Journal of Fluorine Chemistry, 9 (1977) 25–44

Received: July 5, 1976

PREPARATION OF GEM-DIFLUOROCYCLOPROPANES VIA DECOMPOSITION OF METHYL CHLORODIFLUOROACETATE BY ALKALI METAL HALIDES

G. A. WHEATON and D. J. BURTON

Department of Chemistry, University of Iowa, Iowa City, Iowa 52242 (U.S.A.)

SUMMARY

The facile decomposition of methyl chlorodifluoroacetate, induced by either lithium chloride/hexamethylphosphoric triamide complex or potassium fluoride/18-Crown-6 complex, has been carried out in the presence of a variety of olefinic substrates to yield the corresponding gem-difluorocyclopropanes. The ester decomposition has been determined to yield "free" difluorocarbene via a three-step process involving an intermediate chlorodifluoromethide ion.

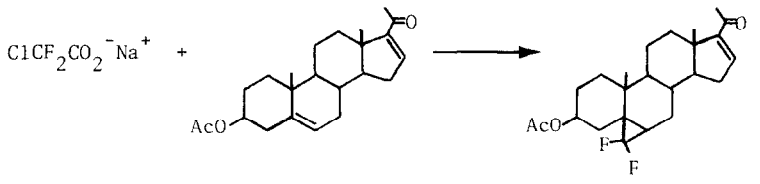
INTRODUCTION

Interest in the introduction of fluorine and fluorinated groups into organic molecules has increased greatly in recent years. A large part of this interest has developed in the area of fluorinated carbenes, particularly difluorocarbene. This intense interest has led to the development of a broad spectrum of methods for the generation of difluorocarbene which have been extensively reviewed [1]. The great majority of difluorocarbene precursors which have been developed suffer from serious limitations insofar as their general synthetic applicability is concerned. In many cases the conditions required for carbene generation are severe, requiring either the presence of strong bases, such as hydroxide or alkoxides, or very high temperatures. Difluorocarbene precursors such as difluorodiazirine [2] or the organometallic reagents Me_3SnCF_3 [3] and $PhHgCF_3$ [4], while yielding highly reactive carbenes under mild, neutral conditions, either require difficult multistep syntheses or are prohibitively expensive for large scale use. Recently, difluorocarbene generation by fluoride ion attack

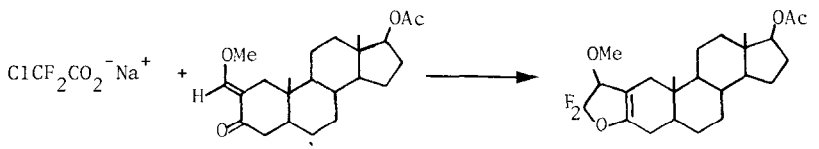
upon bromodifluoromethylphosphonium salts has been reported [5]. This method of carbene generation is advantageous in that it occurs under mild, non-basic conditions, and the precursor is easily and cheaply prepared.

The most widely used sources of difluorocarbene, and perhaps the most generally applicable, however, have been the alkali metal chlorodifluoroacetates. Decarboxylation of sodium chlorodifluoroacetate in the presence of olefins results in the formation of the corresponding gem-difluorocyclopropanes. For example, decarboxylation in the presence of cyclohexene resulted in an 11% yield of 7,7-difluoronorcarane [6]. The use of a large

excess of the acetate salt resulted in an increase in yield to 65%, underscoring one major disadvantage of the acetate salt method of carbene generation. Sodium chlorodifluoroacetate has been used extensively as a source of difluorocarbene for reactions with a variety of steroidal compounds. Decarboxylation of sodium chlorodifluoroacetate in the presence of unsaturated



steroids and transoid enones resulted in formation of the gem-difluorocyclopropane derivatives [7]. The decarboxylation of the sodium salt in the



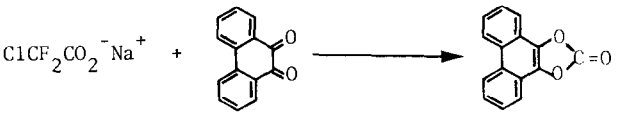
presence of a cisoid enone, however, resulted in the formation of the 1,4-adduct [8] while decarboxylation in the presence of acetylenic steroids resulted in the corresponding gem-difluorocyclopropenyl derivatives [9]. Sodium chlorodifluoroacetate has also been used for various homologation reactions [10].

Decarboxylation of alkali metal chlorodifluoroacetates in the presence of tertiary phosphines and carbonyl compounds resulted in the formation of the corresponding 1,1-difluoromethylene olefins [11]. Utilizing triphenylphosphine, aldehydes and fluorinated ketones could be olefinated.

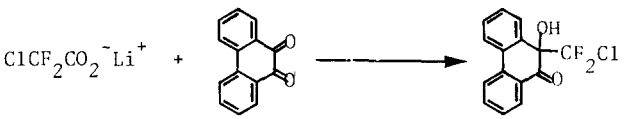
$$ClCF_2CO_2^-M^+ + R_3P \longrightarrow \left[R_3\overset{+}{P}-\overset{-}{C}F_2\right] \xrightarrow{R^1R^2C=O} R^1R^2C=CF_2$$

While these olefinations presumably occurred via an intermediate difluoromethylene ylide, a study by Burton and Herkes [12] suggested that the formation of these ylides did not involve the trapping of difluorocarbene by the phosphines.

Decarboxylation of sodium chlorodifluoroacetate in the presence of 9,10-phenanthrene quinone resulted in the isolation of 9,10-phenanthrene diyl-carbonate while the decarboxylation of the lithium salt in the presence of



the same quinone resulted in isolation of an α-ketodifluoromethyl alcohol [13]. The different products arising from use of the two salts were



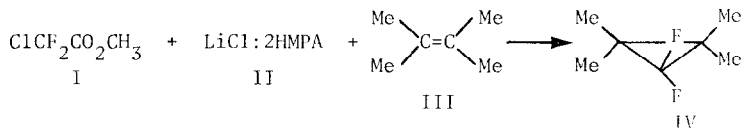
ascribed by the authors to the greater solubility of lithium chloride, relative to sodium chloride, in the solvent used.

The widespread use of chlorodifluoroacetate salts stems from the fact that carbene formation occurs under relatively mild conditions, decarboxylation occurring at a convenient rate at temperatures of ca. 100-130°C. In addition, this method of carbene generation occurs in neutral reaction media making it suitable for use with base sensitive substrates. As previously mentioned, however, the use of large excesses of these acetate salts are required to ensure good yields. Another major disadvantage to their use is the hygroscopic nature of these salts. This hygroscopicity necessitates exhaustive drying of the salts during their preparation and requires that they be handled only under completely anhydrous conditions. Another disadvantage of the use of the alkali metal chlorodifluoroacetates is that the difluorocarbene generated upon decarboxylation has been observed to be less efficiently trapped than the difluorocarbene derived from either difluorodiazirine [2] or organometallic reagents [3,4].

In a previous report [14] we described the decomposition of methyl chlorodifluoroacetate by lithium chloride/hexamethylphosphoric triamide complex (LiCl:2HMPA) as a method of difluorocarbene generation. We now wish to report in greater detail the decomposition of methyl chlorodifluoroacetate by complexed alkali metal halides as a source of difluorocarbene.

RESULTS AND DISCUSSION

Treatment of methyl chlorodifluoroacetate (I) with the lithium chloride/hexamethylphosphoric triamide complex (II) in ethereal aprotic solvents at temperatures of 75° to 80°C results in the formation of methyl chloride and carbon dioxide. When the ester decomposition occurs in the presence of 2,3-dimethyl-2-butene (III) difluorocarbene may be intercepted by the olefin to yield 1,1-difluoro-2,2,3,3-tetramethylcyclopropane (IV). When the decomposition of (I) by (II) was carried out in triglyme, for example, in the presence



of an equimolar amount of olefin (III), a 90% yield of the cyclopropane (IV) was achieved.

Scope and limitations

The ester also undergoes decomposition in the presence of potassium fluoride/18-Crown-6 complex (V) under mild conditions. The yields of cyclopropanes which are obtained upon decomposition of (I) by (V) in the presence of olefins are essentially the same as the yields obtained by decomposition of (I) by (II) in the presence of olefins. The scope and limitations of these ester decomposition reactions as sources of difluorocarbene have been investigated utilizing a series of representative olefins. The results of these cyclopropanation reactions are presented in Table I.

For the generation of difluorocarbene by decomposition of (I) triglyme is the preferred solvent. The yields of cyclopropanes obtained by this method are observed to be greatest in triglyme for reasons which are at present not understood [15]. In addition, the use of triglyme as the solvent results in the easy isolation of these volatile cyclopropanes by flash distillation of the reaction mixtures. The cyclopropanes may then be

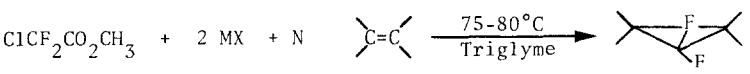
separated from the unreacted olefins by either fractional distillation or by preparative glpc. The product cyclopropanes were identified by either their ^{19}F NMR spectra or by their mass spectra or both. In addition, when authentic samples were available, the cyclopropanes were further identified by comparison of their glpc retention times and ^{19}F NMR spectra with authentic samples.

As is evident from Table I the yields of cyclopropanes obtained from both the tetrasubstituted and trisubstituted ethylenes are excellent. As the amount of substitution about the double bond decreases the yields of cyclopropanes decrease accordingly. This trend is consistent with a highly electrophilic carbene species such as difluorocarbene. The less electron-rich 1,1- and 1,2-disubstituted ethylenes give only modest yields of cyclopropanes at best. Indeed, the isomeric 2-butenes gave extremely low yields of the corresponding cyclopropanes even when large excesses of the olefins were used under forcing conditions. Similarly, cyclohexene was converted to 7,7-difluorobicyclo[4.1.0]heptane in only a 30% yield when a three-fold excess of the olefin was used, while the use of an equimolar amount of cyclohexene gave a poor yield of only 15% of the cyclopropane derivative. The two 1,1-disubstituted olefins, 2-ethyl-1-butene and methylenecyclohexane, gave very nearly the same yields, 40% and 34% respectively. The 40% yield of gem-difluoro-2,2-diethylcyclopropane was obtained utilizing an olefin to ester ratio of 2.0 while the 34% yield of 1,1-difluorospiro[2.5]octane was obtained using an olefin to ester ratio of 0.5 suggesting that the use of either excess olefin or excess ester is equally suited to yield maximization. However, olefins which have boiling points of ca. 55°C or lower must be used in large excesses to ensure a sufficient concentration of olefin is maintained in solution. In the cases of unreactive olefins, which remain in solution at the temperatures required for ester decomposition, the ester may be used in excess in order to ensure reasonable yields as indicated by the reaction utilizing methylenecyclohexane as the olefin substrate. This alternative to the use of large excesses of olefin is welcome in those cases in which the olefin is expensive or difficult to prepare.

The difluorocyclopropanation reactions utilizing E-2-methoxy-2-butene and the cis- and trans-2-butenes resulted in stereospecific addition of the difluoromethylene group across the carbon-carbon double bond. In each of the cases only one cyclopropane isomer was observed as the product of the reaction. None of the other cyclopropane isomer was observed in any of these cases. The cis- and trans-1,1-difluoro-2,3-dimethylcyclopropanes were easily identified by comparison of their ^{19}F NMR spectra with those of authentic samples. The cis-isomer has a spectrum consisting of two signals,

TABLE I

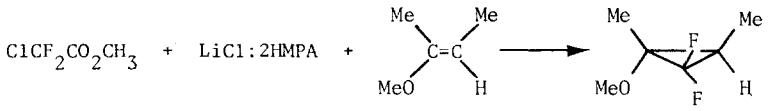
Preparation of 1,1-difluorocyclopropanes



MX	Olefin	N	Yield[a] of Cyclopropane (%)
LiCl:2HMPA	2,3-dimethyl-2-butene	1.0	90
"	"	4.0	ca. 100
"	2-methyl-2-butene	1.0	45
"	"	4.0	93
"	E-2-methoxy-2-butene	1.0	70[b]
"	2-ethyl-1-butene	2.0	40
"	methylenecyclohexene	0.5	34[c]
"	cyclohexene	1.0	15
"	"	4.0	30
"	2,5-dihydrofuran	1.0	trace
"	cis-2-butene[d]	6.0	5[b]
"	trans-2-butene[d]	6.0	4[b]
(K)F[e]	2,3-dimethyl-2-butene	1.0	85
"	2-methyl-2-butene	1.0	38
"	cyclohexene	1.0	15

[a]Glpc yield based on ester. [b]Stereospecific addition of carbene to olefin occurred. [c]Glpc yield based on olefin. [d]Reactions were carried out in an autoclave at an external temperature of 120°C. [e]Potassium fluoride/18-Crown-6 complex (2:1).

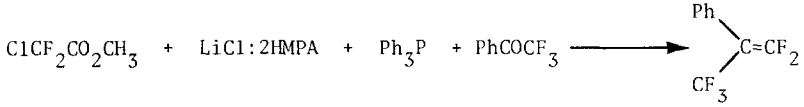
while that of the trans-isomer consists of only one signal. In the case of the product from the ester decomposition in the presence of E-2-methoxy-2-butene, however, the stereochemical assignment of the structure was assumed on the basis of the formation of a single product isomer. The ^{19}F NMR spectrum and the mass spectrum confirm the structure of the cyclopropane, but the isomeric assignment was based solely on the structure of the starting olefin, since total inversion of the stereochemistry about the carbon-carbon



double bond seems highly unlikely. The stereospecificity of the cyclopropanation reaction is suggestive of a singlet carbene species as the cyclopropanating intermediate, although carbenoids also result in stereospecific cyclopropanation.[16]

As indicated in Table I decomposition of ester (I) by either LiCl:2HMPA (II) or KF/18-Crown-6 (V) in the presence of olefins resulted in essentially identical yields of the corresponding gem-difluorocyclopropanes. For example, decomposition of (I) in the presence of an equimolar amount of 2,3-dimethyl-2-butene (III) by (II) and (V) resulted in yields of 1,1-difluorotetramethylcyclopropane (IV) of 90% and 85% respectively. Ester decomposition by (II) and (V) in the presence of equimolar amounts of 2-methyl-2-butene or cyclohexene again resulted in essentially identical yields of cyclopropanes. Thus, the use of either the lithium chloride complex (II) or the potassium fluoride complex (V) to effect decomposition of ester (I) in the presence of olefins results in essentially equal cyclopropanating efficiency. Due, however, to the difficulty associated with the preparation of the Crown ether, the use of the lithium chloride/HMPA complex (II) for the ester decomposition is the method of choice, especially when the cyclopropanation reaction is to be employed on a relatively large scale.

Treatment of ester (I) with complex (II) in triglyme at 80° to 85°C in the presence of triphenylphosphine and α,α,α-trifluoroacetophenone resulted in an 80% yield of 2-phenylpentafluoropropene (VI) after 22 hours. The olefin (VI) was identified by comparison of its glpc retention time



I II VI

and ^{19}F NMR spectrum with those of an authentic sample. Decarboxylation of sodium chlorodifluoroacetate in diglyme at 100°C in the presence of triphenylphosphine and trifluoroacetophenone has been reported to give only a 68% yield of olefin (VI)[12].

As suggested by Burton and Herkes [12], this olefination reaction may indeed not involve difluorocarbene generation and subsequent trapping by triphenylphosphine. In this case, the formation of the difluoromethylene ylide may involve initial reaction of the ester (I) with triphenylphosphine. Un-

like the observations of Burton and Herkes, however, the addition of triphenylphosphine did not significantly accelerate the rate of ester decomposition. Further work on this aspect of the ester:LiCl:HMPA reaction will be reported in a future publication.

Mechanism

Treatment of ester (I) with complex (II) resulted in initial displacement of chlorodifluoroacetate ion from the methyl carbon by chloride ion with subsequent formation of methyl chloride. Treatment of (I) with LiCl:HMPA in THF at 40°C resulted in a 92% yield of methyl chloride [17]. ^{19}F NMR analysis of the reaction mixture using $C_6H_5CF_3$ as an internal standard indicated essentially quantitative formation of a lithium chlorodifluoroacetate/HMPA complex [18]. An analogous complexed acetate salt should be formed in this system, which would undergo decarboxylation upon heating at 80° to generate an intermediate chlorodifluoromethide ion which may be intercepted either by protonation or by reaction with polyfluoromethyl ketones [17]. When ester (I) was treated with complex (II) in

$$ClCF_2CO_2CH_3 + LiCl{:}2HMPA \longrightarrow CH_3Cl + ClCF_2CO_2Li{:}2HMPA$$

$$ClCF_2CO_2Li{:}2HMPA \longrightarrow CO_2 + [ClCF_2^-][Li{:}2HMPA^+] \xrightarrow{H^+} HCF_2Cl$$

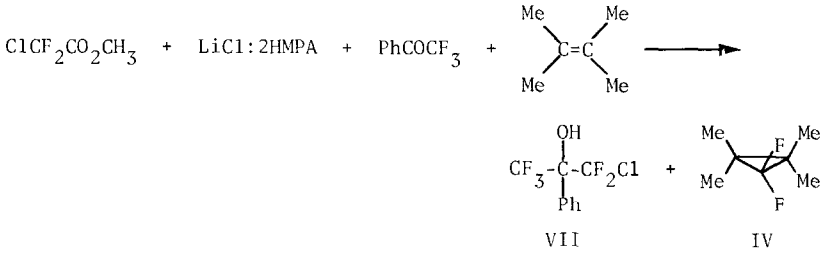
$$[ClCF_2^-] \xrightarrow[2)\ H^+]{1)\ RCOCF_3} CF_3\text{-}C(OH)(R)\text{-}CF_2Cl$$

triglyme in the presence of trifluoroacetophenone a 56% yield of 1-chloro-2-phenylpentafluoro-2-propanol (VII) was isolated upon steam distillation. We have demonstrated in a previous report [17] that the formation of the alcohol (VII) occurs *via* addition of the chlorodifluoromethide ion to the carbonyl carbon rather than by addition of difluorocarbene across the carbon-oxygen double bond to form an oxirane which may then undergo ring-opening to yield the alcohol.

$$ClCF_2CO_2CH_3 + LiCl{:}2HMPA + PhCOCF_3 \longrightarrow CF_3\text{-}C(OH)(Ph)\text{-}CF_2Cl$$

VII

Decomposition of (I) by (II) in the presence of equimolar amounts of both trifluoroacetophenone which is a good carbanion trap and 2,3-dimethyl-2-butene which has been demonstrated to be an excellent trap for difluorocarbene resulted in the formation of alcohol (VII) and cyclopropane (IV) upon acidification of the reaction mixture using dilute HCl. ^{19}F NMR analysis of the acidified reaction mixture showed that (VII) was formed in 48% yield while the cyclopropane was formed in a 30% yield. The results of this



VII IV

competition indicate that the ketone trapped most of the initially formed chlorodifluoromethide ion, while the olefin trapped the difluorocarbene which was formed by decomposition of the untrapped carbanion. The yield of the alcohol obtained in this competition reaction was essentially unchanged from that obtained in the absence of the olefin indicating that indeed the alcohol does not arise by carbene addition to the ketone followed by ring-opening of the oxirane. Conversely, the 30% yield of cyclopropane (IV) obtained in the competition with trifluoroacetophenone is greatly decreased from the 90% yield which was obtained in the absence of the ketone. This severe suppression of the cyclopropanation reaction indicates that the ketone is scavanging either the cyclopropanating species or the intermediate from which the cyclopropanating species is derived.

The intermediate responsible for difluoromethylene transfer in these cyclopropanation reactions may be either a lithium carbenoid or free difluorocarbene. Decarboxylation of the complexed acetate salt might result in the formation of a free chlorodifluoromethide ion which, if not trapped, would collapse to difluorocarbene by loss of chloride ion. Alternatively, decarboxylation of the acetate salt could yield complexed chlorodifluoromethyllithium, a carbenoid [19]. The carbenoid could react preferentially as a typical organolithium reagent in the presence of ketones such as trifluoroacetophenone which are very susceptible to nucleophilic attack, while in the presence of electron-rich olefins such as 2,3-dimethyl-2-butene (III) the carbenoid could transfer the difluoromethylene group to the double bond.

Both of these possibiliities are consistent with the observed cyclopropane yields and with the results of the competition reaction between trifluoroacetophenone and olefin (III).

Moss [20] has recently proposed that carbenic species which have a carbene selectivity index (m_{CXY}) greater than 0.91 are free carbenes, even when generated in the presence of K^+Halide or K^+OR^-, and not carbenoids. Thus, difluorocarbene (m_{CXY}=1.48) [21] may be a free carbene and not a carbenoid when generated in the presence of potassium halides or alkoxides. However, no correlation of carbene selectivity to the nature of carbene species in the presence of lithium halides has been reported. Thus, it is possible that even difluorocarbene may exist as a carbenoid species in the presence of the lithium chloride/HMPA complex (II).

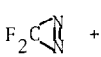
Moss [22] has suggested that potassium alkoxide/18-Crown-6 complex-induced α-eliminations should result in the generation of free carbenes. By analogy, the cyclopropanating species generated by the decomposition of ester (I) induced by the potassium fluoride/18-Crown-6 complex (V) should be free difluorocarbene also. A comparison of the relative reactivities of 2,3-dimethyl-2-butene and 2-methyl-2-butene toward the free difluorocarbene generated by decomposition of ester (I) by the KF/18-Crown-6 complex to the relative reactivities of the same olefin pair toward the cyclopropanating species generated by the decomposition of (I) by the LiCl:2HMPA complex should give some insight into the nature of the latter cyclopropanating species. If the two cyclopropanating species, obtained by decomposition of methyl chlorodifluoroacetate by (II) and (V) respectively, result in significantly different relative reactivity ratios for the olefin pair then the carbene species generated by the LiCl:2HMPA-induced decomposition of the ester (I) is most likely a lithium carbenoid; that is, difluorocarbene either complexed with or very closely associated with the lithium chloride/HMPA complex (II). If a free carbene is also generated upon ester decomposition by (II), then the relative olefin reactivities should be the same or very nearly so.

Methyl chlorodifluoroacetate (I) was treated with potassium fluoride/18-Crown-6 complex (V) in triglyme at 75° to 80°C in the presence of a four-fold excess of both 2,3-dimethyl-2-butene and 2-methyl-2-butene. Ester (I) was similarly treated with the lithium chloride/2HMPA complex (II) in triglyme at 75° to 80°C in the presence of a four-fold excess of both olefins. After heating for two hours the reaction mixtures were analyzed by glpc to determine the ratio of cyclopropanes which were formed. These initial product

ratios were found to have remained unchanged after 24 hours. The results of these relative reactivity determinations are reported in Table II. The reported relative reactivities [23] are the average values of three determinations and the uncertainties are average deviations from the average of these three determinations. The relative reactivity ratio of the olefin pair toward the photolytically generated free difluorocarbene, as determined by Mitsch and Rodgers [24], is included for comparison. As indicated in

TABLE II

Relative reactivities of 2,3-dimethyl-2-butene and 2-methyl-2-butene toward difluorocarbene

$:CF_2$ Source	$K_{\diagup\!=\!\diagdown}/K_{\diagup\!=\!}$
$ClCF_2CO_2CH_3$ + LiCl:2HMPA	4.27±0.03
$ClCF_2CO_2CH_3$ + (K) F[a]	4.18±0.05
 + hν[b]	3.71

[a]Potassium fluoride/18-Crown-6.

[b]Reference [24].

Table II the relative reactivities of the olefins toward the two cyclopropanating species generated upon ester decomposition by either LiCl:2HMPA or KF/18-Crown-6 are the same within experimental error. We conclude from these results that in each case the reactive intermediate in cyclopropanation reactions is indeed free difluorocarbene. The greater selectivity exhibited by the carbene generated by the ester decomposition method relative to that generated by photolysis of difluorodiazirine is most likely a solvent effect. In the case of the diazirine phtolysis excess olefin served as the reaction solvent which should result in a relatively non-solvated carbene. In the ester decomposition method, however, the highly electrophilic difluorocarbene [21] would most likely be at least slightly solvated by triglyme. Such a solvent effect may also account for the somewhat reduced reactivity of the ester-generated carbene relative to difluorocarbene generated by some other methods [2-4].

CONCLUSIONS

Generation of difluorocarbene by the decomposition of methyl chlorodifluoroacetate by either lithium chloride/2HMPA complex or by potassium fluoride/18-Crown-6 complex in the presence of simple alkenes results in better yields than are generally obtained by the decarboxylation of alkali metal chlorodifluoroacetates. The yields of cyclopropanes are essentially the same as those obtained utilizing the fluoride ion decomposition of bromodifluoromethylphosphonium salts [5]. While relatively reactive tetra- and tri-substituted ethylenes give excellent yields of cyclopropanes, the less reactive 1,1- and 1,2-disubstituted ethylenes require the use of excess olefin to ensure reasonable yields of cyclopropanes. Although the overall yields of cyclopropanes using this method are less than those obtained from some difluorocarbene sources, the decomposition of methyl chlorodifluoroacetate by the lithium chloride/2HMPA complex offers several advantages over these other carbene precursors which we feel more than atone for the decreased reactivity of the carbene produced by this method for most applications.

Unlike precursors for the more reactive carbenes, methyl chlorodifluoroacetate may be easily prepared in large quantities, and high purity is easily attained. This carbene precursor is relatively inexpensive to prepare and use, and the ester decomposition method is readily adaptable to large scale applications. Unlike the alkali metal chlorodifluoroacetates, the ester may be conveniently stored and handled, and it has a long shelf-life. In addition, the generation of difluorocarbene by ester decomposition occurs under relatively mild, non-basic conditions.

Experimental results indicate that decomposition of methyl chlorodifluoroacetate by lithium chloride/2HMPA complex results in the initial formation of a short-lived chlorodifluoromethide ion. In the absence of efficient carbanion trapping reagents the methide ion collapses by loss of chloride to generate free difluorocarbene.

EXPERIMENTAL

All boiling points are uncorrected and were obtained during fractional distillation. ^{19}F NMR spectra were recorded on a Varian HA-100 spectrometer operating at 94.075 MHz, and the chemical shifts are reported in Ø* values upfield from an external (capillary) $CFCl_3$ reference. Quantitative analyses

were determined from signal areas relative to an internal $C_6H_5CF_3$ standard. Mass spectral samples were collected by the analytical glpc capillary technique of Burson and Kenner [25], and the spectra were recorded on a Hitachi-Perkin Elmer RMU-66 mass spectrometer operating at 70 ev. Glpc analyses were carried out on an F and M Model 720 Dual Column Chromatograph equipped with thermal conductivity detectors and using helium as a carrier gas. The column used was a 10 ft x 1/4 in o.d. copper column packed with 15% (w/w) silicon rubber SE-30 on 80-100 mesh Chromosorb P support. Quantitative glpc analyses were determined from peak areas relative to toluene as an internal standard employing corrections for differences in thermal conductivities. Triglyme (Ansul Chemical Co.) was distilled from sodium benzophenone ketyl at reduced pressure after pre-drying over anhydrous calcium sulfate. Hexamethylphosphoric triamide (HMPA) (Aldrich) was distilled at reduced pressure from sodium. Lithium chloride and potassium fluoride (anhydrous) (Alpha-Ventron) were dried in a vacuum oven (125°C, ca. 1 mm Hg) for 24 hours then stored in a dissicator over P_2O_5. The lithium chloride and potassium fluoride were handled under dry nitrogen in a glove bag and were transferred via a solids addition tube capped by a rubber septum. The 18-Crown-6 was prepared and purified by the literature method [26]. The olefins utilized in this study were distilled from sodium prior to use.

Methyl chlorodifluoroacetate

A solution of chlorodifluoroacetic acid (Halocarbon Chemical Co.) (130.5 g, 1.00 mole), excess absolute methanol (48.0 g, 1.50 moles), and concentrated sulfuric acid (40 ml) in a 1 liter 1-necked round bottom flask equipped with a Teflon®-coated magnetic stir bar and a reflux condensor topped by a calcium chloride drying tube was refluxed for 18 hours. The reaction mixture was cooled to room temperature then poured into ice water (600 ml), and the lower organic layer was separated, washed with 5% sodium bicarbonate solution (2 x 250 ml) and water (2 x 200 ml), dried over activated 4A molecular sieves for twelve hours, and distilled under nitrogen through a 15 cm Vigreux column to give a 69% (99.8 g, 0.69 mole) yield of methyl chlorodifluoroacetate (b.p. 77.5-78.5°C; lit. b.p. 79-81°C [27].

Preparation of cyclopropanes *via* ester decomposition by LiCl:2HMPA

(a) 1,1-difluoro-2,2,3,3-tetramethylcyclopropane

Anhydrous lithium chloride (4.23 g, 0.10 mole) was added, *via* a solids addition tube, with vigorous stirring to a solution of HMPA (35.8 g, 35.0 ml, 0.20 mole) in a 200 ml of dry triglyme in a 500 ml 2-necked flask equipped with a septum port, a Teflon® -coated magnetic stir bar, a thermometer, and a reflux condensor topped by a glass "tee" connected to a source of dry nitrogen and a mineral oil bubbler. Water from an ice-water bath was circulated through the condenser. The mixture was stirred at room temperature until the lithium chloride had gone into solution, then 2,3-dimethyl-2-butene (16.8 g, 23.8 ml, 0.20 mole) was added to the solution followed by the addition of methyl chlorodifluoroacetate (7.25 g, 5.30 ml, 0.050 mole). The solution was heated to 80°C and stirred for 24 hours. The reaction mixture was flash distilled at *ca*. 2 mm of Hg. Fractionation of the flash distillate through a 15 cm glass helices column gave an 86% (5.7 g, 0.043 mole) isolated yield of 1,1-difluoro-2,2,3,3-tetramethylcyclopropane, b.p. 90-91°C, which was 98% pure by glpc analysis. The ^{19}F NMR spectrum consisted of a multiplet at $\emptyset^*(DCCl_3)$+148.9 ppm. The mass spectrum gave a molecular ion at m/e 134. Repetition of the reaction on a 10 mmole scale using toluene as an internal glpc standard resulted in an essentially quantitative yield of 1,1-difluoro-2,2,3,3-tetramethylcyclopropane.

(b) 1,1-difluoro-2,2,3-trimethylcyclopropane

Treatment of methyl chlorodifluoroacetate (7.25 g, 5.30 ml, 0.050 mole) and 2-methyl-2-butene (14.0 g, 21.0 ml, 0.20 mole) as described above gave a 76% (4.6 g, 0.038 mole) isolated yield of 1,1-difluoro-2,2,3-trimethylcyclopropane, b.p. 69-70°C. The ^{19}F NMR spectrum consisted of two signals: $\emptyset^*(DCCl_3)$+139.0 ppm (d of m), +150.8 ppm (d of m), J(F-C-F)=150.4 Hz. The mass spectrum gave a molecular ion at m/e 120. Repetition of the reaction on a 10 mmole scale using toluene as an internal standard resulted in a 93% glpc yield of the cyclopropane.

(c) 1,1-difluoro-2-methoxy-*cis*-2,3-dimethylcyclopropane

Treatment of methyl chlorodifluoroacetate (2.90 g, 2.12 ml, 0.020 mole) and *E*-2-methoxy-2-butene (1.72 g, 0.020 mole)[28] as described above resulted in a 70% glpc yield of 1,1-difluoro-2-methoxy-*cis*-2,3-dimethylcyclopropane

relative to toluene as an internal standard. The cyclopropane was identified by both its ^{19}F NMR and mass spectra. An analytical sample was collected by preparative glpc on a 10 ft x 1/2 in column packed with 20% (w/w) silicon rubber SE-30 on 80-100 mesh Chromosorb P. The ^{19}F NMR spectrum consisted of two signals: $\emptyset^*(DCCl_3)$+143.8 ppm (d of d of m, F cis- to H); +147.5 ppm (d of m, F trans- to H); J(F, cis-H)=20.0 Hz, J(F-C-F)=159.0 Hz. The mass spectrum gave a molecular ion at m/e 136. None of the trans-isomer was observed in the reaction mixture.

(d) 1,1-difluoro-2,2-diethylcyclopropane

Treatment of methyl chlorodifluoroacetate (1.45 g, 1.06 ml, 0.010 mole) and 2-ethyl-1-butene (Pfaltz and Bauer) (1.68 g, 0.020 mole) as described above resulted in a 40% glpc yield of 1,1-difluoro-2,2-diethylcyclopropane relative to toluene as an internal standard. The ^{19}F NMR spectrum consisted of one signal: $\emptyset^*$(triglyme)+145.2 ppm (t of m), J(F, ring CH_2)=8.4 Hz. The mass spectrum gave a molecular ion at m/e 134.

(e) 1,1-difluorospiro[2.5]octane

Treatment of methyl chlorodifluoroacetate (4.35 g, 3.18 ml, 0.030 mole) and methylenecyclohexane (1.44 g, 0.015 mole)[29] as described above resulted in a 34% glpc yield of 1,1-difluorospiro[2.5]octane relative to toluene as an internal standard. The ^{19}F NMR spectrum consisted of one signal: $\emptyset^*$(triglyme)+140.1 ppm (t of m), J(F, ring CH_2)=8.5 Hz. The mass spectrum gave a molecular ion at m/e 146.

(f) 7,7-difluoronorcarane

Treatment of methyl chlorodifluoroacetate (1.45 g, 1.06 ml, 0.010 mole) and cyclohexene (Phillips) (3.29 g, 0.040 mole) as described above resulted in a 30% glpc yield of 7,7-difluoronorcarane relative to toluene as an internal standard. The ^{19}F NMR spectrum consisted of two signals: $\emptyset^*$(triglyme)+129.2 ppm (d of t, F cis- to H's); + 159.0 ppm (d, F trans- to H's); J(F, cis-H's)=14.0 Hz, J(F-C-F)=163.2 Hz. The mass spectrum gave a molecular ion at m/e 132.

(g) 6,6-difluoro-3-oxa[3.10]bicyclohexane

Treatment of methyl chlorodifluoroacetate (1.45 g, 1.06 ml, 0.010 mole) and 2,5-dihydrofuran (PCR) (0.70 g, 0.010 mole) resulted in the formation of a trace of 6,6-difluoro-3-oxa[3.1.0]bicyclohexane as detected by glpc and

^{19}F NMR analysis. The ^{19}F NMR spectrum consisted of two signals: Ø*(triglyme)+129.1 ppm (d of t of m, F cis to ring H's), +172.1 ppm (d of t, F trans to ring H's); J(F, cis-H's)=13.2 Hz, J(F, trans-H's)=2.0 Hz, J(F-C-F)=173.0 Hz. The mass spectrum gave a molecular ion at m/e 120.

(h) 1,1-difluoro-cis-2,3-dimethylcyclopropane

Lithium chloride (1.70 g, 0.040 mole), HMPA (14.3 g, 14.0 ml, 0.080 mole), methyl chlorodifluoroacetate (2.90 g, 2.12 ml, 0.020 mole), and triglyme (40 ml) were placed in a 128 ml Hastalloy autoclave in a glove bag under nitrogen. The autoclave was sealed under nitrogen then immersed in a liquid nitrogen bath. Cis-2-butene (Matheson Gas, C.P.) (6.73 g, 0.120 mole was then condensed into the autoclave which was then sealed. The autoclave was immersed in an oil bath and was heated at a bath temperature of 120°C for 24 hours. The autoclave was then cooled to 0°C in an ice-water bath and vented. The reaction mixture was analyzed by glpc to give a 5% glpc yield of 1,1-difluoro-cis-2,3-dimethylcyclopropane relative to toluene as an internal standard. The ^{19}F NMR spectrum consisted of two signals: Ø*(triglyme)+128.7 ppm (d of m, F cis- to H's); + 158.3 ppm (d of m, F trans- to H's); J(F, cis-H's)=12.0 Hz, J(F-C-F)=158.7 Hz. None of the trans- isomer was observed.

(i) 1,1-difluoro-trans-2,3-dimethylcyclopropane

Treatment of methyl chlorodifluoroacetate (2.90 g, 2.12 ml, 0.020 mole) and trans-2-butene (Matheson Gas, C.P.) (6.73 g, 0.120 mole) as described above resulted in a 4% glpc yield of 1,1-difluoro-trans-2,3-dimethylcyclopropane relative to toluene as an internal standard. The ^{19}F NMR spectrum consisted of one signal: Ø*(triglyme)+143.1 ppm (m). None of the cis-isomer was observed.

Preparation of cyclopropanes via ester decomposition by KF/18-Crown-6

(a) 1,1-difluoro-2,2,3,3-tetramethylcyclopropane

Potassium fluoride (2.91 g, 0.050 mole) was added via a solids addition tube to a solution of 18-Crown-6 (7.0 g, 0.026 mole) in triglyme (25 ml) in a 50 ml 2-necked flask equipped with a septum port, a thermometer, a Teflon® -coated magnetic stir bar, and a reflux condenser topped by a glass "tee" connected to a source of dry nitrogen and a mineral oil bubbler. Water from

an ice-water bath was circulated through the condenser. After stirring the solution for one-half hour, 2,3-dimethyl-2-butene (1.68 g, 2.38 ml, 0.020 mole) and methyl chlorodifluoroacetate (2.90 g, 2.12 ml, 0.020 mole) were added to the solution. The reaction mixture was then heated to 80°C and stirred at this temperature for 24 hours. Glpc analysis after 24 hours indicated the formation of an 85% glpc yield of 1,1-difluoro-2,2,3,3-tetramethylcyclopropane relative to toluene as an internal standard.

(b) 1,1-difluoro-2,2,3-trimethylcyclopropane

Treatment of methyl chlorodifluoroacetate (1.45 g, 1.06 ml, 0.010 mole) and 2-methyl-2-butene (0.70 g, 0.010 mole) as described above resulted in a 38% glpc yield of 1,1-difluoro-2,2,3-trimethylcyclopropane relative to toluene as an internal glpc standard.

(c) 7,7-difluoronorcarane

Treatment of methyl chlorodifluoroacetate (1.45 g, 1.06 ml, 0.010 mole) and cyclohexene (0.82 g, 0.010 mole) as described above resulted in a 15% glpc yield of 7,7-difluoronorcarane relative to toluene as an internal standard.

Ester decomposition by LiCl:2HMPA in the presence of triphenylphosphine and α,α,α-trifluoroacetophenone

Treatment of methyl chlorodifluoroacetate (1.45 g, 1.06 ml, 0.010 mole) with lithium chloride (0.85 g, 0.020 mole) and HMPA (7.15 g, 7.0 ml, 0.040 mole) in triglyme (25 ml) at 75° to 80°C in the presence of triphenylphosphine (2.62 g, 0.010 mole) and α,α,α-trifluoroacetophenone (1.74 g, 1.38 ml, 0.010 mole) for 22 hours resulted in an 80% glpc yield of 2-phenylpentafluoropropene relative to toluene as an internal standard. The olefin was identified by comparison of its ^{19}F NMR spectrum and glpc retention time with those of an authentic sample.

Ester decomposition by LiCl:2HMPA in the presence of α,α,α-trifluoroacetophenone

Methyl chlorodifluoroacetate (1.45 g, 1.06 ml, 0.010 mole) was added to a solution of lithium chloride (0.85 g, 0.020 mole), HMPA (7.15 g, 7.0 ml, 0.040 mole), and α,α,α-trifluoroacetophenone (1.74 g, 1.38 ml, 0.010 mole) in

triglyme (25 ml) heated to 80°C. The solution was heated with stirring for 24 hours then was steam distilled to give a 56% yield of 1-chloro-2-phenylpentafluoro-2-propanol [30] as determined by ^{19}F NMR using $C_6H_5CF_3$ as an internal standard.

Competition Reactions

(a) Competition between α,α,α-trifluoroacetophenone and 2,3-dimethyl-2-butene

Methyl chlorodifluoroacetate (2.90 g, 2.12 ml, 0.020 mole) was added to a solution of lithium chloride (1.70 g, 0.040 mole), HMPA (14.5 g, 14.0 ml, 0.080 mole), α,α,α-trifluoroacetophenone (11.0 g, 0.080 mole), and 2,3-dimethyl-2-butene (6.72 g, 0.080 mole) in triglyme (25 ml) heated to 80°C. The reaction mixture was stirred at this temperature for 24 hours then was steam distilled. ^{19}F NMR analysis of the steam distillate using $C_6H_5CF_3$ as an internal standard indicated the formation of a 48% yield of 1-chloro-2-phenylpentafluoro-2-propanol and a 30% yield of 1,1-difluoro-2,2,3,3-tetramethylcyclopropane.

(b) Competition between 2,3-dimethyl-2-butene and 2-methyl-2-butene using LiCl:2HMPA

Methyl chlorodifluoroacetate (1.45 g, 1.06 ml, 0.010 mole) was added to a solution of lithium chloride (0.85 g, 0.020 mole), HMPA (7.15 g, 7.0 ml, 0.040 mole), 2,3-dimethyl-2-butene (4.21 g, 5.6 ml, 0.050 mole), and 2-methyl-2-butene (3.51 g, 5.3 ml, 0.050 mole) in triglyme (20 ml) at 80°C. Glpc analysis of the reaction mixture after two hours indicated the formation of 1,1-difluoro-2,2,3,3-tetramethylcyclopropane and 1,1-difluoro-2,2,3-trimethylcyclopropane in a ratio of 4.30. After 24 hours the product ratio had not changed.

(c) Competition between 2,3-dimethyl-2-butene and 2-methyl-2-butene using KF/18-Crown-6

Methyl chlorodifluoroacetate (1.45 g, 1.06 ml, 0.010 mole) was added to a solution of potassium fluoride (1.50 g, 0.026 mole), 18-Crown-6 (7.0 g, 0.026 mole), 2,3-dimethyl-2-butene (4.21 g, 5.6 ml, 0.050 mole), 2-methyl-2-butene (3.51 g, 5.3 ml, 0.050 mole) in triglyme (20 ml) at 80°C. Glpc analysis of the reaction mixture after two hours indicated the formation of 1,1-difluoro-2,2,3,3-tetramethylcyclopropane and 1,1-difluoro-2,2,3-trimethylcyclopropane in a ratio of 4.20. After 24 hours the product ratio had not changed.

ACKNOWLEDGMENT

We would like to thank Professor C. L. Liotta for the preprints of the synthesis and purification of 18-Crown-6.

REFERENCES AND NOTES

1 See, for example: R. D. Chambers, Fluorine in Organic Chemistry, John Wiley and Sons, Inc., New York, 1973, pp. 120-5; J. Hine, Divalent Carbon, Ronald Press, New York, 1964, Ch. 3, pp. 36-65; W. Kirmse, Carbene Chemistry, Academic Press, New York, 1964, Ch. 8; M. Jones, Jr. and R. A. Moss, Carbenes, Vol. II, John Wiley and Sons, Inc., New York, 1975, Ch. 3; W. A. Sheppard and C. M. Sharts, Organic Fluorine Chemistry, W. A. Benjamin, New York, 1969, pp. 237-76; D. Seyferth, Acc. of Chem. Research, 5 (1972) 65.

2 R. A. Mitsch, J. Heterocycl. Chem., 1 (1964) 59.

3 D. Seyferth, J. Y. -P. Mui, M. E. Gordon, and J. M. Burlitch, J. Am. Chem. Soc., 87 (1965) 681; D. Seyferth, H. Dentouzos, R. Suzuki, and J. Y. -P. Mui, J. Org. Chem., 32 (1967) 2980.

4 D. Seyferth, S. P. Hopper, and K. V. Darragh, J. Am. Chem. Soc., 91 (1969) 6536; D. Seyferth and S. P. Hopper, J. Org. Chem., 37 (1972) 4070; D. Seyferth and S. P. Hopper, J. Organomet. Chem., 44 (1972) 97.

5 D. J. Burton and D. G. Naae, J. Am. Chem. Soc., 95 (1973) 8467.

6 J. M. Birchall, G. W. Cross, and R. N. Haszeldine, Proc. Chem. Soc., (1960) 81.

7 L. H. Knox, E. V. Verlarde, S. M. Berger, and D. H. Caudriello, Chem. and Ind., (London), (1962) 860; L. H. Knox, E. V. Verlarde, S. M. Berger, D. H. Caudriello, P. W. Landis, and A. D. Cross, J. Am. Chem. Soc., 85 (1963) 1851; C. Beard, N. H. Dyson, and J. H. Fried, Tetrahedron, 28 (1966) 3281; C. Beard, I. T. Harrison, L. Kirkham, and J. H. Fried, Tetrahedron, 28 (1966) 3287; T. L. Popper, F. E. Carlon, H. M. Marigliano, and M. D. Yudis, Chem. Commun., (1968) 277.

8 P. Hodge, J. A. Edwards, and J. H. Fried, Tetrahedron Lett., (1966) 5175.

9 P. Crabbé, H. Carpio, E. V. Verlarde, and J. H. Fried, J. Org. Chem., 38 (1973) 1478.

10 P. Crabbé, H. Carpio, A. Cervantes, J. Iriarte, and L. Tökes, Chem. Commun., (1968) 79; P. Crabbé, A. Cervantes, A. Cruz, E. Galeazzi, J. Iriarte, and E. V. Verlarde, J. Am. Chem. Soc., 95 (1973) 6655.

11 See, for example: S. A. Fuqua, W. G. Duncan, and R. M. Silverstein, J. Org. Chem., 30 (1965) 1027; S. A. Fuqua, W. G. Duncan, and R. M. Silverstein, J. Org. Chem., 30 (1965) 2543; D. J. Burton and F. E. Herkes, Tetrahedron Lett., (1965) 1883; P. M. Barna, Chem. and Ind., (London), (1966) 2054.

12 D. J. Burton and F. E. Herkes, J. Org. Chem., 32 (1967) 1311.

13 M. Derenberg and P. Hodge, J. Chem. Soc., Perkin Trans., (1972) 1056.

14 G. A. Wheaton and D. J. Burton, J. Fluorine Chem., 8 (1976) 97.

15 Similar observations for the generation of chlorocarbene in diethyl ethe have been reported as well as some possible explanations for this behavior; A. Amaro and K. Grohmann, J. Am. Chem. Soc., 97 (1975) 3830.

16 D. J. Burton and J. L. Hahnfeld, submitted for publication.

17 D. J. Burton and G. A. Wheaton, J. Am. Chem. Soc., 96 (1974) 6787.

18 The isolation and characterization of this complex $ClCF_2CO_2Li$:HMPA will be described in detail in another forthcoming publication.

19 See, for example: O. R. Pierce, E. T. McBee, and G. F. Judd, J. Am. Chem. Soc., 76 (1954) 474; V. Frazen, Angew. Chem., 72 (1960) 566; V. Franzen and L. Fikentscher, Chem. Ber., 95 (1962) 1958; F. Franzen, Chem. Ber., 95 (1962) 1964.

20 R. A. Moss, M. A. Joyce, and F. G. Pilkiewicz, Tetrahedron Lett., (1975) 2425.

21 R. A. Moss and C. B. Mallon, J. Am. Chem. Soc., 97 (1975) 344.

22 R. A. Moss and F. G. Pilkiewicz, J. Am. Chem. Soc., 96 (1974) 5632.

23 W. Kirmse, Carbene Chemistry, Academic Press, New York, 2nd edn., 1971, p. 313.

24 R. A. Mitsch and A. S. Rodgers, Int. J. Chem. Kinet., 1 (1969) 439.

25 K. R. Burson and C. T. Kenner, J. Chromatographic Science, 7 (1969) 63.

26 G. W. Gokel, D. J. Cram, C. L. Liotta, H. P. Harris, and F. L. Cook, J. Org. Chem., 39 (1974) 2445.

27 N. Yarovenko, Zh. Obsch. Khim., 27 (1957) 2796; Chem. Abstr., 52 (1958) 8042b.

28 P. J. Stang and M. G. Mangum, J. Am. Chem. Soc., 97 (1975) 1459.

29 A. Maeicker, Organic Reactions, Vol. 14, R. Adams, Ed., John Wiley and Sons, New York, 1965, p. 395.

30 R. A. Bekker, G. V. Asratyan, B. L. Dyatkin, and I. L. Knunyants, Dokl. Chem., 204 (1972) 439.