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SYNTHESIS OF MONOFLUOROCYCLOPROPANE DERIVATIVES

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INTRODUCTION

In the study of n.m.r. chemical shift and coupling constants of 1-halo-2,2-dimethylcyclopropanes (1) it was of considerable interest to have the monofluoro derivative in order to determine the effect of electronegativity on these parameters. Attempts to prepare monofluorocyclopropanes by fluorination with inorganic fluorides proved unsuccessful.

Tarrant et al. (2) prepared the 1,1-difluoro-2,2-dimethylcyclopropane from 1,3-dibromo-1,1-difluoro-3-methylbutane by the reduction of the dibromide with zinc dust and n-propanol. A systematic approach to the synthesis of fluorocyclopropanes was reported by Misani and co-workers (3). With the development of carbene chemistry, several research workers have prepared difluorocyclopropyl derivatives using fluoromethanes (4), difluorotetrachloroacetone (5),

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[+] Taken in part from the Ph.D. dissertation of U. V. Rao, submitted to Wayne State University (1964).

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dichlorofluoroacetate (6), and difluorodiazirine (7, 8), as convenient sources for the generation of difluoro and chlorofluoro carbenes; however, the synthesis of simple monofluorocyclopropyl derivatives has not been reported. In this note, a simple procedure for the selective reduction of 1-chloro-1-fluorocyclopropanes by organotin hydrides (9, 10) to yield monofluorocyclopropanes is described.

EXPERIMENTAL

1-chloro-1-fluoro-2, 2-dimethylcyclopropane:- 1.0 Mole of isobutylene (Matheson cp grade) was added to a flask cooled to -10° C which contained 0.5 moles of freshly prepared and dried potassium-t-butoxide. Stirring was then started and 0.303 moles of sym-difluorotetrachloroacetone was slowly added while maintaining the temperature between 0° and -10° C. The reaction mixture was stirred for an additional two hours at -10° C, and then allowed to warm slowly to room temperature.

The unreacted olefin was collected in a trap cooled with a dry ice-acetone mixture. After all the olefin had evaporated, 250 ml of pentane was added followed by an equal volume of water. The pentane layer was separated and washed thoroughly with water to remove t-butanol and dried over anydrous magnesium sulfate. The pentane was stripped off and the remaining mixture fractionated on a Holzman column to give 20.0 g (35%) 1-chloro-1-fluoro-2, 2-dimethylcyclopropane, b.p. 78-79°, $n_D^{25.6^\circ}$ = 1.3948. Analysis* of the product gave the following results:

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* Analysis was carried out by Midwest Micro Lab Inc., 600 E. 46 St., Indianapolis, Ind.

Calcd. for C_5H_8ClF: Cl, 28.93; F, 15.50; C, 48.99; H, 6.58

Found: Cl, 28.73; F, 15.41; C, 49.02; H, 6.64.

The gas phase infrared spectrum of the chlorofluorocyclopropane was consistent with the structure (5, 11). The major absorption peaks were as follows: 3.4 (cyclopropane CH), 8.5, 8.9 (C-F), 10.15, 10.70 μ (cyclopropane ring).

This compound was further characterized by its mass spectrum (Atlas CH IV with an ionizing potential of 70 v). The molecular ions occurred at 122 (21.1, relative intesnity) and 124 (6.4) corresponding to the relative abundance of Cl^{35} (3.06) and Cl^{37} (1). Both the proton and fluorine n.m.r. spectra were consistent with the structure.

1-fluoro-2,2-dimethylcyclopropane:- 0.05 moles of the 1-chloro-1-fluorocyclopropane were placed in a 100 ml three-necked flask with 25 ml of solvent. The flask was fitted with a dry ice condenser and a distillation head to allow removal of volatile fluorocyclopropane (B.P. 43°C) from the reaction mixture. An equimolar quantity of the reducing agent was added and the reaction allowed to proceed with the fluorocyclopropane being collected in a dry ice-acetone trap. Final separation was carried out on a preparative v.p.c. using a firebrick column coated with 20% silicone oil. The yields obtained using different reducing agents, solvents, temperatures, and reaction times are shown in Table 1.

TABLE 1

Reducing Agent	Conditions	% Reduction[a]
$(n\text{-}C_4H_9)_3SnH$	2 M in Xylene, 110°C, 48 hrs.	35[b]
$(n\text{-}C_4H_9)_3SnH$	2 M in Heptane, 60°C, 48 hrs.	10[b]
$(C_6H_5)_3SnCl+LiAlH_4$	2 M in n-butylether, 140°C, 10 hrs.	8[b, d]
$(n\text{-}C_4H_9)_3SnCl$ $+LiAlH_4$	2 M in n-butylether, 140°C, 10 hrs.	10[c, d]
$(n\text{-}C_4H_9)_2SnCl_2$ $+LiAlH_4$	2 M in n-butylether, 140°, 10 hrs.	10[d]
$(C_6H_5)_2SnCl_2$ $+LiAlH_4$	2 M in n-butylether, 140°, 10 hrs.	10[d]
$LiAlH_4$	THF, 60°C, 10 hrs.	No reduction
Zn dust	2 M n-propanol, 90°C, 10 hrs.	No reduction

a. Except in 1 and 2, the yields were computed from the areas under vpc curves.

b. 1.5 mole % of catalyst (azobisisobutyronitrile) added.

c. The yield was low because of some mechanical loss of sample.

d. The fluoro derivative is associated with very close boiling fractions thus rendering separation difficult.

Analysis of the product gave the following results:

Calcd. for C_5H_9F: C, 68.14; H, 10.30

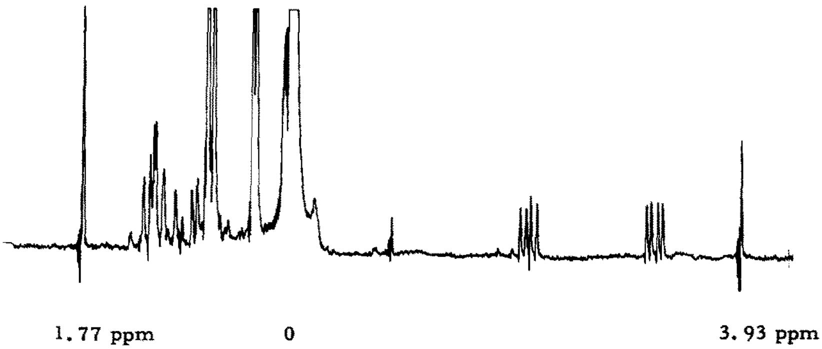
Found: C, 68.88; H, 10.18.

The gas phase infrared spectrum of the monofluorocyclopropane was consistent with the structure. Major absorption peaks were as follows:

3.4 (cyclopropane C-H), 8.7, 9.1 (C-F) 10.25, 11.25 and 11.58 µ (cyclopropane ring). The mass spectrum shows the molecular ion ($C_5H_9F^+$) at 88. Both the proton (Fig. I) and the fluorine n.m.r. spectra are consistent with the structure.

FIG. I

The proton n.m.r. spectrum of 1-fluoro-2,2-dimethylcyclopropane



DISCUSSION

The final synthesis of a simple monofluorocyclopropane has been described and this technique, the reduction with tributyltin hydride, should be applicable to the preparation of a wide variety of alkyl-substituted monofluorocyclopropanes, thus opening this area for investigation.

Preliminary work on the n.m.r. spectra of the 1-fluoro-2,2-dimethylcyclopropane (Fig. I) (20% in 2:1 benzene to cyclohexane solution) shows two quartets centered at 2.07 and 3.17 ppm downfield from cyclohexane arising from the interaction of the fluorine with the geminal proton and the other ring protons. In addition, it should be noted that

H-F coupling takes place with all other protons, including those of the methyl groups.

This has been confirmed by the F^{19} n.m.r. spectrum which consists of two groups of lines arising from the geminal proton coupling centered at 217.9 and 219.0 ppm upfield from Freon 11 (the internal standard). Each of these groups has 28 discernible lines corresponding to splitting by the other ring protons and by the protons on the methyl groups.

Solvent effects on the proton n.m.r. spectrum have been observed which are particularly noticeable in the quartet centered at 2.07 ppm in the fluoride. These changes have also been observed in 1-chloro-2,2-dimethylcyclopropane, but in this case are much smaller. A complete investigation of these effects is now in progress and will be published elsewhere.

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