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Titanocene(II)-Promoted Olefination of ω,ω-Bis(phenylthio)alkyl Alkanoates. A New Method for the Preparation of ω-Hydroxy Ketones

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Abstract—Intramolecular olefination of esters having a thioacetal moiety was studied. The treatment of ω,ω-bis(phenylthio)alkyl alkanoates with $Cp_2Ti[P(OEt)_3]_2$ and the following hydrolysis gave ω-hydroxy ketones in good yields.

Introduction

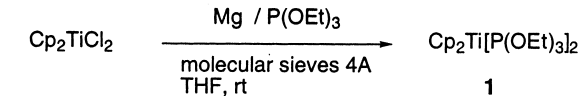
Olefination of carbonyl compounds is one of the most fundamental reactions in organic synthesis. Among a variety of reactions developed to accomplish this transformation, Wittig-type reaction is the most widely used method for this purpose.[1] Wittig olefination, however, suffers one serious drawback that the method can be successfully applied only to the olefination of ketones and aldehydes. Although titanium based reagents such as Tebbe reagent can be used for methylidenation of carbonyl compounds including esters,[2] only a limited number of Tebbe-type reagents which are capable of transforming carbonyl group to alkylidene groups have been developed. For example, a higher homologue of Tebbe reagent can be prepared from $Cp_2TiCl(CH{=}CHMe)$ and diisobutylaluminium hydride, and the resulting reagent can be used for the olefination of ketones in moderate yields.[3] However, these compounds have not yet been much exploited as reagents in organic synthesis owing to the difficulties encountered in their preparations. On the other hand, Utimoto and Takai's unidentified reagent prepared from zinc, dihalomethane, and titanium tetrachloride was shown to be useful for methylidenation of aldehydes and ketones. Modification of this mixture provides reagents that accomplish methylidenation and alkylidenation of carboxylic acid derivatives.[2]

Recently our research group has developed a new method for carbonyl olefination using a thioacetal-$Cp_2Ti[P(OEt)_3]_2$ **1** system.[4] The low-valent titanium species **1** can be prepared by the reduction of commercially available titanocene dichloride with magnesium in the presence of triethyl phosphite (Scheme 1). The organotitanium species formed by the above system are reactive not only toward carbonyl compounds but also carbon–carbon[5] and carbon–nitrogen multiple bonds.[6]

Intramolecular carbonyl olefination is still a big challenge to organic chemists because there is no practical method for intramolecular carbonyl olefination of carboxylic acid derivatives.[7] Recently we have disclosed an intramolecular carbonyl olefination of thiolesters having a diphenyl thioacetal moiety to afford dihydrothiophene derivatives.[8] This result prompted us to apply the thioacetal–titanocene(II) system to the intramolecular olefination of esters. We wish to report here a new synthetic method for the preparation of ω-hydroxy ketones **2** by the olefination of ω,ω-bis(phenylthio)alkyl alkanoates **3** followed by the hydrolysis of the resulting enol ethers (Scheme 2).

Results and Discussion

First we examined the preparation of the cyclic vinyl ether **4** by the olefination of 5,5-bis(phenylthio)pentyl benzoate **3g**. When the reaction of **3g** (0.1 M in THF) was carried out using 3 equiv. of the low-valent titanium reagent **1** at room temperature, a complicated reaction was observed. It is reasonable to assume that not only the intramolecular but also the intermolecular reaction may proceed in this case. In order to suppress the intermolecular reaction, we performed



Scheme 1.

Keywords: esters; olefination; thioacetal; titanium and compounds.
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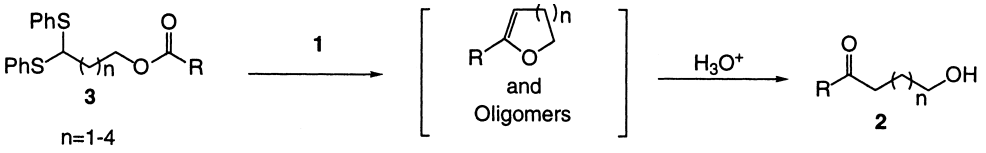
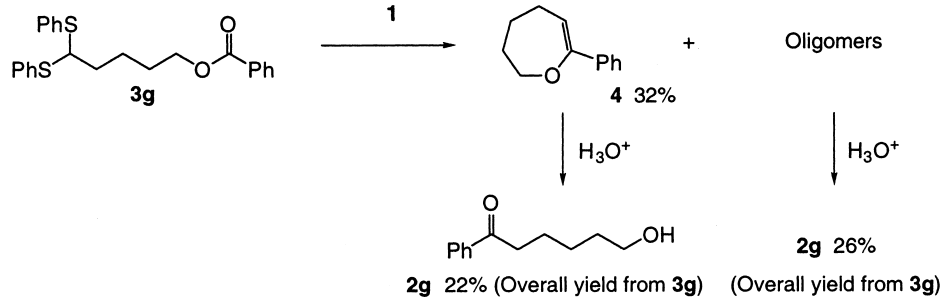
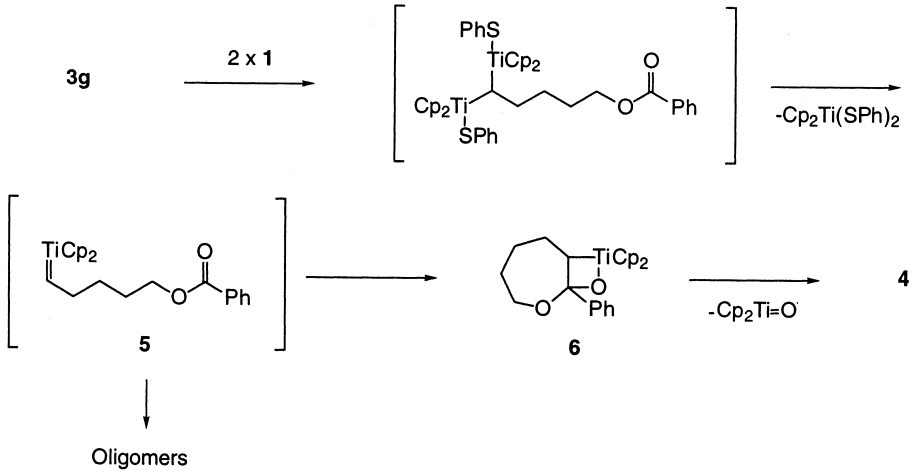


Scheme 2.



Scheme 3.

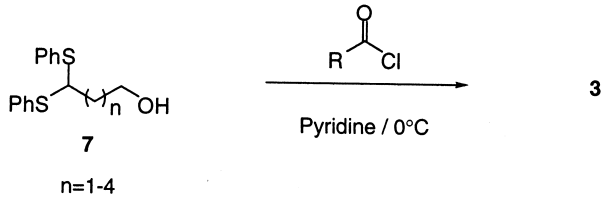


Scheme 4.

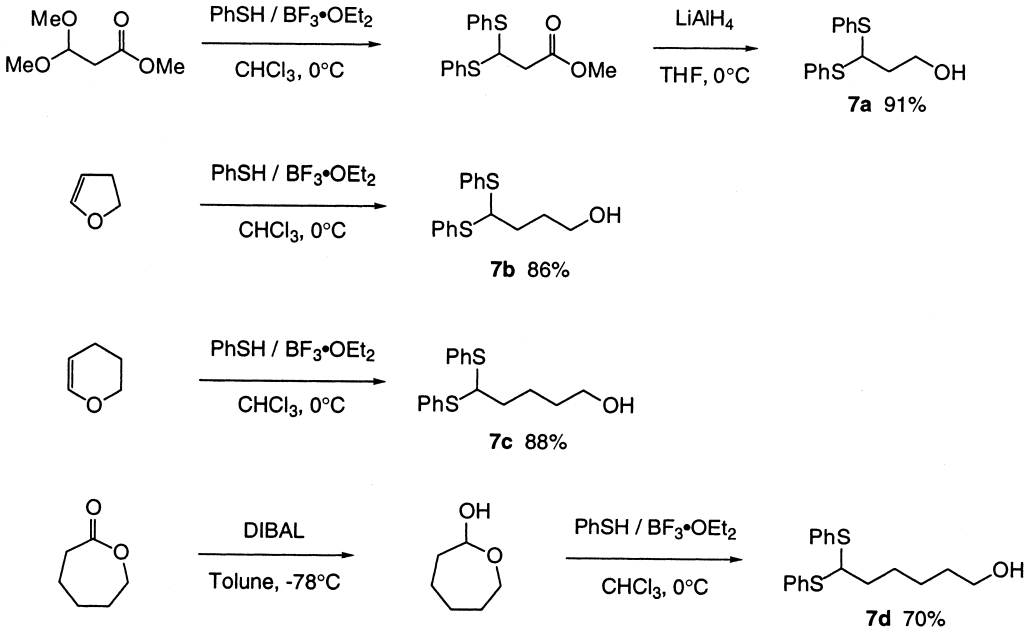
the same reaction under high dilution conditions. Unfortunately, however, we isolated the cyclic vinyl ether **4** only in 32% yield along with a multi-component mixture when the ester **3g** of 0.05 M concentration was added slowly to the low-valent titanium species in THF. The NMR spectrum of the latter mixture suggested that it contained oligomeric vinyl ethers that were formed by the inter- and intramolecular reactions. Then we hydrolyzed these compounds separately and it was confirmed that 6-hydroxy-1-phenylhexanone **2g** was produced by each reaction (Scheme 3).

Despite the further examination using various reaction conditions such as the method of addition and concentration of the substrate, the yield of **4** was not improved. The initial step of the present reaction is assumed to be the formation of carbene complex **5** by the desulfurization of thioacetal **3g** with **1**. The next step is the formation of oxatitanacycle **6** followed by the elimination of titanocene oxide to produce the cyclic vinyl ether **4** (Scheme 4). Unlike the intermolecular reaction, the sterically unfavorable bicyclic titanacycle **6** must be formed during this process. As a result, the intermolecular reaction takes place at the same time even under the high dilution conditions.

As for the preparation of ω-hydroxy ketones, various methods have been explored. The most conventional way



Scheme 5.



Scheme 6.

is the selective oxidation of diols with an inorganic oxidizing agent. For example, Choudary et al. reported the oxidation of diols using *tert*-butyl hydroperoxide in the presence of a catalytic amount of chromia-pillared montmorilonite.[9] It was reported that manganates selectively oxidize diols to hydroxy ketones.[10] Selective oxidations of diols using Br_2-distannoxane[11] and metal nitrates supported on silica gel[12] were also reported. Since ω,ω-bis(phenylthio)alkyl alkanoates **3** are easily prepared from carboxylic acid chlorides with ω,ω-bis(phenylthio)alkanols **7** (**3a**; 88%, **3b**; 91%, **3c**; 88%, **3d**; 91%, **3e**; 92%, **3f**; 88%, **3g**; 92%, **3h**; 89%, **3i**, 82%, **3j**; 90%, **3k**; 81%) (Scheme 5), the above results indicate that the intramolecular olefination of **3** and subsequent hydrolysis constitute a useful method for the transformation of carboxylic acids into ω-hydroxy ketones **2**. The alcohols **7a**–**d** were easily obtained from commercially available methyl 3,3-dimethoxypropanoate, 2,3-dihydrofuran, 3,4-dihydropyran, and ϵ-caprolactone, respectively (Scheme 6). Then we further investigated the present reaction as a method for the preparation of hydroxy ketones **2**.

The reaction of **3g** was carried out using 4 equiv. of the low-valent titanium species **1** in THF for 3 h at room temperature and the resulting crude mixture of enol ethers was treated with HCl in MeOH to produce ω-hydroxy ketone **2g** in 62% yield. The yield of **2g** was increased to 67% when the olefination was performed in refluxing THF. Under the similar reaction conditions, reactions of various ω,ω-bis(phenylthio)alkyl alkanoates **3** were performed and it was found that ω-hydroxy ketones were obtained in moderate to good yields depending on the number of the carbon chain of **7** (Table 1).

In the cases of γ and δ-hydroxy ketones **2a**–**d**, the yields were only moderate (see entries 1–4). We assumed that the relatively stable five- and six-membered cyclic hemiacetals were partially produced during the isolation using silica gel chromatography. Furthermore, it was found that these hydroxy ketones were unstable and easily transformed into unidentified compounds on standing. In order to avoid the formation of hemiacetals, the acetylation of hydroxy ketones was examined. After hydrolysis, the crude products were treated with acetyl chloride in the presence of triethylamine to afford the γ and δ-acetoxy ketones **8** in good yields (Table 2). The fact that the ϵ-acetoxy ketone **8d** was obtained in the yield comparable to the corresponding hydroxy ketone **2f** indicates that the formation of hemiacetal proceeds only in the case of γ- and δ-hydroxy ketones.

Conclusion

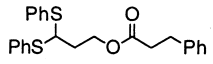
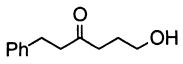
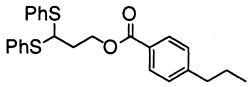
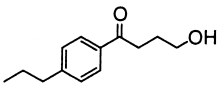
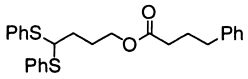
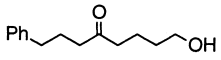
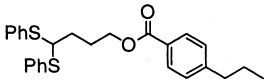
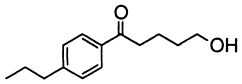
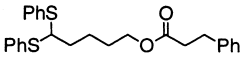
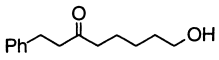
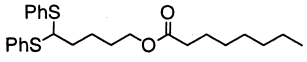
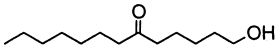
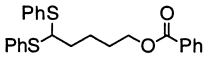
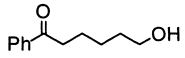
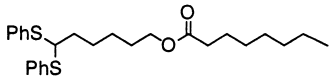
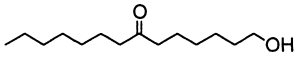
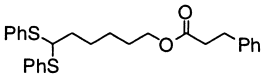
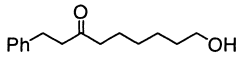
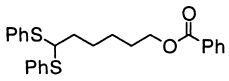
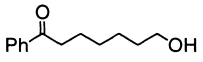
We established a new method for the preparation of ω-hydroxy ketones by the carbonyl olefination of ω,ω-bis(phenylthio)alkyl alkanoates. Since the starting materials are easily prepared by the acylation of ω,ω-bis(phenylthio)alkanols, it should be noted that the present reaction provides a convenient synthetic route to the hydroxy ketones which is completely different from the conventional methods.

Experimental

General

Melting points were determined with a Yanaco MP-S3 micromelting point apparatus. ^1H (500 and 200 MHz) and ^{13}C (125 MHz) NMR spectra were measured in $CDCl_3$ on a Jeol ALPHA-500 and a Jeol FX-200 instruments and are reported in parts per million from tetramethylsilane for ^1H and $CDCl_3$ for ^{13}C spectroscopies. IR spectra were recorded on a Jeol Diamond-20 FT-IR spectrometer; absorptions are reported in cm^{-1}. Elemental analyses were performed by a

Table 1. Preparation of ω-hydroxy ketones **2**

Entry	Ester **3**		ω-Hydroxy ketone **2**		Yield / %
1		**3a**		**2a**	52
2		**3b**		**2b**	55
3		**3c**		**2c**	48
4		**3d**		**2d**	45
5		**3e**		**2e**	67
6		**3f**		**2f**	78
7		**3g**		**2g**	67
8		**3h**		**2h**	69
9		**3i**		**2i**	71
10		**3j**		**2j**	66

Perkin–Elmer 2400II. Wakogel B-5F was used for preparative thin layer chromatography (PTLC) and Merck Si 60 was used for column chromatography as an adsorbent. THF was distilled from sodium and benzophenone. Magnesium turnings were purchased from Nacalai Tesque Inc. (Kyoto, Japan).

Preparation of ω,ω-bis(phenylthio)alkanols 7

Preparation of 3,3-bis(phenylthio)propan-1-ol (7a).[13] To a $CHCl_3$ (30 ml) solution of methyl 3,3-dimethoxypropanoate (4.2 ml, 30 mmol) and thiophenol (6.2 ml, 30 mmol) was added boron trifluoride diethyl etherate (7.4 ml, 60 mmol) at 0°C, and the reaction mixture was stirred overnight. The reaction was quenched by addition of water and organic materials were extracted with $CHCl_3$. The extract was washed with water, dried (Na_2SO_4), and condensed under reduced pressure to give the crude thioacetal. To a THF (30 ml) suspension of $LiAlH_4$ (1.14 g, 30 mmol) was added a THF (20 ml) solution of the crude thioacetal at 0°C under argon. After being stirred overnight, the reaction was quenched by dropwise addition of 1 M NaOH, and the insoluble materials were filtered through Celite and washed with ether. The filtrate was condensed under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc=2:1)

Table 2. Preparation of ω-acetoxy ketones **8**

Entry	Ester **3**	ω-Acetoxy ketone **8**	Yield / %
1	**3a**	**8a**	62
2	**3k**	**8b**	60
3	**3d**	**8c**	63
4	**3f**	**8d**	73

to give **7a** (7.51 g, 91%). **7a**: ^{1}H NMR 1.66 (br s, 1H), 2.10 (q, *J*=6.2 Hz, 2H), 3.89 (br s, 2H), 4.64 (t, *J*=7.0 Hz, 1H), 7.22–7.32 (m, 6H), 7.42–7.47 (m, 4H); ^{13}C NMR 38.36, 55.14, 60.14, 127.82, 128.95, 132.76, 133.81; IR (neat) 3573, 3399, 3073, 3058, 2946, 2883, 1583, 1481, 1438, 1068, 1025, 690. Anal. Calcd for $C_{15}H_{16}S_2O$: C, 65.18; H, 5.83. Found: C, 64.77; H, 5.80.

Preparation of 4,4-bis(phenylthio)butan-1-ol (7b). To a $CHCl_3$ (50 ml) solution of 2,3-dihydrofuran (3.8 ml, 50 mmol) and thiophenol (10.3 ml, 100 mmol) was added boron trifluoride diethyl etherate (5.7 ml, 50 mmol) successively at 0°C. After being stirred for 1 h, the reaction was quenched by addition of water, and the organic materials were extracted with $CHCl_3$. The extract was washed with 1 M NaOH, water, and saturated NaCl solution, and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane/EtOAc=4:1) to give **7b** (12.50 g, 86%). **7b**: ^{1}H NMR 1.64 (br s, 1H), 1.83–1.99 (m, 4H), 3.63 (t, *J*=6.1 Hz, 2H), 4.45 (t, *J*=6.6 Hz, 1H), 7.22–7.32 (m, 6H), 7.41–7.47 (m, 4H); ^{13}C NMR 30.08, 32.31, 58.22, 62.26, 127.72, 128.90, 132.70, 134.13; IR (neat) 3369, 3059, 2949, 2877, 1583, 1439, 1066, 1026, 741, 690. Anal. Calcd for $C_{16}H_{18}S_2O$: C, 66.17; H, 6.25. Found: C, 66.35; H, 6.53.

In a similar manner, 5,5-bis(phenylthio)pentan-1-ol (**7c**)[13] was obtained in 88% yield using 3,4-dihydropyran as a starting material. **7c**: ^{1}H NMR 1.44 (br s, 1H), 1.48–1.58 (m, 2H), 1.63–1.75 (m, 2H), 1.83–1.92 (m, 2H), 3.60 (t, *J*=6.6 Hz, 2H), 4.40 (t, *J*=6.6 Hz, 1H), 7.24–7.34 (m, 6H), 7.42–7.48 (m, 4H); ^{13}C NMR 23.24, 32.01, 35.48, 58.32, 62.51, 127.66, 128.85, 132.69, 134.14; IR (neat) 3369, 3057, 2937, 2861, 1583, 1479, 1439, 1066, 1024, 741, 690. Anal. Calcd for $C_{17}H_{20}S_2O$: C, 67.06; H, 6.62. Found: C, 66.80; H, 6.79.

Preparation of 6,6-bis(phenylthio)hexan-1-ol (7d). To a toluene solution of DIBAL (30 mmol) was added ϵ-caprolactone (3.3 ml, 30 mmol) slowly at −78°C under argon. After being stirred for 4 h, the reaction was quenched by addition of saturated $NaHCO_3$ solution, and the organic materials were extracted with CH_2Cl_2 and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the crude mixture was dissolved in $CHCl_3$ (20 ml), and thiophenol (6.2 ml, 60 mmol) and boron trifluoride diethyl etherate (3.4 ml, 30 mmol) were added successively at 0°C. After being stirred for 2 h, the reaction was quenched by addition of water and the organic materials were extracted with $CHCl_3$. The extract was washed with 1 M NaOH, water, and saturated NaCl solution, and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the crude product was purified by silica gel column chromatography (hexane/EtOAc=4:1) to give **7d** (6.68 g, 70%). **7d**: ^{1}H NMR 1.26–1.36 (m, 2H), 1.46–1.58 (m, 3H), 1.58–1.67 (m, 2H), 1.80–1.90 (m, 2H), 3.58 (t, *J*=6.6 Hz, 2H), 4.40 (t, *J*=6.6 Hz, 1H), 7.22–7.32 (m, 6H), 7.42–7.46 (m, 4H); ^{13}C NMR 25.12, 26.70, 32.37, 35.68, 58.26, 62.60, 127.59, 128.81, 132.61, 134.18; IR (neat) 3356, 3059, 2941, 2860, 1583, 1481, 1439, 1068, 1026, 741, 690. Anal. Calcd for $C_{18}H_{22}S_2O$: C, 67.88; H, 6.96; Found: C, 67.93; H, 7.02.

Preparation of ω,ω-bis(phenylthio)alkyl alkanoates 3

Preparation of 5,5-bis(phenylthio)pentyl benzoate (3g). To a pyridine (5 ml) solution of **7c** (1.52 g, 5 mmol) was added benzoyl chloride (0.64 ml, 5.5 mmol) at 0°C. After being stirred for 1 h, the reaction was quenched by addition of water, and the organic materials were extracted with ether. The extract was washed with 1 M HCl, water, and saturated NaCl solution, and dried (Na_2SO_4). After removal of the solvent, the residue was purified by silica gel column chromatography (hexane/EtOAc=9:1) to give **3g** (1.87 g,

92%). **3g**: ^{1}H NMR 1.69–1.82 (m, 4H), 1.87–1.95 (m, 2H), 4.27 (t, *J*=6.1 Hz, 2H), 4.40 (t, *J*=6.5 Hz, 1H), 7.22–7.31 (m, 6H), 7.40–7.47 (m, 6H), 7.51–7.56 (m, 1H), 8.00–8.05 (m, 2H); ^{13}C NMR 23.60, 28.17, 35.35, 58.27, 64.57, 127.74, 128.32, 128.89, 129.52, 130.34, 132.78, 132.85, 134.05, 166.54; IR (neat) 3058, 2947, 1716, 1583, 1479, 1438, 1274, 1117, 1025, 748, 713, 690. Anal. Calcd for $C_{24}H_{24}S_2O_2$: C, 70.55; H, 5.92. Found: C, 70.63; H, 6.05.

In a similar manner, the following ω,ω-bis(phenylthio)alkyl alkanoates **3** were obtained.

3,3-Bis(phenylthio)propyl 3-phenylpropanoate (3a). ^{1}H NMR 2.11 (dt, *J*=6.1, 7.0 Hz, 2H), 2.56 (t, *J*=7.8 Hz, 2H), 2.88 (t, *J*=7.8 Hz, 2H), 4.31 (t, *J*=6.1 Hz, 2H), 4.43 (t, *J*=7.0 Hz, 1H), 7.14–7.33 (m, 11H), 7.42–7.48 (m, 4H); ^{13}C NMR 30.81, 34.83, 35.72, 55.02, 61.54, 126.25, 127.93, 128.17, 128.47, 128.92, 132.96, 133.54, 140.33, 172.50; IR (neat) 3060, 3028, 2958, 1732, 1583, 1439, 1248, 1161, 748, 692. Anal. Calcd for $C_{24}H_{24}S_2O_2$: C, 70.55; H, 5.92. Found: C, 70.75; H, 6.09.

3,3-Bis(phenylthio)propyl 4-propylbenzoate (3b). ^{1}H NMR 0.94 (t, *J*=7.3 Hz, 3H), 1.66 (tq, *J*=7.3, 7.6 Hz, 2H), 2.28 (dt, *J*=6.1, 7.0 Hz, 2H), 2.64 (t, *J*=7.5 Hz, 2H), 4.55 (t, *J*=6.1 Hz, 2H), 4.59 (t, *J*=7.0 Hz, 1H), 7.20–7.32 (m, 8H), 7.45–7.52 (m, 4H), 7.85–7.90 (m, 2H); ^{13}C NMR 13.70, 24.22, 35.09, 37.99, 55.15, 61.88, 127.48, 127.89, 128.45, 128.95, 129.57, 132.88, 133.69, 148.33, 166.31; IR (neat) 3059, 2962, 1720, 1439, 1275, 1109, 748, 690. Anal. Calcd for $C_{25}H_{26}S_2O_2$: C, 71.05; H, 6.20. Found: C, 71.30; H, 6.34.

4,4-Bis(phenylthio)butyl 4-phenylbutanoate (3c). ^{1}H NMR 1.86–1.98 (m, 6H), 2.24 (t, *J*=7.5 Hz, 2H), 2.62 (t, *J* =7.6 Hz, 2H), 4.04 (t, *J*=6.1 Hz, 2H), 4.40 (t, *J*=6.3 Hz, 1H), 7.14–7.32 (m, 11H), 7.43–7.48 (m, 4H); ^{13}C NMR 26.09, 26.39, 32.15, 33.50, 35.10, 57.88, 63.46, 125.96, 127.81, 128.36, 128.45, 128.90, 132.82, 133.86, 141.28, 173.36; IR (neat) 3060, 2954, 1732, 1583, 1439, 1146, 748, 692. Anal. Calcd for $C_{26}H_{28}S_2O_2$: C, 71.52; H, 6.46. Found: C, 71.67; H, 6.64.

4,4-Bis(phenylthio)butyl 4-propylbenzoate (3d). ^{1}H NMR 0.95 (t, *J*=7.3 Hz, 3H), 1.66 (tq, *J*=7.3, 7.6 Hz, 2H), 1.97–2.04 (m, 2H), 2.04–2.13 (m, 2H), 2.64 (t, *J*=7.6 Hz, 2H), 4.29 (t, *J*=6.3 Hz, 2H), 4.46 (t, *J*=6.6 Hz, 1H), 7.19–7.23 (m, 2H), 7.23–7.31 (m, 6H), 7.43–7.50 (m, 4H), 7.84–7.88 (m, 2H); ^{13}C NMR 13.71, 24.25, 26.22, 32.21, 38.02, 57.84, 63.91, 127.64, 127.79, 128.44, 128.92, 129.57, 132.83, 133.88, 148.22, 166.56; IR (neat) 3059, 2962, 1716, 1439, 1282, 1178, 1113, 748, 692. Anal. Calcd for $C_{26}H_{28}S_2O_2$: C, 71.52; H, 6.46. Found: C, 71.62, H; 6.61.

5,5-Bis(phenylthio)pentyl 3-phenylpropanoate (3e). ^{1}H NMR 1.53–1.68 (m, 4H), 1.81–1.90 (m, 2H), 2.61 (t, *J*=7.8 Hz, 2H), 2.94 (t, *J*=7.8 Hz, 2H), 4.03 (t, *J*=6.4 Hz, 2H), 4.37 (t, *J*=6.6 Hz, 1H), 7.16–7.21 (m, 3H), 7.23–7.33 (m, 8H), 7.42–7.47 (m, 4H); ^{13}C NMR 23.43, 27.97, 30.88, 35.30, 35.77, 58.16, 64.05, 126.16, 127.66, 128.19, 128.39, 128.83, 132.67, 134.04, 140.40, 172.76; IR (neat) 3060, 3030, 2949, 2866, 1732, 1583, 1439, 1161, 748, 692. Anal. Calcd for $C_{26}H_{28}S_2O_2$: C, 71.52; H, 6.46. Found: C, 71.51; H, 6.55.

5,5-Bis(phenylthio)pentyl octanoate (3f). ^{1}H NMR 0.87 (t, *J*=7.0 Hz, 3H), 1.22–1.34 (m, 8H), 1.55–1.72 (m, 6H), 1.87 (dt, *J*=6.7, 8.2 Hz, 2H), 2.28 (t, *J*=7.6 Hz, 2H), 4.03 (t, *J*=6.4 Hz, 2H), 4.39 (t, *J*=6.7 Hz, 1H), 7.24–7.33 (m, 6H), 7.42–7.48 (m, 4 H); ^{13}C NMR 14.03, 22.56, 23.52, 24.97, 28.09, 28.90, 29.09, 31.63, 34.32, 35.38, 58.27, 63.86, 127.71, 128.87, 132.75, 134.10, 173.86; IR (neat) 3059, 2933, 2858, 1739, 1439, 1169, 748, 692. Anal. Calcd for $C_{25}H_{34}S_2O_2$: C, 69.72; H, 7.96. Found C, 69.68; H, 8.11.

6,6-Bis(phenylthio)hexyl octanoate (3h). ^{1}H NMR 0.86 (t, *J*=6.9 Hz, 3H), 1.20–1.40 (m, 10H), 1.52–1.72 (m, 6H), 1.80–1.90 (m, 2H), 2.26 (t, *J*=7.5 Hz, 2H), 4.01 (t, *J*=6.6 Hz, 2H), 4.39 (t, *J*=6.6 Hz, 1H), 7.22–7.38 (m, 6H), 7.40–7.52 (m, 4H); ^{13}C NMR 14.04, 22.56, 24.97, 25.44, 26.63, 28.41, 28.89, 29.08, 31.63, 34.33, 35.66, 58.30, 64.05, 127.64, 128.85, 132.67, 134.23, 173.91; IR (neat) 3059, 2929, 2856, 1734, 1583, 1439, 1169, 748, 692. Anal. Calcd for $C_{26}H_{36}S_2O_2$: C, 70.23; H, 8.16. Found: C, 70.31; H, 8.21.

6,6-Bis(phenylthio)hexyl 3-phenylpropanoate (3i). ^{1}H NMR 1.22–1.31 (m, 2H), 1.52–1.64 (m, 4H), 1.83 (dt, *J*=6.7, 8.9 Hz, 2H), 2.61 (t, *J*=7.8 Hz, 2H), 2.94 (t, *J*=7.9 Hz, 2H), 4.03 (t, *J*=6.6 Hz, 2H), 4.39 (t, *J*=6.7 Hz, 1H), 7.15–7.21 (m, 3H), 7.23–7.33 (m, 8H), 7.42–7.48 (m, 4H); ^{13}C NMR 25.38, 26.61, 28.35, 30.94, 35.63, 35.85, 58.28, 64.29, 126.20, 127.64, 128.23, 128.43, 128.85, 132.65, 134.21, 140.46, 172.89; IR (neat) 3060, 3028, 2939, 2860, 1732, 1583, 1479, 1161, 748, 690. Anal. Calcd for $C_{27}H_{30}S_2O_2$: C, 71.96; H, 6.71. Found: C, 72.05; H, 6.78.

6,6-Bis(phenylthio)hexyl benzoate (3j). ^{1}H NMR 1.38–1.47 (m, 2H), 1.64–1.78 (m, 4H), 1.88 (dt, *J*=6.7, 8.5 Hz, 2H), 4.37 (t, *J*=6.6 Hz, 2H), 4.40 (t, *J*=6.7 Hz, 1H), 7.22–7.31 (m, 6H), 7.39–7.48 (m, 6H), 7.52–7.56 (m, 1H), 8.00–8.05 (m, 2H); ^{13}C NMR 25.52, 26.64, 28.48, 35.64, 58.29, 64.77, 127.64, 128.29, 128.85, 129.49, 130.37, 132.67, 132.79, 134.19, 166.56; IR (neat) 3059, 2939, 2858, 1716, 1583, 1275, 1117, 1026, 748, 714, 690. Anal. Calcd for $C_{25}H_{26}S_2O_2$: C, 71.05; H, 6.20. Found: C, 71.26; H, 6.44.

4,4-Bis(phenylthio)butyl 4-methylbenzoate (3k). ^{1}H NMR 1.95–2.02 (m, 2 H), 2.04–2.11 (m, 2H), 2.40 (s, 3 H), 4.27 (t, *J*=6.1 Hz, 2H), 4.44 (t, *J*=6.4 Hz, 1H), 7.20 (d, *J*=7.9 Hz, 2H), 7.22–7.30 (m, 6H), 7.42–7.49 (m, 4H), 7.82 (d, *J*=7.9 Hz, 2H); ^{13}C NMR 21.66, 26.22, 32.22, 57.87, 63.94, 127.42, 127.81, 128.94, 129.02, 129.57, 132.84, 133.88, 143.54, 166.55; IR (neat) 3060, 2958, 1716, 1614, 1481, 1275, 1109, 841, 752, 690. Anal. Calcd for $C_{24}H_{24}S_2O_2$: C, 70.27; H, 11.01. Found: C, 70.33, H; 11.19.

Carbonyl olefination of ω,ω-bis(phenylthio)alkyl alkanoates 3 followed by hydrolysis

Preparation of 6-hydroxy-1-phenylhexan-1-one (2g). Magnesium turnings (58 mg, 2.4 mmol), finely powdered

molecular sieves 4A (200 mg) and Cp_2TiCl_2 (498 mg, 2 mmol) were placed in a flask and dried by heating with a heat gun under reduced pressure (2–3 mmHg). Care was taken not to sublime Cp_2TiCl_2. After cooling, THF (6 ml) and $P(OEt)_3$ (0.69 ml, 4 mmol) were added successively at room temperature under argon, and the reaction mixture was stirred for 3 h. Then **3g** (204 mg, 0.5 mmol) in THF (10 ml) was added dropwise over 20 min to the mixture. After being refluxed for 3 h, the reaction was quenched by addition of 1 M NaOH (15 ml) and the resulting insoluble materials were filtered through Celite. The organic materials were extracted with ether, and the extract was condensed under reduced pressure. The residue was dissolved in methanol (5 ml) and 3 M HCl (2 ml) was added. After being stirred for 1 h, the reaction mixture was diluted with water. The organic materials were extracted with CH_2Cl_2 and dried (Na_2SO_4). After removal of the solvent, the residue was purified by PTLC (hexane/AcOEt=2:1) to afford **2g** (64 mg, 67%). **2g:** ^{1}H NMR 1.42–1.51 (m, 2H), 1.58–1.67 (m, 2H), 1.73–1.82 (m, 2H), 2.11 (br s, 1H), 2.99 (t, *J*=7.3 Hz, 2H), 3.66 (t, *J*=6.6 Hz, 2H), 7.42–7.49 (m, 2H), 7.52–7.58 (m, 2H), 7.92–7.99 (m, 1H); ^{13}C NMR 23.83, 25.86, 32.38, 38.36, 62.45, 127.95, 128.48, 132.90, 136.87, 200.46; IR (neat) 3407, 3062, 2937, 2864, 1684, 1448, 1221, 1053, 752, 690. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.72; H, 8.76.

In a similar manner, the following ω-hydroxy ketones **2** were obtained.

6-Hydroxy-1-phenylhexan-3-one (2a). ^{1}H NMR 1.82–1.90 (m, 2H), 2.06–2.28 (br, 1H), 2.52 (t, *J*=6.8 Hz, 2H), 2.68–2.98 (m, 4H), 3.60 (t, *J*=6.8 Hz, 2H), 7.11–7.37 (m, 5H); IR (neat) 3442, 3026, 2949, 2881, 1712, 1604, 1496, 1454, 1062, 748, 691.

4-Hydroxy-1-(4-propylphenyl)butan-1-one (2b). ^{1}H NMR 0.94 (t, *J*=7.3 Hz, 3H), 1.66 (tq, *J*=7.3, 7.6 Hz, 2H), 2.01 (tt, *J*=6.1, 6.7 Hz, 2H), 1.95–2.20 (br, 1H), 2.64 (t, *J*=7.6 Hz, 2H), 3.11 (t, *J*=6.7 Hz, 2H), 3.74 (t, *J*=6.1 Hz, 2H), 7.26 (d, *J*=7.6 Hz, 2H), 7.90 (d, *J*=8.2 Hz, 2H); ^{13}C NMR 13.71, 24.17, 26.96, 35.20, 37.98, 62.33, 128.11, 128.21, 128.67, 134.55, 148.60, 200.31; IR (neat) 3529, 2937, 2873, 1684, 1608, 1413, 1182, 1070. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.24; H, 8.53.

8-Hydroxy-1-phenyloctan-4-one (2c). ^{1}H NMR 1.40–2.20 (m, 7H), 2.42 (t, *J*=7.2 Hz, 4H), 2.62 (t, *J*=7.6 Hz, 2H), 3.61 (t, *J*=5.6 Hz, 2H), 7.07–7.35 (m, 5H); ^{13}C NMR 19.64, 25.19, 32.11, 35.07, 41.88, 42.30, 62.28, 125.93, 128.41, 128.44, 141.54, 210.98; IR (neat) 3413, 3030, 2945, 2871, 1714, 1455, 1062, 748, 700. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.01; H, 9.21.

5-Hydroxy-1-(4-propylphenyl)pentan-1-one (2d). ^{1}H NMR 0.94 (t, *J*=7.2 Hz, 3H), 1.50–2.02 (m, 7H), 2.64 (t, *J*=7.5 Hz, 2H), 3.02 (t, *J*=6.9 Hz, 2H), 3.68 (t, *J*=6.1 Hz, 2H), 7.08–7.43 (m, 2H), 7.89 (d, *J*=7.2 Hz, 2H); IR (neat) 3432, 2960, 1683, 1608, 1414, 1182, 1070. Anal. Calcd For $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 75.96, H, 9.27.

8-Hydroxy-1-phenyloctan-3-one (2e). ^{1}H NMR 1.28–1.36 (m, 2H), 1.50–1.62 (m, 4H), 1.95 (br s, 1H), 2.39 (t, *J*=7.3 Hz, 2H), 2.72 (t, *J*=7.6 Hz, 2H), 2.88 (t, *J*=7.6 Hz, 2H), 3.61 (t, *J*=6.6 Hz, 2H), 7.10–7.19 (m, 3H), 7.19–7.29 (m, 2H); ^{13}C NMR 23.26, 25.20, 29.67, 32.28, 42.78, 44.17, 62.40, 125.98, 128.21, 128.38, 140.98, 210.28; IR (neat) 3411, 2937, 2863, 1712, 1496, 1454, 1055, 750, 700. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.00; H, 9.49.

1-Hydroxytridecan-6-one (2f). Mp 39–39.5°C; ^{1}H NMR 0.86 (t, *J*=7.0 Hz, 3H), 1.22–1.40 (m, 10H), 1.52–1.64 (m, 6H), 2.00 (br s, 1H), 2.39 (t, *J*=7.3 Hz, 2H), 2.42 (t, *J*=7.3 Hz, 2H), 3.63 (t, *J*=6.6 Hz, 2H); ^{13}C NMR 13.98, 22.51, 23.35, 23.80, 25.28, 28.98, 29.12, 31.59, 32.33, 42.53, 42.80, 62.42, 211.65; IR (KBr) 3273, 2933, 2850, 1699, 1469, 1382, 1070, 727. Anal. Calcd for $C_{13}H_{26}O_2$: C, 72.85; H, 12.22. Found: C, 72.14; H, 11.54.

1-Hydroxytetradecan-7-one (2h). Mp 52.5–53°C; ^{1}H NMR 0.88 (t, *J*=6.5 Hz, 3H), 1.20–1.41 (m, 12H), 1.52–1.64 (m, 7H), 2.38 (t, *J*=7.6 Hz, 2H), 2.40 (t, *J*=7.3 Hz, 2H), 3.63 (t, *J*=6.6 Hz, 2H); ^{13}C NMR 14.00, 22.55, 23.69, 23.84, 25.49, 28.95, 29.02, 29.17, 31.62, 32.48, 42.58, 42.79, 62.78, 211.69; IR (KBr) 3296, 2933, 2850, 1707, 1465, 1419, 1381, 1074, 729. Anal. Calcd for $C_{14}H_{28}O_2$: C, 73.63; H, 12.36. Found: C, 73.57; H, 12.17.

9-Hydroxy-1-phenylnonan-3-one (2i). Mp 30°C; ^{1}H NMR 1.28–1.39 (m, 4H), 1.50–1.62 (m, 4H), 1.65–1.90 (br, 1H), 2.38 (t, *J*=7.3 Hz, 2H), 2.72 (t, *J*=7.6 Hz, 2H), 2.89 (t, *J*=7.6 Hz, 2H), 3.61 (t, *J*=6.7 Hz, 2H), 7.10–7.37 (m, 5H); ^{13}C NMR 23.57, 25.43, 28.84, 29.70, 32.41, 42.81, 44.16, 62.68, 125.99, 128.23, 128.39, 141.04, 210.34; IR (KBr) 3350, 3031, 2937, 2858, 1697, 1454, 1058, 1043, 989, 733, 702. Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.70; H, 9.61.

7-Hydroxy-1-phenylheptan-1-one (2j). Mp 33.5–34°C; ^{1}H NMR 1.30–1.42 (m, 4H), 1.45–1.58 (m, 2H), 1.62–1.74 (m, 2H), 1.75–1.92 (br, 1H), 2.94 (t, *J*=7.3 Hz, 2H), 3.61 (t, *J*=6.6 Hz, 2H), 7.38–7.48 (m, 2H), 7.48–7.55 (m, 1H), 7.88–7.97 (m, 2H); ^{13}C NMR 24.19, 25.54, 29.03, 32.50, 38.41, 62.77, 127.99, 128.51, 132.89, 136.95, 200.52; IR (KBr) 3402, 2937, 2864, 1684, 1599, 1448, 1221, 1053, 752, 690. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.47; H, 9.08.

The cyclic vinyl ether, 2,3,4,5-tetrahydro-7-phenyloxepin **4**, was obtained by the reaction of **3g** without hydrolysis using the usual work-up and isolation procedures. **4**: mp 125.5–126.5°C; ^{1}H NMR 1.64–1.75 (m, 4H), 2.34 (q, *J*=7.9 Hz, 2H), 3.72 (t, *J*=5.0 Hz, 2H), 5.34 (t, *J*=7.9 Hz, 1H), 7.24–7.30 (m, 1H), 7.31–7.37 (m, 2H), 7.42–7.47 (m, 2H); ^{13}C NMR 24.92, 26.76, 29.13, 68.97, 115.04, 126.21, 127.62, 128.28, 136.39, 153.67; IR (KBr) 3060, 2962, 1718, 1583, 1481, 1438, 1278, 1066, 739, 714, 690. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.48, H, 7.93.

Preparation of ω-acetoxy ketones 8

Preparation of 6-acetoxy-1-phenylhexan-3-one (8a). To an ethereal (2 ml) solution of crude **2a** prepared from **3a** (0.5 mmol) and triethylamine (0.28 ml, 2 mmol) was added

acetyl chloride (0.14 ml, 2 mmol) at 0°C. After being stirred for 1 h, the reaction was quenched by addition of water, and the organic materials were extracted with ether and dried (Na_2SO_4). After removal of the solvent, the residue was purified by PTLC (hexane:EtOAc=9:1) to give **8a** (73 mg, 62%). **8a:** ^{1}H NMR 1.90 (tt, *J*=6.4, 7.0 Hz, 2H), 2.03 (s, 3H), 2.46 (t, *J*=7.2 Hz, 2H), 2.75 (t, *J*=7.6 Hz, 2H), 2.91 (t, *J*=7.6 Hz, 2H), 4.05 (t, *J*=6.4 Hz, 2H), 7.10–7.20 (m, 3H), 7.20–7.28 (m, 2H); ^{13}C NMR 20.87, 22.63, 29.72, 39.14, 44.28, 63.55, 126.10, 128.25, 128.47, 140.89, 170.99, 208.80; IR (neat) 3030, 2960, 1739, 1716, 1455, 1367, 1236, 1041, 752, 702. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.56; H, 7.85.

In a similar manner, the following ω-acetoxy ketones **8** were obtained.

5-Acetoxy-1-(4-methylphenyl)pentan-1-one (8b). Mp 49.5°C; ^{1}H NMR 1.69–1.77 (m, 2H), 1.77–1.86 (m, 2H), 2.04 (s, 3H), 2.41 (s, 3H), 2.98 (t, *J*=7.2 Hz, 2H), 4.11 (t, *J*=6.4 Hz, 2H), 7.21–7.23 (m, 2H), 7.86 (d, *J*=8.2 Hz, 2H); ^{13}C NMR 20.65, 20.92, 21.57, 28.14, 37.71, 64.12, 128.07, 129.22, 134.40, 143.74, 171.13, 199.38; IR (KBr) 2962, 1728, 1674, 1606, 1408, 1377, 1263, 1203, 1184, 829. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 72.05; H, 7.81.

5-Acetoxy-1-(4-propylphenyl)pentan-1-one (8c). Mp 45.5°C; ^{1}H NMR 0.95 (t, *J*=7.3 Hz, 3H), 1.60–1.77 (m, 4H), 1.78–1.86 (m, 2H), 2.04 (s, 3H), 2.64 (t, *J*=7.6 Hz, 2H), 2.99 (t, *J*=7.2 Hz, 2H), 4.11 (t, *J*=6.4 Hz, 2H), 7.24–7.29 (m, 2H), 7.88 (d, *J*=8.2 Hz, 2H); ^{13}C NMR 13.72, 20.68, 20.95, 24.19, 28.17, 37.75, 37.98, 64.16, 128.11, 128.67, 134.66, 148.46, 171.17, 199.45; IR (KBr) 3048, 2960, 1734, 1674, 1606, 1375, 1261, 1249, 1035, 899. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.05; H, 8.47.

1-Acetoxytridecan-6-one (8d). ^{1}H NMR 0.88 (t, *J*=7.0 Hz, 3H), 1.21–1.39 (m, 10H), 1.52–1.68 (m, 6H), 2.04 (s, 3H), 2.38 (t, *J*=7.3 Hz, 2H), 2.41 (t, *J*=7.3 Hz, 2H), 4.05 (t, *J*=6.7 Hz, 2H); ^{13}C NMR 14.02, 20.94, 22.56, 23.35, 23.85, 25.57, 28.43, 29.03, 29.18, 31.64, 42.46, 42.85, 64.28, 171.15, 211.18; IR (neat) 2964, 2862, 1747, 1716, 1471, 1369, 1244, 1047. Anal. Calcd for $C_{15}H_{28}O_3$: C, 70.27; H, 11.01. Found: C, 70.33; H, 11.19.

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