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Remarkable enhancement effect of potassium *tert*-butoxide/THF solution in base-induced Sommelet–Hauser rearrangements

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ABSTRACT

A solution of potassium *tert*-butoxide in THF was shown to remarkably enhance the base-induced Sommelet–Hauser rearrangement of *N*-benzylic amino acid-derived ammonium ylides.

1. Introduction

The base-induced Sommelet–Hauser (S–H) rearrangement of *N*-benzylic ammonium ylides is an interesting and useful transformation in organic synthesis that can provide easy access to *ortho*-substituted aromatic compounds.[1,2] However, the utility of this rearrangement is severely limited by a competing [1,2] Stevens rearrangement, resulting in a distribution of products, that is, dependent on the reaction conditions and the substrate structures.[3] For example, under common reaction conditions in the base-induced rearrangement of *N*-benzylic amino acid-derived ammonium ylides, the [1,2] Stevens rearrangement is known to be favored and produces α-benzylated amino acid derivatives as the major reaction product. Recently, we reported that an electron-withdrawing substituent on the aromatic ring of *N*-benzylic amino acid-derived ammonium ylides enhances the S–H rearrangement.[4] In the course of these investigations, we found that a solution of potassium *tert*-butoxide (*t*-BuOK) in THF had a remarkable enhancement effect on the base-induced S–H rearrangement. Herein, we wish to report that S–H rearrangements promoted by a solution of *t*-BuOK in THF are shown to proceed under mild conditions with minimal competition from the [1,2] Stevens rearrangement. This enhancement effect was observed with a variety of *N*-benzylic amino acid-derived ammonium ylides.

2. Results and discussion

First, we examined the rearrangement of the *N*-benzyl-*N*,*N*-dimethylglycine *tert*-butyl ester-derived ammonium salt **1a**, which was promoted by common bases to afford *N*,*N*-dimethyl-*o*-tolylglycine *tert*-butyl ester (**2a**) as the S–H product and *N*,*N*-dimethylphenylalanine *tert*-butyl ester (**3a**) as the [1,2] Stevens product (Table 1). When the reaction was carried out by addition of solid *t*-BuOK (1.1 equiv)[5] to a THF solution of **1a** at 0 °C for 3 h under an atmosphere of argon (entry 1), the [1,2] Stevens rearrangement proceeded preferably to give **3a** as the major product (43%). The corresponding S–H rearrangement product **2a** was obtained in only 22% yield. The yield of **2a** was slightly improved (40%) by addition of a THF solution of **1a** to a suspension of solid *t*-BuOK in THF (entry 2). Use of solid sodium *tert*-butoxide (*t*-BuONa), LDA, phenyllithium, potassium hydroxide, and potassium carbonate did not result in any improvement (entries 3–7). Interestingly, when the reaction was carried out with a 1.0 M solution of *t*-BuOK in THF,[6] the S–H rearrangement was dramatically accelerated to give **2a** in 80% yield along with the [1,2] Stevens product **3a** in 8% yield (entry 8). However, a *t*-BuOK/THF solution prepared from sublimed grade (99% purity) solid *t*-BuOK (entry 9) or a solid *t*-BuOK obtained by concentration of the commercially available *t*-BuOK/THF solution (entry 10) did not accelerate the S–H rearrangement. Analogue bases, such as a solution of *t*-BuONa in THF (entry 11) or a solution of potassium bis(trimethylsilyl)amide (KHMDS) in toluene (entry 12) did not show any enhancement effects in the S–H rearrangement.

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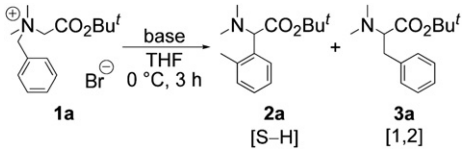
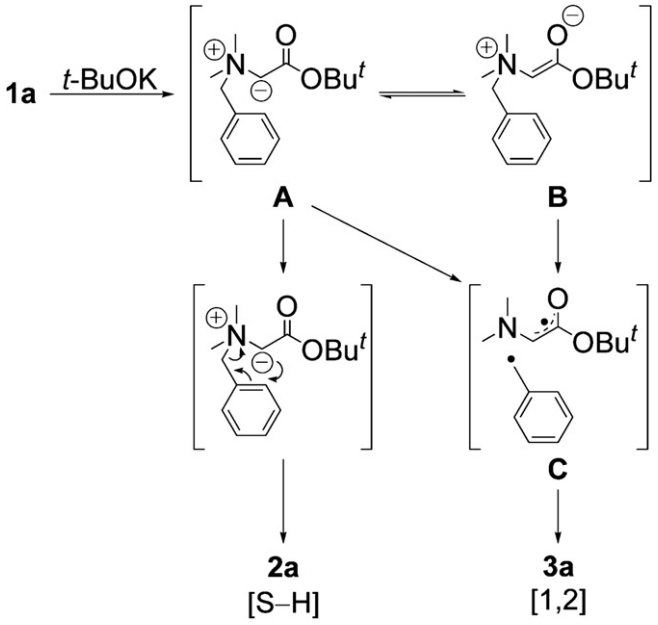
Table 1
Base-induced S–H rearrangement of **1a** with various types of bases



Entry	Base (equiv)[a]	**2a** (%)[b]	**3a** (%)[b]
1	*t*-BuOK solid (1.1)	22	43
2	*t*-BuOK solid (1.1)[c]	40	36
3	*t*-BuONa solid (1.1)	19	43
4	LDA THF solution (1.1)	6	29
5	PhLi cyclohexane–Et_2O solution (1.1)	0	15
6	KOH powder (5)	0	22
7	K_2CO_3 (1.2)	0	0
8	*t*-BuOK THF solution (1.1)[d]	80	8
9	*t*-BuOK THF solution (1.1)[e]	18	42
10	*t*-BuOK solid (1.1)[f]	15	43
11	*t*-BuONa THF solution (1.1)[g]	36	35
12	KHMDS toluene solution (1.1)[h]	15	34

[a] Unless otherwise noted, the bases were added to a THF solution of **1a**.
[b] Isolated yield.
[c] A THF solution of **1a** was added to a suspension of *t*-BuOK in THF.
[d] Commercially available from Aldrich or TCI.
[e] Prepared from sublimed grade solid *t*-BuOK (not clear completely).
[f] Obtained by concentration of *t*-BuOK THF solution prior to use.
[g] Commercially available from Aldrich.
[h] The reaction was carried out in THF–toluene (5:1).

The exact reason for this enhancement effect is unknown at present, however, it is safe to say that a clear solution of *t*-BuOK in THF might be disassociated efficiently[7] to generate ammonium ylide **A** (Scheme 1), which leads to **2a** preferably by [2,3] carbanion rearrangement (S–H rearrangement). Small amount of impurities such as KOH and K_2CO_3 depending on exposure of solid *t*-BuOK to air or moisture would be lowered the solubility in THF. The resulting reagent might stabilize enolate form **B**[8] or promote formation of radical pair **C**, which leads to **3a** by recombination ([1,2] Stevens rearrangement). The following experimental results support these speculations: (1) A reagent grade (97% purity) solid

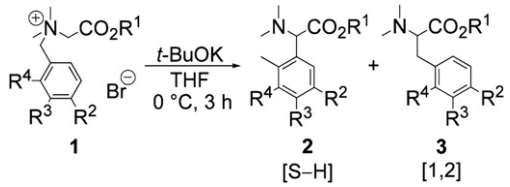


Scheme 1. Base-induced S–H versus [1,2] Stevens rearrangement.

t-BuOK is not soluble in THF so much even if refluxing.[9] (2) A sublimed grade (99% purity) solid *t*-BuOK is more soluble in THF than the reagent grade; however, the resulting mixture did not give a clear solution. (3) Use of a solid *t*-BuOK obtained by concentration of *t*-BuOK/THF solution afforded the similar result with the reagent grade of solid *t*-BuOK. The reagent was not dissolved in THF completely after solidification. (4) When the reactions were carried out using *t*-BuOK/THF solution in the presence of small amount (0.2 equiv) of KOH or K_2CO_3, the yield of **3a** was improved (**2a**: ca. 65%, **3a**: ca. 20%). (5) ^{1}H NMR analysis of *t*-BuOK/THF solution in THF-d_8 showed a single peak of *t*-Bu substituent (δ 1.01, s) without any peaks of impurities.

To demonstrate the enhancement effect of *t*-BuOK/THF solution in S–H rearrangements, we attempted the reaction of various types of amino acid ester-derived ammonium salts **1b–i** with solid or solution based *t*-BuOK (Table 2). In the reaction of benzyl ester-derived ammonium salt **1b**, the use of solid *t*-BuOK gave a mixture of S–H and [1,2] rearrangement products (entry 1, **2b**: 51%, **3b**: 22%). However, the yield of **2b** was improved with a *t*-BuOK/THF solution (entry 2, **2b**: 74%, **3b**: 9%). This effect was also observed using monosubstituted benzylammonium salts as substrates. In the reaction of *para*-chlorobenzyl derivative **1c** with a *t*-BuOK/THF solution; the yield of S–H rearrangement product **2c** was improved to 87% (entry 4) from 60% (entry 3). The effect was clearly observed using deactivated substrates, including electron-donating substituents,[4,10] such as *para*-methyl (**1d**) and *para*-methoxy (**1e**) derivatives. In both cases, the S–H rearrangement was accelerated with the *t*-BuOK/THF solution. For example, the yield of **2d** was improved to 68% (entry 6) from 8% (entry 5), and the yield of **2e** was improved to 45% (entry 8) from 0% (entry 7). Similar results were obtained in the reactions of *meta*- and *ortho*-substituted benzyl derivatives **1f–i** (entries 9–16).

Table 2
Base-induced S–H rearrangement of amino acid ester-derived ammonium salts **1b–i**

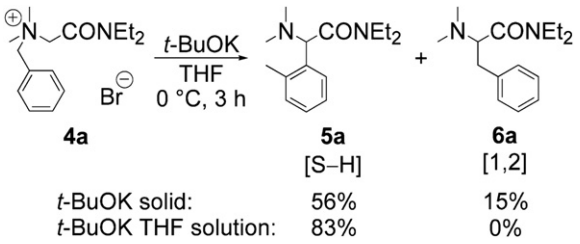


Entry	R^1	R^2	R^3	R^4		*t*-BuOK[a]	**2** (%)[b]	**3** (%)[b]
1	CH_2Ph	H	H	H	**b**	Solid	51	22
2	CH_2Ph	H	H	H	**b**	THF solution	74	9
3	*t*-Bu	Cl	H	H	**c**	Solid	60	22
4	*t*-Bu	Cl	H	H	**c**	THF solution	87	4
5	*t*-Bu	Me	H	H	**d**	Solid	8	59
6	*t*-Bu	Me	H	H	**d**	THF solution	68	20
7	*t*-Bu	OMe	H	H	**e**	Solid	0	53
8	*t*-Bu	OMe	H	H	**e**	THF solution	45	37
9	*t*-Bu	H	Cl	H	**f**	Solid	51	22
10	*t*-Bu	H	Cl	H	**f**	THF solution	71	3
11	*t*-Bu	H	Me	H	**g**	Solid	11	44
12	*t*-Bu	H	Me	H	**g**	THF solution	74	13
13	*t*-Bu	H	H	Cl	**h**	Solid	32	35
14	*t*-Bu	H	H	Cl	**h**	THF solution	87	3
15	*t*-Bu	H	H	Me	**i**	Solid	8	64
16	*t*-Bu	H	H	Me	**i**	THF solution	73	14

[a] Reagent grade of solid *t*-BuOK or commercially available THF solution of *t*-BuOK were used.
[b] Isolated yield.

The enhancement effect of the *t*-BuOK/THF solution on the S–H rearrangement was also shown in the reaction of amino acid amide-derived ammonium salts **4** (Scheme 2). A reaction of glycine

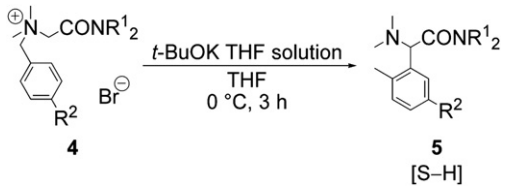
diethylamide-derived ammonium salt **4a** with solid *t*-BuOK afforded the corresponding S–H rearrangement product **5a** in 56% yield along with the [1,2] Stevens product **6a** in 15% yield. Similarly, when the reaction was carried out with a solution of *t*-BuOK in THF, **5a** was obtained in 83% yield without any detectable amount of **6a**.



Scheme 2. *t*-BuOK-induced S–H rearrangement of amino acid amide-derived ammonium salt **4a**.

To further explore the scope and limitations of the *t*-BuOK/THF solution-induced S–H rearrangement of amino acid amide-derived ammonium salts **4**, we prepared a series of substrates **4b**–**h** and tested their reactivity under these reaction conditions (Table 3). A reaction of cyclic tertiary amide **4b** under the same conditions proceeded slowly (entry 1). The product **5b** was obtained in lower yield (58%). By activating the substrates with an electron-withdrawing substituent on the aromatic ring,[4] such as *para*-*tert*-butoxycarbonyl (**4c**: *p*-CO_2^tBu), the yield was improved to 92% (entry 2). Next, we examined the reactions of secondary amide-derived ammonium salts **4d**–**g**. Sterically hindered secondary amides, such as *tert*-butyl amide derivative **4d**, rearranged to **5d** in 83% yield (entry 3); however, *n*-butyl and phenyl amide derivatives **4e** and **4f** resulted in lower yields (entry 4, **5e**: 29%; entry 5, **5f**: 20%). By adding an electron-withdrawing group, the S–H rearrangement proceeded smoothly to give **5g** in 99% yield (entry 6). These results imply that the intermolecular hydrogen bonds caused by amide proton (NH) might inhibit the S–H rearrangement. *tert*-Butyl amide derivative **4d** would not form intermolecular hydrogen bonds due to steric hindrance. Thus, we attempted the reaction with the tertiary amide derivative **4h**. The S–H rearrangement proceeded smoothly without an electron-withdrawing group to afford **5h** in excellent yield (entry 7, 96%).

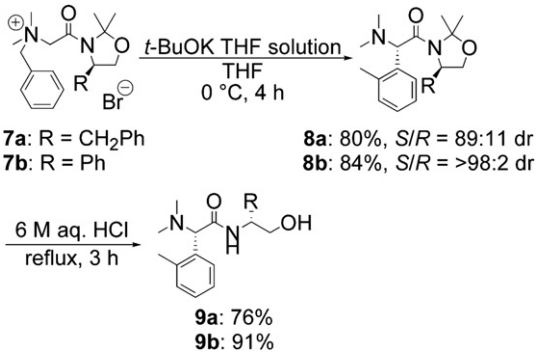
Table 3
t-BuOK/THF solution-induced S–H rearrangement of amino acid amide-derived ammonium salts **4b**–**h**[a]



Entry	NR^1_2	R^2		**5** (%)[b]
1	Pyrrolidin-1-yl	H	**b**	58
2	Pyrrolidin-1-yl	CO_2^tBu	**c**	92
3	NH^tBu	H	**d**	83
4	NH^nBu	H	**e**	29
5	NHPh	H	**f**	20
6	NH^nBu	$CO_2{}^tBu$	**g**	99
7	NMe^nBu	H	**h**	96

[a] Commercially available THF solution of *t*-BuOK was used in the reactions.
[b] Isolated yield.

Finally, we examined the asymmetric S–H rearrangement of the amino acid amide-derived ammonium salts **7a** and **7b** using (*R*)-4-substituted-2,2-dimethyloxazolidine as a chiral auxiliary (Scheme 3) . Treatment of these compounds with a solution of *t*-BuOK in THF afforded **8a** or **8b**, respectively, in good yields with high diastereoselectivities (**8a**: 80%, 2*S*/2*R*=89:11; **8b**: 84%, 2*S*/2*R*=>98:2).[11] Deacetonidation of **8** with 6 M hydrochloric acid gave the corresponding peptide alcohols **9** in good yields (**9a**: 76%, **9b**: 91%) without epimerization.



Scheme 3. Asymmetric S–H rearrangement of amino acid amide-derived ammonium salts **7**.

In conclusion, we have reported the enhancement effect of a potassium *tert*-butoxide/THF solution in base-induced Sommelet–Hauser rearrangements. Under mild reaction conditions, the rearrangements of *N*-benzylic amino acid esters and amide-derived ammonium salts are shown to proceed with minimal competition from the [1,2] Stevens rearrangement. The method provides efficient access to α-aryl amino acid derivatives and expands the synthetic utility of the S–H rearrangement.

3. Experimental section

3.1. General

Infrared spectra were recorded on a Perkin–Elmer Spectrum GX FT-IR spectrometer. ^1H and ^{13}C NMR spectra were measured on a JEOL 270 MHz (^1H: 270 MHz, ^{13}C: 68 MHz), a Varian 400 MHz (^1H: 400 MHz, ^{13}C: 100 MHz), and a Varian 500 MHz (^1H: 500 MHz, ^{13}C: 125 MHz) spectrometers. Splitting patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak. Specific rotations were recorded on a JASCO Polarimeter P–1010. High-resolution mass spectra were measured on a Thermo Fisher Scientific LC/FT-MS spectrometer. Elemental analyses were recorded on a Yanaco CHN Corder MT-3. Reactions involving air- or moisture-sensitive compounds were conducted in appropriate round-bottomed flask with a magnetic stirring bar under an argon atmosphere. Tetrahydrofuran (THF) was purchased from KANTO Chemical Co., Inc., Japan as an anhydrous solvent. A 1.0 M THF solution of potassium *tert*-butoxide was purchased from Aldrich or Tokyo Chemical Industry Co., Ltd (TCI). A reagent grade (97%) of potassium *tert*-butoxide was purchased from KANTO Chemical Co., Inc., Japan. A sublimed grade (99%) of potassium *tert*-butoxide was purchased from Aldrich. A 2.0 M THF solution of sodium *tert*-butoxide was purchased from Aldrich. For thin layer chromatography (TLC) analysis throughout this work, Merck TLC plates (silica gel 60 F_{254}) were used. The products were purified by preparative column chromatography on silica gel (silica gel 60N, spherical neutral, KANTO Chemical Co., Inc., Japan).

3.2. Experimental

*3.2.1. Representative procedure for base-induced Sommelet–Hauser rearrangement of N-benzyl glycine tert-butyl ester-derived ammonium salt **1a**.* A 1.0 M THF solution of potassium *tert*-butoxide (0.36 mL, 0.36 mmol) was added to a solution of **1a** (109 mg, 0.33 mmol) in THF (3.0 mL) at 0 °C. The mixture was stirred for 3 h at the same temperature under an argon atmosphere. The resulting mixture was quenched with saturated aqueous ammonium chloride and extracted with ethyl acetate. The combined extracts were washed with saturated aqueous sodium hydrogen carbonate and brine. The solution was dried over sodium sulfate and concentrated. Purification of the residue by chromatography on silica gel (hexane/ethyl acetate=8:1 to 2:1 as eluent) gave **2a** (65.6 mg, 80% yield) as a pale yellow oil and **3a** (6.8 mg, 8% yield) as a colorless oil.

*3.2.2. tert-Butyl (dimethylamino)(2-methylphenyl)acetate (**2a**).* Pale yellow oil. IR (film) 2978, 2866, 2819, 2771, 1741, 1461, 1392, 1367, 1278, 1256, 1220, 1143, 1103, 1046, 945, 901, 879, 837, 814, 753 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.59–7.51 (1H, m, ArH), 7.23–7.11 (3H, m, ArH), 4.03 (1H, s, NCHCO), 2.42 (3H, s, $ArCH_3$), 2.27 (6H, s, $N(CH_3)_2$), 1.38 (9H, s, *t*-Bu); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.1, 136.9, 135.7, 130.3, 128.0, 127.5, 126.1, 81.0, 71.2, 43.2, 27.9, 19.7. Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.34; H, 9.46; N, 5.52.

*3.2.3. tert-Butyl 2-(dimethylamino)-3-phenylpropanoate (**3a**).* Colorless oil. IR (film) 2977, 2936, 2867, 2831, 2787, 1723, 1454, 1391, 1367, 1256, 1221, 1147, 1064, 1030, 980, 951, 874, 845, 739, 699 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.31–7.15 (5H, m, Ph), 3.31 (1H, dd, *J*=9.8, 5.7 Hz, NCHCO), 3.02 (1H, dd, *J*=13.1, 9.8 Hz, CH_2Ph), 2.88 (1H, dd, *J*=13.1, 5.7 Hz, CH_2Ph), 2.41 (6H, s, $N(CH_3)_2$), 1.34 (9H, s, *t*-Bu); ^{13}C NMR (68 MHz, $CDCl_3$) δ 170.7, 138.3, 129.2, 128.2, 126.3, 80.9, 70.0, 41.8, 36.3, 28.1. Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 71.97; H, 9.43; N, 5.46.

*3.2.4. Benzyl (dimethylamino)(2-methylphenyl)acetate (**2b**).* Colorless oil. IR (film) 3065, 3032, 2953, 2866, 2821, 2774, 1744, 1488, 1458, 1377, 1344, 1258, 1197, 1145, 1102, 1046, 968, 891, 746, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54–7.50 (1H, m, ArH), 7.30–7.25 (3H, m, ArH), 7.22–7.13 (5H, m, ArH), 5.16 (1H, d, *J*=12.4 Hz, CH_2Ph), 5.08 (1H, d, *J*=12.4 Hz, CH_2Ph), 4.23 (1H, s, NCHCO), 2.41 (3H, s, $ArCH_3$), 2.27 (6H, s, $N(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 137.1, 135.8, 134.9, 130.5, 128.4, 128.3, 128.0, 127.87, 127.86, 126.2, 70.5, 66.3, 43.2, 19.7. Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.55; H, 7.55; N, 5.01.

*3.2.5. Benzyl 2-(dimethylamino)-3-phenylpropanoate (**3b**).* Colorless oil. IR (film) 3064, 3031, 2939, 2867, 2831, 2787, 1730, 1496, 1454, 1377, 1349, 1265, 1210, 1160, 1150, 1081, 1065, 1029, 978, 911, 748, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.14 (10H, m, ArH), 5.04 (2H, s, OCH_2Ph), 3.49 (1H, dd, *J*=9.6, 5.6 Hz, NCHCO), 3.07 (1H, dd, *J*=13.4, 9.6 Hz, CH_2Ph), 2.94 (1H, dd, *J*=13.4, 5.6 Hz, CH_2Ph), 2.39 (6H, s, $N(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 138.0, 135.7, 129.1, 128.41, 128.37, 128.3, 128.1, 126.4, 69.5, 65.9, 41.9, 36.2. Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.49; H, 7.58; N, 5.07.

*3.2.6. tert-Butyl (5-chloro-2-methylphenyl)(dimethylamino)acetate (**2c**).* Colorless oil. IR (film) 2979, 2868, 2822, 2775, 1740, 1483, 1457, 1393, 1368, 1349, 1256, 1220, 1145, 1085, 1046, 998, 958, 910, 841, 811, 786 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (1H, d, *J*=2.0 Hz, ArH), 7.14 (1H, dd, *J*=8.4, 2.0 Hz, ArH), 7.07 (1H, d, *J*=8.4 Hz, ArH), 3.96 (1H, s, NCHCO), 2.37 (3H, s, $ArCH_3$), 2.27 (6H, s, $N(CH_3)_2$), 1.39 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 137.5, 135.2, 131.9, 131.5, 128.1, 127.6, 81.4, 71.2, 43.2, 27.9, 19.2. Anal. Calcd for $C_{15}H_{22}ClNO_2$: C, 63.48; H, 7.81; N, 4.94. Found: C, 63.71; H, 7.95; N, 4.97.

*3.2.7. tert-Butyl 3-(4-chlorophenyl)-2-(dimethylamino)propanoate (**3c**).* Colorless oil. IR (film) 2977, 2936, 2869, 2832, 2788, 1726, 1492, 1454, 1392, 1367, 1255, 1222, 1148, 1094, 1046, 1017, 982, 953, 879, 845, 816, 773 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (2H, ddd, *J*=8.6, 2.2, 2.2 Hz, ArH), 7.14 (2H, ddd, *J*=8.6, 2.2, 2.2 Hz, ArH), 3.27 (1H, dd, *J*=9.4, 5.8 Hz, NCHCO), 2.98 (1H, dd, *J*=13.4, 9.4 Hz, CH_2Ph), 2.83 (1H, dd, *J*=13.4, 5.8 Hz, CH_2Ph), 2.40 (6H, s, $N(CH_3)_2$), 1.36 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 136.9, 132.1, 130.6, 128.3, 81.1, 69.7, 41.7, 35.6, 28.2. Anal. Calcd for $C_{15}H_{22}ClNO_2$: C, 63.48; H, 7.81; N, 4.94. Found: C, 63.24; H, 7.92; N, 4.88.

*3.2.8. tert-Butyl (dimethylamino)(2,5-dimethylphenyl)acetate (**2d**).* Pale yellow oil. IR (film) 2977, 2930, 2866, 2819, 2770, 1741, 1502, 1457, 1391, 1367, 1257, 1214, 1144, 1103, 1047, 958, 900, 845, 810, 787 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (1H, d, *J*=1.6 Hz, ArH), 7.02 (1H, d, *J*=8.0 Hz, ArH), 6.97 (1H, dd, *J*=8.0, 1.6 Hz, ArH), 3.97 (1H, s, NCHCO), 2.36 (3H, s, $ArCH_3$), 2.29 (3H, s, $ArCH_3$), 2.26 (6H, s, $N(CH_3)_2$), 1.38 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 135.5, 135.4, 133.7, 130.1, 128.5, 128.2, 80.9, 71.3, 43.3, 27.9, 20.9, 19.3. Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.86; H, 9.65; N, 5.37.

*3.2.9. tert-Butyl 2-(dimethylamino)-3-(4-methylphenyl)propanoate (**3d**).* Pale yellow oil. IR (film) 2976, 2934, 2867, 2831, 2787, 1723, 1516, 1453, 1391, 1367, 1256, 1222, 1147, 1100, 1073, 1045, 1027, 990, 974, 878, 845, 807, 774 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.09 (2H, d, *J*=8.4 Hz, ArH), 7.06 (2H, d, *J*=8.4 Hz, ArH), 3.29 (1H, dd, *J*=9.6, 5.6 Hz, NCHCO), 2.98 (1H, dd, *J*=13.2, 9.6 Hz, CH_2Ar), 2.84 (1H, dd, *J*=13.2, 5.6 Hz, CH_2Ar), 2.40 (6H, s, $N(CH_3)_2$), 2.30 (3H, s, $ArCH_3$), 1.36 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 135.7, 135.2, 129.0, 128.9, 80.8, 70.0, 41.8, 35.9, 28.2, 21.0. Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.74; H, 9.60; N, 5.26.

*3.2.10. tert-Butyl (dimethylamino)(5-methoxy-2-methylphenyl)acetate (**2e**).* Colorless oil. IR (film) 2977, 2867, 2832, 2772, 1739, 1611, 1580, 1501, 1464, 1392, 1367, 1349, 1283, 1248, 1215, 1145, 1109, 1043, 959, 899, 844, 815, 788, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.14 (1H, d, *J*=3.0 Hz, ArH), 7.05 (1H, d, *J*=8.4 Hz, ArH), 6.74 (1H, dd, *J*=8.4, 3.0 Hz, ArH), 3.97 (1H, s, NCHCO), 3.78 (3H, s, OCH_3), 2.34 (3H, s, $ArCH_3$), 2.26 (6H, s, $N(CH_3)_2$), 1.38 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 158.0, 136.6, 131.1, 128.9, 114.1, 112.4, 81.0, 71.5, 55.4, 43.4, 27.9, 18.9. Anal. Calcd for $C_{16}H_{25}NO_3$: C, 68.79; H, 9.02; N, 5.01. Found: C, 68.78; H, 9.10; N, 4.97.

*3.2.11. tert-Butyl 2-(dimethylamino)-3-(4-methoxyphenyl)propanoate (**3e**).* Colorless oil. IR (film) 2976, 2936, 2867, 2833, 2787, 1722, 1613, 1513, 1456, 1391, 1367, 1299, 1248, 1147, 1105, 1072, 1037, 981, 952, 878, 844, 823, 775, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.12 (2H, ddd, *J*=8.4, 2.4, 2.4 Hz, ArH), 6.80 (2H, ddd, *J*=8.4, 2.4, 2.4 Hz, ArH), 3.78 (3H, s, OCH_3), 3.26 (1H, dd, *J*=9.8, 5.6 Hz, NCHCO), 2.96 (1H, dd, *J*=13.5, 9.8 Hz, CH_2Ar), 2.82 (1H, dd, *J*=13.5, 5.6 Hz, CH_2Ar), 2.40 (6H, s, $N(CH_3)_2$), 1.35 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 158.1, 130.3, 130.2, 113.6, 80.8, 70.2, 55.2, 41.8, 35.5, 28.2. Anal. Calcd for $C_{16}H_{25}NO_3$: C, 68.79; H, 9.02; N, 5.01. Found: C, 68.66; H, 9.17; N, 5.22.

*3.2.12. tert-Butyl (4-chloro-2-methylphenyl)(dimethylamino)acetate (**2f**).* Colorless oil. IR (film) 2979, 2868, 2821, 2774, 1741, 1596, 1482, 1455, 1392, 1368, 1256, 1222, 1143, 1046, 947, 882, 859, 836, 789, 736, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (1H, d, *J*=8.0 Hz, ArH), 7.19–7.14 (2H, m, ArH), 3.96 (1H, s, NCHCO), 2.39 (3H, s, $ArCH_3$), 2.25 (6H, s, $N(CH_3)_2$), 1.38 (9H, s, *t*-Bu); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 170.6, 138.8, 134.3, 133.1, 130.1, 129.5, 126.2, 81.3, 70.8, 43.1, 27.9, 19.5; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{23}ClNO_2$: 284.1412. Found: 284.1408.

*3.2.13. tert-Butyl 3-(3-chlorophenyl)-2-(dimethylamino)propanoate (**3f**).* Pale yellow oil. IR (film) 2977, 2936, 2868, 2832, 2788, 1721, 1598, 1573, 1477, 1452, 1391, 1367, 1256, 1221, 1146, 1079, 1046, 983, 952, 845, 780, 698, 686 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22–7.15 (3H, m, ArH), 7.11–7.07 (1H, m, ArH), 3.28 (1H, dd, J=9.6, 5.6 Hz, NCHCO), 2.99 (1H, dd, J=13.6, 9.6 Hz, CH_2Ar), 2.85 (1H, dd, J=13.6, 5.6 Hz, CH_2Ar), 2.40 (6H, s, $N(CH_3)_2$), 1.37 (9H, s, t-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 140.4, 133.9, 129.45, 129.36, 127.4, 126.5, 81.2, 69.7, 41.7, 35.9, 28.1; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{23}ClNO_2$: 284.1412. Found: 284.1409.

*3.2.14. tert-Butyl (dimethylamino)(2,4-dimethylphenyl)acetate (**2g**).* Colorless oil. IR (film) 2978, 2866, 2818, 2770, 1742, 1501, 1457, 1392, 1367, 1276, 1255, 1219, 1143, 1047, 953, 896, 876, 837, 788 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (1H, d, J=8.0 Hz, ArH), 6.99 (1H, d, J=8.0 Hz, ArH), 6.96 (1H, s, ArH), 3.98 (1H, s, NCHCO), 2.38 (3H, s, $ArCH_3$), 2.29 (3H, s, $ArCH_3$), 2.25 (6H, s, $N(CH_3)_2$), 1.38 (9H, s, t-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 137.0, 136.6, 132.6, 131.0, 127.9, 126.8, 80.8, 71.0, 43.2, 27.9, 21.0, 19.6; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{26}NO_2$: 264.1958. Found: 264.1953.

*3.2.15. tert-Butyl 2-(dimethylamino)-3-(3-methylphenyl)propanoate (**3g**).* Pale yellow oil. IR (film) 2977, 2935, 2868, 2831, 2787, 1726, 1609, 1453, 1391, 1367, 1254, 1219, 1145, 1095, 1072, 1044, 979, 871, 845, 779, 740, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.15 (1H, dd, J=7.8, 7.8 Hz, ArH), 7.03–6.98 (3H, m, ArH), 3.30 (1H, dd, J=9.8, 5.4 Hz, NCHCO), 2.98 (1H, dd, J=13.4, 9.8 Hz, CH_2Ar), 2.85 (1H, dd, J=13.4, 5.4 Hz, CH_2Ar), 2.41 (6H, s, $N(CH_3)_2$), 2.30 (3H, s, $ArCH_3$), 1.34 (9H, s, t-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 138.1, 137.6, 130.0, 128.1, 127.0, 126.2, 80.8, 70.0, 41.8, 36.2, 28.1, 21.3; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{26}NO_2$: 264.1958. Found: 264.1953.

*3.2.16. tert-Butyl (3-chloro-2-methylphenyl)(dimethylamino)acetate (**2h**).* Colorless oil. IR (film) 2979, 2869, 2822, 2775, 1730, 1638, 1572, 1453, 1392, 1368, 1256, 1216, 1145, 1050, 1012, 949, 901, 873, 837, 777, 713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (1H, dd, J=8.0, 1.2 Hz, ArH), 7.30 (1H, dd, J=8.0, 1.2 Hz, ArH), 7.12 (1H, dd, J=8.0, 8.0 Hz, ArH), 4.09 (1H, s, NCHCO), 2.47 (3H, s, $ArCH_3$), 2.27 (6H, s, $N(CH_3)_2$), 1.39 (9H, s, t-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 137.8, 135.1, 134.9, 128.6, 126.8, 126.6, 81.3, 71.5, 43.0, 27.9, 15.9; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{23}ClNO_2$: 284.1412. Found: 284.1411.

*3.2.17. tert-Butyl 3-(2-chlorophenyl)-2-(dimethylamino)propanoate (**3h**).* Pale yellow oil. IR (film) 2978, 2938, 2868, 2832, 2787, 1731, 1472, 1455, 1393, 1368, 1257, 1222, 1148, 1052, 978, 953, 884, 845, 752, 683 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.31 (1H, m, ArH), 7.26–7.22 (1H, m, ArH), 7.17–7.12 (2H, m, ArH), 3.44 (1H, dd, J=8.0, 6.8 Hz, NCHCO), 3.11–3.06 (2H, m, CH_2Ar), 2.43 (6H, s, $N(CH_3)_2$), 1.35 (9H, s, t-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 136.0, 134.3, 131.6, 129.4, 127.8, 126.5, 81.0, 67.6, 41.8, 33.6, 28.1; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{23}ClNO_2$: 284.1412. Found: 284.1404.

*3.2.18. tert-Butyl (dimethylamino)(2,3-dimethylphenyl)acetate (**2i**).* Colorless oil. IR (film) 2978, 2933, 2867, 2819, 2771, 1730, 1463, 1391, 1367, 1277, 1251, 1215, 1143, 1098, 1045, 949, 901, 877, 841, 814, 776, 721 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.32 (1H, dd, J=7.2, 2.0 Hz, ArH), 7.09 (1H, dd, J=7.6, 2.0 Hz, ArH), 7.06 (1H, dd, J=7.6, 7.2 Hz, ArH), 4.19 (1H, s, NCHCO), 2.31 (3H, s, $ArCH_3$), 2.28 (3H, s, $ArCH_3$), 2.25 (6H, s, $N(CH_3)_2$), 1.39 (9H, s, t-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 136.7, 135.6, 135.5, 129.2, 126.0, 125.3, 80.9, 71.2, 43.0, 27.9, 20.9, 15.0; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{26}NO_2$: 264.1958. Found: 264.1951.

*3.2.19. tert-Butyl 2-(dimethylamino)-3-(2-methylphenyl)propanoate (**3i**).* Colorless oil. IR (film) 2977, 2936, 2868, 2831, 2786, 1725, 1493, 1454, 1391, 1367, 1257, 1219, 1147, 1069, 1047, 979, 881, 846, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.16–7.05 (4H, m, ArH), 3.29 (1H, dd, J=10.0, 5.2 Hz, NCHCO), 3.03 (1H, dd, J=13.6, 10.0 Hz, CH_2Ar), 2.89 (1H, dd, J=13.6, 5.2 Hz, CH_2Ar), 2.43 (6H, s, $N(CH_3)_2$), 2.34 (3H, s, $ArCH_3$), 1.32 (9H, s, t-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 136.4, 136.3, 130.2, 129.8, 126.4, 125.7, 80.8, 68.6, 41.9, 33.5, 28.1, 19.5; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{26}NO_2$: 264.1958. Found: 264.1956.

*3.2.20. N,N-Diethyl-2-dimethylamino-2-(2-methylphenyl)acetamide (**5a**).* White solid. IR (film) 2972, 2931, 2875, 2829, 2784, 1646, 1450, 1427, 1379, 1361, 1270, 1252, 1220, 1192, 1134, 1096, 1045, 949, 914, 891, 859, 829, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (1H, d, J=7.2 Hz, ArH), 7.25–7.13 (3H, m, ArH), 4.45 (1H, s, NCHCO), 3.52 (1H, dq, J=13.6, 7.2 Hz, CH_2CH_3), 3.20 (1H, dq, J=13.6, 7.2 Hz, CH_2CH_3), 3.14 (1H, dq, J=15.0, 7.2 Hz, CH_2CH_3), 2.95 (1H, dq, J=15.0, 7.2 Hz, CH_2CH_3), 2.43 (3H, s, $ArCH_3$), 2.39 (6H, s, $N(CH_3)_2$), 1.09 (3H, t, J=7.2 Hz, CH_2CH_3), 0.97 (3H, t, J=7.2 Hz, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 137.0, 135.2, 130.6, 128.9, 127.7, 126.0, 66.1, 42.2, 41.0, 40.1, 19.3, 14.0, 12.7. Anal. Calcd for $C_{15}H_{24}N_2O$: C, 72.54; H, 9.74; N, 11.28. Found: C, 72.31; H, 9.81; N, 11.23.

*3.2.21. N,N-Diethyl-2-dimethylamino-3-phenylpropanamide (**6a**).* White solid. IR (film) 2972, 2934, 2869, 2827, 2784, 1637, 1456, 1379, 1360, 1264, 1220, 1138, 1076, 1040, 974, 938, 881, 789, 736, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25–7.13 (5H, m, Ph), 3.53 (1H, dd, J=10.5, 3.5 Hz, NCHCO), 3.33 (1H, dq, J=13.5, 7.0 Hz, CH_2CH_3), 3.26–3.16 (3H, m, CH_2Ph and CH_2CH_3), 2.95 (1H, dq, J=14.8, 7.5 Hz, CH_2CH_3), 2.84 (1H, dd, J=12.5, 3.5 Hz, CH_2Ph), 2.41 (6H, s, $N(CH_3)_2$), 1.04 (3H, t, J=7.0 Hz, CH_2CH_3), 0.80 (3H, t, J=7.5 Hz, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 139.4, 129.4, 128.2, 126.0, 65.8, 41.62, 41.60, 40.4, 32.6, 14.2, 12.9. Anal. Calcd for $C_{15}H_{24}N_2O$: C, 72.54; H, 9.74; N, 11.28. Found: C, 72.36; H, 9.78; N, 11.17.

*3.2.22. N,N-Dimethyl-1-(2-methylphenyl)-2-oxo-2-(pyrrolidin-1-yl) ethanamine (**5b**).* Colorless oil. IR (film) 2951, 2873, 2781, 1646, 1418, 1342, 1308, 1259, 1226, 1190, 1096, 1048, 985, 958, 916, 864, 828, 754, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52–7.48 (1H, m, ArH), 7.23–7.14 (3H, m, ArH), 4.31 (1H, s, NCHCO), 3.59–3.52 (1H, m, NCH_2CH_2), 3.47–3.39 (2H, m, NCH_2CH_2), 3.01–2.94 (1H, m, NCH_2CH_2), 2.44 (3H, s, $ArCH_3$), 2.37 (6H, s, $N(CH_3)_2$), 1.94–1.66 (4H, m, NCH_2CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 137.3, 134.8, 130.4, 129.0, 127.7, 126.2, 68.0, 45.9, 45.6, 42.6, 26.2, 23.8, 19.5. Anal. Calcd for $C_{15}H_{22}N_2O$: C, 73.13; H, 9.00; N, 11.37. Found: C, 72.85; H, 8.99; N, 11.07.

*3.2.23. 1-(5-tert-Butoxycarbonyl-2-methylphenyl)-N,N-dimethyl-2-oxo-2-(pyrrolidin-1-yl)ethanamine (**5c**).* Pale yellow oil. IR (film) 3052, 2977, 2876, 2777, 1710, 1645, 1423, 1368, 1303, 1255, 1185, 1130, 1037, 1001, 987, 944, 850, 763, 736, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (1H, d, J=2.0 Hz, ArH), 7.80 (1H, dd, J=8.0, 2.0 Hz, ArH), 7.23 (1H, d, J=8.0 Hz, ArH), 4.33 (1H, s, NCHCO), 3.57–3.51 (1H, m, NCH_2CH_2), 3.51–3.43 (1H, m, NCH_2CH_2), 3.40–3.34 (1H, m, NCH_2CH_2), 3.07–3.00 (1H, m, NCH_2CH_2), 2.49 (3H, s, $ArCH_3$), 2.37 (6H, s, $N(CH_3)_2$), 1.93–1.69 (4H, m, NCH_2CH_2), 1.58 (9H, s, t-Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 165.8, 142.7, 135.1, 130.6, 130.1, 130.0, 128.6, 80.8, 68.9, 46.0, 45.7, 42.5, 28.2, 26.3, 23.8, 19.8. Anal. Calcd for $C_{20}H_{30}N_2O_3$: C, 69.33; H, 8.73; N, 8.09. Found: C, 69.48; H, 8.98; N, 7.79.

*3.2.24. N-tert-Butyl-2-(dimethylamino)-2-(2-methylphenyl)acetamide (**5d**).* White solid. IR (film) 3339, 3064, 2962, 2870, 2826,

2781, 1681, 1512, 1456, 1391, 1363, 1252, 1228, 1174, 1097, 1040, 916, 888, 759, 738 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.36–7.29 (1H, m, ArH), 7.22–7.10 (3H, m, ArH), 6.92 (1H, br, NH), 3.90 (1H, s, NCHCO), 2.46 (3H, s, $ArCH_3$), 2.21 (6H, s, $N(CH_3)_2$), 1.34 (9H, s, *t*-Bu); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.3, 137.3, 136.2, 130.8, 127.3, 126.9, 126.0, 72.7, 50.5, 43.9, 28.6, 20.5. Anal. Calcd for $C_{15}H_{24}N_2O$: C, 72.54; H, 9.74; N, 11.28. Found: C, 72.42; H, 9.89; N, 11.00.

*3.2.25. N-n-Butyl-2-(dimethylamino)-2-(2-methylphenyl)acetamide (**5e**).* Colorless oil. IR (film) 3313, 3063, 3023, 2956, 2868, 2823, 2776, 1660, 1521, 1463, 1376, 1239, 1176, 1155, 1083, 1041, 982, 895, 743 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 (1H, d, *J*=6.5 Hz, ArH), 7.19–7.11 (3H, m, ArH), 6.96 (1H, br, NH), 4.01 (1H, s, NCHCO), 3.31–3.18 (2H, m, $CH_2CH_2CH_2CH_3$), 2.47 (3H, s, $ArCH_3$), 2.23 (6H, s, $N(CH_3)_2$), 1.54–1.43 (2H, m, $CH_2CH_2CH_2CH_3$), 1.37–1.27 (2H, m, $CH_2CH_2CH_2CH_3$), 0.90 (3H, t, *J*=7.0 Hz, $CH_2CH_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 137.3, 136.0, 130.8, 127.4, 127.1, 126.0, 72.3, 44.0, 38.7, 31.6, 20.4, 20.1, 13.7. Anal. Calcd for $C_{15}H_{24}N_2O$: C, 72.54; H, 9.74; N, 11.28. Found: C, 72.65; H, 9.85; N, 11.00.

*3.2.26. 2-(Dimethylamino)-2-(2-methylphenyl)-N-phenylacetamide (**5f**).* Colorless oil. IR (film) 3320, 3055, 2984, 2956, 2873, 2832, 2787, 1688, 1599, 1519, 1441, 1311, 1266, 1169, 1153, 1098, 1079, 1040, 962, 898, 744, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.00 (1H, br, NH), 7.57 (2H, ddd, *J*=8.0, 1.2, 1.2H, ArH), 7.42–7.38 (1H, m, ArH), 7.31 (2H, ddd, *J*=8.0, 1.2, 1.2 Hz, ArH), 7.22–7.13 (3H, m, ArH), 7.09 (1H, tt, *J*=7.4, 1.2 Hz, ArH), 4.17 (1H, s, NCHCO), 2.51 (3H, s, $ArCH_3$), 2.31 (6H, s, $N(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 137.8, 137.5, 135.2, 131.0, 129.0, 127.8, 127.3, 126.3, 124.0, 119.4, 72.6, 44.0, 20.5. Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 76.07; H, 7.64; N, 10.29.

*3.2.27. 2-(5-tert-Butoxycarbonyl-2-methylphenyl)-N-n-butyl-2-(dimethylamino)acetamide (**5g**).* Pale yellow oil. IR (film) 3339, 3054, 2961, 2872, 2829, 2783, 1711, 1675, 1518, 1460, 1368, 1303, 1263, 1165, 1129, 1039, 947, 891, 849, 737, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (1H, d, *J*=2.0 Hz, ArH), 7.75 (1H, dd, *J*=8.0, 2.0 Hz, ArH), 7.20 (1H, d, *J*=8.0 Hz, ArH), 7.07 (1H, br, NH), 4.02 (1H, s, NCHCO), 3.26 (2H, dt, *J*=6.8, 6.8 Hz, $CH_2CH_2CH_2CH_3$), 2.52 (3H, s, $ArCH_3$), 2.23 (6H, s, $N(CH_3)_2$), 1.58 (9H, s, *t*-Bu), 1.54–1.43 (2H, m, $CH_2CH_2CH_2CH_3$), 1.39–1.27 (2H, m, $CH_2CH_2CH_2CH_3$), 0.89 (3H, t, *J*=7.2 Hz, $CH_2CH_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 165.6, 142.3, 136.3, 130.7, 130.0, 128.4, 128.3, 80.7, 72.1, 44.0, 38.7, 31.6, 28.2, 20.7, 20.1, 13.7. Anal. Calcd for $C_{20}H_{32}N_2O_3$: C, 68.93; H, 9.26; N, 8.04. Found: C, 68.78; H, 9.37; N, 7.82.

*3.2.28. N-n-Butyl-2-(dimethylamino)-N-methyl-2-(2-methylphenyl) acetamide (**5h**).* Pale yellow oil. 6:4 mixture of rotamers. IR (film) 2957, 2929, 2871, 2784, 1650, 1463, 1403, 1293, 1255, 1190, 1137, 1090, 1042, 957, 932, 892, 863, 846, 794, 752 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.43–7.34 (1H, m, ArH), 7.23–7.11 (3H, m, ArH), 4.47 (1H, s, NCHCO), 3.41 (0.6H, dd, *J*=13.5, 7.3 Hz, $CH_2CH_2CH_2CH_3$), 3.30 (0.6H, dd, *J*=13.5, 7.3 Hz, $CH_2CH_2CH_2CH_3$), 3.20–3.04 (0.4H, m, $CH_2CH_2CH_2CH_3$), 2.95–2.77 (0.4H, m, $CH_2CH_2CH_2CH_3$), 2.90 (1.2H, s, NCH_3), 2.73 (1.8H, s, NCH_3), 2.44 (3H, s, $ArCH_3$), 2.39 (6H, s, $N(CH_3)_2$), 1.54–1.08 (4H, m, $CH_2CH_2CH_2CH_3$), 0.91 (1.8H, t, *J*=7.3 Hz, $CH_2CH_2CH_2CH_3$), 0.84 (1.2H, t, *J*=6.9 Hz, $CH_2CH_2CH_2CH_3$); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.8, 171.6, 137.2, 136.8, 135.2, 134.9, 130.6, 130.5, 129.0, 128.8, 127.82, 127.75, 126.1, 126.0, 66.4, 66.2, 48.9, 47.8, 42.3, 42.1, 34.6, 33.4, 30.3, 29.1, 20.0, 19.3, 13.82, 13.79. Anal. Calcd for $C_{16}H_{26}N_2O$: C, 73.24; H, 9.99; N, 10.68. Found: C, 73.12; H, 10.10; N, 10.43.

*3.2.29. (2S,4′R)-2-(4′-Benzyl-2′,2′-dimethyl-1′,3′-oxazolidin-3′-yl)-N,N-dimethyl-1-(2-methylphenyl)-2-oxo-ethanamine [(2S)-**8a**].* White solid. $[\alpha]_{589}^{25}$ +72.1 (*c* 1.00, EtOH); IR (film) 3055, 2984, 2935, 2878, 2786, 1651, 1452, 1403, 1376, 1363, 1347, 1265, 1208, 1190, 1141, 1047, 961, 895, 845, 804, 744, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.30 (3H, m, ArH), 7.28–7.23 (1H, m, ArH), 7.23–7.12 (5H, m, ArH), 4.43 (1H, s, NCHCO), 3.64 (1H, d, *J*=9.2 Hz, $NCHCH_2O$), 3.51 (1H, ddd, *J*=10.0, 4.8, 4.8 Hz, $NCHCH_2O$), 3.40 (1H, ddd, *J*=9.2, 4.8, 1.2 Hz, $NCHCH_2O$), 3.05 (1H, dd, *J*=13.6, 4.8 Hz, CH_2Ph), 2.93 (1H, dd, *J*=13.6, 10.0 Hz, CH_2Ph), 2.45 (3H, s, $ArCH_3$), 2.39 (6H, s, $N(CH_3)_2$), 1.82 (3H, s, $C(CH_3)_2$), 1.58 (3H, s, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 137.7, 137.3, 134.8, 130.9, 129.2, 128.9, 128.3, 128.1, 127.0, 125.9, 95.6, 67.2, 66.4, 57.6, 41.5, 40.7, 27.5, 22.3, 19.3. Anal. Calcd for $C_{23}H_{30}N_2O_2$: C, 75.37; H, 8.25; N, 7.64. Found: C, 75.38; H, 8.39; N, 7.55.

*3.2.30. (2R,4′R)-2-(4′-Benzyl-2′,2′-dimethyl-1′,3′-oxazolidin-3′-yl)-N,N-dimethyl-1-(2-methylphenyl)-2-oxo-ethanamine [(2R)-**8a**].* Colorless oil. $[\alpha]_{589}^{26}$ +20.1 (*c* 0.50, EtOH); IR (film) 3060, 3028, 2980, 2933, 2872, 2783, 1647, 1452, 1404, 1375, 1342, 1308, 1265, 1242, 1207, 1187, 1142, 1077, 1045, 962, 913, 845, 806, 748, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60–7.55 (1H, m, ArH), 7.37–7.14 (6H, m, ArH), 6.97 (2H, d, *J*=7.2 Hz, ArH), 4.84 (1H, s, NCHCO), 4.27–4.19 (1H, m, $NCHCH_2O$), 3.84–3.74 (2H, m, $NCHCH_2O$), 2.55–2.43 (1H, m, CH_2Ph), 2.51 (3H, s, $ArCH_3$), 2.44 (6H, s, $N(CH_3)_2$), 2.27 (1H, dd, *J*=14.0, 2.6 Hz, CH_2Ph), 1.76 (3H, s, $C(CH_3)_2$), 1.66 (3H, s, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 137.8, 137.6, 134.7, 131.0, 129.4, 129.0, 128.7, 128.0, 126.7, 125.8, 96.1, 66.4, 66.0, 59.3, 41.2, 39.7, 26.7, 23.5, 19.5; HRMS–ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{23}H_{31}N_2O_2$: 367.2380. Found: 367.2367.

*3.2.31. (2S,4′R)-N,N-Dimethyl-2-(2′,2′-dimethyl-4′-phenyl-1′,3′-oxazolidin-3′-yl)-1-(2-methylphenyl)-2-oxo-ethanamine [(2S)-**8b**].* Pale yellow oil. $[\alpha]_{589}^{24}$ −33.6 (*c* 1.00, EtOH); IR (film) 2982, 2930, 2873, 2787, 1651, 1604, 1478, 1451, 1397, 1346, 1306, 1246, 1200, 1169, 1140, 1069, 962, 928, 844, 821, 750, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43–7.31 (4H, m, ArH), 7.27–7.16 (5H, m, ArH), 4.30 (1H, dd, *J*=6.4, 2.0 Hz, NCHPh), 4.10 (1H, s, NCHCO), 4.03 (1H, dd, *J*=8.8, 6.4 Hz, CH_2O), 3.72 (1H, dd, *J*=8.8, 2.0 Hz, CH_2O), 2.23 (6H, s, $N(CH_3)_2$), 2.10 (3H, s, $ArCH_3$), 1.96 (3H, s, $C(CH_3)_2$), 1.64 (3H, s, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 141.7, 138.5, 134.5, 130.8, 128.9, 128.2, 128.0, 127.9, 126.0, 125.7, 96.4, 71.3, 67.0, 60.0, 41.2, 25.9, 22.3, 18.8. Anal. Calcd for $C_{22}H_{28}N_2O_2$: C, 74.97; H, 8.01; N, 7.95. Found: C, 74.96; H, 8.19; N, 7.72.

*3.2.32. (2S,1′R)-N-(1′-Benzyl-2′-hydroxyethyl)-2-(dimethylamino)-2-(2-methylphenyl)acetamide (**9a**).* White solid. $[\alpha]_{589}^{26}$ +83.3 (*c* 1.00, EtOH); IR (film) 3363, 3054, 2985, 2954, 2872, 2830, 2785, 1659, 1513, 1462, 1337, 1266, 1174, 1155, 1097, 1042, 959, 896, 741, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.19 (7H, m, ArH), 7.17–7.13 (3H, m, ArH and NH), 4.20–4.10 (1H, m, $NCHCH_2O$), 3.93 (1H, s, NCHCO), 3.64 (1H, dd, *J*=11.0, 3.6 Hz, $NCHCH_2O$), 3.55 (1H, dd, *J*=11.0, 5.2 Hz, $NCHCH_2O$), 3.04–2.50 (1H, br, OH), 2.99 (1H, dd, *J*=14.0, 6.4 Hz, CH_2Ph), 2.82 (1H, dd, *J*=14.0, 9.0 Hz, CH_2Ph), 2.42 (3H, s, $ArCH_3$), 2.01 (6H, s, $N(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 137.6, 137.3, 135.8, 130.9, 129.1, 128.6, 127.6, 127.1, 126.7, 126.2, 71.9, 65.0, 53.0, 43.8, 36.9, 20.4. Anal. Calcd for $C_{20}H_{26}N_2O_2$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.34; H, 8.08; N, 8.47.

*3.2.33. (2S,1′R)-2-(Dimethylamino)-N-(2′-hydroxy-1′-phenylethyl)-2-(2-methylphenyl)acetamide (**9b**).* White solid. $[\alpha]_{589}^{25}$ +5.9 (*c* 1.00, EtOH); IR (film) 3348, 3245, 3055, 2987, 2956, 2870, 2830, 2783, 1669, 1507, 1463, 1335, 1265, 1177, 1155, 1070, 1043, 983, 896, 850, 747, 705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (1H, d, *J*=6.8 Hz, NH), 7.43 (1H, dt, *J*=8.4, 2.0 Hz, ArH), 7.40–7.34 (2H, m, ArH), 7.34–7.28 (3H, m, ArH), 7.24–7.15 (3H, m, ArH), 5.00 (1H, ddd, *J*=6.8, 6.0, 4.6 Hz, NCHPh), 4.08 (1H, s, NCHCO), 3.83 (1H, dd, *J*=11.2, 6.0 Hz, CH_2O), 3.79 (1H, dd, *J*=11.2, 4.6 Hz, CH_2O), 3.00–2.50 (1H, br, OH), 2.48 (3H, s, $ArCH_3$), 2.21 (6H, s, $N(CH_3)_2$); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 173.0, 139.0, 137.4, 135.6, 131.0, 128.9, 127.9, 127.7, 127.3, 126.8, 126.2, 72.0, 66.6, 56.0, 44.0, 20.4. Anal. Calcd for $C_{19}H_{24}N_2O_2$: C, 73.05; H, 7.74; N, 8.97. Found: C, 73.06; H, 7.83; N, 8.71.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.09.105. These data include MOL files and InChIKeys of the most important compounds described in this article.

References and notes

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5. The purity of solid *t*-BuOK did not affect the results. Both the reagent grade (97% purity) and the sublimed grade (99% purity) afforded practically identical results.
6. Commercially available from Aldrich or TCI. Both the reagents afforded practically identical results.
7. Previously, it was reported that both the solid and THF-based solution of *t*-BuOK form tetramers. See: (a) Schmidt, P.; Lochmann, L.; Schneider, B. *J. Mol. Struct.* **1971**, *9*, 403–411; (b) Halaška, V.; Lochmann, L.; Lim, D. *Collect. Czech. Chem. Commun.* **1968**, *33*, 3245–3253. However, our experimental results showed different activities.
8. We attempted the reactions of amino ketone-derived ammonium salts (*tert*-butyl and phenyl ketones) using *t*-BuOK/THF solution instead of ester **1a** and amide **4a**. However, the corresponding S–H products were not obtained. Stabilization of enolate form **B** would inhibit S–H rearrangement.
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11. The stereochemistry of **8b** was determined after deacetonization to **9b**. The 2*S*-configuration of **9b** was determined by ^{1}H NMR comparison with the (*S*)-authentic sample. The configuration of **8a** and **9a** were determined by the analogy with **8b** and **9b**. For experimental details, see Supplementary data.