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## A FACILE ONE-STEP PREPARATION OF CHLOROFLUOROMETHYLENE OLEFINS

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### SUMMARY

The "insitu" reaction of triphenylphosphine, fluorotrichloromethane, zinc dust, and an aldehyde or ketone in dimethylformamide at 60°C provides a facile one-step synthesis of chlorofluoromethylene olefins. A study of representative examples of carbonyl compounds demonstrates that this approach gives yields of olefinic products comparable to other more elaborate or expensive synthetic routes. It should prove to be synthetically useful for the preparation of chlorofluoromethylene olefins from aldehydes and reactive ketones.

### INTRODUCTION

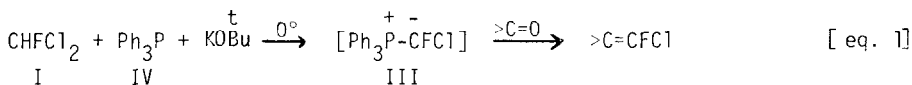
Several recent reports in the chemical literature have been directed to the preparation of chlorofluoromethylene olefins. The initial reports [2] employed lengthy synthetic sequences and are of limited synthetic utility. Later reports have focused on the use of the chlorofluoromethylene ylide in a Wittig type of reaction [3-6]. The ylide was generated by the action of base either on esters of dichlorofluoroacetic acid [4] or dichlorofluoromethane [3,5], or *via* decarboxylation of dichlorofluoroacetate salts [3,5]. A more recent report has also employed phenyl-dichlorofluoromethyl mercury as the ylide precursor [7].

Both aliphatic and aromatic aldehydes give modest yields of chlorofluoromethylene olefins from the ylide approach. Ketones which contain an activating group (electron-withdrawing) alpha to the carbonyl function also give respectable yields of the halogenated olefins, whereas unactivated ketones and cyclic ketones give low yields of olefins. Despite this

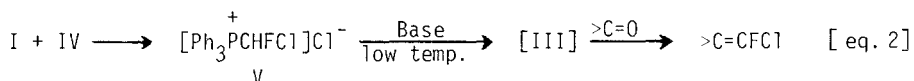
limitation, the ylide approach has been the most productive route yet to a variety of chlorofluoromethylene olefins.

The main drawback to the currently employed ylide approach has been the ease of or expense involved in the preparation of the required precursors. Dichlorofluoroacetic acid is generally prepared either from hexachloroacetone or trichloroacetic acid. Both methods require a fluorination step and generally produce more than one fluorinated product or more than one fluorinated isomer [2]. Consequently, large scale preparations are expensive and inefficient. The organomercurial reagent is also expensive to prepare and presents some hazards for large scale use. The only inexpensive and convenient precursor employed to date has been dichlorofluoromethane [3,5], but, unfortunately, olefin yields via this approach have not been very satisfactory.

These limitations of precursor availability prompted us to search for a cheap, commercially available precursor which could be employed in a simple one-step olefin synthesis. The only two presently commercially available precursors which could potentially achieve this result are dichlorofluoromethane (I) and fluorotrichloromethane (II). Previous work in this laboratory has shown that capture of chlorofluorocarbene, from reaction of base with (I), occurs with tertiary phosphines and generates the required chlorofluoromethylene ylide (III). However, yields of olefinic products via this method are low [5]. In addition, the use of polyfluorinated ketones requires pregeneration of the ylide (III), which exhibits only limited stability under these reaction conditions [3,5], cf. eq. 1.



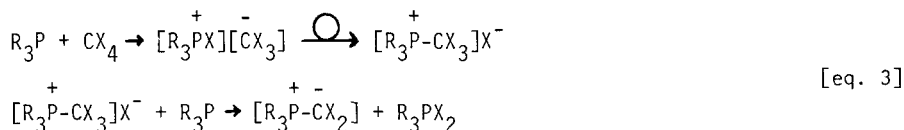
An alternative approach to (III) would involve the alkylation of (IV) by (I) to yield chlorofluoromethyltriphenylphosphonium chloride (V). Subsequent low temperature ylide generation from (V) might enhance the stability of (III) and provide a practical approach to the chlorofluoromethylene olefins, eq. 2.



Although a similar approach has met with some success in the preparation of fluoromethylene olefins [8], all attempts to alkylate (IV) with (I) in

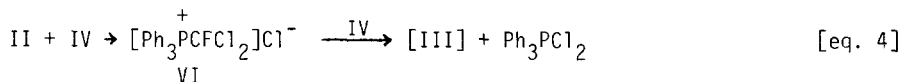
this laboratory have met with limited success. Consequently, (V) cannot be easily prepared by this method, and this route to (III) was abandoned.

Perhalomethanes, such as  $\text{CCl}_4$ ,  $\text{CBr}_4$ ,  $\text{CF}_2\text{Br}_2$ , and  $\text{CFBr}_3$ , are excellent precursors of polyhalogenated phosphonium salts [9-12]. Subsequent dehalogenation of these salts with a second mole of tertiary phosphine generates the ylidic intermediate. Although salt formation appears to be the result of a simple alkylation reaction, in many cases the mechanistic pathway actually involves positive halogen abstraction by the tertiary phosphine from the perhalomethane [9] as illustrated in eq. 3.



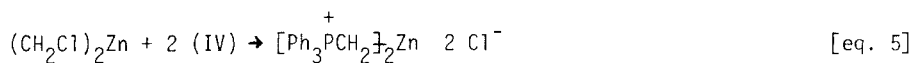
The ease of this type of indirect alkylation is dependent upon the halogen abstracted, the halophilicity of the tertiary phosphine, and the stability of the intermediate methide ion.

Since carbon tetrachloride has been reported to participate so easily in this type of alkylation [12], (II) appeared a likely candidate to undergo a similar type of alkylation reaction. Subsequent dechlorination of the dichlorofluoromethyl triphenylphosphonium chloride (VI) with a second mole of (IV) would give (III), eq. 4.

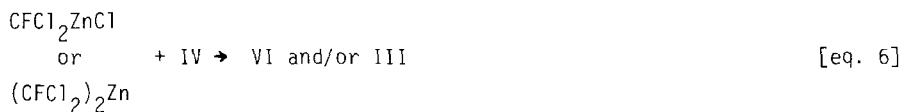
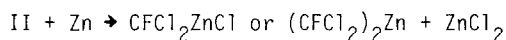


An added advantage of this approach would be that "insitu" generation of (III) could be accomplished, even in the presence of polyfluorinated ketones. Unfortunately, all attempts to prepare (VI) via this type of indirect alkylation again met with limited success. At low temperatures (<65°C) alkylation was totally unsuccessful. At higher temperatures under pressure, a complex mixture of products was obtained. Again, all simple, straightforward approaches to obtain the ylide precursor were unsuccessful.

Several recent literature reports, however, renewed our interest in this project and suggested an alternative indirect approach to resolve this precursor problem. Wittig and Schwarzenbach [13] have reported that bis-(chloromethyl)zinc reacted with (IV) to give a phosphonium salt, eq.5.



More recently, Posta and Paleta [14] have reported that (II) reacts with zinc dust to give (I) - presumably via an organozinc intermediate. Consequently, we rationalized that potentially the reaction of the fluorinated organozinc intermediate from (II) and zinc might react with (IV) to produce (VI) and/or (III) [15], eq. 6.



The results of this organometallic approach are summarized below.

## RESULTS AND DISCUSSION

The reaction of (II), (IV), and trifluoroacetophenone (VII) in dimethylformamide (DMF) at 60°C for 48 hours gave only 5%  $\text{CF}_3\text{C(Ph)=CFC1}$  (VIII). Under similar conditions, (II), zinc dust, and (VII) gave 2% (VIII). However, when (II), (IV), zinc dust, and (VII) were reacted under similar conditions, a 70% yield of (VIII) was obtained. More reactive tertiary phosphines offer no advantages over (IV) under these conditions. Tri-n-butylphosphine consumed (VII), and others have reported similar reactions of (VII) and other activated ketones with tris-(dimethylamino)-phosphine [16].

Although no extensive work was carried out to optimize reaction conditions, the extent of olefination of (VII) was examined in dimethylformamide (DMF), tetrahydrofuran (THF), and triglyme (TG). Attempts to activate the zinc dust were also made. These results are summarized in Table I.

The results reported in Table I indicate that the more polar solvent, DMF, obviously leads to the best yield of olefin (VIII), and that zinc dust itself is most efficient in the resulting olefination of (VII) [17]. Thus, in order to evaluate the generality of this approach, similar reactions were carried out under these conditions with a representative

TABLE I

Preparation of  $\text{CF}_3\text{C}(\text{Ph})=\text{CFC1}$ , Metal and Solvent Survey
$$\begin{array}{ccccccc} \text{CFC1}_3 & + & \text{Ph}_3\text{P} & + & \text{CF}_3\text{COPh} & + & \text{Metal} & \xrightarrow[60^\circ]{\text{Solvent}} & \text{CF}_3\text{C}(\text{Ph})=\text{CFC1} \\ \text{II} & & \text{IV} & & \text{VII} & & & & \text{VIII} \end{array}$$


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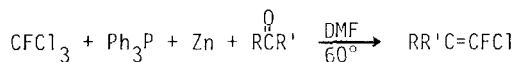
Metal	Solvent	% Yield, VIII <sup>a</sup>	Rx. Time (hrs) <sup>b,c</sup>
Zn	DMF	70	48
Zn	DMF	71	24
Zn	DMF	73	48 <sup>d</sup>
Zn	THF	trace	48
Zn	TG	3	21
Zn(Cu)	DMF	48	36
Zn(Cu)	THF	13	72
Zn(Cu)	TG	11	54
Zn(Hg)	DMF	53	24
Zn(Hg)	THF	2	48
Zn(Hg)	TG	7	90

<sup>a</sup>Glpc yield based on (VII). <sup>b</sup>Time when maximum olefin yield was initially realized in the DMF reactions. <sup>c</sup>Time of termination for the reactions in THF and TG. <sup>d</sup>This reaction was carried out in the presence of an equimolar amount of tetramethylethylene.

aromatic aldehyde, aliphatic aldehyde, non-activated ketone, and cyclic ketone. The results of this survey are summarized in Table II.

The extent of olefination observed via this approach parallels that observed by both Ando [4] and Krutzsch [5]. Aromatic aldehydes and activated ketones exhibit the highest reactivity, while aliphatic aldehydes show somewhat reduced reactivity. Unactivated ketones, as expected, give only low yields of olefin products, consistent with the earlier reports [4,5] that the ease of olefination is directly dependent upon the electrophilicity of the carbonyl group. It can easily be predicted from Ando's competition studies [4] and the work of Krutzsch [5] that electron-withdrawing substituents on the aromatic ring of the

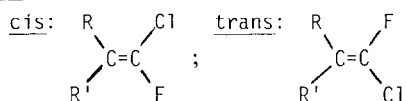
Table II  
Carbonyl Olefination Survey



R	R'	% Yield, Olefin <sup>a</sup>	Rx. Time (hrs) <sup>b</sup>	Cis/Trans Ratio <sup>c</sup>
Ph	CF <sub>3</sub>	71	24	53:47
Ph	H	64	115	53:47
n-C <sub>6</sub> H <sub>13</sub>	H	49	89	41:59 <sup>d</sup>
Ph	H	15	96	43:57
—(CH <sub>2</sub> ) <sub>4</sub> —	—	4	208	—

<sup>a</sup>GlpC yield based on the carbonyl compound. All olefinic products were unambiguously identified by comparison of IR, <sup>1</sup>H NMR, and <sup>19</sup>F NMR spectra with authentic samples. <sup>b</sup>Time when maximum olefin yield is obtained.

<sup>c</sup>Isomer ratio was determined via glpc.,



<sup>d</sup>Isomer ratio was determined via <sup>1</sup>H NMR.

aldehyde or activated ketone will lead to higher yields of olefins. Likewise, other perfluoroalkyl-containing ketones would be expected to exhibit high reactivity, analogous to (VII). Consequently, obvious extensions of this approach to olefination can be easily predicted from these earlier reports.

#### MECHANISM

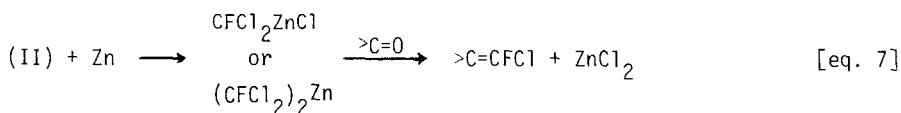
Although no detailed mechanistic study has been carried out on this reaction, several possible mechanistic pathways can be reasonably rationalized to account for the olefination reaction. The most reasonable pathways are discussed below:

### I. Phosphonium Salt Formation Followed by Zinc Dehalogenation:

The primary function of the zinc or zinc couples in these reactions might be to serve as dehalogenation agents of (VI), which could arise from reaction of (IV) and (II). However, when (II) was reacted with (IV) for 40 hours in DMF at 60°, most of (II) remained and a small amount of (I) was observed by  $^{19}\text{F}$  NMR. No (VI) was detected. Consequently, this mechanistic scheme was not considered operative here.

### II. Organozinc Formation With Subsequent Carbonyl Olefination:

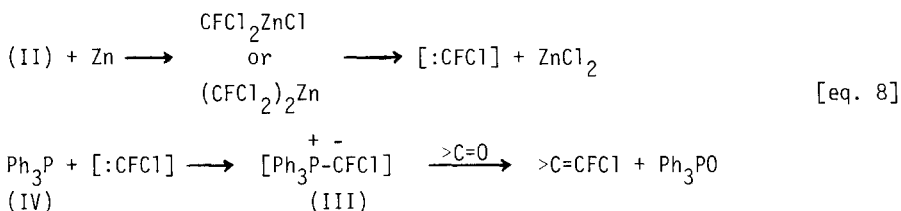
Since Hashimoto and co-workers [18,19] have recently demonstrated that zinc-polyhalomethane complexes can convert aldehydes directly to olefins, it might be reasonable that a similar scheme could account for the description of our observations, eq. 7.



However, when (II), zinc dust and (VII) were reacted for 48 hours in DMF at 60°C, only 2% (VIII) and 7% (I) were detected. Thus, the Hashimoto scheme cannot account for any significant amount of olefinic product in these reactions.

### III. Organozinc Formation Followed by Chlorofluorocarbene Formation:

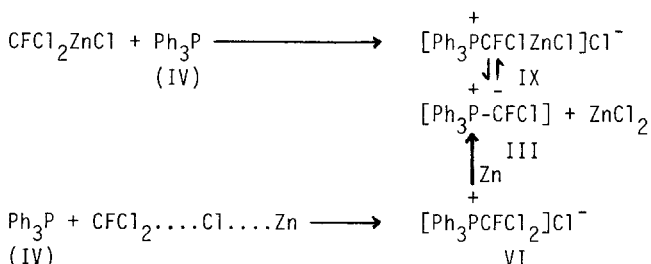
Phosphines are known to be effective trapping agents for carbenes [3-5]. Chlorofluorocarbene could potentially be formed by decomposition or extrusion from an organozinc reagent. Consequently, ylide formation could result from the trapping of the carbene by (IV) with a resultant Wittig reaction to produce the observed chlorofluoromethylene olefins,



eq. 8. However, when (II), zinc dust, and tetramethylethylene (TME) were reacted for 74-91 hours in DMF at 60°C,  $^{19}\text{F}$  NMR revealed no cyclopropane formation. In addition, when (II), zinc dust, (IV), (VII), and TME were reacted in DMF at 60°C for 48 hours, no effect was observed on the yield of (VIII) (cf. Table I). Also, no cyclopropane was detected by  $^{19}\text{F}$  NMR. Since (IV) and TME have been previously shown to be competitive for chlorofluorocarbene [5], the absence of cyclopropane and the absence of any effect on the extent of olefination seem to preclude the intervention of chlorofluorocarbene in these reactions.

#### IV. Zinc Assisted Formation of An Intermediate Ylide Precursor:

Since the presence of both zinc and tertiary phosphine are required for the realization of good chlorofluoromethylene olefin yields, the most reasonable mechanistic scheme to rationalize this reaction is to consider the formation of (VI) or an organozinc analog of (VI), such as (IX), which is formed either by reaction of (IV) with an organozinc intermediate or via polarization of (II) by zinc which facilitates alkylation by (IV).



Further dehalogenation of (VI) would produce ylide (III). Dissociation of IX would also yield (III). Previous work with mercuric salt complexes of ylides has shown spontaneous dissociation in polar solvents to give free ylide [20]. Thus, if (IX) is formed, it would not be surprising that it would easily dissociate to give (III) [21]. The present data cannot distinguish between intermediate formation of (VI) or (IX), however, the stereochemistry of the olefinic products points to (III) as the olefinating intermediate. The cis:trans ratio shown in Table II are identical, within experimental error, to those previously observed in this laboratory from two other independent approaches to the generation of (III) [3,5]. Thus, if (IX) is formed, it must dissociate to give (III).



## CONCLUSION

In DMF, the synergistic effect of zinc dust and triphenylphosphine on fluorotrichloromethane in the presence of aldehydes and activated ketones offers an inexpensive, facile, one-step route to chlorofluoromethylene olefins.

## EXPERIMENTAL:

### Solvents and Reagents:

Since these reactions were found to be extremely moisture sensitive, all solvents and reagents were scrupulously dried before use. DMF (MCB) was distilled from BaO at reduced pressure. THF (MCB) and TG (Ansul) were predried by stirring over sodium followed by distillation from a sodium benzophenone ketyl. All solvents were stored over 4 Å (Linde) molecular sieves in dark, septum-capped bottles under a dry nitrogen atmosphere. Triphenylphosphine was heated at 50°C/0.1 mm overnight and stored in a desiccator under nitrogen over P<sub>2</sub>O<sub>5</sub>. Zinc dust (98%, MCB) was used as received. Zinc-copper couple was prepared by the method of LeGoff [22]; other couples were similarly prepared by the substitution of mercuric acetate for the cupric acetate in the LeGoff procedure. All solid, dried reagents were handled in a glove bag (N<sub>2</sub> atm.) and transferred to reaction flasks via Fieser side-arm addition tubes [23]. The carbonyl compounds were purified by standard literature procedures [24]. Tetramethylethylene (Aldrich, 99%) was stored under nitrogen and used without further purification.

### Analytical Instrumentation:

Glpc analyses were carried out on a Hewlett-Packard Model 5750B Dual Column Gas Chromatograph equipped with thermal conductivity detectors with helium serving as carrier gas. The columns used were 10 ft x 1/4 in. O.D. stainless steel columns packed with 15% Carbowax (w/w) on acid-washed 100-200 mesh Chromosorb P (Column A) or 20% Fluorosilicone (FS-1265, w/w) on 80-100 mesh Chromosorb P (Column B). Quantitative glpc analyses were performed by the use of integrated peak areas (Disc<sup>®</sup> integrator) relative to toluene or mesitylene as internal standards, employing corrections for differences in thermal conductivity. <sup>19</sup>F NMR spectra were recorded on a

Varian HA-100 spectrometer operating at 94.075 MHz, with chemical shifts reported in  $\delta^*$  values upfield from the internal reference,  $\text{CFCl}_3$ . Quantitative NMR analyses were determined from signal areas relative to internal  $\text{C}_6\text{H}_5\text{COCF}_3$  (VII) or  $\text{C}_6\text{H}_5\text{CF}_3$ .

#### Reaction Apparatus and Procedure:

All glassware was dried at  $120^\circ$  overnight and then assembled while hot during a nitrogen purge. The standard reaction apparatus consisted of a two-necked round bottom flask equipped with a septum port, Teflon<sup>®</sup>-coated magnetic stir bar and an Allihn condenser, which was connected via a glass tee to a bubbler and a source of dry nitrogen. Solvents were added via predried syringe, followed by triphenylphosphine (IV) and zinc dust via solid addition tubes. The carbonyl component was then added via syringe, followed by syringe (cooled) addition of fluorotrichloromethane (II).

#### Preparation of Chlorofluoromethylene Olefins:

All survey reactions were carried out with an excess of (II), (IV), and zinc or zinc couple, relative to the carbonyl compound. Olefin yields are based on the carbonyl component. Product olefins were unambiguously identified by comparison of their spectroscopic properties relative to authentic samples.

##### (1) Carbonyl Survey

###### (a) Benzaldehyde

The following procedure is representative. Treatment of benzaldehyde (Fisher) (1.09 g, 10.3 mmol) with (IV) (3.10 g, 11.8 mmol), zinc dust (3.44 g, 52.6 mg-atoms), and (II) (1.5 cc, 2.45 g, 17.8 mmol) in 50 ml of DMF for 115 hours at  $60^\circ\text{C}$  gave (via glpc analysis on Column B) a 64% yield (6.64 mmol) of cis- and trans- $\beta$ -chloro- $\beta$ -fluorostyrene in an isomer ratio of 53:47.

##### (2) Solvent and Metal Couple Survey

###### (a) Trifluoroacetophenone (VII):

The following procedure is representative. Reaction of (VII) (1.78 g, 10.3 mmol), (IV) (3.36 g, 12.8 mmol), zinc-copper couple (2.80 g, 37.1 mg-atoms), and (II) (1.1 cc, 1.80 g, 13.1 mmol) in 50 ml

THF was carried out for 72 hours at 60°C. Glpc analysis (Column A) showed a 13% (1.34 mmoles) yield of cis- and trans-1-chloro-2-phenyltetrafluoropropene (VIII) in a 53:47 cis:trans isomer ratio.

### Control Experiments:

#### (a) Triphenylphosphine (IV) and Fluorotrichloromethane (II):

Triphenylphosphine (IV) (8.18 g, 31.2 mmoles) was reacted with fluorotrichloromethane (II) (1.8 cc, 3.01 g, 21.9 mmoles) for 40 hours in DMF at 60°C. Glpc analysis (Column B) after 40 hours showed 80% (17.6 mmole) (II).  $^{19}\text{F}$  NMR analysis showed no (VI) and small amounts of (I), at  $\delta^* 80.4$  ppm.,  $J_{\text{H},\text{F}} = 57$  Hz.

#### (b) Triphenylphosphine (IV), Fluorotrichloromethane (II) and Trifluoroacetophenone (VII):

(IV) (3.14 g, 12.0 mmoles), (II) (1.5 cc, 2.45 g, 17.8 mmoles) and (VII) (1.05 g, 6.0 mmoles) were reacted for 48 hours in DMF at 60°C. Glpc analysis (Column A) indicated 5% (VIII) and 70% (4.27 mmole) (VII) [25].

#### (c) Zinc Dust, Fluorotrichloromethane (II), and Trifluoroacetophenone (VII):

Zinc dust (1.57 g, 24.0 mg-atoms), (II) (2.0 cc, 3.26 g, 23.7 mmoles) and (VII) (1.04 g, 6.0 mmoles) were reacted for 48 hours in DMF at 60°C. Glpc analysis (Column A) showed 2% (VIII) and 50% (3.0 mmole) (VII) [25].  $^{19}\text{F}$  NMR analysis also revealed 9% (I).

#### (d) Zinc Dust, Fluorotrichloromethane (II), and Tetramethylethylene (TME):

Zinc dust (3.12 g, 47.8 mg-atoms), (II) (1.5 cc, 2.45 g, 17.8 mmoles) and TME (1.91 g, 22.7 moles) were reacted for 72 hours in DMF at 60°C. Glpc analysis (Column B) showed 83% (II) (14.8 mmole) and 88% TME (20.0 mmole). No cyclopropane formation ( $\delta^* 146$  ppm) [26] could be detected by  $^{19}\text{F}$  NMR analysis.

#### (e) Competition Study: Triphenylphosphine (IV) and TME:

Triphenylphosphine (IV) (3.14 g, 12.0 mmoles), zinc dust (2.35 g, 36.0 mg-atoms), (II) (2.0 cc, 3.26 g, 23.7 mmoles), (VII) (1.09 g, 6.3 mmoles) and TME (0.53 g, 6.3 mmoles) were reacted for 48 hours in DMF at 60°C. Glpc analysis (Column A) showed 73% (VIII) (4.59 mmole) and 6% (VII).  $^{19}\text{F}$  NMR analysis showed small amounts of (I) and  $\text{Ph}_3\text{PF}_2$  but no chlorofluorocyclopropane.

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