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A base-induced dearomative [2,3] sigmatropic rearrangement of amino acid ester-derived ammonium salts followed by 1,4elimination produced  $\alpha$ -(*ortho*-vinylphenyl)amino acid esters. The reaction of azetidine-2-carboxylic acid-derived ammonium salt (1*S*,2*S*,1'*R*)-**3b** proceeded with a perfect N-to-C chirality transfer to afford  $\alpha$ -(*ortho*-vinylphenyl)azetidine-2carboxylic acid ester (*R*)-**5** (99% ee). On the other hand, the reaction of glycine-derived ammonium salt (*R*)-**6a**, which involves an efficient chirality transfer from a chiral benzylic carbon to an  $\alpha$ -carbon of an ester carbonyl giving the optically active  $\alpha$ -(*ortho*-vinylphenyl)glycine ester (*R*)-**8a** (85% ee), was demonstrated. Although this dearomative [2,3] rearrangement followed by 1,4-elimination has limitations with regard to the structures of the substrates, our method provides unique access to substituted  $\alpha$ -arylamino acid derivatives.

#### Introduction

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The [2,3] sigmatropic rearrangement involving an aromatic C=C double bond, such as Sommelet–Hauser (S–H) rearrangement,<sup>1-7</sup> is a unique synthetic transformation because the initial [2,3] rearrangement is a dearomative reaction.<sup>8-10</sup> For example, the S–H rearrangement of ylide **A** depicted in Scheme 1 (eqn (1)) proceeds via an initial dearomative [2,3] shift to generate **B** followed by aromatization. These processes result in the formation of a new C–C bond between an aromatic (sp<sup>2</sup>) and an aliphatic (sp<sup>3</sup>) carbon under mild conditions. Furthermore, dearomatized **B** has a cyclohexadienyl fragment, and analogous derivatives could be used as unique building blocks. However, their isolation and synthetic applications have been limited.

As mentioned above, we have reported that the baseinduced S–H rearrangement of *N*-(1'-phenylethyl)azetidine-2carboxylic acid ester-derived ammonium salt, (1*S*,2*S*,1'*S*)-**1**, prepared from (*S*)-(1-phenylethyl)amine gave  $\alpha$ -(2-ethylphenyl) derivative (*R*)-**2** (Scheme 1, eqn (1)).<sup>4b,11</sup> To expand the synthetic scope of this transformation, we attempted the reaction of analogue salt (1*S*,2*S*,1'*R*)-**3a**, which was prepared from (*R*)-2-amino-2-phenylethanol (eqn (2)). Interestingly, the reaction produced *ortho*-vinylphenyl derivative (*R*)-**5** as an unexpected side product along with S–H rearrangement product (*R*)-**4a**. We expected that (*R*)-**5** would be formed via the [2,3] shift of ylide **A'** followed by 1,4-elimination of



dearomatized **B'**, and this transformation will expand the synthetic scope of dearomative [2,3] sigmatropic rearrangements. The formed  $\alpha$ -(*ortho*-vinylphenyl)amino acid derivatives can serve as interesting building blocks via further

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<sup>+</sup>Electronic Supplementary Information (ESI) available: Experimental details of preparation of substrates **3** and **6**, determination of ee, absolute structures, and copy of NMR spectra. See DOI: 10.1039/x0xx00000x

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functionalization of the double bond.<sup>12</sup> Thus, we started to investigate this successive [2,3] rearrangement–1,4-elimination.

#### **Results and discussion**

We examined the S–H rearrangement of (1S,2S,1'R)-3a<sup>13,14</sup> with 1.2 equivalents of tBuOK in THF at 0 °C for the preparation of (R)-4 $a^{15}$  (Table 1, Entry 1). Desired product (R)-4a was obtained in 48% yield with 98% ee via N-to-C chirality transfer. (R)-5<sup>16</sup> was isolated as an unexpected side product in 31% yield with 98% ee. We expected that the yield of (R)-5 would be improved by the addition of excess tBuOK because the base-promoted 1,4-elimination to produce (*R*)-5 would be driven to completion. Thus, substrate (1S,2S,1'R)-3a was treated with 2.0 equivalents of tBuOK; however, this change did not improve the reaction outcome (Entry 2). To enhance the rate of the elimination, we decided to exchange the methoxy leaving group (OMe), as in (15,25,1'R)-3a, for an acetoxy (OAc) moiety. The reaction of acetate (1S,2S,1'R)-3b with 1.2 equivalents of tBuOK gave only (R)-5 in 47% yield with 99% ee (Entry 3). The desired 1,4elimination would proceed smoothly. The 47% yield was reasonable because the maximum yield of (R)-5 is 60% with 1.2 equivalents of tBuOK. As expected, the use of 2.0 equivalents of tBuOK produced desired (R)-5 in 89% yield with 99% ee (Entry 4).



	Entry	ĸ		(equiv)	(R)-4	( <i>R</i> )- <b>5</b>	
	1	Me	а	1.2	48%, 98% ee	31%, 98% ee	
	2	Me	а	2.0	52%, 95% ee	33%, 98% ee	
	3	Ac	b	1.2	0%	47%, 99% ee	
	4	Ac	b	2.0	0%	89%, 99% ee	

<sup>&</sup>lt;sup>a</sup> Isolated yield. The ee were determined by chiral HPLC.

The other enantiomer, (*S*)-**5**, could be obtained from the salt of the other diastereomer, (1R,2R,1'R)-**3b**<sup>13,14</sup> (Scheme 2). The reaction of (1R,2R,1'R)-**3b** with 2.0 equivalents of *t*BuOK gave (*S*)-**5** in 67% yield with 91% ee. In our previous work, the analogous diastereomers of the azetidinium salts were found to be poorly-tolerated in the dearomative [2,3] rearrangement.<sup>4a,17</sup> Thus, the yield and ee would be slightly lower.

To clarify the reaction pathway leading to (*R*)-**5**, we treated (*R*)-**4a** with *t*BuOK to prevent E2 elimination in the conversion of S–H rearrangement product (*R*)-**4a** into (*R*)-**5** (Scheme 3). <sup>1</sup>H NMR analysis of the crude material showed only 2% conversion without any decomposition.







This result, depicted in Scheme 3, indicated that (R)-5 is mainly derived from dearomatized intermediate **B**', which is generated from the initial [2,3] rearrangement of ylide **A**' (Scheme 4). When the leaving group is OMe, as in (1*S*,2*S*,1'*R*)-**3a**, both the aromatization leading to (R)-**4a** and the 1,4elimination leading to (R)-5 could also occur from **B**'. The use of OAc as the leaving group enhanced the rate of the 1,4elimination and afforded only (R)-5 even when 1.2 equivalents of *t*BuOK was used.



Scheme 4 Proposed reaction pathway leading to (R)-5.

With these results in hand, we decided to apply this successive dearomative [2,3] rearrangement–1,4-elimination to acyclic substrates such as glycine-derived ammonium salt (*R*)-**6a**<sup>18</sup> (Scheme 5). The reaction would proceed with chirality transfer from a chiral benzylic carbon to an  $\alpha$ -carbon of the ester carbonyl to afford optically active, S–H rearrangement product **7a** and  $\alpha$ -(*ortho*-vinylphenyl)glycine ester **8a**. First, we examined the reaction of (*R*)-**6a** at -40 °C to avoid the anticipated racemization of **7a** and **8a**. However, the products (**7a**: 5% yield, **8a**: 73% yield) were obtained as racemates. Interestingly, when the reaction was carried out at -78 °C (3 runs), the enantioselective formation of products **7a** and **8a** was achieved, and the desired products were obtained in 88–90%

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ee for (*R*)-**7a**<sup>19</sup> and 69–75% ee for (*R*)-**8a**<sup>20</sup> although the yields of (*R*)-**8a** were slightly lower at this temperature (56–60% yields). The stereochemistries of substrate (*R*)-**6a**, products (*R*)-**7a** and (*R*)-**8a** indicate that the reaction proceeds via intermediate **C**. Desired product (*R*)-**8a** may racemize more easily than (*R*)-**7a** due to conjugation with the vinyl substituent. Finally, we attempted the reaction at –92 °C (3 runs) and obtained (*R*)-**7a** in 7–12% yields with 93–95% ee and (*R*)-**8a** in 48–52% yields with 81–85% ee.



To define the scope and limitations of this reaction for the formation of 8, we prepared various racemic substrates 6 and subjected them to the reaction at -40 °C (Table 2). The reactions of para- and ortho-substituted substrates 6b-f resulted in moderate yields of 8b-f (Entries 1-5, 46-64%). As expected, the reaction of meta-chloro derivative 6g afforded both possible regioisomers 8g (2,4-disubstituted, 34% yield) and 8g' (2,6-disubstituted, 28% yield) (Entry 6). In each of the described S–H reactions above, the corresponding rearrangement products (analogous to 7a) were observed in approximately 10% yields.<sup>21</sup> Finally, we applied this transformation to the construction of an  $\alpha$ -quaternary amino acid (Entry 7). The reaction of alanine-derived ammonium salt 6h (1/1 mixture of diastereomers) under the same conditions gave  $\alpha$ -(*ortho*-vinylphenyl)alanine ester **8h** in 40% yield.

#### Conclusions

In conclusion, the dearomative [2,3] sigmatropic rearrangement followed by 1,4-elimination of ammonium ylides to provide  $\alpha$ -(*ortho*-vinylphenyl)amino acid esters was successfully demonstrated. This result is a new synthetic application of dearomatized compound **B**'. Further studies are necessary to clarify the origin of the chirality transfer from the chiral benzylic carbon of (*R*)-**6a** to an  $\alpha$ -carbon of the ester carbonyl of (*R*)-**7a** and (*R*)-**8a**. These studies will be reported in due course.

Although dearomative [2,3] sigmatropic rearrangements, such as the Sommelet–Hauser rearrangement, still have limited

substrate scopes, our studies will expand the synthetic applications of ammonium ylide rearrangemented by and provide a unique method of synthesizing  $\alpha$ -arylamino acid derivatives.



Experimental

#### General

Infrared spectra were recorded on a Perkin Elmer Spectrum GX FT-IR spectrometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured on a Varian or a Bruker 400 MHz spectrometers (<sup>1</sup>H: 400 MHz, <sup>13</sup>C: 100 MHz). As an internal standard, Me<sub>4</sub>Si was used for <sup>1</sup>H NMR ( $\delta$  0 ppm) and CDCl<sub>3</sub> for <sup>13</sup>C NMR ( $\delta$  77 ppm). 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 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 moisturesensitive compounds were conducted in appropriate roundbottomed flasks with a magnetic stirring bar under an argon atmosphere. Reactions under lower temperature were carried out using a Constant Temp. Bath with Magnetic Stirrer (PSL-1400 and PSL-1800, EYELA, Japan) and a Ultra-Cooling Reacter (UCR-150, Techno Sigma Co., Ltd., Japan). A 1.0 M tBuOK THF solution were purchased from Tokyo Chemical Industry (TCI) Co., Ltd., Japan. THF was purchased from KANTO Chemical Co., Inc., Japan as an anhydrous solvent. For thin layer chromatography (TLC) analysis throughout this work, Merck TLC plates (silica gel 60 F<sub>254</sub>) were used. The products were purified by preparative column chromatography on silica gel (silica gel 60N, spherical neutral, KANTO Chemical Co., Inc., Japan).

#### Representative procedure for the reaction of (1*S*,2*S*,1'*R*)-3a

A solution of (15,25,1'R)-**3a** (102 mg, 0.224 mmol, 97% ee) in THF (2.0 mL) was treated with a 1 M tBuOK THF solution (0.27 mL, 0.27 mmol) at 0 °C under an argon atmosphere and stirred for 3 h at the same temperature. The resulting mixture was

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quenched with saturated NH<sub>4</sub>Cl aq. and extracted with EtOAc. The combined extracts were washed with saturated NaHCO<sub>3</sub> aq. followed by brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The residue was purified by chromatography on silica gel [*n*hexane/EtOAc = 15/1 to 4/1 as the eluent,  $R_{f}$ : (*R*)-**5** > (*R*)-**4a**] to

#### (*R*)-4a (33.1 mg, 48% yield, 98% ee) as a colourless oil. Representative procedure for the reaction of (1*S*,2*S*,1'*R*)-3b

obtain (R)-5 (19.0 mg, 31% yield, 98% ee) as a colourless oil and

A solution of (15,25,1'R)-**3b** (106 mg, 0.219 mmol, 99% ee) in THF (2.0 mL) was treated with a 1 M tBuOK THF solution (0.44 mL, 0.44 mmol) at 0 °C under an argon atmosphere and stirred for 3 h at the same temperature. The resulting mixture was quenched with saturated NH<sub>4</sub>Cl aq. and extracted with EtOAc. The combined extracts were washed with saturated NaHCO<sub>3</sub> aq. followed by brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. <sup>1</sup>H NMR analysis of the crude product showed only (*R*)-**5** as the product. Purification of the crude product by chromatography on silica gel (*n*-hexane/EtOAc = 20/1 to 10/1 as the eluent) afforded (*R*)-**5** (53.1 mg, 89% yield, 99% ee) as a colourless oil.

#### Representative procedure for the reaction of (R)-6a

A 1 M *t*BuOK THF solution (1.05 mL, 1.05 mmol) was added slowly to a solution of (*R*)-**6a** (212 mg, 0.527 mmol, >99% ee) in THF (4.2 mL) at -92 °C under an argon atmosphere and the mixture was stirred for 3 h at the same temperature. The resulting mixture was poured into saturated NH<sub>4</sub>Cl aq. and extracted with EtOAc. The combined extracts were washed with saturated NaHCO<sub>3</sub> aq. followed by brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Purification of the residue by chromatography on silica gel (*n*-hexane/EtOAc = 8/1 to 2/1 as the eluent, *R*<sub>f</sub>: (*R*)-**8a** > (*R*)-**7a**) afforded (*R*)-**8a** (71.0 mg, 52% yield, 85% ee) as a colourless oil and (*R*)-**7a** (11.5 mg, 7% yield, 95% ee) as a colourless oil.

#### (*R*)-*tert*-Butyl 2-(2-(2-methoxyethyl)phenyl)-1-methylazetidine-2carboxylate [(*R*)-4a]

Colourless oil;  $[\alpha]^{25}_{589}$  +143.4 (c 1.0 in EtOH) for 98% ee [determined by HPLC analysis: Daicel Chiralcel OD-H column (25 cm), n-hexane/iPrOH = 99.5/0.5 as the eluent, flow rate = 0.50 mL/min, t<sub>R</sub> = 10.3 min for (R)-4a (98.8%) and 12.6 min for (S)-4a (1.2%)]; IR (film) v<sub>max</sub>/cm<sup>-1</sup> 3065, 2974, 2929, 2853, 2782, 1715, 1482, 1455, 1392, 1367, 1255, 1194, 1162, 1120, 1086, 1039, 974, 922, 908, 845, 762; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.55-7.51 (1H, m, ArH), 7.26-7.15 (3H, m, ArH), 3.55 (2H, t, J = 7.6 Hz, CH<sub>2</sub>O), 3.48 (1H, ddd, J = 8.7, 6.1, 2.4 Hz, 4-H), 3.39-3.32 (1H, m, 4-H), 3.34 (3H, s, OCH<sub>3</sub>), 2.96 (1H, ddd, J = 10.4, 8.0, 2.4 Hz, 3-H), 2.65 (1H, dt, J = 14.4, 7.6 Hz, CH<sub>2</sub>Ar), 2.59 (1H, dt, J = 14.4, 7.6 Hz, CH<sub>2</sub>Ar), 2.49 (3H, s, NCH<sub>3</sub>), 2.21 (1H, ddd, J = 10.4, 8.8, 8.7 Hz, 3-H), 1.44 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.7, 142.6, 134.0, 128.8, 126.7, 126.0, 125.5, 81.8, 75.6, 72.7, 58.5, 52.2, 39.8, 31.7, 29.9, 28.1; HRMS (ESI): calcd for C<sub>18</sub>H<sub>28</sub>NO<sub>3</sub> [M + H]<sup>+</sup> 306.2064, found 306.2054.

## (*R*)-*tert*-Butyl 1-methyl-2-(2-vinylphenyl)azetidine-2-carboxylate [(*R*)-5]

Colourless oil;  $[\alpha]^{19}_{589}$  +158.3 (*c* 1.0 in EtOH) for 99% ee [determined by HPLC analysis: Daicel Chiralcel OD-H column (25 cm), *n*-hexane/*i*PrOH = 99.5/0.5 as the eluent, flow rate = 0.50

mL/min,  $t_{\rm R}$  = 8.4 min for (S)-5 (0.5%) and 8.9 min for (R)-5 (99.5%)]; IR (film) v<sub>max</sub>/cm<sup>-1</sup> 3087, 3062, 2994, 129309, 28528, 21982, 1716, 1626, 1474, 1456, 1412, 1391, 1367, 1289, 1254, 1197, 1164, 1125, 1086, 1043, 1021, 978, 948, 910, 845, 822, 773, 759, 743; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.56 (1H, dd, J = 7.6, 1.2 Hz, ArH), 7.45 (1H, dd, J = 7.6, 1.2 Hz, ArH), 7.29 (1H, ddd, J = 7.6, 7.6, 1.2 Hz, ArH), 7.21 (1H, ddd, J = 7.6, 7.6, 1.2 Hz, ArH), 6.54 (1H, dd, J = 17.1, 11.0, CH=CH<sub>2</sub>), 5.61 (1H, dd, J = 17.1, 1.2 Hz, CH=CH<sub>2</sub>), 5.21 (1H, dd, J = 11.0, 1.2 Hz, CH=CH<sub>2</sub>), 3.48 (1H, ddd, J = 8.4, 6.2, 2.4 Hz, 4-H), 3.33 (1H, ddd, J = 8.8, 8.4, 6.2 Hz, 4-H), 2.97 (1H, ddd, J = 10.5, 8.4, 2.4 Hz, 3-H), 2.48 (3H, s, NCH<sub>3</sub>), 2.19 (1H, ddd, J = 10.5, 8.8, 8.4 Hz, 3-H), 1.37 (9H, s, tBu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.5, 141.6, 134.3, 134.1, 127.5, 126.8, 125.2, 125.1, 115.8, 81.7, 75.4, 52.1, 39.9, 29.7, 28.0; HRMS (ESI): calcd for C<sub>17</sub>H<sub>24</sub>NO<sub>2</sub> [M + H]<sup>+</sup> 274.1802, found 274.1793. (S)-tert-Butyl 1-methyl-2-(2-vinylphenyl)azetidine-2-carboxylate [(*S*)-5]

Colourless oil;  $[\alpha]^{24}_{589}$  –146.9 (*c* 1.0 in EtOH) for 91% ee [determined by HPLC analysis: Daicel Chiralcel OD-H column (25 cm), *n*-hexane/*i*PrOH = 99.8/0.2 as the eluent, flow rate = 0.50 mL/min,  $t_{\rm R}$  = 9.2 min for (*S*)-**5** (95.5%) and 9.9 min for (*R*)-**5** (4.5%)].

#### (*R*)-*tert*-Butyl 2-(2-(2-acetoxyethyl)phenyl)-2-(dimethylamino)acetate [(*R*)-7a]

Colourless oil;  $[\alpha]^{26}_{589}$  –83.1 (*c* 1.0 in EtOH) for 95% ee [determined by HPLC analysis: Daicel Chiralpak AD-H column (25 cm), *n*-hexane/*i*PrOH = 95/5 as the eluent, flow rate = 0.50 mL/min,  $t_{\rm R}$  = 8.5 min for (*S*)-**7a** (2.3%) and 9.7 min for (*R*)-**7a** (97.7%)]; IR (film)  $\nu_{\rm max}$ /cm<sup>-1</sup> 3060, 2978, 2866, 2820, 2773, 1741, 1449, 1391, 1367, 1238, 1143, 1105, 1045, 947, 901, 835, 757; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.61-7.55 (1H, m, ArH), 7.27-7.18 (3H, m, ArH), 4.34 (1H, dt, *J* = 11.0, 7.6 Hz, CH<sub>2</sub>O), 4.26 (1H, dt, *J* = 11.0, 7.6 Hz, CH<sub>2</sub>O), 4.11 (1H, s, NCHCO), 3.10 (2H, dd, *J* = 7.6, 7.6 Hz, CH<sub>2</sub>Ar), 2.28 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 2.07 (3H, s, COCH<sub>3</sub>), 1.38 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.97, 170.95, 136.5, 135.8, 130.3, 128.6, 127.8, 127.0, 81.3, 70.5, 64.7, 43.0, 31.9, 27.9, 21.0; HRMS (ESI): calcd for C<sub>18</sub>H<sub>28</sub>NO<sub>4</sub> [M + H]<sup>+</sup> 322.2013, found 322.2005.

#### (R)-tert-Butyl 2-(dimethylamino)-2-(2-vinylphenyl)acetate [(R)-8a]

Colourless oil;  $[\alpha]^{20}_{589}$  –137.9 (*c* 1.0 in EtOH) for 85% ee [determined by HPLC analysis: Daicel Chiralpak AD-H column (25 cm), *n*-hexane/*i*PrOH = 99.5/0.5 as the eluent, flow rate = 0.50 mL/min,  $t_R$  = 8.1 min for (*S*)-**8a** (7.6%) and 9.2 min for (*R*)-**8a** (92.4%)]; IR (film)  $\nu_{max}/cm^{-1}$  3085, 3063, 2978, 2932, 2866, 2819, 2772, 1741, 1730, 1626, 1479, 1459, 1449, 1413, 1392, 1367, 1256, 1221, 1143, 1089, 1045, 993, 947, 903, 881, 866, 836, 808, 771, 750; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.58-7.53 (1H, m, ArH), 7.50-7.45 (1H, m, ArH), 7.29-7.23 (2H, m, ArH), 7.24 (1H, dd, *J* = 17.1, 10.8 Hz, *CH*=CH<sub>2</sub>), 5.62 (1H, dd, *J* = 17.1, 1.6 Hz, CH=CH<sub>2</sub>), 5.34 (1H, dd, *J* = 10.8, 1.6 Hz, CH=CH<sub>2</sub>), 4.13 (1H, s, NCHCO), 2.26 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 1.37 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.8, 138.0, 134.9, 134.5, 128.4, 127.82, 127.76, 126.3, 116.4, 81.2, 71.1, 43.1, 27.9; HRMS (ESI): calcd for C<sub>16</sub>H<sub>24</sub>NO<sub>2</sub> [M + H]<sup>+</sup> 262.1802, found 262.1792.

### *tert*-Butyl 2-(5-chloro-2-vinylphenyl)-2-(dimethylamino)acetate (8b)

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Colourless oil; IR (film) v<sub>max</sub>/cm<sup>-1</sup> 3086, 2979, 2868, 2823, 2775, 1739, 1625, 1591, 1478, 1415, 1392, 1368, 1255, 1221, 1144, 1117, 1097, 1082, 1045, 990, 955, 914, 866, 827, 785, 753, 734; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.60 (1H, d, J = 2.4 Hz, ArH), 7.41 (1H, d, J = 8.4 Hz, ArH), 7.23 (1H, dd, J = 8.4, 2.4 Hz, ArH), 7.16 (1H, dd, J = 17.4, 10.9 Hz, CH=CH<sub>2</sub>), 5.61 (1H, dd, J = 17.4, 1.6 Hz, CH=CH<sub>2</sub>), 5.36 (1H, dd, J = 10.9, 1.6 Hz, CH=CH<sub>2</sub>), 4.07 (1H, s, NCHCO), 2.27 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 1.39 (9H, s, tBu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.1, 136.3, 136.2, 133.7, 128.3, 128.1, 127.6, 117.1, 81.6, 71.0, 43.1, 27.9; HRMS (ESI): calcd for C<sub>16</sub>H<sub>23</sub>ClNO<sub>2</sub> [M + H]<sup>+</sup> 296.1412, found 292.1404.

#### tert-Butyl 2-(5-bromo-2-vinylphenyl)-2-(dimethylamino)acetate (8c)

Colourless oil; IR (film) v<sub>max</sub>/cm<sup>-1</sup> 3086, 2978, 2868, 2822, 2775, 1739, 1626, 1585, 1556, 1476, 1414, 1392, 1367, 1255, 1220, 1144, 1106, 1080, 1046, 989, 951, 907, 867, 826, 784, 752; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.75 (1H, d, J = 2.0 Hz, ArH), 7.39 (1H, dd, J = 8.6, 2.0 Hz, ArH), 7.34 (1H, d, J = 8.6 Hz, ArH), 7.15 (1H, dd, J = 17.3, 10.9 Hz, CH=CH<sub>2</sub>), 5.62 (1H, dd, J = 17.3, 1.2 Hz, CH=CH<sub>2</sub>), 5.36 (1H, dd, J = 10.9, 1.2 Hz, CH=CH<sub>2</sub>), 4.06 (1H, s, NCHCO), 2.26 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 1.39 (9H, s, tBu); <sup>13</sup>C NMR (100 MHz, CDCl\_3)  $\delta$  170.1, 136.8, 136.5, 133.7, 131.2, 131.0, 127.9, 121.8, 117.1, 81.6, 70.9, 43.1, 27.9; HRMS (ESI): calcd for C<sub>16</sub>H<sub>23</sub>BrNO<sub>2</sub> [M + H]<sup>+</sup> 340.0907, found 340.0897.

#### tert-Butyl 2-(dimethylamino)-2-(5-methyl-2-vinylphenyl)acetate (8d)

Yellow oil; IR (film) v<sub>max</sub>/cm<sup>-1</sup> 3083, 2978, 2866, 2820, 2772, 1740, 1611, 1494, 1456, 1414, 1391, 1367, 1255, 1215, 1144, 1094, 1046, 994, 963, 904, 870, 825, 789, 756; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ 7.38 (1H, s, ArH), 7.37 (1H, d, J = 8.0 Hz, ArH), 7.20 (1H, dd, J = 17.3, 10.9 Hz, CH=CH<sub>2</sub>), 7.07 (1H, dd, J = 8.0, 1.6 Hz, ArH), 5.58 (1H, dd, J = 17.3, 1.6 Hz, CH=CH<sub>2</sub>), 5.28 (1H, dd, J = 10.9, 1.6 Hz, CH=CH<sub>2</sub>), 4.08 (1H, s, NCHCO), 2.33 (3H, s, ArCH<sub>3</sub>), 2.26 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 1.38 (9H, s, tBu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ 170.9, 137.6, 135.0, 134.6, 134.2, 128.7, 128.6, 126.1, 115.5, 81.1, 71.1, 43.3, 27.9, 21.1; HRMS (ESI): calcd for C<sub>17</sub>H<sub>26</sub>NO<sub>2</sub> [M + H]<sup>+</sup> 276.1958, found 276.1950.

#### tert-Butyl 2-(dimethylamino)-2-(5-methoxy-2-vinylphenyl)acetate (8e)

Colourless oil; IR (film) v<sub>max</sub>/cm<sup>-1</sup> 3083, 2977, 2867, 2833, 2773, 1738, 1606, 1569, 1494, 1463, 1392, 1367, 1287, 1245, 1217, 1144, 1099, 1045, 991, 963, 901, 870, 828, 789, 754, 734, 696; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.42 (1H, d, J = 8.6 Hz, ArH), 7.15 (1H, dd, J = 17.3, 10.9 Hz, CH=CH<sub>2</sub>), 7.13 (1H, d, J = 2.8 Hz, ArH), 6.82 (1H, ddd, J = 8.6, 2.8, 0.4 Hz, ArH), 5.53 (1H, dd, J = 17.3, 1.6 Hz, CH=CH<sub>2</sub>), 5.23 (1H, dd, J = 10.9, 1.6 Hz, CH=CH<sub>2</sub>), 4.09 (1H, s, NCHCO), 3.81 (3H, s, OCH<sub>3</sub>), 2.26 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 1.38 (9H, s, *t*Bu);  $^{13}\text{C}$  NMR (100 MHz, CDCl\_3)  $\delta$  170.7, 159.3, 135.7, 134.1, 130.5, 127.4, 114.62, 114.58, 112.3, 81.2, 71.1, 55.3, 43.3, 27.9; HRMS (ESI): calcd for  $C_{17}H_{26}NO_3$  [M + H]<sup>+</sup> 292.1907, found 292.1899.

#### tert-Butyl 2-(3-chloro-2-vinylphenyl)-2-(dimethylamino)acetate (8f)

Colourless oil; IR (film) v<sub>max</sub>/cm<sup>-1</sup> 3086, 3058, 2978, 2867, 2821, 2774, 1740, 1633, 1589, 1562, 1443, 1392, 1367, 1300, 1272, 1253, 1217, 1144, 1096, 1043, 988, 934, 900, 878, 838, 780, 754; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.61 (1H, dd)9<sup>|=1</sup>8.10,31/2892,0A94), 7.34 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.21 (1H, dd, J = 8.0, 8.0 Hz, ArH), 6.75 (1H, dd, J = 17.8, 11.5 Hz, CH=CH<sub>2</sub>), 5.71 (1H, dd, J = 11.5, 1.7 Hz, CH=CH<sub>2</sub>), 5.54 (1H, dd, J = 17.8, 1.7 Hz, CH=CH<sub>2</sub>), 4.29 (1H, s, NCHCO), 2.21 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 1.39 (9H, s, tBu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) *δ*170.7, 137.8, 137.1, 133.2, 132.6, 128.7, 128.0, 127.0, 122.6, 81.3, 70.5, 43.1, 27.9; HRMS (ESI): calcd for  $C_{16}H_{23}CINO_2 [M + H]^+ 296.1412$ , found 292.1402.

#### tert-Butyl 2-(4-chloro-2-vinylphenyl)-2-(dimethylamino)acetate (8g)

Yellow oil; IR (film)  $v_{\rm max}/{\rm cm}^{-1}$  3087, 2978, 2933, 2868, 2822, 2774, 1740, 1626, 1591, 1560, 1476, 1414, 1391, 1368, 1279, 1255, 1221, 1144, 1044, 988, 948, 920, 880, 851, 836, 792, 752, 724; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.52 (1H, d, J = 8.4 Hz, ArH), 7.45 (1H, d, J = 2.2 Hz, ArH), 7.24 (1H, dd, J = 8.4, 2.2 Hz, ArH), 7.17 (1H, dd, J = 17.4, 11.1 Hz, CH=CH<sub>2</sub>), 5.64 (1H, dd, J = 17.4, 1.3 Hz, CH=CH<sub>2</sub>), 5.39 (1H, dd, J = 11.1, 1.3 Hz, CH=CH<sub>2</sub>), 4.06 (1H, s, NCHCO), 2.25 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 1.38 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.4, 139.6, 133.7, 133.6, 133.0, 129.9, 127.8, 126.3, 117.8, 81.5, 70.7, 43.1, 27.9; HRMS (ESI): calcd for C<sub>16</sub>H<sub>23</sub>CINO<sub>2</sub> [M + H]<sup>+</sup> 296.1412, found 292.1406.

#### tert-Butyl 2-(6-chloro-2-vinylphenyl)-2-(dimethylamino)acetate (8g')

Colourless oil; IR (film) v<sub>max</sub>/cm<sup>-1</sup> 3083, 2979, 2866, 2820, 2774, 1742, 1624, 1587, 1559, 1453, 1406, 1392, 1367, 1319, 1251, 1220, 1148, 1090, 1049, 1008, 952, 906, 843, 813, 792, 747, 710; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.64 (1H, dd, J = 17.4, 10.9 Hz, CH=CH<sub>2</sub>), 7.45 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.33 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.18 (1H, ddd, J = 8.0, 8.0, 0.5 Hz, ArH), 5.59 (1H, dd, J = 17.4, 1.5 Hz, CH=CH<sub>2</sub>), 5.30 (1H, dd, J = 10.9, 1.5 Hz, CH=CH<sub>2</sub>), 4.67 (1H, s, NCHCO), 2.28 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 1.32 (9H, s, *t*Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.7, 140.5, 135.9, 135.2, 132.3, 129.0, 128.6, 125.0, 116.0, 81.1, 70.1, 43.9, 27.8; HRMS (ESI): calcd for C<sub>16</sub>H<sub>23</sub>CINO<sub>2</sub> [M + H]<sup>+</sup> 296.1412, found 292.1408. tert-Butyl 2-(dimethylamino)-2-(2-vinylphenyl)propanoate (8h)

Colourless oil; IR (film) v<sub>max</sub>/cm<sup>-1</sup> 3084, 3061, 2978, 2932, 2870, 2833, 2791, 1720, 1622, 1598, 1567, 1475, 1455, 1410, 1391, 1367, 1242, 1163, 1104, 1052, 1023, 977, 908, 844, 808, 757; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ7.53-7.46 (1H, m, ArH), 7.48 (1H, dd, J = 17.4, 10.9 Hz, CH=CH<sub>2</sub>), 7.43-7.36 (1H, m, ArH), 7.25-7.17 (2H, m, ArH), 5.53 (1H, dd, J = 17.4, 1.6 Hz, CH=CH<sub>2</sub>), 5.17 (1H, dd, J = 10.9, 1.6 Hz, CH=CH<sub>2</sub>), 2.34 (6H, s, N(CH<sub>3</sub>)<sub>2</sub>), 1.57 (3H, s, 2-CH<sub>3</sub>), 1.48 (9H, s, tBu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  171.1, 140.6, 137.4, 137.2, 127.4, 127.2, 127.0, 126.9, 114.3, 81.3, 70.8, 39.9, 28.3, 23.3; HRMS (ESI): calcd for C<sub>17</sub>H<sub>26</sub>NO<sub>2</sub> [M + H]<sup>+</sup> 276.1958, found 276.1954.

#### Conflicts of interest

There are no conflicts to declare.

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- 13 The stereochemistry of (1*S*,2*S*,1'*R*)-**3a**–**b** and (1*R*,2*R*,1'*R*)-**3b** were determined by analogy with (1*S*,2*S*,1'*S*)-**1** and analogous ammonium salt derivatives. See ref. 4a, 4b and other references therein.
- 14 Substrates (1*S*,2*S*,1'*R*)-**3a**–**b** and (1*R*,2*R*,1'*R*)-**3b** were prepared by N-quaternization of precursor tertiary amines. The ee of the tertiary amines; (1*S*,2*S*,1'*R*)-**3a**: 97% ee, (1*S*,2*S*,1'*R*)-**3b**: 98% ee and (1*R*,2*R*,1'*R*)-**3b**: 99% ee. Details: see ESI.
- 15 The stereochemistry of (*R*)-4a was determined by analogy with (*R*)-2 and (*R*)-5.
- 16 The stereochemistry of (*R*)-**5** was determined by the specific rotation value after conversion into (*R*)-**2** by hydrogenation. Details: see ESI.
- 17 According to our previous study, the initial [2,3] rearrangement of (1*R*,2*R*,1'*R*)-**3b** would proceed via eclipsed-like conformation which decreases the yield and the rate of chirality transmission. The details: see ref. 4a.
- 18 Substrates (*R*)-**6a** was prepared by N-quaternization of (*R*)-2-(dimethylamino)-2-phenylethyl acetate with *tert*-butyl bromoacetate. The ee of (*R*)-2-(dimethylamino)-2phenylethyl acetate was >99% ee. Details: see ESI.
- 19 The stereochemistry of (*R*)-**7a** was determined by analogy with (*R*)-**8a**.
- 20 The stereochemistry of (*R*)-**8a** was determined by comparison of the specific rotation value with the *S*-authentic sample after conversion into (*R*)-2-(dimethylamino)-2-(2-ethylphenyl)ethanol. Details: see ESI.
- 21 We do not present their spectroscopic characterization in this manuscript because of small amounts.