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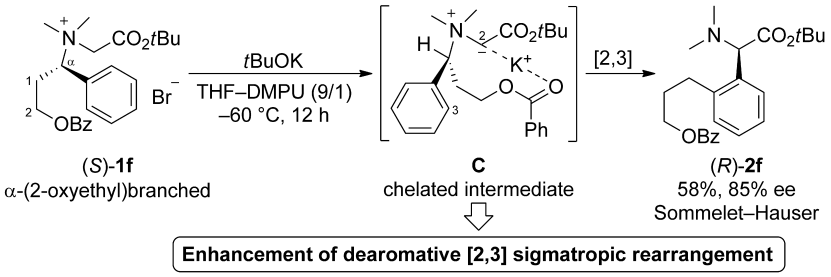

(*S*)-**1f**
α-(2-oxyethyl)branched

C
chelated intermediate

(*R*)-**2f**
58%, 85% ee
Sommelet–Hauser

Enhancement of dearomative [2,3] sigmatropic rearrangement

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Base-induced Sommelet–Hauser rearrangement of *N*-(α-(2-oxyethyl)branched)benzylic glycine ester-derived ammonium salts via a chelated intermediate

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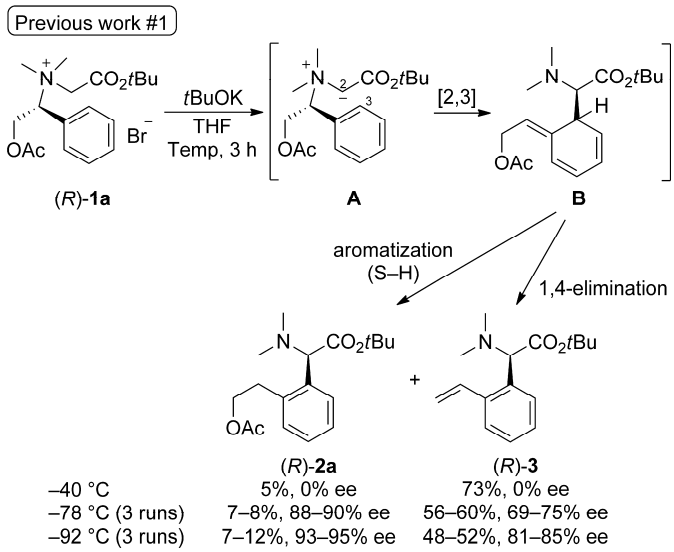
ABSTRACT

The base-induced Sommelet–Hauser (S–H) rearrangement of *N*-(α-branched)benzylic glycine ester-derived ammonium salts **1** was investigated. When the α-branched substituent was a simple alkyl, such as a methyl or butyl, desired S–H rearrangement product **2** was obtained in low yield with formation of the [1,2] Stevens rearranged **4** and Hofmann eliminated products **5** and **6**. However, when the α-branched substituent had a 2-oxy moiety, such as 2-acetoxyethyl or 2-benzoyloxyethyl, the yields of **2** were improved. These results could be explained by formation of chelated intermediate **C** that stabilizes the carbanionic ylide, and the subsequent initial dearomative [2,3] sigmatropic rearrangement would be accelerated. The existence of **C** was supported by mechanistic experiments. This enhancement effect is not very strong or effective; however, it will expand the synthetic usefulness of ammonium ylide rearrangements.

1. Introduction

The base-induced Sommelet–Hauser (S–H) rearrangement of *N*-benzylic tetraalkylammonium salts is one of the unique reactions that proceed via the dearomative [2,3] sigmatropic reaction to generate a dearomatized intermediate followed by re-aromatization. [1–5] This transformation enables the construction of a new C–C bond on an aromatic ring and is applicable to the synthesis of α-aryl amino acid derivatives using *N*-benzylic amino acid-derived tetraalkylammonium salts as a substrate. However, the substrate and product scopes of S–H rearrangement are severely limited because several side reactions are complicated such as [1,2] Stevens rearrangement, Hofmann elimination, and S_N2 substitution. Our group has solved the limitations and successfully improved the yield of S–H rearrangement by discovering of enhancement effects on the rearrangement, such as (i) use of an electron-deficient *N*-benzylic migrating group, [6] (ii) use of a *t*BuOK THF solution as a base, [7] (iii) use of an amino acid amide-derived ammonium salt as the substrate, [7] and (iv) stabilization of the carbanionic ylide by ring strain. [4c] To further expand the synthetic scope and utility of the S–H rearrangement, the discovery of additional enhancement effects are still awaited.

Recently, we reported a reaction of *N*-(α-branched)benzylic glycine-derived ammonium salts (*R*)-**1a** at –40 to –92 °C to give the corresponding S–H product (*R*)-**2a** in 5–12% yields and *o*-vinylphenyl derivative (*R*)-**3** in 48–73% yields (Scheme 1). [4a] The main product (*R*)-**3** was formed via the dearomative [2,3] sigmatropic reaction followed by 1,4-elimination. The results



Scheme 1. Base-induced dearomative [2,3] sigmatropic rearrangement of *N*-(α-branched)benzylic salts (*R*)-**1a**.

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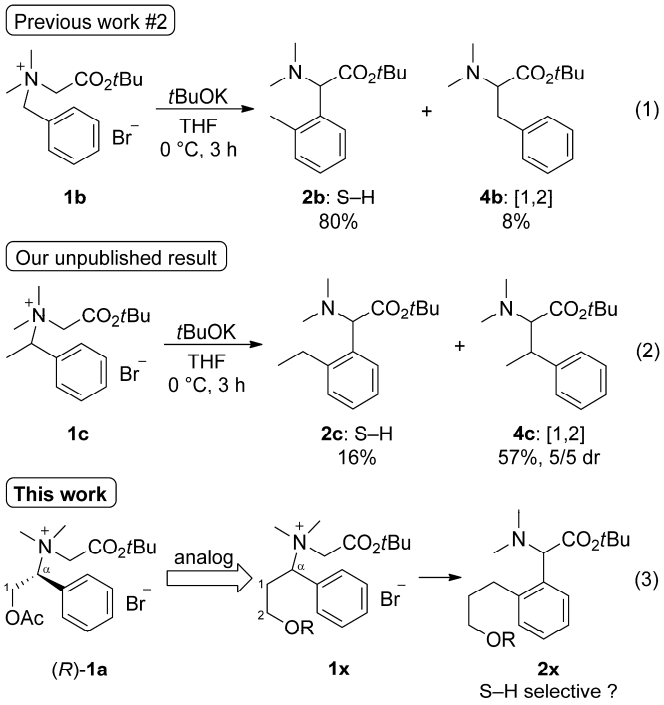
were very surprising to us because the initial dearomative [2,3] rearrangement smoothly proceeded even at –92 °C to provide (*R*)-**2a** and (*R*)-**3**. Our group recognized that an *N*-(α-branched)benzylic migrating group is unfavored for the S–H rearrangement. For example, reaction of *N*-benzylic salt **1b** provided the S–H rearranged **2b** in 80% yield and the [1,2] rearranged **4b** in 8% yield (Scheme 2, Eq. (1)). In contrast, reaction of *N*-(α-methyl-branched)benzylic salt **1c** gave **2c** in only 16% yield and **4c** in 57% yield (Eq. (2)). The ratio of the S–H versus [1,2] Stevens rearrangement products was reversed. Therefore, we expected that an α-(acetoxymethyl)branched substituent, as in (*R*)-**1a** depicted in Scheme 1, might accelerate the inititial dearomative [2,3] sigmatropic rearrangement and provide (*R*)-**2a** and (*R*)-**3** as main products. To verify this expectation, we began to investigate the base-induced S–H rearrangement of *N*-(α-(2-oxyethyl)branched)benzylic derivatives **1x** as an anaologous substrate to eliminate the 1,4-elimination pathway (Eq. (3)).

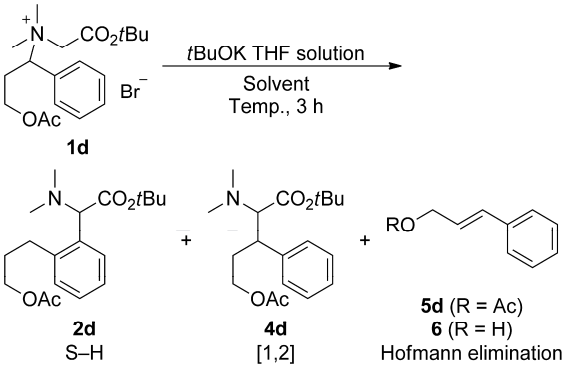


Scheme 2. S–H (**2**) vs. [1,2] Stevens (**4**) in the base-induced rearrangement of **1**.

2. Results and discussion

We prepared α-(2-acetoxyethyl) derivative **1d** as a substrate and carried out reactions to investigate the accelerate effect of the dearomative [2,3] sigmatropic rearrangement by the α-(2-acetoxyethyl)branched substituent, as in **1d**, compared with the α-methyl-branched substituent, as in **1c** dipicted in Scheme 1 (Table 1). First, reaction of **1d** with 1.2 equivalents of *t*BuOK (1 M THF solution) at –40 °C in THF (ca. 0.1 M) for 3 h (Entry 1) was examined according to the conditions depicted in Scheme 1. Contrary to our expectations, the reaction gave the desired S–H rearrangement product **2d** in only 16% yield with formation of side products such as the [1,2] Stevens rearranged **4d** (26%, 6/4 dr), the Hofmann eliminated **5d** (17%), and its acetate cleaved **6** (3%). The total yield of **2d**–**6** was 62%. These yields were determined by ^{1}H NMR analysis of the crude product using mesitylene as an internal standard because 10–20% loss of the *N*,*N*-dimethyl products **2** and **4** accompanied after silica-gel column chromatographic purification. To improve the yield of **2d**, we added 5–20% (v/v) 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU) [8] into THF and carried out their reactions (Entries 2–4). The yields of **2d** were improved to approximately 50%, and the total yield of **2d**–**6** was approximately 80%. To avoid the use of expensive DMPU and simplify the reaction conditions, we attempted to use MeCN as the main reaction solvent which is easily removable by evaporation (Entry 5). [9] The yield of **2d** was successfully improved to 60%, and the total yield of **2d**–**6** was 82%. Thus, we checked the reaction conditions in detail. The reaction with 2.0 equivalents of *t*BuOK or under different temperatures (0 to –40 °C and –78 °C in EtCN) did not show any improvements in the yield of **2d** (Entries 6–9).

Table 1 Optimization of reaction conditions in the base-induced S–H rearrangement of **1d** into **2d**.[a]

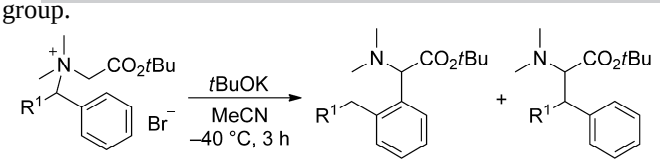


Entry	Solvent	Temp. (°C)	**2d** (%)	**4d** (%, dr[b])	**5d**+**6**[c] (%)
1	THF	–40	16	26, 6/4	17+3
2	THF/DMPU (8/2)	–40	51	12, 7/3	15+2
3	THF/DMPU (9/1)	–40	52	12, 7/3	13+3
4	THF/DMPU (19/1)	–40	47	13, 7/3	11+5
5	MeCN/THF (9/1)	–40	60	11, 6/4	6+5
6[d]	MeCN/THF (8/2)	–40	55	7, 5/5	1+6
7	MeCN/THF (9/1)	–20	43	15, 6/4	9+3
8	MeCN/THF (9/1)	0	24	33, 5/5	9+5
9	EtCN/THF (9/1)	–78	0	23, 5/5	12+2

[a] Determined by ^{1}H NMR analysis of the crude product using mesitylene as an internal standard. [b] Less polar isomer (**4da**)/more polar isomer (**4db**) based on TLC analysis. [c] *Z*-isomers of **5d** and **6** were not observed. [d] 2.0 equivalents of *t*BuOK THF solution were used.

With these results in hand, we next investigated the type of substituent in the migrating group for the S–H rearrangement (Table 2). To clarify that the solvent MeCN itself does not accelerate the desired S–H rearrangement, reaction of α-methyl branched derivative **1c** was examined under the optimized conditions (Entry 1). The reaction produced **2c** in only 10% yield and the [1,2] Stevens rearrangement product **4c** in 30% yield (5/5 dr). To show that the size of the α-branched substituent does not affect this rearrangement, reaction of α-butyl derivative **1e** was also examined (Entry 2). Almost the same result as with **1a** was obtained (**2e**: 15%; **4e**: 30%). The results indicate that the α-(2-acetoxyethyl) substituent, as in **1d**, would accelerate the S–H rearrangement. Thus, we prepared analogous ester derivatives, such as benzoate (Bz: **1f**) and pivalate (Piv: **1g**), and carried out their reactions (Entries 3 and 4). The desired **2f** and **2g** are the main products, respectively (**2f**: 64%, **2g**: 66%). The use of *tert*-butylcarbonate (Boc) derivative **1h** did not lead to any improvements (Entry 5, **2h**: 51%). Unexpectedly, reaction of methyl ether derivative **1i** also afforded **2i** as a main product, although the yield was slightly lowered (Entry 6, **2i**: 46%).

Table 2 Effect of α-branched substituent in the migrating group.



1c–i → **2c–i** S–H + **4c–i** [1,2]

Entry	R^1		**2** (%)[a]	**4** (%)[a], dr[b]
1	Me	**c**	10	30, 5/5
2	*n*Bu	**e**	15	30, 5/5
3	CH_2CH_2OBz	**f**	64	12, 6/4
4	CH_2CH_2OPiv	**g**	66	N.D.
5	CH_2CH_2OBoc	**h**	51	N.D.
6	CH_2CH_2OMe	**i**	46	N.D.

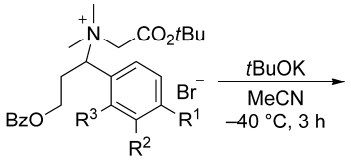
[a] Determined by ^{1}H NMR analysis of the crude product using mesitylene as an internal standard. N.D. = not determined because enough amounts of **4** for identification were not obtained. [b] Less polar isomer (**4ca–4fa**)/more polar isomer (**4cb–4fb**) based on TLC analysis.

To estimate how efficiently these α-(2-oxyethyl) substituents can accelerate the S–H rearrangement, we introduced an electron-withdrawing or -donating group onto the aromatic ring in the migrating group and investigated their reactions (Table 3). Our previous studies on the base-induced S–H rearrangement clarified that an electron-withdrawing group accelerates the S–H rearrangement but that an electron-donating group deactivates the rearrangement. [7] Reactions of *p*-chloro (**1j**) and *p*-bromo (**1k**) derivatives smoothly proceeded to provide the corresponding S–H rearranged **2j** and **2k** as the main products, respectively (Entries 1 and 2); however, reactions of *p*-methyl (**1l**) and *p*-methoxy (**1m**) derivatives did not (Entries 3 and 4). The exact reason is unclear at present, the use of *m*-chloro (**1n**) and *o*-chloro (**1o**) derivatives as substrates resulted in lower yields of **2** (Entries 5 and 6). The enhancement effect of the α-(2-oxyethyl) substituent, as in **1**, would not be as strong, reducing the effect of the aromatic ring substituent.

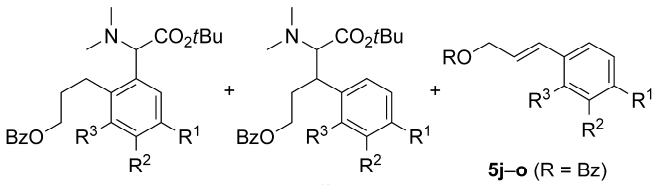
Based on the above described results, we proposed that the rearrangement of α-(2-oxyethyl)branched salts, such as **1d** and **1f**, proceeds via a chelated intermediate **C** that might stabilize the carbanionic ylide leading to the dearomative [2,3] sigmatropic rearrangement (Scheme 3). To demonstrate this proposition, we examined reaction of **1f** in the presence of 18-crown-6 as a potassium ion (K^+) scavenger to inhibit the formation of **C**. The reaction of benzoyl derivative **1f** in THF–DMPU (9/1) [10] proceeded to afford the desired **2f** as a major product (60%). However, when the same reaction was carried out in the presence of 1.2 equivalents of 18-crown-6, which would proceed via an intermediate **D** in resonance with the ammonium ylide and enolate, the yield of **2f** was dramatically decreased (10%). The yields of **2f** and **4f** were similar with the reaction of non-chelatable **1c** and **1e** depicted in Table 2, Entries 1 and 2. Therefore, it is safe to say that the acceleration effect of the dearomative [2,3] sigmatropic rearrangement by the α-(2-benzoyloxyethyl)branched substituent, as in **1f**, was disabled by addition of 18-crown-6. Other words, the chelated carbanionic ylide form **C** would be desired for the initial concerted dearomative [2,3] sigmatropic rearrangement. [11]

Furthermore, we investigated reaction of chiral salt (*S*)-**1f**, which would afford (*R*)-**2f** if the rearrangement proceeds via chelated **C** (Scheme 4). First, reaction of (*S*)-**1f** was examined at –40 °C for 3 h, and the desired (*R*)-**2f** was obtained in 68% yield with 6% ee. Racemization would proceed similarly to the reaction of (*S*)-**1a** depicted in Scheme 1. Thus, the reaction was carried out at a lower temperature to minimize racemization. Although the reaction at –60 °C for 3 h resulted in a low conversion (43%), the ee of (*R*)-**2f** [12] was 90% ee. Finally, when the reaction was performed at –60 °C for 12 h, (*R*)-**2f** was obtained in 58% yield with 85% ee. This result also supports the formation of chelated intermediate **C**. A potassium ion (K^+), as in **C**, coordinates between the ylide carbanion and ester carbonyl. Therefore, the aromatic ring of the migrating group is located toward the front-side of the ylide carbanion, followed by the dearomative [2,3] sigmatropic rearrangement, which produces (*R*)-**2f** as an enantio-enriched form.

Table 3 Effect of substituent on the aromatic ring in the migrating group.



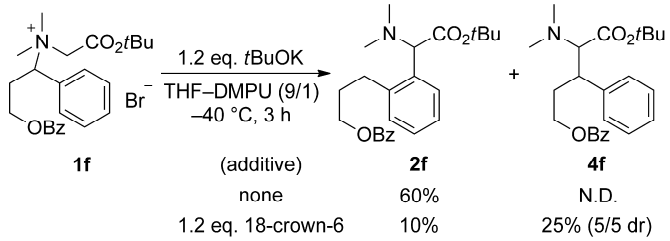
1j–o



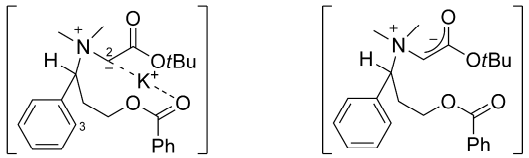
2j–o + **4j–o** + **5j–o** (R = Bz), **6j–o** (R = H)

Entry	R^1	R^2	R^3		**2** (%)[a]	**4** (%), dr[a,b]	**5**+**6** (%)[a,b]
1	Cl	H	H	**j**	53	N.D.	N.D.
2	Br	H	H	**k**	68	N.D.	N.D.
3	CH_3	H	H	**l**	6	31, 6/4	11+0
4	OCH_3	H	H	**m**	0	25, 6/4	10+7
5	H	Cl	H	**n**	17	34, 6/4	N.D.
6	H	H	Cl	**o**	30	N.D.	N.D.

[a] Determined by ^{1}H NMR analysis of the crude product using mesitylene as an internal standard. The Hofmann eliminated **5l**, **6l**, **5m**, and **6m** (Entries 3 and 4) were prepared as authentic samples respectively. [b] N.D. = not determined. Because enough amounts of **4** for identification were not obtained or the authentic Hofmann eliminated samples were not prepared.



1f	(additive)	**2f**	**4f**
	none	60%	N.D.
	1.2 eq. 18-crown-6	10%	25% (5/5 dr)

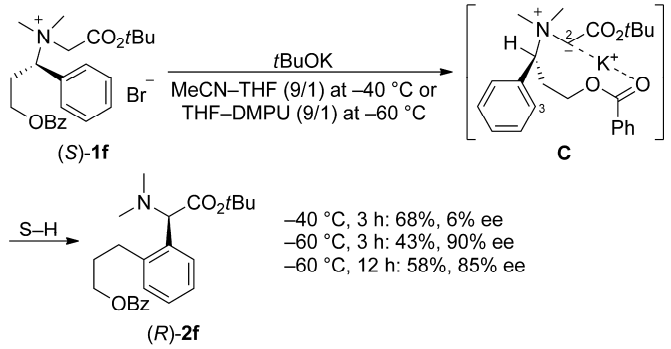


C **D**

Scheme 3. Proposed chelated intermediate **C** obtained by the S–H rearrangement of **1f** in the presence of 18-crown-6.

In conclusion, our studies on the base-induced S–H rearrangement of *N*-(α-branched)benzylic ammonium salts **1** were described. An α-(2-oxyethyl) substituent such as 2-acetoxyethyl or 2-benzoyloxyethyl accelerates the initial

dearomative [2,3] sigmatropic rearrangement and produces the desired S–H rearrangement product **2** in moderate yields. The rearrangement proceeds via the chelated intermediate **C**, that stabilizes the carbanionic ylide leading to the dearomative [2,3] sigmatropic rearrangement. The existence of the chelated intermediate **C** could be supported by mechanistic experiments: (i) the reaction in the presence of 18-crown-6 as a potassium ion (K^+) scavenger and (ii) the reaction via chirality transfer from a chiral benzylic carbon of (*S*)-**1f** to an α-carbon of the ester carbonyl of (*R*)-**2f**. The enhancement effect is not very strong or effective; however, it will expand the synthetic usefulness of ammonium ylide rearrangements and provide a unique method of synthesizing α-arylamino acid derivatives.



Scheme 4. Proposed chelated intermediate **C** obtained by the S–H rearrangement of (*S*)-**1f** into (*R*)-**2f**.

3. Experimental section

General: Infrared spectra (IR) were recorded on a JASCO FT/IR-4600 spectrometer. ^{1}H and ^{13}C NMR spectra were measured on a Varian (^{1}H: 400 MHz, ^{13}C: 100 MHz) or a Bruker (^{1}H: 400 MHz, ^{13}C: 100 MHz) spectrometer. Me_4Si (δ 0 ppm) was used as an internal standard in $CDCl_3$ for ^{1}H NMR. $CDCl_3$ (δ 77.00 ppm) was used as an internal standard for ^{13}C NMR. The splitting patterns are denoted as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad peak. High-resolution mass spectra (ESI) were measured on a Thermo Fisher Scientific LC/FT-MS spectrometer. Specific rotations were recorded on a JASCO polarimeter P-1010. Normal phase HPLC analyses were performed using a JASCO HPLC pump (PU-2080) and a UV/VIS detector (UV-2075). Reactions involving air- or moisture-sensitive compounds were conducted in appropriate round-bottomed flasks with a magnetic stirring bar under an argon (Ar) or a nitrogen (N_2) atmosphere. Reactions under lower temperature were carried out using a constant temperature bath with a magnetic stirrer (PSL-1400 and PSL-1800, EYELA, Japan) and an ultracooling reactor (UCR-150, Techno-Sigma Co., Ltd, Japan). A 1.0 M *t*BuOK THF solution was purchased from Tokyo Chemical Industry (TCI) Co., Ltd, Japan. Tetrahydrofuran (THF) was purchased from KANTO Chemical Co., Inc., Japan as an anhydrous solvent. Acetonitrile (MeCN) was dried over 3 Å molecular sieves activated at 200 °C under vacuum. For the thin layer chromatography (TLC) analysis throughout this work, a FUJIFILM Silicagel 70 TLC Plate-Wako was used. The products were purified by preparative column chromatography on silica gel (60N, spherical neutral) purchased from KANTO Chemical Co., Inc., Japan.

*3.1. Representative procedure for preparation of 3-acetoxy-N-(2-(tert-butoxy)-2-oxoethyl)-N,N-dimethyl-1-phenylpropan-1-aminium bromide (**1d**)* [13]

A mixture of benzaldehyde (3.05 mL, 30.0 mmol), NH_4OAc (3.08 g, 40.0 mmol), and malonic acid (3.12 g, 30.0 mmol) in EtOH (50 mL) was refluxed for 16 h under a N_2 atmosphere. The resulting mixture was cooled to room temperature and filtered. The filtracts were washed with EtOH and dried under reduced pressure to obtain 3-amino-3-phenylpropanoic acid (2.68 g, 54% yield) as a white solid. This product (2.48 g, 15.0 mmol) was added slowly to a suspension of $LiAlH_4$ (0.85 g, 22 mmol) in THF (30 mL) at 0 °C and the mixture was refluxed for 5 h under a N_2 atmosphere. The resulting mixture was cooled to 0 °C, diluted with Et_2O, and quenched with H_2O (0.85 mL). The mixture was treated with 15 wt.% NaOH in H_2O (0.85 mL) followed by H_2O (2.55 mL) and stirred for over 30 min at room temperature. The mixture was and filtered through a pad of Celite and the filtrate was evaporated to obtain 3-amino-3-phenylpropan-1-ol (2.01 g, 89% yield) as colorless crystals. A mixture of this product (1.71 g, 11.3 mmol), 37 wt.% HCHO in H_2O (1.8 mL, ca. 23 mmol) and HCO_2H (1.75 mL, 46.4 mmol) was stirred at 100 °C for 15 h. The resulting mixture was cooled to room temperature and treated with 2 M NaOH in H_2O. The mixture was extracted with CH_2Cl_2 and the combined extracts were washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by bulb-to-bulb distillation under reduced pressure (3 to 5 mmHg, 150 to 180 °C) to afford 3-(dimethylamino)-3-phenylpropan-1-ol (1.85 g, 91% yield) as a colorless oil. A solution of this product (581 mg, 3.24 mmol) and DMAP (79 mg, 0.65 mmol) in CH_2Cl_2 (16 mL) was treated with Ac_2O (0.46 mL, 4.9 mmol) at 0 °C and stirred for 30 min. The resulting mixture was treated with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and evaporated. Purification of the residue by chromatography on silica gel (CH_2Cl_2/MeOH = 20/1 to 10/1 as the eluent) gave 3-(dimethylamino)-3-phenylpropyl acetate (451 mg, 63% yield) as a colorless oil. A solution of this product (473 mg, 2.14 mmol) and *tert*-butyl bromoacetate (347 μL, 2.35 mmol) in MeCN (4.3 mL) was stirred for 3 days at room temperature. The resulting mixture was evaporated and the residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH = 10/1 to 5/1 as the eluent) to afford **1d** (898 mg, quant.) as a white solid. IR (ATR) ν_{max}/cm^{-1} 2977, 2931, 1732, 1459, 1417, 1395, 1368, 1237, 1151, 1070, 1041, 984, 935, 872, 840, 800, 771, 722, 704; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.35 (5H, br m, Ph), 5.49 (1H, dd, *J* = 10.8, 4.4 Hz, NCHPh), 4.81 (1H, d, *J* = 17.2 Hz, NCH_2CO), 4.33 (1H, d, *J* = 17.2 Hz, NCH_2CO), 4.11 (1H, ddd, *J* = 11.4, 5.0, 5.0 Hz, $CHCH_2CH_2$), 3.75 (3H, s, $N(CH_3)_2$), 3.64 (1H, ddd, *J* = 11.4, 8.5, 5.0 Hz, $CHCH_2CH_2$), 3.51 (3H, s, $N(CH_3)_2$), 2.83-2.67 (2H, m, $CHCH_2CH_2$), 1.98 (3H, s, CH_3CO), 1.52 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 163.9, 133.8 (br), 131.4, 129.7 (br), 129.3, 128.1 (br), 85.4, 73.3, 61.1, 60.3, 49.4, 49.3, 27.8, 27.4, 20.6; HRMS (ESI): calcd for $C_{19}H_{30}NO_4$ [M – Br]$^+$ 336.2169, found 336.2166.

*3.2. Representative procedure for preparation of 3-(benzoyloxy)-N-(2-(tert-butoxy)-2-oxoethyl)-N,N-dimethyl-1-phenylpropan-1-aminium bromide (**1f**)* [13]

A solution of 3-(dimethylamino)-3-phenylpropan-1-ol (144 mg, 0.803 mmol), Et_3N (123 μL, 0.882 mmol), and DMAP (5 mg, 0.04 mmol) in THF (4 mL) was treated with BzCl (102 mL, 0.878 mmol) at room temperature. After stirring for 20 h at room temperature, the resulting mixture was diluted with H_2O and extracted with EtOAc. The combined extracts were washed with saturated aqueous $NaHCO_3$ followed by brine and dried over Na_2SO_4. Evaporation of the solvents and purification of the residue by chromatography on silica gel (CH_2Cl_2/MeOH = 50/1 to 20/1 as the eluent) afforded 3-(dimethylamino)-3-phenylpropyl benzoate (190 mg, 84% yield) as a colorless oil. A solution of this product (184 mg, 0.649 mmol) and *tert*-butyl bromoacetate

(115 μL, 0.779 mmol) in MeCN (1.3 mL) was stirred for 3 days at room temperature. The resulting mixture was evaporated and the residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH = 20/1 to 5/1 as the eluent) to obtain **1f** (319 mg, quant.) as a white solid. IR (ATR) ν_{max}/cm^{-1} 2976, 2929, 2874, 1715, 1451, 1415, 1395, 1369, 1342, 1314, 1270, 1251, 1152, 1113, 1070, 1025, 983, 937, 873, 840, 807, 771, 713; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.91 (2H, m, ArH), 7.67 (1H, br, ArH), 7.62-7.48 (2H, br m, ArH), 7.57 (1H, tt, *J* = 7.4, 1.2 Hz, ArH), 7.48-7.38 (4H, m, ArH), 5.66 (1H, dd, *J* = 11.8, 3.8 Hz, NCHPh), 4.89 (1H, d, *J* = 17.2 Hz, NCH_2CO), 4.45-4.32 (2H, m, NCH_2CO and $CHCH_2CH_2$), 3.90 (1H, ddd, *J* = 11.5, 8.9, 4.8 Hz, $CHCH_2CH_2$), 3.80 (3H, s, $N(CH_3)_2$), 3.54 (2H, s, $N(CH_3)_2$), 3.00-2.82 (2H, m, $CHCH_2CH_2$), 1.48 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 164.0, 133.7 (br), 133.1, 131.4, 129.7 (br), 129.5, 129.3, 129.2, 128.3, 85.4, 73.4, 61.2, 61.0, 49.5, 27.9, 27.6; HRMS (ESI): calcd for $C_{24}H_{32}NO_4$ [M – Br]$^+$ 398.2326, found 398.2321.

*3.3. Representative procedure for the base-induced rearrangement of **1d** to obtain pure tert-butyl 5-acetoxy-2-(dimethylamino)-3-phenylpentanoate (**4d**) (Table 1, Entry 1)*

A solution of **1d** (141 mg, 0.339 mmol) in THF (3.0 mL) was treated with a 1.0 M *t*BuOK THF solution (0.41 mL, 0.41 mmol) at –40 °C under an Ar atmosphere and stirred for 3 h at the same temperature. The resulting mixture was poured into saturated aqueous NH_4Cl and extracted with EtOAc. The combined extracts were washed with saturated aqueous $NaHCO_3$ followed by brine, dried over Na_2SO_4, and evaporated. The residue was dissolved in $CDCl_3$ and mesitylene (15.7 μL, 0.113 mmol) was added as an internal standard. ^{1}H NMR analysis of the solution determined the yields of **2d** (16%), **4d** (26%, **4da**/**4db** = 6/4), cinnamyl acetate (**5d**) (17%), and cinnamyl alcohol (**6**) (3%). The $CDCl_3$ solution was evaporated and the residue was purified twice by chromatography on silica gel (1st: CH_2Cl_2/EtOAc = 15/1 to 10/1 as the eluent; 2nd: *n*-hexane/EtOAc = 4/1 to 3/1 as the eluent, R_f: **4da** > **4db**) to afford pure **4da** (7.1 mg, 6% yield) as colorless crystals and **4db** (7.4 mg, 7% yield) as colorless crystals. **4da**: m.p. 48–51 °C; IR (KBr) ν_{max}/cm^{-1} 3060, 3032, 2976, 2936, 2871, 2836, 2794, 1738, 1706, 1499, 1477, 1455, 1392, 1364, 1321, 1241, 1200, 1147, 1060, 1045, 1011, 979, 951, 850, 796, 757, 739, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (2H, dddd, *J* = 7.6, 7.2, 1.6, 1.6 Hz, Ph), 7.21 (1H, tt, *J* = 7.2, 1.6 Hz, Ph), 7.18-7.13 (2H, m, Ph), 3.90 (1H, ddd, *J* = 10.9, 7.2, 4.8 Hz, 5-H), 3.73 (1H, ddd, *J* = 10.9, 8.3, 6.4 Hz, 5-H), 3.33 (1H, d, *J* = 11.0 Hz, 2-H), 3.12 (1H, ddd, *J* = 11.2, 11.0, 3.2 Hz, 3-H), 2.23 (6H, s, $N(CH_3)_2$), 1.97 (3H, s, CH_3CO), 1.93 (1H, dddd, *J* = 13.6, 8.3, 7.2, 3.2 Hz, 4-H), 1.77 (1H, dddd, *J* = 13.6, 11.2, 6.4, 4.8 Hz, 4-H), 1.52 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.2, 141.0, 128.4, 128.1, 126.6, 81.3, 72.6, 62.4, 42.2, 41.2, 32.5, 28.4, 20.9; HRMS (ESI): calcd for $C_{19}H_{30}NO_4$ [M + H]$^+$ 336.2169, found 336.2158. **4db**: m.p. 83–86 °C; IR (KBr) ν_{max}/cm^{-1} 3029, 2977, 2938, 2869, 2832, 2793, 2775, 1734, 1713, 1496, 1455, 1390, 1367, 1256, 1238, 1150, 1092, 1037, 938, 845, 792, 759, 739, 703; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.22 (2H, m, Ph), 7.21-7.14 (3H, m, Ph), 3.96 (1H, ddd, *J* = 11.1, 7.3, 5.2 Hz, 5-H), 3.83 (1H, ddd, *J* =11.1, 7.8, 6.4 Hz, 5-H), 3.28 (1H, d, *J* = 11.6 Hz, 2-H), 3.05 (1H, ddd, *J* = 11.6, 11.4, 3.2 Hz, 3-H), 2.47-2.36 (1H, m, 4-H), 2.41 (6H, s, $N(CH_3)_2$), 1.96 (3H, s, CH_3CO), 1.75 (1H, dddd, *J* = 14.2, 11.4, 6.4, 5.2 Hz, 4-H), 1.11 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 169.3, 140.6, 128.8, 128.3, 126.9, 80.5, 72.6, 62.7, 42.2, 41.2, 31.3, 27.9, 20.9; HRMS (ESI): calcd for $C_{19}H_{30}NO_4$ [M + H]$^+$ 336.2169, found 336.2160.

*3.4. Representative procedure for the base-induced rearrangement of **1d** to obtain pure tert-butyl 2-(dimethylamino)-2-(2-pentylphenyl)acetate (**2d**) (Table 1, Entry 5)*

A solution of **1d** (137 mg, 0.329 mmol) in MeCN (3.0 mL) was treated with a 1.0 M *t*BuOK THF solution (0.39 mL, 0.39 mmol) at –40 °C under an Ar atmosphere and stirred for 3 h at the same temperature. The resulting mixture was poured into saturated aqueous NH_4Cl and extracted with EtOAc. The combined extracts were washed with saturated aqueous $NaHCO_3$ followed by brine, dried over Na_2SO_4, and evaporated. The residue was dissolved in $CDCl_3$ and mesitylene (15.3 μL, 0.110 mmol) was added as an internal standard. ^{1}H NMR analysis of the solution determined the yields of **2d** (60%), **4d** (11%, **4da**/**4db** = 6/4), **5d** (6%), and **6** (5%). The $CDCl_3$ solution was evaporated and the residue was purified by chromatography on silica gel (CH_2Cl_2/EtOAc = 5/1 to 2/1 as the eluent) to obtain pure **2d** (53.2 mg, 48% yield) as a colorless oil. IR (ATR) ν_{max}/cm^{-1} 2977, 2954, 2868, 2819, 2772, 1736, 1459, 1449, 1391, 1366, 1233, 1140, 1033, 948, 903, 835, 795, 754, 731; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.56 (1H, m, ArH), 7.24-7.12 (3H, m, ArH), 4.14 (1H, dt, *J* = 10.8, 6.6 Hz, OCH_2), 4.11 (1H, dt, *J* = 10.8, 6.6 Hz, OCH_2), 4.04 (1H, s, NCHCO), 2.82 (2H, t, *J* = 8.0 Hz, CH_2Ar), 2.27 (6H, s, $N(CH_3)_2$), 2.08 (3H, s, CH_3CO), 2.07-1.90 (2H, m, $CH_2CH_2CH_2$), 1.38 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.13, 171.10, 140.1, 135.2, 129.6, 128.5, 127.8, 126.5, 81.2, 70.4, 63.9, 43.2, 30.1, 29.1, 27.9, 21.0; HRMS (ESI): calcd for $C_{19}H_{30}NO_4$ [M + H]$^+$ 336.2169, found 336.2166.

*3.5. tert-Butyl 2-(dimethylamino)-2-(2-ethylphenyl)acetate (**2c**)*

Colorless oil; IR (ATR) ν_{max}/cm^{-1} 2968, 2933, 2870, 2817, 2769, 1741, 1729, 1448, 1391, 1366, 1347, 1279, 1255, 1219, 1139, 1043, 961, 946, 901, 877, 865, 836, 807, 753; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.57 (1H, m, ArH), 7.25-7.15 (3H, m, ArH), 4.05 (1H, s, NCHCO), 2.78 (2H, q, *J* = 7.6 Hz, CH_2CH_3), 2.26 (6H, s, $N(CH_3)_2$), 1.37 (9H, s, *t*Bu), 1.25 (3H, t, *J* = 7.6 Hz, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 143.0, 134.8, 128.8, 128.2, 127.7, 126.0, 81.0, 70.5, 43.3, 27.8, 25.8, 15.7; HRMS (ESI): calcd for $C_{16}H_{26}NO_2$ [M + H]$^+$ 264.1958, found 264.1956.

*3.6. tert-Butyl 2-(dimethylamino)-3-phenylbutanoate (**4ca**)*

Colorless crystals; M.p. 46–48 °C; IR (ATR) ν_{max}/cm^{-1} 3060, 3027, 3010, 2964, 2931, 2871, 2830, 2776, 1711, 1604, 1497, 1471, 1454, 1389, 1363, 1338, 1297, 1267, 1143, 1100, 1083, 1062, 1041, 1031, 1009, 996, 968, 908, 852, 810, 786, 758, 753, 700; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.27 (2H, m, Ph), 7.23-7.17 (3H, m, Ph), 3.28 (1H, d, *J* = 10.9 Hz, 2-H), 3.12 (1H, dq, *J* = 10.9, 6.8 Hz, 3-H), 2.26 (6H, s, $N(CH_3)_2$), 1.51 (9H, s, *t*Bu), 1.18 (3H, d, *J* = 6.8 Hz, 4-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 144.5, 128.3, 127.3, 126.2, 81.0, 73.4, 41.3, 39.4, 28.4, 20.3; HRMS (ESI): calcd for $C_{16}H_{26}NO_2$ [M + H]$^+$ 264.1958, found 264.1956.

*3.7. tert-Butyl 2-(dimethylamino)-3-phenylbutanoate (**4cb**)*

Colorless oil; M.p. 68–70 °C; IR (ATR) ν_{max}/cm^{-1} 3058, 3030, 3008, 2976, 2930, 2866, 2827, 2792, 2769, 1713, 1495, 1450, 1389, 1365, 1353, 1287, 1264, 1215, 1146, 1089, 1066, 1037, 1019, 1000, 959, 910, 866, 842, 786, 757, 740, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.15 (5H, m, Ph), 3.19 (1H, d, *J* = 11.4 Hz, 2-H), 3.06 (1H, dq, *J* = 11.4, 6.8 Hz, 3-H), 2.42 (6H, s, $N(CH_3)_2$), 1.30 (3H, d, *J* = 6.8 Hz, 4-H), 1.13 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 143.7, 128.1, 126.4, 80.3, 73.7, 41.2, 39.6, 27.9, 19.1; HRMS (ESI): calcd for $C_{16}H_{26}NO_2$ [M + H]$^+$ 264.1958, found 264.1956.

*3.8. tert-Butyl 2-(dimethylamino)-2-(2-pentylphenyl)acetate (**2e**)*

Colorless oil; IR (ATR) ν_{max}/cm^{-1} 2955, 2929, 2861, 2817, 2770, 1741, 1730, 1458, 1391, 1366, 1347, 1279, 1255, 1219, 1139, 1042, 961, 946, 902, 879, 866, 836, 789, 752; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.56 (1H, m, ArH), 7.23-7.12 (3H, m, ArH), 4.04 (1H, s, NCHCO), 2.72 (2H, t, *J* = 8.0 Hz, CH_2Ar), 2.26 (6H, s, $N(CH_3)_2$), 1.75-1.51 (2H, m, CH_2), 1.46-1.30 (4H, m, CH_2), 1.37 (9H, s, *t*Bu), 0.92 (3H, t, *J* = 7.0 Hz, $CH_2CH_2CH_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 141.7, 135.0, 129.5, 128.2, 127.5, 126.0, 80.9, 70.3, 43.3, 32.8, 31.9, 31.1, 27.8, 22.5, 14.0; HRMS (ESI): calcd for $C_{19}H_{32}NO_2$ $[M + H]^+$ 306.2428, found 306.2419.

*3.9. tert-Butyl 2-(dimethylamino)-3-phenylheptanoate (**4ea**)*

Colorless crystals; M.p. 68–71 °C; IR (ATR) ν_{max}/cm^{-1} 2957, 2932, 2861, 2824, 2790, 2766, 1712, 1496, 1454, 1362, 1245, 1207, 1148, 1114, 1098, 1065, 1041, 1026, 1008, 979, 937, 913, 870, 843, 789, 763, 739, 726, 700; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (2H, dddd, *J* = 7.3, 7.3, 1.6, 1.6 Hz, Ph), 7.20 (1H, tt, *J* = 7.3, 1.6 Hz, Ph), 7.18-7.13 (2H, m, Ph), 3.32 (1H, d, *J* = 11.1 Hz, 2-H), 2.95 (1H, ddd, *J* = 11.1, 10.6, 3.2 Hz, 3-H), 2.23 (6H, s, $N(CH_3)_2$), 1.58-1.39 (2H, m, CH_2), 1.52 (9H, s, *t*Bu), 1.32-1.09 (2H, m, CH_2), 1.09-0.93 (2H, m, CH_2), 0.78 (3H, t, *J* = 7.2 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 142.5, 128.13, 128.07, 126.1, 80.9, 72.8, 45.3, 41.2, 33.6, 29.2, 28.4, 22.5, 13.8; HRMS (ESI): calcd for $C_{19}H_{32}NO_2$ $[M + H]^+$ 306.2428, found 306.2420.

*3.10. tert-Butyl 2-(dimethylamino)-3-phenylheptanoate (**4eb**)*

Colorless crystals; M.p. 28–31 °C; IR (ATR) ν_{max}/cm^{-1} 2972, 2951, 2929, 2871, 2857, 2829, 2782, 1715, 1495, 1468, 1454, 1391, 1366, 1330, 1316, 1265, 1251, 1221, 1144, 1100, 1087, 1065, 1033, 1002, 995, 952, 934, 904, 863, 845, 795, 760, 729, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.22 (2H, m, Ph), 7.20-7.15 (3H, m, Ph), 3.26 (1H, d, *J* = 11.6 Hz, 2-H), 2.88 (1H, ddd, *J* = 11.6, 11.6, 3.2 Hz, 3-H), 2.41 (6H, s, $N(CH_3)_2$), 2.02 (1H, dtd, *J* = 14.8, 8.4, 3.2 Hz, 4-H), 1.51-1.39 (1H, m, CH_2), 1.38-1.13 (3H, m, CH_2), 1.10 (9H, s, *t*Bu), 1.09-0.98 (1H, m, CH_2), 0.80 (3H, t, *J* = 7.4 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 141.8, 128.9, 128.0, 126.4, 80.2, 73.0, 45.4, 41.2, 31.9, 29.3, 27.8, 22.7, 14.0; HRMS (ESI): calcd for $C_{19}H_{32}NO_2$ $[M + H]^+$ 306.2428, found 306.2421.

*3.11. 3-(2-(2-(tert-Butoxy)-1-(dimethylamino)-2-oxoethyl)phenyl)propyl benzoate (**2f**)*

Colorless oil; IR (ATR) ν_{max}/cm^{-1} 3062, 2977, 2953, 2867, 2819, 2771, 1716, 1602, 1584, 1451, 1391, 1367, 1314, 1270, 1220, 1176, 1140, 1115, 1069, 1042, 1026, 961, 948, 903, 835, 797, 754, 732, 710; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10-8.06 (2H, m, ArH), 7.63-7.54 (2H, m, ArH), 7.49-7.42 (2H, m, ArH), 7.25-7.17 (3H, m, ArH), 4.39 (2H, t, *J* = 6.2 Hz, OCH_2), 4.08 (1H, s, NCHCO), 2.94 (2H, t, *J* = 7.8 Hz, CH_2Ar), 2.25 (6H, s, $N(CH_3)_2$), 2.23-2.04 (2H, m, $CH_2CH_2CH_2$), 1.36 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 166.5, 140.1, 135.2, 132.9, 130.3, 129.7, 129.6, 128.5, 128.3, 127.8, 126.5, 81.2, 70.4, 64.4, 43.2, 30.4, 29.3, 27.9; HRMS (ESI): calcd for $C_{24}H_{32}NO_4$ $[M + H]^+$ 398.2326, found 398.2320.

*3.12. 5-(tert-Butoxy)-4-(dimethylamino)-5-oxo-3-phenylpentyl benzoate (**4f**)*

Isolated as a 6/4 mixture of diastereomers. White solid; IR (ATR) ν_{max}/cm^{-1} 2974, 2934, 2876, 2827, 2765, 1715, 1602, 1583, 1495, 1473, 1452, 1366, 1313, 1271, 1201, 1143, 1117, 1069, 1024, 976, 941, 866, 846, 793, 756, 710, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.92 (2H, m, ArH), 7.57-7.51 (1H, m, ArH), 7.45-7.38 (2H, m, ArH), 7.33-7.15 (5H, m, ArH), 4.22 (0.4H, ddd, *J* = 11.0, 6.9, 5.0 Hz, 1-H), 4.15 (0.6H, ddd, *J* = 11.1, 6.8, 4.4 Hz, 1-H), 4.09 (0.4H, ddd, *J* = 11.0, 8.5, 6.0 Hz, 1-H), 3.99 (0.6H, ddd, *J* = 11.1, 8.5, 6.0 Hz, 1-H), 3.38 (0.6H, d, *J* = 11.2 Hz, 4-H), 3.33 (0.4H, d, *J* = 11.6 Hz, 4-H), 3.23 (0.6H, ddd, *J* = 11.2, 11.1, 3.2 Hz, 3-H), 3.17 (0.4H, ddd, *J* = 11.6, 11.4, 3.2 Hz, 3-H), 2.60 (0.4H, dddd, *J* = 14.2, 8.5, 6.9, 3.2 Hz, 2-H), 2.43 (2.4H, s, $N(CH_3)_2$), 2.25 (3.6H, s, $N(CH_3)_2$), 2.10 (0.6H, dddd, *J* = 13.8, 8.5, 6.8, 3.2 Hz, 2-H), 1.97-1.83 (1H, m, 2-H), 1.51 (5.4H, s, *t*Bu), 1.12 (3.6H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 169.3, 166.4, 166.3, 141.0, 140.5, 132.8, 132.7, 130.35, 130.30, 129.52, 129.46, 128.8, 128.5, 128.35, 128.26, 128.1, 126.9, 126.7, 81.3, 80.5, 72.74, 72.65, 63.3, 62.9, 42.43, 42.42, 41.26, 41.17, 32.7, 31.5, 28.4, 27.9; HRMS (ESI): calcd for $C_{24}H_{32}NO_4$ $[M + H]^+$ 398.2326, found 398.2317.

*3.13. 3-(2-(2-(tert-Butoxy)-1-(dimethylamino)-2-oxoethyl)phenyl)propyl pivalate (**2g**)*

Colorless oil; IR (ATR) ν_{max}/cm^{-1} 2975, 2934, 2870, 2818, 2771, 1726, 1480, 1459, 1394, 1367, 1282, 1256, 1220, 1140, 1035, 947, 902, 836, 798, 753; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.57 (1H, m, ArH), 7.24-7.18 (2H, m, ArH), 7.18-7.12 (1H, m, ArH), 4.14 (1H, dq, *J* = 11.4, 6.4 Hz, OCH_2), 4.11 (1H, dq, *J* = 11.4, 6.4 Hz, OCH_2), 4.04 (1H, s, NCHCO), 2.83 (2H, t, *J* = 8.0 Hz, CH_2Ar), 2.26 (6H, s, $N(CH_3)_2$), 2.10-1.88 (2H, m, $CH_2CH_2CH_2$), 1.37 (9H, s, *t*Bu), 1.25 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 171.0, 140.2, 135.1, 129.7, 128.5, 127.8, 126.5, 81.1, 70.3, 63.8, 43.2, 38.8, 30.4, 29.3, 27.9, 27.3; HRMS (ESI): calcd for $C_{22}H_{36}NO_4$ $[M + H]^+$ 378.2639, found 378.2634.

*3.14. tert-Butyl 2-(2-(3-((tert-butoxycarbonyl)oxy)propyl)phenyl)-2-(dimethylamino)acetate (**2h**)*

Colorless oil; IR (ATR) ν_{max}/cm^{-1} 2978, 2934, 2869, 2819, 2772, 1737, 1457, 1393, 1367, 1275, 1253, 1220, 1155, 1140, 1097, 1040, 1009, 947, 914, 903, 852, 837, 794, 753, 732; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.55 (1H, m, ArH), 7.25-7.13 (3H, m, ArH), 4.18-4.07 (2H, m, OCH_2), 4.05 (1H, s, NCHCO), 2.84 (2H, t, *J* = 7.8 Hz, CH_2Ar), 2.27 (6H, s, $N(CH_3)_2$), 2.13-1.93 (2H, m, $CH_2CH_2CH_2$), 1.50 (9H, s, *t*Bu), 1.37 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 153.6, 140.0, 135.2, 129.6, 128.4, 127.7, 126.4, 81.8, 81.1, 70.2, 66.4, 43.1, 30.1, 28.9, 27.8, 27.7; HRMS (ESI): calcd for $C_{22}H_{36}NO_5$ $[M + H]^+$ 394.2588, found 394.2578.

*3.15. tert-Butyl 2-(dimethylamino)-2-(2-(3-methoxypropyl)phenyl)acetate (**2i**)*

Colorless oil; IR (ATR) ν_{max}/cm^{-1} 2977, 2929, 2867, 2821, 2770, 1740, 1729, 1478, 1458, 1448, 1391, 1367, 1349, 1280, 1255, 1219, 1139, 1118, 1042, 948, 902, 884, 836, 795, 753; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.55 (1H, m, ArH), 7.25-7.14 (3H, m, ArH), 4.08 (1H, s, NCHCO), 3.44 (1H, dt, *J* = 9.4, 6.4 Hz, OCH_2), 3.41 (1H, dt, *J* = 9.4, 6.4 Hz, OCH_2), 3.37 (3H, s, OCH_3), 2.82 (2H, t, *J* = 7.8 Hz, CH_2Ar), 2.27 (6H, s, $N(CH_3)_2$), 2.01-1.83 (2H, m, $CH_2CH_2CH_2$), 1.37 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 140.8, 135.2, 129.6, 128.3, 127.6, 126.2, 81.0, 71.9, 70.2, 58.4, 43.1, 31.0, 29.1, 27.8; HRMS (ESI): calcd for $C_{18}H_{30}NO_3$ $[M + H]^+$ 308.2220, found 308.2212.

*3.16. 3-(2-(2-(tert-Butoxy)-1-(dimethylamino)-2-oxoethyl)-4-chlorophenyl)propyl benzoate (**2j**)*

Colorless oil; IR (ATR) ν_{max}/cm^{-1} 3062, 2977, 2954, 2897, 2868, 2821, 2774, 1716, 1601, 1483, 1451, 1392, 1367, 1349, 1314, 1270, 1220, 1141, 1111, 1069, 1042, 1026, 959, 912, 899, 838,

813, 790, 736, 710; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-8.04 (2H, m, ArH), 7.65 (1H, d, *J* = 2.4 Hz, ArH), 7.57 (1H, tt, *J* = 7.4, 1.4 Hz, ArH), 7.45 (2H, dddd, *J* = 8.1, 7.4, 1.4, 1.4 Hz, ArH), 7.19 (1H, dd, *J* = 8.2, 2.4 Hz, ArH), 7.13 (1H, d, *J* = 8.2 Hz, ArH), 4.38 (2H, t, *J* = 6.2 Hz, OCH_2), 4.03 (1H, s, NCHCO), 2.97-2.83 (2H, m, CH_2Ar), 2.25 (6H, s, $N(CH_3)_2$), 2.20-2.01 (2H, m, $CH_2CH_2CH_2$), 1.38 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 166.4, 138.6, 137.2, 132.9, 132.4, 130.9, 130.2, 129.5, 128.6, 128.3, 128.0, 81.6, 70.4, 64.2, 43.1, 30.2, 28.8, 27.8; HRMS (ESI): calcd for $C_{24}H_{31}ClNO_4$ $[M + H]^+$ 432.1936, found 432.1921.

*3.17. 3-(4-Bromo-2-(2-(tert-butoxy)-1-(dimethylamino)-2-oxoethyl)phenyl)propyl benzoate (**2k**)*

Colorless oil; IR (ATR) ν_{max}/cm^{-1} 3062, 2977, 2954, 2868, 2821, 2774, 1716, 1602, 1586, 1479, 1451, 1392, 1367, 1348, 1314, 1270, 1220, 1174, 1141, 1110, 1069, 1042, 1026, 960, 905, 890, 837, 809, 735, 710; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (2H, dd, *J* = 7.9, 1.2 Hz, ArH), 7.79 (1H, d, *J* = 2.0 Hz, ArH), 7.57 (1H, t, *J* = 7.6 Hz, ArH), 7.45 (2H, dd, *J* = 7.9, 7.6 Hz, ArH), 7.34 (1H, dd, *J* = 8.2, 2.0 Hz, ArH), 7.07 (1H, d, *J* = 8.2 Hz, ArH), 4.37 (2H, t, *J* = 6.2 Hz, OCH_2), 4.01 (1H, s, NCHCO), 2.96-2.80 (2H, m, CH_2Ar), 2.25 (6H, s, $N(CH_3)_2$), 2.19-2.01 (2H, m, $CH_2CH_2CH_2$), 1.38 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 166.5, 139.1, 137.6, 133.0, 131.5, 131.3, 131.0, 130.3, 129.6, 128.4, 120.4, 81.7, 70.5, 64.2, 43.2, 30.2, 28.9, 27.9; HRMS (ESI): calcd for $C_{24}H_{31}BrNO_4$ $[M + H]^+$ 476.1431, found 476.1410.

*3.18. 3-(2-(2-(tert-Butoxy)-1-(dimethylamino)-2-oxoethyl)-4-methylphenyl)propyl benzoate (**2l**)*

Yellow oil; IR (ATR) ν_{max}/cm^{-1} 2925, 2856, 2819, 2771, 1717, 1638, 1602, 1584, 1501, 1451, 1391, 1367, 1314, 1270, 1215, 1142, 1114, 1069, 1042, 1026, 963, 936, 902, 843, 815, 789, 711; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (2H, dd, *J* = 8.2, 1.4 Hz, ArH), 7.57 (1H, tt, *J* = 7.6, 1.4 Hz, ArH), 7.48-7.41 (3H, m, ArH), 7.07 (1H, d, *J* = 7.6 Hz, ArH), 7.02 (1H, dd, *J* = 7.6, 1.6 Hz, ArH), 4.37 (2H, t, *J* = 6.4 Hz, OCH_2), 4.03 (1H, s, NCHCO), 2.89 (2H, t, *J* = 7.8 Hz, CH_2Ar), 2.30 (3H, s, $ArCH_3$), 2.25 (6H, s, $N(CH_3)_2$), 2.19-2.03 (2H, m, $CH_2CH_2CH_2$), 1.36 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 166.6, 137.0, 136.1, 132.9, 130.4, 129.58, 129.57, 128.9, 128.7, 128.3, 70.5, 64.4, 43.3, 30.4, 29.7, 29.0, 27.9, 21.0; HRMS (ESI): calcd for $C_{25}H_{34}NO_4$ $[M + H]^+$ 412.2482, found 412.2472.

*3.19. 5-(tert-Butoxy)-4-(dimethylamino)-5-oxo-3-(p-tolyl)pentyl benzoate (**4l**)*

Isolated as a 6/4 mixture of diastereomers. Colorless oil; IR (ATR) ν_{max}/cm^{-1} 2969, 2936, 2869, 2832, 2788, 1713, 1602, 1584, 1515, 1471, 1450, 1391, 1365, 1313, 1270, 1149, 1115, 1069, 1048, 1026, 975, 961, 944, 849, 815, 788, 708; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.91 (2H, m, ArH), 7.57-7.49 (1H, m, ArH), 7.46-7.36 (2H, m, ArH), 7.13-7.02 (4H, m, ArH), 4.21 (0.4H, ddd, *J* = 10.9, 6.8, 4.8 Hz, 1-H), 4.15 (0.6H, ddd, *J* = 11.0, 6.9, 4.8 Hz, 1-H), 4.09 (0.4H, ddd, *J* = 10.9, 8.4, 6.0 Hz, 1-H), 4.00 (0.6H, ddd, *J* = 11.0, 8.3, 6.2 Hz, 1-H), 3.37 (0.6H, d, *J* = 11.2 Hz, 4-H), 3.31 (0.4H, d, *J* = 11.6 Hz, 4-H), 3.19 (0.6H, ddd, *J* = 11.2, 11.0, 3.2 Hz, 3-H), 3.13 (0.4H, ddd, *J* = 11.6, 11.4, 3.2 Hz, 3-H), 2.57 (0.4H, dddd, *J* = 14.2, 8.4, 6.8, 3.2 Hz, 2-H), 2.42 (2.4H, s, $N(CH_3)_2$), 2.30 (1.8H, s, $ArCH_3$), 2.28 (1.2H, s, $ArCH_3$), 2.25 (3.6H, s, $N(CH_3)_2$), 2.07 (0.6H, dddd, *J* = 13.5, 8.3, 6.9, 3.2 Hz, 2-H), 1.94-1.80 (1H, m, 2-H), 1.51 (5.4H, s, *t*Bu), 1.13 (3.6H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 169.3, 166.4, 166.3, 137.8, 137.3, 136.3, 136.0, 132.70, 132.66, 130.35, 130.30, 129.5, 129.4, 129.2, 128.9, 128.6, 128.20, 128.19, 127.9, 81.2, 80.4, 72.72, 72.69, 63.3, 62.9, 42.0, 41.9, 41.2, 41.1, 32.7, 31.4, 28.4, 27.9, 21.1, 20.9; HRMS (ESI): calcd for $C_{25}H_{34}NO_4$ $[M + H]^+$ 412.2482, found 412.2472.

*3.20. 5-(tert-Butoxy)-4-(dimethylamino)-3-(4-methoxyphenyl)-5-oxopentyl benzoate (**4m**)*

Isolated as a 5/5 mixture of diastereomers. Yellow oil; IR (ATR) ν_{max}/cm^{-1} 3005, 2962, 2932, 2869, 2833, 2790, 2770, 1712, 1612, 1584, 1513, 1469, 1450, 1390, 1366, 1313, 1271, 1245, 1175, 1145, 1116, 1069, 1035, 1025, 1006, 942, 911, 829, 817, 791, 734, 710; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.92 (2H, m, ArH), 7.58-7.50 (1H, m, ArH), 7.46-7.37 (2H, m, ArH), 7.16-7.08 (2H, m, ArH), 6.84 (1H, ddd, *J* = 8.4, 2.4, 2.4 Hz, ArH), 6.80 (1H, ddd, *J* = 8.4, 2.4, 2.4 Hz, ArH), 4.21 (0.5H, ddd, *J* = 11.1, 6.8, 5.0 Hz, 1-H), 4.16 (0.5H, ddd, *J* = 11.0, 6.6, 4.8 Hz, 1-H), 4.08 (0.5H, ddd, *J* = 11.1, 8.5, 6.0 Hz, 1-H), 4.00 (0.5H, ddd, *J* = 11.0, 8.4, 6.2 Hz, 1-H), 3.76 (1.5H, s, OCH_3), 3.75 (1.5H, s, OCH_3), 3.33 (0.5H, d, *J* = 11.2 Hz, 4-H), 3.29 (0.5H, d, *J* = 11.6 Hz, 4-H), 3.18 (0.5H, ddd, *J* = 11.2, 11.2, 3.2 Hz, 3-H), 3.12 (0.5H, ddd, *J* = 11.6, 11.6, 3.2 Hz, 3-H), 2.57 (0.5H, dddd, *J* = 14.0, 8.5, 6.8, 3.2 Hz, 2-H), 2.42 (3H, s, $N(CH_3)_2$), 2.26 (3H, s, $N(CH_3)_2$), 2.07 (0.5H, dddd, *J* = 14.0, 8.4, 6.6, 3.2 Hz, 2-H), 1.93-1.78 (1H, m, 2-H), 1.51 (4.5H, s, *t*Bu), 1.15 (4.5H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 169.4, 166.4, 166.3, 158.5, 158.2, 132.8, 132.75, 132.71, 132.4, 130.34, 130.29, 129.7, 129.5, 129.4, 128.9, 128.23, 128.22, 113.9, 113.7, 81.3, 80.4, 72.8, 63.3, 62.9, 55.2, 55.0, 41.6, 41.5, 41.2, 41.1, 32.7, 31.4, 28.4, 27.9; HRMS (ESI): calcd for $C_{25}H_{34}NO_5$ $[M + H]^+$ 428.2431, found 428.2422.

*3.21. 3-(2-(2-(tert-Butoxy)-1-(dimethylamino)-2-oxoethyl)-5-chlorophenyl)propyl benzoate (**2n**)*

Colorless oil; IR (ATR) ν_{max}/cm^{-1} 2977, 2954, 2931, 2868, 2820, 2773, 1716, 1597, 1569, 1478, 1451, 1391, 1367, 1314, 1270, 1221, 1140, 1112, 1069, 1043, 1026, 949, 901, 882, 836, 790, 710; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (2H, dd, *J* = 8.0, 1.2 Hz, ArH), 7.60-7.53 (2H, m, ArH), 7.46 (2H, dd, *J* = 8.0, 7.2 Hz, ArH), 7.23-7.18 (2H, m, ArH), 4.40 (2H, t, *J* = 6.2 Hz, OCH_2), 4.02 (1H, s, NCHCO), 2.97-2.83 (2H, m, CH_2Ar), 2.23 (6H, s, $N(CH_3)_2$), 2.20-2.03 (2H, m, $CH_2CH_2CH_2$), 1.36 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 166.5, 142.2, 133.9, 133.6, 133.0, 130.3, 130.1, 129.6, 129.5, 128.4, 126.8, 81.5, 70.1, 64.3, 43.1, 30.2, 29.2, 27.9; HRMS (ESI): calcd for $C_{24}H_{31}ClNO_4$ $[M + H]^+$ 432.1936, found 432.1923.

*3.22. 5-(tert-Butoxy)-3-(3-chlorophenyl)-4-(dimethylamino)-5-oxopentyl benzoate (**4n**)*

Isolated as a 5/5 mixture of diastereomers. Colorless oil; IR (ATR) ν_{max}/cm^{-1} 2975, 2936, 2870, 2833, 2790, 1715, 1598, 1573, 1474, 1452, 1432, 1391, 1367, 1314, 1269, 1144, 1113, 1069, 1046, 1026, 999, 943, 878, 842, 783, 737, 710, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98-7.89 (2H, m, ArH), 7.58-7.51 (1H, m, ArH), 7.46-7.38 (2H, m, ArH), 7.25-7.14 (3H, m, ArH), 7.14-7.05 (1H, m, ArH), 4.24 (0.5H, ddd, *J* = 11.1, 6.2, 5.4 Hz, 1-H), 4.17 (0.5H, ddd, *J* = 11.2, 6.4, 5.0 Hz, 1-H), 4.11 (0.5H, ddd, *J* = 11.1, 8.3, 5.8 Hz, 1-H), 4.02 (0.5H, ddd, *J* = 11.2, 8.2, 5.8 Hz, 1-H), 3.32 (0.5H, d, *J* = 11.4 Hz, 4-H), 3.28 (0.5H, d, *J* = 11.6 Hz, 4-H), 3.21 (0.5H, ddd, *J* = 11.4, 10.6, 3.0 Hz, 3-H), 3.15 (0.5H, ddd, *J* = 11.6, 11.2, 3.0 Hz, 3-H), 2.61 (0.5H, dddd, *J* = 14.5, 8.3, 6.2, 3.0 Hz, 2-H), 2.42 (3H, s, $N(CH_3)_2$), 2.24 (3H, s, $N(CH_3)_2$), 2.09 (0.5H, dddd, *J* = 14.2, 8.2, 6.4, 3.0 Hz, 2-H), 1.99-1.82 (1H, m, 2-H), 1.50 (4.5H, s, *t*Bu), 1.16 (4.5H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 169.0, 166.4, 166.3, 143.4, 143.0, 134.3, 134.2, 132.85, 132.82, 130.2, 130.1, 129.7, 129.6, 129.5, 129.4, 128.9, 128.3, 128.1, 127.1, 127.0, 126.9, 126.5, 81.5, 80.8, 72.6, 72.5, 63.1, 62.8, 42.41, 42.38, 41.3, 41.2, 32.5,

31.3, 28.4, 27.9; HRMS (ESI): calcd for $C_{24}H_{31}ClNO_4$ $[M + H]^+$ 432.1936, found 432.1926.

*3.23. 3-(2-(2-(tert-Butoxy)-1-(dimethylamino)-2-oxoethyl)-6-chlorophenyl)propyl benzoate (**2o**)*

Colorless oil; IR (ATR) ν_{max}/cm^{-1} 2977, 2954, 2931, 2896, 2867, 2820, 2773, 1717, 1451, 1392, 1367, 1314, 1270, 1216, 1141, 1112, 1069, 1044, 1027, 958, 914, 836, 778, 733, 710; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (2H, dd, *J* = 7.7, 1.2 Hz, ArH), 7.61-7.51 (2H, m, ArH), 7.45 (2H, dd, *J* = 7.7, 7.2 Hz, ArH), 7.32 (1H, dd, *J* = 8.0, 1.2 Hz, ArH), 7.16 (1H, dd, *J* = 8.0, 8.0 Hz, ArH), 4.51-4.39 (2H, m, OCH_2), 4.11 (1H, s, NCHCO), 3.17 (1H, ddd, *J* = 13.5, 10.9, 5.6 Hz, CH_2Ar), 3.04 (1H, ddd, *J* = 13.5, 10.9, 5.6 Hz, CH_2Ar), 2.24 (6H, s, $N(CH_3)_2$), 2.20-2.00 (2H, m, $CH_2CH_2CH_2$), 1.37 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 166.6, 138.3, 137.6, 134.8, 132.9, 130.4, 129.6, 129.2, 128.3, 127.3, 127.2, 81.6, 70.7, 64.7, 43.0, 28.6, 27.9, 26.4; HRMS (ESI): calcd for $C_{24}H_{31}ClNO_4$ $[M + H]^+$ 432.1936, found 432.1923.

*3.24. 85% ee of (R)-3-(2-(2-(tert-Butoxy)-1-(dimethylamino)-2-oxoethyl)phenyl)propyl benzoate [(R)-**2f**] (Scheme 4, –60 °C, 12 h)*

Colorless oil; $[\alpha]^{23}_{589}$ –72.6 (*c* 1.0, EtOH) for 85% ee [determined by HPLC analysis: Daicel Chiralpak AD-H column (25 cm), *n*-hexane/*i*PrOH = 90/10 as the eluent, flow rate = 0.50 mL/min, t_R = 8.7 min for (*S*)-**2f** (7.3%) and 10.4 min for (*R*)-**2f** (92.7%)]. Other spectroscopic data: see **2f**.

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8. Previously, we reported that the use of DMPU as a solvent was effective for base-induced S–H rearrangement. See ref. 4c.
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10. 18-Crown-6 did not dissolve in MeCN.
11. Our previous study on carbanionic ylide form versus ammonium enolate form in base-induced S–H rearrangement: see ref. 4c.
12. The stereochemistry of (*R*)-**2f** was tentatively determined by comparison of the specific rotation value with those of the analogous (*R*)- and (*S*)-2-aryl-2-(dimethylamino)ethanol derivatives after conversion into 3-(2-(1-(dimethylamino)-2-hydroxyethyl)phenyl)propan-1-ol [(*R*)-**7**] by $LiAlH_4$ reduction. Details: see Supplementary data.
13. The synthetic schemes: see Supplementary data.

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Supplementary Material

Supplementary data associated with this article can be found online at xxx.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: