PERKIN 1

# Atroposelective attack of nucleophiles on 2-formyl-1-naphthamides and their derivatives: chelation and non-chelation control

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Organometallic nucleophiles attack 2-formyl-1-naphthamides to give secondary alcohols with widely varying atroposelectivity. By careful choice of reagent, selectivities of up to >99 : 1 in favour of either the *anti* or the *syn* atropisomer can be obtained. Ethers and amines may be synthesised atroposelectively from acetals or imines. The sense of the selectivity is determined by the reactive conformation of the Ar–CHO bond, itself dependent on the coordinating and chelating ability of the nucleophile's counterion. The roles of conformation, Lewis acids, and chelation/non-chelation control in relation to stereoselectivity are discussed.

## Introduction

In the previous paper[1] we described the synthesis of secondary alcohols **1** by atroposelective reduction of the corresponding ketones **2** (Scheme 1, disconnection (a)). We had earlier reported the synthesis of the same class of alcohols by atroposelective addition of ortholithiated 1-naphthamides **3** to aldehydes (disconnection (b)).[2,3] In this paper we turn to the third possible route to the alcohols, indicated by disconnection (c)—the addition of an alkyl metal reagent to a 2-formylnaphthamide **4**.[4] We also consider the atroposelective addition of nucleophiles to the oxonium and imine[5] derivatives of **4** (leading to ethers **21** and amines **24**–**27**).

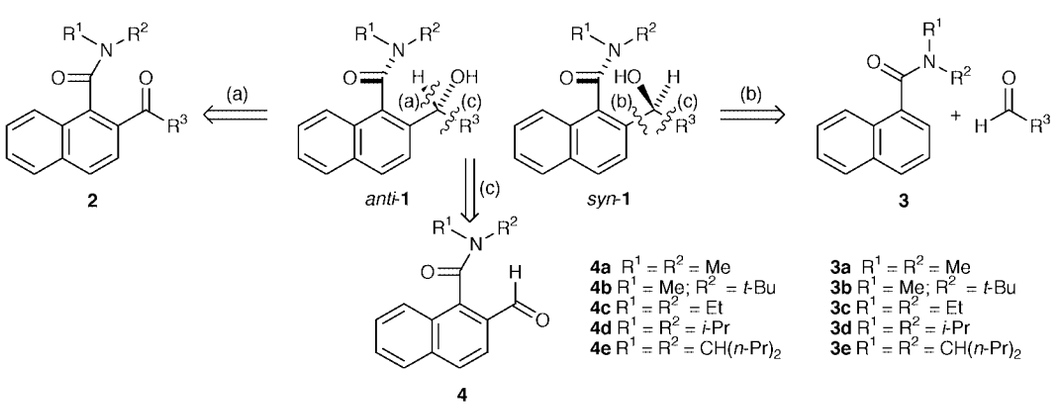
Conformational freedom around the R–CHO bond means that nucleophilic attack on chiral aldehydes[6] only rarely exhibits high levels of stereoselectivity. Additions of Grignard reagents to simple acyclic chiral aldehydes typically give up to 80 : 20 selectivity.[7,8] More complex aldehydes containing bulky *N*,*N*-dibenzylamino groups[9,10] or silyl substituents[11] or lacking free rotation[12] demonstrate rather higher levels of selectivity. Cram and Wilson[13] noted that metal chelation by the aldehyde carbonyl oxygen and a second heteroatom may increase the stereoselectivity considerably, and in favourable cases, simple chiral aldehydes bearing alkoxy substituents may react with >90 : 10 stereoselectivity with Grignard reagents and, to a lesser extent, organolithiums.[14,15] Higher selectivities still may be obtained, for example, by the use of $RTiCl_3$ reagents,[16,17] but in general selectivity in chelation-controlled addition is supremely sensitive to the nature of the organometallic used and to the conditions of the reaction.[18] Examples of additions to chiral aldehydes with high levels of (1,3)-,[15,19,20] and more remote[21,22] asymmetric induction have also been reported. There are a few reports of the use of planar[23,24] or axial[25] chirality to govern the direction of attack on aldehydes.

## Results and discussion

### Synthesis of 2-formyl-1-naphthamides

The aldehydes **4** were very conveniently made from their parent 1-naphthamides **3** by ortholithiation[26] and reaction with DMF (Scheme 2, Table 1). The yield of **4b** and **4e** was lowered by a competing addition of *s*-BuLi to the aromatic ring. The synthesis of **4b**, for example, also produced four diastereoisomers of the amides **5** in 65% yield. Addition to the ring appears to be a problem when one of the *N*-alkyl groups is particularly large, and may be a result of hindrance to O–Li coordination.[27]

Only **4a** could not be made in this way: *N*,*N*-dimethylamides are generally too electrophilic (at the carbonyl group) to undergo ortholithiation.[26] Instead, we made **4a** from 1-bromo-2-methylnaphthalene **6** (Scheme 3). Bromination[29] and Hass–Bender oxidation[30] gave the aldehyde **8**[29,31] which was protected as its dioxolane **9**.[32] Bromine–lithium exchange gave an organolithium which reacted with *N*,*N*-dimethylcarbamoyl chloride to yield naphthamide **10** which was deprotected using acid to give **4a**.

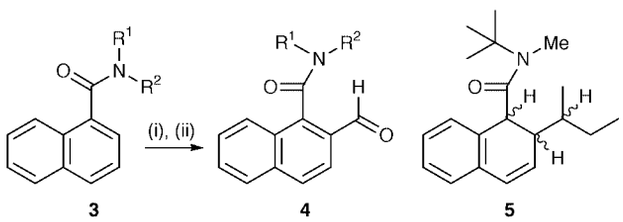



**Scheme 1** Atroposelective routes to **1**.

### Additions of nucleophiles to 2-formyl-1-naphthamides 4

We started by treating the aldehydes **4** with a range of simple organolithium and Grignard reagents in THF at −78 °C as shown in Scheme 4 and Table 2: methyllithium (entry 1), butyllithium (entry 2), octynyllithium (entry 7), phenyllithium (entry 10); and methylmagnesium bromide (entry 12), butylmagnesium chloride (entry 13), phenylmagnesium bromide (entry 17), allylmagnesium bromide (entry 18). The reactions gave moderate to excellent yields of the alcohols **11**–**15** but with selectivities varying greatly, from 140 : 1 *syn* to >99 : 1 *anti*.

The additions have one simple overriding feature: all the Grignard reagents add with *syn*-selectivity, and (apart from PhLi and octynyllithium) the organolithiums add with *anti*-selectivity. Other than this, the trends are much less distinct.



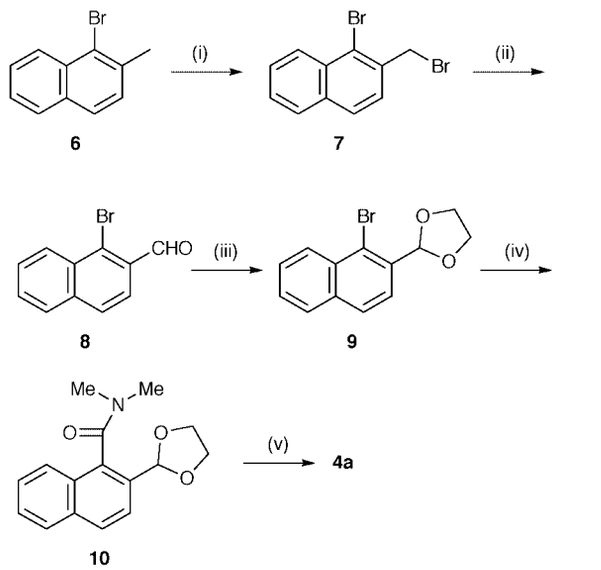

**Scheme 2** Synthesis of aldehydes **4** (i) *s*-BuLi, THF, −78 °C; (ii) $Me_2NCHO$, −78 °C.

**Table 1** Synthesis of aldehydes **4**

| Entry | $R^1$ | $R^2$ | Starting material | Product | Yield (%) |
|---|---|---|---|---|---|
| 1 | Me | *t*-Bu | **3b** | **4b** | 33[a] |
| 2 | Et | Et | **3c** | **4c** | 78 |
| 3 | *i*-Pr | *i*-Pr | **3d** | **4d** | 82[28] |
| 4 | CH(*n*-Pr)$_2$ | CH(*n*-Pr)$_2$ | **3e** | **4e** | 59 or 44[2] |

[a] Plus **5** (65%).

Phenyl and butyl additions are more selective than allyl additions, with the methyl additions lying in between. Selectivity also varies with the *N*-substituents $R^1$ and $R^2$: generally, but by no means always, the N*i*-$Pr_2$ aldehyde **4d** reacts with slightly higher selectivity than the $NEt_2$ aldehyde **4c**. The $N(CHPr_2)_2$ aldehyde **4e** underwent the most *anti*-selective (with MeLi, entry 1) and the most *syn*-selective (with PhMgBr, entry 17) reactions of all, but its reactions with BuLi (entry 2) and BuMgBr (entry 13) were notably unselective, and gave significant amounts of the reduction product **16e**. Our first conclusion, therefore, is that the reactions of **4** are controlled




**Scheme 3** Synthesis of **4a**; (i) NBS, $(PhCO_2)_2$, $CCl_4$, (60%); (ii) 2-nitropropane, NaOEt, EtOH, (62%); (iii) $HOCH_2CH_2OH$, *p*-TsOH, PhH, (91%); (iv) 1. *t*-BuLi × 2, 2. $ClCONMe_2$; (v) *p*-TsOH, AcMe (83% over 2 steps).

**Table 2** Additions of nucleophiles to aldehydes **4**

| | | | From **4c** | | From **4d** | | From **4e** | |
|---|---|---|---|---|---|---|---|---|
| Entry | Reagent | Additives (equiv.) | Product, yield[a] (%) | Ratio[b] *anti*:*syn* | Product, yield[a] (%) | Ratio[b] *anti*:*syn* | Product, yield[a] (%) | Ratio[b] *anti*:*syn* |
| 1 | MeLi | — | **11c** 94 | 71:29 | **11d** 90 | 80:20 | **11e** 99 | >99:1 |
| 2 | *n*-BuLi | — | **12c** 56 | 85:15 | **12d** 83 | 85:15 | **12e** 91 + 6[c] | 49:51 |
| 3 | | HMPA (4) | **12c** 63 | 66:34 | **12d** 65 | 73:27 | — | — |
| 4 | | $BF_3{\cdot}OEt_2$ (1)[d] | **12c** 67 | 57:43 | **12d** 41 | 48:52 | — | — |
| 5 | | $BF_3{\cdot}OEt_2$ (2)[d] | **12c** 49 | 43:57 | **12d** 59 | 45:55 | — | — |
| 6 | | $Me_3Al$ (0.1) | — | — | **12d** 56 | 94:6 | — | — |
| 7 | OctynylLi | — | — | — | **13d** 90 | 20:80 | — | — |
| 8 | | $Me_3Al$ (0.1) | — | — | **13d** 66 | 93:7 | — | — |
| 9 | | *i*-$Bu_2AlH$ (1) | — | — | **13d** 50 | >99:1 | — | — |
| 10 | PhLi | — | **14c** 52 | 19:81 | **14d** 95 | 34:66 | — | — |
| 11 | | HMPA (4) | **14c** —[e] | 27:73 | **14d** —[e] | 33:67 | — | — |
| 12 | MeMgBr | — | **11c** 91 | 25:75 | **11d** 66 | 23:77 | — | — |
| 13 | *n*-BuMgCl | — | **12c** 72 | 14:86 | **12d** 57 | 15:85 | **12e** 33 + 33[c,f] | 34:66 |
| 14 | | HMPA (4) | **12c** 68 | 38:62 | **12d** 62 | 32:68 | — | — |
| 15 | | $MgBr_2$ (1)[d] | **12c** 83 | 43:57 | **12d** 61 | 50:50 | — | — |
| 16 | | $ZnBr_2$ (1)[d] | **12c** 74 | 37:63 | **12d** 89 | 32:68 | — | — |
| 17 | PhMgBr | — | **14c** 81 | 14:86 | **14d** 71 | 3:97 | **14e** 90 | 1:140 |
| 18 | AllylMgBr | — | **15c** 97 | 42:58 | **15d** 94 | 40:60 | — | — |
| 19 | MeTi(O*i*-Pr)$_3$ | — | **11c** 70 | 98:2 | **11d** 99 | 300:1 | **11e** 59 | >99:1 |
| 20 | *n*-BuTi(O*i*-Pr)$_3$ | — | **12c** 64 | 74:26 | **12d** 63 | 125:1 | — | — |
| 21 | OctynylTi(O*i*-Pr)$_3$ | — | **13c** 76 | 95:5 | **13d** 52 | 125:1 | — | — |
| 22 | PhTi(O*i*-Pr)$_3$ | — | **14c** 97 | 11:89 | **14d** 96 | 85:15 | — | — |
| 23 | AllylTi(O*i*-Pr)$_3$ | — | **15c** 92 | 71:29 | **15d** 100 | 77:28 | — | — |
| 24 | $MeTiCl_3$ | [g] | **11c** 48 + 12[h] | 6:94 | **11d** 41 + 13[h] | 65:35 | — | — |
| 25 | $MeTiCl_3$ | [i] | 18[h] | — | 23[h] | — | — | — |

[a] Isolated yield of mixture. [b] Determined by analytical HPLC. [c] Yield of reduction product **16**. [d] $CH_2Cl_2$ in the absence of THF. [e] Product not isolated. [f] *n*-BuMgBr used. [g] Reagent formed *in situ* from MeMgBr + $TiCl_4$. [h] Yield of pinacol product **17**. [i] Reagent formed *in situ* from MeLi + $TiCl_4$.

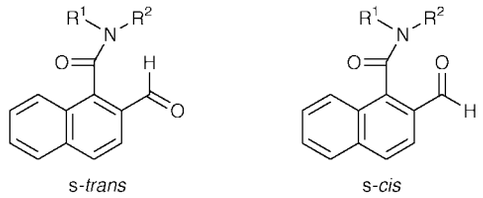
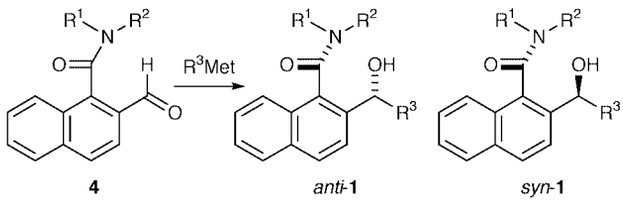
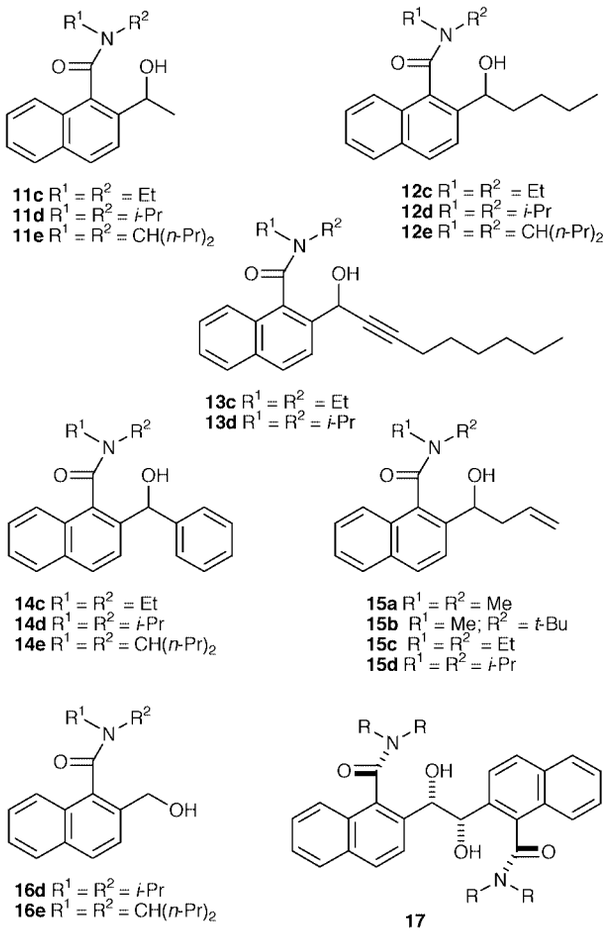



**Fig. 1** Conformation of aldehyde **4**.




**Scheme 4**

principally by the nature of the metal and are influenced relatively little by the size of $R^1$ and $R^2$.

In contrast with the reactions of aldehydes **4** the reactions of ketones **2** all proceed with the same stereochemical sense[1] because all reagents attack **2** from the less hindered face (*syn* to the amide C=O) of its s-*cis* conformation. For aldehyde **4**, both s-*cis* and s-*trans* conformations are accessible (Fig. 1), and **4** may present either face of its electrophilic carbonyl group to an incoming reagent simply by rotation about the Ar–CHO bond. The effect of the metal on the stereoselectivity of the reaction could be a result of the degree of chelation by the metal between the amide and the aldehyde carbonyl groups, which would affect the Ar–CHO torsional angle in the transition state.[33] This being so, additives which promote or dissuade chelation should influence the selectivity accordingly. We added to the reactions of BuLi, PhLi and BuMgCl four equiv. of HMPA (entries 3, 11, 14, Table 2) in an attempt to prevent amide–aldehyde chelation: in all cases selectivity decreased, becoming more *syn*-selective from BuLi and more *anti*-selective from PhLi and BuMgCl. We also repeated the reactions of BuLi and BuMgCl in $CH_2Cl_2$ in the presence of Lewis acids: $BF_3{\cdot}OEt_2$ (1 or 2 equiv., entries 4 and 5) to discourage chelation and $MgBr_2$ and $ZnBr_2$ (entries 15, 16) to encourage it. Again, the only effect was that the selectivity, in whichever direction, decreased.

Organoaluminium reagents can exhibit high levels of stereoselectivity in their additions to aldehydes.[22] Additionally, trimethylaluminium has been shown to be capable of forming five-membered chelates with epoxyalcohol derivatives, increasing their reactivity and controlling the regioselectivity of their reactions.[34] We therefore briefly investigated the effect of organoaluminium reagents on the stereoselectivity of additions to chiral aldehydes. In the presence of one equivalent of DIBAL-H, octynyllithium gave the alcohol **13d** solely as its *anti*-diastereoisomer (entry 9).[35] The reaction was (unsurprisingly) accompanied by a significant amount of reduction to alcohol **16d** and behaved unpredictably, with **16d** sometimes being the sole product.[36] No reaction was observed when DIBAL-H was replaced with trimethylaluminium. However, in the presence of *catalytic* quantities (0.1 equiv.) of trimethylaluminium, reactivity was restored, the *anti* diastereoisomer being produced (entry 8) with slightly lower stereoselectivity than with stoichiometric DIBAL-H. The same enhanced *anti*-stereoselectivity was observed when BuLi was added to **4d** in the presence of catalytic trimethylaluminium (entry 6).

Trialkylaluminiums cannot usually be used as Lewis acids in the presence of organolithiums because of the rapid formation of ate-complexes. However, Maruoka and co-workers[34] have shown that $Me_3Al$ leads to an enhancement of the reactivity of epoxy-alcohol derivatives towards organolithiums which cannot be ascribed to ate complex formation: catalytic quantities of $Me_3Al$ are essential. DIBAL-H–trialkylaluminium complexes have moreover been used to control the selectivity of additions of vinyllithiums to chiral aldehydes.[37] We therefore propose that these are reactions of organolithiums catalysed (and increased in selectivity) by coordination of $R_3Al$ to the aldehyde oxygen, and that the presence of excess $Me_3Al$ leads to the formation of less reactive ate complexes. The highly selective formation of the *anti* diastereoisomer suggests that chelation between the amide and aldehyde carbonyl groups is not involved.

As an alternative to the use of additives, we next turned to reagents designed respectively to avoid and to promote chelation during stereoselective reactions. Alkyltitanium triisopropoxides, whose reactions with α-alkoxyaldehydes proceed *via* non-chelated transition states,[15,38,39] were made by treating MeLi, BuLi, octynyllithium, phenyllithium and allylmagnesium bromide with $ClTi(O\textit{i}\text{-}Pr)_3$. The outcomes of their reactions with **4** are shown in entries 19–23 of Table 2. Apart from one case, the reactions went in the same sense as most of the organolithium reactions—they were *anti*-selective—but with much higher levels of stereocontrol than even the $Me_3Al$-catalysed reactions (entries 6, 8 and 9). $MeTi(O\textit{i}\text{-}Pr)_3$ was the most selective of all, reacting with **4c**, **4d** and **4e** with 50 : 1, 300 : 1 and >99 : 1 selectivity respectively (entry 19), with the $octynylTi(O\textit{i}\text{-}Pr)_3$ performing almost as well (entry 21: the octynyltitanium species reacts with selectivity opposite to that of octynyllithium). $BuTi(O\textit{i}\text{-}Pr)_3$ reacted selectively with the $N\textit{i}\text{-}Pr_2$ aldehyde **4d**, though the selectivity with the $NEt_2$ aldehyde **4c** was less good (entry 20). The allyl reagent (entry 23), as before, was less selective, and the $PhTi(O\textit{i}\text{-}Pr)_3$ (entry 22) exhibited a bizarre switch from *anti*-selectivity with **4d** to *syn*-selectivity with **4c** [PhLi had also proved unusually *syn*-selective (entry 7)].

The alkyltitanium triisopropoxide reactions demonstrate that the key to good *anti*-selectivity in the addition to 2-formyl-1-naphthamides is to avoid chelation. In fact, the results obtained

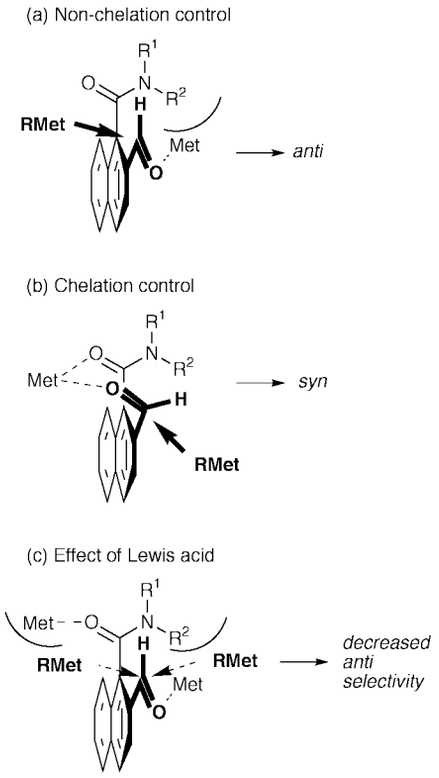



**Fig. 2** Chelation and non-celation control in the attack of organometallics on aldehydes **4**.

here are among the most selective reactions ever observed for chiral aldehydes,[15] and may indeed be the most selective ever of chiral aldehydes without an α-chiral centre. We attribute the exceptionally high levels of stereoselectivity to co-ordination of the bulky titanium reagent to the aldehyde as the reaction takes place, which (along with the titanium's lack of ability to chelate the amide C=O) greatly destabilises the s-*cis* conformation[40] of the aldehyde. Reaction on the less hindered face of **4** then leads solely to the *anti* diastereoisomer.

Alkyltitanium trichlorides, in contrast, favour chelation.[15,16] When we treated **4c** and **4d** with $MeTiCl_3$ made from MeMgBr (entry 24) we got a moderate yield of the desired alcohols **11c** with high *syn*-selectivity and **11d** with moderate *anti*-selectivity, along with some by-product **17**. When the $MeTiCl_3$ was made from MeLi (entry 25), the diol **17** was the only product isolated. An X-ray crystal structure proved that **17** has an *anti* relationship between the hydroxy-bearing centres and the respective amide C=O groups, and is formed as a single *syn* diastereoisomer of the diol. Intramolecular pinacol couplings are rarely stereoselective,[41,42] but Seebach and Raubenheimer[43] have described the use of a low-valent titanium reagent, formed by reduction of $TiCl_4$ with BuLi, to carry out *syn*-selective pinacol couplings. We assume a similar low-valent titanium species is involved here.

Bearing in mind the complexity of the possible metal–amide–aldehyde–solvent aggregates likely in the reaction mixture, detailed speculation on the origin of each individual stereoselectivity is pointless. However, regarding the effect of the metal on the stereoselectivity, we draw the following general conclusions:

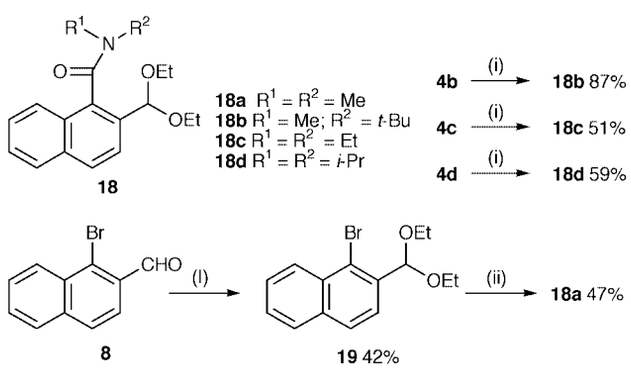
(a) Non-chelating metal atoms (Li, Ti, Al) promote reaction through an s-*trans* conformation approximating to that shown in Fig. 2(a). With Met = $Ti(Oi\text{-}Pr)_3$ or $AlMe_3$, the size of the metal ligand means that this is very much the favoured conformation and high selectivities result.

(b) Chelating metal atoms (Mg) promote reaction through a conformation approximating to that shown in Fig. 2(b) in which the other face of the CHO group is exposed to attack.

(c) The results in the presence of Lewis acids $BF_3{\cdot}OEt_2$, $MgBr_2$ and $ZnBr_2$ are harder to account for. A possible general explanation for the decrease in selectivity observed in all 8 experiments employing these additives is that Lewis acids prefer above all to coordinate to the amide carbonyl group, which is the most basic site in the molecule. This coordination (illustrated in Fig. 2(c)) increases the effective size of the C=O group, lessening the steric distinction between O and $NR^1R^2$, and decreasing the ability of the amide to direct highly selective reactions.[44]

### Lewis-acid mediated additions of allyltrimethylsilane to aldehydes and acetals

An alternative way of avoiding chelation during the additions is to use, instead of the aldehydes, the oxonium ions **20**.[43] These would be made from the corresponding acetals on treatment with Lewis acids,[45] and would allow us to use allyltrimethylsilane as a nucleophile.[46] The acetals **18** were formed straightforwardly from the aldehydes by refluxing with ethanol; **18a** was made directly from the bromoaldehyde **8**[31] which was first converted to the acetal[29] and then to the amide by bromine–lithium exchange and reaction with *N*,*N*-dimethylcarbamoyl chloride (Scheme 5).




**Scheme 5** Synthesis of acetals **18**; (i) EtOH, *p*-TsOH, 4 Å sieves; (ii) 1. 2 × *t*-BuLi, −78 °C, $Et_2O$, 2. $ClCONMe_2$.

We treated each of the aldehydes **4a**–**4d** and each of the acetals **18a**–**18d** with allyltrimethylsilane in the presence of $TiCl_4$ or $SnCl_4$. To ensure completion, 2 equiv. of Lewis acid were required with the aldehydes; one equiv. with the acetals (Scheme 6). The results of the reactions are shown in Table 3.

Unlike the previous results, changing the reagents had no effect on the sense of the selectivity, and relatively little effect on the magnitude of the selectivity. The one remarkable point is that while reactions of $NMe_2$, NMe*t*-Bu and $NEt_2$ amides **4a**–**c** and **18a**–**c** are all *syn*-selective—some highly *syn*-selective—all the reactions with the N*i*-$Pr_2$ amides **4d** and **18d** are *anti*-selective. The fact that both the acetal-derived oxonium ions **20** and the aldehydes **4** react with the same selectivity in each case suggests that none of these reactions is under chelation control, and that the aldehyde is reacting in an extended s-*trans* conformation (this is certainly expected for **20**, whose s-*cis* conformation will be particularly crowded) as shown in Fig. 3. Yet most of the reactions give the *syn* product—possible only if the reagent approaches the face of the aldehyde *syn* to the amide nitrogen. This could be explained if (i) the *N*-substituents (or at least the one *trans* to O) are relatively small (Me or Et, as they are in **4a**–**c**) and (ii) the amide oxygen is made larger by coordination (Fig. 3(a)). Significant complexation between the basic amide oxygen and the strongly Lewis acidic Ti or Sn reagents is to be expected, especially since two equivalents of Lewis acid were needed to ensure completion in the reactions of **4**. We can then rationalise the *anti*-selectivity of **4d** and **18d** by proposing that while the Lewis-acid complexed amide C=O is larger than Me or Et,[44] it is still less efficient at blocking

**Table 3** Lewis acid-promoted additions of allyltrimethylsilane to aldehydes and acetals

| Entry | Starting material | Lewis acid | From **4a** or **18a** Product, yield[a] (%) | Ratio[b] *anti*:*syn* | From **4b** or **18b** Product yield[a] (%) | Ratio[b] *anti*:*syn* | From **4c** or **18c** Product, yield[a] (%) | Ratio[b] *anti*:*syn* | From **4d** or **18d** Product, yield[a] (%) | Ratio[b] *anti*:*syn* |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **4** | $SnCl_4$ | **15a** 62[c] | 3:97 | — | — | **15c** 61 | 20:80 | **15d** 56 | 92:8 |
| 2 | **4** | $TiCl_4$ | **15a** 57[c] | 29:71 | **15b** 81 | 34:66 | **15c** 54 | 12:88 | **15d** 58 | 91:9 |
| 3 | **18** | $TiCl_4$ | **21a** 57 | 12:88 | **21b** 58 | 10:90 | **21c** 73 | 10:90 | **21d** 47 | 93:7 |

[a] Isolated yield. [b] Ratio in $^1$H NMR of crude product. [c] The crude product contained, additionally, traces of the lactone **22**. **15a** lactonised slowly on standing, and **22** was formed almost quantitatively from **15a** after 1 week at 60 °C in $CDCl_3$.

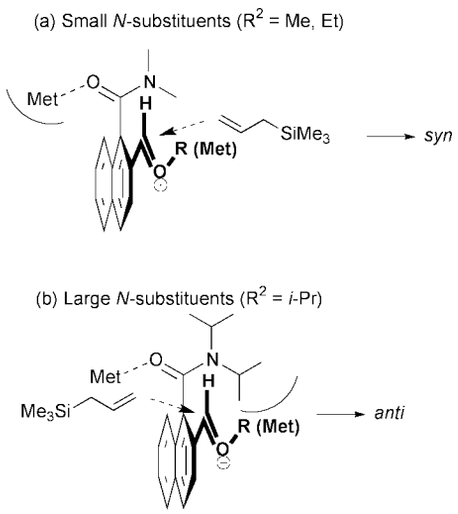
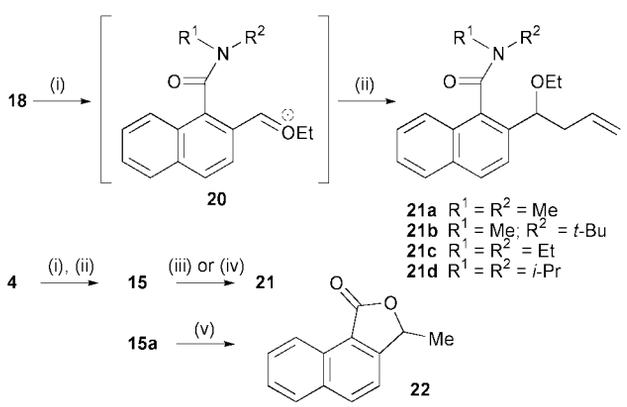



**Fig. 3** Stereoselectivity in the additions of allyltrimethylsilane.




**Scheme 6** Reactions with allyltrimethylsilane; (i) $SnCl_4$ or $TiCl_4$; (ii) allyltrimethylsilane; (iii) MeLi, $Et_3O^+BF_4^-$; (iv) NaH, EtI; (v) $CDCl_3$, 60 °C.

reagent approach than *i*-Pr (Fig. 3(b)). The switch in selectivity does not arise from hindrance to O-complexation by one of the N*i*-Pr groups, since **4b** and **18b**, with an *N*-*t*-Bu group *cis* to oxygen, reacts with the opposite selectivity.

### Assigning the stereochemistry of the alcohols 11–15 and ethers 21

We have previously assigned stereochemistry to the known alcohols **11c**–**e** and **14c**–**e** either by X-ray crystallography (**14d**) or by a method based on polarity and $^{13}$C NMR correlations. We noted that, for alcohols of the general structure **1**, *syn*-**1** is the more polar of the diastereoisomers, and its C=O signal in the $^{13}$C NMR is always downfield of *anti*-**1**'s C=O signal. The X-ray crystal structures (shown in Figs. 4 and 5) of *anti*-**15c** ($\delta_{C=O}$ = 164.6; $t_R$ = 5.9 min [2:1 petrol–EtOAc]; compare *syn*-**15c** $\delta_{C=O}$ = 169.9; $t_R$ = 12.3 min [2:1 petrol–EtOAc]) and *anti*-**15d** ($\delta_{C=O}$ = 164.4; $t_R$ = 3.7 min [2:1 petrol–EtOAc]; compare *syn*-**15d**

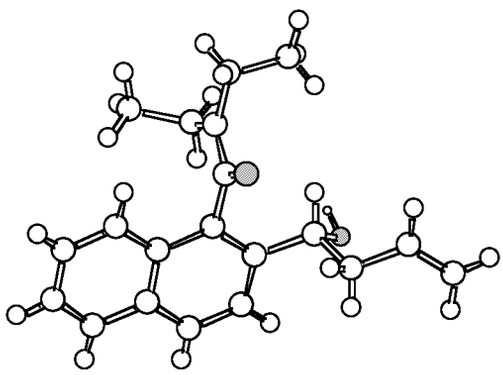


**Fig. 4** X-Ray crystal structure of *anti*-**15c**.

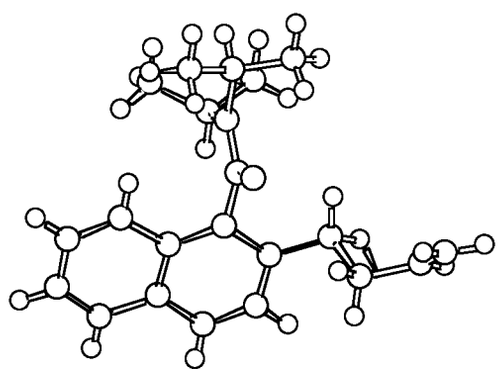


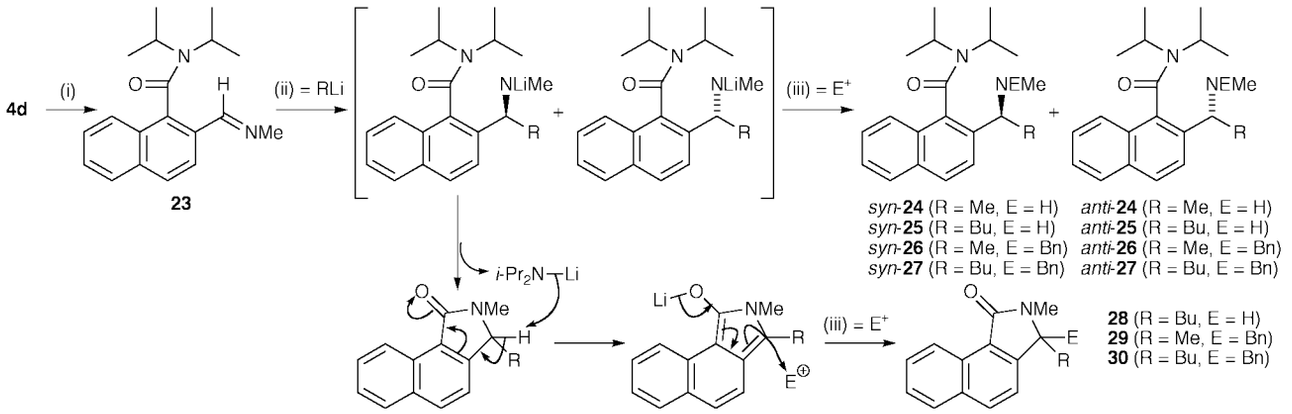
**Fig. 5** X-Ray crystal structure of *anti*-**15d**.

$\delta_{C=O}$ = 165.6; $t_R$ = 6.4 min [2:1 petrol–EtOAc]) were determined and confirm the generality of this method for stereochemical assignment. It was therefore used to assign stereochemistry to the diastereoisomers of the remaining alcohols **12c**–**12e**, **13c**, **13d**, **15a** and **15b**.

The stereochemistry of the ethers **21** was determined by conversion of one diastereoisomer of each of the alcohols **15a**–**15d** (*syn*-**15a**, *anti*-**15b**, *syn*-**15c**, *anti*-**15d**) to single diastereoisomers of the ethers **21a**–**21d** using NaH, EtI, or, for **15a** (which readily lactonises to **22** under these conditions) MeLi and triethyloxonium tetrafluoroborate.

### Organolithium additions to imines

The final part of our investigation concerned the addition of organolithiums to the imine derivatives of 2-formyl-1-naphthamides.[5] Imines typically react with higher stereoselectivity than their parent aldehydes,[47] and we expected the imine **23**, like the oxonium ions **20**, to prefer the extended s-*trans* conformation for steric reasons. Unlike the oxonium ions, however, they could in principle still react under chelation control. 2-Alkoxyimines react under chelation control with Grignards, though their reactions with organolithiums are poorly selective.[48] However, 2-(*N*,*N*-dibenzylamino)imines (unlike their parent aldehydes) react highly selectively under chelation control with organolithiums.[49]




**Scheme 7** Synthesis and reactions of imine **23**; (i) $MeNH_2$, $H_2O$, 60 min; (ii) MeLi or BuLi, −78 °C, 1–3 h; (iii) $NH_4Cl$, −78 °C or BnBr, 0 °C.

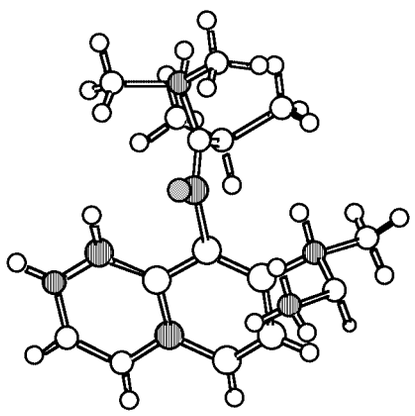


**Fig. 6** X-Ray crystal structure of *syn*-**24**.

**Table 4** Addition of organolithiums to imines **23**

| Entry | RLi | $E^+$ | Product, yield (%) | Ratio *syn*:*anti* | By-product, yield (%) |
|---|---|---|---|---|---|
| 1 | MeLi | $NH_4Cl$ | **24** 92 | >96:4 | — |
| 2 | BuLi | $NH_4Cl$ | **25** 85 | 92:8 | **28**[a] |
| 3 | MeLi | BnBr | **26** 15 | 96:4 | **29** 64 |
| 4 | BuLi | BnBr | **27** 16 | 92:8 | **30** 34 |

[a] Trace amounts of **28** were produced.

We made the *N*-methylimine **23** from **4d** simply by heating the aldehyde with aqueous methylamine. The imine was then treated with MeLi or BuLi in THF at −78 °C for 1–3 h and quenched with ammonium chloride to yield the amines **24** or **25**. Both of the reactions were highly selective (Table 4): it was not possible to detect the minor diastereoisomer from the addition of MeLi to **23**. The product of this reaction, *syn*-**24** was crystalline, and its X-ray crystal structure (Fig. 6) proved the *syn* stereochemistry which we assume to be that of the major isomer of **25** too.

We made the tertiary amines **26** and **27** in a similar way, by quenching the reactions with BnBr. Alkylation reached completion only when the reaction mixtures were warmed to 0 °C for 1–3 h. The tertiary amines **26** and **27** could then be isolated in low yield, but the major products were the lactams **29** and **30**, presumably formed by the mechanism outlined in Scheme 7, which outpaces the *N*-benzylation. Traces of related lactam **28** are formed in the reactions leading to **25**.

Considering the moderate *anti*-selectivity shown by additions of organolithiums to the related aldehydes **4**, the *syn*-selectivity in these reactions is surprising. There are two possible factors at work here. Firstly, repulsion between N*i*-$Pr_2$ and CH=NMe is greater than between N*i*-$Pr_2$ and CH=O, and may be favouring a conformation approaching Fig. 7(b). Secondly, chelation,

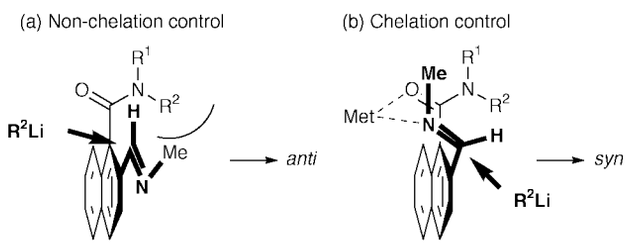
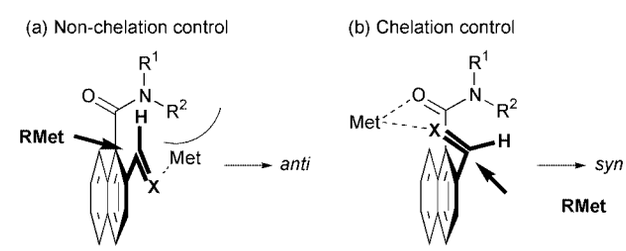



**Fig. 7** Stereoselectivity in the addition of organolithiums to imines.



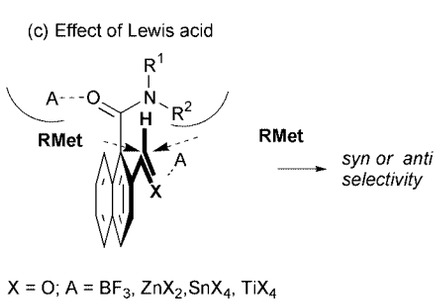




**Fig. 8**

which was absent from the RLi–carbonyl additions, may become important in the late transition states of the imine additions.

## Summary

The stereoselectivity of the reactions of 2-formyl-1-naphthamides is very much subject to the conformational freedom inherent in the Ar–CHO bond. Reagents which limit this freedom, by chelation, for example, or by coordination of Lewis acids to the aldehyde, allow higher levels of selectivity to be obtained. In general, we propose three models for the reactions of aldehydes **4** and their derivatives (Fig. 8): (a), dominated by coordination of a Lewis acidic metal to the aldehyde C=O, which may lead to very high levels of selectivity in favour of the *anti* isomer [aldehydes + RLi, RLi–$AlR_3$, RTi(O*i*-Pr)$_4$]; (b), dominated by chelation of a metal ion by both carbonyl

groups, which may lead to good selectivity for the *syn* isomer [aldehydes + RMgX, imines + RLi]; and (c), dominated by coordination of a Lewis acid to the amide C=O group, which, leads to lowered *anti*-selectivity, and with small $NR_2$ to a switch to *syn*-selectivity [aldehydes + RMet + added Lewis acid, oxonium ions + allylSiMe$_3$ + Lewis acid].

## Experimental

General experimental details have been given before.[1]

### 1-Bromo-2-(bromomethyl)naphthalene 7

By the method of Smith *et al.*[29] a solution of 1-bromo-2-methylnaphthalene (9.720 g, 43.96 mmol), *N*-bromosuccinimide (8.398 g, 47.18 mmol), benzoyl peroxide (0.200 g, 0.83 mmol) and carbon tetrachloride (100 ml) was heated to reflux for 5.5 hours under an atmosphere of nitrogen, cooled, washed with saturated aqueous sodium hydrogen carbonate (3 × 50 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a yellow solid which was recrystallised from petrol to give *bromide* **7** (7.920 g, 60%) as yellow needles, mp 106–107 °C (lit.,[29] 103–105 °C).

### 1-Bromo-2-formylnaphthalene 8

By a modification of the method of Hass and Bender,[30] sodium (0.667 g, 0.029 mol) was carefully added to a flask charged with ethanol (30 ml). When the sodium had dissolved, 2-nitropropane (2.85 ml, 0.032 mol) was added. A white precipitate formed immediately. The mixture was treated with 1-bromo-2-(bromomethyl)naphthalene **7** (7.920 g, 0.026 mol) and heated to reflux for 6 h with occasional agitation of the reaction vessel. The mixture was allowed to cool to ambient temperature, treated with water (30 ml) and the ethanol was removed under reduced pressure. Ether (50 ml) was added and the solution was washed with aqueous 1 M sodium hydroxide (2 × 20 ml) and water (2 × 20 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product in quantitative yield. Recrystallisation from EtOAc gave the *aldehyde* **8** (3.877 g, 62%) as yellow needles, mp 115–117 °C (lit.,[29] 115–116 °C).

### 2-(1-Bromo-2-naphthyl)-1,3-dioxolane 9

By the method of Hartman *et al.*[32] a solution of 1-bromo-2-formylnaphthalene **8** (1.507 g, 6.41 mmol), ethylene glycol (0.50 ml, 8.98 mmol), toluene-*p*-sulfonic acid dihydrate (0.366 g, 1.92 mmol) in benzene (30 ml) was heated to reflux under a Dean–Stark condenser overnight. The mixture was cooled, diluted with ether (30 ml), washed with 10% aqueous sodium hydroxide (3 × 20 ml) and water (5 × 20 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the *dioxolane* **9** as a pale yellow oil (1.636 g, 91%) requiring no further purification, $\nu_{max}$(film)/cm$^{-1}$ 3065, 2953, 2886, 1788; $\delta_H$(300 MHz, $CDCl_3$) 8.44 (1H, *J* 8.4, ArH), 7.92–7.85 (2H, m, ArH), 7.75 (1H, d, *J* 8.5, ArH), 7.70–7.56 (2H, m, ArH), 6.48 (1H, s, C*H*$(OCH_2)_2$), 4.32–4.12 (4H, m, $CH_2CH_2$); $\delta_C$(75 MHz, $CDCl_3$) 134.9, 134.5, 132.1, 128.1, 127.9, 127.5, 127.1, 124.1, 123.9, 103.4, 103.4 and 65.6; *m*/*z* (CI) 279 (100%, M + H$^+$) and 281 (86%, M + H$^+$); *m*/*z* (EI) 278 (13%, M$^+$[$^{79}$Br]), 280 (13%, M$^+$[$^{81}$Br]), 73 (100%, $CH(OCH_2)_2$) and 199 (42%, M − $^{79}$Br) (Found: M$^+$, 277.9942. $C_{13}H_{11}O_2Br$ requires *M*, 277.9943).

### *N*,*N*-Dimethyl-2-(1,3-dioxolan-2-yl)-1-naphthamide 10

A solution of dioxolane **9** (1.314 g, 4.71 mmol) in ether (30 ml) was added dropwise to a solution of *tert*-butyllithium (6.09 ml, 10.36 mmol) in ether (50 ml) at −78 °C under an atmosphere of nitrogen to give an orange–brown solution. The mixture was stirred for an additional 35 minutes, by which time a precipitate had formed. *N*,*N*-Dimethylcarbamoyl chloride (0.96 ml, 10.36 mmol) was added. The mixture was stirred for 5 minutes, warmed to ambient temperature and stirred for a further 1 hour. Saturated aqueous sodium hydrogen carbonate (10 ml) was added and the solvent was removed under reduced pressure. The aqueous phase was extracted with dichloromethane (4 × 20 ml), and the combined organic extracts were washed with brine (50 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give *naphthamide* **10** as a brown oil which was used without further purification, $\nu_{max}$(film)/cm$^{-1}$ 2950, 2938, 2889, 1638; $\delta_H$(300 MHz, $CDCl_3$) 7.92 (1H, d, *J* 8.5, ArH), 7.88 (1H, m, ArH), 7.75 (1H, m, ArH), 7.71 (1H, d, *J* 8.5, ArH), 7.58–7.52 (2H, m, ArH), 6.00 (1H, s, C*H*$(OCH_2CH_2O)$), 4.30–3.90 (4H, m, $CH_2CH_2$), 3.30 (3H, s, $CH_3$), 2.78 (3H, s, $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.5, 134.0, 133.6, 131.3, 129.0, 128.8, 128.2, 127.1, 126.8, 124.9, 123.4, 101.7, 65.7, 65.4, 38.4 and 34.5; *m*/*z* (CI) 272 (100%, M + H$^+$); *m*/*z* (EI) 271 (3%, M$^+$) and 198 (100%, M − $C_3H_6O_2$) (Found: M + H$^+$, 272.1294. $C_{16}H_{17}NO_3$ requires *M* + H, 271.1208).

### *N*,*N*-Dimethyl-2-formyl-1-naphthamide 4a

Toluene-*p*-sulfonic acid dihydrate (215 mg, 1.03 mmol) was added to a solution of crude naphthamide **10** in acetone (50 ml) at ambient temperature. The mixture was stirred for 11 hours. Water (30 ml) was added and the acetone was removed under reduced pressure. The aqueous residue was extracted with ethyl acetate (4 × 20 ml) and the combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (2 × 30 ml), brine (30 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a yellow solid which was recrystallised from ethyl acetate to give the *aldehyde* **4a** (885 mg, 83%) as orange prisms, $\lambda_{max}$/nm ($\varepsilon_{max}$) ($CH_2Cl_2$) 254 (60320), 290 (10800), 340 (2475); mp 111–115 °C (EtOAc); $\nu_{max}$(film)/cm$^{-1}$ 3240, 1689, 1633; $\delta_H$(300 MHz, $CDCl_3$) 10.22 (1H, s, CHO), 8.00–7.85 (4H, m, ArH), 7.7–7.6 (2H, m, ArH), 3.37 (3H, s, $CH_3$), 2.79 (3H, s, $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 190.5, 168.3, 139.9, 136.1, 129.4, 129.3, 129.1, 129.0, 128.5, 128.0, 126.1, 123.3, 38.2 and 34.7; *m*/*z* (CI) 228 (100%, M + H$^+$); *m*/*z* (EI) 227 (6%, M$^+$), 198 (40%, M − CHO), 183 (43%, M − $CON(CH_3)_2$), 127 (100%) (Found: C, 73.9; H, 6.04; N, 6.10%. $C_{14}H_{13}NO_2$ requires C, 74.0; H, 5.7; N, 6.2%).

### *N*-(*tert*-Butyl)-*N*-methyl-2-formyl-1-naphthamide 4b

*sec*-Butyllithium (5.68 ml, 7.39 mmol; 1.3 M solution in hexanes) was added to a solution of naphthamide **3b**[28] (1.619 g, 6.72 mmol) in THF (50 ml) at −78 °C under an atmosphere of nitrogen. After 1 h, DMF (1.0 ml, 12.9 mmol) was added. The mixture was allowed to warm to ambient temperature, quenched with water (20 ml) and stirred overnight. The THF was removed under reduced pressure and the aqueous residue was diluted with ether (60 ml). The layers were separated and the ethereal layer was washed with water (4 × 30 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford the crude product mixture. Purification by flash chromatography on silica gel [10:1 petrol–EtOAc] afforded *the aldehyde* **4b** (602 mg, 33%) as a colourless oil which solidified on standing, mp 122–124 °C; $R_f$ 0.31 [2:1 petrol–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 2963, 2927, 2871, 2850, 1690, 1633; $\delta_H$(300 MHz, $CDCl_3$) 10.27 (1H, s, CHO), 8.00–7.88 (4H, m, ArH), 7.70–7.59 (2H, m, ArH), 2.74 (3H, s, $NCH_3$), 1.72 (9H, s, $C(CH_3)_3$); $\delta_C$(75 MHz, $CDCl_3$) 190.6, 168.5, 142.5, 136.3, 129.3, 128.8, 128.7, 128.4, 127.9, 125.8, 122.8, 58.0, 33.9 and 28.0; *m*/*z* (CI) 270 (100%, M + H$^+$); *m*/*z* (EI) 269 (2%, M$^+$), 212 (100%, M − *t*-Bu) and 183 (94%, M − N(*t*-Bu)Me) (Found: M + H$^+$, 270.1493. $C_{17}H_{19}NO_2$ requires *M* + H, 270.1494).

Also obtained was *N-(tert-butyl)-N-methyl-2-(1-methylpropyl)-1,2-dihydro-1-naphthamide* **5** (1.306 g, 65%) as a brown oil, which contained a mixture of diastereoisomers in a ratio of 56$^a$:23$^b$:10$^c$:7$^d$ (by $^1$H NMR), $R_f$ 0.31 [10:1 petrol–EtOAc];

$\nu_{max}$(film)/cm$^{-1}$ 3028, 2959, 2926, 2873, 1649; $\delta_H$(300 MHz, $CDCl_3$) 7.31–6.93 (4H, m, ArH), 6.58 (1H$^a$, d, *J* 10, C*H*=CHCH), 6.52 (1H$^c$, d, *J* 10, C*H*=CHCH), 6.51 (1H$^b$, d, *J* 10, C*H*=CHCH), 6.50 (1H$^d$, d, *J* 10, C*H*=CHCH), 6.04 (1H$^d$, dd, *J* 10 and 4, CH=C*H*CH), 5.97 (1H$^a$, dd, *J* 10 and 5, CH=C*H*CH), 5.93 (1H$^b$, dd, *J* 10 and 2.5, CH=C*H*CH), 4.42 (1H$^a$, d, *J* 7.5, C*H*CON(*t*-Bu)$CH_3$), 4.33 (1H$^c$, d, *J* 7.5, C*H*CON(*t*-Bu)$CH_3$), 4.12 (1H$^d$, d, *J* 11.5, C*H*CON(*t*-Bu)$CH_3$), 4.10 (1H$^b$, d, *J* 13, C*H*CON(*t*-Bu)$CH_3$), 3.14 (3H$^c$, s, $NCH_3$), 3.09 (3H$^a$, s, $NCH_3$), 3.02 (3H$^b$, s, $NCH_3$), 3.01 (3H$^d$, s, $NCH_3$), 2.70 (1H, m, CH=CHC*H*), 1.82 (1H, m, $CH_3CH_2CH(CH_3)$), 1.56 (9H$^b$, s, *t*-Bu), 1.54 (9H$^d$, s, *t*-Bu), 1.51 (9H$^a$, s, *t*-Bu), 1.45 (9H$^c$, s, *t*-Bu), 1.5–1.2 (2H$^{b,c,d}$, m, $CH_3CH_2$), 0.94 (3H$^a$, t, *J* 7.5, $CH_3CH_2$), 0.75 (3H$^a$, d, *J* 6.5, $CH_3CH_2CH(CH_3)$); $\delta_C$(75 MHz, $CDCl_3$) 172.6, 134.9, 133.9, 129.5, 128.2, 128.1, 127.5, 127.3, 127.1, 127.0, 126.8, 126.6, 126.3, 126.1, 125.9, 125.6, 57.2, 47.5, 45.8, 42.7, 41.7, 40.2, 36.4, 35.8, 32.3, 28.3, 28.2, 27.6, 27.6, 25.1, 15.4, 15.3, 12.1 and 11.9; *m*/*z* (CI) 300 (100%, M + H$^+$); *m*/*z* (EI) 299 (3%, M$^+$) and 57 (100%) (Found: M$^+$, 299.2248. $C_{20}H_{29}NO$ requires *M*, 299.2249).

### *N*,*N*-Diethyl-2-formyl-1-naphthamide 4c

A solution of *N*,*N*-diethyl-1-naphthamide **3c**[2] (3.189 g, 14.03 mmol) in THF (40 ml) was added to a stirred solution of *sec*-butyllithium (11.85 ml of a 1.3 M solution in cyclohexane, 15.44 mmol) in THF (80 ml) at −78 °C under an atmosphere of nitrogen. After 1 hour at −78 °C, the mixture was treated with a solution of DMF (5.24 ml) in THF (20 ml) and allowed to warm to ambient temperature. Water (50 ml) was added and most of the THF was removed under reduced pressure. The residue was extracted with dichloromethane (3 × 50 ml). The combined organic fractions were washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure at room temperature. Flash chromatography [4:1 petrol–EtOAc] afforded the *aldehyde* **4c** as a pale yellow solid (2.771 g, 78%), mp 65–66 °C; $R_f$ 0.23 [2:1 petrol–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 1697, 1630; $\delta_H$(200 MHz, $CDCl_3$) 10.21 (1H, s, CHO), 8.0–7.5 (6H, m, ArH), 3.77 (2H, q, *J* 7.5, $NCH_2$), 3.06 (2H, q, *J* 7.5, $NCH_2$), 1 43 (3H, t, *J* 7.5, $CH_3$), 0.95 (3H, t, *J* 7.5, $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 190.6 (CHO), 167.4 ($CONEt_2$), 140.8, 136.2, 129.5, 129.3, 129.1, 128.6, 127.9, 126.1, 122.8 (aromatics), 43.2 ($CH_2$), 39.3 ($CH_2$), 14.0 ($CH_3$) and 12.9 ($CH_3$); *m*/*z* (CI) 256 (100%, M + H$^+$); *m*/*z* (EI) 255 (4%, M$^+$) and 226 (100%, M − Et) (Found: M + H$^+$, 256.1332. $C_{16}H_{17}NO_2$ requires *M*, 256.1337).

### General procedure for reaction of aldehydes 4 with organolithium or Grignard reagents

A solution of the organolithium or Grignard reagent (0.98 mmol, 1.25 equiv.) was added dropwise to a stirred solution of the aldehyde **4** (0.784 mmol) in dry THF (5 ml) under nitrogen at −78 °C. After 3 hours, saturated aqueous ammonium chloride (5 ml) was added. The layers were separated and the aqueous layer extracted with diethyl ether (2 × 5 ml). The combined organic fractions were washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure without external heating. The crude product was stored in the freezer. Analytical HPLC [1:1–8:1 petrol or hexane–EtOAc] of the crude product gave the diastereoisomeric ratios shown in Table 2; flash chromatography gave the purified products in the yields shown in Table 2, and (where necessary) preparative HPLC afforded the pure separated diastereoisomers.

In this way, with MeLi (1.4 M in $Et_2O$) or with MeMgBr (3 M in $Et_2O$, aldehyde **4c** gave the alcohols **11c**,[2] aldehyde **4d**[28] gave the alcohols **11d**,[2] and the aldehyde **4e**[2] gave the alcohol *anti*-**11e**.[2]

In the same way, with BuLi (1.6 M in hexane), with BuMgCl (2.0 M in THF), or with BuMgBr (2.0 M in THF) aldehyde **4c** gave *(R$_a$*R*)-N,N-diethyl-2-(1′-hydroxypentyl)-1-naphthamide anti*-**12c** as a white solid, mp 85–88 °C; $R_f$ 0.32 [2:1 petrol–EtOAc]; $t_R$ 8.4 min [2:1 petrol–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3425 (OH), 1613 (C=O); $\delta_H$(300 MHz, $CDCl_3$) 8.0–7.4 (6H, m, ArH), 4.83 (1H, dd, *J* 7.5 and 7.5, C*H*(OH)), 3.77 (1H, m, *J* 7.5, $NCH_AH_B$), 3.73 (1H, m, $NCH_AH_B$), 3.14 (1H, m, $NCH_AH_B$), 3.12 (1H, m, $NCH_AH_B$), 2.8 (1H, br m, OH), 1.86 (2H, m, $CH(OH)CH_2$), 1.6–1.3 (4H, m, $CH_2CH_2$), 1.43 (3H, t, *J* 7.5, $NCH_2CH_3$), 0.96 (3H, t, *J* 7.5, $NCH_2CH_3$), 0.91 (3H, t, *J* 7.5, $CH_2CH_2CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.3 ($CONEt_2$), 138.0, 132.8, 131.8, 129.4, 129.0, 128.1, 126.9, 126.2, 125.0, 123.6 (aromatics), 72.4 (CHOH), 43.2, 39.0, 38.8, 28.1, 22.6, 14.1 (2 peaks) and 12.9 ($NEt_2$ and *n*-butyl); *m*/*z* (CI) 314 (100%, M + H$^+$) and 296 (30%, M − OH); *m*/*z* (EI) 313 (8%, M$^+$) (Found: M$^+$, 313.2040. $C_{20}H_{27}NO_2$ requires *M*, 313.2042).

Also obtained was *(R$_a$*S*)-N,N-diethyl-2-(1′-hydroxypentyl)-1-naphthamide syn*-**12c** as a colourless oil, $R_f$ 027 [2:1 petrol–EtOAc]; $t_R$ 13.3 min [2:1 petrol–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3417 (OH), 1613 (C=O); $\delta_H$(300 MHz, $CDCl_3$) 7.9–7.4 (6H, m, ArH), 4.79 (1H, dd, *J* 7.5 and 9.5, C*H*OH), 3.31 (1H, m, $NCH_AH_B$), 3.22 (1H, m, $NCH_AH_B$), 3.10 (2H, q, *J* 7.5, $NCH_2$), 2.05 (1H, m, $CH(OH)CH_AH_B$), 1.79 (1H, m, $CH(OH)CH_AH_B$), 1.5–1.3 (4H, m, $CH_2CH_2$), 1.42 (3H, t, *J* 7.5, $NCH_2CH_3$), 1.00 (3H, t, *J* 7.5, $NCH_2CH_3$), 0.95 (3H, t, *J* 7.5, $CH_2CH_2CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 170.0 ($CONEt_2$), 138.6, 132.7, 132.6, 129.2, 129.1, 128.3, 126.9, 126.2, 124.8, 123.8 (aromatics), 71.0 (CHOH), 43.2, 38.7, 35.8, 28.6, 22.7, 14.1, 13.8 and 12.8 ($NEt_2$ and *n*-butyl); *m*/*z* (CI) 314 (75%, M + H$^+$) and 296 (M − OH); *m*/*z* (EI) 313 (17%, M$^+$) (Found: M$^+$, 313.2038. $C_{20}H_{27}NO_2$ requires *M*, 313.2042).

Similarly, aldehyde **4d**[28] gave *(R$_a$*R*)-N,N-diisopropyl-2-(1′-hydroxypentyl)-1-naphthamide anti*-**12d** as a white solid, mp 117–119 °C, $R_f$ 0.47 [2:1 petrol–EtOAc]; $t_R$ 5.4 min [4:1 petrol–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3436 (OH), 1612 (C=O); $\delta_H$(200 MHz, $CDCl_3$) 7.9–7.4 (6H, m, ArH), 4.91 (1H, t, *J* 7.5, C*H*OH), 3.65 (1H, septet, *J* 7.5, NCH), 3.63 (1H, septet, *J* 7.5, NCH), 2.21 (1H, br s, OH), 1.88 (2H, m, $CH(OH)CH_2$), 1.82 (3H, d, *J* 7.5, $NCHCH_3$), 1.73 (3H, d, *J* 7.5, $NCHCH_3$), 1.51–1.38 (4H, m, $CH_2CH_2$), 1.17 (3H, d, *J* 7.5, $NCHCH_3$), 1.03 (3H, d, *J* 7.5, $NCHCH_3$), 0.93 (3H, t, *J* 7.5, $CH_2CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.0 ($CON^iPr_2$), 137.4, 133.1, 132.9, 129.4, 128.6, 128.1, 126.7, 126.2, 125.2, 123.4 (aromatics), 72.0 (CHOH), 51.1 (NCH), 46.2 (NCH), 38.9, 28.1, 22.5, 20.9, 20.7, 20.6, 20.4 and 14.0 (4 × $CH_3$ and *n*-butyl); *m*/*z* (CI) 342 (100%, M + H$^+$) and 324 (M − OH); *m*/*z* (EI) 341 (18%, M$^+$) (Found: M$^+$, 341.2357. $C_{22}H_{31}NO_2$ requires *M*, 341.2355).

Also obtained was *(R$_a$*S*)-N,N-diisopropyl-2-(1′-hydroxypentyl)-1-naphthamide syn*-**12d** as a white solid, mp 99–102 °C; $R_f$ 0.39 [2:1 petrol–EtOAc]; $t_R$ 7.5 min [4:1 petrol–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3418 (OH), 1611 (C=O); $\delta_H$(300 MHz, $CDCl_3$) 7.9–7.4 (6H, m, ArH), 4.85 (1H, dd, *J* 9 and 6, C*H*OH), 3.68 (1H, septet, *J* 7, NCH), 3.61 (1H, septet, *J* 7, NCH), 2.12 (1H, m, $CH(OH)CH_AH_B$), 1.9–1.7 (2H, m, $CH(OH)CH_AH_BCH_CH_D$), 1.81 (3H, d, *J* 7.5, $NCHCH_3$), 1.75 (3H, d, *J* 7.5, $NCHCH_3$), 1.46 (3H, m, $CH_CH_DCH_2$), 1.11 (6H, d, *J* 7.5, $NCH(CH_3)_2$), 0.98 (3H, t, *J* 7, $CH_2CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 170.2 ($CON^iPr_2$), 137.8, 134.2, 132.8, 129.2, 128.8, 128.2, 126.7, 126.3, 124.9, 123.7 (aromatics), 71.0 (CHOH), 51.4, 46.4, 35.0, 28.9, 22.8, 20.9, 20.6, 20.5 and 14.1 (4 × $CH_3$ and *n*-butyl); *m*/*z* (CI) 342 (9%, M + H$^+$) and 324 (M − OH); *m*/*z* (EI) 341 (15%, M$^+$) (Found: M$^+$, 341.2355. $C_{22}H_{31}NO_2$ requires *M*, 341.2355).

Similarly, the aldehyde **4e**[2] gave *(R$_a$*,1′S*)-N,N-di(4-heptyl)-2-(1′-hydroxypentyl)-1-naphthamide anti*-**12e** as an oil, $R_f$ 0.73 [2:1 petrol–EtOAc]; $t_R$ 8.3 min [6:1 hexane–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3384, 2958, 2932, 2871, 1605; $\delta_H$(300 MHz, $CDCl_3$) 7.9–7.4 (6H, m, ArH), 4.98 (1H, dd, *J* 4 and 9, C*H*OH), 3.03 (2H, quintet, *J* 6.5, 2 × NCH), 2.5–0.6 (22H, m, CH(OH)-$CH_2CH_2CH_2CH_3$ and 2 × $NCH(CH_2CH_2CH_3)_2$), 1.05 (3H, t, *J* 7.5, $CH_3$), 1.01 (3H, t, *J* 7.5, $CH_3$), 0.91 (3H, t, *J* 7.0, $CH_3$),

0.75 (3H, t, *J* 7.5, $CH_3$), 0.36 (3H, t, *J* 7.5, $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.4, 138.4, 132.6, 132.1, 129.3, 128.5, 127.9, 126.1, 125.9, 125.6, 123.1, 71.8, 59.9, 56.8, 39.3, 36.9, 36.7, 35.8, 28.0, 22.3, 21.7, 20.3, 20.2, 14.4, 14.0, 14.0 and 13.2; *m*/*z* (CI) 454 (100%, M + $H^+$) and 436 (17%, M − OH); *m*/*z* (EI) 453 (3%, $M^+$) and 84 (100%) (Found: $M^+$, 453.3596. $C_{30}H_{47}NO_2$ requires *M*, 453.3607).

Also obtained was *(*$R_a$**,1′*R**)-N,N-di(4-heptyl)-2-(1′-hydroxypentyl)-1-naphthamide syn*-**12e** as a colourless oil, $R_f$ 0.69 [2:1 petrol–EtOAc]; $t_R$ 21.7 min [6:1 hexane–EtOAc]; $\nu_{max}$(film)/$cm^{-1}$ 3408, 2958, 2932, 2871, 1605; $\delta_H$(300 MHz, $CDCl_3$) 7.9–7.4 (6H, m, ArH), 4.88 (1H, dd, *J* 3.5 and 9.5, C*H*OH), 3.05 (2H, m, 2 × NCH), 2.35 (2H, m, NCHC$H_2$-$CH_2CH_3$), 2.11 (2H, m, CH(OH)C$H_AH_B$$CH_2$ and NCHC$H_A$-$H_BCH_2CH_3$), 1.94 (1H, m, NCHCC$H_AH_B$$CH_2CH_3$), 1.79 (1H, m, CH(OH)C$H_AH_B$$CH_2CH_2CH_3$), 1.73–0.53 (16H, m, CH-(OH)$CH_2CH_2CH_2CH_3$, 2 × NCHC$H_2CH_2CH_3$, 4 × NCHCH$_2$-C$H_2CH_3$), 1.05 (3H, t, *J* 7.5, $CH_3$), 1.01 (3H, t, *J* 7.5, $CH_3$), 0.97 (3H, t, *J* 7.5, $CH_3$), 0.65 (3H, t, *J* 7, $CH_3$), 0.50 (3H, t, *J* 7, $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 171.0, 138.6, 134.1, 132.4, 129.3, 128.9, 128.1, 126.3, 126.1, 125.0, 123.3, 70.7, 60.4, 57.2, 36.9, 36.8, 36.4, 35.4, 33.5, 28.9, 22.8, 21.7, 20.4, 20.3, 14.4, 14.1, 13.7 and 13.5; *m*/*z* (CI) 454 (14%, M + $H^+$), 438 (100%, M − $CH_3$) and 436 (51%, M − OH) (Found: $M^+$, 453.3596. $C_{30}H_{47}NO_2$ requires *M*, 453.3607).

Also obtained was *N,N-di(4-heptyl)-2-(hydroxymethyl)-1-naphthamide* **16** as a colourless oil, $R_f$ 0.53 [2:1 petrol–EtOAc]; $t_R$ 2.9 min [6:1 hexane–EtOAc]; $\nu_{max}$(film)/$cm^{-1}$ 3412, 2959, 2932, 2871, 1603; $\delta_H$(300 MHz, $CDCl_3$) 7.88–7.78 (3H, m, ArH), 7.57–7.45 (3H, m, ArH), 4.91 (1H, d, *J* 12, C$H_AH_B$OH), 4.54 (1H, d, *J* 12, $CH_AH_B$OH), 3.10–2.92 (2H, m, 2 × NCH), 2.09 (1H, m, NCHC$H_AH_B$$CH_2CH_3$), 1.90 (1H, m, NCHC$H_AH_B$-$CH_2CH_3$), 1.64–0.80 (13H, m, 3 × NCHC$H_2CH_2CH_3$, 3 × NCHCH$_2$C$H_2CH_3$ and NCHCH$_2$C$H_AH_BCH_3$), 1.06 (3H, t, *J* 7, NCHC$H_2CH_2CH_3$), 1.01 (3H, t, *J* 7.5, NCHCH$_2$$CH_2CH_3$), 0.92 (1H, m, NCHCH$_2$$CH_AH_BCH_3$), 0.64 (3H, t, *J* 7, NCH-$CH_2CH_2CH_3$), 0.43 (3H, t, *J* 7, NCHCH$_2$$CH_2CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 170.6, 135.4, 133.8, 132.5, 129.3, 128.9, 128.1, 127.1, 126.3, 126.2, 125.0, 63.9, 60.1, 57.0, 37.0, 36.8, 36.2, 34.9, 21.7, 20.2, 20.0, 14.4, 13.7 and 13.3; *m*/*z* (CI) 398 (20%, M + $H^+$) and 382 (100%, M − $CH_3$); *m*/*z* (EI) 397 (1%, $M^+$), 86 (100%), 84 (100%) and 49 (100%) (Found: M + $H^+$, 398.3055. $C_{26}H_{39}NO_2$ requires *M* + H, 398.3059).

Also obtained was remaining starting material **4e** (30%).

In the same way, with octynyllithium, prepared from oct-1-yne (0.15 ml, 0.98 mmol, 1.3 equiv.) in THF (0.5 ml) and *n*-BuLi (0.57 ml of a 1.6 M solution in hexanes, 0.91 mmol, 1.2 equiv.) at −78 °C stirred together for 30 min and added to the solution of the aldehyde by a cannula, aldehyde **4d**[2] gave *(*$R_a$**,1′*R**)-N,N-diisopropyl-2-(1′-hydroxynon-2′-ynyl)-1-naphthamide anti*-**13d** as a colourless oil, $R_f$ 0.51 [2:1 petrol–EtOAc]; $t_R$ 5.1 min [4:1 hexane–EtOAc]; $\nu_{max}$/$cm^{-1}$ 3388, 3057, 2959, 2931, 2870, 2858, 1612; $\delta_H$(300 MHz, $CDCl_3$) 7.84 (3H, m, ArH), 7.77 (1H, d, *J* 8.5, ArH), 7.50 (2H, m, ArH), 5.64 (1H, m, OH), 3.57 (2H, m, 2 × NCH), 2.87 (1H, d, *J* 5, C*H*OH), 2.23 (2H, td, *J* 7.0 and 1.9, C≡CC$H_2$$(CH_2)_4CH_3$), 1.77 (3H, d, *J* 7, NCHC$H_3$), 1.69 (3H, d, *J* 7, NCHC$H_3$), 1.51 (2H, m, $CH_2CH_2$$(CH_2)_3CH_3$), 1.43–1.19 (6H, m, $(CH_2)_3CH_3$), 1.12 (3H, d, *J* 6.5, NCHC$H_3$), 0.98 (3H, d, *J* 6.5, NCHC$H_3$), 0.89 (3H, t, *J* 6.5, $(CH_2)_5CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 168.8, 134.2, 133.6, 133.0, 129.4, 128.6, 128.0, 126.6, 126.4, 125.3, 125.0, 87.9, 80.3, 62.8, 51.2, 46.2, 31.2, 28.5, 28.4, 22.4, 20.7, 20.4, 20.4, 20.3, 18.9 and 13.9; *m*/*z* (CI) 394 (27%, M + $H^+$), 376 (100%, M − OH) and 284 (87%, M − C≡C$(CH_2)_5CH_3$) (Found: $M^+$, 393.2673. $C_{26}H_{35}$-$NO_2$ requires *M*, 393.2668).

Also obtained was *(*$R_a$**,1′*S**)-N,N-diisopropyl-2-(1′-hydroxynon-2′-ynyl)-1-naphthamide syn*-**13d** as a white solid, mp 90–92 °C; $R_f$ 0.39 [2:1 petrol–EtOAc]; $t_R$ 12.1 min [4:1 hexane–EtOAc]; $\lambda_{max}$/nm ($\varepsilon_{max}$) ($CH_2Cl_2$) 234 (66630), 282 (7965); $\nu_{max}$/$cm^{-1}$ 3312, 2960, 2931, 2870, 2858, 1608; $\delta_H$(300 MHz, $CDCl_3$) 7.89 (1H, d, *J* 8.7, ArH), 7.8 (3H, m, ArH), 7.51 (2H, m, ArH), 5.65 (1H, d, *J* 1.5, C*H*OH), 4.07 (1H, d, *J* 1.5, OH), 3.64 (1H, septet, *J* 6.5, NCH), 3.54 (1H, septet, *J* 6.5, NCH), 2.29 (2H, td, *J* 7.0 and 1.9, CCC$H_2$$(CH_2)_4CH_3$), 1.78 (3H, d, *J* 7, $CH_3$), 1.69 (3H, d, *J* 7, $CH_3$), 1.55 (2H, m, $CH_2CH_2$$(CH_2)_3CH_3$), 1.48–1.22 (6H, m, $CH_2CH_2(CH_2)_3CH_3$), 1.10 (3H, d, *J* 6.5, $CH_3$), 1.04 (3H, d, *J* 6.5, $CH_3$), 0.89 (3H, t, *J* 7.0, $(CH_2)_5CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.4, 135.3, 133.2, 132.9, 128.8, 128.7, 128.2, 126.7, 126.4, 125.0, 124.8, 87.8, 79.0, 62.3, 51.4, 46.4, 31.2, 28.5, 28.4, 22.4, 20.8, 20.5, 20.5, 20.4, 18.8 and 13.9; *m*/*z* (CI) 394 (13%, M + $H^+$), 276 (100%, M − OH) and 284 (64%, M − CC$(CH_2)_5CH_3$) (Found: $M^+$, 393.2662. $C_{26}H_{35}NO_2$ requires *M*, 393.2668).

In the same way, with PhLi (1.8 M in hexane–ether) or with PhMgBr (1.0 M in THF), aldehyde **4c** gave the alcohols **14c**,[2] the aldehyde **4d**[28] gave the alcohols **14d**[2] and the aldehyde **4e**[2] gave the alcohol *syn*-**14e**.[2]

In the same way, with allylMgBr (1.0 M in THF) the aldehyde **4c** gave *(*$R_a$**R*)-N,N-diethyl-2-(1′-hydroxybut-3′-enyl)-1-naphthamide anti*-**15c** as a white solid, mp 107–110 °C; $R_f$ 0.55 (EtOAc); $t_R$ 5.9 min [2:1 petrol–EtOAc]; $\nu_{max}$(film)/$cm^{-1}$ 3402 (OH), 1611 (C=O); $\delta_H$(300 MHz, $CDCl_3$) 7.8–7.4 (6H, m, ArH), 5.80 (1H, m, $CH_2$C*H*=$CH_2$), 5.14 (1H, d, *J* 17.5, $CH_2CH$=C$H^{trans}$H), 5.12 (1H, d, *J* 10, $CH_2CH$=C$HH^{cis}$), 4.74 (1H, t, *J* 3.5, C*H*OH), 3.63 (2H, $ABX_3$, $J_{AX} = J_{BX} = 7$, $NCH_2$), 3.00 (2H, m, $NCH_2$), 2.62 (1H, m, C$H_AH_B$CH=$CH_2$), 2.47 (1H, br s, OH), 2.37 (1H, m, $CH_AH_B$CH=$CH_2$), 1.31 (3H, t, *J* 7, $CH_3$), 0.86 (3H, t, *J* 7, $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 164.6 ($CONEt_2$), 132.5, 130.1, 128.3, 127.3, 124.8, 124.4, 123.7, 122.5, 121.7, 120.4, 119.0, 114.5 (Ar and C=C), 66.1 (CHOH), 39.4, 38.7, 34.5 ($CH_2$), 9.5 ($CH_3$) and 8.4 ($CH_3$); *m*/*z* (CI) 298 (37%, M + $H^+$) and 280 (M − OH); *m*/*z* (EI) 297 (1%, $M^+$) (Found: $M^+$, 297.1735. $C_{22}H_{27}NO_2$ requires *M*, 297.1729).

Also obtained was *(*$R_a$**S*)-N,N-diethyl-2-(1′-hydroxybut-3′-enyl)-1-naphthamide syn*-**15c** as a colourless oil, $R_f$ 0.54 [EtOAc]; $t_R$ 12.3 min [2:1 petrol–EtOAc]; $\nu_{max}$(film)/$cm^{-1}$ 3407 (OH), 1610 (C=O); $\delta_H$(300 MHz, $CDCl_3$) 7.9–7.4 (6H, m, ArH), 5.88 (1H, ddt, *J* 17.5, 11 and 7, $CH_2$C*H*=$CH_2$), 5.17 (1H, dd, *J* 17.5 and 2, $CH_2CH$=C$H^{trans}$H), 5.09 (1H, d, *J* 10, $CH_2CH$=$CHH^{cis}$), 4.87 (1H, t, *J* 5.5, C*H*OH), 3.80 (1H, m, NC$H_AH_B$-$CH_3$), 3.71 (1H, m, $NCH_AH_BCH_3$), 3.65 (1H, br s, OH), 3.09 (2H, m, $NCH_2$), 2.78 (1H, m, C$H_AH_B$CH=$CH_2$), 2.60 (1H, m, $CH_AH_B$CH=$CH_2$), 1.40 (3H, t, *J* 7, $CH_2CH_3$), 0.98 (3H, t, *J* 7, $CH_2CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.9 ($CONEt_2$), 137.7, 134.8, 132.7, 129.2, 129.1, 128.3, 126.9, 126.3, 124.8, 123.8, 117.5 (Ar and C=C), 70.8 (CHOH), 43.3, 40.6, 38.6 ($CH_2$), 13.8 ($CH_3$) and 12.8 ($CH_3$); *m*/*z* (CI) 298 (64%, M + $H^+$), 256 (M − $C_3H_5$) and 280 (M − OH); *m*/*z* (EI) 297 (3%, $M^+$) (Found: $M^+$, 297.1735. $C_{22}H_{27}NO_2$ requires *M*, 297.1729).

Similarly, the aldehyde **4d**[28] gave the *alcohol (*$R_a$**R*)-N,N-diisopropyl-2-(1′-hydroxybut-3′-enyl)-1-naphthamide anti*-**15d** as a white solid, mp 135–139 °C; $R_f$ 0.53 [1:1 petrol–EtOAc]; $t_R$ 3.7 min [2:1 petrol–EtOAc]; $\nu_{max}$(film)/$cm^{-1}$ 3421 (OH), 1611 (C=O); $\delta_H$(300 MHz, $CDCl_3$) 7.9–7.4 (6H, m, ArH), 5.91 (1H, m, $CH_2$C*H*=$CH_2$), 5.27 (1H, d, *J* 17, $CH_2CH$=C$H^{trans}$H), 5.23 (1H, d, *J* 9.5, $CH_2CH$=$CHH^{cis}$), 4.95 (1H, dd, *J* 3.5 and 3, C*H*OH), 3.62 (2H, septet, *J* 6.5, 2 × NCH), 2.75 (1H, m, C$H_AH_B$CH=$CH_2$), 2.46 (2H, m, OH and $CH_AH_B$CH=$CH_2$), 1.79 (3H, d, *J* 6.5, $CH_3$), 1.70 (3H, d, *J* 6.5, $CH_3$), 1.13 (3H, d, *J* 6.5, $CH_3$), 1.03 (3H, d, *J* 6.5, $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 164.4 ($CONiPr_2$), 131.9, 130.3, 128.6, 128.4, 124.8, 124.0, 123.6, 122.2, 121.7, 120.5 (Ar), 118.9, 114.4 (C=C), 66.0 (CHOH), 46.7 ($CH_2$), 41.6 (NCH), 39.5 (NCH), 16.5 ($CH_3$), 16.2 ($CH_3$), 16.1 ($CH_3$) and 15.9 ($CH_3$); *m*/*z* (CI) 326 (33%, M + $H^+$), 284 (M − $C_3H_5$) and 280 (M − OH); *m*/*z* (EI) 325 (2%, $M^+$) (Found: $M^+$, 325.2043. $C_{22}H_{27}NO_2$ requires *M*, 325.2042).

Also obtained was the alcohol *(*$R_a$**S*)-N,N-diisopropyl-2-(1′-hydroxybut-3′-enyl)-1-naphthamide syn*-**15d** as a colourless oil, $R_f$ 0.47 [1:1 petrol–EtOAc]; $t_R$ 6.4 min [2:1 petrol–EtOAc];

$\nu_{max}$(film)/cm$^{-1}$ 3398 (OH), 1608 (C=O); $\delta_H$(300 MHz, $CDCl_3$) 7.9–7.4 (6H, m, ArH), 5.97 (1H, ddt, *J* 17, 10 and 7, $CH_2CH$=$CH_2$), 5.23 (1H, dd, *J* 17 and 1.5, $CH_2CH$=C$H^{trans}$H), 5.14 (1H, d, *J* 10, $CH_2CH$=C$HH^{cis}$), 4.93 (1H, t, *J* 5, C*H*OH), 3.76 (1H, br s, OH), 3.63 (2H, m, 2 × NCH), 2.88 (1H, m, C$H_A$$H_B$CH=$CH_2$), 2.62 (1H, m, $CH_A$$H_B$CH=$CH_2$), 1.79 (3H, d, *J* 7, $CH_3$), 1.66 (3H, d, *J* 7, $CH_3$), 1.09 (6H, m, 2 × $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 165.6 (CON*i*$Pr_2$), 132.5, 130.5, 129.7, 128.4, 124.7, 124.3, 123.7, 122.3, 121.9, 120.4 (Ar), 119.3, 112.9 (C=C), 66.1 (CHOH), 46.9 ($CH_2$), 42.0 (NCH), 35.4 (NCH), 16.4 ($CH_3$), 16.1 ($CH_3$), 16.1 ($CH_3$) and 16.0 ($CH_3$); *m*/*z* (CI) 326 (64%, M + $H^+$), 284 (M − $C_3H_5$) and 280 (M − OH); *m*/*z* (EI) 325 (7%, $M^+$) (Found: $M^+$, 325.2042. $C_{22}H_{27}NO_2$ requires *M*, 325.2042).

### General procedure for addition of organolithium or Grignard reagents in the presence of hexamethylphosphoramide or boron trifluoride–diethyl ether

Hexamethylphosphoramide (0.55 ml, 3.136 mmol) or boron trifluoride–diethyl ether (0.10 ml, 0.784 mmol) was added dropwise to a stirred solution of the aldehyde **4** (200 mg, 0.784 mmol) and in dry THF (5 ml) under nitrogen at −78 °C. After 40 minutes at −78 °C, a solution of organolithium or Grignard reagent (0.94 mmol) was added dropwise. After 3 hours at −78 °C, saturated aqueous ammonium chloride (5 ml) was added and the products were analysed and purified as described above.

### General procedure for addition of Grignard reagents in the presence of magnesium dibromide–diethyl ether or zinc dibromide

Magnesium bromide–diethyl ether (203 mg, 0.784 mmol) or zinc dibromide (177 mg, 0.784 mmol) was added to a stirred solution of the aldehyde **4** (0.784 mmol) in dry dichloromethane (5 ml) under nitrogen at −78 °C. After 40 minutes at −78 °C, *n*-butylmagnesium chloride (0.43 ml of a 2.0 M solution in THF, 0.861 mmol) was added dropwise. After 3 hours at −78 °C, saturated aqueous ammonium chloride (5 ml) was added and the products were analysed and purified as described above.

### Additions of organolithiums to aldehyde 4d in the presence of trimethylaluminium or DIBAL-H

Trimethylaluminium (20 µl of a 2 M solution in hexane) was added to a stirred solution of the *n*-butyllithium (0.34 ml of a 1.6 M solution in hexane) in THF (50 ml) under nitrogen at −78 °C. The aldehyde **4d** (112 mg, 0.4 mmol) was added immediately and the mixture stirred for 1 hour at −78 °C, 2.5 hours at 0 °C, and 1 h at room temperature, poured into 1 M HCl and extracted with dichloromethane (2 × 60 ml). The extracts were washed with sodium bicarbonate solution and with brine, dried ($MgSO_4$) and evaporated under reduced pressure. Analytical HPLC of the crude mixture showed a ratio of 93.8 : 6.2 of *anti*-**12d** : *syn*-**12d**. Purification by flash chromatography [4 : 1 petrol–EtOAc] gave the alcohols **12d** (73 mg, 56%).

In a similar way, oct-1-ynyllithium (prepared as above from *n*-butyllithium (0.26 ml of a 1.6 M solution in hexane) and oct-1-yne (70 µl, 0.5 mmol) and trimethylaluminium (17 µl of a 2 M solution in hexane) gave a crude product containing (by analytical HPLC) a mixture of 93 : 7 *anti*-**13d** : *syn*-**13d**. Purification by flash chromatography [4 : 1 petrol–EtOAc] gave the alcohol (75 mg, 66%) as a colourless oil.

In a similar way, oct-1-ynyllithium (prepared as above from *n*-butyllithium (1 ml of a 1.6 M solution in hexane) and oct-1-yne (0.23 ml, 1.6 mmol) and diisobutylaluminium hydride (1.6 ml of a 1 M solution in hexane) gave a crude product containing (by analytical HPLC) a mixture of >99 : 1 *anti*-**13d** : *syn*-**13d**. Purification by flash chromatography [4 : 1 petrol–EtOAc] gave the alcohol (75 mg, 50%) as a colourless oil.

### General procedure for the addition of alkyltitanium triisopropoxides

Chlorotitanium triisopropoxide (0.41 ml, 0.41 mmol; 1 M solution in dichloromethane) was added to a solution of alkyllithium or Grignard reagent (0.37 mmol) in THF (2.4 ml) at −78 °C under an atmosphere of nitrogen. The mixture was allowed to warm to 0 °C, treated with a solution of aldehyde **4** (0.27 mmol) in THF (1.7 ml) and stirred for a further 4 hours. The mixture was poured into ice-cold aqueous 2 M hydrochloric acid (15 ml) and diethyl ether (30 ml). Most of the solvent was removed under reduced pressure without external heating, and the aqueous residue was extracted with dichloromethane (5 × 20 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure without external heating to give the crude product. Analytical HPLC [2 : 1 hexane–EtOAc] gave the diastereoisomeric ratios (see Table 2), and the crude product was purified by flash chromatography on silica gel [2 : 1 petrol–EtOAc] to give the product alcohols in the yields shown in Table 2.

In this way, with methyllithium (1.4 M solution in ether) the aldehyde **4c** gave alcohols **11c**; aldehyde **4d** gave alcohols **11d** and aldehyde **4e** gave alcohols **11e**.

Similarly, with *n*-butyllithium (0.44 ml, 0.70 mmol; 1.6 M solution in ether), aldehyde **4c** gave alcohols **12c** and aldehyde **4d** gave alcohols **12d**.

Similarly, with oct-1-ynyllithium, prepared as described above, aldehyde **4d** gave the alcohols **13d** and aldehyde **4c** gave *(R$_a$*,1′R*)-N,N-diethyl-2-(1′-hydroxynon-2′-ynyl)-1-naphthamide anti*-**13c** as a pale yellow oil, $R_f$ 0.23 [2 : 1 petrol–EtOAc]; $t_R$ 5.2 [2 : 1 hexane–EtOAc]; $\nu_{max}$/cm$^{-1}$ 3378, 3057, 2954, 2932, 2869, 2858, 1612; $\delta_H$(300 MHz, $CDCl_3$) 7.78 (2H, m, ArH), 7.70 (1H, m, ArH), 7.62 (1H, d, *J* 8.5, ArH), 7.43 (2H, m, ArH), 5.49 (1H, br m, C*H*OH), 3.80–3.55 (2H, m, $CH_2CH_3$), 3.35 (1H, br m, OH), 3.02 (2H, m, $CH_2CH_3$), 2.14 (2H, td, *J* 6 and 1.5, C≡$CCH_2$), 1.44 (2H, m, $CH_2CH_2(CH_2)_3CH_3$), 1.34 (3H, t, *J* 7, $NCH_2CH_3$), 1.3–1.15 (6H, m, $CH_2CH_2(CH_2)_3CH_3$), 0.90 (3H, t, *J* 7, $NCH_2CH_3$), 0.80 (3H, t, *J* 7, $(CH_2)_5CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.5, 135.2, 132.9, 132.6, 129.5, 129.1, 128.1, 126.9, 126.5, 125.5, 125.0, 87.6, 79.9, 63.8, 43.6, 39.0, 31.2, 28.5, 28.4, 22.4, 19.0, 14.0, 13.4 and 12.8; *m*/*z* (CI) 366 (1%, M + $H^+$), 348 (18%, M − OH), 256 (2%, M − C≡$C(CH_2)_5CH_3$) and 74 (100%) (Found: M + $H^+$, 366.2435. $C_{24}H_{31}NO_2$ requires *M* + H, 366.2433).

Also obtained was *(R$_a$*,1′S*)-N,N-diethyl-2-(1′-hydroxynon-2′-ynyl)-1-naphthamide syn*-**13c** as a pale yellow oil, $R_f$ 0.12 [2 : 1 petrol–EtOAc]; $t_R$ 9.1 [2 : 1 hexane–EtOAc]; $\nu_{max}$/cm$^{-1}$ 3426, 3058, 2955, 2931, 2870, 2858, 1610; $\delta_H$(300 MHz, $CDCl_3$) 7.89 (1H, d, *J* 8.5, ArH), 7.82 (1H, d, *J* 8.5, ArH), 7.78 (1H, m, ArH), 7.62 (1H, m, ArH), 7.43 (2H, m, ArH), 5.53 (1H, t, *J* 2, C*H*OH), 3.75 (1H, m, $NCH_AH_BCH_3$), 3.60 (1H, m, $NCH_A$-$H_BCH_3$), 3.03 (1H, q, *J* 7, $CH_AH_BCH_3$), 3.02 (1H, q, *J* 7.2, $NCH_AH_BCH_3$), 2.22 (2H, dt, *J* 7 and 2, C≡$CCH_2$), 1.46 (2H, m, $CH_2CH_2(CH_2)_3CH_3$), 1.34 (3H, t, *J* 7, $NCH_2CH_3$), 1.35–1.15 (6H, m, $CH_2CH_2(CH_2)_3CH_3$), 0.91 (3H, t, *J* 7, $NCH_2CH_3$), 0.81 (3H, t, *J* 7, $(CH_2)_5CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.5, 135.9, 133.0, 132.2, 129.3, 128.9, 128.3, 127.1, 126.5, 124.8, 124.6, 88.0, 78.6, 62.7, 43.3, 39.2, 31.2, 28.5, 28.4, 22.5, 18.8, 14.0, 13.9 and 12.9; *m*/*z* (CI) 348 (9%, M − OH), 256 (2%, M − C≡$C(CH_2)_5CH_3$) and 74 (100%).

Also obtained was recovered aldehyde **4c** (42 mg, 23%).

Similarly, with phenyllithium (1.8 M solution in cyclohexane–ether), aldehyde **4c** gave alcohols **14c**; aldehyde **4d** gave alcohols **14d** and aldehyde **4e** gave alcohols **14e**.

Similarly, with allylmagnesium bromide (1 M solution in ether), aldehyde **4c** gave alcohol **15c** and aldehyde **4d** gave alcohols **15d**.

### Additions of methyltitanium trichloride

Titanium tetrachloride (1.13 ml, 1.13 mmol; 1 M solution in

dichloromethane) was added to a stirred solution of methylmagnesium bromide (0.43 ml, 1.13 mmol; 3 M solution in diethyl ether) or methyllithium (0.81 ml, 1.13 mmol, 1.4 M solution in diethyl ether) in THF (7.3 ml) at −78 °C under an atmosphere of nitrogen. After 10 minutes, a solution of aldehyde **4** (240 mg, 0.64 mmol) in THF (5.9 ml) was added. The mixture was allowed to warm to 0 °C and stirred for a further 2 hours. The mixture was poured into ice-cool aqueous 2 M hydrochloric acid (15 ml) and diethyl ether (30 ml). Most of the solvent was removed under reduced pressure without external heating, and the aqueous residue was extracted with dichloromethane (5 × 20 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure without external heating to give the crude product. Analytical HPLC [2:1 hexane–EtOAc] gave the diastereoisomeric ratio (see Table 2), and the crude product was purified by flash chromatography on silica gel [2:1 petrol–EtOAc] to give the product alcohols in the yield shown in Table 2.

In this way, the aldehyde **4c** and MeMgBr gave the alcohols **11c** along with *(Ra*)-N,N-diethyl-2-((1R*,2R*)-2-{1-[(Ra*)-(diethylamino)carbonyl]-2-naphthyl}-1,2-dihydroxyethyl)-1-naphthamide* **17** (R = Et) (59 mg, 12%) as a colourless oil, $R_f$ 0.17 [1:1 petrol–EtOAc]; $\nu_{max}$/cm$^{-1}$ 3272, 3058, 2974, 2936, 2899, 2855, 2816, 2765, 1601; $\delta_H$(300 MHz, $CDCl_3$) 7.76 (2H, m, ArH), 7.65 (2H, m, ArH), 7.51 (2H, d, *J* 8.5, ArH), 7.45 (4H, m, ArH), 6.85 (2H, d, *J* 8.5, ArH), 6.01 (2H, s, C*H*OH), 5.21 (2H, s, CHO*H*), 3.92 (2H, m, 2 × NC$H_AH_B$CH$_3$), 3.53 (2H, m, 2 × NCH$_A$$H_B$CH$_3$), 2.95 (4H, q, *J* 7.5, 2 × NC$H_2$CH$_3$), 1.39 (6H, t, *J* 7, 2 × CH$_2$C$H_3$), 0.90 (6H, t, *J* 7, 2 × CH$_2$C$H_3$); $\delta_C$(75 MHz, $CDCl_3$) 171.6, 135.1, 132.7, 132.2, 128.3, 127.6, 126.8, 126.6, 126.2, 124.3, 74.1, 45.5, 43.7, 39.7, 14.0 and 13.0; *m/z* (CI) 513 (4%, M + H$^+$), 256 (4%, M − $C_{16}H_{18}NO_2$) and 74 (100%) (Found: M + H$^+$, 513.2754. $C_{32}H_{36}N_2O_4$ requires *M* + H, 513.2753).

With MeLi, only **17** (R = Et) was obtained.

In the same way, the aldehyde **4d** and MeMgBr gave the alcohols **11d** along with *(Ra*)-N,N-diisopropyl-2-((1R*,2R*)-2-{1-[(Ra*)-(diisopropylamino)carbonyl]-2-naphthyl}-1,2-dihydroxyethyl)-1-naphthamide* **17** (R = *i*-Pr) (30 mg, 13%) as a colourless oil, $\nu_{max}$/cm$^{-1}$ 3408, 3060, 3014, 2977, 2930, 2873, 2855; $\delta_H$(300 MHz, $CDCl_3$) 7.80–7.60 (4H, m, ArH), 7.50–7.30 (6H, m, ArH), 6.74 (2H, d, *J* 8.5, ArH), 5.97 (2H, d, *J* 4.5, C*H*OH), 5.22 (2H, d, *J* 4.5, CHO*H*), 3.63 (2H, septet, *J* 7, 2 × NCH), 3.43 (2H, septet, *J* 6.5, 2 × NCH), 1.71 (12H, d, *J* 7, 4 × CH$_3$), 1.03 (6H, d, *J* 6.5, 2 × CH$_3$), 0.94 (6H, d, *J* 6.5, 2 × CH$_3$); $\delta_C$(75 MHz, $CDCl_3$) 172.0, 134.9, 133.1, 132.6, 128.3, 128.2, 127.2, 126.5, 126.2, 126.2, 124.6, 74.9, 51.9, 46.7, 21.3, 20.8, 20.5 and 20.1; *m/z* (CI) 569 (27%, M + H$^+$) and 284 (100%, M − $C_{18}H_{22}NO_2$) (Found: M + H$^+$, 569.3382. $C_{36}H_{44}N_2O_4$ requires *M* + H, 569.3379).

With MeLi, only **17** (R = *i*-Pr) was obtained.

### 1-Bromo-2-(diethoxymethyl)naphthalene 19

1-Bromo-2-formylnaphthamide **8** (1.155 g, 4.91 mmol), toluene-*p*-sulfonic acid monohydrate (131 mg, 0.69 mmol), 4 Å molecular sieves (*ca.* 1 g) and ethanol (15 ml) were heated to reflux for 60 hours and cooled. 10% Aqueous sodium hydroxide (15 ml) was added, the ethanol was removed under reduced pressure, and diethyl ether (40 ml) was added. The layers were separated and the organic portion was washed with 10% aqueous sodium hydroxide (2 × 15 ml), water (3 × 20 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give an oil. Purification by flash chromatography on neutral alumina [4:1 petrol–EtOAc] afforded *the acetal* **19** (634 mg, 42%) as a white solid, $R_f$ 0.32 [80:1 petrol (bp 40–60 °C)–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3061, 2976, 2926, 2896, 2878; $\delta_H$(300 MHz, $CDCl_3$) 8.42 (1H, *J* 8.5, ArH), 7.85 (3H, m, ArH), 7.61 (2H, m, ArH), 6.05 (1H, s, C*H*(OEt)$_2$), 3.80 (2H, m, C$H_2$CH$_3$), 3.69 (2H, m, C$H_2$CH$_3$), 1.32 (6H, t, *J* 7, 2 × CH$_3$); $\delta_C$(75 MHz, $CDCl_3$) 136.2, 134.6, 132.0, 128.0, 127.7, 127.4, 127.3, 126.8, 124.9, 123.3, 102.2, 62.6 and 15.2; *m/z* (EI) 308 (1%, M$^+$) and 49 (100%) (Found: M$^+$, 308.0410. $C_{15}H_{16}O_2Br$ requires *M*, 308.0412).

### *N*,*N*-Dimethyl-2-(diethoxymethyl)-1-naphthamide 18a

A solution of the bromoacetal **19** in diethyl ether (15 ml) was added dropwise over a period of 15 minutes to a solution of *tert*-butyllithium (2.33 ml, 3.96 mmol; 1.7 M solution in pentane) in diethyl ether (10 ml) at −78 °C under an atmosphere of nitrogen. The resulting brown solution was stirred for 70 minutes. *N*,*N*-Dimethylcarbamoyl chloride (0.83 ml, 9.01 mmol) was added in one portion and the mixture stirred for further 10 minutes, warmed to ambient temperature over a period of 60 minutes. Saturated aqueous sodium hydrogen carbonate (5 ml) was added to the orange solution. The layers were separated and the organic portion was washed with saturated aqueous sodium hydrogen carbonate (20 ml) and brine (2 × 20 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a brown oil which was distilled (Kugelrohr, bp 243 °C, 0.5 mmHg) to afford *the acetal* **18a** (353 mg, 47%) as a colourless oil, $\nu_{max}$(film)/cm$^{-1}$ 2974, 2932, 2874, 1629; $\delta_H$(300 MHz, $CDCl_3$) 7.89 (2H, m, ArH), 7.80 (1H, d, *J* 8.7, ArH), 7.73 (1H, m, ArH), 7.53 (2H, m, ArH), 5.67 (1H, s, C*H*(OEt)$_2$), 3.88–3.52 (4H, m, 2 × CH$_2$), 3.30 (3H, s, NCH$_3$), 2.75 (3H, s, NCH$_3$), 1.27 (6H, t, *J* 7.1, 2 × CH$_2$C$H_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.8, 133.3, 133.2, 133.1, 129.0, 128.6, 128.1, 127.0, 126.5, 124.7, 123.5, 100.4, 62.8, 62.5, 38.3, 34.5, 15.1 and 15.0; *m/z* (CI) 256 (100%, M − OEt); *m/z* (EI) 301 (7%, M$^+$), 256 (21%, M − OEt) and 127 (100%) (Found: M$^+$, 310.1673. $C_{18}H_{23}NO_3$ requires *M*, 310.1678).

### *N*-(*tert*-Butyl)-*N*-methyl-2-(diethoxymethyl)-1-naphthamide 18b

By the method given for **19**, a mixture of the aldehyde **4b** (206 g, 0.78 mmol), toluene-*p*-sulfonic acid monohydrate (15 mg, 0.08 mmol), 4 Å molecular sieves (*ca.* 0.5 g) and ethanol (10 ml) were heated to reflux for 2 days. Purification by flash chromatography on neutral alumina [15:1 petrol–EtOAc] afforded *the acetal* **18b** (229 mg, 87%) as a white solid, $R_f$ 0.38 [4:1 petrol (bp 40–60 °C)–EtOAc]; mp 116–120 °C; $\nu_{max}$(film)/cm$^{-1}$ 3060, 2975, 2926, 2876, 1698, 1632; $\delta_H$(300 MHz, $CDCl_3$) 7.90–7.75 (4H, m, ArH), 7.58–7.48 (2H, m, ArH), 5.67 (1H, s, C*H*(OEt)$_2$), 3.90 (1H, m, C$H_AH_B$CH$_3$), 3.66 (2H, m, C$H_2$CH$_3$), 3.54 (1H, m, CH$_A$$H_B$CH$_3$), 2.72 (3H, s, NCH$_3$), 1.72 (9H, s, *t*-Bu), 1.29 (3H, t, *J* 7, CH$_2$C$H_3$), 1.26 (3H, t, *J* 7, CH$_2$C$H_3$); $\delta_C$(75 MHz, $CDCl_3$) 170.0, 135.6, 133.4, 132.2, 128.7, 128.2, 128.1, 126.8, 126.4, 124.6, 123.5, 100.3, 62.9, 62.7, 57.2, 33.8, 28.1, 15.2 and 15.1.

### *N*,*N*-Diethyl-2-(diethoxymethyl)-1-naphthamide 18c

In the same way, aldehyde **4c** (1.329 g, 5.21 mmol), toluene-*p*-sulfonic acid monohydrate (99 mg, 0.52 mmol), 4 Å molecular sieves (*ca.* 1 g) and ethanol (20 ml) were heated to reflux for 24 hours. The crude product was purified by flash chromatography on neutral alumina [4:1 petrol–EtOAc] and afforded *the acetal* **18c** (875 mg, 51%) as a pale yellow oil, $R_f$ 0.36 [4:1 petrol–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 2975, 2932, 2876, 1631; $\delta_H$(300 MHz, $CDCl_3$) 8.0–7.7 (4H, m, ArH), 7.5 (2H, m, ArH), 5.56 (1H, s, C*H*(OEt)$_2$), 4.0–3.4 (6H, m, 3 × CH$_2$), 3.2–3.0 (2H, m, CH$_2$), 1.44 (3H, t, *J* 7, CH$_3$), 1.28 (3H, t, *J* 7, CH$_3$), 1.24 (3H, t, *J* 7, CH$_3$), 0.96 (3H, t, *J* 7, CH$_3$); $\delta_C$(75 MHz, $CDCl_3$) 190.4, 168.8, 133.3, 133.0, 129.1, 128.7, 128.1, 126.7, 126.5, 125.1, 123.6, 100.5, 63.1, 62.5, 43.2, 38.8, 15.1, 15.1, 13.7 and 12.9; *m/z* (CI) 330 (100%, M + H$^+$) and 284 (0.3%, M − OEt); *m/z* (EI) 226 (14%, M − CH(OEt)$_2$), 284 (31%, M − OEt), 300 (15%, M − Et) and 183 (100%) (Found: M + H$^+$ 330.2060. $C_{20}H_{27}NO_3$ requires *M* + H, 330.2069).

### *N*,*N*-Diisopropyl-2-(diethoxymethyl)-1-naphthamide 18d

In the same way, aldehyde **4d** (1.120 g, 3.96 mmol), toluene-*p*-sulfonic acid monohydrate (100 mg, 0.53 mmol), 4 Å molecular sieves (*ca.* 1 g) and ethanol (25 ml) were heated to reflux for 3 days. The crude product was purified by flash chromatography on neutral alumina [7:1 petrol–EtOAc] to give *the acetal* **18d** (834 mg, 59%) as a white solid, $R_f$ 0.54 [4:1 petrol–EtOAc]; mp 135–141 °C; $\nu_{max}$(film)/cm$^{-1}$ 2975, 2931, 2897, 2874, 1629; $\delta_H$(300 MHz, $CDCl_3$) 7.92–7.76 (4H, m, ArH), 7.56–7.50 (2H, m, ArH), 5.56 (1H, s, $CH(OEt)_2$), 4.08 (1H, dq, *J* 14 and 7, $OCH_AH_BCH_3$), 3.70–3.40 (5H, $OCH_AH_BCH_3$, $CH_2$, 2 × NCH), 1.81 (3H, d, *J* 7, $NCHCH_3$), 1.73 (3H, d, *J* 7, $NCHCH_3$), 1.32 (3H, t, *J* 7, $OCH_2CH_3$), 1.21 (3H, t, *J* 7, $OCH_2CH_3$), 1.13 (3H, d, *J* 6.5, $NCHCH_3$), 1.01 (3H, d, *J* 6.5, $NCHCH_3$); $\delta_C$(75 MHz, $CDCl_3$) 168.5, 134.3, 133.4, 132.6, 128.9, 128.5, 128.1, 126.5, 125.2, 123.9, 100.6, 65.8, 63.5, 62.3, 51.2, 46.2, 20.7, 20.5, 20.4, 20.3, 15.1 and 15.0; *m*/*z* (CI) 358 (6%, M + H$^+$) and 312 (100%, M − OEt); *m*/*z* (EI) 312 (5%, M − OEt) and 183 (100%) (Found: C, 73.76; H, 8.66; N, 3.82%. $C_{22}H_{31}NO_3$ requires C, 73.9; H, 8.7; N, 3.9%).

### General procedure for the allylation of aldehydes with allyltrimethylsilane in the presence of $SnCl_4$

A solution of the aldehyde **4** (0.784 mmol) in dry dichloromethane (3 ml) was added dropwise to a solution of stannic chloride (1.57 ml of a 1.0 M solution in dichloromethane, 1.568 mmol) under nitrogen at −78 °C. After 1 hour, allyltrimethylsilane (0.12 ml, 0.862 mmol) was then added in one portion. After stirring at −78 °C for a further 2 hours the mixture was allowed to warm to 0 °C, water (3 ml) was added, the layers were separated, and the aqueous layer extracted with dichloromethane (two 5 ml portions). The combined organic fractions were washed with brine, dried ($MgSO_4$), evaporated under reduced pressure without external heating, analysed and purified as described above.

### General procedure for allylation of aldehydes with allyltrimethylsilane in the presence of $TiCl_4$

Titanium tetrachloride (0.53 ml of a 1.0 M solution in dichloromethane, 0.530 mmol) was added in one portion to a stirring solution of aldehyde **44** (0.265 mmol) in dry dichloromethane (1.69 ml) under nitrogen at −78 °C. After 10 minutes, allyltrimethylsilane (0.1 ml, 0.636 mmol) was added dropwise to the deep red solution over a 15 minute period and the mixture was stirred for 3.5 hours at −78 °C. Saturated aqueous ammonium chloride (2 ml) was added, the layers were separated, and the aqueous layer extracted with dichloromethane (two 5 ml portions). The combined organic fractions were washed with brine, dried ($MgSO_4$), evaporated under reduced pressure without external heating, analysed and purified as described above.

By both of these methods, aldehyde **4a** gave *(R$_a$*,1′R*)-N,N-dimethyl-2-(1′-hydroxybut-3′-enyl)-1-naphthamide anti*-**15a**, $t_R$ 8.8 min [1:1 hexane–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 2972, 2933, 2844, 2736, 1702, 1619; $\delta_H$(300 MHz, $CDCl_3$) 7.88 (2H, m, ArH), 7.67 (2H, m, ArH), 7.53 (2H, m, ArH), 5.91 (1H, ddt, *J* 17, 10 and 6, $CH$=$CH_2$), 5.24 (1H, d, *J* 17, CH=C$H^{trans}$H), 5.21 (1H, d, *J* 10, CH=CH$H^{cis}$), 4.82 (1H, dd, *J* 9 and 4, C*H*OH), 3.29 (3H, s, $CH_3$), 2.78 (3H, s, $CH_3$), 2.72 (1H, m, $CH_AH_B$-CH=$CH_2$), 2.55 (1H, m, $CH_AH_B$CH=$CH_2$); $\delta_C$(75 MHz, $CDCl_3$) 170.1, 137.1, 134.4, 132.7, 131.6, 129.1, 129.0, 128.1, 127.1, 126.2, 124.6, 123.7, 118.8, 71.0, 43.4, 38.3 and 34.6; *m*/*z* (CI) 270 (100%, M + H$^+$) and 252 (17%, M − OH) (Found: M + H$^+$, 269.1412). $C_{17}H_{19}NO_2$ requires *M* + H, 269.1416).

Also obtained was *(R$_a$*,1′S*)-N,N-dimethyl-2-(1′-hydroxybut-3′-enyl)-1-naphthamide syn*-**15a**, $t_R$ 11.2 min [1:1 hexane–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3377, 3061, 2975, 2929, 2851, 1614; $\delta_H$(300 MHz, $CDCl_3$) 7.87 (2H, m, ArH), 7.63 (2H, m, ArH), 7.54 (2H, m, ArH), 5.83 (1H, ddt, *J* 17, 10.5 and 7, $CH$=$CH_2$), 5.15 (1H, dd, *J* 17 and 1.5, CH=C$H^{trans}$H), 5.08 (1H, d, *J* 10.5, CH$H^{cis}$), 4.89 (1H, dd, *J* 7.5 and 6.5, C*H*OH), 3.39 (1H, br m, OH), 3.30 (3H, s, $CH_3$), 2.76 (3H, s, $CH_3$), 2.75 (1H, m, CH(OH)-$CH_AH_B$), 2.62 (1H, m, CH(OH)$CH_AH_B$); $\delta_C$(75 MHz, $CDCl_3$) 170.5, 137.8, 134.5, 132.6, 132.3, 129.1, 128.9, 128.2, 127.1, 126.2, 124.4, 123.8, 117.7, 70.9, 40.9, 38.6 and 34.5; *m*/*z* (CI) 270 (92%, M + H$^+$), 252 (37%, M − OH) and 242 (100%, M − CH=$CH_2$) (Found: C, 76.20; H, 6.85; N, 4.37%; M + H$^+$, 269.1415. $C_{17}H_{19}NO_2$ requires C, 75.8; H, 7.1; N, 5.2%; *M* + H, 269.1416).

The $^1$H NMR of the crude reaction mixture indicated traces of **22**, and samples of **15a** in deuterochloroform lactonised slowly on standing. For example, a solution of alcohols **15a** (67 mg, 0.25 mmol) in deuterochloroform (0.6 ml) was allowed to stand for 1 week at 60 °C. The solvent was removed under reduced pressure to afford a brown oil which was purified by flash chromatography on silica gel [4:1 petrol (bp 40–60 °C)–EtOAc] to afford *3-allyl-1,3-dihydrobenzo[e]isobenzofuran-1-one* **22** (54 mg, 96%) as a colourless oil, $R_f$ 0.27 [4:1 petrol–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3073, 2917, 1749; $\delta_H$(300 MHz, $CDCl_3$) 9.06 (1H, d, *J* 8.4, ArH), 8.18 (1H, d, *J* 8.5, ArH), 8.02 (1H, d, *J* 8, ArH), 7.78 (1H, m, ArH), 7.69 (1H, m, ArH), 7.56 (1H, d, *J* 8.5, ArH), 5.84 (1H, ddt, *J* 17, 10.5 and 6.5, $CH$=$CH_2$), 5.63 (1H, t, *J* 5.5, ArC*H*(OCO)$CH_2CHCH_2$), 5.26 (1H, d, *J* 17.2, CH=C$H^{trans}$H), 5.19 (1H, d, *J* 10.5, CH=CH$H^{cis}$), 2.90 (1H, m, $CH_AH_B$CH=$CH_2$), 2.75 (1H, m, $CH_AH_B$CH=$CH_2$); $\delta_C$(75 MHz, $CDCl_3$) 170.5, 150.9, 135.3, 133.3, 131.2, 129.2, 128.9, 128.4, 127.2, 123.5, 120.4, 119.6, 118.5, 79.4 and 38.3; *m*/*z* (CI) 225 (100%, M + H$^+$); *m*/*z* (EI) 224 (12%, M$^+$) and 183 (100%, M − $CH_2CH$=$CH_2$) (Found: M$^+$, 224.0838. $C_{15}H_{12}O_2$ requires *M*, 224.0837).

By the same methods, aldehyde **4b** gave *(R$_a$*,1′S*)-N-(tert-butyl)-N-methyl-2-(1-hydroxybut-3-enyl)-1-naphthamide anti*-**15b** as a white solid, mp 103–107 °C; $R_f$ 0.21 [1:1 petrol–EtOAc]; $t_R$ 18.9 [8:1 hexane–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3398–3262, 2977, 2960, 2916, 1614; $\delta_H$(300 MHz, $CDCl_3$) 7.86 (2H, m, ArH), 7.75 (1H, m, ArH), 7.65 (1H, d, *J* 8.5, ArH), 7.58–7.48 (2H, m, ArH), 5.86 (1H, ddt, *J* 17, 10.5 and 1, $CH$=$CH_2$), 5.18 (1H, dd, *J* 17 and 1, CH=C$H^{trans}$H), 5.10 (1H, dd, *J* 10.5 and 1, CH=CH$H^{cis}$), 4.95 (1H, m, C*H*OH), 3.25 (1H, br s, OH), 2.84–2.70 (1H, m, $CH_AH_B$CH=$CH_2$), 2.72 (3H, s, $NCH_3$), 2.68–2.56 (1H, m, $CH_AH_B$CH=$CH_2$), 1.69 (9H, s, *t*-Bu); $\delta_C$(75 MHz, $CDCl_3$) 170.1, 137.4, 135.4, 135.3, 129.2, 128.8, 127.7, 126.7, 124.9, 124.3, 118.1, 71.3, 58.1, 41.2, 34.8 and 28.6; *m*/*z* (CI) 312 (43%, M + H$^+$), 294 (100%, M − OH), 270 (27%, M − $CH_2$-$CH$=$CH_2$) and 255 (36%, M − MeN*t*-Bu); *m*/*z* (EI) 311 (1%, M$^+$) and 49 (100%) (Found: M$^+$, 311.1888. $C_{20}H_{25}NO_2$ requires *M*, 311.1885).

Also obtained was *(R$_a$*,1′R*)-N-(tert-butyl)-N-methyl-2-(1-hydroxybut-3-enyl)-1-naphthamide syn*-**15b** as a white solid, mp 139–141 °C; $R_f$ 0.21 [1:1 petrol–EtOAc]; $t_R$ 36.2 [8:1 hexane–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3432–3415, 3058, 2977, 2960, 2923, 1615; $\delta_H$(300 MHz, $CDCl_3$) 7.88 (2H, m, ArH), 7.80 (1H, m, ArH), 7.68 (1H, d, ArH), 7.59–7.49 (2H, m, ArH), 5.93 (1H, m, $CH_2CH$=$CH_2$), 5.32–5.21 (2H, m, CH=C$H_2$), 4.92 (1H, dt, *J* 9 and *J* 3.5, C*H*OH), 2.78 (3H, s, $NCH_3$), 2.83–2.72 (1H, m, $CH_AH_B$CH=$CH_2$), 2.63 (1H, d, *J* 3.5, OH), 2.53 (1H, dt, *J* 14 and 8.5, $CH_AH_B$CH=$CH_2$), 1.71 (9H, s, *t*-Bu); $\delta_C$(75 MHz, $CDCl_3$) 171.0, 136.8, 135.2, 134.5, 133.4, 129.5, 129.0, 128.7, 127.6, 126.6, 125.1, 124.3, 119.3, 71.7, 57.9, 44.0, 34.4 and 28.7; *m*/*z* (CI) 312 (19%, M + H$^+$), 294 (26%, M − OH), 270 (29%, M − $CH_2CH$=$CH_2$), 225 (42%, M − MeN-*t*-Bu) and 88 (100%); *m*/*z* (EI) 311 (1%, M$^+$) and 49 (100%) (Found: M$^+$, 311.1886. $C_{20}H_{25}NO_2$ requires *M*, 311.1885).

By the same methods, aldehyde **4c** gave the alcohols **15c** and aldehyde **4d** gave the alcohols **15d**.

### General procedure for allylation of acetals with allyltrimethylsilane in the presence of $TiCl_4$

Titanium tetrachloride (0.35 ml of a 1.0 M solution in dichloro-

methane, 0.35 mmol) was added in one portion to a stirred solution of acetal **18** (0.265 mmol) in dry dichloromethane (1.7 ml) under nitrogen at −78 °C. After 10 minutes, allyltrimethylsilane (0.1 ml, 0.64 mmol) was added dropwise over a 15 min period to the deep red solution. The mixture was stirred for 3 hours at −78 °C. Saturated aqueous ammonium chloride (5 ml) was added, the layers were separated, and the aqueous layer was extracted with dichloromethane (5 × 10 ml). The combined organic fractions were washed with brine, dried ($MgSO_4$), evaporated under reduced pressure without external heating, analysed and purified as described above.

**($R_a$*,1′*R**)- and ($R_a$*,1′*S**)-*N*,*N*-Dimethyl-2-(1′-ethoxybut-3′-enyl)-1-naphthamide *anti*-21a and *syn*-21a.** By this method, acetal **18a** gave an inseparable (by flash chromatography or HPLC) mixture of the *ethers* **21a**. Purification by flash chromatography on silica gel [2:1 petrol–EtOAc] afforded a mixture of *anti*-**21a** and *syn*-**21a** as a colourless oil, $R_f$ 0.31 [2:1 petrol–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3059, 3012, 2977, 2870, 2855, 1750, 1631; $\delta_H$(300 MHz, $CDCl_3$) *anti*-**21a**: 7.90 (2H, m, ArH), 7.68 (2H, m, ArH), 7.55 (2H, m, ArH), 5.99 (1H, ddt, *J* 17, 10 and 7, C*H*=$CH_2$), 5.1 (2H, m, CH=C$H_2$), 4.47 (1H, dd, *J* 8 and 5, CHOEt), 3.4 (2H, m, C$H_2$$CH_3$), 3.33 (3H, s, $NCH_3$), 2.82 (3H, s, $NCH_3$), 2.61 (2H, m, C$H_2$CH=$CH_2$), 1.25 (3H, t, *J* 7.0, $CH_2$C$H_3$); *syn*-**21a**: 7.90 (2H, m, ArH), 7.68 (2H, m, ArH), 7.55 (2H, m, ArH), 5.89 (1H, ddt, *J* 17, 10 and 6.5, C*H*=$CH_2$), 5.1 (2H, m, CH=C$H_2$), 4.62 (1H, dd, *J* 8 and 5.5, CHOEt), 3.4 (2H, m, C$H_2$$CH_3$), 3.31 (3H, s, $NCH_3$), 2.77 (3H, s, $NCH_3$), 2.71 (1H, m, C$H_A$$H_B$CH=$CH_2$), 2.44 (1H, m, $CH_A$$H_B$CH=$CH_2$), 1.17 (3H, t, *J* 7.0, $CH_2$C$H_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.7, 169.6, 136.7, 136.5, 135.0, 133.1, 132.7, 129.1, 129.0, 128.8, 128.2, 128.1, 127.0, 127.0, 126.2, 126.1, 124.6, 124.5, 124.0, 123.5, 116.8, 116.6, 79.2, 77.9, 64.5, 64.2, 41.8, 41.7, 38.6, 38.1, 34.5, 34.4, 15.2 and 15.2; *m*/*z* (CI) 298 (86%, M + $H^+$) and 242 (100%); *m*/*z* (EI) 256 (M − $CH_2$CH=$CH_2$) and 183 (31%) (Found: M + $H^+$, 298.1814. $C_{19}H_{23}NO_2$ requires *M* + H, 298.1807). Assignments in the $^1$H NMR spectrum were made by COSY.

**($R_a$*,1′*R**)- and ($R_a$*,1′*S**)-*N*-(*tert*-Butyl)-*N*-methyl-2-(1′-ethoxybut-3′-enyl)-1-naphthamide *anti*-21b and *syn*-21b.** In the same way, acetal **18b** gave a crude product which was purified by flash chromatography on silica gel [7:1 petrol–EtOAc] to give a mixture of the two *ethers anti*-**21b** and *syn*-**21b** as a white solid. Preparative HPLC [16:1 hexane–EtOAc] gave *anti*-**21b** as a sticky white solid, $R_f$ 0.25 [7:1 petrol (bp 40–60 °C)–EtOAc]; $t_R$ 7.4 min [16:1 hexane–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3057, 2975, 2918, 2871, 1634; $\delta_H$(300 MHz, $CDCl_3$) 7.87 (2H, m, ArH), 7.76 (1H, m, ArH), 7.67 (1H, d, *J* 8.5, ArH), 7.53 (2H, m, ArH), 6.00 (1H, ddt, *J* 17, 10 and 7, C*H*=$CH_2$), 5.14 (1H, dd, *J* 17 and 2, CH=C$H^{trans}$H), 5.07 (1H, d, *J* 10, CH=CH$H^{cis}$), 4.55 (1H, dd, *J* 9 and 4, C*H*OEt), 3.50–3.29 (2H, m, C$H_2$$CH_3$), 2.78 (3H, s, $NCH_3$), 2.68–2.48 (2H, m, C$H_2$CH=$CH_2$), 1.70 (9H, s, *t*-Bu), 1.26 (3H, t, *J* 7, $CH_2$C$H_3$); $\delta_C$(75 MHz, $CDCl_3$) 170.0, 135.8, 135.3, 134.8, 132.8, 129.0, 128.3, 128.1, 126.9, 126.0, 124.4, 123.4, 116.4, 79.1, 64.5, 57.1, 41.9, 33.5, 28.1 and 15.2; *m*/*z* (CI) 340 (100%, M + $H^+$) and 294 (12%, M − OEt) (Found: M + $H^+$, 340.2275. $C_{22}H_{29}NO_2$ requires *M* + H, 340.2276).

Also obtained was *syn*-**21b** as a white solid, mp 105–107 °C; $R_f$ 0.25 [7:1 petrol–EtOAc]; $t_R$ 9.0 min [16:1 hexane–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 2973, 2955, 2919, 2870, 2850, 1626; $\delta_H$(300 MHz, $CDCl_3$) 7.88 (2H, m, ArH), 7.74 (1H, m, ArH), 7.67 (1H, d, *J* 8.5, ArH), 7.53 (2H, m, ArH), 5.93 (1H, ddt, *J* 17, 10 and 7.5, C*H*=$CH_2$), 5.17–5.05 (2H, m, CH=C$H_2$), 4.68 (1H, dd, *J* 8.5 and 5, C*H*OEt), 3.41 (2H, m, C$H_2$$CH_3$), 2.72 (3H, s, $NCH_3$), 2.70 (1H, m, C$H_A$$H_B$CH=$CH_2$), 2.40 (1H, m, $CH_A$$H_B$CH=$CH_2$), 1.70 (9H, s, *t*-Bu), 1.16 (3H, t, *J* 7, $CH_2$C$H_3$); $\delta_C$(75 MHz, $CDCl_3$) 170.2, 135.5, 135.3, 132.8, 128.8, 128.4, 128.1, 126.9, 126.1, 124.5, 123.9, 116.6, 64.1, 57.3, 41.7, 34.1, 29.6, 28.0 and 15.1; *m*/*z* (CI) 340 (55%, M + $H^+$) and 294 (100%, M − OEt) (Found: M + $H^+$, 340.2276. $C_{22}H_{29}NO_2$ requires *M* + H, 340.2276).

**($R_a$*,1′*R**)- and ($R_a$*,1′*S**)-*N*,*N*-Diethyl-2-(1′-ethoxybut-3′-enyl)-1-naphthamide *anti*-21c and *syn*-21c.** In the same way, acetal **18c** gave a crude product which was purified by flash chromatography on silica gel [7:1 petrol–EtOAc] to give a mixture of the two *ethers* **21c** which were separated by preparative HPLC [2:1 hexane–EtOAc] to afford *anti*-**21c** as a colourless oil, $R_f$ 0.47 [3:2 petrol–EtOAc]; $t_R$ 28.4 [16:1 hexane–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3058, 2975, 2934, 2895, 2873, 1632; $\delta_H$(300 MHz, $CDCl_3$) 7.88 (2H, m, ArH), 7.77 (1H, m, ArH), 7.70 (1H, d, *J* 8.5, ArH), 7.52 (2H, m, ArH), 5.99 (1H, ddt, *J* 17, 10 and 6.5, C*H*=$CH_2$), 5.14 (1H, d, *J* 17, CH=C$H^{trans}$H), 5.07 (1H, d, *J* 10.2, CH=CH$H^{cis}$), 4.49 (1H, dd, *J* 8.5 and 4, CHOEt), 3.96 (1H, m, C$H_A$$H_B$$CH_3$), 3.60 (1H, m, $CH_A$$H_B$$CH_3$), 3.43 (2H, m, C$H_2$$CH_3$), 3.15 (2H, m, C$H_2$$CH_3$), 2.66 (1H, m, C$H_A$$H_B$-CH=$CH_2$), 2.54 (1H, m, $CH_A$$H_B$CH=$CH_2$), 1.42 (3H, t, *J* 7, $CH_3$), 1.26 (3H, t, *J* 7, $CH_3$), 1.00 (3H, t, *J* 7, $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 168.7, 136.6, 135.1, 132.7, 132.4, 129.4, 128.7, 128.0, 126.6, 126.0, 124.9, 123.4, 116.5, 79.1, 64.6, 42.8, 41.9, 38.4, 15.3, 14.0 and 12.7; *m*/*z* (CI) 326 (100%, M + $H^+$) and 280 (22%, M − OEt); *m*/*z* (EI) 325 (3%, $M^+$) and 284 (100%, M − $CH_2$CH=$CH_2$) (Found: $M^+$, 325.2042. $C_{21}H_{27}NO_2$ requires *M*, 325.2042).

Also obtained was *syn*-**21c** as a colourless oil, $R_f$ 0.47 [3:2 petrol–EtOAc]; $t_R$ 34.6 [16:1 hexane–EtOAc]; $\nu_{max}$(film)/cm$^{-1}$ 3058, 2974, 2934, 2896, 2875, 1630; $\delta_H$(300 MHz, $CDCl_3$) 7.85 (2H, m, ArH), 7.74 (1H, m, ArH), 7.65 (1H, m, ArH), 7.50 (2H, m, ArH), 5.94 (1H, ddt, *J* 17.5, 10 and 7.5, C*H*=$CH_2$), 5.08 (2H, m, CH=C$H_2$), 4.56 (1H, dd, *J* 9 and 4, C*H*OEt), 4.00 (1H, m, C$H_A$$H_B$$CH_3$), 3.50 (1H, m, $CH_A$$H_B$$CH_3$), 3.39 (2H, m, C$H_2$$CH_3$), 3.07 (2H, m, C$H_2$$CH_3$), 2.70 (1H, m, C$H_A$$H_B$CH=$CH_2$), 2.35 (1H, m, $CH_A$$H_B$CH=$CH_2$), 1.38 (3H, t, *J* 7, $CH_3$), 1.11 (3H, t, *J* 7, $CH_3$), 1.0 (3H, t, *J* 7, $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 168.9, 136.1, 135.2, 133.4, 132.8, 128.8, 128.0, 126.6, 126.2, 125.1, 123.9, 116.6, 64.1, 43.0, 41.6, 38.4, 38.1, 15.1 and 13.8; *m*/*z* (CI) 326 (100%, M + $H^+$) and 280 (29%, M − OEt); *m*/*z* (EI) 325 (3%, $M^+$) and 284 (100%, M − $CH_2$CH=$CH_2$) (Found: $M^+$, 325.2044. $C_{21}H_{27}NO_2$ requires M, 325.2042).

**($R_a$*,1′*R**)- and ($R_a$*,1′*S**)-*N*,*N*-Diisopropyl-2-(1′-ethoxybut-3′-enyl)-1-naphthamide *anti*-21d and *syn*-21d.** In the same way, acetal **18d** gave a crude product which was purified by flash chromatography on silica gel [7:1 petrol–EtOAc] to yield a mixture of the two naphthamides **21d**. Preparative HPLC [25:1 hexane–EtOAc] gave *(Ra*,1′R*)-N,N-diisopropyl-2-(1′-ethoxybut-3′-enyl)-1-naphthamide syn*-**21d** as a white solid, mp 112–113 °C; $\nu_{max}$(film)/cm$^{-1}$ 3073, 3057, 2975, 2931, 2895, 2872, 1627; $\delta_H$(300 MHz, $CDCl_3$) 7.85 (3H, m, ArH), 7.71 (1H, d, *J* 8.5, ArH), 7.51 (2H, m, ArH), 6.01 (1H, ddt, *J* 17, 10 and 6.5, C*H*=$CH_2$), 5.15 (1H, dd, *J* 17 and 2, CH=C$H^{trans}$H), 5.07 (1H, d, *J* 10, CH=CH$H^{cis}$), 4.59 (1H, dd, *J* 9 and 3, C*H*OEt), 3.68 (2H, m, 2 × NCH), 3.50 (2H, q, *J* 7, C$H_2$$CH_3$), 1.81 (3H, d, *J* 7, NCHC$H_3$), 1.71 (3H, d, *J* 7, NCHC$H_3$), 1.30 (3H, t, *J* 7, $CH_2$C$H_3$), 1.17 (3H, d, *J* 6.5, NCHC$H_3$), 1.05 (3H, d, *J* 6.5, NCHC$H_3$); $\delta_C$(75 MHz, $CDCl_3$) 168.5, 136.3, 135.4, 133.3, 132.7, 129.5, 128.2, 128.0, 126.4, 125.9, 124.9, 123.3, 116.4, 79.4, 64.5, 50.9, 46.1, 42.0, 21.2, 21.1, 20.6, 20.5 and 15.5; *m*/*z* (CI) 354 (100%, M + $H^+$) and 308 (15%, M − OEt); *m*/*z* (EI) 353 (3%, $M^+$), 312 (32%, M − $CH_2$CH=$CH_2$) and 270 (100%) (Found: $M^+$, 353.2346. $C_{23}H_{31}NO_2$ requires *M*, 353.2355).

Also obtained was *(Ra*,1′R*)-N,N-diisopropyl-2-(1′-ethoxybut-3′-enyl)-1-naphthamide anti*-**21d** as a white solid, mp 125–128 °C; $\nu_{max}$(film)/cm$^{-1}$ 3084, 2977, 2959, 2926, 2871, 2856, 1625; $\delta_H$(300 MHz, $CDCl_3$) 7.86 (3H, m, ArH), 7.66 (1H, d, *J* 8.5, ArH), 7.53 (2H, m, ArH), 6.10 (1H, ddt, *J* 17, 10.5 and 6.5, C*H*=$CH_2$), 5.18 (2H, m, CH=C$H_2$), 4.61 (1H, dd, *J* 10.5 and 2, C*H*OEt), 3.63 (2H, septet, *J* 7, 2 × NCH), 3.43 (2H, m,

$CH_2CH_3$), 2.82 (1H, m, $CH_AH_BCH{=}CH_2$), 2.30 (1H, dd, *J* 14.5 and 6.5, $CH_AH_BCH{=}CH_2$), 1.83 (3H, d, *J* 6.5, $NCHCH_3$), 1.72 (3H, d, *J* 6.5, $NCHCH_3$), 1.14 (6H, m, $NCHCH_3$ and $CH_2CH_3$), 1.05 (3H, d, *J* 6.5, $NCHCH_3$); $\delta_C$(75 MHz, $CDCl_3$) 168.7, 135.5, 134.4, 133.0, 129.1, 128.5, 128.0, 126.5, 126.2, 125.3, 124.0, 116.3, 76.8, 64.1, 50.8, 46.3, 41.3, 21.1, 20.9, 20.5, 20.3 and 15.1; *m*/*z* (CI) 354 (100%, $M + H^+$) and 308 (40%, M − OEt); *m*/*z* (EI) 353 (3%, $M^+$), 312 (25%, $M - CH_2CH{=}CH_2$) and 49/84/86 (100%) (Found: $M^+$, 353.2347. $C_{23}H_{31}NO_2$ requires *M*, 353.2355).

### Correlation of stereochemistry by ethylation of alcohols 15. Method 1

Methyllithium (0.40 ml, 0.63 mmol; 1.6 M solution in diethyl ether) and triethyloxonium tetrafluoroborate (144 mg, 0.76 mmol) were added to a solution of the alcohol *syn*-**15a** (170 mg, 0.63 mmol) in THF (8 ml) at −78 °C under an atmosphere of nitrogen. After 10 min, the mixture was allowed to warm to 0 °C. After 20 minutes water (10 ml) was added to the white suspension. The mixture was extracted with dichloromethane (5 × 10 ml), and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure without external heating to give the crude product. Purification by flash column chromatography on silica gel [2:1 petrol (bp 40–60 °C)–EtOAc] afforded *syn*-**21a** (120 mg, 64%) as a colourless oil. Also obtained was lactone **22** (36 mg, 25%).

### Correlation of stereochemistry by ethylation of alcohols 15. Method 2

Sodium hydride (16 mg, 2.05 mmol) was added to a solution of the alcohol *anti*-**15b** (15 mg, 0.05 mmol) in DMF (2 ml) at 0 °C under an atmosphere of nitrogen. After 30 minutes, ethyl iodide (0.30 ml, 3.75 mmol) was added to the yellow solution. After 4 h, saturated aqueous ammonium chloride (5 ml) was added and the mixture was extracted with dichloromethane (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure without external heating to give a crude product which was purified by flash column chromatography on silica gel [7:1 petrol–EtOAc] to yield *anti*-**21b** (15 mg, 94%) as a colourless oil.

By method 2, the alcohol *syn*-**15c** (31 mg, 0.10 mmol) in THF (1.4 ml) gave, after 9 h, the ethyl ether *syn*-**21c** (30 mg, 89%) as a colourless oil.

By method 2, the alcohol *anti*-**15d** (445 mg, 1.40 mmol) gave, after 16 h, a crude product which was purified by flash chromatography [3:1 petrol–EtOAc] to yield *anti*-**21d** (467 mg, 97%) as a white solid.

### *N*,*N*-Diisopropyl-2-(*N*-methylformimidoyl)-1-naphthamide 23

Aldehyde **4d**[28] (1.564 g, 5.23 mmol) was added to 40% aqueous methylamine (15.7 g, 203 mmol) to form a white suspension which clarified on heating on a steam bath for 60 minutes. The solution was cooled to ambient temperature and the white precipitate isolated by filtration and dissolved in dichloromethane. This solution was dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a white solid which was recrystallised from ethyl acetate to afford the *imine* **23** (1.308 g, 80%) as very fine white needles, mp 188–190 °C (ethyl acetate); $\lambda_{max}$/nm ($\varepsilon_{max}$) ($CH_2Cl_2$) 254 (47080), 290 (11670); $\nu_{max}$(film)/$cm^{-1}$ 3058, 3021, 2988, 2965, 2937, 2906, 2867, 2770, 1639, 1619; $\delta_H$(300 MHz, $CDCl_3$) 8.57 (1H, br m, $CH{=}NCH_3$), 8.12 (1H, d, *J* 9, ArH), 7.94–7.82 (3H, m, ArH), 7.56 (2H, m, ArH), 3.67 (1H, septet, *J* 7, NCH), 3.59 (3H, d, *J* 1.5, $CH{=}NCH_3$), 3.54 (1H, septet, *J* 6.5, NCH), 1.82 (3H, d, *J* 6.5, $NCHCH_3$), 1.75 (3H, d, *J* 7, $NCHCH_3$), 1.04 (3H, d, *J* 6.5, $NCHCH_3$), 1.03 (3H, d, *J* 6.5, $NCHCH_3$); $\delta_C$(75 MHz, $CDCl_3$) 168.3, 160.0, 137.5, 134.4, 129.3, 128.9, 128.2, 128.2, 127.4, 127.0, 125.3, 122.8, 51.3, 48.6, 46.4, 20.8, 20.6 and 20.4; *m*/*z* (CI) 297 (100%, $M + H^+$); *m*/*z* (EI) 296 (5%, $M^+$) and 196 ($M - N(CH(CH_3)_2)_2$) (Found: C, 77.14; H, 8.34; N, 9.42%. $C_{19}H_{24}N_2O$ requires C, 77.0; H, 8.1; N, 9.5%).

### ($R_a$*,1′*R**)- and ($R_a$*,1′*S**)-*N*,*N*-Diisopropyl-2-[1′-(methylamino)ethyl]-1-naphthamide *anti*-24 and *syn*-24

Methyllithium (0.48 ml, 0.77 mmol; 1.6 M solution in diethyl ether) was added dropwise over 5 minutes to a solution of imine **23** (189 mg, 0.64 mmol) in THF (7 ml) at −78 °C under an atmosphere of nitrogen. The resulting yellow solution was stirred for 3 hours, saturated aqueous ammonium chloride (5 ml) was added and the mixture warmed to ambient temperature. The THF was removed under reduced pressure without external heating and the aqueous residue was extracted with dichloromethane (5 × 10 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure at ambient temperature to give the crude product, which contained (by $^1$H NMR) >96:4 *syn*-**24**:*anti*-**24**. Purification by flash chromatography on silica gel [1:1 petrol–EtOAc + 1% triethylamine] gave *syn*-**24** (183 mg, 92%) as a pale brown solid. Recrystallisation from ethyl acetate afforded the amine as pale brown rhombic prisms, mp 163–165 °C (EtOAc); $\nu_{max}$(film)/$cm^{-1}$ 3316, 3052, 3009, 2968, 2934, 2899, 2873, 2799, 1617; $\delta_H$(300 MHz, $CDCl_3$) 7.87–7.80 (3H, m, ArH), 7.59 (1H, d, *J* 8.7, ArH), 7.49 (2H, m, ArH), 3.96 (1H, q, *J* 6.5, $ArCH(NHCH_3)CH_3$), 3.63 (2H, m, 2 × NCH), 2.35 (3H, s, $NCH_3$), 1.80 (3H, d, *J* 7, $NCHCH_3$), 1.72 (3H, d, *J* 7, $NCHCH_3$), 1.49 (3H, d, *J* 6.5, $ArCH(NHCH_3)CH_3$), 1.13 (3H, d, *J* 6.5, $NCHCH_3$), 1.03 (3H, d, *J* 7, $NCHCH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.1, 137.6, 134.5, 132.6, 129.3, 128.4, 127.9, 126.4, 125.9, 125.1, 123.4, 55.6, 50.8, 46.1, 34.2, 21.2, 20.9, 20.8, 20.4 and 20.4; *m*/*z* (CI) 314 (100%, $M + H^+$) (Found: C, 76.60; H, 9.04; N, 9.13%. $C_{20}H_{28}N_2O$ requires C, 76.9; H, 9.0; N, 9.0%).

Heating *syn*-**24** in $CDCl_3$ for 5 days at 60 °C produced enough *anti*-**24** to allow identification of its $NCH_3$ $^1$H NMR signal at $\delta$ 2.43 (3H, s).

### ($R_a$*,1′*R**)- and ($R_a$*, 1′*S**)-*N*,*N*-Diisopropyl-2-[1′-(methylamino)pentyl]-1-naphthamide *anti*-25 and *syn*-25

In the same way, imine **23** (89 mg, 0.30 mmol) and *n*-butyllithium (0.23 ml, 0.36 mmol; 1.6 M solution in hexanes) gave, after 1 h, a crude product containing a ratio of 92:8 *syn*-**25**:*anti*-**25**. Purification by flash chromatography on silica gel [1:1 petrol–EtOAc + 1% triethylamine] gave *syn*-**25** (187 mg, 85%) as a pale brown solid, mp 110–111 °C; $R_f$ 0.29 [1:1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine]; $\nu_{max}$(film)/$cm^{-1}$ 3326, 3057, 2961, 2933, 2872, 2859, 2797, 1624; $\delta_H$(300 MHz, $CDCl_3$) 7.83 (3H, m, ArH), 7.54 (1H, d, *J* 8.8, ArH), 7.48 (2H, m, ArH), 3.77 (1H, dd, *J* 8.5 and 4.5, $CH(NHCH_3)$), 2.30 (3H, s, $NCH_3$), 1.90 (2H, m, $CH_AH_BCH_AH_BCH_2CH_3$), 1.80 (3H, d, *J* 7, $NCHCH_3$), 1.71 (3H, d, *J* 6.5, $NCHCH_3$), 1.60 (1H, m, $CH_AH_B(CH_2)_2CH_3$), 1.36 (3H, m, $CH_2CH_AH_BCH_2CH_3$), 1.12 (3H, d, *J* 6.5, $NCHCH_3$), 1.02 (3H, d, *J* 6.5, $NCHCH_3$), 0.94 (3H, t, *J* 7, $(CH_2)_3CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.1, 137.2, 134.8, 132.5, 129.4, 128.2, 127.9, 126.3, 125.9, 125.1, 123.8, 60.9, 50.9, 46.1, 35.1, 33.9, 29.6, 23.0, 21.0, 20.9, 20.5, 20.3 and 14.0; *m*/*z* (CI) 355 (100%, $M + H^+$), 324 (1%, $M - NHCH_3$) and 254 (8%, $M - N^iPr_2$); *m*/*z* (EI) 354 (2%, $M^+$) and 196 (100%) (Found: $M^+$, 354.2677. $C_{23}H_{34}N_2O$ requires *M*, 354.2671).

Also obtained was *3-butyl-2-methyl-2,3-dihydro-1H-benzo[e]-isoindol-1-one* **28** (10 mg, 4%), $R_f$ 0.60 [1:1 petrol–EtOAc + 1% triethylamine]; $\nu_{max}$(film)/$cm^{-1}$ 3056, 2956, 2930, 2862, 1679; $\delta_H$(300 MHz, $CDCl_3$) 9.30 (1H, d, *J* 8.5, ArH), 8.01 (1H, d, *J* 8.4, ArH), 7.94 (1H, d, *J* 8, ArH), 7.69 (1H, t, *J* 7.5, ArH), 7.58 (1H, t, *J* 7.5, ArH), 7.51 (1H, d, *J* 8.5, ArH), 4.47 (1H, t, *J* 4.3, $CH(CH_2)_3CH_3$), 3.19 (3H, s, $NCH_3$), 2.09 (2H, m, $CHCH_2CH_2CH_2CH_3$), 1.26 (2H, m, $CH(CH_2)_2CH_2CH_3$), 1.04 (1H, m, $CHCH_AH_B(CH_2)_2CH_3$), 0.82 (3H, t, *J* 7.5, $(CH_2)_3CH_3$),

0.76 (1H, m, $CH_AH_B(CH_2)_2CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.5, 145.3, 133.0, 131.9, 129.2, 127.9, 127.7, 126.6, 126.3, 123.9, 119.1, 61.0, 29.8, 27.0, 24.2, 22.5 and 13.8; *m/z* (CI) 254 (100%, M + $H^+$) and 196 (4%, M − $C_4H_9$); *m/z* (EI) 253 (14%, $M^+$), 196 (100%, M − $C_4H_9$) (Found: $M^+$, 253.1472. $C_{17}H_{19}NO$ requires *M*, 253.1467).

Heating *syn*-**25** in $CDCl_3$ for 5 days at 60 °C produced enough *anti*-**25** to allow identification of its $NCH_3$ $^1$H NMR signal at $\delta$ 2.40 (3H, s).

### ($R_a$*,1′*R**)- and ($R_a$*,1′*S**)-*N*,*N*-Diisopropyl-2-{1-[benzyl-(methyl)amino]ethyl}-1-naphthamide *anti*-26 and *syn*-26

Methyllithium (0.52 ml, 0.83 mmol; 1.6 M solution in diethyl ether) was added dropwise over 5 minutes to a solution of imine **23** (204 mg, 0.69 mmol) in THF (7 ml) at −78 °C under an atmosphere of nitrogen. After 3 hours benzyl bromide (0.13 ml, 1.10 mmol) was added and after a further 5 minutes the mixture was warmed to 0 °C. After 30 minutes saturated aqueous ammonium chloride (5 ml) was added and the solvent was removed under reduced pressure without external heating. The aqueous residue was extracted with dichloromethane (5 × 10 ml) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product which contained (by analytical HPLC (10:1 hexane–EtOAc + 1% triethylamine)) a ratio of 96:4 *syn*-**26**:*anti*-**26**. Purification by flash chromatography on silica gel [15:1 petrol–EtOAc + 1% triethylamine] afforded *syn*-**26** (41 mg, 15%) as a colourless oil that solidified on standing, $R_f$ 0.26 [4:1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine]; $t_R$ 5.2 min [10:1 hexane–EtOAc + 1% triethylamine]; $\nu_{max}$(film)/$cm^{-1}$ 3059, 3027, 2975, 2933, 2873, 2837, 2790, 1629; $\delta_H$(300 MHz, $CDCl_3$) 7.80–7.66 (4H, m, ArH), 7.42–7.34 (2H, m, ArH), 7.20 (5H, m, ArH), 3.65–3.46 (4H, m, 2 × NCH, $CH_AH_BPh$ and $CH(CH_3)N$), 3.17 (1H, d, *J* 13.7, $CH_AH_BPh$), 2.08 (3H, s, $NCH_3$), 1.71 (3H, d, *J* 6.9, $NCHCH_3$), 1.63 (3H, d, *J* 6.7, $NCHCH_3$), 1.42 (3H, d, *J* 6.5, $CH_3CHN$), 1.07 (3H, d, *J* 6.5, $NCHCH_3$), 0.93 (3H, d, *J* 6.5, $NCHCH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.0, 140.5, 138.4, 133.7, 132.7, 129.4, 128.7, 128.3, 127.9, 127.9, 126.3, 125.9, 125.2, 124.6, 60.7, 59.6, 50.6, 46.2, 39.4, 22.0, 21.3, 20.9, 20.5 and 20.4; *m/z* (CI) 403 (10%, M + $H^+$) and 302 (100%, M − $N(CH(CH_3)_2)_2$); *m/z* (EI) 210 (100%) and 91 (49%, $CH_2Ph$) (Found: M + $H^+$, 403.2756. $C_{27}H_{34}N_2O$ requires *M* + H, 403.2749).

Also obtained was *3-benzyl-2,3-dimethyl-2,3-dihydro-1H-benzo[e]isoindol-1-one* **29** (133 mg, 54%) as a pale yellow solid, $R_f$ 0.11 [4:1 petrol–EtOAc + 1% triethylamine]; $\lambda_{max}$/nm ($\varepsilon_{max}$) ($CH_2Cl_2$) 236 (45640), 300 (7623); $\nu_{max}$/$cm^{-1}$ 3060, 3029, 2968, 2929, 1678; $\delta_H$(300 MHz, $CDCl_3$) 9.04 (1H, d, *J* 7.7, ArH), 7.88 (1H, d, *J* 8.5, ArH), 7.79 (1H, d, *J* 8, ArH), 7.51 (1H, m, ArH), 7.43 (1H, m, ArH), 7.32 (1H, d, *J* 8.5, ArH), 6.96–6.88 (3H, m, ArH), 6.70–6.64 (2H, m, ArH), 3.22 (1H, d, *J* 14, $CH_AH_BPh$), 3.08 (3H, s, $NCH_3$), 3.05 (1H, d, *J* 14, $CH_AH_BPh$), 1.54 (3H, s, $CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 168.7, 149.2, 135.1, 132.9, 131.7, 129.4, 129.1, 127.8, 127.7, 126.7, 126.3, 125.6, 124.1, 118.9, 64.9, 43.3, 24.6 and 23.9; *m/z* (CI) 301 (100%, M + $H^+$) and 210 (8%, M − $CH_2Ph$); *m/z* (EI) 210 (100%, M − $CH_2Ph$) (Found: M + $H^+$, 302.1545. $C_{21}H_{19}NO$ requires *M* + H, 302.1545).

Heating *syn*-**26** in $CDCl_3$ for 5 days at 60 °C produced enough *anti*-**26** to allow identification of its $NCH_3$ $^1$H NMR signal at $\delta$ 2.24 (3H, s) and to assign its retention time as $t_R$ [10:1 hexane–EtOAc + 1% triethylamine] 4.3 min.

### ($R_a$*,1′*R**)- and ($R_a$*,1′*S**)-*N*,*N*-Diisopropyl-2-{1′-[benzyl-(methyl)amino]pentyl}-1-naphthamide *anti*-27 and *syn*-27

In the same way, imine **23**, *n*-butyllithium (0.55 ml, 0.88 mmol; 1.6 M solution in hexanes) and benzyl bromide (0.13 ml, 1.10 mmol) gave a crude product containing a ratio of 92:8 *syn*-**27**:*anti*-**27** (by analytical HPLC) which was purified by flash chromatography on silica gel [15:1 petrol–EtOAc + 1% triethylamine] to afford *(Ra*,1′S*)-N,N-diisopropyl-2-{1-[benzyl-(methyl)amino]pentyl}-1-naphthamide syn*-**27** (51 mg, 16%) as a sticky pale yellow solid, $R_f$ 0.18 [4:1 petrol (bp 40–60 °C)–EtOAc + 1% triethylamine]; $t_R$ 3.0 min [15:1 hexane–EtOAc + 1% triethylamine]; $\nu_{max}$(film)/$cm^{-1}$ 3059, 3026, 2960, 2934, 2870, 2858, 2792, 1709, 1630; $\delta_H$(300 MHz, $CDCl_3$) 7.80–7.70 (3H, m, ArH), 7.52 (1H, d, *J* 8.5, ArH), 7.42–7.34 (2H, m, ArH), 7.25–7.06 (5H, m, ArH), 3.87 (1H, dd, *J* 9.5 and 4.5, C*H*N), 3.60 (1H, d, *J* 13.5, $PhCH_AH_B$), 3.6–3.4 (2H, m, 2 × NCH), 3.43 (1H, d, *J* 13.5, $PhCH_AH_B$), 2.06 (3H, s, $NCH_3$), 2.1 (1H, m, $CH_AH_B(CH_2)_2CH_3$), 1.71 (3H, d, *J* 6.9, $NCHCH_3$), 1.7 (1H, m, $CH_2CH_AH_BCH_2CH_3$), 1.6 (1H, m, $CH_AH_B(CH_2)_2CH_3$), 1.58 (3H, d, *J* 7, $NCHCH_3$), 1.5–1.2 (3H, m, $CH_2CH_AH_BCH_2CH_3$), 1.05 (3H, d, *J* 6.6, $NCHCH_3$), 0.90–0.84 (6H, m, $NCHCH_3$ and $(CH_2)_3CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.2, 135.0, 134.8, 132.5, 129.8, 128.5, 128.4, 127.9, 127.8, 127.3, 126.3, 126.0, 125.9, 125.6, 125.5, 64.9, 58.3, 50.7, 46.2, 37.8, 33.4, 29.1, 23.1, 21.1, 21.1, 20.7, 20.4 and 14.1; *m/z* (CI) 445 (100%, M + $H^+$); *m/z* (EI) 387 (6%, M − $C_4H_9$), 353 (2%, M − $CH_2Ph$) and 49 (100%) (Found: M + $H^+$, 445.3223. $C_{30}H_{46}N_2O$ requires *M* + H, 445.3219).

Also obtained was *3-benzyl-3-butyl-2-methyl-2,3-dihydro-1H-benzo[e]isoindol-1-one* **30** (134 mg, 54%) as a pale yellow solid, $R_f$ 0.17 [4:1 petrol–EtOAc + 1% triethylamine]; $\nu_{max}$(film)/$cm^{-1}$ 3061, 3030, 2955, 2930, 2861, 1679; $\delta_H$(300 MHz, $CDCl_3$) 9.18 (1H, dd, *J* 8 and 1, ArH), 8.01 (1H, d, *J* 8, ArH), 7.91 (1H, d, *J* 7.5, ArH), 7.66–7.52 (2H, m, ArH), 7.44 (1H, d, *J* 8.5, ArH), 7.03 (3H, m, ArH), 6.77 (2H, m, ArH), 3.34 (1H, d, *J* 14, $CH_AH_BPh$), 3.18 (1H, d, *J* 14, $CH_AH_BPh$), 3.17 (3H, s, $NCH_3$), 2.16 (2H, m, $CH_2(CH_2)_2CH_3$), 1.22 (2H, m, $(CH_2)_2CH_2CH_3$), 0.84 (1H, m, $CH_2CH_AH_BCH_2CH_3$), 0.77 (3H, t, *J* 7.3, $(CH_2)_3CH_3$), 0.49 (1H, m, $CH_2CH_AH_BCH_2CH_3$); $\delta_C$(75 MHz, $CDCl_3$) 169.4, 147.5, 134.8, 132.9, 131.7, 129.5, 129.0, 127.9, 127.8, 127.6, 126.7, 126.6, 126.2, 124.1, 118.9, 68.2, 43.4, 35.7, 24.8, 24.7, 22.4 and 13.8; *m/z* (CI) 344 (100%, M + $H^+$) and 252 (6%, M − $CH_2Ph$); *m/z* (EI) 252 (100%, M − $CH_2Ph$) (Found: M + $H^+$, 344.2017. $C_{24}H_{25}NO$ requires *M* + H, 344.2014).

Heating *syn*-**27** in $CDCl_3$ for 5 days at 60 °C produced enough *anti*-**27** to allow identification of its $NCH_3$ $^1$H NMR signal at $\delta$ 2.22 (3H, s) and to assign its retention time as $t_R$ 3.0 min [15:1 hexane–EtOAc + 1% triethylamine].

### Crystal data for *anti*-15c†

Single crystals of *anti*-**15c** were grown from ethyl acetate, mounted on a thin glass fibre and transferred to the cold gas stream of the diffractometer. $C_{19}H_{23}NO_2$, $M = 297.38$, monoclinic, $a = 10.1424(14)$, $b = 16.7857(13)$, $c = 10.7011(15)$ Å, $\beta = 114.446(9)°$, $U = 1658.5(4)$ Å$^3$, $T = 123(1)$ K, space group $P2_1/c$ (no. 14), $Z = 4$, $D_c = 1.191$ g cm$^{-3}$, $\mu$(Mo-K$\alpha$) = 0.077 mm$^{-1}$. Data collected on a Rigaku AFC7R diffractometer, 4038 reflections measured, $\theta_{max} = 26.99°$, 3609 reflections unique ($R_{int} = 0.0108$).[50] Final agreement factors for 227 parameters gave $R_1 = 0.0562$, $wR^2 = 0.1036$ and GOF = 1.010 based on all 3609 data, final difference map +0.28 and −0.24 e Å$^{-3}$.[51]

### Crystal data for *anti*-15d†

Single crystals of *anti*-**15d** were grown from ethyl acetate, mounted on a thin glass fibre and transferred to the cold gas stream of the diffractometer. $C_{21}H_{27}NO_2$, $M = 325.44$, monoclinic, $a = 11.4254(4)$, $b = 20.1558(6)$, $c = 16.4936(5)$ Å, $\beta = 99.506(1)°$, $U = 3746.1(2)$ Å$^3$, $T = 123(1)$ K, space group $P2_1/c$ (no. 14), $Z = 8$, $D_c = 1.154$ g cm$^{-3}$, $\mu$(Mo-K$\alpha$) = 0.073 mm$^{-1}$.

† CCDC reference number 207/413. See http://www.rsc.org/suppdata/p1/b0/b000669f for crystallographic files in .cif format.

Data collected on a Bruker AXS SMART CCD diffractometer, 31581 reflections measured, data truncated to 0.80 Å ($\theta_{max}$ 26.37°, 99.8% complete), 7639 reflections unique ($R_{int} = 0.0441$).[50] Final agreement factors for 501 parameters gave $R_1 = 0.0490$, $wR^2 = 0.1078$ and GOF = 1.007 based on all 7639 data, final difference map +0.37 and −0.22 e Å$^{-3}$.[51]

### Crystal data for *syn*-24†

Single crystals of *syn*-**24** were grown from ethyl acetate, mounted on a thin glass fibre and transferred to the cold gas stream of the diffractometer. $C_{20}H_{28}N_2O$, $M = 312.44$, orthorhombic, $a = 16.219(3)$, $b = 11.966(3)$, $c = 18.823(3)$ Å, $U = 3653(1)$ Å$^3$, $T = 123(1)$ K, space group *Pbca* (no. 61), $Z = 8$, $D_c = 1.136$ g cm$^{-3}$, $\mu$(Mo-Kα) = 0.070 mm$^{-1}$. Data collected on a Bruker AXS SMART CCD diffractometer, 19092 reflections measured, data truncated to 0.80 Å ($\theta_{max}$ 26.37°, 99.5% complete), 3715 reflections unique ($R_{int} = 0.0238$).[50] Final agreement factors for 218 parameters gave $R_1 = 0.0473$, $wR^2 = 0.1014$ and GOF = 1.000 based on all 4011 data, absolute structure not determined, final difference map +0.25 and −0.22 e Å$^{-3}$.[51]

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