phenone and 2-heptanone catalyzed by **5**, BH_3-THF and BMS provided the best results for the rate of reduction and enantioselection as compared to those by catecholborane, 9-BBN and dibromoborane. To obtain the best enantioselectivities, Lewis basic solvents (*e.g.* THF or DME) for BMS and nonpolar solvents (*e.g.* toluene or hexane) for catecholborane were preferable.

Acknowledgment. This work was generously supported by OCRC/KOSEF.

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Stereocontrolled Synthesis of Conjugated *E*-Dienoate Esters *Via* Double Alkylation and then Pyrolysis of Methyl Phenylsulfinylacetate

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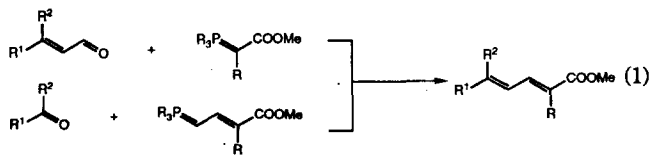
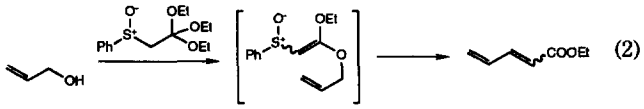
Conjugated dienoate moieties are frequently found in naturally occurring compounds having a wide range of biological activity and in many synthetic intermediates.[1] Sarcopytol A, a 14-membered cyclic terpene cembranoid[2], has a dienoate unit. So far only one synthesis of Sarcopytol A was reported using the Horner-Simmons reaction.[3] Manumycin has been also identified as potent and selective inhibitors of Ras farnesyltransferase, and its aminoacyl side chain having a α-methyldienoate substructure was proposed as pharmocores.[4] A decadienoate has been used in the synthesis of a natural insecticide.[5] The syntheses of these dienoate moieties are generally made by the Wittig or its related reactions[6] as shown in Eq. 1.



(1)

All of these methods involve the addition of a carbanion unit to the carbonyl compounds, followed by some type of elimination. Although these usually proceed with high chemo- and stereo-selectivity in many cases, the application to the dienoate synthesis often encounters some serious problems. In general, allylic ylides do form the conjugated dienes with a moderate degree of stereoselectivity.[7] Furthermore, 2-alkylsubstituted ylides are not only difficult to prepare but diminish the selectivity in many cases.[8] Recently, Posner and his coworkers reported an easy process for dienoate synthesis using Claisen rearrangement of the ketene acetal derived from phenylsulfinyl orthoacetate with various allylic alcohols (Eq. 2).[9] This method has been proven to be a highly efficient process when two-carbon homologated dienoates were desired. They further applied this method to the syntheses of vitamin D analogs. However, their method resulted in the formation of a stereoisomeric mixtures possibly due to the required high temperature in the Claisen rearrangement.

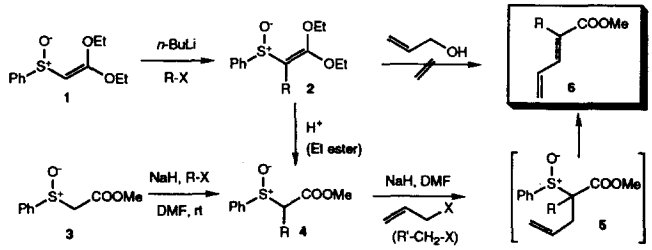


(2)

It was well-known that sulfoxides readily undergo *syn* elimination with a β-hydrogen atom on pyrolysis to form olefins *via* a concerted cyclic pathway.[10] Also pyrolysis of sulfoxides having an α-carbonyl group provides the α,β-unsaturated carbonyl compounds.[11] The *E*-olefins usually predominates in disubstituted ethylenes, but a mixtures of isomers are obtaind in tri- and tetra-substituted compounds. Similar, even better, results could be obtained by using selenoxides.[12] Although these procedures take place under comparatively mild conditions, these have been mostly used in introducing a double bond in a molecule.

We have been interested in synthesizing 2-alkyl substituted dienoates esters and now report a highly stereocontrolled process to the dienoate esters using consecutive alkylations of methyl phenylsulfinylacetate. Scheme 1 shows a general sequence for our new methodology.

Our approach involves consecutive bisalkylation of methyl phenylsulfinylacetate (**3**) with alkyl halides and then allyl halides and followed by spontaneous elimination of phenylsulfenic acid to yield the α-alkyl substituted dienoate esters **6**. Initially, we have tried to alkylate a ketene acetal[13], 2,2-diethoxyvinyl phenylsulfoxide (**1**), to obtain the α-alkyl ketene acetals **2**. The ketene acetal **1** seemed to be smoothly deprotonated by *n*-butyllithium and reacted with electrophiles to form the α-alkyl ketene acetal **2**.[14] The alkylated ketene acetals **2** were too unstable to be isolated and were



Scheme 1.

Table 1. Reactions of 3 with Various Alkyl Halides in DMF to form Dienoate 6

	R-X	R'-CH_2-X	% Yield of 6[a]	Product
1	CH_2=$CHCH_2Br$	CH_2=$CHCH_2Br$	56	**6a**
2	PhCH=$CHCH_2Br$	PhCH=$CHCH_2Br$	90	**6b**
3	$PhCH_2Br$	$PhCH_2Br$	77	**6c**[b]
4	n-C_9H_{19}-I	CH_2=$CHCH_2Br$	61	**6d**
5	$HCC(CH_2)_4$-I	CH_2=$CHCH_2Br$	65	**6e**
6	CH_2=$CH(CH_2)_2Br$	CH_2=$CHCH_2Br$	73	**6f**
7	c-C_6H_{11}-I	CH_2=$CHCH_2Br$	16	**6g**

[a] Represents isolated yields of *E* isomers. [b] Methyl α-benzylcinnamate was the product (**6c**).

easily converted to a diastereomeric mixture of the corresponding ester **4** in high yields. The same result was obtained from classical alkylation of methyl phenylsulfinylacetate (**3**) with alkyl iodides or reactive alkyl bromides.[15] Both diastereomers **4** were further reacted with allylic halides, and spontaneous elimination of sulfenic acid under the reaction conditions (below room temperature) formed the dienoates **6**. Among various alkylations we employed, a successful alkylation was obtained using NaH as a base and DMF as a solvent. After the monoalkylation was complete by TLC analysis, the subsequent addition of allylic halides to the reaction mixture resulted in the formation of the dienoates. Those results are summarized in Table 1.

It seemed that the bisalkylated intermediate underwent a rapid elimination under the reaction conditions (below room temperature) to produce stereoselectively a new double bond. When two equivalents of allyllic bromides (entries 1, 2) were used as electrophiles, only the corresponding single products were obtained by the NMR analysis, respectively. A benzylic bromide also was a good electrophile for this process (entry 3). The sodium enolate of methyl phenylsulfinylacetate was reacted with typical reactive alkyl iodides, n-nonyl (entry 4), and 5-hexynyl (entry 5), and a reactive alkyl bromide, 1-bromo-3-butene (entry 6). This was, however, slowly reacted with a secondary alkyl iodide (entry 7). Addition of allyl bromide to the monoalkylated products resulted in the rapid formation of the corresponding dienoates (entry 4-6) in high yields.[16] A typical procedure is given for entry 4. To 60% sodium hydride in mineral oil (49.3 mg, 1.2 mmol) in dry DMF (0.5 m*l*) was added methyl phenylsulfinylacetate (96.9 mg, 0.48 mmol) in dry DMF (1.0 m*l*) *via* cannula at 0 ℃ under argon atmosphere. The resulting sodium enolate solution was treated with n-nonyl iodide (149.1 mg, 0.58 mmol) in DMF (0.5 m*l*) *via* a cannula. The resulting solution was stirred for 2-15 h at room temperature until all starting material was gone. The solution was cooled to 0 ℃ and treated with allyl bromide (100 μ*l*, 1.1 mmol) *via* a gas tight syringe. Additional stirring for 2 h at room temperature afforded the corresponding dienoate. The extractive workup and flash chromatography on silica gel gave the single isomeric product **6e** (71.3 mg, 61%). The stereochemistry of the dienoates was excellent in which a new double bond was formed with only *E* configuration without interrupting the original configuration of allylic halide (entry 2). No corresponding *Z* isomers were detected by the 200 MHz NMR analysis of the crude reaction products.

In conclusion, we have shown for the first time that the ketene acetal could be deprotonated and alkylated with some typical electrophiles to the corresponding α-alkylated ketene acetals. The effectiveness and efficiency of the protocol in Scheme 1 for tandem, one-flask bisalkylations of methyl phenylsulfinylacetate followed by spontaneous β-elimination of benzenesulfenic acid represents a simple, and convenient stereoselective synthesis of α-alkylated dienoate esters without isolating any intermediates. The extension and application of this methodology is underway.

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16. Spectral data of the products are given. **6a**: IR (neat, cm^{-1}) 2905, 2840, 1705, 1632, 1428, 1255, 1200; ^1H NMR (200 MHz) δ 7.24 (d, *J*=11.5 Hz, 1H), 6.55 (ddd, *J*=16.5,

11.5, 9.8 Hz, 1H), 5.82 (m, 1H), 5.58 (d, J=16.5 Hz, 1H), 5.46 (d, J=11.5 Hz, 1H), 5.00 (d, J=16.0 Hz, 1H), 4.95 (d, J=9.6 Hz, 1H), 3.71 (s, 3H), 3.17 (d, J=10.0 Hz, 2H). **6b**: IR (neat, cm^{-1}) 3050, 3020, 2950, 1700, 1620, 1430, 1280, 1230, 1190, 1080, 965, 745; ^1H NMR (200 MHz) δ 7.50-7.42 (m, 3H), 7.37-7.11 (m, 8H), 7.07 (d, J=11.1 Hz, 1H), 6.88 (d, J=15.4 Hz, 1H), 6.45 (d, J=15.8 Hz, 1H), 6.14 (dt, J=15.8, 5.9 Hz, 1H), 3.77 (s, 3H), 3.42 (d, J=5.9 Hz, 2H). **6c**: IR (neat, cm^{-1}) 2995, 1693, 1602, 1420, 1240, 1185, 1065, 745; ^1H NMR (200 MHz) δ 7.93 (s, 1H), 7.35-7.20 (m, 10H), 3.95 (s, 2H), 3.74 (s, 3H). **6d**: IR (neat, cm^{-1}) 2900, 1700, 1245; ^1H NMR (200 MHz) δ 7.16 (d, J=11.4 Hz, 1H), 6.66 (ddd, J=16.8, 11.4, 10.0 Hz, 1H), 5.56 (dd, J=16.8, 1.2 Hz, 1H), 5.45 (dd, J=10.0, 1.2 Hz, 1H), 3.76 (s, 3H), 2.41 (t, J=7.3 Hz, 2H), 1.26 (s, 14H), 0.88 (t, J=6.2 Hz, 3H). **6e**: IR (neat, cm^{-1}) 3280, 2940, 2850, 1700, 1635, 1430; ^1H NMR (200 MHz) δ 7.17 (d, J=11.5 Hz, 1H), 6.65 (ddd, J=16.6, 11.4, 10.0 Hz, 1H), 5.58 (dd, J=16.6, 1.5 Hz, 1H), 5.45 (dd, J=10.2, 1.5 Hz, 1H), 3.73 (s, 3H), 2.40 (t, J=7.2 Hz, 2H), 2.23 (m, 2H), 1.93 (t, J=2.5 Hz, 1H), 1.90-1.35 (m, 4H). **6f**: IR (neat, cm^{-1}) 2890, 1680, 1240, 720; ^1H NMR (200 MHz) δ 7.19 (d, J=11.4 Hz, 1H), 6.65 (ddd, J=16.7, 11.4, 10.0 Hz, 1H), 5.81 (ddt, J=17.0, 10.2, 6.8 Hz, 1H), 5.58 (d, J=16.6 Hz, 1H), 5.46 (d, J=10.2 Hz, 1H), 5.02 (dt, J=17.1, 1.5 Hz, 1H), 4.96 (dt, J=9.1, 1.5 Hz, 1H), 3.77 (s, 3H), 2.52 (t, J=7.5 Hz, 2H), 2.18 (q, J=6.8 Hz, 2H).

The Nucleophilic Reaction of β,β-Difluoro-α-phenylvinyl Sulfide with Heteroatom (O, N, S) Nucleophiles

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Fluoroolefins substituted by two fluorines at terminal olefinic carbon have a unique reactivity toward nucleophiles and thus can be used as a useful synthetic block for further synthesis of fluorinated or nonfluorinated compounds.[1] Although considerable efforts have included investigation of nucleophilic reaction of *gem*-difluoroolefins for last two decades, most of these reactions are related to stereochemistry of addition-elimination products,[2] proton exchange reactions of resultant carbanion in alcoholic media,[3] and study on ease of β-defluorination of resultant carbanion.[4] However, a study on the doubly nucleophilic substitution reaction of *gem*-difluoroolefins with more than two equivalents of heteroatom nucleophiles has not been reported. Only one example has been reported on the reaction of symmetrical *gem*-dichlorinated and *gem*-difluorinated ketene dithioacetals with only a bidentate sulfur nucleophile in recent years.[5] Of particular interests in connection with a study on the doubly nucleophilic substitution reaction of *gem*-difluoroolefins is β,β-difluoro-α-phenylvinyl sulfide **1**, because this sulfide **1** is a novel compound and thus reactivity of **1** toward ionic species has not been studied yet. Recently, we found that β,β-difluoro-α-phenylvinyl sulfide **1** can be easily prepared from the reaction of 2,2,2-trifluoro-1,1-bis(phenylthio)ethylbenzene with a mixture of 2 equiv. $TiCl_4$ and 4 equiv. $LiAlH_4$.[6] In this communication, we wish to describe about reactions of **1** with various types of heteroatom (N, O, S) nucleophiles.

Treatment of **1** with 1 equiv. of oxygen nucleophiles, such as alkoxides or phenoxides, in acetonitrile at room temperature for 4 hours resulted in the formation of only monosubstituted vinyl sulfides **2** *via* addition-elimination reaction in good yields. The use of sulfur nucleophile in this reaction caused to formation of disubstituted vinyl sulfide **3**, even though minor product, as well as formation of **2** along with recovery of 5% starting material **1**. The formation of **3** indicates that sulfur substituted vinyl sulfide **2g** is more reactive than oxygen substituted vinyl sulfides **2a-f** for the further reaction with nucleophile. When **1** was reacted with 2 equiv. of nucleophile under the same reaction condition, unexpected results were obtained. Therefore, the reaction of **1** with 2 equiv. of unbranched alkoxides, such as methoxide or ethoxide, afforded a mixture **2a** and **2b** and α-phenylthio substituted esters **4a** and **4b**. Complete conversion of **2a** and **2b**[7] to **4a** and **4b**[8] was achieved by the use of large excess (4 equiv.) of nucleophile. In contrast, the similar reactions of **1** with 2 equiv. of branched alkoxides, such as *i*-propoxide or *t*-butoxide, under the same reaction condition did not provide esters **4c** and **4d**, but only **2c** and **2d** were obtained in 81% and 78% isolated yields, respectively. Progress did not occur even if 4 equiv. of nucleophile was used in this reaction. However, **1** was reacted with more than 2 equiv. of nucleophiles, such as 2,2,2-trifluoroethoxide, phenoxide, or thioethoxide, to yield only disubstituted vinyl sulfides **3e**, **3f**, and **3g** in good yields. The formation of **4** was not detected in these reactions. This result is probably due to the blocking effect of 2,2,2-trifluoromethyl or phenyl group of **2** against dealkylation reaction by nucleophiles as well as activating effect of 2,2,2-trifluoromethoxy and phenoxy group on vinyl carbon atom. The reactions of **1** with several types of nucleophiles are summarized in Table 1.

From these results, it is recognized that structure of monosubstituents (R_1) of **2** affects the further reaction with another equiv. of nucleophile. The formation of **4a** and **4b** can be rationalized by the reaction of ketene(I) which might be generated *via* dealkylation of alkoxy group of **2**, followed by dehalogenation, with nucleophile. Although the isolation of ketene(I) was failed because of high reactivity of ketene in this reaction system, the corresponding alkyl ethers which are formed *via* the dealkylation reaction of **2** with alkoxides were isolated in excellent yields and then identified by ^1H NMR and mass spectroscopy. Therefore, it seems likely that dealkylation of alkoxy group of **2** is most important step to approach the products **4**. No formation of **4c** and **4d** provides a good evidence to support this speculation because *i*-propyl and *t*-butyl group are too bulky to undergo the dealkylation of alkoxy group of **2**. After products **2b** and **2c** were isolated,