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A new synthesis of β,γ-alkenyl carboxylic acids from α,β-alkenyl carboxylic acid chlorides and α,β-alkenyl aldehydes with one-carbon elongation

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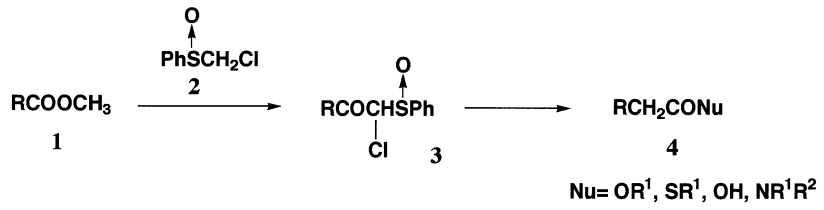
Abstract—Reaction of the lithium α-sulfinyl carbanion of chloromethyl phenyl sulfoxide with α,β-alkenyl carboxylic acid chlorides gave γ,δ-alkenyl α-chloro-β-keto sulfoxides in variable yields. The keto sulfoxides were also synthesized from α,β-alkenyl aldehydes in two steps in good overall yields: addition of the lithium α-sulfinyl carbanion of chloromethyl phenyl sulfoxide to α,β-alkenyl aldehydes followed by oxidation of the adducts with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone or Dess–Martin periodinane. These products were treated in sequence with potassium hydride, *tert*-butyllithium, and 5% aqueous sodium hydroxide, in one flask to give β,γ-alkenyl carboxylic acids with one-carbon elongation in good yields. The procedure offers a new method for synthesizing β,γ-alkenyl carboxylic acids from α,β-alkenyl carboxylic acid chlorides and α,β-alkenyl aldehydes with one-carbon elongation.

Carboxylic acids and their derivatives are undoubtedly among the most important and fundamental compounds in organic chemistry.[1] Among carboxylic acids, the unsaturated ones are even more important in synthetic organic chemistry. α,β-Alkenyl carboxylic acids and their derivatives are synthesized from saturated carboxylic acids[2] or from aldehydes and ketones by Horner–Wadsworth–Emmons reaction[3] with two-carbon elongation. Thus, the synthesis of α,β-alkenyl carboxylic acids and their derivatives is thought to be relatively easy.

On the other hand, how can we produce β,γ-alkenyl carboxylic acids?[4] One published method is the ester homologation using dibromomethyllithium as a one-carbon homologating agent by Kowalski.[5] He reported a synthesis of ethyl esters of β,γ-alkenyl carboxylic acids from α,β-alkenyl ones with one-carbon homologation. However, the reaction was somewhat troublesome and the yields were reported to be moderate.[5]

We recently reported a versatile procedure for one-carbon elongation of *saturated* methylesters **1** to esters, thioesters, carboxylic acids, and amides **4** through the β-keto sulfoxides **3** (Scheme 1).[6] In continuation of our studies for the homologation of carbonyl compounds using aryl 1-chloroalkyl sulfoxides as homologating agents,[7] herein we report a new synthesis of β,γ-alkenyl carboxylic acids from α,β-alkenyl carboxylic acid chlorides and α,β-alkenyl aldehydes with one-carbon elongation using chloromethyl phenyl sulfoxide **2** as the one-carbon homologating agent. The whole sequence is illustrated in Scheme 2.

A summary of the presented procedure is as follows. The reaction of α,β-alkenyl carboxylic acid chlorides **5** with the



Scheme 1. One-carbon homologation of saturated methylesters to esters, thioesters, carboxylic acids, and amides.

Keywords: β,γ-alkenyl carboxylic acid; sulfoxide; sulfoxide–lithium exchange; alkylidene carbenoid; one-carbon elongation.
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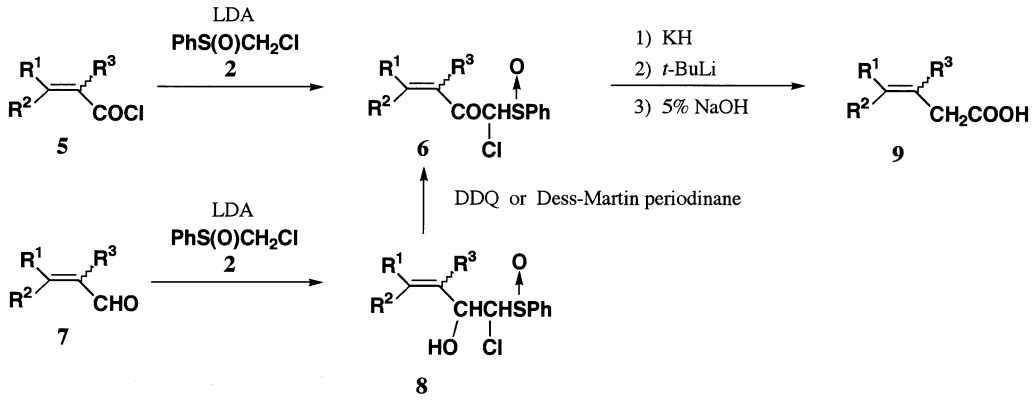
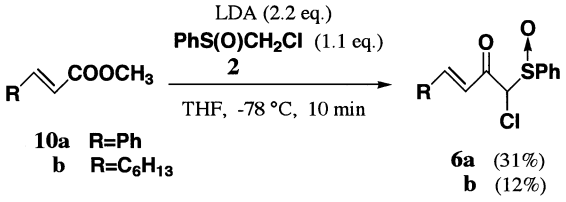


Scheme 2. One-carbon elongation of α,β-alkenyl carboxylic acid chlorides **5** and α,β-alkenyl aldehydes **7** to β,γ-alkenyl carboxylic acids **9**.



Scheme 3. Reaction of α,β-alkenyl methylesters with the lithium carbanion of chloromethyl phenyl sulfoxide **2**.

lithium α-sulfinyl carbanion of chloromethyl phenyl sulfoxide **2** leads to the formation of γ,δ-alkenyl β-keto sulfoxides **6** in variable yields. The reaction of α,β-alkenyl aldehydes **7** with the lithium carbanion of **2** gives the adducts **8** in almost quantitative yields. The hydroxyl group of the adducts **8** can be oxidized with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) or Dess–Martin periodinane to give the same ketones **6** in good yields. The ketones **6** are converted, in three operations in one flask, to the desired β,γ-alkenyl carboxylic acids **9** in good yields.

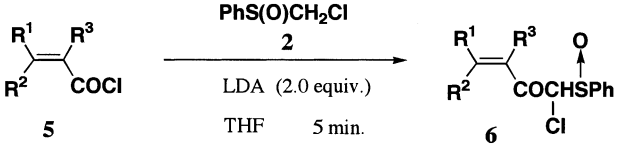
1. Results and discussion

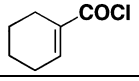
1.1. One-carbon elongation of α,β-alkenyl carboxylic acid chlorides and α,β-alkenyl aldehydes to β,γ-alkenyl carboxylic acids

As shown in Scheme 1, we reported a new method for one-carbon elongation of methylesters **1** to carboxylic acids and their derivatives **4** through α-chloro-β-keto sulfoxide **3**.[6] In this study, we investigated the chemistry by using *saturated* alkyl carboxylic acid methyl esters and aryl carboxylic acid methyl esters. The reaction of the lithium carbanion of **2** with these methylesters **1** gave quite good yields of the β-keto sulfoxides **3**.

As an extension of this method to a synthesis of β,γ-alkenyl carboxylic acids and their derivatives from α,β-alkenyl carboxylic acid derivatives with one-carbon elongation, we first investigated the reaction of the lithium carbanion of **2** with α,β-alkenyl carboxylic acid methyl esters **10** (Scheme 3). Methyl cinnamate **10a** was added to a solution of the lithium carbanion of **2** and excess lithium

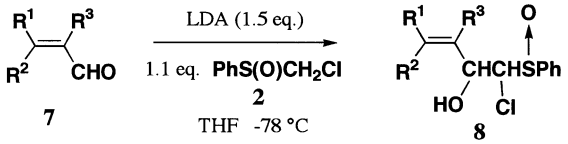
Table 1. Synethesis of γ,δ-alkenyl α-chloro-β-keto sulfoxides **6** from α,β-alkenyl carboxylic acid chlorides **5**

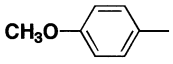
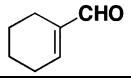


Entry	5				PhS(O)CH_2Cl (equivalents)	Temperature (°C)	6 (Yield/%)[a]	
		R^1	R^2	R^3				
1	**5a**	Ph	H	H	1.1	−78	**6a**	62
2	**5a**	Ph	H	H	1.1	−90[b]	**6a**	71
3	**5a**	Ph	H	H	1.5	−90[b]	**6a**	72
4	**5a**	Ph	H	H	1.5	−100[b]	**6a**	72
5	**5b**	C_6H_{13}	H	H	1.5	−100[b]	**6b**	55
6	**5c**	Ph	H	Ph	1.5	−100[b]	**6c**	75
7	**5d**	Ph	H	CH_3	1.5	−100[b]	**6d**	58
8	**5e**				1.5	−100[b]	**6e**	90

[a] Isolated purified yield after column chromatography.
[b] Methanol and liquid nitrogen were used as a cooling bath.

Table 2. Addition of the lithium carbanion of chloromethyl phenyl sulfoxide **2** to α,β-alkenyl aldehydes **7**



7				8 (Yield/%)	
	R^1	R^2	R^3		
7a	Ph	H	H	**8a**	93
7b	C_6H_{13}	H	H	**8b**	95
7c		H	H	**8c**	90
7d	Ph	H	CH_3	**8d**	98
7e	Ph	Ph	H	**8e**	93
7f				**8f**	87

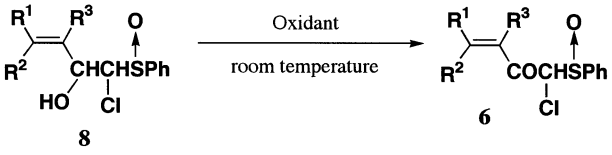
diisopropylamide (LDA) at −78°C and the reaction mixture was stirred for 10 min. In contrast to the result with the saturated relative (the yield of this reaction with methyl 3-phenylpropionate was 95%),[8] the reaction gave a complex mixture, from which the desired product **6a** (a mixture of two diastereomers) was obtained in only 31% yield. The reaction with methyl 2-nonenoate **10b** gave an even poorer yield of **6b** with several unknown by-products.

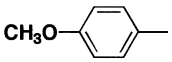
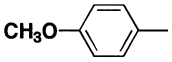
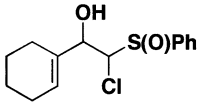
We then investigated other α,β-alkenyl carboxylic acid derivatives and found that acid chlorides were the compounds of choice (Table 1). Cinnamoyl chloride **5a** was added to a solution of the lithium carbanion of **2** (1.1 equivalents) with excess LDA (2 equivalents) at −78°C. This reaction gave a rather clean reaction mixture and the desired product **6a** was obtained in 62% yield (entry 1). Lowering the reaction temperature to −90°C showed some good effect to give a better yield of the product (entry 2). Using 1.5 equivalents of **2** gave a slightly better yield (entries 3 and 4). From the results shown in entries 1–4, we decided to apply the conditions in entry 4 to other α,β-alkenyl carboxylic acid chlorides. Although the best conditions described above were applied to some other α,β-alkenyl carboxylic acid chlorides, the yields of the desired products **6b–e** were found to be variable (entries 5–8).

As described above, the results for the synthesis of **6** from α,β-alkenyl carboxylic acid chlorides were not satisfactory, and we next planned a two-step synthesis of **6** from α,β-alkenyl aldehydes **7** via the adducts **8** (see Scheme 2). First, reaction of the lithium α-sulfinyl carbanion of **2** with α,β-alkenyl aldehydes **7** was investigated, and the results are summarized in Table 2. To the lithium carbanion of **2**, generated from 1.1 equivalents of **2** with 1.5 equivalents of LDA in THF at −78°C, was added the α,β-alkenyl aldehydes **7a–f**. All the aldehydes gave the desired adducts **8** (a mixture of diastereomers) in almost quantitative yields without any Michael-type adducts.

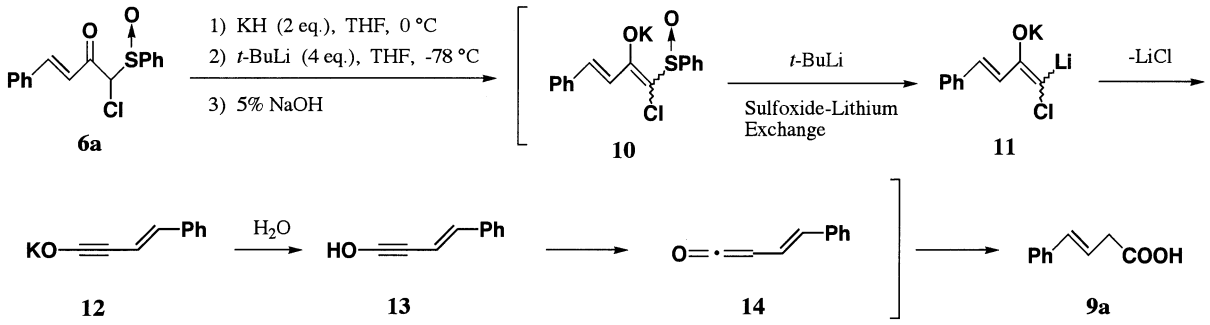
Oxidation of the hydroxyl group of **8** to a ketone group was found to be troublesome. Chromium(VI) oxidation of the alcohol **6** with PCC[9] or PDC[10] gave only a complex mixture. The Swern oxidation[11] also gave a complex mixture. Activated MnO_2 did not work. Finally, we found that

Table 3. Oxidation of **8** with DDQ or Dess–Martin periodinane



Entry	8				Oxidant[a]	Solvent	Time (h)	6 (Yield/%)	
		R^1	R^2	R^3					
1	**8a**	Ph	H	H	A	THF	17	**6a**	76
2	**8a**	Ph	H	H	A	CH_2Cl_2	19	**6a**	93
3	**8b**	C_6H_{13}	H	H	A	CH_2Cl_2	o.n.[b]	**6b**	0[c]
4	**8b**	C_6H_{13}	H	H	A	Benzene	o.n.[b]	**6b**	0[c]
5	**8b**	C_6H_{13}	H	H	B	CH_2Cl_2	0.5	**6b**	72
6	**8c**		H	H	A	CH_2Cl_2	o.n.[b]	**6f**	0[c]
7	**8c**		H	H	B	CH_2Cl_2	0.5	**6f**	68 (95)[d]
8	**8d**	Ph	H	CH_3	A	CH_2Cl_2	16	**6d**	84
9	**8e**	Ph	Ph	H	A	CH_2Cl_2	o.n.[b]	**6g**	0[c]
10	**8e**	Ph	Ph	H	B	CH_2Cl_2	0.5	**6g**	52 (85)[d]
11	**8f**				B	CH_2Cl_2	0.5	**6e**	91 (98)[d]

[a] Oxidant: A, 1.2 Equivalents of DDQ; B, Dess–Martin periodinane.
[b] Over night.
[c] No reaction was observed.
[d] The yield in parenthesis is the conversion yield.



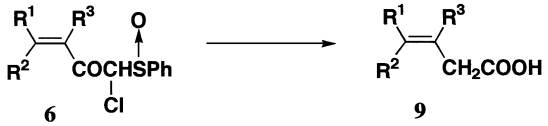
Scheme 4. Synthesis of (*E*)-4-phenyl-3-butenoic acid **9a** from γ,δ-alkenyl α-chloro-β-keto sulfoxide **6a**.

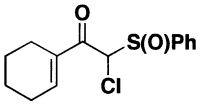
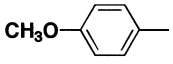
DDQ [12] and Dess–Martin periodinane[13] worked to give the desired ketone **6** (Table 3).

First, the alcohol **8a** derived from cinnamaldehyde was treated with 1.2 equivalents of DDQ in THF at room temperature for 17 h (entry 1). This reaction gave a rather clean reaction mixture from which the desired ketone **6a** was obtained in 76% yield. This reaction gave better yield when CH_2Cl_2 was used as the solvent (entry 2). We applied this oxidation to other alcohols **8b–e**. Quite interestingly, this DDQ-oxidation was found to be highly sensitive with the structure of the alcohols **8**. As shown in Table 3, in the alcohols **8b–f**, only **8d** was smoothly oxidized to give the ketone **6d** in good yield (entry 8). In the other cases (entries 3, 4, 6, and 9), almost no reaction was observed even when the reaction was conducted in refluxing solvent.

The Dess–Martin oxidation[13] was applied to the alcohols that could not be oxidized with DDQ (Table 3; entries 5, 7, 10, and 11). As shown in Table 3, the oxidation worked; however, the yields of the desired ketones were moderate to good, although the conversion yields were high. In addition, it was found that the ketones **6** are rather unstable under basic conditions and they dissolve in aqueous sodium hydroxide solution. This fact means that the hydrogen on the carbon bearing the sulfinyl group of **6** must be highly acidic. Because of the acidic nature of **6**, in the work-up of the oxidation, we had to use not a sodium hydroxide solution but a sodium hydrogencarbonate solution for removing the benzoic acid derivatives from the Dess–Martin periodinane.

Table 4. Synthesis of β,γ-alkenyl carboxylic acids **9** from γ,δ-alkenyl α-chloro-β-keto sulfoxides **6**



	6			9	
	R^1	R^2	R^3		(Yield/%)
6a	Ph	H	H	**9a**	60
6b	C_6H_{13}	H	H	**9b**	65
6c	Ph	H	Ph	**9c**	53
6d	Ph	H	CH_3	**9d**	80
6e				**9e**	69
6f		H	H	**9f**	85
6g	Ph	Ph	H	**9g**	69

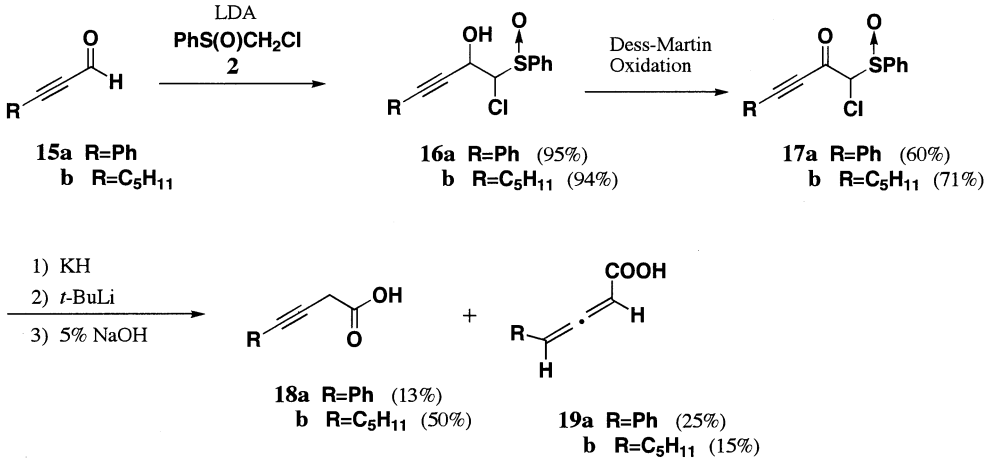
1.2. Trial to make β,γ-alkynyl carboxylic acids

We next investigated an extension of the above procedure to produce β,γ-alkynyl carboxylic acids starting from phenylpropargyl aldehyde **15a** and 2-octynal **15b** (Scheme 5). Addition of the lithium carbanion of **2** to these aldehydes gave the adduct **16** in quantitative yields. The oxidation of these alcohols **16** with DDQ gave only complex mixtures. The Dess–Martin oxidation of **16** worked; however, the yields of the ketones **17** were not high. In addition, it was found that the stability of the ketones **17** was found to be even lower compared with the ketones **6**.

The ketones **17** were treated with potassium hydride followed by *tert*-butyllithium in the same way as described above. We obtained the carboxylic acids; however, they

With several kinds of γ-alkenyl α-chloro-β-keto sulfoxides **6a–g** in hand, we investigated the final reaction (see Scheme 4).[6] A solution of **6a** in THF was added to a suspension of KH in dry THF at 0°C and the suspension was stirred for 30 min. Hydrogen gas evolution was observed within 30 min and in this treatment, **6a** was converted to the potassium enolate **10**. The solution was then cooled to −78°C and *tert*-butyllithium was added carefully to the solution. The sulfoxide–lithium exchange took place to give lithium alkylidene carbenoid **11**, which was then rearranged to the alkynolate **12**. After 10 min, 5% aqueous sodium hydroxide solution was added to the reaction mixture and the solution was slowly allowed to warm to room temperature. By this treatment, the alkynolate **12** was converted to the alkynol **13**, which was converted to the ketene **14**. The ketene **14** reacts with the water to give the desired carboxylic acid **9a** as crystals.

The results are summarized in Table 4. As shown in the table, all the ketones **6** gave the desired β,γ-alkenyl carboxylic acid in 53–85% yields. As described above, in our previous study,[6] we synthesized esters, thio esters, and amides by adding alcohols, thiols, and amine hydrochlorides instead of 5% aqueous sodiun hydroxide solution. We investigated also these reactions to produce β,γ-alkenyl carboxylic acid derivatives; however, adding those reagents instead of 5% NaOH gave only complex mixtures.



Scheme 5. One-carbon elongation of alkynals **15** to β,γ-alkynyl acids **18** and allenic acids **19**.

were a mixture of the β,γ-alkynyl carboxylic acid **18** and allenic carboxylic acid **19** and the yields were not good. Unfortunately, these carboxylic acids were very difficult to separate on silica gel. From these results, we concluded that the synthesis of β,γ-alkynyl carboxylic acids by the presented method is quite difficult.

2. Experimental

Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H NMR spectra were measured in a $CDCl_3$ solution with JEOL JNM-LA 400 and 500 spectrometer. Electron-impact mass spectra (MS) were obtained at 70 eV by direct insertion. Silica gel 60 (MERCK) containing 0.5% fluorescence reagent 254 and a quartz column were used for column chromatography and the products having UV absorption were detected by UV irradiation. In experiments requiring a dry solvent, THF was distilled from benzophenone ketyl; HMPA and diisopropylamine were distilled from CaH_2. α,β-Ethylenic carboxylic acid chlorides were synthesized from α,β-ethylenic carboxylic acids with $SOCl_2$ and distilled under vacuum before use.

2.1. Synthesis of γ,δ-alkenyl α-chloro-β-keto sulfoxides 6 from α,β-alkenyl carboxylic acid methylesters 10

A synthesis of (*E*)-1-chloro-4-phenyl-1-(phenylsulfinyl)but-3-ene-2-one (**6a**) is described. A solution of chloromethyl phenyl sulfoxide **2** (567 mg; 3.3 mmol) in 2 mL of THF was added dropwise to a solution of LDA (6.6 mmol) in 15 mL of dry THF at −78°C. The reaction mixture was stirred for 10 min, then methyl cinnamate **10a** (487 mg, 3 mmol) in 1.5 mL of dry THF was added to the reaction mixture and the solution was stirred at −78°C for 10 min. The reaction was quenched by adding saturated aqueous NH_4Cl and the whole was extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and the solvent was evaporated to give an oil. The product was separated by silica gel column chromatography to give **6a** (280 mg; 31%) as a colorless oil (about 2:3 diastereomeric mixture). IR (neat) 1688 (CO), 1606, 1089, 1056 (SO), 748, 688 cm^{-1}; ^{1}H NMR δ 5.23 (0.6H, s), 5.24 (0.4H, s), 6.97 (0.4H, d, *J*=15.6 Hz), 6.99 (0.6H, d, *J*=15.6 Hz), 7.39–7.73 (11H, m). MS *m/z* (%) 304 (M^+, 5), 178 (17), 131 (100), 115 (57). Calcd for $C_{16}H_{13}ClO_2S$: M, 304.0323. Found: *m/z* 304.0312.

2.1.1. 1-Chloro-1-(phenylsulfinyl)dec-3-ene-2-one (6b). Light yellow oil (about 2:3 diastereomeric mixture); IR (neat) 1693 (CO), 1621, 1089, 1058 (SO), 748, 689 cm^{-1}; ^{1}H NMR δ 0.89 (3H, t, *J*=7.0 Hz), 1.26–1.33 (6H, m), 1.42–1.46 (2H, m), 2.21–2.27 (2H, m), 5.14 (0.6H, s), 5.15 (0.4H, s), 6.37 (0.6H, d, *J*=15.6 Hz), 6.38 (0.4H, d, *J*=15.6 Hz), 7.02 (0.6H, dt, *J*=15.6, 7.0 Hz), 7.07 (0.4H, dt, *J*=15.6, 7.0 Hz), 7.51–7.70 (5H, m). MS *m/z* (%) 312 (M^+, 17), 139 (79), 125 (100). Calcd for $C_{16}H_{21}ClO_2S$: M, 312.0949. Found: *m/z* 312.0945.

2.2. Synthesis of γ,δ-alkenyl α-chloro-β-keto sulfoxides 6 from α,β-alkenyl carboxylic acid chlorides 5

A synthesis of **6a** from cinnamoyl chloride and chloromethyl phenyl sulfoxide **2** is described. A solution of chloromethyl phenyl sulfoxide **2** (262 mg; 1.5 mmol) in 1 mL of dry THF was added dropwise to a solution of LDA (3 mmol) in 8 mL of dry THF at −78°C. The mixture was stirred for 10 min, then the solution was cooled to −100°C. Cinnamoyl chloride (**5a**) (167 mg; 1 mmol) in 1 mL of dry THF was added to the solution and the reaction mixture was stirred at −100°C for 5 min. The reaction was quenched by adding saturated aqueous NH_4Cl and the solution was extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$, and the solvent was evaporated to give an oil, which was purified by silica gel column chromatography to afford **6a** (221 mg; 72%) as a light yellow oil.

2.2.1. (*E*)-1-Chloro-3,4-diphenyl-1-(phenylsulfinyl)but-3-ene-2-one (6c). Colorless oil (about 2:3 diastereomeric mixture); IR (neat) 1674 (CO), 1585, 1568, 1446, 1088, 1056 (SO), 751, 687 cm^{-1}; ^{1}H NMR δ 5.28 (0.6H, s), 5.29 (0.4H, s), 6.88–7.80 (16H, m). MS *m/z* (%) 380 (M^+, 1), 255 (22), 207 (39), 179 (100), 178 (85). Calcd for $C_{22}H_{17}ClO_2S$: M, 380.0638. Found: *m/z* 380.0640.

2.2.2. (*E*)-1-Chloro-3-methyl-4-phenyl-1-(phenylsulfinyl)-but-3-ene-2-one (6d). Colorless oil (about 3:7 diastereomeric

mixture); IR (neat) 1663 (CO), 1617, 1087, 1045 (SO), 749, 689 cm^{-1}; ^1H NMR δ 1.90 (2.1H, d, J=1.2 Hz), 2.15 (0.9H, d, J=1.2 Hz), 5.68 (0.3H, s), 5.84 (0.7H, s), 7.37–7.81 (11H, m). MS m/z (%) 318 (M^+, trace), 193 (53), 145 (55), 129 (100), 115 (65). Calcd for $C_{17}H_{15}ClO_2S$: M, 318.0481. Found: m/z 318.0483.

2.2.3. 2-Chloro-1-(1-cyclohexenyl)-2-(phenylsulfinyl)-ethanone (6e). Colorless oil (about 2:3 diastereomeric mixture); IR (neat) 1660 (CO), 1629, 1087, 1058 (SO), 752, 689 cm^{-1}; ^1H NMR δ 1.52–1.68 (4H, m), 1.86–2.35 (4H, m), 5.50 (0.4H, s), 5.63 (0.6H, s), 6.84 (0.6H, m), 7.05 (0.4H, m), 7.48–7.77 (5H, m). MS m/z (%) 282 (M^+, 7), 157 (8), 125 (53), 109 (100). Calcd for $C_{14}H_{15}ClO_2S$: M, 282.0481. Found: m/z 282.0491.

2.3. Addition of the lithium carbanion of chloromethyl phenyl sulfoxide 2 to α,β-alkenyl aldehydes 7

A synthesis of (*E*)-1-chloro-4-phenyl-1-(phenylsulfinyl)but-3-ene-2-ol (**8a**) is described. A solution of chloromethyl phenyl sulfoxide (576 mg; 3.3 mmol) in 1 mL of dry THF was added dropwise to a solution of LDA (4.5 mmol) in 10 mL of dry THF at −78°C. The mixture was stirred for 10 min, then cinnamaldehyde (**7a**) (0.4 mL; 3 mmol) in 1 mL of dry THF was added to the solution, and the reaction mixture was stirred at −78°C for 2 h. The reaction was quenched by adding saturated aqueous NH_4Cl, and the solution was extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and the solvent was evaporated to give oil, which was purified by silica gel column chromatography to afford **8a** (856 mg; 93%) as a colorless oil (about 1:1 diastereomeric mixture). IR (neat) 3343 (OH), 1444, 1086, 1047 (SO), 747, 690 cm^{-1}; ^1H NMR δ 3.12 (0.5H, d, J=4.5 Hz, OH), 4.28 (0.5H, d, J=4.5 Hz, OH), 4.51–4.54 (1H, m), 4.73–4.78 (0.5H, m), 4.93–4.97 (0.5H, m), 6.30 (0.5H, dd, J=15.4, 6.4 Hz), 6.32 (0.5H, dd, J=15.4, 6.4 Hz), 6.78 (0.5H, d, J=15.4 Hz), 6.80 (0.5H, d, J=15.4 Hz), 7.26–7.70 (10H, m). MS m/z (%) 306 (M^+, trace), 180 (31), 145 (46), 126 (100), 117 (52). Calcd for $C_{16}H_{15}ClO_2S$: M, 306.0481. Found: m/z 306.0472.

2.3.1. (*E*)-1-Chloro-1-(phenylsulfinyl)dec-3-ene-2-ol (8b). Colorless oil (a mixture of diastereomeric isomers); IR (neat) 3369 (OH), 1444, 1085, 1040 (SO), 747, 689 cm^{-1}; ^1H NMR δ 0.87 (3H, CH_3), 1.22–1.44 (8H, CH_2), 2.04–2.11 (2H, allyl-H), 4.35–4.68 (2H), 5.53–5.66 (1H, vinyl-H), 5.82–5.96 (1H, vinyl-H), 7.46–7.75 (5H, m). MS m/z (%) 314 (M^+, trace), 126 (100), 78 (18). Calcd for $C_{16}H_{23}ClO_2S$: M, 314.1106. Found: m/z 314.1095.

2.3.2. (*E*)-1-Chloro-4-(4-methoxyphenyl)-1-(phenylsulfinyl)but-3-ene-2-ol (8c). One of the isomers was separated as colorless crystals; mp 98–99.5°C (AcOEt–hexane). IR (KBr) 3328 (OH), 2832, 1605, 1084, 1033 (SO), 748, 687 cm^{-1}; ^1H NMR δ 2.87 (1H, d, J=4.4 Hz, OH), 3.82 (3H, s), 4.51 (1H, d, J=4.4 Hz), 4.90–4.94 (1H, m), 6.17 (1H, dds, J=16.0, 6.8 Hz), 6.74 (1H, d, J=16.0 Hz), 6.87 (2H, d, J=8.8 Hz), 7.36 (2H, d, J=8.8 Hz), 7.56–7.69 (5H, m). Anal. Calcd for $C_{17}H_{17}ClO_2S$: C, 60.62; H, 5.09; Cl, 10.53; S, 9.52. Found: C, 60.44; H, 4.73; Cl, 10.61; S, 9.64.

2.3.3. (*E*)-1-Chloro-3-methyl-4-phenyl-1-(phenylsulfinyl)-but-3-ene-2-ol (8d). Colorless oil (about 2:3 diastereomeric mixture); IR (neat) 3361, 1599, 1087, 1046 (SO), 746, 699 cm^{-1}; ^1H NMR δ 1.92 (3H, CH_3), 4.56–4.79 (2H, m), 6.58 (0.4H, s, vinyl-H), 6.78 (0.6H, s, vinyl-H), 7.20–7.75 (10H, m). MS m/z (%) 320 (M^+, 1), 159 (49), 126 (100). Calcd for $C_{17}H_{17}ClO_2S$: M, 320.0625. Found: m/z 320.0637.

2.3.4. 1-Chloro-4,4-diphenyl-1-(phenylsulfinyl)but-3-ene-2-ol (8e). Colorless oil (about 3:7 diastereomeric mixture); IR (neat) 3344 (OH), 1444, 1086, 1032 (SO), 754, 700 cm^{-1}; ^1H NMR δ 4.39 (0.3H, d, J=3.4 Hz), 4.44 (0.7H, d, J=3.4 Hz), 4.65–4.76 (1H, m), 6.13 (0.3H, d, J=9.3 Hz), 6.22 (0.7H, d, J=8.8 Hz), 7.14–7.72 (15H, m). MS m/z (%) 382 (M^+, trace), 282 (5), 256 (13), 221 (100), 115 (64). Calcd for $C_{22}H_{19}ClO_2S$: M, 382.0794. Found: m/z 382.0778.

2.3.5. 2-Chloro-1-(1-cyclohexenyl)-2-(phenylsulfinyl)-ethanol (8f). Colorless oil (about 1:1 diastereomeric mixture); IR (neat) 3368 (OH), 2930, 1478, 1445, 1088, 1052 (SO), 746, 688 cm^{-1}; ^1H NMR δ 1.52–2.23 (8H, m), 4.37–4.53 (2H, m), 5.80 (0.5H, s, vinyl-H), 5.98 (0.5H, s, vinyl-H), 7.54–7.72 (5H, m). MS m/z (%) 284 (M^+, trace), 157 (7), 126 (100), 78 (24). Calcd for $C_{14}H_{17}ClO_2S$: M, 284.0638. Found: m/z 284.0638.

2.4. Oxidation of 8 with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone

A synthesis of ketone **6a** from the alcohol **8a** is described. DDQ (259 mg; 1.14 mmol) was added to a solution of **8a** (291 mg; 0.95 mmol) in 10 mL of dry CH_2Cl_2 at room temperature with stirring. The solution was stirred for 19 h, then the reaction was quenched by adding 5% saturated aqueous $NaHCO_3$, and the solution was extracted with $CHCl_3$. The organic layer was washed once with saturated aqueous NH_4Cl. The solution was dried over $MgSO_4$, and the solvent was evaporated to give an oil, which was purified by silica gel column chromatography to afford **6a** (267 mg; 93%) as a yellow oil.

2.5. Oxidation of 8 with Dess–Martin periodinane

A synthesis of (*E*)-1-chloro-4-(4-methoxyphenyl)-1-(phenylsulfinyl)but-3-ene-2-one (**6f**) is described. Dess–Martin periodinane (550 mg; 1.3 mmol) was added to a solution of **8c** in 6 mL of dry CH_2Cl_2 at room temperature with stirring. The solution was stirred for 30 min, then the reaction was quenched by adding saturated aqueous $NaHCO_3$: $Na_2S_2O_3$ (1:1) and the solution was extracted with $CHCl_3$. The solution was purified by silica gel column chromatography to afford **6f** (203 mg; 68%, conversion yield 95%) as a light yellow oil (about 4.5:5.5 diastereomeric mixture); IR (neat) 2838, 1681 (CO), 1591, 1258, 1088, 1056 (SO), 748 cm^{-1}; ^1H NMR δ 3.86 (3H, s), 5.19 (0.55H, s), 5.24 (0.45H, s), 6.83 (0.45H, d, J=15.6 Hz), 6.87 (0.55 H, d, J=15.6 Hz), 6.92 (2H, d, J=8.9 Hz), 7.50–7.72 (8H, m). MS m/z (%) 334 (M^+, 3), 250 (3), 211 (9), 181 (22), 161 (100). Calcd for $C_{17}H_{15}ClO_3S$: M, 334.0428. Found: m/z 334.0427.

2.5.1. 1-Chloro-4,4-diphenyl-1-(phenylsulfinyl)but-3-ene-

2-one (6g) Colorless oil (about 4.5:5.5 diastereomeric mixture); IR (neat) 1682 (CO), 1584, 1567, 1088, 1056 (SO), 750, 696 cm^{-1}; ^1H NMR δ 4.88 (0.55H, s), 4.91 (0.45H, s), 6.68 (0.55H, s), 6.70 (0.45H, s), 7.13–7.67 (15H, m). MS *m/z* (%) 380 (M^+, trace), 254 (75), 207 (100), 191 (68). Calcd for $C_{22}H_{17}ClO_2S$: M, 380.0638. Found: *m/z* 380.0633.

2.6. Synthesis of β,γ-alkenyl carboxylic acids 9 from γ,δ-alkenyl α-chloro-β-keto sulfoxides 6

A synthesis of (*E*)-4-phenyl-3-butenoic acid (**9a**) is described. To a suspension of KH (32 mg; 0.8 mmol) in 3 mL of dry THF was added dropwise with stirring a solution of **6a** (122 mg; 0.4 mmol) in 1 mL of THF at 0°C. The suspension was stirred at 0°C for 15 min, then the solution was cooled to −78°C. *t*-BuLi (1.6 mmol) was added the reaction mixture was stirred at −78°C for 10 min, and at 0°C for 10 min. To the reaction mixture were added 5 mL of 5% NaOH and a mixture of ether–benzene (20 mL). The whole was stirred vigorously with a magnetic stirrer. The solution was transferred into a separatory funnel and the aqueous layer was separated. The organic layer was extracted once with 5% NaOH (5 mL). The combined aqueous layer was acidified with 10% HCl and extracted with ether–benzene. The organic layer was washed once with saturated aqueous NH_4Cl and dried over $MgSO_4$. Evaporation of the solvent gave **9a**[14,15] (36 mg; 60%) as a light yellow crystals. Mp 84–86°C (AcOEt–hexane); IR (KBr) 3060, 2957, 1704, 1650, 1224, 976, 745, 693 cm^{-1}; ^1H NMR δ 3.30 (2H, d, *J*=7.1 Hz), 6.28 (1H, dt, *J*=15.7, 7.1 Hz), 6.52 (1H, d, *J*=15.7 Hz), 7.22–7.38 (5H, m). MS *m/z* (%) 162 (M^+, 51), 117 (100), 115 (42), 91 (25). Calcd for $C_{10}H_{10}O_2$: M, 162.0680. Found: *m/z* 162.0674.

2.6.1. (*E*)-3-Decenoic acid (9b).[4] Yellow oil; IR (neat) 2928, 1716, 1143, 968, 690, 668 cm^{-1}; ^1H NMR δ 0,88 (3H, t, *J*=7.0 Hz), 1.21–1.40 (8H, m), 2.01–2.05 (2H, m), 3.02 (2H, d, *J*=5.8 Hz), 5.48–5.63 (2H, m).

2.6.2. (*Z*)-3,4-Diphenyl-3-butenoic acid (9c). Colorless crystals; mp 131.5–133°C (hexane), (lit.[16] mp 134.5–136°C). IR (KBr) 3054, 3022, 2920, 1705, 1303, 793, 760, 702, 659 cm^{-1}; ^1H NMR δ 3.52 (2H, s), 6.60 (1H, s), 6.95–7.30 (10H, m). MS *m/z* (%) 238 (M^+, 100), 178 (80), 115 (80). Calcd for $C_{16}H_{14}O_2$: M, 238.0993. Found: *m/z* 238.1004.

2.6.3. (*E*)-3-Methyl-4-phenyl-3-butenoic acid (9d). Colorless crystals; mp 111–112°C (AcOEt–hexane); IR (KBr) 2961, 2867, 1730, 1694, 1667, 1445, 1218, 747, 702 cm^{-1}; ^1H NMR δ 1.97 (3H, s), 3.23 (2H, s), 6.43 (1H, s), 7.20–7.35 (5H, m). MS *m/z* (%) 176 (M^+, 94), 131 (100), 116 (52), 91 (61). Calcd for $C_{11}H_{12}O_2$: M, 176.0830. Found: *m/z* 176.0836. Anal. Calcd for $C_{11}H_{12}O_2$: C, 75.03; H, 6.87. Found: C, 74.66; H, 6.69.

2.6.4. (1-Cyclohexenyl)acetic acid (9e). Light yellow low melting solid, (lit.[17] mp 34–35°C). IR (neat) 2929, 2859, 2838, 1708, 1437, 1408, 1294, 1224, 959, 921, 651 cm^{-1}; ^1H NMR δ 1.54–1.68 (4H, m), 2.01–2.06 (4H, m), 2.99 (2H, s), 5.61 (1H, s). MS *m/z* (%) 140 (M^+, 21), 81 (39), 80 (100). Calcd for $C_8H_{12}O_2$: M, 140.0836. Found: *m/z* 140.0846.

2.6.5. (*E*)-4-(4-Methoxyphenyl)-3-butenoic acid (9f). Colorless crystals; mp 101–103°C (hexane), (lit.[18] mp 102–104°C). IR (KBr) 2962, 2935, 1723, 1599, 1513, 1251, 1174, 1032, 831, 756 cm^{-1}; ^1H NMR δ 3.27 (2H, d, *J*=7.0 Hz), 3.81 (3H, s), 6.14 (1H, dt, *J*=15.9, 7.0 Hz), 6.46 (1H, d, *J*=15.9 Hz), 6.85 (2H, d, *J*=8.9 Hz), 7.31 (2H, d, *J*=8.6 Hz). MS *m/z* (%) 192 (M^+, 68), 147 (100), 91(18). Calcd for $C_{11}H_{12}O_3$: M, 192.0784. Found: *m/z* 192.0781.

2.6.6. 4,4-Diphenyl-3-butenoic acid (9g). Colorless crystals; mp 115–116°C (hexane), (lit.[19] 114.5–115.5°C). IR (KBr) 3058, 3025, 1706, 1584, 1567, 1445, 760, 698 cm^{-1}; ^1H NMR δ 3.21 (2H, d, *J*=7.3 Hz), 6.24 (1H, t, *J*=7.3 Hz), 7.12–7.48 (10H, m). MS *m/z* (%) 238 (M^+, 91), 193 (100), 178 (38), 115 (82). Calcd for $C_{16}H_{14}O_2$: M, 238.0986. Found: *m/z* 238.0992.

2.6.7. 1-Chloro-4-phenyl-1-(phenylsulfinyl)but-3-yn-2-ol (16a). Yellow oil; IR (neat) 3262 (OH), 2230, 1489, 1442, 1070, 1028 (SO), 690 cm^{-1}; ^1H NMR δ 3.99 (1H, s, OH), 4.63–4.71 (1H, m), 5.03–5.34 (1H, m), 7.28–7.86 (10H, m). MS *m/z* (%) 304 (M^+, trace), 290 (18), 226 (24), 126 (100), 125 (65), 115 (90).

2.6.8. 1-Chloro-1-(phenylsulfinyl)non-3-yn-2-ol (16b). Yellow oil; IR (neat) 3332 (OH), 2232, 1444, 1086, 1041 (SO), 749, 689 cm^{-1}; ^1H NMR δ 0.89 (3H, CH_3), 1.24–1.58 (6H, CH_2), 2.14 (1H, OH), 2.19–2.29 (2H, m), 4.38–4.69 (2H, m), 7.45–7.87 (5H, m). MS *m/z* (%) 299 (M^+, trace), 152 (9), 126 (100), 78 (32). Calcd for $C_{15}H_{20}ClO_2S$: M, 299.0872. Found: *m/z* 299.0860.

2.6.9. 1-Chloro-4-phenyl-1-(phenylsulfinyl)but-3-yn-2-one (17a). Yellow oil (about 2:3 diastereomeric mixture; IR (neat) 2205, 1672 (CO), 1444, 1286, 1089, 1058 (SO), 760, 688 cm^{-1}; ^1H NMR δ 5.20 (0.6H, s), 5.42 (0.4H, s), 7.39–7.75 (10H, m). MS *m/z* (%) 302 (M^+, 1), 210 (9), 149 (17), 129 (100), 125 (48). Calcd for $C_{16}H_{11}ClO_2S$: M, 302.0169. Found: *m/z* 302.0158.

2.6.10. 1-Chloro-1-(phenylsulfinyl)non-3-yn-2-one (17b). Yellow oil (about 1:1 diastereomeric mixture); IR (neat) 2208, 1681 (CO), 1444, 1090, 1059 (SO), 746, 689 cm^{-1}; ^1H NMR δ 0.92 (3H, t, *J*=7.2 Hz), 1.31–1.39 (4H, m), 1.56–1.59 (2H, m), 2.38–2.41 (2H, m), 5.02 (0.5H, s), 5.25 (0.5H, s), 7.53–7.72 (5H, m). MS *m/z* (%) 296 (M^+, trace), 125 (100), 123 (29). Calcd for $C_{15}H_{17}ClO_2S$: M, 296.0637. Found: *m/z* 296.0648.

2.6.11. A mixture of acetylene 18a and 19a. Only selected data can be described. Colorless oil; IR (neat) 2204 (acetylene), 1978 (allene), 1707 (CO), 1173, 758, 687 cm^{-1}; ^1H NMR δ 3.58 (s, propargyl-H), 6.03 (d, *J*=6.1 Hz), 6.69 (d, *J*=6.1 Hz). MS *m/z* (%) 160 (M^+, 50), 122 (61), 115 (96), 105 (100). Calcd for $C_{10}H_8O_2$: M, 160.0524. Found: *m/z* 160.0538.

2.6.12. A mixture of acetylene 18b and 19b. Only selected data can be described. Colorless oil; IR (neat) 2240 (acetylene), 1958 (allene; lit.[20] 1955), 1722, 1714 (CO), 1284,

1228, 935 cm^{-1}; ^1H NMR δ 3.32 (t, J=2.4 Hz, propargyl-H; lit.[21] 3.31 (t, J=2.5 Hz)), 5.58 (m, vinyl-H), 5.68 (m, vinyl-H). MS m/z (%) 154 (M^+, trace), 122 (38), 105 (43), 94 (100).

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