Supporting Information

A Stereocontrolled Synthesis of (–)-Galanthamine

Vachiraporn Satcharoen,[†] Neville J. McLean,[†] Stephen C. Kemp,[†] Nicholas P. Camp[‡] and Richard C. D. Brown^{*†}

[†] School of Chemistry, University of Southampton, Highfield, Southampton SO17 1BJ, UK

[‡] Lilly Research Centre, Erl Wood Manor, Sunninghill Road, Windlesham, Surrey, UK

Corresponding author rcb1@soton.ac.uk; FAX: +44 (0)23 80594108

Page	Contains	Page	Contains
S2	General Methods	S29	¹ H & ¹³ C NMR for compound 7
S3	Experimental and data for compound 3	S30	¹ H & ¹³ C NMR for compound 8
S4	Experimental and data for compound 4a	S31	¹ H & ¹³ C NMR for compound 9
S5	Experimental and data for compound 6	S32	¹ H & ¹³ C NMR for compound 10
S6	Experimental and data for compound 7	S33	¹ H & ¹³ C NMR for compound 11
S7	Experimental and data for compound 8	S34	¹³ C NMR for <i>N</i> -Methoxy- <i>N</i> -methylhex-5-enamide
S8	Experimental and data for compound 9	S35	¹ H & ¹³ C NMR for 1-(trimethylsilyl)oct-7-en-1-yn-3-one
S9–10	Experimental and data for compound 10	S36	¹ H & ¹³ C NMR for compound 13
S11	Experimental and data for compound 11	S37	¹ H & ¹³ C NMR for compound 14
S12	Experimental and data for <i>N</i> -Methoxy- <i>N</i> -methylhex-5-enamide	S38	¹ H & ¹³ C NMR for compound 15
S13	Experimental and data for 1-(Trimethylsilyl)oct-7-en-1-yn-3-one	S39	¹ H & ¹³ C NMR for compound 16
S14	Experimental and data for compound 13	S40	¹ H & ¹³ C NMR for compound 17
S15	Derivatisation and <i>e.e.</i> determination for 13	S41	¹ H & ¹³ C NMR for compound 18
S16	Experimental and data for compound 14	S42	¹ H & ¹³ C NMR for compound 19
S17	Experimental and data for compound 15	S43	¹ H & ¹³ C NMR for mono-mesylates
S18	Experimental and data for compound 16	S44	¹ H & ¹³ C NMR for compound 1
S19	Experimental and data for compound 17		
S20	Experimental and data for compound 18		
S21–22	Experimental and data for compound 19		
S23–24	Experimental and data for mesylate		
S25–26	Experimental and data for compound 1		
S27	¹ H & ¹³ C NMR for compound 3		
S28	¹ H & ¹³ C NMR for compound 6		

General Methods

All reactions were carried out under an inert atmosphere in oven dried glassware. THF and Et₂O were distilled from sodium-benzophenone prior to use. Triethylamine and dichloromethane were dried by distillation from CaH₂. All other solvents and reagents were purified, if required, using standard methods.¹ Column chromatography was carried out using Merck Kieselgel 60 and column dimensions are quoted in cm (width x depth). Thin layer chromatography was carried out on Merck silica gel 60 F₂₅₄ and visualised under UV illumination (254 nm) and stained with potassium permanganate. ¹H-NMR and ¹³C-NMR spectra (300 and 75 MHz respectively) were recorded in CDCl₃ solutions using a Bruker AC300 and AV300 or on a Bruker DPX400 (400 and 100 MHz). Chemical shifts are reported in δ units using CHCl₃ as an internal standard (δ 7.27 ppm ¹H, δ 77.36 ppm ¹³C). Coupling constants (*J*) were recorded in Hz. The following abbreviations for the multiplicity of the peaks are s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), br (broad) and m (multiplet). Infrared spectra were recorded on a Nicolet 380 fitted with a Diamond platform, as solids or neat liquids. The IR spectra are reported in wavenumbers (cm⁻¹). The abbreviations, (s) strong, (m) medium, (w) weak and (br) broad were used when reporting the spectra. Melting points were obtained using a Gallenkamp Electrothermal apparatus and are uncorrected. Electron impact and chemical ionisation mass spectra were obtained using a Fisons VG platform single quadropole mass spectrometer. Electrospray mass spectra were obtained using a Micromass platform mass analyser with an electrospray ion source.

Enantiomeric excesses were determined with chiral HPLC analysis, performed on a Hewlett-Packard 1090 series II HPLC and Daicell Chemical Industries Chiralcel OD-H column, eluting with IPA/hexane.

¹ Armarego, W. L. F.; Perrin, D. D.; Perrin, D. R. *Purification of Laboratory Chemicals*; 4th ed.; Butterworth-Heinemann Ltd: Oxford, 1997.

***tert*-Butyl 3-hydroxy-2-iodo-4-methoxybenzyl(methyl)carbamate (3)** C₁₄H₂₀INO₄

M.w. = 393.22 g/mol

White Solid

NMR spectra exhibited broadening due to restricted rotation

To a suspension of 3-hydroxy-2-iodo-4-methoxybenzaldehyde² (2.00 g, 7.19 mmol) in MeOH (10 mL) was added methylamine (7.19 mL of a 2.0 M soln. in MeOH, 14.39 mmol) dropwise producing a red solution which was stirred for 20 h leading to an orange suspension. The reaction was concentrated *in vacuo* then redissolved in MeOH (100 mL). To the solution were added 4 Å molecular sieves and the solution was stirred 15 min before the addition of NaBH₄ (598 mg, 15.81 mmol). The resultant amber solution was stirred for 22 h before concentration *in vacuo* giving a beige solid. The solid was dissolved in dioxane (35 mL) and 1 N NaOH (18 mL) before the addition of (Boc)₂O (1.82 mL, 7.91 mmol) and the reaction was stirred for 16 h. The crude mixture was passed through a pad of celite flushing with EtOAc and the phases were separated. The aqueous was extracted with EtOAc (4 x 30 mL) then CH₂Cl₂ (3 x 30 mL). The combined organic phases were dried (MgSO₄) and concentrated *in vacuo* giving a brown solid. Purification by flash column chromatography on silica gel (4.0 cm x 6 cm) eluting with EtOAc/hexane (3:7) afforded the desired Boc protected benzylic amine **3** as a white solid (2.47 g, 6.28 mmol, 87%). **Mpt** 108–111 °C; **FT-IR** (neat) ν_{max} 3337 (br), 3003 (w), 2974 (w), 2935 (w), 2839 (w), 1678 (s), 1597 (w), 1481 (s) cm⁻¹; **¹H NMR** (300 MHz, CDCl₃) δ 6.83 (1H, d, *J* = 6.8 Hz, C5_{Ar}H), 6.71 (1H, m, C6_{Ar}H), 6.24 (1H, br s, -OH), 4.42 (2H, br s, -CH₂N), 3.90 (3H, s, OCH₃), 2.85 (3H, br s, -NCH₃), 1.45 (9H, br s, -OC(CH₃)₃) ppm; **¹³C NMR** (75 MHz, CDCl₃, C2_{Ar} not observed) δ 156.32 (C, -C=O), 145.94 (C, C3/4_{Ar}), 145.29 (C, C3/4_{Ar}), 132.76 (C, C1_{Ar}), 119.17 & 118.57 (CH, C6_{Ar}), 110.73 (C, C5_{Ar}), 80.07 (C, -OC(CH₃)₃), 57.42 (CH₂, -NCH₂), 56.69 (CH₃, -OCH₃), 34.53 (CH₃, -NCH₃), 28.76 (CH₃, -OC(CH₃)₃) ppm; **LRMS** (ES⁺) *m/z* 416 [M+Na⁺].

² Markovich, K. M.; Tantishaiyakul, V.; Hamada, A.; Miller, D. D.; Romstedt, K. J.; Shams, G.; Shin, Y.; Fraundorfer, P. F.; Doyle, K.; Feller, D. R. *J. Med. Chem.* **1992**, 35, 466-479.

(±)-Oct-7-en-1-yn-3-ol (4a) C₈H₁₂O

M.w. = 124.18 g/mol

Pale yellow oil

A solution of 5-hexenal (790 mg, 8.07 mmol) in THF (10 mL) was added dropwise to a solution of ethynylmagnesium bromide (0.5 M in THF, 19.36 mL, 9.68 mmol) at $-60\text{ }^{\circ}\text{C}$. After stirring for an hour at $-60\text{ }^{\circ}\text{C}$, the reaction mixture was allowed to warm to rt, sat'd NH_4Cl (10mL) and H_2O (10 mL) were then added. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were washed with brine, dried (MgSO_4) and concentrated under reduced pressure to give the crude product as a brown oil. Purification by flash chromatography on silica gel (15 g) eluting with Et_2O /hexane (1:19) afforded the title compound **4a** as a pale yellow oil (450 mg, 3.62 mmol, 45%). Spectroscopic data were consistent with those reported in the literature.³

³ Padwa, A.; Lipka, H.; Watterson, S. H.; Murphree, S. S. *J. Org. Chem.* **2003**, 68, 6238-6250.

(±)-3-[1-(1-Ethynyl)-5-hexenyl]-2-iodo]-4-methoxybenzaldehyde (6) $C_{16}H_{17}IO_3$

M.w. = 384.21 g/mol

Yellow oil

To a stirred solution of 3-hydroxy-2-iodo-4-methoxybenzaldehyde (1.12 g, 4.03 mmol) in THF (30 mL) was added *n*-Bu₃P (1.2 mL, 4.84 mmol) and a solution of **4a** (500 mg, 4.03 mmol) in THF (10 mL). After stirring for 5 minutes, a solution of DBAD (1.85 g, 8.05 mmol) in THF (10 mL) was added dropwise. The reaction mixture was stirred for 15 h and then quenched with H₂O (10 mL). The organic phase was separated and the aqueous phase was extracted with Et₂O (3 x 20 mL). The combined organic phases were washed with brine, dried (MgSO₄) and concentrated under reduced pressure to give the crude product as a yellow oil. Purification by flash chromatography on silica gel (20 g) eluting with Et₂O/hexane (15:85) afforded the title arylether **6** as a yellow oil (865 mg, 2.25 mmol, 56%). **IR** (neat) $\nu_{\max}$ 3288 (m), 2936 (m), 2842 (m), 1677 (s), 1572 (s), 1270 (s), 1243 (s), 1049 (w) cm⁻¹; **¹H NMR** (300 MHz, CDCl₃) δ 10.15 (1H, s, ArCHO), 7.72 (1H, d, *J* = 8.4 Hz, ArH), 6.98 (1H, d, *J* = 8.4 Hz, ArH), 5.87 (1H, ddt, *J* = 17.2, 10.2, 6.6 Hz, H₂C=CHCH₂), 5.24 (1H, td, *J* = 6.2, 2.2 Hz, HC(O)), 5.07 (1H, ddt, *J* = 16.8, 1.8, 1.5 Hz, H_AH_BC=CHCH₂), 5.03-4.97 (1H, m, H_AH_BC=CHCH₂), 3.90 (3H, s, ArOCH₃), 2.36 (1H, d, *J* = 2.2 Hz, HC_{alkyne}), 2.19 (2H, qt, *J* = 6.6, 1.5 Hz, H₂C=CHCH₂), 2.11-2.02 (2H, m, H₂C=CH(CH₂)₂CH₂), 1.89-1.69 (2H, m, H₂C=CHCH₂CH₂); **¹³C NMR** (75 MHz, CDCl₃) δ 195.5 (CHO), 157.5 (C_{Ar}OCH₃), 145.9 (C_{Ar}(O)), 138.4 (H₂C=CHCH₂), 128.0 (C_{Ar}CHO), 127.2 (CH_{Ar}), 114.9 (H₂C=CHCH₂), 111.9 (CH_{Ar}), 102.0 (C_{Ar}I), 81.3 (C_{alkyne}), 75.9 (CH(O)), 71.4 (CH_{alkyne}), 56.2 (OCH₃), 35.3 (H₂C=CH(CH₂)₂CH₂), 35.3 (H₂C=CHCH₂), 24.4 (H₂C=CHCH₂CH₂); **LRMS** (ES⁺) *m/z* 407 [M+Na]⁺; **HRMS** (ES⁺) Calcd. for C₁₆H₁₇IO₃Na: 407.01145, found 407.01180.

(±)-2-Iodo-4-methoxy-3-[(2-vinyl-2-cyclohexenyl)oxy]benzaldehyde (7) $C_{16}H_{17}IO_3$

M.w. = 384.21 g/mol

White solid

To a stirred solution of **6** (65 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) was added a solution of the first generation Grubbs catalyst **12** (14 mg, 17 μ mol) in CH_2Cl_2 (2 mL). The reaction mixture was heated at reflux for 12 h and concentrated under reduced pressure to yield the crude product as a black oil. Purification by flash chromatography on silica gel (6 g) eluting with Et_2O /hexane (1:19) afforded the cyclised product **7** as a white solid (40 mg, 0.10 mmol, 62%). **Mpt.** = 114 °C (Et_2O :Hexane); **IR** (neat) ν_{max} 2936 (m), 2840 (w), 1681 (s), 1571 (s), 1473 (m), 1271 (s), 1246 (s), 1021 (m) cm^{-1} ; **1H NMR** (300 MHz, $CDCl_3$) δ 10.10 (1H, s, ArCHO), 7.64 (1H, d, J = 8.8 Hz, ArH), 6.95 (1H, d, J = 8.8 Hz, ArH), 6.30 (1H, dd, J = 17.6, 11.0 Hz, $H_2C=CH$), 6.04 (1H, dd, J = 4.8, 2.6 Hz, $HC=C(HC=CH_2)$), 5.42 (1H, t, J = 3.3 Hz, $HC(O)$), 5.16 (1H, d, J = 17.6 Hz, $H_AH_B C=CH$), 4.83 (1H, d, J = 11.0 Hz, $H_AH_B C=CH$), 3.96 (3H, s, $ArOCH_3$), 2.42-2.03 (4H, m, $C=CH(CH_2)_2CH_2$, $C=CHCH_2$), 1.69-1.48 (2H, m, $C=CHCH_2CH_2$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 195.9 (CHO), 157.0 ($C_{Ar}OCH_3$), 144.7 ($C_{Ar}(O)$), 138.2 ($HC=$), 135.7 ($C=CH$), 133.0 ($=CH$), 129.4 ($C_{Ar}CHO$), 126.0 (CH_{Ar}), 111.6 (CH_{Ar}), 111.5 ($H_2C=CH$), 101.8 ($C_{Ar}I$), 72.9 ($CH(O)$), 56.0 (OCH_3), 28.3 (CH_2), 25.8 (CH_2), 17.6 (CH_2); **LRMS** (ES^+) m/z 791 [$2M+Na$] $^+$; **HRMS** (ES^+) Calcd. for $C_{16}H_{17}IO_3Na$: 407.01145, found 407.01179.

4-Methoxy-5a,6,7,9a-tetrahydridibenzo[b,f]oxepine-1-carbaldehyde (8) $C_{16}H_{16}O_3$

M.w. = 256.30 g/mol

Colourless oil

A solution of ($\pm$)-**2-bromo-4-methoxy-3-[(2-vinyl-2-cyclohexenyl)oxy]-benzaldehyde** (130 mg, 338 μ mol), $Pd(OAc)_2$ (11 mg, 51 μ mol), 1,3-bis(diphenylphosphino)propane (21 mg, 51 μ mol) and $AgCO_3$ (279 mg, 1.02 mmol) in toluene was heated at reflux for 1 h. The solvent was removed *in vacuo* leaving a black residue which was purified on silica (1 x 9 cm) eluting with EtOAc/hexane (3:7) to give the title compound **8** as a colourless oil (43 mg, 169 μ mol, 50%). **FT-IR** (neat) ν_{max} 2942 (w), 2868 (w), 2835 (w), 1683 (m), 1556 (m), 1438 (m), 1274 (s) cm^{-1} ; **1H NMR** (400 MHz, $CDCl_3$) δ 10.16 (1H, s, **CHO**), 7.50 (1H, d, J = 8.3 Hz, **ArH**), 7.23 (1H, d, J = 12.0 Hz, **-CH=CHC=**), 6.88 (1H, d, J = 8.3 Hz, **ArH**), 6.51 (1H, d, J = 12.3 Hz, **-CH=CHC=**), 5.96 (1H, t, J = 3.8 Hz, **=CHCH₂**), 4.41 (1H, t, J = 6.8 Hz, **OCHCH₂**), 3.93 (3H, s, **OCH₃**), 2.24-2.35 (2H, m, **=CHCHH** and **-OCHCHH**), 2.11-2.20 (1H, m, **=CHCHH**), 2.01 (1H, tdd, J = 12.3, 9.3, 3.3 Hz, **-OCHCHH**), 1.82-1.90 (1H, m, **CH₂CHHCH₂**), 1.58-1.69 (1H, m, **CH₂CHHCH₂**) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 191.78 (**CHO**), 155.68 (**C_{Ar}OCH₃**), 149.07 (**-CH=CHC=**), 139.35 (**C_{Ar}(O)**), 135.77 (**-CH=CHC=**), 131.90 (**=CHCH₂**), 131.39 (**C_{Ar}H**), 131.32 (**C_{Ar}CHO**), 127.40 (**C_{Ar}CH=**), 119.89 (**-CH=CHC=**), 109.65 (**C_{Ar}H**), 81.28 (**CH(O)**), 56.37 (**OCH₃**), 30.03 (**CH₂**), 25.97 (**CH₂**), 20.92 (**CH₂**) ppm; **LRMS** (CI) m/z 257 [**M+H**]⁺; **HRMS** (ES+) for $C_{16}H_{16}NaO_3$, found 279.0997, calculated 279.0991.

(±)-(2-Iodo-4-methoxy-3-(2-vinylcyclohex-2-enyloxy)benzyloxy)(*tert*-butyl)dimethylsilane (9)

$C_{22}H_{33}IO_3Si$

M.w. = 500.49 g/mol

White solid

To a solution of (2-iodo-4-methoxy-3-(2-vinylcyclohex-2-enyloxy)phenyl)methanol (463 mg, 1.20 mmol) in CH_2Cl_2 (10 mL) was added DMAP (15 mg, 0.12 mmol), imidazole (82 mg, 1.20 mmol) and Et_3N (167 μL , 1.20 mmol). After stirring for 10 minutes, TBDMSCl (181 mg, 1.20 mmol) was added. The reaction mixture was stirred for 12 h then quenched with saturated NH_4Cl (15 mL) and H_2O (15 mL). The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (3 x 15 mL). The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product as a brown oil. Purification by flash chromatography on silica gel (10 g) eluting with Et_2O /hexane (1:9) afforded the title compound **9** as a white solid (570 mg, 1.14 mmol, 95%). **Mpt.** = 95 °C (Et_2O :hexane); **IR** (neat) ν_{max} 2953 (m), 2929 (m), 1475 (s), 1252 (s), 1209 (s), 1029 (s), 836 (s), 775 (s) cm^{-1} ; **1H NMR** (300 MHz, $CDCl_3$) δ 7.16 (1H, d, J = 8.4 Hz, ArH), 6.91 (1H, d, J = 8.4 Hz, ArH), 6.34 (1H, dd, J = 17.6, 11.0 Hz, $H_2C=CH$), 6.03 (1H, dd, J = 4.0, 3.3 Hz, $HC=C(HC=CH_2)$), 5.46 (1H, t, J = 3.3 Hz, $HC(O)$), 5.16 (1H, d, J = 17.6 Hz, $H_AH_BC=CH$), 4.87 (1H, d, J = 11.3 Hz, $H_AH_BC=CH$), 4.63 (1H, d, J = 15.1 Hz, $ArCH_AH_BOTBS$), 4.57 (1H, d, J = 15.1 Hz, $ArCH_AH_BOTBS$), 3.90 (3H, s, $ArOCH_3$), 2.39-2.00 (4H, m, $C=CH(CH_2)_2CH_2$, $C=CHCH_2$), 1.63-1.43 (2H, m, $C=CHCH_2CH_2$), 0.98 (9H, s, $C(CH_3)_3$), 0.13 (6H, s, 2 x CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 151.4 ($C_{Ar}(O)$), 146.2 ($C_{Ar}OCH_3$), 138.2 ($HC=C(HC=CH_2)$), 136.2 ($C_{Ar}CH_2OTBS$ and $HC=C(HC=CH_2)$), 132.4 ($HC=C(HC=CH_2)$), 121.4 (CH_{Ar}), 112.1 (CH_{Ar}), 111.8 ($H_2C=CH$), 95.8 ($C_{Ar}I$), 72.6 ($CH(O)$), 69.7 (CH_2OTBS), 55.9 (OCH_3), 28.1 (CH_2), 26.0 ($C(CH_3)_3$), 25.9 (CH_2), 18.4 ($C(CH_3)_3$), 17.8 (CH_2), -5.0 (2 x CH_3); **LRMS** (ES^+) m/z 500 $[M+H]^+$; **HRMS** (ES^+) Calcd. for $C_{22}H_{33}IO_3SiNa$: 523.1136, found 523.1133.

(±)-2-(2-(2-(*tert*-Butyldimethylsilyloxy)ethyl)cyclohex-2-enyloxy)-4-((*tert*-butyldimethylsilyloxy)methyl)-3-iodo-1-methoxybenzene (10)

$C_{28}H_{49}IO_4Si_2$

M.w. = 632.22 g/mol

Colourless oil

To a stirred solution of diene **9** (514 mg, 1.03 mmol) in THF (7 mL) was added a solution of 9-BBN (3 mL, 1.54 mmol, 0.5M in THF). The reaction mixture was stirred for 15 h at rt. NaOH (3M, 6 mL) was added dropwise and chilled H_2O_2 (30%, 6 mL) was added slowly. The solution was stirred at rt for 3 h, then H_2O (15 mL) was added. The organic phase was separated and the aqueous phase was extracted with Et_2O (3 x 15 mL). The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product as a brown oil. Purification by flash chromatography on silica gel (10 g) eluting with Et_2O /hexane (1:3) afforded **2-(6-(3-((*tert*-butyldimethylsilyloxy)methyl)-2-iodo-6-methoxyphenoxy)cyclohex-1-enyl)ethanol** as a yellow oil (450 mg, 0.87 mmol, 84%). **IR** (neat) ν_{max} 3391 (br), 2925 (m), 2852 (m), 1467 (m), 1250 (m), 1025 (m), 833 (s), 731 (s) cm^{-1} ; **1H NMR** (300 MHz, $CDCl_3$) δ 7.18 (1H, d, J = 8.4 Hz, ArH), 6.91 (1H, d, J = 8.4 Hz, ArH), 5.85-5.80 (1H, m, HC=C(CH₂)), 5.05 (1H, t, J = 4.0 Hz, HC(O)), 4.63 (1H, d, J = 13.9 Hz, ArCH_AH_BOTBS), 4.51 (1H, d, J = 13.9 Hz, ArCH_AH_BOTBS), 3.83 (3H, s, ArOCH₃), 3.81-3.72 (2H, m, CH₂OH), 2.66 (1H, dt, J = 13.9, 6.2 Hz, CH_AH_BCH₂OH), 2.45 (1H, dt, J = 13.9, 7.3 Hz, CH_AH_BCH₂OH), 1.58-1.39 (5H, m, C=CH(CH₂)₂CH₂, C=CHCH₂, CH₂OH), 2.24-1.83 (2H, m, C=CHCH₂CH₂), 0.96 (9H, s, C(CH₃)₃), 0.12 (6H, s, 2 x CH₃); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 150.8 (C_{Ar}(O)), 145.7 (C_{Ar}OCH₃), 136.2 (HC=C(HC=CH₂)), 134.3 (C_{Ar}CH₂OTBS), 130.1 (HC=C(CH₂)), 122.0 (CH_{Ar}), 112.2 (CH_{Ar}), 95.8 (C_{Ar}I), 76.6 (CH(O)), 69.6 (C_{Ar}CH₂OTBS), 61.8 (CH₂OH), 55.8 (OCH₃), 38.0 (CH₂), 28.1 (CH₂CH₂OH), 26.0 (C(CH₃)₃), 25.6 (CH₂), 18.7 (CH₂), 15.3 (C(CH₃)₃), -4.5 (2 x CH₃); **LRMS** (ES⁺) m/z 541 [M+Na]⁺; **HRMS** (ES⁺) Calcd. for $C_{22}H_{35}IO_4SiNa$: 541.1241, found 541.1232.

To a stirred solution of **2-(6-(3-((*tert*-butyldimethylsilyloxy)methyl)-2-iodo-6-methoxyphenoxy)cyclohex-1-enyl)ethanol** (95 mg, 0.18 mmol) in CH_2Cl_2 (5 mL) was added DMAP (3 mg, 0.18 mmol), imidazole (12 mg, 0.18 mmol) and Et_3N (26 μ L, 0.18

mmol). After stirring for 10 minutes, TBDMSCl (27 mg, 0.18 mmol) was added. The reaction mixture was stirred for 12 h and then quenched with saturated NH_4Cl (10 mL) and water (10 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were washed with brine, dried (MgSO_4) and concentrated under reduced pressure to give the crude product as a brown oil. Purification by flash chromatography on silica gel (10 g) eluting with Et_2O /hexane (1:9) afforded the title compound **10** as a colourless oil (100 mg, 0.16 mmol, 88%). **IR** (neat) ν_{max} 2928 (m), 2855 (m), 1472 (m), 1251 (m), 1101 (m), 833 (s) (cm^{-1}); **^1H NMR** (300 MHz, CDCl_3) δ 7.18 (1H, d, J = 8.4 Hz, ArH), 6.92 (1H, d, J = 8.4 Hz, ArH), 5.75 (1H, m, $\text{HC}=\text{C}(\text{CH}_2)$), 4.95 (1H, t, J = 4.0 Hz, $\text{HC}(\text{O})$), 4.63 (1H, d, J = 13.9 Hz, $\text{ArCH}_\text{A}\text{H}_\text{B}\text{OTBS}$), 4.57 (1H, d, J = 13.9 Hz, $\text{ArCH}_\text{A}\text{H}_\text{B}\text{OTBS}$), 3.84 (3H, s, ArOCH_3), 3.82-3.73 (2H, m, CH_2OTBS), 2.60 (1H, dt, J = 13.9, 6.2 Hz, $\text{CH}_\text{A}\text{H}_\text{B}\text{CH}_2\text{OTBS}$), 2.39 (1H, dt, J = 13.9, 7.3 Hz, $\text{CH}_\text{A}\text{H}_\text{B}\text{CH}_2\text{OTBS}$), 2.23-1.87 (4H, m, $\text{C}=\text{CH}(\text{CH}_2)_2\text{CH}_2$, $\text{C}=\text{CHCH}_2$), 1.59-1.39 (2H, m, $\text{C}=\text{CHCH}_2\text{CH}_2$), 0.98 (9H, s, $\text{C}(\text{CH}_3)_3$), 0.89 (9H, s, $\text{C}(\text{CH}_3)_3$), 0.14 (6H, s, 2 x CH_3), 0.04 (6H, s, 2 x CH_3); **^{13}C NMR** (75 MHz, CDCl_3) δ 150.9 ($\text{C}_\text{Ar}(\text{O})$), 146.6 ($\text{C}_\text{Ar}\text{OCH}_3$), 136.1 ($\text{HC}=\text{C}(\text{HC}=\text{CH}_2)$), 134.5 ($\text{C}_\text{Ar}\text{CH}_2\text{OTBS}$), 128.9 ($\text{HC}=\text{C}(\text{CH}_2)$), 121.7 (CH_Ar), 112.2 (CH_Ar), 95.8 ($\text{C}_\text{Ar}\text{I}$), 76.7 ($\text{CH}(\text{O})$), 69.7 (ArCH_2OTBS), 63.0 (CH_2OTBS), 55.7 (OCH_3), 37.7 (CH_2), 28.5 ($\text{CH}_2\text{CH}_2\text{OTBS}$), 26.0 (2 x $\text{C}(\text{CH}_3)_3$), 25.6 (CH_2), 18.8 (CH_2), 18.4 ($\text{C}(\text{CH}_3)_3$), 18.3 ($\text{C}(\text{CH}_3)_3$), -4.5 (4 x CH_3); **LRMS** (ES^+) m/z 655 [$\text{M}+\text{Na}$] $^+$; **HRMS** (ES^+) Calcd. for $\text{C}_{28}\text{H}_{49}\text{IO}_4\text{Si}_2\text{Na}$: 655.2106, found 655.2090.

[[9a-(2-[[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy]ethyl)-4-methoxy-5a, 6, 7, 9a-tetrahydrodibenzo[*b,d*]furan-1-yl]methoxy](*tert*-butyl)dimethylsilane (11)

$C_{28}H_{48}O_4Si_2$

M.w. = 504.85 g/mol

Yellow oil

To a stirred solution of **10** (300 mg, 0.47 mmol) in toluene (15 mL) was added Ag_2CO_3 (389 mg, 1.41 μ mol), dppp (29 mg, 0.07 mmol) and $Pd(OAc)_2$ (16 mg, 0.07 mmol). The reaction mixture was evacuated and flushed with argon 3 times. The mixture was heated at reflux for 15 h and allowed to cool to rt. The reaction mixture was concentrated under reduced pressure to give the crude product as a black oil. Purification by flash chromatography on silica gel (12 g) eluting with Et_2O /hexane (1:9) to afford the title compound **11** as a yellow oil (210 mg, 0.42 mmol, 89%). **IR** (neat) ν_{max} 2928 (m), 2856 (m), 1505 (m), 1278 (m), 1253 (m), 1085 (s), 833 (s), 774 (s) cm^{-1} ; **1H NMR** (300 MHz, $CDCl_3$) δ 6.83 (1H, d, J = 8.0 Hz, ArH), 6.71 (1H, d, J = 8.0 Hz, ArH), 5.82 (2H, s, HC=CH), 4.95 (1H, dd, J = 5.1, 3.0 Hz, HC(O)), 4.51 (1H, d, J = 14.1 Hz, ArCH_AH_BOTBS), 4.44 (1H, d, J = 14.1 Hz, ArCH_AH_BOTBS), 3.85 (3H, s, ArOCH₃), 3.68 (1H, dt, J = 10.0, 7.5 Hz, CH_AH_BOTBS), 3.62 (1H, dt, J = 10.6, 7.0 Hz, CH_AH_BOTBS), 2.30-2.03 (4H, m, CH₂CH₂OTBS, HC=CHCH₂CH₂), 1.99-1.80 (2H, m, HC=CHCH₂CH₂), 0.94 (9H, s, C(CH₃)₃), 0.86 (9H, s, C(CH₃)₃), 0.10 (6H, s, 2 x CH₃), -0.09 (6H, s, 2 x CH₃); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 147.6 (C_{Ar}OCH₃), 144.6 (C_{Ar}(O)), 131.6 (C_{Ar}CH₂OTBS), 130.1 (HC=CH), 127.8 (C_{Ar}), 120.8 (CH_{Ar}), 111.0 (CH_{Ar}), 85.6 ((O)CH(CH₂)), 62.6 (ArCH₂OTBS), 60.3 (CH₂OTBS), 56.1 (OCH₃), 49.7 (C), 40.3 (CH₂CH₂OTBS), 26.3 (C(CH₃)₃), 26.2 (C(CH₃)₃), 24.5 (CH₂), 19.9 (CH₂), 18.7 (C(CH₃)₃), 18.5 (C(CH₃)₃), -4.8 (2 x CH₃), -5.1 (2 x CH₃); **LRMS** (ES⁺) m/z 527 [M+Na]⁺; **HRMS** (ES⁺) Calcd. for $C_{28}H_{48}O_4Si_2Na$: 527.2983, found 527.2989.

***N*-Methoxy-*N*-methylhex-5-enamide** $\text{C}_8\text{H}_{15}\text{NO}_2$

M.w. = 157.21 g/mol

Colourless oil

To a solution of 5-hexenoic acid (200 mg, 1.75 mmol) in CH_2Cl_2 (10 mL) was added EDCI (503 mg, 2.63 mmol), DMAP, (321 mg, 2.63 mmol) and *N,O*-dimethylhydroxyamine hydrochloride (256 mg, 2.63 mmol). The resultant mixture was stirred for 2.5 h before being quenched with brine (10 mL). The phases were separated and the aqueous phase extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with 2 M HCl (10 mL) and brine (10 mL) before being dried (MgSO_4) and concentrated *in vacuo* giving a pale yellow oil. Purification by flash column chromatography on silica gel (3.0 cm x 6 cm) eluting with EtOAc/hexane (4:6) yielded the title amide as a colourless oil (257 mg, 1.63 mmol, 93%). **FT-IR** (neat) ν_{max} 3077 (w), 2938 (w), 1661 (s) cm^{-1} ; **^1H NMR** (400 MHz, CDCl_3) δ 5.81 (1H, ddt, J = 17.1, 10.3, 6.8 Hz, $\text{H}_2\text{C}=\text{CH}-$), 5.04 (1H, dq, J = 17.1 Hz, 2.0 Hz, H_a), 4.98 (1H, ddt, J = 10.3, 2.0, 1.3 Hz, H_b), 3.68 (3H, s, $-\text{NOCH}_3$), 3.18 (3H, s, $-\text{NCH}_3$), 2.43 (2H, t, J = 7.5 Hz, $-\text{CH}_2\text{C}(\text{O})\text{N}-$), 2.12 (2H, q, J = 7.1 Hz, $\text{H}_2\text{C}=\text{CHCH}_2-$), 1.75 (2H, qn, J = 7.5 Hz, $\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_2-$) ppm; **^{13}C NMR** (100 MHz, CDCl_3) δ 181.92 (C, $-\text{C}=\text{O}$), 138.49 (CH, $\text{H}_2\text{C}=\text{CH}-$), 115.38 (CH_2 , $\text{H}_2\text{C}=\text{CH}-$), 61.54 (CH_3 , $-\text{NOCH}_3$), 33.64 (CH_2 , $\text{H}_2\text{C}=\text{CHCH}_2-$), 32.60 (CH_3 , $-\text{NCH}_3$), 31.49 (CH_2 , $-\text{CH}_2\text{C}(\text{O})\text{N}-$), 24.05 (CH_2 , $\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_2-$) ppm; **LRMS** (ES^+) m/z 180 [$\text{M}+\text{Na}^+$].

1-(Trimethylsilyl)oct-7-en-1-yn-3-one C₁₁H₁₈OSi

M.w. = 194.35 g/mol

Colourless oil

A solution of TMS acetylene (3.456 g, 35.2 mmol) in THF (110 mL) at $-40\text{ }^{\circ}\text{C}$ was treated with *n*-BuLi (15.43 mL of a 2.28 M soln. in hexane, 35.19 mmol) dropwise. This solution was stirred for 2 h allowing the mixture to warm to $0\text{ }^{\circ}\text{C}$. The mixture was cooled to $-10\text{ }^{\circ}\text{C}$ before the dropwise addition of a solution of *N*-methoxy-*N*-methylhex-5-enamide (3.69 g, 23.5 mmol) in THF (28 mL) giving a colourless solution. After stirring at $-10\text{ }^{\circ}\text{C}$ for 3 h the reaction was quenched with NH_4Cl (30 mL). The phases were separated before the aqueous phase was extracted with Et_2O (3 x 25 mL). The combined organic phases were washed with brine (15 mL), dried (MgSO_4) and concentrated *in vacuo* giving a yellow oil. Purification by flash column chromatography on silica gel (5.0 cm x 9 cm) eluting with CH_2Cl_2 gave the title ketone as a colourless oil (3.88 g, 20.0 mmol, 85%). **FT-IR** (neat) ν_{max} 3078 (w), 2961 (w), 1676 (s), 1642 (m) cm^{-1} ; **^1H NMR** (400 MHz, CDCl_3) δ 5.78 (1H, ddt, $J = 17.1, 10.3, 6.7\text{ Hz}$, $\text{H}_2\text{C}=\text{CH}-$), 5.08-4.97 (2H, m, $\text{H}_2\text{C}=\text{CH}-$), 2.57 (2H, t, $J = 7.3\text{ Hz}$, $\text{TMSC}\equiv\text{CC}(\text{O})\text{CH}_2-$), 2.10 (2H, br q, $J = 7.0\text{ Hz}$, $\text{H}_2\text{C}=\text{CHCH}_2-$), 1.78 (2H, qn, $J = 7.3\text{ Hz}$, $\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_2-$), 0.25 (9H, s, $-\text{Si}(\text{CH}_3)_3$) ppm; **^{13}C NMR** (100 MHz, CDCl_3) δ 187.97 (C, $-\text{C}=\text{O}$), 137.95 (CH, $\text{H}_2\text{C}=\text{CH}-$), 115.83 (CH_2 , $\text{H}_2\text{C}=\text{CH}-$), 102.40 (C, $-\text{C}\equiv\text{CTMS}$), 98.05 (C, $-\text{C}\equiv\text{CTMS}$), 44.83 (CH_2 , $\text{TMSC}\equiv\text{CC}(\text{O})\text{CH}_2-$), 33.15 (CH_2 , $\text{H}_2\text{C}=\text{CHCH}_2-$), 23.37 (CH_2 , $\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_2-$), -0.41 (CH_3 , $-\text{Si}(\text{CH}_3)_3$) ppm; **LRMS** (ES^+) m/z 195 [$\text{M}+\text{H}^+$].

(R)-1-(Trimethylsilyl)oct-7-en-1-yn-3-ol (13) C₁₁H₂₀OSi

M.w. = 196.36 g/mol

Colourless oil

1-(Trimethylsilyl)oct-7-en-1-yn-3-one (1.00 g, 5.15 mmol) was cooled to 0 °C before treatment with *R*-Alpine borane (20.6 mL of a 0.5 M soln. in THF, 10.3 mmol) followed by immediate concentration *in vacuo* giving a yellow oil. The oil was stirred for 18 h at rt before quenching at 0 °C with acetaldehyde (1.5 mL). The mixture was stirred for 15 min at 0 °C before Et₂O (50 mL) and ethanolamine (0.68 mL, 11.32 mmol) were added. The reaction mixture was warmed to rt and stirred for 1.5 h producing a white precipitate and yellow solution. The heterogeneous mixture was filtered through a pad of celite, eluting with Et₂O. The organic phase was washed with H₂O (10 mL) and brine (10 mL), dried (MgSO₄) and concentrated *in vacuo* giving a yellow oil. Purification by flash column chromatography on silica gel (5.0 cm x 8 cm) eluting with EtOAc/hexane (1:19) afforded the desired alcohol **13** as a colourless oil (901 mg, 4.59 mmol, 89%). The enantiomeric excess was estimated to be 92% *ee* from chiral HPLC analysis (OD-H chiral column) of a phenyl ether derivative prepared by Mitsunobu coupling with 3-hydroxy-2-iodo-4-methoxybenzaldehyde (see below). NMR data for alcohol **13** are consistent with those reported in the literature for the racemic material.⁴ [α]_D = +1.5 (*c* 1.0, CHCl₃, 22 °C; 92% *e.e.*); **FT-IR** (neat) ν_{max} 3331 (br), 2957 (w), 2172 (w), 1641 (w), 1250 (m) cm⁻¹; **¹H NMR** (400 MHz, CDCl₃) δ 5.82 (1H, ddt, *J* = 17.1, 10.3, 6.7 Hz, H₂C=CH-), 5.04 (1H, dq, *J* = 17.1, 1.8 Hz), 4.97 (1H, ddt, *J* = 10.3, 2.0, 1.1 Hz), 4.37 (1H, q, *J* = 7.0 Hz, -CHOH), 2.11 (2H, qt, *J* = 6.8, 1.5 Hz, H₂C=CHCH₂-), 1.77-1.67 (2H, m, -CH₂C(OH)-), 1.64-1.50 (2H, m, H₂C=CHCH₂CH₂-), 0.18 (9H, s, -Si(CH₃)₃) ppm; **¹³C NMR** (100 MHz, CDCl₃) δ 138.76 (CH, H₂C=CH-), 115.13 (CH₂, H₂C=CH-), 107.10 (C, -C $\equiv$ CTMS), 89.83 (C, -C $\equiv$ CTMS), 63.12 (CH, -COH), 37.45 (CH₂, -CH₂C(OH)-), 24.71 (CH₂, H₂C=CHCH₂CH₂-), 0.23 (CH₃, -Si(CH₃)₃) ppm; **LRMS** (ES⁺) *m/z* 219 [M+Na⁺], 431 [2M+K⁺].

⁴ Young, D. G. J.; Burlison, J. A.; Peters, U. *J. Org. Chem.* **2003**, 68, 3494-3497.

3-((*S*)-1-Trimethylsilyl)oct-7-en-1-yn-3-yloxy)-2-iodo-4-methoxybenzaldehyde C₁₉H₂₅IO₃Si

M.w. = 456.39 g/mol

Colourless oil

To a solution of 3-hydroxy-2-iodo-4-methoxybenzaldehyde (200 mg, 0.72 mmol) in THF (6 mL) was added PPh₃ (315 mg, 1.20 mmol) and a solution of alcohol **13** (118 mg, 0.60 mmol) in THF (1.5 mL) dropwise. The resultant mixture was stirred for 5 min. before the dropwise addition of DIAD (0.24 mL, 1.20 mmol). The mixture was heated to reflux and stirred for 14 h before the reaction was concentrated *in vacuo* giving a yellow oil. Purification by flash column chromatography on silica gel (2.0 cm x 9 cm) eluting with EtOAc/hexane (3:97) gave the title aryl ether as a colourless oil (91 mg, 0.20 mmol, 33%). [α]_D +30.0 (*c* 6.0, CHCl₃, 21 °C); **FT-IR** (neat) ν_{max} 2953 (w), 2843 (w), 1683 (s), 1640 (w), 1573 (s), 1475 (m) cm⁻¹; **¹H NMR** (400 MHz, CDCl₃) δ 10.07 (1H, s, -CHO), 7.72 (1H, d, *J* = 8.6 Hz, CHOCCHCH-), 6.96 (1H, d, *J* = 8.6 Hz, CHOCCHCH-), 5.88 (1H, ddt, *J* = 17.0, 10.3, 6.6 Hz, H₂C=CH-), 5.22 (1H, t, *J* = 6.4 Hz, ArOCHCH₂-), 5.08 (1H, dq, *J* = 17.0, 1.7 Hz, H_a), 5.01 (1H, ddt, *J* = 10.3, 2.0, 1.5 Hz, H_b), 3.94 (3H, s, ArOCH₃), 2.20 (2H, q, *J* = 7.0 Hz, -CH₂CH=CH₂), 2.15-1.95 (2H, m, ArOCHCH₂-), 1.85-1.65 (2H, m, ArOCHCH₂CH₂-), 0.02 (9H, s, -Si(CH₃)₃) ppm; **¹³C NMR** (100 MHz, CDCl₃) δ 195.93 (CH, -CHO), 158.04 (C, -COMe + CHOCCO-), 138.85 (CH, -CH=CH₂), 129.47 (C, CHOC-), 127.40 (CH, CHOCCHCH-), 115.15 (CH₂, -CH=CH₂), 111.85 (CH, CHOCCHCH-), 103.26 (C, -CI), 103.02 (C, -C $\equiv$ CTMS), 93.61 (C, -C $\equiv$ CTMS), 72.53 (CH, ArOCHCH₂), 56.50 (CH₃, ArOCH₃), 35.63 (CH₂, ArOCHCH₂-), 33.71 (CH₂, -CH₂CH=CH₂), 24.90 (CH₂, ArOCHCH₂CH₂-), -0.03 (CH₃, -Si(CH₃)₃) ppm; **LRMS** (ES⁺) *m/z* 479 [M+Na⁺], 495 [M+K⁺].

The enantiomeric excess of the aryl ether was estimated to be 92% *ee* from chiral HPLC analysis (OD-H chiral column; *i*PrOH/hexane).

(S)-tert-Butyl 2-iodo-4-methoxy-3-(1-(trimethylsilyl)oct-7-en-1-yn-3-yloxy)benzyl (methyl)carbamate (14) C₂₅H₃₈INO₄Si

M.w. = 571.56 g/mol

Colourless oil

NMR spectra exhibited broadening / doubling of peaks due to restricted rotation

To a solution of phenol **3** (774 mg, 1.97 mmol) in THF (18 mL) was added PPh₃ (938 mg, 3.58 mmol) and a solution of the propargylic alcohol **13** (351 mg, 1.79 mmol) in THF (4 mL). This solution was stirred for 5 min before the dropwise addition of DIAD (0.70 mL, 3.58 mmol). The reaction was then heated to reflux and stirred for 3.5 h. The reaction mixture was cooled and concentrated *in vacuo* giving a brown orange oil. Purification by flash column chromatography on silica gel (5.0 cm x 8 cm) eluting with EtOAc/hexane (1:19→1:10) afforded the desired ether (**14**) as a colourless oil (835 mg, 1.46 mmol, 74%). [α]_D = +11.5 (*c* 0.5, CHCl₃, 27 °C); **FT-IR** (neat) ν_{max} 2957 (w), 2934 (w), 2865 (w), 2838 (w), 2175 (w), 1696 (s), 1640 (w), 1589 (w), 1476 (m), 1389 (m) cm⁻¹; **¹H NMR** (400 MHz, CDCl₃) δ 6.87 (1H, br d, *J* = 6.7 Hz, C5_{Ar}H), 6.81 (1H, m, C6_{Ar}H), 5.87 (1H, ddt, *J* = 17.1, 10.3, 6.7 Hz, H₂C=CH-), 5.20 (1H, m, ArOCH), 5.07 (1H, dq, *J* = 17.1, 1.8 Hz), 4.99 (1H, ddt, *J* = 10.3, 1.8, 1.3 Hz), 4.46 (2H, br, -NCH₂-), 3.84 (3H, s, OCH₃), 2.83 (3H, br, -NCH₃), 2.18 (2H, br q, *J* = 6.7 Hz, H₂C=CHCH₂-), 2.10-1.93 (2H, m, OCHCH₂-), 1.86-1.65 (2H, m, OCHCH₂CH₂-), 1.51 & 1.44 (9H, br, -OC(CH₃)₃), 0.04 (9H, s, -Si(CH₃)₃) ppm; **¹³C NMR** (100 MHz, CDCl₃, C2_{Ar} not observed) δ 156.34 (C, -C=O), 151.83 (C, C4_{Ar}), 146.63 (C, C3_{Ar}), 138.98 (CH, H₂C=CH-), 132.71 (C, C1_{Ar}), 123.52 & 122.49 (CH, C6_{Ar}), 115.00 (CH₂, H₂C=CH-), 112.46 (CH, C5_{Ar}), 104.07 (C, -C≡CTMS), 92.60 (C, -C≡CTMS), 80.06 (C, -C(CH₃)₃), 72.21 (CH, ArOCH-), 57.99 & 56.92 (CH₂, -NCH₂-), 56.36 (CH₃, OCH₃), 35.67 (CH₂, OCHCH₂), 34.44 (CH₃, -NCH₃), 28.79 (CH₃, -C(CH₃)₃), 24.90 (CH₂, H₂C=CHCH₂CH₂-), 0.06 (CH₃, -Si(CH₃)₃) ppm; **LRMS** (ES⁺) *m/z* 572 [M+H⁺], 594 [M+Na⁺]; **HRMS** (ES⁺) for C₂₅H₃₈INNaO₄Si, calculated 594.1507, found 594.1504 Da.

(S)-tert-Butyl 2-iodo-4-methoxy-3-(oct-7-en-1-yn-3-yloxy)benzyl(methyl) carbamate
(15)

$C_{22}H_{30}INO_4$

M.w. = 499.38 g/mol

Pale yellow oil

NMR spectra exhibited broadening / doubling of peaks due to restricted rotation

To a solution of phenolic ether **14** (800 mg, 1.40 mmol) in MeOH (8 mL) was added K_2CO_3 (213 mg, 1.54 mmol) in one portion. The heterogeneous mixture was stirred for 4 h at rt giving a white opaque mixture. The reaction was quenched with NH_4Cl (10 mL) then concentrated *in vacuo* before dissolving in EtOAc (30 mL) and H_2O (10 mL). The phases were separated and the aqueous phase was extracted with EtOAc (3 x 40 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo* giving the title compound **15** as a pale yellow oil which required no further purification (675 mg, 1.35 mmol, 97%). $[\alpha]_D^{25} = -1.1$ (c 0.5, $CHCl_3$, 26 °C). **FT-IR** (neat) ν_{max} : 3290 (w), 3236 (w), 3076 (w), 2974 (w), 2932 (w), 2866 (w), 2838 (w), 2111 (w), 1690 (s), 1640 (w), 1589 (m), 1476 (m) cm^{-1} ; **1H NMR** (400 MHz, $CDCl_3$) δ 6.92-6.80 (2H, m, $C5_{Ar}H$ & $C6_{Ar}H$), 5.87 (1H, ddt, $J = 17.1, 10.3, 6.7$ Hz, $H_2C=CH-$), 5.23 (1H, br t, $J = 5.5$ Hz, $ArOCHCH_2-$), 5.07 (1H, dq, $J = 17.1, 1.8$ Hz, $CH=CH_EH_Z$), 5.00 (1H, ddt, $J = 10.3, 1.8, 1.3$ Hz, $CH=CH_EH_Z$), 4.60-4.30 (2H, br, $-NCH_2-$), 3.85 (3H, s, OCH_3), 2.86 (3H, br, $-NCH_3$), 2.35 (1H, d, $J = 2.0$ Hz, $-C\equiv CH$), 2.18 (2H, q, $J = 7.0$ Hz, $H_2C=CHCH_2-$), 2.07-2.00 (2H, m, $OCHCH_2-$), 1.88-1.65 (2H, m, $OCHCH_2CH_2-$), 1.50 & 1.43 (9H, br s, $-OC(CH_3)_3$) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.41 (C, $-C=O$), 151.66 (C, $C4_{Ar}$), 146.34 (C, $C3_{Ar}$), 138.84 (CH, $H_2C=CH-$), 133.15 (C, $C1_{Ar}$), 122.95 (CH, $C6_{Ar}$), 115.12 (CH_2 , $H_2C=CH-$), 112.69 (CH, $C5_{Ar}$), 82.25 (C, $-C\equiv CH$), 80.06 (C, $-C(CH_3)_3$), 75.54 (CH, $-C\equiv CH$), 71.55 (CH, $-OCHCH_2-$), 57.91 & 57.03 (CH_2 , $-NCH_2-$), 56.39 (CH_3 , OCH_3), 35.68 (CH_2 , $-OCHCH_2-$), 34.56 (CH_3 , $-NCH_3$), 33.74 (CH_2 , $H_2C=CHCH_2-$), 28.78 (CH_3 , $-OC(CH_3)_3$), 24.80 (CH_2 , $H_2C=CHCH_2CH_2-$) ppm; **LRMS** (ES^+) m/z 500 $[M+H^+]$, 522 $[M+Na^+]$; **HRMS** (ES^+) for $C_{22}H_{30}INNaO_4$, calculated 522.1112, found 522.1119 Da.

(S)-tert-Butyl 2-iodo-4-methoxy-3-(2-vinylcyclohex-2-enyloxy)benzyl(methyl) carbamate (16) C₂₂H₃₀INO₄

M.w. = 499.38 g/mol

Colourless oil

NMR spectra exhibited broadening / doubling of peaks due to restricted rotation

To a solution of enyne **15** (532 mg, 1.07 mmol) in CH₂Cl₂ (32 mL) was added Grubb's 1st generation catalyst (26 mg, 0.03 mmol) in one portion and the resultant purple solution was stirred for 3 h at rt. The reaction was concentrated *in vacuo* giving a brown oil. Purification by flash column chromatography on silica gel (4.0 cm x 10 cm) eluting with EtOAc/hexane (1:9) gave the desired diene **16** as a colourless oil (453 mg, 0.91 mmol, 85%). [α]_D = -140.2 (*c* 0.6, CHCl₃, 26 °C); **FT-IR** (neat) $\nu_{\max}$ 3003 (w), 2973 (w), 2935 (w), 2866 (w), 2835 (w), 1694 (s), 1644 (w), 1587 (w), 1475 (m) cm⁻¹; **¹H NMR** (400 MHz, CDCl₃) δ 6.87 (1H, d, *J* = 8.3 Hz, C5_{Ar}H), 6.78 (1H, m, C6_{Ar}H), 6.33 (1H, dd, *J* = 17.7, 11.2 Hz, H₂C=CH-), 6.03 (1H, dd, *J* = 4.9, 2.9 Hz, -CH₂CH=C-), 5.45 (1H, t, *J* = 3.4 Hz, OCHCH₂-), 5.24 (1H, br d, *J* = 17.7 Hz), 4.84 (1H, d, *J* = 11.2 Hz), 4.39 (2H, br, -NCH₂Ar), 3.87 (3H, s, OCH₃), 2.85 & 2.80 (3H, br s, -NCH₃), 2.34 (1H, m, =C-CH₂-), 2.26-2.00 (5H, m, =C-CH₂CH₂CH₂-), 1.51 & 1.43 (9H, br s, -OC(CH₃)₃) ppm; **¹³C NMR** (100 MHz, CDCl₃) δ 156.32 & 155.88 (C, -C=O), 151.17 (C, C4_{Ar}), 147.16 (C, C3_{Ar}), 138.57 (CH, H₂C=CHC-), 136.42 (C, H₂C=CHC-), 133.21 (C, C1_{Ar}), 132.86 (CH, -CH₂CH=C-), 122.17 & 121.61 (CH, C6_{Ar}), 112.53 (CH, C5_{Ar}), 111.96 (CH₂, H₂C=CHCH-), 80.00 (C, -OC(CH₃)₃), 73.04 (CH, ArOCH-), 58.10 & 57.18 (CH₂, -NCH₂Ar), 56.21 (CH₃, OCH₃), 34.48 (CH₃, -NCH₃), 28.78 (CH₃, -OC(CH₃)₃), 28.56 (CH₂, OCHCH₂-), 26.22 (CH₂, =CHCH₂-), 18.11 (CH₂, -CH₂CH₂CH₂-) ppm; **LRMS** (ES⁺) *m/z* 500 [M+H⁺], 522 [M+Na⁺]; **HRMS** (ES⁺) for C₂₂H₃₀INNaO₄, calculated 522.1112, found 522.1111 Da.

(S)-tert-butyl 3-(2-(2-hydroxyethyl)cyclohex-2-enyloxy)-2-iodo-4-methoxybenzyl(methyl) carbamate (17) $C_{22}H_{32}INO_5$

M.w. = 517.40 g/mol

Colourless oil

NMR spectra exhibited broadening / doubling of peaks due to restricted rotation

To a solution of diene **16** (436 mg, 0.87 mmol) in THF (6 mL) was added 9-BBN (2.62 mL of 0.5 M in THF, 1.31 mmol) dropwise, the resultant pale yellow solution was stirred for 17 h. To the mixture was added 3 M NaOH (5 mL) followed by H_2O_2 (5 mL) leading to an exothermic reaction. The reaction was stirred for 3 h before the addition of H_2O (15 mL). The mixture was extracted with Et_2O (4 x 25 mL) and the combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo* giving a colourless oil. Purification by flash column chromatography on silica gel (3.5 cm x 9 cm) eluting with $EtOAc$ /hexane (1:1) gave the desired alcohol **17** as a colourless oil (410 mg, 0.79 mmol, 91%). $[\alpha]_D = -50.4$ (c 1.2, $CHCl_3$, 26 °C); **FT-IR** (neat) ν_{max} 3436 (br), 2973 (w), 2933 (m), 2867 (w), 2835 (w), 1678 (s), 1586 (m), 1474 (m) cm^{-1} ; **1H NMR** (400 MHz, $CDCl_3$) δ 6.89 (1H, d, J = 8.5 Hz, $C5_{Ar}H$), 6.81 (1H, br d, J = 8.5 Hz, $C6_{Ar}H$), 5.84 (1H, dd, J = 3.8, 3.5 Hz, $CH_2CH=C$), 5.07 (1H, br t, J = 4.1 Hz, $ArOCH-$), 4.41 (2H, br, $-NCH_2Ar$), 3.85 (3H, s, OCH_3), 3.84-3.70 (2H, m, $-CH_2OH$), 2.86 (3H, br, $-NCH_3$), 2.66 (1H, dt, J = 13.9, 5.3 Hz, $-CH_2CH_2OH$), 2.46 (1H, dt, J = 13.9, 6.5 Hz, $-CH_2CH_2OH$), 2.20 (1H, m, CH_2), 2.12-1.97 (2H, m, CH_2), 1.96-1.84 (2H, m, CH_2), 1.60-1.34 (10H, m, CH_2 and $-OC(CH_3)_3$) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.29 (C, $-C=O$), 151.23 (C, $C4_{Ar}$), 146.61 (C, $C3_{Ar}$), 134.52 (C, $-CH=CCH_2-$), 133.23 (C, $C1_{Ar}$), 130.53 (CH, $-CH=CCH_2-$), 122.43 & 122.05 (CH, $-C6_{Ar}$), 112.66 (CH, $C5_{Ar}$), 80.08 (C, $-OC(CH_3)_3$), 77.01 (CH, $ArOCHCH_2-$), 62.15 (CH_2 , $-CH_2OH$), 58.20 & 57.36 (CH_2 , $-NCH_2Ar$), 56.16 (CH_3 , OCH_3), 38.40 (CH_2 , $-CH_2CH_2OH$), 34.64 (CH_3 , $-NCH_3$), 28.77 (CH_3 , $-OC(CH_3)_3$), 28.51 (CH_2 , $OCHCH_2-$), 25.89 (CH_2 , $-CH_2CH=C$), 19.06 (CH_2 , $-CH_2CH_2CH=C$) ppm; **LRMS** (ES^+) m/z 540 [$M+Na^+$]; **HRMS** (ES^+) for $C_{22}H_{32}INNaO_5$, calculated 540.1217, found 540.1230 Da.

Heck reaction to give tricycle 18 $C_{22}H_{31}NO_5$

M.w. = 389.49 g/mol

Pale yellow oil

NMR spectra exhibited broadening / doubling of peaks due to restricted rotation

To a solution of iodide **17** (388 mg, 0.75 mmol) in toluene (24 mL) was added Ag_2CO_3 (620 mg, 2.25 mmol), dppp (46 mg, 0.11 mmol) and $Pd(OAc)_2$ (25 mg, 0.11 mmol). The green heterogeneous mixture was heated to reflux and stirred for 16 h giving a black solution. The solution was concentrated *in vacuo* giving a black oil. Purification by flash column chromatography on silica gel (3.5 cm x 12 cm) eluting with EtOAc/hexane (3:2) afforded the desired tricyclic product **18** as a pale yellow oil (169 mg, 0.43 mmol, 58%). $[\alpha]_D = -26.5$ (c 1.2, $CHCl_3$, 26 °C); **FT-IR** (neat) ν_{max} 3442 (br), 2972 (w), 2931 (m), 2839 (w), 1690 (s), 1622 (m), 1581 (w), 1505 (s) cm^{-1} ; **1H NMR** (400 MHz, $CDCl_3$) δ 6.72 (1H, d, $J = 8.5$ Hz, $C5_{Ar}H$), 6.58 (1H, d, $J = 8.5$ Hz, $C6_{Ar}H$), 5.87 (1H, ddd, $J = 11.0, 4.3, 2.8$ Hz - $CCH=CH-$), 5.81 (1H, d, $J = 11.0$ Hz, - $CCH=CH-$), 4.85 (1H, dd, $J = 5.5, 3.6$ Hz, $ArOCHCH_2-$), 4.58 (1H, br d, $J = 15.7$ Hz, - NCH_2Ar), 4.43 (1H, d, $J = 15.7$ Hz, - NCH_2Ar), 3.86 (3H, s, OCH_3), 3.69-3.57 (2H, m, - CH_2OH), 2.82 (3H, br s, - NCH_3), 2.27-1.92 (5H, m, - CH_2-), 1.85 (1H, m, - CH_2-), 1.48 (9H, s, - $OC(CH_3)_3$) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.40 (C, - $C=O$), 147.86 (C, $C3_{Ar}$), 144.51 (C, $C4_{Ar}$), 131.58 (C, $C2_{Ar}$), 129.39 (CH, - $CCH=CH-$), 128.65 (CH, - $CCH=CH-$), 126.54 (C, $C1_{Ar}$), 120.64 (CH, br, $C6_{Ar}$), 111.46 (CH, $C5_{Ar}$), 85.76 (CH, $ArOCHCH_2-$), 80.23 (C, - $OC(CH_3)_3$), 59.96 (CH_2 , - CH_2OH), 56.18 (CH_3 , OCH_3), 49.53 (C, - $CCH=CH-$), 48.90 (CH_2 , - CH_2N-), 40.84 (CH_2 , - CH_2CH_2OH), 34.32 (CH_3 , - NCH_3), 28.78 (CH_3 , - $OC(CH_3)_3$), 24.87 (CH_2 , $OCHCH_2CH_2-$), 20.11 (CH_2 , $OCHCH_2CH_2-$) ppm; **LRMS** (ES^+) m/z 390 [$M+H^+$], 412 [$M+Na^+$]; **HRMS** (ES^+) for $C_{22}H_{32}NO_5$, calculated 390.2275, found 390.2264 Da.

Allylic oxidation to afford mixture of epimeric allylic alcohols (19) C₂₂H₃₁NO₆

M.w. = 405.48 g/mol

Peach oil

NMR spectra exhibited broadening / of peaks due to restricted rotation.

To a solution of the cyclohexene **18** (25 mg, 64.19 μ mol) in dioxane (0.6 mL) was added NaH₂PO₄ (8 mg, 64.19 μ mol), SeO₂ (7 mg, 64.19 μ mol) and quartz sand (29 mg). The yellow heterogeneous mixture was flushed with argon and sealed before heating to 150 °C with stirring for 1 h. A further addition of SeO₂ (7 mg, 64.19 μ mol) and quartz sand (29 mg) was made and the tube was flushed with argon, resealed then heated to 150 °C for an additional 1 h. A final addition of SeO₂ (7 mg, 64.19 μ mol) and quartz sand (29 mg) was made before the tube was flushed with argon, resealed then heated to 150 °C for a further 1 h. After cooling the reaction mixture was passed through a plug of celite eluting with EtOAc and the resulting solution was concentrated *in vacuo* giving an orange oil. The oil was dissolved in CH₂Cl₂ (30 mL) and washed with 1 N NaOH (10 mL). The aqueous phase was extracted with CH₂Cl₂ (3 x 20 mL) and the combined organic phase was washed with a mixture of brine (5 mL) and H₂O (5 mL), dried (Na₂SO₄) and concentrated *in vacuo* giving a brown oil. Purification by flash column chromatography on silica gel (1.5 cm x 6 cm) eluting with EtOAc/hexane (1:1) gave the desired diols **19α/β** (16 mg, 39.46 μ mol, 61%, *dr* = 4.8:1) as an unseparated mixture of diastereoisomers. Data were obtained from the mixture of diastereoisomers (4.8:1): [α]_D = -0.1 (*c* 0.35, CHCl₃, 26 °C); **FT-IR** (neat) ν_{max} 3399 (br), 2931 (m), 1670 (s), 1623 (m), 1581 (w), 1505 (m) cm⁻¹; **¹H NMR** (for major diastereoisomer **19α**, 400 MHz, CDCl₃) δ 6.75 (1H, d, *J* = 8.3 Hz, C5_{Ar}H), 6.64 (1H, d, *J* = 8.3 Hz, C6_{Ar}H), 5.96 (1H, dd, *J* = 10.0, 4.0 Hz, -CCH=CH-), 5.85 (1H, d, *J* = 10.0 Hz, -CCH=CH-), 4.90 (1H, dd, *J* = 6.3, 3.4 Hz, ArOCHCH₂-), 4.55 (1H, d, *J* = 15.8 Hz, -NCH₂Ar), 4.46 (1H, d, *J* = 15.8 Hz, -NCH₂Ar), 4.20 (1H, dt, *J* = 4.6, 4.0 Hz, -CH(OH)-), 3.85 (3H, s, OCH₃), 3.72-3.58 (2H, m, -CH₂CH₂OH for both diastereoisomers), 2.81 (3H, s, -NCH₃), 2.31 (1H, ddd, *J* = 14.3, 6.3, 4.6 Hz, -CH₂CH(OH)-), 2.22-2.12 (2H, m, -CH₂CH(OH) & -CH₂CH₂OH), 1.96 (1H, dt, *J* = 14.3, 7.0 Hz, -CH₂CH₂OH), 1.47 (9H, s, -OC(CH₃)₃) ppm; Selected ¹H NMR data for minor diastereoisomer: δ 6.60 (1H, d, *J* = 8.3 Hz, C6_{Ar}H), 5.04 (1H, dd, *J* = 4.0, 5.4

Hz, ArOCHCH₂-), 2.44 (1H, dt, $J = 5.4$ Hz, -CH₂CH(OH)-), 1.89 (1H, ddd, $J = 3.5, 8.0, 13.5$, -CH₂CH₂OH) ppm; ¹³C NMR (for major diastereoisomer **19α**, 100 MHz, CDCl₃) δ 156.34 (C, -C=O), 147.15 (C, C3_{Ar}), 144.91 (C, C4_{Ar}), 130.02 (CH, -CCH=CH-), 129.80 (CH, -CCH=CH-), 126.34 (C, C1_{Ar}), 121.14 (CH, br, C6_{Ar}), 111.82 (CH, C5_{Ar}), 85.15 (CH, ArOCHCH₂-), 80.42 (C, -OC(CH₃)₃), 63.16 (CH, -CH(OH)-), 59.59 (CH₂, -CH₂CH₂OH), 56.23 (CH₃, -OCH₃), 49.88 (C, -CCH=CH-), 49.11 (CH₂, -NCH₂Ar), 39.25 (CH₂, -CH₂CH₂OH), 34.27 (CH₃, -NCH₃), 32.67 (CH₂, ArOCHCH₂-), 28.77 (CH₃, -OC(CH₃)₃) ppm. (C2_{Ar} was not observed); Selected ¹³C NMR data for minor diastereoisomer: δ 111.60 (CH, C5_{Ar}), 84.24 (CH, ArOCHCH₂-), 62.92 (CH, -CH(OH)-), 59.90 (CH₂, -CH₂CH₂OH), 49.68 (C, -CCH=CH-) ppm; LRMS (ES⁺) m/z 428 [M+Na⁺]; HRMS (ES⁺) for C₂₂H₃₁NNaO₆, calculated 428.2044, found 428.2041 Da.

Reaction of diastereoisomeric diols **19 with methanesulfonyl chloride** $C_{23}H_{33}NO_8S$

M.w. = 483.58 g/mol

Colourless oil

NMR spectra exhibited broadening / of peaks due to restricted rotation.

To a solution of the diols **19α/β** (30 mg, 73.90 μ mol, *dr* = 4.8:1) in THF (1.6 mL) at 0 °C was added Et₃N (11 μ L, 78.30 μ mol) and MsCl (6 μ L, 78.30 μ mol) dropwise. The beige cloudy mixture was stirred for 1 h at 0 °C before the addition of Et₃N (21 μ L, 147.8 μ mol) and the reaction was stirred for a further 4.5 h 0 °C. After this time a further addition of MsCl (2 μ L, 26.10 μ mol) was made and the reaction was warmed to rt then stirred for 2 h. After which two further additions of MsCl (2 μ L, 26.10 μ mol) at 2 h and 48 h were made respectively. H₂O (5 mL) was added and the mixture was extracted with EtOAc (4 x 10 mL), the combined organic phase was dried (MgSO₄) and concentrated *in vacuo*. It was found that the crude was a 3:1 mixture of starting material and product. The crude material was dissolved in CH₂Cl₂ (1.6 mL) and treated with Et₃N (31 μ L, 222 μ mol) and MsCl (4 μ L, 51.73 μ mol) and stirred for 16 h at rt before a further addition of MsCl (2 μ L, 25.87 μ mol) was made and the reaction was stirred for 16 h. H₂O (5 mL) was added and the mixture was extracted with EtOAc (4 x 10 mL), the combined organic phase was dried (MgSO₄) and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (2.0 cm x 10 cm) eluting with EtOAc/hexane (7:3) afforded the desired mesylate (12 mg, 24.81 μ mol, 34%), starting material **19** (3 mg, 7.39 μ mol, 10%) and dimesylate (7 mg, 12.46 μ mol, 17%). Data were obtained from the mixture of diastereoisomers (4.8:1): [α]_D = -2.3 (*c* 0.5, CHCl₃, 26 °C); **FTIR** (neat) $\nu_{\max}$ 3421 (br), 2973 (w), 2935 (w), 2838 (w), 1682 (s), 1623 (w), 1581 (w), 1506 (m), 1355 (s), 1173 (s) cm⁻¹; **¹H NMR** (Data for major α diastereoisomer, 400 MHz, CDCl₃) δ 6.77 (1H, d, *J* = 8.4 Hz, C5_{Ar}H), 6.67 (1H, d, *J* = 8.4 Hz, C6_{Ar}H), 6.01 (1H, dd, *J* = 10.3, 3.8 Hz, -CCH=CH-), 5.90 (1H, br d, *J* = 10.3 Hz, -CCH=CH-), 4.84 (1H, dd, *J* = 6.5, 4.0 Hz, ArOCHCH₂-), 4.55 (1H, br d, *J* = 15.3 Hz, -NCH₂Ar), 4.44 (1H, d, *J* = 15.3 Hz, -NCH₂Ar), 4.27-4.14 (3H, m, CH(OH)- & -CH₂CH₂OMs), 3.86 (3H, s, OCH₃), 2.94 (3H, s, -OSO₂CH₃), 2.81 (3H, s, -NCH₃), 2.40 (1H, m, -CH₂CH₂OMs), 2.31-2.18 (2H, m, ArOCHCH₂CH(OH)-), 2.13 (1H, dt, *J* = 14.8, 7.3 Hz, -CH₂CH₂OMs), 1.48 (9H, s, -

OC(CH₃)₃) ppm; ¹³C NMR (Data for major diastereoisomer, 100 MHz, CDCl₃) δ 156.19 (C, -C=O), 147.19 (C, C3_{Ar}), 145.09 (C, C4_{Ar}), 141.09 (C, C2_{Ar}), 131.30 (CH, -CCH=CH-), 128.70 (CH, -CCH=CH-), 126.31 (C, C1_{Ar}), 121.68 (CH, br, C6_{Ar}), 112.68 (CH, C5_{Ar}), 84.68 (CH, ArOCHCH₂-), 80.45 (C, -C(CH₃)₃), 66.68 (CH₂, -CH₂OMs), 63.21 (CH, -CH(OH)-), 56.30 (CH₃, OCH₃), 49.54 (C, -CCH=CH-), 49.29 (CH₂, -NCH₂Ar), 37.75 (CH₃, -OSO₂CH₃), 36.03 (CH₂, -CH₂CH₂OMs), 34.17 (CH₃, -NCH₃), 33.13 (CH₂, ArOCHCH₂-), 28.78 (CH₃, -OC(CH₃)₃) ppm; **LRMS** (ES⁺) *m/z* 506 [M+Na⁺]; **HRMS** (ES⁺) for C₂₃H₃₃NNaO₈S, calculated 506.1819, found 506.1825 Da.

(-)-Galanthamine (1) $C_{17}H_{21}NO_3$

M.w. = 287.35 g/mol

White solid

To a solution of 1° monomesylate derivatives of diols **19α/β** (10 mg, 20.68 μmol) in CH_2Cl_2 (0.2 mL) at 0 °C was added TFA (31 μL, 413.58 μmol) dropwise. The mixture was warmed to rt and stirred for 1.5 h. The reaction was cooled to 0 °C before the addition of $CHCl_3$ (0.3 mL) and $NaHCO_3$ (0.3 mL), then allowed to warm to rt and stirred for 3 h. The reaction was diluted with H_2O (3 mL) and $CHCl_3$ (5 mL) and the organic phase was separated, re-extracting the aqueous phase with $CHCl_3$ (3 x 5 mL). The combined organic phase was dried ($MgSO_4$) and concentrated *in vacuo* giving a waxy solid. Purification by flash column chromatography on silica gel (1.2 cm x 8 cm) eluting with $MeOH/CH_2Cl_2$ (1:19→1:9) afforded (-)-galanthamine (**1**, 92% *e.e.*) as a white solid (4 mg, 13.92 μmol, 67%) and *epi*-galanthamine (**20**) (1 mg, 3.48 μmol, 17%). Spectroscopic and analytical data were consistent with those reported previously (NMR⁵). **Mpt.** 125-127 °C; (Lit: 125-127 °C, 128-129 °C);^{6,7} $[\alpha]_D = -81.3$ (*c* 0.15, $CHCl_3$, 24 °C; 92% *e.e.*) (Lit:⁷ -93.4 *c* 1.0, $CHCl_3$, 25 °C, 99% *e.e.*); **FT-IR** (neat) ν_{max} 3384 (br), 3025 (w), 2916 (m), 1623 (m), 1591 (w), 1507 (s), 1438 (s), 1282 (s) cm^{-1} ; **¹H NMR** (400 MHz, $CDCl_3$) δ 6.67 (1H, d, *J* = 8.0 Hz, C5_{Ar}H), 6.63 (1H, d, *J* = 8.0 Hz, C6_{Ar}H), 6.08 (1H, dd, *J* = 10.3, 1.3 Hz, -CCH=CH-), 6.01 (1H, ddd, *J* = 10.3, 5.0, 1.3 Hz, -CCH=CHCH₂-), 4.62 (1H, s, ArOCHCH₂-), 4.15 (1H, br t, *J* = 5.0 Hz, -CHCH(OH)-), 4.10 (1H, d, *J* = 15.1 Hz, -NCH₂Ar), 3.84 (3H, s, OCH₃), 3.69 (1H, d, *J* = 15.1 Hz, -NCH₂Ar), 3.28 (1H, ddd, *J* = 14.3, 12.8, 1.8 Hz, -CH₂CH₂N-), 3.06 (1H, dt, *J* = 14.3, 3.3 Hz, -CH₂CH₂N-), 2.70 (1H, ddd, *J* = 15.6, 3.5, 1.5 Hz, -CH₂CH(OH)-), 2.41 (3H, s, -NCH₃), 2.10 (1H, td, *J* = 13.6, 3.3 Hz, -CH₂CH₂N-), 2.02 (1H, ddd, *J* = 15.6 Hz, 5.0, 2.5 Hz, CH₂CH(OH)-), 1.65 (1H, br s, -OH), 1.59 (1H, ddd, *J* = 13.6, 4.0, 1.8 Hz, -CH₂CH₂N-) ppm; **¹³C NMR** (100 MHz, $CDCl_3$) δ 146.23 (C, -COCH₃), 144.51 (C, -

⁵ Trost, B. M.; Tang, W. P.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 14785-14803.

⁶ Kobayashi, S.; Yuasa, K.; Sato, K.; Imakura, Y.; Shingu, T. *Heterocycles* **1982**, *19*, 1219-1222.

⁷ Shieh, W.-C.; Carlson, J. A. *J. Org. Chem.* **1994**, *59*, 5463-5465.

COCHCH₂CH(OH)-), 133.44 (C, -NCH₂CCCCH=CH-), 129.69 (C, -NCH₂C-), 128.00 (CH, -CCHC=CHCH(OH)-), 127.24 (CH, -CCH=CHCH(OH)-), 122.42 (CH, -NCH₂CCHCH-), 111.64 (CH, -NCH₂CCHCH-), 89.11 (CH, ArOCHCH₂-), 62.46 (CH, ArOCHCH₂CH(OH)-), 61.01 (CH₂, -NCH₂Ar), 56.30 (CH₃, ArOCH₃), 54.22 (CH₂, -NCH₂CH₂-), 48.60 (C, -C CH=CH-), 42.50 (CH₃, -NC H₃), 34.22 (CH₂, ArOCHCH₂CH(OH)-), 30.33 (CH₂, -NCH₂CH₂-) ppm; **LRMS** (ES⁺) *m/z* 288 (100%) [M+H⁺], 310 (30%) [M+Na⁺].

^1H and ^{13}C NMR for compound **3** *Tert-butyl 3-hydroxy-2-iodo-4-methoxybenzylmethylcarbamate* *Tert-butyl 3-hydroxy-2-iodo-4-methoxybenzylmethylcarbamate*

^1H and ^{13}C NMR for compound **6**

vs4203-97 compound 6

vs4203-97 compound 6

^1H and ^{13}C NMR for compound **7**

vs4203-100 compound 7

vs4203-100 compound 7

^1H and ^{13}C NMR for compound **8**

sck4033/42 nv2904sck2 dpx400

sck4033/42 nv2904sck2 dpx400

^1H and ^{13}C NMR for compound **9**

vs4372-55 compound 9

vs4372-55 compound 9

^1H and ^{13}C NMR for compound **10**

vs4372-61 compound 10

vs4372-61 compound 10

^1H and ^{13}C NMR for compound **11**

vs4372-62B compound 11

vs4372-62B compound 11

^{13}C NMR for *N*-Methoxy-*N*-methylhex-5-enamide*N*-methoxy-*N*-methylhex-5-enamide

^1H & ^{13}C NMR for 1-(trimethylsilyl)oct-7-en-1-yn-3-one *1-(trimethylsilyl)oct-7-en-1-yn-3-one* *1-(trimethylsilyl)oct-7-en-1-yn-3-one*

^1H and ^{13}C NMR for compound **13** *(R)*-1-(trimethylsilyl)oct-7-en-1-yn-3-ol *(R)*-1-(trimethylsilyl)oct-7-en-1-yn-3-ol

^1H and ^{13}C NMR for compound **14**

Tert-butyl-3-((S)-1-(trimethylsilyl)oct-7-en-1-yn-3-yloxy)-2-iodo-4-methoxybenzylmethylcarbamate

Tert-butyl-3-((S)-1-(trimethylsilyl)oct-7-en-1-yn-3-yloxy)-2-iodo-4-methoxybenzylmethylcarbamate

^1H and ^{13}C NMR for compound **15**

Tert-butyl-3-((S)-oct-7-en-1-yn-3-yloxy)-2-iodo-4-methoxybenzylmethylcarbamate

Tert-butyl-3-((S)-oct-7-en-1-yn-3-yloxy)-2-iodo-4-methoxybenzylmethylcarbamate

^1H and ^{13}C NMR for compound **16**

Tert-butyl-3-((S)-2-vinylcyclohex-2-enyloxy)-2-iodo-4-methoxybenzylmethylcarbamate

Tert-butyl-3-((S)-2-vinylcyclohex-2-enyloxy)-2-iodo-4-methoxybenzylmethylcarbamate

^1H and ^{13}C NMR for compound **17**

Tert-butyl-3-((S)-2-(2-hydroxyethyl)cyclohex-2-enyloxy)-2-iodo-4-methoxybenzylmethylcarbamate

Tert-butyl-3-((S)-2-(2-hydroxyethyl)cyclohex-2-enyloxy)-2-iodo-4-methoxybenzylmethylcarbamate

^1H and ^{13}C NMR for compound **18**

1,1-dimethylethyl-N-(((5aS,9aS)-9a-(hydroxyethyl)-4-(methoxy)-5a,6,7,9a-tetrahydrodibenzo[b,d]furan-1-yl)methyl)-N-methylcarbamate

1,1-dimethylethyl-N-(((5aS,9aS)-9a-(hydroxyethyl)-4-(methoxy)-5a,6,7,9a-tetrahydrodibenzo[b,d]furan-1-yl)methyl)-N-methylcarbamate

^1H and ^{13}C NMR for compound **19**

1,1-dimethylethyl-N-(((5aS,7R,9aS)-7-hydroxy-9a-(2-hydroxyethyl)-4-(methoxy)-5a,6,7,9a-tetrahydrodibenzo[b,d]furan-1-yl)methyl)-N-methylcarbamate

1,1-dimethylethyl-N-(((5aS,7R,9aS)-7-hydroxy-9a-(2-hydroxyethyl)-4-(methoxy)-5a,6,7,9a-tetrahydrodibenzo[b,d]furan-1-yl)methyl)-N-methylcarbamate

^1H and ^{13}C NMR for mono-mesylates

2-[(3R4aS,9bS)-9-([(1,1-dimethylethyl)oxy]carbonyl)(methylamino)methyl]-3-hydroxy-6-(methoxy)-3,4,4a,9b-tetrahydrodibenzo[b,d]furan-9-yl]ethyl methanesulfonate

2-[(3R4aS,9bS)-9-([(1,1-dimethylethyl)oxy]carbonyl)(methylamino)methyl]-3-hydroxy-6-(methoxy)-3,4,4a,9b-tetrahydrodibenzo[b,d]furan-9-yl]ethyl methanesulfonate

^1H and ^{13}C NMR for (-)-galanthamine (**1**)

(-)-Galanthamine

^{13}C NMR for (-)-galanthamine (**1**)

(-)-Galanthamine