Journal of Fluorine Chemistry, *29* (1985) 273–286

Received: December 5, 1984; accepted: February 18, 1985

NUCLEOPHILIC REACTIONS OF FLUOROOLEFINS.
VI. REACTIONS OF 1-PHENYLPENTAFLUOROPROPENE WITH LITHIUM ALUMINIUM HYDRIDE . REGIO- AND STEREOSELECTIVE SUBSTITUTION OF VINYLIC FLUORINES BY HYDROGEN

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SUMMARY

1-Phenylpentafluoropropene 1 reacted readily with lithium aluminium hydride in glyme to give products of the displacement of vinylic fluorine atoms by hydrogen. In the temperature range between -20°C and -10°C, the substitution of one vinylic fluorine occurred, either at carbon C-1 or C-2, to give predominantly monohydrofluoroalkenes 2 and 3 while at 20° *ca*. 97% conversion to 1,2-dihydrofluoroalkenes 4 took place. The substitution of the first fluorine proceeded with high degree of regio- and stereoselectivity. Subsequent substitution of monohydroalkenes gave mostly isomer 4E with only little formation of 4Z.

INTRODUCTION

Lithium aluminium hydride and sodium borohydride, common carriers of hydride ion, have been shown to be excellent rea-

0022-1139/85/$3.30

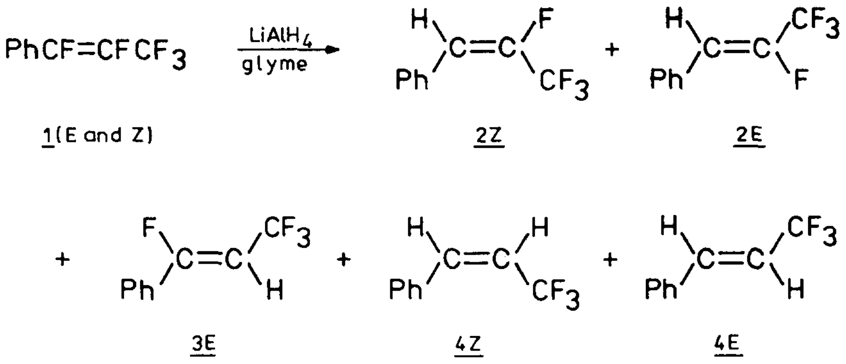
gents for nucleophilic displacement of vinylic or allylic fluorine atoms by hydride to give mono- and di-hydrofluoroalkenes; large numbers of such reactions have been reported and reviewed [1, 2]. These reactions apparently involve carbanion intermediates and, in contrast to catalytic hydrogenation of unsaturated fluorocompounds [3, 4], usually no products of the addition of hydrogen across the double bond are formed.

As the continuation of studies on the influence of the bulk of attacking nucleophile on the regioselectivity of the substitution of vinylic fluorines in 1-phenylpentafluoropropenes [5, 6] it was deemed of interest to study the reaction with hydride ion. Since 1-phenylpentafluoropropene 1 showed relatively small nucleophilic reactivity as compared to perhaloalkenes, lithium aluminium hydride, which has been reported [1] to be more reactive than sodium borohydride, was choosen for this study as the reducing agent. Another purpose of the present work was a facile synthesis of 1-phenyl-3,3,3-trifluoropropene 4, required for further work, from the readily available alkene 1 [7].

RESULTS AND DISCUSSION

Reaction of 1-phenylpentafluoropropene 1 with lithium aluminium hydride in refluxing diethyl ether was very sluggish; after three hours the GLC analysis of the reaction mixture showed 76% of the unreacted alkene 1. In contrast, the reaction proceeded readily in ethylene glycol dimethyl ether (glyme) and even at -20° it was complete in two hours. In general, five products were formed: three monohydroalkenes, viz. 1-phenyl-2,3,3,3-tetrafluoropropenes 2Z and 2E, and 1-phenyl-1,3,3,3-

-tetrafluoropropene 3E, and two dihydroalkenes, *viz*. 1-phenyl-3,3,3-trifluoropropenes 4Z and 4E.



The reaction was found to be strongly temperature-sensitive (Table 1). In the range between -20° and -10° reduction of one of the vinylic fluorines, either at carbon C-1 or C-2, occurred with more than total 90% selectivity for monohydroalkenes 2 and 3 with only little formation of dihydroalkenes 4. At 20° and higher temperature, substitution of both vinylic fluorines by hydrogen atoms took place and mixtures of products which consisted of *ca*. 97% of dihydroalkenes 4 were obtained.*

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*This is a clear illustration that removal of one vinylic fluorine reduces nucleophilic reactivity of the double bond of alkene 1, therefore, substitution of the second vinylic fluorine requires higher activation energy. In the reactions of 1 with alkyllithiums [5] and lithium dialkylamides [6] at 20° no double substitution was observed.

TABLE 1

Reactions of 1-phenylpentafluoropropene 1 with lithium aluminium hydride in glyme

Run	Ratio of 1E/1Z	Reaction temp., °C	Product distribution (%)[a] 2Z	2E	3E	4Z	4E	Yield mol (%)[b]
1	76/24	-12 to -10	21.1	3.7	67.3	0.4	7.3	
2	95/5	0 to 30			1.4	2.0	95.4	64.0
3	81/19	0 to 40			1.1	2.7	94.1	77.5
4	99%E	-15 to -10	0.8	1.3	93.7		4.0	
5	99%Z	-20 to -15	84.2	10.3	1.3		4.2	

[a] GLC estimate in the crude reaction mixture

[b] Yields of the distilled mixture of products

Compounds 2Z, 3E, and 4E were isolated by distillation and purified by preparative GLC; their physical properties and analyses are given in Table 2.

TABLE 2

Physical properties and analyses of compounds 2, 3, and 4

Compd.	B.p. °C	ν(C=C) cm^{-1}	Found (calculated), % C	H	F
2Z	143-144	1695	56.8(56.8)	3.1 (3.2)	40.2(40.0)
3E	174-175	1688	56.8(56.8)	3.1(3.2)	39.9(40.0)
4E	165	1662	63.0(62.8)	4.1(4.1)	33.2(33.1)

The structure of all compounds 2, 3, and 4 were elucidated from their ^{1}H and ^{19}F NMR spectral data (Table 3). These data have shown that, from amongst five compounds which were formed, three of them contained one vinylic fluorine and one vinylic proton that identified them as monohydroalkenes. The vinylic fluorine signals of the main low-temperature product appeared at apparently lower field than the corresponding signals of the two other monohydroalkenes, and by the comparison with earlier reported data [5, 6], this compound should be 1-phenyl-1,3,3,3-tetrafluoropropene and the two others should be 1-phenyl-2,3-3,3-tetrafluoropropenes. Large H-F and F-CF_3 coupling constants identified the former compound as 3E. Assignment of configurations 2Z and 2E for the latter compounds was based on the characteristic magnitude of the *cis* and *trans* proton-to-fluorine coupling constants [8]. The major final product of the reaction of alkene 1 with lithium aluminium hydride at ambient temperature exhibited a single fluorine signal in the range of the CF_3 groups and two signals of vinylic protons. Structure 4E has been assigned to this compound on the basis of a typical *trans* proton-to-proton coupling constant [9]. Similarly, coupling constant J/H-H/ suggested structure 4Z for the minor product.

The ratios of monohydroalkenes 2 and 3 and of the isomers Z to E of these alkenes, which were obtained in the reaction conducted at -10° (Table 1, run 1), suggested that the reaction proceeds with high regio- and stereoselectivity. This suggestion has been fully confirmed by conducting the reactions with isomers 1E and 1Z of 99% purity (runs 4 and 5). In both cases, if considering the presence of *ca.* 1% of the other iso-

TABLE 3

^{19}F and ^{1}H NMR data on compounds 2, 3, and 4

Compd.	Chemical shifts (ppm)[a,b]	Coupling const.(Hz)
2Z	$\phi(CF_3)$ = 66.6(d), $\phi(F)$ = 124.4(dq) $\delta(H)$ = 6.75(d)	J(H-F) = 20.6 $J(F\text{-}CF_3)$ = 9.6
2E	$\phi(CF_3)$ = 71.9(d), $\phi(F)$ = 131.0(dq) $\delta(H)$ = 6.32(d)	$J(F\text{-}CF_3)$ = 11.3
3E	$\phi(CF_3)$ = 57.3(dd), $\phi(F)$ = 103.0(dq) $\delta(H)$ = 5.60(dq)	J(H-F) = 33.1 $J(F\text{-}CF_3)$ = 16.6 $J(H\text{-}CF_3)$ = 7.5
4Z	$\phi(CF_3)$ = 57.6(d) $\delta(H)$ = 6.82(d)[c]	J(H-H) = 12.0 $^{gem}J(H\text{-}CF_3)$ = 9.6
4E	$\phi(CF_3)$ = 63.3(dd) $\delta(H)$ = 6.12(dq) and 7.10(dq)	J(H-H) = 16.0 $^{gem}J(H\text{-}CF_3)$ = 6.5 $^{vic}J(H\text{-}CF_3)$ = 2.0

d - doublet, q - quartet

[a] From internal CCl_3F for ^{19}F (positive upfield) and from internal TMS for ^{1}H .

[b] All compounds exhibited signals of aromatic protons within the range of 7.3 - 7.5 ppm .

[c] A signal of the second vinylic proton was not detected.

mer, a 98.8% regioselectivity for the substitution at carbon C-2 of isomer <u>1E</u> and a 99.7% regioselectivity for the substitution at carbon C-1 of isomer <u>1Z</u> were obtained. Thus, the substitution of hydrogen for fluorine in alkenes <u>1</u> is practically regiospecific. In these reactions, which involve hydride ion as a nucleophile,* steric factors must be very small, if any, and the orientation is governed exclusively by the polarisation of the double bond of the reactant alkenes <u>1</u>. In the <u>E</u> form, conjugation of the double bond with the benzene ring opposes and overwhelms inductive polarisation by the <u>trans</u>-CF_3 group and carbon C-2 becomes more positive than carbon C-1 and therefore more susceptible to nucleophilic attack. This counterbalancing effect is much less efficient in the <u>Z</u> form in which steric interactions between the CF_3 group and the benzene ring may force the latter out of the plane of the double bond, thus decreasing the effect of conjugation [10] and, therefore, the activation of carbon C-1 by inductive influence of the CF_3 group predominates.

It is rather difficult to make straightforward comparison of the regioselectivity of the substitution of fluorine in alkenes <u>1</u> by hydride ion (or AlH_4^- anion) with the substitution by carbanions reported earlier [5], firstly, because of the difference in the <u>E</u>/<u>Z</u> ratio of the starting alkenes used, secondly, because of the difference in the reaction conditions (solvent, temperature). However, when considering the present results

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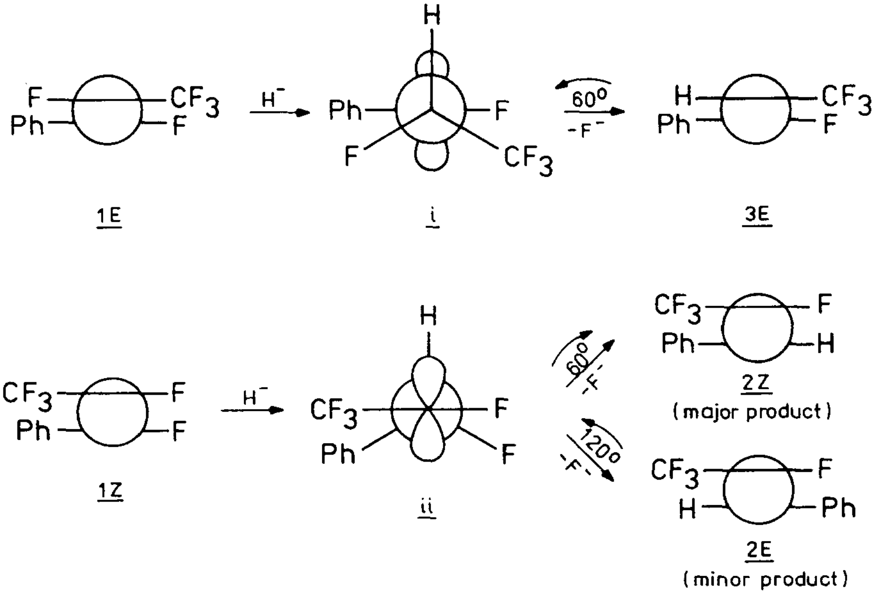
*Even if the nucleophilic species is the AlH_4^- anion, the electrophilic centre is attacked not by the aluminium but by the hydrogen atom of this anion [12].

(Table 1, runs 4 and 5) and recent results obtained from the reactions of high purity isomers of 1 with methyllithium and tert-butyllithium [11], it is evident that, for the reactions with 1Z, the increasing bulk of a nucleophile shifts the regioselectivity from the 100% C-1 for hydride ion to the C-1/C-2 = = 80/20 for methyl anion to the C-1/C-2 = 30/70 for tert-butyl anion. The bulk of the attacking nucleophile (hydride ion and carbanions) has shown rather small and not unequivocal influence on the regioselectivity of the substitution at isomer 1E, with carbon C-2 being always the favoured side. Present results do not contradict previous explanations of the effect of the bulk of a nucleophile on the regioselectivity in nucleophilic reactions of alkene 1, but show that the overall regioselectivity is governed mostly by isomer 1Z.

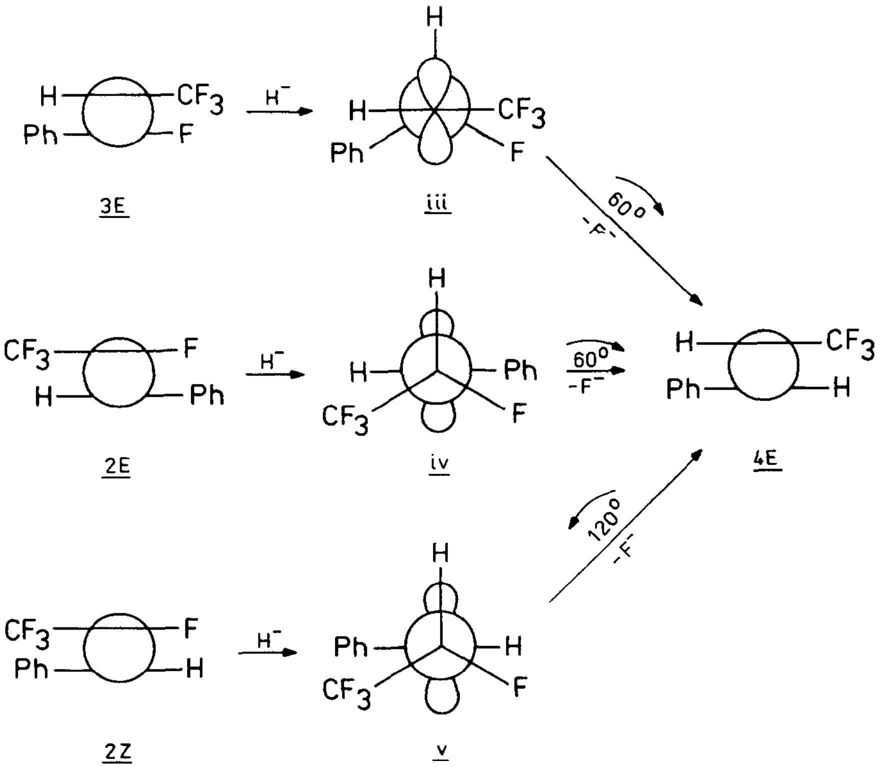
The stereochemical outcome of the substitution of fluorine at position C-2 in alkene 1E by hydrogen was the complete retention of the configuration. Retention also predominates in the substitution at C-1 in 1Z; retained and inverted products 2Z and 2E were formed in the ratio of 8.4 : 1 (Table 1, runs 4 and 5). This is in agreement with the results of recent studies [13, 14, 15] and calculations [16, 17] which have shown that in nucleophilic vinylic substitution, internal rotation of the initially formed carbanion by 60° and then, expulsion of leaving group to give a retained product, is preferred to the 120° rotation leading to an inverted product. In both intermediates i and ii (Scheme 1) which are formed by the attack of hydride ion on the C-2 carbon of 1E and on the C-1 carbon of 1Z, respectively, the 60° rotation ('least motion process') will be



Scheme 1. Stereochemistry of the reaction of alkenes 1 with hydride ion.

preferred to the 120° rotation. However, in the latter case, stereoelectronic repulsion between the CF_3 and the phenyl groups somewhat increases a barrier to the 60° rotation which should lead to a fluoride ion elimination, and the competing 120° rotation contributes to the formation of small amounts of the inverted product 2E.

Results obtained at 20° and 40° (Table 1) suggest that subsequent substitution of alkene 3E by hydride ion also proceeds with retention of the configuration, while in the case of compounds 2 stereoconvergence takes place. Alkene 4E was formed as almost the only product. The stereochemical reaction pathway is shown in Scheme 2. It seems reasonable that the driving force for nearly exclusive 120° rotation of intermediate v leading to the inverted alkene 4E, besides repulsion between the CF_3 and the phenyl groups, is the mutual attraction of the hydrogen and fluorine atoms. It is not clear from which alkene, 2Z, 2E, or 3E, small amounts of 4Z are formed.



Scheme 2. Stereochemistry of the reactions of alkenes 2 and 3 with hydride ion.

Finally, this work resulted in developing of facile, regio- and stereoselective synthesis of 1-phenyl-2,3,3,3-tetrafluoropropene 2Z (nc), 1-phenyl-1,3,3,3-tetrafluoropropene 3E (nc), and particularly 1-phenyl-3,3,3-trifluoropropene 4E. In relation to the latter, it seems to be a more convenient method than the three-step synthesis reported by Yagupolskii and Fiyalkov [18].

EXPERIMENTAL

Boiling points were determined in capillaries by Sivoloboff's method and are uncorrected. NMR spectra were recorded with a JEOL-4H-100 spectrometer and IR spectra with a Beckmann IR Acculab TM-1 spectrometer. GLC separations were performed with a Chromatron GCHF.18.3.4 instrument (GDR) using a 3.5 m x 4 mm column for analytical work and 4.0 m x 10 mm column for preparative work, both columns packed with Chromosorb G coated with 3 % silicon oil SE-52.

Synthesis of a mixture of 1-phenylpentafluoropropenes 1Z and 1E has been described previously [7]. The isomers were separated by distillation through a Büchi Fisher type column. Lithium aluminium hydride was pure grade commercial reagent (FLUKA). Ethylene glycol dimethyl ether (glyme) was purified by refluxing with sodium metal until blue with benzophenone and distillation. Finally, the solvent was redistilled from lithium aluminium hydride.

Reduction of 1-phenylpentafluoropropenes 1Z and 1E with lithium aluminium hydride

The reactions were carried out in a round-bottomed flask equipped with reflux condenser, magnetic stirring bar, thermometer and dropping funnel. Before the reaction, the apparatus was swept with dry argon and a slow stream of argon was maintained during the course of the reaction.

Low-temperature reactions

25 ml of glyme and 1.5 g (0.04 mole) of lithium aluminium hydride were placed in the reaction flask and cooled down to -20° by means of an ethanol-water-dry ice bath. Then, 6.4 g (0.03 mole) of alkene 1 (E or Z or their mixture) was added dropwise while stirring at such a rate as to keep the temperature within the range from -20° to -10° (exothermic reaction). After addition, the reaction mixture was stirred at this same range of temperature for two hours and then quenched by careful addition of diluted (1 : 1) hydrochloric acid. The bottom organic layer was extracted with chloroform, washed with water and dried over magnesium sulphate. After removal of the major part of the solvent by distillation under atmospheric pressure, the residue was subjected to GLC and NMR investigations. Analytical samples of alkenes 2Z (from 1Z) and 3E (from 1E) were obtained by distillation followed by preparative GLC purification.

Ambient-temperature reactions. Synthesis of 1-phenyl-3,3,3-trifluoropropene 4E

A suspension of 10.0 g (0.26 mole) of lithium aluminium hydride in 250 ml of glyme was cooled down to 0° and then 63.0 g (0.3 mole) of a mixture of alkenes 1E and 1Z was added dropwise over 30 - 45 minutes. The temperature increased to 30 - 40° and was self-maintained within this range by the heat of the reaction for four hours. Thereafter, heating was applied to keep the temperature of 40° for additional two hours. The reaction mixture was worked up as described above. Distillation under reduced pressure gave 40 g (yield ca. 77%) of alkene 4 (the E/Z ratio = ca. 40 : 1) of 97% purity.

ACKNOWLEDGMENT

This work has been supported by the Polish Academy of Sciences within the project MR-I-12.

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