

New synthetic routes to optically active α -quaternary α -aryl amino acid derivatives via the diastereoselective Stevens and Sommelet–Hauser rearrangements

Eiji Tayama,^{*a} Kiwako Orihara^a and Hiroshi Kimura^a

⁵ Received (in XXX, XXX) 1st January 2007, Accepted 1st January 2007

First published on the web 1st January 2007

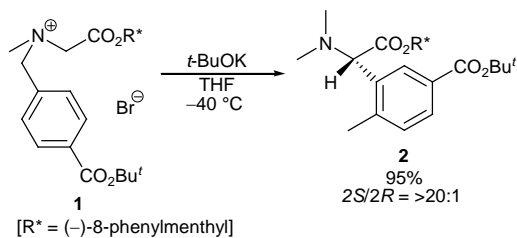
DOI: 10.1039/b000000x

The Stevens rearrangement of *N*-allylic α -aryl amino acid-derived ammonium salts and the Sommelet–Hauser rearrangement of *N*-benzylic α -alkyl amino acid-derived ammonium salts are shown to proceed with remarkably high levels of diastereoselectivity. The methods presented in this work provide new routes to optically active α -quaternary α -aryl amino acid derivatives.

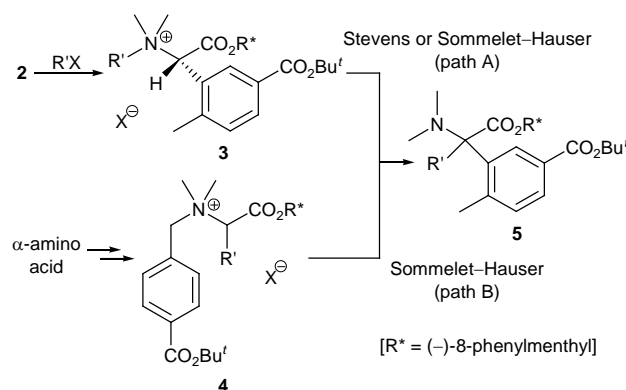
Introduction

Optically active α -quaternary α -aryl amino acid derivatives are a class of the most attractive target compounds in organic synthesis due to their interesting biological properties but limited routes for synthesis. The most well-studied synthetic method for α -quaternary α -aryl amino acid derivatives involves enantio- or diastereoselective cyanation of ketoimines to produce optically active α -quaternary α -aryl α -amino nitriles as amino acid precursors.^{1,2} While several methods or chiral catalysts for asymmetric cyanation have been developed, other routes to α -quaternary α -aryl amino acid derivatives have been limited.

Recently, we reported that the asymmetric Sommelet–Hauser rearrangement of *N*-benzylic glycine-derived ammonium salts **1** proceeds with high levels ($2S/2R = >20:1$) of diastereoselectivity to afford the optically active α -arylglycine esters **2** (Scheme 1).³ With this method, we have examined two routes to α -quaternary α -aryl amino acid esters **5** (Scheme 2). One route (path A) is the diastereoselective Stevens or Sommelet–Hauser rearrangement of the α -arylglycine-derived ammonium salt **3** which was prepared by quaternization of **2** with allylic or benzylic halides ($R'X$).^{4,5} The other route (path B) is the Sommelet–Hauser rearrangement of α -alkyl-substituted ammonium salts **4** which were prepared by quaternization of α -amino acid esters. We now report that the rearrangement of **3** or **4** with potassium *tert*-butoxide in THF provides the corresponding α -quaternary α -aryl amino acid derivatives **5** in high diastereoselectivities.



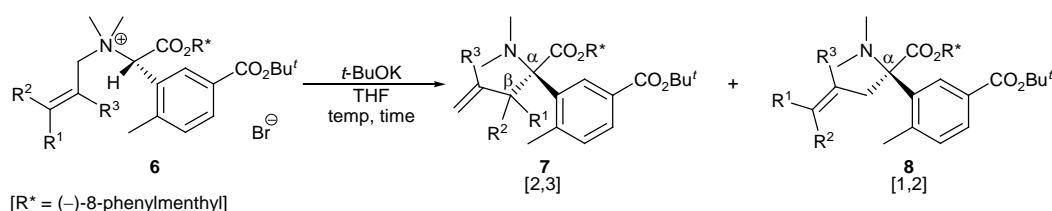
Scheme 1 Previous report of the asymmetric Sommelet–Hauser rearrangement of *N*-benzylic ammonium salts **1**



Scheme 2 Two routes to optically active α -quaternary α -aryl amino acid derivatives **5** via the diastereoselective Stevens and Sommelet–Hauser rearrangements

Results and discussion

First, we carried out the Stevens rearrangement of *N*-(*E*)-crotyl- α -arylglycine-derived ammonium salt **6a** ($E/Z = 85:15$) prepared by quaternization of **2** with (*E*)-crotyl bromide in quantitative yield.⁶ Treatment of **6a** with potassium *tert*-butoxide in THF at -40 °C (Table 1, entry 1), the corresponding [2,3] rearrangement product **7a** was obtained in 83% yield ($2R/2S = >20:1$,⁷ 9:1 dr for the β -position⁸), together with 17% of the [1,2] rearrangement product **8a** ($2R/2S = >20:1$, $E/Z = 1:1$),⁹ respectively. Next, we examined the rearrangement of a *N*-(*Z*)-crotyl derivative **6b** ($E/Z = 15:85$) under the same conditions as described above (entry 2). Interestingly, the yield of the [2,3] rearrangement product **7b** was decreased (52% yield, $2R/2S = >20:1$, 3:7 dr for the β -position), and the yield of the [1,2] rearrangement product **8b**¹⁰ was increased (42% yield, $2R/2S = >20:1$, $E/Z = 1:>20$). The [2,3] and [1,2] rearrangements proceeded stereospecifically. The diastereomer ratios of product **7** or **8** (β -position or E/Z) are determined by the E/Z ratio of the starting material **6a** or **6b**. To define the scope and limitations of the present method, we prepared a series of substrates **6c–6e** and carried out their reactions with potassium *tert*-butoxide. The rearrangement of *N*-methallyl- (entry 3, **6c**) and *N*-allyl

Table 1 Diastereoselective Stevens rearrangement of *N*-allylic α -aryl amino acid-derived ammonium salts **6**^a

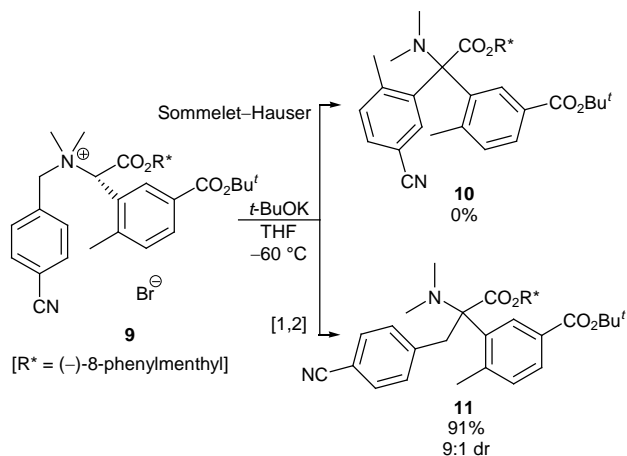
[R* = (-)-8-phenylmenthyl]

Entry	R ¹	R ²	R ³	a ^f	temp, time (°C, h)	yield (%) ^b	7		yield (%) ^b	8	
							dr (α) ^{c,d}	dr (β) ^{c,e}		dr (α) ^{c,d}	<i>E/Z</i> ^c
1	Me	H	H	a ^f	-40, 4	83	>20:1	9:1	17	>20:1	1:1
2	H	Me	H	b ^g	-40, 4	52	>20:1	3:7	42	>20:1	1:>20
3	H	H	Me	c	-40, 4	95	>20:1	–	0	–	–
4	H	H	H	d	-78, 1	91	>20:1	–	0	–	–
5	Ph	H	H	e	-78, 6	0	–	–	69	>20:1	>20:1

^a Reactions were conducted using 1.5 equiv. of *t*-BuOK. ^b Isolated yield. ^c The ratios were determined by ¹H NMR assay. ^d 2*R*/2*S*. ^e The absolute configuration was not determined. ^f *E/Z* = 85:15 mixture. ^g *E/Z* = 15:85 mixture.

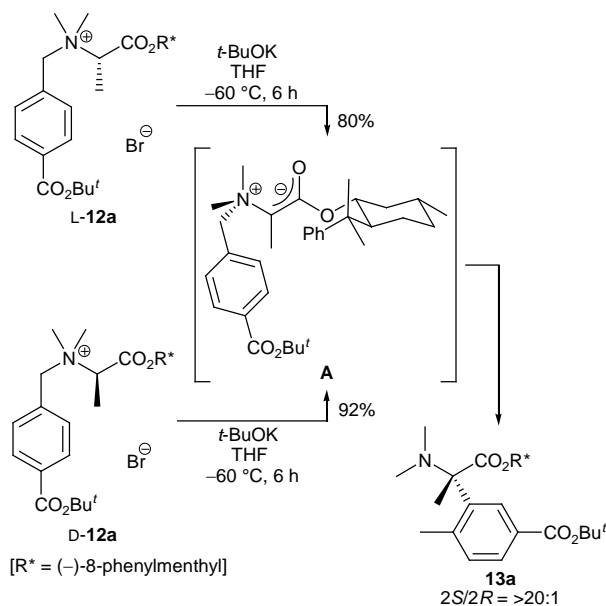
(entry 4, **6d**) derivatives provided the corresponding 5 rearrangement products **7c** and **7d** in excellent yields with equally high α -diastereoselectivities ($2R/2S = >20:1$). However, in the rearrangement of a *N*-(*E*)-cinnamyl derivative **6e** (entry 5) at -78°C , the [1,2] Stevens product **8e** was obtained in 69% yield exclusively with high α - and *E/Z*-selectivities ($2R/2S = >20:1$, *E/Z* = $>20:1$). The [2,3] Stevens product **7e** was not detected. The radical stabilization group (Ph) on the allylic substituent might accelerate the [1,2] Stevens rearrangement.

Next, we attempted the Sommelet–Hauser rearrangement of 15 *N*-benzylic α -aryl amino acid-derived ammonium salts **9** to produce α,α -diaryl amino acid derivative **10** (Scheme 3). Unfortunately, however, when the rearrangement of **9** with potassium *tert*-butoxide was carried out in THF at -60°C , the [1,2] Stevens rearrangement proceeded exclusively to give the 20 α -benzylic α -aryl amino acid ester **11** in 91% yield with reasonable α -diastereoselectivity (9:1 dr).¹¹ No detectable amount of the Sommelet–Hauser product **10** was observed.

**Scheme 3** Rearrangement of a *N*-benzylic α -aryl amino acid-derived ammonium salt **9**

To explore another synthetic route to optically active α -quaternary α -aryl amino acid derivatives, we prepared *N*-benzylic α -alkyl amino acid-derived ammonium salts **12a**

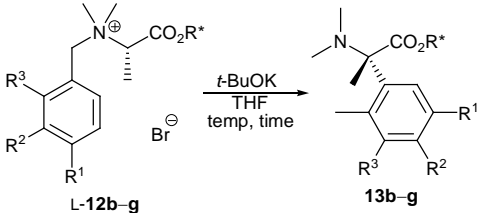
from L- and D-alanine and examined their Sommelet–Hauser 30 rearrangement (Scheme 4). The rearrangements of L-**12a** and D-**12a** in THF at -60°C were found to produce the same rearrangement product **13a** (α -arylalanine ester) in good yields (80% yield from L-**12a**; 92% yield from D-**12a**) with excellent α -diastereoselectivities ($2S/2R = >20:1$).⁷ The high 35 α -selectivity, though the exact origin is unclear at present, suggests that the rearrangement proceeds via the same intermediate **A** (ammonium ylide¹²) generated from ammonium salts L-**12a** and D-**12a** by deprotonation with potassium *tert*-butoxide. The (-)-8-phenylmenthyl moiety 40 would block the *Re*-face (front side of **A**) of the ammonium ylide, thus leading exclusively to the 2*S*-isomer of **13a**.

**Scheme 4** Diastereoselective Sommelet–Hauser rearrangement of *N*-benzylic L- and D- α -alanine-derived ammonium salts **12a**

45 The scope of substrates was further explored as shown in Table 2. The reactions of *para*- and *ortho*-cyano-*N*-benzylic ammonium salt **12b** and **12c** were found to afford the corresponding Sommelet–Hauser rearrangement product in good yields (entries 1, 2) with moderate α -

diastereoselectivities (9:1 dr for **13b**, 6:1 dr for **13c**). However, the rearrangement of *meta*-cyano ammonium salt **12d** proceeded with a high diastereoselectivity to produce 2,4-disubstituted regioisomer **13d**¹³ as an only detectable rearrangement product (entry 3, 82% yield, >20:1 dr). The reaction of *para*-methoxycarbonyl (**12e**) and trifluoromethyl (**12f**) derivatives also afforded the corresponding product **13e** (entry 4, 57% yield) or **13f** (entry 5, 98% yield) respectively with equally high diastereoselectivities (>20:1 dr). In the absence of an electron-withdrawing substituent on the aromatic ring such as **12g** (entries 6, 7), the reaction did not give the Sommelet–Hauser product **13g**. The [1,2] Stevens rearrangement product was obtained as an only detectable product.

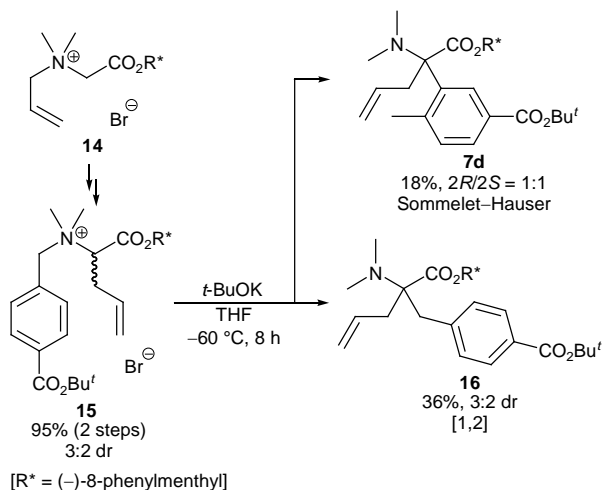
Table 2 Diastereoselective Sommelet–Hauser rearrangement of various types of *N*-benzylic α -alanine-derived ammonium salts **12b–12g**^a



[R* = (-)-8-phenylmenthyl]

Entry	R ¹	R ²	R ³		temp, time (°C, h)	yield ^b (%)	dr ^c (2 <i>S</i> /2 <i>R</i>)
1 ^d	CN	H	H	b	-60, 4	80	9:1
2	H	H	CN	c	-60, 4	82	6:1
3	H	CN	H	d	-60, 4	82	>20:1
4	COOMe	H	H	e	-60, 4	57	>20:1
5 ^d	CF ₃	H	H	f	-60, 8	98	>20:1
6	H	H	H	g	-60, 12	0 ^e	–
7	H	H	H	g	-40, 12	0 ^e	–

^a Reactions were conducted using 1.5 equiv. of *t*-BuOK. ^b Isolated yield. ^c The ratios were determined by ¹H NMR assay. ^d The reactions were carried out in THF–CH₂Cl₂ (2:1) because of the low solubility of the ammonium salts. ^e The corresponding [1,2] Stevens rearrangement product was obtained (19% yield for entry 6, 81% yield for entry 7) with no diastereoselectivities (2:1 dr). The spectroscopic data was noted in experimental section.



Scheme 5 Diastereoselective Sommelet–Hauser rearrangement of an α -allylglycine-derived ammonium salt **15**

Finally, we attempted the rearrangement of an α -allylglycine derivative **15** (3:2 dr mixture) prepared via the [2,3] Stevens rearrangement of **14** (Scheme 5). Unfortunately, however, the rearrangement did not proceed smoothly under the same conditions as described in Scheme 4. The Sommelet–Hauser rearrangement product **7d** and the [1,2] Stevens product **16** were obtained in 18% (2*R*/2*S* = 1:1) and 36% yield (3:2 dr), respectively.

Conclusions

We have shown that the Stevens rearrangement of *N*-allylic α -aryl amino acid-derived ammonium salts **6** and the Sommelet–Hauser rearrangement of *N*-benzylic α -alanine-derived ammonium salts **12** proceeded with remarkably high levels of diastereoselectivity. The scope and limitations of these two synthetic methods are defined. The present method provides new routes to optically active α -quaternary α -aryl amino acid derivatives, and expands the synthetic scope of the Sommelet–Hauser rearrangement.

Experimental

General

Infrared (IR) spectra were recorded on a HITACHI Infrared Spectrometer 270–30. ¹H and ¹³C NMR spectra were measured on a JEOL JMN–Excalibur (¹H: 270 MHz, ¹³C: 68 MHz) and a Varian UNITY plus–500SW (¹H: 500 MHz, ¹³C: 125 MHz) spectrometers. Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak. Specific rotations were recorded on a JASCO Polarimeter P–1010. For thin layer chromatography (TLC) analysis throughout this work, Merck TLC plates (silica gel 60F₂₅₄) were used. The products were purified by preparative column chromatography on silica gel (silica gel 60N, spherical neutral, KANTO Chemical Co., Inc., Japan). The elemental analyses were recorded on a Yanaco CHN order MT–3. Reactions involving air- or moisture-sensitive compounds were conducted in appropriate round-bottomed flask with a magnetic stirring bar under an atmosphere of dry argon. Tetrahydrofuran (THF) was purchased from KANTO Chemical Co., Inc., Japan as anhydrous solvent.

Representative procedure for the diastereoselective Stevens rearrangement of *N*-allylic α -aryl amino acid-derived ammonium salt

A solution of **6a** (136 mg, 0.212 mmol) in THF (2.1 mL) was cooled to –40 °C and treated with a 1.0 M THF solution of potassium *tert*-butoxide (0.32 mL, 0.32 mmol). The mixture was stirred for 4 h at the same temperature under an argon atmosphere. The resulting mixture was added to stirred ice-cold saturated aqueous ammonium chloride and the mixture was extracted with ether. The combined extracts were washed with saturated aqueous sodium hydrogen carbonate and brine, dried over sodium sulfate, and concentrated. Purification of the residue by chromatography on silica gel (hexane/ethyl acetate = 20:1 to 10:1 as eluent) gave **7a** (99 mg, 83% yield) as a white solid and **8a** (20 mg, 17% yield) as a white solid.

(2R)-2-(5'-tert-Butoxycarbonyl-2'-methylphenyl)-2-dimethyl-amino-3-methylpent-4-enoic acid (-)-8-phenylmenthol ester (7a)

white solid (Found: C, 77.2; H, 9.3; N, 2.2. Calc. for $C_{36}H_{51}NO_4$: C, 77.0; H, 9.15; N, 2.5%); mp 49–51 °C; $[\alpha]_{589}^{23}$ –30.9 (c 1.00 in $CHCl_3$); ν_{max} (film)/ cm^{-1} 3016, 2968, 2924, 2872, 2796, 1708, 1608, 1454, 1368, 1304, 1272, 1256, 1210, 1160, 1142, 1030, 978, 960, 914, 848, 758, 700; δ_H (270 MHz, $CDCl_3$, Me_4Si) 8.14 (1H, s, Ar-H), 7.72 (1H, dd, $J = 7.8$, 1.6 Hz, Ar-H), 7.36–7.19 (4H, m, Ar-H), 7.19–7.10 (2H, m, Ar-H), 5.78 (1H, ddd, $J = 17.3$, 10.0, 7.8 Hz, 4-H), 5.05–4.86 (3H, m, 5-H and COOCH), 3.30 (1H, dq, $J = 7.8$, 6.5 Hz, 3-H), 2.51 (3H, s, Ar- CH_3), 2.40–2.24 (1H, m, 8-Ph-Men-H), 2.34 (6H, s, $(CH_3)_2N$), 2.17–2.03 (1H, m, 8-Ph-Men-H), 1.64–0.75 (6H, m, 8-Ph-Men-H), 1.59 (9H, s, *t*-Bu), 1.37 (3H, s, 8-Ph-Men- CH_3), 1.28 (3H, s, 8-Ph-Men- CH_3), 0.87 (3H, d, $J = 7.6$ Hz, 8-Ph-Men- CH_3), 0.82 (3H, d, $J = 6.5$ Hz, 3- CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 167.8, 166.1, 150.8, 143.8, 140.0, 135.2, 133.6, 132.5, 128.0, 127.8, 127.3, 125.7, 125.4, 114.9, 80.4, 78.6, 50.4, 43.3, 40.9, 40.2, 39.9 (2C), 34.4, 31.5, 30.2, 28.3 (3C), 27.9, 23.7, 23.5, 22.0 (2C), 18.8.

(2R)-2-(5'-tert-Butoxycarbonyl-2'-methylphenyl)-2-dimethyl-aminohex-4-enoic acid (-)-8-phenylmenthol ester (8a)

E/Z = 1:1 mixture; white solid (Found: C, 76.7; H, 9.2; N, 2.4. Calc. for $C_{36}H_{51}NO_4$: C, 77.0; H, 9.15; N, 2.5%); ν_{max} (film)/ cm^{-1} 2924, 2870, 2792, 1710, 1608, 1452, 1390, 1366, 1304, 1254, 1208, 1160, 1136, 1092, 1012, 972, 895, 850, 762, 736, 700; δ_H (270 MHz, $CDCl_3$, Me_4Si) 8.24 (0.5H, d, $J = 1.9$ Hz, Ar- $H_{(Z)}$), 8.18 (0.5H, d, $J = 1.4$ Hz, Ar- $H_{(E)}$), 7.74–7.66 (1H, m, Ar-H), 7.39–7.21 (4H, m, Ar-H), 7.19–7.08 (2H, m, Ar-H), 5.31 (0.5H, dq, $J = 10.9$, 6.5 Hz, 5- $H_{(Z)}$), 5.15 (0.5H, dtd, $J = 10.9$, 6.5, 1.6 Hz, 4- $H_{(Z)}$), 5.07–4.89 (2H, m, 4- $H_{(E)}$, 5- $H_{(E)}$, and COOCH), 2.83 (0.5H, dd, $J = 16.1$, 6.5 Hz, 3- $H_{(Z)}$), 2.64 (0.5H, dd, $J = 16.7$, 4.9 Hz, 3- $H_{(E)}$), 2.35 (3H, s, $(CH_3)_2N_{(Z)}$), 2.33 (3H, s, $(CH_3)_2N_{(E)}$), 2.32 (1.5H, s, Ar- $CH_{3(Z)}$), 2.28 (1.5H, s, Ar- $CH_{3(E)}$), 2.26–2.10 (2.5H, m, 3-H and 8-Ph-Men-H), 2.01–1.89 (0.5H, m, 3- $H_{(E)}$ or 8-Ph-Men- $H_{(E)}$), 1.64–1.19 (6H, m, 8-Ph-Men-H and 6-H), 1.58 (9H, s, *t*-Bu), 1.46 (1.5H, s, 8-Ph-Men- $CH_{3(Z)}$), 1.39 (1.5H, s, 8-Ph-Men- $CH_{3(E)}$), 1.27 (1.5H, s, 8-Ph-Men- $CH_{3(Z)}$), 1.23 (1.5H, s, 8-Ph-Men- $CH_{3(E)}$), 1.15–0.75 (6H, m, 8-Ph-Men-H and 8-Ph-Men- CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 167.5 $_{(E)}$, 167.4 $_{(Z)}$, 166.3, 151.3 $_{(E)}$, 151.1 $_{(Z)}$, 141.1 $_{(E)}$, 141.0 $_{(Z)}$, 139.0 $_{(E)}$, 138.9 $_{(Z)}$, 131.7, 130.8 $_{(E)}$, 130.7 $_{(Z)}$, 128.6 $_{(Z)}$, 128.5 $_{(E)}$, 128.1, 127.8 $_{(E)}$, 127.4 $_{(Z)}$, 127.3 $_{(E)}$, 125.7 $_{(Z)}$, 125.6 $_{(E)}$, 125.42 $_{(Z)}$, 125.40 $_{(Z)}$, 125.37 $_{(E)}$, 124.8 $_{(Z)}$, 80.4 $_{(Z)}$, 80.3 $_{(E)}$, 77.4 $_{(Z)}$, 77.2 $_{(E)}$, 72.0 $_{(E)}$, 71.7 $_{(Z)}$, 50.2 $_{(Z)}$, 49.9 $_{(E)}$, 44.2 $_{(Z)}$, 44.1 $_{(E)}$, 40.3 $_{(Z)}$, 40.1 $_{(E)}$, 39.8 $_{(Z)}$, 39.7 $_{(E)}$, 35.7 $_{(E)}$, 34.6 $_{(E)}$, 34.5 $_{(Z)}$, 34.1 $_{(E)}$, 31.5 $_{(Z)}$, 30.3 $_{(Z)}$, 29.6 $_{(Z)}$, 28.3 $_{(E)}$, 28.2, 27.5 $_{(Z)}$, 27.4 $_{(E)}$, 25.6 $_{(E)}$, 24.4 $_{(Z)}$, 22.3, 21.9, 18.0 $_{(E)}$, 12.8 $_{(Z)}$.

(2R)-2-(5'-tert-Butoxycarbonyl-2'-methylphenyl)-2-dimethyl-amino-3-methylpent-4-enoic acid (-)-8-phenylmenthol ester (7b)

3:7 mixture of stereoisomers; white solid (Found: C, 77.0; H, 9.4; N, 2.4. Calc. for $C_{36}H_{51}NO_4$: C, 77.0; H, 9.15; N, 2.5%); ν_{max} (film)/ cm^{-1} 3056, 2964, 2868, 2796, 1706, 1608, 1454, 1392, 1368, 1300, 1256, 1206, 1160, 1140, 1094, 1030, 978,

910, 850, 762, 732, 700; δ_H (270 MHz, $CDCl_3$, Me_4Si) 8.16 (1H, s, Ar-H), 7.76–7.68 (1H, m, Ar-H), 7.34–7.06 (6H, m, Ar-H), 5.78 (0.3H, ddd, $J = 17.3$, 10.1, 7.8 Hz, 4-H), 5.61 (0.7H, ddd, $J = 17.0$, 10.7, 6.8 Hz, 4-H), 5.06–4.80 (3H, m, 5-H and COOCH), 3.40–3.24 (1H, m, 3-H), 2.51 (0.9H, s, Ar- CH_3), 2.48 (2.1H, s, Ar- CH_3), 2.41–2.24 (1H, m, 8-Ph-Men-H), 2.34 (1.8H, s, $(CH_3)_2N$), 2.32 (4.2H, s, $(CH_3)_2N$), 2.17–1.95 (1H, m, 8-Ph-Men-H), 1.64–0.72 (6H, m, 8-Ph-Men-H), 1.60 (6.3H, s, *t*-Bu), 1.59 (2.7H, s, *t*-Bu), 1.37 (0.9H, s, 8-Ph-Men- CH_3), 1.28 (0.9H, s, 8-Ph-Men- CH_3), 1.23 (2.1H, s, 8-Ph-Men- CH_3), 1.20 (2.1H, s, 8-Ph-Men- CH_3), 0.91 (2.1H, d, $J = 7.0$ Hz, 3- CH_3 or 8-Ph-Men- CH_3), 0.87 (3H, d, $J = 7.6$ Hz, 8-Ph-Men- CH_3), 0.82 (0.9H, d, $J = 6.8$ Hz, 3- CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 168.4 (0.7C), 167.8 (0.3C), 166.2 (0.7C), 166.1 (0.3C), 150.7 (0.3C), 150.5 (0.7C), 143.8 (0.3C), 143.6 (0.7C), 140.1 (0.7C), 140.0 (0.3C), 135.2 (0.3C), 135.0 (0.7C), 133.6 (1.0C), 132.5 (0.3C), 132.3 (0.7C), 128.0 (0.6C), 127.9 (1.4C), 127.8 (0.3C), 127.5 (0.7C), 127.25 (0.3C), 127.19 (0.7C), 125.64 (0.6C), 125.58 (1.4C), 125.3 (0.3C), 125.2 (0.7C), 115.8 (0.7C), 114.9 (0.3C), 80.35 (0.3C), 80.31 (0.7C), 78.6 (0.3C), 78.0 (0.7C), 50.3 (0.3C), 50.2 (0.7C), 43.2 (0.3C), 42.2 (0.6C), 41.5 (0.7C), 40.9 (0.3C), 40.2 (1.0C), 40.1 (0.7C), 39.8 (0.7C), 34.4 (0.3C), 34.1 (0.7C), 31.5 (0.7C), 31.4 (0.3C), 31.1 (0.7C), 30.3 (0.7C), 30.1 (0.3C), 28.3 (2.1C), 28.2 (0.9C), 27.9 (0.3C), 27.5 (0.7C), 23.8 (0.7C), 23.7 (0.3C), 23.5 (0.3C), 23.4 (0.7C), 22.0 (1.4C), 21.9 (0.6C), 18.7 (0.3C), 14.6 (0.7C).

(2R, 4Z)-2-(5'-tert-Butoxycarbonyl-2'-methylphenyl)-2-dimethylaminohex-4-enoic acid (-)-8-phenylmenthol ester (8b)

colorless crystals (Found: C, 77.2; H, 9.4; N, 2.4. Calc. for $C_{36}H_{51}NO_4$: C, 77.0; H, 9.15; N, 2.5%); mp 147–149 °C; $[\alpha]_{589}^{24}$ –11.6 (c 1.00 in $CHCl_3$); ν_{max} (film)/ cm^{-1} 2952, 2924, 2868, 2792, 1710, 1608, 1454, 1368, 1308, 1262, 1210, 1160, 1138, 1014, 978, 958, 850, 762, 736, 700; δ_H (270 MHz, $CDCl_3$, Me_4Si) 8.24 (1H, d, $J = 1.9$ Hz, Ar-H), 7.71 (1H, dd, $J = 7.7$, 1.9 Hz, Ar-H), 7.43–7.25 (4H, m, Ar-H), 7.22–7.10 (2H, m, Ar-H), 5.31 (1H, dq, $J = 10.9$, 6.5 Hz, 5-H), 5.21–5.09 (1H, m, 4-H), 4.99 (1H, td, $J = 10.5$, 3.8 Hz, COOCH), 2.83 (1H, dd, $J = 16.1$, 6.5 Hz, 3-H), 2.35 (6H, s, $(CH_3)_2N$), 2.32 (3H, s, Ar- CH_3), 2.26–2.10 (3H, m, 3-H and 8-Ph-Men-H), 1.64–1.21 (3H, m, 8-Ph-Men-H), 1.58 (9H, s, *t*-Bu), 1.46 (3H, s, 8-Ph-Men- CH_3), 1.28 (3H, d, $J = 6.5$ Hz, 6-H), 1.27 (3H, s, 8-Ph-Men- CH_3), 1.15–0.75 (3H, m, 8-Ph-Men-H), 0.88 (3H, d, $J = 5.9$ Hz, 8-Ph-Men- CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 167.4, 166.4, 151.1, 141.1, 138.9, 131.7, 130.8, 128.6, 128.1, 127.5, 125.7, 125.43, 125.41, 124.8, 80.4, 77.4, 71.7, 50.2, 44.2, 40.3, 39.8, 34.5, 31.5, 30.3, 29.6, 28.2, 27.5, 24.4, 22.3, 21.9, 12.8.

(2R)-2-(5'-tert-Butoxycarbonyl-2'-methylphenyl)-2-dimethyl-amino-4-methylpent-4-enoic acid (-)-8-phenylmenthol ester (7c)

white solid (Found: C, 77.1; H, 9.45; N, 2.4. Calc. for $C_{36}H_{51}NO_4$: C, 77.0; H, 9.15; N, 2.5%); mp 57–59 °C; $[\alpha]_{589}^{24}$ 37.1 (c 1.00 in $CHCl_3$); ν_{max} (film)/ cm^{-1} 3056, 2964, 2792, 1708, 1608, 1454, 1392, 1368, 1304, 1264, 1206, 1160, 1136, 1096, 1032, 992, 954, 896, 850, 762, 736, 700; δ_H (270 MHz, $CDCl_3$, Me_4Si) 8.17 (1H, d, $J = 1.9$ Hz, Ar-H), 7.68 (1H, dd, $J = 7.8$, 1.9 Hz, Ar-H), 7.40–7.22 (4H, m, Ar-H), 7.16–7.06 (2H,

m, Ar-H), 4.96 (1H, td, $J = 10.5$, 4.1 Hz, COOCH), 4.44 (1H, s, 5-H), 4.17 (1H, s, 5-H), 2.64 (1H, d, $J = 15.4$ Hz, 3-H), 2.39 (6H, s, (CH₃)₂N), 2.30-2.17 (2H, m, 8-Ph-Men-H), 2.28 (3H, s, Ar-CH₃), 1.87 (1H, d, $J = 15.4$ Hz, 3-H), 1.66-1.20 (3H, m, 8-Ph-Men-H), 1.57 (9H, s, *t*-Bu), 1.44 (3H, s, 4-CH₃ or 8-Ph-Men-CH₃), 1.43 (3H, s, 4-CH₃ or 8-Ph-Men-CH₃), 1.23 (3H, s, 8-Ph-Men-CH₃), 1.17-0.83 (3H, m, 8-Ph-Men-H), 0.89 (3H, d, $J = 6.2$ Hz, 8-Ph-Men-CH₃); δ_{C} (68 MHz, CDCl₃, CHCl₃) 167.1, 166.3, 151.4, 141.0, 140.9, 138.6, 131.4, 131.2, 128.4, 128.2, 127.2, 125.5, 125.3, 115.1, 80.3, 77.5, 72.9, 49.7, 44.2, 40.4, 40.0, 38.2, 34.6, 31.5, 28.2, 27.7, 27.3, 26.5, 24.1, 22.5, 21.9.

(2R)-2-(5'-tert-Butoxycarbonyl-2'-methylphenyl)-2-dimethylaminopent-4-enoic acid (-)-8-phenylmenthol ester [(R)-7d]

white solid (Found: C, 77.0; H, 9.15; N, 2.4. Calc. for C₃₅H₄₉NO₄: C, 76.7; H, 9.0; N, 2.6%); mp 140–143 °C; $[\alpha]_{589}^{24}$ 12.4 (*c* 1.00 in CHCl₃); ν_{max} (film)/cm⁻¹ 3064, 2952, 2872, 2796, 1712, 1608, 1454, 1392, 1368, 1304, 1256, 1218, 1162, 1140, 990, 956, 912, 850, 756, 700; δ_{H} (270 MHz, CDCl₃, Me₄Si) 8.21 (1H, d, $J = 1.9$ Hz, Ar-H), 7.71 (1H, dd, $J = 7.8$, 1.9 Hz, Ar-H), 7.40-7.20 (4H, m, Ar-H), 7.18-7.08 (2H, m, Ar-H), 5.38 (1H, ddt, $J = 17.0$, 10.5, 6.8 Hz, 4-H), 4.96 (1H, td, $J = 10.5$, 4.2 Hz, COOCH), 4.81 (1H, dd, $J = 10.5$, 1.4 Hz, 5-H), 4.74 (1H, dd, $J = 17.0$, 1.4 Hz, 5-H), 2.61 (1H, dd, $J = 15.8$, 7.0 Hz, 3-H), 2.40-2.12 (2H, m, 8-Ph-Men-H), 2.33 (6H, s, (CH₃)₂N), 2.28 (3H, s, Ar-CH₃), 1.97 (1H, dd, $J = 15.8$, 6.2 Hz, 3-H), 1.67-0.78 (6H, m, 8-Ph-Men-H), 1.58 (9H, s, *t*-Bu), 1.40 (3H, s, 8-Ph-Men-CH₃), 1.22 (3H, s, 8-Ph-Men-CH₃), 0.89 (3H, d, $J = 5.9$ Hz, 8-Ph-Men-CH₃); δ_{C} (68 MHz, CDCl₃, CHCl₃) 167.3, 166.3, 151.4, 141.1, 138.9, 133.6, 131.8, 130.6, 128.6, 128.2, 127.5, 125.5, 125.3, 117.1, 80.4, 77.3, 71.7, 49.8, 44.1, 40.0, 39.7, 36.7, 34.6, 31.5, 28.2, 27.5, 27.3, 26.5, 22.3, 21.9.

(2S)-2-(5'-tert-Butoxycarbonyl-2'-methylphenyl)-2-dimethylaminopent-4-enoic acid (-)-8-phenylmenthol ester [(S)-7d]

white solid (Found: C, 77.0; H, 9.1; N, 2.6. Calc. for C₃₅H₄₉NO₄: C, 76.7; H, 9.0; N, 2.6%); mp 45–47 °C; $[\alpha]_{589}^{22}$ -36.1 (*c* 1.00 in CHCl₃); ν_{max} (film)/cm⁻¹ 3052, 2956, 2924, 2868, 2788, 1708, 1610, 1454, 1390, 1368, 1302, 1278, 1254, 1190, 1164, 1138, 982, 952, 912, 850, 760, 736, 700; δ_{H} (270 MHz, CDCl₃, Me₄Si) 7.90 (1H, d, $J = 1.6$ Hz, Ar-H), 7.69 (1H, dd, $J = 7.8$, 1.6 Hz, Ar-H), 7.28-7.07 (6H, m, Ar-H), 5.52 (1H, ddt, $J = 16.9$, 10.4, 6.9 Hz, 4-H), 5.00 (1H, td, $J = 10.4$, 3.8 Hz, COOCH), 4.79 (1H, d, $J = 16.9$ Hz, 5-H), 4.77 (1H, d, $J = 10.4$ Hz, 5-H), 2.82-2.61 (2H, m, 3-H), 2.51 (3H, s, Ar-H), 2.48-2.26 (1H, m, 8-Ph-Men-H), 2.37 (6H, s, (CH₃)₂N), 2.05-1.91 (1H, m, 8-Ph-Men-H), 1.64-0.67 (6H, m, 8-Ph-Men-H), 1.57 (9H, s, *t*-Bu), 1.27 (3H, s, 8-Ph-Men-CH₃), 1.17 (3H, s, 8-Ph-Men-CH₃), 0.90 (3H, d, $J = 6.2$ Hz, 8-Ph-Men-CH₃); δ_{C} (68 MHz, CDCl₃, CHCl₃) 172.0, 165.7, 151.1, 142.1, 138.5, 134.9, 132.2, 130.4, 128.9, 128.0, 127.6, 125.4, 125.2, 116.3, 80.5, 77.6, 74.3, 50.6, 42.1, 40.4, 40.2, 39.5, 34.5, 31.5, 29.7, 28.2, 27.6, 23.5, 21.8, 21.6.

(2R, 4E)-2-(5'-tert-Butoxycarbonyl-2'-methylphenyl)-2-dimethylamino-5-phenylpent-4-enoic acid (-)-8-phenylmenthol ester (8e)

white solid (Found: C, 78.9; H, 8.8; N, 2.0. Calc. for C₄₁H₅₃NO₄: C, 78.9; H, 8.6; N, 2.25%); mp 61–64 °C; $[\alpha]_{589}^{24}$ 82.0 (*c* 1.00 in CHCl₃); ν_{max} (film)/cm⁻¹ 3020, 2964, 2868, 2796, 1708, 1606, 1494, 1452, 1392, 1368, 1306, 1256, 1214, 1160, 1136, 966, 900, 848, 756, 698; δ_{H} (270 MHz, CDCl₃, Me₄Si) 8.25 (1H, d, $J = 1.6$ Hz, Ar-H), 7.70 (1H, dd, $J = 7.8$, 1.6 Hz, Ar-H), 7.40-7.08 (11H, m, Ar-H), 5.99 (1H, d, $J = 15.9$ Hz, 5-H), 5.79 (1H, dt, $J = 15.9$, 6.5 Hz, 4-H), 4.98 (1H, td, $J = 10.5$, 4.1 Hz, COOCH), 2.76 (1H, dd, $J = 15.7$, 6.5 Hz, 3-H), 2.36 (6H, s, (CH₃)₂N), 2.31 (3H, s, Ar-CH₃), 2.27-2.16 (2H, m, 8-Ph-Men-H), 2.03 (1H, dd, $J = 15.7$, 6.5 Hz, 3-H), 1.67-0.82 (6H, m, 8-Ph-Men-H), 1.54 (9H, s, *t*-Bu), 1.42 (3H, s, 8-Ph-Men-CH₃), 1.24 (3H, s, 8-Ph-Men-CH₃), 0.90 (3H, d, $J = 7.0$ Hz, 8-Ph-Men-CH₃); δ_{C} (68 MHz, CDCl₃, CHCl₃) 167.2, 166.2, 151.5, 141.0, 138.8, 137.8, 132.2, 131.9, 130.6, 128.6, 128.3, 128.2, 127.6, 126.8, 125.9, 125.8, 125.5, 125.4, 80.4, 77.4, 72.1, 49.8, 44.1, 40.0, 39.8, 35.8, 34.6, 31.5, 28.2, 27.5, 27.3, 26.5, 22.3, 21.9.

2-(5'-tert-Butoxycarbonyl-2'-methylphenyl)-3-(4''-cyano-phenyl)-2-dimethylaminopropionic acid (-)-8-phenylmenthol ester [11 (major isomer)]

white solid (Found: C, 77.1; H, 8.4; N, 4.2. Calc. for C₄₀H₅₀N₂O₄: C, 77.1; H, 8.1; N, 4.5%); mp 88–91 °C; $[\alpha]_{589}^{23}$ 126.1 (*c* 1.00 in CHCl₃); ν_{max} (film)/cm⁻¹ 3052, 2960, 2868, 2796, 2224, 1710, 1608, 1454, 1392, 1368, 1304, 1266, 1208, 1178, 1160, 1130, 1000, 954, 898, 850, 824, 762, 734, 700; δ_{H} (270 MHz, CDCl₃, Me₄Si) 7.57 (1H, dd, $J = 7.8$, 1.6 Hz, Ar-H), 7.431 (1H, d, $J = 1.6$ Hz, Ar-H), 7.430 (2H, d, $J = 7.8$ Hz, Ar-H), 7.28-7.16 (4H, m, Ar-H), 7.04 (1H, d, $J = 8.1$ Hz, Ar-H), 6.92 (1H, t, $J = 7.2$ Hz, Ar-H), 6.58 (2H, d, $J = 7.8$ Hz, Ar-H), 5.01 (1H, td, $J = 10.5$, 3.8 Hz, COOCH), 3.03 (1H, d, $J = 15.1$ Hz, CH₂Ar), 2.47-2.21 (2H, m, CH₂Ar and 8-Ph-Men-H), 2.40 (6H, s, (CH₃)₂N), 2.15 (3H, s, Ar-CH₃), 1.87-1.67 (3H, m, 8-Ph-Men-H), 1.51 (9H, s, *t*-Bu), 1.47 (3H, s, 8-Ph-Men-CH₃), 1.33-0.85 (4H, m, 8-Ph-Men-H), 1.20 (3H, s, 8-Ph-Men-CH₃), 0.94 (3H, d, $J = 6.2$ Hz, 8-Ph-Men-CH₃); δ_{C} (68 MHz, CDCl₃, CHCl₃) 167.0, 165.6, 151.9, 142.7, 141.0-140.7 (m), 137.1, 131.6, 131.3, 131.1, 130.7, 128.3, 128.2, 127.4, 125.4, 125.3, 119.0, 109.5, 80.4, 77.8, 49.1, 43.9, 40.28, 40.23, 39.7, 36.9-36.6 (m), 34.6, 31.5, 29.4, 28.1, 26.9, 24.9, 22.1, 22.0.

2-(5'-tert-Butoxycarbonyl-2'-methylphenyl)-3-(4''-cyano-phenyl)-2-dimethylaminopropionic acid (-)-8-phenylmenthol ester [11 (minor isomer)]

white solid (The elemental analysis was not performed due to little amount.); mp 65–68 °C; $[\alpha]_{589}^{23}$ -55.9 (*c* 1.00 in CHCl₃); ν_{max} (film)/cm⁻¹ 3048, 2952, 2920, 2792, 2224, 1708, 1608, 1494, 1456, 1392, 1368, 1300, 1266, 1178, 1132, 1050, 1002, 952, 930, 906, 848, 762, 736, 700; δ_{H} (270 MHz, CDCl₃, Me₄Si) 7.60 (1H, dd, $J = 7.8$, 1.6 Hz, Ar-H), 7.43 (1H, s, Ar-H), 7.26 (2H, d, $J = 8.1$ Hz, Ar-H), 7.20-7.10 (4H, m, Ar-H), 7.09-6.96 (1H, m, Ar-H), 7.00 (1H, d, $J = 7.8$ Hz, Ar-H), 6.77 (2H, d, $J = 8.1$ Hz, Ar-H), 4.91 (1H, td, $J = 10.4$, 3.8 Hz, COOCH), 3.27 (1H, d, $J = 13.8$ Hz, CH₂Ar), 3.11 (1H, d, $J = 13.8$ Hz, CH₂Ar), 2.62-2.51 (1H, m, 8-Ph-Men-H), 2.45 (6H, s, (CH₃)₂N), 2.16 (3H, s, Ar-CH₃), 2.12-1.98 (1H, m, 8-Ph-Men-H), 1.64-1.44 (2H, m, 8-Ph-Men-H), 1.52 (9H, s, *t*-Bu), 1.37-

0.76 (4H, m, 8-Ph-Men-H), 1.21 (3H, s, 8-Ph-Men-CH₃), 1.05 (3H, s, 8-Ph-Men-CH₃), 0.93 (3H, d, *J* = 5.9 Hz, 8-Ph-Men-CH₃); δ_{C} (68 MHz, CDCl₃, CHCl₃) 169.4, 165.2, 151.2, 143.2, 136.8, 132.2, 131.7, 131.0, 130.7, 128.8, 128.5, 128.0, 127.7, 125.3, 125.2, 119.1, 109.6, 80.7, 78.9, 50.9, 42.3, 41.8, 40.0, 34.6, 31.6, 28.9, 28.13, 28.10, 27.8, 26.9, 24.0, 21.9, 20.9.

Representative procedure for the diastereoselective Sommelet–Hauser rearrangement of *N*-benzylic α -alkyl amino acid-derived ammonium salt

A solution of L-12a (97 mg, 0.16 mmol) in THF (1.6 mL) was cooled to -60°C and treated with a 1.0 M THF solution of potassium *tert*-butoxide (0.27 mL, 0.27 mmol). The mixture was stirred for 6 h at the same temperature under an argon atmosphere. The resulting mixture was added to stirred ice-cold saturated aqueous ammonium chloride and the mixture was extracted with ether. The combined extracts were washed with saturated aqueous sodium hydrogen carbonate and brine, dried over sodium sulfate, and concentrated. Purification of the residue by chromatography on silica gel (dichloromethane/methanol = 30:1 to 10:1 as eluent) gave 13a (67 mg, 80% yield) as a white solid.

(2*S*)-2-(5'-*tert*-Butoxycarbonyl-2'-methylphenyl)-2-dimethylaminopropionic acid (–)-8-phenylmenthol ester (13a)

white solid (Found: C, 76.2; H, 9.2; N, 2.55. Calc. for C₃₃H₄₇NO₄: C, 76.0; H, 9.1; N, 2.7%); mp 41–44 $^{\circ}\text{C}$; $[\alpha]_{589}^{23}$ 24.5 (*c* 1.00 in CHCl₃); ν_{max} (film)/cm⁻¹ 2952, 2784, 1708, 1608, 1452, 1392, 1368, 1304, 1276, 1244, 1222, 1166, 1142, 1086, 1050, 976, 954, 918, 848, 752, 700; δ_{H} (270 MHz, CDCl₃, Me₄Si) 7.94 (1H, d, *J* = 1.6 Hz, Ar-H), 7.73 (1H, dd, *J* = 7.7, 1.6 Hz, Ar-H), 7.30–7.20 (4H, m, Ar-H), 7.18–7.10 (2H, m, Ar-H), 4.91 (1H, td, *J* = 10.5, 4.6 Hz, COOCH), 2.61 (3H, s, Ar-CH₃), 2.24 (6H, s, (CH₃)₂N), 1.94–1.74 (2H, m, 8-Ph-Men-H), 1.60 (9H, s, *t*-Bu), 1.53–1.17 (3H, m, 8-Ph-Men-H), 1.44 (3H, s, 8-Ph-Men-CH₃), 1.22 (6H, s, 3-H and 8-Ph-Men-CH₃), 1.02–0.83 (2H, m, 8-Ph-Men-H), 0.77 (3H, d, *J* = 6.2 Hz, 8-Ph-Men-CH₃), 0.68 (1H, td, *J* = 12.2, 11.1 Hz, 8-Ph-Men-H); δ_{C} (68 MHz, CDCl₃, CHCl₃) 172.4, 165.9, 151.0, 143.4, 140.4, 132.3, 129.2, 128.9, 128.0, 127.9, 125.6, 125.3, 80.6, 76.0, 70.7, 49.9, 41.1, 40.1, 39.8, 34.3, 31.2, 29.2, 28.2, 27.3, 24.5, 21.7, 21.3, 16.7.

2-(5'-Cyano-2'-methylphenyl)-2-dimethylaminopropionic acid (–)-8-phenylmenthol ester (13b)

(2*S*)/(2*R*) = 9:1 mixture; colorless gum (Found: C, 78.2; H, 8.8; N, 6.0. Calc. for C₂₉H₃₈N₂O₂: C, 78.0; H, 8.6; N, 6.3%); ν_{max} (film)/cm⁻¹ 2948, 2868, 2784, 2224, 1718, 1600, 1488, 1444, 1370, 1226, 1204, 1162, 1086, 1048, 974, 952, 904, 820, 764, 732, 698; δ_{H} (270 MHz, CDCl₃, Me₄Si) 7.87 (0.1H, d, *J* = 1.6 Hz, Ar-H), 7.59 (0.9H, d, *J* = 1.6 Hz, Ar-H), 7.42 (1H, dd, *J* = 7.8, 1.6 Hz, Ar-H), 7.33–7.09 (6H, m, Ar-H), 4.88 (1H, td, *J* = 10.5, 4.3 Hz, COOCH), 2.61 (2.7H, s, Ar-CH₃), 2.45 (0.3H, s, Ar-CH₃), 2.29 (0.6H, s, (CH₃)₂N), 2.23 (5.4H, s, (CH₃)₂N), 2.14–2.00 (0.2H, m, 8-Ph-Men-H), 2.00–1.85 (0.9H, m, 8-Ph-Men-H), 1.79–1.67 (0.9H, m, 8-Ph-Men-H), 1.56–0.83 (5H, m, 8-Ph-Men-H), 1.34 (3H, s, 8-Ph-Men-CH₃), 1.19 (6H, s, 3-H and 8-Ph-Men-CH₃), 0.78 (3H, d, *J* = 6.5 Hz, 8-Ph-Men-CH₃), 0.66 (1H, td, *J* = 12.0, 11.1 Hz, 8-Ph-Men-H); δ_{C}

(68 MHz, CDCl₃, CHCl₃) 171.6, 150.8, 144.2, 141.8, 133.1, 131.7, 130.4, 128.1, 125.5, 125.3, 119.2, 109.4, 76.5, 70.5, 49.7, 41.1, 40.0, 39.7, 34.2, 31.2, 28.4, 27.2, 25.2, 21.7, 21.6, 16.3.

2-(3'-Cyano-2'-methylphenyl)-2-dimethylaminopropionic acid (–)-8-phenylmenthol ester (13c)

(2*S*)/(2*R*) = 6:1 mixture; colorless gum (Found: C, 77.7; H, 8.8; N, 6.1. Calc. for C₂₉H₃₈N₂O₂: C, 78.0; H, 8.6; N, 6.3%); ν_{max} (film)/cm⁻¹ 3052, 2948, 2868, 2784, 2220, 1716, 1598, 1440, 1370, 1264, 1224, 1182, 1154, 1110, 1088, 1048, 974, 908, 846, 764, 734, 700; δ_{H} (270 MHz, CDCl₃, Me₄Si) 7.76 (0.14H, d, *J* = 8.1 Hz, Ar-H), 7.56–7.44 (1.86H, m, Ar-H), 7.33–7.06 (6H, m, Ar-H), 4.89 (1H, td, *J* = 10.5, 4.3 Hz, COOCH), 2.81 (2.58H, s, Ar-CH₃), 2.62 (0.42H, s, Ar-CH₃), 2.28 (0.84H, s, (CH₃)₂N), 2.25 (5.16H, s, (CH₃)₂N), 2.14–1.96 (2.28H, m, 8-Ph-Men-H), 1.95–1.74 (1.72H, m, 8-Ph-Men-H), 1.62–0.83 (5H, m, 8-Ph-Men-H), 1.39 (3H, s, 8-Ph-Men-CH₃), 1.20 (3H, s, 3-H or 8-Ph-Men-CH₃), 1.19 (3H, s, 3-H or 8-Ph-Men-CH₃), 0.80 (3H, d, *J* = 6.2 Hz, 8-Ph-Men-CH₃), 0.69 (1H, q, *J* = 11.5 Hz, 8-Ph-Men-H); δ_{C} (68 MHz, CDCl₃, CHCl₃) 171.9, 150.8, 142.2, 142.1, 132.0, 131.7, 128.1, 125.9, 125.5, 125.3, 118.6, 115.4, 76.7, 70.8, 49.9, 40.0, 39.8, 39.7, 34.2, 31.2, 28.8, 27.3, 24.7, 21.8, 19.0, 17.3.

(2*S*)-2-(4'-Cyano-2'-methylphenyl)-2-dimethylaminopropionic acid (–)-8-phenylmenthol ester (13d)

colorless gum (Found: C, 78.3; H, 8.7; N, 6.1. Calc. for C₂₉H₃₈N₂O₂: C, 78.0; H, 8.6; N, 6.3%); $[\alpha]_{589}^{25}$ –19.6 (*c* 1.00 in CHCl₃); ν_{max} (film)/cm⁻¹ 2948, 2868, 2784, 2224, 1714, 1600, 1492, 1444, 1368, 1264, 1222, 1178, 1090, 1046, 974, 952, 886, 844, 758, 734, 698; δ_{H} (500 MHz, DMSO-*d*₆, Me₄Si) 7.65 (1H, d, *J* = 8.5 Hz, Ar-H), 7.63 (1H, s, Ar-H), 7.44 (1H, d, *J* = 8.5 Hz, Ar-H), 7.30–7.19 (4H, m, Ar-H), 7.13 (1H, t, *J* = 6.5 Hz, Ar-H), 4.76 (1H, td, *J* = 10.3, 4.0 Hz, COOCH), 2.51 (3H, s, Ar-CH₃), 2.16 (6H, s, (CH₃)₂N), 1.90 (1H, td, *J* = 11.3, 3.0 Hz, 8-Ph-Men-H), 1.72–1.64 (1H, m, 8-Ph-Men-H), 1.48–1.41 (1H, m, 8-Ph-Men-H), 1.40–1.20 (2H, m, 8-Ph-Men-H), 1.34 (3H, s, 8-Ph-Men-CH₃), 1.14 (3H, s, 3-H or 8-Ph-Men-CH₃), 1.13 (3H, s, 3-H or 8-Ph-Men-CH₃), 0.99–0.89 (1H, m, 8-Ph-Men-H), 0.75 (3H, d, *J* = 6.5 Hz, 8-Ph-Men-CH₃), 0.73–0.64 (2H, m, 8-Ph-Men-H); δ_{C} (68 MHz, CDCl₃, CHCl₃) 171.6, 150.8, 145.9, 139.5, 135.6, 129.2, 128.5, 128.1, 125.5, 125.3, 118.8, 110.9, 76.6, 70.9, 49.8, 41.1, 40.0, 39.7, 34.2, 31.2, 28.8, 27.3, 24.8, 21.7, 21.1, 16.9.

(2*S*)-2-Dimethylamino-2-(5'-methoxycarbonyl-2'-methylphenyl)propionic acid (–)-8-phenylmenthol ester (13e)

colorless gum (Found: C, 75.4; H, 8.8; N, 2.9. Calc. for C₃₀H₄₁NO₄: C, 75.1; H, 8.6; N, 2.9%); $[\alpha]_{589}^{25}$ 11.2 (*c* 1.00 in CHCl₃); ν_{max} (film)/cm⁻¹ 3048, 2948, 2780, 1720, 1608, 1572, 1492, 1434, 1370, 1296, 1266, 1242, 1218, 1172, 1108, 1050, 972, 906, 834, 756, 698; δ_{H} (270 MHz, CDCl₃, Me₄Si) 7.93 (1H, s, Ar-H), 7.81 (1H, dd, *J* = 8.0, 1.6 Hz, Ar-H), 7.31–7.10 (6H, m, Ar-H), 4.94 (1H, td, *J* = 10.5, 4.6 Hz, COOCH), 3.90 (3H, s, COOCH₃), 2.63 (3H, s, Ar-CH₃), 2.26 (6H, s, (CH₃)₂N), 1.98–1.81 (2H, m, 8-Ph-Men-H), 1.56–1.15 (3H, m, 8-Ph-Men-H), 1.44 (3H, s, 8-Ph-Men-CH₃), 1.23 (6H, s, 3-H and 8-Ph-Men-CH₃), 1.07–0.60 (3H, m, 8-Ph-Men-H), 0.80

(3H, d, $J = 6.2$ Hz, 8-Ph-Men-CH₃); δ_C (68 MHz, CDCl₃, CHCl₃) 172.5, 167.1, 150.9, 143.9, 140.8, 132.7, 128.8, 128.2, 128.0, 127.4, 125.5, 125.3, 76.2, 71.0, 51.9, 49.8, 41.2, 40.1, 39.7, 34.3, 31.2, 29.1, 27.3, 24.6, 21.8, 21.4, 17.6.

5 **(2S)-2-Dimethylamino-2-(2'-methyl-5'-trifluoromethylphenyl)propionic acid (-)-8-phenylmenthol ester (13f)**

colorless gum (Found: C, 71.35; H, 7.9; N, 2.8. Calc. for C₂₉H₃₈F₃NO₂: C, 71.1; H, 7.8; N, 2.9%); [α]_D²⁶ -14.5 (c 1.00 in CHCl₃); ν_{\max} (film)/cm⁻¹ 2952, 2870, 2784, 1718, 1618, 1598, 1494, 1452, 1406, 1370, 1328, 1288, 1220, 1162, 1120, 1050, 976, 954, 904, 824, 760, 736, 698; δ_H (270 MHz, CDCl₃, Me₄Si) 7.52 (1H, s, Ar-H), 7.38 (1H, d, $J = 7.8$ Hz, Ar-H), 7.32-7.10 (6H, m, Ar-H), 4.93 (1H, td, $J = 10.5, 4.3$ Hz, COOCH), 2.62 (3H, s, Ar-CH₃), 2.28 (6H, s, (CH₃)₂N), 1.99-1.83 (2H, m, 8-Ph-Men-H), 1.60-1.15 (3H, m, 8-Ph-Men-H), 1.40 (3H, s, 8-Ph-Men-CH₃), 1.21 (3H, s, 3-H or 8-Ph-Men-CH₃), 1.20 (3H, s, 3-H or 8-Ph-Men-CH₃), 1.05-0.63 (3H, m, 8-Ph-Men-H), 0.80 (3H, d, $J = 6.2$ Hz, 8-Ph-Men-CH₃); δ_C (68 MHz, CDCl₃, CHCl₃) 172.2, 150.9, 142.2 (q, $J = 1$ Hz), 141.5, 132.9, 128.0, 127.7 (q, $J = 32$ Hz), 125.5, 125.3, 124.6 (q, $J = 4$ Hz), 124.4 (d, $J = 270$ Hz), 123.7 (q, $J = 4$ Hz), 76.5, 71.1, 49.8, 41.2, 40.1, 39.7, 34.3, 31.2, 28.9, 27.3, 24.7, 21.6, 21.3, 17.9.

2-Dimethylamino-2-methyl-3-phenylpropionic acid (-)-8-phenylmenthol ester ([1,2] Stevens rearrangement product in Table 2, entries 6 and 7)

2:1 mixture of stereoisomers; colorless oil (Found: C, 79.7; H, 9.6; N, 3.3. Calc. for C₂₈H₃₉NO₂: C, 79.8; H, 9.3; N, 3.3%); ν_{\max} (film)/cm⁻¹ 3052, 2948, 2868, 2784, 1708, 1600, 1492, 1452, 1370, 1260, 1212, 1154, 1130, 1088, 1046, 1030, 978, 958, 906, 844, 762, 740, 696; δ_H (270 MHz, CDCl₃, Me₄Si) 7.43-7.05 (10H, m, Ar-H), 4.99-4.81 (1H, m, COOCH), 3.26 (0.33H, d, $J = 13.1$ Hz, CH₂Ph), 2.89 (0.67H, d, $J = 13.6$ Hz, CH₂Ph), 2.70 (0.33H, d, $J = 13.1$ Hz, CH₂Ph), 2.66 (0.67H, d, $J = 13.6$ Hz, CH₂Ph), 2.40 (1.98H, s, (CH₃)₂N), 2.38 (4.02H, s, (CH₃)₂N), 2.17-1.85 (1.33H, m, 8-Ph-Men-H), 1.85-1.70 (0.67H, m, 8-Ph-Men-H), 1.57-1.15 (3H, m, 8-Ph-Men-H), 1.35 (2 H, s, 2-CH₃ or 8-Ph-Men-CH₃), 1.21 (2H, s, 2-CH₃ or 8-Ph-Men-CH₃), 1.10-0.58 (3H, m, 8-Ph-Men-H), 1.07 (1H, s, 2-CH₃ or 8-Ph-Men-CH₃), 1.04 (2H, s, 2-CH₃ or 8-Ph-Men-CH₃), 0.99 (1H, s, 2-CH₃ or 8-Ph-Men-CH₃), 0.95 (1H, s, 2-CH₃ or 8-Ph-Men-CH₃), 0.85 (1H, d, $J = 5.9$ Hz, 8-Ph-Men-CH₃), 0.81 (2H, d, $J = 6.5$ Hz, 8-Ph-Men-CH₃); δ_C (68 MHz, CDCl₃, CHCl₃) 173.4 (0.67C), 172.2 (0.33C), 151.1 (0.67C), 151.0 (0.33C), 137.6 (0.33C), 137.4 (0.67C), 131.0 (0.66C), 130.9 (1.34C), 128.1 (1.34C), 127.9 (0.66C), 127.9 (0.66C), 127.7 (1.34C), 126.3 (0.33C), 126.2 (0.67C), 125.5 (1.34C), 125.4 (0.66C), 125.3 (0.67C), 125.1 (0.33C), 76.1 (0.33C), 75.8 (0.67C), 66.2 (0.33C), 66.0 (0.67C), 42.7 (0.33C), 42.0 (0.33C), 41.9 (0.67C), 41.7 (0.67C), 40.03 (0.67C), 39.98 (0.33C), 39.7 (1.33C), 39.6 (0.67C), 34.4 (0.33C), 34.3 (0.67C), 31.4 (0.33C), 31.2 (0.67C), 28.9 (0.33C), 28.4 (0.67C), 27.2 (0.33C), 27.1 (0.67C), 25.5 (0.67C), 24.4 (0.33C), 21.8 (0.33C), 21.7 (0.67C), 18.8 (0.67C), 18.5 (0.33C).

2-(4'-tert-Butoxycarbonylbenzyl)-2-dimethylaminopent-4-enoic acid (-)-8-phenylmenthol ester (16)

3:2 mixture of stereoisomers; white solid (Found: C, 76.45; H, 9.0; N, 2.5. Calc. for C₃₅H₄₉NO₄: C, 76.7; H, 9.0; N, 2.6%); ν_{\max} (film)/cm⁻¹ 3056, 2952, 2868, 2788, 1708, 1610, 1454, 1390, 1368, 1292, 1254, 1210, 1168, 1116, 1046, 1020, 956, 910, 848, 732, 700; δ_H (270 MHz, CDCl₃, Me₄Si) 7.87 (0.8H, d, $J = 8.4$ Hz, Ar-H), 7.86 (1.2H, d, $J = 8.4$ Hz, Ar-H), 7.33-7.02 (7H, m, Ar-H), 5.94-5.66 (1H, m, CH₂CH=CH₂), 5.18-4.84 (3H, m, CH₂CH=CH₂ and COOCH), 3.38 (0.4H, d, $J = 13.5$ Hz, CH₂Ar), 2.92 (0.6H, d, $J = 14.3$ Hz, CH₂Ar), 2.71 (0.6H, d, $J = 14.3$ Hz, CH₂Ar), 2.66 (0.4H, d, $J = 13.5$ Hz, CH₂Ar), 2.46 (0.6H, dd, $J = 14.7, 6.6$ Hz, CH₂CH=CH₂), 2.39 (3.6H, s, (CH₃)₂N), 2.37 (2.4H, s, (CH₃)₂N), 2.23 (0.4H, dd, $J = 16.2, 6.9$ Hz, CH₂CH=CH₂), 2.15-1.93 (2.6H, m, CH₂CH=CH₂ and 8-Ph-Men-H), 1.82 (0.4H, dd, $J = 16.2, 6.1$ Hz, CH₂CH=CH₂), 1.68-0.68 (6H, m, 8-Ph-Men-H), 1.58 (5.4H, s, *t*-Bu), 1.57 (3.6H, s, *t*-Bu), 1.36 (1.2H, s, 8-Ph-Men-CH₃), 1.21 (1.8H, s, 8-Ph-Men-CH₃), 1.09 (1.2H, s, 8-Ph-Men-CH₃), 1.02 (1.8H, s, 8-Ph-Men-CH₃), 0.87 (1.2H, d, $J = 7.8$ Hz, 8-Ph-Men-CH₃), 0.85 (1.8H, d, $J = 6.5$ Hz, 8-Ph-Men-CH₃); δ_C (68 MHz, CDCl₃, CHCl₃) 171.9 (0.6C), 171.1 (0.4C), 165.8 (1.0C), 151.10 (0.4C), 151.08 (0.6C), 142.7 (0.4C), 142.5 (0.6C), 134.0 (0.6C), 133.5 (0.4C), 130.8 (0.8C), 130.7 (1.2C), 130.1 (0.4C), 129.9 (0.6C), 129.0 (0.8C), 128.8 (1.2C), 128.1 (1.2C), 128.0 (0.8C), 125.5 (1.2C), 125.4 (0.8C), 125.2 (0.6C), 125.1 (0.4C), 118.3 (0.6C), 118.0 (0.4C), 80.68 (0.4C), 80.64 (0.6C), 76.73 (0.4C), 76.65 (0.6C), 68.4 (0.4C), 68.2 (0.6C), 49.6 (0.4C), 49.5 (0.6C), 43.0 (0.4C), 42.4 (0.6C), 40.0 (0.6C), 39.8 (0.4C), 39.7 (1.2C), 39.5 (0.8C), 37.9 (0.4C), 36.8 (0.6C), 36.0 (0.6C), 34.5 (0.4C), 34.4 (0.6C), 34.1 (0.4C), 31.4 (0.4C), 31.3 (0.6C), 28.2 (3.0C), 28.1 (0.6C), 27.7 (0.4C), 27.2 (0.6C), 27.1 (0.4C), 26.0 (0.6C), 25.7 (0.4C), 21.83 (0.4C), 21.77 (0.6C).

Acknowledgements

This work was supported by Grant-in-Aid for Young Scientists (19750029) from the Ministry of Education, Culture, Sports, Science and Technology, Japan and The Asahi Glass Foundation.

Notes and references

^a Graduate School of Science and Technology, Niigata University, Niigata 950-2181, Japan. Fax: 81 25 262 7741; Tel: 81 25 262 7741; E-mail: tayama@gs.niigata-u.ac.jp

† Electronic Supplementary Information (ESI) available. See DOI: 10.1039/b000000x/

- For review, see: C. Spino, *Angew. Chem. Int. Ed.*, 2004, **43**, 1764 and references therein.
- Previous examples of optically active α -quaternary α -aryl amino nitriles by asymmetric cyanation of ketoimines: J. Wang, X. Hu, J. Jiang, S. Gou, X. Huang, X. Liu, X. Feng, *Angew. Chem. Int. Ed.*, 2007, **46**, 8468; J. Huang, X. Liu, Y. Wen, B. Qin, X. Feng, *J. Org. Chem.*, 2007, **72**, 204; N. Kato, T. Mita, M. Kanai, B. Therrien, M. Kawano, K. Yamaguchi, H. Danjo, Y. Sei, A. Sato, S. Furusho, M. Shibasaki, *J. Am. Chem. Soc.*, 2006, **128**, 6768; X. Huang, J. Huang, Y. Wen, X. Feng, *Adv. Synth. Catal.*, 2006, **348**, 2579; N. Kato, M. Suzuki, M. Kanai, M. Shibasaki, *Tetrahedron Lett.*, 2004, **45**, 3153; N. Kato, M. Suzuki, M. Kanai, M. Shibasaki, *Tetrahedron Lett.*, 2004,

45, 3147; S. Masumoto, H. Usuda, M. Suzuki, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.*, 2003, **125**, 5634; P. Vachal, E. N. Jacobsen, *J. Am. Chem. Soc.*, 2002, **124**, 10012; P. Vachal, E. N. Jacobsen, *Org. Lett.*, 2000, **2**, 867; J. J. Byrne, M. Chavarot, P.-Y. Chavant, Y. Vallée, *Tetrahedron Lett.*, 2000, **41**, 873.

3 E. Tayama, H. Kimura, *Angew. Chem. Int. Ed.*, 2007, **46**, 8869.

4 For reviews, see: I. E. Markó, In *Comprehensive Organic Synthesis*; B. M. Trost, I. Fleming Eds.; Pergamon, Oxford, 1991, Vol. 3, Chap. 3.10; J. A. Vanecko, H. Wan, F. G. West, *Tetrahedron*, 2006, **62**, 1043.

5 Recent examples of base-induced diastereoselective Stevens and Sommelet–Hauser rearrangement: J. B. Sweeney, A. Tavassoli, J. A. Workman, *Tetrahedron*, 2006, **62**, 11506; S. Hanessian, C. Talbot, P. Saravanan, *Synthesis*, 2006, 723; E. Tayama, S. Nanbara, T. Nakai, *Chem. Lett.*, 2006, **35**, 478; J. A. Workman, N. P. Garrido, J. Sançon, E. Roberts, H. P. Wessel, J. B. Sweeney, *J. Am. Chem. Soc.*, 2005, **127**, 1066.

6 Details, see Electronic supplementary information.

7 The absolute configuration at the α -position of **7**, **8**, and **13** were determined by analogy of the ^1H NMR chemical shifts with that of such known compounds as (2*R*)-**8a** and (2*R*)-**8b**. For more details, see Electronic supplementary information.

8 The absolute configurations at the β -position of **7a** and **7b** were not determined.

25 9 Hydrogenation of **8a** afforded the corresponding reduced compound (α -*n*-butyl derivative) as a single stereoisomer. Thus, **8a** was found to be a 1:1 mixture of *E*- and *Z*-isomer. The absolute configuration at α -position was determined as the *R* because the absolute configuration of *Z*-isomer **8b** was determined as the *R* by a single crystal X-ray diffraction (see, ref. 10). For experimental details, see Electronic supplementary information.

30 10 The absolute configuration of **8b** at α -position was determined as the *R* by a single crystal X-ray diffraction. CCDC-xxxxxx contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

35 11 The absolute configuration of α -benzylic product **11** at α -position was not determined.

12 The geometries of carbonyl-stabilized ammonium ylides were similar to those of phosphonium ylides, see: N. A. Bailey, S. E. Hull, G. F. Kersting, J. Morrison, *Chem. Comm.*, 1971, 1429.

40 13 The assignment of the 2,4-disubstituted regioisomer **13d** was made by ^1H NMR analysis; **13d** showed a singlet peak of an aromatic proton (3-H: δ_{H} 7.63 in DMSO-*d*₆).

45