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A CONVENIENT METHOD FOR THE SYNTHESIS OF CARBOXAMIDES AND THIOESTERS BY USING TETRAKIS(2-METHYLIMIDAZOL-1-YL)SILANE

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Dedicated to Professor Barry M. Trost on the occasion of his 65th birthday

Abstract – Tetrakis(2-methylimidazol-1-yl)silane [Si(2-Me-Im)$_4$], a new dehydrating reagent having silicon–imidazole linkage, reacted readily with carboxylic acids at room temperature to form the corresponding 1-acyl-2-methylimidazole intermediates, which smoothly underwent subsequent condensation with nucleophiles such as amines or thiols to afford the corresponding carboxamides or thioesters in good to excellent yields, respectively.

INTRODUCTION

To form carboxylic acid derivatives such as carboxamides, thioesters, or esters is one of the most fundamental and important synthetic steps for the synthesis of useful natural and unnatural organic molecules, and condensation reactions between carboxylic acids and nucleophiles under mild conditions have significantly been advanced in accordance with the development of new dehydrating reagents.[1,2] Among activated derivatives of carboxylic acids, acyl azolides, particularly 1-acylimidazoles, are versatile and have widely been used as useful synthetic intermediates for the preparation of amides, dipeptides, esters, etc.[3] The classical azolide method is carried out generally by using 1,1'-carbonyldiimidazole (CDI) as a condensation reagent and requires stepwise operation: that is, (i) carboxylic acids are first treated with CDI in a 1 : 1 molar ratio to generate the corresponding 1-acylimidazole intermediates by the elimination of carbon dioxide and imidazole; (ii) after evolution of

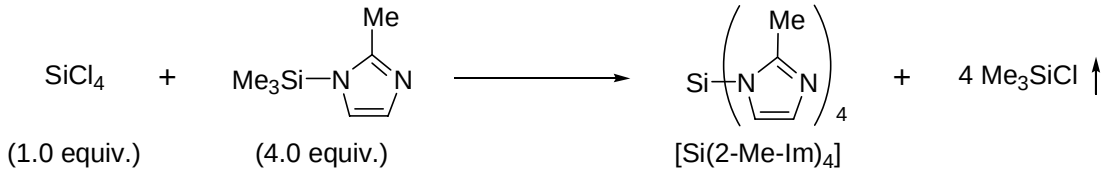
carbon dioxide having been stopped, an equimolar amount of amine is added. In this procedure, the use of excess amounts of CDI should be carefully avoided since the unreacted CDI reacts directly with amine to form undesired urea that may cause purification of the product difficult.[4]

Several useful methods have been developed for the preparation of carboxamides by using silicon-containing dehydrating reagents;[5] e.g., hexamethyldisilazane (HMDS),[6] silicon tetrachloride ($SiCl_4$),[7] dichlorodimethylsilane (Me_2SiCl_2),[8] etc. These conventional reagents, however, have following synthetic limitations: (i) in the reaction with HMDS, high reaction temperature and long reaction time are required; (ii) in the case when chlorosilanes such as $SiCl_4$ or Me_2SiCl_2 are used, the solvent has often been limited to pyridine for neutralization of liberated hydrogen chloride. Therefore, it is still an important topic to develop more efficient silicon-containing dehydrating reagents for the synthesis of carboxylic acid derivatives under mild conditions. Quite recently, it was reported from our laboratory that various imidazolylsilane derivatives were easily synthesized by trans-silylation between 1-(trimethylsilyl)imidazoles and chlorosilanes.[9] It was revealed there that novel reagents having silicon–imidazole linkage were effectively utilized as dehydrating reagents to form carboxamides from carboxylic acids and amines *via* the formation of active 1-acylimidazole intermediates under mild conditions. Although a conventional azolide method that uses CDI requires strict stepwise operation and precise amount of CDI so as to prevent the side-reaction of forming undesired urea, the new method that uses novel dehydrating reagents having silicon–imidazole linkage proceeds just by mixing carboxylic acids, amines, and imidazolylsilanes at a time. Then, the desired carboxamides are afforded in high yields without any side-products even when the amount of the dehydrating reagent is excess. Further, the work-up procedure is quite simple and carboxamides are obtained in almost pure form if tetrakis(2-methylimidazol-1-yl)silane [$Si(2\text{-}Me\text{-}Im)_4$] is used since the co-products of the reaction are 2-methylimidazole and silica [$(SiO_2)_n$]. 2-Methylimidazole thus formed can be removed by washing with dilute acid. In addition, the silica is insoluble in any common solvents and it can therefore be removed easily just by filtration. Here, we would like to describe in detail the results of our continuous investigations on an efficient method for the preparation of carboxamides from carboxylic acids and amines by using easily available $Si(2\text{-}Me\text{-}Im)_4$ as a new dehydrating reagent and also further development of the above reaction applied to the thioesterification between carboxylic acids and thiols.

RESULTS AND DISCUSSION

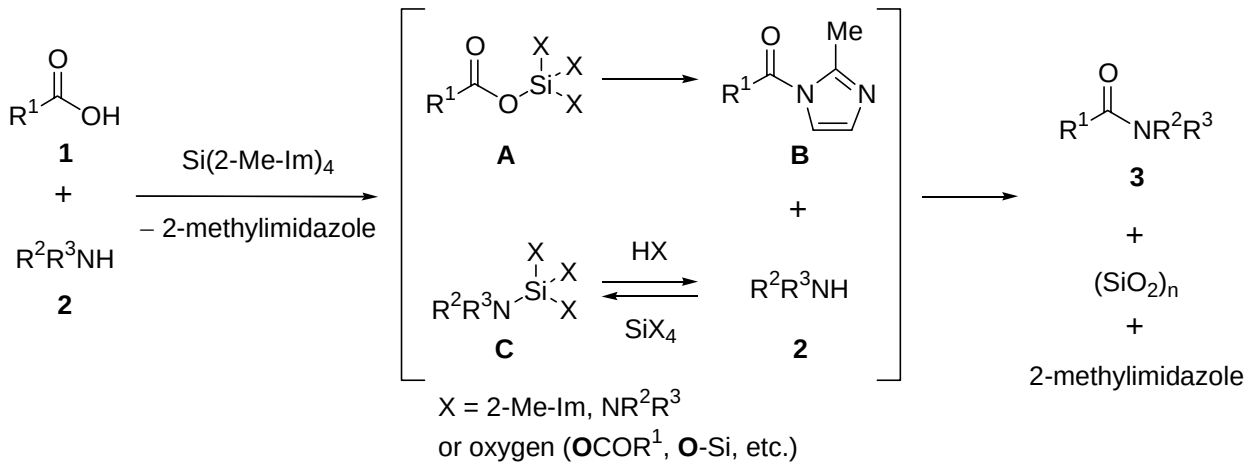
Tetrakis(2-methylimidazol-1-yl)silane [$Si(2\text{-}Me\text{-}Im)_4$] was easily synthesized in almost quantitative yield by trans-silylation between $SiCl_4$ and 2-methyl-1-trimethylsilyl-imidazole in the molar ratio of 1 : 4 in dry

toluene (Scheme 1). After removal of the solvent and formed chlorotrimethylsilane (Me_3SiCl), the resulted solid product can be stored in a sealed bottle for several weeks without decomposition and is used directly for condensation reactions.



Scheme 1.

The proposed mechanism for the formation of carboxamides from carboxylic acids and amines by using $Si(2\text{-Me-Im})_4$ is as follows (Scheme 2). Carboxylic acids (**1**) react with $Si(2\text{-Me-Im})_4$ to form silyl ester intermediates (**A**), which in turn are readily transformed into the corresponding 1-acyl-2-methylimidazoles (**B**) by either intramolecular rearrangement of **A** or nucleophilic attack of liberated 2-methylimidazole to the carbonyl carbon. It is also considered that amines (**2**) are readily silylated in situ by imidazolylsilanes to form silylated amines (**C**), which can easily undergo desilylation to reproduce reactive free amines (**2**) since the intermolecular exchange is favored to shift toward free amine (**2**) by the irreversible formation of carboxamides (**3**) and silica [$(SiO_2)_n$].

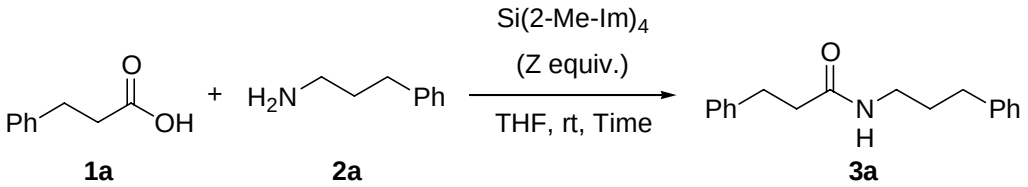


Scheme 2.

As a preliminary experiment, the reaction of 3-phenylpropanoic acid (**1a**) (1.0 equiv.) with 3-phenylpropylamine (**2a**) (1.2 equiv.) was examined in THF by using $Si(2\text{-Me-Im})_4$ (0.6 equiv.) at room temperature. The corresponding carboxamide (**3a**) was obtained in 90% yield after disappearance of the in situ formed 1-acyl-2-methylimidazole intermediate that was monitored by TLC (Table 1, Entry 1). It

was found that the amount of $Si(2\text{-Me-Im})_4$ was reduced to 0.5 equivalents while the yield remained (Entry 2). On the other hand, the use of larger molar amounts of $Si(2\text{-Me-Im})_4$ caused prolongation of

Table 1. Effect of Molar Ratios of Substrates and $Si(2\text{-Me-Im})_4$

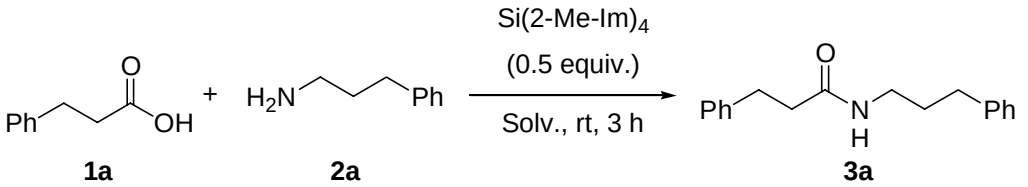


1a (X equiv.) + **2a** (Y equiv.) → **3a**

Entry	X	Y	Z	Time /h	Yield[a] /%
1	1.0	1.2	0.6	4	90
2	1.0	1.2	0.5	3	91
3	1.0	1.2	0.4	3	79
4	1.0	1.2	0.3	3	64
5	1.0	1.2	0.8	8	57 (78)[b]
6	1.0	1.2	1.0	8	53
7	1.0	1.0	0.5	3	90
8	1.1	1.0	0.5	3	96
9	1.2	1.0	0.5	3	99

[a]Isolated yield. [b]Reaction was carried out for 24 h.

Table 2. Effect of Solvents



1a (1.2 equiv.) + **2a** (1.0 equiv.) → **3a**

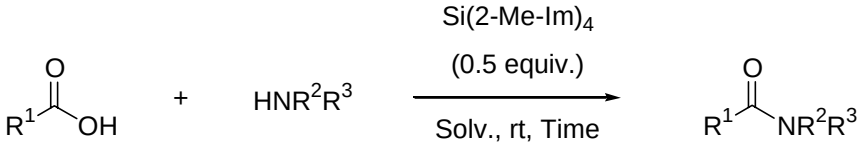
Entry	Solv.	Yield[a] /%
1	THF	99
2	Et_2O	92
3	DMF	90
4	MeCN	96
5	CH_2Cl_2	96
6	toluene	82 (96)[b]

[a]Isolated yield. [b]Reaction was carried out for 9 h.

reaction time because an excess amount of $Si(2\text{-Me-Im})_4$ reacted directly with amine (**2a**) to form silylated amine intermediates and to suppress the desired condensation (Entries 5 and 6). After the molar ratios of carboxylic acid, amine, and $Si(2\text{-Me-Im})_4$ were respectively examined in detail, it was revealed that the desired product was obtained in nearly quantitative yield by employing a slightly excess amount of the carboxylic acid (Entries 8 and 9).

Next, effect of solvents including polar and nonpolar ones were examined by taking the reaction of **1a** with **2a** in the presence of $Si(2\text{-Me-Im})_4$ under the optimized conditions (Table 2). It was found that a wide range of solvents such as THF, Et_2O, DMF, MeCN, CH_2Cl_2, and toluene were successfully used in

Table 3. Synthesis of various carboxamides by using $Si(2\text{-Me-Im})_4$



1 (1.2 equiv.) + **2** (1.0 equiv.) → **3**

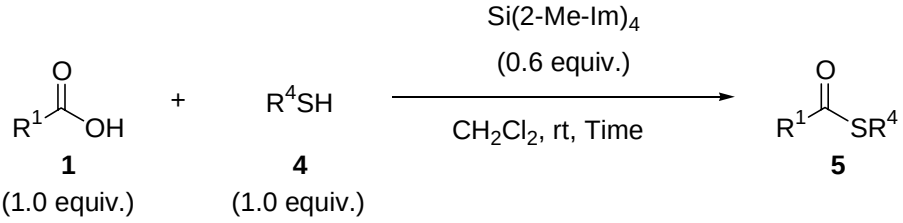
Entry	Carboxylic acid	Amine	Solv.	Time /h	Product	Yield[a] /%
1	$Ph(CH_2)_2CO_2H$ (**1a**)	$Ph(CH_2)_3NH_2$ (**2a**)	THF	3	**3a**	99
2	**1a**	$PhCH_2NH_2$ (**2b**)	THF	3	**3b**	quant.
3	**1a**	Ph_2CHNH_2 (**2c**)	THF	24	**3c**	84
4	**1a**	$PhCHMeNH_2$ (**2d**)	THF	12	**3d**	93
5	**1a**	$PhCH_2NHMe$ (**2e**)	THF	12	**3e**	99
6	**1a**	Piperidine (**2f**)	THF	6	**3f**	96
7	**1a**	$PhNH_2$ (**2g**)	THF	24	**3g**	71
8	**1a**	$EtNH_2$･HCl (**2h**)	CH_2Cl_2	12	**3h**	77
9	**1a**	$PhNH_2$･HCl (**2i**)	CH_2Cl_2	24	**3g**	71
10	**1a**	Gly-OEt･HCl (**2j**)	CH_2Cl_2	24	**3i**	88[b]
11	*c*-$C_6H_{11}CO_2H$ (**1b**)	**2a**	THF	24	**3j**	93
12	**1b**	**2f**	THF	24	**3k**	77
13	*t*-$BuCO_2H$ (**1c**)	**2a**	THF	24	**3l**	78
14	**1c**	**2b**	THF	12	**3m**	84
15	$PhCO_2H$ (**1d**)	**2a**	THF	24	**3n**	87
16	**1d**	**2f**	THF	6	**3o**	93

[a]Isolated yield. [b]Amine･HCl (1.2 equiv.) was added to the mixture of carboxylic acid (1.0 equiv.) and $Si(2\text{-Me-Im})_4$ (0.6 equiv.)

this reaction and the reactions mostly proceeded smoothly to provide the desired carboxamide (**3a**) in high yields except toluene which required longer reaction time due to the poor solubility of $Si(2\text{-Me-Im})_4$. Several examples of carboxamides (**3a–o**) obtained by using $Si(2\text{-Me-Im})_4$ as a dehydrating reagent are listed in Table 3, which clearly shows the efficiency and general applicability of the present method. It is noted that hydrogen chloride salts of amines (**2h–j**) instead of free amines are directly used in this procedure in the absence of other bases such as triethylamine to capture liberated hydrogen chloride since in situ formed 2-methylimidazole works as a hydrogen chloride scavenger (Entries 8–10).

In order to further demonstrate the synthetic utility and versatility of this novel dehydrating reagent, $Si(2\text{-Me-Im})_4$, it was applied to the synthesis of thioesters from carboxylic acids and thiols. Then, thioesterification of carboxylic acids (**1**) (1.0 equiv.) with thiols (**4**) (1.0 equiv.) was tried in CH_2Cl_2 by using $Si(2\text{-Me-Im})_4$ (0.6 equiv.) at room temperature (Table 4). In most cases, the reactions proceeded smoothly under mild conditions to afford the corresponding thioesters (**5**) in good to excellent yields.

Table 4. Synthesis of various thioesters by using $Si(2\text{-Me-Im})_4$



Entry	Carboxylic acid	Thiol	Time /h	Product	Yield[a] /%
1	$Ph(CH_2)_2CO_2H$ (**1a**)	$Me(CH_2)_7SH$ (**4a**)	24	**5a**	86
2	**1a**	$PhCH_2SH$ (**4b**)	6	**5b**	98
3	**1a**	*c*-$C_6H_{11}SH$ (**4c**)	24	**5c**	73
4	**1a**	PhSH (**4d**)	3	**5d**	97
5	*c*-$C_6H_{11}CO_2H$ (**1b**)	**4b**	6	**5e**	83
6	**1b**	**4d**	6	**5f**	98
7	$PhCO_2H$ (**1d**)	**4b**	6	**5g**	86
8	**1d**	**4d**	3	**5h**	93

[a]Isolated yield.

Thus, a novel dehydrating reagent having silicon–imidazole linkage, $Si(2\text{-Me-Im})_4$, was easily prepared by trans-silylation between $SiCl_4$ and 2-methyl-1-trimethylsilylimidazole, and was used very conveniently for the preparation of various carboxamides directly from free carboxylic acids and amines

under mild conditions. In addition, this method was efficiently applied also to the thioesterification between carboxylic acids and thiols.

EXPERIMENTAL

All melting points were measured on a micro melting point apparatus (Yanaco MP-S3) and were not corrected. IR spectra were recorded on a SENSIR TECHNOLOGIES TravelIR Portable FT-IR spectrometer (Attenuated Total Reflection). ^{1}H NMR spectra were recorded on a JEOL JNM-EX270L (270 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C NMR spectra were recorded on a JEOL JNM-EX270L (68 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$; δ = 77.0 ppm). The optical rotations were measured with a JASCO P-1020 polarimeter. HRMS spectra were recorded on a JEOL JMS-700 mass spectrometer. Analytical TLC was performed on Merck preparative TLC plates (silica gel 60 GF254, 0.25 mm). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. Dry solvents were purchased from Kanto Chemical. All reagents were purchased from Tokyo Kasei Kogyo, Kanto Chemical, Kokusan Chemical, Wako Pure Chemical Industries, or Aldrich Chemical. 2-Methyl-1-trimethylsilyl-imidazole was prepared according to the literature procedures.[10]

Preparation of tetrakis(2-methylimidazol-1-yl)silane [Si(2-Me-Im)$_4$].

To a solution of 2-methyl-1-trimethylsilyl-imidazole (10.0 g, 64.8 mmol) in toluene (5.0 mL) was added slowly $SiCl_4$ (1.86 mL, 16.2 mmol) at rt under argon. The precipitation of a white solid was observed. After the mixture was stirred at 80 °C for 1 h, the generated Me_3SiCl and the solvent were removed under reduced pressure to give a white powder in almost quantitative yield (5.71 g). The reagent can be handled for brief periods in the air though it is sensitive to moisture. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.18 (s, 4H), 6.84 (s, 4H), 2.09 (s, 12H). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 149.7, 132.3, 120.9, 15.4. HRMS (EI^+) calcd for $C_{16}H_{20}N_8Si$ $[M]^+$ 352.1580, found *m*/*z* 352.1582.

Typical experimental procedure for the preparation of carboxamides by using Si(2-Me-Im)$_4$ (Table 3, Entry 1).

To a stirred suspension of Si(2-Me-Im)$_4$ (88.0 mg, 0.25 mmol) in THF (0.75 mL) were successively added 3-phenylpropanoic acid (**1a**) (90.1 mg, 0.6 mmol) and a solution of 3-phenylpropylamine (**2a**) (67.6 mg, 0.5 mmol) in THF (0.75 mL) at rt. The reaction mixture was stirred for 3 h at the same temperature, followed by the addition of water. Precipitated silica was filtered off and washed with

EtOAc, and then the filtrate was extracted with EtOAc. The organic layer was washed with 1 M HCl *aq*, saturated $NaHCO_3$ *aq*, and brine, dried over anhydrous Na_2SO_4. After filtration, the solvent was removed under reduced pressure to give 3-Phenyl-*N*-(3-phenylpropyl)propanamide (**3a**) (132 mg, 99%) in almost pure form.

3-Phenyl-*N*-(3-phenylpropyl)propanamide (3a).[2a]

Colorless crystals, mp 55–56 °C. IR (ATR) 3306, 1629, 1537, 1452 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.28–7.09 (m, 10H), 5.64 (br s, 1H), 3.25–3.17 (m, 2H), 2.92 (t, J = 7.6 Hz, 2H), 2.54 (t, J = 7.6 Hz, 2H), 2.40 (t, J = 7.6 Hz, 2H), 1.76–1.70 (m, 2H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.8, 141.2, 140.7, 128.3, 128.2, 128.1, 126.0, 125.8, 39.1, 38.4, 33.2, 31.7, 31.0. Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.89; H, 8.17; N, 5.26.

***N*-Benzyl-3-phenylpropanamide (3b).**[2a]

Colorless crystals, mp 81–82 °C. IR (ATR) 3290, 1638, 1541, 1453 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.27–7.07 (m, 10H), 6.14 (br s, 1H), 4.31 (d, J = 5.9 Hz, 2H), 2.92 (t, J = 7.6 Hz, 2H), 2.46 (t, J = 7.6 Hz, 2H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.8, 140.6, 138.0, 128.4, 128.3, 128.2, 127.4, 127.1, 126.0, 43.4, 38.2, 31.7. Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.10; H, 7.22; N, 5.82.

***N*-(Diphenylmethyl)-3-phenylpropanamide (3c).**[2a]

Colorless crystals, mp 146–147 °C. IR (ATR) 3306, 1642, 1534, 1494 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.30–7.07 (m, 15H), 6.26–6.15 (m, 1H), 6.12 (br s, 1H), 2.96 (t, J = 7.3 Hz, 2H), 2.52 (t, J = 7.3 Hz, 2H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 170.8, 141.2, 140.5, 128.4, 128.3, 127.2, 127.2, 126.1, 56.8, 38.4, 31.6. Anal. Calcd for $C_{22}H_{21}NO$: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.66; H, 6.78; N, 4.47.

3-Phenyl-*N*-[(1*S*)-1-phenylethyl]propanamide (3d).[2a]

Colorless crystals, $[\alpha]_D^{29}$ = –63.9° (*c* 1.02 EtOH). mp 83–84 °C. IR (ATR) 3306, 1635, 1535 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.29–7.12 (m, 10H), 5.96 (br s, 1H), 5.08–5.02 (m, 1H), 2.92 (t, J = 7.6 Hz, 2H), 2.43 (t, J = 7.6 Hz, 2H), 1.36 (d, J = 6.8 Hz, 3H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 170.9, 142.9, 140.6, 128.3, 128.3, 128.2, 127.0, 126.0, 125.9, 48.5, 38.4, 31.7, 21.6. Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.39; H, 7.55; N, 5.41.

***N*-Benzyl-*N*-methyl-3-phenylpropanamide (3e).**[2a]

Colorless oil, a mixture of two stereoisomers A and B. IR (ATR) 1641, 1452, 1403 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.27–7.07 (m, 10H, A+B), 4.58 (s, 2aH, A), 4.44 (s, 2bH, B), 3.02–2.96 (m, 2H, A+B), 2.93 (s, 3bH, B), 2.82 (s, 3aH, A), 2.70–2.63 (m, 2H, A+B). ^{13}C NMR (68 MHz, $CDCl_3$) δ 172.2, 171.9, 141.1, 141.0, 137.1, 136.3, 128.7, 128.3, 128.2, 128.2, 127.8, 127.3, 127.1, 126.0, 125.9, 125.9, 53.1, 50.7, 35.7, 35.3, 34.9, 34.7, 33.9, 31.5, 31.3. HRMS (DEI^+) calcd for $C_{17}H_{19}NO$ $[M]^+$ 253.1467, found *m*/*z* 253.1467.

1-(3-Phenylpropanoyl)piperidine (3f).[2a]

Colorless oil, IR (ATR) 2933, 1632, 1438 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.28–7.22 (m, 5H), 3.56–3.54 (m, 2H), 3.33–3.31 (m, 2H), 2.96 (t, J = 8.0 Hz, 2H), 2.61 (t, J = 8.0 Hz, 2H), 1.66–1.44 (m, 6H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 170.1, 141.2, 128.2, 128.2, 125.8, 46.5, 42.6, 35.1, 31.5, 26.3, 25.5, 24.5. HRMS (DEI^+) calcd for $C_{14}H_{19}NO$ $[M]^+$ 217.1467, found m/z 217.1467.

_N_,3-diphenylpropanamide (3g).[2a]

Colorless crystals, mp 95–96 °C. IR (ATR) 3321, 1650, 1599, 1526, 1495, 1440 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.80 (br s, 1H), 7.42 (d, J = 7.8 Hz, 2H), 7.24–7.12 (m, 7H), 7.07 (t, J = 7.3 Hz, 1H), 2.98 (t, J = 7.8 Hz, 2H), 2.59 (t, J = 7.8 Hz, 2H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 170.6, 140.4, 137.7, 128.7, 128.4, 128.1, 126.1, 124.1, 120.0, 39.2, 31.6. Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.73; H, 6.60; N, 5.90.

_N_-Ethyl-3-phenylpropanamide (3h).[11]

Colorless crystals, mp 55–56 °C. IR (ATR) 3298, 1638, 1550 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.29–7.16 (m, 5H), 5.77 (br s, 1H), 3.27–3.17 (m, 2H), 2.94 (t, J = 7.8 Hz, 2H), 2.44 (t, J = 7.8 Hz, 2H), 1.05 (t, J = 7.3 Hz, 3H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.8, 140.7, 128.3, 128.1, 126.0, 38.4, 34.3, 31.8, 14.8. Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.20; H, 8.54; N, 7.76.

Ethyl N-(3-phenylpropanoyl)glycinate (3i).

Colorless crystals, mp 50–51 °C. IR (ATR) 3313, 1722, 1635, 1546, 1298, 1253, 1228, 1038, 1028 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.27–7.17 (m, 5H), 6.18 (br s, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.99 (d, J = 5.1 Hz, 2H), 2.97 (t, J = 7.8 Hz, 2H), 2.54 (t, J = 7.8 Hz, 2H), 1.26 (t, J = 7.2 Hz, 2H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 172.0, 169.7, 140.5, 128.3, 128.1, 126.0, 61.4, 41.3, 37.9, 31.4, 14.1. Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.33; H, 6.99; N, 5.96.

_N_-(3-Phenylpropyl)cyclohexanecarboxamide (3j).

Colorless crystals, mp 80–82 °C. IR (ATR) 3297, 2930, 2853, 1639, 1549 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.30–7.14 (m, 5H), 5.82 (br s, 1H), 3.30–3.22 (m, 2H), 2.62 (t, J = 7.6 Hz, 2H), 2.08–1.98 (m, 1H), 1.88–1.63 (m, 7H), 1.46–1.15 (m, 5H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 175.9, 141.3, 128.2, 128.1, 125.7, 45.4, 38.9, 33.3, 31.2, 29.6, 25.7. Anal. Calcd for $C_{16}H_{23}NO$: C, 78.32; H, 9.45; N, 5.71. Found: C, 78.18; H, 9.09; N, 5.70.

1-(Cyclohexylcarbonyl)piperidine (3k).[12]

Colorless oil, IR (ATR) 2927, 2853, 1630, 1438, 1252, 1213 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 3.58–3.54 (m, 2H), 3.44–3.40 (m, 2H), 2.52–3.42 (m, 1H), 1.89–1.22 (m, 16H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 174.1, 46.3, 42.6, 40.4, 29.4, 26.8, 25.9, 25.9, 25.6, 24.7. HRMS (DEI^+) calcd for $C_{12}H_{21}NO$ $[M]^+$ 195.1623, found m/z 195.1625.

2,2-Dimethyl-_N_-(3-phenylpropyl)propanamide (3l).

Colorless crystals, mp 77–78 °C. IR (ATR) 3322, 2944, 1630, 1538, 1212 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.30–7.15 (m, 5H), 5.72 (br s, 1H), 3.27 (q, J = 7.6 Hz, 2H), 2.64 (t, J = 7.6 Hz, 2H), 1.89–1.78

(m, 2H), 1.14 (s, 9H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 178.0, 141.3, 128.3, 128.1, 125.8, 39.2, 38.5, 33.4, 31.1, 27.5. Anal. Calcd for $C_{14}H_{21}NO$: C, 76.67; H, 9.65; N, 6.39. Found: C, 76.55; H, 9.23; N, 6.36.

***N*-Benzyl-2,2-dimethylpropanamide (3m).**[13]

Colorless crystals, mp 82–83 °C. IR (ATR) 3298, 2962, 1634, 1538, 1218 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.34–7.22 (m, 5H), 6.10 (br s, 1H), 4.41 (d, J = 5.4 Hz, 2H), 1.22 (s, 9H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 178.0, 138.5, 128.4, 127.3, 127.1, 43.4, 38.6, 27.6. Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.24; H, 9.35; N, 7.29.

***N*-(3-Phenylpropyl)benzamide (3n).**[14]

Colorless crystals, mp 40–41 °C. IR (ATR) 3296, 1633, 1548, 1313 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.69 (d, J = 7.8 Hz, 2H), 7.45–7.11 (m, 8H), 6.64 (br s, 1H), 3.47–3.39 (m, 2H), 2.66 (t, J = 7.6 Hz, 2H), 1.95–1.86 (m, 2H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 167.3, 141.3, 134.4, 131.0, 128.3, 128.2, 128.1, 126.7, 125.7, 39.8, 33.4, 31.0. Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.06; H, 6.99; N, 5.79.

1-Benzoylpiperidine (3o).[15]

Colorless crystals, mp 39–40 °C. IR (ATR) 2935, 2857, 1618, 1575, 1427, 1274 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.38 (s, 5H), 3.70 (br s, 2H), 3.33 (br s, 2H), 1.75–1.45 (m, 6H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 169.9, 136.2, 129.0, 128.1, 126.5, 48.6, 43.0, 26.4, 25.5, 24.5. Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 75.93; H, 7.70; N, 7.34.

Typical experimental procedure for the preparation of thioesters by using Si(2-Me-Im)$_4$ (Table 4, Entry 1).

To a stirred suspension of Si(2-Me-Im)$_4$ (88.0 mg, 0.25 mmol) in CH_2Cl_2 (0.75 mL) were successively added 3-phenylpropanoic acid (**1a**) (90.1 mg, 0.6 mmol) and a solution of 1-octanethiol (**4a**) (73.1 mg, 0.5 mmol) in CH_2Cl_2 (0.75 mL) at rt. The reaction mixture was stirred for 24 h at the same temperature, followed by the addition of water. Precipitated silica was filtered off and washed with EtOAc, and then the filtrate was extracted with EtOAc. The organic layer was washed with 1 M HCl *aq*, saturated $NaHCO_3$ *aq*, and brine, dried over anhydrous Na_2SO_4. After filtration of the mixture and evaporation of the solvent, the crude product was purified by thin-layer chromatography to afford *S*-octyl 3-phenylpropionthioate (**5a**) (120 mg, 86%).

***S*-Octyl 3-phenylpropanethioate (5a).**[2b]

Colorless oil, IR (ATR) 2924, 2855, 1688, 1453, 1045, 971 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.37–7.14 (m, 5H), 3.01–2.83 (m, 6H), 1.67–1.49 (m, 2H), 1.45–1.19 (m, 10H), 0.88 (t, J = 7.0 Hz, 3H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 198.4, 140.0, 128.4, 128.2, 126.2, 45.5, 31.8, 31.5, 29.6, 29.2, 29.1, 29.0, 28.8, 22.7, 14.2. HRMS (DEI$^+$) calcd for $C_{17}H_{26}OS$ [M]$^+$ 278.1704, found *m*/*z* 278.1702.

***S*-Benzyl 3-phenylpropanethioate (5b).**[16]

Colorless oil, IR (ATR) 1687, 1043, 972 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.38–7.11 (m, 10H), 4.10 (s, 2H), 3.00–2.93 (m, 2H), 2.87–2.81 (m, 2H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 197.5, 139.7, 137.4, 128.6, 128.4, 128.3, 128.1, 127.1, 126.2, 45.2, 33.1, 31.4. HRMS (DEI^+) calcd for $C_{16}H_{16}OS$ $[M]^+$ 256.0922, found *m*/*z* 256.0925.

_S_-Cycrohexyl 3-phenylpropanethioate (5c).[2b]

Colorless oil, IR (ATR) 2928, 2853, 1682, 1449, 1044, 970 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.37–7.15 (m, 5H), 3.63–3.46 (m, 1H), 3.01–2.91 (m, 2H), 2.84–2.78 (m, 2H), 1.99–1.81 (m, 2H), 1.74–1.51 (m, 3H), 1.50–1.20 (m, 5H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 198.2, 140.0, 128.3, 128.2, 126.1, 45.6, 42.3, 33.0, 31.5, 26.0, 25.6. HRMS (DEI^+) calcd for $C_{15}H_{20}OS$ $[M]^+$ 248.1235, found *m*/*z* 248.1234.

_S_-Phenyl 3-phenylpropanethioate (5d).[17]

Colorless crystals, mp 44–45 °C. IR (ATR) 1712, 1048, 959 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.39 (s, 5H), 7.36–7.18 (m, 5H), 3.04–2.92 (m, 4H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 196.4, 139.8, 134.3, 129.3, 129.1, 128.4, 128.3, 127.5, 126.3, 45.2, 31.4. Anal. Calcd for $C_{15}H_{14}OS$: C, 74.34; H, 5.82. Found: C, 74.29; H, 5.85.

_S_-Benzyl cyclohexanecarbothioate (5e).[18]

Colorless oil, IR (ATR) 2929, 2854, 1684, 1450, 967 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.28–7.19 (m, 5H), 4.09 (s, 2H), 2.49 (tt, J = 11.3, 3.5 Hz, 3H), 1.95–1.88 (m, 2H), 1.79–1.74 (m, 2H), 1.70–1.60 (m, 1H), 1.53–1.40 (m, 2H), 1.33–1.20 (m, 3H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 202.1, 137.7, 128.6, 128.4, 127.0, 52.4, 32.8, 29.6, 25.7, 25.5. HRMS (DEI^+) calcd for $C_{14}H_{18}OS$ $[M]^+$ 234.1078, found *m*/*z* 234.1079.

_S_-Phenyl cyclohexanecarbothioate (5f).[19]

Colorless crystals, mp 36–37 °C. IR (ATR) 2932, 2850, 1692, 1478, 1441, 960 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.38 (s, 5H), 2.65–2.55 (m, 1H), 2.03–1.96 (m, 2H), 1.86–1.77 (m, 2H), 1.70–1.61 (m, 1H), 1.60–1.44 (m, 2H), 1.40–1.19 (m, 3H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 200.4, 134.4, 129.0, 128.9, 127.8, 52.5, 29.6, 25.6, 25.5. Anal. Calcd for $C_{13}H_{16}OS$: C, 70.87; H, 7.32. Found: C, 70.80; H, 7.00.

_S_-Benzyl benzenecarbothioate (5g).[20]

Colorless crystals, mp 36–37 °C. IR (ATR) 1651, 1206, 905 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 7.69 (d, J = 7.0 Hz, 2H), 7.56–7.20 (m, 8H), 4.31 (s, 2H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 191.0, 137.3, 136.6, 133.3, 128.8, 128.5, 128.5, 127.2, 127.1, 33.3. Anal. Calcd for $C_{14}H_{12}OS$: C, 73.65; H, 5.30. Found: C, 73.64; H, 5.19.

_S_-Phenyl benzenecarbothioate (5h).[20]

Colorless crystals, mp 54–55 °C. IR (ATR) 1664, 1198, 1176, 890 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 8.02 (d, J = 7.0 Hz, 2H), 7.58–7.43 (m, 8H). ^{13}C NMR (68 MHz, $CDCl_3$) δ 189.8, 136.4, 134.9, 133.5, 129.4, 129.1, 128.6, 127.3, 127.2. Anal. Calcd for $C_{13}H_{10}OS$: C, 72.87; H, 4.70. Found: C, 72.83; H, 4.79.

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REFERENCES

1. (a) G. Benz, "Comprehensive Organic Synthesis," Pergamon, ed. by B. M. Trost and I. Fleming, Oxford, 1991, Vol. 6, pp. 381-417. (b) S-Y. Han and Y-A. Kim, *Tetrahedron*, 2004, **60**, 2447. (c) E. Haslam, *Tetrahedron*, 1980, **36**, 2409.
2. For recent reports, see: (a) I. Shiina and Y. Kawakita, *Tetrahedron*, 2004, **60**, 4729 and references cited therein. (b) K. Wakasugi, A. Iida, T. Misaki, Y. Nishii, and Y. Tanabe, *Adv. Synth. Catal*., 2003, **345**, 1209. (c) K. Wakasugi, A. Nakamura, A. Iida, Y. Nishii, N. Nakatani, S. Fukushima, and Y. Tanabe, *Tetrahedron*, 2003, **59**, 5337. (d) I. Shiina, M. Kubota, H. Oshiumi, and M. Hashizume, *J. Org. Chem.*, 2004, **69**, 1822. (e) I. Shiina and Y. Kawakita, *Tetrahedron Lett.*, 2003, **44**, 1951.
3. (a) H. A. Staab, H. Bauer, and K. M. Schneider, "Azolides in Organic Synthesis and Biochemistry," Wiley-VCH, Weinheim, 1998, pp. 129-208. (b) H. A. Staab, *Angew. Chem., Int. Ed. Engl.*, 1962, **1**, 351. (c) T. Kitagawa, H. Kuroda, H. Sasaki, and K. Kawasaki, *Chem. Pharm. Bull.*, 1987, **35**, 4294. (d) A. K. Saha, H. Rapoport, and P. Schultz, *J. Am. Chem. Soc.*, 1989, **111**, 4856.
4. R. Paul and G. W. Anderson, *J. Am. Chem. Soc*., 1960, **82**, 4596.
5. H. Vorbrüggen, "Silicon-mediated Transformations of Functional Groups," Wiley-VCH, Weinheim, 2004.
6. (a) W.-C. Chou, M. C. Chou, Y.-Y. Lu, and S.-F. Chen, *Tetrahedron Lett.*, 1999, **40**, 3419. (b) R. Pellegata, M. Pinza, and G. Pifferi, *Synthesis*, 1978, 614. (c) B. D. Harris, K. L. Bhat, and M. M. Joullie, *Synth. Commun.*, 1986, **16**, 1815. (d) J. W. Lampe, P. F. Hughes, C. K. Biggers, S. H. Smith, and H. Hu, *J. Org. Chem.*, 1994, **59**, 5147.
7. (a) T. H. Chan and L. T. L. Wong, *J. Org. Chem.*, 1969, **34**, 2766. (b) I. Azumaya, H. Kagechika, K. Yamaguchi, and K. Shudo, *Tetrahedron Lett.*, 1996, **37**, 5003.
8. S. H. van Leeuwen, P. J. L. M. Quaedflieg, Q. B. Broxterman, and R. M. J. Liskamp, *Tetrahedron Lett.*, 2002, **43**, 9203.
9. T. Tozawa, Y. Yamane, and T. Mukaiyama, *Chem. Lett.*, 2005, **34**, 734.
10. (a) A. F. Janzen, G. N. Lypka, and R. E. Wasylishen, *Can. J. Chem.*, 1980, **58**, 60. (b) R. E. Wasylishen, G. S. Birdi, and A. F. Janzen, *Inorg. Chem.*, 1976, **15**, 3054. (c) L. Birkofer, P. Richter, and A. Ritter, *Chem. Ber.*, 1960, **93**, 2804.
11. J. Werry, H. Stamm, P.-Y. Lin, R. Falkenstein, S. Gries, and H. Irngartinger, *Tetrahedron*, 1989, **45**, 5015.

12. (a) G. Montaudo, P. Finocchiaro, P. Maravigna, and C. G. Overberger, *Macromolecules*, 1972, **5**, 197. (b) K. Matsumoto, S. Hashimoto, T. Uchida, T. Okamoto, S. Gries, and S. Otani, *Chem. Ber.*, 1989, **122**, 1357.
13. I. Shiina, Y. Suenaga, M. Nakano, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, 2000, **73**, 2811.
14. G. Schlueter and W. Meise, *Liebigs. Ann. Chem.*, 1988, 833.
15. (a) M. Masui, S. Hara, and S. Ozaki, *Chem. Pharm. Bull.*, 1986, **34**, 975. (b) Z. Zhang, Z. Yin, J. F. Kadow, N. A. Meanwell, and T. Wang, *J. Org. Chem.*, 2004, **69**, 1360.
16. M. Yamada, S. Yahiro, T. Yamano, Y. Nakatani, and G. Ourisson, *Bull. Soc. Chim. Fr.*, 1990, **6**, 824.
17. M. Miyashita, I. Shiina, S. Miyoshi, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 1516.
18. H.-J. Liu and S. I. Sabesan, *Can. J. Chem.*, 1980, **58**, 2645.
19. A. Mendoza and D. S. Matteson, *J. Org. Chem.*, 1979, **44**, 1352.
20. A. R. Katritzky, A. A. Shestopalov, and K. Suzuki, *Synthesis*, 2004, **11**, 1806.