

STEREOCHEMICAL STUDIES OF FLUORIDE ION-ASSISTED REDUCTIONS OF KETONES

BY ORGANOSILICON HYDRIDES¹

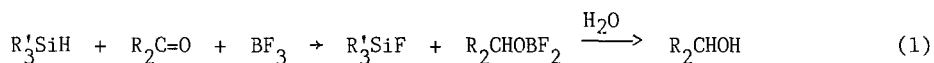
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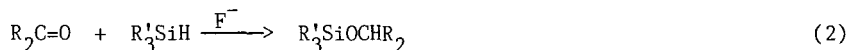
Abstract: The stereochemistry at the silicon and carbon centers has been studied in the fluoride ion-catalyzed reaction between (R)-(+)- α -naphthylphenylmethylsilane and several prochiral aromatic ketones which gives alkoxysilane product.

Organosilicon hydrides are frequently used as reducing agents toward electrophilic carbon centers, but much remains obscure about the mechanistic details of such reactions. Aldehydes and ketones can be reduced to alcohols (or even hydrocarbons) by the action of organosilicon hydrides in the presence of boron trifluoride.² In the process, the organosilicon hydrides are transformed into their respective fluorosilanes (eq 1). When optically active α -naphthyl-

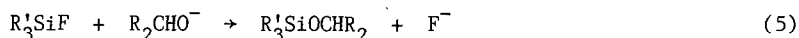
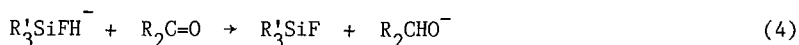


phenylmethylsilane was used to reduce several aldehydes, the fluorosilane product was formed with a small (3-8%) predominance of inversion of configuration.³ This suggests that perhaps boron trifluoride plays a dual role in such reductions - both to enhance the electrophilicity of the carbonyl carbon by bonding with the carbonyl oxygen and to enhance the nucleophilicity of the silicon hydride bond by acting as a donor of fluoride toward the silicon center.

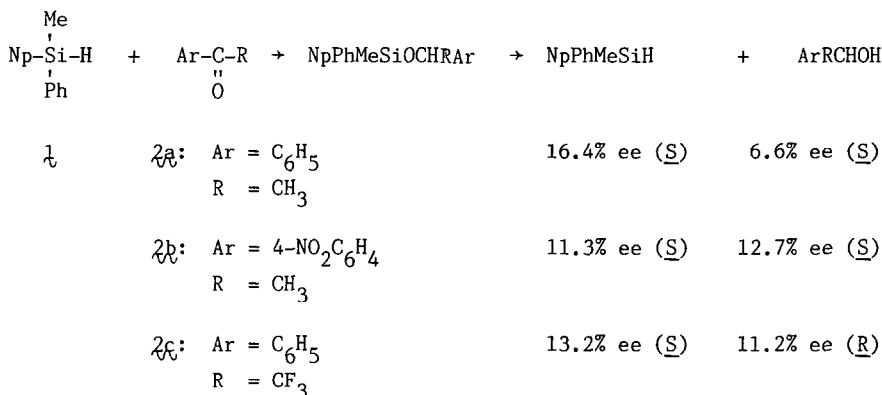
Consistent with this view are the reports by Vol'pin and coworkers that fluoride ion alone can catalyze the formation of alkoxysilanes from organosilicon hydrides and certain aldehydes and ketones (eq 2).⁴ In later work, Corriu and coworkers have shown that this technique can be used even under heterogeneous reaction conditions without solvents to promote synthetically useful selective reductions of aldehydes, ketones, and even esters to alkoxysilanes which yield alcohol products upon hydrolysis.⁵



A reasonable explanation of the role played by fluoride ion in these reactions is given in equations 3-5, below. Initial interaction of fluoride ion with the organosilicon hydride to form a kinetically active, valence-expanded pentacoordinate fluorohydrosilanide ion (eq 3) might be expected to precede the delivery of hydride to the carbonyl center (eq 4). Finally, nucleophilic attack on the fluorosilane by alkoxide ion would form the observed alkoxysilane product and regenerate the fluoride ion to function as catalyst (eq 5).

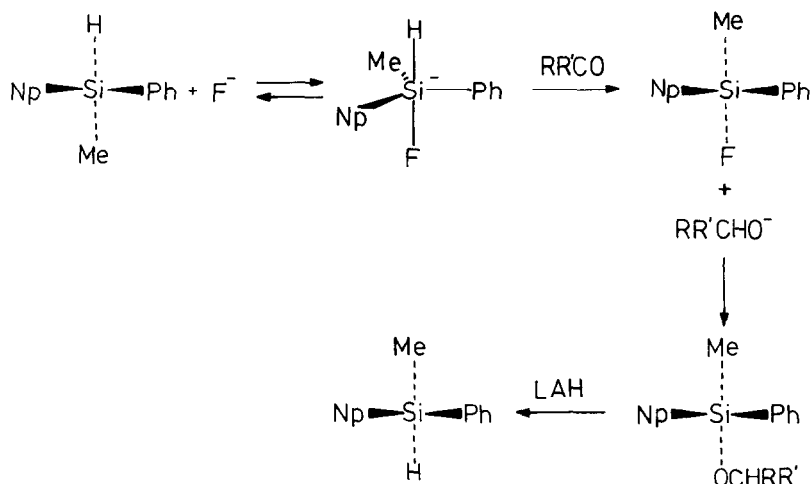


In an effort to better understand the nature of this reducing system, we have studied the fluoride ion-promoted reaction of (R)-(+)- α -naphthylphenylmethylsilane (1)⁶ with several prochiral aromatic ketones (2a-c) and have observed the stereochemical outcome at both the silicon and carbon centers. A solution of 1 (6 mmol) and 2 (5 mmol) in anhydrous acetonitrile (8 mL) saturated with anhydrous cesium fluoride (previously dried at 450°C for 1.5 h) was held under nitrogen in an ultrasonic bath overnight. The alkoxy silane products were then isolated by flash column chromatography on silica gel (ether-hexane solvent)⁷ and cleaved with lithium aluminum hydride to recover the silane and to obtain free alcohol. The optical activities of the alcohol and silane products were then measured and related to their absolute configurations and optical purities. The alkoxy silane product derived from 1 and 2b was divided into two portions: one portion was cleaved by LAH and the silane product was examined; the other portion was hydrolyzed with 2M HCl in acetone and the nitroalcohol was collected and examined. The stereochemical results are shown below as the averages of duplicate experiments.

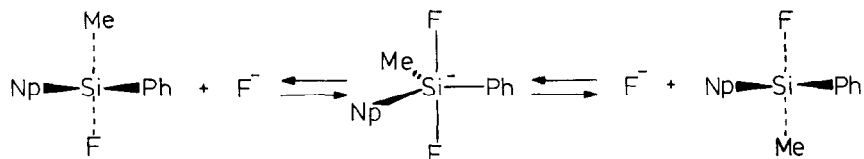


It is noteworthy that in all the cases observed, the organosilicon hydride product had predominantly inverted stereochemistry compared to the starting organosilicon hydride. As the LAH cleavage of alkoxy silanes to organosilicon hydrides and alcohols as used in this work is known to proceed with retention of configuration at silicon,⁸ this can only mean that the alkoxy silane products themselves were formed with predominant inversion.

The fact that the new chiral carbon center was formed in each case with some enantioselectivity indicates that the actual reducing species must be chiral. A reasonable mechanism based on equations 3-5 may be put forth to explain these results. As shown below, we propose that fluoride ion may interact with 1 to give a chiral trigonal bipyramidal pentacoordinate species which can then transfer hydride to the carbonyl center to give fluorosilane and alkoxide ion. If the fluorine and hydrogen ligands were both to occupy axial positions in the reactive intermediate, as seems likely, the result should be that the fluorosilane should be formed with inversion of configuration. Subsequent displacement of fluoride by alkoxide is known to occur with retention of configuration in the absence of alcohol in the medium.⁹



Variable amounts of racemization in the final silicon product are to be expected if any of the intermediate fluorosilane is intercepted by fluoride ion to reversibly form an achiral pentavalent difluoro species prior to reaction with alkoxide ion. It is likely that other known cases of cesium fluoride-induced isomerization of fluorosilanes proceed by similar reversible formation of pentavalent intermediates.¹⁰



Finally, it is worth mentioning that the reducing species derived from 1, regardless of its exact nature, in each case transferred hydride to sterically similar enantiotopic faces of the prochiral ketones; the re faces in the cases of $2a$ and $2b$ and the si face of $2c$. Similar enantioface discriminations have been observed in the reductions of simple prochiral carbenium ions by 1 .¹¹

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References and Notes

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