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A CONVENIENT PREPARATION OF DEUTERATED FLUOROOLEFINS

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SUMMARY

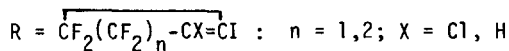
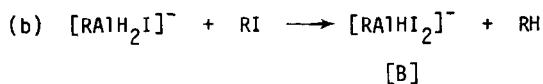
The reduction of iodo-containing fluoroolefins with NaAlH_4 in diglyme followed by hydrolysis with D_2O provides a convenient preparative procedure to the corresponding deuterated fluoroolefin.

INTRODUCTION

Polyfluorinated olefins generally react with complex metal hydrides either via nucleophilic displacement of vinylic halogen by hydrogen or allylic displacement of fluorine through an $\text{SN}2'$ type reaction [1,2]. Olefins that contain vinylic iodide, however, do not undergo nucleophilic substitution when reacted with LiAlH_4 in ether. Instead, they form aluminum complexes, which are stable in solution. Evidence for this alternate mode of reaction was obtained from GLPC analysis of the reaction mixture before and after hydrolysis, measurement of the hydrogen gas evolved during the reaction, and an investigation of the amount of deuterated vs. protonated product obtained if hydrolysis of the reaction mixture was carried out with D_2O [3,4].

The reactions of the iodine-containing olefins can be rationalized via the scheme first described by Hauptschien and co-workers [5], Scheme 1. The deuterated olefin observed, when hydrolysis of the reaction mixture is carried out with D_2O , presumably arise from hydrolysis of complex [B] with D_2O .

Since the deuterated products are of interest in mechanistic studies of these olefins, it would be convenient to have a synthetic method to prepare reasonable quantities of the deuterated olefin without recourse to large amounts of the expensive complex metal deuterides. This report focuses on this question and provides a useful preparative entry to these labeled olefins.



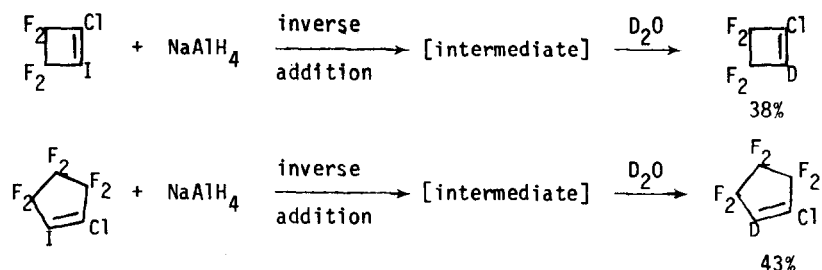
SCHEME 1

RESULTS AND DISCUSSION

We have also demonstrated that $NaAlH_4$ in diglyme reacts with fluoroolefins in a manner analogous to $LiAlH_4$ in ether [6]. The substitution of $NaAlH_4$ for $LiAlH_4$ in these reactions allows the use of diglyme (bp $161^\circ C$) as a solvent and facilitates removal of volatile olefins from reaction mixtures. $LiAlH_4$ is only very slightly soluble in diglyme [7].

We have taken two approaches to solve this problem. The initial approach, Method [I], attempted to remove (via vacuum evaporation) all of the initially formed reduction product (RH in step (b) of Scheme 1), followed by hydrolysis of complex [B] with D_2O . The olefin 1-chloro-2-iodohexafluorocyclopentene (see Experimental) was reacted in this manner, and pure 1-deutero-2-chlorohexafluorocyclopentene was obtained via preparative GLPC [8]. The method works reasonably well; it is, however, complicated by formation of large quantities of the initial reduction product, which hinders the isolation of the deuterated product and lowers the yield of the deuterated product.

An alternate approach, Method [II], merely involves inverse addition. If the reaction proceeds as outlined in Scheme 1, then reaction of equimolar amounts of olefin and hydride should give only intermediate [A] and a mole of hydrogen - providing the olefin is added to the hydride solution and that the AlH_4^- is a better reducing agent than [A]. No reduced olefin should be formed before hydrolysis. The results of this approach are illustrated in the following equations.



The isolated yield of the deuterated olefin is acceptable. The purity of the labelled product is excellent. No evidence of the protonated analog was detected by infrared analysis.

Method (II) appears to be the preferred method. It is easy to carry out experimentally, can be scaled up with no problem, and isolation of the deuterated product is merely a simple distillation. We recommend this procedure to researchers in need of such labelled materials.

EXPERIMENTAL

Method [I]

In a typical reaction, 11.4 ml (12.5 mmoles) of 1.1 M NaAlH_4 in dry diglyme was added slowly at 0-5°C to a stirred solution of 8.40 g (25 mmoles) of 1-chloro-2-iodohexafluorocyclopentene in 25 ml diglyme. After stirring for 1/2 hour, the 1-hydro-2-chlorohexafluorocyclopentene formed was removed under reduced pressure (ca. 1 mm for 24 hours). When GLPC indicated that all of this latter material had been removed, the reaction mixture was hydrolyzed by the slow addition of 2.0 ml of D_2O . Following hydrolysis, the reaction mixture was again subjected to reduced pressure. The distillate (product and diglyme) was subjected to preparative GLPC. A sample of 1-deutero-2-chlorohexafluorocyclopentene was isolated. Its infrared spectrum was identical to an authentic sample and showed no absorptions characteristic of 1-hydro-2-chlorohexafluorocyclopentene [9].

Method [II]

A solution of 33.6 g (100 mmoles) of 1-chloro-2-iodohexafluorocyclopentene in 100 ml of dry diglyme was added slowly to 112 ml (110 mmoles) of 0.987 M NaAlH_4 in diglyme, keeping the temperature of the reaction below

10°C. After the addition of olefin was completed, GLPC analysis of the reaction mixture showed trace amounts of 1-chloro-5,5-dihydropentafluorocyclopentene and 1,5,5-trihydropentafluorocyclopentene, but no 1-hydro-2-chlorohexafluorocyclopentene was observed [10]. The reaction mixture was then slowly hydrolyzed with 8.0 ml D₂O [11]. The reaction mixture was then stirred for one hour at room temperature. The olefinic mixture was then subjected to steam distillation; the organic distillate layer dried over molecular sieves, and then distilled on a spinning band column to give 9.0 g (43%) of 1-deutero-2-chlorohexafluorocyclopentene. The infrared spectrum of this material showed no evidence of any 1-hydro-2-chlorohexafluorocyclopentene [9].

Preparation of 1-deutero-2-chlorotetrafluorocyclobutene

A similar reaction with 100 mmoles of 1-chloro-2-iodotetrafluorocyclobutene and 110 mmoles of NaAlH₄ was carried out as described above to give 6.1 g (38%) of the titled product [12], isolated by preparative GLPC.

ACKNOWLEDGEMENT

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REFERENCES AND NOTES

- 1 D.J. Burton and R.L. Johnson, J. Amer. Chem. Soc., 86 (1964) 6361.
- 2 D.J. Burton and R.L. Johnson, Tetrahedron Letts., (1966) 2681.
- 3 D.J. Burton and F.J. Mettillie, Inorg. and Nucl. Chem. Letts., (1968) 9.
- 4 Cf. S. Natarajan and R.L. Soulen, J. Fluorine Chem., 17 (1981) 447 for related reductions with sodium trimethoxyborohydride. These authors suggest that the results in reference [3] contradict the conclusions of reference [2]. However, it should be noted that in the LiAlH₄/iodo-olefin reactions, attack is on halogen (see [3] for details), whereas the earlier conclusions were based on systems where initial attack is on carbon [2]. Thus, since there is a mechanism change, it's not surprising that the results differ. The conclusions described in reference [2] can only be applied to systems in which attack by hydride is on carbon.

- 5 M. Hauptschien, A.J. Saggiomo, and C. Stokes, J. Amer. Chem. Soc., 78 (1956) 680.
- 6 Unpublished work of F.J. Mettillie in this laboratory.
- 7 The use of ether makes the isolation and purification of the product olefins more difficult. Also, when ether is used, the initially formed reduction products cannot be safely removed [3] by vacuum evaporation [see Method I]. There is nothing magical about the use of NaAlH_4 /diglyme here. Diglyme is merely used because of its higher boiling point, and NaAlH_4 is used because of its solubility in diglyme. We have accomplished a similar selective deuteration of 1-chloro-2-iodotetrafluorocyclobutene via Method [I] using LiAlH_4 in an ether/di-n-butyl ether mixture, followed by hydrolysis with D_2O .
- 8 Trans-2-hydro-3-iodohexafluorobutene-2 gave trans-2-deutero-3-hydrohexafluorobutene-2 via a similar procedure.
- 9 $-\text{CD}=\text{CCl}-$, 1613 cm^{-1} ; $-\text{CH}=\text{CCl}-$, 1631 cm^{-1} for the cyclopentene derivatives. A pure sample of the deuterated olefin was prepared from 1,2-dichlorohexafluorocyclopentene and LiAlD_4 for comparison purposes.
- 10 Apparently, trace amounts of 1-hydro-2-chlorohexafluorocyclopentene are formed, but this olefin is further reduced by the excess hydride present and presents no problem.
- 11 Large amounts of $\text{Al}(\text{OH})_3$ formed; the reaction mixture was transferred to a larger flask for the steam distillation. Presumably, a higher yield of product could be obtained by flash distillation of the reaction mixture, but steam distillation provides a facile method of separation of the product from the $\text{Al}(\text{OH})_3$.
- 12 $-\text{CD}=\text{CCl}-$, 1562 cm^{-1} ; $-\text{CH}=\text{CCl}-$, 1589 cm^{-1} for the cyclobutene derivatives. A pure sample of the deuterated olefin was prepared from 1,2-dichlorotetrafluorocyclobutene and LiAlD_4 for comparison purposes.