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(*S*)-2-(Dibenzylamino)-3-phenylpropanal as a chiral auxiliary: a new strategy for the asymmetric synthesis of 2-substituted alcohols

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Abstract

The high levels of 1,2-stereocontrol observed in nucleophilic additions to (*S*)-2-(dibenzylamino)-3-phenylpropanal (available in three high-yielding steps from L-phenylalanine) can be converted to remote 1,4-stereocontrol by a stereospecific rearrangement if the nucleophile is a vinyl anion equivalent. Ozonolysis of the product followed by reductive work-up returns an enantiomerically pure 2-substituted alcohol, along with the (*S*)-2-(dibenzylamino)-3-phenylpropan-1-ol precursor to the starting aldehyde, which functions as a chiral auxiliary. The sequence provides a new strategy for the use of aldehydes as chiral auxiliaries in the synthesis of chiral alcohols bearing oxygen- or carbon-based 2-substituents.

1. Introduction

Two things are required of chiral auxiliaries above all else: they must induce high levels of stereocontrol and they must be straightforwardly removable. These two requirements can sit uneasily together, since straightforward removal usually means an amide or ester linkage, which in turn necessarily introduces unhelpfully non-stereogenic atoms between the auxiliary and the nearest point on the substrate at which reaction can occur. The best auxiliaries take all this in their stride, and levels of 1,4-asymmetric induction of >95:5 are the norm for, for example, chiral oxazolidinones.[1]

We set out to avoid the problem of spatial separation between auxiliary and new stereogenic centre by developing a new chiral auxiliary strategy which would exploit the high levels of 1,2-asymmetric induction characteristic of nucleophilic additions to some chiral aldehydes.[2] Our plan is outlined in Scheme 1. A stereospecific rearrangement converts the 1,2-relationship created by the addition into

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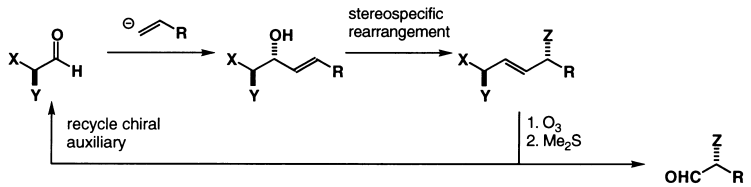
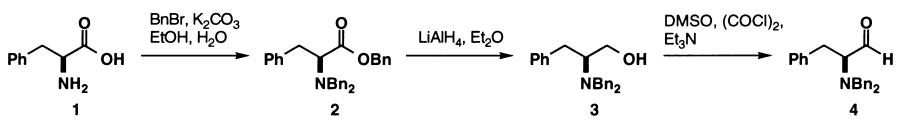
a 1,4-relationship across a *trans* double bond.[3] Ozonolysis removes the aldehyde auxiliary from the functionalised substrate, which is also a 2-substituted aldehyde. The stereospecific rearrangement means that in principle the same degree of stereocontrol should be obtainable whatever substituent Z we choose to introduce, and in this paper we describe our success in applying this strategy to the synthesis of esters, amides and alcohols.



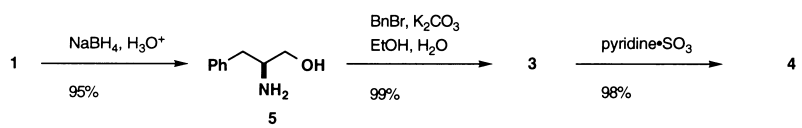
Scheme 1. Exploiting 1,2-asymmetric induction in a new chiral auxiliary strategy

2. Results and discussion

Stereocontrol in the additions of nuleophiles to α-chiral aldehydes is well understood in terms of the Felkin–Anh transition state[4–6] and (depending on aldehyde and nucleophile) chelation control.[7,8] Reetz has described a group of 2-amino aldehydes[9,10] whose reactions are characterised by high 1,2-stereoselectivity and which can be made straightforwardly from available amino acids,[11] and we chose one of these, (*S*)-2-(dibenzylamino)-3-phenylpropanal **4**, as our auxiliary. Reetz's route[10,12] to **4** is shown in Scheme 2, but we found that the aldehyde product from the Swern oxidation of **3** was hard to purify, and while it could be used crude, it could not be stored for later use. We prefer the method of Beaulieu and Wernic[13] (Scheme 3), which proceeds via dibenzylation of phenylalaninol **5** and avoids both the $LiAlH_4$ reduction of **2** (with stoichiometric production of benzyl alcohol) and the Swern oxidation of Reetz's route. We found that the aldehyde **4** made by pyridine–sulfur trioxide oxidation of **3** needed no purification and could be stored for several weeks without decomposition.

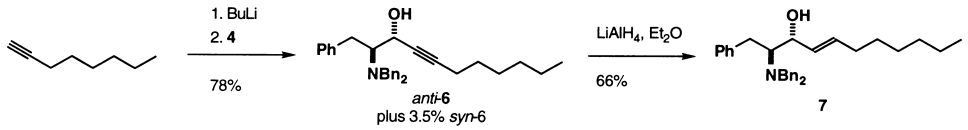


Scheme 2. Reetz's route to **4**



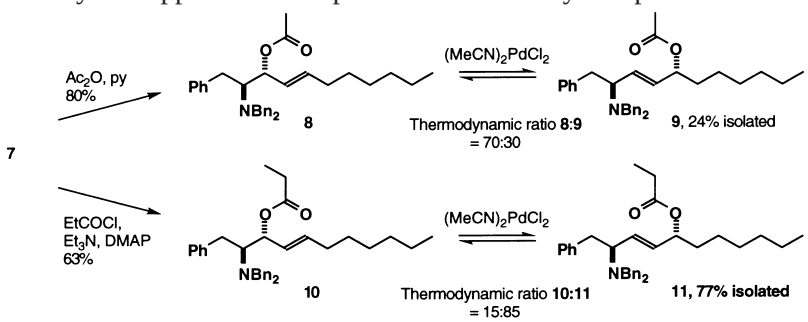
Scheme 3. Beaulieu and Wernic's route to **4**

We needed to add a vinyl anion equivalent to aldehyde **4** (Scheme 1). Noting that lithiated phenylacetylene gives >96:4 *anti* diastereoselectivity on addition to **4**,[9,10,14] we decided to use a lithiated alkyne and subsequently to reduce to the alkene. Reaction of **4** with lithiated 1-octyne gave a 96:4 ratio of diastereoisomers by HPLC, which were separable by chromatography, allowing us to isolate *anti*-**6**[15] in 78% yield. We found that $LiAlH_4$ was a more reliable *E*-selective reducing agent[16] for this alkyne than RedAl®[17] giving the *E*-allylic alcohol **7** in 66% yield.[18]



Stereospecific [2,3] and [3,3]-sigmatropic rearrangements[19–21] and related stereospecific allylic substitutions of derivatives of allylic alcohols have been used to introduce oxygen,[22–25] carbon,[26–32] nitrogen,[33–37], hydrogen,[38] silicon,[39,40] and sulfur[41]-based functional groups. We chose to investigate methods for the first two, and examined the application of three reactions: palladium(II)-catalysed allylic ester rearrangement[22] and the Johnson[42] and Eschenmoser[43] variants of the Claisen[26] rearrangement.

Palladium(II)-catalysed rearrangement of allylic esters is reliably stereospecific,[23–25,44,45] and with both the starting material and product of the reaction being esters the course of the reaction is controlled largely by the relative degree of steric encumbrance they experience.[23,44] We made acetate **8** from **7** and treated it with a Pd(II) catalyst, $(MeCN)_2PdCl_2$, in THF at 20°C. After 24 h, a product **9** was evident by TLC, and after 96 h this product accounted for 30% of the reaction mixture. However, this 70:30 ratio appeared to represent thermodynamic equilibrium between starting material **8** and product **9**, and remained unchanged even after a further 96 h. Heating the mixture did not improve the situation, and resulted in poor recovery and apparent decomposition of the catalyst to palladium metal.



The steric driving force for the reaction — repulsion between the migrating carboxylate and the allylic NBn_2 group — is evidently insufficient to drive this reaction to completion. Aiming to increase steric hindrance, we made the propionate ester **10**, and tried rearranging that. The result was much more encouraging, and after 72 h, the reaction mixture contained 85% of the rearranged product **11**, which we were able to isolate in 77% yield.

Unlike this stepwise[46,47] palladium(II)-catalysed rearrangement, the Claisen rearrangement,[26] and its Johnson[42,48] (using orthoesters to produce esters) and Eschenmoser[43,49] (using amide acetals to produce amides) variants are true stereospecific [3,3]-sigmatropic processes. Both the Johnson–Claisen and Eschenmoser–Claisen rearrangements were attractive to us in the context of this project since they provide single step methods for the stereospecific replacement, with allylic rearrangement, of the oxygen functionality of our allylic alcohol with a carbon-based fragment.

We treated allylic alcohol **7** with triethyl orthoacetate and heated it to 100°C in toluene.[30,42,48] After 20 h, we were able to isolate the rearranged γ,δ-unsaturated ester **12** in 79% yield. The amide **13** could be formed similarly in 87% yield by heating the allylic alcohol with dimethyl acetamide diethyl acetal.[43,49]

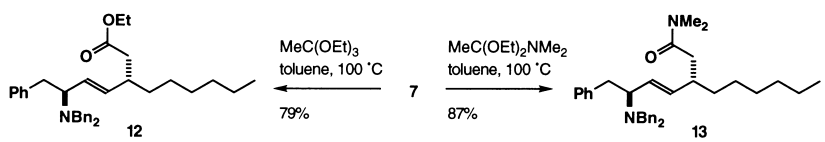


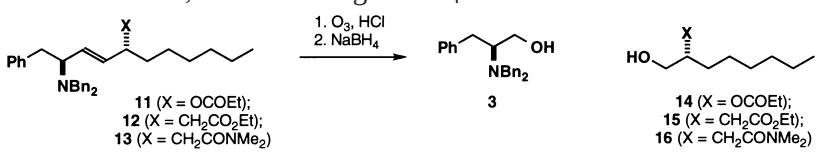
Table 1
Cleavage of **11**–**13** by ozonolysis to 2-substituted alcohols **14**–**16** and auxiliary precursor **3**

entry	starting material	HCl (equiv.)	temp. (°C)	time (min)	isolated product(s) and yield (%)	recovered **3** (%)	remaining S.M. (%)
1	**11**	0	0	60	– (0)	0[a]	3
2	**11**	2	0	60	**14+17** (33)	71	26
3	**11**	2	0	80	**14+17** (84)	0	0
4	**11**	3	0	80	**14+17** (84)	17	0
5	**11**	4	0	80	**17** (68)	30	19
6	**11**	3	–78	80	**14+17** (28)	39	44
7	**11**	3	–78	120	**14+17** (43)	44	11
8	**12**	3	–78	150	**15+19** (78)	33	4
9	**13**	3	–78	180	**16** (75)	63	0

[a]Benzyl alcohol (0.3 mmol) was recovered from the reaction of **11** (0.42 mmol) under these conditions

The three rearranged products — two esters **11**, **12** and an amide **13** — all appeared to be single diastereoisomers by ^{1}H and ^{13}C NMR, though we had to wait till we had cleaved auxiliary from product to be confident that the rearrangements had been fully stereospecific.

This was the next task, and we set out to use ozonolysis to do it. Tertiary amines, and particularly tertiary benzylamines, are susceptible to oxidation by ozone either at nitrogen or, in the case of benzylamines, at the benzylic carbon adjacent to the nitrogen atom.[50,51] We sought to prevent these unwanted oxidations by carrying out our ozonolysis in the presence of 1–5 equiv. of HCl, which we introduced by adding acetyl chloride to the methanol solvent. Although ozonolysis with dimethyl sulfide work-up would be expected to regenerate our aldehyde auxiliary, we envisaged difficulties isolating the two aldehyde products without racemisation or decomposition, so we decided to reduce the ozonide directly to two alcohols **3** and **14**, **15** or **16** using $NaBH_4$.



11 (X = OCOEt);
12 (X = CH_2CO_2Et);
13 (X = CH_2CONMe_2)

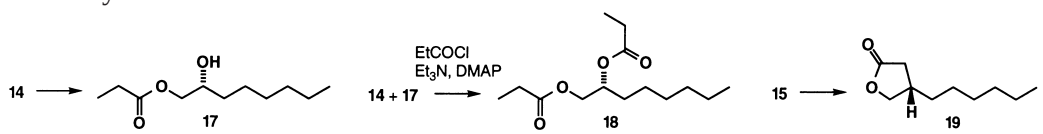
3

14 (X = OCOEt);
15 (X = CH_2CO_2Et);
16 (X = CH_2CONMe_2)

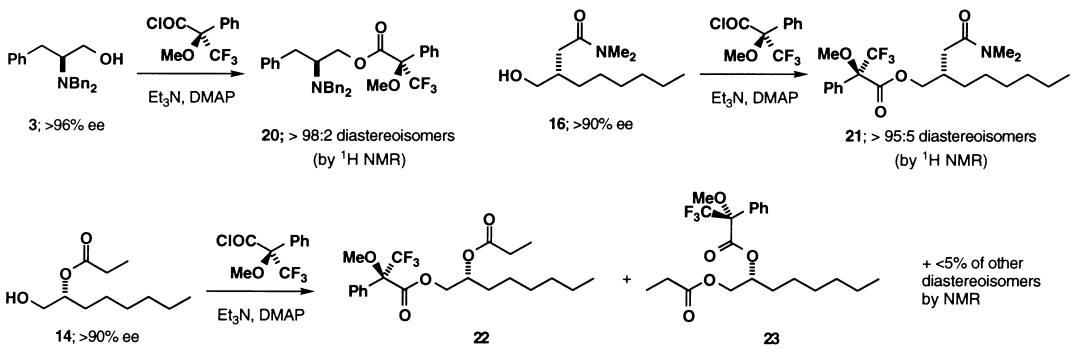
The results of our attempts are shown in the Table 1. The addition of HCl was essential for a clean reaction — without it, the only identifiable product was benzyl alcohol (entry 1), presumably originating from oxidation of the NBn_2 group. Adding 2–3 equiv. of HCl slowed oxidation at nitrogen to the point where reasonable recoveries of the auxiliary **3** could be achieved (71% in entry 2), and it is notable that reactions returning starting material also gave better yields of **3**: presumably, alkene oxidation is faster than oxidation of the protonated amine but not by much. Protonation at nitrogen evidently also slowed the rate of oxidation of the alkene too, and to get acceptable yields of the products it was necessary to lengthen reaction time to 80 minutes or more (entries 3–5). The cleaner, but yet slower, reactions at −78°C were the best compromise and gave acceptable yields of products from **11**, **12** and **13** (entries 7–9).

The products **14** and **15** were susceptible to further reaction under the conditions of the ozonolysis. Cleavage of **11** to the 2-acyloxy alcohol **14** was always accompanied by acyl transfer to the primary

hydroxyl group, giving variable yields of **17**, and **17** was the sole product in the presence of 4 equiv. of HCl. We were able to convert mixtures of **14** and **17** to the bis-propionate **18** for characterisation. The ester **15** was susceptible to lactonisation to give **19**, and varying amounts of **19** accompanied **15** isolated from the ozonolysis of **12**.



The enantiomeric excess of the products confirmed the stereoselectivity of the addition and stereospecificity of the rearrangement. Mosher's MTPA esters[52,53] **20** and **21** of alcohols **3** and **16** with (±)-MTPACl gave two clear sets of NMR signals in the ^{1}H NMR, and the absence of one of these sets of signals from the NMR of the esters made with ozonolysis products and with (+)-MTPACl confirmed that the enantiomeric excess of recovered **3** was >96% and that of **16** was >90% (Fig. 1). Alcohol **14** gave a mixture of inseparable regioisomeric MTPA esters **22** and **23**, but the absence of diastereoisomeric signals from the mixture of **22** and **33** made from **14** with (+)-MTPACl indicated an *ee* of >90%. We were unable to make the MTPA ester from the lactonisable ester **15**, though comparison of the optical rotation of known lactone **19**[54] with its literature value did at least enable us to confirm the configuration of the new chiral centre, which we had assigned using the known[9,10] preference for *anti* product formation from **3**, along with the stereospecificity of the rearrangements.



While **14** could be more simply made by asymmetric dihydroxylation[55] (notwithstanding the question of selective protection[56]), the ester **15** (or lactone **19**) and amide **16** are not available by another straightforward route. In principle, many other related products are available simply by varying the nature of the rearrangement. Similar rearrangement-based approaches to 1,2-difunctionalised compounds have been employed by Thomas[36,37] and by Larchevêque,[57] but ours is the first demonstration of the use of an aldehyde as a recyclable chiral auxiliary. We are currently investigating other aldehydes which show very high diastereofacial bias[58] as auxiliaries for use with this strategy.

3. Experimental

Infra-red spectra were recorded on an ATi Genesis Series FTIR. NMR spectra were recorded at 300 MHz on a Varian XL300 spectrometer (^{1}H) or at 75 MHz on a Bruker XC300 spectrometer (^{13}C). All chemical shifts are quoted in parts per million downfield from tetramethylsilane. Mass spectra were recorded using chemical ionisation (CI) on a Fisons VG Trio 2000 (EI/CI) or a Concept IS (HRMS) spectrometer.

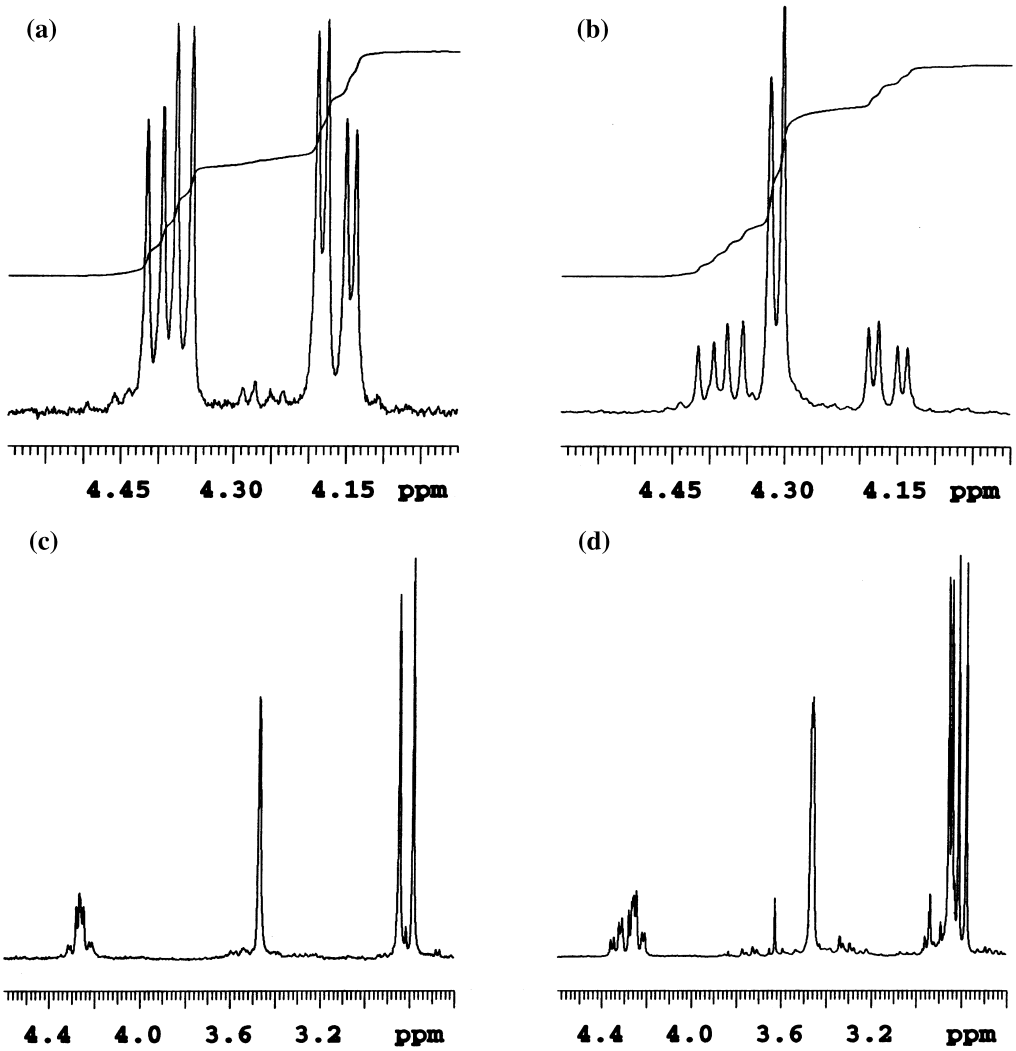


Fig. 1. Portions of the ^{1}H NMR spectrum of (a) ester **20** from recovered **3** and (+)-MTPA; (b) ester **20** from **3** and (±)-MTPA; (c) ester **21** from **16** and (+)-MTPA; (d) ester **21** from **16** and (±)-MTPA

High-performance liquid chromatography was carried out on a Waters Z module (10 cm by 8 mm, packed SiO_2 stationary phase) at room temperature using a Waters 510 pump, eluting with 4:1 hexane:ethyl acetate, flow rate 2 ml/min, 20 μl injection, detection Perkin–Elmer LC-480 Diode Array system using UV absorbance at 255 nm. Flash chromatography[59] was performed using Merck silica gel 60H (40–63 μ, 230–300 mesh) as the stationary phase. Thin layer chromatography (TLC) was performed using Macherey–Nagel 0.25 mm silica gel pre-coated plastic sheets with fluorescent indicator UV_{254}.

Tetrahydrofuran (THF) and diethylether were dried over sodium and distilled under dry nitrogen using benzophenone as an indicator. Dichloromethane was distilled from calcium hydride. Toluene was dried and distilled using a Dean–Stark apparatus and stored over 4 Å molecular sieves. DMSO was distilled and stored over 4 Å molecular sieves.

3.1. (S)-2-Amino-3-phenylpropan-1-ol **5**

The title compound was prepared by the method of Beaulieu and Wernic.[13] L-Phenylalanine (20 g, 0.121 mol) was added to a stirred suspension of $NaBH_4$ (11.45 g, 0.303 mol) in THF (250 ml) at room temperature. The flask was immersed in a ice-water bath and a solution of carefully prepared conc. H_2SO_4 (8.06 ml, 0.151 mol) in ether (22 ml) was added dropwise at such a rate to maintain the reaction mixture below 20°C (addition time approx. 30 min). The reaction mixture was stirred at room temperature overnight and MeOH (10 ml) was carefully added to destroy excess borane. The solvent was removed under reduced pressure, 6 M NaOH (100 ml) was added and mixture heated to reflux for 3 h. The solution was allowed to cool, filtered through a pad of Celite, and extracted with dichloromethane. The combined extracts were washed with water (100 ml) and evaporated under reduced pressure to yield the title compound as a pale yellow oil (17.3 g, 95%); $[\alpha]_D^{25}=-20$ (c=4, EtOH); δ_H (300 MHz; $CDCl_3$), 7.4–7.0 (5H, m, ArH), 3.65 (1H, dd, *J* 10.5 and 4, CH_AH$_B$OH), 3.4 (1H, dd, *J* 10.5 and 7, CH$_A$$H_B$OH), 3.2 (1H, tdd, *J* 8, 5 and 4, C*H*NH$_2$), 2.8 (1H, dd, *J* 13.5 and 5, PhCH_AH$_B$) and 2.55 (1H, dd, *J* 13.5 and 8.5, PhCH$_A$$H_B$); δ_C (75 MHz; $CDCl_3$) 132.0, 129.1, 128.5, 126.3 (Ar), 66.4 (CH_2OH), 54.1 (CHN) and 40.9 (Ph*C*H$_2$); *m*/*z* 152 (100%, *M*+1). [Found: $(M+H)^+$, 152.1082. $C_9H_{13}NO$ requires *M*+H, 152.1075.]

3.2. (S)-2-(Dibenzylamino)-3-phenylpropan-1-ol **3**

By the method of Beaulieu and Wernic,[13] benzyl bromide (37.2 ml, 0.312 mol) was added to a stirred mixture of the crude amino alcohol **5** (21.4 g, 0.142 mol) and anhydrous potassium carbonate (49 g, 0.355 mol) in ethanol (600 ml). After stirring for 3 days at room temperature, the suspension was filtered and concentrated under reduced pressure. Ethyl acetate was added and the solution was washed with water, sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate and evaporated under reduced pressure to give a crystalline yellow solid, which was recrystallised from ethyl acetate to yield the alcohol **3** (47 g, 99%) as a yellow solid, m.p. 69–72°C (lit.[13], 72–74°C); $[\alpha]_D^{25}=+7.6$ (c=4, EtOH); ν_{max}/cm^{-1} (evap. film) 3430 (OH), 3026 (CH), 1602 (Ar) and 1453; δ_H (300 MHz; $CDCl_3$), 7.6–7.0 (15H, m, ArH), 4.0 [2H, d, *J* 14, N(CH_AH$_B$Ph)$_2$], 3.6 [2H, d, *J* 14, N(CH$_A$$H_B$Ph)$_2$], 3.6 (1H, m, C$H_AH_B$OH), 3.4 (1H, dd, *J* 11.8 and 4, CH$_A$$H_B$OH), 3.2 (2H, m, PhC$H_AH_B$C*H*N) and 2.5 (1H, dd, *J* 14, 10.5, PhCCH$_A$$H_B$); δ_C (75 MHz; $CDCl_3$) 139.1, 139.0, 129.1, 129.0, 128.6, 128.5, 127.3, 126.2 (Ar), 60.9 (CH_2OH), 60.4 (CHN), 53.3 [N(*C*H$_2$Ph)$_2$], 31.8 (Ph*C*H$_2$CHN); *m*/*z* 332 (100%, *M*+1) [Found: $(M+H)^+$, 332.2017. $C_{23}H_{25}NO$ requires *M*+H, 332.2014.]

3.3. (S)-2-(Dibenzylamino)-3-phenylpropanal **4**

By the method of Beaulieu and Wernic,[13] pyridine–sulfur trioxide complex (15.9 g, 0.10 mol) in DMSO (60 ml) was added in small portions over 20–30 mins to a solution of (*S*)-2-(dibenzylamino)-3-phenylpropan-1-ol **3** (20 g, 0.06 mol) and Et_3N (15.3 ml, 0.11 mol) in DMSO (60 ml) at 0°C. The mixture was allowed to warm to room temperature, and after 2 h the reaction was quenched with ice–water (100 ml) and extracted with ethyl acetate (3×40 ml). The extracts were washed with water (100 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to yield the aldehyde **4** (19.3 g, 98%) which was used without further purification; $[\alpha]_D^{25}=-88.0$ (c=2, EtOH); ν_{max}/cm^{-1} (film) 1729 (C=O), 1494 and 1453; δ_H (300 MHz; $CDCl_3$) 9.8 (1H, s, CHO), 7.35–7.0 (15H, m, ArH), 3.9 [2H, d, *J* 14, N(CH_AH$_B$Ph)$_2$], 3.75 [2H, d, *J* 14, N(CH$_A$$H_B$Ph)$_2$], 3.62 (1H, t, *J* 7.3, CHN), 3.2 (1H, dd, *J* 14.5 and 8, PhCH_AH$_B$) and 3.0 (1H, dd, *J* 14.5 and 6.5, PhCH$_A$$H_B$); δ_C (75 MHz; $CDCl_3$) 202.1

(C=O), 139.0, 139.8, 129.4, 129.2, 128.5, 128.3, 127.3, 126.2 (Ar), 68.4 (CHN), 54.8 (CH_2N) and 30.0 (PhCH_2CHN); *m*/*z* 330 (100%, *M*+1). [Found: $(M+H)^+$, 330.1860. $C_{23}H_{23}NO$ requires *M*+1, 330.1858.]

3.4. (2S,3R)-2-(Dibenzylamino)-1-phenylundec-4-yn-3-ol **6**

Butyl lithium (43 ml of a 1.6 M solution, 0.069 mol) was added to a solution of 1-octyne (10.2 ml, 0.069 mol) in THF (150 ml) at −78°C. After 30 min, a solution of the aldehyde **4** (15 g, 0.046 mol) in THF (150 ml) was added dropwise. The mixture was stirred at −78°C for 20 min and warmed to room temperature. After 20 min, saturated ammonium chloride solution (300 ml) was added and the mixture was extracted with dichloromethane (3×200 ml). The combined organic fractions were washed with water, dried over sodium sulfate and evaporated under reduced pressure to give a crude product which was purified by flash chromatography [95:5 petroleum ether (b.p. 40–60°C): ether] to give the alkyne **6** (15.7 g, 78%) as a yellow oil, R_f [95:5 petroleum ether (b.p. 40–60°C): ether] 0.32; $[\alpha]_D^{25}$=+23.2 (c=2, EtOH); ν_{max} (film)/cm^{-1} 3400 (OH), 2250 (C≡C), 1601 (Ar), 1494 and 1453; δ_H (300 MHz; $CDCl_3$) 7.5–7.0 (15H, m, Ar), 4.3 [2H, d, *J* 14, N(C$H_A$$H_B$Ph)$_2$], 4.0 (1H, fine m, C*H*OH), 3.4 [2H, d, *J* 14, N(C$H_A$$H_B$Ph)$_2$], 3.1 (1H, dd, *J* 12 and 3.5, PhC$H_A$$H_B$), 3.0 (1H, m, CHN), 2.9 (1H, dd, *J* 12 and 10, PhC$H_A$$H_B$), 2.15 (2H, dt, *J* 2 and 7, CHOHCH_2), 1.4–1.0 [8H, m, (CH_2)$_4$Me] and 0.8 (3H, t, *J* 7, Me); δ_C (75 MHz; $CDCl_3$) 139.0, 138.8, 129.2, 129.1, 128.9, 128.4, 127.3, 126.3 (Ar), 87.6, 79.9 (C≡C), 62.5 (CHOH), 60.4 (CHN), 54.9 (CH_2N), 31.6, 31.3, 28.6, 28.5, 22.4, 18.8 and 13.9 [(CH$_2$)$_5$Me+PhCH_2CH]; *m*/*z* 440 (100%, *M*+1). [Found: $(M+H)^+$, 440.2945. $C_{31}H_{37}NO$ requires *M*+H, 440.2953.]

HPLC analysis of the crude product indicated a 96:4 ratio of diastereoisomers.

3.5. (E,2S,3R)-2-(Dibenzylamino)-1-phenylundec-4-en-3-ol **7**

A solution of the alkyne **6** (4.6 g, 10 mmol) in THF (100 ml) was added to a stirred solution of $LiAlH_4$ (1.58 g, 42 mmol) in THF (100 ml) at 0°C. The mixture was heated to reflux for 5 h and cooled. Saturated sodium bicarbonate solution (0.5 ml) was carefully added and a dense white precipitate formed. The mixture was filtered through a pad of Celite and concentrated under reduced pressure. Flash chromatography [4:1 petroleum ether (b.p. 40–60°C): ether] gave the alkene **7** (2.89 g, 66%) as a yellow oil; R_f [4:1 petroleum ether (b.p. 40–60°C): ether] 0.32; $[\alpha]_D^{25}$=−16.0 (c=2, EtOH); ν_{max} (film)/cm^{-1} 3400 (OH), 1601 (Ar) and 1453; δ_H (300 MHz; $CDCl_3$) 7.4–7.0 (15H, m, Ar), 5.8 (1H, dt, *J*15.5 and 7, CH=C*H*CH_2), 5.65 (1H, dd, *J*15.5 and 7, C*H*=$CHCH_2$), 4.0 (1H, m, C*H*OH), 3.9 [2H, d, *J* 14, N(C$H_A$$H_B$Ph)$_2$], 3.6 [2H, d, *J* 14, N(C$H_A$$H_B$Ph)$_2$], 3.1 (2H, m, PhC$H_A$$H_B$C*H*N), 2.8 (1H, dd, *J* 15 and 8, PhC$H_A$$H_B$), 2.0 (2H, q, *J* 17, CH=CHCH_2), 1.3 [8H, m, (CH_2)$_4$Me] and 0.9 (3H, t, *J* 7, Me); δ_C (75 MHz; $CDCl_3$) 140.0, 139.5, 132.3, 130.1, 129.3, 128.9, 128.4, 128.3, 127.1, 126.1 (Ar and C=C), 71.1 (CHOH), 63.4 (CHN), 55.0 (CH_2N), 32.4, 31.9, 31.7, 29.2, 28.9, 22.6, 14.1 [(CH$_2$)$_5$Me and PhCH_2CH]; *m*/*z* 442 (100%, *M*+1). [Found: $(M+H)^+$, 442.3110. $C_{31}H_{39}NO$ requires *M*+H, 442.3119.]

3.6. (E,2S,3R)-2-(Dibenzylamino)-1-phenylundec-4-en-3-yl acetate **8**

Acetic anhydride (4.3 ml, 45 mmol) was added dropwise to a solution of the alcohol **7** (1.0 g, 2.27 mmol) in pyridine (4 ml) and the mixture was stirred under nitrogen for 24 h. Ethyl acetate (20 ml) was added, and the solution washed with 2 M HCl (3×20 ml), saturated aqueous sodium bicarbonate solution, 20% aqueous copper sulfate soln. and brine. The organic fractions were dried (Na_2SO_4) and the solvent evaporated under reduced pressure to give a crude product. Flash chromatography [4:1 petroleum ether (b.p. 40–60°C): ether] gave the acetate **8** (0.88 g, 80%) as a yellow oil, R_f [5:1 petroleum ether (b.p.

40–60°C): ether] 0.34; $[\alpha]_D^{25}$=+13.2 (c=2, EtOH); ν_{max}/cm^{-1} (film) 1737 (C=O), 1494 and 1453; δ_H (300 MHz; $CDCl_3$) 7.4–7.0 (15H, m, Ar), 5.7 (2H, m, C*H*=CHC*H*OAc), 5.4 (1H, dd, *J* 15.5 and 7, CH=C*H*CHOAc), 3.7 [4H, AB m, N(CH_2Ph)$_2$], 3.1 (2H, m, PhCH_AH$_B$C*H*N), 2.8 (1H, dd, *J* 14 and 5, PhCH$_A$$H_B$CNH), 2.1 (2H, m, CH=CHC$H_2$), 2.0 (3H, s, OCOMe), 1.3 [8H, m, (CH_2)$_4$] and 0.9 (3H, t, *J* 7, CH$_2$*Me*); δ_C (75 MHz; $CDCl_3$) 170.1 (C=O), 140.4, 139.6, 134.2, 129.2, 128.6, 128.2, 128.1, 128.0, 127.6, 126.8, 125.7 (C=C and Ar), 74.3 (*C*HOAc) 61.6 (CHN), 53.9 (CH_2N), 32.6, 32.2, 31.6, 28.8, 28.7, 22.5, 21.3, 14.0 [(CH$_2$)$_4$Me+PhCH$_2$CH+OCO*Me*]; *m*/*z* 484 (100%, *M*+1). [Found: $(M+H)^+$, 484.3215. $C_{33}H_{41}NO_2$ requires *M*+H, 484.3222.]

*3.7. (*E,*2*S,*5*R*)-2-(Dibenzylamino)-1-phenylundec-3-en-5-yl acetate **9***

Bis(acetonitrile) palladium(II) chloride (6.5 mg, 0.025 mmol) was added to a stirred solution of the acetate **8** (0.158 g, 0.25 mmol) in dry THF (4 ml) at room temperature under nitrogen. The red–brown mixture was stirred under nitrogen for 4 days at 30°C and evaporated under reduced pressure to yield a crude product which ^{1}H NMR showed to contain a 70:30 mixture of **8** and **9**. Flash chromatography [1:4 petroleum ether (b.p. 40–60°C): ether] gave the rearranged acetate **9** (31 mg, 24%) as a yellow oil, R_f [1:4 petroleum ether (b.p. 40–60°C): ether] 0.34; δ_H (300 MHz; $CDCl_3$) 7.3–7.0 (15H, m, Ar), 5.7 (1H, dd, *J* 14.5 and 8.5, C*H*=CHCHOAc) 5.2 (2H, m, CH=C*H*C*H*OAc), 3.8 [2H, d, *J* 14, N(CH_AH$_B$Ph)$_2$], 3.3 [2H, d, *J* 14, N(CH$_A$$H_B$Ph)$_2$], 3.3 (1H, m, C*H*NBn$_2$), 2.9 (1H, dd, *J* 14 and 7, PhCH_AH$_B$), 2.7 (1H, m, PhCH$_A$$H_B$), 2.0 (3H, s, OCOMe), 1.5 (2H, m, AcOCHCH_2), 1.2 [8H, m, (CH$_2$)$_4$] and 0.8 (3H, t, *J* 7, Me).

The 70:30 ratio remained unchanged after a further 48 h, and heating the THF to 50°C gave a black precipitate of palladium metal.

*3.8. (*E,*2*S,*3*R*)-2-(Dibenzylamino)-1-phenylundec-4-en-3-yl propionate **10***

Triethylamine (0.32 ml, 2.27 mmol), 4-(*N*,*N*-dimethylamino)pyridine (14 mg, 0.11 mmol) and propionyl chloride (0.2 ml, 2.27 mmol) were added to a stirred solution of the alcohol (0.5 g, 1.13 mmol) in dichloromethane (5 ml) at room temperature. After 3 days the dichloromethane (20 ml) was added and the solution was washed with water (3×20 ml) and dried (Na_2SO_4) The solvent was removed under reduced pressure and the crude product was purified by flash chromatography [6:1 petroleum ether (b.p. 40–60°C): ether] to give the propionate **10** as a yellow oil (1.56 g, 63%), R_f [6:1 petroleum ether (b.p. 40–60°C): ether] 0.42; $[\alpha]_D^{25}$=−29.6 (c=2, EtOH); ν_{max}/cm^{-1} (film) 1736 (C=O); δ_H (300 MHz; $CDCl_3$) 7.2–6.9 (15H, m, Ar), 5.6 (2H, m, C*H*=CHC*H*OAc), 5.3 (1H, dd, *J* 15.5 and 7, CH=C*H*CHOAc), 3.65 [2H, d, *J* 14, N(CH_AH$_B$Ph)$_2$], 3.5 [2H, d, *J* 14, N(CH$_A$$H_B$Ph)$_2$], 3.0 (2H, m, PhC$H_AH_B$C*H*N), 2.75 (1H, dd, *J* 14 and 5, PhCH$_A$$H_B$CNH), 2.2 (2H, ABX$_3$, J_{AB} 16.4, J_{AX} 7.5 and J_{BX} 7.5, OCOCH_2Me), 2.0 [2H, q, *J* 7, CH_2(CH$_2$)$_4$Me], 1.2 [8H, m, (CH$_2$)$_4$], 1.0 (3H, t, *J* 7.5, OCOCH$_2$*Me*) and 0.9 [3H, t, *J* 7, (CH$_2$)$_4$*Me*]; δ_C (75 MHz; $CDCl_3$) 173.4 (C=O), 140.5, 139.5, 133.9, 129.3, 128.6, 128.3, 127.9, 127.7, 126.7, 125.7 (Ar and C=C), 73.8 (OCH), 61.7 (CHN), 53.9 (CH_2N), 32.6 (OCO*C*H$_2$Me), 32.2, 31.6, 29.6, 28.8, 27.9, 22.5, 14.0 and 8.9 [(CH$_2$)$_5$Me+PhCH$_2$+OCOCH$_2$*Me*]; *m*/*z* 498 (100%, *M*+1). [Found: $(M+H)^+$, 498.3364. $C_{34}H_{43}NO_2$ requires *M*+H, 498.3372.]

*3.9. (*E,*2*S,*5*R*)-2-(Dibenzylamino)-1-phenylundec-3-en-5-yl propionate **11***

Bis(acetonitrile) palladium(II) chloride (45 mg, 0.08 mmol) was added to a stirred solution of the propionate **10** (0.4 g, 0.8 mmol) in dry THF (50 ml) at room temperature under nitrogen. The red–brown

mixture was stirred under nitrogen for 3 days at room temperature and evaporated under reduced pressure to yield a crude product which was purified by flash chromatography [4:1 petroleum ether (b.p. 40–60°C): ether] to give the rearranged propionate **11** (0.3 g, 77%) as a yellow oil, R_f [7:1 petroleum ether (b.p. 40–60°C): ether] 0.25; $[\alpha]_D^{25}=-32.8$ (c=2, EtOH); ν_{max}/cm^{-1} (film) 1735 (C=O); δ_H (300 MHz; $CDCl_3$) 7.2–6.9 (15H, m, Ar), 5.7 (1H, dd, *J* 14.5 and 8.5 C*H*=CHCHOCOEt), 5.2 (2H, m, CH=C*HCH*OCOEt), 3.7 [2H, d, *J* 14, N(C$H_A$$H_B$Ph)$_2$], 3.3 [2H, d, *J* 14, N(C$H_A$$H_B$Ph)$_2$], 3.3 (1H, m, NCH), 2.9 (1H, dd, *J* 14 and 7, PhC$H_A$$H_B$), 2.7 (1H, dd, *J* 15 and 7, PhC$H_A$$H_B$), 2.2 (2H, ABX_3 m, OCOCH_2Me), 1.5 (2H, m, OCHCH_2), 1.2 [8H, m, $(CH_2)_4$], 1.1 (3H, t, *J* 7, OCOCH_2*Me*), 0.8 [3H, t, *J* 7, $(CH_2)_4$*Me*]; δ_C (75 MHz; $CDCl_3$) 173.6 (C=O), 139.9, 139.4, 132.4, 130.4, 129.5, 128.4, 128.1, 127.9, 126.6, 125.8 (Ar and C=C), 74.1 (*C*HOCO), 61.2 (CHN), 53.6 (CH_2N), 38.6 (CO*C*H_2Me), 34.5, 31.7, 28.9, 27.9, 25.1, 22.5, 14.0 and 9.2 [$(CH_2)_5$Me+COCH_2*Me*+PhCH_2CH]; *m*/*z* 498 (100%, *M*+1). [Found: $(M+H)^+$, 498.3367. $C_{34}H_{43}NO_2$ requires *M*+H, 498.3372.]

3.10. (E,3S,3′S)-Ethyl-3-(3′-dibenzylamino-4′-phenylbut-1′-en-1′-yl)nonanoate **12**

Triethyl orthoacetate (0.25 ml, 1.36 mmol) and propionic acid (2 μl, 0.03 mmol) were added to a solution of alcohol **7** (0.2 g, 0.45 mmol) in toluene (20 ml). The solution was heated to reflux for 20 h, cooled, concentrated under reduced pressure and purified by flash chromatography [4:1 petroleum ether (b.p. 40–60°C): ether] to give the ester **12** as a pale yellow oil (0.18 g, 79%); R_f [4:1 petroleum ether (b.p. 40–60°C): ether] 0.48; $[\alpha]_D^{25}=-30.8$ (c=2, EtOH); ν_{max}/cm^{-1} (film) 1735 (C=O); δ_H (300 MHz; $CDCl_3$) 7.2–7.0 (15H, m, Ar), 5.4 (1H, dd, *J* 15.5 and 8.5, NCHC*H*=CH), 5.1 (1H, dd, *J* 15.5 and 8.5, NCHCH=C*H*), 4.0 (2H, ABX_3 m, OCH_2), 3.8 [2H, d, *J* 14, N(C$H_A$$H_B$Ph)$_2$], 3.3 [2H, d, *J* 14, N(C$H_A$$H_B$Ph)$_2$], 3.2 (1H, m, CHN), 2.9 (1H, dd, *J* 14 and 8, PhC$H_A$$H_B$), 2.6 (1H, dd, *J* 14 and 7.5, PhC$H_A$$H_B$), 2.5 (1H, m, CH=CHC*H*$CH_2$), 2.2 (1H, dd, *J* 14.5 and 6.3, EtOCOC$H_A$$H_B$), 2.1 (1H, dd, *J* 14.5 and 6.3, EtOCOC$H_A$$H_B$), 1.2 [10H, m, $(CH_2)_5$], 1.1 (3 H, t, *J* 7, OCH_2*Me*) and 0.8 (3H, t, *J* 7, CH_2CH_2*Me*); δ_C (75 MHz; $CDCl_3$) 172.5 (C=O), 140.1, 139.6, 136.9, 129.5, 128.4, 128.0, 127.8, 126.6, 126.5, 125.7 (C=C and Ar), 61.3 (CH_2O), 60.1 (CNH), 53.5 (CH_2N), 40.5 (*C*H_2CO_2Et), 39.4, 38.9, 34.7, 31.8, 29.0, 27.2, 22.6, 14.2 and 14.0 [(CH_2)$_5$Me+PhCH_2+OCH_2*Me*]; *m*/*z* 512 (100%, *M*+1) and 420 (80, M−Bn). [Found: $(M+H)^+$, 512.3532. $C_{35}H_{45}NO_2$ requires *M*+H, 512.3528.]

3.11. (E,3S,3′S)-N,N-Dimethyl-3-(3′-dibenzylamino-4′-phenylbut-1′-en-1′-yl)nonanamide **13**

N,*N*-Dimethylacetamide dimethyl acetal (0.2 ml, 1.22 mmol) was added to a solution of alcohol **7** (0.2 g, 0.45 mmol) in toluene (10 ml). The solution was heated to reflux for 20 h, cooled, and poured into dichloromethane (25 ml) and saturated aqueous NH_4Cl (25 ml). The layers were separated, and the aqueous layer extracted with dichloromethane (2×25 ml). The combined organic fractions were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Purification by flash chromatography [2:1 petroleum ether (b.p. 40–60°C):ether] yielded the amide **13** as a pale yellow oil (0.2 g, 87%); R_f (EtOAc) 0.27; $[\alpha]_D^{25}=28.8$ (c=2, EtOH); ν_{max}/cm^{-1} (film) 1648 (C=O), 1493 and 1453; δ_H (300 MHz; $CDCl_3$) 7.2–7.0 (15H, m, Ar), 5.4 (1H, dd, *J* 15 and 8.7, NCHC*H*=CH), 5.1 (1H, dd, *J* 15 and 8.8, NCHCH=C*H*), 3.7 [2H, d, *J* 14, N(C$H_A$$H_B$Ph)$_2$], 3.3 [2H, d, *J* 14, N(C$H_A$$H_B$Ph)$_2$], 3.2 (1H, m, CHN), 2.9 (1H, dd, *J* 13.5 and 9, PhC$H_A$$H_B$), 2.8 (6H, s, NMe_2), 2.6 (1H, dd, *J* 14 and 7.7, PhC$H_A$$H_B$), 2.5 (1H, m, CH=CHC*H*$CH_2$), 2.1 (2H, d, *J* 7, C$H_2$$CONMe_2$), 1.2 [10H, m, $(CH_2)_5$] and 0.8 (3H, t, *J* 7, CH_2*Me*); δ_C (75 MHz; $CDCl_3$) 171.9 (C=O), 140.2, 139.8, 137.7, 129.5, 128.5, 128.0, 127.8, 127.6, 126.6, 125.7 (Ar and C=C), 61.6 (CHN), 53.5 (CH_2N), 39.7, 39.2, 39.1, 37.4, 34.8, 31.9, 29.2, 27.5,

22.7, 14.1 [(CH_2)$_5$Me+PhCH_2CH+CHCONMe$_2$]; *m*/*z* 511 (100%, *M*+1) and 419 (80, M−Bn). [Found: (M+H)$^+$, 511.3680. $C_{35}H_{43}N_2O$ requires *M*+H, 511.3688.]

3.12. *Ozonolysis of (*E,2S,5R*)-2-(dibenzylamino)-1-phenylundec-3-en-5-yl propionate* **11**

Acetyl chloride (29 μl, 0.4 mmol) was added dropwise to methanol (8 ml) under nitrogen at room temperature. The mixture was stirred for 1 h and was then added dropwise to a solution of the ester **11** (0.1 g, 0.2 mmol). After 30 min, the reaction mixture was cooled to 0°C and was treated with a steady stream of ozone in oxygen for 60 min. Excess ozone was removed by passing a stream of oxygen through the reaction mixture for 10 min, and the reaction mixture diluted with 50% aqueous ethanol (8 ml). Sodium borohydride (76 mg, 2 mmol) was carefully added, the reaction mixture was allowed to warm to 23°C and was stirred for a further 1 h. Concentrated hydrochloric acid (0.5 ml) and EtOAc (30 ml) were added. The solution was washed with saturated aqueous $NaHCO_3$ (10 ml), water (10 ml) and brine (10 ml), dried (Na_2SO_4) and concentrated under reduced pressure to give a crude product mixture. Flash chromatography [2:1 petroleum ether (b.p. 40–60°C):ether] gave (*S*)-2-(dibenzylamino)-3-phenylpropan-1-ol **3** (46 mg, 71%) as a white solid, $[\alpha]_D^{25}=-14.4$ (c=2, EtOH), spectroscopically identical with the material derived directly from L-phenylalanine.

Also obtained was a mixture of the esters **14** and **17** (13 mg, 33%).

In the same way but with acetyl chloride (43 μl, 0.6 mmol), ozonolysis for 2 h at −78°C gave, after purification by flash chromatography, (*S*)-2-(dibenzylamino)-3-phenylpropan-1-ol **3** (29 mg, 44%).

Also obtained was (*R*)-1-hydroxyoct-2-yl propionate **14** as a yellow oil (11 mg, 28%); R_f [1:4 petroleum ether (b.p. 40–60°C): ether] 0.31; $[\alpha]_D^{25}=-17.2$ (c=2, EtOH); δ_H (300 MHz; $CDCl_3$) 4.8 (1H, dq, *J* 3 and 6.5, C*H*OCOEt), 3.6 (2H, m, CH_2OH), 2.3 (2H, q, *J* 7.5 and 15, OCOCH_2CH$_3$), 1.5 [2H, m, CH_2(CH$_2$)$_4$Me], 1.2 [8H, m, (CH_2)$_4$Me], 1.1 (3H, t, *J* 7.5, OCOCH$_2$*Me*) and 0.8 (3H, t, *J* 7, (CH$_2$)$_4$*Me*); δ_C (75 MHz; $CDCl_3$) 174.8 (C=O), 75.5 (*C*HOCO), 64.9 (CH_2OH), 31.6, 30.4, 29.0, 27.7, 25.2, 22.4, 13.9, 9.1 [(CH$_2$)$_5$Me+Et]; *m*/*z* 203 (100%, *M*+1). [Found: (M+H)$^+$, 203.1649. $C_{11}H_{22}O_3$ requires *M*+H, 203.1569.]

Also obtained was (*R*)-2-hydroxyoct-1-yl propionate **17** as a yellow oil (6 mg, 15%); R_f [3:1 petroleum ether (b.p. 40–60°C): ether] 0.26; $[\alpha]_D^{25}=-12.8$ (c=2, EtOH); δ_H (300 MHz; $CDCl_3$) 4.1 (1H, dd, *J* 11 and 4, EtOCOCH_AH$_B$), 3.9 (1H, dd, *J* 11 and 4, EtOCOCH$_A$$H_B$), 3.8 (1H, m, C*H*OH), 2.3 (2H, dd, *J* 7.5 and 3, OCOCH_2CH$_3$), 1.4 [2H, m, CH_2(CH$_2$)$_4$Me], 1.2 [8H, m, (CH_2)$_4$Me], 1.1 (3H, t, *J* 7.5, OCH$_2$*Me*) and 0.8 (3H, t, *J* 7, OCCH$_2$*Me*); δ_C (75 MHz; $CDCl_3$) 174.5 (C=O), 68.4 (CHOH), 64.5 (*C*H$_2$OCO), 33.5, 32.0, 28.5, 27.5, 25.0, 22.5, 14.0, 9.0 [(CH$_2$)$_5$Me+Et]; *m*/*z* 203 (100%, *M*+1). [Found: (M+H)$^+$, 203.1647. $C_{11}H_{22}O_3$ requires *M*+H, 203.1569.]

3.13. *Ozonolysis of (*E,3S,3′S*)-ethyl-3-(3′-dibenzylamino-4′-phenylbut-1′-en-1′-yl)nonanoate* **12**

In the same way but with acetyl chloride (43 μl, 0.6 mmol), ozonolysis for 2 h 30 min at −78°C gave, after purification by flash chromatography, (*S*)-2-(dibenzylamino)-3-phenylpropan-1-ol **3** (22 mg, 33%).

Also obtained was the unstable (*R*)-ethyl-2-hydroxymethylnonanoate **15** (20 mg, 47%) as a yellow oil; R_f [3:1 petroleum ether (b.p. 40–60°C): ether] 0.25; δ_H (300 MHz; $CDCl_3$) 4.1 (2H, q, *J* 7.5, OCH_2CH$_3$), 3.6 (1H, dd, *J* 10.5 and 4, CH_AH$_B$OH), 3.4 (1H, m, CH$_A$$H_B$OH), 2.3 (2H, m, EtOCOC$H_2$), 1.9 (1H, m, HOCH$_2$C*H*), 1.5 (2H, m, C$H_2$(CH$_2$)$_4$Me), 1.2 [11H, m, OCH$_2CH_3$+($CH_2$)$_4$Me] and 0.8 [3H, t, *J* 7, (CH$_2$)$_4$*Me*].

Also obtained was (*R*)-4-hexylfuran-2-one **19** (13 mg, 31%) as a yellow oil; R_f [3:1 petroleum ether (b.p. 40–60°C): ether] 0.48; $[\alpha]_D^{25}=+2.8$ (c=1, EtOH) [lit.[54] $[\alpha]_D^{25}=+4.7$ (c=1.69, $CHCl_3$)]; δ_H (300

MHz; $CDCl_3$) 4.3 (1H, dd, *J* 9 and 8, C$H_A$$H_B$O), 3.8 (1H, dd, *J* 9 and 8, CH_AH_BO), 2.6 (1H, dd, *J* 16.5 and 8, C$H_A$$H_B$CO), 2.5 (1H, septet, *J* 7.5, C*H*CH_2O), 2.1 (1H, dd, *J* 7.5 and 16, CH_AH_BCO), 1.4 [2H, m, C$H_2$$(CH_2)_4$Me], 1.2 [8H, m, (C$H_2$$)_4$Me] and 0.8 (3H, t, *J* 7, Me); δ_C (75 MHz; $CDCl_3$) 164.5 (C=O), 73.4 (CH_2O) 35.7 (*C*H_2CO), 34.5, 33.1, 31.5, 29.1, 27.3, 22.5 and 13.9 [$(CH_2)_5$Me]; *m*/*z* 188 (100%, M+18).

*3.14. Ozonolysis of (*E,*3*S,*3′*S*)-N,N-*dimethyl-3-(3′-dibenzylamino-4′-phenylbut-1′-en-1′-yl)nonanamide **13***

In the same way, but with acetyl chloride (43 μl, 0.57 mmol), ozonolysis for 80 min at 0°C gave, after purification by flash chromatography [2:1 petroleum ether (b.p. 40–60°C): ether], (*S*)-2-(dibenzylamino)-3-phenylpropan-1-ol **3** (50 mg, 63%).

Also obtained was (*R*)-2-hydroxymethyl-*N*,*N*-dimethylnonanamide **16** (25 mg, 75%) as a yellow oil; R_f [3:2 petroleum ether (b.p. 40–60°C): ether] 0.44; $[\alpha]_D^{25}=-14.4$ (c=2, EtOH); ν_{max}/cm^{-1} (film) 1628 (C=O); δ_H (300 MHz; $CDCl_3$) 3.7 (1H, dd, *J* 11 and 4, C$H_A$$H_B$OH), 3.5 (1H, dd, *J* 11 and 8, CH_AH_BOH), 3.1 (3H, s, N*Me*$_A$$Me_B$), 3.0 (3H, s, NMe_A*Me*$_B$), 2.5 (1H, dd, *J* 16 and 4, OCC$H_A$$H_B$), 2.4 (1H, dd, *J* 16 and 9, OCH_AH_B), 2.1 (1H, m, $HOCH_2$C*H*), 1.3 [10H, m, (C$H_2$$)_5$] and 0.8 (3H, t, *J* 7, CH_2*Me*); δ_C (75 MHz; $CDCl_3$) 173.7 (C=O), 66.7 (CH_2OH), 37.6 (*C*$H_2$$CONMe_2$), 37.5, 36.9, 35.6, 32.0, 31.7, 29.4, 27.0, 22.5, 14.0 [$(CH_2)_5$Me+*C*H*C*H_2CON*Me*$_2$]; *m*/*z* 216 (100%, *M*+1). [Found: $(M+H)^+$, 216.1968. $C_{12}H_{25}NO_2$ requires *M*+H, 216.1963.]

*3.15. (*S*)-Octane-1,2-diyl dipropionate **18***

Triethylamine (41 μl, 0.3 mmol), 4-(dimethylamino)pyridine (2 mg, 0.015 mmol) and propionyl chloride (27 μl, 0.3 mmol) were added to a mixture of the isomeric hydroxyesters **14** and **17** (31 mg, 0.15 mmol) in dichloromethane (5 ml) at room temperature. After 3 days, dichloromethane (10 ml) was added and the mixture was washed with water (3×10 ml) and dried (Na_2SO_4) and the solvent was removed under reduced pressure. Flash chromatography [1:1 petroleum ether (b.p. 40–60°C): ether] gave the diester **18** (31.6 mg, 82%) as a yellow oil, R_f [2:1 petroleum ether (b.p. 40–60°C): ether] 0.36; δ_H (300 MHz; $CDCl_3$) 5.0 (1H, dq, *J* 3 and 6, C*H*OCOEt), 4.2 (1H, dd, *J* 9 and 3.5, C$H_A$$H_B$OCOEt), 4.0 (1H, dd, *J* 12 and 9, CH_AH_BOCOEt), 2.2 (4H, q, *J* 8, CH_3CH_2CO×2), 1.5 [2H, m, C$H_2$$(CH_2)_4$Me], 1.2 [8H, m, (C$H_2$$)_4$Me], 1.05 (3H, t, *J* 8), 1.04 (3H, t, *J* 8) (C$H_3$$CH_2$CO×2) and 0.8 [3H, m, (C$H_2$$)_4$Me]; δ_C (75 MHz; $CDCl_3$) 174.0 (C=O); 71.0 (*C*HOCOEt), 65.0 (*C*H_2OCOEt), 32.0, 31.4 (Me*C*H_2CO×2), 29.8, 29.4, 27.4, 27.2, 25.0, 22.2, 14.0 and 9.5; *m*/*z* 276 (100%, M+18). [Found: $(M+H)^+$, 259.1922. $C_{14}H_{26}O_4$ requires *M*+H, 259.1909.]

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