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On the Faciality of Intramolecular Palladium(0)-Catalysed "Metallo-Ene-Type" Cyclisations

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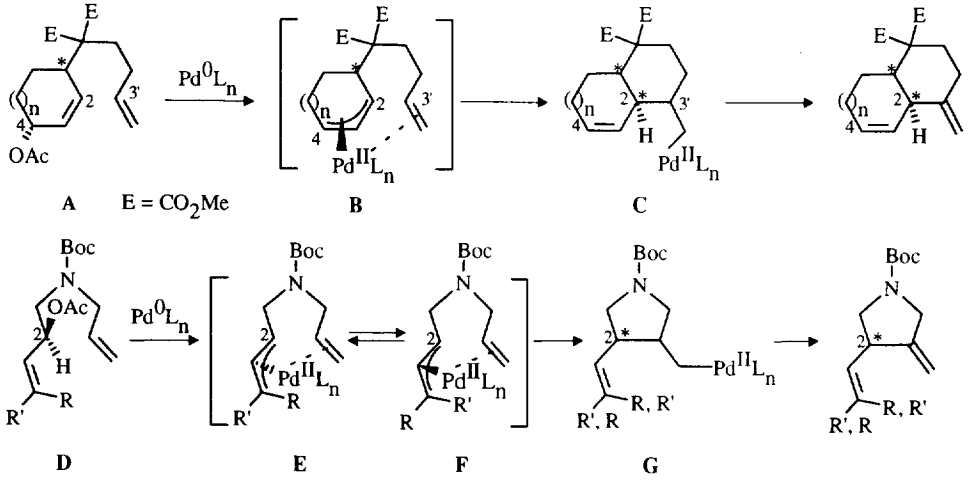
Abstract: The palladium-catalysed "metallo-ene" step in a cyclisation/β-elimination reaction sequence has been shown to be suprafacial with respect to the olefinic component. This reaction has been applied to the synthesis of a trisubstituted exocyclic alkenyl pyrrolidine with complete stereocontrol.

Introduction

Palladium- and nickel-catalysed intramolecular alkene allylations, combined with β-elimination[3], vinylstannane coupling[4], allylzincations[5] or CO-insertion[6] reactions, offer an attractive stereocontrolled route to usefully functionalised five- and six-membered carbo- and heterocyclic systems. We have formalised these transformations as "metallo-ene-type" cyclisations.[7]

It has been demonstrated that palladium-catalysed intramolecular, terminal alkene additions to cyclic 1,3-disubstituted allyl acetates proceed with clean transfer of chirality from C-4 (in **A**, Scheme 1) to C-2 and C-3' (in **C**):[8] Displacement of the acetate by Pd(0) with inversion (**A** → **B**) is followed by suprafacial attack of the alkene moiety onto the allyl unit (**B** → **C**).



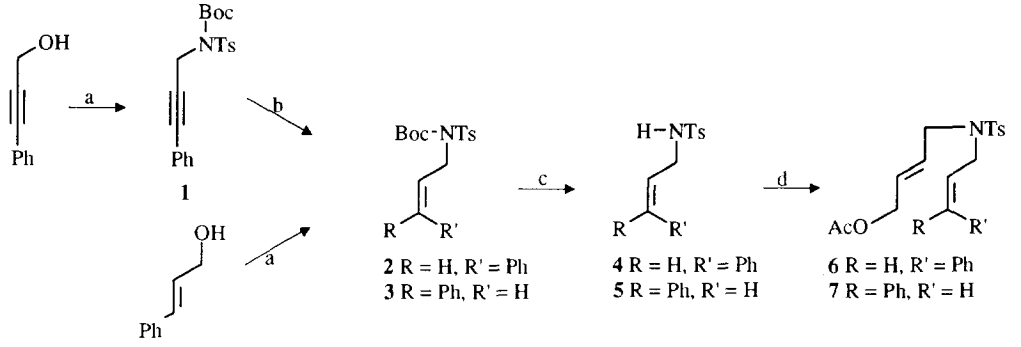
Scheme 1

This stereospecific tandem oxidative addition/alkylation was also extended to acyclic 1,3-disubstituted allyl acetates **D**.[9] As with the cyclic substrates, initial displacement of the acetate group (in **D**, Scheme 1) proceeds with inversion. For the (*E*)-configured substrate (**D**, R' = Me, R = H) the palladium complex **E** immediately undergoes suprafacial allyl palladium-olefin insertion to **G**, resulting in inversion of the configuration at C-2. For the (*Z*)-configured substrate (**D**, R' = H, R = Me) the allyl palladium complex isomerises to give the more stable intermediate **F** *prior* to suprafacial insertion, resulting in overall retention of the configuration at C-2.

These studies showed that the ring closure occurred in a suprafacial manner and under complete stereocontrol relative to the allyl unit. We were interested in the integrity of stereochemically defined (*E*)- or (*Z*)-configured alkenes (the 'enophile') in their palladium-mediated addition to allylic acetates which we also anticipated to be suprafacial.

Synthesis

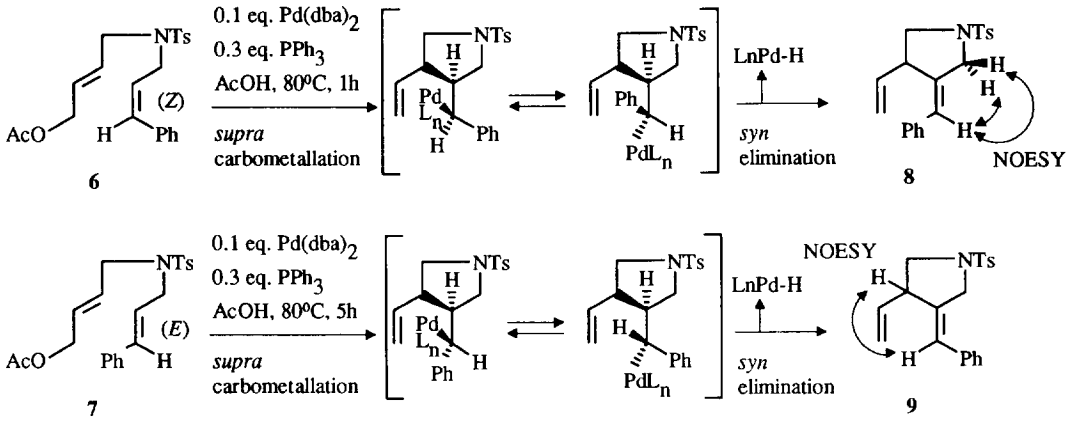
To establish if this was indeed the case we investigated the cyclisation of substrates **6** and **7** (Scheme 2) which contain stereochemically defined terminal substituents on the 'enophile' moiety. These cyclisation substrates were prepared from the corresponding *N*-Boc-tosylamides **2** and **3** by treatment with TFA followed by alkylation with (*Z*)-1-acetoxy-4-chloro-2-butene.[10] *N*-Boc-tosylamide **2** was prepared stereoselectively by Mitsunobu type reaction of *N*-Boc-tosylamide[11] with 3-phenyl-2-propyn-1-ol[12] (to give alkyne **1**) followed by partial hydrogenation over Lindlar's catalyst. Synthesis of **3** was performed starting from commercially available (*E*)-cinnamyl alcohol *via* an analogous Mitsunobu reaction.



Scheme 2. *Reagents:* a) HNTs(Boc), DEAD, PPh_3, THF; b) H_2, Lindlar, EtOAc; c) TFA, CH_2Cl_2; d) NaH, (*Z*)-1-acetoxy-4-chloro-2-butene, $Pd(PPh_3)_4$, THF.

The results of our cyclisation studies are summarised in Scheme 3. Pd(0)-catalysed cyclisation of the (*Z*)-configured substrate **6** furnished (*E*)-benzylidenepyrrolidine **8** as the only product. The corresponding (*Z*)-benzylidenepyrrolidine **9** was obtained as the exclusive product from the cyclisation of the (*E*)-configured substrate **7**.[13]

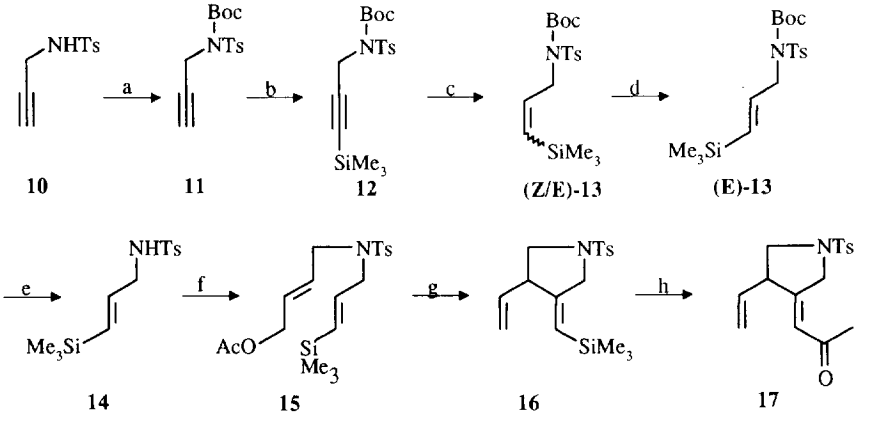
The complete fidelity and sense of transfer of stereochemical information (inherent in the 'enophile' geometry of **6** and **7**), *via* the chiral secondary alkyl palladium intermediate through to the stereochemically defined benzylidenepyrrolidine products, is consistent with a suprafacial cyclisation process (*i.e.* proceeding *via* C-C and Pd-C bond formation on the same face of the alkene) followed by *syn* elimination of palladium hydride.



Scheme 3

We have utilised the suprafaciality of this type of cyclisation reaction for the stereospecific preparation of synthetically useful vinylsilanes.[14] Tosylamide **10**[15] was converted into the *N*-Boc-tosylamide **11**, and the lithium anion of this amide quenched with TMS chloride to provide silane **12**. Reduction of this alkyne[16] provided a mixture of (*E*)- and (*Z*)-vinylsilanes which could be equilibrated to the (*E*)-isomer **13** using NBS ((*E*)/(*Z*) ratio 97:3 by ^{1}H NMR).[17] Treatment with TFA followed by alkylation with (*Z*)-1-acetoxy-4-chloro-2-butene[10] furnished cyclisation precursor **15**. Pd(0)-catalysed cyclisation of **15** proceeded smoothly to give (*Z*)-vinylsilane **16** ((*Z*)/(*E*) ratio 96:4 by ^{1}H NMR) as the exclusive product.

The utility of vinylsilane **16** was demonstrated by performing a Friedel-Crafts acetylation reaction, known to take place with retention of configuration about the alkene,[14] which provided the trisubstituted exocyclic alkenyl pyrrolidine **17** with complete stereocontrol.



Scheme 4. *Reagents:* a) NaH, Boc_2O; b) LiHMDS, Me_3SiCl, THF; c) 1. $(Cy)_2BH$, THF; 2. AcOH, reflux; 3. H_2O_2, NaOH; d) NBS, Pyr, Et_2O, hv; e) TFA, CH_2Cl_2; f) NaH, (*Z*)-1-acetoxy-4-chloro-2-butene, $Pd(PPh_3)_4$, THF; g) 0.1 eq. $Pd(dba)_2$, 0.3 eq. P(o-furyl)$_3$, AcOH, 80°C, 21h; h) $AlCl_3$, AcCl, CH_2Cl_2.

In summary, we have demonstrated that palladium-catalysed "metallo-ene-type" cyclisations proceed in a suprafacial manner relative to the 'enophile' moiety, and this, in conjunction with the known stereospecificity of initial allyl palladium formation, can be used for the predictable construction of heterocyclic systems containing stereochemically defined trisubstituted exocyclic alkenes.

EXPERIMENTAL

General. All reactions were carried out under Ar with magnetic stirring, unless otherwise specified. Solvents were dried by distillation from drying agents as follows: Et_2O, THF (Na-benzophenone), toluene (Na), DMF, CH_2Cl_2 (CaH_2), MeOH (Mg). "Degassing" refers to repeated freeze-thawing until evolution of dissolved gas ceased. "Work up" denotes extraction with an organic solvent, drying ($MgSO_4$) and evaporation *in vacuo*. Column flash chromatography (FC): SiO_2 (*Merck 9385 Kieselgel* 60, 30-60 μm,). GC: *Hewlett-Packard 5790 A*, integrator *HP 3390*, capillary column (fused silica, *OV-1* (12m x 0.2mm), 10 psi H_2, 5 min 200°C, 10°C/min to 270°C, unless otherwise specified. M.p.: *Kofler* hot stage; uncorrected. IR: *Perkin-Elmer 1600*, in $CHCl_3$, unless otherwise specified. ^1H NMR (Bruker AMX-400) in $CDCl_3$, unless otherwise specified, standard $CHCl_3$ and TMS (d = 7.27 or 0 ppm), *J* in Hz. ^{13}C NMR at 100.62 MHz in $CDCl_3$, unless otherwise specified. MS: *Varian CH-4* or *Finnigan 4023* at 70 eV, *m/z* (rel.-%). HR-MS: *VG 7070-E*.

N-tert-Butoxycarbonyl-N-[(3-phenyl-2-propynyl]-4-methylphenylsulfonamide (**1**): PPh_3 (4.11 g, 15.65 mmol, 2 eq.) was added to a solution of N-Boc-toluenesulfonamide[11] (2.13 g, 7.84 mmol, 1 eq.) in dry THF (60 ml). The mixture was cooled under argon to -78°C, and 3-phenyl-2-propynyl-1-ol[12] (1.04 g, 7.84 mmol, 1 eq.) was added followed by DEAD (2.44 g, 14.03 mmol, 1.8 eq.). The reaction mixture was stirred for 1.5 h between -78 and -60°C, warmed up to room temp., concentrated *in vacuo*, and the residue purified by FC (hexane/EtOAc 4:1) to give **1** (1.93 g, 64 %). M.p.: 91°C (EtOAc/hexane). IR: 3032, 2984, 2933, 1731, 1598, 1490, 1363, 1154. ^1H NMR: 1.37 (*s*, 9 H), 2.42 (*s*, 3 H), 4.85 (*s*, 2 H), 7.26-7.33 (*m*, 7 H), 7.97 (*d*, *J* = 8, 2 H). ^{13}C NMR: 150.3 (*s*), 144.3 (*s*), 136.8 (*s*), 131.7 (*2d*), 129.1 (*2d*), 128.5 (*d*), 128.3 (*4d*), 122.5 (*s*), 84.7 (*s*), 84.4 (*s*), 83.8 (*s*), 36.7 (*t*), 27.9 (*3q*), 21.6 (*q*). MS: 330 (4, $[C_{21}H_{23}NO_4S\text{-}C_4H_7]^{+\cdot}$), 175 (9), 174 (75), 139 (9), 130 (13), 115 (23), 105 (14), 103 (36), 96 (23), 91 (41), 65 (23), 57 (100). HR-MS: 330.0773 ($[C_{21}H_{23}NO_4S\text{-}C_4H_7]^{+\cdot}$, calc. 330.0800).

N-tert-Butyloxycarbonyl-N-[3-phenyl-(2Z)-propenyl]-4-methylphenylsulfonamide (**2**): Alkyne **1** (1.55 g, 4.02 mmol) and quinoline (0.11 g, 0.85 mmol) were vigorously stirred in EtOAc (20 ml) at room temp. under H_2 atmosphere (1 atm.) for 24 h. Filtration through Celite, evaporation of the solvent and FC (hexane/EtOAc 4:1) furnished the (*Z*)-alkene **2** (1.33 g, 85%). The reaction was monitored by GC ((min): 8.27 (**2**), 8.68 (**1**)). M.p.: 120°C (CH_2Cl_2/hexane). IR: 3029, 3011, 2984, 2932, 1727, 1598, 1495, 1357, 1155. ^1H NMR: 1.31 (*s*, 9 H), 2.43 (*s*, 3 H), 4.77 (*dd*, *J* = 6, 2, 2 H), 5.70 (*dt*, *J* = *11.5, 6*, 1 H), 6.57 (*d*, *J* = 11.5, 1 H), 7.21-7.39 (*m*, 5 H), 7.35 (*d*, *J* = 8.5, 2 H), 7.80 (*d*, *J* = 8.5, 2 H). ^{13}C NMR: 150.8 (*s*), 144.1 (*s*), 137.3 (*s*), 136.3 (*s*), 131.0 (*d*), 129.2 (*2d*), 128.8 (*2d*), 128.3 (*3d*), 128.0 (*2d*), 127.2 (*d*), 84.2 (*s*), 45.3 (*t*), 27.8 (*3q*), 21.6 (*q*). MS: 331 (5, $[C_{21}H_{25}NO_4S\text{-}C_4H_8]^{+\cdot}$), 287 (4), 176 (100), 155 (6), 115 (44), 91 (38), 57 (40). HR-MS: 331.0900 ($[C_{21}H_{25}NO_4S\text{-}C_4H_8]^{+\cdot}$, calc. 331.0878).

N-[3-Phenyl-(2Z)-propenyl]-4-methylphenylsulfonamide (**4**): TFA (2.5 ml, 3.7 g, 32.5 mmol) was added to N-Boc-tosylamide **2** (992 mg, 2.56 mmol), dissolved in CH_2Cl_2 (5 ml). The mixture was stirred at room temp. for 30 min. Evaporation of the solvent was followed by FC (hexane/EtOAc 4:1) to provide tosylamide **4** (727 mg, 99%). M.p.: 52°C (CH_2Cl_2/hexane). IR: 3373, 3279, 3025, 3016, 2926, 1599, 1494, 1402, 1333, 1160. ^{1}H NMR: 2.43 (*s*, 3 H), 3.85 (*ddd*, *J* = 7, 6, 1, 2 H), 4.59 (*t* broad, *J* = 6, 1 H), 5.55 (*dt*, *J* = 12, 7, 1 H), 6.52 (*d*, *J* = 12, 1 H), 7.08 (*d*, *J* = 8, 2 H), 7.21-7.32 (*m*, 5 H), 7.72 (*d*, *J* = 8, 2 H). ^{13}C NMR: 143.5 (*s*), 136.8 (*s*), 135.8 (*s*), 132.7 (*d*), 129.8 (2*d*), 128.6 (2*d*), 128.3 (2*d*), 127.2 (*d*), 127.2 (2*d*), 126.4 (*d*), 41.3 (*t*), 21.5 (*q*). MS: 287 (2, $C_{16}H_{17}NO_2S^{+\cdot}$), 184 (8), 155 (5), 133 (12), 132 (100), 130 (58), 117 (24), 116 (15), 115 (24), 105 (54), 92 (13), 91 (63), 77 (32), 65 (43). HR-MS: 287.0996 ($C_{16}H_{17}NO_2S^{+\cdot}$, calc. 287.0980).

N-[4-Acetoxy-(2E)-butenyl]-N-[3-phenyl-(2Z)-propenyl]-4-methylphenylsulfonamide (**6**): NaH (55%, 70 mg, 1.60 mmol) was added portionwise at room temp. to a solution of tosylamide **4** (320 mg, 1.12 mmol) in THF (24 ml). After stirring the mixture at room temp. for 30 min (Z)-1-acetoxy-4-chloro-2-butene[10] (250 mg, 1.68 mmol) and $Pd(PPh_3)_4$ (60 mg, 0.052 mmol) were added under argon. Stirring of the mixture for 1 h, addition of water (5 ml), extraction (Et_2O) and drying of the combined organic layers, followed by FC of the residue (hexane/EtOAc 5:1) provided acetoxydiene **6** as oil (414 mg, 93%). IR: 3025, 3014, 2927, 1735, 1599, 1494, 1343, 1247, 1159. ^{1}H NMR: 1.99 (*s*, 3 H), 2.43 (*s*, 3 H), 3.72 (*d*, *J* = 6, 2 H), 4.06 (*dd*, *J* = 6.5, 1.5, 2 H), 4.23 (*dd*, *J* = 5.5, 1, 2 H), 5.31 (*dt*, *J* = 15.5, 5.5, 1 H), 5.41 (*m*, 1 H), 5.47 (*dt*, *J* = 12, 6.5, 1 H), 6.57 (*d*, *J* = 12, 1 H), 7.13 (*d*, *J* = 8, 2 H), 7.22-7.34 (*m*, 5 H), 7.68 (*d*, *J* = 8.5, 2 H). ^{13}C NMR: 170.4 (*s*), 143.3 (*s*), 137.3 (*s*), 136.0 (*s*), 132.8 (*d*), 129.7 (2*d*), 128.8 (*d*), 128.7 (2*d*), 128.3 (2*d*), 127.9 (*d*), 127.3 (*d*), 127.2 (2*d*) 126.9 (*d*), 63.5 (*t*), 48.3 (*t*), 44.2 (*t*), 21.5 (*q*), 20.8 (*q*). MS: 399 (1, $C_{22}H_{25}NO_4S^{+\cdot}$), 340 (5), 244 (17), 184 (25), 155 (9), 130 (35), 117 (76), 116 (11), 115 (37), 91 (100), 77 (11), 65 (30). HR-MS: 399.1496 ($C_{22}H_{25}NO_4S^{+\cdot}$, calc. 399.1504)

N-tert-Butoxycarbonyl-N-[3-phenyl-(2E)-propenyl]-4-methylphenylsulfonamide (**3**): Employing the Mitsunobu reaction as described for the preparation of **1**, cinnamyl alcohol (676 mg, 5.04 mmol) was treated with N-Boc-tosylamide (1.35 g, 4.97 mmol), PPh_3 (2.60 g, 9.93 mmol) and DEAD (1.55 g, 8.90 mmol) in THF (35 ml) to give the diprotected amide **3** (1.48 g, 76%). M.p.: 123°C (CH_2Cl_2/hexane). IR: 3029, 3010, 2984, 2932, 1725, 1598, 1496, 1370, 1218, 1164. ^{1}H NMR: 1.36 (*s*, 9 H), 2.42 (*s*, 3 H), 4.60 (*dd*, *J* = 7, 1, 2 H), 6.28 (*m*, 1 H), 6.66 (*d*, *J* = 16, 1 H), 7.22-7.41 (*m*, 7 H), 7.80 (*d*, *J* = 8, 2 H). ^{13}C NMR: 150.8 (*s*), 144.1 (*s*), 137.5 (*s*), 136.4 (*s*), 133.9 (*d*), 129.2 (2*d*), 128.6 (2*d*), 128.1 (2*d*), 127.9 (*d*), 126.6 (2*d*), 124.3 (*d*), 84.3 (*s*), 48.5 (*t*), 27.9 (3*q*), 21.6 (*q*). MS: 388 (0.2, $C_{21}H_{25}NO_4S^{+\cdot}$), 332 (7), 286 (1), 176 (80), 158 (6), 132 (26), 117 (40), 115 (64), 105 (12), 91 (52), 77 (13), 65 (24), 57 (100). HR-MS: 287.0984 ($[C_{21}H_{25}NO_4S\text{-}C_5H_8O_2]^{+\cdot}$, calc. 287.0980).

N-[3-Phenyl-(2E)-propenyl]-4-methylphenylsulfonamide (**5**): Employing the deprotection reaction as described for the preparation of **4**, the N-Boc-tosylamide **3** (1.51 g, 3.89 mmol) was treated with TFA (2.5 ml, 3.7 g, 32.5 mmol) in CH_2Cl_2 (5 ml). Evaporation of the solvent and the acid, followed by FC (hexane/EtOAc 2:1), furnished the tosylamide **5** (722 mg, 65%). M.p.: 109-110°C (CH_2Cl_2/hexane). IR: 3386, 3240, 3020, 2926, 1599, 1495, 1406, 1334, 1161. ^{1}H NMR: 2.41 (*s*, 3 H), 3.75 (*dd*, *J* = 6, 5, 2 H), 4.65 (*s* broad, 1 H), 6.02 (*dt*, *J* = 16, 6, 1 H), 6.44 (*d*, *J* = 16, 1 H), 7.23-7.31 (*m*, 7 H), 7.78 (*d*, *J* = 8, 2 H). ^{13}C NMR: 143.5 (*s*), 137.1

(*s*), 136.1 (*s*), 133.1 (*d*), 129.8 (*2d*), 128.6 (*2d*), 128.0 (*d*), 127.2 (*2d*), 126.4 (*2d*), 124.1 (*d*), 45.5 (*t*), 21.6 (*q*). MS: 287 (5, $C_{16}H_{17}NO_2S^{+\cdot}$), 155 (4), 133 (11), 132 (100), 130 (65), 115 (23), 105 (52), 104 (14), 91 (61), 77 (26), 65 (36). HR-MS: 287.0977 ($C_{16}H_{17}NO_2S^{+\cdot}$, calc. 287.0980).

N-[4-Acetoxy-(2E)-butenyl]-N-[3-phenyl-(2E)-propenyl]-4-methylphenylsulfonamide (**7**): NaH (55%, 71 mg, 1.63 mmol) was added portionwise at room temp. to a solution of amide **5** (319 mg, 1.11 mmol) in THF (24 ml). After stirring the mixture at room temp. for 20 min, $Pd(PPh_3)_4$ (62 mg, 0.054 mmol), followed by (*Z*)-1-acetoxy-4-chloro-2-butene (278 mg, 1.87 mmol) were added under Ar. Stirring of the mixture for 2.5 h, quenching with water (20 ml), extraction (EtOAc) and drying of the extracts followed by FC of the residue (hexane/EtOAc 4:1) provided acetoxydiene **7** (343 mg, 77%). M.p.: 49-50°C (EtOAc/hexane). IR: 3028, 3012, 2926, 1736, 1598, 1495, 1339, 1236, 1159. ^{1}H NMR: 2.03 (*s*, 3 H), 2.43 (*s*, 3 H), 3.85 (*d*, *J* = 6, 2 H), 3.96 (*dd*, *J* = 6.5, 1, 2 H), 4.50 (*dd*, *J* = 5.5, 0.5, 2 H), 5.61 (*dt*, *J* = 15.5, 6, 1 H), 5.67 (*dt*, *J* = 15.5, 4.5, 1 H), 5.94 (*dt*, *J* = 16, 6.5, 1 H), 6.40 (*d*, *J* = 16, 1 H), 7.21-7.35 (*m*, 7 H), 7.73 (*d*, *J* = 8, 2 H). ^{13}C NMR: 170.5 (*s*), 143.3 (*s*), 137.3 (*s*), 136.1 (*s*), 134.1 (*d*), 129.7 (*2d*), 128.8 (*d*), 128.6 (*2d*), 128.5 (*d*), 127.9 (*d*), 127.2 (*2d*), 126.4 (*2d*), 123.7 (*d*), 63.8 (*t*), 49.2 (*t*), 48.3 (*t*), 21.5 (*q*), 20.8 (*q*). MS: 399 (14, $C_{22}H_{25}NO_4S^{+\cdot}$), 340 (18), 244 (67), 184 (47), 155 (17), 130 (51), 117 (87), 115 (41), 91 (100), 68 (16), 65 (20). HR-MS: 399.1501 ($C_{22}H_{25}NO_4S^{+\cdot}$, calc. 399.1504)

(Z)-3-Benzylidene-1-(4-methylphenylsulfonyl)-4-vinylpyrrolidine (**8**): The allylic acetate **6** (32 mg, 0.080 mmol), $Pd(dba)_2$ (5 mg, 0.009 mmol, 0.1 eq.) and PPh_3 (6 mg, 0.023 mmol, 0.3 eq.) were dissolved in degassed AcOH (1 ml) and stirred at 80°C for 1 h. Evaporation of the solvent and FC (hexane/EtOAc 20:1) furnished pyrrolidine **8** (16 mg, 59%). M.p.: 81-82°C. (Et_2O/pentane). IR: 3030, 2926, 2857, 1598, 1495, 1346, 1159. ^{1}H NMR: 2.43 (*s*, 3 H), 3.26 (*dd*, *J* = 10, 6.5, 1 H), 3.46 (*dd*, *J* = 10, 1.5, 1 H), 3.63 (*m* broad, 1 H), 3.86 (*dd*, *J* = 14, 2, 1 H), 4.15 (*d*, *J* = 14, 1 H), 5.05 (*d*, *J* = 10, 1 H), 5.08 (*d*, *J* = 17, 1 H), 5.74 (*ddd*, *J* = 17, 10, 6, 1 H), 6.43 (*s* broad, 1 H), 7.18-7.35 (*m*, 7 H), 7.72 (*d*, *J* = 8, 2 H). ^{13}C NMR: 143.6 (*s*), 137.7 (*s*), 136.5 (*d*), 136.0 (*s*), 133.2 (*s*), 129.6 (*2d*), 128.3 (*2d*), 128.3 (*2d*), 127.8 (*2d*), 127.2 (*d*), 124.8 (*d*), 116.6 (*t*), 54.5 (*t*), 53.1 (*t*), 44.4 (*d*), 21.5 (*q*). MS: 339 (6, $C_{20}H_{21}NO_2S^{+\cdot}$), 248 (4), 184 (31), 183 (16), 156 (17), 155 (35), 141 (17), 130 (31), 115 (35), 104 (27), 92 (11), 91 (100), 77 (18), 65 (40). HR-MS: 339.1264 ($C_{20}H_{21}NO_2S^{+\cdot}$, calc. 339.1293).

(E)-3-Benzylidene-1-(4-methylphenylsulfonyl)-4-vinylpyrrolidine (**9**): The allylic acetate **7** (39 mg, 0.098 mmol), $Pd(dba)_2$ (6 mg, 0.010 mmol, 0.1 eq.) and PPh_3 (8 mg, 0.030 mmol, 0.3 eq.) were dissolved in degassed AcOH (1 ml) and stirred at 80°C for 5 h. Evaporation of the solvent and FC (hexane/EtOAc 20:1) furnished pyrrolidine **9** (20 mg, 60%). M.p.: 101-102°C (Et_2O/pentane). IR: 3030, 3011, 2926, 2853, 1599, 1494, 1346, 1161. ^{1}H NMR: 2.43 (*s*, 3 H), 2.85 (*dd*, *J* = 9, 9, 1 H), 3.43 (*m* broad, *J* = 7.5, 1 H), 3.64 (*dd*, *J* = 9, 7.5, 1 H), 4.00 (*dt*, *J* = 15, 2, 1 H), 4.31 (*d*, *J* = 15, 1 H), 5.19 (*d*, *J* = 16, 1 H), 5.20 (*d*, *J* = 10, 1 H), 5.58 (*m*, 1 H), 6.19 (*s* broad, 1 H), 7.13 (*d*, *J* = 8, 2 H), 7.21-7.38 (*m*, 5 H), 7.72 (*d*, *J* = 8, 2 H). ^{13}C NMR: 143.7 (*s*), 139.0 (*s*), 136.3 (*s*), 136.0 (*d*), 132.9 (*s*), 129.8 (*2d*), 128.6 (*2d*), 128.1 (*2d*), 127.8 (*2d*), 127.2 (*d*), 124.2 (*d*), 118.6 (*t*), 52.1 (*t*), 50.7 (*t*), 49.3 (*d*), 21.6 (*q*). MS: 339 (6, $C_{20}H_{21}NO_2S^{+\cdot}$), 248 (6), 184 (26), 183 (14), 156 (13), 155 (32), 141 (13), 130 (32), 115 (32), 104 (24), 92 (11), 91 (100), 77 (16), 65 (34). HR-MS: 339.1280 ($C_{20}H_{21}NO_2S^{+\cdot}$, calc. 339.1293).

N-tert-Butoxycarbonyl-N-(2-propynyl)-4-methylphenylsulfonamide (**11**): To a solution of N-(2-propynyl)-toluene sulfonamide **10**[15] (3.50 g, 16.72 mmol) in DMF (150 ml) was added NaH (55% suspension in oil, 0.80 g, 18.33 mmol) at 0°C. After 30 min the reaction was warmed up to room temp., and Boc_2O (4.40 g, 20.16 mmol) was added. The mixture was stirred for 1 h. Addition of water (150 ml), extraction (Et_2O), washing of the combined organic layers with brine, drying and FC (hexanes/EtOAc 3:1) furnished the diprotected amide **11** (4.68 g, 91%). M.p. 95-96°C (CH_2Cl_2/pentane). IR: 3308, 2984, 1731, 1598, 1457, 1362, 1157. ^{1}H NMR: 1.35 (*s*, 9 H), 2.33 (*t*, *J* = 2.5, 1 H), 2.45 (*s*, 3 H), 4.63 (*d*, *J* = 2.5, 2 H), 7.31 (*d*, *J* = 8, 2 H), 7.91 (*d*, *J* = 8, 2 H). ^{13}C NMR: 150.1 (*s*), 144.4 (*s*), 136.7 (*s*), 129.9 (*2d*), 128.2 (*2d*), 84.9 (*s*), 78.9 (*s*), 74.0 (*d*), 35.7 (*t*), 27.8 (*3q*), 21.6 (*q*). MS: 213 (2, $[C_{15}H_{19}NO_4S\text{-}C_7H_{12}]^{+\cdot}$), 210 (5), 189 (28), 155 (23), 145 (37), 144 (10), 108 (28), 91 (42), 65 (12), 57 (100). HR-MS: 189.0790($[C_{15}H_{19}NO_4S\text{-}C_4H_8O_2S]^{+\cdot}$, calc. 189.0789).

N-tert-Butoxycarbonyl-N-(3-trimethylsilyl-2-propynyl)-4-methylphenylsulfonamide (**12**): To a solution of alkyne **11** (2.02 g, 6.53 mmol) in THF (30 ml) at -78°C was added LiHMDS (1 M in THF, 7.2 ml, 7.2 mmol). After 5 min Me_3SiCl (0.92 ml, 0.79 g, 7.3 mmol) was added. After 10 min the mixture was hydrolysed with NH_4Cl (15 ml), extracted (Et_2O) and dried. FC (hexanes/EtOAc 4:1) provided the alkynylsilane **12** (2.47 g, 99%). M.p. 84-85°C (Et_2O/pentane). IR: 2983, 1732, 1599, 1456, 1361, 1156. ^{1}H NMR: 0.18 (*s*, 9 H), 1.36 (*s*, 9 H), 2.45 (*s*, 3 H), 4.63 (*s*, 2 H), 7.29 (*d*, *J* = 8, 2 H), 7.96 (*d*, *J* = 8, 2 H). ^{13}C NMR: 150.1 (*s*), 144.2 (*s*), 136.8 (*s*), 129.1 (*2d*), 128.3 (*2d*), 100.6 (*s*), 88.8 (*s*), 84.6 (*s*), 36.7 (*t*), 27.8 (*3q*), 21.6 (*q*), -0.2 (*3q*). MS: 325 (4, $[C_{18}H_{27}NO_4SiS\text{-}C_4H_8]^{+\cdot}$), 266 (10), 217 (2), 170 (18), 155 (7), 149 (5), 139 (12), 126 (8), 108 (14), 91 (28), 73 (16), 65 (12), 57 (100). HR-MS: 325.0805 ($[C_{18}H_{27}NO_4SiS\text{-}C_4H_8]^{+\cdot}$, calc. 325.0804).

N-tert-Butoxycarbonyl-N-[3-trimethylsilyl-2-propenyl]-4-methylphenylsulfonamide (**13**): Dicyclohexylborane was prepared by addition of cyclohexene (0.80 ml, 0.65 g, 7.9 mmol) to a solution of $BH_3{\cdot}Me_2S$ (10 M in THF, 0.40 ml, 4.0 mmol) in THF (5 ml) which had been cooled to -20°C. After stirring for 3 h at 0°C, the mixture was cooled to -20°C and the alkyne **12** (1.51 g, 3.95 mmol) in THF (5 ml) was added. After stirring at room temp. for 2 h, the THF was removed *in vacuo* leaving a viscous residue which was dissolved in glacial acetic acid (2 ml), and the mixture was refluxed for 1 h. After being poured into ice water, the mixture was treated with 3 N NaOH (1.4 ml) and 30% H_2O_2 (0.9 ml) and stirred 30 min at room temp. Ether was added and the layers separated. The aqueous layer was extracted with Et_2O and the combined organic layers were washed sequentially with 20% NaOH, 2 N HCl, saturated $NaHCO_3$ solution and brine. Drying followed by FC (hexanes/EtOAc 6:1→4:1) provided vinylsilane **13** (1.01 g, 67%) as a mixture of (*E*)- and (*Z*)-isomers. ^{1}H NMR: 0.07 (*s*, 9 H, E), 0.20 (*s*, 9 H, Z), 1.34 (*s*, E and Z), 2.44 (*s*, E and Z), 4.48 (*dd*, *J* = 5, 1.5, 2 H, E), 4.54 (*dd*, *J* = 6, 2, 2 H, Z), 5.70 (*dt*, *J* = 14.5, 1.5 1 H, Z), 5.84 (*dt*, *J* = 19.5, 1.5, 1 H, E), 6.02 (*dt*, *J* = 19.5, 5, 1 H, E), 6.27 (*dt*, *J* = 14.5, 6, 1 H, Z), 7.2-7.3 (*2d*, Z and E), 7.7-7.8 (*2d*, Z and E).

N-tert-Butoxycarbonyl-N-[3-trimethylsilyl-(2E)-propenyl]-4-methylphenylsulfonamide ((*E*)-**13**): To a solution of vinylsilane **13** (1.01 g, 2.64 mmol) in Et_2O (12 ml) was added pyridine (210 µl, 0.21 g, 2.61 mmol). While irradiation with a U.V. sunlamp (500 W), the mixture was treated at 25-30°C (water bath, cooled with ice as needed) with three 5 mol-% portions of NBS (75 mg, 0.424 mmol) at 15 min intervals over a 45 min period.

After irradiating for further 30 min the reaction mixture was washed with 10% HCl, 1 M NaOH and brine. FC (hexanes/EtOAc 4:1) furnished vinylsilane (*E*)-**13** (0.96 g, 95%). (*E*)/(*Z*) ratio: 97:3 (GC (min): 6.69 (*Z*) and 7.57 (*E*)). M.p.: 47-48°C (Et_2O/pentane). IR: 3024, 3020, 2984, 2957, 1725, 1599, 1456, 1359, 1154. ^1H NMR: 0.07 (*s*, 9 H), 1.35 (*s*, 9 H), 2.44 (*s*, 3 H), 4.48 (*dd*, *J* = 5, 1.5, 2 H), 5.84 (*dt*, *J* = 19.5, 1.5, 1 H), 6.02 (*dt*, *J* = 19.5, 5, 1 H), 7.29 (*d*, *J* = 8, 2 H), 7.80 (*d*, *J* = 8, 2 H). ^{13}C NMR: 150.8 (*s*), 144.1 (*s*), 140.2 (*d*), 137.2 (*s*), 132.8 (*d*), 129.1 (*2d*), 128.3 (*2d*), 84.0 (*s*), 50.8 (*t*), 27.8 (*3q*), 21.6 (*q*), -1.4 (*3q*). MS: 327 (7, $[C_{18}H_{29}NO_4SiS\text{-}C_4H_8]^{+\cdot}$), 312 (9), 270 (9), 268 (90), 228 (22), 180 (41), 172 (62), 155 (34), 149 (97), 128 (47), 112 (26), 91 (100), 73 (74), 57 (56). HR-MS: 327.0957 ($[C_{18}H_{29}NO_4SiS\text{-}C_4H_8]^{+\cdot}$, calc. 327.0961).

N-[3-Trimethylsilyl-(2E)-propenyl]-4-methylphenylsulfonamide (**14**): TFA (1 ml) was added to the diprotected amide (*E*)-**13** (1.04 g, 2.714 mmol), dissolved in CH_2Cl_2 (10 ml). The mixture was stirred at room temp. for 2 h. Purification by FC (hexanes/EtOAc 5:1) provided amide **14** as oil (0.77 g, 92%). IR: 3391, 3025, 3015, 2957, 1620, 1599, 1495, 1331, 1160. ^1H NMR: 0.01 (*s*, 9 H), 2.44 (*s*, 3 H), 3.64 (*ddd*, *J* = 6, 6, 1, 2 H), 4.69 (*t* broad, *J* = 6, 1 H), 5.76 (*d*, *J* = 18, 1 H), 5.84 (*dt*, *J* = 18, 5, 1 H), 7.32 (*d*, *J* = 8, 2 H), 7.77 (*d*, *J* = 8, 2 H). ^{13}C NMR: 143.4 (*s*), 139.9 (*d*), 137.2 (*s*), 133.0 (*d*), 129.6 (*2d*), 127.1 (*2d*), 47.6 (*t*), 21.4 (*q*), -1.6 (*3q*). MS: 268 (27, $[C_{13}H_{21}NO_2SiS\text{-}CH_3]^{+\cdot}$), 228 (9), 180 (26), 155 (12), 149 (47), 128 (61), 112 (20), 98 (23), 91 (100), 73 (91), 65 (52), 59 (32). HR-MS: 268.0808 ($[C_{13}H_{21}NO_2SiS\text{-}CH_3]^{+\cdot}$, calc. 268.0827).

N-[4-Acetoxy-(2E)-butenyl]-N-[3-trimethylsilyl-(2E)-propenyl]-4-methylphenylsulfonamide (**15**): NaH (55% suspension in oil, 135 mg, 3.09 mmol) was added portionwise at 0°C to a solution of amide **14** (665 mg, 2.35 mmol) in THF (10 ml). After stirring the mixture at 0°C for 30 min, $Pd(PPh_3)_4$ (140 mg, 0.121 mmol, 5 mol%) was added, followed by (*Z*)-1-acetoxy-4-chloro-2-butene (370 mg, 2.49 mmol). Warming up to room temp., stirring of the mixture for 30 min, addition of water (10 ml), extraction (Et_2O) and drying of the combined organic layers, followed by FC (hexanes/EtOAc 5:1→ 4:1) gave acetate **15** as oil (815 mg, 88%). IR: 3024, 3016, 2956, 1735, 1618, 1599, 1494, 1346, 1158. ^1H NMR: 0.01 (*s*, 9 H), 2.05 (*s*, 3 H), 2.43 (*s*, 3 H), 3.78 (*d*, *J* = 6, 2 H), 3.81 (*d*, *J* = 4, 2 H), 4.48 (*dd*, *J* = 5.5, 1, 2 H), 5.56-5.78 (*m*, 4 H), 7.29 (*d*, *J* = 8, 2 H) , 7.69 (*d*, *J* = 8, 2 H). ^{13}C NMR: 170.5 (*s*), 143.2 (*s*), 139.7 (*d*), 137.4 (*s*), 135.0 (*d*), 129.7 (*2d*), 128.9 (*d*), 128.3 (*d*), 127.2 (*2d*), 63.9 (*t*), 51.9 (*t*), 48.4 (*t*), 21.5 (*q*), 20.8 (*q*), -1.5 (*3q*). MS: 322 (3, $[C_{19}H_{29}NO_4SiS\text{-}C_3H_5O_2]^{+\cdot}$), 256 (15), 240 (45), 228 (15), 180 (89), 155 (31), 149 (56), 139 (20), 117 (26), 113 (54), 91 (100), 73 (85), 59 (40). HR-MS: 322.1310 ($[C_{19}H_{29}NO_4SiS\text{-}C_3H_5O_2]^{+\cdot}$, calc. 322.1297).

(Z)-3-(2-Trimethylsilyl)-ethylidene-4-vinyl-1-(4-methylphenylsulfonyl)-pyrrolidine (**16**): The allylic acetate **15** (47 mg, 0.120 mmol), $Pd(dba)_2$ (7 mg, 0.012 mmol, 0.1 eq.) and PPh_3 (8 mg, 0.035 mmol, 0.3 eq.) were dissolved in degassed AcOH and stirred at 80°C for 21 h. Evaporation of the solvent and FC (hexanes/EtOAc 50:1) furnished pyrrolidine **16** (23 mg, 57%). IR: 3030, 3018, 2956, 1633, 1598, 1473, 1347, 1163. ^1H NMR: 0.07 (*s*, 9 H), 2.43 (*s*, 3 H), 2.78 (*dd*, *J* = 10, 10, 1 H), 3.21 (*dd* broad, *J* = 8.5, 8.5, 1 H), 3.61 (*dd*, *J* = 10, 8.5, 1 H), 3.69 (*ddd*, *J* = 14.5, 2.5, 2, 1 H), 4.00 (*ddd*, *J* = 14.5, 2, 1, 1 H), 5.08 (*d*, *J* = 17, 1 H), 5.13 (*dd*, *J* = 10, 1.5, 1 H), 5.33 (*dt*, *J* = 2.5, 2, 1 H), 5.43 (*ddd*, *J* = 17, 10, 8.5, 1 H), 7.35 (*d*, *J* = 8, 2 H), 7.71 (*d*, *J* = 8, 2 H). ^{13}C NMR: 154.1 (*s*), 143.7 (*s*), 135.9 (*d*), 132.6 (*s*), 129.6 (*2d*), 127.8 (*2d*), 122.4 (*d*), 118.3 (*t*),

52.4 (*t*), 51.3 (*t*), 50.5 (*d*), 21.5 (*q*), -0.8 (*3q*). MS: 335 (4, $C_{17}H_{25}NO_2SiS^{+\cdot}$), 320 (2), 256 (3), 228 (3), 180 (37), 149 (24), 107 (17), 91 (68), 73 (100), 59 (41). HR-MS: 335.1364 ($C_{17}H_{25}NO_2SiS^{+\cdot}$, calc. 335.1375).

(Z)-3-(2-Methylcarbonyl)-ethylidene-4-vinyl-1-(4-methylphenylsulfonyl)-pyrrolidine (**17**): $AlCl_3$ (50 mg, 0.365 mmol, dried *in vacuo*) and AcCl (22 µl, 24 mg, 0.310 mmol, refluxed for several hours over PCl_5 and distilled) were dissolved in CH_2Cl_2 (0.2 ml). The vinylsilane **16** (35 mg, 0.104 mmol), dissolved in CH_2Cl_2 (4 ml), was added over a period of 2.5 h *via* syringe pump. After further 30 min the mixture was hydrolysed with $NaHCO_3$. Work-up (CH_2Cl_2), drying and FC provided ketone **17** (21 mg, 66%). IR: 3024, 3016, 2926, 1692, 1629, 1599, 1350, 1164. ^{1}H NMR: 2.18 (*s*, 3 H), 2.43 (*s*, 3 H), 2.75 (*dd*, *J* = 9.5, 9, 1 H), 3.41 (*dt* broad, *J* = 8.5, 8.5, 1 H), 3.68 (*dd*, *J* = 9, 8, 1 H), 4.03 (*ddd*, *J* = 19, 2.5, 2.5, 1 H), 4.47 (*dd*, *J* = 19, 2, 1 H), 5.20 (*d*, *J* = 17, 1 H), 5.23 (*d*, *J* = 9.5, 1 H), 5.49 (*ddd*, *J* = 17, 9.5, 8, 1 H), 6.04 (*dt*, *J* = 2.5, 2, 1 H), 7.33 (*d*, *J* = 8, 2 H), 7.73 (*d*, *J* = 8, 2 H). ^{13}C NMR: 197.1 (*s*), 158.6 (*s*), 143.8 (*s*), 134.3 (*d*), 132.4 (*s*), 129.8 (*2d*), 128.0 (*2d*), 120.8 (*d*), 119.7 (*t*), 53.2 (*t*), 51.6 (*t*), 49.2 (*d*), 31.1 (*q*), 21.5 (*q*). MS: 305 (14, $C_{16}H_{19}NO_3S^{+\cdot}$), 277 (6), 262 (26), 155 (38), 150 (22), 122 (19), 108 (25), 91 (100), 65 (22). HR-MS: 305.1039 ($C_{16}H_{19}NO_3S^{+\cdot}$, calc. 305.1086).

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