Diastereoselective synthesis of atropisomers containing two non-biaryl stereogenic axes: stereochemical relay through stereogenic centres in dihydrostilbene-2,2′-dicarboxamides

Jonathan Clayden,*[a] Neil Westlund,[a] Christopher S. Frampton[b] and Madeleine Helliwell[a]

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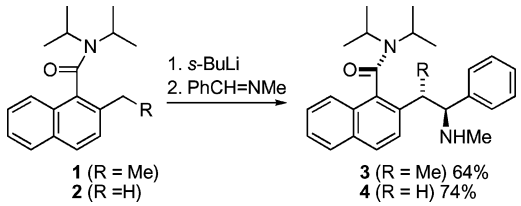
Addition of laterally lithiated tertiary aromatic amides to benzaldimines controls the formation of a new stereogenic centre adjacent to the benzaldimine aromatic ring. Drawing on the fact that such amino-substituted stereogenic centres may themselves control the conformation of amides, with amido-substituted benzaldimines we found it becomes possible to relay stereochemistry from one amide to another *via* this intervening stereogenic centre. A group of dihydrostilbene-2,2′-dicarboxamide derivatives bearing one or two stereogenic axes are made by this method, which demonstrates the use of combined kinetic and thermodynamic control for the relay of stereochemical information.

Introduction

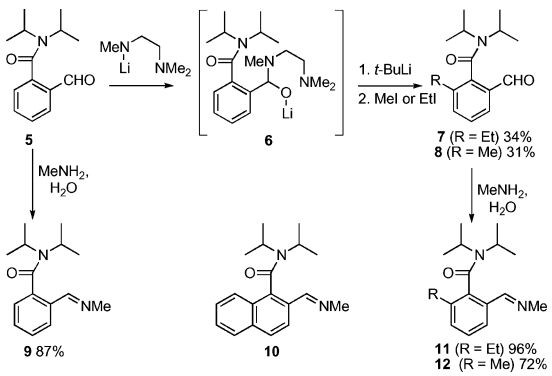
A stereogenic amide axis can both control[1–5] and be controlled by[6–8] a nearby stereogenic centre,[9] and in an accompanying publication[8] we reported the details of how relayed stereocontrol may result from combining these two features of amide stereochemistry: a stereogenic axis controls the conformation of the amide, which in turn controls the formation of a new stereogenic centre. In this paper we show that it is also possible to combine these two aspects of stereochemical control in reverse order, *i.e.* to allow an amide axis to control a new centre and then to allow that centre to control a new amide axis.† This strategy allows axial stereochemistry to be relayed, *via* a stereogenic centre, to a new stereochemically defined axis, and allows the diastereoselective synthesis of atropisomers bearing more than one non-biaryl stereogenic axis.‡[13]

The addition of laterally lithiated amides **1** and **2** to imines (*e.g.*, Scheme 1) generates, highly stereoselectively, amines **3** and **4** with a new stereogenic centre adjacent to an aromatic ring, a necessary requirement for using the stereochemistry of that centre to control a new amide axis.[5,14] That centre bears an NHMe group, which we know to be at least moderately effective in governing the conformation of an adjacent atropisomeric amide.[8] We therefore chose to use the addition of laterally lithiated amides **1** and **2** to 2-amidobenzaldimines **9**–**12** to investigate the potential of an axis-to-axis stereochemical relay.

Four imines **9**–**12** were made by condensing the corresponding aldehydes[3,7] with aqueous methylamine (Scheme 2)[3] Aldehydes **7** and **8** were made in moderate yield from aldehyde **5**[7] by ortholithiation, protecting the formyl group as its trimethylethylenediamine adduct **6**.§[18]



Scheme 1 Diastereoselective lateral lithiation–imine addition.[5,14]



Scheme 2 Synthesis of 2-imino benzamides.

Lithiation of **1**[19] and of **2**[1] and additions to the imine **9** proceeded stereoselectively and gave, as expected,[5] a single diastereoisomer of **13** and of **14** with respect to the atropisomeric Ar–CO axis (marked "axis *a*" in Scheme 3) and the new stereogenic centre(s).¶ The ^{1}H

[a]*School of Chemistry, University of Manchester, Oxford Road, Manchester, UK M13 9PL. E-mail: clayden@man.ac.uk; Fax: +44 161 275 4939*
[b]*Department of Chemistry, University of Southampton, Highfield, Southampton, UK SO17 1BJ*

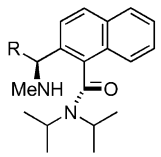
† Preliminary communication: ref. 10.

‡ The stereoselective synthesis of atropisomers containing several biaryl axes have been reported recently: see ref. 11. For diastereoisomeric naphthamides with two atropisomeric axes, see ref. 12.

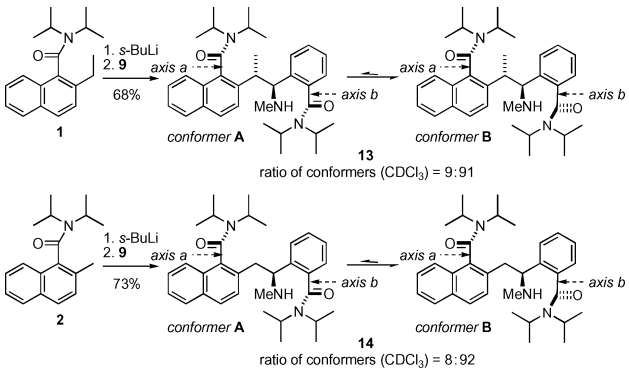
§ We have previously published (ref. 7) an approach to similar compounds by formylation of an alkylated benzamide, a method which required silyl protection of the alkyl group from lateral lithiation (ref. 15 and 16) and which suffers equally from poor yields. Our currently favoured method for similar syntheses involves protection of the aldehyde as its ephedrine-derived oxazolidine (see accompanying paper, ref. 17).

¶ Short reaction times gave the best results: after 3 h the product consists mainly of the corresponding lactam formed by attack of the lithioamine on the amide carbonyl group (see ref. 3).

NMR spectrum of the products clearly showed that they exist as mixtures of conformers about the non-stereogenic benzamide Ar–CO axis marked "axis *b*", though one conformer was preferred to the extent of 91 : 9 for **13** and 92 : 8 for **14**.



15 (R = Me or *n*-Bu)
(favoured conformer)



Scheme 3 Relaying stereochemistry form a naphthamide axis to a benzamide axis.

Comparable imines **15**[8] have showed an apparently hydrogen-bond directed conformational preference for the isomer shown here as conformer A.[8] However, in compounds **13** and **14** the alkyl substituent at the NHMe-bearing stereogenic centre is significantly larger than the R = methyl or *n*-butyl group of **15**. In the X-ray crystal structure of **14** (Fig. 1) axis *b* adopts the orientation shown in conformer B, and on the basis of this evidence, in conjunction with further results presented below, we propose that **13** and **14** exist as >90% conformer B, with steric factors and not hydrogen-bonding governing the preferred orientation of axis *b* (Fig. 2). The

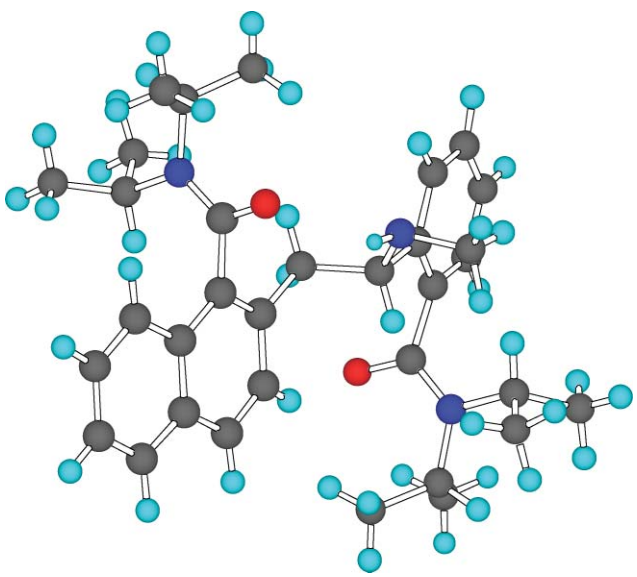


Fig. 1 X-ray crystal structure of **14**.

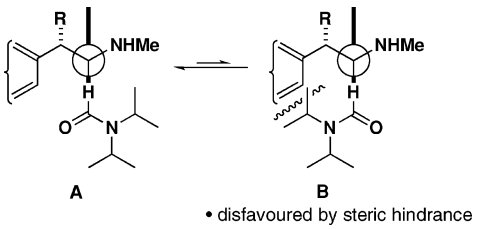
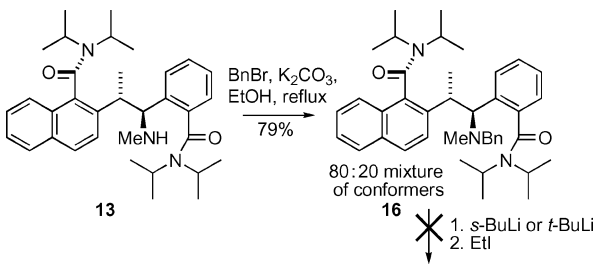


Fig. 2 Conformational preference at axis *b* of **13**, **14**, **17**, **18** and **19**.

X-ray crystal structure of **14** also confirms that the new stereogenic centre is governed by axis *a* in the same sense as **4**.[5]

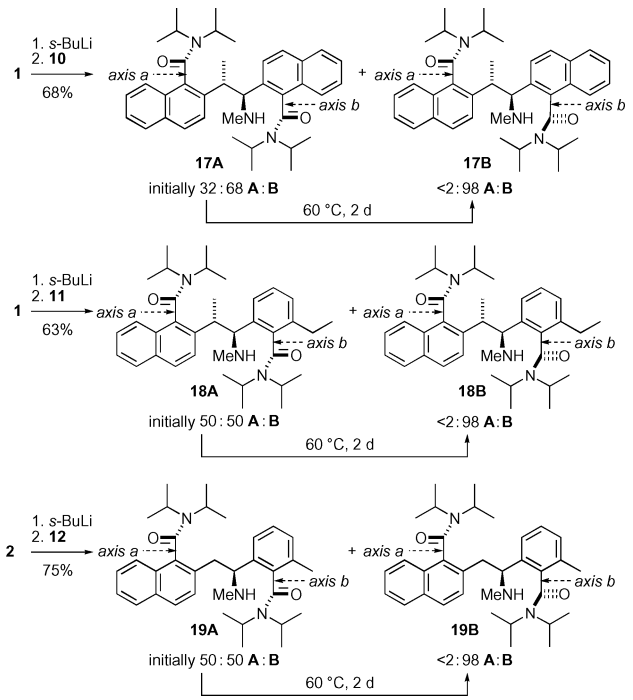
These results indicate that an amide Ar–CO axis is indeed, as hoped, able to govern the preferred orientation of another axis 5 bond lengths away. In order to use convert this conformational preference into a "relayed" diastereoselective reaction, and to allow the formation of a new stereogenic axis, rotation about the benzamide axis (axis *b*) needs to be prevented by the presence of a 6-substituent (we have employed a similar strategy in our asymmetric synthesis of atropisomers under thermodynamic control[6,8]). We attempted functionalisation of **13**, first protecting the amine nitrogen as its *N*-benzyl derivative (Scheme 14). Tertiary amine **16** was formed as an 80 : 20 mixture of conformers (presumably the NMeBn group now comes closer to rivalling the substituted benzyl group on steric grounds[8]), but attempted ortholithiation (Scheme 4) of **16** failed.



Scheme 4 Attempted ortholithiation.

We therefore proceeded to carry out additions of laterally lithiated derivatives of amides **1** and **2** to imines **10**–**12**, which already bear *ortho* substituents. Diastereoisomeric pairs of products of the diamides **17**–**19** were formed, as shown in Scheme 5.

Necessarily, in these reactions, at least two diastereosiomers of **17**–**19** arise because both **10**–**12** and lithiated **1** and **2** are chiral, racemic compounds, at least on the timescale of their addition.[20,21] Two forms of diastereoselectivity are now operative, because both axis *a* and axis *b* can exert kinetic control over the face-selectivity of the addition to the imino group.[3] However, it is evident that the stereoselectivity of the electrophilic attack on lithiated **1** and **2**[5] wins out over the stereoselectivity of nucleophilic attack on **10**–**12**[3] because the products are formed as single diastereoisomers with respect to axis *a* and the stereogenic centre(s) but as mixtures of diastereoisomers at axis *b* with respect to the same centre. The kinetic products of the reaction are *ca.* 1 : 1 mixtures of diastereoisomers. However, from the precedent of **13** and **14**, it seemed likely that one of each pair of diastereosiomers would be favoured at equilibrium. The atropisomeric mixtures were therefore heated in $CDCl_3$ at 60 °C for 2 d. In all three cases rotation about axis *b* resulted in a single diastereoisomer of the



Scheme 5 Atropisomeric stilbene-2,2′-dicarboxamides.

products. An X-ray crystal structure (Fig. 3) confirmed the relative orientation of the amides in **17B**, whose stereochemistry is in accordance with the proposed dominance of steric over hydrogen-bonding effects (Fig. 2) in these systems.

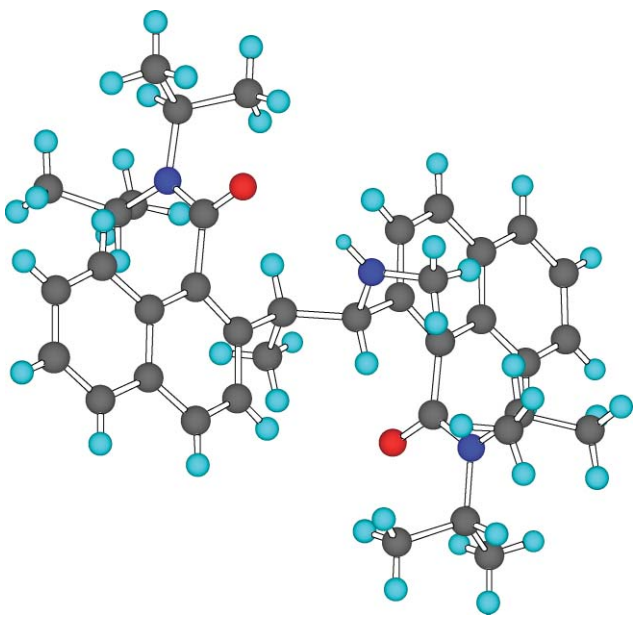
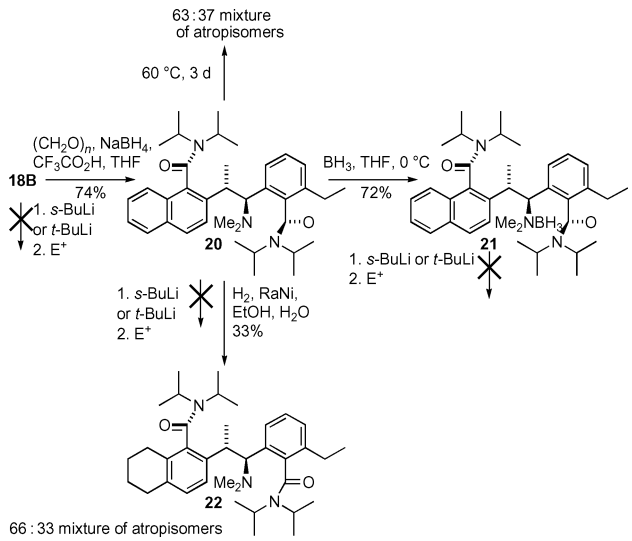


Fig. 3 X-ray crystal structure of **17B**.

Kinetically, axis *a* is also presented with the possibility of epimerisation under these conditions. However, it finds itself adjacent to a stereogenic centre bearing H, Me and a bulky group, which, in accordance with precedent,[8] presumably exerts a thermodynamic control over axis *a* which as a result maintains its relative orientation.

These syntheses represent the first diastereoselective syntheses of compounds bearing two non-biaryl stereogenic axes. Diastereoisomeric atropisomers in which stereochemistry is defined by the configuration of more than one stereogenic axis are known in the biaryl series, for example the michellamine alkaloids[22] and the octinaphthalenes synthesised by Fuji *et al.*[23]

This paper has shown that stereochemistry may be relayed from one axis to another, *via* intervening centres (though one of the centres is inessential to the method, as the synthesis of **19B** shows). Further iterative extension of the relay method was hampered by our inability to lithiate **18** or **19**, even after protection of the amino group as a tertiary amine **20** or a tertiary amine–borane complex **21** (Scheme 6).[24] Attempted hydrogenolysis of the C–N bond to remove altogether the amino group led to the tetralin **22**. However, the strategy shows how a combination of kinetic and therodyamic control may be used to relay stereochemistry through simple molecules, and future publications will describe full details of how this strategy can be harnessed more effectively.*



Scheme 6 Further functionalisation.

X-Ray crystallography††

14. Crystal data $C_{33}H_{45}N_3O_3$; M = 515.74; monoclinic P21/n; a = 7.626(4) Å; b = 20.455(4) Å; c = 19.100(6) Å; β = 93.27(4)°; V = 2974(1) Å^3; T = 296.2 K; Z = 4; μ = 0.555 mm^{-1}; 6639 reflections; R_{int} = 0.02020; CCDC reference number 286019

17B. Crystal data $C_{38}H_{51}N_3O_2$; M = 581.82; orthorhombic Pna21; a = 15.179(3) Å; b = 7.728(2) Å; c = 28.337(6) Å; V = 3324.3(12) Å^3; T = 123(1) K; Z = 4; μ = 0.071 mm^{-1}; 32058 reflections; R_{int} = 0.0335; $R(F)$ 0.0442; CCDC reference number 286020

* This work has been published in preliminary form: ref. 25.

†† CCDC reference numbers 286019 and 286020. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b514561a

Experimental

General methods have been published previously[7]

***N*,*N*-Diisopropyl-2-ethyl-6-formylbenzamide (7).** A solution of *N*,*N*,*N*-trimethylethylenediamine (2.43 ml, 19.15 mmol) in THF (90 ml) at −78 °C under an atmosphere of nitrogen was treated with *n*-butyllithium (11.3 ml, 18.04 mmol; 1.6 M solution in hexanes) and stirred for a further 10 min. To the reaction vessel was added a solution of aldehyde **5**[7] (4.056 g, 17.41 mmol) in THF (30 ml) and stirred for a further 35 min to give a pale yellow coloured solution. To the reaction mixture was added *tert*-butyllithium (12.3 ml, 20.89 mmol; 1.7 M solution in pentane) to give a red-brown coloured solution, and stirred for a further 3 h. The reaction mixture was treated with ethyl iodide (2 ml, 25 mmol) to give a yellow solution and stirred for a further 10 min and allowed to warm to ambient temperature. Water (30 ml) was added to the solution and allowed to stir overnight. The THF was removed under reduced pressure and the aqueous was extracted with diethylether (3 × 30 ml). The combined organic extracts were washed successively with aqueous 2 M hydrochloric acid (3 × 20 ml), saturated aqueous sodium hydrogen carbonate (2 × 20 ml), water (20 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product as an oil. Purification by flash chromatography on silica gel [2 : 1 petrol (bp 40–60 °C)–EtOAc] and recrystallisation from ethyl acetate afforded benzamide **11** (1.545 g, 34%) as colourless oil that crystallised on standing, R_f 0.48 [1 : 1 petrol (bp 40–60 °C)–EtOAc], mp 89–90 °C, ν_{max} (film)/cm^{-1} 3067, 2971, 2936, 2876, 2822, 2749, 1702, 1631, 1591; δ_H(300 MHz, $CDCl_3$) 10.07 (1H, s, CHO), 7.77 (1H, d, *J* 7.6, ArH), 7.54 (1H, d, *J* 7.1, ArH), 7.44 (1H, t, *J* 7.6, ArH), 3.54 (2H, m, 2 × NCH), 2.77 (1H, m, $CHHCH_3$), 2.63 (1H, m, $CHHCH_3$), 1.66 (3H, d, *J* 6.9, $NCHCH_3$), 1.62 (3H, d, *J* 6.9, $NCHCH_3$), 1.29 (3H, t, *J* 7.6, CH_2CH_3), 1.13 (3H, d, *J* 6.7, $NCHCH_3$), 1.04 (3H, d, *J* 6.7, $NCHCH_3$); δ_C(75 MHz, $CDCl_3$) 190.8, 167.5, 140.7, 139.9, 134.3, 131.9, 128.3, 126.7, 51.0, 46.2, 25.0, 20.7, 20.4, 20.4, 20.1 and 14.8; *m*/*z* (CI) 262 (100%, M + H$^+$); *m*/*z* (EI) 261 (1%, M$^+$), 161 (4%, M–N^{i}Pr$_2$) and 49 (100%) (found: C, 73.41; H, 8.69; N, 5.31%; M + H$^+$, 262.1809. $C_{16}H_{23}NO_2$ requires C, 73.6; H, 8.8; N, 5.4%; M + H, 262.1807). Also obtained was recovered benzamide **5** (2.555 g, 63%).

***N*,*N*-Diisopropyl-2-formyl-6-methylbenzamide (8).** In a similar way, N,N,*N*-trimethylethylenediamine (2.29 ml, 18.04 mmol) in THF (90 ml), *n*-butyllithium (11.3 ml, 18.04 mmol; 1.6 M solution in hexanes), aldehyde **5**[26] (3.821 g, 16.40 mmol) in THF (30 ml), *tert*-butyllithium (11.6 ml, 19.68 mmol; 1.7 M solution in pentane) and methyl iodide (2 ml, 32 mmol) gave the crude product as an oil. Purification by flash chromatography on silica gel [2 : 1 petrol (bp 40–60 °C)–EtOAc] afforded nearly pure product. Further purification was achieved by recrystallisation from ethyl acetate to afford pure benzamide **12** (154 mg, 31%) as a colourless blades, R_f 0.41 [1 : 1 petrol (bp 40–60 °C)–EtOAc], mp 107–109 °C, λ_{max}, nm (ε_{max}) (CH_2Cl_2) 246 (32150) 302 (7900), ν_{max} (film)/cm^{-1} 2978, 2934, 1707, 1623; δ_H(300 MHz, $CDCl_3$) 10.07 (1H s, CHO), 7.76 (1H, d, *J* 7.6, ArH), 7.47 (1H, d, *J* 7.0, ArH), 7.40 (1H, t, *J* 7.6, ArH), 3.65–3.45 (2H, m, 2 × NCH), 2.39 (3H, s, $ArCH_3$), 1.67 (3H, d, *J* 6.9, $NCHCH_3$), 1.63 (3H, d, *J* 6.7, $NCHCH_3$), 1.16 (3H, d, *J* 6.6, $NCHCH_3$), 1.05 (3H, d, *J* 6.6, $NCHCH_3$); δ_C(75 MHz, $CDCl_3$) 190.8, 167.7, 140.3, 136.2, 134.7, 132.0, 128.1, 126.9, 51.1, 46.2, 20.8, 20.5, 20.4, 20.1 and 18.3; *m*/*z* (CI) 248 (100%, M + H$^+$); *m*/*z* (EI) 248 (0.004%, M$^+$) and 49 (100%) (found: C, 72.75; H, 8.78; N, 5.55%; M$^+$, 248.1650. $C_{15}H_{21}NO_2$ requires C, 72.9; H, 8.5; N, 5.7%; M, 248.1650). Also obtained was recovered benzamide **5** (252 mg, 53%).

***N*,*N*-Diisopropyl-2-[(methylimino)methyl]benzamide (9).** 2-Formyl-*N*,*N*-diisopropyl-1-benzamide (**5**)[7,21] (4.831 g, 20.73 mmol) was treated with 40% aqueous methylamine (60g, 770 mmol). The usual work-up gave imine **9** (4.454 g, 87%) as a white solid that required no further purification, mp 73–75 °C (EtOAc); ν_{max} (film)/cm^{-1} 2988, 2972, 2939, 2905, 2869, 1649, 1621, 1596; δ_H(300 MHz, $CDCl_3$) 8.37 (1H, bq, *J* 1.7, CH=NCH_3), 7.95 (1H, m, ArH), 7.40 (2H, m, ArH), 7.21 (1H, m, ArH), 3.64 (1H, septet, *J* 6.6, NCH), 3.54 (1H, m, NCH), 3.51 (3H, d, *J* 1.7, CH=NCH_3), 1.61 (3H, d, *J* 6.7, $NCHCH_3$), 1.59 (3H, d, *J* 6.6, $NCHCH_3$), 1.08 (6H, m, 2 × $NCHCH_3$); δ_C(75 MHz, $CDCl_3$) 169.4, 159.7, 139.2, 132.1, 130.3, 128.3, 126.9, 125.2, 50.9, 48.3, 45.9, 20.6, 20.5, 20.3 and 20.2; *m*/*z* (CI) 247 (100%, M + H$^+$); *m*/*z* (EI) 246 (2%, M$^+$) and 203 (11%, M–$CHCH_3$) 49 (100%) (found: M$^+$, 246.1735. $C_{15}H_{22}N_2O$ requires M, 246.1732).

6-Ethyl-2-[(methylimino)methyl]-*N*,*N*-diisopropyl-1-benzamide (11). In the same way, aldehyde **7** (910 mg, 3.49 mmol) was refluxed with 40% aqueous methylamine (12 g, 150 mmol). Work up in the usual manner afforded imine **11** (919 mg, 96%) which required no further purification, mp 84–86 °C, λ_{max}, nm (ε_{max}) (CH_2Cl_2) 234 (11200) 252 (11790) 288 (1582), ν_{max} (film)/cm^{-1} 2967, 2936, 2903, 2876, 2836, 2768, 1650, 1623, 1589; δ_H(300 MHz, $CDCl_3$) 8.38 (1H, bq, *J* 1.5, $CHNCH_3$), 7.83 (1H, m, ArH), 7.34 (2H, m, ArH), 3.52 (2H, m, 2 × NCH), 2.74 (1H, m, $CHHCH_3$), 2.60 (1H, m, $CHHCH_3$), 1.65 (6H, m, 2 × $NCHCH_3$), 1.30 (3H, 3H, t, *J* 7.4, CH_2CH_3), 1.11 (3H, d, *J* 6.7, $NCHCH_3$), 1.02 (3H, d, *J* 6.6, $NCHCH_3$); δ_C(75 MHz, $CDCl_3$) 168.6, 160.5, 139.7, 138.2, 131.8, 130.2, 128.7, 123.8, 50.8, 48.3, 46.0, 25.3, 20.8, 20.4, 20.2 and 14.9; *m*/*z* (CI) 275 (100%, M + H$^+$) and 174 (4%, M–N^{i}Pr$_2$); *m*/*z* (EI) 174 (39%, M–N^{i}Pr$_2$) and 49 (100%) (found: M + H$^+$, 275.2032. $C_{17}H_{1726}N_2O$ requires M + H, 275.2023).

6-Methyl-2-[(methylimino)methyl]-1-benzamide (12). In the same way as for compound **9**, benzamide **8** (700 mg, 2.83 mmol) was treated with 40% aqueous methylamine (10 g, 130 mmol). Work-up in the usual manner afforded imine **12** (565 mg, 77%) as a white solid that required no further purification, mp 81–83 °C, ν_{max} (film)/cm^{-1} 2968, 2934, 2878, 1629, 1592; δ_H(300 MHz, $CDCl_3$) 8.37 (1H, bq, *J* 1.7, $CHNCH_3$), 7.82 (2H, m, ArH), 7.28 (1H, m, ArH), 3.57 (2H, m, 2 × NCH), 3.51 (3H, d, *J* 1.7, $CHNCH_3$), 2.35 (3H, s, $ArCH_3$), 1.65 (6H, m, 2 × $NCHCH_3$), 1.13 (3H, d, *J* 6.7, $NCHCH_3$), 1.03 (3H, d, *J* 6.7, $NCHCH_3$); δ_C(75 MHz, $CDCl_3$) 168.8, 160.3, 138.7, 133.6, 132.1, 131.9, 127.9, 123.8, 50.9, 48.3, 46.1, 20.9, 20.5, 20.4, 20.3 and 18.5; *m*/*z* (CI) 261 (100%, M + H$^+$) and 160 (4%, M–N^{i}Pr$_2$); *m*/*z* (EI) 160 (92%, M–N^{i}Pr$_2$) and 49 (100%) (found: M$^+$, 261.1969. $C_{16}H_{24}N_2O$ requires M, 261.1967).

(a*R*′)-*N*,*N*-Diisopropyl-2-[(1*S*′,2*S*′)-2-{2-[diisopropylamino)-carbonyl]phenyl}-1-methyl-2-(methylamino]ethyl-1-naphthamide (13). A solution of naphthamide **1**[4] (190 mg, 0.67 mmol) in THF (10 ml) at −78 °C under an atmosphere of nitrogen

was treated with *sec*-butyllithium (0.60 ml, 0.67 mmol; 1.12 M solution in hexanes) to give a dark green–blue solution and stirred for a further 60 min. The lithiated intermediate was treated with a solution of imine **9** (165 mg, 0.67 mmol) in THF (5 ml) to give a red-brown solution and stirred for a further 15 min, quenched with saturated aqueous ammonium chloride (5 ml) and warmed to ambient temperature. The THF was removed at ambient temperature and the aqueous was extracted with dichloromethane (5 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to the crude product as a solid. Purification by flash chromatography on silica gel [3 : 1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine] afforded naphthamide **13** (261 mg, 74%) as a white solid. ^{1}H NMR showed **13** to consist of two conformers in a ratio of 11 : 1, R_f 0.43 [1 : 1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine]; ν_{max} (film)/cm^{-1} 3323, 3053, 2968, 2934, 2891, 2876, 1624; δ_H(300 MHz, $CDCl_3$) 7.91–7.67 (5H, m, ArH), 7.56–7.40 (3H, m, ArH), 7.29 (1H, m, ArH), 7.18 (1H, m, ArH), 3.83 (1H, d, *J* 8.9, $CH(NHCH_3)^{major}$), 3.82 (1H, m, NCH^{major}), 3.74–3.50 (3H, m, 3 × NCH^{major}), 3.29 (1H, bm, $CH(CH_3)CH(NCHCH_3)^{minor}$), (3.07 (1H, m, $CH(CH_3)CH(NCHCH_3)^{major}$), 2.23 (1H, bs, NH^{major}), 1.85 (3H, d, *J* 6.6, CH_3^{major}), 1.84 (3H, d, *J* 6.6, CH_3^{major}), 1.73 (3H, d, *J* 6.9, CH_3^{major}), 1.69 (3H, d, *J* 6.9, CH_3^{major}), 1.17 (6H, m, 2 × CH_3^{major}),1.10 (6H, m, 2 × CH_3^{major}), 1.04 (3H, d, *J* 6.6, $NCHCH_3$); δ_C^{major}(75 MHz, $CDCl_3$) 170.4, 170.1, 141.3, 139.4, 138.6, 134.1, 132.1, 129.2, 128.9, 128.6, 127.9, 127.4, 126.3, 125.6, 125.0, 124.7, 124.5, 67.5, 51.0, 50.6, 46.2, 45.8, 44.0, 35.5, 21.1, 20.9, 20.9, 20.8, 20.7, 20.5, 20.5 and 19.4; *m*/*z* (CI) 530 (100%, M + H$^+$) (found: M + H$^+$, 530.3743. $C_{34}H_{47}N_3O_2$ requires M + H, 530.3746).

(a*R*′)-*N*,*N*-Diisopropyl-2-[(2*S*′)-2-{2-[(diisopropylamino)carbonyl]-phenyl}-2-(methylamino)ethyl]-1-naphthamide (14). In the same way as for compound **13**, the lithiated species formed from naphthamide **2**[1] (184 mg, 0.68 mmol) in THF (15 ml) at −78 °C and *sec*-butyllithium (0.61 ml, 0.68 mmol; 1.12 M solution in hexanes) was treated with a solution of imine **9** (168 mg, 0.68 mmol) in THF (5 ml) and stirred for a further 10 min. After work-up in the usual way, purification by flash chromatography on silica gel [3 : 1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine] afforded naphthamide **14** (258 mg, 73%) as a white solid. ^{1}H NMR showed **14** to be present as two conformers in a ratio of 10 : 1, mp >230 °C; ν_{max} (film)/cm^{-1} 3336, 3055, 2969, 2933, 2874, 2847, 2789, 1625; δ_H(300 MHz, $CDCl_3$) 7.90–7.76 (5H, m, ArH), 7.50 (2H, m, ArH), 7.43 (1H, dd, *J* 7.8 and 1.2, ArH), 7.30 (1H, dt, *J* 8.7 and 1.2, ArH), 7.16 (1H, dd, *J* 7.5 and 0.9, ArH), 4.26 (1H, dd, *J* 8.7 and 5.7, $CH(NHMe)^{minor}$), 3.92 (1H, dd, *J* 10.4 and 1.9, $CH(NHMe)^{major}$), 3.86 (1H, septet, *J* 6.6, NCH^{major}), 3.62 (2H, septet, *J* 6.9, 2 × NCH^{major}), 3.47 (1H, septet, *J* 6.6, NCH^{major}), 3.38 (1H, dd, *J* 13.3 and 2.2, $CHHCH(NHMe)^{major}$), 3.12 (1H, dd, *J* 13.5 and 8.7, $CHHCH(NHMe)^{minor}$), 3.02 (1H, dd, *J* 13.5 and 5.7, $CHHCH(NHMe)^{minor}$), 2.73 (1H, dd, *J* 13.3 and 10.6, $CHHCH(NHMe)^{major}$), 2.11 (3H, s, $NHCH_3^{major}$), 2.21 (1H, bs, NH^{major}), 1.83 (3H, d, *J* 6.7, CH_3^{major}), 1.82 (3H, d, *J* 6.9, CH_3^{major}), 1.78 (3H, d, *J* 6.7, CH_3^{major}), 1.69 (3H, d, *J* 6.7, CH_3^{major}), 1.17 (6H, m, 2 × CH_3^{major}), 0.98 (6H, m, 2 × CH_3^{major}); δ_C^{major}(75 MHz, $CDCl_3$) 170.7, 169.9, 142.1, 137.5, 135.0, 133.5, 132.1, 129.3, 128.7, 128.1, 127.9, 127.8, 126.8, 126.5, 126.4, 125.6, 124.8, 124.4, 64.6, 51.2, 50.8, 46.1, 45.7, 42.3, 35.4, 21.3, 21.0, 21.0, 20.7, 20.6, 20.4 and 20.3; *m*/*z* (CI) 516 (100%, M + H$^+$) (found M + H$^+$, 516.3592. $C_{33}H_{45}N_3O_2$ requires M + H, 516.3590). Also obtained was recovered starting naphthamide **2** (20 mg, 11%).

(a*R*′)-*N*,*N*-Diisopropyl-2-((1*S*′,2*S*′)-2-[benzyl(methyl)amino]-2-{2-[(diisopropylamino)carbonyl]phenyl}-1-methylethyl)-1-naphthamide (16). A solution of naphthamide **13** (111 mg, 0.21 mmol), benzyl bromide (0.15 ml, 1.26 mmol), potassium carbonate (116 mg, 0.84 mmol) and ethanol (12 ml) was refluxed overnight, cooled to ambient temperature and diluted with water (10 ml). The solvent was removed under reduced pressure and the aqueous was diluted with diethylether (20 ml). The layers were separated and the ethereal layer was washed with aqueous 0.5 M hydrochloric acid (5 × 5 ml). The acidified aqueous layer was made alkaline (pH >10) by the addition of 15% aqueous sodium hydroxide and extracted with diethylether (5 × 10 ml). The combined ethereal extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel [4 : 1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine] afforded tertiary amine **16** (103 mg, 79%) as a pale yellow oil. ^{1}H NMR showed **16** to exist as as two conformers in a ratio of 4.1 : 1; ν_{max} (film)/cm^{-1} 3058, 2967, 2927, 2873, 2853, 2789, 2244, 1622; δ_H(300 MHz, $CDCl_3$) 7.76 (3H, m, ArH), 7.62 (1H, d, *J* 8.5, ArH), 7.50 (1H, d, *J* 7.6, ArH), 7.37 (3H, m, ArH), 7.22 (2H, m, ArH), 6.9–6.6 (3H, m, ArH), 6.45 (2H, d, *J* 7.0, ArH), 4.76 (1H, d, *J* 10.6, $CHNMeBn^{major}$), 4.25 (1H, d, *J* 10.2, $CHNMeBn^{minor}$), 3.99 (1H, quintet, *J* 6.5, $CH(Me)CHNMeBn^{major}$), 3.7–3.4 (5H, m, 4 × NCH^{major}, $CHHPh^{major}$), 3.39 (1H, d, *J* 12.9, $CHHPh^{major}$), 1.84 (3H, s, NCH_3^{major}), 1.73 (3H, d, *J* 6.6, CH_3^{major}), 1.68 (3H, d, *J* 6.7, CH_3^{major}), 1.56 (6H, bm, 2 × CH_3^{major}), 1.18 (3H, bm, CH_3^{major}), 1.09 (3H, d, *J* 6.7, CH_3^{major}), 1.02 (3H, d, *J* 6.5, CH_3^{major}), 0.94 (3H, d, *J* 6.3, CH_3^{major}), 0.89 (3H, d, *J* 6.3, CH_3^{major}); δ_C^{major}(75 MHz, $CDCl_3$) 170.5, 169.7, 140.2, 139.8, 139.3, 137.1, 133.5, 132.0, 129.9, 128.7, 128.4, 128.1, 127.8, 127.8, 127.5, 127.3, 126.0, 125.7, 125.3, 125.3, 125.2, 69.0, 57.9, 50.9, 50.4, 46.1, 46.0, 38.7, 38.1, 30.3, 29.6, 21.3, 21.1, 20.8, 20.7, 20.6, 20.5 and 20.3; *m*/*z* (CI) 620.6 (100%, M + H$^+$) (found: M$^+$, 620.4208. $C_{41}H_{53}N_3O_2$ requires M, 620.4216).

(a*R*′)-*N*,*N*-Diisopropyl-2-((1*R*′,2*S*′)-2-{1-[(a*S*′)-(diisopropylamino)-carbonyl]-2-naphthyl}-1-methylpropyl)-1-naphthamide and (a*R*′)-*N*,*N*-diisopropyl-2-((1*R*′,2*S*′)-2-{1-[(a*R*′)-(diisopropylamino)carbonyl]-2-naphthyl}-1-methylpropyl)-1-naphthamide (17B and 17A). A solution of naphthamide **1**[4] (204 mg, 0.72 mmol) in THF (15 ml) at −78 °C under an atmosphere of nitrogen was treated with *sec*-butyllithium (0.66 ml, 0.79 mmol; 1.2 M solution in hexanes) to give a dark green-blue solution and stirred for a further 1 h. The lithiated intermediate was treated with a solution of imine **10**[3] (256 mg, 0.87 mmol) in THF (5 ml) to give a purple-pink solution and stirred for a further 2 h. The reaction mixture was treated with saturated aqueous ammonium chloride (5 ml), warmed to ambient temperature, the THF was removed at ambient temperature and the aqueous was extracted with dichloromethane (5 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford the crude product as a solid. ^{1}H NMR showed the atropisomers were present in a ratio of *ca.* 2.1 : 1 **17B** : **17A**. Trituration of the crude mixture in diethyl ether (10 ml) and heating in hot ethylacetate for 30 min gave naphthamide

17B (138 mg, 68%) as a white solid, mp >230 °C (EtOAc) contaminated with a small amount of **17A**; ν_{max} (film)/cm^{-1} 2968, 1620; δ_H(300 MHz, $CDCl_3$) 7.94–7.76 (8H, m, ArH), 7.58–7.46 (4H, m, ArH), 4.01 (1H, d, *J* 9.3, CH(NHCH$_3$)^A), 3.96 (1H, d, *J* 9.3, CH(NHCH$_3$)^B), 3.78–3.60 (4H, m, 4 × NCH^B), 3.09 (1H, m, CHCH$_3^B$), 2.08 (3H, s, NHCH$_3^B$), 2.02 (3H, s, NHCH$_3^A$), 1.91 (3H, d, *J* 6.7, NCHCH$_3^B$), 1.88–1.83 (9H, m, 3 × NCHCH$_3^B$), 1.15–1.00 (12H, m, 4 × NCHCH$_3^B$); $\delta_C{}^B$(75 MHz, $CDCl_3$) 170.2, 169.4, 139.4, 138.0, 134.5, 134.1, 132.6, 132.2, 129.6, 129.3, 128.6, 128.0, 126.5, 126.1, 125.7, 125.7, 125.5, 125.0, 124.8, 124.6, 67.7, 51.0, 50.8, 46.2, 44.2, 35.7, 21.6, 21.1, 21.0, 20.8, 20.7, 20.5, 20.4 and 19.4; *m*/*z* (CI) 580.6 (100%, M + H$^+$) and 297.2 (46%, M–$C_{19}H_{24}NO$); *m*/*z* (EI) 297.4 (2.4%, M–$C_{19}H_{24}NO$) and 91 (100%) (found: M + H$^+$, 580.3910. $C_{38}H_{49}N_3O_2$ requires M + H, 580.3903). Heating amine **17** in $CDCl_3$ for 2 d at 60 °C produces a ratio of >27 **17B** : <1 **17A** (^{1}H NMR).

(a*R*′)-*N*,*N*-Diisopropyl-2-[(1*S*′,2*S*′)-2-{2-[(a*S*′)-(diisopropylamino)-carbonyl]-3-ethylphenyl}-1-methyl-2-(methylamino)ethyl]-1-naphthamide and (a*R*′)-*N*,*N*-diisopropyl-2-[(1*S*′,2*S*′)-2-{2-[(a*R*′)-(diisopropylamino)carbonyl]-3-ethylphenyl}-1-methyl-2-(methylamino)ethyl]-1-naphthamide (18B and 18A). In the same way, the lithiated species formed from naphthamide **1** (252 mg, 0.89 mmol) THF (10 ml) and *sec*-butyllithium (0.75 ml, 0.98 mmol; 1.3 M solution in hexanes) was treated with a solution of imine **11** (268 mg, 0.98 mmol) in THF (6 ml). After work-up in the usual manner, ^{1}H NMR the crude product showed the atropisomers to be present in a ratio of *ca.* 1 : 1 Purification by flash chromatography on silica gel [3 : 1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine] and subsequent heating in ethyl acetate for 30 min afforded naphthamide **18B** contaminated with a small amount of **18A** (371 mg, 75%) as a white solid, mp >230 °C; λ_{max}, nm (ε_{max}) (CH_2Cl_2) 234 (77230) 274 (10020); ν_{max} (film)/cm^{-1} 2967, 2934, 2876, 1621; δ_H(300 MHz, $CDCl_3$) 7.85 (3H, m, ArH), 7.72 (1H, d, *J* 8.7, ArH), 7.50 (3H, m, ArH), 7.38 (1H, t, *J* 7.6, ArH), 7.21 (1H, d, *J* 7.4, ArH), 3.80–3.55 (5H, m, 4 × NCH^B and CH(NHCH$_3$)^B), 2.97 (1H, quintet, *J* 7.7, CHCH$_3$CH(NHCH$_3$)^B), 2.76 (1H, m, CHHCH$_3^B$), 2.65 (1H, m, CHHCH$_3^B$), 2.22 (1H, bs, NH^B), 2.06 (3H, s, NHCH_3^A), 2.01 (3H, s, NHCH_3^B), 1.85 (3H, d, *J* 6.9, NCHCH_3^B), 1.80 (6H, m, 2 × NCHCH_3^B), 1.72 (3H, d, *J* 6.7, NCHCH_3^B), 1.30 (3H, t, *J* 7.6, CH$_2$CH_3^B), 1.16–1.00 (15H, m, 4 × NCHCH_3^B and CHCH_3CH(NHCH$_3$)^B); $\delta_C{}^B$(75 MHz, $CDCl_3$) 170.3, 169.8, 139.5, 137.1, 133.9, 132.1, 129.3, 128.4, 127.9, 126.4, 125.6, 125.0, 124.8, 124.1, 67.3, 51.0, 50.3, 46.2, 45.9, 45.5, 35.5, 26.1, 21.7, 21.0, 20.8, 20.8, 20.6, 20.5, 20.2, 19.5 and 15.4; *m*/*z* (CI) 558 (100%, M + H$^+$) (found: M + H$^+$, 558.4055. $C_{36}H_{51}N_3O_2$ requires M + H, 558.4059). Also obtained was recovered naphthamide **1** (20 mg, 8%). Heating amine **18** in $CDCl_3$ for 2 d at 60 °C produced **18B** only (^{1}H NMR).

(a*S*′)-*N*,*N*-Diisopropyl-2-[(2*S*′)-2-{2-[(a*S*′)-(diisopropylamino)-carbonyl]-3-methylphenyl}-2-(methylamino)ethyl]-1-naphthamide and (a*S*′)-*N*,*N*-diisopropyl-2-[(2*S*′)-2-{2-[(a*R*′)-(diisopropylamino)-carbonyl]-3-methylphenyl}-2-(methylamino)ethyl]-1-naphthamide (19B and 19A). In the same, the lithiated species formed from naphthamide **2**[1] (197 mg, 0.73 mmol) in THF (15 ml) at −78 °C and *sec*-butyllithium (0.67 ml, 0.81 mmol; 1.2 M solution in hexanes) was treated with a solution of imine **12** (210 mg, 0.81 mmol) in THF (5 ml) and stirred for a further 10 min. After work-up in the usual manner, ^{1}H NMR of the crude product showed the atropisomers to be present in a ratio of *ca.* 1 : 1. Purification by flash chromatography on silica gel [1 : 1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine] afforded and subsequent heating in ethyl acetate for 30 min afforded naphthamide **19B** contaminated with a small amount of **19A** (243 mg, 63%) as a white solid, mp >230 °C; ν_{max} (film)/cm^{-1} 2969, 2932, 2873, 1621; δ_H(300 MHz, $CDCl_3$) 7.82 (4H, m, ArH), 7.67 (1H, d, *J* 7.8, ArH), 7.50 (2H, m, ArH), 7.31 (1H, t, *J* 7.6, ArH), 7.14 (1H, d, *J* 7.4, ArH), 4.05 (1H, m, C*H*NHCH$_3^A$), 3.91 (1H, dd, *J* 10.4 and 2.1, C*H*NHCH$_3^B$), 3.80 (1H, septet, *J* 6.6^B, NCH), 3.65 (1H, m, NCH^B), 3.60 (1H, m, NCH^B), 3.44 (1H, septet, *J* 6.7, NCH^B), 3.33 (1H, dd, *J* 13.5 and 2.2, C*H*HCH(NHCH$_3$)^B), 2.62 (1H, dd, *J* 13.3 and 10.6, CH*H*CH(NHCH$_3$)^B), 2.39 (3H, s, NCHCH_3^B), 2.15 (3H, s, CH$_3^B$), 1.89 (3H, d, *J* 6.9, NCHCH_3^B), 1.81 (3H, d, *J* 6.9, NCHCH_3^B), 1.74 (3H, d, *J* 6.9, NCHCH_3^B), 1.73 (3H, d, *J* 6.7, NCHCH_3^B), 1.19 (6H, d, *J* 6.6, 2 × NCHCH_3^B), 0.98 (3H, d, *J* 6.7, NCHCH_3^B), 0.94 (3H, d, *J* 6.7, NCHCH_3^B); $\delta_C{}^B$(75 MHz, $CDCl_3$) 170.3, 170.0, 136.7, 134.9, 133.4, 133.1, 132.1, 129.4, 128.6, 128.2, 128.0, 127.9, 127.8, 126.5, 125.6, 124.8, 123.6, 64.1, 51.2, 50.7, 46.0, 46.0, 43.0, 35.2, 21.8, 21.6, 20.9, 20.7, 20.7, 20.6, 20.3, 20.1 and 19.1; *m*/*z* (CI) 530 (100%, M + H$^+$) (found: M + H$^+$, 530.3751. $C_{34}H_{47}N_3O_2$ requires M + H, 530.3746). Also obtained was recovered naphthamide **2** (20 mg, 11%). Heating amine **19** in $CDCl_3$ for 2 d at 60 °C produced **19B** only (^{1}H NMR).

(a*R*′)-*N*,*N*-Diisopropyl-2-[(1*S*′,2*S*′)-2-{(a*S*′)-(diisopropylamino)-carbonyl]-3-ethylphenyl}-1-methyl-2-(dimethylamino)ethyl]-1-naphthamide and (a*R*′)-*N*,*N*-diisopropyl-2-[(1*S*′,2*S*′)-2-{(a*R*′)-(diisopropylamino)carbonyl]-3-ethylphenyl}-1-methyl-2-(dimethylamino)-ethyl]-1-naphthamide (20). To a stirred mixture of naphthamide **18B** (211 mg, 0.38 mmol), paraformaldehyde (114 mg, 3.79 mmol), sodium borohydride (72 mg, 1.89 mmol) and THF (15 ml) under an atmosphere of nitrogen at ambient temperature was added TFA over a period of 20 min and stirred for a further 25 h. The mixture was poured into a solution of 25% aqueous sodium hydroxide (10 ml) and ice, and diluted with brine (10 ml). The mixture was extracted with dichloromethane (4 × 20 ml) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography on silica gel [4 : 1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine] afforded tertiary amine **20** (160 mg, 74%) as a white solid, mp 179–182 °C; R_f 0.49 [1 : 1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine]; ν_{max} (film)/cm^{-1} 3057, 2975, 2935, 2876, 2840, 2797, 1622, 1614; δ_H(300 MHz, $CDCl_3$) 7.82 (3H, m, ArH), 7.69 (1H, d, *J* 8.8, ArH), 7.46 (2H, m, ArH), 7.36–7.25 (2H, m, ArH), 7.20 (1H, d, *J* 7.3, ArH), 4.51 (1H, d, *J* 10.0, CHNMe$_2$), 3.75–3.50 (5H, m, 4 × NCH and CH(Me)CHNMe$_2$), 2.78 (1H, m, CHHCH$_3$), 2.66 (1H, m, CHHCH$_3$), 2.20 (6H, s, NMe$_2$), 1.86 (6H, m, 2 × CHCH$_3$), 1.75 (3H, d, *J* 6.9, CHCH$_3$), 1.71 (3H, d, *J* 6.9, CHCH$_3$), 1.30 (3H, t, *J* 7.6, CH$_2$CH$_3$), 1.14 (6H, m, 2 × CHCH$_3$), 1.07 (3H, d, *J* 6.5, CHCH$_3$), 0.99 (3H, d, *J* 6.5, CHCH$_3$), 0.94 (3H, d, *J* 6.9, CHCH$_3$); δ_C(75 MHz, $CDCl_3$) 170.1, 169.7, 140.8, 139.8, 138.8, 137.5, 132.4, 132.0, 130.0, 127.9, 127.8, 126.8, 126.2, 126.0, 125.9, 125.4, 125.2, 125.0, 69.4, 51.1, 50.3, 46.2, 45.8, 41.3, 35.5, 26.0, 22.6, 21.1, 21.0, 20.8, 20.8, 20.4, 20.1 and 15.1; *m*/*z* (CI) 572 (100%, M + H$^+$) (found: M + H$^+$, 572.4214. $C_{37}H_{53}N_3O_2$ requires M + H, 572.4216). Also obtained was

recovered naphthamide **18B** (34 mg, 16%). Heating amine **20** in $CDCl_3$ for 2 d at 60 °C produced a ratio of atropisomers 1.7 : 1 (^{1}H NMR); *epi*-**20**, δ_H(300 MHz, $CDCl_3$) 1.96 (6H, s, NMe_2).

(a*R*′)-*N*,*N*-Diisopropyl-2-[(1*S*′,2*S*′)-2-{(a*R*′)-(diisopropylamino)-carbonyl]-3-ethylphenyl}-1-methyl-2-(dimethylaminoborane)ethyl]-1-naphthamide (21). A solution of naphthamide **20** (132 mg, 0.23 mmol) in THF (2 ml) at 0 °C under an atmosphere of nitrogen was treated with borane (0.46 ml, 0.46 mmol; 1 M solution in THF) and stirred for a further 40 min. The solvent was removed at ambient temperature under reduced pressure, and the crude product was purified by flash chromatography on silica gel [1 : 1 petrol (bp 40–60 °C)–EtOAc] to afford pure amine–borane complex **21** (97 mg, 72%) as a white solid, ν_{max} (film)/cm^{-1} 3053, 2976, 2934, 2875, 2395, 2334, 2285, 1615; δ_H(300 MHz, $CDCl_3$) 7.89 (1H, d, *J* 8.8, ArH), 7.78 (1H, d, *J* 8.8, ArH), 7.74–7.64 (2H, m, ArH), 7.36 (3H, m, ArH), 7.23 (1H, t, *J* 7.7, ArH), 7.13 (1H, d, *J* 7.4, ArH), 4.88 (1H, d, *J* 9.6, CHN^+Me_2), 3.81 (1H, septet, *J* 6.3, NCH), 3.64–3.40 (4H, m, $CH(Me)CHN^+Me_2$ and 3 × NCH), 2.86 (3H, s, $^+$NMe), 2.74 (1H, m, CHHMe), 2.61 (1H, m, CHHMe), 2.32 (3H, s, $^+$NMe), 1.71 (9H, m, 3 × $CHCH_3$), 1.62 (3H, d, *J* 6.7, $CHCH_3$), 1.50 (3H, bs, BH_3) 1.12 (3H, d, *J* 6.3, $CHCH_3$), 1.08 (3H, d, *J* 6.5, $CHCH_3$), 1.06 (3H, t, *J* 7.6, CH_2CH_3), 0.95 (3H, d, *J* 6.6, $CHCH_3$), 0.89 (3H, d, *J* 6.5, $CHCH_3$), 0.72 (3H, d, *J* 7.0, $CHCH_3$); δ_C(75 MHz, $CDCl_3$) 169.9, 169.9, 141.3, 141.1, 138.3, 136.6, 132.0, 130.8, 129.7, 129.0, 128.0, 127.7, 127.6, 126.5, 125.9, 125.8, 125.0, 124.6, 74.6, 55.3, 50.7, 50.3, 46.8, 46.3, 46.2, 38.0, 29.6, 27.6, 23.1, 21.7, 21.3, 21.1, 20.9, 20.8, 20.7, 20.2, 20.1 and 16.5; *m*/*z* (CI) 572 (100%, M–BH_3); *m*/*z* (EI) 572 (1%, M–BH_3) and 49 (100%).

***N*,*N*-Di(1-methylethyl)-2-[(1*S*′,2*S*′)-2-(dimethylamino)-2-(2-{[di(1-methylethyl)amino]carbonyl}-3-ethylphenyl)-1-methylethyl}-5,6,7,8-tetrahydro-1-naphthalenecarboxamide (22).** A suspension of naphthamide **20** (66 mg, 0.116 mmol), Raney Nickel (4.6 g; 50% slurry in water), and ethanol was stirred at ambient temperature for 27.5 h (TLC indicated no reaction). The reaction mixture was refluxed for 4 h (TLC indicated no starting material), cooled to ambient temperature, filtered (Celite) and washed through with ethanol then diethylether. The solvent was removed under reduced pressure at ambient temperature to afford the crude product. Purification by flash chromatography [4 : 1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine] afforded tetralin **22** (22 mg, 33%) as a colourless oil (*ca.* 3 : 7 mixture of atropisomers), ν_{max} (film)/cm^{-1} 2973, 2934, 2874, 1625; δ_H(200 MHz, $CDCl_3$) 7.90–7.75 (1H, m, ArH), 7.60–7.5 (1H, m, ArH), 7.40–7.00 (3H, m, ArH), 4.06 (1H, d, *J* 10.9, $CHNMe_2^{minor}$), 3.90 (1H, d, *J* 10.7, $CHNMe_2^{major}$), 3.85–3.35 (5H, m, 4 × NCH and $CH(Me)CHNMe_2$), 3.90–2.50 (4H, m, CH_2CH_3 and $CH_2(CH_2)_3$), 2.08 (6H, s, NMe_2), 1.90–1.60 (16H, m, 4 × CH_3 and 2 × $CH_2CH_2CH_2CH_2$), 1.35–0.95 (20H, m, $CH_2CH_2CH_2CH_2$ and 6 × CH_3); δ_C(75 MHz, $CDCl_3$) 170.2, 169.9, 169.4, 169.1, 140.8, 140.7, 139.5, 138.8, 137.5, 137.0, 135.8, 134.8, 133.7, 133.0, 132.6, 131.8, 129.8, 129.5, 128.6, 128.1, 127.7, 126.9, 126.5, 126.0, 125.7, 125.2, 123.9, 123.6, 122.7, 69.9, 69.3, 50.9, 50.4, 50.0, 49.9, 49.7, 46.1, 45.9, 45.8, 45.6, 42.2, 41.8, 41.0, 38.0, 37.3, 34.2, 29.5, 29.2, 26.6, 26.4, 26.3, 25.8, 23.1, 22.9, 22.8, 22.7, 22.5, 21.8, 21.4, 21.3, 21.2, 21.0, 20.9, 20.8, 20.6, 20.6, 20.2, 20.0, 20.0, 19.9, 19.8, 15.4, 15.3 and 15.0; *m*/*z* (CI) 576 (100%, M + H$^+$), 289 (27%, M–$C_{19}H_{28}NO$) and 286 (16%, M–$C_{18}H_{29}N_2O$); *m*/*z* (EI) 289 (1%, M–$C_{19}H_{28}NO$) and 49 (100%) (found: M + H$^+$, 576.4524. $C_{37}H_{57}N_3O_2$ requires M + H, 576.4529).

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