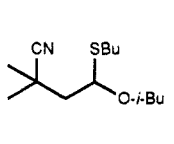
nation to form 4. Notably, only the 5-*exo* ring closure can lead to regeneration of the thiyl radical.

In support of this mechanism, the minor byproducts **10**, **11**, and **12** have been isolated from a reaction employing 1 equiv of dibutyl disulfide. The formation of these byproducts was minimized by using minimum amounts of dibutyl disulfide.



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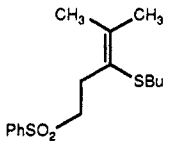

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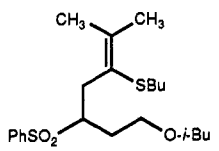

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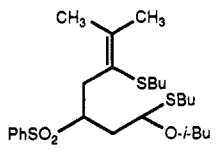

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These mild reaction conditions should be tolerant of many functional groups. Because the reaction is effective with equimolar amounts of unactivated olefins, this and related reactions should be useful for the annulation of complex molecules. Radical chain reactions employing an addition–series of reactions–fragmentation sequence seem ideally suited for accomplishing intricate processes because the intermediate radicals are permitted long lifetimes while the chain transfer is very fast.[11] A wide range of methylenecyclopropanes may undergo similar reactions,[12] and there is potential for influencing the reaction's stereochemistry through the choice of catalyst. We are continuing to study the intriguing features of this reaction.

Acknowledgment is made to the Robert A. Welch Foundation and the donors of The Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Supplementary Material Available: Experimental procedures and spectral data for **1**, **2**, **4**, and **13–18** (4 pages). Ordering information is given on any current masthead page.

(11) For a discussion of ideality in free-radical chain reactions, see ref 4a, p 499.

(12) We have observed that the parent 2-(phenylsulfonyl)-1-methylenecyclopropane also annulates olefins in good yield. These studies will be reported in due course.

The Stereoselective Construction of (*Z*)-3-Aryl-2-fluoroalkenoates

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Summary: The use of 2,4,6-trimethylphenyl α-silyl-α-fluoroacetate in the Peterson olefination reaction leads to the highly stereoselective formation of (*Z*)-3-aryl-2-fluoroalkenoates via an aldol reaction most likely proceeding through an open transition state since stereocontrol of the enolate geometry was not possible.

Even though the stereoselective construction of 2-fluoroalkenoates may have broad general applicability in the preparation of biologically active materials[1] such as prostaglandins,[2] insect sex pheromones,[3] or steroids,[4] there are relatively few methods available for the synthesis of 2-fluoroalkenoate building blocks[5] or monofluoroalkenes generally.[6]

Table I. Products of Peterson Olefination Reaction of the Lithium Enolate of Ethyl α-(Trimethylsilyl)-α-fluoroacetate

$LiC(Si(CH_3)_3)FCO_2CH_2CH_3 + RR'CO \rightarrow RR'C{=}CFCO_2CH_2CH_3$

R	R′	*E*:*Z* stereoselectivity[a]
H	4-CH_3Ph	1:1.4
H	C_2H_5	1:4.0
H	Ph	1:2.7

[a] Determined by ^{19}F NMR spectroscopy.

Results and Discussion

We have found that α-fluoro-α-silylacetates **1** can be utilized in a highly stereoselective Peterson olefination procedure[7,8] to form (*Z*)-3-aryl-2-fluoroalkenoates and a

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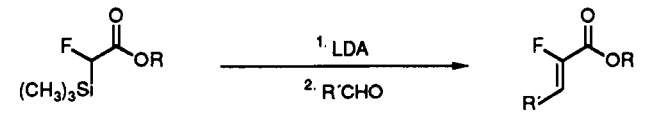
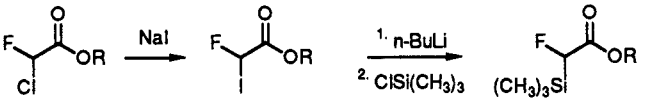
(*E,Z*)-2-fluoroalkadienoate **2**. Previously as part of a



1 **a** R = CH_2CH_3
b R = 2,6-di-*t*-butyl-4-methylphenyl
c R = 2,4,6-trimethylphenyl

2

program to determine the effect of fluorination on the reactivity of enolates we have reported the reactions of lithium enolates of fluorinated esters,[9] amides,[10] and ketones[11] with carbonyl compounds. Chlorotrimethylsilane treatment of the ester or amide enolates, formed by deprotonation with lithium amide bases, generally gave only low yields of a mixture of silylated products including the silyl ketene acetals. In contrast, however, deprotonation of allylic fluoroacetates with lithium diisopropylamide (LDA) gave high yields of C-silylated materials.[12] From previous work it was apparent that the conjugate acid of the amide base could interfere in the reaction of fluoroacetates.[13] Additionally, it has been reported that zinc enolates prepared from α-fluoro-α-bromoacetates gave exclusively the silyl ketene acetal in high yield.[14] Other workers have shown that acetate enolates generally react to form C-silylated products.[15] In order to improve the preparation of the necessary α-fluoro-α-silylacetates, ethyl α-fluoro-α-iodoacetate **4a** was prepared by simple Finkelstein reaction of ethyl α-chloro-α-fluoroacetate,[16] **3a**. Transmetalation of **4** with *n*-butyllithium in THF at −100 °C yielded a solution of an anion that cleanly underwent directed aldol condensation with aldehydes and ketones. The diastereoselectivity and the yields of the reactions were nearly identical with that previously reported.[9a]



3a **4a** **1a**

Table II. Products of Peterson Olefination Reaction of the Lithium Enolate of 2,4,6-Trimethylphenyl α-(Trimethylsilyl)-α-fluoroacetate

$LiC(Si(CH_3)_3)FCO_2TMP + RR'CO \rightarrow RR'C{=}CFCO_2TMP$

R	R'	% yield[a]	*E:Z* stereoselectivity[b]
H	furyl	40	1:50
H	PhCH=CH	28	1:11
H	naphthyl	73	1:16
H	4-CH_3OPh	90	1:32
H	4-CH_3Ph	33	1:40
H	2-CH_3Ph	63	1:13
H	$(CH_3)_3C$	55	1:24
H	C_6H_{13}	50	1:1.4
CH_3	C_5H_{11}	51	1:1
H	Ph	49	1:29
Ph	Ph	25	-
C_3H_7	Ph	82	1:1.3

[a] Isolated yield. [b] ^{19}F NMR spectroscopy.

Chlorotrimethylsilane quenching of a THF solution of the anion, formed by transmetalation, yielded a mixture of O- and C-silylated products. This was surprising in light of Burton's work where exclusive O-silylation occurred with zinc enolates and our own findings of C-silylation with the lithium enolate of allylic fluroacetates. The use of methyllithium–lithium bromide complex in diethyl ether was ineffective at promoting transmetalation while the use of *tert*-butyllithium afforded no improvement in yield or selectivity. The addition of hexamethylphosphoramide to the reaction media was also fruitless. However when pentane and *n*-butyllithium were used for the transmetalation, the ratio of C-silylated to O-silylated products was as high as 18:1. Deprotonation of the resultant ethyl α-fluoro-α-silylacetate with LDA at −78 °C followed by addition of an aldehyde and warming to −40 °C yielded a mixture of (*E*)- and (*Z*)-2-fluoroalkenoates.

The selectivity of the Peterson olefination reaction is directly related to the diastereoselectivity of the aldol process which may in turn be dependent upon control of enolate geometry, which has proven extremely difficult to control in the deprotonation of fluoroacetates. The highest diastereoselectivity in the aldol reaction of fluoroacetates[9c] found to date occurs when the 2,6-di-*tert*-butyl-4-methylphenyl (BHT) esters introduced by Heathcock[17] are employed. The BHT α-chloro-α-fluoroacetate, **3b**, was prepared in the usual manner following preparation of α-chloro-α-fluoroacetyl chloride available from the acid formed on hydrolysis of the ethyl ester.[18] Unfortunately under all conditions examined the Finkelstein reaction failed, presumably as a result of the steric hindrance afforded by the flanking *tert*-butyl groups. However, the Finkelstein reaction proceeded smoothly on the slightly less sterically demanding 2,4,6-trimethylphenyl α-chloro-α-fluoroacetate[19] to yield the crystalline iodide.[20]

(8) General procedure for the synthesis of fluoro olefins. To 50 mL of anhydrous THF containing 3.15 mmol, of lithium diisopropylamide under an argon atmosphere at −100 °C was added 2.15 mmol of 2,4,6-trimethylphenyl α-fluoro-α-trimethylsilylacetate dissolved in 5 mL of anhydrous THF at such a rate that the temperature did not exceed −100 °C. The mixture was allowed to stir 5 min, and then the appropriate aldehyde (1.1 equiv) was quickly added dissolved in a minimum amount of THF. The temperature of the reaction mixture was allowed to warm to −10 °C at which time the reaction mixture was quenched by pouring the mixture thru a short column of silica gel. The crude product eluted from the column with dichloromethane. On evaporation of the solvent, the crude material was dissolved in ether washed with sodium bisulfite to remove unreacted aldehyde (3 × 20 mL) and followed by brine (20 mL). After drying (magnesium sulfate), concentration in vacuo yielded the crude 2-fluoroalkenoate. The crude material was purified by recrystallization or chromatography as appropriate.

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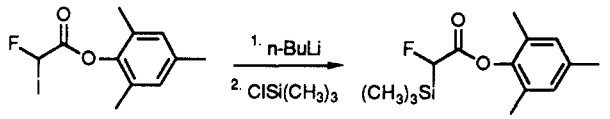
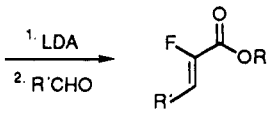
(18) After the method of Takeuchi, Yoshio, Toyama Medical University, private communication. To 10.0 g (0.0712 mol) of ethyl α-chloro-α-fluoroacetate was added 125 mL of 1 N HCl. The resultant mixture was heated under reflux overnight; on cooling to room temperature, the mixture was made basic to litmus paper by the addition of solid sodium hydroxide. Following extraction of the basic solution with 4 portions (25 mL) of ethyl acetate, the mixture was acidified with concentrated HCl. The product α-chloro-α-fluoroacetic acid was isolated by extraction with ethyl acetate (4 portions, 25 mL each). After drying ($MgSO_4$), the ethyl acetate was removed by cautious distillation through a Vigreux column. The residue was distilled (bp 78–82 °C at 5 mm) to yield 2.39 g (30%) of α-chloro-α-fluoroacetic acid.

Transmetalation and silylation were easily effected to yield the TMP α-silyl-α-fluoroacetate which was easily purified by bulb-to-bulb distillation.[21] Deprotonation with LDA at −100 °C followed by addition of the aldehyde yielded on warming to −40 °C the (*Z*)-2-fluoroalkenoate with excellent stereoselectivity[22] in most cases. To test the stability of the products to the reaction conditions, an *E*/*Z* mixture of 2-fluorononenoates was treated with LDA at 0 °C for 1 h, conditions more rigorous than those of the reaction. The *E* to *Z* olefin ratios were unchanged under these harsh circumstances. This selectivity is in sharp contrast to the lack of selectivity previously reported in the reaction of *tert*-butyl α-silyl-α-chloroacetates.[23]

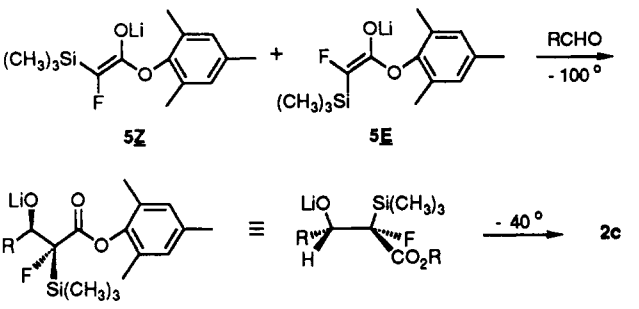


4c 1c



2c

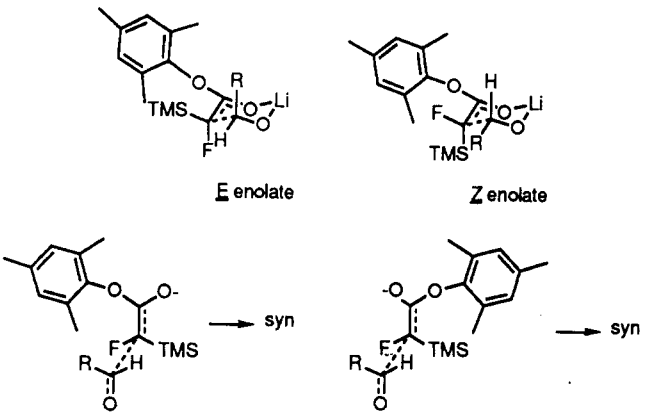
Low-temperature ^{19}F NMR[24] spectroscopy of a solution of the anion **5** indicated that there was a mixture of enolates present. The relative proportion of the two enolates formed was invariant over the temperature range −80 to −40 °C. When benzaldehyde was added to the enolate mixture at −40 °C, olefin formation, and disappearance of the resonances attributed to the enolates, was immediate and the selectivity was equivalent to that reported in Table II. The remarkable preference for formation of the *Z* olefin requires an equally high bias for formation of the



5Z 5E

6 2c

syn[25] aldolate **6** if the commonly accepted syn elimination mechanism for the Peterson olefination reaction is invoked.[7a] Thus we tentatively propose that the high selectivity of the olefination reaction implies that a closed transition state[26] is not likely to be involved in the aldol reaction but rather that the reaction occurs via an open transition state of the type proposed by Noyori[27] where enolate geometry is not important. The bulk of the trimethylsilyl group controls the approach of the aldehyde with the result that only the required syn aldolate is formed irregardless of the enolate geometry.



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Supplementary Material Available: Experimental data for compounds in this paper (5 pages). Ordering information is given on any current masthead page.

(19) **3c** may be prepared in the following manner. To 8.47 g (0.075 mol) of α-chloro-α-fluoroacetic acid was added 18.02 g (1.2 equiv, 0.090 mol) of phthaloyl chloride. The mixture was heated together under reflux for 4 h and then was distilled (bp 65–67 °C) to yield 8.58 g (88%) of the α-chloro-α-fluoroacetyl chloride. 2,4,6-Trimethylphenol (3.63 g, 0.032 mol) dissolved in 50 mL of THF, which had been deprotonated at 0 °C with *n*-butyllithium (0.038 mol., 15.4 mL of a 2.5 M solution in hexane), was treated dropwise with α-chloro-α-fluoroacetyl chloride (5.00 g, 0.038 mol) at 0 °C. The mixture was allowed to warm to room temperature overnight with stirring. The reaction was quenched with saturated ammonium chloride (20 mL) and was extracted with ether (4 portions, 20 mL each). The combined organic extracts were washed with saturated sodium bicarbonate (4 portions, 20 mL each) and brine (20 mL) and were concentrated to yield 5.21 g (85%) of **3c**.

(20) mp 65–66 °C.

(21) bp 90–110 °C at 0.025 mm.

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(24) ^{19}F NMR δ −220 and −218 ppm.

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A Simple Method for Producing Cycloalkenyllithiums from Cycloalkanones via Reductive Lithiation of Enol Phenyl Thioethers

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Received May 29, 1990

Summary: Cyclohexenyl, cycloheptenyl, and cyclooctenyl phenyl sulfides, readily prepared from the corresponding cycloalkanones, are reductively lithiated by lithium *p,p'*-di-*tert*-butylbiphenylide to produce cycloalkenyllithiums in good yields.

Until recently, there has been virtually only a single method to generate the very synthetically useful cyclo-

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