

Article

## Facile Palladium-Mediated Conversion of Ethanethiol Esters to Aldehydes and Ketones

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O tratamento de ésteres etanotiólicos com trietilsilano e paládio sobre carbono, a temperatura ambiente, fornece aldeídos. Adicionalmente, uma variedade de cetonas foram preparadas por reações de ésteres etanotiólicos com reagentes organozinco catalisados por paládio. Vários grupos funcionais, incluindo ésteres, cetonas, haletos aromáticos e aldeídos são tolerados em ambas as transformações. Essas novas reações podem também ser aplicadas na síntese de derivados  $\alpha$ -amino aldeídicos e  $\alpha$ -amino cetônicos utilizando os correspondentes ésteres. (L)- $\alpha$ -amino tióis sem causar racemização.

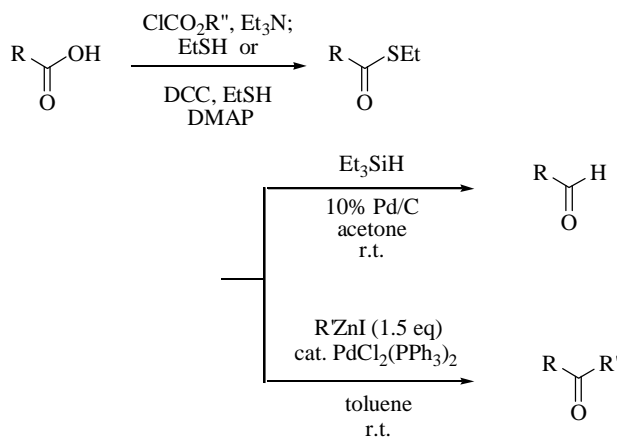
Treatment of ethanethiol esters with triethylsilane and palladium on carbon at ambient temperature furnished aldehydes. In addition, a variety of ketones have been prepared by a palladium-catalyzed reaction of ethanethiol esters with organozinc reagents. Various functional groups, including esters, ketones, aromatic halides and aldehydes, tolerate both transformation reactions. These novel reactions can also be applied to the synthesis of  $\alpha$ -amino aldehyde and  $\alpha$ -amino ketone derivatives using the corresponding L- $\alpha$ -amino thiol esters without causing racemization.

**Keywords:** thiol ester, aldehyde, ketone, triethyl silane, organozinc reagent, palladium-catalyst

### Introduction

Transformations of carboxylic acids to aldehydes have been the subject of intensive investigation among synthetic organic chemists. With a few exceptions<sup>1</sup>, derivatives of acid chlorides, amides, and esters are usually converted to aldehydes by selective reduction. Although a number of synthetic methods have been reported to date, none seems to be generally applicable to multifunctional compounds. In this paper we describe a highly efficient reduction of ethanethiol esters to aldehydes with triethylsilane and a catalytic amount of palladium on carbon (Scheme 1). During the course of this investigation, it occurred to us that the combination of thiol esters, transition metal catalysts, and appropriate organometallic reagents could be used for the synthesis of ketones<sup>2</sup>. The novel ketone-forming reaction we could successfully develop is exceptionally mild and can be applied to the synthesis of ketones bearing

aldehyde, ester, ketone, and arylbromide functionalities (Scheme 1)<sup>3</sup>.



Scheme 1.

## Results and Discussions

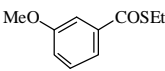
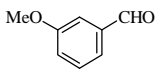
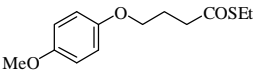
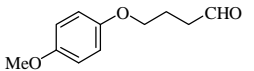
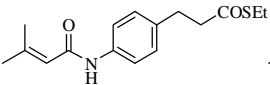
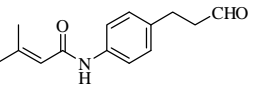
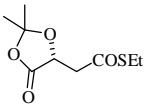
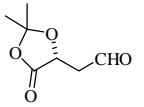
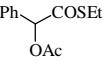
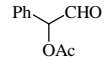
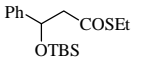
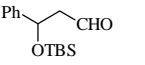
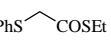
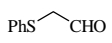
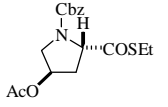
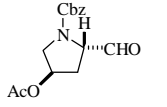
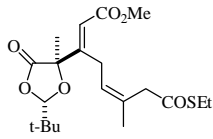
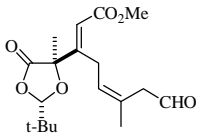
Ethanethiol esters can be conveniently prepared in 60–85% yields from the corresponding acids via mixed anhydride in a one-pot procedure (EtOCOCl or *i*-BuOCOCl (1.2 equiv), Et<sub>3</sub>N (2.4 equiv), CH<sub>2</sub>Cl<sub>2</sub>, 0 °C, 10 min; EtSH (2.3 equiv), then DMAP (0.1 equiv), 0 °C, 10 min). For the conversion of protected amino acids and more valuable acids, Steglich's method (DCC, DMAP, EtSH) was employed<sup>4</sup>.

Thiol ester reduction was performed at room temperature in acetone or CH<sub>2</sub>Cl<sub>2</sub> under argon using 10% Pd on carbon and two to three equivalents of triethylsilane. As shown in Table 1, a variety of functional groups survive the essentially neutral reduction conditions. Our method is particularly suited for the conversion of optically active amino acids to amino aldehyde derivatives that are known to racemize even under mild conditions<sup>5</sup>. For example, the optically pure thiol ester **1** derived from L-glutamic acid 5-methyl ester was converted to the dimethyl acetal **2** in 95% yield in a 40 g-scale experiment (Eq 1). The optical purity of **2** was virtually 100% based on the <sup>1</sup>H-NMR studies of the corresponding (*R*)-(+)- $\alpha$ -methylbenzylamide derivative **3**. While the <sup>1</sup>H-NMR spectrum of the racemic amides **3** exhibited two signals at 3.33 and 3.41 ppm for the dimethyl acetal, the amide **3** derived from L-glutamic acid 5-methyl ester showed only a singlet at 3.33 ppm, and no trace of a peak at 3.41 ppm was observed.

The usefulness of our procedure was demonstrated in our total syntheses of neothramycins<sup>3a</sup> and leinamycin<sup>6</sup> as well as in other recent reports on synthesis of complex natural products<sup>7</sup>.

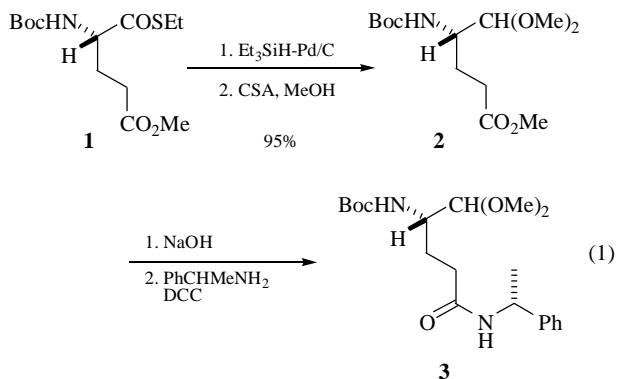
Since the combination of thiol ester and palladium catalyst works quite well for the mild reduction system, we envisioned that replacement of triethylsilane with organometallic reagents would lead to the formation of the corresponding ketones. Thus, we then focused our efforts on a transition metal-catalyzed synthesis of ketones.

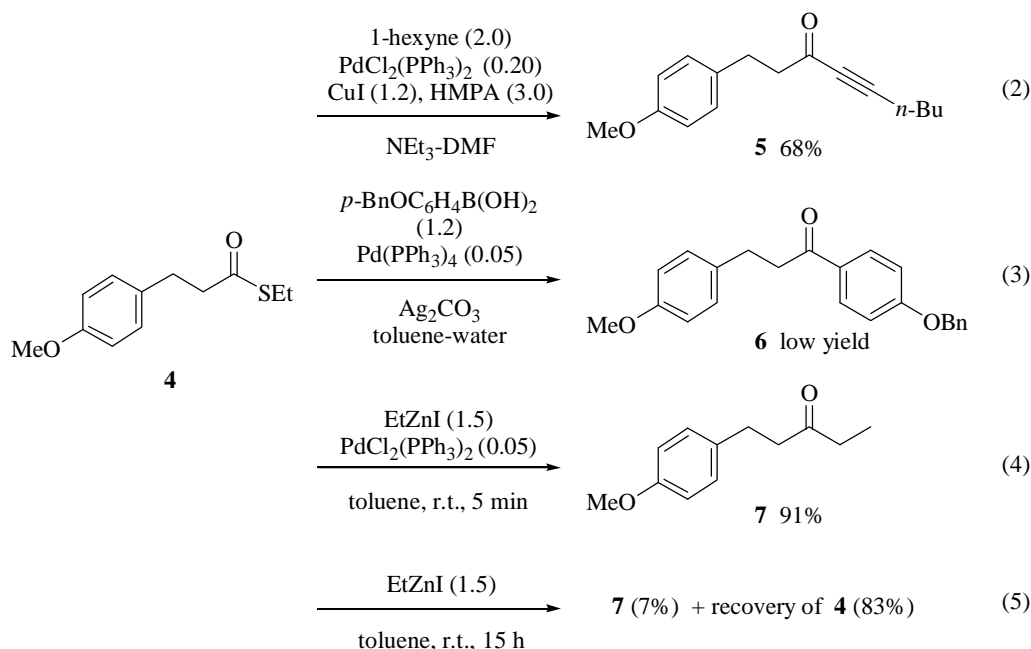
In order to explore catalytic system for a novel ketone formation, we initially screened various combinations of transition metal catalysts and organometallic reagents using ethanethiol ester **4** as a test substrate. While Sonogashira coupling conditions gave acetylenic ketone **5** in 68% yield (Eq. 2), Suzuki-coupling conditions afforded aryl ketone **6** in low yield (Eq. 3). Finally, we have found that treatment of thiol ester **4** with a catalytic amount of PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (5 mol%) and EtZnI (1.5 eq) in toluene at room temperature for 5 min furnished the corresponding ethyl ketone **7** in 91% isolated yield (Eq. 4). When commercially available THF solution of Et<sub>2</sub>Zn was used instead of EtZnI, the corresponding aldehyde was isolated in moderate yield. Mechanistic details of this unexpected reduction are still not clear. The rate of the reaction was dependent upon the choice of the solvent. While the rate

Substrate	Product	Yield (%) <sup>a</sup>
		91 <sup>b,c</sup>
		94
		97
		93 <sup>d</sup>
		84
		88
		75 <sup>e</sup>
		88 <sup>f</sup>
		92

**Table 1.** Reduction of ethanethiol esters with triethylsilane and palladium on carbon.

<sup>a</sup>Isolated yields after chromatographic purification. Pd/C (2 mol%) and Et<sub>3</sub>SiH (3 eq) in acetone were used unless noted otherwise. <sup>b</sup>Et<sub>3</sub>SiH (2 eq) was used. <sup>c</sup>Isolated as tosylhydrazone. <sup>d</sup>5.8-g-scale reaction. Pd/C (0.5 mol%) and Et<sub>3</sub>SiH (1.5 eq) were used. CH<sub>2</sub>Cl<sub>2</sub> was used as solvent. <sup>e</sup>4 mol% of Pd/C was used. <sup>f</sup>Formation of the *cis* isomer was not observed.

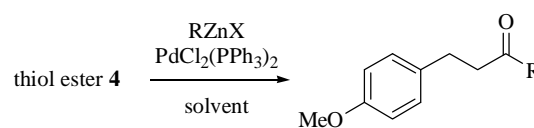




was comparable in CH<sub>2</sub>Cl<sub>2</sub> and CH<sub>3</sub>CN, the reaction proceeded considerably more slowly in THF and benzene. The reaction in DMF did not proceed at all. In the absence of the catalyst, however, only a minute amount of **7** was formed (7%) with recovery of 83% of **4** even after 15 h of stirring at room temperature (Eq. 5).

As shown in Table 2, ethylzinc iodide as well as *i*-butyl-, benzyl-, phenyl-, β-phenethyl-, and vinylzinc halides reacted smoothly to afford the corresponding ketones<sup>8</sup>. Ester- and protected amine-containing zinc reagents could also be used<sup>9,10</sup>. On the other hand, a range of ethanethiol esters such as alkyl, aryl, and α,β-unsaturated thiol esters could be converted into the corresponding ethyl ketones in good to excellent yields (Table 3). It should be noted that a variety of sensitive functional groups including ketone, α-acetate, sulfide, aromatic bromide, chloride and even aldehyde are compatible with this protocol. This remarkable chemoselectivity indicates that the ketone formation is much faster than oxidative addition of palladium to aromatic bromide or nucleophilic addition of zinc reagents to aldehydes.

We next examined a conversion of thiol ester derivatives of *N*-protected L-α-amino acids into the corresponding amino ketone derivatives. The ketone formation proceeded smoothly to give the desired α-amino ketones in good to high isolated yields from the optically pure *N*-Cbz-L-α-phenylalanine thiol esters without appreciable racemization (Table 4, entries 1 and 2). Combinations of functionalized organozinc reagents and L-glutamic acid or L-proline derivatives afforded structurally intriguing amino ketones in good yields.



RZn	(eq)	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> , (eq)	solvent, time (min)	% yield
EtZnI	1.5	0.05	toluene, 5	91
EtZnI	1.5	0.05	THF, 5	74
<i>i</i> -BuZnI	2.0	0.05	THF, 15	90
EtO <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> ZnI	1.5	0.1	CH <sub>2</sub> Cl <sub>2</sub> , 15	92
	1.5	0.1	toluene, 5	87
	2.0	0.1	toluene, 120	79
PhZnI	2.0	0.1	toluene, 60	50
PhCH <sub>2</sub> ZnBr	3.0	0.1	toluene, 60	86
PhCH <sub>2</sub> CH <sub>2</sub> ZnI	2.0	0.1	toluene, 30	50
PhthN(CH <sub>2</sub> ) <sub>3</sub> ZnI	2.0	0.1	toluene, 40	83

**Table 2.** Palladium-catalyzed ketone synthesis with various organozinc reagents.

thiol ester	EtZnI (eq)	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> (eq) solvent, time (min)	%yield	thiol ester	EtZnI (eq)	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> (eq) solvent, time (min)	%yield
	1.5	0.05 toluene, 10	99		1.5	0.05 THF, 60	76
	2.0	0.05 toluene, 50	75		2.0	0.1 toluene, 15	83
	2.0	0.1 toluene, 30	78		3.0	0.1 toluene, 45	79
	2.0	0.05 toluene, 7	98		1.5	0.1 THF, 205	69
	1.5	0.05 toluene, 5	91		1.5	0.05 THF, 30	67

**Table 3.** Palladium-catalyzed ketone synthesis with various thiol esters.

entry	thiol ester <sup>a</sup>	R'ZnI	(eq)	time (min)	% yield
1		EtZnI	2.5	15	88 <sup>b</sup>
2			2.0	40	88 <sup>c</sup>
3			2.0	15	82 <sup>d</sup>
4		PhZnI	3.0	90	58 <sup>d</sup>
5			3.0	90	64 <sup>d</sup>
6		EtZnI	2.0	90	82 <sup>d</sup>
7			2.0	90	82 <sup>d</sup>
8		EtZnI	2.0	180	73 <sup>e</sup>
9			2.0	110	64 <sup>d</sup>

**Table 4.** Synthesis of  $\alpha$ -amino ketones from L- $\alpha$ -amino thiol esters.

<sup>a</sup>For entries 1-5 and 8-9, ee of the starting thiol esters were determined to be 99%. <sup>b</sup>99% ee. <sup>c</sup>98% ee. <sup>d</sup>The ee of the products were not determined. <sup>e</sup>99% ee.<sup>11</sup>,  $[\alpha]_D^{22}$  -43.8° (*c* 1.26, CHCl<sub>3</sub>).

## Experimental

### *Typical procedure for the conversion of carboxylic acids into ethanethiol esters using mixed anhydride method.*

#### *4-[(4-methoxy)-phenoxy]-butanoic acid ethanethiol ester*

To 1.91 g (9.1 mmol) of 4-[(4-methoxy)-phenoxy]-butanoic acid dissolved in 50 mL of dry  $\text{CH}_2\text{Cl}_2$  at 0 °C was added ethyl chloroformate (1.04 mL, 10.9 mmol), followed by rapid dropwise addition of 3.1 mL (22.3 mmol) of triethylamine. After stirring for 10 min, ethanethiol (1.6 mL, 21.6 mmol) and DMAP (111 mg, 0.91 mmol) were added and the mixture was stirred for 10 min at room temperature. The reaction mixture was partitioned between  $\text{CH}_2\text{Cl}_2$  and a 1:1 mixture of 3 N HCl and brine, followed by an extraction of the aqueous layer with  $\text{CH}_2\text{Cl}_2$ . The combined organic extracts were washed with saturated aqueous  $\text{NaHCO}_3$ , and dried over  $\text{MgSO}_4$ . Filtration and evaporation left a crude material. Mplc separation (20–40% ether/hexane gradient) afforded the desired ethanethiol ester as a colorless oil (1.84 g, 80%); IR ( $\text{CH}_2\text{Cl}_2$ ,  $\text{cm}^{-1}$ ) 1680, 1495, 1100;  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.27 (t,  $J = 7$  Hz, 3 H), 2.13 (m, 2 H), 2.77 (t,  $J = 7$  Hz, 2 H), 2.90 (q,  $J = 7$  Hz, 2 H), 3.78 (s, 3 H), 3.95 (t,  $J = 6$  Hz, 2 H), 6.84 (s, 4 H); EI-MS  $m/z$  (relative abundance): 254 (10,  $\text{M}^+$ ), 193 (8), 165 (2), 151 (1), 150 (2), 137 (13), 131 (38), 29 (100).

### *Typical procedure for the reduction of ethanethiol esters to aldehydes. 4-[(4-methoxy)-phenoxy]-butanal*

To an acetone solution (1 mL) of 4-[(4-methoxy)-phenoxy]-butanoic acid ethanethiol ester (187 mg, 0.73 mmol) was added 15.9 mg (0.015 mmol, 2 mol%) of 10% palladium on carbon, followed by addition of triethylsilane (352  $\mu\text{L}$ , 2.20 mmol, 3.0 equiv) at room temperature under argon. After stirring for 8 min at room temperature, the catalyst was filtered off through Celite and washed with acetone. Evaporation and separation on mplc (60% ether/hexane) gave the desired aldehyde in 94% yield (133 mg); IR ( $\text{CH}_2\text{Cl}_2$ ,  $\text{cm}^{-1}$ ) 2730, 1725, 1590, 1500, 1105;  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  2.09 (m, 2 H), 2.64 (t,  $J = 7$  Hz, 2 H), 3.76 (s, 3 H), 3.94 (t,  $J = 6$  Hz, 2 H), 6.82 (s, 4 H), 9.82 (s, 1 H); EI-MS  $m/z$  (relative abundance) 194 (43,  $\text{M}^+$ ), 150 (2), 137 (3), 124 (96), 109 (100).

#### *N-Boc-1-ethylthio-5-methyl-L-glutamate (1)*

To a stirred mixture of 25 g (155 mmol) of L-glutamic acid 5-methyl ester and 22.7 mL of (163 mmol, 1.05 eq) of triethylamine in 300 mL of DMF at room temperature was added 35.5 g of (163 mmol, 1.05 eq) of di-*tert*-butyl dicarbonate. As the reaction proceeded, the starting materials went into solution, and within two hours the reaction was complete. DMF was removed by evaporation under reduced pressure, and the residue was partitioned between  $\text{CH}_2\text{Cl}_2$  and a dilute HCl-NaCl solution. Organic extracts

were dried over  $\text{MgSO}_4$ , filtered, and evaporated. The crude product from above, together with 17.2 mL (232 mmol, 1.50 eq) of ethanethiol and 0.947 g (7.75 mmol, 0.05 eq) of DMAP was dissolved in 300 mL of acetonitrile. To this solution was added 32.0 g (155 mmol, 1.00 eq) of DCC in portions at 0 °C. Upon completion, solid 1,3-dicyclohexylurea was filtered off through Celite column, followed by concentration of the filtrate. Ether was added to bring about more precipitation. The urea was filtered off again through a Celite column. Separation on a silica gel column (60% ether in hexane) gave 44.0 g (92.9%) of the desired thiolester (**1**) as a white solid;  $[\alpha]_D^{25}$  (c 0.0122,  $\text{CHCl}_3$ )  $-16.9^\circ$ ; IR ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ) 3440, 2980, 2930, 1740, 1720, 1680, 1440;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  1.25 (t,  $J = 7.4$  Hz, 3 H), 1.45 (s, 9 H), 1.82 (m, 1 H), 2.17 (m, 1 H), 2.41 (m, 1 H), 2.87 (q,  $J = 7.4$  Hz, 2 H), 3.68 (s, 3 H), 4.35 (br s, 1 H), 5.12 (br d, 1 H); EI-MS  $m/z$  (relative abundance): 306 (6,  $\text{M}^+ + 1$ ), 305 (1,  $\text{M}^+$ ), 250 (25), 216 (84), 206 (25), 160 (100), 116 (100), 100 (35); HR-MS Calcd. for  $\text{C}_{13}\text{H}_{23}\text{NO}_5\text{S}$ : 305.1297. Found: 305.1301.

### *Dimethyl acetal (2). A large scale procedure for the reduction of ethanethiol ester*

To a stirred mixture of 40 g of *N*-Boc-1-ethylthio-5-methyl-L-glutamate (**1**) and 2.78 g (2 mol%) of 10% palladium on carbon in 250 mL of acetone under argon atmosphere at room temperature was slowly added 31.3 mL (197 mmol, 1.5 eq) of triethylsilane over a period of 1 h. Upon completion of the reaction, the catalyst was filtered off through a Celite column. The solvent was carefully evaporated under reduced pressure. The residue was dissolved in 500 mL of methanol, and to this solution was added 43.0 mL (393 mmol, 3 eq) of trimethyl orthoformate and 1.52 g (6.56 mmol, 0.5 eq) of camphorsulfonic acid. The reaction went to completion in 6 h at room temperature. Solid sodium carbonate was added to neutralize the acid. The reaction mixture was evaporated under reduced pressure to a smaller volume, and partitioned between  $\text{CH}_2\text{Cl}_2$  and water. The organic phase was dried over  $\text{MgSO}_4$ , filtered, concentrated and chromatographed on a silica gel column (80% ether in hexane) to yield 36.4 g (95.4%) of the dimethyl acetal **2**;  $[\alpha]_D^{25}$  (c 0.0193,  $\text{CHCl}_3$ )  $-13.2^\circ$ ; IR ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ) 2980, 2950, 2930, 1730, 1710, 1430;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  1.44 (s, 9 H), 1.65–1.72 (m, 1 H), 1.92–2.02 (m, 1 H), 2.40 (t,  $J = 6.0$  Hz, 2 H), 3.43 (s, 6 H), 3.67 (s, 3 H), 3.70–3.81 (m, 1 H), 4.20 (d,  $J = 3.2$  Hz, 1 H), 4.67 (d,  $J = 9.0$  Hz, 1 H); EI-MS  $m/z$  (relative abundance): 291 (1,  $\text{M}^+$ ), 260 (2), 217 (1), 75 (100); HR-MS Calcd. for  $\text{C}_{13}\text{H}_{25}\text{NO}_6$ : 291.1681. Found: 291.1709.

### *Diastereomeric acetal amides (3)*

To a solution of 500 mg of ( $\pm$ ) **2** in 5 mL of methanol and water (4:1) was added 0.5 mL of 3N NaOH. After 30

min, this mixture was acidified with 3N HCl to pH ~5, and evaporated to dryness under reduced pressure. The resulting acid was taken up in CH<sub>2</sub>Cl<sub>2</sub>, dried through Na<sub>2</sub>SO<sub>4</sub> column, and evaporated. To a stirred solution of the acid and 345 mg (1.72 mmol, 1 eq) of DCC in CH<sub>2</sub>Cl<sub>2</sub> was added 332 μL (2.58 mmol, 1.5 eq) of (+)-α-methylbenzylamine at 0 °C. After 20 min, the reaction mixture was partitioned between CH<sub>2</sub>Cl<sub>2</sub> and diluted HCl. The organic layer was washed with a saturated aqueous NaHCO<sub>3</sub>, dried through a Na<sub>2</sub>SO<sub>4</sub> column and evaporated. Purification on a silica gel column with ether as an eluant gave a 1:1 mixture of **3a** and **3b**. The optically active (-)-**2** (250 mg) prepared from **1** was converted to the corresponding amide following the procedure described above. A single compound **3** was obtained, which was also purified on a silica gel column; **3a**, IR (CHCl<sub>3</sub>, cm<sup>-1</sup>) 3310, 3060, 2930, 1690, 1645; <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ 1.46 (s, 9 H), 1.49 (d, *J* = 7.0 Hz, 3 H), 1.66 (m, 1 H), 1.92 (m, 1 H), 2.25 (m, 2 H), 3.32 (s, 6 H), 3.70 (m, 1 H), 3.70 (m, 1 H), 4.12 (d, *J* = 3.2 Hz, 1 H), 4.82 (d, 1 H), 5.11 (m, 1 H), 6.82 (d, 1 H), 7.32-7.37 (m, 5 H); EI-MS *m/z* (relative abundance): 348 (1, M<sup>+</sup>-32), 305 (26), 292 (10), 249 (10), 205 (67), 105 (100); **3b**, IR (CHCl<sub>3</sub>, cm<sup>-1</sup>) 3310, 3080, 2930, 1690, 1655; <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ 1.45 (s, 9 H), 1.51 (d, *J* = 6.8 Hz, 3 H), 1.67 (m, 1 H), 2.01 (m, 1 H), 2.27 (m, 2 H), 3.41 (s, 6 H), 3.88 (m, 1 H), 4.22 (d, 1 H), 4.87 (d, 1 H), 4.87 (d, 1 H), 5.15 (m, 1 H), 6.82 (d, 1 H), 7.33-7.42 (m, 5 H); EI-MS *m/z* (relative abundance): 381 (M<sup>+</sup>+1), 348 (1), 305 (19), 292 (7), 249 (17), 205 (45), 105 (100).

#### Typical procedure for the conversion of ethanethiol esters to the corresponding ethyl ketones

A dry, Ar-purged 50 mL flask containing a magnetic stirring bar is charged with *N*-Cbz-L-phenylalanine ethanethiol ester<sup>12</sup> (1.00 g, 2.91 mmol), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (284 mg, 10 mol%), and toluene (10 mL). To the mixture was added EtZnI (0.90 M in THF, 8.09 mL, 2.5 eq) at room temperature and stirring was continued for 15 min. EtZnI was prepared by heating activated zinc powder<sup>10</sup> (3.1 g) and ethyl iodide (1.93 mL) in refluxing THF (24 mL) for 2 h. The concentration of the reagent was estimated by titration) Diethyl ether (20 mL) was added and the suspension was passed through a pad of Celite. The filtrate was washed with 1N HCl, saturated aqueous NaHCO<sub>3</sub>, brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. Filtration and concentration on a rotary evaporator afforded a crude product. Purification on silica gel column chromatography (15~25% EtOAc in hexane gradient) gave the desired ketone (800 mg, 88% yield). The enantiomeric excess of the product was determined by HPLC analyses using racemic compound as a reference (DAICEL Chiralcel-OJ, 4.6 mm I.D. x 250 mm, 90/10 *n*-hexane/2-propanol, 1.0 mL/min, 40 °C). Retention times of the ketones derived from L-phenylalanine and D-pheny-

lalanine are 12.55 and 17.02 minutes, respectively; Mp, 62-63 °C (benzene-hexane); [α]<sub>D</sub><sup>25</sup> +72.5° (*c* 1.01, CHCl<sub>3</sub>); IR (film, cm<sup>-1</sup>) 3333, 3063, 3031, 2939, 1714, 1604, 1504, 1455, 1248, 1070, 1027, 744, 699; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ 1.01 (t, *J* = 7.0 Hz, 3 H), 2.20-3.20 (m, 2 H), 3.00 (dd, *J* = 6.1, 13.9 Hz, 1 H), 3.07 (dd, *J* = 6.8, 13.9 Hz, 1 H), 4.25 (dd, *J* = 6.8, 13.9 Hz, 1 H), 5.08 (dd, *J* = 12.5, 14.9 Hz, 2 H), 5.39 (br s, 1 H), 7.00-7.50 (m, 10 H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) δ 7.29, 34.08, 37.96, 60.19, 66.85, 127.05, 128.00, 128.12, 128.48, 128.63, 129.14, 135.87, 136.24, 155.65, 209.22; Anal. Calcd. for C<sub>19</sub>H<sub>21</sub>NO<sub>3</sub>: C, 72.99; H, 6.79; N, 4.44. Found: C, 73.29; H, 6.80; N, 4.50.

## Conclusion

In summary, we have demonstrated efficient methodologies for the synthesis of aldehydes and ketones from thiol esters. Since acids can be readily converted to ethanethiol esters under mild conditions and our procedures possess unusually high chemoselectivity, these protocols provide powerful alternatives to the arsenal of synthetic chemists for transformation of acids to aldehydes and ketones, and may find widespread use in organic synthesis.

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11. HPLC analysis was performed with a chiral HPLC column using a racemic mixture as references (DAICEL Chiralcel-OD, 4.6 mm I.D. x 250 mm, 95/5 *n*-hexane/2-propanol, 1.0 mL/min, 40 °C).
12. The thiol ester was prepared from *N*-Cbz-L-phenylalanine via mixed anhydride.