A Convenient and Efficient α-Sulfenylation of Carbonyl Compounds

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Abstract: A method for the α-sulfenylation of carbonyl compounds by 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinanane-2-disulfanyl derivatives has been developed. Readily available reagents, mild reaction conditions, and excellent yields with high selectivity make this method quite simple, convenient and practical.

Key words: thioethers, sulfides, sulfenylation, thiols, carbonyl compounds

The development of new reactions that produce convenient and versatile building blocks from simple and readily available reagents is currently one of the most important tasks for contemporary organic synthesis. α-Sulfenylated carbonyl compounds are particularly interesting synthetic intermediates since they have been used for a variety of organic transformations.[1] Preparation of these compounds very often involves S_N2 displacement of α-halogenated carbonyl compounds with sulfides anions.[2] Other methods are based on the reaction of enolates or enamines with various electrophilic sulfenylating reagents such as commercially available dimethyl disulfide, diphenyl disulfide, *N*-(phenylsulfanyl)phthalimide [3] or *S*-methyl methanethiosulfonate, *N*-(phenylsulfanyl)caprolactam, *N*-(phenylsulfanyl)succinimide,[4] and sulfenyl chlorides (e.g., PhSCl).[5] In recent years, some attention has been paid to the enantioselective α-sulfenylation of carbonyl compounds (aldehydes, ketones, lactones, lactams, and 1,3-dicarbonyl compounds) using chiral organocatalysts[6] and also titanium(IV) catalysts.[7] Although a wide range of sulfenylating reagents is available, many of them required multistep sequences for their preparation. Moreover, their reactivity is often compromised by their stability[6b] or the presence of additional functional groups.

We have previously prepared functionalized unsymmetrical dialkyl disulfides, alkyl aryl disulfides,[8] 'bioresistant' disulfides,[9] unsymmetrical disulfides based on L-cysteine and L-cystine derivatives,[10] and diaryl disulfides[11] using of 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives in reactions with aliphatic, aromatic thiols and thiol groups from cysteine derivatives. The presence of additional functional groups such as amino, hydroxy, or carboxy did not disturb the unsymmetrical disulfide bond formation.

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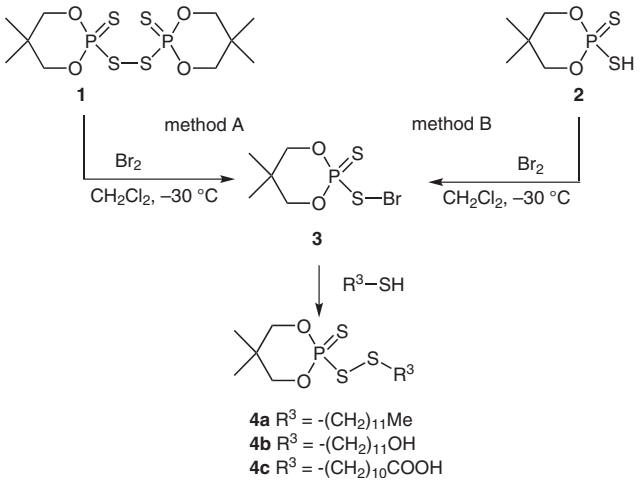
The presence of enolizable C–H bonds in aldehydes, ketones, and α-acidic hydrogens in β-keto esters allows the possibility for reactions with different classes of electrophilic sulfenylating reagents leading to the formation of C–S bonds. Herein, we report a convenient and efficient method for the preparation of α-oxo sulfides from enolizable carbonyl compounds and 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives.

Treatment of the stable and readily available bis(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl) disulfide (**1**) (method A) or 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinane **2** (method B) with bromine at –30 °C quantitatively affords 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-sulfenyl bromide (**3**) (Scheme 1). Subsequent treatment, without prior isolation, of sulfenyl bromide **3** with dodecane-1-thiol, 11-sulfanylundecan-1-ol, or 11-sulfanylundecanoic acid provides the corresponding 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives **4a**–**c**, which can be isolated in very good yields[12] (92–100%, Scheme 1).



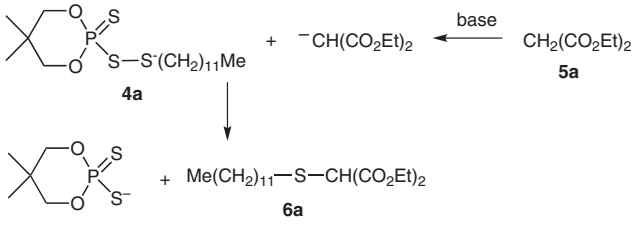
Scheme 1 The synthesis of 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinane-2-disulfanyl derivatives **4a**–**c**

These compounds are stable at room temperature for several months; decomposition by moisture or formation of symmetrical disulfides was not observed.

Initially, we attempted the sulfenylation of diethyl malonate (**5a**) with disulfide **4a** using stoichiometric amounts of reagents. After three hours at room temperature, product **6a** was isolated only in 42% yield (54% of starting material **4a** was recovered) (Table 1, entry 1). When the

reaction of disulfide **4a** was performed with a three-fold excess of diethyl malonate (**5a**), diethyl (dodecylsulfanyl)malonate (**6a**) was obtained in 81% yield (Table 1, entry 3) after 30 minutes at room temperature.

Table 1 The Reactions of Disulfide **4a** with Diethyl Malonate (**5a**)



Entry	Ratio **5a**/**4a**	Base	Solvent	Yield (%)
1	1:1	NaH	THF	42
2	3:2	NaH	THF	64
3	3:1	NaH	THF	81
4	1:1	DBU	toluene	54
5	3:1	DBU	toluene	71
6	1:1	LDA	THF	47
7	3:1	LDA	THF	83
8	1:1	NaOEt	EtOH	41
9	3:1	NaOEt	EtOH	85

As the data in Table 1 demonstrates, the reaction medium did not show a great impact on the α-sulfenylation process. Reactions in tetrahydrofuran and ethanol proceeded in high yields, while toluene was only slightly less efficient. The generation of an enolate anion from diethyl malonate was achieved by several bases, such as NaH, DBU, LDA, and NaOEt, but from a practical point of view sodium hydride and sodium ethoxide were the most convenient.

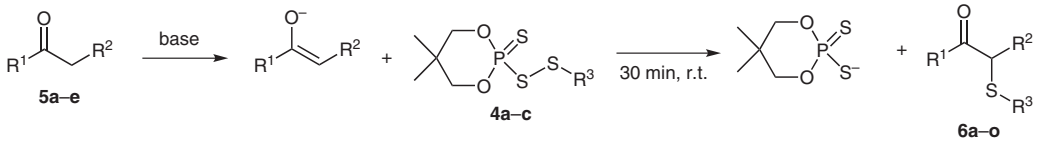
To demonstrate the scope of this new α-sulfenylation reaction, we reacted compounds **5a–e** with sulfenylating reagents **4a–c**. Three equivalents of the enolate anion were generated in tetrahydrofuran or ethanol by means of sodium hydride or sodium ethoxide, respectively. Then treatment with disulfides **4a–c** at room temperature for 30 minutes afforded products **6a–o**. The results are summarized in Table 2.

Generally, high yields (64–98%) were obtained for reactions of carbonyl compounds **5a–e** with sulfenylating reagents **4a–c** (Table 2). Interestingly, in the case of acetophenone (**5b**), the α,α-disulfenylated products were also isolated in ca. 30% yield for reactions with **4a–c**. Probably, the smaller steric hindrance of the enolates obtained from α-sulfenylated acetophenones **6b**, **6g**, and **6l** is responsible for α,α-disulfenylated product formation. Diethyl malonate (**5a**), acetylacetone (**5c**), ethyl 3-oxobutanoate (**5d**), and triethyl phosphonoacetate (**5e**) did not show formation of α,α-disulfenylated products under the same conditions.

To our knowledge, the reactions of disulfides **4b** and **4c** with enolates anions are the first examples of sulfenylation of carbonyl compounds with reagents possessing additional functional groups such as hydroxy or carboxy (Table 2). The reported methods in the literature for the α-sulfenylation of carbonyl compounds are based on the introduction of arylsulfanyl,[3–5] alkylsulfanyl[6,7] or phthalimidosulfanyl[7b] groups without additional functionalities.

In summary, a simple, efficient, and selective method for α-sulfenylation of carbonyl compounds has been developed. Moreover, the presence of additional functional groups such as hydroxy or carboxy did not disturb the course of reaction and allowed preparation of more elaborate structures.

Table 2 α-Sulfenylation of Carbonyl Compounds **5a–e**



	R^1	R^2	Product[a] [isolated yield (%)]		
			4a $R^3 = (CH_2)_{11}Me$[a]	**4b** $R^3 = (CH_2)_{11}OH$[a]	**4c** $R^3 = (CH_2)_{10}CO_2H$[b]
5a	OEt	CO_2Et	**6a** [81]	**6f** [77]	**6k** [90]
5b	Ph	H	**6b** [66]	**6g** [64]	**6l** [65]
5c	Me	Ac	**6c** [97]	**6h** [92]	**6m** [87]
5d	Me	CO_2Et	**6d** [76]	**6i** [81]	**6n** [90]
5e	OEt	$PO(OEt)_2$	**6e** [98]	**6j** [69]	**6o** [80]

[a] NaH as a base in THF.
[b] NaOEt as a base in EtOH.

Dodecane-1-thiol, 11-sulfanylundecan-1-ol, 11-sulfanylundecanoic acid, and NaH (60% in mineral oil) are commercially available from Aldrich. Bis(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl) disulfide (**1**),[13] 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphorinane (**2**),[13] 1-[(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl]dodecane (**4a**), 11-[(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl]undecan-1-ol (**4b**), and 11-[(5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-yl)disulfanyl]undecanoic acid (**4c**)[12] were synthesized by described procedures. THF and EtOH were dried and distilled by standard procedures. Melting points are uncorrected. NMR spectra were recorded on a Varian Gemini 500 MHz or 200 MHz spectrometer. The residual solvent peak was used as internal reference ($CDCl_3$: δ = 7.26 for ^1H, δ = 77.0 for ^{13}C); ^{31}P NMR used an external standard as reference (85% H_3PO_4: δ = 0). ESI-MS spectra were recorded on a Mariner PerSeptve Biosystem. Column chromatography was performed with silica gel 60 (230–400 mesh, Merck). Preparative TLC chromatography was performed with silica gel Polygram SIL G/UV254 (Macherey-Nagel). Petroleum ether = PE.

α-Sulfenylation of Carbonyl Compounds 5a–e with 4a or 4b; General Procedure

A soln of carbonyl compound **5a–e** (3.0 mmol) in anhyd THF (5 mL) was added dropwise to a suspension of NaH (0.12 g, 3.0 mmol) in anhyd THF (15 mL) at r.t. under an N_2 atmosphere. When the evolution of H_2 had ceased, a soln of **4a** (0.398 g, 1.0 mmol) or **4b** (0.400 g, 1.0 mmol) in anhyd THF (5 mL) was added. The mixture was stirred at r.t. for 3 h and evaporated under vacuum. The residue was dissolved in EtOAc (50 mL), washed with sat. aq NH_4Cl, dried ($MgSO_4$), filtered, and concentrated. The products were purified by column chromatography (Table 2).

Diethyl (Dodecylsulfanyl)malonate (6a)

Chromatography (PE–CH_2Cl_2, 2:1); oil; yield: 81%.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.20–1.35 (m, 16 H, CH_2), 1.31 (t, *J* = 7.3 Hz, 6 H, OCH_2CH_3), 1.35–1.45 (m, 2 H, CH_2), 1.55–1.65 (m, 2 H, CH_2), 2.74 (t, *J* = 7.3 Hz, 2 H, SCH_2), 4.17 (s, 1 H, SCH), 4.27 (q, *J* = 7.3 Hz, 4 H, OCH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 167.0, 62.2, 53.0, 31.9, 31.8, 29.6, 29.5, 29.4, 29.3, 29.1, 28.9, 28.7, 22.7, 14.1, 14.0. Signals: expected, 16; observed, 15.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{36}NaO_4S$: 383.2232; found: 383.2237.

2-(Dodecylsulfanyl)-1-phenylethanone (6b)

Chromatography (PE–CH_2Cl_2, 2:1); white solid; yield: 66%; mp 31–32 °C (Lit.[14] 31–32 °C).

^1H NMR (200 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 6.5 Hz, 3 H, CH_3), 1.15–1.45 (m, 18 H, CH_2), 1.50–1.70 (m, 2 H, CH_2), 2.57 (t, *J* = 7.3 Hz, 2 H, SCH_2), 3.79 (s, 2 H, $COCH_2S$), 7.40–7.65 (m, 3 H, Ar), 7.90–8.05 (m, 2 H, Ar).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 194.6, 135.3, 133.2, 128.8, 128.6, 37.1, 32.4, 31.9, 29.6, 29.6, 29.5, 29.3, 29.2, 29.0, 28.7, 22.7, 14.1. Signals: expected, 18; observed, 17.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{32}NaOS$: 343.2072; found: 343.2081.

3-(Dodecylsulfanyl)pentane-2,4-dione (6c)

Chromatography (PE–CH_2Cl_2, 2:1); oil; yield: 97%; only enol isomer is observed.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.24–1.34 (m, 16 H, CH_2), 1.35–1.44 (m, 2 H, CH_2), 1.51–1.59 (m, 2 H, CH_2), 2.45 (s, 6 H, CH_3), 2.50 (t, *J* = 7.3 Hz, 2 H, SCH_2), 17.09 (s, 1 H, C=COH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 197.4, 104.7, 36.9, 31.9, 29.6, 29.5, 29.3, 29.3, 29.2, 28.9, 24.5, 22.7, 14.1. Signals: expected, 15; observed, 13.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{32}NaO_2S$: 323.2021; found: 323.2027.

Ethyl 2-(Dodecylsulfanyl)-3-oxobutanoate (6d)

Chromatography (PE–CH_2Cl_2, 1:1); oil; yield: 76%; both enol and keto isomers were observed with ratio 1:1.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.20–1.45 (m, 21 H, CH_2, $OCCH_3$), 1.57–1.65 (m, 2 H, CH_2), 2.367 and 2.373 (s, 3 H, $COCH_3$, C=CCH_3), 2.54 (t, *J* = 7.3 Hz, 2 H, SCH_2), 4.11 (s, 0.56 H, SCH), 4.23–4.38 (m, 2 H, OCH_2), 13.54 (s, 0.44 H, C=COH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 197.3, 182.1, 173.3, 167.5, 94.1, 62.1, 61.4, 58.1, 35.6, 31.9, 31.6, 29.6, 29.5, 29.4, 29.3, 29.3, 29.1, 29.1, 28.9, 28.8, 28.7, 26.7, 22.7, 21.0, 14.2, 14.1, 14.0. Signals from both isomers: expected, 27; observed, 27.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{34}NaO_3S$: 353.2126; found: 353.2131.

Ethyl 2-(Diethoxyphosphoryl)-2-(dodecylsulfanyl)acetate (6e)

Chromatography (PE–CH_2Cl_2, 1:1); oil; yield: 98%.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.20–1.35 (m, 18 H, CH_2), 1.31 (t, *J* = 7.3 Hz, 3 H, $COOCH_2CH_3$), 1.36 (t, *J* = 7.3 Hz, 6 H, $POCH_2CH_3$), 1.55–1.63 (m, 2 H, CH_2), 2.68–2.80 (m, 2 H, SCH_2), 3.67 (d, $^2J_{P\text{-}C}$ = 20.0 Hz, 1 H, PCH), 4.20–4.30 (m, 6 H, OCH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.7, 63.8 (d, $^2J_{P\text{-}C}$ = 7.6 Hz), 63.7 (d, $^2J_{P\text{-}C}$ = 7.6 Hz), 62.1, 44.7 (d, $J_{P\text{-}C}$ = 141.0 Hz), 33.4 (d, $^3J_{P\text{-}C}$ = 5.5 Hz), 31.9, 29.6, 29.5, 29.4, 29.3, 29.1, 28.9, 28.6, 22.6, 16.3 (d, $^3J_{P\text{-}C}$ = 5.9 Hz), 14.1, 14.0. Signals: expected, 20; observed, 18.

^{31}P NMR (202 MHz, $CDCl_3$): δ = 18.10.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{41}NaO_5PS$: 447.2310; found: 447.2315.

Diethyl [11-Hydroxyundecyl)sulfanyl]malonate (6f)

Chromatography (EtOAc–CH_2Cl_2, 1:6); oil; yield: 77%.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.20–1.45 (m, 20 H, CH_2, OCH_2CH_3), 1.52–1.74 (m, 4 H, CH_2), 2.74 (t, *J* = 7.3 Hz, 2 H, SCH_2), 3.38 (s, 1 H, OH), 3.65 (t, *J* = 6.6 Hz, 2 H, OCH_2), 4.17 (s, 1 H, SCH), 4.27 (q, *J* = 7.3 Hz, 4 H, OCH_2).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 167.0, 63.0, 62.2, 51.0, 32.7, 31.7, 29.5, 29.4, 29.1, 28.9, 28.7, 28.4, 25.7, 14.0. Signals: expected, 15; observed, 14.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{34}NaO_5S$: 385.2025; found: 385.2028.

2-[(11-Hydroxyundecyl)sulfanyl]-1-phenylethanone (6g)

Chromatography ($CHCl_3$); white solid; yield: 64%; mp 47–49 °C.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.20–1.42 (m, 14 H, CH_2), 1.52–1.66 (m, 5 H, CH_2, OH), 2.58 (t, *J* = 7.3 Hz, 2 H, SCH_2), 3.66 (t, *J* = 6.8 Hz, 2 H, OCH_2), 3.81 (s, 2 H, $COCH_2S$), 7.50 (t, *J* = 7.8 Hz, 2 H, *m*-H), 7.60 (t, *J* = 7.8 Hz, 1 H, *p*-H), 8.00 (d, *J* = 7.8 Hz, 2 H, *o*-H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 194.6, 135.2, 133.3, 128.8, 128.7, 63.0, 37.1, 32.7, 32.3, 29.5, 29.4, 29.4, 29.4, 29.1, 28.9, 28.7, 25.7. Signals: expected, 17; observed, 17.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{30}NaO_2S$: 345.1864; found: 345.1871.

3-[(11-Hydroxyundecyl)sulfanyl]pentane-2,4-dione (6h)
Chromatography (EtOAc–CH_2Cl_2, 1:6); oil; yield: 92%; only enol isomer is observed.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20–1.43 (m, 14 H, CH_2), 1.48–1.62 (m, 4 H, CH_2), 1.90 (br s, 1 H, OH), 2.42 (s, 6 H, CH_3), 2.48 (t, *J* = 7.3 Hz, 2 H, SCH_2), 3.62 (t, *J* = 6.8 Hz, 2 H, OCH_2), 17.10 (s, 1 H, C=COH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.5, 104.6, 62.9, 36.8, 32.7, 29.5, 29.4, 29.3, 29.2, 29.1, 28.8, 25.6, 24.5. Signals: expected, 14; observed, 13.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{30}NaO_3S$: 325.1813; found: 325.1817.

Ethyl 2-[(11-Hydroxyundecyl)sulfanyl]-3-oxobutanoate (6i)
Chromatography (EtOAc–CH_2Cl_2, 1:6); oil; yield: 81%; both enol and keto isomers were observed with ratio 1:1.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20–1.45 (m, 18 H, CH_2, OH, $OCCH_3$), 1.47–1.62 (m, 4 H, CH_2), 2.366 and 2.373 (s, 3 H, $COCH_3$, C=CCH_3), 2.54 (t, *J* = 7.3 Hz, 2 H, SCH_2), 3.66 (t, *J* = 6.8 Hz, 2 H, OCH_2), 4.12 (s, 0.55 H, SCH), 4.23–4.38 (m, 2 H, OCH_2), 13.54 (s, 0.45 H, C=COH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 197.2, 182.0, 173.2, 167.4, 94.0, 63.0, 62.1, 61.4, 58.1, 35.6, 31.9, 31.6, 29.6, 29.5, 29.4, 29.3, 29.1, 29.1, 28.9, 28.8, 28.7, 26.7, 22.7, 21.0, 14.2, 14.0. Signals from both isomers: expected, 26; observed, 26.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{32}NaO_4S$: 355.1919; found: 355.1925.

Ethyl 2-(Diethoxyphosphoryl)-2-[(11-hydroxyundecyl)sulfanyl]acetate (6j)
Chromatography (EtOAc–CH_2Cl_2, 1:3); oil; yield: 69%.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20–1.46 (m, 23 H, CH_2, $COOCH_2CH_3$, $POCH_2CH_3$), 1.50–1.70 (m, 5 H, CH_2, OH), 2.74 (t, *J* = 7.3 Hz, 2 H, SCH_2), 3.64 (t, *J* = 6.8 Hz, 2 H, OCH_2), 3.66 (d, $^2J_{P\text{-}C}$ = 19.9 Hz, 1 H, PCH), 4.10–4.35 (m, 6 H, OCH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.8, 63.8 (d, $^2J_{P\text{-}C}$ = 7.6 Hz), 63.7 (d, $^2J_{P\text{-}C}$ = 7.6 Hz), 63.0, 62.1, 44.7 (d, $J_{P\text{-}C}$ = 141.0 Hz), 33.4 (d, $^3J_{P\text{-}C}$ = 5.5 Hz), 31.9, 29.6, 29.5, 29.3, 29.1, 28.9, 28.6, 22.6, 16.3 (d, $^3J_{P\text{-}C}$ = 5.9 Hz), 14.0. Signals: expected, 19; observed, 17.

^{31}P NMR (202 MHz, $CDCl_3$): δ = 18.09.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{39}NaO_6PS$: 449.2103; found: 449.2197.

α-Sulfenylation of Carbonyl Compounds 5a–e with 4c; General Procedure
A soln of carbonyl compound **5a–e** (3.0 mmol) in anhyd EtOH (5 mL) was added dropwise to a soln of NaOEt [NaH (0.16 g, 4.0 mmol) was dissolved in EtOH] in anhyd EtOH (15 mL) at r.t. under N_2 atmosphere. Then a soln of **4c** (0.414 g, 1.0 mmol) in anhyd EtOH (5 mL) was added. The mixture was stirred at r.t. for 3 h and evaporated under vacuum. The residue was dissolved in EtOAc (50 mL), washed with sat. aq NH_4Cl, dried ($MgSO_4$), filtered, and concentrated. The products were purified by column chromatography (Table 2).

Diethyl [(10-Carboxydecyl)sulfanyl]malonate (6k)
Chromatography (EtOAc–CH_2Cl_2, 1:10); oil; yield: 90%.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20–1.45 (m, 18 H, CH_2, OCH_2CH_3), 1.50–1.75 (m, 4 H, CH_2), 2.36 (t, *J* = 7.4 Hz, 2 H, $OOCCH_2$), 2.73 (t, *J* = 7.3 Hz, 2 H, SCH_2), 4.16 (s, 1 H, SCH), 4.26 (q, *J* = 7.1 Hz, 4 H, OCH_2), 6.65 (br s, 1 H, COOH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 179.7, 167.0, 62.2, 51.0, 34.0, 31.7, 29.3, 29.3, 29.1, 29.0, 29.0, 28.9, 28.7, 24.6, 14.0. Signals: expected, 15; observed, 15.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{32}NaO_6S$: 399.1817; found: 399.1821.

2-[(10-Carboxydecyl)sulfanyl]-1-phenylethanone (6l)
Chromatography ($CHCl_3$); yield: 65%

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20–1.42 (m, 12 H, CH_2), 1.53–1.66 (m, 4 H, CH_2), 2.35 (t, *J* = 7.4 Hz, 2 H, $OOCCH_2$), 2.58 (t, *J* = 7.3 Hz, 2 H, SCH_2), 3.80 (s, 2 H, $COCH_2S$), 6.70 (br s, 1 H, COOH), 7.50 (t, *J* = 7.8 Hz, 2 H, *m*-H), 7.60 (t, *J* = 7.8 Hz, 1 H, *p*-H), 8.00 (d, *J* = 7.8 Hz, 2 H, *o*-H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 194.6, 179.6, 135.2, 133.3, 128.8, 128.7, 37.1, 32.7, 32.3, 29.5, 29.4, 29.4, 29.3, 29.1, 28.9, 28.7, 24.7. Signals: expected, 17; observed, 17.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{28}NaO_3S$: 359.1657; found: 359.1653.

3-[(10-Carboxydecyl)sulfanyl]pentane-2,4-dione (6m)
Chromatography (EtOAc–CH_2Cl_2, 1:10); white solid; yield: 87%; mp 42–44 °C; only enol isomer is observed.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20–1.45 (m, 12 H, CH_2), 1.46–1.74 (m, 4 H, CH_2), 2.36 (t, *J* = 7.4 Hz, 2 H, $OOCCH_2$), 2.44 (s, 6 H, CH_3), 2.49 (t, *J* = 7.3 Hz, 2 H, SCH_2), 7.60 (br s, 1 H, COOH), 17.08 (s, 1 H, C=COH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 197.4, 179.9, 104.7, 36.9, 34.0, 29.4, 29.3, 29.2, 29.1, 29.0, 28.9, 24.6, 24.5. Signals: expected, 14; observed, 13.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{28}NaO_4S$: 339.1606; found: 339.1616.

Ethyl 2-[(10-Carboxydecyl)sulfanyl]-3-oxobutanoate (6n)
Chromatography (EtOAc–CH_2Cl_2, 1:10); oil; yield: 90%; both enol and keto isomers were observed with ratio 1:1.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20–1.45 (m, 15 H, CH_2, $OCCH_3$), 1.45–1.62 (m, 4 H, CH_2), 2.35 and 2.36 (s, 3 H, $COCH_3$, C=CCH_3), 2.36 (t, *J* = 7.4 Hz, 2 H, $OOCCH_2$), 2.45–2.70 (m, 2 H, SCH_2), 4.11 (s, 0.55 H, SCH), 4.20–4.38 (m, 2 H, OCH_2), 8.10 (br s, 1 H, COOH), 13.52 (s, 0.45 H, C=COH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 199.2, 182.8, 179.6, 173.2, 167.5, 94.0, 62.2, 61.4, 58.0, 35.6, 33.9, 31.6, 29.4, 29.3, 29.2, 29.1, 29.0, 28.9, 28.8, 28.7, 26.7, 24.6, 21.0, 14.2, 14.0. Signals from both isomers: expected, 26; observed, 25.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{30}NaO_5S$: 369.1712; found: 369.1719.

Ethyl 2-[(10-Carboxydecyl)sulfanyl]-2-(diethoxyphosphoryl)acetate (6o)
Chromatography (EtOAc–CH_2Cl_2, 1:3); oil; yield: 80%.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20–1.46 (m, 21 H, CH_2, $COOCH_2CH_3$, $POCH_2CH_3$), 1.50–1.70 (m, 4 H, CH_2), 2.35 (t, *J* = 6.8 Hz, 2 H, CH_2COOH), 2.73 (t, *J* = 7.3 Hz, 2 H, SCH_2), 3.65 (d, $^2J_{P\text{-}C}$ = 19.9 Hz, 1 H, PCH), 4.10–4.35 (m, 6 H, OCH_2), 6.90 (br s, 1 H, COOH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 179.6, 167.9, 63.7 (d, $^2J_{P\text{-}C}$ = 7.6 Hz), 63.6 (d, $^2J_{P\text{-}C}$ = 7.6 Hz), 62.1, 44.6 (d, $J_{P\text{-}C}$ = 141.0 Hz), 33.3 (d, $^3J_{P\text{-}C}$ = 5.5 Hz), 31.9, 29.6, 29.5, 29.3, 29.1, 28.9, 28.6, 22.6, 16.2 (d, $^3J_{P\text{-}C}$ = 5.9 Hz), 14.0. Signals: expected, 19; observed, 17.

^{31}P NMR (202 MHz, $CDCl_3$): δ = 18.11.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{37}NaO_7PS$: 463.1895; found: 463.1883.

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References

(1) (a) Trost, B. M. *Chem. Rev.* **1978**, *78*, 363. (b) Trost, B. M. *Acc. Chem. Res.* **1978**, *11*, 453. (c) Coates, R. M. *Angew. Chem., Int. Engl. Ed.* **1973**, *12*, 586. (d) Woodward, R. B.; Pachter, I. J.; Scheinbaum, M. L. *J. Org. Chem.* **1971**, *36*, 1137. (e) Midgley, J. M.; Millard, B. J.; Whalley, W. B.; Smith, C. J. *J. Chem. Soc. C* **1971**, 19. (f) Kane, V. V.; Singh, V.; Martin, A.; Doyle, D. L. *Tetrahedron* **1983**, *39*, 345. (g) Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.

(2) (a) Asinger, F.; Thiel, M.; Kalzendorf, I. *Justus Liebigs Ann. Chem.* **1957**, *610*, 25. (b) Asinger, F.; Schaefer, W.; Triem, H. *Monatsh. Chem.* **1966**, *97*, 1510. (c) Truce, W. E.; Knospe, R. H. *J. Am. Chem. Soc.* **1955**, *77*, 5063.

(3) Wang, W.; Li, H.; Wang, J.; Liao, L. *Tetrahedron Lett.* **2004**, *45*, 8229.

(4) Huang, Ch. H.; Liao, K.-S.; De, S. K.; Tsai, Y.-M. *Tetrahedron Lett.* **2000**, *41*, 3911.

(5) (a) Yadav, J. S.; Subba Reddy, B. V.; Jain, R.; Baishya, G. *Tetrahedron Lett.* **2008**, *49*, 3015. (b) Tan, J.; Liang, F.; Wang, Y.; Cheng, X.; Liu, Q.; Yuan, H. *Org. Lett.* **2008**, *10*, 2485.

(6) (a) Sobhani, S.; Fielenbach, D.; Marigo, M.; Wabnitz, T. C.; Jørgensen, K. A. *Chem. Eur. J.* **2005**, *11*, 5689. (b) Marigo, M.; Wabnitz, T. C.; Fielenbach, D.; Jørgensen, K. A. *Angew. Chem.* **2005**, *117*, 804.

(7) (a) Jereb, M.; Togni, A. *Chem. Eur. J.* **2007**, *13*, 9384. (b) Srisailam, S. K.; Togni, A. *Tetrahedron Asymmetry* **2006**, *17*, 2603. (c) Jereb, M.; Togni, A. *Org. Lett.* **2005**, *7*, 4041.

(8) Antoniow, S.; Witt, D. *Synthesis* **2007**, 363.

(9) Kowalczyk, J.; Barski, P.; Witt, D.; Grzybowski, B. A. *Langmuir* **2007**, *23*, 2318.

(10) Szymelfejnik, M.; Demkowicz, S.; Rachon, J.; Witt, D. *Synthesis* **2007**, 3528.

(11) Demkowicz, S.; Rachon, J.; Witt, D. *Synthesis* **2008**, 2033.

(12) Kertmen, A.; Lach, S.; Rachon, J.; Witt, D. *Synthesis* **2009**, in press.

(13) Edmundson, R. S. *Tetrahedron* **1965**, *21*, 2379.

(14) Seshadri, R.; Pegg, W. J.; Israel, M. *J. Org. Chem.* **1981**, *46*, 2596.