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

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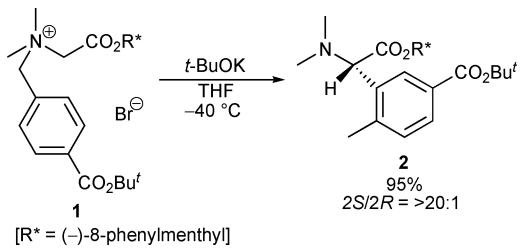
The Stevens rearrangement of *N*-allylic α-aryl amino acid-derived ammonium salts and the Sommelet–Hauser rearrangement of *N*-benzylic α-alkyl amino acid-derived ammonium salts are shown to proceed with remarkably high levels of diastereoselectivity. The methods presented in this work provide new routes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

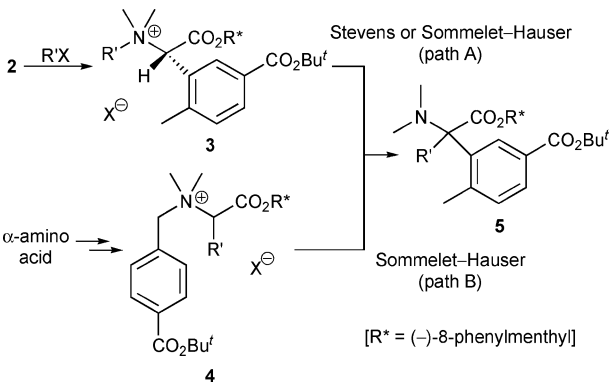
Introduction

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** with 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 the *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] After 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-position[8]), 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 an *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 diastereomeric

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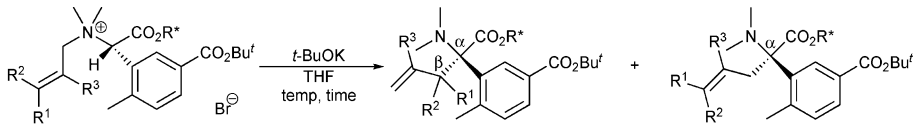
† Electronic supplementary information (ESI) available: Details of the determinations of absolute configuration; table summarizing the ^{1}H NMR data of the rearrangement products; further experimental and characterization details. CCDC reference number 693575. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b811162f

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



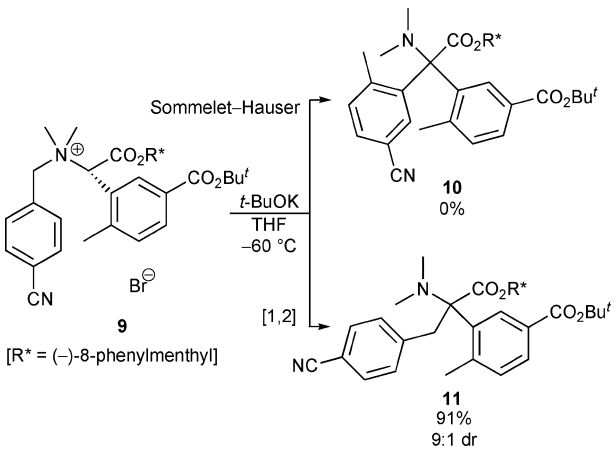
						7			8		
Entry	R^1	R^2	R^3		Temp/°C, time/h	Yield (%)[b]	dr (α)[c,d]	dr (β)[c,e]	Yield (%)[b]	dr (α)[c,d]	*E* : *Z*[c]
1	Me	H	H	**a**[f]	–40, 4	83	> 20 : 1	9 : 1	17	> 20 : 1	1 : 1
2	H	Me	H	**b**[g]	–40, 4	52	> 20 : 1	3 : 7	42	> 20 : 1	1 : >20
3	H	H	Me	**c**	–40, 4	95	> 20 : 1	—	0	—	—
4	H	H	H	**d**	–78, 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 ^{1}H 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.

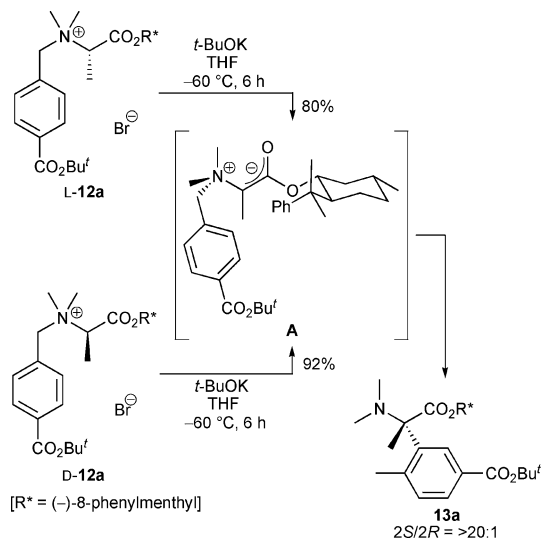
ratios of product **7** or **8** (β-position or *E* : *Z*) are determined by the *E* : *Z* ratio of the starting material **6a** or **6b**. To define the scope and limitations of the present method, we prepared a series of substrates **6c–e** and carried out their reactions with potassium *tert*-butoxide. The rearrangement of *N*-methallyl- (entry 3, **6c**) and *N*-allyl (entry 4, **6d**) derivatives provided the corresponding rearrangement products **7c** and **7d** in excellent yields with equally high α-diastereoselectivities (2*R* : 2*S* = >20 : 1). However, in the rearrangement of an *N*-(*E*)-cinnamyl derivative **6e** (entry 5) at –78 °C, the [1,2] Stevens product **8e** was obtained exclusively in 69% yield with high α- and *E*/*Z*- selectivities (2*R* : 2*S* = >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 *N*-benzylic α-aryl amino acid-derived ammonium salt **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 to give exclusively the 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.

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 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 (2*S* : 2*R* = >20 : 1).[7] Though the exact origin is unclear at present, the high α-selectivity suggests that the rearrangement proceeds *via* the same intermediate **A** (ammonium ylide[12]) generated from ammonium salts L-**12a** and D-**12a** by deprotonation with potassium *tert*-butoxide. The (–)-8-phenylmenthol moiety would block the *re*-face (front side of **A**) of the ammonium ylide, thus leading exclusively to the 2*S*-isomer of **13a**.

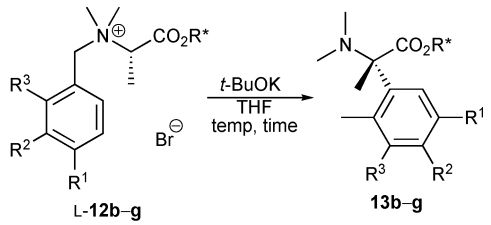


Scheme 3 Rearrangement of an *N*-benzylic α-aryl amino acid-derived ammonium salt **9**



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

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

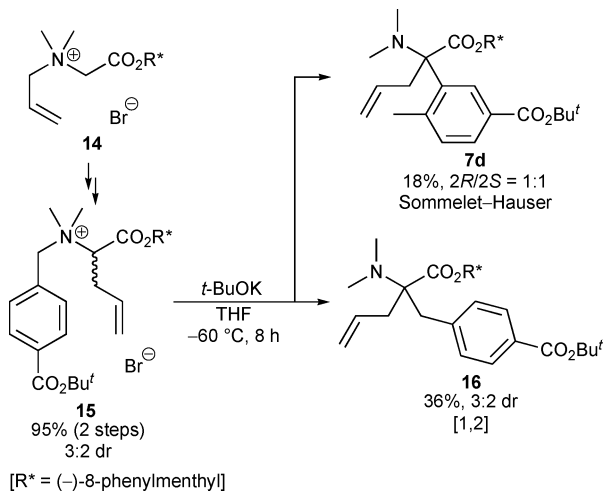


Entry	R^1	R^2	R^3		Temp/°C, time/h	Yield[b] (%)	dr[c] (2*S* : 2*R*)
1[d]	CN	H	H	**b**	–60, 4	80	9 : 1
2	H	H	CN	**c**	–60, 4	82	6 : 1
3	H	CN	H	**d**	–60, 4	82	> 20 : 1
4	COOMe	H	H	**e**	–60, 4	57	> 20 : 1
5[d]	CF_3	H	H	**f**	–60, 8	98	> 20 : 1
6	H	H	H	**g**	–60, 12	0[e]	—
7	H	H	H	**g**	–40, 12	0[e]	—

[a] Reactions were conducted using 1.5 equiv. of *t*-BuOK. [b] Isolated yield. [c] The ratios were determined by ^{1}H NMR assay. [d] The reactions were carried out in THF–CH_2Cl_2 (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 diastereoselectivity (2 : 1 dr). The spectroscopic data is noted in the experimental section.

The scope of substrates was further explored as shown in Table 2. The reactions of *para*- and *ortho*-cyano-*N*-benzylic ammonium salts **12b** and **12c** were found to afford the corresponding Sommelet–Hauser rearrangement products 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 high diastereoselectivity to produce the 2,4-disubstituted regioisomer **13d**[13] as the 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 products **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 in **12g** (entries 6, 7), the reaction did not give the Sommelet–Hauser product **13g**; the [1,2] Stevens rearrangement product was the only detectable product obtained.

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 rearrangement product **16** were obtained in 18% (2*R* : 2*S* = 1 : 1) and 36% yield (3 : 2 dr), respectively.



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

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 were 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. ^{1}H and ^{13}C NMR spectra were measured on JEOL JMN–Excalibur (^{1}H: 270 MHz, ^{13}C: 68 MHz) and Varian UNITY plus-500SW (^{1}H: 500 MHz, ^{13}C: 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 $60F_{254}$) were used. The products were purified by preparative column chromatography on silica gel (silica gel 60 N, spherical neutral, KANTO Chemical Co., Inc., Japan). The elemental analyses were recorded on a Yanaco CHN corder, MT-3. Reactions involving air- or moisture-sensitive

compounds were conducted in an 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 an 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 the eluent) gave **7a** (99 mg, 83% yield) as a white solid and **8a** (20 mg, 17% yield) as a white solid.

(2*R*)-2-(5′-*tert*-Butoxycarbonyl-2′-methylphenyl)-2-dimethylamino-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.

(2*R*)-2-(5′-*tert*-Butoxycarbonyl-2′-methylphenyl)-2-dimethylaminohex-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$_{(Z)}$.

(2*R*)-2-(5′-*tert*-Butoxycarbonyl-2′-methylphenyl)-2-dimethylamino-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 (0.7C), 41.5 (0.7C), 40.9 (0.3C), 40.2 (1.0C), 40.1 (0.7C), 39.8 (0.6C), 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).

(2*R*, 4*Z*)-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.

(2*R*)-2-(5′-*tert*-Butoxycarbonyl-2′-methylphenyl)-2-dimethylamino-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, $(CH_3)_2N$), 2.30–2.17 (2H, m, 8-Ph-Men-H), 2.28 (3H, s, Ar-CH_3), 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-CH_3 or 8-Ph-Men-CH_3), 1.43 (3H, s, 4-CH_3 or 8-Ph-Men-CH_3), 1.23 (3H, s, 8-Ph-Men-CH_3), 1.17–0.83 (3H, m, 8-Ph-Men-H), 0.89 (3H, d, $J = 6.2$ Hz, 8-Ph-Men-CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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.

(2*R*)-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 $C_{35}H_{49}NO_4$: C, 76.7; H, 9.0; N, 2.6%); mp 140–143 °C; $[\alpha]_{589}^{24}$ +12.4 (*c* 1.00 in $CHCl_3$); 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, $CDCl_3$, Me_4Si) 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, $(CH_3)_2N$), 2.28 (3H, s, Ar-CH_3), 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-CH_3), 1.22 (3H, s, 8-Ph-Men-CH_3), 0.89 (3H, d, $J = 5.9$ Hz, 8-Ph-Men-CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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.

(2*S*)-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 $C_{35}H_{49}NO_4$: C, 76.7; H, 9.0; N, 2.6%); mp 45–47 °C; $[\alpha]_{589}^{22}$ −36.1 (*c* 1.00 in $CHCl_3$); 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, $CDCl_3$, Me_4Si) 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, $(CH_3)_2N$), 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-CH_3), 1.17 (3H, s, 8-Ph-Men-CH_3), 0.90 (3H, d, $J = 6.2$ Hz, 8-Ph-Men-CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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.

(2*R*, 4*E*)-2-(5′-*tert*-Butoxycarbonyl-2′-methylphenyl)-2-dimethylamino-5-phenylpent-4-enoic acid (−)-8-phenyl-menthol ester (8e)

White solid (found: C, 78.9; H, 8.8; N, 2.0. Calc. for $C_{41}H_{53}NO_4$: C, 78.9; H, 8.6; N, 2.25%); mp 61–64 °C; $[\alpha]_{589}^{24}$ +82.0 (*c* 1.00 in $CHCl_3$); 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, $CDCl_3$, Me_4Si) 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, $(CH_3)_2N$), 2.31 (3H, s, Ar-CH_3), 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-CH_3), 1.24 (3H, s, 8-Ph-Men-CH_3), 0.90 (3H, d, $J = 7.0$ Hz, 8-Ph-Men-CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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″-cyanophenyl)-2-dimethylaminopropionic acid (−)-8-phenylmenthol ester [11 (major isomer)]

White solid (found: C, 77.1; H, 8.4; N, 4.2. Calc. for $C_{40}H_{50}N_2O_4$: C, 77.1; H, 8.1; N, 4.5%); mp 88–91 °C; $[\alpha]_{589}^{23}$ +126.1 (*c* 1.00 in $CHCl_3$); 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, $CDCl_3$, Me_4Si) 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, CH_2Ar), 2.47–2.21 (2H, m, CH_2Ar and 8-Ph-Men-H), 2.40 (6H, s, $(CH_3)_2N$), 2.15 (3H, s, Ar-CH_3), 1.87–1.67 (3H, m, 8-Ph-Men-H), 1.51 (9H, s, *t*-Bu), 1.47 (3H, s, 8-Ph-Men-CH_3), 1.33–0.85 (4H, m, 8-Ph-Men-H), 1.20 (3H, s, 8-Ph-Men-CH_3), 0.94 (3H, d, $J = 6.2$ Hz, 8-Ph-Men-CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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″-cyanophenyl)-2-dimethylaminopropionic acid (−)-8-phenylmenthol ester [11 (minor isomer)]

White solid (elemental analysis was not performed due to the small amount); mp 65–68 °C; $[\alpha]_{589}^{23}$ −55.9 (*c* 1.00 in $CHCl_3$); 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, $CDCl_3$, Me_4Si) 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, CH_2Ar), 3.11 (1H, d, J = 13.8 Hz, CH_2Ar), 2.62–2.51 (1H, m, 8-Ph-Men-H), 2.45 (6H, s, $(CH_3)_2N$), 2.16 (3H, s, Ar-CH_3), 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-CH_3), 1.05 (3H, s, 8-Ph-Men-CH_3), 0.93 (3H, d, J = 5.9 Hz, 8-Ph-Men-CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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 the 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 $C_{33}H_{47}NO_4$: C, 76.0; H, 9.1; N, 2.7%); mp 41–44 °C; $[\alpha]_{589}^{23}$ +24.5 (*c* 1.00 in $CHCl_3$); 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, $CDCl_3$, Me_4Si) 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-CH_3), 2.24 (6H, s, $(CH_3)_2N$), 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-CH_3), 1.22 (6H, s, 3-H and 8-Ph-Men-CH_3), 1.02–0.83 (2H, m, 8-Ph-Men-H), 0.77 (3H, d, J = 6.2 Hz, 8-Ph-Men-CH_3), 0.68 (1H, td, J = 12.2, 11.1 Hz, 8-Ph-Men-H); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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 $C_{29}H_{38}N_2O_2$: 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, $CDCl_3$, Me_4Si) 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-CH_3), 2.45 (0.3H, s, Ar-CH_3), 2.29 (0.6H, s, $(CH_3)_2N$), 2.23 (5.4H, s, $(CH_3)_2N$), 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-CH_3), 1.19 (6H, s, 3-H and 8-Ph-Men-CH_3), 0.78 (3H, d, J = 6.5 Hz, 8-Ph-Men-CH_3), 0.66 (1H, td, J = 12.0, 11.1 Hz, 8-Ph-Men-H); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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 $C_{29}H_{38}N_2O_2$: 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, $CDCl_3$, Me_4Si) 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-CH_3), 2.62 (0.42H, s, Ar-CH_3), 2.28 (0.84H, s, $(CH_3)_2N$), 2.25 (5.16H, s, $(CH_3)_2N$), 2.14–1.96 (0.28H, 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-CH_3), 1.20 (3H, s, 3-H or 8-Ph-Men-CH_3), 1.19 (3H, s, 3-H or 8-Ph-Men-CH_3), 0.80 (3H, d, J = 6.2 Hz, 8-Ph-Men-CH_3), 0.69 (1H, q, J = 11.5 Hz, 8-Ph-Men-H); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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 $C_{29}H_{38}N_2O_2$: C, 78.0; H, 8.6; N, 6.3%); $[\alpha]_{589}^{25}$ −19.6 (*c* 1.00 in $CHCl_3$); 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, Me_4Si) 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-CH_3), 2.16 (6H, s, $(CH_3)_2N$), 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-CH_3), 1.14 (3H, s, 3-H or 8-Ph-Men-CH_3), 1.13 (3H, s, 3-H or 8-Ph-Men-CH_3), 0.99–0.89 (1H, m, 8-Ph-Men-H), 0.75 (3H, d, J = 6.5 Hz, 8-Ph-Men-CH_3), 0.73–0.64 (2H, m, 8-Ph-Men-H); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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 $C_{30}H_{41}NO_4$: C, 75.1; H, 8.6; N, 2.9%); $[\alpha]_{589}^{25}$ +11.2 (*c* 1.00 in $CHCl_3$); 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, $CDCl_3$, Me_4Si) 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, $COOCH_3$), 2.63 (3H, s, Ar-CH_3), 2.26 (6H, s, $(CH_3)_2N$), 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-CH_3), 1.23 (6H, s, 3-H and 8-Ph-Men-CH_3), 1.07–0.60 (3H, m, 8-Ph-Men-H), 0.80 (3H, d, J = 6.2 Hz, 8-Ph-Men-CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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.

(2*S*)-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 $C_{29}H_{38}F_3NO_2$: C, 71.1; H, 7.8; N, 2.9%); $[\alpha]_{589}^{26}$ −14.5 (c 1.00 in $CHCl_3$); 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, $CDCl_3$, Me_4Si) 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-CH_3), 2.28 (6H, s, $(CH_3)_2N$), 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-CH_3), 1.21 (3H, s, 3-H or 8-Ph-Men-CH_3), 1.20 (3H, s, 3-H or 8-Ph-Men-CH_3), 1.05–0.63 (3H, m, 8-Ph-Men-H), 0.80 (3H, d, J = 6.2 Hz, 8-Ph-Men-CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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 $C_{28}H_{39}NO_2$: 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, $CDCl_3$, Me_4Si) 7.43–7.05 (10H, m, Ar-H), 4.99–4.81 (1H, m, COOCH), 3.26 (0.33H, d, J = 13.1 Hz, CH_2Ph), 2.89 (0.67H, d, J = 13.6 Hz, CH_2Ph), 2.70 (0.33H, d, J = 13.1 Hz, CH_2Ph), 2.66 (0.67H, d, J = 13.6 Hz, CH_2Ph), 2.40 (1.98H, s, $(CH_3)_2N$), 2.38 (4.02H, s, $(CH_3)_2N$), 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 (2H, s, 2-CH_3 or 8-Ph-Men-CH_3), 1.21 (2H, s, 2-CH_3 or 8-Ph-Men-CH_3), 1.10–0.58 (3H, m, 8-Ph-Men-H), 1.07 (1H, s, 2-CH_3 or 8-Ph-Men-CH_3), 1.04 (2H, s, 2-CH_3 or 8-Ph-Men-CH_3), 0.99 (1H, s, 2-CH_3 or 8-Ph-Men-CH_3), 0.95 (1H, s, 2-CH_3 or 8-Ph-Men-CH_3), 0.85 (1H, d, J = 5.9 Hz, 8-Ph-Men-CH_3), 0.81 (2H, d, J = 6.5 Hz, 8-Ph-Men-CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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 $C_{35}H_{49}NO_4$: 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, $CDCl_3$, Me_4Si) 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, CH_2CH=CH_2), 5.18–4.84 (3H, m, CH_2CH=CH_2 and COOCH), 3.38 (0.4H, d, J = 13.5 Hz, CH_2Ar), 2.92 (0.6H, d, J = 14.3 Hz, CH_2Ar), 2.71 (0.6H, d, J = 14.3 Hz, CH_2Ar), 2.66 (0.4H, d, J = 13.5 Hz, CH_2Ar), 2.46 (0.6H, dd, J = 14.7, 6.6 Hz, CH_2CH=CH_2), 2.39 (3.6H, s, $(CH_3)_2N$), 2.37 (2.4H, s, $(CH_3)_2N$), 2.23 (0.4H, dd, J = 16.2, 6.9 Hz, CH_2CH=CH_2), 2.15–1.93 (2.6H, m, CH_2CH=CH_2 and 8-Ph-Men-H), 1.82 (0.4H, dd, J = 16.2, 6.1 Hz, CH_2CH=CH_2), 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-CH_3), 1.21 (1.8H, s, 8-Ph-Men-CH_3), 1.09 (1.2H, s, 8-Ph-Men-CH_3), 1.02 (1.8H, s, 8-Ph-Men-CH_3), 0.87 (1.2H, d, J = 7.8 Hz, 8-Ph-Men-CH_3), 0.85 (1.8H, d, J = 6.5 Hz, 8-Ph-Men-CH_3); δ_C (68 MHz, $CDCl_3$, $CHCl_3$) 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).

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Notes and references

1 For a review, see: C. Spino, *Angew. Chem., Int. Ed.*, 2004, **43**, 1764 and references therein.
2 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 and X. Feng, *Angew. Chem., Int. Ed.*, 2007, **46**, 8468; J. Huang, X. Liu, Y. Wen, B. Qin and 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 and M. Shibasaki, *J. Am. Chem. Soc.*, 2006, **128**, 6768; X. Huang, J. Huang, Y. Wen and X. Feng, *Adv. Synth. Catal.*, 2006, **348**, 2579; N. Kato, M. Suzuki, M. Kanai and M. Shibasaki, *Tetrahedron Lett.*, 2004, **45**, 3153; N. Kato, M. Suzuki, M. Kanai and M. Shibasaki, *Tetrahedron Lett.*, 2004, **45**, 3147; S. Masumoto, H. Usuda, M. Suzuki, M. Kanai and M. Shibasaki, *J. Am. Chem. Soc.*, 2003, **125**, 5634; P. Vachal and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2002, **124**, 10012; P. Vachal and E. N. Jacobsen, *Org. Lett.*, 2000, **2**, 867; J. J. Byrne, M. Chavarot, P.-Y. Chavant and Y. Vallée, *Tetrahedron Lett.*, 2000, **41**, 873.
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6 For details, see the ESI†.
7 The absolute configurations at the α-position of **7**, **8**, and **13** were determined by analogy between their ^{1}H NMR chemical shifts and those of such known compounds as (2*R*)-**8a** and (2*R*)-**8b**. For more details, see the ESI†.
8 The absolute configurations at the β-position of **7a** and **7b** were not determined.
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 the α-position was determined as *R* because the absolute configuration of the *Z*-isomer **8b** was determined as *R* by a single crystal X-ray diffraction (see ref. 10). For experimental details, see the ESI†.
10 The absolute configuration of **8b** at the α-position was determined as *R* by a single crystal X-ray diffraction. CCDC-693575 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.
11 The absolute configuration of the α-benzylic product **11** at the α-position was not determined.
12 The geometries of the carbonyl-stabilized ammonium ylides were similar to those of phosphonium ylides, see: N. A. Bailey, S. E. Hull, G. F. Kersting and J. Morrison, *J. Chem. Soc. D*, 1971, 1429.
13 The assignment of the 2,4-disubstituted regioisomer **13d** was made by ^{1}H NMR analysis; **13d** showed a singlet peak for an aromatic proton (3-H: δ_H 7.63 in DMSO-d_6).

