Atropisomeric diastereoisomers from nucleophilic attack on 8-acyl-1-naphthamides

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

[a] *Department of Chemistry, University of Manchester, Oxford Rd., Manchester, UK M13 9PL*
[b] *Roche Discovery Welwyn, 40 Broadwater Rd., Welwyn Garden City, Herts, UK AL7 3AY*

Received (in Cambridge, UK) 24th January 2000, Accepted 10th March 2000

Restricted rotation about the Ar–CO bond means that 1-naphthamides bearing chiral 8-substituents may exist as pairs of diastereoisomeric atropisomers. These atropisomers are formed with good to excellent stereoselectivity for the *syn*-diastereoisomer by the reaction of 8-formyl-1-naphthamides with organolithiums and Grignard reagents. The reduction of 8-acyl-1-naphthamides also proceeds with *syn*-selectivity. The product alcohols are prone to lactonisation and also to epimerisation, and some of the apparent diastereoselectivities may be the result of thermodynamic, rather than kinetic, control.

Introduction

In the previous two papers[1] we described the atroposelective attack of nucleophiles and some electrophiles on 1-naphthamides bearing prochiral 2-substituents. In this paper we turn to the effect of the stereogenic amide axis of 8-substituted 1-naphthamides on the atroposelectivity of the reactions at prochiral 8-substituents.[2] Axially chiral 1,8-disubstituted naphthalenes have been used successfully as reagents for asymmetric protonation,[3] as chiral auxiliaries for asymmetric conjugate addition reactions,[4] and as chiral ligands for metal-catalysed asymmetric reactions.[5] The 8-substituents of 1-naphthamides are nearer the amide axis than the 2-substituents, and we hoped that this would mean the stereoselectivities of their reactions would be correspondingly higher.

In the event, some were, but the closeness in space of the 1- and 8-substituents led to other problems of reactivity. In addition, it is well known from the binaphthyl series[6–11] that the barrier to rotation provided by an 8-substituent is significantly lower than that provided by a comparable 2-substituent,[12] and in some reactions we were unable to be sure whether the observed selectivities were purely kinetic or whether they arose through thermodynamic equilibration between the diastereoisomeric product atropisomers.

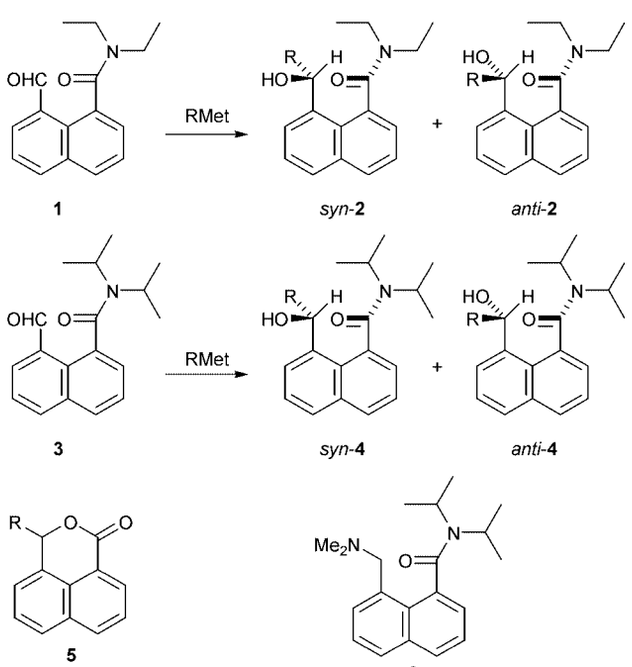
Rotational restriction in 1,8-*biaryl* naphthalenes has been studied in detail. 1,8-Di-*o*-tolylnaphthalene can exist as two diastereoisomeric atropisomers: the *trans* is favoured 3.21 : 1 over the *cis* at 40 °C, and the *cis* isomer converts to the *trans* with a barrier of 100.8 kJ mol^{-1} at this temperature.[13] Barriers to interconversion of naphthalenes bearing *meta*-substituted phenyl[14,15] or pyridyl[16–18] rings at the 1- and 8-positions are much lower, and these compounds do not exist as atropisomeric diastereoisomers. The conformation[19,20] and racemisation[21] of enantiomeric atropisomers of 8-substituted-1-naphthamides and their thioamide derivatives[22] have been described by Mannschreck and Kiefl, but there are no reported examples of diastereoisomeric non-biaryl atropisomers based on a 1,8-disubstituted naphthalene system.

8-Substituted naphthamides are most conveniently made either by a Lossen-type rearrangement[23,24] of 1,8-naphthalimide *N*-oxide or by perilithiation of 1-(dimethylaminomethyl)naphthalene.[24,25] We used both of these methods to make a small group of amides which we proved to be chiral, and whose rate of racemisation turned out to be influenced by the degree of bonding interaction between the amide and the 8-substituent.[26] In the current study, none of the 8-substituted naphthamides has a nucleophilic 8-substituent, and we expected the rates of racemisation or epimerisation to be fast. We therefore kept reaction times to a minimum and ensured that the products remained cold throughout the work-up.

Results and discussion

Addition of alkyllithiums and Grignard reagents to 8-formyl-1-naphthamides

The starting 8-substituted aldehydes were made by our published perilithiation–Polonovski reaction sequence from dimethylaminomethylnaphthalene.[24] We treated each of the two aldehydes **1** and **3** with alkyllithiums or Grignard reagents, as shown in Scheme 1, and obtained mixtures of the atropisomeric



Scheme 1 Reactions of 8-formyl-1-naphthamides with organometallics.

DOI: 10.1039/b000670j

Table 1 Additions to 8-formyl-1-naphthamides

Entry	RMet	Reaction with **1**			Reaction with **3**			Thermodynamic
		Product	Ratio *syn*-:*anti*-**2**	Yield	Product	Ratio *syn*-:*anti*-**4**	Yield	Ratio *syn*-:*anti*-**4**
1	MeLi	**2a**	82:18	76	**4a**	56:44	99	89:11
2	MeLi[a]	—	—	—	**4a**	76:24	99	89:11
3	*n*-BuLi	**2b**	89:11	68	**4b**	90:10	79	85:15
4	PhLi	**2c**	>99:1	69	**4c**	>99:1	55	>99:1
5	MeMgBr	**2a**	83:17	83	**4a**	83:17	81	89:11
6	*n*-BuMgCl	**2b**	83:17	64	**4b**	75:25	61	85:15
7	PhMgBr	**2c**	>99:1	77	**4c**	>99:1	78	>99:1

[a] In the presence of HMPA (4 equiv.).

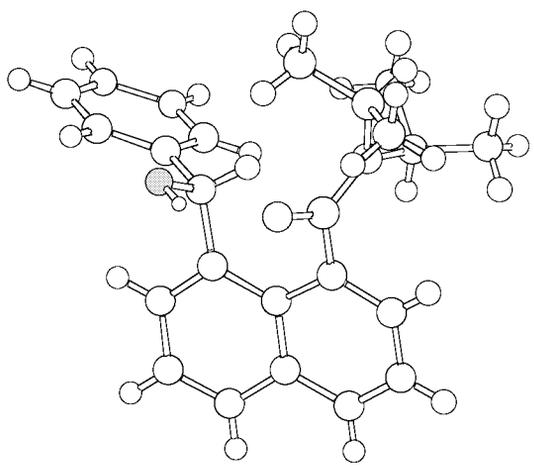


Fig. 1 X-Ray crystal structure of *syn*-**4c**.

diastereoisomers of the products **2** and **4**, generally in good yield (Table 1). The ratios were determined by extracting an aliquot immediately after the reactions had been quenched, performing a rapid mini-workup, and analysing the aliquot immediately by HPLC, keeping the sample on ice. The alcohols **4** could be purified, but slowly cyclised, even as solids at −18 °C in the freezer, to the lactones **5**. The alcohols **3**, with the rather less hindered *N*,*N*-diethylamide group, were much less stable, and even attempted purification on silica resulted in cyclisation to **5**.

Stereochemistry was assigned to *syn*-**4c** on the basis of its X-ray crystal structure, shown in Fig. 1. There is an intramolecular hydrogen bond in this structure, and the hydrogen bonded proton appears as a sharp signal in the ^{1}H NMR at δ 5.2. This sharp OH signal was a common feature of the major product diastereoisomers, and allowed us to be confident that **1** and **3** react with *syn*-stereoselectivity in every case.

Less certain was whether the ratios in Table 1 truly represent the kinetic product ratios from the reactions. The half-life for racemisation of a representative 8-alkyl-1-naphthamide, 8-(*N*′,*N*′-dimethylaminomethyl)-*N*,*N*-diisopropyl-1-naphthamide **6**, is only 5 min at 20 °C,[12,26] and 8-substituted naphthamides racemise significantly faster than similarly substituted 2-naphthamides.[12,26] We gained an estimate of the barrier to epimerisation of **4** (by rotation about Ar–CO) by following the equilibration at 10 °C in toluene of a 72:18 mixture of *syn*-**4a** and *anti*-**4a**. Over a period of a few days, this mixture approached thermodynamic equilibrium. Using the method described previously,[12] we obtained barriers to rotation $\Delta G^{\ddagger}_{syn} = 92$ kJ mol^{-1} and $\Delta G^{\ddagger}_{anti} = 89$ kJ mol^{-1}. These correspond to a half-life for epimerisation of 13 h at 10 °C, or approximately 3 h at 20 °C, assuming $\Delta G^{\ddagger}$ remains constant with temperature. This barrier, while it is about 15–20 kJ mol^{-1} lower than the barrier to epimerisation of the isomeric 2-substituted alcohols,[12] is sufficiently large that, at least for **4a**–**c** we can be confident that the product ratios still represent closely the kinetically controlled product ratio.

We determined the equilibrium ratios of *syn*- and *anti*-**4a**–**c** by allowing solutions of the mixtures of diastereoisomers to stand in $CDCl_3$ until there was no further change in composition of the mixture. This was not possible for **2a**–**c** because they very rapidly cyclised to **5** under these conditions, and we cannot be sure that the products **2** have not already reached thermodynamic equilibrium. The equilibrated ratios of the diastereoisomers of **4** are given in the final column of Table 1. Apart from **4a** made with MeLi, it turns out that all the reactions of **3** give product ratios close to the equilibrium value. Our ability to obtain a ratio for **4a** significantly different from the equilibrium ratio, adds to our confidence that the work-up conditions avoid total equilibration of **4a**–**c**, but we still cannot be certain that the ratios of **2a**–**c** are under purely kinetic control.

The strong thermodynamic preference for one atropisomer mirrors results reported for binaphthyls bearing chiral 8-substituents,[10,27] and is a further result of the proximity in space of the 1- and 8-substituents. The stereochemical effect of this strong *peri*-interaction is observable in unsymmetrically substituted 1,8-diaminonaphthalenes.[28] Its effect on reactivity is even more widespread: this same class of compounds (the "proton sponges") owe their powerful basicity to non-bonded 1,8-interactions between nitrogen lone pairs,[29] and similar effects are apparent in naphthalenes bearing sulfur or selenium atoms in the 1- and 8-positions.[30,31] Non-bonded interactions force 1,8-di-*tert*-butylnaphthalene to adopt a twisted structure[32] with the two *tert*-butyl groups staggered by 40° and are the cause of the remarkably high reactivity of the aromatic rings of 1,8-disubstituted naphthalenes toward reduction,[33,34] and of the unreactivity of trigonal 8-substituents towards nucleophilic attack.[24,35] The crystal structure of *syn*-**4c** (Fig. 1) displays properties consistent with severe repulsion between the *peri*-substituents. The dihedral angle between the two *peri* C–C bonds is 21°, and the bonds are splayed out in the plane of the ring. The amide is twisted away from perpendicularity to avoid Ph–N*i*-Pr$_2$ interactions.†

Conversely, when the two *peri*-substituents are capable of a bonding interaction, that interaction is highly favoured. 1,8-Cyclisations are particularly rapid[24,35] – hence the instability of **2** towards lactonisation. Dunitz and co-workers[36] observed *peri*-bonding interactions even between poorly nucleophilic and electrophilic groups, and we have shown that these interactions slow the racemisation of some 8-substituted-1-naphthamides very significantly.[26] The attractive *peri* π–π interactions[37,38] between electron-rich and -poor aryl substituents have been proposed as the basis for the development of new non-linear optic devices.[39]

† Using Dunitz's notation[36] to describe the geometry of the *peri*-disubstituted system, which we have employed before,[26] $\theta_1 = 115.9°$, $\theta_2 = 122.5°$, $\theta_3 = 123.0°$, $\theta_4 = 118.2°$, $\alpha = 74.0°$, $\beta = 49.9°$, $\gamma = 68.7°$, $\delta = 68.8°$.

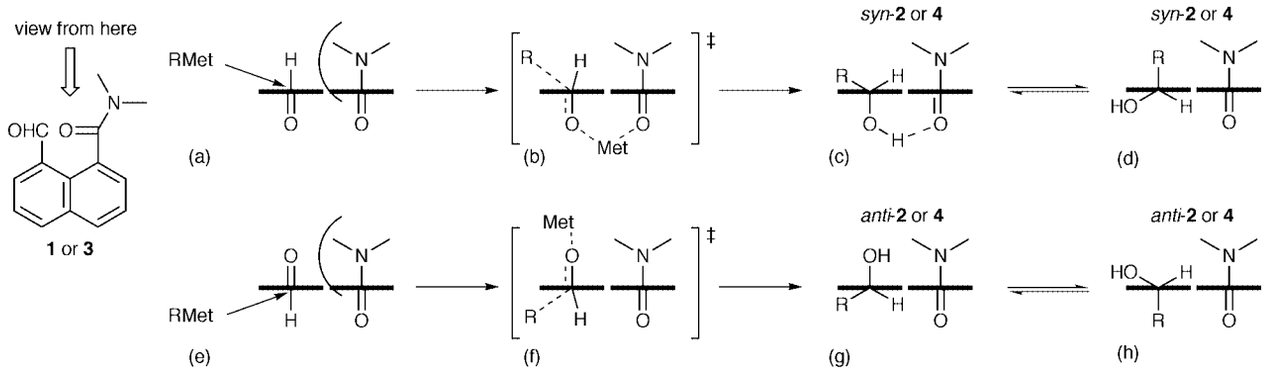


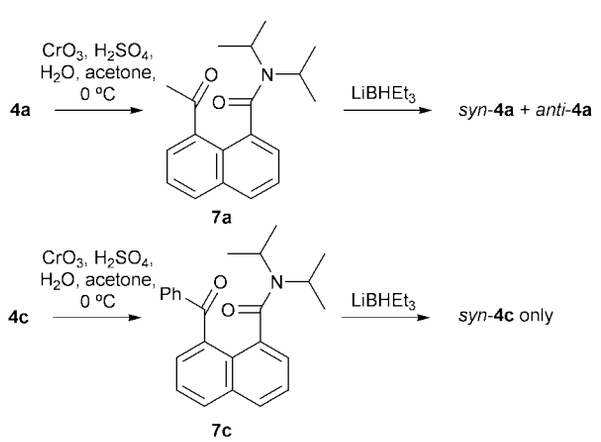
Fig. 2 Stereoselectivity in the attack of nucleophiles on aldehydes **1** and **3**.

In contrast with the reactions of 2-formyl substituted 1-naphthamides, in which the sense of stereoselectivity is highly dependent on the metal, it is almost certain that the sense of the stereoselectivity is the same in every reaction of Table 1, irrespective of the organometallic employed. Steric hindrance in the starting material **2** or **4** means the formyl group must twist out of the plane of the naphthalene ring.[19,20] A suggested transition state for the formation of the *syn*-diastereoisomer is shown in Fig. 2(b): the organometallic approaches from the least hindered direction, away from the amide, and as the new bond forms, only the H atom of the aldehyde has to move closer to the amide NR_2. The corresponding transition state (f) for the *anti*-isomer places the new O–Met bond *syn* to the NR_2 group. *syn*-Selectivity may also be favoured by chelation, which can stabilise (b) but not (f). In one experiment, we added HMPA to the reaction of MeLi and **3**, and indeed noted increased *syn*-selectivity, but it is not clear whether this arises from disruption of chelated complexes or simply from a change in the aggregation state of the nucleophile.

We have no clear explanation for the thermodynamic preference for *syn* over *anti*: it seems likely that conformers (c) and (d) or (g) and (h) are populated for either *syn*- or *anti*-product. But the most stable are probably (c) and (h), since they have the most hindered site occupied by H. Conformer (c) may furthermore be stabilised by a hydrogen bond – this certainly corresponds closely to the conformation in the X-ray crystal structure, but we have no data on whether the *anti*-isomer is more favoured in hydrogen-bonding solvents.

Reduction of 8-acyl-1-naphthamides

Alcohols **4a** and **4c** were oxidised with Jones' reagent at 0 °C (higher temperatures led to significant formation of the lactones **5**) to give the 8-acyl-1-naphthamides **7a** and **7c**. These ketones were reduced using $LiBHEt_3$ (found to be the best reagent for selective reduction of 2-acyl-1-naphthamides[1,40]) back to mixtures of the alcohols **4a** and **4c** (Scheme 2). As with



Scheme 2 Stereoselective reduction of ketones **7**.

all other reactions producing **2c** or **4c**, the reduction of **7c** gave solely **4c** in 90% yield. The reduction of **7a** was, by contrast, almost entirely unselective, giving a 54 : 46 mixture of *syn*- : *anti*-**4a** in 91% yield.

While epimerisation towards thermodynamic equilibrium may still be playing a role in determining product mixtures, kinetic selectivity of this sort can be easily explained again by considering conformation in the transition states leading to *syn*- and *anti*-**4** (Fig. 3). This time, we presume the size of R means (c) and (d) are favoured over (a) and (b), but more so for R = Ph than R = Me, for which (b) and (d) are approximately equally stable.

Conclusion

Both kinetic stereoselectivity and thermodynamically-controlled equilibration favour the formation of *syn* atropisomeric alcohols from nucleophilic additions to 8-acyl substituted naphthamide. However, the products are unstable with respect to epimerisation of the products and cyclisation to lactones.

Experimental

General experimental details have been described before.[1]

(S_a*,1′*S**)- and (S_a*,1′*R**)-*N*,*N*-Diethyl-8-(1′-hydroxyethyl)-1-naphthamide, *anti*-2a and *syn*-2a

A solution of aldehyde **1**[24] (81 mg, 0.32 mmol) in THF (2.0 ml) at −78 °C under an atmosphere of nitrogen was treated with methyllithium (0.27 ml; 1.4 M solution in ether) and stirred for 3 hours. The reaction mixture was then treated with more methyllithium (0.27 ml, 1.4 M solution in ether), stirred for a further 10 minutes, treated with saturated aqueous ammonium chloride (5 ml) and allowed to warm to ambient temperature. After extraction with dichloromethane (4 × 5 ml) the combined organic extracts were dried ($MgSO_4$), filtered, concentrated under reduced pressure to afford a mixture of the *alcohols anti*-**2a** and *syn*-**2a** (66 mg, 76%) as a brown oil [18 (*anti*-**2a**): 82 (*syn*-**2a**) by ^{1}H NMR] containing trace amount of lactone **5a**, ν_{max} (film)/cm^{-1} 3406, 3055, 2978, 2933, 2875, 2850, 1607; δ_H(300 MHz, $CDCl_3$) 7.80 (1H, d, *J* 8.1, ArH), 7.73 (2H, d, *J* 7.7, ArH), 7.45 (1H, t, *J* 7.6, ArH), 7.36 (1H, t, *J* 7.3, ArH), 7.24 (1H, d, *J* 7.0, ArH), 5.51 (1H, q, *J* 6.0, $CHOH^{minor}$), 5.28 (1H, q, *J* 6.5, $CHOH^{major}$), 3.78 (1H, m, $CH_AH_BCH_3^{major}$), 3.42 (1H, m, $CH_AH_BCH_3^{major}$), 3.25 (2H, q, *J* 7.0, $CH_2CH_3^{major}$), 3.06 (1H, m, $CH_AH_BCH_3^{minor}$), 1.55 (3H, d, *J* 6.3, $CH(OH)CH_3^{major}$), 1.50 (3H, d, *J* 6.1, $CH(OH)CH_3^{minor}$), 1.28 (3H, t, *J* 7.1, $CH_2CH_3^{major}$), 1.05 (3H, t, *J* 7.1, $CH_2CH_3^{major}$), 0.91 (3H, t, *J* 7.1, $CH_2CH_3^{minor}$); δ_C^{major}(75 MHz, $CDCl_3$) 173.9, 140.7, 135.1, 132.6, 130.7, 129.1, 128.2, 126.2, 125.5, 125.3, 124.1, 63.8, 43.5, 39.4, 21.8, 13.3 and 11.7; *m*/*z* (CI) 272 (15%, M + H$^+$), 254 (65%, M − OH) and 74 (100%) (Found: M$^+$, 271.1570. $C_{17}H_{21}NO_2$ requires *M*, 271.1572).

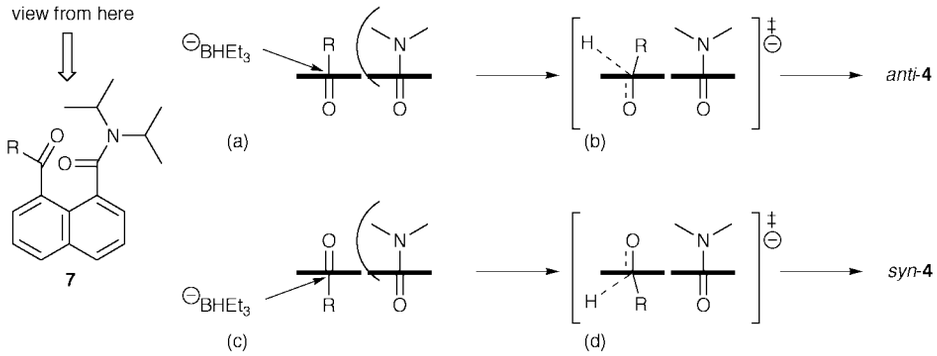


Fig. 3 Stereoselectivity in the attack of nucleophiles on ketones **7**.

Alternatively, a solution of aldehyde **1** (81 mg, 0.32 mmol) in THF (2.0 ml) was treated with methylmagnesium bromide (0.13 ml, 0.38 mmol; 3 M solution in THF), stirred for 3 hours, and treated with more methylmagnesium bromide (0.13 ml, 0.38 mmol; 3 M solution in THF). Work-up in the usual manner afforded *alcohols* **2a** (72 mg, 83%) as a mixture of diastereoisomers [17 (*anti*-**2a**): 83 (*syn*-**2a**) by ^{1}H NMR] containing trace amount of lactone **5a**.

(*S*$_a$*,1′*S**)- and (*S*$_a$*,1′*R**)-*N*,*N*-Diethyl-8-(1′-hydroxypentyl)-1-naphthamide, *anti*-2b and *syn*-2b

In the same way, a solution of aldehyde **1** (85 mg, 0.33 mmol) in THF (2.0 ml) at −78 °C under an atmosphere of nitrogen was treated with *n*-butyllithium (0.26 ml, 0.42 mmol; 1.6 M solution in hexanes), stirred for 3 hours, treated with more *n*-butyllithium (0.26 ml, 0.42 mmol; 1.6 M solution in hexanes) and stirred for a further 10 minutes. Work up in the usual manner gave the crude product as a brown oil. The product was dried under high vacuum overnight to afford the *alcohols anti*-**2b** and *syn*-**2b** (70 mg, 68%) as a brown oil and as a mixture of diastereoisomers [11 (*anti*-**2b**): 89 (*syn*-**2b**) by ^{1}H NMR] containing trace amounts of lactone **5b**, ν_{max} (film)/cm^{-1} 3426, 3053, 2956, 2934, 2870, 1721, 1690, 1607; δ_H(300 MHz, $CDCl_3$) 7.81 (1H, d, *J* 8.1, ArH), 7.72 (1H, d, *J* 8.1, ArH), 7.67 (1H, d, *J* 7.3, ArH), 7.45 (1H, t, *J* 7.8, ArH), 7.35 (1H, t, *J* 7.4, ArH), 7.24 (1H, d, *J* 7.0, ArH), 5.32 (1H, br m, C*H*OH^{minor}), 4.94 (1H, br m, C*H*OH^{major}), 4.35 (1H, br s, OH^{major}), 3.76 (1H, m, NCH_AH$_B$CH$_3$^{major}), 3.45 (1H, m, NCH$_A$$H_BCH_3$^{major}), 3.36 (1H, m, NCH_AH$_B$CH$_3$^{major}), 3.27 (1H, m, NCH$_A$$H_BCH_3$^{major}), 2.07 (1H, m, CH_AH$_B$(CH$_2$)$_2$CH$_3$^{major}), 1.80 (1H, m, CH$_A$$H_B$(CH$_2$)$_2$-CH$_3$^{major}), 1.5–1.0 (4H, m, CH$_2$(CH_2)$_2$CH$_3$^{major}), 1.30 (3H, t, *J* 7.1, NCH$_2$CH_3^{major}), 1.11 (3H, t, *J* 7.1, NCH$_2$CH_3^{major}), 0.81 (3H, t, *J* 7.0, (CH$_2$)$_3$CH_3^{major}); δ_C^{major}(75 MHz, $CDCl_3$) 174.0, 140.0, 135.2, 132.6, 130.8, 128.9, 128.9, 126.3, 125.9, 125.5, 124.0, 68.4, 43.5, 39.4, 35.3, 29.1, 22.7, 14.0, 13.4 and 11.9; *m*/*z* (CI) 314 (1%, M + H$^+$), 296 (2%, M − OH), 241 (7%, M − NEt$_2$) and 74 (100%); *m*/*z* (EI) 313 (0.05%, M$^+$) and 49 (100%) (Found: M$^+$, 313.2040. $C_{20}H_{27}NO_2$ requires *M*, 313.2042).

Alternatively, a solution of aldehyde **1** (67 mg, 0.26 mmol) in THF (2.0 ml) was treated with *n*-butylmagnesium chloride (0.16 ml, 0.32 mmol; 2 M solution in THF), stirred for 3 hours, and treated with more *n*-butylmagnesium bromide (0.16 ml, 0.32 mmol; 2 M solution in THF). Work-up in the usual manner afforded *alcohols* **2b** (52 mg, 64%) as a mixture of diastereoisomers [17 (*anti*-**2b**): 83 (*syn*-**2b**) by ^{1}H NMR] containing trace amount of lactone **5b**.

(*S*$_a$*,1′*R**)-*N*,*N*-Diethyl-8-[hydroxy(phenyl)methyl]-1-naphthamide *syn*-2c

In the same way, a solution of aldehyde **1** (83 mg, 0.33 mmol) in THF (2.0 ml) at −78 °C under an atmosphere of nitrogen was treated with phenyllithium (0.20 ml, 0.36 mmol; 1.8 M solution in cyclohexane–diethyl ether), stirred for 3 hours, treated with more phenyllithium (0.20 ml, 0.36 mmol; 1.8 M solution in cyclohexane–diethyl ether) and stirred for a further 10 minutes. Work-up in the usual manner afforded the *alcohol syn*-**2c** (76 mg, 69%) as a brown oil and as a single diastereoisomer (by ^{1}H NMR) containing a trace amount of lactone **5c**, ν_{max} (film)/cm^{-1} 3426, 3410, 3060, 3030, 2977, 2930, 2874, 2850, 1603; δ_H(300 MHz, $CDCl_3$) 7.83 (1H, d, *J* 8.1, ArH), 7.69 (1H, d, *J* 8.1, ArH), 7.45–7.15 (8H, m, ArH), 7.10 (1H, d, *J* 7.3, ArH), 6.35 (1H, s, C*H*OH), 3.66 (1H, m, CH_AH$_B$CH$_3$), 3.50 (1H, m, CH$_A$$H_BCH_3$), 3.36 (1H, m, C$H_AH_BCH_3$), 3.27 (1H, m, CH$_A$$H_B$-CH$_3$), 1.19 (3H, t, *J* 7.1, CH$_2$CH_3), 1.10 (3H, t, *J* 7.2, CH$_2$CH_3); δ_C(75 MHz, $CDCl_3$) 174.0, 143.2, 141.1, 135.0, 132.5, 130.9, 129.6, 129.1, 128.7, 128.0, 126.7, 126.6, 126.2, 125.7, 124.2, 70.4, 43.7, 39.6, 13.6 and 11.9; *m*/*z* (CI) 334 (M + H$^+$, 3%), 316 (3%, M − OH), 261 (4%, M − NEt$_2$) and 74 (100%); *m*/*z* (EI) 333 (1%, M$^+$), 316 (1%, M − OH), 261 (9%, M − NEt$_2$) and 49 (100%) (Found: M, 333.1734. $C_{22}H_{23}NO_2$ requires *M*, 333.1729).

Alternatively, a solution of aldehyde **1** (83 mg, 0.33 mmol) in THF (2.0 ml) was treated with phenylmagnesium bromide (0.39 ml, 0.39 mmol; 1 M solution in THF), stirred for 3 hours, and treated with more phenylmagnesium bromide (0.39 ml, 0.39 mmol; 1 M solution in THF). Work-up in the usual manner afforded *alcohol syn*-**2c** (85 mg, 77%) as a single diastereoisomer (by ^{1}H NMR) containing trace amounts of lactone **5c**.

(*S*$_a$*,1′*S**)- and (*S*$_a$*,1′*R**)-*N*,*N*-Diisopropyl-8-(1′-hydroxyethyl)-1-naphthamide, *anti*-4a and *syn*-4a

A solution of aldehyde **3** (176 mg, 0.62 mmol) in THF (3 ml) at −78 °C under an atmosphere of nitrogen was treated with methyllithium (0.50 ml, 0.81 mmol; 1.6 M solution in diethyl ether) dropwise, stirred for a further 3 hours, quenched with saturated aqueous ammonium chloride (5 ml) and allowed to warm to ambient temperature. The aqueous was extracted with dichloromethane (4 × 5 ml) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product as an oil. ^{1}H NMR of the crude product showed the atropisomers to be present in a ratio of 24 (*anti*-**4a**): 76 (*syn*-**4a**). Purification by flash chromatography [4:1 petrol–EtOAc] afforded a mixture of the *alcohols anti*-**4a** and *syn*-**4a** (184 mg, 99%) as a white solid, mp 90–92 °C; R_f 0.39 [2:1 petrol (bp 40–60 °C)–EtOAc]; ν_{max} (film)/cm^{-1} 3426, 2972, 2932, 1605; δ_H(300 MHz, $CDCl_3$) 7.97–7.80 (3H, m, ArH), 7.57 (1H, m, ArH), 7.47 (1H, m, ArH), 7.29 (1H, m, ArH), 5.81 (1H, q, *J* 6.0, C*H*OH^{minor}), 5.58 (1H, dq, *J* 3.7, 6.5, C*H*OH^{major}), 4.67 (1H, d, *J* 3.7, CHO*H*^{major}), 4.01 (1H, septet, *J* 6.7, NCH^{major}), 3.78 (1H, septet, *J* 6.6, NCH^{minor}), 3.67 (1H, m, NCH^{major}), 1.71 (6H, d, *J* 6.7, 2 × CH$_3$^{major}), 1.69 (3H, m, CH$_3$^{minor}), 1.67 (3H, m, CH$_3$^{minor}), 1.65 (3H, m, CH$_3$^{minor}), 1.24 (3H, d, *J* 6.6, CH$_3$^{major}), 1.19 (3H, d, *J* 6.7, CH$_3$^{minor}), 1.18 (3H, d, *J* 6.7, CH$_3$^{major}), 1.13 (3H, d, *J* 6.6, CH$_3$^{major}); δ_C(75 MHz, $CDCl_3$) 173.8^{major}, 171.8^{minor}, 143.2, 140.4, 135.2, 134.7, 134.0,

130.4, 129.9, 129.1, 128.7, 128.1, 126.2, 126.0, 125.0, 124.8, 124.5, 124.3, 66.4, 63.5, 51.6, 51.0, 46.3, 45.9, 26.0, 21.0, 20.3, 20.2, 20.2, 20.1, 19.9, 19.7 and 19.4; *m*/*z* (CI) 300 (97%, M + H^+) and 282 (100%, M − OH); *m*/*z* (EI) 299 (3%, M^+) and 49 (100%) (Found: M^+, 299.1891. $C_{19}H_{25}NO_2$ requires *M*, 299.1885).

Alternatively, a solution of aldehyde **3** (67 mg, 0.22 mmol) in THF (1.5 ml) was treated with methylmagnesium bromide (0.39 ml, 0.39 mmol; 1 M solution in THF), stirred for 3.5 hours and quenched with saturated aqueous ammonium chloride (5 ml). After work-up in the usual manner, ^{1}H NMR of the crude product showed the atropisomers to be present in a ratio of 17 (*anti*-**4a**): 83 (*syn*-**4a**). Purification by flash chromatography [4:1 petrol–EtOAc] afforded the *alcohols* **4a** (52 mg, 81%) as a white solid.

Alternatively, a solution of aldehyde **3** (110 mg, 0.39 mmol) and HMPA (0.35 ml, 2.02 mmol) in THF (3 ml) at −78 °C under an atmosphere of nitrogen was treated with methyllithium (0.32 ml, 0.51 mmol; 1.6 M solution in diethyl ether) dropwise, stirred for a further 4 hours, quenched with saturated aqueous ammonium chloride (5 ml) and allowed to warm to ambient temperature. The aqueous was extracted with diethyl ether (4 × 5 ml) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product as an oil. ^{1}H NMR of the crude product showed the atropisomers to be present in a ratio of 24 (*anti*-**4a**): 76 (*syn*-**4a**). Purification by flash chromatography [4:1 petrol–EtOAc] afforded the alcohols **4a** (184 mg, 99%) as a white solid.

Alternatively, a solution of ketone **7a** (23 mg, 0.08 mmol) in THF (1.5 ml) at −78 °C under an atmosphere of nitrogen was treated with Super Hydride® (0.20 ml, 0.20 mmol; 1 M solution in THF) dropwise, stirred for a further 5 hours, warmed to ambient temperature and added to a solution of 30% hydrogen peroxide (1 ml) and 10% aqueous sodium hydroxide (1 ml). The aqueous was extracted with dichloromethane (4 × 5 ml) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product as an oil. ^{1}H NMR of the crude product showed the atropisomers to be present in a ratio of 46 (*anti*-**4a**): 54 (*syn*-**4a**). Purification by flash chromatography [4:1 petrol–EtOAc] afforded the *alcohols* **4a** (21 mg, 91%) as a white solid.

(*S*$_a$*,1′*S**)- and (*S*$_a$*,1′*R**)-*N*,*N*-Diisopropyl-8-(1′-hydroxypentyl)-1-naphthamide, *anti*-4b and *syn*-4b

By the method described above, a solution of aldehyde **3** (66 mg, 0.23 mmol) in THF (1.5 ml) was treated with *n*-butyllithium (0.18 ml; 1.6 M solution in hexanes), stirred for 3 hours and quenched with saturated aqueous ammonium chloride (5 ml). Work-up in the usual manner gave the crude product as a brown oil. ^{1}H NMR of the crude product showed the atropisomers to be present in a ratio of 10 (*anti*-**4b**): 90 (*syn*-**4b**). Purification by flash chromatography [4:1 petrol–EtOAc] afforded a mixture of the *alcohols anti*-**4b** and *syn*-**4b** (62 mg, 79%) as a colourless oil, R_f 0.47 [2:1 petrol–EtOAc]; ν_{max} (film)/cm^{-1} 3428, 3053, 2961, 2934, 2871, 1606; δ_H(300 MHz, $CDCl_3$) 7.79 (1H, dd, *J* 8.2 and 1.1, ArH), 7.72 (1H, d, *J* 8.1, ArH), 7.66 (1H, d, *J* 7.3, ArH), 7.45 (1H, t, *J* 7.7, ArH), 7.35 (1H, t, *J* 7.1, ArH), 7.19 (1H, dd, *J* 7.3 and 1.2, ArH), 5.53 (1H, dd, *J* 8.4 and 3.3, C*H*OH^{minor}), 5.10 (1H, m, C*H*OH^{major}), 4.65 (1H, d, *J* 3.2, OH^{major}), 3.98 (1H, septet, *J* 6.6, NCH^{major}), 3.57 (1H, septet, *J* 6.9, NCH^{major}), 2.14 (1H, m, CH_AH$_B$(CH$_2$)$_2$CH$_3$^{major}), 1.83 (1H, m, CH$_A$$H_B$(CH$_2$)$_2CH_3$^{major}), 1.62 (3H, d, *J* 6.9, NCHCH_3^{major}), 1.53 (3H, d, *J* 6.7, NCHCH_3^{major}), 1.5–1.0 (4H, m, CH$_2$(CH_2)$_2$CH$_3$^{major}), 1.15 (3H, d, *J* 6.6, NCHCH_3^{major}), 1.10 (3H, d, *J* 6.7, NCHCH_3^{major}), 0.84 (3H, t, *J* 7.3, CH$_2$(CH$_2$)$_2$-CH_3^{major}); δ_C^{major}(75 MHz, $CDCl_3$) 173.8, 140.1, 135.3, 134.0, 130.5, 129.0, 128.7, 126.3, 125.6, 124.7, 124.1, 68.4, 51.6, 46.3, 35.3, 29.4, 23.1, 20.5, 20.2, 20.1, 20.0 and 14.0; *m*/*z* (CI) 342 (46%, M + H^+) and 324 (100%, M − OH); *m*/*z* (EI) 341 (5%, M^+), 324 (11%, M − OH) and 86 (100%) (Found: M^+, 341.2361. $C_{22}H_{31}NO_2$ requires *M*, 341.2355).

Alternatively, a solution of aldehyde **3** (47 mg, 0.17 mmol) in THF (1.1 ml) was treated with *n*-butylmagnesium chloride (0.10 ml, 0.20 mmol; 2 M solution in THF), stirred for 3 hours and quenched with saturated aqueous ammonium chloride (5 ml). Work up in the usual manner gave the crude product as a brown oil. ^{1}H NMR of the crude product showed the atropisomers to be present in a ratio of 25 (*anti*-**4b**): 75 (*syn*-**4b**). Purification by flash chromatography [4:1 petrol–EtOAc] afforded a mixture of the *alcohols* **4b** (35 mg, 61%) as a colourless oil.

(*S*$_a$*,1′*R**)-*N*,*N*-Diisopropyl-8-[1′-hydroxy(phenyl)methyl]-1-naphthamide *syn*-4c

In the same way, a solution of aldehyde **3** (47 mg, 0.17 mmol) in THF (1.1) was treated with phenyllithium (0.11 ml, 0.20 mmol; 1.8 M solution in cyclohexane–diethyl ether), stirred for 3 hours and quenched with saturated aqueous ammonium chloride (5 ml). Work up in the usual manner gave the crude product as a brown oil. ^{1}H NMR of the crude product showed the presence of only one diastereoisomer. Purification by flash chromatography [4:1 petrol–EtOAc] afforded the *alcohol syn*-**4c** (33 mg, 55%) as an off-white solid. Recrystallisation from ethyl acetate by slow evaporation afforded the product as colourless blades, ν_{max} (film)/cm^{-1} 3426, 3054, 2963, 2934, 2871, 1606; δ_H(300 MHz, $CDCl_3$) 7.94 (1H, dd, *J* 8.2 and 1.2, ArH), 7.73 (1H, dd, *J* 8.1 and 1.1, ArH), 7.42–7.16 (8H, m, ArH), 7.15 (1H, dd, *J* 7.4 and 1.4, ArH), 6.50 (1H, s, C*H*OH), 5.29 (1H, s, OH), 4.19 (1H, septet, *J* 6.7, NCH), 3.67 (1H, septet, *J* 6.9, NCH), 1.67 (3H, d, *J* 6.9, CH_3), 1.63 (3H, d, *J* 6.9, CH_3), 1.30 (3H, d, *J* 6.5, CH_3), 1.14 (3H, d, *J* 6.7, CH_3); δ_C(75 MHz, $CDCl_3$) 173.9, 143.1, 141.4, 135.2, 133.8, 130.6, 129.6, 129.1, 128.6, 127.9, 126.6, 126.2, 124.8, 124.3, 70.2, 51.8, 46.4, 29.6, 20.4, 20.2, 20.7 and 19.8.

Alternatively, by the method used for the reduction of **7a**, a solution of ketone **7c** (51 mg, 0.14 mmol) in THF (2 ml) and Super Hydride® (0.28 ml, 0.28 mmol; 1 M solution in THF) gave a crude product as an oil. ^{1}H NMR of the crude product showed a single atropisomer, *anti*-**4c**. Purification by flash chromatography [2:1 petrol–EtOAc] gave the *alcohol anti*-**4c**(46 mg, 90%) as a white solid.

3-Methyl-1*H*,3*H*-benzo[*de*]isochromen-1-one 5a

Alcohols **2a** (56 mg, 0.21 mmol) were eluted through silica gel [2:1 petrol (bp 40–60 °C)–EtOAc] to give *the lactone* **5a** (39 mg, 94%) as a sticky pale yellow solid, λ_{max}/nm (ε_{max}) (CH_2Cl_2) 238 (19940), 314 (5647); ν_{max} (film)/cm^{-1} 3238, 3216, 1719; δ_H(300 MHz, $CDCl_3$) 8.46 (1H, dd, *J* 7.1 and 1.1, ArH), 8.17 (1H, dd, *J* 8.4 and 1.1, ArH), 7.91 (1H, d, *J* 8.2, ArH), 7.70 (1H, dd, *J* 8.1 and 7.3, ArH), 7.62 (1H, dd, *J* 8.2 and 7.3, ArH), 7.43 (1H, *J* 7.1, ArH), 6.05 (1H, q, *J* 6.7, C*H*CH$_3$), 1.86 (3H, d, *J* 6.7, CH_3); δ_C(75 MHz, $CDCl_3$) 164.1, 133.5, 132.4, 132.1, 129.1, 127.5, 126.8, 126.5, 126.4, 122.1, 120.2 and 24.5; *m*/*z* (CI) 199 (100%, M + H^+) and 183 (M − CH_3); *m*/*z* (EI) 198 (31%, M^+), 183 (99%, M − CH_3) and 127 (100%) (Found: M^+, 198.0680. $C_{13}H_{10}O_2$ requires *M*, 198.0681).

3-Butyl-1*H*,3*H*-benzo[*de*]isochromen-1-one 5b

Alcohols **2b** (42 mg, 0.13 mmol) were eluted through silica gel [2:1 petrol–EtOAc] to give *the lactone* **5b** (30 mg, 97%) as a pale yellow solid, R_f 0.51 [2:1 petrol–EtOAc]; ν_{max} (film)/cm^{-1} 3057, 2956, 2931, 2870, 2861, 1758, 1729; δ_H(300 MHz, $CDCl_3$) 8.44 (1H, dd, *J* 7.2 and 1.1, ArH), 8.14 (1H, dd, *J* 8.4 and 1.1, ArH), 7.88 (1H, d, *J* 8.2, ArH), 7.68 (1H, dd, *J* 8.2 and 7.3, ArH), 7.60 (1H, dd, *J* 8.2 and 7.1, ArH), 7.40 (1H, d, *J* 7.1, ArH), 5.92 (1H, t, *J* 5.9, C*H*(CH$_2$)$_3$CH$_3$), 2.07 (2H, m, CHCH_2(CH$_2$)$_2$CH$_3$), 1.60–1.24 (4H, m, CHCH$_2$(CH_2)$_2$CH$_3$), 0.90 (3H, t, *J* 7.3, CH_3); δ_C(75 MHz, $CDCl_3$) 164.3, 133.5, 132.1, 131.3, 128.9, 127.9,

126.7, 126.4, 126.3, 122.3, 81.1, 39.0, 26.4, 22.3 and 13.8; *m/z* (CI) 241 (100%, M + H^+) and 183 (3%, M − C_4H_9); *m/z* (EI) 240 (14%, M^+) and 183 (100%, M − C_4H_9) (Found: M^+, 240.1146. $C_{16}H_{16}O_2$ requires *M*, 240.1150).

3-Phenyl-1*H*,3*H*-benzo[*de*]isochromen-1-one 5c

Alcohol *syn*-**2c** (63 mg, 0.19 mmol) was eluted through silica gel [2 : 1 petrol–EtOAc] to give the *lactone* **5c**[41] (47 mg, 95%) as a pale yellow solid, ν_{max} (film)/cm^{-1} 3058, 3033, 2972, 2928, 2872, 2851, 1725; δ_H(300 MHz, $CDCl_3$) 8.41 (1H, dd, *J* 7.3 and 1.1, ArH), 8.10 (1H, dd, *J* 8.4 and 1.0, ArH), 7.82 (1H, d, *J* 8.4, ArH), 7.63 (1H, dd, *J* 8.2 and 7.4, ArH), 7.44 (1H, m, ArH), 7.30 (5H, m, ArH), 7.12 (1H, d, *J* 7.1, ArH), 6.77 (1H, s, CHPh); δ_C(75 MHz, $CDCl_3$) 167.2, 139.9, 133.7, 130.5, 129.5, 128.9, 128.8, 128.4, 127.7, 127.2, 126.5, 124.5 and 120.4; *m/z* (CI) 216 (100%, M + H^+); *m/z* (EI) 260 (29%, M^+) and 86 (100%) (Found: M^+, 260.0835. $C_{18}H_{12}O_2$ requires *M*, 260.0837).

N,*N*-Diisopropyl-8-acetyl-1-naphthamide 7a

A solution of alcohols **4a** (161 mg) in acetone (5.5 ml) at 0 °C was treated with Jones reagent (0.87 ml of a solution of CrO_3 (2.5 g): conc. H_2SO_4 (2 ml): water (8 ml); 1.71 mmol) and stirred for a further 45 minutes. The reaction mixture was added to a solution of saturated aqueous sodium hydrogen carbonate (50 ml) and extracted with ethyl acetate (4 × 30 ml). The combined organic extracts were washed with water (50 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel [3 : 1 petrol–EtOAc] afforded the *ketone* **7a** (115 mg, 72%) as a white solid, λ_{max}/nm (ε_{max}) (CH_2Cl_2) 232 (22600), 294 (6111); R_f 0.39 [2 : 1 petrol–EtOAc]; ν_{max} (film)/cm^{-1} 2996, 2978, 2928, 1691, 1621; δ_H(300 MHz, $CDCl_3$) 7.81 (1H, d, *J* 8.1, ArH), 7.76 (1H, d, *J* 8.0, ArH), 7.48 (1H, d, *J* 7.0, ArH), 7.41–7.30 (3H, m, ArH), 4.18 (1H, septet, *J* 6.6, NCH), 3.46 (1H, septet, *J* 6.9, NCH), 2.63 (3H, s, $COCH_3$), 1.54 (3H, d, *J* 6.7, NCHCH_3), 1.41 (3H, d, *J* 6.7, NCHCH_3), 1.36 (3H, d, *J* 6.6, NCHCH_3), 1.22 (3H, d, *J* 6.6, NCHCH_3); δ_C(75 MHz, $CDCl_3$) 203.6, 171.5, 140.0, 135.3, 135.2, 131.1, 129.8, 126.8, 125.4, 125.1, 124.9, 124.5, 51.5, 45.8, 29.7, 20.8, 20.7 and 20.3; *m/z* (CI) 298 (100%, M + H^+), 254 (4%, M − $COCH_3$) and 197 (11%, M − N^iPr_2); *m/z* (EI) 254 (10%, M − $COCH_3$) and 197 (49%, M − N^iPr_2) (Found: M + H^+, 298.1806. $C_{19}H_{23}NO_2$ requires *M* + H, 298.1807).

N,*N*-Diisopropyl-8-benzoyl-1-naphthamide 7c

In the same way, a solution of alcohols **4c** (175 mg, 0.49 mmol) in acetone (5 ml) at 0 °C was treated with Jones' reagent (0.78 ml). Work-up and purification by flash chromatography [3 : 1 petrol–EtOAc] afforded the *ketone* **7c** (140 mg, 81%) as a white solid, mp 143–145 °C, R_f 0.35 [3 : 1 petrol–EtOAc]; ν_{max} (film)/cm^{-1} 3056, 2973, 2930, 2876, 1663, 1624; δ_H(300 MHz, $CDCl_3$) 8.1–7.9 (5H, m, ArH), 7.7–7.4 (6H, m, ArH), 4.36 (1H, septet, *J* 6.6, NCH), 3.50 (1H, septet, *J* 6.9, NCH), 1.58 (3H, d, *J* 6.6, CH_3), 1.40 (3H, d, *J* 6.9, CH_3), 1.34 (3H, d, *J* 6.6, CH_3), 1.28 (3H, d, *J* 6.9, CH_3); δ_C(75 MHz, $CDCl_3$) 196.4, 171.0, 137.6, 137.3, 135.5, 135.4, 132.5, 131.1, 130.1, 129.8, 128.5, 127.9, 127.8, 125.3, 125.0, 124.1, 51.5, 45.7, 20.9, 20.9, 20.5 and 20.2; *m/z* (CI) 360 (100%, M + H^+) and 259 (86%, M − N^iPr_2); *m/z* (EI) 359 (6%, M^+) and 259 (100%, M − N^iPr_2) (Found: M^+, 359.1882. $C_{24}H_{25}NO_2$ requires *M*, 359.1885).

Crystal data for *syn*-4c ‡

Single crystals of *syn*-**4c** were grown from ethyl acetate, mounted on a thin glass fibre and transferred to the cold gas stream of the diffractometer. $C_{24}H_{27}NO_2$, $M = 361.47$, monoclinic, $a = 9.358(2)$, $b = 11.813(3)$, $c = 9.917(3)$ Å, $\beta = 114.44(2)°$, $U = 998.0(5)$ Å^3, $T = 123(1)$ K, space group $P2_1$ (no. 4), $Z = 2$, $D_c = 1.203$ g cm^{-3}, μ(Mo-Kα) = 0.076 mm^{-1}. Data collected on a Bruker AXS SMART CCD diffractometer, 10012 reflections measured, data truncated to 0.80 Å (θ_{max} 26.37°, 99.8% complete), 4011 reflections unique ($R_{int} = 0.0140$).[42] Final agreement factors for 252 parameters and 1 restraint gave $R_1 = 0.0279$, $wR^2 = 0.0734$ and GOF = 1.004 based on all 4011 data, final difference map +0.31 and −0.44 eÅ^{-3}.[43]

‡ CCDC reference number 207/414. See http://www.rsc.org/suppdata/p1/b0/b000670j for crystallographic files in .cif format.

Acknowledgements

We are grateful to the EPSRC and Roche Discovery (Welwyn) for a CASE award (to N. W.), to Zeneca for an unrestricted grant, to the Royal Society for an Equipment Grant, and to Dr Francis Wilson for helpful discussions.

References

1 See the two preceding papers: J. Clayden, N. Westlund, R. L. Beddoes and M. Helliwell, *J. Chem. Soc.*, *Perkin Trans. 1*, 2000, DOI: 10.1039/b000668h; J. Clayden, C. McCarthy, N. Westlund and C. S. Frampton, *J. Chem. Soc.*, *Perkin Trans. 1*, 2000, DOI: 10.1039/b000669f.
2 Preliminary communication: J. Clayden, N. Westlund and F. X. Wilson, *Tetrahedron Lett.*, 1999, **40**, 7883.
3 K. Fuji, T. Kawabata, A. Kuroda and T. Taga, *J. Org. Chem.*, 1995, **60**, 1914.
4 K. Fuji, X.-S. Yang, K. Tanaka, N. Asakawa and X.-J. Hao, *Tetrahedron Lett.*, 1996, **37**, 7373.
5 K. Fuji and T. Kawabata, *Tetrahedron Lett.*, 1998, **39**, 6323.
6 A. S. Cooke and M. M. Harris, *J. Chem. Soc.*, 1963, 2365.
7 Y. Badar, A. S. Cooke and M. M. Harris, *J. Chem. Soc.*, 1965, 1412.
8 M. M. Harris, R. Z. Mazengo and A. S. Cooke, *J. Chem. Soc.* (*C*), 1967, 2575.
9 A. S. Cooke and M. M. Harris, *J. Chem. Soc.* (*C*), 1967, 988.
10 A. I. Meyers and M. J. McKennon, *Tetrahedron Lett.*, 1995, **36**, 5869.
11 K. Fuji, M. Sakurai, N. Tohkai, A. Kuroda, T. Kawabata, Y. Fukuzawa, T. Kinoshita and T. Tada, *Chem. Commun.*, 1996, 1609.
12 A. Ahmed, R. A. Bragg, J. Clayden, L. W. Lai, C. McCarthy, J. H. Pink, N. Westlund and S. A. Yasin, *Tetrahedron*, 1998, **54**, 13277.
13 R. J. Clough and J. B. Roberts, *J. Am. Chem. Soc.*, 1976, **98**, 1018.
14 H. O. House and R. W. Bashe, *J. Org. Chem.*, 1965, **30**, 2942.
15 H. O. House, W. J. Campbell and M. Gall, *J. Org. Chem.*, 1970, **35**, 1815.
16 J. M. Zoltewicz, N. M. Maier and W. M. F. Fabian, *J. Org. Chem.*, 1996, **61**, 7018.
17 J. A. Zoltewicz, N. Maier and W. M. F. Fabian, *Tetrahedron*, 1996, **52**, 8703.
18 J. A. Zoltewicz, N. Maier and W. M. F. Fabian, *J. Org. Chem.*, 1998, **63**, 4985.
19 S. B. Bulgarevich, N. A. Ivanova, D. Y. Movshovich, A. Mannschreck, L. Kiessl, H. Zinner and C. Kiefl, *J. Mol. Struct.*, 1992, **265**, 417.
20 S. B. Bulgarevich, N. A. Ivanova, D. Y. Movshovich, A. Mannschreck and C. Kiefl, *J. Mol. Struct.*, 1994, **326**, 17.
21 A. Mannschreck, H. Zinner and N. Pustet, *Chimia*, 1989, **43**, 165.
22 C. Kiefl and A. Mannschreck, *Synthesis*, 1995, 1033.
23 A. J. Birch, M. Salahud-Din and D. C. C. Smith, *J. Chem. Soc.* (*C*), 1966, 523.
24 J. Clayden, C. S. Frampton, C. McCarthy and N. Westlund, *Tetrahedron*, 1999, **55**, 14161.
25 R. L. Gay and C. R. Hauser, *J. Am. Chem. Soc.*, 1967, **89**, 2297.
26 J. Clayden, C. McCarthy and M. Helliwell, *Chem. Commun.*, 1999, 2059.
27 A. I. Meyers and A. Price, *J. Org. Chem.*, 1998, 412.
28 J. P. H. Charmant, G. C. Lloyd Jones, T. M. Peakman and R. L. Woodward, *Tetrahedron Lett.*, 1998, **39**, 4233.
29 R. W. Alder, *Chem. Rev.*, 1989, **89**, 1215.
30 T. Fujii, H. Sakuragi and N. Furukawa, *Tetrahedron Lett.*, 1995, **36**, 8039.
31 W. Nakanishi, S. Hayashi and S. Toyota, *J. Org. Chem.*, 1998, **63**, 8790.
32 J. Handal, J. G. White, R. W. Franck, Y. H. Yuh and N. L. Allinger, *J. Am. Chem. Soc.*, 1977, **99**, 3345.

33 A. J. Kirby and J. M. Percy, *Tetrahedron*, 1988, **44**, 6911.
34 J. V. Popovici-Müller and T. A. Spencer, *Tetrahedron Lett.*, 1997, **38**, 8161.
35 A. J. Kirby and J. M. Percy, *Tetrahedron*, 1988, **44**, 6903.
36 W. B. Schweizer, G. Procter, M. Kaftory and J. D. Dunitz, *Helv. Chim. Acta*, 1978, **61**, 2783.
37 R. H. Mitchell, T. K. Vinod and G. W. Bushell, *J. Am. Chem. Soc.*, 1990, **112**, 3847.
38 F. Cozzi, M. Cinquini, R. Annunziata and J. S. Siegel, *J. Am. Chem. Soc.*, 1993, **115**, 5330.
39 A. Bahl, W. Grahn, S. Stadler, F. Feiner, G. Bowhill, C. Bräuchle, A. Reisner and P. G. Jones, *Angew. Chem.*, *Int. Ed. Engl.*, 1995, **34**, 1485.
40 J. Clayden, N. Westlund and F. X. Wilson, *Tetrahedron Lett.*, 1996, **37**, 5577.
41 M. Watanabe and V. Snieckus, *J. Am. Chem. Soc.*, 1980, **102**, 1457.
42 SMART, SAINT and SADABS area-detector control and integration software, Bruker AXS Inc., Madison, WI 53719, USA, 1997.
43 G. M. Sheldrick. SHELXTL, Bruker AXS Inc., Madison, WI 53719, USA, 1997.