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Synthesis of Chiral 1,3-Dienes through Ring-Closing Metathesis of Enantioenriched Enynes: Potential Precursors of Morphane Analogs

MARÍA JESÚS GARCIA-MUÑOZ,[1,2,3] ANA SIRVENT,[1,2,3] FRANCISCO FOUBELO[1,2,3] and MIGUEL YUS[1,3]

[1] Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, Apdo. 99, 03080 Alicante, Spain
[2] Instituto de Síntesis Orgánica/ISO,Universidad de Alicante, Apdo. 99, 03080 Alicante, Spain
[3] Centro de Innovación en Química Avanzada (ORFEO-CINQA), Universidad de Alicante, Apdo. 99, 03080 Alicante, Spain

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ABSTRACT

A simple methodology for the synthesis of enynes by indium mediated diastereoselective allylation of aromatic *N-tert*-butanesulfinylimines bearing alkenyl groups at *ortho*-position with allyl bromide has been developed. The addition of the allyl indium intermediate to the chiral imine took place with excellent diastereoselectivity. Ruthenium-catalyzed ring-closing metathesis of the resulting enynes provided the expected cyclic 1,3-dienes in good to moderate yields. These chiral dienes are potential precursors of biologically and pharmacologically active morphane derivatives.

Key words: allylation, imines, dienes, enynes, metathesis, alkaloids.

INTRODUCTION

Ring closing metathesis (Schmalz 1995) is an important tool in organic synthesis because cyclic unsaturated compounds could be accessed from linear hydrocarbons with double or triple bonds at the terminal positions. When the ring closing metathesis is performed on an enyne system, the resulting cyclic 1,3-dienes with one exocyclic double bond are of special interest (Kaliappan 2005). These dienes are versatile synthetic intermediates and could be involved in a wide variety of process, such as cycloaddition reactions, electrophilic additions, etc. The first ring closing metathesis of enynes was performed by Katz and Sivavec in 1985 by means of a tungsten Fischer carbene complex (Katz and Sivavec 1985). More recently, Grubbs developed more efficient catalysts of ruthenium to perform olefin metathesis in different types of solvents (Vougioukalakis and Grubbs 2010). In addition, these catalysts were air-tolerant, avoiding the tedious work under inert atmospheres, and also compatible with a wide range of functional groups (Hoveyda et al. 2004). In 2010, Tan and co-workers studied the ring-closing metathesis of chiral propargyl amines bearing allyl and *tert*-butanesulfinyl groups bonded to the nitrogen atom, using a second generation ruthenium catalyst (Bauer et al. 2010). In this way, vinylpyrrolines were obtained as reaction products

Correspondence to: Francisco Foubelo
E-mail: foubelo@ua.es
Miguel Yus
E-mail: yus@ua.es

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in high yields (Figure 1a). The group of Fustero reported the synthesis of enantiopure cyclic dienes through the ring-closing metathesis of homoallylic benzylic alcohols with an alkenyl group at *ortho*-position of the aromatic ring (Rodriguez et al. 2016), using Grubbs second generation catalyst in the presence of 1,7-octadiene as additive (Figure 1b). More recently, the same group performed the ring-closing metathesis of structural related *N-tert*-butanesulfinyl amino derivatives under similar reaction conditions (Lazaro et al. 2017), producing the expected dienes in high yields (Figure 1c). On the other hand, our research group reported the stereoselective allylation (Foubelo and Yus 2004) and propargylation (Garcia-Muñoz et al. 2013) of *N-tert*-butanesulfinyl aldimines and ketimines (Sirvent et al. 2012) with brominated precursors by means of indium metal, leading to homoallylic and homopropargylic amine derivatives, respectively, with high diastereoselectivity. These compounds were used as precursors in the synthesis of natural products (Foubelo and Yus 2014) and other structurally diverse nitrogen-containing compounds (Garcia-Muñoz et al. 2016). Continuing our interest in this topic, and prompted by the latest results from the group of Fustero, we report herein our approach to the synthesis enantioenriched 1,3-dienes with a *N-tert*-butanesulfinamide group through an enyne ring-closing metathesis.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES

(R_S)-*tert*-Butanesulfinamide was a gift of Medalchemy (> 99% ee by chiral HPLC on a Chiracel AS column, 90:10 *n*-hexane/*i*-PrOH, 1.2 mL/min, l = 222 nm). TLC was performed on silica gel 60 F_{254}, using aluminium plates and visualized with phosphomolybdic acid (PMA) stain. Flash chromatography was carried out on handpacked columns of silica gel 60 (230- 400 mesh). Melting points are uncorrected. Optical rotations were

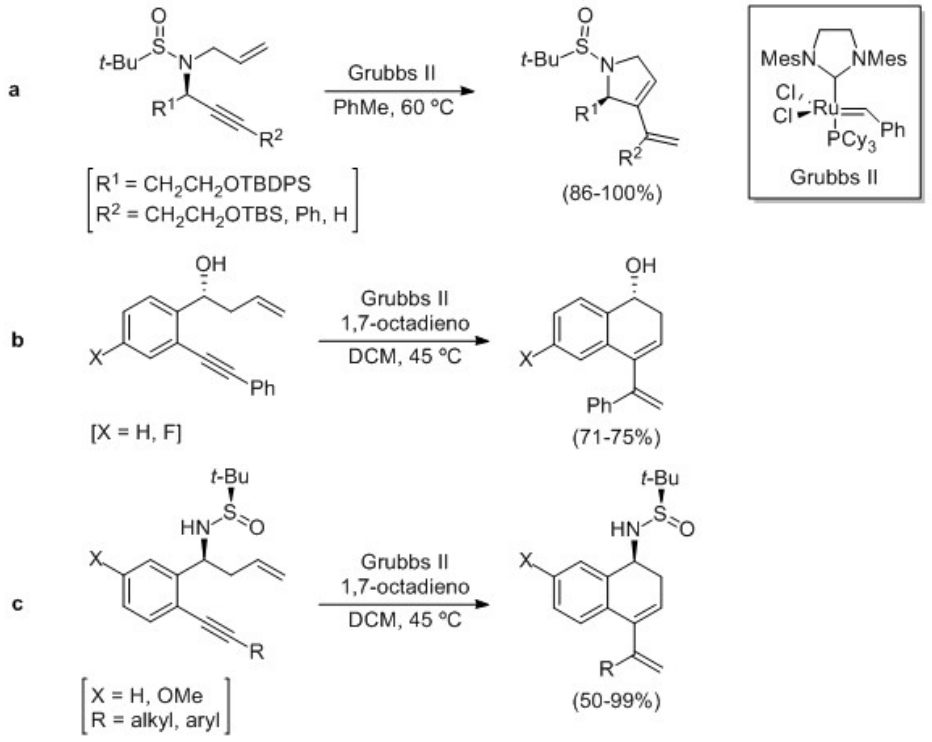


Figure 1 - Examples of ring-closing metathesis in *N-tert*-butasulfinamides bearing enyne moiety**.**

measured using a polarimeter with a thermally jacketed 5 cm cell at approximately 20 ºC and concentrations (*c*) are given in g/100 mL. Infrared analyses were performed with a spectrophotometer equipped with an ATR component; wave numbers are given in cm^{-1}. Low-resolution mass spectra (EI) were obtained at 70 eV, and fragment ions in *m/z* with relative intensities (%) in parentheses. High-resolution mass spectra (HRMS) were also carried out in the electron impact mode (EI) at 70 eV and on an apparatus equipped with a time of flight (TOF) analyzer and the samples were ionized by ESI techniques and introduced through an ultra-high pressure liquid chromatography (UPLC) model. ^{1}H NMR spectra were recorded at 300 or 400 MHz for ^{1}H NMR and 75 or 100 MHz for ^{13}C NMR, using $CDCl_3$ as the solvent and TMS as internal standard (0.00 ppm). The data are being reported as: s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet or unresolved, br s = broad signal, coupling constant(s) in Hz, integration. ^{13}C NMR spectra were recorded with ^{1}H-decoupling at 100 MHz and referenced to $CDCl_3$ at 77.16 ppm. DEPT-135 experiments were performed to assign CH, CH_2 and CH_3.

SYNTHESIS OF 2-VINYLBENZALDEHYDE (**3A**)

To a solution of *o*-bromostyrene (**2a**, 0.915 g, 0.626 mL, 5.0 mmol) in anhydrous THF (15 mL) was added drop wise a 2.5 M solution of *n*-BuLi in hexane (2.2 mL, 5.5 mmol) at -78 ºC. The reaction mixture was stirred at this temperature for 1 h, and after that, dry dimethylformamide (DMF, 0.456 g, 0.483 mL, 6.25 mmol) was also added dropwise. Stirring was continued for 20 min at the same temperature and the reaction was hydrolyzed with a saturated aqueous NH_4Cl solution (6 mL), and extracted with diethyl ether (3×10 mL). The organic layer was washed with brine (2×10 mL), dried over anhydrous magnesium sulfate and evaporated (15 Torr) to yield almost pure 2-vinylbenzaldehyde (**3a**) as a pale yellow oil (0.587 g, 4.45 mmol, 89%): R_F 0.50 (hexane/AcOEt 10:1); IR (film) ν 2917, 2858, 2750, 1691, 1595, 1565, 1479, 1205, 1186, 922, 861, 770, 741 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.28 (1H, s, COH), 7.82 (1H, dt, *J* = 7.5, 1.0 Hz, ArH), 7.59-7.49 (3H, m, ArH), 7.45-7.38 (1H, m, C*H*=CH_2), 5.70 (1H, dd, *J* = 17.4, 1.2 Hz, CH=CH*H*), 5.51 (1H, dd, *J* = 11.0, 1.2 Hz, CH=C*H*H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 192.3 (CH), 140.4 (C), 133.7, 133.3 (CH), 132.8 (C), 131.1, 127.8, 127.4 (CH), 119.3 (CH_2); LRMS (EI) *m/z* 132 (M^+, 31%), 131 (14), 104 (21), 103 (24), 91 (17), 77 (15), 71 (24), 70 (21), 69 (18), 57 (28), 55 (20), 45 (19), 43 (100).

GENERAL PROCEDURE FOR THE PREPARATION OF ALDEHYDES **9**

To a solution of the corresponding *o*-bromobenzaldehyde **3** (7.0 mmol) in freshly distilled Et_3N (28 mL) was successively added the corresponding terminal alkyne **8** (8.4 mmol), CuI (0.0133 g, 0.07 mmol) and $Pd(PPh_3)_4$ (0.161 g, 0.14 mmol). The resulting mixture was stirred at 50 ºC for 5 h and after that, a white solid was filtered off through a short plug of celite, washed with ethyl acetate (3×10 mL) and concentrated (15 Torr). The residue was purified by column chromatography (hexane/ethyl acetate) to yield pure compounds **9**. Yields for these compounds **9** are given on Table I. Physical and spectroscopic data follow.

2-(*Trimethylsilylethynyl*)*benzaldehyde* (**9a**): yellow solid; mp 42–43 ºC (hexane/CH_2Cl_2); R_F 0.58 (hexane/AcOEt 20:1); IR (KBr) ν 2957, 2854, 2761, 2151, 1697, 1592, 1247, 866, 845, 763 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.56 (1H, d, *J* = 0.9 Hz, COH), 7.93-7.89 (1H, m, ArH), 7.60-7.51 (1H, m, ArH), 7.46-7.41 (1H, m, ArH), 0.28 [9H, s, $Si(CH_3)_3$]; ^{13}C-NMR (101 MHz, $CDCl_3$) δ 192.0 (CH), 136.3 (C), 133.8 (CH), 133.6 (CH), 129.0 (C), 127.0 (C), 126.9 (CH), 102.5 (C), 100.2 (C), 0.1 (CH_3); LRMS (EI) *m/z* 202 (M^+, 4%), 201 (18), 188 (18), 187(100), 161 (11), 128 (27).

2-(Oct-1-yn-1-yl)benzaldehyde (**9b**): colourless oil; R_F 0.62 (hexane/AcOEt 10:1); IR (film) ν 2957, 2929, 2856, 1697, 1594, 1192, 823, 761, 726 637 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.54 (1H, d, *J* = 0.8 Hz, COH), 7.88 (1H, dt, *J* = 7.9, 1.0 Hz, ArH), 7.55-7.45 (2H, m, ArH), 7.37 (1H, dddd, *J* = 7.8, 5.8, 2.8, 0.9 Hz, ArH), 2.48 (2H, t, *J* = 7.1 Hz, CH_2), 1.71-1.54 (2H, m, CH_2), 1.52-1.38 (2H, m, CH_2), 1.39-1.26 (4H, m, 2 × CH_2), 0.91 (3H, t, *J* = 7.0 Hz, CH_3); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 192.2 (CH), 135.9 (C), 133.6, 133.2 (CH), 127.9 (C), 127.8, 126.8 (CH), 98.2, 76.3 (C), 31.3, 28.6, 28.5, 22.5, 19.6 (CH_2), 14.0 (CH_3); LRMS (EI) *m/z* 214 (M^+, 8%), 185 (12), 167 (11), 157 (40), 145 (25), 144 (100), 143 (15), 131 (13), 129 (18), 128 (27), 116 (28), 115 (63).

2-(Phenylethynyl)benzaldehyde (**9c**): yellow oil; R_F 0.47 (hexane/AcOEt 10:1); IR (film) ν 3060, 2843, 1695, 1591, 1492, 1264, 1192, 817, 753, 688, 637 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.65 (1H, d, *J* = 0.8 Hz, COH), 7.94 (1H, ddd, *J* = 7.8, 1.4, 0.6 Hz, ArH), 7.65-7.61 (1H, m, ArH), 7.60-7.52 (3H, m, ArH), 7.47-7.41 (1H, m, ArH), 7.40-7.34 (3H, m, ArH); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 191.6 (CH), 135.8 (C), 133.7, 133.2, 131.6, 129.0, 128.5, 128.4, 127.2 (CH), 126.8, 122.3, 96.3, 84.8 (C); LRMS (EI) *m/z* 206 (M^+, 60%), 205 (27), 180 (11), 178 (30), 177 (26), 176 (26), 167 (16), 165 (12), 152 (18), 151 (18), 150 (14), 149 (50), 137 (11), 135 (10), 127 (13), 125 (16), 123 (17), 111 (27), 109 (25), 83 (36), 77 (14), 71 (49), 57 (68), 44 (44), 43 (100).

5-Methoxy-2-(phenylethynyl)benzaldehyde (**9d**): yellow solid; mp 77–79 ºC (hexane/CH_2Cl_2); R_F 0.38 (hexane/AcOEt 10:1); IR (KBr) ν 2848, 1685, 1604, 1594, 1499, 1323, 1226, 1164, 1023, 830, 753, 746, 684, 619 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.61 (1H, s, COH), 7.58-7.50 (3H, m, ArH), 7.42 (1H, d, *J* = 2.8 Hz, ArH), 7.38-7.33 (3H, m, ArH), 7.13 (1H, dd, *J* = 8.6, 2.8 Hz, ArH), 3.87 (3H, s, CH_3); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 191.5 (CH), 159.7, 137.1 (C), 134.5, 131.4, 128.7, 128.4 (CH), 122.6 (C), 121.7 (CH), 119.6 (C), 109.8 (CH), 94.8, 84.8 (C), 55.6 (CH_3); LRMS (EI) *m/z* 236 (M^+, 100%), 222 (13), 221 (67), 193 (27), 165 (63), 164 (17), 163 (19), 149 (24), 139 (11), 70 (15), 43 (65).

2-[(4-Methoxyphenyl)ethynyl]benzaldehyde (**9e**): yellow solid; mp 44–46 ºC (hexane/CH_2Cl_2); R_F 0.32 (hexane/AcOEt 10:1); IR (KBr) ν 2843, 1695, 1603, 1591, 1507, 1248, 1018, 839, 766, 635 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.64 (1H, d, *J* = 0.8 Hz, COH), 7.93 (1H, ddd, *J* = 7.8, 1.5, 0.6 Hz, ArH), 7.61 (1H, ddd, *J* = 7.8, 1.4 0.6 Hz, ArH), 7.56 (1H, td, *J* = 7.5, 1.4 Hz, ArH), 7.50 (2H, d, *J* = 8.9 Hz, ArH), 7.46-7.37 (1H, m, ArH), 6.90 (2H, d, *J* = 8.8 Hz, ArH), 3.83 (3H, s, CH_3); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 191.8 (CH), 160.2, 135.6 (C), 133.7, 133.2, 133.0, 128.2 (CH), 127.3 (C), 127.2 (CH), 114.3 (C), 114.2 (CH), 96.5, 83.7 (C), 55.3 (CH_3); LRMS (EI) *m/z* 236 (M^+, 100%), 221 (61), 193 (19), 165 (57), 164 (15), 163 (17).

SYNTHESIS OF 2-[2-(OCT-1-YL)PHENYL] ACETALDEHYDE (**13**)

A 1 M solution of potassium hexamethyldisilazide (KHMDS, 2.0 mL, 2.0 mmol) was added to a suspension of (methoxymethyl) triphenylphosphonium chloride (0.684 g, 2.0 mmol) in THF (4 mL) at -78 ºC. The reaction mixture was stirred at the same temperature for 1 h. After that, a solution of aldehyde **9b** (0.214 g, 1.0 mmol) in THF (8 mL) and stirring was maintained for 3 h allowing the system to reach 0 ºC. The resulting mixture was filtered through a short plug of celite, washed with hexane (3×15 mL) and concentrated (15 Torr). The residue was dissolved in THF (1.5 mL), treated with a 3 M solution of HCl (0.25 mL, 0.75 mmol) and the resulting solution was stirred at 78 ºC for 18 h. After that, the reaction mixture was cooled down to room temperature, basified with a saturated sodium bicarbonate aqueous solution and extracted with ethyl acetate (3×15 mL). The organic layer was washed with brine (2×10 mL), dried over

anhydrous magnesium sulfate and evaporated (15 Torr) to yield aldehyde **16** which was used in the next step without purification.

GENERAL PROCEDURE FOR THE PREPARATION OF N-TERT-BUTANESULFINYL ALDIMINES **4A** AND **14**

To a solution of (*R*)-*tert*-butanesulfinamide (**1**, 0.601 g, 5.0 mmol) and the corresponding aldehyde (5.5 mmol) in THF (20 mL) was added $Ti(OEt)_4$ (2.28 g, 2.08 mL, 10.0 mmol) at room temperature under argon. The resulting mixture was stirred for 5 h at the same temperature, and after that, quenched with brine (3.0 mL), and diluted with ethyl acetate (50.0 mL). The resulting suspension was filtered through a short plug of Celite and concentrated Then, the reaction mixture was filtered through a short plug of Celite and the solvent was evaporated (15 Torr). The residue was purified by column chromatography (hexane/EtOAc) to yield pure compounds **4a** and **14**. Yields for compounds **4a** and **14** are given in Figures 2 and 4, respectively. Physical and spectroscopic data follow.

(R_S)-N-(tert-*Butanesulfinyl*)-N-(*2-vinylbenzyliden*)*amine* (**4a**): yellow oil; R_F 0.32 (hexane/AcOEt 9:1); = -166.5 (*c* 1.05, CH_2Cl_2); IR (film) ν 3060, 2981, 2962, 2932, 2864, 1602, 1584, 1474, 1363, 1221, 1183, 1082, 983, 920, 769, 715 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.93 (1H, s, CNH), 7.95 (1H, dd, *J* = 7.8, 1.5 Hz, ArH), 7.55 (1H, dd, *J* = 7.7, 1.4 Hz, ArH), 7.48 (1H, td, *J* = 7.6, 1.5 Hz, ArH), 7.43-7.32 (2H, m, ArH, C*H*=CH_2), 5.67 (1H, dd, *J* = 17.3, 1.2 Hz, CH=CH*H*), 5.47 (1H, dd, *J* = 11.0, 1.2 Hz, CH=C*H*H), 1.28 [9H, s, $C(CH_3)_3$]; ^{13}C-NMR 161.3 (CH), 139.7 (C), 133.6, 132.1 (CH), 131.0 (C), 129.1, 127.9, 127.3 (CH), 118.9 (CH_2), 57.7 (C), 22.6 (CH_3); LRMS (EI) *m/z* 235 (M^+, 1%), 179 (21), 149 (16), 132 (12), 131 (18), 130 (51), 116 (30), 115 (10), 77 (11), 70 (19), 61 (16), 57 (52), 45 (17), 43 (100), 41 (16).

(R_S)-N-(tert-*Butanesulfinyl*)-N-{*2*-[*2*-(*1-octynyl*)*phenyl*]*ethyliden*}*amine* (**14**): yellow oil; R_F 0.31 (hexane/AcOEt 9:1); = -186.0 (*c* 1.05, CH_2Cl_2); IR (film) ν 2955, 2928, 2858, 1697, 1619, 1457, 1087, 756 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.14 (1H, t, *J* = 4.9 Hz, CNH), 7.45-7.39 (1H, m, ArH), 7.26-7.15 (3H, m, ArH), 4.00 (2H, t, *J* = 4.8 Hz, CH_2), 2.42 (2H, t, *J* = 7.1 Hz, CH_2), 1.67-1.53 (2H, m, CH_2), 1.51-1.41 (2H, m, CH_2), 1.37-1.27 (4H, m, 2 × CH_2), 1.17 [9H, s, $C(CH_3)$], 0.95-0.84 (3H, m, CH_3); ^{13}C-NMR 167.3 (CH), 136.7 (C), 132.4, 129.4, 127.8, 127.0 (CH), 124.3, 95.4, 78.8, 56.8 (C), 41.3, 31.3, 28.7, 28.6 22.5 (CH_2), 22.4 (CH_3), 19.5 (CH_2), 14.0 (CH_3); LRMS (EI) *m/z* 275 ($M^+C_4H_8$, 5%), 230 (11), 229 (62), 227 (11), 226 (37), 170 (15), 169 (16), 168 (13), 167 (15), 157 (22), 156 (27), 155 (22), 154 (14), 143 (19), 142 (14), 141 (22), 131 (14), 130 (20), 129 (29), 128 (37), 127 (18), 116 (12), 115 (30), 113 (22), 85 (16), 57 (100), 55 (20), 43 (51), 41 (30).

SYNTHESIS OF (1*S*,R_S)-N-(TERT-BUTANESULFINYL)-1-(2-VINYLPHENYL)-4-(TRIMETHYLSILYL)BUT-3-YN-1-AMINE (**6A**)

A mixture of imine **4a** (0.118 g, 0.5 mmol), 3-bromo-1-trimethylsilyl-1-propyne (**5**; 313 mg, 0.275 mL, 1.65 mmol), and indium (189 mg, 1.65 mmol) was sonicated in dry THF (2 mL) for 7 h. Then the resulting mixture was hydrolyzed with H_2O (5 mL) and extracted with ethyl acetate (3×15 mL). The organic phase was washed with brine (3×10 mL), dried with anhydrous magnesium sulfate, and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield pure compound **6a** as a pale yellow oil (0.082 g, 0.35 mmol, 70%): R_F 0.50 (hexane/AcOEt 2:1); = -78.3 (*c* 2.24, CH_2Cl_2); IR (film) ν 3193, 2958, 2897, 2868, 2174, 1474, 1411, 1363, 1249, 1053, 840, 759 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.48-7.43 (1H, m, ArH), 7.42-7.37 (1H, m, ArH), 7.31-7.25 (2H, m, ArH), 7.13 (1H, dd, *J* = 17.2, 10.9 Hz, C*H*=CH_2), 5.61 (1H, dd, *J* = 17.2, 1.5 Hz, CH=CH*H*), 5.36 (1H, dd, *J* = 10.9, 1.5 Hz, CH=C*H*H), 4.89 (1H, ddd, *J* = 8.2, 5.1, 3.0 Hz, CH), 4.23 (1H, d, *J* = 3.0 Hz, NH), 2.73 (1H,

dd, *J* = 16.9, 5.1 Hz, CH*H*), 2.63 (1H, dd, *J* = 16.9, 8.4 Hz, C*H*H), 1.24 [9H, s, $C(CH_3)_3$], 0.16 [9H, s, $Si(CH_3)_3$]; ^{13}C-NMR (75 MHz, $CDCl_3$) δ 137.3, 137.2 (C), 134.1, 128.0, 127.7, 127.2, 126.8 (CH), 117.5 (CH_2), 102.1, 86.2, 55.8 (C), 52.4 (CH), 29.2 (CH_2), 22.6, -0.08 (CH_3); LRMS (EI) *m/z* 243 ($M^+C_4H_8OS$, 4%), 228 (11), 207 (13), 180 (25), 179 (19), 167 (16), 165 (12), 164 (100), 132 (37), 131 (25), 130 (66), 128 (15), 117 (23), 116 (39), 115 (26), 77 (15), 73(76).

GENERAL PROCEDURE FOR THE AMINOALLYLATION OF ALDEHYDES **9**: SYNTHESIS OF ENYNES **11**

A mixture of indium powder (173 mg, 1.50 mmol), (R_S)-*N*-*tert*-butanesulfinamide (**1**, 0.121 g, 1.0 mmol), the corresponding aldehyde **9** (1.15 mmol), and $Ti(OEt)_4$ (0.456 g, 0.450 mL, 2.0 mmol) in THF (2 mL) was stirred under argon for 1 h at 23 ºC. At this time, allyl bromide (**10**, 0.254 g, 0.18 mL, 1.50 mmol) was added and the reaction mixture heated for 5 h at 60 ºC. The mixture was allowed to cool to room temperature, quenched with brine (2 mL), and diluted with ethyl acetate. The resulting suspension was filtered through a short plug of Celite and the solvent evaporated (15 Torr). The residue was purified by column chromatography (hexane/EtOAc) to yield pure compounds **11**. Yields are given on Table I. Physical and spectroscopic data follow.

(*1*S,R_S)-N-(tert-*Butanesulfinyl*)-*1*-[*2*-(*trimethylsilylethynyl*)*phenyl*]*but-3-en-1-amine* (**11a**): colourless oil; R_F 0.38 (hexane/AcOEt 2:1); = -68.0 (*c* 1.10, CH_2Cl_2); IR (film) ν 3075, 2958, 2154, 1475, 1447, 1249, 1053, 862, 840, 758, 644 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.46 (1H, ddd, *J* = 7.5, 1.4, 0.6 Hz, ArH), 7.38-7.26 (2H, m, ArH), 7.20 (1H, ddd, *J* = 7.6, 6.9, 2.0 Hz, ArH), 5.87-5.60 (1H, m, C*H*=CH_2), 5.23-5.11 (2H, m, CH=CH_2), 5.02-4.90 (1H, m, CH), 3.80 (1H, d, *J* = 3.9 Hz, NH), 2.84-2.69 (1H, m, CH*H*), 2.63-2.46 (1H, m, C*H*H), 1.21 [9H, s, $C(CH_3)_3$], 0.27 [9H, s, $Si(CH_3)_3$]; ^{13}C-NMR (75 MHz, $CDCl_3$) δ 144.2 (C), 134.3, 133.0, 128.5, 127.0, 126.8 (CH), 121.8 (C), 119.0 (CH_2), 102.8, 100.2 (C), 55.9 (CH), 41.7 (CH_2), 22.6 (CH_3), -0.08 (CH_3); LRMS (EI) *m/z* 291 (M^+–C_4H_8, 1%), 235 (17), 234 (100), 231 (17), 230 (24), 218 (54), 202 (25), 200 (21), 186 (32), 160 (20), 156 (97), 143 (23), 75 (21), 73 (75), 59 (16).

(*1*S,R_S)-N-(tert-*Butanesulfinyl*)-*1*-[*2*-(*oct-1-yn-1-yl*)*phenyl*]*but-3-en-1-amine* (**11b**): colourless oil; R_F 0.43 (hexane/AcOEt 2:1); = -59.3 (*c* 1.12, CH_2Cl_2); IR (film) ν 3065, 2955, 2929, 2858, 1638, 1448, 1362, 1055, 910, 757 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40 (1H, dd, *J* = 7.6, 1.5 Hz, ArH), 7.31 (1H, dd, *J* = 7.7, 1.7 Hz, ArH), 7.23 (1H, dd, *J* = 7.6, 1.6 Hz, ArH), 7.18 (1H, td, *J* = 7.3, 1.7 Hz, ArH), 5.83-5.64 (1H, m, C*H*=CH_2), 5.23-5.10 (2H, m, CH=CH_2), 5.04-4.94 (1H, m, CH), 3.77 (1H, d, *J* = 3.9 Hz, NH), 2.82-2.66 (1H, m, CH*H*), 2.61-2.47 (1H, m, C*H*H), 2.45 (2H, t, *J* = 7.1 Hz, CH_2), 1.68-1.57 (3H, m, CH_2, CH*H*), 1.51-1.42 (1H, m, C*H*H), 1.38-1.28 (4H, m, 2 × CH_2), 1.20 (9H, s, $C(CH_3)_3$), 0.96-0.85 (3H, m, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 143.4 (C), 134.3, 132.6, 127.5, 126.9, 126.6 (CH), 122.8 (C), 118.9 (CH_2), 96.1, 55.8 (C), 55.6 (CH), 42.0, 31.3, 28.7, 28.6 (CH_2), 22.6 (CH_3), 22.5, 19.6 (CH_2), 14.1 (CH_3); LRMS (EI) *m/z* 287 (M^+–C_5H_{12}, 3%), 262 (23), 246 (26), 243 (18), 242 (100), 227 (20), 226 (99), 214 (29), 213 (22), 212 (21), 183 (30), 172 (20), 170 (29), 168 (25), 157 (20), 156 (84), 155 (22), 154 (20), 144 (14), 143 (48), 142 (36), 141 (22), 130 (36), 129 (24), 128 (24).

(*1*S,R_S)-N-(tert-*Butanesulfinyl*)-*1*-[*2*-(*phenylethynyl*)*phenyl*]*but-3-en-1-amine* (**11c**): colourless oil; R_F 0.25 (hexane/AcOEt 2:1); = -42.9 (*c* 1.61, CH_2Cl_2); IR (film) ν 3214, 3061, 2960, 2922, 2867, 1638, 1492, 1473, 1261, 1053, 912, 755, 689 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.57-7.51 (3H, m, ArH), 7.41-7.27 (6H, m, ArH), 5.84-5.70 (1H, m, C*H*=CH_2), 5.23-5.13 (2H, m, CH=CH_2), 5.12-5.04 (1H, m, CH), 3.80 (1H, d, *J* =

3.7 Hz, NH), 2.81 (1H, dt, *J* = 14.1, 5.9 Hz, CH*H*), 2.62 (1H, dt, *J* = 14.8, 7.9 Hz, C*H*H), 1.21 [9H, s, $C(CH_3)_3$]; ^{13}C-NMR (75 MHz, $CDCl_3$) δ 143.6 (C), 134.2, 132.6, 131.5, 128.5, 128.4, 128.3, 127.1, 126.9 (CH), 123.0, 122.1 (C), 119.1 (CH_2), 94.7, 87.1, 55.8 (C), 55.7 (CH), 42.0 (CH_2), 22.6 (CH_3); LRMS (EI) *m/z* 247 (M^+–C_4H_8SO, 6%), 237 (15), 236 (17), 235 (24), 234 (100), 219 (18), 218 (22), 207 (23), 205 (57), 204 (69), 203 (19), 202 (23), 176 (18).

(*1*S,R$_S$)-N-(tert-*Butanesulfinyl*)-*1*-[*5-methoxy-2-*(*phenylethynyl*)*phenyl*]*but-3-en-1-amine* (**11d**): colourless oil; R_F 0.23 (hexane/AcOEt 2:1); = -41.8 (*c* 2.08, CH_2Cl_2); IR (film) ν 3075, 2951, 2834, 1732, 1606, 1595, 1498, 1292, 1233, 1032, 914, 821, 755, 690 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.54-7.45 (3H, m, ArH), 7.37-7.30 (3H, m, ArH), 6.95 (1H, d, *J* = 2.7 Hz, ArH), 6.79 (1H, dd, *J* = 8.5, 2.6 Hz, ArH), 5.90-5.68 (1H, m, C*H*=CH_2), 5.25-5.13 (2H, m, CH=C*H*$_2$), 5.08-4.99 (1H, m, CH), 3.82 (3H, s, CH_3), 2.81 (1H, dt, *J* = 14.5, 6.0 Hz, CH*H*), 2.59 (1H, dt, *J* = 14.8, 8.0 Hz, C*H*H), 1.22 [9H, s, $C(CH_3)_3$]; ^{13}C-NMR (75 MHz, $CDCl_3$) δ 159.7, 145.5 (C), 134.2, 134.0, 131.3, 128.3, 128.1 (CH), 123.3 (C), 119.1 (CH_2), 114.1 (C), 112.8, 112.6 (CH), 93.4, 87.1 (C), 55.9 (C), 55.7 (CH), 55.3 (CH_3), 42.0 (CH_2), 22.6 (CH_3); LRMS (EI) *m/z* 277 (M^+–C_4H_8OS, 10%), 237 (25), 236 (100), 235 (18), 215 (12), 192 (13), 191 (13), 57 (20).

(*1*S,R$_S$)-N-(tert-*Butanesulfinyl*)-*1*-{*2*-[(*4-methoxyphenyl*)*ethynyl*]*phenyl*}*but-3-en-1-amine* (**11e**): colourless oil; R_F 0.19 (hexane/AcOEt 2:1); = -22.2 (*c* 1.38, CH_2Cl_2); IR (film) ν 3213, 3065, 2976, 2957, 2908, 2209, 1605, 1509, 1459, 1286, 1248, 1174, 1054, 1030, 913, 831, 758 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.53-7.45 (3H, m, ArH), 7.37 (1H, dd, *J* = 7.7, 1.5 Hz, ArH), 7.30 (1H, td, *J* = 7.5, 1.5 Hz, ArH), 7.26-7.21 (1H, m, ArH), 6.91-6.85 (2H, m, ArH), 5.87-5.69 (1H, m, C*H*=CH_2), 5.24-5.13 (2H, m, CH=C*H*$_2$), 5.11-5.02 (1H, m, CH), 3.83 (4H, s, CH_3, NH), 2.84-2.76 (1H, m, CH*H*), 2.62 (1H, dt, *J* = 14.8, 7.9 Hz, C*H*H), 1.20 [9H, s, $C(CH_3)_3$]; ^{13}C-NMR (101 MHz, $CDCl_3$) δ 159.7, 143.3 (C), 134.3, 133.0, 132.4, 128.0, 127.1, 126.8 (CH), 122.4 (C), 119.0 (CH_2), 115.1 (C), 114.0 (CH), 94.8, 85.8, (C), 55.8 (CH), 55.3 (CH_3), 42.0 (CH_2), 22.7 (CH_3); LRMS (EI) *m/z* 277 (M^+–C_4H_8OS, 24%), 276 (84), 246 (13), 237 (17), 236 (100), 235 (34), 215 (14), 57 (18).

ALLYLATION OF IMINE **14**: SYNTHESIS OF HOMOALLYL AMINE DERIVATIVE **15**

A mixture of imine **14** (0.166 g, 0.5 mmol), allyl bromide (**10**; 0.127 g, 0.090 mL, 0.75 mmol) and indium (0.063 g, 0.55 mmol) was stirred in THF (2 mL) for 6 h at 60 ºC. Then the resulting mixture was hydrolyzed with H_2O (5 mL) and extracted with ethyl acetate (3×15 mL). The organic phase was washed with brine (3×10 mL), dried with anhydrous magnesium sulfate, and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield pure compound **15** as a colourless oil (0.093 g, 0.25 mmol, 50%): R_F 0.41 (hexane/AcOEt 2:1); = -12.3 (*c* 1.10, CH_2Cl_2); IR (film) ν 2954, 2928, 2858, 1638, 1448, 1363, 1051, 914, 756 cm^{-1}; ^{1}H-RMN (400 MHz, $CDCl_3$) δ 7.47-7.31 (1H, m, ArH), 7.23-7.09 (3H, m, ArH), 5.69-5.75 (1H, m, C*H*=CH_2), 5.24-5.16 (2H, m, CH=C*H*$_2$), 3.77-3.62 (1H, m, CH), 3.37 (1H, d, *J* = 7.2 Hz, NH), 2.98 (1H, dd, *J* = 13.5, 8.4 Hz, CH*H*), 2.92 (1H, dd, *J* = 13.5, 6.3 Hz, C*H*H), 2.48-2.39 (4H, m, 2 × CH_2), 1.68-1.58 (4H, m, 2 × CH_2), 1.52-1.42 (4H, m, 2 × CH_2), 1.04 [9H, s, $C(CH_3)_3$], 0.95-0.87 (3H, m, CH_3); ^{13}C-RMN (101 MHz, $CDCl_3$) δ 140.4 (C), 134.1, 132.2, 129.9, 127.5, 126.2 (CH), 124.2 (C), 119.3 (CH_2), 94.6, 79.4 (C), 56.8 (CH), 55.8 (C), 40.8, 40.2, 31.4, 28.8, 28.7, 22.6 (CH_2), 22.4 (CH_3), 19.6 (CH_2), 14.1 (CH_3); LRMS (EI) *m/z* 317 (M^+–C_4H_8, 3%), 275 (23), 242 (27), 226 (23), 207 (33), 186 (13), 157 (12), 156 (12), 141 (21), 131 (14), 129 (20), 128 (34), 118 (100), 115 (18), 102 (34).

GENERAL PROCEDURE FOR THE DESILYLATION OF COMPOUNDS **6A** AND **11A**: SYNTHESIS OF TERMINAL ALKYNES **6B** AND **11F**

A suspension of potassium carbonate (0.005 g, 0.036 mmol) in methanol (4 mL) was added dropwise to a solution of compounds **6a** or **11a** (0.5 mmol) in THF (4 mL). The reaction mixture was stirred for 12 h at room temperature and then it was hydrolyzed with a 1 M NH_4Cl aqueous solution (8 mL) and extracted with methyl *tert*-butyl ether (3×15 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc, 2:1) to yield pure compounds **6b** or **11f** in 69 and >95% yield, respectively. Physical and spectroscopic data follow.

(*1*S,R_S)-N-(tert-*Butanesulfinyl*)-*1*-(*2-vinylphenyl*)*but-3-yn-1-amine* (**6b**): yellow oil; R_F 0.26 (hexane/AcOEt 2:1); = -80.9 (*c* 1.20, CH_2Cl_2); IR (film) ν 3296, 3218, 2981, 2962, 2922, 2864, 1624, 1474, 1452, 1364, 1053, 916, 762, 637 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.48-7.44 (1H, m, ArH), 7.42-7.39 (1H, m, ArH), 7.32-7.27 (2H, m, ArH), 7.12 (1H, dd, *J* = 17.2, 10.9 Hz, C*H*=CH_2), 5.62 (1H, dd, *J* = 17.2, 1.4 Hz, CH=CH*H*), 5.37 (1H, dd, *J* = 11.0, 1.4 Hz, CH=C*H*H), 4.92 (1H, ddd, *J* = 8.4, 5.1, 3.6 Hz, CH), 4.06 (1H, d, *J* = 3.6 Hz, NH), 2.74 (1H, ddd, *J* = 16.9, 5.2, 2.6 Hz, CH*H*), 2.65 (1H, ddd, *J* = 16.9, 8.1, 2.6 Hz, C*H*H), 2.12 (1H, t, *J* = 2.6 Hz, CH), 1.24 [9H, s, $C(CH_3)_3$]; ^{13}C-NMR (75 MHz, $CDCl_3$) δ 137.3, 137.1 (C), 134.0, 128.1, 127.8, 126.9, 126.8 (CH), 117.6 (CH_2), 79.9 (C), 72.2 (CH), 55.9 (C), 52.8 (CH), 27.7 (CH_2), 22.6 (CH_3); LRMS (EI) *m/z* 171 (M^+–C_4H_8OS, 2%), 131 (12), 130 (100), 128 (11), 116 (19), 115 (19), 77 (10).

(*1*S,R_S)-N-(tert-*Butanesulfinyl*)-*1*-(*2-ethynylphenyl*)*but-3-en-1-amine* (**11f**): colourless oil; R_F 0.22 (hexane/AcOEt 2:1); = -94.2 (*c* 1.45, CH_2Cl_2); IR (film) ν 3292, 3203, 2976, 2957, 2868, 1638, 1474, 1446, 1363, 1054, 914, 759 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50 (1H, dd, *J* = 7.4, 1.1 Hz, ArH), 7.39-7.30 (2H, m, ArH), 7.23 (1H, ddd, *J* = 7.6, 6.9, 1.9 Hz, ArH), 5.82-5.68 (1H, m, C*H*=CH_2), 5.22-5.14 (2H, m, CH=CH_2), 5.03 (1H, ddd, *J* = 8.5, 5.4, 3.4 Hz, CH), 3.77 (1H, d, *J* = 3.5 Hz, NH), 3.35 (1H, s, CH), 2.78-2.67 (1H, m, CH*H*), 2.60-2.46 (1H, m, C*H*H), 1.20 [9H, s, $C(CH_3)_3$]; ^{13}C-NMR (101 MHz, $CDCl_3$) δ (101 MHz, $CDCl_3$) δ 144.4 (C), 134.1, 133.2, 128.8, 127.1, 126.8 (CH), 121.0 (C), 119.2 (CH_2), 82.6 (C), 81.3 (CH), 55.8 (C), 55.2 (CH), 42.1 (CH_2), 22.6 (CH_3); LRMS (EI) *m/z* 219 (M^+–C_4H_8, 3%), 178 (93), 177 (28), 171 (13), 170 (14), 161 (39), 160 (26), 159 (27), 158 (60), 130 (60), 129 (100), 128 (48), 115 (27), 103 (20), 102 (30), 101 (15), 77 (23).

GENERAL PROCEDURE FOR THE RING-CLOSING METATHESIS OF ENYNES **11** AND **15**: SYNTHESIS OF DIENES **12** AND **16**

A mixture of the corresponding enyne **11** or **15** (0.1 mmol), ruthenium Grubbs second generation catalyst (0.0085 g, 0.01 mmol) in dry toluene (10 mL) was stirred at 120 ºC under argon for 1 h. Then the solvent was evaporated (15 Torr) and the resulting residue was purified by column chromatography (silica gel, hexane/AcOEt) to yield pure compounds **12** and **16**. Yields are given on Table II. Physical and spectroscopic data follow.

(*1*S,R_S)-N-(tert-*Butanesulfinyl*)-*4*-(*oct-1-en-2-yl*)-*1,2-dihydronaphthalen-1-amine* (**12b**): colourless oil; R_F 0.53 (hexane/AcOEt 1:1); = -10.3 (*c* 1.12, CH_2Cl_2); IR (film) ν 3208, 2954, 2926, 2856, 1451, 1362, 1052, 898, 772, 747 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40-7.36 (1H, m, ArH), 7.31-7.19 (3H, m, ArH), 5.86 (1H, t, *J* = 4.5 Hz, C=C*H*), 5.09 (1H, dt, *J* = 2.5, 1.3 Hz, C=CH*H*), 5.00 (1H, d, *J* = 2.4 Hz, C=C*H*H), 4.50-4.40 (1H, m, CH), 3.45 (1H, d, *J* = 8.8 Hz, NH), 2.74 (1H, ddd, *J* = 17.0, 5.7, 4.2 Hz, CH*H*), 2.58 (1H, ddd, *J* = 17.0, 7.1, 4.9 Hz, C*H*H), 2.23 (2H,

t, J = 7.3 Hz, CH_2), 1.40-1.21 (8H, m, 4 × CH_2), 1.19 [9H, s, $C(CH_3)_3$], 0.90-0.82 (3H, m, CH_3); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 148.7, 140.8, 136.3, 133.3 (C), 127.9, 127.3, 126.6, 125.7, 122.0 (CH), 114.1 (CH_2), 56.0 (C), 54.7 (CH), 35.8, 32.4, 31.7, 28.9, 28.3 (CH_2), 22.6, 14.0 (CH_3); LRMS (EI) *m/z* 303 (M^+–C_4H_8, 4%), 240 (25), 239 (100), 238 (38), 169 (14), 168 (19), 167 (27), 155 (36), 154 (13), 153 (20), 152 (11), 142 (10), 141 (67), 129 (13), 57 (31), 43 (11), 41 (13).

(*1*S,R$_S$)-N-(tert-*Butanesulfinyl*)-*4*-(*1*-*phenylvinyl*)-*1,2-dihydronaphthalen-1-amine* (**12c**): colourless oil; R_F 0.33 (hexane/AcOEt 1:1); = -12.5 (*c* 1.34, CH_2Cl_2); IR (film) ν 3198, 2962, 2922, 2864, 1474, 1447, 1262, 1047, 900, 770, 696 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42-7.37 (3H, m, ArH), 7.25-7.22 (3H, m, ArH), 7.17 (1H, td, *J* = 7.4, 1.4 Hz, ArH), 7.10 (1H, td, *J* = 7.5, 1.5 Hz, ArH), 7.00 (1H, dd, *J* = 7.7, 1.4 Hz, ArH), 6.09 (1H, t, *J* = 4.5 Hz, C=CH), 5.67 (1H, d, *J* = 1.6 Hz, C=CH*H*), 5.35 (1H, d, *J* = 1.6 Hz, C=*H*H), 4.58 (1H, q, *J* = 7.1 Hz, CH), 3.49 (1H, d, *J* = 8.1 Hz, NH), 2.89 (1H, ddd, *J* = 17.1, 5.7, 4.1 Hz, CH*H*), 2.67 (1H, ddd, *J* = 17.2, 7.1, 4.8 Hz, C*H*H), 1.23 [9H, s, $C(CH_3)_3$]; ^{13}C-NMR (101 MHz, $CDCl_3$) δ 147.9, 139.7, 139.6, 135.6, 133.4 (C), 128.3, 128.0, 127.7, 127.3, 126.7, 126.6, 126.3, 125.1 (CH), 115.4 (CH_2), 56.1 (C), 54.3 (CH), 32.6 (CH_2), 22.6 (CH_3); LRMS (EI) *m/z* 295 (M^+–C_4H_8, 3%), 232 (25), 231 (92), 230 (65), 229 (29), 228 (10), 215 (15), 153 (39), 152 (13), 104 (10), 103 (100), 77 (13), 71 (17), 69 (14), 57 (45), 55 (15), 43 (27), 41 (18).

(*1*S,R$_S$)-N-(tert-*Butanesulfinyl*)-*7-methoxy-4*-(*1-phenylvinyl*)-*1,2-dihydronaphthalen-1-amine* (**12d**): colourless oil; R_F 0.38 (hexane/AcOEt 1:1); = -13.5 (*c* 1.34, CH_2Cl_2); IR (film) ν 3198, 3030, 2951, 2922, 2863, 2834, 1607, 1569, 1492, 1261, 1250, 1039, 897, 735, 696 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42-7.37 (2H, m, ArH), 7.25-7.20 (3H, m, ArH), 6.97 (1H, dd, *J* = 2.7, 0.8 Hz, ArH), 6.91 (1H, d, *J* = 8.5 Hz, ArH), 6.61 (1H, dd, *J* = 8.5, 2.7 Hz, ArH), 5.97 (1H, t, *J* = 4.5 Hz, C=CH), 5.64 (1H, d, *J* = 1.7 Hz, C=CH*H*), 5.34 (1H, d, *J* = 1.7 Hz, C=C*H*H), 4.54 (1H, td, *J* = 8.2, 5.7 Hz, CH), 3.76 (3H, s, CH_3), 3.48 (1H, d, *J* = 8.5 Hz, NH), 2.87 (1H, ddd, *J* = 16.9, 5.8, 4.5 Hz, CH*H*), 2.62 (1H, ddd, *J* = 16.9, 8.0, 4.6 Hz, C*H*H), 1.25 [9H, s, $C(CH_3)_3$]; ^{13}C-NMR (101 MHz, $CDCl_3$) δ 158.7, 148.0, 139.8, 139.2, 137.7 (C), 128.3, 127.7, 126.6 (CH), 126.5 (C), 122.7 (CH), 115.2 (CH_2), 112.7, 112.3 (CH), 56.1 (C), 55.2 (CH), 54.9 (CH_3), 32.7 (CH_2), 22.7 (CH_3); LRMS (EI) *m/z* 277 (M^+–C_4H_8OS, 4%), 262 (45), 261 (87), 260 (100), 229 (15), 215 (12), 202 (14), 183 (27), 103 (88), 97 (18), 85 (18), 83 (16), 77 (12), 71 (24), 70 (19), 69 (19), 57 (54), 55 (22), 43 (78).

(*1*S,R$_S$)-N-(tert-*Butanesulfinyl*)-*4*-[*1*-(*4-methoxyphenyl*)*vinyl*]-*1,2-dihydronaphthalen-1-amine* (**12e**): colourless oil; R_F 0.30 (hexane/AcOEt 1:1); = -13.1 (*c* 1.53, CH_2Cl_2); IR (film) ν 3213, 2957, 2927, 2859, 1604, 1509, 1458, 1247, 1176, 1031, 897, 835, 755, 737 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40-7.37 (1H, m, ArH), 7.33 (2H, d, *J* = 8.9 Hz, ArH), 7.17 (1H, td, *J* = 7.4, 1.5 Hz, ArH), 7.11 (1H, td, *J* = 7.5, 1.5 Hz, ArH), 7.00 (1H, dd, *J* = 7.7, 1.4 Hz, ArH), 6.77 (2H, d, *J* = 8.8 Hz, ArH), 6.08 (1H, t, *J* = 4.5 Hz, C=CH), 5.57 (1H, d, *J* = 1.7 Hz, C=CH*H*), 5.24 (1H, d, *J* = 1.7 Hz, C=C*H*H), 4.58 (1H, q, *J* = 7.2 Hz, CH), 3.77 (3H, s, CH_3), 3.48 (1H, d, *J* = 8.1 Hz, NH), 2.88 (1H, ddd, *J* = 17.2, 5.8, 4.2 Hz, CH*H*), 2.66 (1H, ddd, *J* = 17.1, 7.3, 4.8 Hz, C*H*H), 1.23 [9H, s, $C(CH_3)_3$]; ^{13}C-NMR (101 MHz, $CDCl_3$) δ 159.3, 147.2, 139.8, 135.6, 133.5, 132.2 (C), 127.9, 127.8, 126.6, 126.3, 124.8, 113.6 (CH), 113.5 (CH_2), 56.0 (C), 55.2 (CH), 54.4(CH_3), 32.6 (CH_2), 22.6 (CH_3); LRMS (EI) *m/z* 277 (M^+–C_4H_8OS, 8%), 263 (15), 261 (56), 260 (47), 259 (26), 153 (16), 135 (14), 133 (100), 70 (13), 57 (35), 43 (57).

(*1*S,R$_S$)-N-(tert-*Butanesulfinyl*)-*4-vinyl-1,2-dihydronaphthalen-1-amine* (**12f**): colourless oil; R_F 0.33 (hexane/AcOEt 1:1); = -6.9 (*c* 1.57, CH_2Cl_2); IR (film) ν 3208, 2955, 2864, 1736, 1474,

1450, 1362, 1241, 1046, 911, 747 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.45-7.36 (2H, m, ArH), 7.37-7.19 (2H, m, ArH), 6.62 (1H, dd, *J* = 17.3, 10.9 Hz, C*H*=CH_2), 6.12 (1H, t, *J* = 4.8 Hz, C=CH), 5.55 (1H, dd, *J* = 17.3, 1.8 Hz, CH=CH*H*), 5.24 (1H, dd, *J* = 10.9, 1.7 Hz, CH=C*H*H), 4.45 (1H, dt, *J* = 8.9, 6.4 Hz, CH), 3.43 (1H, d, *J* = 9.1 Hz, NH), 2.77 (1H, dt, *J* = 17.2, 5.2 Hz, CH*H*), 2.63 (1H, dt, *J* = 17.2, 6.2 Hz, C*H*H), 1.19 [9H, s, $C(CH_3)_3$]; ^{13}C-NMR (75 MHz, $CDCl_3$) δ 136.5, 136.1 (C), 134.7 (CH), 133.2 (C), 127.9, 127.5, 126.8, 124.4, 122.6 (CH), 116.1 (CH_2), 56.1 (C), 54.7 (CH), 32.5 (CH_2), 22.6 (CH_3); LRMS (EI) *m/z* 171 (M^+–C_4H_8OS, 1%), 168 (30), 155 (22), 154 (100), 153 (71), 152 (29), 141 (11), 115 (14).

(*6*S,R_S)-N-(tert-*Butanesulfinyl*)-*9*-(*oct-1-en-2-yl*)-*6,7-dihydro-5*H*benzo*[*7*]*anulen-7-amine* (**16**): colourless oil; R_F 0.54 (hexane/AcOEt 1:1); = -9.5 (*c* 1.76, CH_2Cl_2); IR (film) ν 3208, 2954, 2926, 2858, 1449, 1362, 1055, 900, 752, 730 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28-7.21 (1H, m, ArH), 7.20-7.17 (3H, m, ArH), 6.16 (1H, t, *J* = 7.3 Hz, C=CH), 5.04-4.98 (1H, m, C=CH*H*), 4.92 (1H, d, *J* = 2.2 Hz, C=C*H*H), 4.15-4.05 (1H, m, CH), 3.16 (1H, d, *J* = 6.7 Hz, NH), 2.89 (1H, dd, *J* = 13.2, 6.2 Hz, CH*H*), 2.60 (1H, dd, *J* = 13.2, 5.3 Hz, C*H*H), 2.29-2.19 (3H, m, CH_2, CH*H*), 1.95-1.85 (1H, m, C*H*H), 1.43-1.34 (2H, m, CH_2), 1.32-1.24 (6H, m, 3 × CH_2), 1.23 [9H, s, $C(CH_3)_3$], 0.92-0.81 (3H, m, CH_3); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 148.9, 145.0, 139.1, 137.5 (C), 129.2, 129.1, 127.0, 126.2, 123.1 (CH), 114.6 (CH_2), 63.4 (CH), 55.6 (C), 39.9, 34.5, 34.1, 31.7, 28.9, 28.1 (CH_2), 22.6 (CH_3), 22.6 (CH_2), 14.1 (CH_3); LRMS (EI) *m/z* 269 (M^+–C_4H_8OS, 2%), 267 (16), 252 (29), 251 (38), 182 (32), 181 (49), 179 (13), 168 (26), 167 (100), 166 (18), 165 (33), 156 (16), 155 (26), 154 (16), 153 (28), 152 (19), 141 (36), 128 (24), 115 (21).

RESULTS AND DISCUSSION

Homopropargylamine derivatives **6a** and **6b** were prepared first starting from *ortho*-bromostyrene **2a**. The reaction of **2a** with *n*-BuLi in THF (an aromatic organolithium compound is formed through a bromine-lithium exchange), followed by reaction with *N,N*-dimethylformamide (DMF) and final hydrolysis with water gave *ortho*-vinylbenzaldehyde (**3a**) in 89% yield. Condensation of aldehyde **3a** with (*R*)-*N*-*tert*-butanesulfinamide (**1**) in the presence of $Ti(OEt)_4$ led to *N*-*tert*-butanesulfinyl imine **4a** in 75% yield. Further indium promoted propargylation of **4a** with trimethylsilylpropargyl bromide (**5**) gave rise to the expected compound **6a** with high diastereoselectivity (>98:2) and yield (70%). Finally, treatment of **6a** with potassium carbonate in a mixture of THF and methanol for 12 hours led to the formation of terminal alkyne **6b** in 89% yield (Figure 2).

Unfortunately, all the attempts to perform a ring-closing metathesis in enynes **6a** and **6b**, under the reaction conditions described by Bolm in the synthesis of cyclic sulfoximines with Grubbs second generation catalyst failed to produce the desired cyclic dienes **7** (Furger and Bolm 2009). Instead of that, starting compounds were recovered unaltered (Figure 3).

We decided to study the enyne ring-closing metathesis in other compounds different to **6a** and **6b**. These compounds were prepared in two synthetic operations starting from *ortho*-bromobenzaldehyde (**3b**, R^2 = H) and 2-bromo-5-methoxybenzaldehyde (**3c**, R^2 = OMe). First, the palladium catalyzed Sonogashira coupling reaction of aromatic aldehydes **3** with terminal alkynes **8** led to *ortho*-alkynyl aldehydes in high yields. After that, enynes **11** were obtained by aminoallylation of aldehyde **9** by successive reaction with (*R*)-*N*-*tert*-butanesulfinamide (**1**) in the presence of $Ti(OEt)_4$ at room temperature for 1 hour, followed by addition of indium metal and allyl bromide (**10**),

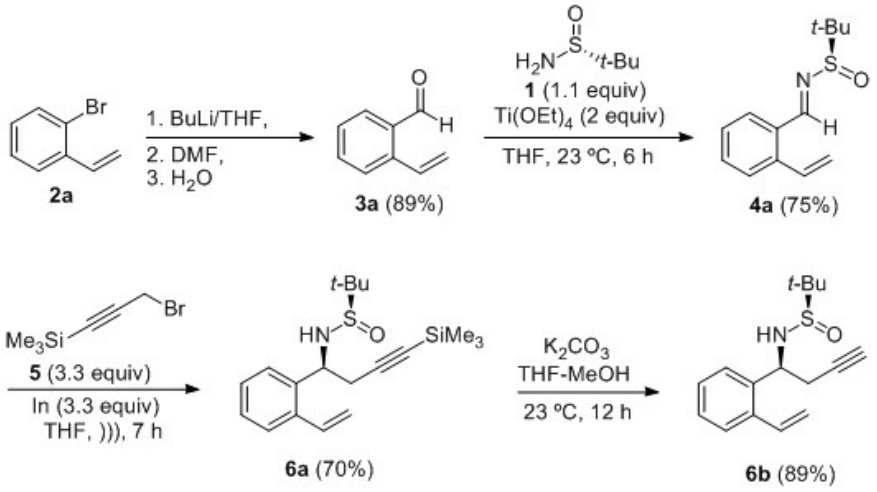


Figure 2 - Synthesis of enyne **6b**.

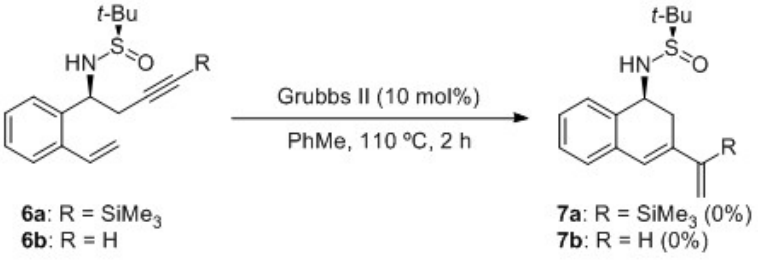


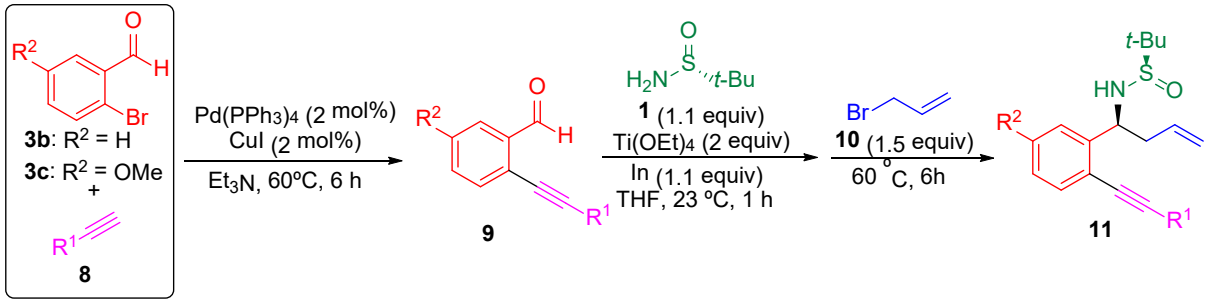
Figure 3 - Attempt to perform ring-closing metathesis of enynes **6**.

and further reaction of the resulting mixture at 60 ºC for 6 hours, in a one-pot process. The reaction was monitorized by TLC and it was not necessary to isolate the imine intermediate. The expected enynes **11** were obtained in good to moderate yields. The aminoallylation of aldehyde **9d** with an electron-donating substituent at the aromatic ring took place in only 30% yield, leading to enyne **11d**. On the other hand, enyne **11f** was obtained in quantitative yield by desilylation of **11a** (Table I).

The treatment of compounds **11** with a catalytic amount of Grubbs second generation catalyst in toluene a 110 ºC for 1 hour led to the expected cyclic dienes **12** in variable yields, but for silylated derivative **11a** ($R^1 = SiMe_3$) which did not undergo ring-closing metathesis and was recovered at the end of the reaction. The highest yields were obtained for enynes **11b** [$R^1 = (CH_2)_5Me$] and **11f** (R^1 = H), which derived from aliphatic alkynes **8**, leading to dienes **12b** and **12f**, in 70 and 69% yield, respectively. On the other hand, lower yields were found for enynes **11d** and **11e** with electron-donating methoxy groups in one of the aromatic rings (Table II).

Ring-closing metathesis of all enynes **11** shown on Table I produced six-membered cycles. With the aim of widen the scope of this reaction, we prepared an enyne system which after ring-closing metathesis would generate a seven-membered ring. For this purpose, aromatic aldehyde **9b** was transformed into aldehyde **13**. This homologation process was carried out through a Wittig reaction with methoxymethyl triphenylphosphonium chloride, followed by acidic hydrolysis. After that, the imine **14** was prepared in 64% yield by condensation with (*R*)-*N*-*tert*-butanesulfinamide

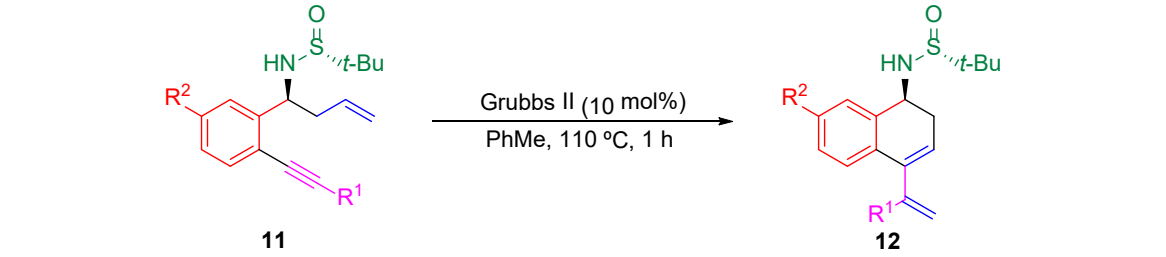
TABLE I
Synthesis of enynes 11.

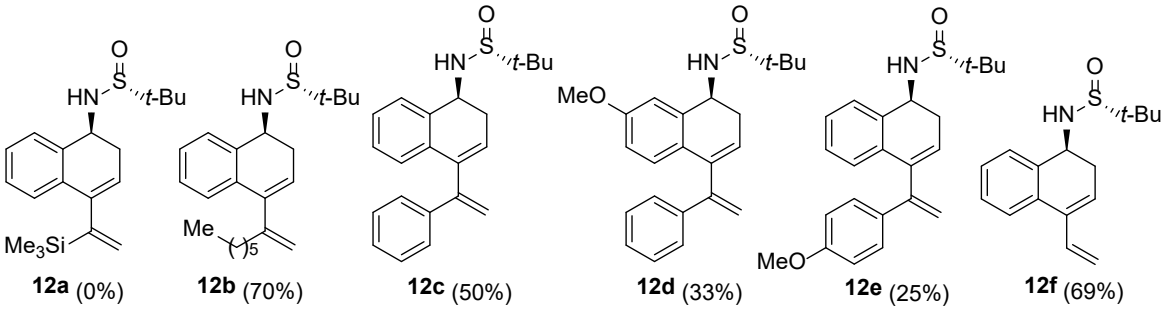


Entry	R^1	R^2	Aldehyde **9**		Enyne **11**	
			No.	Yield (%)[a]	No.	Yield (%)[a]
1	Me_3Si	H	**9**[a]	50	**11a**	55
2	$Me(CH_2)_5$	H	**9b**	88	**11b**	51
3	Ph	H	**9c**	98	**11c**	82
4	Ph	OMe	**9d**	85	**11d**	30
5	4-$MeOC_6H_4$	H	**9e**	93	**11e**	64
6	H	H			**11f**	>98[b]

[a] Isolated yield after column chromatography purification. [b] Compound 11f was obtained by desilylation of 11a under basis conditions.

TABLE II
Synthesis of dienes 12.[a]





[a] Isolated yield after column chromatography purification.

(**1**) in the presence of $Ti(OEt)_4$. Allylation of this imine with allyl bromide (**10**) in the presence of indium metal gave the expected enyne **15** in 50% yield. Finally, the ring-closing metathesis of **15** under the reactions conditions depicted on Table II led to diene **16** upon formation of a seven-membered ring. Surprisingly this metathesis took place in higher yield (78%) than for compounds **12**, in spite of the higher stability of six-membered rings (Figure 4). Importantly, two stereogenic centers are present in dienes **12** and **16** (the carbon atom bonded to the nitrogen, and the sulfur atom), and are of potential interest in Diels-Alder reactions with different dienophiles, because high levels of regio- and stereoselectivity could be achieved in these transformations.

In conclusion, second generation Grubbs catalyst demonstrated to be effective in the ring-closing metathesis of *N*-*tert*-butanesulfinyl homoallylamine derivatives bearing *ortho*-alkynyl substituted aryl groups. The resulting dienes **12** and **16** are of potential interest in Diels-Alder reactions with different dienophiles, because high levels of regio- and stereoselectivity could be achieved in these transformations due to the presence of two stereogenic centers (the sulfur atom and the carbon atom bonded to the nitrogen). These chiral dienes are interesting precursors for the asymmetric synthesis of the skeleton present in some alkaloids, such as **17** (Foubelo and Yus 2014, 2016), and particularly in morphane derivatives (see, e.g. morphine; Figure 5) (Abate et al. 2012).

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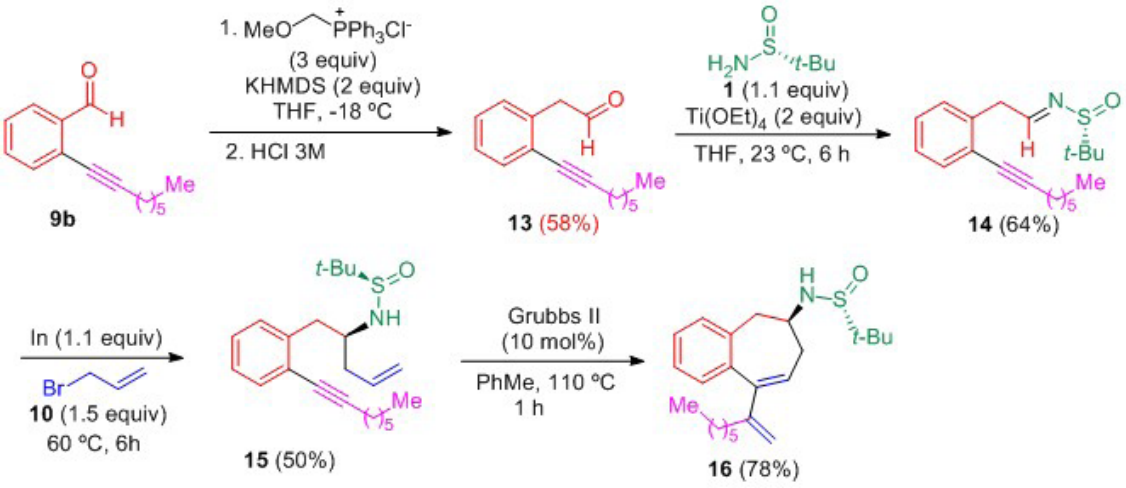

Figure 4 - Synthesis of diene **16**.

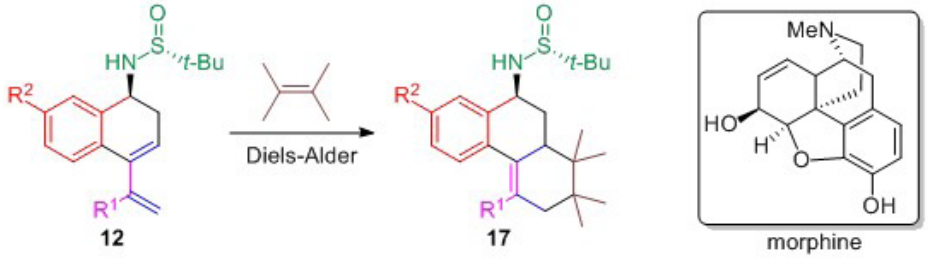

Figure 5 - Potential synthetic applications of dienes **12**.

CONSOLIDER INGENIO 2010-CDS2007-00006, CTQ2011-24165), the Ministerio de Economía y Competitividad (MINECO; projects CTQ2014-53695-P, CTQ2014-51912-REDC, CTQ2016-81797-REDC, CTQ2017-85093-P), FEDER, the Generalitat Valenciana (PROMETEO 2009/039, PROMETEOII/2014/017), and the University of Alicante.

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