Tetrahedron Letters, Vol.32, No.24, pp 2735-2736, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

THE HYDROGENATION OF FLUOROOLEFINS

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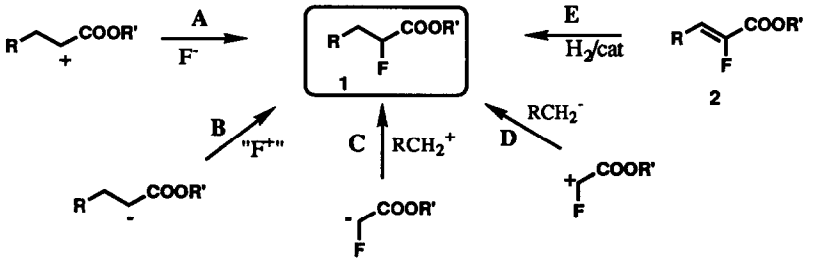
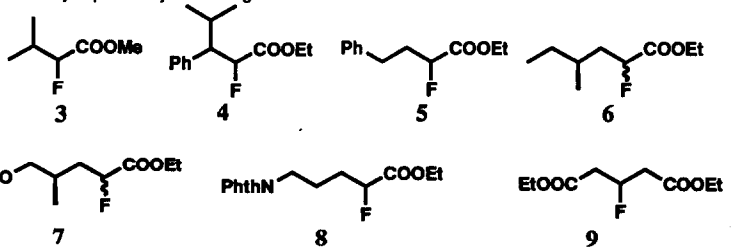
Abstract. Palladium catalysts are found to selectively hydrogenate fluoroolefins without hydrogenolytic cleavage of the carbon-fluorine bond. Since a large number of methods are available for the preparation of unsaturated organofluoro compounds this constitutes a general synthetic route to sp^3-fluorinated molecules.

There continues to be a great interest in selectively fluorinated molecules for biological application.[2] In particular, α-fluoro carbonyl compounds turned out to be useful targets and intermediates. The different pathways for the preparation of α-fluoro carboxylates **1** are shown in the following scheme. Route **A** refers to the nucleophilic displacement of α-bromo, hydroxy and amino acids using various sources of fluoride anions[3-5] whereas in route **B**, showing reversed polarity, esterenolates and their synthetic equivalents (alkylated malonates, nitro- and cyano-acetates, keteneacetals) are reacted with electrophilic fluorinating agents.[3,6-10] Since fluoroacetate anions themselve (**C**) are known to undergo direct alkylation reactions only moderately[11,12] some improvements have been reported.[13-15]To complete the scheme fluoroacetate cation equivalents (**D**) are known as well;[16] difluoroketene thioacetals (CF_2=CXSR, X=SR or OMe) react with alkyllithium reagents to give compounds **1** after hydrolysis.



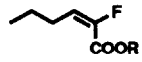
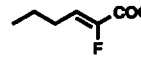
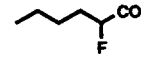
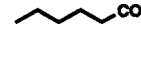
Surprisingly the catalytic hydrogenation of fluoroolefins **2** in order to get **1** (route **E**) was reported only a few times.[17-19] This may be due to the hydrogenolyic lability of vinylic fluorine compared to the saturated counterpart.[20] Since a vast variety of methods is now available for the preparation of α-fluoro-α,β-unsaturated carbonyl compounds like **2**,[21-23] we undertook a more systematic examination of hydrogenation conditions. The results for E and Z- alkyl 2-fluoro-2-hexenoates as model compounds are listed in the table.

The results clearly indicate that among all catalysts tested palladium catalysts are best in order to avoid hydrogenolytic cleavage of the carbon-fluorine bond. Compounds **3-10** represent further examples of compounds we prepared by hydrogenation of the corresponding fluoroolefins.[24] The method is not only applicable to α-fluoro-α,β-unsaturated esters and acids; for the examples **9** and **10** it is extended to β-fluoro and non conjugated systems.[26] The application of this strategy for the preparation of fluorinated dipeptide isosteres was recently reported by our collegue.[28]

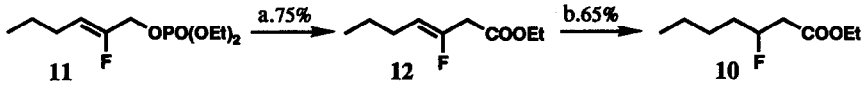


Acknowledgement: We wish to thank B. Eng for carrying out the hydrogenation experiments.

Table. Product Distribution in the Hydrogenation of 2-Fluoro-2-hexenoic Acid Esters[a]

entry	catalyst[b]						R
1	-	c.	90.5	9.5			Et
2	Pd-C	d.	-	-	99-99.4	1-0.6	Et
3	$Pd-BaSO_4$		-	-	99.6	0.4	Et
4	Rh-C	e.	-	0.26	98.6	1.2	Et
5	Rh-Alox	e.	-	3.0	93.7	3.3	Et
6	Pt-C	e.	26	13.8	13.7	46.5	Et
7	PtO_2	e.	9.3	22.6	14.2	55.9	Et
8	-	f.	9.7	90.3			Me
9	$Pd-BaSO_4$		-	-	99.75	0.25	Me
10	Pt-C	g.	-	-	12.5	87.5	Me

a. The reactions were run in ethyl acetate as solvent under atmospheric pressure of hydrogen at room temperature; compositions were determined by glc techniques using authentic samples as reference; b. 5% metal on carrier, supplied by Engelhard if not stated otherwise; c. ethyl 2-fluoro-2-hexenoate prepared using Machleidt's procedure;[21] d. different suppliers: Engelhard (4522), Johnson Matthey (Typ 56), Degussa (E 101 N/D); e. hydrogenation interrupted at approximately 100% uptake; f. methyl 2-fluoro-2-hexenoate prepared using Ishihara's procedure ;[22] g. reaction until no further hydrogen was absorbed.



a. $Pd_2(dba)_3{\cdot}CHCl_3$, PPh_3, cat. NaBr, EtOH, CO, 50°C; b. H_2/$Pd-BaSO_4$, isolated yield.

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(Received in Germany 16 January 1991)