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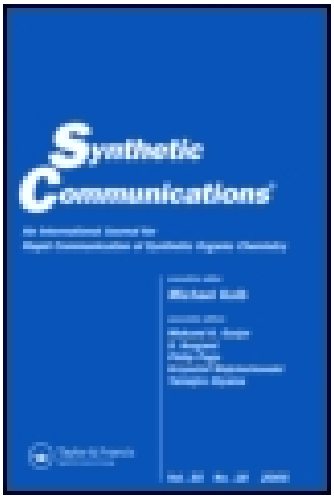

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Utilizing the Asymmetric Amino-Cope Rearrangement as a Novel Approach to Enantiomerically Enriched 3-Substituted Aldehydes

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UTILIZING THE ASYMMETRIC AMINO-COPE REARRANGEMENT AS A NOVEL APPROACH TO ENANTIOMERICALLY ENRICHED 3-SUBSTITUTED ALDEHYDES

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We report the asymmetric amino-Cope rearrangement of some novel 3-amino-1,5-diene substrates to yield enantiomerically enriched 3-alkyl and 3-aryl aldehyde products. We have developed a system that gives excellent and comparable levels of product enantiomeric excess (ee) for both alkyl- and aryl-substituted products. Our results have implications for the control of the mechanistic pathway of the amino-Cope rearrangement and thus its potential utility in asymmetric synthesis.

Keywords: Aldehyde; aminoalcohol; amino-Cope; asymmetric; rearrangement

There is considerable interest in asymmetric variants of sigmatropic rearrangements,[1] and we have pioneered the amino-Cope rearrangement as a new synthetic protocol. Scheme 1 summarizes our ultimate goal: the one-pot asymmetric synthesis of acyclic aldehyde targets containing up to three contiguous chiral centres via amino-Cope rearrangement (step 1) and subsequent enamine derivatization and hydrolysis (step 2).

Our group has pioneered the key steps of this protocol, including a successful tandem amino-Cope rearrangement–enamine derivatization reaction.[2] We have established that an anionic variant of the amino-Cope rearrangement is possible and that high asymmetric induction can be achieved at an asymmetric center created during the rearrangement of a diastereoisomerically pure substrate.[3] We have also reported applications of our methodology in the synthesis of enantiomerically enriched heterocyclic targets.[4]

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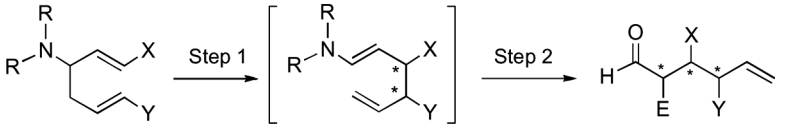

Scheme 1. Synthetic potential of the amino-Cope rearrangement.

Given our own work in this area, and that of Dobson et al.[5] and Yoo et al.,[6] there remains a question over the mechanisms involved in the anionic amino-Cope rearrangement. Whereas Yoo et al. have suggested a dissociation/recombination mechanism rather than a concerted [3,3]-rearrangement,[6] Dobson et al. prefer a competitive [1,3]-, not [3,3]-, rearrangement mechanism.[5] In our own work, a methyl group marker within the 3-amino-1,5-diene substrate gave further evidence of a competing mechanism to the expected [3,3]-rearrangement.[7]

So far we have *only* reported the asymmetric rearrangement of substrates bearing a phenyl substituent at the 1-position of the 3-amino-1,5-diene system (i.e., compound **2a**, R=Ph). High enantiomeric excess (*ee*) values can be obtained on rearrangement of this substrate,[3b] but clearly the *same* product is achieved on rearrangement of this substrate by *any* of the suggested mechanisms (Scheme 2). We have proposed the chairlike transition-state conformation, **4**, to rationalize the observed stereochemical outcome of the rearrangement; indeed we have shown that the absolute stereochemistry of the product aldehyde **3a** can be predicted using this rule of thumb, if one knows the absolute stereochemistry of the amine stereocenter in the 1,3-diene unit.[3]

Clearly, our overall proposal outlined in Scheme 1 relies heavily upon the control of the reaction mechanism, with the [3,3]-route being highly desirable. One would expect to observe higher *ee* values in reactions that proceed by a concerted [3,3]-rearrangement mechanism than one in which competitive dissociation played a major role, because dissociation of the substrate could lead to some loss of stereochemical information from within the diene unit. One would then be left with a remote chiral auxiliary as sole contributor to stereochemical induction in this process. A competing [1,3]-shift mechanism would also prove problematic for us because our proposal calls for the creation of neighboring stereocenters during amino-Cope rearrangement (at positions X and Y in Scheme 1). The work of Dobson et al. has suggested that the identity of the solvent can play an important role in

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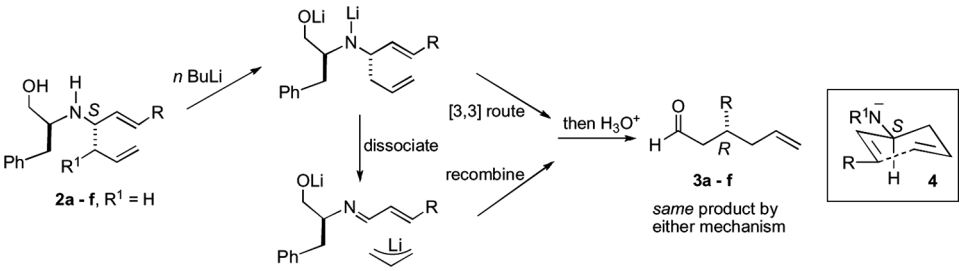


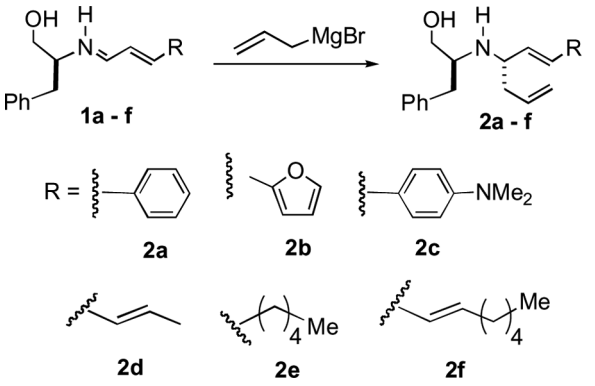
Scheme 2. Asymmetric amino-Cope rearrangement.

determining which mechanistic pathway is followed ([1,3] vs. [3,3]) on rearrangement of certain substrates. Tetrahydrofuran (THF) as solvent appears to promote the [1,3]-rearrangement, whereas the [3,3]-route can be favored by a solvent such as hexane.[5]

In this article, we report our own work in this area. It is important at the outset to note the differences between our substrates in this study, which lack any additional substituent at the 4-position of the 3-amino-1,5-diene substrates (Scheme 2, $R^1 = H$), and those of Dobson et al. that bear a thiophenol group in this position ($R^1 = SPh$). Interestingly, it is known in anionic oxy-Cope rearrangement chemistry that the presence of a sulfur-based substituent in this critical position (i.e., a Dobson-type substrate) promotes the dissociative heterolytic cleavage pathway as a result of the strong stabilizing effect of the divalent sulfur.[8]

Preparation of the 3-amino-1,5-diene substrates was accomplished through a previously reported route.[3b] A series of imines derived from phenylalaninol and unsaturated aldehydes were reacted with allyl magnesium bromide to yield the desired amino-dienes **2a**–**f** (Scheme 3). Rearrangement of substrates **2a**–**f** was performed on treatment with 2.5 eq. BuLi in the appropriate solvent system at −78 °C, followed by warming to ambient temperature before aqueous workup and product isolation by column chromatography (Scheme 2). The *ee* and absolute stereochemistry of the target aldehydes **3a**–**f** (Table 1) were determined by conversion to the corresponding diastereoisomeric oxazolidine derived from 1*R*,2*S*-(–)-ephedrine, as described by Agami et al.[9]

As can be appreciated from Table 1, THF remains the solvent of choice, with toluene and hexanes generally giving lesser yields and product *ee* values (in five out of the six cases). In THF, the lowest *ee* is observed with substrate **2d**, with arguably the least sterically demanding substituent (a 3-carbon unit). As the chain length of the substituent increases (i.e., in substrates **2e** and **2f**), the *ee* increases above that of substrate **2d**. The observation that the *ee* is slightly lower with the longer chain substituent **2f** (a 7-carbon unit) than with **2e**, the 6-carbon unit, is perhaps due to an increase in effective steric bulk of the 6-carbon alkyl substituent on removing the conjugating (planar) alkene moiety present in **2f**; thereby **2e** may have slightly



Scheme 3. Preparation of 3-amino-1,5-diene substrates.

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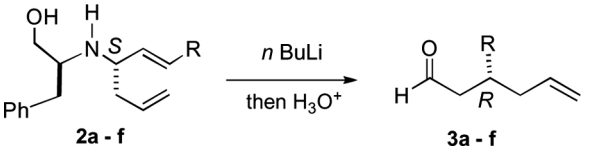
Table 1. Asymmetric anionic amino-Cope rearrangement of substrates **2a–f**



2a - f **3a - f**

Product	R	THF		Toluene		Hexanes	
		Yield (%)	*ee* (%)	Yield (%)	*ee* (%)	Yield (%)	*ee* (%)
3a	Ph	69	82 (*R*)	69	60	44	39
3b	-2-Furyl	53	67 (*R*)	32	56	19	52
3c	-Ph-4-N(Me)$_2$	65	75 (*R*)	59	60	53	65
3d	-CH=CHMe	35	44 (*R*)	16	36	8	55
3e	-(CH$_2$) $_4$Me	21	89 (*R*)	22	87	8	77
3f	-CH=CH(CH$_2$)$_4$Me	54	70 (*R*)	37	66	12	63

more degrees of freedom as a substituent, and its influence on the transition state of the rearrangement may be more keenly felt. The cyclic aromatic substituents present in substrates **2a–c** give comparable levels of *ee* in THF, with furan being lowest of all, perhaps because of its slightly smaller steric bulk. These arguments could be applied to rationalize the observed *ee* values if one continued to apply the chairlike conformational model, **4**, noted previously, with the bulkier substituents expected to occupy a pseudo-equatorial orientation. In all cases, the induced product stereochemistry was as predicted by our usual model, **4**.

Since the *ee* varied significantly in THF across the range of substrates, we decided to investigate the addition of a cosolvent. In the Dobson study, the use of a cosolvent such as N,N,N′,N′-tetramethylethylenediamine (TMEDA) or hexamethylphosphoramide (HMPA) gave an increase in the [3,3]- to [1,3]-product ratio in toluene and hexanes, but with THF the use of a cosolvent actually favored the [1,3]-process.[5] We chose to investigate the rearrangement of three of the substrates noted earlier: our previously favored model **2a**, the furan derivative **2b** (because this gave the lowest *ee* of the aryl substituents), and **2d** (the substrate giving the lowest *ee* of all, 8% *ee*, in hexanes). We chose to use 1,3-dimethyl-3,4,5,6-tetrahydro-2-(1H)-pyrimidinone (DMPU) as a cosolvent (in varying amounts) in our study, as a replacement for HMPA, and THF as the main solvent because hexanes and toluene had given inferior yields in our initial screen of solvents. Our results are presented in Table 2.

The addition of DMPU as a cosolvent reduced product yield in all cases, but this was accompanied by significant increases in the *ee* of the product aldehydes. The method of choice is to reduce the amount of cosolvent to just 2.5 equivalents in THF solvent. Under these conditions, we observed an excellent increase in *ee* from 35% in THF alone to 83% *ee* in THF-DMPU with substrate **2d**. Although the product yields have been sacrificed somewhat, we do observe an increase in the product yield with all substrates as the amount of cosolvent is decreased to 2.5 equivalents in THF.

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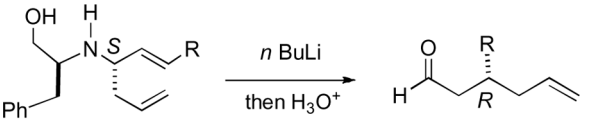
Table 2. Effect of DMPU as a cosolvent in the amino-Cope rearrangement in THF



2a, b, d **3a, b, d**

		10 eq. DMPU		5 eq. DMPU		2.5 eq. DMPU	
Product	R	Yield (%)	*ee* (%)	Yield (%)	*ee* (%)	Yield (%)	*ee* (%)
3a	-Ph	6	84	29	86	50	89
3b	-2-Furyl	11	75	32	82	41	82
3d	-CH=CHMe	8	72	10	81	18	83

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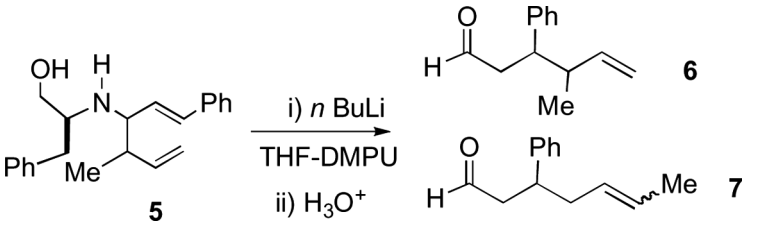
As noted in Scheme 2, the possibility exists of competing rearrangement mechanisms, leading to the formation of products **3a**–**f** via alternative, non-[3,3]-routes. We reasoned that the presence of a methyl group marker at position 4 of the 3-amino-1,5-diene (Scheme 4) would allow us to detect the involvement of alternative reaction pathways during rearrangement in the now favored THF-DMPU solvent system. Amino-diene **5** was prepared as previously described by us.[7] Clearly, a concerted [3,3]-rearrangement of substrate **5** would lead to product **7**, with the methyl group marker ultimately located at the terminal alkene position. Formation of isomeric product **6** would indicate the involvement of alternative mechanistic pathways for rearrangement.

Previous work with the corresponding amino-diene derivative of valinol had shown that rearrangement in THF alone proceeded to give a 1:1 mixture (57% yield) of the available isomeric products, confirming that in THF alone the rearrangement could not proceed solely by a [3,3]-mechanism.[7] However, on treating amino-diene substrate **5** under typical rearrangement conditions in THF-DMPU, we observed a yield of 49% for the reaction, with preferential formation of the [3,3]-product **7**. The observed ratio of **7**:**6**, at >9:1, clearly demonstrates the enhanced control of the reaction that is attainable in this mixed solvent system.

In summary, we have investigated a range of solvent systems for the asymmetric amino-Cope rearrangement of some novel 3-amino-1,5-diene substrates and have developed a new route for the asymmetric synthesis of 3-alkyl and 3-aryl aldehydes. We have discovered that a solvent system of THF-DMPU (2.5 equivalents) produces



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Scheme 4. Marker experiment with the THF-DMPU solvent system.

better and comparable levels of *ee* for the 3-aryl or 3-alkyl substituted aldehyde products. The consistency of the product *ee* across the substrate types, the predictive capacity of the conformational model used by us, and our results obtained when using a methyl group marker support the premise that the rearrangement is proceeding predominantly through a [3,3]-mechanism in the THF-DMPU cosolvent system developed herein.

EXPERIMENTAL

General Experimental Details

All solvents were dried, distilled, and stored over 4-Å molecular sieves prior to use. Analytical thin layer chromatography (TLC) was carried out using aluminium-backed plates coated with 0.2 mm silica. Plates were visualized under ultraviolet (UV) light (at 254 nm) or by staining with either potassium permanganate solution or PMA (phosphomolybdic acid). Flash-column chromatography was carried out using Merck Kieselgel (70–230 mesh ASTM). Samples were applied as saturated solutions in an appropriate solvent or pre-adsorbed onto the minimum quantity of silica. Hand bellows were used to apply pressure when required at the column. Infrared (IR) spectra were recorded in the range from 4000 to 600 cm^{-1}. Solid samples were run as nujol mull, and liquids were run as thin films. Nuclear magnetic resonance (NMR) spectra (^{1}H and ^{13}C) were recorded using either Bruker AC-250 or DPX-400 instruments. Multiplicities were recorded as broad peaks (br), singlets (s), doublets (d), triplets (t), and multiplets (m). All NMR samples were made up in deuterated chloroform with all values quoted in parts per million relative to tetramethylsilane (TMS) as internal reference, unless otherwise stated. Coupling constants (*J* values) are reported in hertz (Hz). Diastereoisomer ratios were calculated from the integration of suitable peaks in the proton NMR.

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(*S*,2*E*)-2-((*E*)-3-Phenylallylideneamino)-3-phenylpropan-1-ol 1a

trans-Cinnamaldehyde (1.66 mL, 13.2 mmol) was added dropwise to a stirred solution of (*S*)-2-amino-3-phenylpropan-1-ol (2.0 g, 13.2 mmol) in dicholoromethane (DCM; 50 mL) at room temperature. The solution was stirred for 10 min, anhydrous magnesium sulfate was added, and the reaction mixture was stirred for an additional 10 min. Filtration and removal of solvent under reduced pressure produced the target compound as a yellow solid (3.48 g, 99%), a sample of which was recrystallized from DCM/hexanes to yield white crystals: mp 115–116 °C; $[\alpha]_D^{25} = -220$ (*c* 1.0, $CHCl_3$); IR (nujol) 3220, 3026, 2921, 2856, 1635, 1450, 749 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) 2.78 (1H, dd, *J* 13.6, 8.8), 2.92 (1H, dd, *J* 13.6, 5.2), 3.40–3.44 (1H, m), 3.78 (1H, dd, *J* 11.2, 3.6), 3.85 (1H, dd, *J* 11.2, 7.6), 6.64 (1H, d, *J* 16.0), 6.77 (1H, dd, *J* 16.0, 8.8), 7.12–7.37 (10H, m), 7.63 (1H, d, *J* 8.8); ^{13}C NMR ($CDCl_3$, 100 MHz) 39.4, 66.2, 74.9, 126.6, 127.5, 127.6 (2), 128.8 (2), 129.1 (2), 129.5, 129.9 (2), 135.9, 138.9, 142.8, 164.4; HRMS (EI) 265 (M^+, 7%), 174 (100%). Calcd for $C_{18}H_{19}NO$: 265.1467; found: 265.1468.

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(*S,2E*)-2-((*E*)-3-(Furan-2-yl)allylideneamino)-3-phenylpropan-1-ol 1b

3-(2-Furyl)acrolein (1.62 g, 13.2 mmol) was added to a stirred solution of (*S*)-2--amino-3-phenylpropan-1-ol (2.0 g, 13.2 mmol) in DCM (50 mL) at room temperature. The solution was stirred for 10 min, anhydrous magnesium sulfate was added, and the reaction mixture was stirred for an additional 10 min. Filtration and removal of solvent under reduced pressure produced the target compound as a yellow solid (3.31 g, 98%), a sample of which was recrystallized from diethyl ether/hexanes to yield yellow crystals: mp 75–78 °C; $[\alpha]_D^{25} = -245.6$ (*c* 1.4, $CHCl_3$); IR (nujol) 3227, 2855, 1628, 1016, 745, 701 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 2.78 (1H, dd, *J* 13.4, 8.6), 2.92 (1H, dd, *J* 13.4, 8.4), 3.38–3.41 (1H, m), 3.76 (1H, dd, *J* 11.3, 3.5), 3.83 (1H, dd, *J* 11.3, 7.5), 6.38–6.41 (2H, m), 6.50 (1H, d, *J* 15.9), 6.67 (1H, dd, *J* 15.9, 9.1), 7.11–7.26 (5H, m), 7.41 (1H, s), 7.58 (1H, d, *J* 9.1); ^{13}C NMR ($CDCl_3$, 100 MHz) 38.9, 65.8, 74.3, 111.9 (2), 125.4, 126.1, 128.2 (2), 129.0, 129.6 (2), 138.5, 143.8, 151.7, 163.6; HRMS (EI) 255 (M^+, 18%), 164 (100%). Calcd for $C_{16}H_{17}NO_2$: 255.1259; found: 255.1258.

(*S,2E*)-2-((*E*)-3-(4-(Dimethylamino)phenyl)allylideneamino)-3-phenylpropan-1-ol 1c

4-Dimethylaminocinnamaldehyde (2.32 g, 13.2 mmol) was added to a stirred solution of (*S*)-2-amino-3-phenylpropan-1-ol (2.0 g, 13.2 mmol) in DCM (50 mL) at room temperature. The solution was stirred for 10 min, anhydrous magnesium sulfate was added, and the reaction mixture was stirred for an additional 10 min. Filtration and removal of solvent under reduced pressure produced the target compound as a yellow solid (3.96 g, 97%), a sample of which was recrystallized from diethyl ether/hexanes to yield yellow crystals: mp 161–164 °C; $[\alpha]_D^{25} = -217.0$ (*c* 1.1, $CHCl_3$). $C_{20}H_{24}N_2O$ requires C, 77.89; H, 7.84; N, 9.08%; found: C, 77.61; H, 7.86; N, 9.07. IR (nujol) 3156, 2922, 2843, 1631, 1603, 1367, 981, 814 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) 2.79 (1H, dd, *J* 13.4, 8.0), 2.92 (1H, dd, *J* 13.4, 5.6), 3.00 (6H, s), 3.37–3.42 (1H, m), 3.74–3.83 (2H, m), 6.63–6.70 (4H, m), 7.15–7.34 (7H, m), 7.68 (1H, d, *J* 7.6); ^{13}C NMR ($CDCl_3$, 100 MHz) 39.6, 40.7 (2), 66.4, 74.8, 112.3 (2), 123.0, 124.0, 126.5, 128.7 (2), 129.2 (2), 130.1 (2), 139.2, 143.6, 151.4, 165.2; HRMS (EI) 308 (M^+, 42%), 217 (100%). Calcd. for $C_{20}H_{24}N_2O$: 308.1889; found: 308.1893.

(*S,2E*)-2-((*2E,4E*)-Hexa-2,4-dienylideneamino)-3-phenylpropan-1-ol 1d

trans,trans-2,4-Hexadienal (1.46 mL, 13.2 mmol, containing a trace of the minor *trans, cis* isomer) was added dropwise to a stirred solution of (*S*)-2-amino-3-phenylpropan-1-ol (2.0 g, 13.2 mmol) in DCM (50 mL) at room temperature. The solution was stirred for 10 min, anhydrous magnesium sulfate was added, and the reaction mixture was stirred for an additional 10 min. Filtration and removal of solvent under reduced pressure produced the target compound as a yellow oil (2.86 g, 94%), which was used without further purification: $[\alpha]_D^{25} = -146.8$ (*c* 0.9, $CHCl_3$); IR (neat) 3244, 3025, 2914, 2856, 1628, 1453, 995, 737, 701 cm^{-1}; ^1H NMR ($CDCl_3$,

400 MHz) 1.81 (3H, d, *J* 8.0), 2.75 (1H, dd, *J* 13.5, 8.2), 2.89 (1H, dd, *J* 13.5, 5.4), 3.31–3.37 (1H, m), 3.69–3.78 (2H, m), 5.88–5.94 (1H, m), 6.10–6.20 (2H, m), 6.43 (1H, dd, *J* 10.7, 5.3), 7.11–7.27 (5H, m), 7.56 (1H, d, *J* 9.1); ^{13}C NMR ($CDCl_3$, 100 MHz) 18.5, 39.0, 65.9, 74.0, 126.1, 128.2 (2), 128.5, 129.6 (2), 130.8, 135.7, 138.5, 142.9, 164.3; HRMS (EI) 230 [$(M+1)^+$, 100%]. Calcd. for $C_{15}H_{20}NO$: 230.1545; found: 230.1540.

(*S*, 2*E*)-2-((*E*)-Oct-2-enylideneamino)-3-phenylpropan-1-ol 1e

trans-2-Octenal (1.97 mL, 13.2 mmol) was added dropwise to a stirred solution of (*S*)-2-amino-3-phenylpropan-1-ol (2.0 g, 13.2 mmol) in DCM (50 mL) at room temperature. The solution was stirred for 10 min, anhydrous magnesium sulfate was added, and the reaction mixture was stirred for an additional 10 min. Filtration and removal of solvent under reduced pressure produced the target compound as a yellow oil (3.25 g, 95%), which was used without further purification: $[\alpha]_D^{25} = -102.5$ (*c* 1.5, $CHCl_3$); IR (neat) 3237, 2953, 2925, 2856, 1653, 1495, 1453, 1080, 1046, 747 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) 0.88 (3H, t, *J* 7.2), 1.23–1.50 (6H, m), 2.03–2.14 (2H, m), 2.73 (1H, dd, *J* 13.5, 8.4), 2.89 (1H, dd, *J* 13.5, 5.3), 3.27–3.37 (1H, m), 3.71 (1H, dd, *J* 11.4, 3.6), 3.79 (1H, dd, *J* 11.4, 7.6), 5.97–6.04 (1H, m), 6.11 (1H, dd, *J* 15.6, 8.5), 7.10–7.28 (5H, m), 7.44–7.48 (1H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) 14.0 (CH_3), 22.4, 28.1, 31.3, 32.5, 39.0, 65.6, 74.1, 126.4, 128.2 (2), 129.7 (2), 129.8, 138.6, 146.8, 164.3; HRMS (EI) 259 (M^+, 3%), 168 (100%). Calcd. for $C_{17}H_{25}NO$: 259.1936; found: 259.1932.

(*S*,2*E*)-2-((2*E*,4*E*)-Deca-2,4-dienylideneamino)-3-phenylpropan-1-ol 1f

trans,trans-2,4-Decadienal (2.30 mL, 13.2 mmol) was added dropwise to a stirred solution of (*S*)-2-amino-3-phenylpropan-1-ol (2.0 g, 13.2 mmol) in DCM (50 mL) at room temperature. The solution was stirred for 10 min, anhydrous magnesium sulfate was added, and the reaction mixture was stirred for an additional 10 min. Filtration and removal of solvent under reduced pressure produced the target compound as a yellow oil (3.74 g, 99%), which was used without further purification: $[\alpha]_D^{25} = -101.6$ (*c* 1.2, $CHCl_3$); IR (neat) 3276, 2924, 2855, 1629, 1453, 1046, 995, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) 0.88 (3H, t, *J* 7.2), 1.25–1.41 (6H, m), 2.08–2.13 (2H, m), 2.73 (1H, dd, *J* 13.4, 8.3), 2.88 (1H, dd, *J* 13.4, 5.1), 3.29–3.36 (1H, m), 3.70–3.81 (2H, m), 5.82–5.90 (1H, m), 6.04–6.23 (2H, m), 6.37 (1H, dd, *J* 16.0, 8.0), 7.10–7.26 (5H, m), 7.49 (1H, d, *J* 9.1); ^{13}C NMR ($CDCl_3$, 100 MHz) 14.0, 22.4, 28.5, 31.3, 32.8, 38.9, 65.7, 74.3, 126.1, 128.2 (2), 128.4, 129.3, 129.5 (2), 138.5, 141.2, 143.1, 164.2; HRMS (EI) 286 [$(M+1)^+$, 100%]. Calcd. for $C_{19}H_{28}NO$: 286.2171; found: 286.2170.

(*S*)-2-((*S*,*E*)-1-Phenylhexa-1,5-dien-3-ylamino)-3-phenylpropan-1-ol 2a

(*S*,2*E*)-2-((*E*)-3-Phenylallylideneamino)-3-phenylpropan-1-ol (3.0 g, 11.3 mmol) was dissolved in a 4:1 mixture of dry toluene/diethyl ether (75 mL) under a nitrogen

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atmosphere. Magnesium turnings (0.91 g, 37.3 mmol) and a catalytic amount of iodine were added to the solution. Allyl bromide (3.16 mL, 37.3 mmol) was cautiously added, and the mixture was stirred for 18 h. The reaction was quenched with water until a gelatinous precipitate formed. The organic layer was decanted, and the gelatinous residue was rinsed with diethyl ether (2×50 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$(2×75 mL), dried over anhydrous sodium sulfate, and filtered. The solvent was removed under reduced pressure, and a yellow solid was obtained, which was recrystallized from diethyl ether/hexanes to yield the target compound **2a** as white crystals (2.74 g, 79%): mp 73–74 °C; $[\alpha]_D^{25}$ −43.3 (*c* 1.6, $CHCl_3$); IR (nujol) 3320, 3024, 2924, 1494, 1453, 1030, 967, 748, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 2.22–2.25 (2H, m), 2.71–2.81 (2H, m), 2.99–3.04 (1H, m), 3.22–3.27 (1H, m), 3.34 (1H, dd, *J* 10.6, 3.5), 3.63 (1H, dd, *J* 10.6, 3.5), 5.04–5.10 (2H, m), 5.68 (1H, dd, *J* 15.9, 8.3), 5.73–5.81 (1H, m), 6.28 (1H, d, *J* 15.9), 7.13–7.33 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$) 38.9, 40.9, 56.4, 57.7, 62.0, 117.5, 126.3 (2C), 126.4, 127.4, 128.49 (2C), 128.52 (2C), 129.2 (2C), 130.7, 132.0, 134.8, 136.7, 138.6; HRMS (EI) 308 ($[M+1]^+$, 100%). Calcd. for $C_{21}H_{26}NO$: 308.2014; found: 308.2012.

(*S*)-2-((*S,E*)-1-(Furan-2-yl)hexA-1,5-dien-3-ylamino)-3-phenylpropan-1-ol 2b

(*S*)-2(*E*)-2-((*E*)-3-(Furan-2-yl)allylideneamino)-3-phenylpropan-1-ol (3.0 g, 11.8 mmol) was dissolved in a 4:1 mixture of dry toluene/diethyl ether (75 mL) under a nitrogen atmosphere. Magnesium turnings (0.94 g, 38.8 mmol) and a catalytic amount of iodine were added to the solution. Allyl bromide (3.28 mL, 38.8 mmol) was cautiously added, and the mixture was stirred for 18 h. The reaction was quenched with water until a gelatinous precipitate formed. The organic layer was decanted, and the gelatinous residue was rinsed with diethyl ether (2×50 mL). The combined organic layers were washed twice with a saturated solution of $NaHCO_3$ (2×75 mL), dried over anhydrous sodium sulfate, and filtered. The solvent was removed under reduced pressure, and a brown solid was obtained, which was recrystallized from diethyl ether/hexanes to yield the target compound **2b** as yellow crystals (2.56 g, 78%); mp 88–90 °C; $[\alpha]_D^{25}$ −103.2 (*c* 1.0, $CHCl_3$); IR (nujol) 3386, 2923, 1453, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 2.22 (2H, m), 2.70–2.81 (2H, m), 2.97–3.03 (1H, m), 3.20–3.25 (1H, m), 3.32 (1H, dd, *J* 10.7, 3.5), 3.60 (1H, dd, *J* 10.7, 3.8), 5.04–5.10 (2H, m), 5.69–5.81 (2H, m), 6.03 (1H, d, *J* 16.1), 6.13 (1H, d, *J* 3.2), 6.36 (1H, d, *J* 3.2), 7.15–7.28 (5H, m), 7.33 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) 38.8, 40.9, 56.5, 57.4, 61.9, 107.5, 111.2, 117.6, 119.1, 126.4, 128.5 (2C), 129.2 (2C), 130.7, 134.8, 138.5, 141.7, 152.3; HRMS (EI) 298 ($[M+1]^+$, 83%), 147 (100%). Calcd. for $C_{19}H_{24}NO_2$: 298.1807; found 298.1818.

(*S*)-2-(*S,E*)-1-(4-(Dimethylamino)phenyl)hexa-1,5-dien-3-ylamino)-3-phenylpropan-1-ol 2c

(*S*,2*E*)-2-((*E*)-3-(4-(Dimethylamino)phenyl)allylideneamino)-3-phenylpropan-1-ol (3.0 g, 9.7 mmol) was dissolved in a 4:1 mixture of dry toluene/Et_2O

(75 mL) under a nitrogen atmosphere. Magnesium turnings (0.78 g, 32.1 mmol) and a catalytic amount of iodine were added to the solution. Allyl bromide (2.72 mL, 32.1 mmol) was cautiously added, and the mixture was stirred for 18 h. The reaction was quenched with water, and a gelatinous precipitate formed. The organic layer was decanted, and the gelatinous residue was rinsed with diethyl ether (2×50 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$(2×75 mL), dried over anhydrous sodium sulfate, and filtered. The solvent was removed under reduced pressure, and a yellow solid was obtained, which was recrystallized from diethyl ether/hexanes to yield the target compound **2c** as orange crystals (3.04 g, 89%); mp 116–118 °C; $[\alpha]_D^{25}$–65.7 (*c* 1.0, $CHCl_3$); IR (nujol) 2891, 1611, 1523, 1354, 965, 804, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 2.24–2.29 (2H, m), 2.79–2.81 (2H, m), 2.99 (6H, s), 3.02–3.08 (1H, m), 3.24–3.26 (1H, m), 3.36 (1H, dd, *J* 10.4, 3.2), 3.66 (1H, dd, *J* 10.4, 4.0), 5.06–5.09 (2H, m), 5.53 (1H, dd, *J* 15.8, 8.4), 5.78–5.84 (1H, m), 6.23 (1H, d, *J* 15.8), 6.72 (2H, d, *J* 4.8), 7.18–7.31 (7H, m); ^{13}C NMR (100 MHz, $CDCl_3$) 39.3, 41.0 (2C), 41.6, 56.7, 58.5, 62.3, 112.9 (2C), 117.7, 125.6, 126.8, 127.7 (2C), 128.1, 129.0 (2C), 129.8 (2C), 131.2, 135.7, 139.1, 150.5; HRMS (EI) 350 (M^+, 1%), 309 (100%). Calcd. for $C_{23}H_{30}N_2O$: 350.2358; found: 350.2365.

(*S*)-2-((*S*,5*E*,7*E*)-Nona-1,5,7-trien-4-ylamino)-3-phenylpropan-1-ol 2d

(*S*,2*E*)-2-((2*E*,4*E*)-Hexa-2,4-dienylideneamino)-3-phenylpropan-1-ol (2.50 g, 10.9 mmol) was dissolved in a 4:1 mixture of dry toluene/diethyl ether (75 mL) under a nitrogen atmosphere. Magnesium turnings (0.87 g, 36.0 mmol) and a catalytic amount of iodine were added to the solution. Allyl bromide (3.04 mL, 36.0 mmol) was cautiously added, and the mixture was stirred for 18 h. The reaction was quenched with water until a gelatinous precipitate formed. The organic layer was decanted, and the gelatinous residue was rinsed with Et_2O (2×50 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$ (2×75 mL), dried over anhydrous sodium sulfate, and filtered. The solvent was removed under reduced pressure, and a yellow solid was obtained, which was adsorbed onto silica and purified by flash-column chromatography (4:1, hexanes/EtOAc) to produce a yellow solid. Traces of a minor isomer, resulting from the presence of traces of *trans,cis*-2,4-hexadienal in the original commercial reagents, were partially removed by recrystallization from hexanes, yielding the target compound **2d** as white crystals (1.91 g, 65%); mp 74–75 °C; $[\alpha]_D^{25}$ −35.8 (*c* 1.6, $CHCl_3$). Calcd. for $C_{18}H_{25}NO$: C, 79.66; H, 9.28; N, 5.16; found: C, 79.67; H, 9.29; N, 5.09. IR (nujol) 3403, 3023, 2927, 1639, 1495, 1453, 1265, 1030, 990, 739, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 1.75 (3H, dd, *J* 6.7, 1.7), 2.13–2.17 (2H, m), 2.68–2.78 (2H, m), 2.93–2.98 (1H, m), 3.07–3.12 (1H, m), 3.28 (1H, dd, *J* 10.7, 3.5), 3.51 (1H, dd, *J* 10.7, 3.8), 5.02–5.09 (3H, m), 5.59–5.75 (2H, m), 5.84–5.98 (2H, m), 7.15–7.31 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) 18.1, 38.8, 40.9, 56.3, 57.3, 61.7, 117.3, 126.4, 128.5 (2C), 129.1, 129.3 (2C), 130.8, 131.2, 132.8, 135.0, 138.5; HRMS (FAB) 272 ($[M+1]^+$, 37%), 92 (100%). Calcd. for $C_{18}H_{26}NO$: 272.2014; found: 272.2012.

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(*S*)-2-((*S,E*)-Undeca-1,5-dien-4-ylamino)-3-phenylpropan-1-ol 2e

(*S*,2*E*)-2-((*E*)-Oct-2-enylideneamino)-3-phenylpropan-1-ol (3.0 g, 11.6 mmol) was dissolved in a 4:1 mixture of dry toluene/Et_2O (75 mL) under a nitrogen atmosphere. Magnesium turnings (0.93 g, 38.2 mmol) and a catalytic amount of iodine were added to the solution. Allyl bromide (3.23 mL, 38.2 mmol) was cautiously added, and the mixture was stirred for 18 h. The reaction was quenched with water until a gelatinous precipitate formed. The organic layer was decanted, and the gelatinous residue was rinsed with diethyl ether (2×50 mL). The combined organic layers were washed with a saturated solution of $NaHCO_3$ (2×75 mL), dried over anhydrous sodium sulfate, and filtered. The solvent was removed under reduced pressure, and a yellow oil was obtained, which was adsorbed onto silica and purified by flash-column chromatography (9:1, hexanes/EtOAc). The target compound **2e** was isolated as yellow crystals (2.15 g, 62%), a portion of which was recrystallized from diethyl ether/hexanes to yield pale yellow needles: mp 54–57 °C; $[\alpha]_D^{25}$ −44.7 (*c* 1.6, $CHCl_3$). Calcd. for $C_{20}H_{31}NO$: C, 79.68; H, 10.36; N, 4.65; found: C, 79.58; H, 10.68; N, 4.67. IR (nujol) 3028, 2924, 1463, 1118, 967, 914, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* 6.8), 1.24–1.34 (6H, m), 1.93–1.98 (2H, m), 2.04–2.17 (2H, m), 2.69–2.79 (2H, m), 2.94–2.98 (1H, m), 3.00–3.05 (1H, m), 3.28 (1H, dd, *J* 10.6, 3.6), 3.55 (1H, dd, *J* 10.6, 3.9), 4.93 (1H, dd, *J* 15.3, 8.4), 5.00–5.06 (2H, m), 5.31–5.38 (1H, m), 5.67–5.78 (1H, m), 7.15–7.30 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) 14.5, 22.9, 29.4, 31.8, 32.6, 39.7, 41.4, 56.6, 57.9, 62.1, 117.4, 126.8, 128.9 (2C), 129.7 (2C), 132.4, 132.7, 135.7, 139.0; HRMS (EI) 300 ($[M-1]^+$, 1%), 260 (100%). Calcd. for $C_{20}H_{30}NO$: 300.2327; found: 300.2323.

(*S*)-2-((*S,5E,7E*)-Trideca-1,5,7-trien-4-ylamino)-3-phenylpropan-1-ol 2f

(*S*,2*E*)-2-((2*E*,4*E*)-Deca-2,4-dienylideneamino)-3-phenylpropan-1-ol (3.5 g, 12.3 mmol) was dissolved in a 4:1 mixture of dry toluene/diethyl ether (100 mL) under a nitrogen atmosphere. Magnesium turnings (0.98 g, 40.5 mmol) and a catalytic amount of iodine were added to the solution. Allyl bromide (3.42 mL, 40.5 mmol) was cautiously added, and the mixture was stirred for 18 h. The reaction was quenched with water until a gelatinous precipitate formed. The organic layer was decanted, and the gelatinous residue was rinsed with diethyl ether (2×50 mL).). The combined organic layers were washed with a saturated solution of $NaHCO_3$(2×75 mL), dried over anhydrous sodium sulfate, and filtered. The solvent was removed under reduced pressure, and a yellow solid was obtained, which was adsorbed onto silica and purified by flash-column chromatography (4:1, hexanes/EtOAc) followed by recrystallization from hexanes to yield the target compound **2f** as white crystals (2.69 g, 67%): mp 62–63 °C; $[\alpha]_D^{25}$–32.1 (*c* 1.1, $CHCl_3$). Calcd. for $C_{22}H_{33}NO$: C, 80.68; H, 10.16; N, 4.28; found: C, 80.83; H, 9.98; N, 4.15. IR (nujol) 3319, 2954, 2924, 1495, 1454, 989, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* 6.9), 1.24–1.43 (6H, m), 2.03–2.09 (2H, m), 2.12–2.17 (2H, m), 2.68–2.78 (2H, m), 2.93–2.98 (1H, m), 3.07–3.12 (1H, m), 3.28 (1H, dd, *J* 10.6, 3.5), 3.57 (1H, dd, *J* 10.6, 3.8), 5.02–5.11 (4H, m), 5.56–5.64 (1H, m), 5.67–5.78 (1H, m), 5.84–5.96 (2H, m), 7.15–7.31 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$,)

14.1, 22.5, 28.9, 31.4, 32.6, 38.9, 40.9, 56.3, 57.3, 61.8, 117.2, 126.4, 128.5 (2C), 129.28 (2C), 129.33, 131.3, 133.0, 134.8, 135.0, 138.6; HRMS (EI) 328 ($[M+1]^+$, 100%). Calcd. for $C_{22}H_{34}NO$: 328.2640; found: 328.2649.

(*R*)-3-Phenylhex-5-enal 3a

(*S*)-2-((*S,E*)-1-Phenylhexa-1,5-dien-3-ylamino)-3-phenylpropan-1-ol **2a** (2.50 g, 8.1 mmol) was dried in vacuo for 1 h, dissolved in dry THF (40 mL) under a nitrogen atmosphere, and cooled to −78 °C. A 2.5 M solution of *n*-BuLi in hexanes (8.13 mL, 20.3 mmol) was added dropwise, and the mixture was stirred for 10 min before warming to room temperature. The resultant solution was heated at reflux for 1 h, quenched with water, dried over anhydrous sodium sulfate, and filtered through a small pad of celite, eluting with DCM. The solvent was removed under reduced pressure, and an orange oil was obtained, which was adsorbed onto silica and purified by flash-column chromatography (9:1, light petroleum/diethyl ether) to yield the target compound **3a** as a pale yellow oil (0.98 g, 69%): $[\alpha]_D^{25}$ −21.3 (*c* 1.7, $CHCl_3$); IR (neat) 3028, 2923, 1724, 1494, 1453, 915, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 2.34–2.46 (2H, m), 2.68–2.81 (2H, m), 3.26–3.33 (1H, m), 4.93–5.04 (2H, m), 5.55–5.70 (1H, m), 7.18–7.32 (5H, m), 9.60 (1H, t, *J* 1.9); ^{13}C NMR (100 MHz, $CDCl_3$) 40.13, 41.3, 49.7, 117.6, 126.7, 127.5 (2C), 128.5 (2C), 136.1, 143.8, 202.1; HRMS (EI) 174 (M^+, 8%), 105 (100%). Calcd for $C_{12}H_{14}O$: 174.1045; found: 174.1046.

Following rearrangements and isolation, the *ee* values of all aldehyde products were immediately determined by conversion to the diastereoisomeric oxazolidine derivative of 1*R*, 2*S*-(–)-ephedrine, as described by Agami et al.[9]

The same procedure was conducted separately in toluene, hexanes, and THF/DMPU. In each case, the solvents were removed under reduced pressure, and the crude orange oil was adsorbed onto silica and purified by flash-column chromatography (9:1, light petroleum/diethyl ether) to yield the target compound **3a** as a pale yellow oil. Spectroscopic data were identical to those previously obtained for **3a**.

(*R*)-3-(Furan-2-yl)hex-5-enal 3b

(*S*)-2-((*S,E*)-1-(Furan-2-yl)hexa-1,5-dien-3-ylamino)-3-phenylpropan-1-ol **2b** (1.0 g, 3.4 mmol) was dried in vacuo for 1 h, dissolved in dry THF (30 mL) under a nitrogen atmosphere, and cooled to −78 °C. A 2.5 M solution of *n*-BuLi in hexanes (3.36 mL, 8.4 mmol) was added dropwise, and the mixture was stirred for 10 min before warming to room temperature. The resultant solution was heated at reflux for 1 h, quenched with water, dried over anhydrous sodium sulfate, and filtered through a small pad of celite, eluting with DCM. The solvent was removed under reduced pressure, and an orange oil was obtained, which was adsorbed onto silica and purified by flash-column chromatography (9:1, light petroleum/diethyl ether) to yield the target compound **3b** as a pale yellow oil (0.29 g, 53%): $[\alpha]_D^{25}$ −13.6 (*c* 1.0, $CHCl_3$); IR (neat) 2923, 1724, 1506, 1011, 920, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 2.33–2.41 (1H, m), 2.46–2.54 (1H, m), 2.66–2.78 (2H, m), 3.39–3.46 (1H, m), 5.03–5.08 (2H, m), 5.64–5.75 (1H, m), 6.04 (1H, d, *J* 3.2), 6.28

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(1H, dd, *J* 3.2, 1.8), 7.32 (1H, dd, *J* 1.8, 0.7), 9.73 (1H, t, *J* 1.9); ^{13}C NMR (100 MHz, $CDCl_3$) 32.9, 38.0, 46.6, 105.4, 110.0, 117.5, 135.1, 141.3, 156.3, 201.3; HRMS (EI) 164 (M^+, 11%), 95 (100%). Calcd. for $C_{10}H_{12}O_2$: 164.0837; found: 164.0835.

The same procedure was conducted separately in toluene, hexane, and tetrahydrofuran/DMPU. In each case, the solvents were removed under reduced pressure, and the crude orange oil was adsorbed onto silica and purified by flash-column chromatography (9:1, light petroleum/diethyl ether) to yield the target compound **3b** as a pale yellow oil. Spectroscopic data were identical to those previously obtained for **3b**.

(*R*)-3-(4-(Dimethylamino)phenyl)hex-5-enal 3c

(*S*)-2-(*S,E*)-1-(4-(Dimethylamino)phenyl)hexa-1,5-dien-3-ylamino)-3-phenylpropan-1-ol **2c** (1.0 g, 2.9 mmol) was dried in vacuo for 1 h, dissolved in dry THF (20 mL) under a nitrogen atmosphere, and cooled to −78 °C. A 2.5 M solution of *n*-BuLi in hexanes (2.85 mL, 7.1 mmol) was added dropwise, and the mixture was stirred for 10 min before warming to room temperature. The resultant solution was heated at reflux for 1 h, quenched with water, dried over anhydrous sodium sulfate, and filtered through a small pad of celite, eluting with DCM. The solvent was removed under reduced pressure, and an orange oil was obtained, which was adsorbed onto silica and purified by flash-column chromatography (9:1, light petroleum/diethyl ether) to yield the target compound **3c** as a pale yellow oil (0.41 g, 65%): $[\alpha]_D^{25}$ −13.8 (*c* 1.4, $CHCl_3$); IR (neat) 2921, 1721, 1614, 1518, 1444, 1348, 1164, 947, 816 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 2.30–2.43 (2H, m), 2.62–2.75 (2H, m), 2.92 (6H, s), 3.16–3.24 (1H, m), 4.98–5.04 (2H, m), 5.63–5.73 (1H, m), 6.69 (2H, d, *J* 8.6), 7.06 (2H, d, *J* 8.6), 9.65 (1H, t, *J* 2.2); ^{13}C NMR (100 MHz, $CDCl_3$) 38.9, 40.6 (2C), 41.2, 49.5, 112.8 (2C), 116.8, 128.0 (2C), 131.1, 136.2, 149.4, 202.5; HRMS (EI) 217 (M^+, 23%), 176 (100%). Calcd. for $C_{14}H_{19}NO$: 217.1467; found: 217.1467.

The same procedure was conducted separately in toluene and in hexane. In each case, the solvent was removed under reduced pressure, and the crude orange oil was adsorbed onto silica and purified by flash-column chromatography (9:1, light petroleum/diethyl ether) to yield the target compound **3c** as a pale yellow oil. Spectroscopic data were identical to those previously obtained for **3c**.

(*R*)-3-((*E*)-Prop-1-enyl)hex-5-enal 3d

(*S*)-2-((*S*,5*E*,7*E*)-Nona-1,5,7-trien-4-ylamino)-3-phenylpropan-1-ol **2d** (1.5 g, 5.5 mmol) was dried in vacuo for 1 h, dissolved in dry THF (40 mL) under a nitrogen atmosphere, and cooled to −78 °C. A 2.5 M solution of *n*-BuLi in hexanes (5.53 mL, 13.8 mmol) was added dropwise, and the mixture was stirred for 10 min before warming to room temperature. The resultant solution was heated at reflux for 1 h, quenched with water, dried over anhydrous sodium sulfate, and filtered through a small pad of celite, eluting with DCM. The solvent was removed under reduced pressure, and an orange oil was obtained, which was adsorbed onto silica and purified by flash-column chromatography (9.5:1, light petroleum/diethyl ether) to yield the target compound **3d** as a pale yellow oil (0.27 g, 35%): $[\alpha]_D^{25}$ −15.7 (*c* 1.1, $CHCl_3$);

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IR (neat) 2916, 1724, 1686, 1439, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 1.65 (3H, d, *J* 4), 2.05–2.20 (2H, m), 2.28–2.38 (1H, m), 2.43–2.52 (1H, m), 2.64–2.73 (1H, m), 4.99–5.07 (2H, m), 5.28–5.35 (1H, m), 5.44–5.57 (1H, m), 5.68–5.79 (1H, m), 9.70 (1H, t, *J* 2); ^{13}C NMR (100 MHz, $CDCl_3$) 17.9, 36.9, 39.6, 48.0, 116.9, 126.0, 133.1, 135.9, 202.8.

Traces of a minor aldehyde isomer were present, resulting from the presence of traces of substrate analogs produced from the minor amounts of *trans, cis*-2,4-hexadienal present in the original commercial reagents used in the preparation of the parent amino-diene substrate **2d**.

The same procedure was conducted separately in toluene, hexane, and tetrahydrofuran/DMPU. The solvents were removed under reduced pressure, and the crude orange oil was adsorbed onto silica and purified by flash-column chromatography (9.5:1, light petroleum/diethyl ether) to yield the target compound **3d** as a pale yellow oil. Spectroscopic data were identical to those previously obtained for **3d**. Because of problems of instability of the product aldehyde, we were unable to obtain high-resolution mass spectral (HRMS) data.

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(*R*)-3-Allyloctanal 3e

(*S*)-2-((*S,E*)-Undeca-1,5-dien-4-ylamino)-3-phenylpropan-1-ol **2e** (1.5 g, 5.0 mmol) was dried in vacuo for 1 h, dissolved in dry THF (40 mL) under a nitrogen atmosphere, and cooled to −78°C. A 2.5 M solution of *n*-BuLi in hexanes (5.0 mL, 12.4 mmol) was added dropwise, and the mixture was stirred for 10 min before warming to room temperature. The resultant solution was heated at reflux for 1 h, quenched with water, dried over anhydrous sodium sulfate, and filtered through a small pad of celite, eluting with DCM. The solvent was removed under reduced pressure, and a yellow oil was obtained, which was adsorbed onto silica and purified by flash-column chromatography (9.5:1, light petroleum/diethyl ether) to yield the target compound **3e** as a pale yellow oil (0.17 g, 21%): $[\alpha]_D^{25}$ −10.7 (*c* 1.3, $CHCl_3$); IR (neat) 2955, 2925, 2856, 1725, 913 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7.0), 1.27–1.32 (8H, m), 1.99–2.10 (2H, m), 2.13–2.19 (1H, m), 2.36 (2H, m), 5.01–5.06 (2H, m), 5.70–5.77 (1H, m), 9.76 (1H, t, *J* 2.3); ^{13}C NMR (100 MHz, $CDCl_3$) 14.1, 22.6, 26.4, 31.9, 32.8, 34.0, 38.5, 48.1, 117.1, 136.2, 203.1.

The same procedure was conducted separately in toluene and in hexane. In each case, the solvent was removed under reduced pressure, and the crude yellow oil was adsorbed onto silica and purified by flash-column chromatography (9.5:1, light petroleum/diethyl ether) to yield the target compound **3e** as a pale yellow oil. Spectroscopic data were identical to those previously obtained for **3e**. Because problems of instability of the aldehyde, we were unable to obtain HRMS data.

(*R,E*)-3-Allyldec-4-enal 3f

(*S*)-2-((*S*,5*E*,7*E*)-Trideca-1,5,7-trien-4-ylamino)-3-phenylpropan-1-ol **2f** (0.70 g, 2.1 mmol) was dried in vacuo for 1 h, dissolved in dry THF (30 mL) under a nitrogen atmosphere, and cooled to −78°C. A 2.5 M solution of *n*-BuLi in hexanes (2.14 mL, 5.3 mmol) was added dropwise, and the mixture was stirred for 10 min before

warming to room temperature. The resultant solution was heated at reflux for 1 h, quenched with water, dried over anhydrous sodium sulfate, and filtered through a small pad of celite, eluting with DCM. The solvent was removed under reduced pressure, and a yellow oil was obtained, which was adsorbed onto silica and purified by flash-column chromatography (9.5:1, light petroleum/diethyl ether) to yield the target compound **3f** as a pale yellow oil (0.23 g, 54%): $[\alpha]_D^{25}$ −20.8 (*c* 1.2, $CHCl_3$); IR (neat) 2955, 2925, 2855, 1726, 1440, 971, 914 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 7), 1.20–1.37 (6H, m), 1.95–2.00 (2H, m), 2.10–2.18 (2H, m), 2.35 (1H, m), 2.46 (1H, m), 2.65–2.71 (1H, m), 5.01–5.05 (2H, m), 5.25–5.31 (1H, m), 5.42–5.49 (1H, m), 5.68–5.79 (1H, m), 9.70 (1H, t, *J* 3); ^{13}C NMR (100 MHz, $CDCl_3$) 14.1, 22.5, 29.1, 31.3, 32.4, 37.0, 39.7, 48.1, 116.9, 131.7, 131.8, 135.9, 202.7; HRMS (EI) 194 (M^+, 2%), 109 (100%). Calcd. for $C_{13}H_{22}O$: 194.1671; found: 194.1675.

The same procedure was conducted separately in toluene and in hexane. In each case, the solvent was removed under reduced pressure, and the crude yellow oil was adsorbed onto silica and purified by flash-column chromatography (9.5:1, light petroleum/diethyl ether) to yield the target compound **3f** as a pale yellow oil. Spectroscopic data were identical to those previously obtained for **3f**.

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