Simple, Mild, and Practical Esterification, Thioesterification, and Amide Formation Utilizing *p*-Toluenesulfonyl Chloride and *N*-Methylimidazole

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Supporting information for this article is available on the WWW under http://asc.wiley.vch.de or from the author.

Abstract: We have developed an efficient method for the esterification or thioesterification of equimolar amounts of carboxylic acids and alcohols or thiols using a novel reagent, *p*-toluenesulfonyl chloride (TsCl) together with *N*-methylimidazole. The present method is simple, mild, and reactive, uses readily available and economical reagents. The choice of amine is critical for the present method. The amine, *N*-methylimidazole, has two roles: (i) as an HCl scavenger for the initial smooth generation of mixed anhydrides between carboxylic acids and TsCl and (ii) successive formation of highly reactive ammonium intermediates from mixed anhydrides. This method could be applied to various types of carboxylic acids, alcohols, and thiols: a) several functionalities were tolerated; b) two *N*-Cbz amino acids were smoothly esterified without racemization; and c) the labile 1β-methylcarbapenem key intermediate and a pyrethroid insecticide, prallethrin, were successfully prepared. The related amide formation between carboxylic acids and primary or secondary amines was also performed. The proposed reaction mechanism involves a novel method for producing the reactive acylammonium intermediates. The production of these intermediates was rationally supported by a careful ^{1}H NMR monitoring study.

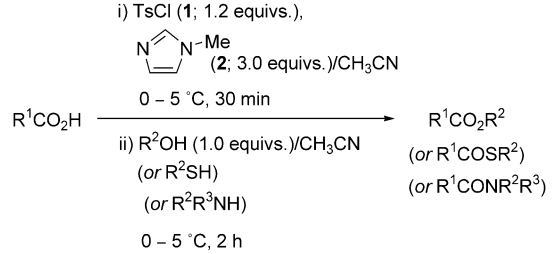
Keywords: amide formation; esterification; *N*-methylimidazole; synthetic methods; thioesterification; *p*-toluenesulfonyl chloride

From the standpoint of elaborate complex natural product synthesis and process chemistry, direct esterification between equimolar amounts of carboxylic acids and alcohols is well recognized as an important unit reaction for a wide range of organic syntheses.[1] Much effort has been invested in the development of efficient methods; e.g., the use of DCC,[2] halopyridinium salts,[3] *N,N*-carbonyldiimidazole,[4] 2,4,6-trichlorobenzoyl chloride,[5] BOP-Cl,[6] DPC,[7] DPTC,[8] MNBA,[9] etc.

In view of process chemistry, there remains a strong need for simpler, more reactive, convenient, and inexpensive agents. The mixed anhydride method, composed of different acids, is a rational process: Use of sulfonic acid as a counter acid moiety is a promising candidate for an efficient esterification due to its simplicity, ready availability and low cost of the reagents.

To this end, we focused our attention on the use of an easily accessible reagent, *p*-toluenesulfonyl chloride (TsCl; **1**)/a specific amine. Here, we present an efficient method for the esterification and thioesterification of equimolar amounts of carboxylic acids and alcohols or thiols, respectively, using TsCl (**1**)/*N*-methylimidazole (**2**).[10] The related amide formation between carboxylic acids and primary or secondary amines was also successfully performed (*vide supra*).

A related reagent, CH_3SO_2Cl, was not suitable due to the undesirable side sulfene dimerization.[11] The choice of amine is critical for the present method, because the amine has two roles: (i) as an HCl scavenger for the initial smooth generation of mixed anhydrides between carboxylic acids and **1** and (ii) the successive formation



Scheme 1. Esterification or thioesterification using readily available TsCl (**1**)/*N*-methylimidazole (**2**).

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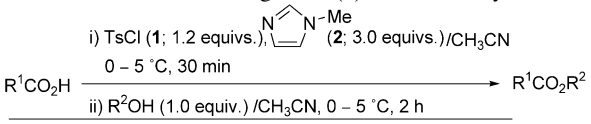
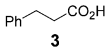
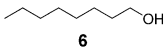
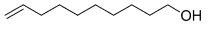
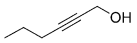
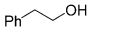
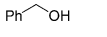
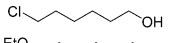
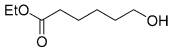
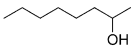
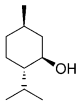
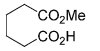
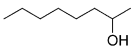
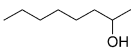
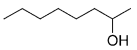
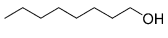
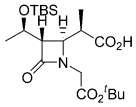
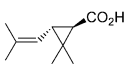
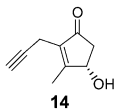
Table 1. Esterification between equimolar amounts of carboxylic acids and alcohols using TsCl (**1**) and *N*-methylimidazole (**2**).



R^1CO_2H	R^2OH	Yield/%[a]
 **3**	 **6**	84[b]
		93(70)
		92
		87
		93
		96
	PhOH	95
		95
		82
		93[c](40)
		91[c]
		87[c]
		87[d]
PhCO2H		89[d]
 **10**	MeOH	89[e]
		87[e]
 **11**	MeOH	91[e]
 **12**		95[d](70)
 **13**	 **14**	91[d](13)

[a] Parentheses indicate the reaction using TsCl (**1**; 1.2 equivs.)/Et_3N (3.0 equivs.)/cat. DMAP (0.1 equiv.) under identical conditions (see Supporting Information).
[b] 2.4 equivalents of *N*-methylimidazole (**2**) were used.
[c] Step ii) 20–25 °C for 2 h.
[d] Step i) 20–25 °C for 30 min and ii) 20–25 °C for 2 h.
[e] In CH_2Cl_2, i) −40 to −35 °C for 30 min and ii) −40 to −35 °C for 2 h. In all examples, >99% ee by HPLC analyses (see Experimental Section).

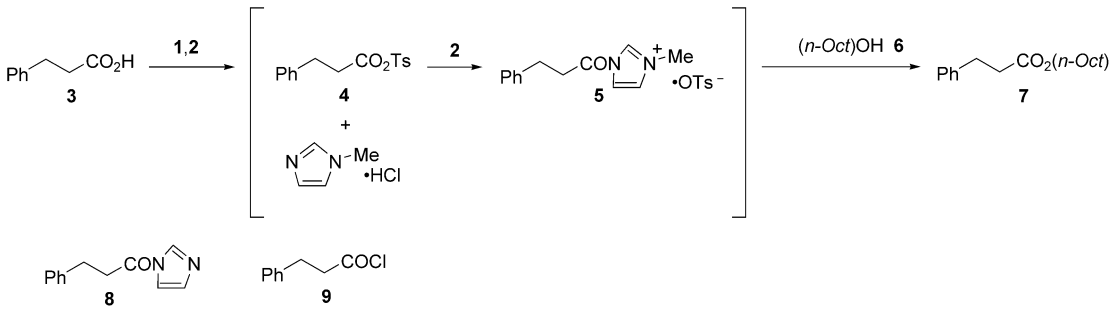
of reactive ammonium intermediates from mixed anhydrides. We expected that *N*-methylimidazole (**2**) would fulfill both roles.

Indeed, the reaction of 3-phenylpropanoic acid (**3**) with 1-octanol (**6**; 1.0 equiv.) using TsCl (**1**) (1.2 equivs.) and *N*-methylimidazole (**2**; 3.0 equivs.) in CH_3CN at 0–5 °C resulted in esterification in 93% yield. Table 1 lists the results of the esterification using various carboxylic acids and alcohols. As solvents, CH_3CN and CH_2Cl_2 were somewhat superior to toluene and THF. Although the use of **1**/Et_3N/catalytic *N,N*-dimethylaminopyridine (DMAP) might be expected to fulfill this role, some comparable experiments under identical conditions demonstrated the superiority of the present method (see Supporting Information).

The proposed reaction mechanism, exemplified using **3** and **6**, is as follows (Scheme 2). The mixed anhydride **4** between **3** and **1** is initially produced with the formation of the HCl salt of **2**. Anhydride **4** is in turn transformed into acylammonium salt **5**. The highly reactive intermediate **5** immediately condenses with **6** to produce octyl 3-phenylpropanoate (**7**). This marked switching behavior is characteristic of *N*-methylimidazole **2**. Due to the electron withdrawing effect of the cationic ammonium, the intermediate **5** is likely to be more reactive than the corresponding anhydride **4** and acylimidazole **8**, which is a reactive acylating substrate.[4] Bigg and their coworkers reported that activation of acylimidazoles with methyl trifluoromethanesulfonate (CH_3OTf) contributes to the aminoacylations.[12] The advantage of the present protocol is that it eliminates the use of CH_3OTf and generates acylammonium **5** in a one-pot process.

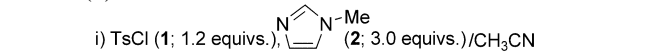
A ^1H NMR monitoring study using 3-phenylpropanoic acid **3** and its analogues **4**, **5**, **8**, and **9** rationally supported the hypothesis of the generation of **5**. The chemical shift of the α-position of these compounds progressively shifted downfield from acid **3** ($\delta =$ 2.54 ppm), mixed anhydride **4** (2.74), acylimidazaole **8** (3.05), acyl chloride **9** (3.20), and acylammonium **5** (3.66) (see Supporting Information). This shift is considered to be proportional to the acylating reactivity of these analogues.

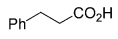
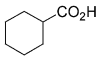
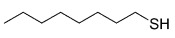
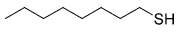
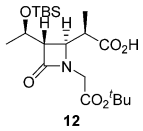
The salient features of the present esterification are as follows. (i) Several esters of primary and secondary alcohols were prepared in good to excellent yield under mild and practical conditions. (ii) Several functionalities such as a double or a triple bond, a halogen, and an ester were tolerated. (iii) *N*-Cbz alanine (**10**) and proline (**11**), which are prone to racemization under basic conditions, were smoothly esterified with complete retention of their chiral centers. (iv) The labile 1β-methylcarbapenem key intermediate[13] and a pyrethroid insecticide, prallethrin,[14] were successfully prepared from azetidinone **12** and by the reaction between (1*R*,3*R*)-chrysanthemic acid (**13**) and (*S*)-hydroxycyclopentenone **14**, respectively (see Supporting Information). Direct and



Scheme 2. Proposed reaction mechanism.

Table 2. Thioesterification between equimolar amounts of carboxylic acids and thiols using TsCl (**1**) and *N*-methylimidazole (**2**).

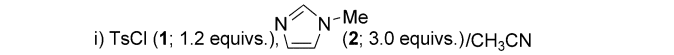


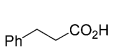
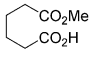
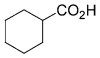
R^1CO_2H	R^2SH	Yield/%[a]
		94(29)
		92
	PhSH	90
		92[b](25)
		90
		87[b]
		95[c]
		92[c]
$PhCO_2H$		90[c]
		94[c]
 12		94[c](13)

[a] Parentheses indicate the reaction using TsCl (**1**; 1.2 equivs.)/Et_3N (3.0 equivs.)/cat. DMAP (0.1 equiv.) under identical conditions (see Supporting Information).
[b] Step ii) 20–25 °C for 2 h.
[c] Step i) 20–25 °C for 30 min and ii) 20–25 °C for 2 h.

mild esterification of these compounds is an important subject in the fine chemical area. (v) DMAP, a popular acylation-step catalyst was not used; avoidance of

Table 3. Amide formation between equimolar amounts of carboxylic acids and primary or secondary amines using TsCl (**1**) and *N*-methylimidazole (**2**).



R^1CO_2H	R^2R^3NH	Yield/%
		95
		95
	$^tBuNH_2$	90[a]
	$PhNH_2$	95
		94
		93[b]
$PhCO_2H$		94[b]

[a] Step ii) 20–25 °C for 2 h.
[b] Step i) 20–25 °C for 30 min and ii) 20–25 °C for 2 h.

DMAP is strongly desired by many process chemists due to its cost and toxicity. (vi) The reaction of **3** with tertiary alcohols such as *t*-butyl alcohol and linalool, however, resulted in low yields under standard conditions ($< 10\%$).

Compared with a related method using Me_2NSO_2Cl/Me_2NR/cat. DMAP,[11b,c] the present method has other merits as well: (i) higher reactivity; (ii) operationally simpler; (iii) economical (including the elimination of expensive DMAP during the acylation step, the total cost of the condensation reagent is reduced to approximately 10%); and (iv) lower toxicity of TsCl (**1**) compared to Me_2NSO_2Cl.[15]

We then extended this protocol to a related thioesterification, and amide formation between equimolar amounts of carboxylic acids and thiols, as well as primary or secondary amines (Tables 2 and 3).

The present method was successful, while the Me_2NSO_2Cl method failed to produce thioesterification (no reaction). The results of the thioesterification method using **1**/Et_3N/cat. DMAP did not reach a practical revel, as shown in Table 2. The reactivity of the present amide formation was higher than esterification and thioesterification, so that it proceeded with good to excellent yields.

In conclusion, various carboxylic esters, thioesters, and amides can be practically and conveniently prepared in good to excellent yield between carboxylic acids and equimolar amounts of alcohols, thiols, and amines, respectively, under very mild conditions using a simple and easily accessible reagent, *p*-TsCl (**1**) and *N*-methylimidazole (**2**), wherein the reactions proceed through a new type of highly reactive acylammonium intermediate pathway.

Experimental Section

The following esters, thioesters, and amides obtained in this work are known compounds: 1-octyl 3-phenylpropanoate,[16] 9-decen-1-yl 3-phenylpropanoate,[11c] 2-hexyn-1-yl 3-phenylpropanoate,[11c] 2-phenylethyl 3-phenylpropanoate,[17] benzyl 3-phenylpropanoate,[18] phenyl 3-phenylpropanoate,[19] 6-chlorohexyl 3-phenylpropanoate,[11c] ethyl 6-(3-phenylpropanoyloxy)hexanoate,[11c] 2-octyl 3-phenylpropanoate,[20] l-menthyl 3-phenylpropanoate,[11c] 1-octyl cyclohexanecarboxylate,[21] 2-octyl benzoate,[22] *N*-carbobenzyloxy-*l*-alanine methyl ester,[23] *N*-carbobenzyloxy-*l*-proline methyl ester,[23] (3*S*,4*S*)-4-[(1*R*)-1-benzyloxycarbonylethyl]-1-(*tert*-butoxycarbonylmethyl)-3-[(1*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone,[13] *S*)-2-methyl-4-oxo-3-(2-propynyl)cyclopent-2-enyl (1*R*,3*R*)-chrysanthemate,[14] *S*-benzyl 3-phenylpropanethioate,[24] *S*-phenyl 3-phenylpropanethioate,[25] *S*-1-octyl cyclohexanecarbothioate,[26] *S*-cyclohexyl cyclohexanecarbothioate,[27] *S*-1-octyl benzothioate,[28] *S*-cyclohexyl benzothioate,[29] *N*-(3-phenylpropanoyl)-(1*S*)-phenylethylamine,[11c] *N*-(3-phenylpropanoyl)piperidine,[11c] *N*-(1,1-dimethylethyl)-3-phenylpropionamide,[11c] 5-(methoxycarbonyl)pentanilide,[30] *N*-(cyclohexanecarbonyl)piperidine,[11c] *N*-(benzoyl)piperidine.[11c]

Typical Procedure for Esterification

TsCl (**1**; 229 mg, 1.2 mmol) in CH_3CN (1.0 mL) was added to the stirred solution of 3-phenylpropanoic acid (**3**; 150 mg, 1.0 mmol) and *N*-methylimidazole (**2**; 246 mg, 3.0 mmol) in CH_3CN (1.0 mL) at 0–5 °C under an Ar atmosphere, and the mixture was stirred for 30 min. To the stirred mixture 1-octanol (**6**; 130 mg, 1.0 mmol) in CH_3CN (1.0 mL) was added at 0–5 °C, and the mixture was stirred at the same temperature for 2 h. Water was added to the stirred mixture, and extracted with ether. The organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane:ether, 40:1) to give 1-octyl 3-phenylpropanonate;[16] Yield: 243 mg (93%).

N-Carbobenzyloxy-*l*-alanine Methyl Ester[23]

TsCl (**1**; 229 mg, 1.2 mmol) in CH_2Cl_2 (1.0 mL) was added to a stirred solution of *N*-Cbz-*l*-alanine (**10**; 223 mg, 1.0 mmol) and *N*-methylimidazole (**2**; 246 mg, 3.0 mmol) in CH_2Cl_2 (1.0 mL) at −40 to −35 °C under an Ar atmosphere, and the mixture was stirred for 30 min. CH_3OH (32 mg, 1.0 mmol) in CH_2Cl_2 (1.0 mL) was added to the mixture at −40 to −35 °C, followed by stirring at the same temperature for 2 h. The reaction mixture was poured into the stirred ice/water (reverse quench), which was extracted with ether. The organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane:EtOAc; 4:1) to give the desired product; yield: 210 mg (89%). HPLC analyses were performed using Shimadzu HPLC system (consisting of the following: SLC-10A, DGU-4A, LC-10AD, SIL-10A, CTO-10A, and detector SPD-10AV, measured at 254 nm) and DAICEL Chiracel OD column (4.6 mm i.d. × 25 cm) at 30 °C (column oven temperature). >99% ee by HPLC analysis [flow rate 1.50 mL/min, solvent: *n*-hexane/2-propanol, 70/30, t_R (racemic) = 6.18 min and 6.88 min, respectively, t_R (*N*-carbobenzyloxy-*l*-alanine methyl ester) = 6.24 min]. Colorless oil; $[\alpha]_D^{23}$: −33.9 (*c* 1.00, CH_3OH) [lit. $[\alpha]_D^{22}$: −36 (*c* 1, CH_3OH)]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (3H, d, *J* = 7.3 Hz), 3.75 (3H, s), 4.40 (1H, m), 5.09 (1H, d, J_{gem} = 12.5 Hz), 5.13 (1H, d, J_{gem} = 12.5 Hz), 5.32 (1H d, *J* = 5.4 Hz), 7.29–7.41 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.63, 49.55, 52.38, 66.87, 128.06, 128.12, 128.48, 136.24, 155.54, 173.41; IR (neat): ν = 3343, 2953, 1723, 1530, 1454, 1215, 1071 cm^{-1}.

N-Carbobenzyloxy-*l*-alanine Octyl Ester

A similar reaction using 1-octanol (130 mg, 1.0 mmol) instead of CH_3OH produced the desired product; yield: 290 mg (87%). >99% ee by HPLC analysis [flow rate 1.50 mL/min, solvent: *n*-hexane/2-propanol, 80/20, t_R (racemic) = 3.65 min and 5.11 min, respectively, t_R (*N*-carbobenzoxy-*l*-alanine octyl ester) = 3.66 min]. Colorless oil; $[\alpha]_D^{23}$: −25.6 (*c* 1.00, CH_3OH); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (3H, t, *J* = 6.8 Hz), 1.21–1.38 (10H, m), 1.41 (3H, d, *J* = 7.1 Hz), 1.56–1.68 (2H, m), 4.13 (2H, t, *J* = 6.3 Hz), 4.38 (1H, m), 5.09 (1H, d, J_{gem} = 12.7 Hz), 5.34 (1H, d, J_{gem} = 12.7 Hz), 7.28–7.38 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.05, 18.80, 22.59, 25.75, 28.48, 29.11, 31.73, 49.67, 65.61, 66.85, 128.07, 128.12, 128.49, 136.29, 155.55, 173.02; IR (neat): ν = 3345, 2928, 2857, 1728, 1528, 1454, 1211, 1071 cm^{-1}. Anal. found: C 59.2, H 5.9, N 6.0%; calcd. for $C_{11}H_{13}NO_4$: C 59.19, H 5.87, N 6.27%.

^{1}H NMR Monitoring Study

^{1}H NMR spectra of **4** and **6** (*in situ* generated) were measured for the ratios of **3**:**1**:**2** (=1:1:1) and (=1:1:3), respectively, in $CDCl_3$ at 20–25 °C. These ^{1}H NMR spectra are available as PDF files (Supporting Information). Actually, the use of *N*-

methylimidazole (**2**) showed a higher generation of mixed anhydride **4** than the use of Et_3N.

Typical Procedure for Thioesterification

A similar reaction using 1-octanethiol (146 mg, 1.0 mmol) instead of 1-octanol in the case of esterification resulted in the production of *S*-octyl 3-phenylpropionthioate, yield: 252 mg (94%). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.88$ (3H, t, $J = 6.8$ Hz), 1.21 – 1.38 (10H, m), 1.55 (2H, m), 2.83 – 2.89 (4H, m), 2.97 (2H, m), 7.16 – 7.22 (3H, m), 7.25 – 7.31 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.06, 22.62, 28.79, 28.91, 29.06, 29.13, 29.51, 31.49, 31.78, 45.52, 126.28, 128.30, 128.49, 140.14, 198.73$; IR (neat): $\nu = 2926, 2855, 1690, 1454, 1047, 974, 698$ cm^{-1}. Anal. found: C 73.1, H 9.3%; calcd. for $C_{17}H_{26}OS$: C 73.33, H 9.41%.

Typical Procedure of Amide Formation

A similar reaction using piperidine (85 mg, 1.0 mmol) instead of 1-octanol in the case of esterification resulted in the production of *N*-(3-phenylpropanoyl)piperidine;[11c] yield: 206 mg (95%).

Methyl 2-Octyladipate

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.88$ (3H, t, $J = 6.6$ Hz), 1.19 (3H, d, $J = 6.3$ Hz), 1.22 – 1.34 (8H, m), 1.41 – 1.61 (2H, m), 1.63 – 1.71 (4H, m), 2.26 – 2.37 (4H, m), 3.67 (3H, s), 4.90 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.03, 19.97, 22.55, 24.38, 24.50, 25.34, 29.09, 31.71, 33.68, 34.28, 35.91, 51.49, 70.95, 172.95, 173.75$; IR (neat): $\nu = 2932, 2861, 1736, 1460, 1437, 1177, 1078$ cm^{-1}. Anal. found: C 66.8, H 6.0%; calcd. for $C_{13}H_{14}O_4$: C 66.66, H 6.02%.

S-Cyclohexyl 3-Phenylpropanethioate

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.20 – 1.47$ (5H, m), 1.54 – 1.62 (1H, m), 1.64 – 1.74 (2H, m), 1.85 – 1.94 (2H, m), 2.81 (2H, m), 2.96 (2H, m), 3.52 (1H, m), 7.16 – 7.22 (3H, m), 7.25 – 7.31 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 25.52, 25.89, 31.49, 33.00, 42.26, 45.61, 126.25, 128.30, 128.47, 140.20, 198.44$; IR (neat): $\nu = 2930, 2855, 1686, 1451, 1046, 972, 698$ cm^{-1}. Anal. found: C 72.1, H 7.9%; calcd. for $C_{15}H_{20}OS$: C 72.53, H 8.12%.

S-1-Octyl 5-(Methoxycarbonyl)pentanethioate

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.88$ (3H, t, $J = 6.9$ Hz), 1.22 – 1.39 (10H, m), 1.53 – 1.59 (2H, m), 1.62 – 1.74 (4H, m), 2.33 (2H, m), 2.56 (2H, m), 2.86 (2H, t, $J = 7.3$ Hz), 3.67 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.05, 22.61, 24.19, 25.03, 28.82, 28.86, 29.05, 29.12, 29.54, 31.76, 33.64, 43.59, 51.52, 173.65, 199.21$; IR (neat): $\nu = 2928, 2857, 1742, 1690, 1458, 1437, 995, 666$ cm^{-1}. Anal. found: C 62.2, H 9.7%; calcd. for $C_{15}H_{28}O_3S$: C 62.46, H 9.78%.

S-Cyclohexyl 5-(Methoxycarbonyl)pentanethioate

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.21 – 1.73$ (12H, m), 1.86 – 1.95 (2H, m), 2.32 (2H, m), 2.53 (2H, m), 3.50 (1H, m), 3.67 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 24.19, 25.02, 25.52, 25.91, 33.04, 33.65, 42.20, 43.67, 51.52, 173.68, 198.95$; IR (neat): $\nu = 2932, 2855, 1740, 1686, 1449, 997, 700$ cm^{-1}. Anal. found: C 60.1, H 8.7%; calcd. for $C_{13}H_{22}O_3S$: C 60.43, H 8.58%.

(3*S*,4*S*)-4-[(1*R*)-1-Cyclohexylthiocarbonylethyl]-1-(*tert*-butoxycarbonylmethyl)-3-[(1*R*)-1-*tert*-butyldimethylsilyloxyethyl]-2-azetidinone

Colorless oil; $[\alpha]_D^{23}$: -28.5 (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.08$ (6H, s), 0.87 (9H, s), 1.20 (3H, d, $J = 7.1$ Hz), 1.23 (3H, d, $J = 6.3$ Hz), 1.91 – 1.32 (2H, m), 1.35 – 1.44 (4H, m), 1.45 (9H, s), 1.64 – 1.73 (2H, m), 1.83 – 1.92 (2H, m), 2.96 (1H, dd, $J = 3.4$ Hz, 7.1 Hz), 2.98 (1H, dd, $J = 2.1$ Hz, 7.1 Hz), 3.47 (1H, m), 3.74 (1H, d, $J_{gem} = 17.8$ Hz), 4.04 (1H, dd, $J = 2.1$ Hz, 3.4 Hz), 4.09 (1H, d, $J_{gem} = 17.8$ Hz), 4.15 (1H, dd, $J = 6.3$ Hz, 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = -4.76$, $-4.27, 12.37, 17.89, 22.69, 25.46, 25.81, 28.02, 32.75, 32.99, 42.53, 43.38, 49.65, 57.44, 61.10, 66.54, 81.88, 167.24, 167.95, 201.16$; IR (neat): $\nu = 2932, 2857, 1767, 1680, 1451, 1370, 1157, 837$ cm^{-1}. Anal. found: C 60.5, H 9.1, N 2.5%; calcd. for $C_{26}H_{47}NO_5SSi$: C 60.78, H 9.22, N 2.73%.

N-(5-Methoxycarbonylpentanoyl)piperidine

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.49 – 1.73$ (10H m), 2.30 – 2.39 (4H, m), 3.36 – 3.41 (2H m), 3.52 – 3.57 (2H, m), 3.66 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 24.55, 24.74, 24.82, 25.56, 26.52, 32.93, 33.85, 42.61, 46.61, 51.46, 170.76, 173.92$; IR (neat): $\nu = 2938, 2857, 1738, 1642, 1439, 1254, 1013$ cm^{-1}. Anal. found: C 63.2, H 9.2, N 6.0%; calcd. for $C_{12}H_{21}NO_3$: C 63.41, H 9.31, N 6.16%.

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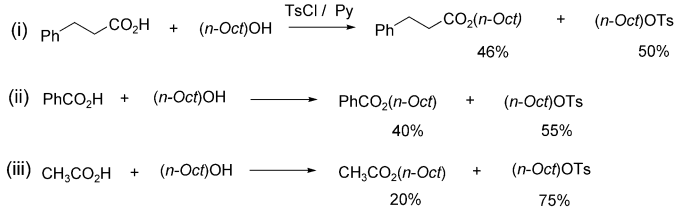

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