*Tetrahedron* Vol. 47, No 9, pp 1629-1648, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00


# CARBENOID ENTRY INTO TRIFLUOROMETHYLATED MOLECULES: PREPARATION OF FUNCTIONALIZED $CF_3$-CONTAINING $\gamma,\delta$-UNSATURATED CARBOXYLIC ESTERS BY RHODIUM-CATALYZED REACTION OF ETHYL 3,3,3-TRIFLUORO-2-DIAZO-PROPIONATE WITH ALLYLIC SULFIDES AND THEIR FURTHER FACILE CONVERSION TO TRIFLUOROMETHYLATED CONJUGATED DIENOIC ESTERS

Guoqiang Shi, Yuanyao Xu* and (in part)Ming Xu[1]

Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Academia Sinica, 345 Lingling Lu, Shanghai 200032, China

(*Received in Japan* 6 *August* 1990)

**Abstract:** The [2,3]-sigmatropic rearrangement of sulfonium ylides derived from rhodium-catalyzed decomposition of ethyl 3,3,3-trifluoro-2-diazo-propionate in the presence of allylic sulfides affords a variety of functionalized $CF_3$-containing $\gamma,\delta$-unsaturated carboxylic esters which have been further converted to synthetically useful trifluoromethylated dienoic esters via the dehydrosulfenylation sequence. For the synthetic application, a novel fluorinated retinoid was synthesized.

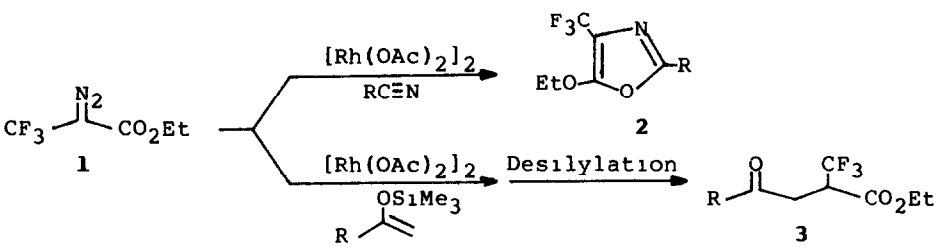
## Introduction

The biological activity of many trifluoromethyl-substituted compounds has resulted in considerable effort in the development of synthetic routes to compounds of this category.[2] The synthesis of specifically trifluoromethylated materials is an ongoing area of research, which, on one hand, has led to innovative method for introducing a $CF_3$ group to the aromatic compounds by direct trifluoromethylation and, on the other hand has revealed a conspicuous lack of appropriate means for constructing various $CF_3$-containg aliphatic compounds. For example, trifluoromethylation of aromatics could be achieved rather readily with a variety of methods most notably by using trifluoromethyl copper and related organometallics[3] and by transformations of trichloromethyl group with hydrogen fluoride and carboxyl group with sulfur tetrafluoride.[4] However, although a few methods[5] are available for the direct introduction of $CF_3$ group into aliphatic molecules, new approaches that allow access to trifluoromethylated aliphatic compounds under mild conditions and with a tolerance of functionalities are still highly desirable. As a result, the preparation of $CF_3$-containing intermediates and their utilization as building blocks has become an important strategy for the construction of

trifluoromethylated aliphatic molecules. In this context, a limited number of intermediates are known as useful $CF_3$-containing building blocks,[6] however, most of them tend to have restricted reactivities and applicabilities either because of their limited availability or because of the frustrating fact that the carbon-carbon bond formation on a trifluoromethyl substituted anionic or cationic carbon is problematic due to the propensity of fluorine towards $\beta$-elimination or due to its high electronegativity.

Very recently, we have found an easy preparation of a $CF_3$-containing diazo compound, ethyl 3 3,3-trifluoro-2-diazo-propionate(**1**), from readily obtainable starting materials and demonstrated its feasibility for the production of a reactive $CF_3$-substituted carboethoxy carbenoid by rhodium catalysis and its utilization for the synthesis of trifluoromethylated oxazole derivatives[7] (**2**) and 1,4-dicarbonyl compounds[8] (**3**)(Scheme 1). In

Scheme 1



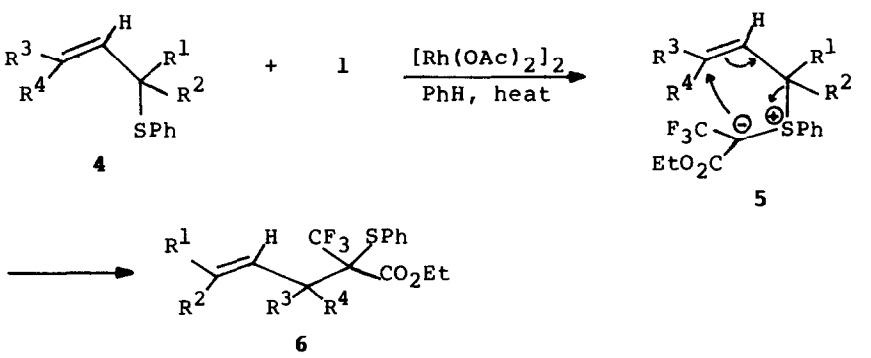

these reactions, compound **1** has manifested itself as a viable source of a $CF_3$-substituted carbenoid which has the normal reactivities characteristic of those already widely employed in many transformations and, what is more, possesses a functionalizable ester group. In attempts to expand the scope of its further synthetic utilities based on the broad spectrum of synthetically useful transformations that could be carried out with diazo compounds,[9] we have explored the reaction of **1** with a variety of allylic sulfides catalyzed by rhodium(II) acetate and the further transformation of the products thus obtained. Herein, we report the details of our investigation.

## Results and Discussion

**[2,3]-Sigmatropic Rearrangement of Allylic Sulfonium Ylides Derived from Rhodium-Catalyzed Decomposition of 1 in the Presence of Allylic Sulfides.** The Symmetry allowed [2,3]-sigmatropic rearrangement of sulfur ylide is widely recognized as a facile bond reorganization process; and it has undergone a renaissance with the discovery of metal complexes, rhodium(II) acetate in particular, as highly effective catalysts for the

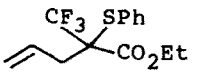
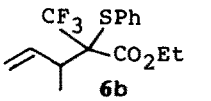
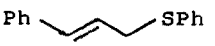
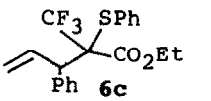
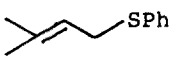
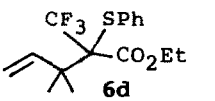
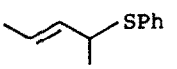
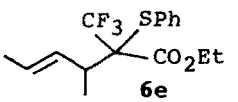
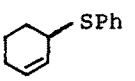
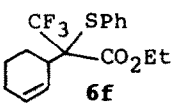
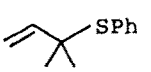
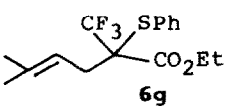
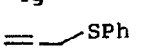
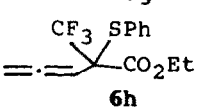
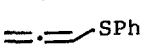
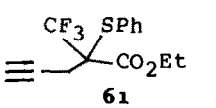
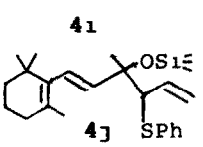
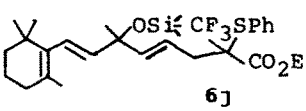
ylide generation in lieu of the widely employed base promoted methodologies.[9,10] For the synthetic manipulation of **1** modeled after this rearrangement reaction, a variety of allylic sulfides were prepared by ordinary sulfenylation methods or by the addition of the allyl sulfide to a carbonyl compound.[11] The [2,3]-sigmatropic rearrangement was then carried out by first stirring a mixture of an allylic substrate and a catalytic amount of rhodium(II) acetate in dry benzene until the solution became homogeneously purplish red, introducing 1.1-2.0 equivalents of diazo compound **1** and then heating the reaction mixture to the temperature at which a smooth nitrogen evolution was maintained. In all cases, the reaction was completed within one hour and afforded the trifluoromethylated products **6** resulting from the expected [2,3]-sigmatropic rearrangement of the sulfur ylide **5** derived from the entrapment of the $CF_3$-substituted carboethoxy carbenoid intermediate by the divalent sulfur compound **4** (Scheme 2).

Scheme 2




The reaction was successful with a wide range of substrates and the results were summarized in Table 1. As can been seen from the Table, besides simple allylic sulfides, the structurally analogous propargyl and allenyl sulfides can also successfully trap the carbenoid intermediate and subsequently undergo the symmetry-allowed [2,3]-sigmatropic rearrangement. Furthermore, the reaction can be extended to a more complex allylic substrate **4j** which also possesses nonallylic double bonds and a protected hydroxy group(Table 1, entry 10). This case serves to demonstrate that, by having an allylic sulfide moiety in a complex molecule, a rapid entry into the rearrangement products can be obtained, in which a biologically important $CF_3$ group is incorporated along with an ester moiety capable of further synthetic elaboration.

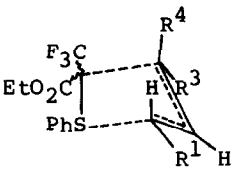
Table 1. Products from Rhodium(II) Acetate Catalyzed Reaction of **1** with Allylic Sulfides

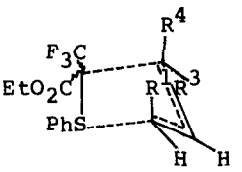
| Entry | Allylic Sulfides **4** | Reaction Conditions equiv. of **1**,[a] T(°C)/t(h) | | Products **6**[b] | Yield[c] (%) |
|---|---|---|---|---|---|
| 1 |  **4a** | 1.2 | 68/0.4 |  **6a** | 96 |
| 2 |  **4b** | 1.2 | 65/0.4 |  **6b** | 97 (24:76) |
| 3 |  **4c** | 1.1 | 70/0.4 |  **6c** | 99 (22:78) |
| 4 |  **4d** | 1.2 | 65/0.5 |  **6d** | 95 |
| 5 |  **4e** | 1.3 | 45/0.5 |  **6e** | 98 (28:72) |
| 6 |  **4f** | 1.4 | 55/0.5 |  **6f** | 93 (36:64) |
| 7 |  **4g** | 1.8 | 35/0.6 |  **6g** | 80 |
| 8 |  **4h** | 1.3 | 60/0.5 |  **6h** | 85 |
| 9 |  **4i** | 2.0 | 35/0.7 |  **6i** | 82 |
| 10 |  **4j** | 1.8 | 40/0.6 |  **6j** | 90 (32:68) |

a) Mole equivalent based on **4**. b) All products were fully characterized by $^{1}H$ NMR, $^{19}F$ NMR, IR, MS and C, H, F elemental analyses. c) Isolated product yield based on **4** (ratio of diastereoisomers determined by $^{19}F$ NMR and/or $^{1}H$ NMR given in parentheses).

Since allylic sulfides tend to compete with the diazo compound for available coordination sites on the rhodium catalyst and hence cause a deactivation of the catalyst to various extent depending on the complexing ability of the sulfides, the reaction temperatures have been found to vary with the structure of the substrates. Thus, in the cases of less hindered sulfides(for instance, entry 1-4 in Table 1) which tend to combine with the catalyst more strongly, higher reaction temperatures than those in the cases of more hindered substrates(for instance, entry 7,10 in Table 1) were required in order to make the catalytic decomposition of 1 become more favorable. The exceptionally low reaction temperature required in the case of allenyl sulfide seems not to be resulted from the steric hindrance but from the diminished complexing ability of sulfur caused by the substitution of a more electronegative $sp^2$ carbon.

In the case where the allylic sulfide has an $\alpha$-alkyl substituent. (Table 1, entry 5 and 10), the rearrangement leads to the exclusive formation of a product with the newly formed double bond in a trans configuration. This stereospecificity has also been observed in a number of related [2,3]-sigmatropic rearrangement systems[12] and can be rationalized by invoking a five membered ring transition state with the $\alpha$-substituent preferentially occupied at the equatorial position.[13] Moreover,



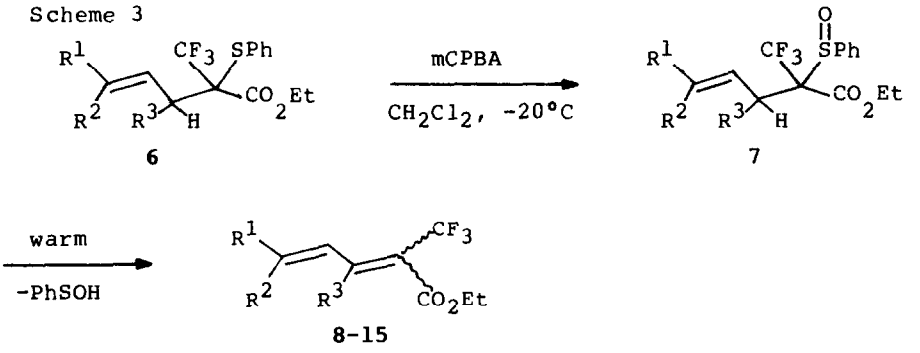

diastereoselectivity has been observed in the reactions which produce a product with two chiral centers. The diastereoisomeric ratios have been determined by $^{19}F$ NMR and/or $^{1}H$ NMR measurement based on the different chemical shift of each diastereoisomer and they appeared to be comparable with those obtained from the rhodium-catalyzed reactions of ethyl diazoacetate with allylic amines and allylic oxygen ethers.[13,14,15]

**Conversion of the Rearrangement Products 6 to Trifluoromethylated Dienoic Esters.** The multifunctionality possessed by the rearrangement products **6** has brought about many possibilities for their further transformation to other synthetically valuable $CF_3$-containing intermediates. We have chosen to evaluate the synthetic potential of **6** by applying the dehydrosulfenylation sequence which involved the oxidation of the sulfide to sulfoxide followed by a syn elimination of sulfenic acid so that a variety of $\alpha$-trifluoromethyl-substituted conjugated

dienoic esters were easily obtained which have been otherwise difficult to prepare and nevertheless are reminiscent of the popularity enjoyed by their nonfluorinated counterparts in the field of synthetic organic chemistry.[16]

The oxidation of sulfides to sulfoxides is a relatively facile transformation for which many reagents have been employed, notably sodium metaperiodate and m-chloroperbenzoic acid (mCPBA).[16] However, because of the steric hindrance and the electronic effect exerted on the sulfur atom that caused by the geminal substitution of a $CF_3$ group, oxidation of **6** with sodium metaperiodate failed to afford any fruitful results and treatment of a methylene chloride solution of **6** with mCPBA at -78°C only gave rise to a very sluggish reaction although the same reaction conditions led to a rapid oxidation of their nonfluorinated counterparts.[17] Fortunately, the situation with the latter was easily ameliorated upon raising the reaction temperature from -78°C to -20°C. At this temperature, the oxidation took place smoothly and was completed within several hours. The double bond at $\gamma$-position of **6**, which might have been expected to react in competition for the peracid, appeared to be rendered inert presumably by the inductive effect transmitted from the $\alpha$-carbon which has been substituted by three highly electron-withdrawing

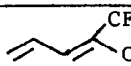
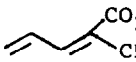
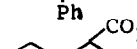
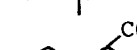
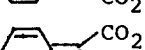
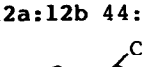
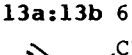
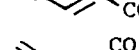
Scheme 3




groups. However, a remote double bond such as that in the case of compound **6j** has been found to be unable to survive during the oxidation step. Thus, the reaction of **6j** with mCPBA followed by eliminative desulfinylation resulted in a product with the cyclohexene ring epoxidized (Table 2, entry 8).

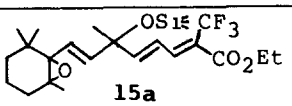
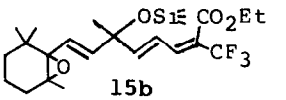
It should be noted that all the sulfoxide intermediates **7** produced are quite thermally labile and undergo elimination readily. In some cases the elimination step was virtually completed during the work up of the

Table 2 Preparation of α-Trifluoromethyl-substituted Conjugated Dienoic Esters and Their NMR Spectral Data

| Entry | Sulfides 6 | Equiv.of mCPBA[a] | Products[b] | Yield[c] (%) | Spectral Data $^{19}F$ NMR ($CCl_4$)[d] | $^1H$ NMR($CDCl_3$) γ-H, | β-H |
|---|---|---|---|---|---|---|---|
| 1 | **6a** | 1.2 |  **8a** | 77 | -18.8 | 6.97 | 7.48 |
| | | |  **8b** | | -13.5 | 7.39 | 7.07 |
| | | | **(8a:8b** 58:42) | | | | |
| 2 | **6b** | 1.5 |  **9a** | 89 | -20.8 | 6.61 | — |
| | | |  **9b** | | -22.6 | 6.88 | — |
| | | | **(9a:9b** 75:25) | | | | |
| 3 | **6c** | 1.6 |  **10a** | 95 | -12.1 | 6.90 | — |
| | | |  **10b** | | -12.6 | 6.97 | — |
| | | | **(10a:10b** 22:78) | | | | |
| 4 | **6e** | 1.5 |  **11a** | 90 | -21.0 | 6.35 | — |
| | | |  **11b** | | -22.3 | 6.57 | — |
| | | | **(11a:11b** 69:31) | | | | |
| 5 | **6f** | 1.7 |  **12a** | 90 | -21.4 | 6.42 | — |
| | | |  **12b** | | -22.4 | 6.58 | — |
| | | | **(12a:12b** 44:56) | | | | |
| 6 | **6g** | 1.5 |  **13a** | 75 | -18.3 | 6.52 | 7.85 |
| | | |  **13b** | | -13.0 | 7.01 | 7.42 |
| | | | **(13a:13b** 65:35) | | | | |
| 7 | **6i** | 1.2 |  **14a** | 77 | -15.3 | — | 7.08 |
| | | |  **14b** | | -12.5 | — | 6.65 |
| | | | **(14a:14b** 82:18) | | | | |

To be continued on the following page

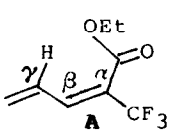
Table 2 continued

| Entry | Sulfides 6 | Equiv.of mCPBA[a] | Products[b] | Yield[c] | Spectral Data $^{19}F$ NMR ($CCl_4$)[d] | $^1H$ NMR($CDCl_3$) $\gamma$-H | $\beta$-H |
|---|---|---|---|---|---|---|---|
| 8 | **6j** | 2.5 |  **15a** | 66 | -19.6 | 6.78 | 7.45 |
| | | |  **15b** | | -13.8 | 7.29 | 7.09 |
| | | | **(15a:15b** 65:35) | | | | |

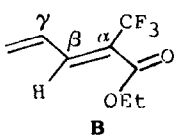
a) Mole equivalent based on **6**. b) For entry 1, 6, 7 and 8, the two geometric isomers were separated by flash column chromatography and for the rest entries, they were obtained as a mixture. All products were fully characterized by $^1H$ NMR, $^{19}F$ NMR, IR, MS and C, H, F elemental analyses. c) Total isolated yield of the two isomers based on **6**. d) Trifluoroacetic acid ( $\delta$ 0.00)was used as an external standard and downfield shifts were designated as negative.

oxidation reaction; and in others a brief warming of the crude oxidation product in $CCl_4$ could effect the complete elimination of sulfenic acid. Compared with the elimination temperature required for simple $\alpha$-sulfinyl carbonyl compound, the enhanced facilitation of the present elimination process is explicable in terms of the conjugative stablization of the incoming double bond synergistically conferred by the carbonyl group and the innate carbon-carbon double bond and the effect of enhanced dipole-dipole interactions exerted by a highly electron-withdrawing $CF_3$ group on the energy and conformation of the ground state of the sulfoxide.

The elimination product has been found to consist of a pair of geometric isomers for which the Z/E ratio and the stereochemistry of the newly introduced double bond have been determined on the basis of $^1H$ NMR and $^{19}F$ NMR spectroscopic analyses. It was found that for each pair of isomers, the $^1H$ NMR signal of the $\gamma$-proton in one isomer and the $\beta$-proton in the other have been considerably shifted downfield as compared to each other isomer (Table 2). This could be resulted from a syn arrangement between the proton in question and the carbonyl group as shown in structure **A** and **B** respectively, so that the protons were situated right in the



**A**



**B**

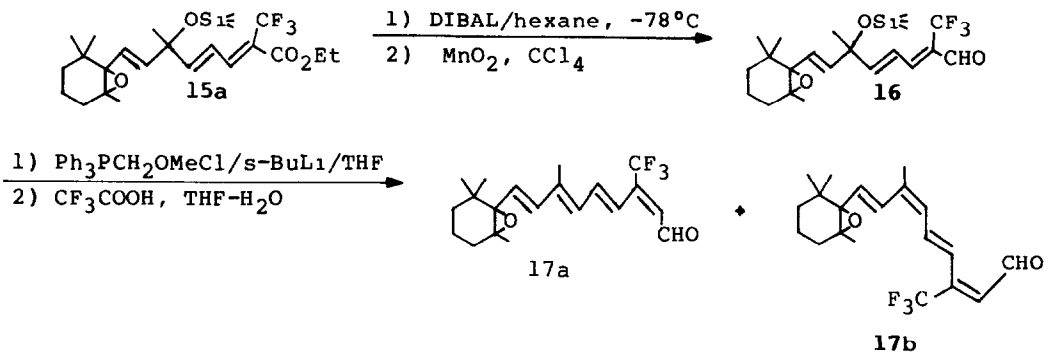
deshielding cone of the carbonyl group and hence resonanced at lower field than it would do otherwise.[18] Based on this interpretation of $^1$H NMR data, which has been frequently invoked for configuration assignment of unsaturated carbonyl compounds,[19] we are able to deduce the geometry of the newly formed double bond for each isomer as depicted in Table 2. Supportive evidence for this $^1$H NMR-based assignement of Z,E configuration has been found in the corresponding $^{19}$F NMR spectra. It has been well documented that the $^{19}$F NMR signal of a $CF_3$ group attached to a double bond will be shifted downfield when it is cis to the bulkier one of the two vicinal double bond substituents as compared with that when they are in a trans orientation.[20] This generalization has served to be a rule of thumb for the assignment of the geometry of a $CF_3$-substituted double bond[18] although the theoretical backgrounds are not yet well founded. As would be expected, the two isomers produced in each elimination reaction have displayed a $^{19}$F NMR chemical shift difference whose magnititude appeared to be related with that of the difference in the steric interaction of the $CF_3$ group with its neighbouring cis substituent (Table 2). Accordingly, the configurations of each pair of isomers can be determined by assuming the steric bulkiness relative to the cis adjacent $CF_3$ group in the order of alkyl, aryl $>$ alkenyl, alkynyl $>$ H; and the geometries so deduced have turned out to be well in agreement with those derived on the basis of $^1$H NMR analysis as is already mentioned above.

It should be noted that the coupling constants between the fluorine and the olefinic proton ($^4J_{HF}$) in all of the present $CF_3$-substituted unsaturated compounds appeared to be too small to be clearly identified and are, therefore, of little diagnostic value for the assigment of E, Z configuration although in some previous cases it has been cited for such purpose.[21]

**Application to the Synthesis of 20,20,20-Trifluoro-5,6-epoxyretinal.** The structural modifications of retinal, such as by replacement of a 5, 9 or 20 methyl group with a $CF_3$ group, have been the subject of several important papers published in recent years.[22] Also, there have been reports that 5,6-epoxyretinal was able to combine with cattle opsin to form rhodopsin pigments analogs.[23] We envisaged that the present approach to the synthesis of trifluoromethylated dienoic esters would offer an interesting access to a fluorinated analog of 5,6-epoxyretinal, which, being modified with fluorine and an epoxy ring, might show some interesting biological properties in its binding study against the parent retinal. Thus, further elaboration of compound **15a**[24] has been carried out as follows:reduction of **15a** with diisobutylaluminum hydride(DIBAL) to the corresponding alcohol followed by oxidation with activated manganese

dioxide readily afforded an aldehyde **16** in 70% yield. One carbon homologation of **16** by its Wittig reaction with methoxymethylene triphenylphosphorane followed by acid hydrolysis gave an 8:2 isomeric mixture of the fluorinated retinoids **17a** and **17b** in 34% yield (Scheme 4). The structure of **17a** and **17b** have been well confirmed by comparison of their 400 MHz $^1$H NMR spectra with related known compounds.[25,19a,20d]

Scheme 4




## Conclusion

We have studied the [2,3]-sigmatropic rearrangement of sulfonium ylide intermediates derived from catalytic decomposition of the $CF_3$-containing diazo compound **1** in the presence of allylic sulfides and explored the use of the trifluoromethylated rearrangement products for the synthesis of trifluoromethylated conjugated dienoic esters. As previously reported [7,8] the present utilization of **1** as a $CF_3$-containing building block via the ylide route has once again turned out to be a successful strategy for the construction of trifluoromethylated molecules, which has been featured by the easy availability of the starting materials as well as the facility with which the transformations have been carried out. In addition to ylides derived from sulfides, those from tertiary amines, bromides, iodides, acetals and even oxygen ethers can also be generated from diazo compounds with rhodium(II) carboxylates under very mild conditions and undergo subsequent [2,3]-sigmatropic rearrangement or [1,2]-Stevens rerrangement with high efficiency and apparent synthetic advangtages.[9,13,14] Therefore, the success of the present carbenoid entry into trifluoromethylated organic molecules has revealed the great potential for new synthetic developments in the field of synthetic organofluorine chemistry.

## Experimental Section

$^1H$ NMR spectra were recorded on a JEOL FX-90, Varian XL-200 or Bruker AM-400 spectrometer with $Me_4Si$ as an internal standard; and $^{19}F$ NMR spectra were obtained on a Varian EM-360L spectrometer with trifluoroacetic acid($\delta$,0.00) as an external standard, downfield shifts were designated as negative. Infrared spectra were taken on a Shimadzu IR-440 spectrometer and mass spectra(MS) and high resolution mass spectra (HRMS) were run respectively on a Finnigan 4021 GC/MS/DC and a Varian MAT 212 instruments with an ionizing voltage of 70ev. All reactions as well as column chromatography were monitored routinely with the aid of TLC or $^{19}F$ NMR spectroscopy.

Benzene was dried over sodium wire and THF was distilled from sodium/benzophenone. Ethyl 3,3,3-trifluoro-2-diazo-propionate(**1**) was prepared as described in our previous paper[8] and rhodium acetate was obtained by the method of Wilkinson.[26] Allylic sulfides were generally prepared by the reaction of allylic halides with sodium thiophenolate( from thiophenol and NaH) in THF except **4i**, which was prepared by isomerization of **4h**[27], and **4e**, which was obtained by acid catalyzed addition of thiophenol to isoprene;[28] the preparation of **4j** was described as follows.

**Preparation of (5E)-4-methyl-3-(phenylthio)-6-(2,6,6-trimethyl-1-cyclohexen-1-yl)-4-(trimethylsiloxy)-1,5-hexadiene(4j):**[11] To a solution of allyl phenyl sulfide (15 mmol) in dry THF(100 mL) was added a hexane solution of s-BuLi(1 M, 15 mL) dropwise over 10 min. and the orange mixture was stirred at -78°C for an additional 30 min. Titanium(IV) isopropoxide(15 mmol) was introduced via syringe at -78°C and the resulting solution was stirred at -78°C for 10 min. $\beta$-ionone(12 mmol) was added over a period of 5 min. and the mixture was first stirred at -78°C for 10 min. and then at 0°C for 1 h. After usual work up and chromatagraphic separation on silica gel (9:1 petroluem ether(60-90°C)/ethyl acetate as the eluent), the isolated product was dissolved in dry hexane(5 mL) and pyridine(2 mL). Hexamethyl disilazane(8 mmol) and trimethylchlorosilane(6 mmol) were then introduced to the solution. The resulting mixture was stirred at 70°C overnight and then all the volatile materials were removed at 70°C(2 mmHg). The residue was then dissolved in dry hexane and the white precipitate was removed by filtration. Concentration of the filtrate gave essentially pure **4j** as a 6:4 mixture of diastereoisomers in 90% yield(based on $\beta$-ionone). **4j**: Oil; $^1H$ NMR($CDCl_3$, 200MHz) 0.05(s, 3.6H,$SiMe_3$) and 0.14(s, 5.4H,$SiMe_3$), 1.02(s,1.8H,6'-$CH_3$) and 1 06(s,1.2H, 6'-$CH_3$), 1.04(s,3H,6'-$CH_3$), 1.40-1.68(m,4H,2 $CH_2$), 1.51(s,1.2H,4-$CH_3$) and 1.58(s,1.8H, 4-$CH_3$), 1.69(s,1.8H,2'-$CH_3$) and 1.73(s,1.2H,2'-$CH_3$), 1.86-2.1(m,2H,$CH_2$), 3.49(d,J=9.8Hz,0.4H,3-H) and 3.50(d,J=10.0Hz,0.6H,3-H), 4.74(d,J=17.4Hz,0.6H,1-H) and 4.78(d,J=17.4Hz,0.4H,1-H) 4.90(d,J=10.0Hz,

0.6H,1-H) and 4.95(d,J=10.0Hz,0.4H,1-H), 5.55(d,J=16.0Hz,0.6H, 5-H) and 5.66(d,J=16.0,0.4H,5-H), 5.78-6.0(m,1H,2-H), 6.08(br d,J=16.0Hz,1H,6-H), 7.12-7.45(m,5H,ArH). MS,m/z(relative intensity) 399(M-Me,1), 325(2), 305 (3), 289(2), 266(23), 265 (100), 175(15), 149(4), 147(3), 143(6), 117(8), 109(4), 73(22). Anal. calcd for $C_{25}H_{38}OSSi$: C,72.46; H,9.18. Found: C, 72.23; H,9.53.

**Reaction of Ethyl 3,3,3-Trifluoro-2-diazo-propionate(1) with Allylic Phenyl Sulfides(4) Catalyzed by $[Rh(OAc)_2]_2$. General Procedure:** A mixture of allylic sulfide(4 mmol) and rhodium acetate(0.5 mol% based on **1**) in dry benzene (10 ml) was stirred until a purple homogeneous solution was formed. Diazo compound **1**(4.4-8.0 mmol) was then introduced in one portion and the resulting mixture was stirred and heated under nitrogen to the desired temperature as is indicated in Table 1 until gas evolution had ceased. The solvent was then removed under reduced pressure and the residue was subjected to silica gel chromatography using 9:1 petroleum ether(60-90°C)/ethyl acetate as the eluent to give trifluoromethylated product **6a-j**.

**Ethyl 2-(phenylthio)-2-(trifluoromethyl)-4-pentenoate(6a):** Oil; $^1H$ NMR($CDCl_3$, 90Hz) $\delta$ 1.18(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 2.64 and 2.88 (AB portion of ABX system, J=14.4 and 7.0Hz,2H,2 3-H), 3.98 (q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 5.08(d,J=10.8Hz,1H,5-H), 5.11(d,J=16.2Hz,1H,5-H), 5.50-6.04(m,1H,4-H), 7.12-7.70(m, 5H,ArH); $^{19}F$ NMR($CCl_4$) $\delta$ -11.0; IR(neat) 1740(s),1664(m); MS, m/z(relative intensity): 304(M, 16), 231(10), 217(11), 189(32), 148 (13), 136(42), 109(100), 77(17), 69(14), 65(28). Anal. calcd for $C_{14}H_{15}O_2F_3S$: C,55.26; H,4.93; F,18.75. Found:C,54.81; H,4.89; F,19.03.

**Ethyl 3-methyl-2-(phenylthio)-2-(trifluoromethyl)-4-pentenoate(6b):** Obtained as a 24:76 mixture of diastereoisomers. Oil; $^1H$ NMR($CDCl_3$,90MHz) $\delta$ 1.10(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 1.20-1.40(m,3H,3-$CH_3$), 3.02-3.48(m,1H,3-H), 3.92(q,J=7.2Hz,2H, $O\underline{CH_2}CH_3$), 4.95-5.32(m,2H,5-H), 5.66-6.14(m,1H,4-H), 7.12-7.68(m,5H,ArH); $^{19}F$ NMR($CCl_4$) $\delta$ -15.7 and -15.9(ratio 76:24); IR(neat) 1740(s), 1640(w); MS, m/z(relative intensity) 318(M, 31), 264 (33), 244(25), 217(18), 191(15), 189(61), 136(30), 127(34), 110(42), 109 (83), 77(21), 69(15), 65(48), 55(100); Anal. calcd for $C_{15}H_{17}O_2F_3S$: C, 56.60; H,5.35; F,17.92. Found: C,56.60; H,5.29, F,17.82.

**Ethyl 3-phenyl-2-(phenylthio)-2-(trifluoromethyl)-4-pentenoate(6c):** Obtained as a 22:78 mixture of diastereoisomers. Oil; $^1H$ NMR($CDCl_3$,90MHz) $\delta$ 1.04(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 3.89(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 4.22(d,J=9.0Hz, 0.78H, 3-H) and 4.50(d,J=9.5Hz,0.22H,3-H), 5.10(d,J=17.5Hz,1H,5-H), 5.13 (d,J=10.8Hz,1H,5-H), 6.22-6.80(m,1H,4-H), 7.10-7.68(m,10H,ArH); $^{19}F$ NMR ($CCl_4$) $\delta$ -15.9 and -16.6(ratio 78:22); IR(neat) 1740(s), 1640(w), MS, m/z(relative intensity) 381(M+1, 9), 271(5), 117(100), 91(5), 77(2);

Anal. calcd for $C_{20}H_{19}O_2F_3S$: C,63.15; H,5.00; F,15.00. Found: C,62.73, H, 4.91; F,15.27.

**Ethyl 3,3-dimethyl-2-(phenylthio)-2-(trifluoromethyl)-4-pentenoate (6d):** $^1$H NMR($CDCl_3$, 90MHz) $\delta$ 1.14(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 1.32(br s,3H,3-$CH_3$), 1.37(br s,3H,3-$CH_3$), 4.00(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 5.02(d,J=17.1Hz, 1H,5-H), 5.03(d,J=10.8Hz,1H,5-H), 6.14(dd,J=17.1Hz and 10.8Hz,1H,4-H), 7.08-7.70(m, 5H,ArH); $^{19}$F NMR($CCl_4$) $\delta$ -19.5; IR(neat) 1740(s), 1640(m), MS, m/z(relative intensity) 332(M, 2), 264(46), 244(20), 223(13), 189 (6), 110(11), 109(22), 69(100); Anal. calcd for $C_{16}H_{19}O_2F_3S$: C,57.83; H,5.72; F,17.17. Found: C,57.51; H,5.73; F,17.48.

**Ethyl (4E)-3-methyl-2-(phenylthio)-2-(trifluoromethyl)-4-hexenoate (6e):** Obtained as a 28:72 mixture of diastereoisomers. Oil; $^1$H NMR($CDCl_3$, 90MHz) $\delta$1.11(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 1.26(dq,J=7.1Hz, $J_{HF}$=1.5Hz,3H,3-$CH_3$), 1.65(d,J=4.7Hz,3H,3×6-H),3.10-3.38(m,1H,3-H), 3.97(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 5.50(m, 1H,4-H), 5.66(dq,J=16Hz and 4.7Hz,1H,5-H), 7.20-7.74(m,5H,ArH); $^{19}$F NMR($CCl_4$) $\delta$ -15.4 and -15.5(ratio 72:28); IR(neat) 1740(s); MS, m/z(relative intensity) 332(M, 3), 264(36), 244(8), 109(15), 69(100); Anal. calcd for $C_{16}H_{19}O_2F_3S$: C,57.83; H,5.72; F,17.17. Found: C,57.63; H, 5.77; F,17.50.

**Ethyl 2-(2-cyclohexen-1-yl)-2-(phenylthio)-3,3,3-trifluoropropionate (6f):** Obtained as a 36:64 mixture of diastereoisomers. Oil; $^1$H NMR($CDCl_3$, 90MHz) $\delta$ 1.11(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 1.46-2.18(m,6H,3×$CH_2$), 3.04-3.42(m, 1H,methine), 3.98(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 5.66-5.90(m,2H,$C\underline{H}$=$C\underline{H}$), 7.14-7.76 (m,5H,ArH); $^{19}$F NMR($CCl_4$) $\delta$-16.0 and -16.2(ratio 64:36); IR(neat) 1740 (s); MS, m/z(relative intensity) 344(M, 4), 264(64), 244(21), 168(8), 142 (5), 127(6), 110(15), 109(22), 81(100). Anal. calcd for $C_{17}H_{19}O_2F_3S$: C, 59.30; H,5.52; F,16.57. Found: C,58.96; H,5.66; F,16.96.

**Ethyl 5-methyl-2-(phenylthio)-2-(trifluoromethyl)-4-hexenoate (6g):** Oil; $^1$H NMR($CDCl_3$, 90MHz) $\delta$ 1.10(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 1.56(s,3H,$CH_3$), 1.67(s,3H,$CH_3$), 2.72(d,J=7.0Hz,2H,2×3-H), 3.98(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 5.12(t,J=7.0Hz,1H,4-H), 7.12-7.70(m,5H,ArH); $^{19}$F NMR($CCl_4$) $\delta$ -11.0; IR(neat) 1740(s); MS, m/z(relative intensity) 332(M, 3), 264(30), 244 (21), 223(59), 216(3), 150(8), 127(10), 110(36), 108(42), 69(100). Anal. calcd for $C_{16}H_{19}O_2F_3S$: C,57.83; H,5.72; F,17.17. Found: C,57.89; H,5.72; F,17.41.

**Ethyl 2-(phenylthio)-2-(trifluoromethyl)-3,4-pentadienoate(6h):** Oil; $^1$H NMR($CDCl_3$, 90MHz) $\delta$ 1.09(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 3.98(q,J=7.2Hz,2H, $O\underline{CH_2}CH_3$), 4.76(d,J=6.9Hz,2H,2×5-H), 5.38(t,J=6.9Hz,1H,3-H), 7.15-7.72(m, 5H,ArH). $^{19}$F NMR($CCl_4$) $\delta$ -9.2; IR(neat) 1960(m), 1740(s), 850(s); MS, m/z(relative intensity) 302(M, 11), 229(38), 193(83), 189(17), 165(100), 147(13), 145(77), 134(19), 123(10), 117(23), 110(46), 109(82), 91(27), 77

(20), 69(29), 65(57), 51(33). Anal. calcd for $C_{14}H_{13}O_2F_3S$: C, 55.63; H, 4.30; F,19.00. Found: C,55.73; H,4.32; F,18.68.

**Ethyl 2-(phenylthio)-2-(trifluoromethyl)-4-pentynoate(6i):** Oil; $^1$H NMR($CDCl_3$, 90MHz) $\delta$ 1.10(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 1.96(t,2.3Hz,1H,5-H), 2.76(d,J=2.3Hz,2H,2×3-H), 3.98(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$); 7.15-7.72(m,5H, ArH); $^{19}$F NMR($CCl_4$) $\delta$ -9.8; IR(neat) 3300(s), 1740(s); MS, m/z(relative intensity) 302(M, 28), 229(44), 209(15), 189(37), 165(16), 160(24), 145 (13), 134(27), 109(100), 110(40), 77(19), 69(25). Anal. calcd for $C_{14}H_{13}O_2F_3S$: C,55.63; H,4.30; F,19.00. Found: C,55.67; H,4.37; F,19.28.

**Ethyl (4E,7E)-6-methyl-8-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2-(phenylthio)-2-(trifluoromethyl)-6-(trimethylsiloxy)-4,7-octadienoate(6j):** Obtained as a 32:68 mixture of diastereoisomers. $^1$H NMR($CCl_4$, 60MHz) $\delta$ 0.04(s,2.88H,$SiMe_3$) and 0.10(s,6.12H,$SiMe_3$), 1.10(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 1.23(s,6H,2 6'-$CH_3$), 1.82(s,3H,$CH_3$) 1.87(br s, 3H,$CH_3$), 1.46-1.66(m,2H, $CH_2$), 1.85-2.25(m,4H,2×$CH_2$), 2.85(br d,J=7.0Hz,2H,2×3-H), 4.00(q,J=7.2Hz, 2H,$O\underline{CH_2}CH_3$), 5.70(d,J=16.0Hz,1H,7-H), 5.91(d,J=16.0Hz,1H,8-H), 6.25(br d, J=15.0Hz,1H,5-H), 6.65(br dt,J=15.0 and 7.0Hz,1H,4-H), 7.20-7.70(m,5H, ArH); $^{19}$F NMR($CCl_4$) $\delta$ -11.0; IR(neat) 1740(s), 1630(w); MS, m/z(relative intensity) 569(M+1, 15), 554(11), 479(13), 291(30), 265(21), 215(57), 161 (12), 159(32), 147(13), 145(19), 117(37), 129(25), 73(100). Anal. calcd for $C_{30}H_{43}O_3F_3SSi$· C,63.38; H,7.57; F,10.03. Found: C,63.88; H,7.72; F, 10.46.

**Conversion of the Rearrangement Products to Trifluoromethylated Conjugated Dienoic Esters. General Procedure:** A Solution of the rearrangement product **6**(3 mmol) in methylene chloride (40 mL) was cooled to -40°C and mCPBA (3.6-6.6 mmol) was added. The resulting reaction mixture was then stirred at -20°C for a period of 6-10 h. The progress of the reaction can be monitored by $^{19}$F NMR. If there was still starting material remaining in the reaction mixture after the consumption of added mCPBA (negative test of KI-starch indicator paper), additional amount of mCPBA was added to ensure a complete reaction. The cold reaction mixture was poured into a separatory funnel containing 120 mL ether and 100 mL of 5% aqueous sodium sulfite solution and the organic layer was separated and the aqueous layer was extracted twice with ether. The combined organic layer was washed with saturated aqueous sodium bicarbonate solution, dried over anhydrous sodium sulfate and concentrated in vacuo to give a residue which was in some cases (Table 2, entry 2, 3 and 4) directly chromatographed on silica gel and in others (Table 2, entry 1, 5, 6, 7 and 8) dissolved in 50mL carbon tetrachloride and briefly warmed at 50°C for a few minutes before chromatographic separation. The eluents for chromatography usually consist of 19:1 to 9:1 petroluem ether(60-90°C)/

ethyl acetate except those for low boiling products (Table 2, entry 1 and 7) which were composed of 8:2 pentane/methylene chloride.

**Ethyl (2Z/E)-2-(trifluoromethyl)-2,4-pentadienoate(8):** The product was separated into two isomeric compounds **8a** and **8b** (ratio 58:42). **8a** (Z isomer): Oil. $^1$H NMR($CDCl_3$, 200MHz) $\delta$ 1.34(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 4.29 (q,J=7.2Hz,2H, $O\underline{CH_2}CH_3$), 5.80(d,J=10.0Hz,1H,5-H), 5.86(d,J=15.6Hz,1H,5-H), 6.97(dddq,J=10.0, 11.7 and 15.6Hz,$J_{HF}$=1.7Hz,1H,4-H), 7.48(d,J=11.7Hz,1H, 3-H); IR(neat) 1730(s), 1650(m); MS, m/z(relative intensity) 194(M, 30), 175(25), 166(20), 149(100), 127(40), 121(50), 101(45), 69(20). Anal. calcd for $C_8H_9O_2F_3$: C,49.48; H,4.61; F,29.38. Found: C,49.59; H,4.96; F, 29.80. **8b**(E isomer): Oil; $^1$H NMR($CDCl_3$, 200MHz) $\delta$ 1.36(t,J=7.2Hz,3H, $OCH_2\underline{CH_3}$), 4.31(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 5.78(d,J=10.6Hz,1H,5-H), 5.80(d, J=17.5Hz,1H,5-H), 7.07(br d,J=11.6Hz,1H,3-H), 7.39(ddd,J=17.5, 11.6 and 10.6Hz,1H,4-H); IR(neat) 1730(s); MS, m/z(relative intensity) 194(M, 20), 175(28), 166(53), 149(100), 146(50), 127(29), 121(52), 119(36), 101 (45), 69(15). Anal. calcd for $C_8H_9O_2F_3$: C,49.48; H,4.61; F,29.38. Found: C,49.02; H,4.72; F,29.84.

**Ethyl (2E/Z)-3-methyl-2-(trifluoromethyl)-2,4-pentadienoate (9):** Obtained as a 75:25 isomeric mixture of **9a** and **9b.** Oil; $^1$H NMR($CDCl_3$, 200MHz) $\delta$ 1.33(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 2.02(q,$J_{HF}$=1.5Hz,0.75H,3-$CH_3$) and 2.08(q,$J_{HF}$=1.9Hz,2.25H,3-$CH_3$), 4.31(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 5.51(d,J= 10.5Hz,0.75H,5-H) and 5.57(d,J=10.5Hz,0.25H,5-H), 5.71(d,J=17.1Hz,1H, 5-H), 6.61(dd,J=10.4 and 17.1Hz,0.75H,4-H) and 6.88(ddq,J=10.5 and 17.1Hz, $J_{HF}$=1.2Hz,0.25H,4-H); IR(neat) 1730(s), 1640(m), 1600(m); MS, m/z (relative intensity) 208(M, 30), 189(12), 180(52), 170(12), 165(31), 163 (100), 160(55), 145(36), 141(33), 139(38), 115(39), 95(20), 43(54). Anal. calcd for $C_9H_{11}O_2F_3$: C,51.92; H,5.28; F,27.40. Found: C,51.67; H,5.01; F,27.72.

**Ethyl (2E/Z)-3-phenyl-2-(trifluoromethyl)-2,4-pentadienoate (10):** Obtained as a 22:78 isomeric mixture of **10a** and **10b.** Oil; $^1$H NMR($CDCl_3$, 200MHz) $\delta$ 0.85(t,J=7.3Hz,0.66H,$OCH_2\underline{CH_3}$) and 1.36(t,J=7.2Hz,2.34H,$OCH_2\underline{CH_3}$), 3.87(q,J=7.3Hz,0.44H,$O\underline{CH_2}CH_3$) and 4.37(q,J=7.2Hz,1.56H,$O\underline{CH_2}CH_3$), 5.03(d, J=16.9Hz,0.22H,5-H) and 5.15(d,J=17.1Hz,0.78H,5-H), 5.56(d,J=10.5Hz, 0.22H,5-H) and 5.62(d,J=10.8Hz,0.78H,5-H), 6.90(dd,J=17.1 and 10.8Hz, 0.22H,4-H) and 6.97(dd,J=16.9 and 10.5Hz,0.88H,4-H), 7.10-7.43(m,5H, ArH); IR(neat) 1740(s), 1725(s); MS, m/z(relative intensity) 270(M, 41), 250(40), 225(49), 222(23), 205(31), 204(36), 202(100), 196(24), 177 (45), 146(32), 139(40), 128(34), 91(14). Anal. calcd for $C_{14}H_{13}O_2F_3$: C, 62.22; H,4.81; F,21.11. Found: C,62.60; H,4.54; F,20.95.

**Ethyl (2E/Z, 4E)-3-methyl-(trifluoromethyl)-2,4-hexadienoate (11):** Obtained as a 69:31 isomeric mixture of **11a** and **11b.** Oil; $^1$H NMR($CDCl_3$,

200MHz) δ 1.32(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 1.86(d,J=5.7Hz,2.1H,5-$CH_3$) and 1.90 (d,J=6.0Hz,0.9H,5-$CH_3$), 1.99(q,$J_{HF}$=2.0Hz,0.9H,3-$CH_3$) and 2.06(q,$J_{HF}$=2.0Hz, 2.1H,3-$CH_3$), 4.30(q,J=7,2Hz,2H,$OCH_2CH_3$), 6.21(dq,J=6.0 and 16.0Hz,0.31H, 5-H) and 6.26(dq,J=5.7 and 15.9Hz,0.69H,5-H), 6.35(d,J=15.9Hz,0.69H,4-H) and 6.57(br d,J=16.0Hz,0.31H,4-H); IR(neat) 1730(s), 1650(w); MS, m/z (relative intensity) 222(M, 54), 207(44), 203(38), 194(16), 179(55), 177 (100), 159(79), 155(29), 149(20), 129(21). Anal. calcd for $C_{10}H_{13}O_2F_3$: C,54.05; H,5.86; F,25.68. Found: C,54.45; H,5.57; F,25.62.

**Ethyl 2-(2-cyclohexen-1-ylidene)-3,3,3-trifluoro-propionate (12):** Obtained as a 44:56 isomeric mixture of **12a** and **12b**. Oil; $^1H$ NMR($CDCl_3$, 200MHz)δ 1.32(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 1.72-1.86(m,2H,5'-$CH_2$), 2.18-2.30(m, 2H,4'-$CH_2$), 2.45-2.54(m,1.12H,6'-$CH_2$) and 2.56-2.66(m,0.88H,6'-$CH_2$), 4.28 (q,J=7.2Hz,1.12H,$O\underline{CH_2}CH_3$) and 4.29(q,J=7.2Hz,0.88H,$O\underline{CH_2}CH_3$), 6.29-6.40(m, 1H,3'-H), 6.42(d,J=10.2Hz,0.44H,2'-H) and 6.58(dq,J=10.2Hz,$J_{HF}$=2.1Hz, 0.56H,2'-H); IR(neat) 1730(s), 1630(s), 1600(m); MS, m/z(relative intensity) 234(M, 48), 215(37), 214(49), 190(100), 186(32), 167(62), 141 (34), 91(33). Anal. calcd for $C_{11}H_{13}O_2F_3$: C,56.41; H,5.55; F,24.36.

**Ethyl (2E/Z)-5-methyl-2-(trifluoromethyl)-2,4-hexadienoate (13):** The product was separated into two isomeric compounds **13a** and **13b** (ratio 65:35). **13a** (Z isomer): Oil; $^1H$ NMR($CDCl_3$, 200MHz) δ 1.33(t,J=7.2Hz,3H, $OCH_2\underline{CH_3}$), 1.98(s,6H, 2×$CH_3$), 4.29(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 6.52(br d,J= 12.6Hz,1H,4-H), 7.85(d,J=12.6Hz,1H,3-H); IR(neat) 1730(s), 1635(m); MS, m/z(relative intensity) 223(M+1, 100), 222(M, 80), 207(40), 189(15), 203(59), 179(62), 177(81), 159(79), 155(25), 149(68), 129(77), 109(43), 79(47). Anal. calcd for $C_{10}H_{13}O_2F_3$: C,54.05; H,5.85; F,25.67. Found: C,54.30; H,5.70; F,25.70. **13b**(E isomer): Oil. $^1H$ NMR($CDCl_3$, 200MHz) δ 1.34(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 1.94(s,3H,$CH_3$), 1.98(s,3H,$CH_3$),4.30(q,J=7.2Hz, 2H,$O\underline{CH_2}CH_3$), 7.01(br d,J=11.7Hz,1H,4-H), 7.42(d,J=11.7Hz,1H,3-H); IR (neat) 1728(s), 1635(s), 1605(m); MS, m/z(relative intensity) 223(M+1, 100), 222(M, 26), 207(25), 203(32), 179(23), 177(54), 159(42), 149(29), 129(39), 109(23), 79(20). Anal. calcd for $C_{10}H_{13}O_2F_3$: C,54.05; H,5.86; F, 25.68. Found: C,54.07; H,5.80; F,25.26.

**Ethyl (2E/Z)-2-(trifluoromethyl)-2-penten-4-yn-oate(14):** The product was separated into two isomeric compounds **14a** and **14b**(ratio 82:18). **14a** (Z isomer). Oil. $^1H$ NMR($CDCl_3$, 200MHz) δ 1.32(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 3.88 (dq,J=2.7Hz, $J_{HF}$=1.5Hz,1H,C-CH), 4.29(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 7.08(d,J= 2.7Hz,3-H); IR(neat) 3300(s), 2090(s), 1730(s), 1625(s); MS, m/z(relative intensity) 192(M, 3), 164(50), 147(100), 69(33). Anal. calcd for $C_8H_7O_2F_3$: C,50.00; H,3.65; F,29.69. Found: C,50.25; H,3.80; F,29.20. **14b** (E isomer): Oil. $^1H$ NMR($CDCl_3$, 200MHz) δ 1.32(t,J=7.2Hz,3H,$OCH_2\underline{CH_3}$), 3.82 (d,J=2.8Hz,1H, C-CH), 4.33(q,J=7.2Hz,2H,$O\underline{CH_2}CH_3$), 6.65(dq,J=2.8Hz,$J_{HF}$=

1.8Hz,1H,3-H); IR(neat) 3300(m), 2100(m), 1730(s), 1630(m); MS, m/z (relative intensity) 193(M+1, 18), 192(M, 1), 165(29), 164(16), 147(100), 69(62). Anal. calcd for $C_8H_7O_2F_3$: C,50.00; H,3.65; F,29.69. Found: C, 49.88; H,3.85; F,29.30.

**Ethyl (2 Z/E, 4E, 7E)-8-(1,2-epoxy-2,6,6-trimethyl-cyclohex-1-yl)-6-methyl-2-(trifluoromethyl)-6-(trimethylsiloxy)-2, 4, 7-octatrienoate(15):** Obtained according to the general procedure described above except that in the work-up step aqueous solution of sodium bicarbonate, instead of sodium sulfite, was added to the cold reaction mixture to render it alkaline (pH=9) and a mitxure of 19:1 petroleum ether(60-90°C)/ethyl acetate (containing a few drops of triethylamine) was used as the eluent for chromatography. The product was separated into two isomeric compounds **15a** and **15b**(ratio 65:35). **15a**(Z isomer): Obtained as a 6:5 mixture of diastereoisomers. Oil; $^1$H NMR($CDCl_3$, 200MHz) $\delta$ 0.09(s,4.1H,$SiMe_3$) and 0.10(s,4.9H,$SiMe_3$), 0.87(s,3H,6'-$CH_3$), 1.02(s,3H,6'-$CH_3$), 1.08(s,3H, 2'-$CH_3$), 1.27(t,J=7.1Hz, 3H,$OCH_2\underline{CH_3}$), 1.41(s,3H,6-$CH_3$), 1.25-1.45(m,4H, 2 $CH_2$), 1.59-1.90(m,2H,$CH_2$), 4.23(q,J=7.1Hz,2H,$O\underline{CH_2}CH_3$), 5.62(d,J=15.5Hz, 0.45H,7-H) and 5.63(d,J=15.5Hz,0.55H,7-H), 5.83(d,J=15.5Hz,1H,8-H), 6.25 (d,J=14.9Hz,0.45H,5-H) and 6.28(d,J=14.9Hz,0.55H,5-H), 6.78(br dd,J= 14.9Hz and 12.1Hz,1H,4-H), 7.45(d,J=12.1Hz,1H,3-H); IR(neat) 1730(s), 1635(s), 1605(m); MS, m/z(relative intensity) 474(M, 4), 459(2), 347(3), 335(6), 322(6), 293(6), 183(10), 165(7), 157(7), 143(6), 117(6), 73(37), 69(7), 43(100). HRMS calcd for $C_{24}H_{37}O_4F_3Si$: 474.2414; found: 474.2428. **15b**(E isomer): Obtained as a 6:5 mixture of diastereoisomers. Oil; $^1$H NMR($CDCl_3$, 200MHz) $\delta$ 0.16(s,4.1H,$SiMe_3$) and 0.17(s,4.9H,$SiMe_3$), 0.93(s,3H,6'-$CH_3$), 1.07(s,3H,6'-$CH_3$), 1.14(s,3H,2'-$CH_3$), 1.25(t,J=7.1Hz, 3H,$OCH_2\underline{CH_3}$), 1.48(s,3H,6-$CH_3$), 1.24-1.52(m,4H,2x$CH_2$), 1.62-1.98(m,2H,$CH_2$), 4.30(q,J=7.1Hz,2H,$O\underline{CH_2}CH_3$), 5.68(d,J=15.5Hz,1H,7-H), 5.88(d,J=15.5Hz,1H, 8-H), 6.24(d,J=15.1Hz,0.45H,5-H) and 6.26(d,J=15.1Hz,0.55H,5-H), 7.09 (d,J=11.6Hz, 1H,3-H), 7.29(dd,J=11.6 and 15.1Hz,1H,4-H); IR(neat) 1730 (s), 1640(m), 1605(w); MS, m/z(relative intensity) 475(M+1, 10), 459(5), 335(11), 322(11), 315(5), 293(12), 265(7), 249(7), 209(6), 197(9), 183 (18), 165(14), 157(14), 143(14), 73(100), 69(18), 43(71). HRMS calcd for $C_{24}H_{37}O_4F_3Si$: 474.2414; found: 474.2419.

**(2Z, 4E, 7E)-6-methyl-8-(1,2-epoxy-2,6,6-trimethyl-cyclohex-1-yl)-2-(trifluoromethyl)-2,4,7-octatrienal(16):** To a stirred solution of **15a** (1.38 mmol) in THF(20 mL) cooled at -78°C was added a hexane solution of diisobutylaluminium hydride (DIBAL) (1.0 M, 2.8 mL) dropwise over 10 min. and the reaction mixture was stirred at -78°C for an additional 30 min. After then, TLC analysis (19:1 petroleum ether/ethyl acetate) showed complete loss of the starting material spot at $R_f$ 0.7. 10% Aqueous

ammonium chloride (60 mL) was then added and the insoluble material was filtered off with the aid of ethyl acetate (50 mL). The organic layer was separated, washed with brine, dried over anhydrous sodium sulfate and concentrated in vacuo to give a residue which showed only one spot at $R_f$ 0.2 by TLC analysis (19:1 petroleum ether/ethyl acetate). The residue was taken up in carbon tetrachloride (20 mL) and freshly prepared manganese dioxide[29] (5 g) was added. The heterogeneous reaction mixture was stirred at room temperature for 30 min. and then filtered. The filtrate was concentrated in vacuo to yield a residue which was subjected to column chromatographic separation on silica gel using a 9:1 mixture of petroleum ether(60-90°C) and ethyl acetate(containing a few drops of triethylamine) as the eluent to afford **16** as a 6:5 mixture of diastereoisomers in 70% yield. Oil; $^1$H NMR($CDCl_3$, 400MHz) 0.16(s,9H,$SiMe_3$), 1.03(s,3H,6'-$CH_3$), 1.07(s,1.64H,6'-$CH_3$) and 1.08(s,1.36H,6'-$CH_3$), 1.13(s,3H,2'-$CH_3$), 1.39-1.48(m,4H,2 $CH_2$), 1.49(s,3H,6-$CH_3$), 1.69-1.93(m,2H,$CH_2$), 5.68(d,J=16.0Hz, 0.45H,7-H) and 5.70(d,J=16.0Hz,0.55H,7-H), 5.90(d,J=16.0Hz,1H,8-H), 6.45 (d,J=15.7Hz,0.45H,5-H) and 6.49(d,J=15.7Hz,0.55H,5-H), 6.89(br dd,J=12.7 and 15.7Hz,1H,4-H), 7.30(d,J=12.7Hz,1H,3-H), 9.54(s,1H,1-H); $^{19}$F NMR ($CDCl_3$) -18.0, IR(neat) 1705(s), 1640(s), 1600(m); MS, m/z(relative intensity) 430(M ,3), 341(M-$OSiMe_3$, 6), 303(6), 265(6), 213(9), 183(15), 165(15), 149(13), 143(17), 117(14), 73(100), 43(69). HRMS calcd for $C_{22}H_{33}O_3F_3Si$: 430.2152; found: 430.2139.

**(7E,9E/Z,11E,13E)-5,6-epoxy-20,20,20-trifluororetinal (17):** To a stirred suspension of methoxymethyl triphenylphosphonium chloride (2.5 mmol) in THF(20 mL) cooled at -78°C was added s-BuLi in hexane(1 M, 2.5 mL) over 5 min. After addition was complete, stirring was continued at -78°C for an additional 1 h to result in a deep red solution. The aldehyde **16**(0.62 mmol) in THF(2 mL) was then added and the mixture was stirred at -78°C for 10 min. and was then allowed to warm to room temperature during 2 h. Usual alkaline work up of the reaction mixture afforded a viscous oil which was triturated with 9:1 hexane/ether and passed through a short column of silica gel. The filtrate was concentrated to give a colourless oil which was dissolved in 20 mL aqueous THF (THF:$H_2O$ 9.1) containing 0.5 mL trifluoroacetic acid and the reaction mixture was stirred at room temperature for 24 h. Water(20 mL) was added and three extractions with ether was carried out. The organic layer was washed with sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate and concentrated. The residual oil was chromatographed on silica gel to afford a 80:20 isomeric mixture of **17a** and **17b**(ratio 80:20) as an intensely yellow oil in 34% yield(based on **16**). $^1$H NMR($CDCl_3$, 400MHz) **17a:** 0.91(s,3H,1-$CH_3$), 1.09(s,3H,1-$CH_3$), 1.14(s,3H,5-$CH_3$),

1.38-1.42(m,4H,2 and 3-$CH_2$), 1.70-1.88(m,2H,4-$CH_2$), 1.97(s,3H,9-$CH_3$), 6.12(d,J=15.5Hz,1H,7-H), 6.22(d,J=11.5Hz,1H,10-H), 6.28(d,J=6.8Hz,1H, 14-H), 6.30(d,J=15.5Hz,1H,8-H), 6.88(d,J=15.4Hz,1H,12-H), 7.13(br dd,J= 11.5Hz and 15.4Hz,1H,11-H), 10.12(d,J=6.8Hz,1H,15-H). **17b**: 0.92(s,3H, 1-$CH_3$), 1.09(s,3H,1-$CH_3$), 1.13(s,3H,5-$CH_3$), 1.38-1.42(m,4H,2 and 3-$CH_2$), 1.70-1.88(m,2H,4-$CH_2$), 1.99(s,3H,9-$CH_3$), 6.12(d,J=15.5Hz,1H,7-H), 6.14 (d,J=11.5Hz,1H,10-H), 6.28(d,J=6.8Hz,1H,14-H), 6.74(d,J=15.5Hz,1H,8-H), 6.80(d,J=15.4Hz,1H,12-H), 7.23(br dd,J=11.5 and 15.4Hz,1H,11-H), 10.01(d, J=6.8Hz,1H,15-H); $^{19}F$ NMR($CDCl_3$) **17a**: -12.4, **17b**: -12.3; IR(neat) 1680(s), 1590(s), 1180(s), 1140(s); MS, m/z(relative intensity) 354(M, 100), 311(15), 325(50), 269(19), 205(45), 149(20), 109(15), 69(18), 43(47). HRMS calcd for $C_{20}H_{25}O_2F_3$: 354.1808; found: 354.1825

**Acknowledgment:** We thank National Natural Science Foundation of China and Academia Sinica for their financial support.

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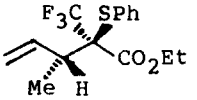
15. The relative configurations of the diastereomers may be deduced on the basis of the Z/E ratio of the elimination products assuming that the elimination proceeds in a syn fashion (vide infra). As an example, the relative configuration of the major diastereomer of **6b** can be assigned as:

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24. Somewhat surprisingly, although the reduction of **15b** by DIBAL can also proceed smoothly to produce the corresponding alcohol, the oxidation of the alcohol by $MnO_2$ under exactly the same condition as was used in the case of its isomer **15a** did not take place to any appreciable extent presumably because of steric reasons.
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