

Configurational Stability

On the Configurational Stability of Chiral, Nonracemic Fluoro- and Iodo-[D₁]Methyllithiums

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Abstract: Enantiomerically pure fluoro- $[D_1]$ methyllithium and iodo- $[D_1]$ methyllithiums of up to 92% *ee* were generated by transmetalation of the corresponding stannanes with MeLi in THF at various temperatures. The intermediate halo- $[D_1]$ methyllithiums were trapped with benzaldehyde or acetophenone already present in excess in the reaction mixture to either give halohydrins or to disintegrate to carbene. The fluoro- $[D_1]$ methyllithiums were found to be microscopically

Introduction

Chiral, nonracemic α -heteroatom-substituted organolithiums are valuable reagents for synthesis.^[1] Their preparation, reactions, the determination of their configurational stability and mechanisms of enantiomerization, as well as their aggregation states have attracted much attention since their first observation^[2] by Stille and Sreekumar. By far the most important are organolithiums α -substituted with oxygen or nitrogen. We have accessed homochiral oxygen-^[3] [D₁]**1 a**, sulfur-^[4] [D₁]**1 b** and nitrogen substituted^[5] [D₁]methyllithiums [D₁]**1 c** and evaluated their micro- and macroscopic configurational stability (Figure 1). Chloro-^[6] and bromo-[D₁]methyllithiums,^[4] ([D₁]**1 d**) and ([D₁]**1 e**), were found to be chemically very labile at -78 °C, but configurationally stable.

Herein, we present our results for chiral fluoro- ($[D_1]$ **1** f) and iodo- $[D_1]$ methyllithiums ($[D_1]$ **1** g). While α -fluoroalkyllithiums are unknown compounds, α -fluorocyclopropyllithiums could

Figure 1. Chiral heteroatom-substituted [D₁]methyllithiums.

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configurationally stable within the tested range of -95 to 0°C, but chemically only stable at temperatures below -95°C due to a rapidly increasing portion disintegrating to carbene. The iodo-[D₁]methyllithiums were configurationally labile relative to the rate of addition to PhCHO at all temperatures tested (-95 to -30°C). Disintegration to carbene interfered as well.

be generated by bromine-lithium exchange.^[7] Unlabeled fluoromethyllithium was claimed^[8,9] not to be detectable by NMR spectroscopy at -120° C, but to give ethene, without providing experimental evidence. ICH₂M (M=Li^[10], ZnX^[11]) were prepared preferably from diiodomethane and used for syntheses. (lodomethyl)triphenyltin was found to furnish triphenylstannylmethyllithium when treated with *n*BuLi at -50 °C in Et₂O and a mixture of triphenylstannylmethyl- and iodomethyllithium in THF.^[12] Evidently, configurationally stable 1-iodoalkyllithiums and the corresponding Grignard reagents were prepared by Hoffmann's group.^[13] The structures of unlabeled carbenoids 1, their aggregation, solvation, and addition^[8,14] to alkenes have been calculated extensively, especially for FCH₂Li.^[8] Boche et al. found that the calculated barrier to planarization for FCH2-(13.6 kcal mol⁻¹) which reflects configurational stability was highest from all heteroatom-substituted carbanions (N: 11.0; O 11.0, S: 2.8; H: 3 kcal mol⁻¹).^[15] This finding could so far not be corroborated experimentally because neither chiral fluoromethyl- nor an α -fluoroalkyllithium could be generated.

Results and Discussion

To access chiral fluoro- $[D_1]$ methyllithiums we decided to prepare them from (*R*)- and (*S*)-tributylstannyl- $[D_1]$ methanol^[3,4] of 99% *ee*, by tin–lithium exchange. The reactions were optimized in the unlabeled series first. Reaction of tributylstannylmethanol (**2**)^[16] with bis(2-methoxyethyl)aminosulfur trifluoride (Deoxo-Fluor®)^[17] furnished fluoromethylstannane **3** in 68% yield (Scheme 1).

It was treated with MeLi (4 equiv) at -78 °C in THF to give fluoromethyllithium which was trapped in situ with benzaldehyde (4 equiv) to yield fluorohydrin (±)-**4** and 1-phenylethanol [(±)-**7**a] derived from benzaldehyde by addition of MeLi $\begin{array}{c} R^{1} R^{2} \\ R^{2} \\ R^{3} \\ R^{3} \\ R^{3} \\ R^{1} \\ R^{2} \\ R^{1} \\ R^{2} \\ R^{1} \\ R^{2} \\ R$

Scheme 1. Preparation of fluoromethylstannanes 3 from stannylmethanols 2.



Scheme 2. Conversion of fluoromethylstannanes 3 to fluoromethyllithiums 1 f and their in situ trapping with benzaldehyde/ketones.

(Scheme 2). The composition of the crude product as determined by ¹H NMR (400 MHz) is given in Table 1, entry 1.

Only part of the fluoromethyllithium generated in situ was converted to fluorohydrin (\pm) -4. Evidently, the remaining portion decomposed to methylene. The yield could not be improved significantly by adding lithium-complexing 12-crown-4 as ligand (Table 1, entry 2) or by replacing MeLi by MeLi-LiBr (Table 1, entry 3). When tin-lithium-exchange was performed with nBuLi/12-crown-4 (Table 1, entry 4) the yield was only 17% with a high degree of decomposition (83%), as no residual starting material could be detected. In the case of adding benzaldehyde after tinlithium exchange and aging of the intermediate fluoromethyllithium for 30 sec no fluorohydrin was formed. In all cases fluorohydrin 4 and 1-phenylethanol were isolated as a mixture inseparable by flash chromatography. In summary, our initial experiments proved that fluoromethyllithium can be generated and intercepted with benzaldehyde, despite being chemically very labile.

In the labeled series, enantiomerically pure stannylmethanols (*R*)- and (*S*)-[D₁] $2^{[3a,4]}$ were converted to (*S*)- and (*R*)-[D₁]3 in similar yields (73%) of 98% *ee* consistently, when they were first reacted with Et₂NTMS^[18] and then with Deoxo-Fluor[®]. However, omission of silylation gave fluoro-[D₁]methylstannanes with *ee* values of 88–98%. The *ee* values of the chiral, nonracemic [D₁]3 were evalu-

Table 1. Transmetalation of 3 in presence of benzaldehyde (4 equiv) in
THF at −78 °C.

Entry	Fluorohydrin (\pm)- 4 ^[a]	Stannane 3 ^[a]	Decomposition ^[a,b]
1	1.0 (38)	0.6	1.0
2	1.0 (43)	-	1.3
3	1.0 (32)	0.7	1.4
4	1.0 (17)	-	5.0

[a] The ratios of fluorohydrin (±)-4/starting fluoromethylstannane 3 and decomposition were determined by ¹H NMR spectroscopy of the crude product [(±)-4 was standardized to 1.0]; yields are given in parenthesis. [b] Calculated from difference between MeSnBu₃ and product 4 formed.

ated by converting them with lithium (*R*)-1-(2-naphthyl)ethanethiolate^[6] to diastereomeric sulfides, whose ratios were determined by ¹H NMR spectroscopy. Similarly to the experiments in the unlabeled series, MeLi was added to a mixture of fluoromethylstannane (*R*)-[D₁]**3** and benzaldehyde in THF at -78 °C without and at -70 °C with 12-crown-4. The ¹H NMR spectrum of the crude product obtained by the reaction performed at -78 °C indicated that only half of the starting stannane was transmetalated and that only 30% of the fluoro-[D₁]methyllithium formed was added to benzaldehyde to give fluorohydrin (2*S*)-[2-D₁]**4** (Table 2, entry 1).

In the case of the experiment with [12]crown-4 as ligand, all the starting material was transmetalated and only 20% of the generated FCHDLi was added to benzaldehyde (Table 2, entry 2). For the sake of clarity, it is more convenient here for the deuterated fluoro- and later for the deuterated iodohydrins as well to give the *ee* value for each chiral center individually.

Table 2. Molar ratios of starting stannanes 3, fluorohydrins 4/5/6, and MeSnBu₂ in crude products for conversion of 3 to 4/5/6 as determined by ¹H NMR spectroscopy (400 MHz). Entry Electrophile T [°C] Stannane 3 Fluorohydrin 4/5/6 MeSnBu₃ (R)-[D₁]3 (2S)-[2-D1]3 1 -78 1.0 1.1 0.3 benzaldehyde (R)-[D₁]3 (2S)-[2-D₁]4 2 -701.0 0 0.2 3 5 3 1.0 -95 1.2 1.0 acetophenone (1R)-[1-D₁]5 (S)-[D₁]3 4 -30 1.0 4.0 0.6 3 6 5 -95 1.0 0.5 1.0 *t*butylphenylketone 3 6 6 -78 1.0 0.9 0.7 (R)-[D₁]3 (1S)-[1-D₁]5 7 -78 1.0 0.2 0.4 (R)-[D₁]3 (1S)-[1-D₁]5 1.0 8 -30acetophenone 0.7 0.3 (R)-[D₁]3 (1S)-[1-D₁]5 9 0 1.0 0.1 0.1



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As the enantioselectivity of the addition of the chiral carbanion (S)-[D₁]**1 f** to benzaldehyde is zero, (*R*)- and (S)-configuration at C-1 were always formed in equal amounts, resulting in a product with zero "*ee*" at C-1, that is, racemic at C-1. The yields of labeled fluorohydrins (2S)-[2-D₁]**4** of "*ee*" >95% at C-2 were 10% and 20%, respectively. The *ee* value was determined by derivatization with (S)-Mosher chloride [(S)-MTPACI] and ¹H NMR spectroscopy (400 MHz). Similarly, reference samples of fluorohydrins^[19] (±)-**4** and (*R*)-**4** (98% *ee*) were derivatized (Figure 2).



Figure 2. Signals of CH₂F and CHDF groups in the ¹H {¹⁸F} NMR spectra (600 MHz, CDCl₃) of (*R*)-Mosher esters derived from A) (*R*)-4 of 98% *ee*; B) (*S*)-4 of 85% *ee*; C) mixture of (15,25)-[2-D₁]4·MTPA-(*R*)/(1*R*,25)-[2-D₁]4·MTPA-(*R*) = 5:3 (enrichment of one diastereomer by PTLC); *ee* value (at C-2) > 95%.

Fluoro-[D₁]methyllithium seems to be microscopically configurationally stable for the short life time between generation and addition to benzaldehyde, but chemically very labile. Transmetalation follows a retentive course.^[2,20] We assume that the same is true for the addition of FCHDLi to benzaldehyde. It was found by Reich and Phillips^[21] and others^[22] that tin ate complexes form in quantities detectable by NMR spectroscopy only under special conditions, e.g., presence of HMPA as additive in THF, increasing number of phenyl substituents at tin, and low temperature (-80 °C). Furthermore, tributyltin compounds do not favor the formation of ate complexes, which are substantially less reactive^[21] than lithium reagents. These facts indicate that salt free species or aggregates of heteroatom-substituted methyllithiums are produced, neglecting the LiF formed by decomposition of FCH₂Li.

To influence the ratio of the addition of MeLi to different electrophiles relative to transmetalation of the stannane, benzaldehyde was replaced by acetophenone (reaction conditions: stannane **3** (1 equiv), acetophenone (2 equiv), temperatures of -95 and -30 °C, one drop of MeLi (2 equiv, 1 m) per 5 sec) and *tert*-butyl phenyl ketone (-95 and -78 °C). The molar ratios of fluoromethylstannane **3**/fluorohydrin (±)-**5**/MeSnBu₃ are collected in Table 2. In all four cases (Table 2, entries 3–6) some fluoromethylstannane **3** was recovered. Furthermore, fluoromethyllithium is chemically stable at temperatures ≤ -95 °C, as the fluorohydrin and tributylmethylstannane are formed in equal molar amounts. However, at -30 °C already 40% of the fluoromethyllithium generated decomposed (ratio of fluorohydrin/tributylmethylstannane 0.6:1.0). These data show qualitatively that decomposition of fluoromethyllithium increases with increasing temperature as expected. Unlabeled (±)-**5** could be esterified with (*S*)-MTPACI under forcing conditions (DMAP, 50 °C, 9 h, 1,4-dioxane) with partial resolution of the fluorohydrin and in low yield, both of which did not influence the determination of the *ee* value in the labeled series later on.

At -95 °C, all the fluoromethyllithium formed by transmetalation was trapped by *tert*-butyl phenyl ketone. At -78 °C however, the decomposition (to carbene) already interfered with addition to ketone. FCH₂Li was only partially added to the ketone, 31% decomposed to methylene. Surprisingly, these data are similar to those for acetophenone, even though the *t*Bu group is sterically more demanding than the methyl group. As this sterically hindered alcohol could not be derivatized with (*S*)-MTPACI to test whether the Mosher ester could be used in the labeled series to determine the *ee* value, the remaining experiments were performed with acetophenone as electrophile at -78, -30, and 0 °C (Table 2, entries 7–9; Figure 3).

FCHDLi was chemically unstable already at -78 °C and disintegration increased from 60% at -78 °C to 90% at 0 °C. The yield was very low at 0 °C, but all three fluorohydrins (1*S*)-[1-D₁]**5** had 98% *ee* as determined by derivatization with (*S*)-MTPACI and ¹H NMR spectroscopy (Figure 3). These experiments prove that fluoromethyllithium is microscopically configurationally stable at all temperatures tested (-95 to 0 °C), even

Table 3. Molar ratios of starting stannanes 8, iodohydrins 10, and $MeSnBu_3$ in crude products for conversion of 8 to 10 as determined by

¹ H NMR spectroscopy (400 MHz).				
Entry	T [°C]	Stannane 8	lodohydrin 10	MeSnBu ₃
1	-78	8 14.4	10 0.7	1.0
2	-50	8 5.0	10 0.45	1.0
3	-78	(<i>S</i>)-[D ₁] 8 0.0	(2S)-[2-D ₁] 10 0.65	1.0
4	-50	(<i>S</i>)-[D ₁] 8 1.3	(2S)-[2-D ₁] 10 0.44	1.0
5	-95	(<i>R</i>)-[D ₁] 8 3.5	(2 <i>R</i>)-[2-D ₁] 10 0.72	1.0
6	-50	(<i>R</i>)-[D ₁] 8 1.4	(2 <i>R</i>)-[2-D ₁] 10 0.56	1.0
7	-30	(<i>R</i>)-[D ₁] 8 0.1	(2 <i>R</i>)-[2-D ₁] 10 0.1	1.0

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Figure 3. Signals of CH₂F and CHDF groups in the ¹H NMR spectra (400 MHz in case of A, 600 MHz in case of B, C and D, CDCl₃) of (*R*)-Mosher esters derived from A) (\pm)-**5**, B) (1*R*)-[1-D₁]**5** of 90% *ee*, 95% D₁; C) zoom of spectrum shown in B to show the peaks of the unlabeled species marked with "o" and those of the two (1*S*)-[1-D₁]diastereomers marked with "x"; D) (1*S*)-[1-D₁]**5** of 98% *ee*.

more so than the diisopropylcarbamoyloxy-substituted methyllithium.^[3] It is therefore the most configurationally stable heteroatom-substituted methyllithium.

The preparation of chiral, nonracemic iodo- $[D_1]$ methyllithiums and the determination of their configurational stability turned out to be experimentally very challenging as in the case of fluoro- $[D_1]$ methyllithiums because of low reproducibility attributed to the chemical lability of the species involved. Two preliminary experiments were performed before optimizing the experiments in the unlabeled series as before (Scheme 3).

To test transmetalation of iodomethylstannane (for preparation see Scheme 4), MeLi was added to a solution of **8** in THF at -78 °C, followed by CF₃CO₂D 30 sec later. The ¹H NMR spectrum of the crude product showed that it was a mixture of tributylmethylstannane (50%) containing no deuterium and two stannanes of unknown structure. No starting iodomethyl-



Scheme 3. Testing of transmetalation of stannane 8 and chemical stability of lithium alkoxide derived from 10.



Scheme 4. Preparation of iodomethylstannanes 8, their conversion to iodomethyllithiums 1 f and in situ trapping with benzaldehyde.

stannane could be detected. This experiment indicated that 1) tin-lithium exchange is very rapid and 2) the tributylmethylstannane (9) was formed by exchange of the iodomethyl for the Me substitutent and not by quenching of intermediate tributylstannylmethyllithium with CF₃CO₂D, formed by lithiumiodine exchange. Additionally, racemic iodohydrin $\mathbf{10}^{^{[23]}}$ was mixed with MeLi (1.5 equiv) at -78 °C and guenched with CF₃CO₂H after 5 min. The isolated product was identical (¹H NMR, TLC) to the starting iodohydrin and did not contain phenyloxirane $[(\pm)-11]$, corroborated by spiking with authentic phenyloxirane. Clearly, the lithium alcoholate formed from the iodohydrin, was stable toward ring closure, normally requiring warming up to room temperature.^[13a, 24] As such, isolation of the iodohydrin formed by addition of iodomethyllithium to benzaldehyde should not pose a problem in later experiments. Stannylmethanol 2 was converted to iodomethylstannane 8 in 89% yield, using Ph₃P/NIS^[25] (Scheme 4).

MeLi (4 equiv) was slowly added dropwise (one drop per one second) to a stirring mixture of iodomethylstannane (1 equiv) and excess benzaldehyde (4 equiv) in THF at -78 °C. After 5 min a solution of CF₃CO₂H in CH₂Cl₂ (2 M) and water (5 mL) were added. The crude product (for ratio of components see Table 3, entry 1) was purified by flash chromatography to yield iodohydrin **10** (15%) always in admixture (ca. 50%) with tin containing compounds of unknown structure, which were once removed by preparative thin layer chromatography in the labeled series to get an analytical sample of homogenous iodohydrin.

The mixture was routinely used for the preparation of the (*R*)-Mosher esters, from which the tin-containing impurities could by separated easily by flash chromatography. When the reaction was performed at -50 °C, the yield was again 15%, although the products and starting materials had different ratios (Table 3, entry 2). These two experiments demonstrate that iodomethyllithium is formed as an intermediate by Sn–Li exchange and that it was trapped by benzaldehyde to yield iodohydrin **10**. As expected, the competing addition of MeLi to benzaldehyde was predominant and part of the iodomethyl-

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lithium decomposed in a temperature dependent proportion. At -78 °C, 70% of the iodomethyllithium ended up in the iodohydrin, however at -50 °C only 45%.

We anticipated that chiral iodo-[D1]methylstannanes were prone to substitution with excess iodide in the reaction mixture, which could lead to partial racemization. To avoid this, short reaction times at temperatures as low as possible for its preparation from chiral stannyl-[D1]methanol and purification were aimed for. The optimized Mitsunobu reaction^[26] following an S_N2 mechanism was performed with tris(4-chlorophenyl)phosphine/diisopropyl azodicarboxylate/HI^[27] (solution in CH_2CI_2) in a mixture of toluene/ CH_2CI_2 at -78 °C for 20 min. The reaction was quenched with a few drops of dry methanol and immediately applied to a silica gel column kept in dim light, cooled to -78 °C in the upper part, and using an eluent also cooled to -78 °C. lodomethylstannanes (R)- and (S)-[D₁]8 were obtained from the corresponding stannylmethanols (R)and (S)-[D1]2 in yields of 64% and 55%, respectively (iodine has priority over tin in CIP nomenclature). Their enantiomeric excesses determined by combining reaction with lithium (R)-1-(2-naphthyl)ethanethiolate^[6] and ¹H NMR spectroscopy, were 86 and 92%, respectively. These iodo-[D1]methylstannanes transmetalated and the intermediate were iodo-[D₁]methyllithiums were trapped at various temperatures with benzaldehyde already present in the reaction mixture. The ratios of products in the crude reaction mixture of 5 experiments with chiral, nonracemic ICHDLi are compiled in Table 3 (entries 3-7). As can be seen easily from entries 1-5 in Table 4, the yields were low and part of the starting material was not consumed, but the deuterated iodohydrins were not racemic at C-2 (but at C-1) as determined by ¹H NMR spectroscopy of their (R)-Mosher esters.

Table 4. Ge [D ₁]methyllin drins [D ₁] 10	neration and tra thiums (<i>R</i>)- and (<i>S</i>)-[[pping of c D ₁] 1 g with PhC	hiral, nonracemic CHO in THF to give io	iodo- odohy-
Entry	[D ₁] 1 g Conf./ <i>ee</i> [%]	Temp. [°C]	[D ₁] 10 Conf./ <i>ee</i> [%]	Yield [%] ^[a]
1	(S)/92	-78	(S)/49	55
2	(S)/92	-50	(<i>S</i>)/33	27
3	(<i>R</i>)/84	-95	(<i>R</i>)/61	22
4	(<i>R</i>)/84	-50	(<i>R</i>)/33	22
5	(<i>R</i>)/84	-30	(<i>R</i>)/28	9
[a] Mixture of iodohydrin and tin-containing impurity (1:1).				

The "ee" at C-2 of the five halohydrins decreased with increasing the temperature (Table 4). Surprisingly, the "ee" was still 28% at -30 °C starting from an iodo-[D₁]methylstannane of 84% ee (Table 4, entry 5). Despite the short lifetime of the iodo-[D₁]methyllithium, part of the molecules enantiomerized (Figure 4). Therefore, they are microscopically configurationally labile, contrary to the fluoro-, chloro-, and bromomethyllithiums. We assume that addition of these species to benzalde-hyde follows a retentive course. The rate of desintegration of iodomethyllithiums, which are also carbenoids, increased with



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Figure 4. Signals of CH₂I and CHDI groups in the ¹H NMR spectra (400 MHz, toluene-D₆) of (*R*)-Mosher esters derived from A) (\pm)-**10**; B) (2S)-[2-D₁]**10** of 49% *ee* (at C-2); C) (2*R*)-[2-D₁]**10** of 61% *ee* (at C-2). Signals of B) and C) broadened by deuterium coupling.

increasing temperature, as judged from the ratio of tributylmethylstannane and iodohydrin.

Conclusion

In conclusion, we present our findings on the microscopic configurational stability (configurational stability relative to the addition to benzaldehyde or acetophenone) of enantiomerically pure fluoro-[D1]methyllithiums prepared by tin-lithium exchange in the presence of excess benzaldehyde or acetophenone. Only part of the fluoromethylstannane was transmetalated as addition of MeLi to the electrophiles interfered. Depending on the reaction temperature, a portion of the generated fluoro-[D1]methyllithiums was added to the electrophiles to give fluorohydrins, the remaining portions disintegrated to carbene and LiF. Fluoro-[D₁]methyllithiums were found to be configurationally stable up to 0°C relative to the addition to acetophenone. At that temperature, carbene formation was heavily interfering, which could be avoided when keeping the temperature below -95 °C. lodo-[D₁]methyllithiums prepared similarly from tributyl-(iodo-[D1]methyl)stannanes of up to 92% ee were found to be configurationally labile relative to the addition to benzaldehyde at all temperatures investigated (-95°C to -30 °C). The rate of disintegration of ICHDLi to deuterated carbene and Lil increased significantly with increasing temperature.

Experimental Section

General procedure for the generation and addition of fluoromethyl- (1 f) and (*S*)-fluoro-[D₁]methyllithium {(*S*)-[D₁]1f} to benzaldehyde - (\pm)-2-fluoro-1-phenylethanol [(\pm)-(4)] and (1*R*/*S*,2*S*)-2-fluoro-1-phenyl-[1-D₁]ethanol {(2*S*)-[2-D₁]4}

A solution of tributyl(fluoromethyl)stannane **3** (97 mg, 0.30 mmol), (for entries 2 and 4: a stoichiometric amount of [12]crown-4 rela-

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tive to MeLi or nBuLi), and freshly distilled benzaldehyde (127 mg, 121 μ L, 1.2 mmol) in dry THF (1.5 mL) was cooled to the respective temperature under argon. MeLi [Entry 1, 0.75 mL, 1.6 M solution in Et₂O, 1.20 mmol; entry 3: 4 equivalents MeLi·LiBr (1.5 м, in Et₂O) relative to fluoromethylstannane instead of MeLi; entry 4: 4 equiv of nBuLi (1.6 м in hexanes)] was slowly added drop by drop. The mixture was stirred for 10 min at bath temperature before addition of water (3 mL). The organic phase was separated, the aqueous one extracted with Et₂O, and the combined organic layers were dried (MgSO₄). After removal of the solvent under reduced pressure, the crude product was in some cases purified by flash chromatography (CH₂Cl₂, $R_f = 0.24$). The other experiments of Table 1 were performed with similar quantities of 3 analogously, except for the changes given in the Table. The ratios of compounds in the crude products were evaluated by ¹H NMR spectroscopy and the yields calculated accordingly (Table 1). As 1-phenylethanol (major portion) and (relatively volatile) fluorohydrin 4 had the same R_{fr} both were isolated as a mixture. Signals of labeled or unlabeled $^{\scriptscriptstyle 5}$ fluorohydrin 4 could be seen in the ¹H NMR spectrum.

Similarly, fluoro- $[D_1]$ methylstannane (*R*)- $[D_1]$ **3** (0.105 g, 0.32 mmol) gave a crude mixture of (*R*)- $[D_1]$ **3**, fluorohydrin (2*S*)- $[2-D_1]$ **4**, MeSnBu₃, benzaldehyde, and 1-phenylethanol {ratio in Table 2, Entry 1; 0.230 g, calculated yield of (2*S*)- $[2-D_1]$ **4**: 10%} at -78 °C.

Similarly, fluoro- $[D_1]$ methylstannane (*R*)- $[D_1]$ **3** (0.105 g, 0.32 mmol) gave a crude mixture of (*R*)- $[D_1]$ **3**, fluorohydrin [(2*S*)-[2- D_1]**4**, MeSnBu₃, benzaldehyde, and 1-phenylethanol {ratio in Table 2, Entry 2; 0.210 g, calculated yield of (2*S*)- $[2-D_1]$ **4**: 20%} at -70° C, and in presence of [12]crown-4 (0.226 g, 1.28 mmol).

Full experimental procedures and spectroscopic data, copies of NMR spectra.

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