



Cite this: *Org. Biomol. Chem.*, 2015, **13**, 10548

## Synthesis and applications of secondary amine derivatives of (+)-dehydroabietylamine in chiral molecular recognition†

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(+)-Dehydroabietylamine (**1a**), the novel derivatives (**2a–6a**) and their NTf<sub>2</sub> salts (**1b–6b**) were tested as chiral NMR solvating agents for the resolution of enantiomers of the model compound Mosher's acid (**7**) and its *n*-Bu<sub>4</sub>N salt (**8**). Best enantiomeric discrimination of **7** was obtained using bisdehydroabietyl-amino-*N*<sup>1</sup>,*N*<sup>2</sup>-ethane-1,2-diamine (**6a**), and of **8** using *N*-(dehydroabietyl)-2-(dehydroabietylaminio)ethanaminium bis((trifluoromethyl)-sulfonyl)-amide (**6b**). For the maximal resolution of enantiomers of **8**, 1.0 eq. of **6b** were needed. However, 0.5 eq. of **6a** sufficed for the maximal resolution of enantiomers of **7**. Enantiomeric excess studies were successfully conducted using **6a** and **6b**. The capability of **6a** and **6b** to recognize the enantiomers of various  $\alpha$ -substituted carboxylic acids and their *n*-Bu<sub>4</sub>N salts were examined. Best resolutions were observed for aliphatic and aromatic carboxylic acids bearing an electronegative  $\alpha$ -substituent. Now the ee studies on such non-aromatic carboxylic acids are also feasible.

Received 7th August 2015,  
Accepted 24th August 2015

DOI: 10.1039/c5ob01667c

www.rsc.org/obc

## Introduction

Analytical enantiomeric purity determinations are of great interest particularly in organic, medicinal and biological chemistry, where stereocontrol is important. Compared to commonly used techniques such as HPLC, NMR is more versatile, and the development of more sensitive instruments has made it a potential competitor for the traditional methods in chiral recognition. As NMR can provide fast and easy enantiomeric excess (ee) measurements (up to 94–99% ee),<sup>1</sup> it is the ideal tool for quick ee determinations when developing new asymmetric synthesis or when studying the efficacy of a new chiral catalyst. Also, if the enantiomeric resolution cannot be efficiently performed with traditional methods, NMR can be used as an alternative.<sup>2</sup>

In NMR, two general methods to investigate the enantiomeric purity of a compound may be applied. One is to use an enantiomerically pure chiral derivatising agent to produce two diastereomers. However, this method is time consuming and also may cause concerns of kinetic resolution and racemization. The second, more convenient and faster method is provided by chiral solvating agents (CSAs) where the resolving ability is based on the supramolecular complexation between

two enantiomers of a chiral guest and a chiral host.<sup>3,4</sup> Since complex formation is strongly dependent on interactions between a host and a guest, CSAs may contain hydrogen bond acceptor and donor groups (such as –NH<sub>2</sub>, –OH, –COOH), aromatic functionality for  $\pi$ – $\pi$  stacking, and ionic and dipole groups for ion–ion, dipole–dipole and ion–dipole interactions.<sup>4,5</sup> However, the functional groups of the host and guest are not solely responsible for an efficient enantiomeric discrimination, but also the deuterated solvent used, concentration, molar ratio of host and guest, temperature and the anion (if present) of the chiral host<sup>6</sup> have an effect on the resolution.<sup>3</sup> The non-ionic and ionic CSAs are often derived from chiral natural compounds such as amino acids, menthol or mandelic acid. These compounds are generally not only chiral but also contain suitable functionalities for complex formation.

In this study we have used the readily available softwood resin derivative (+)-dehydroabietylamine<sup>7</sup> (**1a**, Scheme 1) as a starting material to create novel CSAs for the enantiomeric resolution of racemic carboxylic acids by NMR. As only few of the reported amine based CSAs are ionic, and it being thought advisable to see if ionic functionalities might provide better resolution, protonated forms of our amines were also tested.

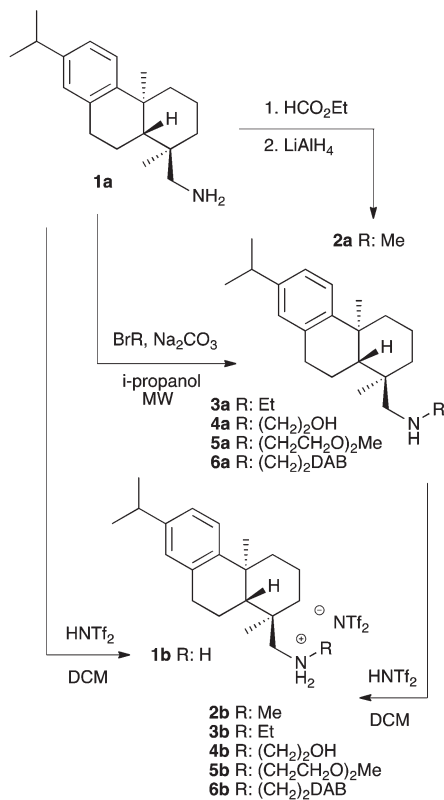
## Results and discussion

Five secondary amine derivatives **2a–6a** of **1a** were prepared and converted along with **1a** to bis(trifluoromethane)-sulfonyl-

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† Electronic supplementary information (ESI) available: NMR data, chiral recognition, titration, enantiomeric excess studies, separation of carboxylic acids. See DOI: 10.1039/c5ob01667c





**Scheme 1** Preparation of (+)-dehydroabietylamine based secondary amines and their corresponding NTf<sub>2</sub> salts. (DAB = (+)-dehydroabietylamine, BrR = BrEt, Br(CH<sub>2</sub>)<sub>2</sub>OH, Br(CH<sub>2</sub>CH<sub>2</sub>O)<sub>2</sub>Me, Br(CH<sub>2</sub>)<sub>2</sub>Br).

amide (NTf<sub>2</sub>) salts (**1b–6b**) to give CSAs with ionic functionality. NTf<sub>2</sub> was chosen for a counter anion as it has been found to provide better enantiomeric resolution with an ionic CSA.<sup>7,8</sup> Compounds **3a–6a** were readily prepared by an expedient one step reaction with suitable alkyl bromides in a microwave reactor (Scheme 1). Compound **2a** was synthesized in two steps by the conversion of **1a** to formamide followed by reduction. Physical data of the compounds are listed in Table 1, showing that when the amines are converted to NTf<sub>2</sub> salts the melting points increase and the optical rotations decrease.

The ability of compounds **1–6a** and **b** to recognize the chirality of ionic and non-ionic racemic carboxylic acids was examined using Mosher's acid **7** and its *n*-Bu<sub>4</sub>N salt **8**. The effect of concentration of CSA was also investigated, as according to literature, the magnitude of non-equivalence ( $\Delta\delta$ ) increases when the concentration of host is higher than that of the guest.<sup>3,4</sup> CDCl<sub>3</sub> was chosen as solvent for the experiments because it is known that polar solvents can solvate ions and protic solvents may interfere in hydrogen bond formation which are important for complex formation.<sup>9</sup> NMR experiments were performed by taking 0.5 mL (1.0 eq., 22.0 mM) of a stock solution containing **7** or **8** (guest) and dissolved CSA (host) (1.0 or 2.0 eq.). Both <sup>1</sup>H and <sup>19</sup>F NMR spectra were recorded (Table 2). Results indicate that **1–6a** and **b** form a dia-

**Table 1** (+)-Dehydroabietylamine derivatives and their physical data

No.	R	Anion	mp (°C)	$[\alpha]_D^{22}$ <sup>a</sup>	$[M]_D^{22}$ <sup>b</sup>
<b>1a</b>	—	—	44.2	+44.35	+126.60
<b>1b</b>	—	NTf <sub>2</sub>	197.2	+17.11	+96.96
<b>2a</b>	Me	—	Liquid at rt.	+50.64	+151.65
<b>2b</b>	Me	NTf <sub>2</sub>	180.3	+10.86	+63.06
<b>3a</b>	Et	—	Liquid at rt.	+49.47	+155.10
<b>3b</b>	Et	NTf <sub>2</sub>	180.9	+9.80	+58.35
<b>4a</b>	(CH <sub>2</sub> ) <sub>2</sub> OH	—	74.0	+42.05	+138.57
<b>4b</b>	(CH <sub>2</sub> ) <sub>2</sub> OH	NTf <sub>2</sub>	160.7	+7.03	+42.92
<b>5a</b>	(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> Me	—	Liquid at rt.	+34.07	+132.05
<b>5b</b>	(CH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub> Me	NTf <sub>2</sub>	Viscous liquid at rt.	+7.03	+47.00
<b>6a</b>	(CH <sub>2</sub> ) <sub>2</sub> DAB <sup>c</sup>	—	63.8	+43.32	+258.58
<b>6b</b>	(CH <sub>2</sub> ) <sub>2</sub> DAB <sup>c</sup>	NTf <sub>2</sub>	237.3	+13.54	+118.93

<sup>a</sup> *c* = 1.0, CHCl<sub>3</sub>. <sup>b</sup> Molar rotation calculated from  $[\alpha]_D^{22} \times M/100$ , where *M* is the molar mass. <sup>c</sup> DAB = (+)-Dehydroabietylamine.

stereometric salt pair with the model compound (**7** or **8**) as no resolution was detected between a non-ionic CSA (**1a–6a**) and **8**, or an ionic CSA (**1b–5b**) and **7**. This is most probably caused by the lack of suitable interactions in forming a salt pair. However, the ionic **6b** resolved the non-ionic **7** presumably because the former has a non-ionic amine group to be protonated by **7** and is therefore able to resolve the enantiomers of **7**. Due to the poor solubility of **6b** in CDCl<sub>3</sub> the resolution of **7** under 2 : 1 conditions could not be determined. No significant increase in the chemical shift difference between *R* and *S* enantiomers ( $\Delta\delta$ ) was detected when the concentration of host was doubled. In some cases the increase of concentration even led to a decrease in  $\Delta\delta$ . This was especially notable in the case of compounds **6a** and **6b**. Among the non-ionic CSAs, **1a**, **2a** and **6a** resolved the enantiomers of **7** highly efficiently. Especially **6a** worked exceptionally well (host : guest ratio 1 : 1) both in <sup>1</sup>H NMR (0.14 ppm, 71.8 Hz) and in <sup>19</sup>F NMR (0.045 ppm, 21.2 Hz). The extent of resolution decreased both in <sup>1</sup>H NMR and in <sup>19</sup>F NMR when the molar ratio was increased to 2 : 1. For the resolution of **8** the corresponding NTf<sub>2</sub> salts **1b**, **2b** and **6b** gave best results. In this case the highest resolution was obtained with **6b** both in <sup>1</sup>H NMR (0.16 ppm, 81.1 Hz) and in <sup>19</sup>F NMR (0.076 ppm, 35.8 Hz). As in the case of **6a**, an increase in concentration lowered  $\Delta\delta$  in <sup>1</sup>H NMR; however, in <sup>19</sup>F NMR  $\Delta\delta$  was increased to 0.32 ppm (149.9 Hz).

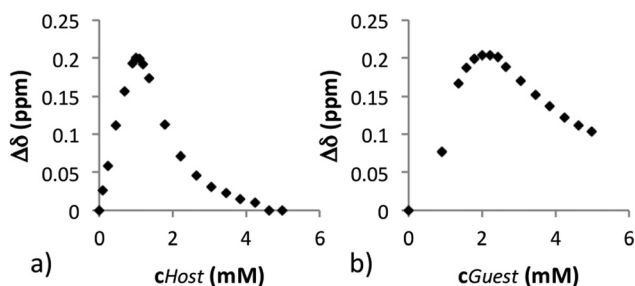
As compounds **6a** and **6b** gave the best results, their enantiomeric discrimination ability in NMR was further investigated. To find out how much guest is needed for maximum resolution and to obtain information about the composition of complex (e.g. 2 : 1 vs. 1 : 1 complex), the guest **7** (0.5 mL, 2.0 mM) was titrated with host **6a** (46.6 mM). Due to the poor solubility of **6b** in CDCl<sub>3</sub>, titration was performed in an opposite manner compared to **6a** (i.e., titrating a 2.0 mM solution of host **6b** with a 46.6 mM solution of guest **8**) (Fig. 1). Titration results from both <sup>1</sup>H and <sup>19</sup>F NMR spectra indicate that the maximal resolution with host **6a** occurs at the point where the molar ratio of host and guest was 0.5 : 1 (0.200 ppm,



**Table 2** The magnitude of non-equivalence ( $\Delta\delta$ ) between *R* and *S* enantiomers of racemic Mosher's acid (**7**) and its *n*-Bu<sub>4</sub>N salt (**8**) in the presence of different CSAs (**1–6a** and **b**) in CDCl<sub>3</sub> at 27 °C

CSA	Host : Guest	7 (ppm, (Hz))		8 (ppm, (Hz))	
		<sup>1</sup> H	<sup>19</sup> F	<sup>1</sup> H	<sup>19</sup> F
<b>1a</b>	1 : 1	0.024 (12.1)	0.074 (34.6)	nd	nd
	2 : 1	0.022 (10.9)	0.064 (30.3)	nd	nd
<b>1b</b>	1 : 1	nd	nd	0.014 (6.8)	0.051 (23.9)
	2 : 1	nd	nd	0.016 (8.0)	0.059 (27.7)
<b>2a</b>	1 : 1	0.037 (18.7)	nd	nd	nd
	2 : 1	0.04 (20.0)	0.029 (13.5)	nd	nd
<b>2b</b>	1 : 1	nd	nd	0.033 (16.6)	0.019 (8.7)
	2 : 1	nd	nd	0.025 (12.7)	nd
<b>3a</b>	1 : 1	0.013 (6.7)	nd	nd	nd
	2 : 1	0.016 (7.8)	nd	nd	nd
<b>3b</b>	1 : 1	nd	nd	0.014 (6.9)	nd
	2 : 1	nd	nd	0.0074 (3.7)	nd
<b>4a</b>	1 : 1	0.0059 (3.0)	0.017 (8.0)	nd	nd
	2 : 1	0.0092 (4.6)	0.0066 (3.1)	nd	nd
<b>4b</b>	1 : 1	nd	nd	0.0051 (2.5)	nd
	2 : 1	nd	nd	0.0068 (3.4)	nd
<b>5a</b>	1 : 1	0.015 (7.5)	nd	nd	nd
	2 : 1	0.013 (6.3)	nd	nd	nd
<b>5b</b>	1 : 1	nd	nd	0.0082 (4.1)	nd
	2 : 1	nd	nd	0.014 (6.8)	nd
<b>6a</b>	1 : 1	0.14 (71.8)	0.045 (21.2)	nd	nd
	2 : 1	0.027 (12.3)	0.028 (13.3)	nd	nd
<b>6b</b>	1 : 1	0.023 (11.3)	0.035 (16.6)	0.16 (81.1)	0.076 (35.8)
	2 : 1	— <sup>a</sup>	— <sup>a</sup>	0.038 (22.2)	0.32 (149.9)

<sup>a</sup> Could not be measured since **6b** was not soluble in CDCl<sub>3</sub> at high concentrations. nd (no resolution was detected).



**Fig. 1** (a) The chiral resolution of enantiomers of **7** with **6a** (<sup>1</sup>H NMR) and (b) chiral resolution of enantiomers of **8** with **6b** (<sup>1</sup>H NMR).

99.9 Hz in <sup>1</sup>H NMR and 0.088 ppm, 41.2 Hz, in <sup>19</sup>F NMR), and with **6b** at the molar ratio 1 : 1 (0.204 ppm, 101.8 Hz in <sup>1</sup>H NMR and 0.093 ppm, 43.7 Hz in <sup>19</sup>F NMR) (see ESI 3.1 and 3.2†). Commercially available CSAs are often expensive, and the ability of **6a** to resolve enantiomers at the host:guest molar ratio 0.5 : 1 is a clear improvement as a minimum of 1.0 eq. (and in some cases an excess up to 24 eq.) of host is needed to obtain a maximal resolution.<sup>3</sup> Since  $\Delta\delta$  between the enantiomers of **7** (and of **8**) decreased in <sup>1</sup>H NMR when the concentration of **6a** (or **6b**) increased, it is assumed that

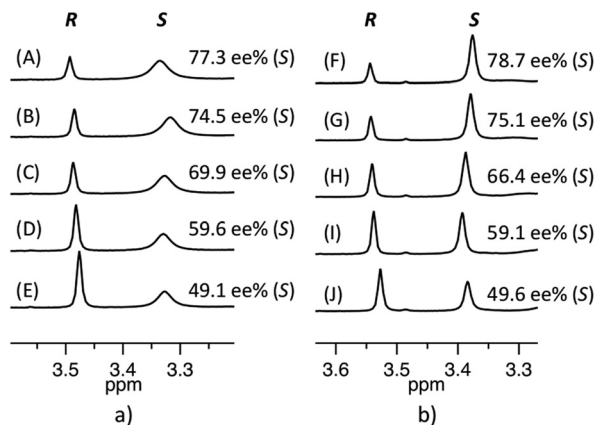
the supramolecular complexation pattern changes when the concentration of host increases.

The suitability of CSAs **6a** and **6b** for enantiomeric excess (ee) NMR measurements was tested with **7** and **8**. Both **6a** and **6b** can be used to detect the enantiomeric composition of samples with excellent reliability (Fig. 2a and b; see ESI 4.1 and 4.2†).

The resolution of racemic  $\alpha$ -substituted carboxylic acids or their *n*-Bu<sub>4</sub>N salts by **6a** and **6b**, respectively, is presented in Table 3 and ESI 5.1 and 5.2.† CSAs **6a** and **6b** discriminate best carboxylic acids having an electronegative atom (e.g. O, N, Br) at the  $\alpha$ -position (**11–15a** and **b**). Such aromatic or non-aromatic carboxylic acids were discriminated equally well. This is a major improvement as it has been suggested that the presence of an aromatic ring is necessary for good signal separation.<sup>10</sup> In any case the resolution of non-aromatic carboxylic acids, especially using amine based CSAs, has been largely neglected.<sup>4,9,11</sup>

The carboxylic acids **9a** and **b**, **10a** and **b** were discriminated by the corresponding host only moderately (1–7 Hz). This may be due to the lack of suitable interactions between the host and guest. This, however, is not a problem for ee determination as certain specialized NMR experiments are now available and can be used when the multiplet resolution





**Fig. 2** Validation of enantiomeric composition of (a) **7** in the presence of **6a** (expected ee%: (A) 80, (B) 75, (C) 70, (D) 60, (E) 50) and (b) **8** in the presence of **6b** (expected ee%: (F) 50, (G) 58, (H) 67, (I) 75, (J) 79) by  $^1\text{H}$  NMR (500 MHz) in  $\text{CDCl}_3$  at 27 °C. (The peak of *S* enantiomer is wider due to strong binding with **6a**, see ESI 3.1.1.†)

needs improvement or when the overlapping of CSA and substrate is an issue.<sup>12</sup> Compound **6b** resolves the enantiomers of **9–12b** better than its non-ionic form **6a** resolves those of compounds **9–12a**, indicating that stronger interaction can be obtained between the ionic CSA and ionic substrate. This can be used to advantage if the resolution of non-ionic CSA and substrate is not sufficient. CSA **6a** resolves the enantiomers of **13–15a** better than the corresponding ionic CSA **6b** those of **13–15b**. Interestingly **6a** resolved the prochiral  $\text{CH}_2$  hydrogens in compound **9a**. Since CSAs are usually able to resolve  $\alpha$ -substituted carboxylic acids at the chiral  $\alpha$ -site<sup>13</sup> only, this is an additional advantage.

## Conclusions

A number of derivatives (**2a–6a**) of (+)-dehydroabietylamine (**1a**) and their  $\text{NTf}_2$  salts (**1b–6b**) were prepared for use in chiral molecular recognition studies, the syntheses being carried out by highly expedient microwave techniques. The ability of the CSAs **1–6a** and **b** to resolve racemic **7** and **8** was examined by  $^1\text{H}$  and  $^{19}\text{F}$  NMR. **6a** showed excellent discrimination ability for **7** and its corresponding  $\text{NTf}_2$  salt **6b** for **8**. Optimum conditions for enantiomeric discrimination with **6a** and **6b** were determined by titration. **6b** gives best results at a 1 : 1 host : guest molar ratio whereas **6a** gave best resolution at a 0.5 : 1 host : guest molar ratio. This is a useful result since usually at least 1.0 eq. of CSA are needed for maximum resolution. **6a** and **6b** are highly useful in ee determination as well. In resolving various  $\alpha$ -substituted racemic carboxylic acids using **6a** or **6b**, best results were given by acids bearing an electronegative  $\alpha$ -substituent. In general, acids bearing or lacking an aromatic moiety performed equally well. For carboxylates, somewhat better results were obtained when ionic CSA **6b** was used for the resolution than when using **6a** for non-ionic sub-

strates. In future, the applicability of compounds **6a** and **6b** in resolution by NMR will be further investigated, and the development of new (+)-dehydroabietylamine based CSAs are being continued.

## Experimental

### Materials and methods

All reagents and solvents were obtained from commercial suppliers and were used without further purification unless otherwise stated. Dehydroabietylamine was purchased (Sigma Aldrich) as 60% grade and purified by a method described in the literature<sup>14</sup> with slight modifications (see below). Flash chromatography was performed on 40–63 mesh silica gel. Microwave oven reactions were performed using the CEM Focused Microwave<sup>TM</sup> Synthesis System (Model Discover). Melting points were determined on a digital melting point apparatus (Büchi B 545). Optical rotations were determined on a digital polarimeter (JASCO DIP-1000) at 22 °C in  $\text{CHCl}_3$  or MeOH as solvent. Exact masses were obtained using high-resolution mass spectrometry (Bruker MicroTOF LC) with electrospray ionisation (ESI).

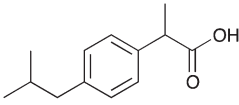
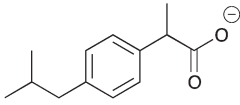
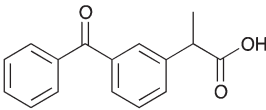
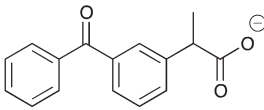
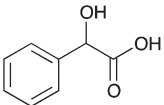
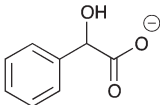
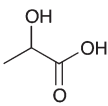
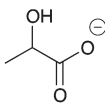
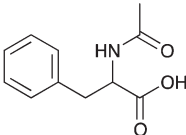
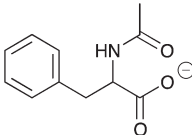
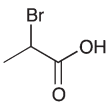
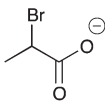
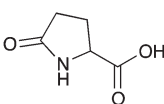
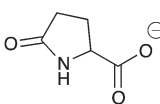
### Synthesis of chiral solvating agents

**Purification of (+)-dehydroabietylamine 1a.** 60% (+)-dehydroabietylamine (42.0 g) was dissolved in toluene (70.0 mL) and acetic acid (9.65 g) in toluene (30.0 mL) was slowly added. The salt was let to crystallize in fridge. The product was filtered and washed with hexane. (+)-Dehydroabietylamine acetate was recrystallized from MeOH. (+)-Dehydroabietylamine acetate (21.0 g) was dissolved in hot water and 10% NaOH solution (28.0 mL) was added. (+)-Dehydroabietylamine was extracted by  $\text{Et}_2\text{O}$  and the organic phase was washed with water until neutral. The organic phase was dried over  $\text{Na}_2\text{SO}_4$ . The solvent was evaporated and (+)-dehydroabietylamine was dried under vacuum; mp 44.2 °C (lit. 44–45 °C);<sup>15</sup> HRMS-ESI ( $m/z$ ) calc. for  $\text{C}_{20}\text{H}_{32}\text{N}$  [ $\text{M} + \text{H}$ ]<sup>+</sup> 286.2529, found 286.2540; [ $\alpha_{\text{D}}^{22}$  +44.3480 ( $c$  1.0 in  $\text{CHCl}_3$ ) (lit. +58.0,  $c$  0.2 in DMSO, 20 °C);<sup>15</sup>  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 0.891 (s, 3H,  $\text{CH}_3$ ), 1.220 (s, 3H,  $\text{CH}_3$ ), 1.224 (d,  $J = 6.98$  Hz, 6H,  $2 \times \text{CH}_3$ ), 1.331 (m, 2H,  $\text{CH}_2$ ), 1.386 (m, 1H,  $\text{CHH}$ ), 1.521 (dd,  $J = -11.75, 3.31$  Hz, 1H,  $\text{CH}$ ), 1.688 (m, 2H,  $\text{CH}_2$ ), 1.736 (m, 2H,  $\text{CH}_2$ ), 2.289 (dt,  $J = -13.14, 1.72$  Hz, 1H,  $\text{CHH}$ ), 2.395 (d,  $J = -13.46$  Hz, 1H,  $\text{CHH}$ ), 2.607 (d,  $J = -13.46$  Hz, 1H,  $\text{CHH}$ ), 2.822 (sep,  $J = 6.98$  Hz, 1H,  $\text{CH}$ ), 2.884 (m, 2H,  $\text{CH}_2$ ), 6.891 (d,  $J = 1.94$  Hz, 1H,  $\text{CH}_{\text{Ar}}$ ), 6.996 (dd,  $J = 8.08, 1.94$  Hz, 1H,  $\text{CH}_{\text{Ar}}$ ), 7.183 (d,  $J = 8.08$  Hz, 1H,  $\text{CH}_{\text{Ar}}$ );  $^{13}\text{C}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 18.777 ( $\text{CH}_2$ ), 18.895 ( $\text{CH}_3$ ), 18.895 ( $\text{CH}_2$ ), 24.107 ( $\text{CH}_3$ ), 24.130 ( $\text{CH}_3$ ), 25.374 ( $\text{CH}_3$ ), 30.311 ( $\text{CH}_2$ ), 33.575 ( $\text{CH}$ ), 35.355 ( $\text{CH}_2$ ), 37.355 ( $\text{C}$ ), 37.527 ( $\text{C}$ ), 38.699 ( $\text{CH}_2$ ), 45.003 ( $\text{CH}$ ), 53.998 ( $\text{CH}_2$ ), 123.959 ( $\text{CH}_{\text{Ar}}$ ), 124.382 ( $\text{CH}_{\text{Ar}}$ ), 126.937 ( $\text{CH}_{\text{Ar}}$ ), 134.840 ( $\text{C}_{\text{Ar}}$ ), 145.668 ( $\text{C}_{\text{Ar}}$ ), 147.626 ( $\text{C}_{\text{Ar}}$ ).

**Dehydroabietyl-N-methanamine 2a.** (+)-Dehydroabietylamine (1.82 g, 6.38 mmol, 1.0 eq.) and ethyl formate (1.01 g, 1.10 mL, 12.76 mmol, 2.0 eq.) were measured to a flask and



**Table 3** The magnitude of non-equivalencies of aromatic and non-aromatic racemic carboxylic acids in the presence of **6a** and their *n*-Bu<sub>4</sub>N salts in the presence of **6b** (<sup>1</sup>H 500 MHz NMR, CDCl<sub>3</sub> at 27 °C)

Cmpd. <sup>a</sup>	Racemic carboxylic acid	$\Delta\delta$		Cmpd. <sup>b</sup>	<i>n</i> -Bu <sub>4</sub> N salt of racemic carboxylic acid	$\Delta\delta$			
		ppm	Hz			ppm	Hz		
<b>9a</b>		Me H CH <sub>2</sub>	0.0020 0.0052 0.0062	1.1 2.6 3.1	<b>9b</b>		Me H CH <sub>2</sub>	0.0099 0.0053 — <sup>c</sup>	5.0 2.6 — <sup>c</sup>
<b>10a</b>		Me H	0.014 nd	7.2 nd	<b>10b</b>		Me H	0.01 nd	5.1 nd
<b>11a</b>		H	0.084	42.1	<b>11b</b>		H	0.10	50.8
<b>12a</b>		H Me	0.014 0.0062	6.9 3.1	<b>12b</b>		H Me	0.038 — <sup>c</sup>	19.1 — <sup>c</sup>
<b>13a</b>		H NH Me	0.01 0.052 0.033	5.1 26.1 16.3	<b>13b</b>		H NH Me	nd 0.051 0.033	nd 25.5 16.5
<b>14a</b>		H Me	0.014 0.077	6.1 38.7	<b>14b</b>		H Me	0.016 — <sup>c</sup>	8.2 — <sup>c</sup>
<b>15a</b>		H NH	0.016 0.088	8.2 43.8	<b>15b</b>		H NH	0.017 0.072	8.4 36.2

<sup>a</sup> 11.0 μL of a 46.6 mM **6a** solution was added to 0.5 mL of a 2.0 mM solution of the analyte studied, to give an 0.5 : 1 host : guest molar ratio.

<sup>b</sup> 22.5 μL of a 46.6 mM solution of the analyte studied was added to 0.5 mL of a 2.0 mM solution of **6b**, to give a 1 : 1 host : guest molar ratio.

<sup>c</sup> Peak overlapped with host peaks; nd (no resolution was detected).

refluxed at 65 °C over night. The excess ethylformate was evaporated and product dried under vacuum (yield 99.8%). (+)-Dehydroabietylformamide (2.01 g, 6.41 mmol, 1.0 eq.) in THF (20 mL) was added dropwise to a flask containing LiAlH<sub>4</sub> suspension (0.26 g, 6.74 mmol, 1.05 eq.) in THF (15 mL) at 0 °C, refluxed for 6 h and let to cool to rt. MeOH was added to reaction mixture, which was stirred for 10 min.

#### General procedure for the preparation of secondary amines under microwave irradiation

The mixture was filtered and solvent evaporated. The crude product was dissolved in Et<sub>2</sub>O, dried over MgSO<sub>4</sub> and filtered. The solvent was evaporated and the product dried under vacuum, and purified by column chromatography (1 : 9 MeOH : DCM). Yield 0.60 g, 42.0%; colourless liquid; calc. for C<sub>21</sub>H<sub>34</sub>N

[M + H]<sup>+</sup> 300.2686, found 300.2690; [α]<sub>D</sub><sup>22</sup> +50.6360 (*c* = 1.0, CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ ppm 0.951 (s, 3H, CH<sub>3</sub>), 1.223 (s, 3H, CH<sub>3</sub>), 1.229 (d, *J* = 6.90 Hz, 6H, 2 × CH<sub>3</sub>), 1.406 (m, 1H, CHH), 1.431 (m, 2H, CH<sub>2</sub>), 1.543 (dd, *J* = −12.27, 2.54 Hz, 1H, CH), 1.771 (m, 2H, CH<sub>2</sub>), 1.789 (m, 2H, CH<sub>2</sub>), 2.334 (d, *J* = −11.72 Hz, 1H, CHH), 2.433 (s, 3H, CH<sub>3</sub>), 2.457 (d, *J* = −11.72 Hz, 1H, CHH), 2.826 (sep *J* = 6.90 Hz, 1H, CH), 2.893 (m, 2H, CH<sub>2</sub>), 6.885 (d, *J* = 2.11 Hz, 1H, CH<sub>Ar</sub>), 6.986 (dd, *J* = 8.20, 2.11 Hz, 1H, CH<sub>Ar</sub>), 7.172 (d, *J* = 8.20 Hz, 1H, CH<sub>Ar</sub>); <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>) δ ppm 19.008 (CH<sub>3</sub>), 19.091 (CH<sub>2</sub>), 19.218 (CH<sub>2</sub>), 24.146 (2 × CH<sub>3</sub>), 25.409 (CH<sub>3</sub>), 30.361 (CH<sub>2</sub>), 33.590 (CH), 36.520 (CH<sub>2</sub>), 37.094 (C), 37.580 (C), 37.879 (CH<sub>3</sub>), 38.664 (CH<sub>2</sub>), 46.061 (CH), 64.881 (CH<sub>2</sub>), 123.902 (CH<sub>Ar</sub>), 124.355 (CH<sub>Ar</sub>), 126.896 (CH<sub>Ar</sub>), 134.908 (C<sub>Ar</sub>), 145.582 (C<sub>Ar</sub>), 147.694 (C<sub>Ar</sub>).



### General procedure for preparation of secondary amines under microwave radiation

(+)-Dehydroabietylamine (1.0 eq.), 1-bromoethane (1.05 eq.) and  $\text{Na}_2\text{CO}_3$  (0.6 eq.) were added to a microwave tube with isopropanol (in the case of **6a** (+)-dehydroabietylamine (2.0 eq.), 1,2-dibromoethane (1.0 eq.) and  $\text{Na}_2\text{CO}_3$  (1.0 eq.) were used). The reaction mixture was microwave irradiated (110 W at 110 °C) for 2 h. The solvent was evaporated and the residue triturated with ether, filtered and mixed with  $\text{Et}_2\text{O}$ . The separated phases and organic phase was washed with water until neutral. The organic phase was dried over  $\text{Na}_2\text{SO}_4$  and filtered, the solvent evaporated and the product dried under vacuum.

**Dehydroabietyl-N-ethanamine 3a.** Yield 2.47 g 74.9%; colourless liquid; calc. for  $\text{C}_{22}\text{H}_{36}\text{N}$   $[\text{M} + \text{H}]^+$  314.2842, found 314.2834;  $[\alpha]_{\text{D}}^{22} +49.4720$  ( $c = 1.0$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 0.938 (s, 3H,  $\text{CH}_3$ ), 1.082 (t,  $J = 6.93$  Hz, 3H,  $\text{CH}_3$ ), 1.225 (s, 3H,  $\text{CH}_3$ ), 1.235 (d,  $J = 7.04$  Hz, 6H,  $2 \times \text{CH}_3$ ), 1.410 (m, 1H,  $\text{CHH}$ ), 1.425 (m, 2H,  $\text{CH}_2$ ), 1.595 (dd,  $J = -12.09$ , 2.49 Hz, 1H,  $\text{CH}$ ), 1.666 (m, 2H,  $\text{CH}_2$ ), 1.785 (m, 2H,  $\text{CH}_2$ ), 2.277 (dt,  $J = -12.22$  Hz, 3.65, 1H,  $\text{CHH}$ ), 2.327 (d,  $J = -11.74$  Hz, 1H,  $\text{CHH}$ ), 2.512 (d,  $J = -11.74$  Hz, 1H,  $\text{CHH}$ ), 2.626 (q,  $J = 6.93$ , 2H,  $\text{CH}_2$ ), 2.832 (sep  $J = 7.02$  Hz, 1H,  $\text{CH}$ ), 2.892 (m, 2H,  $\text{CH}_2$ ), 6.893 (d,  $J = 2.20$  Hz, 1H,  $\text{CH}_{\text{Ar}}$ ), 6.993 (dd,  $J = 8.14$ , 2.20 Hz, 1H,  $\text{CH}_{\text{Ar}}$ ), 7.185 (d,  $J = 8.14$  Hz, 1H,  $\text{CH}_{\text{Ar}}$ );  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 15.641 ( $\text{CH}_3$ ), 18.959 ( $\text{CH}_2$ ), 19.040 ( $\text{CH}_3$ ), 19.380 ( $\text{CH}_2$ ), 24.146 ( $2 \times \text{CH}_3$ ), 25.466 ( $\text{CH}_3$ ), 30.459 ( $\text{CH}_2$ ), 33.590 ( $\text{CH}$ ), 36.447 ( $\text{CH}_2$ ), 37.054 ( $\text{C}$ ), 37.588 ( $\text{C}$ ), 38.697 ( $\text{CH}_2$ ), 45.324 ( $\text{CH}_2$ ), 45.721 ( $\text{CH}$ ), 61.881 ( $\text{CH}_2$ ), 123.910 ( $\text{CH}_{\text{Ar}}$ ), 124.428 ( $\text{CH}_{\text{Ar}}$ ), 126.904 ( $\text{CH}_{\text{Ar}}$ ), 134.997 ( $\text{C}_{\text{Ar}}$ ), 145.557 ( $\text{C}_{\text{Ar}}$ ), 147.491 ( $\text{C}_{\text{Ar}}$ ).

**Dehydroabietylamine-N-ethanol 4a.** Recrystallized from  $\text{Et}_2\text{O}$  pentane mixture. Yield 0.25 g, 71.0%; white solid; mp. 74.0 °C; calc. for  $\text{C}_{22}\text{H}_{36}\text{NO}$   $[\text{M} + \text{H}]^+$  330.2791, found 330.2804;  $[\alpha]_{\text{D}}^{22} +42.0520$  ( $c = 1.0$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 0.935 (s, 3H,  $\text{CH}_3$ ), 1.225 (s, 3H,  $\text{CH}_3$ ), 1.231 (d,  $J = 6.86$  Hz, 6H,  $2 \times \text{CH}_3$ ), 1.402 (m, 1H,  $\text{CHH}$ ), 1.410 (m, 2H,  $\text{CH}_2$ ), 1.636 (dd,  $J = -11.45$ , 2.75 Hz, 1H,  $\text{CH}$ ), 1.672 (m, 2H,  $\text{CH}_2$ ), 1.753 (m, 2H,  $\text{CH}_2$ ), 2.289 (dt,  $J = -12.53$  Hz, 3.22, 1H,  $\text{CHH}$ ), 2.307 (d,  $J = -11.78$  Hz, 1H,  $\text{CHH}$ ), 2.512 (d,  $J = -11.78$  Hz, 1H,  $\text{CHH}$ ), 2.763 (m, 2H,  $\text{CH}_2$ ), 2.832 (m, 1H,  $\text{CH}$ ), 2.897 (m, 2H,  $\text{CH}_2$ ), 3.578 (m, 2H,  $\text{CH}_2$ ), 6.892 (d,  $J = 1.98$  Hz, 1H,  $\text{CH}_{\text{Ar}}$ ), 6.995 (dd,  $J = 8.20$ , 1.98 Hz, 1H,  $\text{CH}_{\text{Ar}}$ ), 7.185 (d,  $J = 8.20$  Hz, 1H,  $\text{CH}_{\text{Ar}}$ );  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 18.951 ( $\text{CH}_2$ ), 18.983 ( $\text{CH}_3$ ), 19.485 ( $\text{CH}_2$ ), 24.114 ( $\text{CH}_3$ ), 24.138 ( $\text{CH}_3$ ), 25.490 ( $\text{CH}_3$ ), 30.426 ( $\text{CH}_2$ ), 33.582 ( $\text{CH}$ ), 36.382 ( $\text{CH}_2$ ), 37.151 ( $\text{C}$ ), 37.564 ( $\text{C}$ ), 38.800 ( $\text{CH}_2$ ), 45.397 ( $\text{CH}$ ), 51.661 ( $\text{CH}_2$ ), 60.603 ( $\text{CH}_2$ ), 60.975 ( $\text{CH}_2$ ), 123.975 ( $\text{CH}_{\text{Ar}}$ ), 124.404 ( $\text{CH}_{\text{Ar}}$ ), 126.961 ( $\text{CH}_{\text{Ar}}$ ), 134.859 ( $\text{C}_{\text{Ar}}$ ), 145.654 ( $\text{C}_{\text{Ar}}$ ), 147.613 ( $\text{C}_{\text{Ar}}$ ).

**Dehydroabietylamine-N-2-(2-methoxyethoxy)ethanamine 5a.** Yield 0.23 g, 57.5%; yellow liquid; calc. for  $\text{C}_{25}\text{H}_{42}\text{NO}_2$   $[\text{M} + \text{H}]^+$  388.3210, found 388.3214;  $[\alpha]_{\text{D}}^{22} +34.0680$  ( $c = 1.0$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 0.923 (s, 3H,  $\text{CH}_3$ ), 1.217 (s, 3H,  $\text{CH}_3$ ), 1.228 (d,  $J = 6.95$  Hz, 6H,  $2 \times \text{CH}_3$ ), 1.400 (m, 1H,  $\text{CHH}$ ),

1.430 (m, 2H,  $\text{CH}_2$ ), 1.609 (dd,  $J = -11.58$ , 2.32 Hz, 1H,  $\text{CH}$ ), 1.662 (m, 2H,  $\text{CH}_2$ ), 1.765 (m, 2H,  $\text{CH}_2$ ), 2.275 (dt,  $J = -13.08$  Hz, 3.51, 1H,  $\text{CHH}$ ), 2.305 (d,  $J = -11.62$  Hz, 1H,  $\text{CHH}$ ), 2.532 (d,  $J = -11.62$  Hz, 1H,  $\text{CHH}$ ), 2.778 (t,  $J = 5.33$  Hz, 2H,  $\text{CH}_2$ ), 2.825 (sep  $J = 6.95$  Hz, 1H,  $\text{CH}$ ), 2.880 (m, 2H,  $\text{CH}_2$ ), 3.374 (s, 3H,  $\text{CH}_3$ ), 3.535 (m, 2H,  $\text{CH}_2$ ), 3.561 (m, 2H,  $\text{CH}_2$ ), 3.599 (m, 2H,  $\text{CH}_2$ ), 6.884 (d,  $J = 2.08$  Hz, 1H,  $\text{CH}_{\text{Ar}}$ ), 6.986 (dd,  $J = 8.15$ , 2.08 Hz, 1H,  $\text{CH}_{\text{Ar}}$ ), 7.176 (d,  $J = 8.15$  Hz, 1H,  $\text{CH}_{\text{Ar}}$ );  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 18.935 ( $\text{CH}_2$ ), 19.040 ( $\text{CH}_2$ ), 19.380 ( $\text{CH}_3$ ), 24.138 ( $2 \times \text{CH}_3$ ), 25.490 ( $\text{CH}_3$ ), 30.467 ( $\text{CH}_2$ ), 33.582 ( $\text{CH}$ ), 36.334 ( $\text{CH}_2$ ), 37.200 ( $\text{C}$ ), 37.588 ( $\text{C}$ ), 38.680 ( $\text{CH}_2$ ), 45.510 ( $\text{CH}$ ), 50.451 ( $\text{CH}_2$ ), 59.187 ( $\text{CH}_2$ ), 61.809 ( $\text{CH}_2$ ), 70.367 ( $\text{CH}_2$ ), 70.824 ( $\text{CH}_2$ ), 72.078 ( $\text{CH}_2$ ), 123.894 ( $\text{CH}_{\text{Ar}}$ ), 124.452 ( $\text{CH}_{\text{Ar}}$ ), 126.896 ( $\text{CH}_{\text{Ar}}$ ), 135.037 ( $\text{C}_{\text{Ar}}$ ), 145.533 ( $\text{C}_{\text{Ar}}$ ), 147.783 ( $\text{C}_{\text{Ar}}$ ).

**Bisdehydroabietylaminone- $N^1,N^2$ -ethane-1,2-diamine 6a.** Purified by flash chromatography (1 : 9 MeOH : DCM). Yield 0.78 g 74.3%; white solid; mp. 63.8 °C; calc. for  $\text{C}_{42}\text{H}_{65}\text{N}_2$   $[\text{M} + \text{H}]^+$  597.5142, found 597.5132;  $[\alpha]_{\text{D}}^{22} +43.3160$  ( $c = 1.0$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 0.914 (s, 6H,  $2 \times \text{CH}_3$ ), 1.204 (s, 6H,  $2 \times \text{CH}_3$ ), 1.229 (d,  $J = 7.02$  Hz, 12H,  $4 \times \text{CH}_3$ ), 1.336 (m, 2H,  $2 \times \text{CHH}$ ), 1.375 (m, 4H,  $2 \times \text{CH}_2$ ), 1.565 (dd,  $J = -12.25$ , 2.66 Hz, 2H,  $2 \times \text{CH}$ ), 1.603 (m, 4H,  $2 \times \text{CH}_2$ ), 1.713 (m, 2H,  $2 \times \text{CHH}$ ), 1.753 (m, 2H,  $2 \times \text{CHH}$ ), 2.233 (dt,  $J = -12.83$ , 3.27 Hz, 2H,  $2 \times \text{CHH}$ ), 2.319 (d,  $J = -11.80$  Hz, 2H,  $2 \times \text{CHH}$ ), 2.509 (d,  $J = -11.80$  Hz, 2H,  $2 \times \text{CHH}$ ), 2.696 (s, 4H,  $2 \times \text{CH}_2$ ), 2.824 (sep  $J = 7.02$  Hz, 2H,  $2 \times \text{CH}$ ), 2.876 (m, 4H,  $2 \times \text{CH}_2$ ), 6.872 (d,  $J = 1.85$  Hz, 2H,  $2 \times \text{CH}_{\text{Ar}}$ ), 6.983 (dd,  $J = 8.13$ , 1.85 Hz, 2H,  $2 \times \text{CH}_{\text{Ar}}$ ), 7.158 (d,  $J = 8.13$  Hz, 2H,  $2 \times \text{CH}_{\text{Ar}}$ );  $^{13}\text{C}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 18.983 ( $4 \times \text{CH}_2$ ), 19.348 ( $2 \times \text{CH}_3$ ), 24.138 ( $4 \times \text{CH}_3$ ), 25.466 ( $2 \times \text{CH}_3$ ), 30.459 ( $2 \times \text{CH}_2$ ), 33.582 ( $2 \times \text{CH}$ ), 36.390 ( $2 \times \text{CH}_2$ ), 37.167 ( $2 \times \text{C}$ ), 37.548 ( $2 \times \text{C}$ ), 38.583 ( $2 \times \text{CH}_2$ ), 45.624 ( $2 \times \text{CH}$ ), 50.018 ( $\text{CH}_2$ ), 61.606 ( $2 \times \text{CH}_2$ ), 123.910 ( $2 \times \text{CH}_{\text{Ar}}$ ), 124.412 ( $2 \times \text{CH}_{\text{Ar}}$ ), 126.888 ( $2 \times \text{CH}_{\text{Ar}}$ ), 134.883 ( $\text{C}_{\text{Ar}}$ ), 145.541 ( $2 \times \text{C}_{\text{Ar}}$ ), 147.637 ( $2 \times \text{C}_{\text{Ar}}$ ).

### General procedure of $\text{NTf}_2$ salts

Primary amine **1a** or secondary amine **2a–6a** (1.0 eq.) was dissolved to DCM (0.5 mL).  $\text{HNTf}_2$  (1.0 eq.) was added at 0 °C. Reaction mixture was stirred for 1 h at rt. The layers were separated and the organic phase washed with water ( $3 \times 2.0$  mL). The organic solvent was evaporated and product dried in vacuum.

**Dehydroabietylaminium bis((trifluoromethyl)sulfonyl)amide 1b.** Yield 0.18 g, 93.1%; white solid; mp. 197.2 °C; calc. for  $\text{C}_{20}\text{H}_{32}\text{N}$   $[\text{M} - \text{NTf}_2]^+$  286.2529, found 286.2537; calc. for  $\text{C}_2\text{F}_6\text{NO}_4\text{S}_2$   $[\text{NTf}_2]$  279.9167, found 279.9178;  $[\alpha]_{\text{D}}^{22} +17.1120$  ( $c = 1.0$ ,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 1.062 (s, 3H,  $\text{CH}_3$ ), 1.213 (m, 1H,  $\text{CHH}$ ), 1.225 (d,  $J = 6.78$  Hz, 6H,  $2 \times \text{CH}_3$ ), 1.230 (s, 3H,  $\text{CH}_3$ ), 1.371 (dd,  $J = -12.42$ , 2.50 Hz, 1H,  $\text{CH}$ ), 1.408 (m, 1H,  $\text{CHH}$ ), 1.592 (td,  $J = -12.74$ , 3.16 Hz, 1H,  $\text{CHH}$ ), 1.655 (td,  $J = 7.30$ , 1.96 Hz, 1H,  $\text{CHH}$ ), 1.681 (td,  $J = 7.30$ , 1.96 Hz, 1H,  $\text{CHH}$ ), 1.752 (m, 2H,  $\text{CH}_2$ ), 2.329 (dt,  $J = -13.01$ , 3.35 Hz, 1H,  $\text{CHH}$ ), 2.822 (sep  $J = 6.78$  Hz,  $\text{CH}$ ), 2.829 (d,  $J = -12.89$  Hz, 1H,  $\text{CHH}$ ), 2.904 (m, 2H,  $\text{CH}_2$ ), 3.167 (d,  $J = -12.89$  Hz, 2H,  $\text{CHH}$ ), 6.888 (d,  $J = 1.81$  Hz, 1H,  $\text{CH}_{\text{Ar}}$ ), 6.998 (dd,  $J = 8.17$ ,



1.81 Hz, 1H,  $CH_{Ar}$ ), 7.141 (d,  $J = 8.17$  Hz, 1H,  $CH_{Ar}$ );  $^{13}C$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  ppm 17.001 ( $CH_3$ ), 18.166 ( $CH_2$ ), 19.089 ( $CH_2$ ), 24.049 ( $CH_3$ ), 24.090 ( $CH_3$ ), 25.174 ( $CH_3$ ), 29.609 ( $CH_2$ ), 33.598 ( $CH$ ), 35.201 ( $CH_2$ ), 35.678 ( $C$ ), 37.572 ( $C$ ), 37.912 ( $CH_2$ ), 47.008 ( $CH$ ), 52.834 ( $CH_2$ ), 119.552 (q,  $J = 320.75$ ,  $CF_3$ ), 124.137 ( $CH_{Ar}$ ), 124.258 ( $CH_{Ar}$ ), 126.977 ( $CH_{Ar}$ ), 134.074 ( $C_{Ar}$ ), 146.188 ( $C_{Ar}$ ), 146.245 ( $C_{Ar}$ ).

**Dehydroabietyl-N-methanaminium bis((trifluoromethyl)sulfonyl)amide 2b.** Yield 0.098, g 88.6%; white solid; mp. 180.3 °C; calc. for  $C_{21}H_{34}N [M - NTF_2]^+$  300.2686, found 300.2696 calc. for  $C_2F_6NO_4S_2 [NTf_2]$  279.9167, found 279.9167;  $[\alpha]_D^{22} +10.8600$  ( $c = 1.0$ ,  $CHCl_3$ );  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  ppm 1.102 (s, 3H,  $CH_3$ ), 1.218 (d,  $J = 7.06$  Hz, 6H,  $2 \times CH_3$ ), 1.227 (s, 3H,  $CH_3$ ), 1.278 (m, 1H,  $CHH$ ), 1.371 (dd,  $J = -12.49$ , 2.30 Hz, 1H,  $CH$ ), 1.408 (m, 1H,  $CHH$ ), 1.656 (m, 1H,  $CHH$ ), 1.662 (m, 1H,  $CHH$ ), 1.753 (m, 2H,  $CH_2$ ), 1.824 (m, 1H,  $CHH$ ), 2.332 (dt,  $J = -13.14$ , 3.08 Hz, 1H,  $CHH$ ), 2.717 (d,  $J = -12.06$  Hz, 1H,  $CHH$ ), 2.823 (sep  $J = 7.06$  Hz,  $CH$ ), 2.827 (s, 3H,  $CH_3$ ), 2.906 (m, 2H,  $CH_2$ ), 3.142 (d,  $J = -12.06$  Hz, 1H,  $CHH$ ), 6.887 (d,  $J = 1.68$  Hz, 1H,  $CH_{Ar}$ ), 6.998 (dd,  $J = 8.29$ , 1.68 Hz, 1H,  $CH_{Ar}$ ), 7.138 (d,  $J = 8.29$  Hz, 1H,  $CH_{Ar}$ );  $^{13}C$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  ppm 17.106 ( $CH_3$ ), 18.118 ( $CH_2$ ), 19.291 ( $CH_2$ ), 24.057 ( $CH_3$ ), 24.082 ( $CH_3$ ), 25.198 ( $CH_3$ ), 29.666 ( $CH_2$ ), 33.598 ( $CH$ ), 35.719 ( $CH_2$ ), 36.059 ( $CH_3$ ), 36.334 ( $C$ ), 37.588 ( $C$ ), 37.823 ( $CH_2$ ), 47.445 ( $CH$ ), 63.694 ( $CH_2$ ), 119.658 (q,  $J = 321.38$ ,  $CF_3$ ), 124.315 ( $CH_{Ar}$ ), 124.112 ( $CH_{Ar}$ ), 126.961 ( $CH_{Ar}$ ), 133.945 ( $C_{Ar}$ ), 146.221 ( $2 \times C_{Ar}$ ).

**Dehydroabietyl-N-ethanaminium bis((trifluoromethyl)sulfonyl)amide 3b.** Yield 0.18 g, 96.9%; white solid; mp. 180.9 °C; calc. for  $C_{22}H_{36}N [M - NTF_2]^+$  314.2842, found 314.2847; calc. for  $C_2F_6NO_4S_2 [NTf_2]$  279.9167, found 279.9167;  $[\alpha]_D^{22} +9.8120$  ( $c = 1.0$ ,  $CHCl_3$ );  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  ppm 1.113 (s, 3H,  $CH_3$ ), 1.222 (d,  $J = 7.05$  Hz, 6H,  $2 \times CH_3$ ), 1.233 (s, 3H,  $CH_3$ ), 1.241 (m, 1H,  $CHH$ ), 1.371 (dd,  $J = -13.00$ , 2.33 Hz, 1H,  $CH$ ), 1.400 (t,  $J = 7.32$  Hz, 3H,  $CH_3$ ), 1.415 (m, 1H,  $CHH$ ), 1.664 (m, 1H,  $CHH$ ), 1.719 (m, 1H,  $CHH$ ), 1.752 (m, 2H,  $CH_2$ ), 1.829 (m, 1H,  $CHH$ ), 2.332 (dt,  $J = -12.75$ , 3.31 Hz, 1H,  $CHH$ ), 2.696 (d,  $J = -12.34$  Hz, 1H,  $CHH$ ), 2.825 (sep  $J = 7.05$  Hz,  $CH$ ), 2.864 (m, 1H,  $CHH$ ), 2.944 (ddd,  $J = -17.16$ , 7.27, 1.28 Hz, 1H,  $CHH$ ), 3.163 (d,  $J = -12.34$  Hz, 1H,  $CHH$ ), 3.206 (dq,  $J = 7.32$ , 4.51 Hz, 2H,  $CH_2$ ), 6.889 (d,  $J = 1.94$  Hz, 1H,  $CH_{Ar}$ ), 7.005 (dd,  $J = 8.22$ , 1.94 Hz, 1H,  $CH_{Ar}$ ), 7.146 (d,  $J = 8.22$  Hz, 1H,  $CH_{Ar}$ );  $^{13}C$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  ppm 10.697 ( $CH_3$ ), 17.041 ( $CH_3$ ), 18.085 ( $CH_2$ ), 19.323 ( $CH_2$ ), 24.057 ( $CH_3$ ), 24.090 ( $CH_3$ ), 25.174 ( $CH_3$ ), 29.706 ( $CH_2$ ), 33.598 ( $CH$ ), 35.767 ( $CH_2$ ), 36.204 ( $C$ ), 37.612 ( $C$ ), 37.855 ( $CH_2$ ), 45.697 ( $CH_2$ ), 47.606 ( $CH$ ), 60.749 ( $CH_2$ ), 119.662 (q,  $J = 320.21$ ,  $CF_3$ ), 124.128 ( $CH_{Ar}$ ), 124.323 ( $CH_{Ar}$ ), 126.945 ( $CH_{Ar}$ ), 133.912 ( $C_{Ar}$ ), 146.221 ( $C_{Ar}$ ), 146.261 ( $C_{Ar}$ ).

**Dehydroabietyl-2-hydroxy-N-ethanaminium bis((trifluoromethyl)sulfonyl)amide 4b.** 0.18 g, 98.26%; white solid; mp. 160.7 °C; calc. for  $C_{22}H_{36}NO [M - NTF_2]^+$  330.2791, found 330.2783; calc. for  $C_2F_6NO_4S_2 [NTf_2]$  279.9167, found 279.9165;  $[\alpha]_D^{22} +7.0280$  ( $c = 1.0$ ,  $CHCl_3$ );  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  ppm 1.114 (s, 3H,  $CH_3$ ), 1.216 (d,  $J = 7.05$  Hz, 6H,  $2 \times CH_3$ ), 1.233 (s, 3H,  $CH_3$ ), 1.300 (m, 1H,  $CHH$ ), 1.386 (dd,  $J = -12.42$ , 2.35 Hz, 1H,  $CH$ ), 1.411 (m, 1H,  $CHH$ ), 1.673 (m, 1H,  $CHH$ ),

1.691 (m, 1H,  $CHH$ ), 1.774 (m, 2H,  $CH_2$ ), 1.820 (m, 1H,  $CHH$ ), 2.344 (dt,  $J = -13.08$ , 3.38 Hz, 1H,  $CHH$ ), 2.815 (d,  $J = -12.20$  Hz, 1H,  $CHH$ ), 2.820 (sep  $J = 7.05$  Hz,  $CH$ ), 2.872 (m, 1H,  $CHH$ ), 2.946 (ddd,  $J = -17.25$ , 7.02, 1.29 Hz, 1H,  $CHH$ ), 3.177 (d,  $J = -12.20$  Hz, 1H,  $CHH$ ), 3.272 (ddd,  $J = 6.19$  Hz, 1H,  $CHH$ ), 3.326 (ddd,  $J = -13.04$ , 6.19, 4.17 Hz, 1H,  $CHH$ ), 3.932 (m, 2H,  $CH_2$ ), 6.887 (d,  $J = 1.95$  Hz, 1H,  $CH_{Ar}$ ), 6.997 (dd,  $J = 8.10$ , 1.95 Hz, 1H,  $CH_{Ar}$ ), 7.143 (d,  $J = 8.10$  Hz, 1H,  $CH_{Ar}$ );  $^{13}C$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  ppm 17.367 ( $CH_3$ ), 18.127 ( $CH_2$ ), 19.200 ( $CH_2$ ), 24.049 ( $CH_3$ ), 24.083 ( $CH_3$ ), 25.183 ( $CH_3$ ), 29.612 ( $CH_2$ ), 33.594 ( $CH$ ), 35.652 ( $CH_2$ ), 36.446 ( $C$ ), 37.633 ( $C$ ), 37.847 ( $CH_2$ ), 47.094 ( $CH$ ), 51.202 ( $CH_2$ ), 56.368 ( $CH_2$ ), 60.758 ( $CH_2$ ), 119.612 (q,  $J = 321.32$ ,  $CF_3$ ), 124.315 ( $CH_{Ar}$ ), 124.120 ( $CH_{Ar}$ ), 126.957 ( $CH_{Ar}$ ), 133.952 ( $C_{Ar}$ ), 146.196 ( $C_{Ar}$ ), 146.249 ( $C_{Ar}$ ).

**Dehydroabietyl-amino-N-2-(2-methoxyethoxy)ethanaminium bis((trifluoromethyl)sulfonyl)-amide 5b.** Yield 0.082 g, 95.1%; yellow liquid; calc. for  $C_{25}H_{42}NO_2 [M - NTF_2]^+$  388.3210 found 388.3216; calc. for  $C_2F_6NO_4S_2 [NTf_2]$  279.9167, found 279.9156;  $[\alpha]_D^{22} +7.0280$  ( $c = 1.0$ ,  $CHCl_3$ );  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  ppm 1.118 (s, 3H,  $CH_3$ ), 1.213 (d,  $J = 6.82$  Hz, 6H,  $2 \times CH_3$ ), 1.236 (s, 3H,  $CH_3$ ), 1.321 (m, 2H,  $CH_2$ ), 1.386 (dd,  $J = -12.66$ , 2.45 Hz, 1H,  $CH$ ), 1.414 (m, 1H,  $CHH$ ), 1.685 (m, 1H,  $CHH$ ), 1.784 (m, 2H,  $CH_2$ ), 1.834 (m, 1H,  $CHH$ ), 2.341 (dt,  $J = -13.73$ , 3.31 Hz, 1H,  $CHH$ ), 2.819 (sep  $J = 6.82$  Hz,  $CH$ ), 2.828 (d,  $J = -12.37$  Hz, 1H,  $CHH$ ), 2.880 (m, 1H,  $CHH$ ), 2.946 (m, 1H,  $CHH$ ), 3.109 (d,  $J = -12.37$  Hz, 1H,  $CHH$ ), 3.260 (s, 3H,  $CH_3$ ), 3.293 (m, 1H,  $CHH$ ), 3.407 (m, 1H,  $CHH$ ), 3.488 (t,  $J = 4.48$  Hz, 2H,  $CH_2$ ), 3.688 (m, 2H,  $CH_2$ ), 3.824 (m, 2H,  $CH_2$ ), 6.884 (d,  $J = 1.84$  Hz, 1H,  $CH_{Ar}$ ), 6.993 (dd,  $J = 8.07$ , 1.84 Hz, 1H,  $CH_{Ar}$ ), 7.144 (d,  $J = 8.07$  Hz, 1H,  $CH_{Ar}$ );  $^{13}C$  NMR (300 MHz,  $CDCl_3$ )  $\delta$  ppm 17.585 ( $CH_3$ ), 18.211 ( $CH_2$ ), 19.185 ( $CH_2$ ), 24.072 ( $CH_3$ ), 24.114 ( $CH_3$ ), 25.084 ( $CH_3$ ), 29.482 ( $CH_2$ ), 33.609 ( $CH$ ), 35.644 ( $CH_2$ ), 36.453 ( $C$ ), 37.602 ( $C$ ), 37.961 ( $CH_2$ ), 46.846 ( $CH$ ), 48.503 ( $CH_2$ ), 59.006 ( $CH_3$ ), 59.701 ( $CH_2$ ), 63.732 ( $CH_2$ ), 69.643 ( $CH_2$ ), 71.257 ( $CH_2$ ), 119.766 (q,  $J = 322.24$ ,  $CF_3$ ), 124.300 ( $CH_{Ar}$ ), 124.094 ( $CH_{Ar}$ ), 126.908 ( $CH_{Ar}$ ), 133.990 ( $C_{Ar}$ ), 146.284 ( $C_{Ar}$ ), 146.326 ( $C_{Ar}$ ).

**N-(Dehydroabietyl)-2-(dehydroabietyl-amino)ethanaminium bis((trifluoromethyl)sulfonyl)-amide 6b.** Yield 0.16 g, 83.4%; white solid; mp. 237.3 °C; calc. for  $C_{42}H_{65}N_2 [M - NTF_2]^+$  597.5142, found 597.5160; calc. for  $C_2F_6NO_4S_2 [NTf_2]$  279.9167, found 279.9173;  $[\alpha]_D^{22} +13.5440$  ( $c = 1.0$ ,  $MeOH$ );  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  ppm 1.015 (s, 6H,  $2 \times CH_3$ ), 1.185 (s, 6H,  $2 \times CH_3$ ), 1.208 (d,  $J = 76.98$  Hz, 12H,  $4 \times CH_3$ ), 1.230 (m, 2H,  $2 \times CHH$ ), 1.314 (m, 2H,  $2 \times CHH$ ), 1.369 (dd,  $J = -11.78$ , 2.27 Hz, 2H,  $2 \times CH$ ), 1.555 (dt,  $J = -11.55$  Hz, 2H,  $2 \times CHH$ ), 1.664 (m, 4H,  $2 \times CH_2$ ), 1.769 (m, 4H,  $2 \times CH_2$ ), 2.267 (dt,  $J = -12.89$  Hz, 2H,  $2 \times CHH$ ), 2.677 (d,  $J = -11.76$  Hz, 2H,  $2 \times CHH$ ), 2.813 (sep  $J = 7.05$  Hz, 2H,  $2 \times CH$ ), 2.832 (m, 2H,  $2 \times CHH$ ), 2.926 (dd,  $J = -16.91$ , 6.86 Hz, 2H,  $2 \times CHH$ ), 2.952 (m, 2H,  $2 \times CHH$ ), 3.269 (s, 4H,  $2 \times CH_2$ ), 6.866 (d,  $J = 1.81$  Hz, 2H,  $2 \times CH_{Ar}$ ), 6.987 (dd,  $J = 8.13$ , 1.81 Hz, 2H,  $2 \times CH_{Ar}$ ), 7.113 (d,  $J = 8.13$  Hz, 2H,  $2 \times CH_{Ar}$ );  $^{13}C$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  ppm 17.908 ( $2 \times CH_3$ ), 18.311 ( $2 \times CH_2$ ), 19.158 ( $2 \times CH_2$ ), 24.099 ( $4 \times CH_3$ ), 25.225 ( $2 \times CH_3$ ), 29.802 ( $2 \times CH_2$ ), 33.601 ( $2 \times CH$ ), 36.201 ( $2 \times CH_2$ ), 36.705 ( $2 \times C$ ), 37.560 ( $2 \times C$ ),



38.045 ( $2 \times \text{CH}_2$ ), 46.304 ( $2 \times \text{CH}_2$ ), 46.945 ( $2 \times \text{CH}$ ), 61.499 ( $2 \times \text{CH}_2$ ), 119.606 (q,  $J = 320.98$ ,  $\text{CF}_3$ ), 124.170 ( $2 \times \text{CH}_{\text{Ar}}$ ), 124.246 ( $2 \times \text{CH}_{\text{Ar}}$ ), 126.960 ( $2 \times \text{CH}_{\text{Ar}}$ ), 134.081 ( $2 \times \text{C}_{\text{Ar}}$ ), 146.131 ( $2 \times \text{C}_{\text{Ar}}$ ), 146.501 ( $2 \times \text{C}_{\text{Ar}}$ ).

### Synthesis of guests

*N*-Acetylation of phenylalanine was performed according to literature.<sup>16</sup> Preparation of  $[\text{NBu}_4]^+$  salts was performed by adding tetrabutylammoniumhydroxide (1.0 M in MeOH, 1.0 eq.) to racemic acid (1.0 eq.) in MeOH. After stirring for 1–3 h, the solvent was evaporated and product was dried in vacuum.

## Acknowledgements

TL is grateful for the support of the University of Helsinki and The Finnish Society of Sciences and Letters.

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