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PRELIMINARY NOTE

Methyl Chlorodifluoroacetate as a Precursor for the Generation of Difluorocarbene

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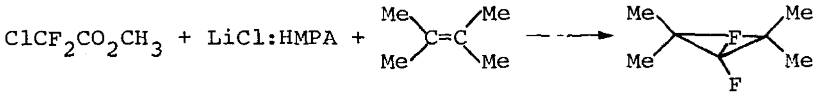
The interest in the development of methods for the generation of difluorocarbene has greatly increased in recent years. Many precursors of difluorocarbene have been investigated [1], but the great majority of them suffer serious limitations. Difluorocarbene precursors such as difluorodiazirine [2], Me_3SnCF_3 [3], and $PhHgCF_3$ [4], involve multistep syntheses or are prohibitively expensive for large scale use. Alkali metal chlorodifluoroacetates, while by far the most commonly employed sources of difluorocarbene, are very hygroscopic and must be used in large excesses to obtain good yields [5]. Much more recently bromodifluoromethylphosphonium bromides have been utilized as sources of difluorocarbene [6]. These salts offer the advantages of ease of preparation and mild reaction conditions. We now wish to report a mild, convenient, one-step method for the generation of difluorocarbene utilizing the easily prepared, inexpensive precursor methyl chlorodifluoroacetate (I).

When ester (I) was treated with lithium chloride/hexamethylphosphoric triamide (HMPA) complex (II) in refluxing dichloromethane in the presence of 2,3-dimethyl-2-butene (III),

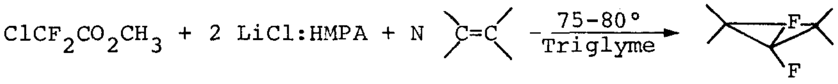


I II III IV

a 78% yield of cyclopropane IV was obtained. The by-products of the reaction were CO_2 and methyl chloride. The same reaction employing triglyme as the solvent at ca. 80° C resulted in a 90% yield of (IV). This cyclopropanation reaction has been investigated utilizing a series of representative olefins. The yields of some typical reactions are presented in Table I.

TABLE I

The formation of 1,1-difluorocyclopropanes [7]



Olefin	N	Yield[a] of Cyclopropane (%)
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]
E-3-methyl-2-pentene	1.0	50[b]
2-ethyl-1-butene	2.0	40
methylenecyclohexane	0.5	34[c]
cyclohexene	1.0	15
"	4.0	30

[a] Glpc yield based on ester. [b] Stereospecific addition of carbene to olefin occurred. [c] Glpc yield based on olefin.

As is evident from Table I both tetra- and trisubstituted ethylenes are converted to cyclopropanes in good yields. The 1,1- and 1,2-disubstituted ethylenes gave only moderate yields of cyclopropane adducts. Olefins with low boiling points or those which are very unreactive must be present in large excess to ensure relatively good yields. Stereospecific addition of difluorocarbene to both E-2-methoxy-2-butene and E-3-methyl-2-pentene occurred to give only one cyclopropane isomer. When excesses of 2,3-dimethyl-2-butene and 2-methyl-2-butene were allowed to compete for the difluorocarbene generated by the decomposition of methyl chlorodifluoroacetate the observed reactivity ratio was 4.3 [8]. The carbene generated in this system is slightly more selective than the carbene generated by the vapor-phase photolysis of difluorodiazirine which gave a reactivity ratio of 3.7 for these same two olefins [9].

The following general procedure is described to provide operational detail for the generation of difluorocarbene by this method, and is adaptable to a wide variety of substrate olefins.

Anhydrous lithium chloride (4.2 g, 0.10 mol) was added with stirring to a solution of hexamethylphosphoric triamide (35.8 g, 35.0 ml, 0.20 mol) in 200 ml of dry triglyme. The mixture was stirred at room temperature under dry nitrogen until all of the lithium chloride had gone into solution, then 2-methyl-2-butene (14.0 g, 21.0 ml, 0.20 mol) was added to the solution, followed by the addition of methyl chlorodifluoroacetate (7.3 g, 5.5 ml, 0.05 mol). The solution was heated to 80° C and stirred for 24 hr then flash distilled at *ca.* 2 mm. Fractionation of the flash distillate gave 4.6 g (0.038 mol, 76%) of 1,1-difluorotrimethylcyclopropane, b.p. 69-70° C, which was 99% pure by glpc analysis. The ^{19}F nmr spectrum (in $DCCl_3$ with $CFCl_3$ capillary) consisted of two signals: Φ*139.0 ppm (d of m) and Φ*150.8 ppm (d of m) with geminal-fluorine coupling of 150.4 Hz, which agrees well with the reported spectrum [6]. The mass spectrum gave a molecular ion at m/e 120.

Although the yields of cyclopropanes obtained by this method are not too different than those obtained *via* the alkali metal chlorodifluoroacetate or phosphonium salt methods, this procedure does offer several advantages. The ester decomposition method is one which may easily be adapted to large scale preparations. The ester may easily be obtained in large quantities and high purity [10]. It is conveniently stored and handled, and has a long shelf-life. Ester decomposition to generate difluorocarbene occurs under relatively mild, nonbasic conditions.

Investigations are presently under way to determine the mechanism of this decomposition, the nature of the cyclopropanating species, and whether this method can be extended to the generation of other fluorocarbenes.

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7 All of the cyclopropanes were unambiguously identified by nmr and mass spectral analysis.

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10 Chlorodifluoroacetic acid is commercially available from Halocarbon Chemical, Hackensack, New Jersey, and can be esterified by conventional methods.