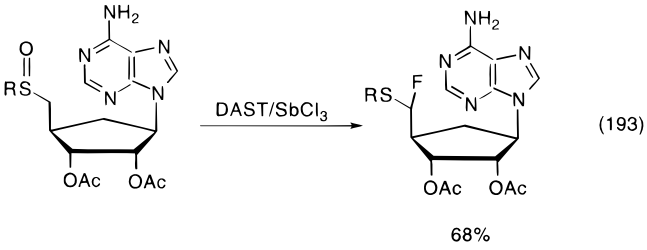


(191)

McCarthy and co-workers have discovered a useful conversion of sulfoxides into α-fluoro thioethers by treatment with DAST (eq 192).[285−287] A variety of primary alkyl phenyl sulfoxides and methyl alkyl sulfoxides gave excellent yields of α-fluoro sulfides. Functional groups such as nitrile, ester, amide, and ether could be tolerated under the reaction conditions. Introduction of the methoxy group into the phenyl ring of the alkyl phenyl sulfoxides dramatically increased the rate of the reaction, which indicated the reaction involved a sulfonium cation intermediate. Lewis acids such as $ZnI_2$ also catalyzed this conversion. However, sulfoxides could be reduced by iodide in some cases, but the use of $SbCl_3$ circumvented this side reaction (eq 193).[286,288]

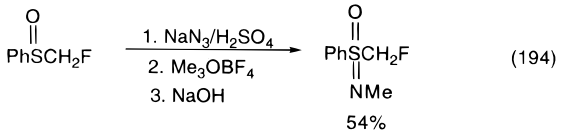


(192)



(193)

Oxidation of the sulfides with 1 equiv of MCPBA at low temperature gave the corresponding sulfoxides. The sulfones were obtained by treatment with 2 equiv of MCPBA. The sulfoxides also were transformed into sulfoximine by consecutive treatment with $NaN_3/H_2SO_4$, $Me_3OBF_4$, and then NaOH (eq 194).[289]



(194)

## 2. Applications of Anions of α-Fluoralkyl Sulfoxides, Sulfones, and Sulfoximines

### *2.1. Applications of α-Fluoroalkyl Sulfoxides*

**2.1.1. Prearation of Anions of α-Fluoroalkyl Sulfoxides.** The lithium anion of α-fluoromethyl phenyl sulfoxide **136** was first generated by reaction of α-fluoromethyl phenyl sulfoxide with LDA in THF at −78 °C. The anion, **136**, was reported to be stable at low temperature and at 0 °C for at least 1 h in an

early paper.[290] Later, the isotopically labeled anion of **136** was also prepared, which was used as a probe to investigate its thermal stability and structure by NMR. Seebach and co-workers found the $^{13}C$ NMR signal of the lithiated carbon atom rapidly became smaller at −90 °C and disappeared at −60 °C, indicative that the anion was much less stable than the early description.[291] The use of cosolvents such as HMPA, DMPU, and TMEDA were found to improve the thermal stability and facilitate functionalization reactions.[290] Seebach also claimed that the lithium cation was located at the oxygen atom of the anion based on the lack of the carbon−lithium coupling.[291]

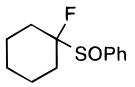
**2.1.2. Reactions with Alkyl Halides or Acyl Halides.** Alkylation of **136** readily occurred with a variety of primary or benzyl halides (eq 195). The yields of alkylated products were good when a cosolvent such as HMPA and TMEDA was used in THF at −78 °C. With α,ω-dihalides, a stepwise cycloalkylation was achieved, giving cyclic α-fluorosulfoxides upon further treatment of primary alkylated products with LDA (eq 196).[290]

$$\mathrm{PhSOCHFLi + CH_3(CH_2)_{10}CH_2I \xrightarrow[-78\ \text{to}\ -20^oC]{HMPA} CH_3(CH_2)_{10}CH_2CHFSOPh} \quad (195)$$

85%

$$\mathrm{Cl(CH_2)_nCH_2Br \xrightarrow{PhSOCHFLi} Cl(CH_2)_nCH_2CHFSOPh \xrightarrow[THF/HMPA]{LDA}}$$

65-68%

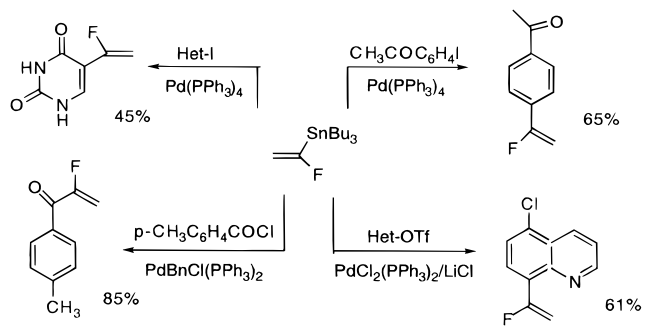


(196)

n = 4, 59%

When the α-fluoroalkyl sulfoxide **137** reacted with ethyl chloroformate, a more hindered base such as lithium 2,2,6,6-tetramethylpiperidide (LTMP) was used at −100 °C to prevent an attack of the base on the sulfoxide group (eq 197).[292] Raising the reaction temperature to −78 °C significantly decreased the yields of the desired products. Pyrolysis of the alkylated products gave the corresponding vinyl fluorides as a mixture of (*E*)- and (*Z*)-isomers.[284,290,293] The anion also reacted with trialkyltin halides or triflate to give α-stannyl sulfoxides, which readily underwent protodestannylation reaction due to the weak carbon−tin bond. The α-stannyl sulfoxides could be pyrolyzed in refluxing toluene in the presence of (*i*-Pr)$_2$NEt to form α-fluorovinyl(trialkyl)tins (eq 198), which were useful synthons to make fluoroolefins through palladium-catalyzed coupling reactions with aromatic or acyl halides (Scheme 68).[286]

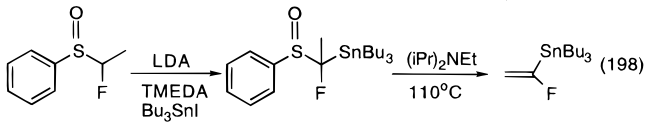
**Scheme 68**




$$\mathrm{PhSOCHFHCH_2Ph + ClCO_2Et \xrightarrow{LTMP} PhSOCFCH_2Ph} \quad (197)$$

$$\mathrm{CO_2Et}$$

76%




(198)

**2.1.3. Reactions with Carbonyl Substrates.** The anions of **137** also condensed with carbonyl compounds such as linear or cyclic aliphatic and aromatic aldehydes to give β-hydroxy-α-fluorosulfoxides (Table 41). The resultant β-hydroxy-α-fluoro sulfoxides were useful intermediates for the prepara-

**Table 41. Reaction of Anions of α-Fluoro Sulfoxides or Sulfones with Carbonyl Compounds**

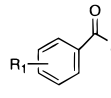
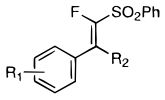
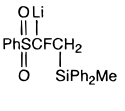
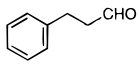
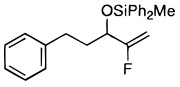
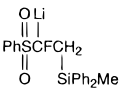
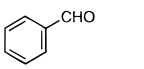
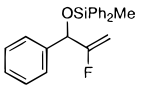
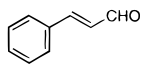
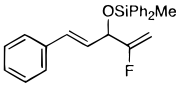
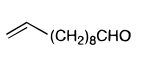
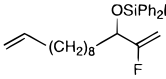
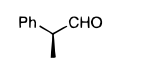
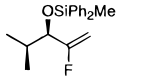
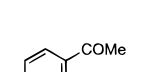
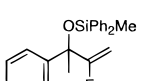
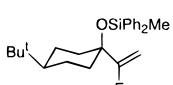
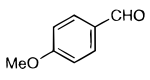
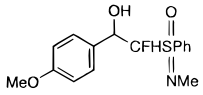
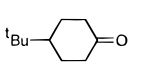
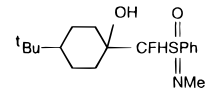
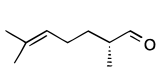
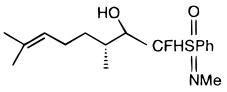
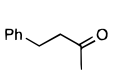
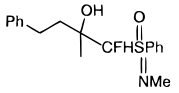
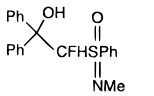
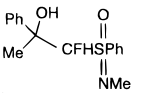
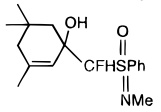
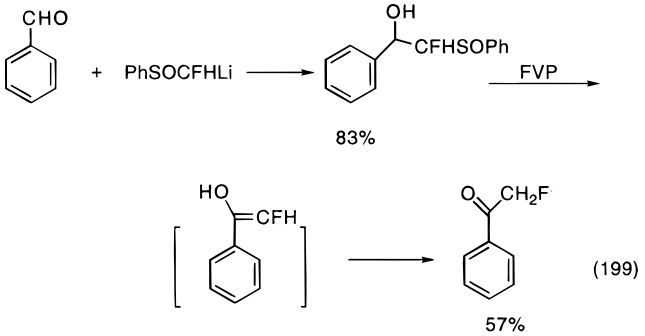
| Anion | Carbonyl Compund | Product | Yield (%) | Ref |
|---|---|---|---|---|
| $C_6H_5SOCFHLi$ | RCHO | $C_6H_5SOCFH(OH)R$ | | |
| | R = $C_2H_5$ | | 58 | 290 |
| | R = n-$C_5H_{11}$ | | 64 | 290 |
| | R = n-$C_7H_{13}$ | | 68 | 290 |
| | R = Ph | | 55 | 290 |
| | R = n-$C_8H_{17}$ | | 82 | 294 |
| | R = n-$C_{11}H_{23}$ | | 74 | 294 |
| | R = n-$C_{13}H_{27}$ | | 49 | 294 |
| | R = Ph | | 83 | 294 |
| | R = $PhCH_2$ | | 91 | 294 |
| $C_6H_5SOCFLi$(Bu) | R = $PhCH_2CH_2$ | $C_6H_5SOCF(Bu)CH(OMs)R$ | 78 | 296 |
| | R = n-$C_9H_{19}$ | | 74 | 296 |
| $C_6H_5SOCFLi$($CH_3$) | R = $PhCH_2CH_2$ | $C_6H_5SOCF(CH_3)CH(OMs)R$ | 39 | 296 |
| | R = n-$C_9H_{19}$ | | 39 | 296 |
| $C_6H_5SOCFHLi$ | R = $PhCH_2CH_2$ | $C_6H_5SOCFHCOR$ | 90 | 298 |
| | R = n-$C_9H_{19}$ | | 81 | 298 |
| | R = c-$C_6H_{11}$ | | 96 | 298 |
| | R = Ph | | 78 | 298 |
| $C_6H_5SO_2CFHLi$ |  |  | | |
| | $R_1$ = H, $R_2$ = H | | 67 | 273 |
| | $R_1$ = 4-Cl, $R_2$ = H | | 80 | 273 |
| | $R_1$ = 3,4-$(OMe)_2$, $R_2$ = H | | 71 | 273 |
| | $R_1$ = $F_5$, $R_2$ = H | | 78 | 273 |
| | $R_1$ = H, $R_2$ = Ph | | 92 | 273 |
|  |  |  | 71 | 298 |
|  |  |  | 93 | 298 |
| |  |  | 71 | 298 |
| |  |  | 74 | 298 |
| |  |  | 74 | 298 |
| |  |  | 72 | 298 |
| |  |  | 89 | 298 |

**Table 42. Reaction of Anions of α-Fluoro Sulfoximine with Carbonyl Compounds**

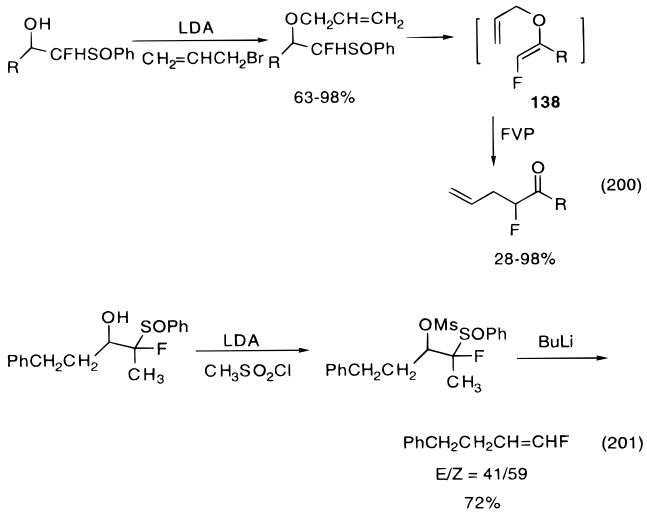
| Anion | Carbonyl Compund | Product | Yield (%) |
|---|---|---|---|
|  |  |  | 79 |
| |  |  | 93 |
| |  |  | 83 |
| |  |  | 91 |
| |  |  | 86 |
| |  |  | 92 |
| |  |  | 95 |

tion of other fluoro compounds. Pyrolysis of β-hydroxy-α-fluoro sulfoxides gave phenylsulfenic acid and α-fluoroenols, which rapidly isomerized to α-fluoro ketones. Although phenylsulfenic acid was isolated in good yield, only low yields of the desired α-fluoro ketones were obtained when the pyrolysis was conducted in a sealed tube at 180 °C.[290] That is probably due to decomposition of α-fluoro ketones upon prolonged heating at 180 °C. The use of flash vacuum pyrolysis (FVP) significantly improved the yields of α-fluoro ketones (eq 199).[294]




(199)

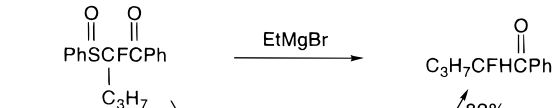
Allylation of the formed hydroxy sulfoxides with various allyl halides afforded the corresponding allyl ethers which were flash vacuum pyrolyzed to give α-fluoroalkenyl ketones via a Claisen intermediate **138** (eq 200).[295] β-Hydroxy sulfoxides were readily converted to β-methyloxy sulfoxides by treatment with $MeSO_2Cl$ (Table 42).[296] When the β-mesyloxy sulfoxide was treated with butyllithium, the butyl group exclusively attacked a sulfur atom and resulted in the formation of fluoroolefin as a mixture of (*E*)- and (*Z*)-isomers (eq 201).[296]




(200)

(201)

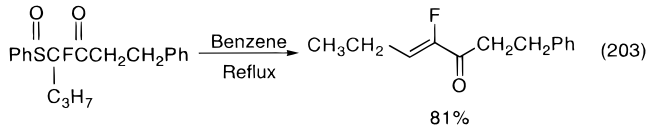
After Swern oxidation of the hydroxy group of the adducts (eq 202), the sulfenyl group could be readily removed by treatment with ethyl Grignard reagent to give α-fluoro ketones in high yields.[297] The mechanism of the desulfinylation probably involved a ligand exchange reaction of sulfoxide to give a magnesium enolate. Interestingly, the enolate was formed regioselectively between the carbonyl carbon and the carbon bearing the sulfenyl group, which was a useful intermediate for Aldol condensations (Scheme 69).[297] The α-fluoro-α-sulfinyl ketones also underwent a thermal elimination reaction in refluxing benzene solution to give α-fluoro-α,β-unsaturated ketones in 75−91% yields (eq 203, Table 41).[297]




(202)

**Scheme 69**



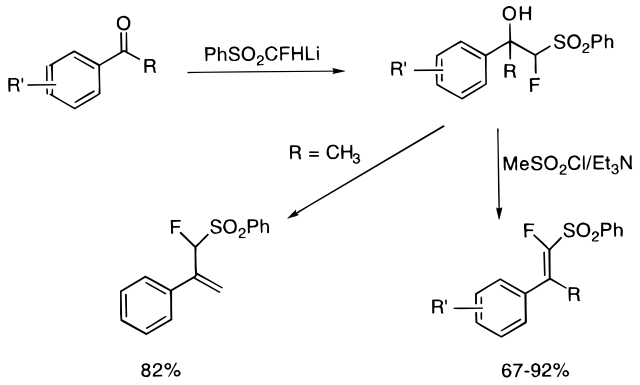




(203)

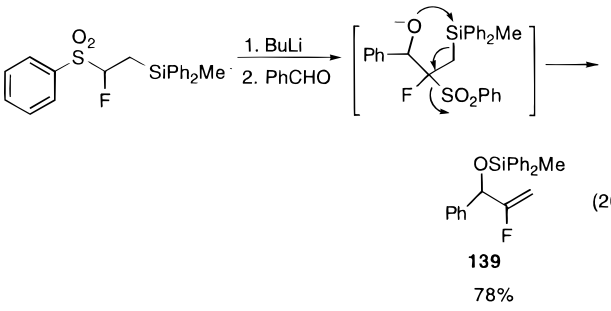
### *2.2. Applications of Anions of α-Fluoro Sulfones or Sulfoximine*

Anions of fluoromethyl phenyl sulfone and sulfoximine could be generated by treatment of appropriate precursors with BuLi or LDA in THF at low temperatures.[273,289] The sulfone anion readily added to carbonyl compounds to give high yields of α-fluoro-β-hydroxy sulfones. After mesylation, the hydroxy sulfones were converted to α-fluorovinyl sulfones with base (Table 41).[273] However, the condensation product from acetophenone formed α-fluoroallyl sulfone under similar conditions (Scheme 70).[273]

**Scheme 70**

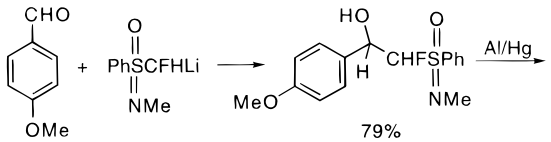


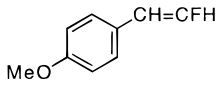

When α-fluoro-β-silylethyl phenyl sulfone was treated with BuLi in THF at −78 °C followed by addition of various aldehydes and ketones, fluoroolefins **139** were obtained upon warming the reaction mixture to room temperature. The mechanism for this conversion probably involved the adduct intermediate, which carbon−sulfur bond cleavage occurred with synchronous migration of silyl group from the carbon to oxygen (eq 204, Table 41).[298]



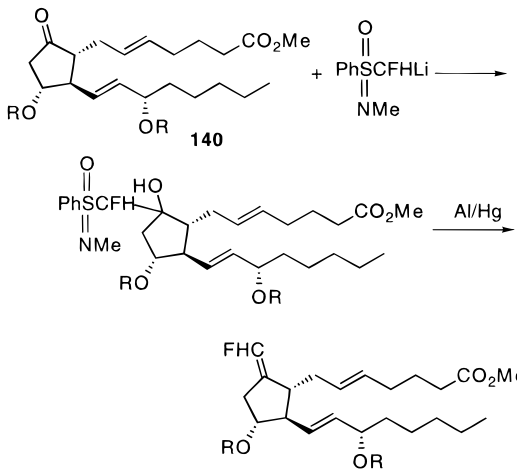

(204)

The anion of fluoromethyl phenyl sulfoximine also condensed with aromatic or aliphatic aldehydes and ketones to afford the adducts in excellent yields (eq 205, Table 42).[289] With an α,β-unsaturated ketone, only the 1,2-adduct was formed. The anion exclusively attacked the carbonyl group when reacted with **140**.[289] Subsequent treatment of the β-hydroxy-α-fluoro sulfoximines with aluminum amalgam produced good yields of the desired fluoroalkenes (eq 206). These compounds are precursors for making $PGE_2$ derivatives which have better chemical stability but a similar dipole monment at C-9 compared to natural $PGE_2$. The β-hydroxy-α-fluoro sulfoximines from aromatic ketones and α,β-ketones, however, gave poor yields of the fluoroalkenes under similar conditions.



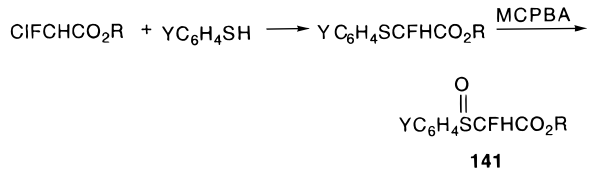

(205)




(206)

## 3. Applications of Stabilized Anions of Phenyl α-Fluoro Sulfoxides $PhSOCFHCO_2Et$

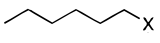
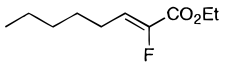
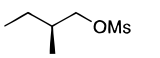
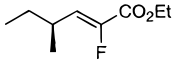
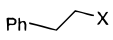
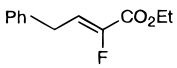
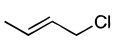
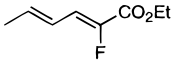
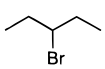
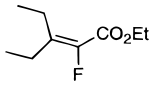
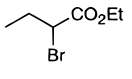
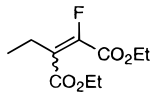
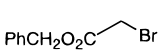
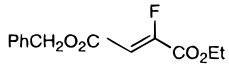
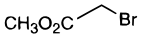
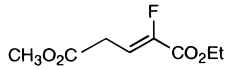
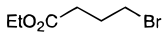
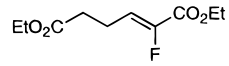
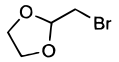
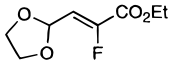
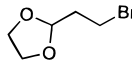
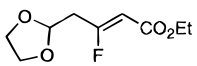
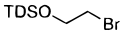
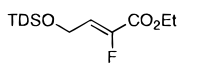
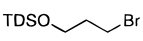
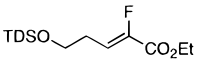
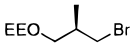
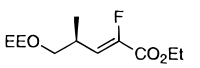
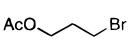
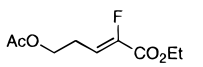
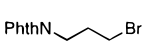
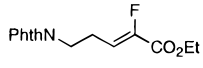
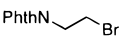
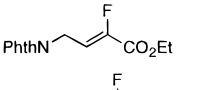
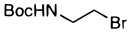
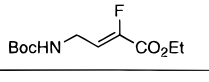
Sodium thiophenolates reacted with chlorofluoroacetates in ethanol at room temperature to form α-(phenylthio)-α-fluoroacetates which were cleanly oxidized with percarboxylic acids at −60 °C to give α-(phenylsulfinyl)-α-fluoroacetates **141** (eq 207).[299,300]




(207)

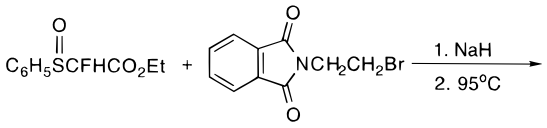
Alkylation of **141** (Y = H) was studied in a variety of solvents with several bases and halides. Although DME, $CH_2Cl_2$, acetone, and toluene were used as solvents, DMF and acetonitrile generally gave superior results. Sodium hydride was the most employed base, but NaOEt, $K_2CO_3$, and amine were also effective. Primary alkyl iodides and bromides worked well, while chlorides or mesylates gave only modest yields of the products. Secondary bromides reacted sluggishly and sterically hindered alkyl halides such as neopentyl iodide did not react at all. Ester, acetate, silyl ether, imide, and amide groups could be tolerated under these conditions, and no racemization occurred with a chiral halide. The resulting alkylated products subsequently underwent an elimination reaction by heating at 96−100 °C to give

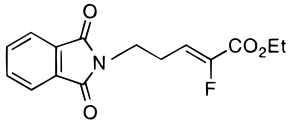
**Table 43. Preparation of α-Fluoro-α,β-unsaturated Esters from PhSOCFHCO$_2$Et[299]**

| substracte | Product | Yield (%) |
|---|---|---|
|  |  | |
| X = Cl | | 44 |
| X = Br | | 77 |
| X = I | | 73 |
|  |  | 24 |
|  |  | |
| X = Cl | | 24 |
| X = Br | | 76 |
|  |  | 70 |
|  |  | 28 |
|  |  | 56 |
|  |  | 28 |
|  |  | 24 |
|  |  | 85 |
|  |  | 76 |
|  |  | 63 |
|  |  | 44 |
|  |  | 70 |
|  |  | 61 |
|  |  | 47 |
|  |  | 73 |
|  |  | 63 |
|  |  | 90 |

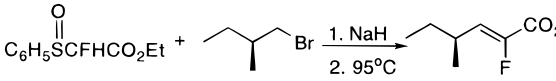
α-fluoro-α,β-unsaturated esters with high (*E*)-stereoselectivity (eqs 208 and 209 and Table 43).[299]

Compound **141** also underwent a Michael addition with α,β-unsaturated esters, nitriles, and ketones in the presence of catalytic amounts of NaOEt in ethanol at room temperature. Subsequent regiospecific elimination could be achieved by heating in



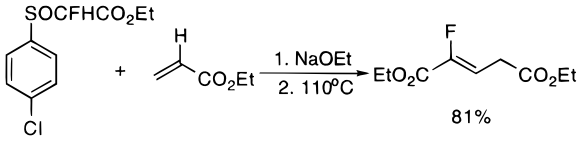




51% (208)




64% (209)

toluene at 110 °C to give functionalized unsaturated esters containing a vinylic fluorine atom (eqs 210 and 211).[299]




81% (210)




45% (211)

Desulfinylation of **141** with a magnesium reagent gave α-fluoro esters in good yields (eq 212).[292]




58% (212)

## *VIII. α,α-Difluoro Phosphonates and Sulfones and Their Anions*

### 1. (α,α-Difluoromethyl)phosphonates and Their Anions

#### *1.1. Preparation and Stability of Anion of (α,α-Difluoromethyl)phosphonate*

Diethyl (difluoromethyl)phosphonate was readily prepared from dialkyl phosphites and chlorodifluoromethane. Although the reaction appears to be an $S_N2$ type displacement, the mechanism involves generation and capture of difluorocarbene (Scheme 71).[301]

**Scheme 71**




Reaction of trialkyl phosphites with difluorodibromomethane gave (bromodifluoromethyl)phosphonates in excellent yields (eq 213).[302] The mechanism was similar to that of the reaction with chlorodifluoromethane via a carbene trapping sequence. These two phosphonates have been widely used as precur-

sors for the preparation of the anion of (difluoromethyl)phosphonate.

$$(RO)_3P + CF_2Br_2 \longrightarrow (RO)_2POCF_2Br \quad (213)$$

When (difluoromethyl)phosphonate was treated with LDA in THF at −78 °C, (dialkoxyphosphinyl)-(difluoromethyl)lithium **142** was generated.[303] Compound **142** was less stable than the corresponding lithiomonofluoro analog $(RO)_2P(O)CFHLi$, but exhibited slightly greater stability than lithium (chlorofluoromethyl)phosphonate, $(RO)_2P(O)CFClLi$.[304] At 0 °C **142** rapidly dissociated to give difluorocarbene, although it was recovered substantially unchanged from reaction quenched with aqueous $KH_2PO_4$ at −70 °C.[304] Coordinating solvents such as HMPA can modestly stabilize the anion, and alkylation with primary iodide occurred at −25 °C but only low yield of product was observed.[305] Thus the generation and capture reaction are best conducted at −78 °C. On the other hand, lithium anion of (difluoromethyl)-diphenylphosphine oxide was a little more stable, and the preparation and functionalization could be carried out in THF at −50 °C without significant decomposition.[306]

### *1.2. Applications of Anion of (α,α-Difluoromethyl)-phosphonates*

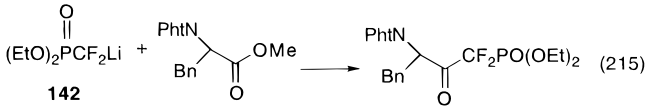
**1.2.1. Reactivities of Anion of (α,α-Difluoromethyl)phosphonates.** Obayashi and co-workers first reported that the anion **142** reacted with $Me_3SiCl$, $Bu_3SnCl$, or $(EtO)_2POCl$ to give high yields of functionalized phosphonates (eq 214).[303,307]

$$(EtO)_2P(O)CF_2Li \ (\mathbf{142}) + EX \xrightarrow[-78°C]{} (EtO)_2P(O)CF_2E \quad (214)$$

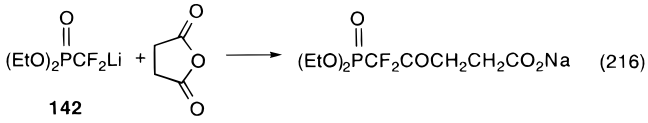
| EX | |
|---|---|
| $Me_3SiCl$: | 87% |
| $Bu_3SnCl$: | 77% |
| $(EtO)_2POCl$: | 74% |

Blackburn reacted **142** with ethyl isocycanate to give diethyl *N*-ethylphosphonodifluoroacetamide in satisfactory yield.[304] However, reaction of the anion with *S*-methyl (diisopropoxyphosphonoyl)dithioformate failed to give the desired fluoro thioketone. Although the reaction with benzoyl chloride gave a 25% yield of (α-benzoyl-α,α-difluoromethyl)phosphonate, acetyl chloride was insufficiently reactive. The use of ethyloxalyl chloride resulted in the decomposition of the starting material. With ethyl chloroformate, only low yield of the desired product was observed, and the major products were tetraethyl difluoromethylenebisphosphonate **143** and tetrafluoro-2,2-dihydropropane-1,3-diylbisphosphonate **144**. Obviously, the initially formed phosphonodifluoroacetate ester further reacted with **142** to lead to **143** and **144** (Scheme 72).[304]

Although **142** could react with protected amino carboxylate[308] or succinic anhydride[309] to give the corresponding adducts (eqs 215 and 216), the best method so far for the preparation of these phosphonodifluoroacetates was the reaction of acyl chlorides with thermally stable phosphono(difluoromethyl)zinc reagents in the presence of CuBr.[310]

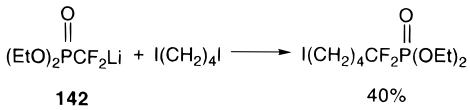


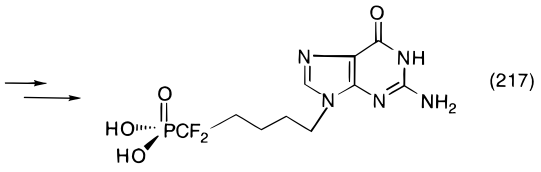

(215)




(216)

**1.2.2. Reactions with Alkyl Halides or Triflates.** Obayashi and co-workers[303] claimed in 1982 that alkylation of the anion **142** with ethyl and butyl bromide occurred readily at −78 °C to give 66% and 82% yields of the desired products, respectively, but the full paper has never appeared since then. Many workers in this field have discovered that Obayashi's work is not repeatable at the published yields. Subsequent workers have found that the anion does not generally undergo displacement reactions with primary alkyl halides due to its weak nucleophilicity at low temperature. The reported yields ranged from 23% to 40% with simple primary alkyl iodides (eq 217, Table 44)[305,311] and no products were obtained when reacted with glycidyl halides.[312]



(217)

**Scheme 72**

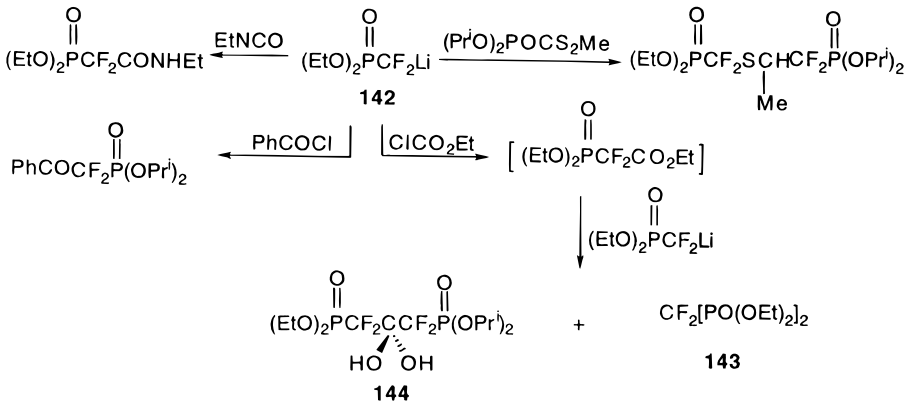
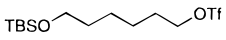
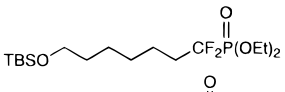
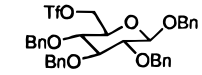
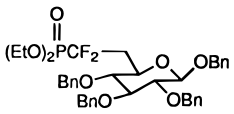
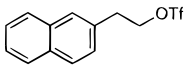
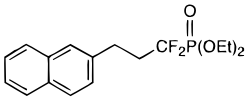
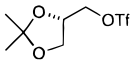
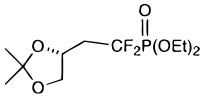
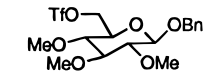
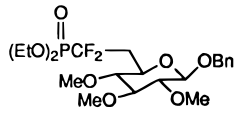
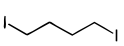
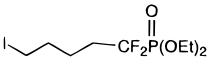
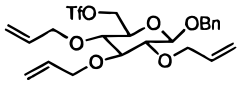
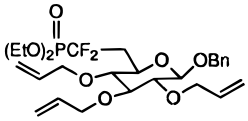
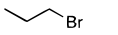
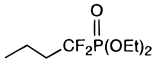
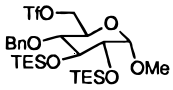
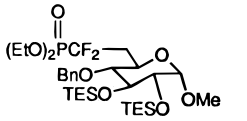
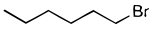
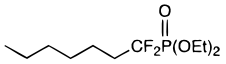
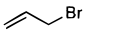
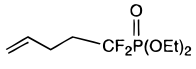
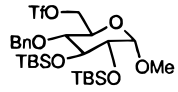
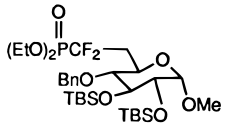
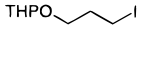
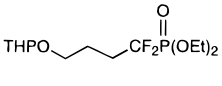
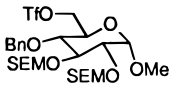
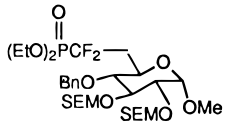
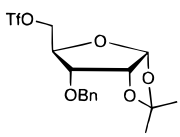
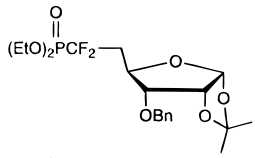
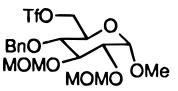
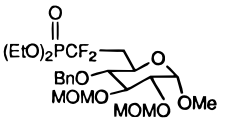
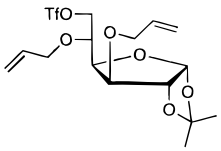
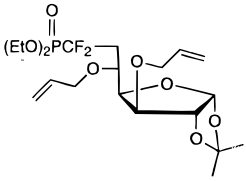
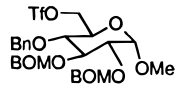
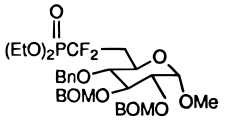
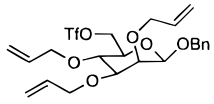
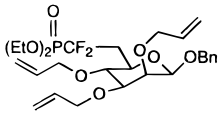
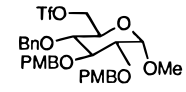
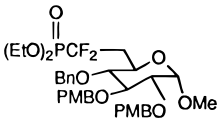


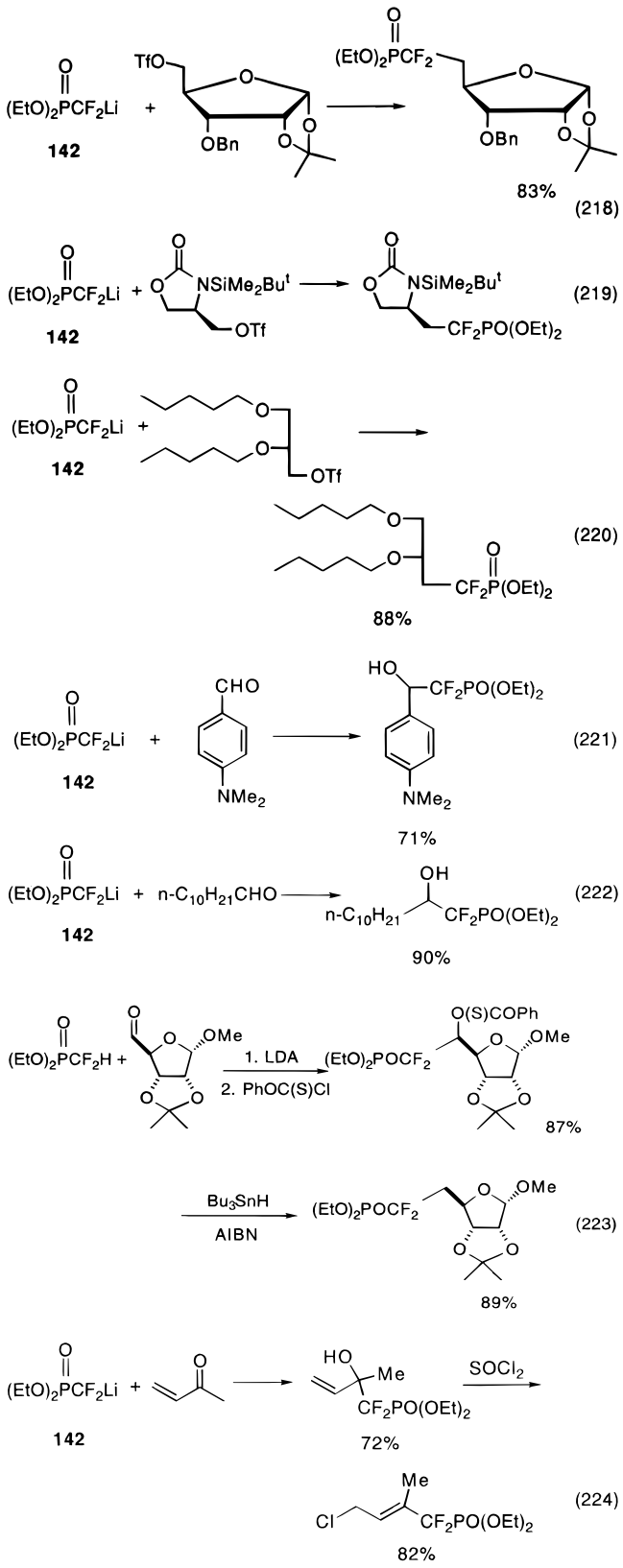
**Table 44. Alkylation of $LiCF_2P(O)(OEt)_2$**

| Triflate or Halide | Phosphonate | Yield (%) | Ref | Triflate | Phosphonate | Yield (%) | Ref |
|---|---|---|---|---|---|---|---|
|  |  | 60 | 313 |  |  | 79 | 313 |
|  |  | 59 | 313 | | | | |
|  |  | 63 | 314 |  |  | 78 | 313 |
|  |  | 40 | 311 |  |  | 82 | 313 |
|  |  | 82 | 303 |  |  | 59 | 313 |
|  |  | 66 | 303 | | | | |
|  |  | 23 | 303 |  |  | 70 | 313 |
|  |  | 23 | 305 |  |  | 69 | 313 |
|  |  | 83 | 313 |  |  | 81 | 313 |
|  |  | 65 | 313 |  |  | 80 | 313 |
|  |  | 74 | 313 |  |  | 71 | 313 |
| | 288 | | | | | | |

More reactive triflates, however, reacted smoothly with the anion at −78 °C within 5−10 min (eqs 218−220).[313−315] The alkylation also depended upon the solvents and counterions. THF was far superior to diethyl ether or 1,2-bis(methyloxy)ethane, and lithium salts gave satisfactory yields but reactions failed when KHMDS, NaHMDS, or phosphazonium base were used. Regardless of the use of stabilizers such as HMPA and TMEDA, the displacement reaction was complete within 5−10 min and yields were good to excellent as summarized in the Table 44. More recently, the anion of diallyl (difluoromethyl)phosphonate was reacted with a protected sugar triflate to give α,α-difluorophosphonic acid after hydrolysis with palladium catalysis.[316] However, displacement with secondary sugar triflates failed.[313]

**1.2.3. Reactions with Carbonyl Substrates.** Compound **142** also readily added to a variety of carbonyl compounds. Aromatic and aliphatic aldehydes and ketones could be used as substrates but aldehydes bearing a nitro group or a pyridine ring gave only traces of the desired products.[303] With α,*β*-unsaturated aldehydes or ketones, only 1,2-adducts were obtained and no 1,4-adducts could be detected in the crude reaction mixture. Upon heating the THF solution of the adducts, the Wadsworth−Emmons reaction occurred producing 1,1-difluoroolefins as described in the Table 45.

When the workup was carried out at room temperature or below, the diethyl (2,2-difluoro-3-hydroxyalkyl)phsphonates were obtained (eqs 221 and 222, Table 45).[303] The hydroxy phosphonates could either be isolated or further functionalized. Trapping of the alkoxide adducts *in situ* with phenyl chlorothionoformate gave the thiocarbonates (Table 45). Subsequent Barton deoxygenation produced the desired (α,α-difluoroalkyl)phosphonates in 81−89% yields when treated with $Bu_3SnH$ and AIBN in refluxing toluene (eq 223).[312] The phosphonoallyl alcohols were regio- and stereospecifically converted into the allyl chlorides upon treatment with $SOCl_2$ (eq 224).[317] Cerium chloride-mediated reaction of **142**



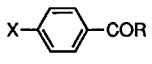
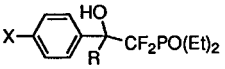
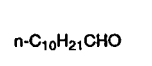
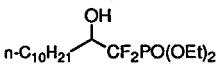
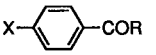
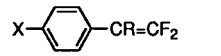
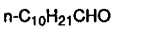
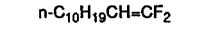
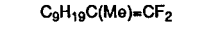
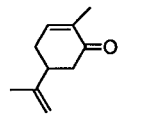
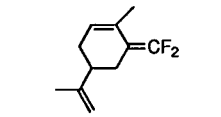
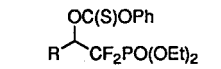
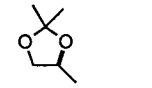
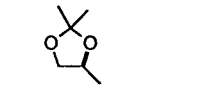

with aliphatic and aromatic esters give α,α-difluoro-β-keto phosphonates in good yields.[317b] With a α,β-unsaturated ester, a mixture of 1,2- and 1,4-adducts was formed in moderate yield. Interestingly, *N*,*N*-dimethylformamide could also be used as a substrate in the cerium-mediated reaction. After acid workup, α,α-difluoro-β-dihydroxy phosphonate was obtained in 80%.

Reaction of *p*-$BuOC_6H_4CH(OH)CF_2P(O)(OEt)_2$ with LDA or BuLi gave the olefin **145** exclusively in 60–77% yields. When LiH was used as a base, phosphonyl rearrangment product **146** was formed in 87% yield (Scheme 73). The use of NaH, KH, and Bu$^t$OK resulted in the formation of a mixture of **145** and **146**. Interestingly, $C_6H_5CH(OH)CF_2PO(OEt)_2$ and *p*-$NO_2C_6H_4CH(OH)CF_2PO(OEt)_2$ only afforded olefins with these bases.[303]

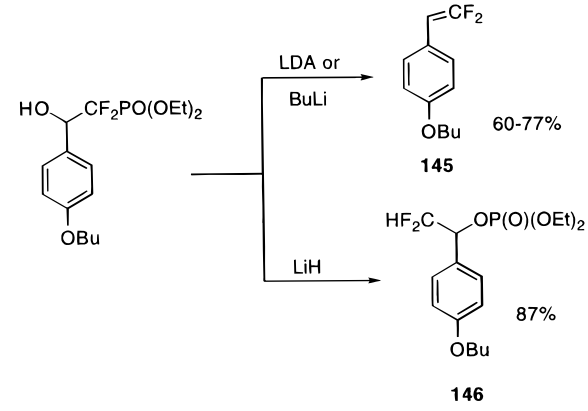
Oxidation of hydroxyphosphonate with pyridinium chlorochromate gave the corresponding ketone. Treatment of the ketone with BuLi followed by thermal elimination afforded the difluoroolefin (eq 225).[303]

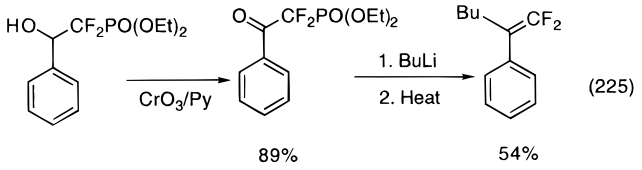
Although **142** failed to react with *p*-nitrobenzaldehyde, the 4-pyridinecarbaldehyde, $Me_3SiCF_2P(O)(OEt)_2$ readily reacted with these aldehydes in the presence

**Table 45. Reaction of $LiCF_2P(O)(OEt)_2$ with Carbonyl Compounds**

| Carbonyl Compund | Product | Yield (%) | Ref |
|---|---|---|---|
|  |  | | 303 |
| X = OBu, R = H | X = OBu, R = H | 76 | |
| X = $NO_2$, R = H | X = $NO_2$, R = H | 8 | |
| X = H, R = H | X = H, R = H | 83 | |
| X = Cl, R = Me | X = Cl, R = Me | 77 | |
| X = OMe, R = Me | X = OMe, R = Me | 86 | |
|  |  | 90 | 303 |
|  |  | | 303 |
| X = $NMe_2$, R = H | X = $NMe_2$, R = H | 67 | |
| X = OBu, R = H | X = OBu, R = H | 61 | |
| X = $NO_2$, R = H | X = $NO_2$, R = H | 0 | |
| X = OMe, R = Me | X = OMe, R = Me | 62 | |
| X = Br, R = Me | X = Br, R = Me | 54 | |
| X = H, R = $C_3H_7$ | X = H, R = $C_3H_7$ | 62 | |
| X = $NO_2$, R = Me | X = $NO_2$, R = Me | 0 | |
| X = H, R = Ph | X = H, R = Ph | 64 | |
|  |  | 71 | 303 |
|  |  | 75 | 303 |
|  |  | 54 | 303 |
|  |  | | 312 |
| R = n-$C_6H_{13}$ | R = n-$C_6H_{13}$ | 90 | |
| R = $Ph_2MeSiOCH_2CH_2$ | R = $Ph_2MeSiOCH_2CH_2$ | 71 | |
| R = c-$C_6H_{11}$ | R = c-$C_6H_{11}$ | 87 | |
| R = Ph | R = Ph | 85 | |
|  |  | 83 | |

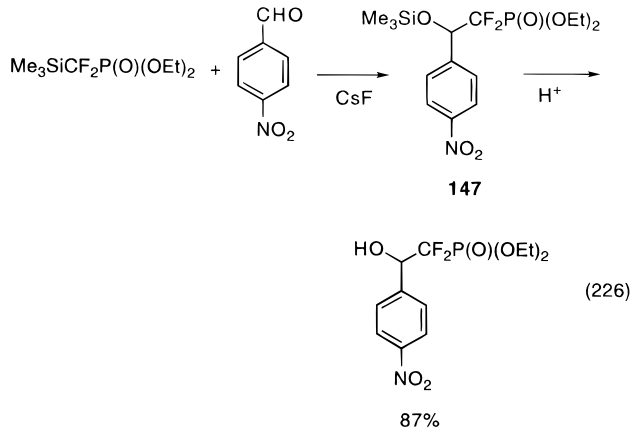
**Scheme 73**





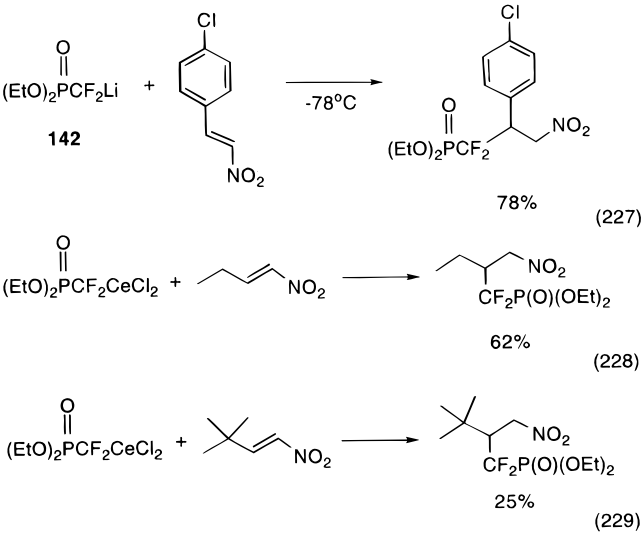

(225)

of catalytic amounts of CsF to give silyl ethers **147**, which hydrolyzed with acid to form hydroxy phosphonates (eq 226). $Me_3SiCF_2P(O)(OEt)_2$ was also utilized to make [1-$^{14}$C]-2,2-difluoroethylene from $^{14}CH_2O$.[318]




(226)

**1.2.4. Reaction with Nitroalkene.** Compound **142** underwent Michael addition to $\beta$-chloronitrostyene derivative to give 1,4-addition products (eq 227).[319] However, the reaction required a 3-fold excess of **142** to complete conversion of nitrostyenes and no desired adducts were obtained with nonaromatic nitroalkenes. Lequeux and Percy improved this process by using cerium reagent, prepared by reaction of **142** with $CeCl_3$ in THF at −78 °C.[320] The resultant ceiurm reagent readily added to nitroalkenes in moderate to good yields with both aromatic and aliphatic nitroalkenes (eq 228). When sterically hindered nitroalkenes were used as substrates, adducts were also obtained but in low yields (eq 229).[320] The resulting Michael adducts could be used to prepare 3-amino-1,1-difluorophosphonic acids.




(227)

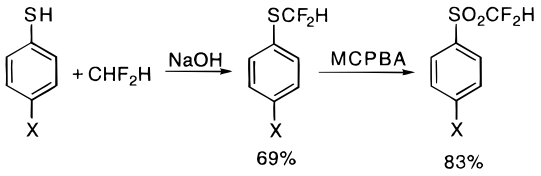
(228)

(229)

## 2. α,α-Difluoromethyl Sulfones and Their Anions

### 2.1. Preparation of α,α-Difluoromethyl Sulfones

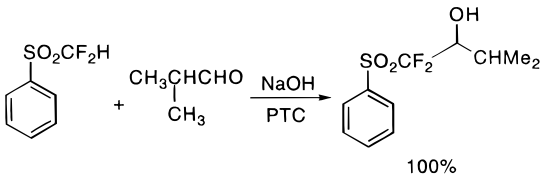
α,α-Difluoromethyl sulfone was readily prepared by oxidation of difluoromethyl sulfides, which were generated by reaction of thiophenoxide with halodifluoromethane in phase-transfer conditions or polar aprotic solvents such as DMF (eq 230).[321−323]



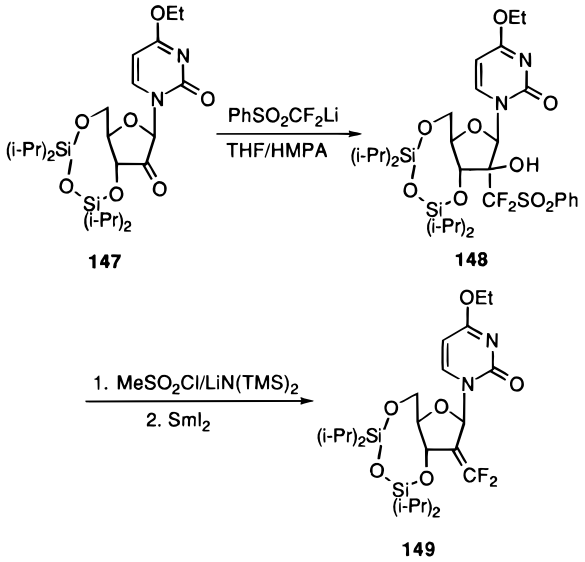

(230)

### 2.2. Applications of Anions of α,α-Difluoromethyl Sulfones

The difluoro sulfone condensed with aldehydes under phase-tranfer conditions to give $\beta$-hydroxy-α,α-difluoro sulfone. Aqueous 50% NaOH solution was used as a base for this reaction in the presence of a catalytic amount of tricaprylylmethylammonium chloride. When a variety of aromatic and aliphatic aldehydes were employed as substrates, good yields of the $\beta$-hydroxy-α,α-difluoro sulfones were formed (eq 231).[321] Ketone **147** also reacted with α,α-difluoromethyl sulfone when 2 equiv of $LiN(SiMe_3)_2$ was added in THF−HMPA at −70 °C to give nucleoside **148** which could be converted into compound **149** by treatment with methanesulfonyl chloride and then $SmI_2$ (eq 232).[324] The similar conversion of the ketone **147** into **149** was unsuccessful by Wadsworth−Emmons olefination using (difluoromethyl)-diphenylphosphine oxide.[324]




(231)

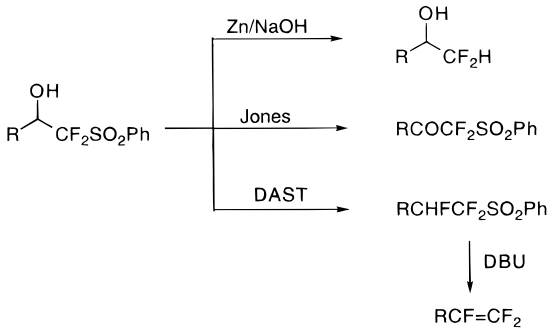



(232)

$\beta$-Hydroxy-α,α-difluoro sulfones could be oxidized with Jones reagent to afford $\beta$-keto sulfones, from which α,α-difluoromethyl ketones were readily prepared by treatment with Al−Hg. The hydroxy group

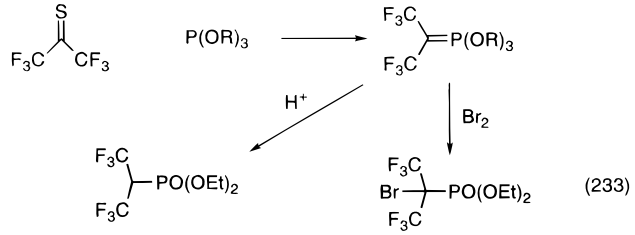
of the adducts were also fluorinated with DAST to give $\beta$-fluoro-$\alpha,\alpha$-difluoro sulfones, which reacted with a base to give trifluoroalkenes (Scheme 74).[321]

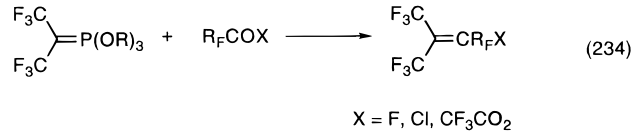
**Scheme 74**



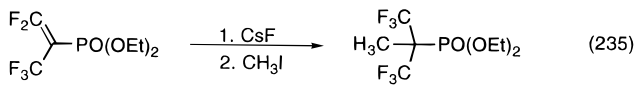

## IX. [$\alpha,\alpha$-Bis(trifluoromethyl)methyl]phosphonates and Their Anions

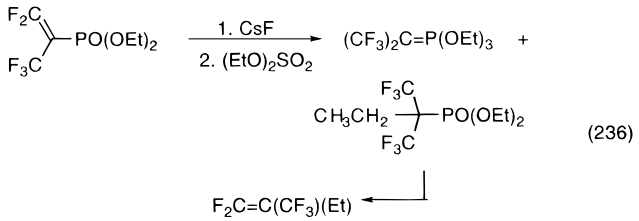
Hexafluorothioacetone reacted smoothly and rapidly with trialkyl-phosphites to give good yields of trialkoxy[bis(trifluoromethyl)methylene]phosphoranes, which were easily hydrolyzed with aqueous acid and added bromine to give readily the corresponding phosphonates (eq 233).[325] The phosphoranes underwent Wittig reaction with perfluoroacyl halide and anhydrides to give olefins (eq 234).[326]

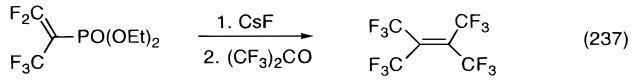



The anion of the phosphonate was generated by addition of fluoride to pentafluoroisopropenylphosphonate in a polar aprotic solvent at low temperatures.[327] The anion was stable at −78 °C and decomposed at 20 °C over 2 days. Although methylation of the anion exclusively occurred at the carbon atom with methyl iodide or dimethyl sulfate, ethylation was more difficult and gave a mixture carbon-ethylated and oxygen-ethylated products (eqs 235 and 236). With hexafluoroacetone or benzaldehyde, the Wittig−Horner reaction products were obtained in low yields (eq 237).[327]




## X. Conclusion

The previously summarized material presents the first overall review of fluorinated ylides. It should be useful to workers attempting to introduce one, two, or three fluorines into an organic compound or for the introduction of perfluoroalkyl or perfluorocycloalkyl groups. We have attempted to summarize methods for the preparation of fluorinated ylide precursors, methods of ylide generation, reactivity and stability of various fluorinated ylides, and a comprehensive summary of fluorinated ylide reactions. Where appropriate, we have attempted to illustrate mechanistic pathways of ylide generation as well as ylide reactions. In addition, stereospecificity of fluorinated ylide reactions has been included and rationales for the observed specificity were outlined where appropriate.

Forty years ago fluorinated ylide chemistry began with feeble attempts to produce simple fluoromethylene ylides. Since that time a vast array of functionalized fluorinated ylides have been developed, and this useful reaction intermediate is a mainstay in the arsenal of synthetic chemists for the introduction of fluorine and the preparation of fluorine-containing multifunctionalized compounds. As yet, many of the methods summarized in this article lack complete stereochemical control, and the future will surely see significant improvements in the stereospecificity of fluorinated ylide reactions.

We hope that this review proves useful to both synthetic and mechanistic chemists and provides a stimulus for new and exciting work in fluorinated ylide chemistry.

## Acknowledgments

D.J.B. thanks the National Science Foundation for support of Ylide research at the University of Iowa and Margaret A. Burton for assistance in the preparation of this manuscript. D.J.B. also acknowledges the contributions of his co-workers for their dedicated research work and their enthusiasm in keeping his laboratory a lively place for research. Z.Y.Y. and W.Q. thank Dr. P. A. Morken for critical comments.

## References

(1) Wittig, G.; Geissler, G. *Justus Liebigs Ann. Chem.* **1953**, *580*, 44.
(2) Tyuleneva, V. V.; Rokhlin, E. M.; Knunyants, I. L. *Russ. Chem. Review* **1981**, *50*, 280.
(3) Burton, D. J. *J. Fluorine Chem.* **1983**, *23*, 339.
(4) Franzen, V. *Angew. Chem.* **1960**, *72*, 566.
(5) Franzen, V. *Ber. Dtsch. Chem. Ges.* **1962**, *95*, 1964.

(6) Speziale, A. J.; Ratts, K. W. *J. Am. Chem. Soc.* **1962**, *84*, 854.
(7) Markanov, S. P.; Yakubovich, A. Ya.; Ginsburg, V. A.; Filatov, A. S.; Englin, M. A.; Privezentsevia, N. F.; Nikoforova, T. Ya. *Doklady Akad. Nauk SSSR* **1961**, *141*, 357.
(8) Mark, V. *Tetrahedron Lett.* **1964**, 3139.
(9) Ramirez, F.; Smith, C. P.; Meyerson, S. *Tetrahedron Lett.* **1966**, 3651.
(10) Fuqua, S. A.; Duncan, W. G.; Silverstein, R. M. *Tetrahedron Lett.* **1964**, 1461.
(11) Fuqua, S. A.; Duncan, W. G.; Silverstein, R. M. *J. Org. Chem.* **1965**, *30*, 1027.
(12) Herkes, F. E.; Burton, D. J. *J. Org. Chem.* **1967**, *32*, 1311.
(13) Fuqua, S. A.; Duncan, W. G.; Silverstein, R. M. *Tetrahedron Lett.* **1965**, 521.
(14) Fuqua, S. A.; Duncan, W. G.; Silverstein, R. M. *J. Org. Chem.* **1965**, *30*, 2543.
(15) Burton, D. J.; Herkes, F. E.; Klabunde, K. J. *J. Am. Chem. Soc.* **1966**, *88*, 5042.
(16) Burton, D. J.; Herkes, F. E. *Tetrahedron Lett.* **1965**, 1883.
(17) Klabunde, K. J.; Burton, D. J. *J. Am. Chem. Soc.* **1972**, *94*, 820.
(18) Burton, D. J.; Herkes, F. E. *Tetrahedron Lett.* **1965**, 4509.
(19) Burton, D. J.; Herkes, F. E. *J. Org. Chem.* **1968**, *33*, 1854.
(20) Burton, D. J.; Headley, J. A. *J. Fluorine Chem.* **1981**, *18*, 323.
(21) Burton, D. J.; Zawistowski, E. A. *J. Fluorine Chem.* **1971/72**, *1*, 347.
(22) Zawistowski, E. A. Ph.D. Thesis, University of Iowa, 1969.
(23) Rabinowitz, R.; Marcus, R. *J. Am. Chem. Soc.* **1962**, *84*, 1312.
(24) Rabinowitz, R. U.S. Patent 3,225,106, 1965.
(25) Naae, D. G. Ph.D. Thesis, University of Iowa, 1972.
(26) Flynn, R. M.; Manning, R. G.; Kessler, R. M.; Burton, D. J.; Hansen, S. W. *J. Fluorine Chem.* **1981**, *18*, 525.
(27) Kesling, H. S., Jr. Ph.D. Thesis, University of Iowa, 1975.
(28) Riesel, L.; Vogt, H.; Kolleck, V. *Z. Anorg. Allg. Chem.* **1989**, *574*, 143.
(29) Lauritsen, K.; Vogt, H.; Riesel, L. *Z. Anorg. Allg. Chem.* **1994**, *620*, 1103.
(30) Van Hamme, M. J. Ph.D. Thesis, University of Iowa, 1974.
(31) Vander Haar, R. W., Jr. Ph.D. Thesis, University of Iowa, 1973.
(32) Cox, D. G. Ph.D. Thesis, University of Iowa, 1984.
(33) Naae, D. G.; Burton, D. J. *J. Fluorine Chem.* **1971/72** *1*, 123.
(34) Naae, D. G.; Burton, D. J. *Synth. Commun.* **1973**, *3*, 197.
(35) Naae, D. G.; Kesling, H. S.; Burton, D. J. *Tetrahedron Lett.* **1975**, 3789.
(36) Burton, D. J.; Naae, D. G.; Flynn, R. M.; Smart, B. E.; Brittelli, D. R. *J. Org. Chem.* **1983**, *48*, 3616.
(37) Burton, D. J.; Kesling, H. S.; Naae, D. G. *J. Fluorine Chem.* **1981**, *18*, 293.
(38) Suda, M. *Tetrahedron Lett.* **1981**, 1421.
(39) Suda, M.; Fukushima, A. *Chem. Lett.* **1981**, 103.
(40) Begue, J. P.; Bonnet-Delpon, D.; Percy, J. M.; Rock, M. H.; Wilkes, R. D. *J. Chem. Soc., Chem. Commun.* **1995**, 1857.
(41) Motherwell, W. B.; Tozer, M. J.; Ross, B. C. *J. Chem. Soc., Chem. Commun.* **1989**, 1437.
(42) Houlton, J. S.; Motherwell, W. B.; Ross, B. C.; Tozer, M. J. *Tetrahedron* **1993**, *49*, 8087.
(43) Vinson, W. A.; Prickett, K. S.; Spahic, B.; Ortiz de Montellano, P. R. *J. Org. Chem.* **1983**, *48*, 4661.
(44) Schlosser, M.; Zimmermann, M. *Synthesis* **1969**, 75.
(45) Burton, D. J.; Greenlimb, P. E. *J. Org. Chem.* **1975**, *40*, 2796.
(46) Burton, D. J.; Wiemers, D. M. *J. Fluorine Chem.* **1985**, *27*, 85.
(47) Greenlimb, P. E., III. Ph.D. Thesis, University of Iowa, 1972.
(48) Burton, D. J.; Greenlimb, P. E. *J. Fluorine Chem.* **1973/74**, *3*, 447.
(49) Schlosser, M.; Christmann, K. F. *Synthesis* **1969**, 38.
(50) Krutzsch, H. C. Ph.D. Thesis, University of Iowa, 1968.
(51) Vander Haar, R. W.; Burton, D. J.; Naae, D. G. *J. Fluorine Chem.* **1971/72**, *1*, 381.
(52) Burton, D. J.; Flynn, R. M.; Manning. R. G.; Kessler, R. M. *J. Fluorine Chem.* **1982**, *21*, 371.
(53) Yamanaka, H.; Ando, T.; Funasaka, W. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 756.
(54) Burton, D. J.; Krutzsch, H. C. *Tetrahedron Lett.* **1968**, 71.
(55) Burton, D. J.; Krutzsch, H. C. *J. Org. Chem.* **1970**, *35*, 2125.
(56) Van Hamme, M. J.; Burton, D. J. *J. Fluorine Chem.* **1977**, *10*, 131.
(57) Van Hamme, M. J.; Burton, D. J. *J. Fluorine Chem.* **1979**, *13*, 407.
(58) Van Hamme, M. J.; Burton, D. J. *J. Organomet. Chem.* **1979**, *169*, 123.
(59) Cox, D. G.; Burton, D. J. *J. Org. Chem.* **1988**, *53*, 366.
(60) Cox, D. G.; Gurusamy, N.; Burton, D. J. *J. Am. Chem. Soc.* **1985**, *107*, 2811.
(61) Burton, D. J.; Cox, D. G. *J. Am. Chem. Soc.* **1983**, *105*, 650.
(62) Cox, D. G.; Sprague, L. G.; Burton, D. J. *J. Fluorine Chem.* **1983**, *23*, 383.
(63) Jeong, I. H.; Burton, D. J.; Cox, D. G. *Tetrahedron Lett.* **1986**, *27*, 3709.
(64) Burton, D. J.; Jeong, I. H. *J. Fluorine Chem.* **1993**, *62*, 259.
(65) Jeong, I. H. Ph.D. Thesis, University of Iowa, 1987.
(66) Dixon, D. A.; Smart, B. E. *J. Am. Chem. Soc.* **1986**, *108*, 7172.
(67) Burton, D. J.; Herkes, F. E. *Org. Synth.* **1968**, *48*, 116.
(68) Burton, D. J.; Inouye, Y.; Headley, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 3980.
(69) Headley, J. A. Ph.D. Thesis, University of Iowa, 1975.
(70) Hudlicky, M., Pavlath, A. E., Eds. *Chemistry of Organic Fluorine Compounds II*; American Chemical Society: Washington, DC, 1995; p 586.
(71) Filler, R.; Lin, S.; Zhang, Z. *J. Fluorine Chem.* **1995**, *74*, 69.
(72) Tronchet, J. M. J.; Schwarzenbach, D.; Barbalat-Rey, F. *Carbohydr. Res.* **1976**, *46*, 9.
(73) Tronchet, J. M. J.; Bonenfant, A. P. *Helv. Chim. Acta* **1980**, *63*, 1644.
(74) Tronchet, J. M. J.; Bonenfant, A. P.; Barbalat-Rey, F. *Carbohydr. Res.* **1978**, *67*, 564.
(75) Fried, J.; Kittisopikul, S.; Hallinan, E. A. *Tetrahedron Lett.* **1984**, *25*, 4329.
(76) Hayashi, S.; Nakai, T.; Ishikawa, N.; Burton, D. J.; Naae, D. G.; Kesling, H.S. *Chem. Lett.* **1979**, 983.
(77) Barna, P. M. *Chem. Ind.* **1966**, 2054.
(78) Burton, D. J.; Shinya, S.; Howells, R. D. *J Am. Chem. Soc.* **1979**, *101*, 3689.
(79) Stockel, R. F.; Megson, F.; Beachem, M. T. *J. Org. Chem.* **1968**, *33*, 4395.
(80) (a) Howells, M. A.; Howells, R. D.; Baenziger, N. C.; Burton, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 5366. (b) Howells, R. D. Ph.D. Thesis, University of Iowa, 1973. (c) Vander Valk, P. D. Ph.D. Thesis, University of Iowa, 1974.
(81) Angerer, I. D. *Diss. Abstr.* **1969**, *29B*, 4583.
(82) Henry, R. A. *J. Chem. Eng. Data* **1976**, *21*, 503.
(83) Burton, D. J.; Inouye, Y. *Tetrahedron Lett.* **1979**, 3397.
(84) Inouye, Y. Ph.D. Thesis, University of Iowa, 1978.
(85) Gale, D. M.; Middleton, W. J.; Krespan, C. G. *J. Am. Chem. Soc.* **1966**, *88*, 3617.
(86) Gale, D. M; Milddleton, W. J.; Krespan, C. R. *J. Am. Chem. Soc.* **1965**, *87*, 657.
(87) Hanack, M.; Korhummel, C. *Synthesis* **1984**, 944.
(88) Mack, H.; Hanack, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 184.
(89) Korhummel, C.; Hanack, M. *Chem. Ber.* **1989**, *122*, 2187.
(90) Escoula, B.; Rico, I.; Laval, J. P.; Lattes, A. *Synth. Commun.* **1985**, *15*, 35.
(91) Cecutti, C.; Rico, I.; Lattes, A. *J. Dispersion Sci. Technol.* **1986**, *7*, 307.
(92) Kubota, T.; Yamamoto, M. *Tetrahedron Lett.* **1992**, *33*, 2603.
(93) Qiu, W.; Burton, D. J. *J. Fluorine Chem.* **1993**, *65*, 143.
(94) Burton, D. J.; Lee, T. M. *J. Fluorine Chem.* **1976**, *8*, 189.
(95) Birum, G. H.; Matthews, C. N. *J. Org. Chem.* **1967**, *32*, 3554.
(96) Filler, R.; Heffern, E. W. *J. Org. Chem.* **1967**, *32*, 3249.
(97) Schmidbaur, H.; Zybill, C. E. *Chem. Ber.* **1981**, *114*, 3589.
(98) Shen, Y.; Qiu, W. *Synthesis* **1987**, 42.
(99) Nesmeyanov, N. A.; Bergman, S. T.; Reutov, O. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1972**, 605.
(100) Shen, Y.; Xiang, Y. *J. Chem. Soc., Perkin Trans. 1* **1991**, 665.
(101) Shen, Y.; Qiu, W. *J. Fluorine Chem.* **1988**, *38*, 175.
(102) Shen, Y.; Wang, T. *J. Fluorine. Chem.* **1994**, *67*, 33.
(103) Vicente, J.; Chicote, M. T.; Fernandez-Baeza, J.; Fernandez-Baeza, A. *J. Am. Chem. Soc.* **1993**, *115*, 794.
(104) Vicente, J.; Chicote, M. T.; Fernandez-Baeza, J.; Fernandez-Baeza, A. *New J. Chem.* **1994**, *18*, 263.
(105) Burton, D. J.; Vander Valk, P. D. *J. Fluorine Chem.* **1981**, *18*, 413.
(106) Sun, W.; Prestwich, G. D. *Tetrahedron Lett.* **1990**, *31*, 801.
(107) Kolodyazhnyl, O. I.; Shevchuk, L. I.; Kukhar, V. P. *Zh. Obsh. Khim.* **1977**, *47*, 723.
(108) Leroy, J.; Wakselman, C. *Synthesis* **1982**, 496.
(109) (a) Thenappan, A.; Burton, D. J. *Tetrahedron Lett.* **1989**, *30*, 3641. (b) Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1990**, *55*, 2311.
(110) Miyano, M.; Stealey, M. A. *J. Org. Chem.* **1975**, *40*, 2840.
(111) Shen, Y.; Qiu, W.; Xin, Y.; Huang, Y. *Synthesis* **1984**, 924.
(112) Zhang, P.; Tong, W.; Ding, W. *Shanghai Keji Daxue Xuebao* **1988**, *11*, 105; *Chem. Abstr.* **1990**, *112*, 77372.
(113) Filler, R.; Heffern, E. W. *J. Org. Chem.* **1967**, *32*, 3249.
(114) (a) Huang, Y.; Shen, Y.; Chen, K.; Wang, C. *Huaxue Xuebao* **1979**, *37*, 47. (b) Huang, Y.; Shen, Y.; Cen, W. *Huaxue Xuebao* **1983**, *41*, 187; *Chem. Abstr.* **1983**, *99*, 38008.
(115) (a) Huang, Y.; Shen, Y.; Ding, W.; Zheng, J. *Tetrahedron Lett.* **1981**, *22*, 5283. (b) Shen, Y.; Zheng, J.; Huang, Y. *J. Fluorine Chem.* **1988**, *41*, 363.
(116) (a) Shen, Y.; Xin, Y.; Cen, W.; Huang, Y. *Synthesis* **1984**, 35. (b) Shen, Y.; Cen, W.; Huang, Y. *Synthesis* **1985**, 159.
(117) Shen, Y.; Lin, Y.; Xin, Y. *Tetrahedron Lett.* **1985**, *26*, 5137.
(118) Shen, Y.; Cen, W.; Huang, Y. *Synthesis* **1987**, 626.
(119) Shen, Y.; Zheng, J. *J. Fluorine Chem.* **1987**, *35*, 513.
(120) Xin, Y.; Wu, X.; Shen, Y. *J. Fluorine Chem.* **1988**, *40*, 15.
(121) Braga, A. L.; Comasseto, J. V.; Petragnani, N. *Synthesis* **1984**, 240.
(122) Shen, Y.; Qiu, W. *Synthesis* **1987**, 42.
(123) Shen, Y.; Xiang, Y.; Qiu, W. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2965.
(124) Shen, Y.; Gao, S. *J. Fluorine Chem.* **1993**, *61*, 105.

(125) Ding, W.; Cai, W.; Dai, J.; Huang, Y.; Zhen, J. *Huaxue Xuebao* **1983**, *41*, 67; *Chem. Abstr.* **1983**, *98*, 179520.
(126) Huang, Y.; Shen, Y.; Xin, Y. *Huaxue Xuebao* **1981**, *39*, 659; *Chem. Abstr.* **1982**, *97*, 198275.
(127) Shen, Y.; Qiu, W. *Tetrahedron Lett.* **1987**, *28*, 4283.
(128) (a) Hamper, B. C. *J. Org. Chem.* **1988**, *53*, 5558. (b) Hamper, B. C. *Org. Synthesis* **1992**, *70*, 246.
(129) Huang, Y.; Shen, Y. *Adv. Organomet. Chem.* **1982**, *20*, 115.
(130) Ding, W.; Pu, J.; Kong, X. *Huaxue Xuebao* **1986**, *44*, 62; *Chem. Abstr.* **1987**, *106*, 33177.
(131) Ding, W.; Pu, J.; Zhang, P. *Youji Huaxue* **1987**, 435; *Chem. Abstr.* **1988**, *109*, 190495.
(132) Ding, W.; Zhang, P.; Cao, W. *Tetrahedron Lett.* **1987**, *28*, 81.
(133) (a) Ding, W.; Pu, J.; Zhang, C. *Synthesis* **1992**, 635. (b) Ding, W.; Pu, J.; Zhang, C.; Cao, W. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1369.
(134) (a) Ding, W.; Pu, J.; Kong, X. *Huaxue Xuebao* **1986**, *44*, 255; *Chem. Abstr.* **1986**, *105*, 191290. (b) One of the referees suggested that the water adduct of ylide **93** could eliminate MeOH and $Ph_3AsO$ intramolecularly via a six-member ring mechanism to form a ketene which cyclized to afford pyrone product.
(135) Ding, W.; Wei, J.; Pu, J. *Huaxue Xuebao* **1987**, *45*, 1035; *Chem. Abstr.* **1988**, *109*, 73549.
(136) Trabelsi, H.; Bollens, E.; Cambon, A. *Synthesis* **1990**, 623.
(137) Ding, W.; Pu, J.; Wang, T. *Shanghai Keji Daxue Xuebao* **1989**, *12*, 31; *Chem. Abstr.* **1990**, *113*, 172156.
(138) Kadyrov, A. A.; Rokhlin, E. M.; Knunyants, I. L. *Izv. Akad. Nauk. SSSR. Ser. Khim.* **1981**, 2653.
(139) (a) Ding, W.; Zhang, P.; Cao, W. *Shanghai Keji Daxue Xuebao* **1988**, *11*, 99; *Chem. Abstr.* **1989**, *111*, 77584. (b) Ding, W.; Cao, W.; Xu, Z.; Shi, Z.; Yao, Y. *Chin. J. Chem.* **1993**, *11*, 81; *Chem. Abstr.* **1994**, *120*, 76981.
(140) Ding, W.; Cao, W.; Xu, Z.; Yao, Y.; Shi, Z.; Han, Z. *J. Chem. Soc., Perkin Trans. 1* **1993**, 854.
(141) Shen, Y.; Wang, T. *Tetrahedron Lett.* **1989**, *30*, 7203.
(142) Shen, Y.; Wang, T. *Tetrahedron Lett.* **1990**, *31*, 5925.
(143) Shen, Y.; Wang, T. *J. Chem. Soc., Perkin Trans. 1* **1991**, 487.
(144) Shen, Y.; Wang, T. *J. Chem. Res. (S)* **1993**, 490.
(145) Shen, Y.; Gao, S. *J. Fluorine Chem.* **1993**, *61*, 273.
(146) Shen, Y.; Gao, S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1473.
(147) Shen, Y.; Gao, S. *J. Org. Chem.* **1993**, *58*, 4564.
(148) Shen, Y.; Qi, M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3.
(149) Shen, Y.; Wang, T. *Tetrahedron Lett.* **1990**, *31*, 3161.
(150) (a) Thenappan, A.; Burton, D. J. *Tetrahedron Lett.* **1989**, *30*, 6113. (b) Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1991**, *56*, 273.
(151) Belletire, J. L.; Namie, M. W. *Synth. Commun.* **1983**, *13*, 87.
(152) Shen, Y.; Qiu, W. *Tetrahedron Lett.* **1987**, *28*, 449.
(153) Shen, Y.; Qiu, W. *J. Chem. Soc., Chem. Commun.* **1987**, 703.
(154) Shen, Y.; Xiang, Y. *J. Fluorine Chem.* **1991**, *52*, 221.
(155) Shen, Y.; Xiang, Y. *J. Fluorine Chem.* **1992**, *56*, 321.
(156) Shen, Y.; Liao, Q.; Qiu, W. *J. Chem. Soc., Perkin Trans. 1* **1990**, 695.
(157) Shen, Y.; Qiu, W. *Huaxue Xuebao* **1993**, *51*, 1209; *Chem. Abstr.* **1994**, *121*, 34417.
(158) (a) Shen, Y.; Liao, Q. *J. Fluorine Chem.* **1990**, *47*, 137. (b) Shen, Y.; Liao, Q. *J. Fluorine Chem.* **1995**, *73*, 251.
(159) Shen, Y.; Gao, S.; Xiang, Y. *J. Fluorine Chem.* **1993**, *63*, 151.
(160) Shen, Y.; Xiang, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 1384.
(161) Shen, Y.; Xiang, Y.; Qiu, W. *Tetrahedron Lett.* **1991**, *32*, 4953.
(162) Qiu, W.; Shen, Y. *J. Fluorine Chem.* **1988**, *38*, 249.
(163) (a) Vicente, J.; Chicote, T.; Fernandez-Baeza, J.; Fernandez-Baeza, A.; Jones, P. G. *J. Am. Chem. Soc.* **1993**, *115*, 794. (b) Vicente, J.; Chicote, T.; Fernandez-Baeza, J.; Fernandez-Baeza, A.; Jones, P. G. *New J. Chem.* **1994**, *18*, 263.
(164) Shao, M; Jin, X.; Tang, Y.; Huang, Q.; Huang, Y. *Tetrahedron Lett.* **1982**, *23*, 5343.
(165) Xia, Z.; Zhang, Z.; Shen, Y. *Huaxue Xuebao* **1984**, *42*, 1223; *Chem. Abstr.* **1985**, *102*, 158435.
(166) Trabelsi, H.; Rouvier, E.; Cambon, A. *J. Fluorine Chem.* **1988**, *39*, 1.
(167) Bollens, E.; Szonyi, F.; Trabelsi, H.; Cambon, A. *J. Fluorine Chem.* **1994**, *67*, 177.
(168) Ding, W.; Pu, J.; Wang, T. *Shanghai Keji Daxue Xuebao* **1989**, *12*, 124; *Chem. Abstr.* **1990**, *112*, 179258.
(169) Ding, W.; Cao, W.; Zhu, D.; Tong, W. *Chem. Res. Chin. Univ.* **1992**, *8*, 224; *Chem. Abstr.* **1993**, *118*, 254650.
(170) Ding, W.; Zhang, P.; Pu, J.; Zhang, C.; Mao, S.; Wang, Y.; Shen, W. *Huaxue Xuebao* **1991**, *49*, 284; *Chem. Abstr.* **1991**, *115*, 49850.
(171) Ding, W.; Pu, J.; Zhang, P. *Huaxue Xuebao* **1987**, *45*, 47; *Chem. Abstr.* **1988**, *108*, 55471.
(172) Shen, Y.; Fan, Z.; Qiu, W. *J. Organomet. Chem.* **1987**, *320*, 21.
(173) Bansal, R. K.; Bhagchandani, G. *J. Prakt. Chem.* **1981**, 49.
(174) Starzewski, K.-H. A. O.; Richter, W.; Schmidbaur, H. *Chem. Ber.* **1976**, *109*, 473.
(175) Shen. Y.; Qiu, W. *Synthesis* **1987**, 65.
(176) Nesmeyanov, N. A.; Berman, S. T.; Reutov, O. A. *Izv. Akad. Nauk SSSR. Ser. Khim.* **1972**, 605.
(177) (a) Schmidbaur, H.; Richter, W.; Wolf, W.; Kohler, F. H. *Chem. Ber.* **1975**, *108*, 2649. (b) Yamamoto, Y.; Schmidbaur, H. *J. Chem. Soc., Chem. Commum.* **1975**, 608.
(178) Xia, Z.; Zhang, Z. *Huaxue Xuebao* **1983**, *41*, 577; *Chem. Abstr.* **1983**, *99*, 113979.
(179) Gosney, I.; Lloyd, D. *Tetrahedron* **1973**, *29*, 1697.
(180) Fan, Z.; Shen, Y. *Huaxue Xuebao* **1984**, *42*, 759; *Chem. Abstr.* **1984**, *101*, 181583.
(181) Zeng, W.; Tao, W. *Gaodeng Xuexiao Huaxue Xuebao* **1991**, *12*, 921; *Chem. Abstr.* **1992**, *116*, 105704.
(182) (a) Kuang, F.; Tao, W.; Zuo, Z.; Xiong, H. *Youji Huaxue* **1988**, *8*, 344; *Chem. Abstr.* **1989**, *110*, 135397. (b) Kuang, F.; Wu, K.; Lou, X.; Tao, W. *Wuhan Daxue Xuebao, Ziran Kexuebao (1)* **1988**, 140; *Chem. Abstr.* **1989**, *110*, 38823.
(183) Burton, D. J.; Vander Valk, P. D. *J. Fluorine Chem.* **1981**, *18*, 413.
(184) Cioaner, E. *J. Org. Chem.* **1970**, *35*, 1725.
(185) Qiu, W.; Shen, Y. *Huaxue Xuebao* **1989**, *47*, 1131; *Chem. Abstr.* **1990**, *113*, 24066.
(186) Huang, Y.; Ding, W.; Cai, W.; Ma, J.; Wang, Q. *Sci. Sin. (Engl. Ed.)* **1981**, *24*, 189; *Chem. Abstr.* **1981**, *95*, 97923.
(187) (a) Shen, Y.; Xiang, Y. *J. Fluorine Chem.* **1991**, *53*, 429. (b) Shen, Y.; Xiang, Y. *Synth. Commum.* **1991**, *21*, 1403.
(188) Shen, Y.; Liao, Q.; Qiu, W. *J. Chem. Soc., Chem. Commun.* **1988**, 1309.
(189) (a) Shen, Y.; Xiang, Y. *Tetrahedron Lett.* **1990**, *31*, 2305. (b) Shen, Y.; Xiang, Y. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2493.
(190) Shen, Y.; Xiang, Y. *J. Chem. Res. (S)* **1994**, 198.
(191) Zhang, P.; Ding, W.; Cao, P.; Mao, S. *Shanghai Keji Daxue Xuebao* **1989**, *12*, 21; *Chem. Abstr.* **1990**, *113*, 172225.
(192) Ding, W.; Cai, W.; Peng, X. *Huaxue Xuebao* **1986**, *44*, 261; *Chem. Abstr.* **1986**, *105*, 191291.
(193) Wittmann, H.; Ziegler, E.; Peters, K.; Peters, E. M.; Schnering, H. G. *Monatsh. Chem.* **1983**, *114*, 1097.
(194) Izzo, P.; Lee, V. J. *J. Heterocycl. Chem.* **1988**, *25*, 289.
(195) Burton, D. J.; Howells, R. D.; Vander Valk, P. D. *J. Am. Chem. Soc.* **1977**, *99*, 4830.
(196) Cullen, W. R.; Soulen, R. L. *J. Fluorine Chem.* **1981**, *17*, 453.
(197) Ellzey, S. E., Jr.; Guice, W. A. *J. Org. Chem.* **1966**, *31*, 1300.
(198) Bansal, R. K.; Bhagchandani, G. *Indian J. Chem.* **1980**, *19B*, 801.
(199) Bansal, R. K.; Bhagchandani, G. *Indian J. Chem.* **1979**, *18B*, 362.
(200) Bansal, R. K.; Sharma, S. K. *J. Organomet. Chem.* **1978**, *155*, 293.
(201) Banks, R. E.; Thomson, J. *J. Fluorine Chem.* **1984**, *26*, 499.
(202) Banks, R. E.; Thomson, J. *J. Chem. Res.* **1985**, (S) *33*; (M) 0671.
(203) Banks, R. E.; Pritchard, R. G.; Thomson, J. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1769.
(204) Wittmann, H.; Ziegler, E. *Monatsh. Chem.* **1981**, *112*, 1333.
(205) Wittmann, H.; Ziegler, E. *Monatsh. Chem.* **1982**, *113*, 1451.
(206) Wittmann, H.; Ziegler, E. *Monatsh. Chem.* **1983**, *114*, 1223.
(207) Ziegler, E.; Wittmann, H.; Peters, K. *Monatsh. Chem.* **1983**, *114*, 783.
(208) Ziegler, E.; Wittmann, H. *Monatsh. Chem.* **1985**, *116*, 821.
(209) Shi, G.; Xu, Y.; Xu, M. *Tetrahedron* **1991**, *47*, 1629.
(210) Wittmann, H.; Ziegler, E.; Sterk, H.; Peters, K.; Peters, E. M.; Schnering, H. G. *Monatsh. Chem.* **1985**, *116*, 1189.
(211) Ziegler, E.; Wittmann, H.; Sterk, H. *Monatsh. Chem.* **1987**, *118*, 115.
(212) Wittmann, H.; Ziegler, E. *Monatsh. Chem.* **1986**, *117*, 821.
(213) Ziegler, E.; Wittmann, H. *Monatsh. Chem.* **1986**, *117*, 653.
(214) Wittmann, H.; Ziegler, E. *Oesterr. Chem. Ztg.* **1988**, *89*, 259.
(215) Pavlenko, N. V.; Yagupol'skii, Y. L. *Russ. J. Gen. Chem.* **1994**, *64*, 1148.
(216) Middleton, W. J. *J. Org. Chem.* **1975**, *40*, 574.
(217) Abramov, V. S. *Khim. Primen. Fosfororgan Soedinenii, Akad. Nauk. SSSR* **1955**, 218.
(218) Blackburn, G. M.; Kent, D. E. *J. Chem. Soc., Chem. Commum.* **1981**, 511.
(219) Blackburn, G. M.; Kent, D. E. *J. Chem. Soc., Perkin Trans. 1* **1986**, 219.
(220) Sanders, T. C.; Hammond, G. B. *J. Org. Chem.* **1993**, *58*, 5598.
(221) Takeuchi, Y.; Nagata, K.; Koizumi, T. *J. Org. Chem.* **1987**, *52*, 5061.
(222) McKenna, C. E.; Shen, P. D. *J. Org. Chem.* **1981**, *46*, 4573.
(223) Grell, W.; Machleidt, H. *Liebigs Ann. Chem.* **1966**, *693*, 134.
(224) Koizumi, T.; Hagi, T.; Horie, Y.; Takeuchi, Y. *Chem. Pharm. Bull.* **1987**, *35*, 3959.
(225) Differding, E.; Duthaler, R. O.; Krieger, A.; Ruegg, G. M.; Schmit, C. *Synlett* **1991**, 395.
(226) Davis, F. A.; Han, W.; Murphy, C. K. *J. Org. Chem.* **1995**, *60*, 4730.
(227) Xu, Z. Q.; DesMarteau, D. D. *J. Chem. Soc., Perkin Trans. 1* **1992**, 312.
(228) Burton, D. J.; Flynn, R. M. *J. Fluorine Chem.* **1977**, *10*, 329.
(229) Patois, C.; Savignac, P. *J. Chem. Soc., Chem. Commun.* **1993**, 1711.
(230) Patois, C.; Savignac, P. *Synth. Commun.* **1994**, *24*, 1317.
(231) Machletdt, H.; Wessendorf, R. *Liebigs Ann. Chem.* **1964**, *674*, 1.
(232) Elkik, E.; Imbeaux, M. *Synthesis* **1989**, 861.
(233) Thenappan, A. Ph.D. Thesis, University of Iowa, 1989.
(234) Hall, C. R.; Inch, T. D.; Williams, N. E. *J. Chem. Soc., Perkin Trans. 1* **1985**, 233.

(235) Blackburn, G. M.; Parratt, M. J. *J. Chem. Soc., Chem. Commun.* **1983**, 866.
(236) Blackburn, G. M.; Parratt, M. J. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1425.
(237) Elkik, E.; Freancesch, C. *Bull. Soc. Chim. Fr.* **1985**, 783.
(238) Thenappan, A. Ph. D. Thesis, University of Iowa, 1989.
(239) McKenna, C. E.; Khawli, L. A. *Phosphorus Sulfur* **1983**, *18*, 483.
(240) McKenna, C. E.; Khawli, L. A. *J. Org. Chem.* **1986**, *51*, 5467.
(241) Moghadam, G. E.; Penne, J. S. *Bull. Soc. Chim. Fr.* **1985**, 448.
(242) Morikawa, T.; Sasaki, H.; Mori, K.; Shiro, M.; Taguchi, T. *Chem. Pharm. Bull.* **1992**, *40*, 3189.
(243) Taguchi, T.; Takigawa, T.; Igarashi, A.; Kobayashi, Y.; Tanaka, Y.; Jubiz, W.; Briggs, R. C. *Chem. Pharm. Bull.* **1987**, *35*, 1666.
(244) Piva, O. *Synlett* **1994**, 729.
(245) Pirrung, M. C.; Rowley, E. G.; Holmes, C. P. *J. Org. Chem.* **1993**, *58*, 5683.
(246) Allmendinger, T.; Furet, P.; Hungerbohler, E. *Tetrahedron Lett.* **1990**, *31*, 7279.
(247) Baader, E.; Bartmann, W.; Beck, G.; Below, B. P.; Bergmann, A.; Jendralla, H.; Kebeler, K.; Wess, G. *Tetrahedron Lett.* **1989**, *30*, 5115.
(248) Camps, F.; Coll. J.; Fabrias, G.; Guerrero, A. *Tetrahedron* **1984**, *40*, 2871.
(249) Patrick, T. B.; Lanahan, M. V.; Yang, C.; Walker, J. K. *J. Org. Chem.* **1994**, *59*, 1210.
(250) Asato, A. E.; Matsumoto, H.; Denny, M.; Liu, R. S. H. *J. Am. Chem. Soc.* **1978**, *100*, 5957.
(251) Asato, A. E.; Kini. A.; Denny, M.; Liu, R. S. H. *J. Am. Chem. Soc.* **1983**, *105*, 2923.
(252) Liu, R. S. H.; Matsumoto, H.; Asato, A. E.; Denny, M.; Shichida, Y.; Yoshizawa, T.; Dahlquist, F. W. *J. Am. Chem. Soc.* **1981**, *103*, 7195.
(253) Mead, D.; Loh, R.; Asato, A. E.; Liu, R. S. H. *Tetrahedron Lett.* **1985**, *26*, 2873.
(254) Massoudi, H. H.; Cantacuzene, D.; Wakselman, C.; Tour, C. B. *Synthesis* **1983**, 1010.
(255) Schlosser, M. *Tetrahedron* **1978**, *34*, 3.
(256) Thenappan, A.; Burton, D. J. *Tetrahedron Lett.* **1989**, *30*, 5571.
(257) Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1990**, *55*, 4639.
(258) Grison, Ph. C. C.; Sauvetre, R. *J. Organomet. Chem.* **1987**, *332*, 1.
(259) Grison, Ph. C. C. *Tetrahedron Lett.* **1988**, *29*, 2655.
(260) Patrick, T. B.; Nadji, S. *J. Fluorine Chem.* **1990**, *49*, 147.
(261) Thenappan, A.; Burton, D. J. *Tetrahedron Lett.* **1989**, *30*, 3641.
(262) Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1990,** *55*, 2311
(263) Welch, J. T. *Selective Fluorination in Organic & Bioorganic Chemistry*; American Chemical Society: Washington, DC, 1991; Chapter 7.
(264) Thenappan, A.; Burton, D. J. *Tetrahedron Lett.* **1989**, *30*, 6113.
(265) Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1991**, *56*, 273
(266) Tsai, H. J.; Thenappan, A.; Burton, D. J. *Tetrahedron Lett.* **1992**, *33*, 6579.
(267) Tsai, H. J.; Thenappan, A.; Burton, D. J. *J. Org. Chem.* **1994**, *59*, 7085.
(268) Blackburn, G. M.; Parratt, M. J. *J. Chem. Soc., Chem. Commun.* **1982**, 1270.
(269) Blackburn, G. M.; Parratt, M. J. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1417.
(270) Blackburn, G. M.; Rashid, A. *J. Chem. Soc., Chem. Commun.* **1989**, 40.
(271) McCarthy, J. R.; Matthews, D. P.; Edwards, M. L.; Stemerick, D. M.; Jarvi. E. T. *Tetrahedron Lett.* **1990**, *31*, 5449.
(272) Schmidt, C. *Synlett* **1994**, 241.
(273) Inbasekaran, M.; Peet, N. P.; McCarthy, J. R.; LeTourneau, M. E. *J. Chem. Soc., Chem. Commun.* **1985**, 678.
(274) Moor, W. R.; Schatzman, G. L.; Jarvi, E. T.; Gross, R. S.; McCarthy, J. R. *J. Am. Chem. Soc.* **1992**, *144*, 360.
(275) McCarthy, J. R.; Matthews, D. P.; Stemerick, D. M.; Huber, E. W.; Bey, P.; Lippert, B. J.; Snyder, R. D.; Sunkara, P. S. *J. Am. Chem. Soc.* **1991**, *113*, 7439.
(276) Khrimian, A. P.; DeMilo, A. B.; Waters, R. M.; Liquido, N. J.; Nicholson, J. M. *J. Org. Chem.* **1994**, *59*, 8034.
(277) Matthews, D. P.; Gross, R. S.; McCarthy, J. R. *Tetrahedron Lett.* **1994**, *35*, 1027.
(278) Wemple, J.; More, K. M. *Synthesis* **1977**, 791.
(279) Fujita, M.; Suzuki, M.; Ogata, K.; Ogura, K. *Tetrahedron Lett.* **1991**, 32, 1463.
(280) Janzen, A. F.; Wang, P. M. C.; Lemire, A. E. *J. Fluorine Chem.* **1983**, *22*, 557.
(281) Zupan, M. *J. Fluorine Chem.* **1976**, *8*, 305.
(282) Umemoto, T.; Tomizawa, G. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3625.
(283) Fuchigami, T. *Org. Synth. Jpn.* **1994**, *52*, 59
(284) Purrington, S. T.; Pittman, J. H. *Tetrahedron Lett.* **1987**, *28*, 3901.
(285) McCarthy, J. R.; Peet, N. P.; LeTourneau, M. E.; Inbasekaran, M. *J. Am. Chem. Soc.* **1985**, *107*, 735.
(286) Matthews, D. P.; Waid, P. P.; Sabol, J. S.; McCarthy, J. R. *Tetrahedron Lett.* **1994**, *35*, 5177.
(287) (a) McCarthy, J. R.; Matthews, D. P.; Paolini, J. P. *Org. Synth.* **1993**, 72, 209. (b) Matthews, D. P.; McCarthy, J. R. *J. Org. Chem.* **1990**, *55*, 2973.
(288) Robins, M. J.; Wnuk, S. F. *Tetrahedron Lett.* **1988**, *29*, 5729.
(289) Boys, M. L.; Collington, E. W.; Finch, H.; Swanson, S.; Whitehead, J. F. *Tetrahedron Lett.* **1988**, *29*, 3365.
(290) Reutrakul, V.; Rukachaisirikul, V. *Tetrahedron Lett.* **1983**, *24*, 725.
(291) Najera, C.; Yus, M.; Hassig, R.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 1100.
(292) Satoh, T.; Kitoh, Y.; Onda, K.; Takano, K.; Yamakawa, K**.** *Tetrahedron* **1994**, *50*, 4957.
(293) Krishnan, G.; Sampson, P. *Tetrahedron Lett.* **1990**, *31*, 5609.
(294) Reutrakul, V.; Kruahong, T.; Pohmakotr, M. *Tetrahedron Lett.* **1994**, *35*, 4851.
(295) Reutrakul, V.; Kruahong, T.; Pohmakotr, M. *Tetrahedron Lett.* **1994**, *35*, 4853.
(296) Satoh, T.; Itoh, N.; Onda, K.; Kitoh, Y.; Yamakawa, K. *Tetrahedron Lett.* **1992**, *33*, 1483.
(297) Satoh, T.; Itoh, N.; Onda, K.; Kitoh, Y.; Yamakawa, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2800.
(298) Fujii, A.; Usuki, Y.; Iio, H. Tokoroyama, T. *Synlett* **1994**, 725.
(299) Allmendinger, T. *Tetrahedron* **1991**, *47*, 4905.
(300) Takeuchi, Y.; Ogura, H.; Ishii, Y.; Koizumi, T. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1721.
(301) Flynn, R. M. Ph.D. Thesis, University of Iowa, 1979.
(302) Burton, D. J.; Flynn, R. M. *J. Fluorine Chem.* **1977**, *16*, 329.
(303) Obayashi, M.; Ito, E.; Matsui, K.; Kondo, K. *Tetrahedron Lett.* **1982,** *23*, 2323.
(304) Blackburn, G. M.; Brown, D.; Martin, S. J.; Parratt, M. J. *J. Chem. Soc., Perkin Trans. 1* **1987**, 181.
(305) Kim, C. U.; Luh, B. Y.; Misco, P. F.; Nronson, J. J.; Hitchcock, M. J. M.; Ghazzouli, I.; Martin, J. C. *J. Med. Chem.* **1990**, *33*, 1207.
(306) Edwards, M. L.; Stemerick, D. M.; Jarvi, E. T.; Matthews, D. P.; McCarthy, J. R. *Tetrahedron Lett.* **1990**, *31*, 5571.
(307) Obayashi, M.; Kondo, K. *Tetrahedron Lett.* **1982**, *23*, 2327.
(308) Chen, S.; Yuan, C. *Phosphorus, Sulfur, Silicon* **1993**, *82*, 73.
(309) Moriarty, R. M.; Condeiu, C.; Liu, K.; Tuladhar, S.; Lenz,D.; Brimfeld, A. *Abstracts of Paper,* 210th National Meeting of The American Chemical Society, Chicago, IL; American Chemical Society (Division of Organic Chemistry): Washington, DC, 1995, p 277.
(310) Burton, D. J.; Sprague, L. G. *J. Org. Chem.* **1988**, *53*, 1523.
(311) Halazy, S.; Ehrhard, A.; Danzin, C. *J. Am. Chem. Soc.* **1991**, *113*, 315.
(312) Martin, S.; Dean, D. W.; Wagman, A. S. *Tetrahedron Lett.* **1992**, *33*, 1839.
(313) Berkowitz, D. B.; Eggen, M.; Shen, Q.; Sloss, D. G. *J. Org. Chem.* **1993**, *58*, 6174.
(314) Berkowitz, D. B.; Shen, Q.; Maeng, J. *Tetrahedron Lett.* **1994**, *35*, 6445.
(315) Vinod, T. K.; Griffith, O. H.; Keana, J. F. W. *Tetrahedron Lett.* **1994**, *35*, 7193.
(316) Berkowitz, D. B.; Sloss, D. G. *J. Org. Chem.* **1995**, *60*, 7047.
(317) (a) Halazy, S.; Gross-Berges, V. *J. Chem. Soc., Chem. Commun.* **1992**, 743. (b) Lequeux, T. P.; Percy, J. M. *J. Chem. Soc., Chem. Commun.* **1995**, 2111.
(318) Ruzicka, J. A.; Qiu, W.; Baker, M. T.; Burton, D. J. *J. Labelled Compd. Radiopharm.* **1994**, *XXXIV*, 59.
(319) Howson, W.; Hills, J. M. *Bioorg. Med. Chem. Lett.* **1991**, *1*, 501.
(320) Lequeux, T. P.; Percy, J. M. *Synlett* **1995**, 361.
(321) Stahly, G. P.; Rouge, B. U.S. Patent 4,837,327, 1989.
(322) Rico, I.; Cantacuzene, D.; Wakselman, C. *J. Org. Chem.* **1983**, *48*, 1979.
(323) Langlois, B. R. *J. Fluorine Chem.* **1988**, *41*, 247.
(324) Sabol, J. S.; McCarthy, J. R. *Tetrahedron Lett.* **1992**, *33*, 3101.
(325) Middleton, W. J.; Sharkey, W. H. *J. Org. Chem.* **1965**, *30*, 1384.
(326) Volkonskii, A. Y.; Mysov, E. I.; Rokhlin, E. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1984**, 1356.
(327) Kadyrov, A. A.; Rokhlin, E. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1983**, 1353.

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