Aldol-type condensation reactions of lithium eneselenolates generated from selenoamides with aldehydes

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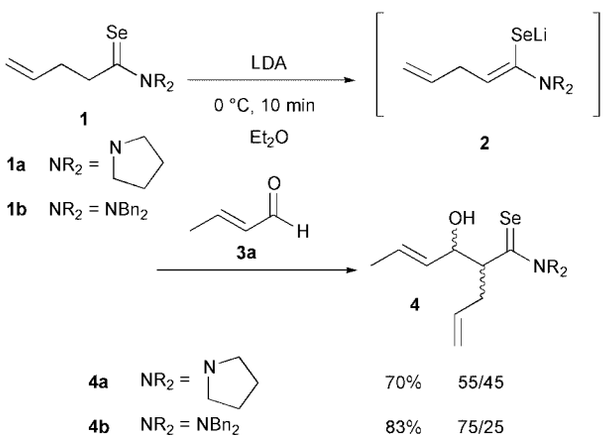
Aldol-type condensation reactions of α-monosubstituted selenoamides with a variety of aldehydes are examined to furnish β-hydroxy selenoamides in good to high yields. The use of selenoamides derived from dibenzylamine exhibits high stereoselectivity. As for the reaction with aliphatic aldehydes selenoamides show better yields and selectivity compared with ordinary amides. Conversion of the resulting β-hydroxy selenoamides to 1,3-amino alcohols is also described.

Introduction

Aldol condensation reactions of lithium enolates[1] have been studied in great depth. Similar reactions using lithium thioenolates have also been explored.[2] In contrast, much less attention has been paid to the chemistry of the selenium counterparts of enolates, *i.e.*, eneselenolates. However, recent studies on the organoselenium compounds[3] have proved their importance in a variety of fields such as material chemistry, biological chemistry and organic synthesis. As a result, synthetic reactions leading to new types of organoselenium compounds are in demand, and eneselenolates can be key reactive species in such reactions. Generation of metal eneselenolates has been generally attained by the insertion reaction of a selenium atom into vinyl metallic species.[4] In contrast, only limited examples of the deprotonation of selenocarbonyl compounds have been studied[5] despite the recent ongoing progress of their chemistry.[6] This is partly because of the instability of enolizable selenocarbonyl compounds and of the lack of methods for their simple synthesis. Very recently, we established efficient methods for the synthesis of selenoamides [RC(Se)NR′$_2$][7] and selenothioic acid *S*-esters [RC(Se)SR′][8] starting from terminal acetylenes. Deprotonation of the obtained selenocarbonyl compounds[9,10] proceeded in a similar way to that of ordinary carbonyl and thiocarbonyl compounds. The reaction of lithium eneselenolates of a selenoacetamide with aldehydes took place accompanied by dehydration to give α,β-unsaturated selenoamides, and β-hydroxy selenoamides were not obtained as products.[9a] We have further disclosed that Michael addition of lithium eneselenolates of α-monosubstituted selenoamides to α,β-unsaturated ketones and esters was complete within a few seconds with high efficiency.[9b] We report herein aldol-type condensation reactions of lithium eneselenolates of α-monosubstituted selenoamides and their stereoselectivity. The conversion of the resulting β-hydroxy selenoamides to 1,3-amino alcohols is also described.

Results and discussion

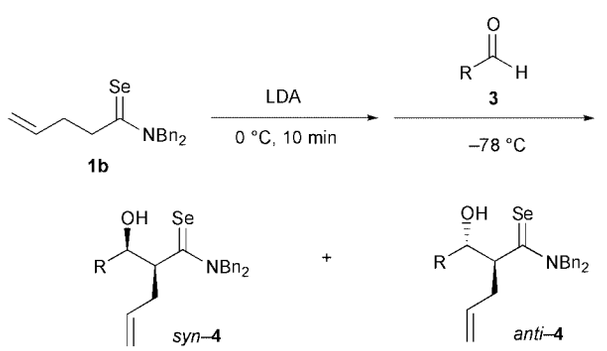
At the outset, the reaction of lithium eneselenolates generated from pent-4-eneselenoamides **1** with crotonaldehyde **3a** was carried out in Et_2O (Scheme 1). The reaction of **2a** with **3a** was complete within a few seconds to give 1,2-adduct **4a** in 70% yield as a stable mixture of two diastereomers in a ratio of 55 : 45. No product derived from the Michael addition of **2a** to **3a** was detected. To improve the stereoselectivity of the



Scheme 1

reaction, selenoamides bearing a variety of amino groups were synthesized according to the literature[7d] and were treated with LDA and aldehyde **3a**. As a result, the use of *N*,*N*-dibenzylpent-4-eneselenoamide **1b** gave β-hydroxy selenoamide **4b** in 83% yield with better diastereoselectivity.

Then, a wide range of aldehydes **3** were employed as substrates for the aldol condensation reaction of selenoamide **1b** (Scheme 2). The results are summarized in Table 1. Initially, α,β-unsaturated aldehydes **3b**–**3f** were treated with lithium eneselenolate **2b** (entries 1–7). In all cases the 1,2-addition of **2b** to aldehydes **3b**–**3f** proceeded smoothly to give the products **4c**–**4g** in moderate to good yields with selectivities from 71 : 29



Scheme 2

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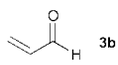
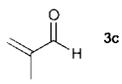
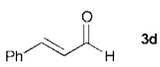
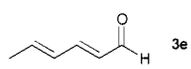
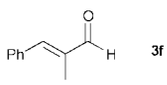
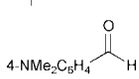
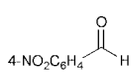
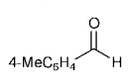
Table 1 Reaction of pent-4-eneselenoamide **1b** with aldehydes **3**[a]

Entry	Aldehyde	Product yield (%)[b]	Diastereomer ratio (*threo* : *erythro*)[c]
1	 **3b**	**4c** 70	88 : 12
2	 **3c**	**4d** 81	93 : 7
3	 **3d**	**4e** 78	74 : 26
4	 **3e**	**4f** 57	77 : 23
5		**4f** 64[d]	68 : 32
6	 **3f**	**4g** 81	71 : 29
7		**4g** 45[d]	4 : 96
8	 **3g**	**4h** 84	89 : 11
9	 **3h**	**4i** 87	94 : 6
10	 **3i**	**4j** 27[e]	>99 : <1
11	 **3j**	**4k** 29	95 : 5
12	 **3k**	**4l** 49	83 : 17

[a] Selenoamide **1b** (1 mmol) was treated with LDA (1.2 mmol) in Et_2O or THF (5 mL) at 0 °C for min, then to the reaction mixture was added an aldehyde **3** (1.2 mmol) at −78 °C and stirred for 10 min at −78 °C. [b] Isolated yield. [c] The ratio of diastereomers was determined by ^{1}H NMR spectroscopy of crude products. [d] The reaction was carried out in the presence of TMEDA (2.4 mmol). [e] After the addition of aldehyde **3i** the reaction mixture was stirred for 10 min at −78 °C, raised to 0 °C, and stirred for 5 min at 0 °C.

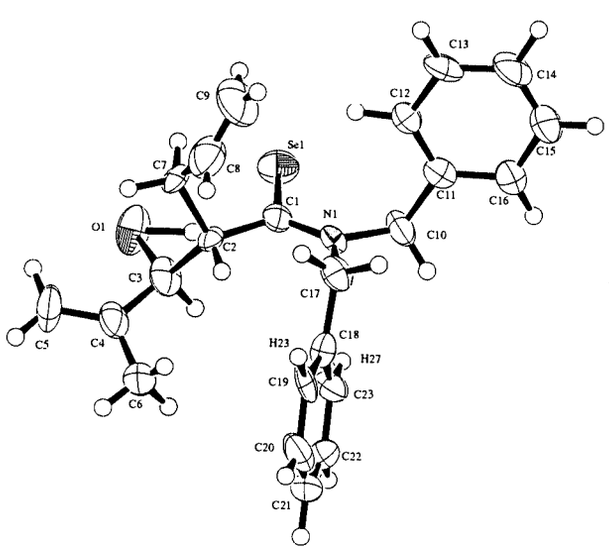


Fig. 1 ORTEP drawing of compound **4d** with atomic-numbering scheme.

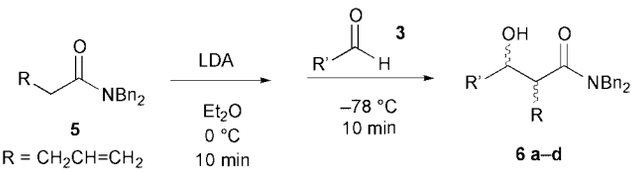
to 93 : 7 (entries 1–4, 6). The α,β-unsaturated aldehydes with substituents at the β-position exhibited low selectivity, whereas aldehyde **3c** gave a highly stereoselective reaction. The X-ray structure of the crystalline product **4d** confirmed that the *syn* isomer of **4d** was selectively formed (Fig. 1). The stereochemistry of all other products **4** was determined on the basis of the similarities of ^{1}H NMR and ^{13}C NMR chemical shifts.[11]

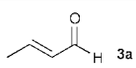
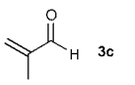
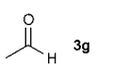
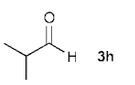
The effect of an additive on the diastereoselectivity in the aldol reaction of **2** was next examined. However, the addition of TMEDA to the reaction mixture lowered the selectivity. For example, the diastereoselectivity of the product **4f** decreased to 68 : 32 from 77 : 23 (entry 5). As an exceptional case the reaction with (*E*)-α-methylcinnamaldehyde **3f** in the presence of TMEDA gave the *anti* isomer of the product **4g** with a selectivity of 4 : 96 (entry 7). The stereoselectivity of the reaction with aliphatic and aromatic aldehydes was also examined. The use of acetaldehyde **3g** and isobutyraldehyde **3h** as aliphatic aldehydes gave β-hydroxy selenoamides **4h** and **4i** with high stereoselectivity and in good yields (entries 8 and 9). The reaction of aromatic aldehydes **3i** and **3k** also showed high stereoselectivities, although the yields of the products **4j**–**4l** were moderate (entries 10–12). The applicability of the diastereoselective aldol-type condensation of selenoamides was further examined. *N*,*N*-Dibenzyl-α-phenyl(selenoacetamide) **1c** was treated with LDA and aldehyde **3h** to give the corresponding β-hydroxy selenoamide **4m** in 86% yield as a mixture of diastereomers in a ratio of 77 : 23 (Scheme 3).

To compare the reactivity and selectivity of lithium eneselenolates **2b** with those of the lithium enolate generated from amide **5** the enolate was treated with aldehydes. The results are summarized in Table 2. In the reaction of the lithium enolate generated from **5** with aldehydes **3a** and **3c** both the yields and diastereoselectivity of the products **6a** and **6b** were nearly equal to those obtained with lithium eneselenolate **2b** (entries 1 and 2). On the other hand, in the reaction with aldehydes **3g** and **3h**, selenoamide **1b** gave both higher yields and better diastereoselectivity.

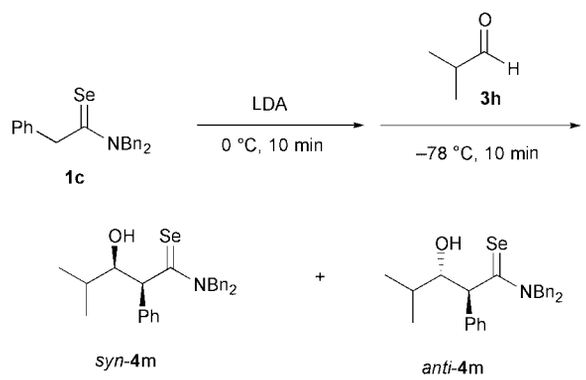
Finally, β-hydroxy selenoamides were converted to 1,3-amino alcohols, which have been one of the most important classes of compounds in organic synthesis,[12] by reduction with $LiAlH_4$ (Scheme 4). When β-hydroxy selenoamide **4d** was treated with

Table 2 Reaction of amide **5** with aldehydes **3**[a]

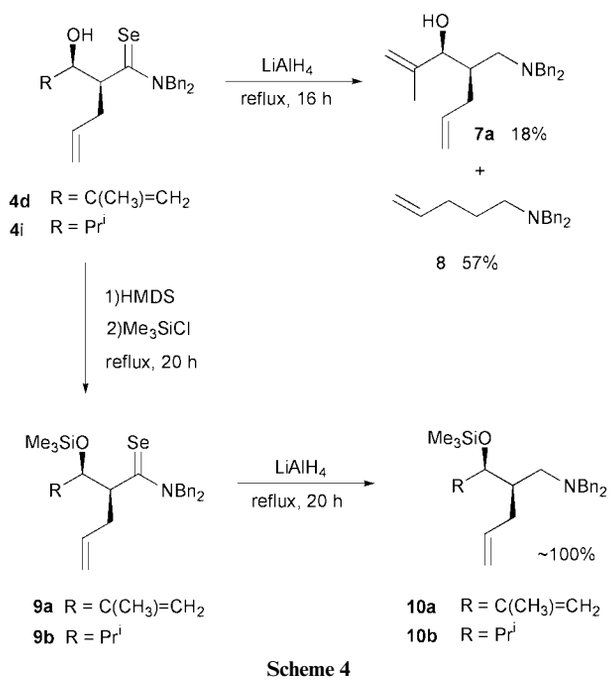


Entry	Aldehyde	Product yield (%)[b]	Diastereomer ratio (*syn* : *anti*)[c]
1	 3a	76	80 : 20
2	 3c	62	99 : 1
3	 3g	27	74 : 26
4	 3h	40[d]	75 : 25

[a] Amide **5** (1 mmol) was treated with LDA (1.2 mmol) in Et_2O (5 mL) at 0 °C for 10 min, then to the reaction mixture was added an aldehyde **3** (1.2 mmol) at −78 °C and stirred for 10 min at −78–0 °C. [b] Isolated yield. [c] The ratio of diastereomers was determined by ^{1}H NMR. [d] The starting material **5** was recovered in 17% recovery.



Scheme 3



Scheme 4

$LiAlH_4$, it gave amino alcohol **7a** in low yield (18%) along with a 57% yield of alkenylamine **8**, the result of the retro-aldol reaction of **4d**. Then, β-siloxy selenoamide **9a** derived from **4d** was treated with $LiAlH_4$ to furnish TMS-protected 1,3-amino alcohol **10a** in high yield. A similar transformation of **4i** was successful to give **10b** quantitatively *via* siloxy selenoamides **9b**. In these cases the stereochemistry of the starting β-hydroxy selenoamides was retained.

In summary, the aldol-type condensation reaction of lithium eneselenolates generated from pent-4-eneselenoamides has provided a new route to β-hydroxy selenoamides. The highly stereoselective reaction was attained with *N*,*N*-dibenzyl selenoamide **1b**. In particular, the use of aliphatic aldehydes gave products with better diastereoselectivities and yields than those of the reaction of these aldehydes with ordinary amides. Reduction of the obtained β-hydroxy selenoamides with $LiAlH_4$ successfully led to 1,3-amino alcohols.

Experimental

General

IR spectra were obtained on a Perkin-Elmer FT-IR 1640 spectrophotometer. ^{1}H NMR spectra were measured on a JEOL *α*-400 (399.7 MHz) for samples in $CDCl_3$. Chemical shifts of protons are reported in *δ*-values referred to tetramethylsilane as internal standard, and the following abbreviations are used; s: singlet, d: doublet, m: multiplet. *J*-values are given in Hz ^{13}C NMR spectra were measured on a JEOL *α*-400 (100.4 MHz). Mass spectra (MS) were taken on Shimadzu GCMS QP1000 (EI mode) or GCMS 9020DF high-resolution mass spectrometers. High-resolution mass spectra were taken on the 9020DF spectrometer. Elemental analyses were carried out by the Elemental Analysis Center of Kyoto University. High-performance liquid chromatography (HPLC) was performed using a Japan Analytical Industry LC-908 recycling preparative HPLC coupled to RI indicator and UV detecter (256 nm). The selenoamides **1** were prepared by the procedure in the literature.[7] Other substrates were commercially available.

General procedure for the aldol reaction of lithium eneselenolates 2

A representative experimental procedure is described for the preparation of 1-[3-hydroxy-2-(prop-2-enyl)-1-selenoxohex-4-enyl]pyrrolidine **4a**. To a THF solution (5 mL) of diisopropylamine (0.17 mL, 1.2 mmol) was added BuLi (1.6 M hexane solution; 0.75 mL, 1.2 mmol) at 0 °C, and the mixture was

stirred for 10 min at this temperature. Pent-4-eneselenoamide **1a** (0.216 g, 1.0 mmol) was added, and the mixture was stirred for 10 min at 0 °C. Then, crotonaldehyde **3a** (0.1 mL, 1.2 mmol) and water (1 mL) were added successively at −78 °C. The resulting mixture was poured into saturated aq. NaCl, and extracted with Et_2O three times. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (SiO_2; hexane–Et_2O = 3 : 1) to give **4a** (0.201 g, 70%, diastereomer ratio *syn* : *anti* = 55 : 45) as a yellow oil, R_f = 0.46, 0.58 (hexane–Et_2O = 1 : 3); δ_H (400 MHz; $CDCl_3$) 1.72 (3 H, d, *J* 6.6, CH_3), 2.00–2.20 (4 H, m, CH_2), 2.50–2.60 (1 H, m, CH_2C=C), 2.80–2.90 (1 H, m, CH_2C=C), 3.08–3.15 (1 H, m, CHC=Se), 3.50–3.70 (2 H, m, CH_2), 3.80–4.00 (2 H, m, CH_2), 4.30–4.40 (1 H, m, CHO), 4.40–4.50 (1 H, s, OH), 4.97 (1 H, dd, *J* 10.4, CH_2=), 5.11 (1 H, d, *J* 15.6, CH_2=), 5.50–5.60 (1 H, m, CH), 5.65–5.83 (2 H, m, CH_2); δ_C (100 MHz; $CDCl_3$) *syn* isomer 17.8, 23.9, 26.1, 34.4, 52.4, 57.7, 57.7, 73.1, 117.1, 127.5, 131.1, 135.9, 206.0; *anti* isomer 17.8, 23.9, 26.0, 37.9, 52.4, 57.7, 73.1, 117.4, 127.5, 131.1, 135.9, 204.4; ν_{max}/cm^{-1} 3394, 2974, 1638, 1560, 1329, 1258, 1170, 969, 920; *m*/*z* (EI) 287 (Found: C, 54.33; H, 7.26. $C_{13}H_{21}NOSe$ requires C, 54.54; H, 7.39%).

***N*,*N*-Dibenzyl-3-hydroxy-2-(2-prop-2-enyl)hex-4-eneselenoamide 4b.** A *yellow oil*; δ_H (400 MHz; $CDCl_3$) *syn* isomer 1.58 (3 H, d, *J* 6.4, CH_3), 2.50–2.65 (1 H, m, CH_2), 2.90–3.00 (1 H, m, CH_2), 3.20–3.30 (1 H, m, CHC=Se), 4.24 (1 H, d, *J* 5.3, CHO), 4.66 (1 H, d, *J* 17.1, NCH_2), 4.84 (1 H, s, OH), 4.89 (1 H, d, *J* 14.4, NCH_2), 5.01 (1 H, dd, *J* 1.5, and 10.7, CH_2=C), 5.17 (1 H, d, *J* 18.5, CH_2=C), 5.25 (1 H, dd, *J* 1.5 and 5.3, CH=C), 5.40–5.80 (3 H, m, CH, NCH_2), 6.27 (1 H, d, *J* 14.4, NCH_2), 7.00–7.40 (10 H, m, Ph); *anti* isomer 1.70 (3 H, d, *J* 6.3, 3H, CH_3), 2.50–2.65 (2 H, m, CH_2), 3.20–3.30 (1 H, m, CHC=Se), 4.46 (1 H, t, *J* = 6.5, CHO), 4.66 (1 H, d, *J* 17.1, NCH_2), 4.80–4.90 (2 H, m, OH, NCH_2), 4.90–5.10 (2 H, m, CH_2=C), 5.18–5.22 (1 H, m, CH), 5.40–5.80 (3 H, m, CH=CH, NCH_2), 6.27 (1 H, d, *J* 14.2, NCH_2), 7.00–7.40 (10 H, m, Ph); ν_{max}/cm^{-1} 3421, 3030, 2367, 2344, 1497, 1449, 1354, 1220, 1169, 1079, 1029, 917, 734, 697; *m*/*z* (EI) 413 (Found: M^+, 413.12683. $C_{23}H_{27}NOSe$ requires *M*, 413.12565).

***N*,*N*-Dibenzyl-3-hydroxy-2-(prop-2-enyl)pent-4-eneselenoamide 4c.** A *yellow oil*; δ_H (400 MHz; $CDCl_3$) *syn* isomer 2.45–2.55 (1 H, m, =CH_2), 2.85–2.95 (1 H, m, CH_2), 3.44–3.60 (1 H, m, CHC=Se), 4.25–4.30 (1 H, m, CHO), 4.66 (1 H, d, *J* 17.0, NCH_2), 4.81 (1 H, d, *J* 14.6, NCH_2), 4.88 (1 H, d, *J* 17.0, NCH_2), 4.95–5.05 (3 H, m, OH, CH_2=C), 5.07–5.10 (1 H, m, CH_2=C), 5.16 (1 H, dd, *J* 2.0 and 16.8, CH_2=C), 5.44–5.55 (1 H, m, C=CH), 5.60–5.75 (1 H, m, C=CH), 6.37 (1 H, d, *J* 14.6, NCH_2), 7.07–7.41 (10 H, m, Ph); *anti* isomer 2.45–2.55 (1 H, m, CH_2), 2.85–2.95 (1 H, m, CH_2), 3.44–3.60 (1 H, m, CHC=Se), 4.25–4.30 (1 H, m, CHO), 4.60–5.25 (8 H, m, NCH_2, OH, CH_2=C, CH_2=C), 5.60–5.75 (1 H, m, C=CH), 5.85–5.95 (1 H, m, C=CH), 6.20 (1 H, d, *J* 14.6, NCH_2), 7.07–7.41 (10 H, m, Ph); δ_C (100 MHz; $CDCl_3$) *syn* isomer 35.0, 54.7, 55.3, 60.6, 73.3, 115.8, 118.0, 126.0–134.4, 135.4, 137.8, 215.4; *anti* isomer 38.5, 54.4, 55.6, 59.9, 75.5, 117.5, 118.1, 126.7–134.5, 134.5, 138.5, 213.1; MS *m*/*z* 399 (Found: M^+, 399.10924. $C_{22}H_{25}NOSe$ requires *M*, 399.11001).

***N*,*N*-Dibenzyl-3-hydroxy-4-methyl-2-(prop-2-enyl)pent-4-eneselenoamide 4d.** A *yellow oil*; δ_H (400 MHz; $CDCl_3$) *syn* isomer 1.17 (3 H, s, CH_3), 2.40–2.48 (1 H, m, CH_2), 2.85–2.95 (1 H, m, CH_2), 3.26–3.33 (1 H, dd, *J* 2.9 and 10.7, CHC=Se), 4.15 (1 H, s, OH), 4.66 (1 H, d, *J* 17.3, NCH_2), 4.76 (1 H, d, *J* 14.5, NCH_2), 4.88 (1 H, s, OCH), 4.90–5.00 (2 H, m, NCH_2, CH_2=C), 5.10–5.20 (2 H, m, CH_2=C), 5.42 (1 H, s, CH_2=C), 5.60–5.75 (1 H, m, CH=C), 6.46 (1 H, d, *J* 14.5, NCH_2), 7.05–7.45 (10 H, m, Ph); *anti* isomer 1.27 (3 H, s, CH_3), 2.24–2.34 (1 H, m, CH_2), 2.60–2.72 (1 H, m, CH_2), 3.32–3.40 (1 H, m, CH=Se), 4.15 (1 H, s, OH), 4.66–5.20 (7 H, m, NCH_2, OCH, CH_2=C, CH_2=C), 5.42 (1 H, s, CH_2=C), 5.46–5.60 (1 H, m, =CH), 6.46 (1 H, d, *J* 14.6, NCH_2), 7.05–7.45 (10 H, m, Ph); δ_C (100 MHz; $CDCl_3$) *syn* isomer 19.3, 34.5, 52.3, 54.4, 60.8, 74.6, 112.8, 118.0, 125.7, 128.1, 128.3, 128.3, 128.9, 129.4, 135.6, 133.8, 134.4, 143.1, 216.2; ν_{max}/cm^{-1} 3276, 1642, 1496, 1446, 1233, 1000, 912, 733, 696, 588; *m*/*z* (EI) 412 (Found: C, 66.74; H, 6.55. $C_{23}H_{27}NOSe$ requires C, 66.98; H, 6.60%).

***N*,*N*-Dibenzyl-3-hydroxy-5-phenyl-2-(prop-2-enyl)pent-4-eneselenoamide 4e.** A *yellow oil*; δ_H (400 MHz; $CDCl_3$) *syn* isomer 2.58–2.64 (1 H, m, CH_2), 2.95–3.06 (1 H, m, CH_2), 4.30 (1 H, d, *J* 5.5, OH), 4.60–5.10 (6 H, m, CHC=Se, CHO, NCH_2), 5.45 (1 H, d, *J* 14.0, C=CH_2), 5.60–5.70 (2 H, m, CH=, C=CH_2), 6.32 (1 H, dd, *J* 7.6 and 16.1, CH_2=), 6.67 (1 H, d, *J* 16.1, CH=C), 7.14–7.49 (15 H, m, Ph); δ_C (100 MHz; $CDCl_3$) *syn* isomer 35.7, 54.7, 56.1, 60.7, 73.6, 118.0, 126.1–136.6, 215.2; *anti* isomer 38.7, 54.4, 55.8, 60.2, 74.7, 118.2, 126.1–135.4, 212.9; ν_{max}/cm^{-1} 3344, 3028, 2250, 1678, 1626, 1495, 1450, 1354, 1221, 1167, 1124, 970, 918, 845, 749, 696; *m*/*z* (EI) 475 (Found: M^+, 475.13881. $C_{28}H_{29}NOSe$ requires *M*, 475.14129).

***N*,*N*-Dibenzyl-3-hydroxy-2-(prop-2-enyl)octa-4,6-dieneselenoamide 4f.** A *yellow oil*; δ_H (400 MHz; $CDCl_3$) *syn* isomer 1.64 (3 H, d, *J* 6.3, CH_3), 2.40–2.50 (1 H, m, CH_2), 2.80–2.90 (1 H, m, CH_2), 3.15–3.20 (1 H, m, CHC=Se), 4.24 (1 H, d, *J* 5.9, CHO), 4.38 (1 H, s, OH), 4.50–6.00 (10 H, m, CH, NCH_2), 6.23 (1 H, d, *J* 14.6, NCH_2), 7.00–7.40 (10 H, m, Ph); *anti* isomer 1.70 (3 H, d, *J* 6.8, CH_3), 2.50–2.60 (1 H, m, CH_2), 3.00–3.10 (1 H, m, CH_2), 3.20–3.30 (1 H, m, CHC=Se), 4.31 (1 H, d, *J* 4.9 Hz, CHO), 4.50–6.00 (11 H, m, CH_2=CH, CH=CH, OH, NCH_2), 6.23 (1 H, d, *J* 14.6, NCH_2), 7.00–7.40 (10 H, m, Ph); δ_C (100 MHz; $CDCl_3$) *syn* isomer 18.1, 35.5, 54.6, 56.0, 60.6, 73.3, 115.4–137.5, 215.3; *anti* isomer 13.5, 32.5, 54.4, 55.8, 60.5, 73.3, 115.4–137.5, 213.0; ν_{max}/cm^{-1} 2968, 2371, 1654, 1560, 1508, 1499, 1458, 990, 734 cm^{-1}; *m*/*z* (EI) 439 (Found: M^+, 439.14394. $C_{25}H_{29}NOSe$ requires *M*, 439.14129).

***N*,*N*-Dibenzyl-3-hydroxy-4-methyl-5-phenyl-2-(prop-2-enyl)-pent-4-eneselenoamide 4g.** A *yellow oil*; δ_H (400 MHz; $CDCl_3$) *syn* isomer 1.29 (3 H, s, CH_3), 2.50–2.60 (1 H, m, CH_2), 2.85–2.97 (1 H, m, CH_2), 3.39 (1 H, dd, *J* 2.6 and 10.0, CH=CSe), 4.29 (1 H, s, OH), 4.65–5.20 (6 H, m, NCH_2,CH_2=C, PhCH), 5.50–5.75 (2 H, m, =CH, CHO), 6.45 (1 H, d, *J* 14.4 Hz, NCH_2), 6.50–7.50 (15 H, m, Ph); δ_C (100 MHz; $CDCl_3$) *syn* isomer 15.2, 34.7, 52.6, 60.8, 76.0, 118.0–134.3, 216.0; *anti* isomer 13.6, 39.0, 54.4, 60.5, 82.5, 117.9–134.3, 214.4; ν_{max}/cm^{-1} 3428, 3028, 2978, 1507, 1449, 1247, 1159, 1029, 742, 697; *m*/*z* (EI) 489 (Found: C, 71.39; H, 6.40. $C_{29}H_{31}NOSe$ requires C, 71.30; H, 6.40%).

***N*,*N*-Dibenzyl-2-(1-hydroxyethyl)pent-4-eneselenoamide 4h.** A *yellow oil*; δ_H (400 MHz; $CDCl_3$) *syn* isomer 0.94 (3 H, d, *J* 6.8, CH_3), 2.49–2.56 (1 H, m, CH_2), 2.85–2.95 (1 H, m, CH_2), 3.13 (1 H, ddd, *J* 1.5, 3.4, and 10.2, CHC=Se), 3.88–3.93 (1 H, m, CHO), 4.63 (1 H, d, *J* 16.6, NCH_2), 4.82 (1 H, d, *J* 14.4, NCH_2), 4.88 (1 H, d, *J* 16.6, NCH_2), 5.02 (1 H, dd, *J* 2.1 and 10.5, CH_2=C), 5.19 (1 H, dd, *J* 2.1 and 17.1, CH_2=C), 5.60–5.80 (1 H, m, =CH), 6.35 (1 H, d, *J* 14.4, NCH_2), 7.05–7.45 (10 H, m, Ph); δ_C (100 MHz; $CDCl_3$) *syn* isomer 20.9, 35.0, 54.6, 55.9, 60.5, 68.9, 117.9, 125.9–134.5, 135.5, 216.4; *anti* isomer 20.9, 38.7, 54.2, 57.6, 59.7, 70.5, 117.9, 126.9–134.7, 134.6, 213.8; ν_{max}/cm^{-1} 3320, 2970, 1638, 1605, 1499, 1445, 1360, 1330, 1296, 1235, 1176, 995, 920, 909, 737, 697, 633, 564, 458; *m*/*z* (EI) 386 (Found: C, 65.05; H, 6.46 $C_{21}H_{25}NOSe$ requires C, 65.28; H, 6.52%).

***N*,*N*-Dibenzyl-2-(1-hydroxy-2-methylpropyl)pent-4-eneselenoamide 4i.** A *yellow oil*; δ_H (400 MHz; $CDCl_3$) *syn* isomer 0.44 (3 H, d, *J* 6.8, CH_3), 0.93 (3 H, d, *J* 6.8, CH_3), 1.60–1.70 (1 H, m, CH), 2.27 (1 H, s, OH), 2.40–2.50 (1 H, m, CH_2), 2.90–3.00 (1 H, m, CH_2), 3.31 (1 H, d, *J* 8.8, CHO), 3.41 (1 H, dd, *J* 3.9 and 10.3, CSeCH), 4.64 (1 H, d, *J* 17.1, NCH_2), 4.94 (1 H, d,

J 14.6, NCH_2), 5.13 (1 H, d, *J* 17.1, NCH_2), 4.90–5.00 (2 H, m, CH_2=C), 5.60–5.70 (1 H, m, CH_2=C), 6.23 (1 H, d, *J* 14.6, NCH_2), 7.00–7.50 (10 H, m, Ph); *anti* isomer 0.82 (3 H, d, *J* 6.8, CH_3), 1.00 (3 H, d, *J* 6.8, CH_3), 1.95–2.05 (1 H, m, CH), 2.27 (1 H, s, OH), 2.30–2.40 (1 H, m, CH_2), 2.60–2.70 (1 H, m, CH_2), 3.30–3.40 (1 H, m, CHO), 3.97 (1 H, dd, *J* 3.2 and 8.6, CSeCH), 4.60–5.40 (4 H, m, NCH_2, CH_2=C), 5.33 (1 H, d, *J* 14.4, NCH_2), 5.50–5.60 (1 H, m, =CH), 6.52 (1 H, d, *J* 14.4, NCH_2), 7.00–7.50 (10 H, m, Ph); δ_C (100 MHz; $CDCl_3$) 18.6, 19.8, 31.5, 35.0, 51.7, 54.2, 60.5, 77.9, 117.7, 125.7–134.5, 135.8, 216.7; ν_{max}/cm^{-1} 3854, 3650, 2959, 1654, 1560, 1498, 1225, 734, 697 cm^{-1}; *m*/*z* (EI) 414 (Found: C, 66.55; H, 7.10. $C_{23}H_{29}NOSe$ requires C, 66.66; H, 7.05%).

***N*,*N*-Dibenzyl-2-[(4-dimethylaminophenyl)hydroxymethyl]-prop-4-eneselenoamide 4j.** A *yellow solid*; δ_H (400 MHz; $CDCl_3$) 2.30–2.40 (1 H, m, CH_2), 2.55–2.65 (1 H, m, 1H, CH_2), 2.93 (6 H, s, CH_3), 3.45–3.55 (1 H, m, CHC=Se), 3.78–3.84 (1 H, m, OH), 4.61 (1 H, d, *J* 16.6, NCH_2), 4.72 (1 H, d, *J* 16.6, NCH_2), 4.88 (1 H, d, *J* 10.2, CH_2=), 4.96 (1 H, d, *J* 17.1, CH_2=C), 5.00–5.10 (1 H, m, CHO), 5.40–5.60 (3 H, m, NCH_2, C=CH), 6.65–7.40 (14 H, m, ArH); δ_C (100 MHz; $CDCl_3$) 39.0, 40.6, 54.2, 58.0, 60.2, 77.1, 112.5, 117.8, 126.7, 127.8, 128.2, 128.7, 129.1, 134.2, 134.6, 134.7, 213.8; ν_{max}/cm^{-1} 3854, 3650, 3451, 2902, 1612, 1506, 1449, 1348, 1252, 1166, 1028, 821, 740, 697, 572, 464; *m*/*z* (EI) 492 (Found: M^+, 492.16669. $C_{28}H_{32}NO$ requires *M*, 492.16782).

***N*,*N*-Dibenzyl-2-[hydroxy(4-nitrophenyl)methyl]prop-4-ene-selenoamide 4k.** A *yellow solid*; δ_H (400 MHz; $CDCl_3$) *syn* isomer 2.15–2.20 (1 H, m, CH_2), 2.90–3.00 (1 H, m, CH_2), 3.31 (1 H, ddd, *J* 1.0, 3.9, and 10.7, CHC=Se), 4.60 (1 H, d, *J* 14.6, NCH_2), 4.74 (1 H, d, *J* 17.1, NCH_2), 4.86 (1 H, s, OH), 4.74 (1 H, d, *J* 17.1, NCH_2), 4.96 (1 H, dd, *J* 2.0 and 10.2, CH_2=C), 5.08 (1 H, dd, *J* 2.0 and 17.1, CH_2=C), 5.40–5.60 (1 H, m, C=CH), 5.81 (1 H, s, CHO), 6.55–8.00 (15 H, m, NCH_2, ArH); *anti* isomer 2.40–2.60 (2 H, m, CH_2), 3.55–3.60 (1 H, m, CHC=Se), 4.50–5.05 (6 H, m, NCH_2, CH_2=C, CHOH), 5.40–5.60 (1 H, m, C=CH), 5.81 (1 H, s, CHO), 6.55–8.00 (15 H, m, NCH_2, ArH); δ_C (100 MHz; $CDCl_3$) *syn* isomer 33.9, 54.9, 56.5, 61.5, 73.2, 118.8, 123.2, 125.6, 126.8, 128.2, 128.4, 128.5, 128.9, 129.7, 134.0, 134.2, 146.9, 149.1, 214.8; ν_{max}/cm^{-1} 3342, 3069, 1604, 1515, 1451, 1413, 1343, 1237, 1169, 1070, 854, 739, 694; *m*/*z* (EI) 369 ($M^+ - PhNO_2$) (Found: M^+, 494.11021. $C_{26}H_{26}N_2O_3Se$ requires *M*, 494.11074).

***N*,*N*-Dibenzyl-2-[hydroxy(4-methylphenyl)methyl]prop-4-ene-selenoamide 4l.** A yellow solid; δ_H (400 MHz; $CDCl_3$) *syn* isomer 2.26 (3 H, s, CH_3), 2.25–2.40 (1 H, m, CH_2), 2.95–3.05 (1 H, m, CH_2), 3.30–3.40 (1 H, m, CHC=Se), 4.50–5.00 (6 H, m, NCH_2, OH, CH_2=, CHO), 5.08 (1 H, d, *J* 17.1, NCH_2), 5.45–5.60 (1 H, m, C=CH), 6.52 (1 H, d, *J* 14.1, NCH_2), 6.60–7.50 (14 H, m, ArH); δ_C (100 MHz; $CDCl_3$) *syn* isomer 21.0, 34.3, 54.6, 57.3, 60.9, 74.2, 118.0–139.2, 215.8; *anti* isomer 21.0, 34.8, 54.46, 57.5, 60.2, 76.4, 118.1–139.2, 134.4, 213.1; ν_{max}/cm^{-1} 1499, 1442, 1418, 1358, 1236, 1169, 998, 916, 816, 735, 694, 586, 462; *m*/*z* (EI) 343 [$M^+ - (CH_2$=$CHCH_2 + Ph)$] (Found: M^+, 463.13953. $C_{27}H_{29}NOSe$ requires *M*, 463.14129).

***N*,*N*-Dibenzyl-3-hydroxy-4-methyl-2-phenylpentaneseleno-amide 4m.** A *yellow solid*; δ_H (400 MHz; $CDCl_3$) *syn* isomer 0.61 (3 H, d, *J* 6.3, CH_3), 0.86 (3 H, d, *J* 6.3, CH_3), 1.50–1.60 (1 H, m, CH), 4.02 (1 H, dd, *J* 1.6 and 9.0, 1H, CHO), 4.23 (1 H, d, *J* 1.6, CHC=Se), 4.39 (1 H, d, *J* 15.6, NCH_2), 4.49 (1 H, d, *J* 15.6, NCH_2), 4.87 (1 H, d, *J* 17.1, NCH_2), 6.63 (1 H, d, *J* 17.1, NCH_2), 7.70–7.60 (15 H, m, Ph); *anti* isomer 0.70 (3 H, d, *J* 6.3 CH_3), 0.93 (3 H, d, *J* 6.8, CH_3), 1.40–1.50 (1 H, m, CH), 4.11 (1 H, d, *J* 9.3, CHC=Se), 4.56 (1 H, d, *J* 9.3, CHO), 4.68 (1 H, d, *J* 15.6, NCH_2), 4.43 (1 H, d, *J* 15.1, NCH_2), 5.13 (1 H, d, *J* 15.6, NCH_2), 6.29 (1 H, d, *J* 15.1, NCH_2), 7.70–7.60 (15 H, m, Ph); δ_C (100 MHz; $CDCl_3$) *syn* isomer 19.1, 19.3, 29.7, 54.9, 57.4, 60.2, 79.5, 125.5–134.5, 213.4; *anti* isomer 14.7, 21.0, 27.8, 54.2, 59.9, 60.5, 79.9, 125.5–134.5, 211.5; ν_{max}/cm^{-1} 3374, 2960, 1496, 1450, 1354, 1221, 1165, 1078, 1030, 999, 733, 696; *m*/*z* 450 (EI) (Found: C, 69.07; H, 6.44. $C_{26}H_{29}NOSe$ requires C, 69.32; H, 6.49%).

***N*,*N*-Dibenzyl-4-methyl-2-(prop-2-enyl)-3-(trimethylsiloxy)-pent-4-enamine 10a.** A solution of selenoamide **4d** (0.124 g, 0.3 mmol), HMDS (0.06 mL, 0.3 mmol) and a catalytic amount of trimethylsilyl chloride was stirred under reflux for 20 h. The reaction mixture was concentrated *in vacuo*. To a THF solution of the reaction mixture was added $LiAlH_4$ (0.023 mg, 0.60 mmol) at 0 °C. The reaction mixture was stirred under reflux for 20 h. The residue was poured into saturated aq. NaCl, and extracted with Et_2O three times. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to give **10a** (0.142 g, <100%) as a colourless oil, $R_f = 0.88$ (hexane–Et_2O 1 : 1); δ_H (400 MHz; $CDCl_3$) 0.00 [9 H, s, $(CH_3)_3SiO$], 1.60 [3 H, s, C=C(CH_3)], 1.75–1.85 (1 H, m, CH), 2.05–2.40 (4 H, m, CH_2), 3.27 (2 H, d, *J* 13.7, NCH_2), 3.66 (2 H, d, *J* 13.7, NCH_2), 3.91 (1 H, d, *J* 6.4, CHO), 4.70–4.90 (4 H, m, CH_2=C), 5.50–5.65 (1 H, m, C=CH), 7.10–7.20 (10 H, m, Ph); δ_C (100 MHz; $CDCl_3$) 0.2, 18.0, 31.7, 39.4, 55.0, 58.8, 77.4, 112.4, 115.8, 126.9, 128.2, 129.2, 139.6, 146.3, 137.4; ν_{max}/cm^{-1} 3065, 3028, 2960, 1638, 1495, 1452, 1372, 1250, 1070, 902, 842, 747, 698; *m*/*z* (EI) 406, 210 (Found: M^+, 407.26615. $C_{26}H_{37}NOSi$ requires *M*, 407.26426).

***N*,*N*-Dibenzyl-2-[2-methyl-1-(trimethylsiloxy)propyl]pent-4-enamine 10b.** A *colourless oil*; δ_H (400 MHz; $CDCl_3$) 0.00 [9 H, s, $(CH_3)_3SiO$], 0.82 (3 H, d, *J* 6.8, CH_3), 0.82 (3 H, d, *J* 6.3, CH_3), 1.60–2.50 (6 H, m, CH, CH_2), 3.38–3.45 (1 H, m, CHO), 3.48 (2 H, d, *J* 13.7, NCH_2), 3.57 (2 H, d, *J* 13.7, NCH_2), 4.80–5.00 (2 H, m, CH_2=C), 5.70–5.90 (1 H, m, C=CH), 7.20–7.40 (10 H, m, Ph); δ_C (100 MHz; $CDCl_3$) 0.8, 19.0, 20.2, 31.9, 32.8, 39.5, 57.3, 58.7, 79.5, 115.2, 126.9, 128.2, 129.6, 138.9, 139.5; ν_{max}/cm^{-1} 2958, 1640, 1495, 1453, 1385, 1250, 1057, 840, 746, 698; *m*/*z* 409 (EI) (Found: M^+, 409.27925. $C_{26}H_{39}NOSi$ requires *M*, 409.27990).

X-Ray structure analysis †

The measurement was carried out on a Rigaku AFC7R four-circle diffractometer with graphite-monochromated Mo-Kα radiation ($\lambda = 0.710\,69$ Å). The structure was solved and refined using the teXsan® crystallographic software package on an IRIS Indigo computer. X-Ray quality crystals of **4d** were obtained by recrystallization from hexane–Et_2O (1 : 1). A full-matrix least-squares refinement was executed with non-hydrogen atoms being anisotropic. The final least-squares cycle included fixed hydrogen atoms at calculated positions of which each isotropic thermal parameter was set to 1.2 times that of the connecting atom. The crystal data are as follows: empirical formula: $C_{23}H_{27}NOSe$; formula weight: 412.43; crystal dimensions: $0.02 \times 0.14 \times 0.11$ mm; crystal system: monoclinic; lattice parameters: $a = 7.445(2)$, $b = 10.865(2)$, $c = 13.339(1)$ Å, space group: $P2_1$(#4); $Z = 2$; μ(Mo-Kα) = 17.82 cm^{-1}; temperature of data collection: −80 °C; residuals: *R*1; $R_w = 0.049$; 0.068; no. of observed reflections: 3200; $R_{int} = 0.030$.

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† CCDC reference number 158064. See http://www.rsc.org/suppdata/p1/b1/b100198l/ for crystallographic files in .cif or other electronic format.

Notes and references

1 For reviews: (*a*) C. H. Heathcock, *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 2, p. 181; (*b*) C. H. Heathcock, *Modern Synthetic Methods*, ed. R. Scheffold, VCH, New York, 1992, p. 3; (*c*) S. Saito and H. Yamamoto, *Chem. Eur. J.*, 1999, **5**, 1959.

2 For reviews (*a*) P. Metzner and A. Thuillier, *Sulfur Reagents in Organic Synthesis*, ed. A. R. Katritzky, O. Meth-Cohn and C. W. Rees, Academic Press, New York, 1994; (*b*) P. Metzner, *Top. Curr. Chem.*, 1999, **204**, 127.

3 For reviews (*a*) A. Krief, *Comprehensive Organometallic Chemistry*, ed. W. W. Abel, F. G. A. Stone and G. Wilkinson, Pergamon Press, Oxford, 1995, vol. 11, p. 515; (*b*) K. El-Bayoumy, *Drugs Fut.*, 1997, **22**, 539; (*c*) *Organoselenium Chemistry: A Practical Approach*, ed. T. G. Back, Oxford University Press, UK, 1999.

4 (*a*) J. V. Comasseto, L. W. Ling, N. Petragnani and H. A. Stefani, *Synthesis*, 1997, 373; (*b*) K. Shimada, M. Asahida, K. Takahashi, Y. Sato, S. Aoyagi, Y. Takikawa and C. Kabuto, *Chem. Lett.*, 1998, 513.

5 (*a*) D. J. R. Barton, P.-E. Hansen and K. Picker, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1723; (*b*) R. S. Sukhai and L. Brandsma, *Synthesis*, 1979, 455; (*c*) M. Sekiguchi, A. Ogawa, S. Fujiwara, I. Ryu, N. Kambe and N. Sonoda, *Chem. Lett.*, 1990, 2053; (*d*) T. Kanda, T. Ezaka, T. Murai and S. Kato, *Tetrahedron Lett.*, 1995, **36**, 2807.

6 For reviews (*a*) F. S. Guziec, Jr. and L. J. Guziec, *Comprehensive Organic Functional Group Transformations*, ed. A. R. Katritzky, O. Meth-Cohn and C. W. Rees, Pergamon Press, Oxford, 1995, vol. 3, p. 381; (*b*) A. Ishii and J. Nakayama, *Comprehensive Organic Functional Group Transformations*, ed. A. R. Katritzky, O. Meth-Cohn and C. W. Rees, Pergamon Press, Oxford, 1995, vol. 5, p. 505; (*c*) C. P. Dell, *Comprehensive Organic Functional Group Transformations*, ed. A. R. Katritzky, O. Meth-Cohn and C. W. Rees, Pergamon Press, Oxford, 1995, vol. 5, p. 565; (*d*) T. Murai and S. Kato, *Top. Curr. Chem.*, 2000, **208**, 177.

7 (*a*) T. Murai, T. Ezaka, N. Niwa, T. Kanda and S. Kato, *Synlett*, 1996, 865; (*b*) T. Murai, T. Ezaka, T. Kanda and S. Kato, *Chem. Commun.*, 1996, 1809; (*c*) T. Murai, T. Mori and S. Kato, *Synlett*, 1998, 619; (*d*) T. Murai, T. Ezaka and S. Kato, *Bull. Chem. Soc. Jpn.*, 1998, **71**, 1193.

8 T. Murai and S. Kato, *Sulfur Rep.*, 1998, **20**, 397 and references cited therein.

9 (*a*) T. Murai, T. Ezaka, T. Ichimiya and S. Kato, *Synlett*, 1997, 775; (*b*) T. Murai, A. Suzuki, T. Ezaka and S. Kato, *Org. Lett.*, 2000, **2**, 311.

10 (*a*) S. Kato, T. Komuro, T. Kanda, H. Ishihara and T. Murai, *J. Am. Chem. Soc.*, 1993, **115**, 3000; (*b*) T. Murai, M. Fujii and S. Kato, *Chem. Lett.*, 1997, 545; (*c*) T. Murai, H. Endo, M. Ozaki and S. Kato, *J. Org. Chem.*, 1999, **64**, 2130.

11 The protons attached to the α-carbon atom to the selenocarbonyl group of *syn* isomers were observed at higher fields than those of *anti* isomers. In the ^{13}C NMR spectra, the carbon atoms of the selenocarbonyl group of *syn* isomers were observed at lower fields than those of *anti* isomers.

12 For recent examples of the synthesis of 1,3-amino alcohols: (*a*) J. Barluenga, F. Fernández-Marí, A. L. Viado, E. Aguilar and B. Olano, *J. Org. Chem.*, 1996, **61**, 5659; (*b*) B. F. Bonini, M. Comes-Franchini, G. Mazzanti, A. Ricci and M. Sala, *J. Org. Chem.*, 1996, **61**, 7242; (*c*) S. Cicchi, S. Crea, A. Goti and A. Brandi, *Tetrahedron: Asymmetry*, 1997, **8**, 293; (*d*) C. Lutz, V. Lutz and P. Knochel, *Tetrahedron*, 1998, **54**, 6385; (*e*) P. R. Carlier, M.-C. Lo, P. C.-K. Lo, E. Richelson, M. Tatsumi, I. J. Reynolds and T. A. Sharma, *Bioorg. Med. Chem. Lett.*, 1998, **8**, 487; (*f*) X. Li, C.-H. Yeung, A. S. C. Chan and T.-K. Yang, *Tetrahedron: Asymmetry*, 1999, **10**, 759; (*g*) J.-L. Toujas, L. Toupet and M. Vaultier, *Tetrahedron*, 2000, **56**, 2665; (*h*) T.-P. Loh, J.-M. Huang S.-H. Goh and J. J. Vittal, *Org. Lett.*, 2000, **2**, 1291.