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Hydroboration and Suzuki–Miyaura Coupling Reactions with the Electronically Modulated Variant of an Ynamine: The Synthesis of (*E*)-β-Arylenamides

Bernhard Witulski,* Nicole Buschmann and Uwe Bergsträßer

Fachbereich Chemie, Universität Kaiserslautern, Erwin Schrödinger Straße, D-67663 Kaiserslautern, Germany

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Abstract—The first hydroboration of an 1-alkynylamide—the electronically modulated variant of an ynamine—is described. This hydroboration in combination with a Suzuki–Miyaura cross-coupling reaction with aryl bromides or aryl iodides allows a flexible synthesis of (*E*)-β-arylenamides and 3-(2′-amidovinyl)indoles with high degree of molecular diversity.

Introduction

The sequence of a chemo- and regioselective monohydroboration of alkynes followed by a palladium-catalysed cross-coupling reaction with aryl or vinyl halides (Suzuki–Miyaura coupling) provides a highly efficient and flexible access to vinyl aryls or conjugated dienes via the formation of a new carbon–carbon bond.[1] The usefulness of this method for the synthesis of natural products and drug related targets arises from the fact that many functional groups are tolerated by this two step procedure, and that cross-couplings proceed without the loss of a predefined stereochemistry.[2] Although numerous functionalised alkynes have been subjected to the Suzuki–Miyaura cross-coupling protocol, only a few reports appeared using synthetically profitable alkynes bearing a heteroatom adjacent to the carbon–carbon triple bond.

Monohydroborations of 1-halogeno-1-alkynes proceeded regio- and stereoselectively to give the corresponding (*Z*)-1-halogeno-1-alkenyl boranes,[3] that have been used for the synthesis of (*Z*)-1-halogeno-1-alkenes,[4] 1,1-dihalogeno-1-alkenes,[5] and (*Z*)-1-alkenylboronic esters[6]—each one being a versatile building block for transition metal catalysed cross-coupling reactions. The direct hydroboration of 1-alkoxy-1-alkynes with catecholborane afforded 2-alkoxyvinyl boronic esters that were coupled with aryl halides to the corresponding β-arylvinyl ethers with retention of configuration of the olefinic component.[7] Similarly, the catalytic hydroboration of 1-alkylthio-1-alkynes and the subsequent cross-coupling reaction with organic halides provided access to stereodefined β-arylvinyl sulphides.[8]

However, neither a hydroboration nor the use of 1-alkynylamines **1** (ynamines) in Suzuki–Miyaura cross-coupling reactions has been reported so far. This lack of attention is presumably attributed to the electron richness of the ynamine carbon–carbon triple bond, that is responsible for the extraordinary reactivity and extreme sensitivity towards hydrolysis of these otherwise attractive building blocks for organic chemistry.[9]

Recently we described a practicable synthesis for *N*-functionalised 1-alkynylamides (ynamides) of type **2** and **3**, a new set of electronically tuneable alkynes whose protecting groups (PG) serve both in masking the amine functionality and in tuning the electron density, and hence the reactivity, of the adjacent carbon–carbon triple bond (Scheme 1).[10] These electronically modulated variants of ynamines have been used by us in intramolecular Pauson–Khand reactions for the construct of proline derivatives,[11] as well as in rhodium- and ruthenium-catalysed crossed alkyne cyclotrimerisations for the chemo- and regioselective synthesis of highly substituted indolines.[12] Given our interest in the chemistry and reactivity of *N*-functionalised 1-alkynylamides, we considered their application as building blocks in Suzuki–Miyaura cross-coupling reactions for the formation of stereodefined (*E*)-β-arylenamides. β-Arylenamides are important structural features of a wide variety of organic molecules with significance to organic synthesis and medicinal chemistry, and they can be found as a structural motif in natural products like tuberine, erbstatin and aspergillamide.[13] β-Arylenamides have been prepared by a number of different methods and mostly multistep procedures were employed.[14] However, two metal assisted couplings for the formation of β-arylenamides were

Keywords: ynamines; hydroboration; catalysis; palladium; 1-alkynylamides; cross-coupling reaction.

* Corresponding author. Tel.: +49-631-205-2032; fax: +49-631-205-3921; e-mail: witulski@rhrk.uni-kl.de

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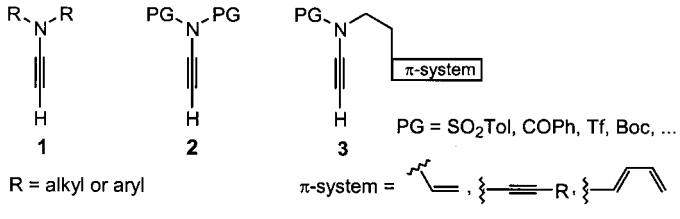


Scheme 1.

reported including the direct vinylic substitution of β-arylvinyl bromides by phthalimides and the Heck arylation of *N*-vinyloxyazolone.[15,16]

Herein we report the first introduction of an enamide group into arenes based on a Suzuki–Miyaura cross-coupling protocol using an ynamide as a CH=CH–N(PG)$_2$ building block.

Results and Discussion

The synthesis of ynamide **7** needed for the hydroboration and cross-coupling studies relied on our recently developed approach to *N*-functionalised 1-alkynylamides via the direct *N*-ethynylation with alkynyliodonium salts (Scheme 2).[10,17]

Ynamide **6** was obtained in gram quantities in 75% yield after adding **5** to the lithium salt of the amide **4** in toluene at room temperature. Following its isolation, a desilylation with TBAF in wet THF resulted in the desired 1-alkynylamide **7** in 96% yield. Unlike its *N*,*N*-dialkyl-substituted analogues, ynamide **7** is easy to handle, withstands aqueous work-up procedures as well as chromatographic purification on silica gel. This atypical stability towards hydrolysis strongly indicates that **7** is an electron deficient variant of an ynamine.

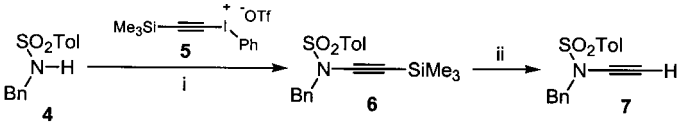
Hydroboration of **7** with catecholborane (**8**) (1–1.5 equiv.) in THF at 70°C for 2 h proceeded chemo- and regioselectively to the (*E*)-vinylborane **9**. The completion of the reaction was confirmed by observing the disappearance of alkyne **7** by TLC and the stereochemical outcome of the reaction was examined by the isolation of **9** via bulb to bulb distillation (225–260°C, 10^{-3} Torr) and ^{1}H NMR analysis.[18]

The direct hydroboration of **7** with catecholborane (**8**) gave only the monohydroboration product **9** with *E*-configuration as indicated by a doublet at δ=8.05 (J=16.55 Hz) in the ^{1}H NMR spectra recorded in $CDCl_3$. However, the isolation of vinylborane **9** turned out to be less favourable for the anticipated cross-coupling reactions due to its instability and difficulties of storage and purification. Therefore, a one-flask procedure was envisaged.

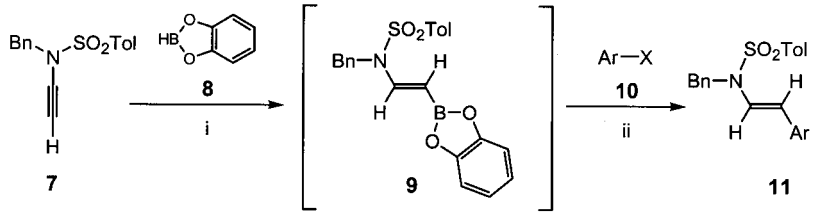
The optimum conditions for carrying out the cross-coupling reactions in a two-step one-flask procedure along Scheme 3 started with the hydroboration of alkyne **7** with catecholborane (**8**) (1–1.5 equiv.) in THF at 70°C as described above. The in situ formed organoborane complex **9** (1.5 equiv.) was then coupled at 70–80°C with an aryl iodide or aryl bromide after addition of a catalytic amount of $Pd(PPh_3)_4$ (10 mol%) and freshly powdered NaOH (3 equiv.). Cross-coupling reactions could also be achieved when an aqueous 3 M NaOH solution was used as base, however in some cases the yields were lower and side products resulting from a protodeboration became dominant.

Electron deficient as well as electron rich aryl iodides were efficiently coupled using this protocol in overall yields of 61–80% (Table 1). In all cases the cross-coupling reactions proceeded with the retention of configuration of the intermediate vinylborane **9** giving exclusively the corresponding (*E*)-β-arylenamides **11a–d**. Suzuki–Miyaura cross-couplings were less efficient for the aryl bromides **10c** and **10e**, however they still could be accomplished in moderate to good yields (Table 1, entry 3 and 5).

Finally we applied this cross-coupling protocol to the synthesis of 3-(2′-amidovinyl)indoles **15**, compounds of

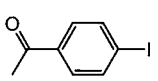
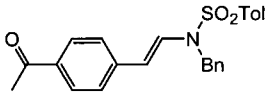
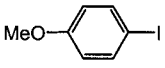
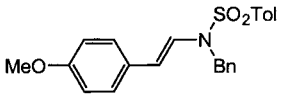
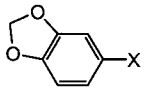
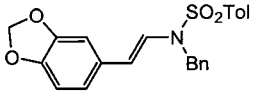
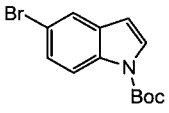
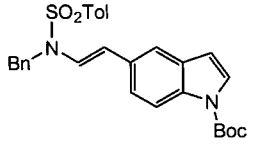


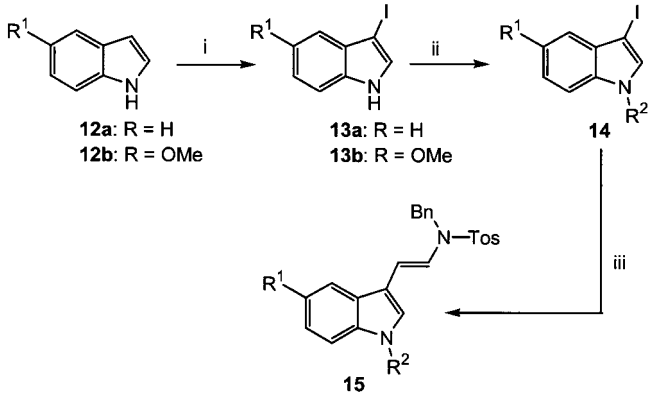
Scheme 2. *Reagents and conditions:* (i) *n*BuLi (1.1 equiv.), toluene, 0°C, then addition of **5** (1.2 equiv.); (ii) TBAF, wet THF, 0°C, 20 min.



Scheme 3. *Reagents and conditions:* (i) catecholborane (**8**) (1.5 equiv.), THF, 70°C, 2 h; (ii) aryl halogenide (X=Br, I), $NaOH_{solid}$ (3 equiv.); $Pd(PPh_3)_4$ (10 mol%), 80°C, 4 h, sealed tube.

Table 1. Aminoethenylation of arenes according to Scheme 3

Entry	Arylhalogenide **10**	Conditions	Arylated (*E*)-Enamide **11**	Yield [%]
1	 **10a**	4h (80 °C)	 **11a**	80
2	 **10b**	4h (80 °C)	 **11b**	61
3	 **10c** (X = Br)	4h (80 °C)	 **11c**	56
4	**10d** (X = I)	4h (80 °C)	**11c**	75
5	 **10e**	4h (80 °C)	 **11d**	75



Scheme 4. *Reagents and conditions:* (i) I_2, KOH, DMF, 20°C, 0.45 h (100%); (ii) R^2=Boc: Boc_2O, Et_3N, DMAP (10 mol%), CH_2Cl_2, 20°C, 0.5 h, (88–98%); R^2=SO_2Tol: TosCl, NaOH, CH_2Cl_2, 20°C, 5 h, (60–80%); (iii) **7** and catecholborane (**8**), THF, 70°C, 2 h, then addition of **14**, $NaOH_{solid}$ (3 equiv.), $Pd(PPh_3)_4$ (10 mol%), 70°C, 10–40 h, sealed tube, (58–84%).

synthetic and medicinal interest since they possess the structural feature of dehydrotryptamin, serotonin and bufotenin. Furthermore 3-(2′-amidovinyl)indoles **15** might be useful as 4π-electron components in Diels–Alder reactions for the formation of carbazoles.[19]

3-Iodoindoles **14** were obtained by direct iodination of the indoles **12a** and **12b** followed by protecting the *N*-1 position at the indole nucleus. *N*-protection was necessary to allow the anticipated cross-coupling reactions (Scheme 4). The products **15a–d** were obtained in yields of 58–84% after isolation and purification with column chromatography following the above described one flask procedure of the Suzuki–Miyaura cross-coupling reaction (Table 2). Again in all cases the desired 3-vinylindoles **15** were received with complete retention of the configuration of the stereochemistry of the initial vinyl borane complex **9**. Notably, cross-coupling reactions with the *N*-tosylated 3-iodoindoles **14b** and **14d** were faster than those having a *N*-Boc protecting group at the indole nucleus (**14a** and **14c**). Obviously the more pronounced electron-withdrawing character of the *N*-tosyl group enhanced the rate of reaction for the oxidative addition of the palladium catalyst into the indoyl–iodine bond and therefore favouring the overall catalytic process.

Suitable crystals for X-ray diffraction studies were obtained from indole **15d** after crystallisation from $CHCl_3$/pentane at −20°C.[20] The indole ring of **15d** is approximately planar (mean deviation from best plane=1.6 pm). The

Table 2. Aminoethenylation of 3-iodo-1H-indoles **14** to 3-(2′-amidovinyl)indoles **15** (all reactions were carried out in sealed Schlenk tubes using 1.5 equiv. of **9** with respect to the amount of **7**, 10 mol% $Pd(PPh_3)_4$, and 3 equiv. of solid NaOH)

Entry	**14**	R^1	R^2	Conditions	**15**	Yield (%)
1	**14a**	H	Boc	THF, 70°C, 40 h	**15a**	58
2	**14b**	H	SO_2Tol	THF, 70°C, 20 h	**15b**	71
3	**14c**	OMe	Boc	THF, 70°C, 26 h	**15c**	74
4	**14d**	OMe	SO_2Tol	THF, 70°C, 10 h	**15d**	84

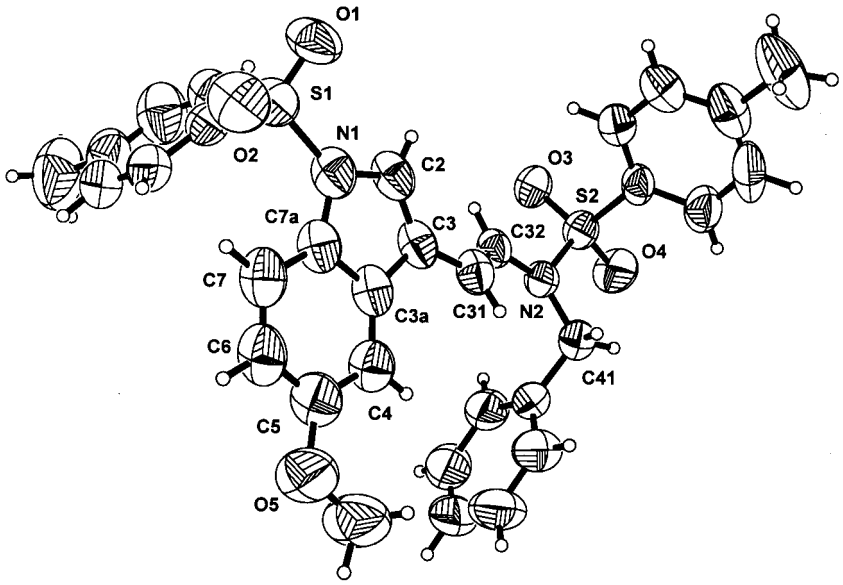


Figure 1. Molecular structure of **15d**.[20] Selected bond lengths (pm) and angles (°): N1–C2 141.5(3), C2–C3 135.3(4), C3–C31 145.8(4), C31–C32 130.0(3), C32–N2 141.3(3) N2–C41 146.6(3); N1–C2–C3 109.7(3), C2–C3–C3a 107.1(2), C2–C3–C31 130.5(3), C3–C31–C32 127.2(3), C31–C32–N2 125.5(3), C32–N2–C41 118.2(2).

conformation of the diene unit C2═C3–C31═C32 is s-*cis*-synclinal with a torsional angle of −32.1°, the bond length of the central C3–C31 bond has the typical butadiene value of 145.8(4) pm. The bond angles C2–C3–C31 (130.5°) and C3–C31–C32 (127.2°) are relatively large. The methylene group of the benzyl substituent at N2 is nearly coplanar with the alkene unit, the torsional angle C41–N2–C32–C31 being −3.9°. The bond length N2–C32 [141.3(3) pm] are in a comparable region with the endocyclic indole nitrogen/carbon atom bond lengths (see Fig. 1).

Conclusion

In summary, by taking advantage of the electronic deficient properties of 1-alkynylamide **7** the first hydroboration of an ynamine became possible. The combination of hydroboration and Suzuki–Miyaura cross-coupling reaction in a one flask procedure afforded a convenient access with high molecular diversity to (*E*)-β-arylenamides **11** and to the corresponding 3-(2′-amidovinyl)indoles **15**, compounds with potent interest in synthetic and medicinal chemistry. Applications of this strategy in more elaborated syntheses of indole alkaloids are part of our current research programs.

Experimental

General procedures

Reactions requiring anhydrous conditions were performed using flame-dried glassware and conducted under an atmosphere of nitrogen. Anhydrous solvents were prepared in accordance with standard protocols. Compounds were purified by chromatography on silica gel 60 (63–230 mesh). Melting points were measured on a Büchi melting-point apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer FT-IR spectrometer 16PC. Spectra were recorded as thin films or in KBr pellets. NMR spectra were recorded in $CDCl_3$ as solvent on Bruker AMX 400 and Bruker AC 200 spectrometers with either TMS or solvent as internal reference; *J*-values are given in Hz with an accuracy of ±0.2. Assignments were supported by DEPT spectra. Elemental analyses were carried out on a Perkin–Elmer elemental analyser EA 240 and on a Perkin–Elmer 2400 CHN elemental analyser. Mass spectra were recorded under EI conditions on a Finnigan MAT 90 spectrometer. The syntheses of the 3-iodo-1*H*-indoles **13a–b** and **14a–d** were carried out in analogy to published methods.[23]

***N*-Benzyl-*N*-trimethylsilanylethynyl-4-methylbenzenesulphonamide (6).** *N*-benzyl-4-methylbenzenesulphonamide (**4**) (1.51 g, 5.78 mmol) was dissolved in toluene (50 mL) and *n*BuLi (4.1 mL, 1.6 M in hexane) was added at 0°C via syringe. After 20 min, the alkynyliodonium salt **5** (3.12 g, 6.92 mmol) was added to the reaction mixture in small portions and thereafter stirred overnight at room temperature. The reaction mixture was filtered through a plug of silica gel and the crude product purified by chromatography (SiO_2, hexanes:diethyl ether=9:1 (v/v)) yielding ynamide **6** (1.55 g, 75%) as a colourless solid, mp 58–60°C. ^{1}H NMR (400 MHz): δ=7.72 (d, *J*=8.3 Hz, 2H), 7.3 (m, 7H), 4.47 (s, 2H), 2.43 (s, 3H), 0.08 (s, 9H); ^{13}C NMR (100 MHz): δ=144.5 (s), 134.6 (s), 134.3 (s), 129.5 (d), 128.9 (d), 128.3 (d), 128.2 (d), 127.8 (d), 95.3 (s), 73.9 (s), 55.4 (t), 21.6 (q), 0.1 (q); IR (KBr): ν=3062, 3013, 2109, 1597, 1496, 1363, 1374, 1253, 1188, 1176, 1090, 1049, 946 cm^{-1}; MS (EI), *m/z* (%): 357 (M^+, 10), 202 (6), 155 (16), 149 (9), 91 (100), 73 (10); Anal. Calcd. for $C_{19}H_{23}NO_2SSi$ (357.542): C, 63.83; H, 6.48; N, 3.92. Found: C, 63.45, H, 6.45, N, 3.83.

***N*-Benzyl-*N*-ethynyl-4-methylbenzenesulphonamide (7).** Ynamide **6** (552 mg, 1.54 mmol) was dissolved in oxygen free wet THF (50 mL) and treated at 0°C with TBAF (2 mL

of a 1 M solution in THF). The progress of the desilylation was followed by TLC and after 10 min diethyl ether and brine were added. The organic phase was separated, dried with $MgSO_4$ and after evaporation of the solvent the crude product was purified by column chromatography (SiO_2, hexanes:diethyl ether=9:1) yielding ynamide **7** (423 mg, 96%) as a colourless solid, mp 95–96°C. ^{1}H NMR (200 MHz): δ=7.82 (d, J=8.4 Hz, 2H), 7.32–7.40 (m, 7H), 4.55 (s, 2H), 2.74 (s, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz): δ=144.7 (s), 134.6 (s), 134.2 (s); 129.7 (d), 128.6 (d), 128.5 (d), 128.3 (d), 127.7 (d), 76.2 (s), 59.7 (d), 55.2 (t), 21.6 (q); IR (KBr): ν=3277, 3062, 2928, 2134, 1596, 1495, 1452, 1431, 1359, 1189, 1171, 1088, 1048, 931 cm^{-1}; MS (EI), *m/z* (%): 285 (M^+, 10), 155 (35), 130 (14), 91 (100); Anal. Calcd. for $C_{16}H_{15}NO_2S$ (285.36): C, 67.35; H, 5.30; N, 4.91. Found: C, 67.48, H, 5.16, N, 4.83.

***tert*-Butyl 5-bromo-1*H*-indole-1-carboxylate (10e).** 5-Bromoindole (1.00 g, 5.10 mmol) was dissolved in CH_2Cl_2 (100 mL) and thereafter Boc_2O (1.34 g, 6.15 mmol) and DMAP (124 mg, 1.02 mmol) were added. The mixture was stirred at room temperature overnight. The solvent was evaporated and the crude product was chromatographed over silica gel (SiO_2, hexanes:diethyl ether=8:2 (v/v)) to afford **10e** (1.37 g, 91%) as colourless solid, mp 55–57°C, R_f 0.76 (hexanes:diethyl ether=8:2 (v/v). ^{1}H NMR (400 MHz): δ=8.01 (d, J=8.8 Hz, 1H), 7.68 (d, J=1.9 Hz, 1H), 7.58 (d, J=3.7 Hz, 1H), 7.40 (dd, J=8.8 Hz, J=1.9 Hz, 1H), 6.50 (d, J=3.7 Hz, 1H), 1.66 (s, 9H); ^{13}C NMR (100 MHz): δ=149.8 (s), 134.3 (s), 132.7 (d), 127.4 (d), 123.9 (d), 117.0 (d), 116.4 (s), 106.9 (d), 84.5 (s), 28.6 (q); MS (EI), *m/z* (%): 295 (M^+, 94), 238 (100), 224 (75), 196 (96).

***N*-[(*E*)-2-(4-Acetylphenyl)ethenyl]-*N*-benzyl-4-methylbenzenesulphonamide (11a).** *General procedure:* Ynamide **7** (63 mg, 0.22 mmol) was introduced into a Schlenk tube with screw cap and THF (2 mL) was added. Under nitrogen atmosphere catechol borane (**8**) (0.33 mL of a 1 M solution in THF) was introduced via syringe and the sealed tube kept at 70–80°C for 2 h. Thereafter, NaOH (17.6 mg, 0.44 mmol), $Pd(PPh_3)_4$ (17 mg, 0.02 mmol), 4-iodoacetophenone (**10a**) (37 mg, 0.15 mmol) and additional THF (3 mL) were added and the mixture kept for additional 4 h at 80°C. After cooling diethyl ether (20 mL) and NaOH (3N, 20 mL) were added and the mixture washed with brine. The organics were dried with $MgSO_4$ and concentrated. The crude product was chromatographed on silica gel (hexanes:diethyl ether=95:5 (v/v)) to afford **11a** (49 mg, 80%) as colourless solid; mp 154–155°C; R_f 0.21 (hexanes:ethyl acetate=8:2 (v/v)). ^{1}H NMR (400 MHz): δ=7.82 (d, J=8.5 Hz, 2H), 7.72 (d, J=8.0 Hz, 2H), 7.64 (d, J=14.6 Hz, 1H), 7.22–7.32 (m, 9H), 5.64 (d, J=14.5 Hz, 1H), 4.67 (s, 2H), 2.54 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz): δ=197.3 (s), 144.3 (s), 141.4 (s), 135.7 (s), 134.9 (s), 134.8 (s), 130.0 (d), 129.0 (d), 128.8 (d), 128.7 (d), 127.6 (d), 127.0 (d), 126.7 (d), 125.2 (d), 110.3 (d), 49.4 (t), 26.4 (q), 21.5 (q); IR (neat): ν: 3034, 1677, 1638, 1599, 1495, 1360, 1325, 1270, 1181, 1165, 1090, 1047, 944, 872 cm^{-1}; MS (EI), *m/z* (%): 405 (M^+, 59), 277 (9), 262 (15), 224 (16), 208 (11), 106 (36), 91 (100); Anal. Calcd. for $C_{24}H_{23}NO_3S$ (405.51): C, 71.08; H, 5.72; N, 3.45. Found: C, 70.82, H, 5.44, N, 3.38.

***N*-Benzyl-*N*-[(*E*)-2-(4-methoxyphenyl)ethenyl]-4-methylbenzenesulphonamide (11b).** Prepared according to the general procedure using **7** (73 mg, 0.26 mmol), **8** (0.38 mL of a 1 M solution in THF) and additional THF (2 mL). Thereafter NaOH (21 mg, 0.51 mmol), $Pd(PPh_3)_4$ (20 mg, 0.02 mmol), 4-iodoanisole (**10b**) (40 mg, 0.17 mmol) and THF (3 mL) were added. The crude product was chromatographed on silica gel (hexanes:diethyl ether=95:5 (v/v)) to afford **11b** (41 mg, 61%) as colourless solid; mp 119–120°C; R_f 0.37 (hexanes:ethyl acetate=8:2 (v/v)). ^{1}H NMR (400 MHz): δ=7.69–7.71 (m, 2H), 7.23–7.33 (m, 8H), 7.09–7.11 (m, 2H), 6.76–6.79 (m, 2H), 5.62 (d, J=14.6 Hz, 1H), 4.61 (s, 2H), 3.76 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz): δ=158.4 (s), 143.9 (s), 135.9 (s), 135.4 (s), 129.9 (d), 128.8 (s), 128.6 (d), 127.4 (d), 127.0 (d), 126.9 (d), 126.5 (d), 124.9 (d), 114.0 (d), 112.2 (d), 55.3 (q), 49.5 (t), 21.5 (q); IR (neat): ν=3033, 2925, 1644, 1608, 1512, 1454, 1356, 1249, 1163, 1091, 1031, 943, 807 cm^{-1}; MS (EI), *m/z* (%): 393 (M^+, 21), 238 (38), 121 (6), 91 (100); Anal. Calcd. for $C_{23}H_{23}NO_3S$ (393.50): C, 70.20; H, 5.89; N, 3.56. Found: C, 69.96, H, 5.67, N, 3.45.

***N*-[(*E*)-2-(1,3-Benzodioxol-5-yl)ethenyl)-*N*-benzyl-4-methylbenzenesulphonamide (11c).** From 4-bromo-1,2-methylenedioxybenzene (**10c**): Prepared according to the general procedure using **7** (61 mg, 0.21 mmol), **8** (0.32 mL of a 1 M solution in THF) and THF (2 mL). Thereafter NaOH (17 mg, 0.42 mmol), $Pd(PPh_3)_4$ (16 mg, 0.01 mmol), 4-bromo-1,2-methylenedioxybenzene (**10c**) (0.017 mL, 0.14 mmol) and additional THF (3 mL) were added. The crude product was chromatographed on silica gel (hexanes:diethyl ether=95:5 (v/v)) to afford **11c** (32 mg, 56%) as colourless solid.

From 4-iodo-1,2-methylenedioxybenzene (**10d**): Prepared according to the general procedure using **7** (70 mg, 0.24 mmol), **8** (0.37 mL of a 1 M solution in THF) and THF (2 mL). Thereafter NaOH (20 mg, 0.49 mmol), $Pd(PPh_3)_4$ (19 mg, 0.02 mmol), 4-iodo-1,2-methylenedioxybenzene (**10d**) (40 mg, 0.16 mmol) and additional THF (3 mL) were added. The crude product was chromatographed on silica gel (hexanes:diethyl ether=95:5 (v/v)) to afford **11c** (50 mg, 75%) as colourless solid; mp 163–164°C; R_f 0.32 (hexanes:ethyl acetate=8:2 (v/v)). ^{1}H NMR (400 MHz): δ=7.70 (d, J=8.4 Hz, 2H), 7.21–7.31 (m, 8H), 6.73 (d, J=1.5 Hz, 1H), 6.66 (d, J=8.0 Hz, 1H), 6.56 (dd, J=8.0 Hz, J=1.5 Hz, 1H), 5.89 (s, 2H), 5.58 (d, J=14.4 Hz, 1H), 4.60 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz): δ=148.0 (s), 146.3 (s), 144.0 (s), 135.9 (s), 135.3 (s), 130.5 (d), 129.9 (d), 128.6 (d), 127.5 (d), 127.0 (d), 126.8 (d), 125.3 (d), 119.7 (d), 112.3 (d), 108.3 (d), 105.0 (d), 101.0 (t), 49.5 (t), 21.5 (q); IR (neat): ν=2919, 1644, 1504, 1492, 1446, 1352, 1252, 1164, 1090, 1038, 812, 768, 737 cm^{-1}; MS (EI), *m/z* (%): 407 (M^+, 26), 332 (33), 252 (19), 222 (19), 91 (100), 77 (20), 32 (90); Anal. Calcd. for $C_{23}H_{21}NO_4S$ (407.49): C, 67.79; H, 5.19; N, 3.44. Found: C, 67.44, H, 5.31, N, 3.44.

***tert*-Butyl 5-((*E*)-2-{benzyl-[4-methylphenyl)sulphonyl]-amino}-ethenyl)-1*H*-indole-1-carboxylate (11d).** Prepared

according to the general procedure using **7** (62 mg, 0.22 mmol), **8** (0.32 mL of a 1 M solution in THF) and THF (2 mL). Thereafter NaOH (17 mg, 0.43 mmol), $Pd(PPh_3)_4$ (17 mg, 0.015 mmol), **10e** (43 mg, 0.15 mmol) and additional THF (3 mL) were added. The crude product was chromatographed on silica gel (hexanes:diethyl ether=95:5 (v/v)) to afford **11d** (55 mg, 75%) as colourless solid; mp 164–166°C; R_f 0.6 (hexanes:ethyl acetate=8:2 (v/v)). ^{1}H NMR (400 MHz): δ=7.98 (d, J=8.0 Hz, 1H), 7.73 (d, J=8.0 Hz, 2H), 7.53 (d, J=3.8 Hz, 1H), 7.45 (d, J=14.6 Hz, 1H), 7.22–7.36 (m, 8H), 7.15 (dd, J=8.7 Hz, J=1.6 Hz, 1H), 6.46 (d, J=3.8 Hz, 1H), 5.76 (d, J=14.6 Hz, 1H), 4.65 (s, 2H), 2.41 (s, 3H), 1.65 (s, 9H); ^{13}C NMR (100 MHz): δ=150.0 (s), 144.3 (s), 136.4 (s), 135.9 (s), 131.3 (s), 130.3 (d), 129.1 (s), 129.06 (d), 127.9 (d), 127.6 (s), 127.4 (d), 127.3 (d), 126.1 (d), 122.3 (d), 118.1 (d), 115.6 (d), 113.2 (d), 107.5 (d), 84.1 (s), 50.0 (t), 28.6 (q), 22.0 (q); IR (neat): ν=3303, 2979, 1731, 1643, 1470, 1369, 1258, 1227, 1164, 1132, 1087, 1025, 938, 734 cm^{-1}; MS (EI), m/z (%): 502 (M^+, 7), 402 (23), 291 (22), 247 (44), 156 (25), 106 (19), 91 (100); Anal. Calcd. for $C_{29}H_{30}N_2O_4S$ (502.63): C, 69.30; H, 6.02; N, 5.57. Found: C, 68.99, H, 5.60, N, 5.41.

***tert*-Butyl 3-iodo-1*H*-indole-1-carboxylate (14a) and 3-iodo-1-[(4-methylphenyl)sulphonyl]-1*H*-indole (14b).** A solution of I_2 (4.39 g, 17.28 mmol) in DMF (30 mL) was dropped into a solution of 1*H*-indole (**12a**) (2 g, 17.07 mmol) and KOH (2.39 g, 42.7 mmol) in DMF (30 mL) at room temperature and stirred for 0.45 h. The reaction mixture was poured into ice and water (400 mL) containing ammonia (0.5%) and sodium metabisulphite (0.1%). The white precipitate was filtered and washed with cold water. The obtained 3-iodo-1*H*-indole (**13a**) (4.15 g, 100%) was used without further purification.

3-Iodo-1*H*-indole (**13a**) (1.57 g, 6.46 mmol) was dissolved in CH_2Cl_2 (150 mL) and treated with Boc_2O (1.57 g, 7.17 mmol), triethylamine (2.7 mL), and DMAP (79.8 mg, 0.65 mmol) and was stirred at room temperature for 0.5 h. The solution was then washed twice with sodium metabisulphite (5%), dried with $MgSO_4$ and concentrated. Chromatography over silica gel (SiO_2, hexanes:diethyl ether=8:2 (v/v)) followed by crystallisation from pentane gave **14a** (1.94 g, 88%) as colourless solid, mp 36–40°C. ^{1}H NMR (400 MHz): δ=8.13 (d, J=8.1 Hz, 1H), 7.73 (s, 1H), 7.29–7.43 (m, 3H), 1.68 (s, 9H); ^{13}C NMR (100 MHz): δ=148.7 (s), 134.9 (s), 132.1 (s), 130.1 (d), 125.3 (d), 123.3 (d), 121.5 (d), 115.1 (d), 65.4 (s), 28.14 (q); MS (EI), m/z (%): 343 (M^+, 69), 287 (100), 270 (13), 243 (98), 116 (28), 57 (98); Anal. Calcd. for $C_{13}H_{14}INO_2$ (343.16): C, 45.50; H, 4.11; N, 4.08. Found: C, 45.37, H, 3.66, N, 3.96.

To a solution of 3-iodo-1*H*-indole (**13a**) (4.15 g, 17.07 mmol) in CH_2Cl_2 (50 mL) was added NaOH (819 mg, 20.46 mmol) and 4-methylbenzenesulphonyl chloride (3.96 g, 20.77 mmol) and stirred at room temperature for 5 h. The solution was washed with brine, dried with $MgSO_4$ and concentrated. Chromatography over silica gel (SiO_2, hexanes:diethyl ether=6:1 (v/v)) produced the desired product **14b**. An analytical pure sample (2.69 g, 40%) was obtained after crystallisation from CH_2Cl_2/pentane mp 238–139°C. ^{1}H NMR (400 MHz): δ=7.96 (d, J=8.7 Hz, 1H), 7.78 (d, J=8.7 Hz, 2H), 7.70 (s, 1H), 7.22–7.39 (m, 5H), 2.34 (s, 3H); ^{13}C NMR (100 MHz): δ=145.3 (s), 134.9 (s), 134.3 (s), 132.4 (s), 130.0 (d), 129.7 (d), 126.9 (d), 125.6 (d), 123.9 (d), 122.0 (d), 113.4 (d), 84.3 (s), 66.8 (s), 21.6 (q); MS (EI), m/z (%): 396 (M^+, 100), 242 (78), 155 (25), 115 (26), 91 (37); Anal. Calcd. for $C_{15}H_{12}INO_2S$ (397.23): C, 45.35; H, 3.04; N, 3.53. Found: C, 45.35, H, 2.81, N, 3.41.

***tert*-Butyl 3-iodo-5-methoxy-1*H*-indole-1-carboxylate (14c) and 3-iodo-5-methoxy-1-[(4-methylphenyl)sulphonyl]-1*H*-indole (14d). 14c** was prepared according to the above procedure using 3-iodo-5-methoxy-1*H*-indole (**13b**) (917 mg, 3.36 mmol), Boc_2O (879 mg, 4.02 mmol) and DMAP (82 mg, 0.67 mmol). Chromatography over silica gel (SiO_2, hexanes:diethyl ether=6:1(v/v) produced the desired product **14c** (1.23 g, 98%); mp 112–113°C. ^{1}H NMR (400 MHz): δ=8.03 (d, J=9.0 Hz, 1H), 7.71 (s, 1H), 6.99 (dd, J=9.0 Hz, J=2.5 Hz, 1H), 6.86 (d, J=2.5 Hz, 1H), 3.92 (s, 3H), 1.68 (s, 9H); ^{13}C NMR (100 MHz): δ=156.5 (s), 148.6 (s), 133.0 (s), 130.6 (d), 116.0 (d), 114.5 (d), 103.7 (d), 84.1 (s), 65.1 (s), 55.7 (d), 28.1 (q).

14d was prepared according to the above procedure using 5-methoxy-1*H*-indole (**12b**) (942 mg, 6.40 mmol), I_2 (1.64 g, 6.48 mmol) and KOH (661 mg, 11.77 mmol) giving 3-iodo-5-methoxy-1H-indole (**13b**) (1.53 g, 87%). The obtained crude product was immediately tosylated by using 3-iodo-5-methoxy-1*H*-indole (**13b**) (716 mg, 2.62 mmol), 4-methylbenzenesulphonyl chloride (750 mg, 3.93 mmol) and NaOH (126 mg, 3.15 mmol) in CH_2Cl_2. After column chromatography (SiO_2, hexanes:ethyl acetate=8:2 (v/v)) and crystallisation from CH_2Cl_2 **14d** (660 mg, 60%) was obtained as colourless solid, mp 174–175°C, R_f 0.46 (hexanes:ethyl acetate=8:2 (v/v)), ^{1}H NMR (400 MHz) δ=7.87 (d, J=9.0 Hz, 1H), 7.77 (d, J=8.4 Hz, 2H), 7.67 (s, 1H), 7.25 (d, J=9.0 Hz, J=2.5 Hz, 1H), 6.80 (d, J=2.5 Hz, 1H), 3.87 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz): δ=157.5 (s), 146.6 (s), 135.3 (s), 133.9 (s), 130.8 (d), 130.4 (d), 129.3 (s), 127.3 (d), 115.6 (d), 114.9 (d), 104.3 (d), 67.3 (s), 56.1 (q), 22.0 (q).

***tert*-Butyl 3-((*E*)-2-{benzyl-[(4-methylphenyl)sulphonyl]-amino}ethenyl)-1*H*-indole-1-carboxylate (15a).** Prepared according to the general procedure using **7** (154 mg, 0.54 mmol), **8** (0.54 mL of a 1 M solution in THF) and THF (2 mL). Thereafter NaOH (43 mg, 1.08 mmol), $Pd(PPh_3)_4$ (42 mg, 0.036 mmol), **14a** (124 mg, 0.36 mmol) and additional THF (5 mL) were added. The crude product was chromatographed on silica gel (hexanes:diethyl ether=19:1 (v/v)) to afford **15a** (104 mg, 58%) as colourless solid; mp 129–131°C; R_f 0.46 (hexanes:ethyl acetate=8:2 (v/v)). ^{1}H NMR (400 MHz): δ=8.12 (d, J=7.9 Hz, 1H), 7.74 (d, J=8.1 Hz, 2H), 7.49–7.55 (m, 2H), 7.42 (s, 1H), 7.21–7.37 (m, 9H), 5.73 (d, J=14.8 Hz, 1H), 4.67 (s, 2H), 2.41 (s, 3H), 1.64 (s, 9H); ^{13}C NMR (100 MHz): δ=149.5 (s), 144.1 (s), 135.8 (s), 135.7 (s), 135.3 (s), 130.0 (d), 128.7 (d), 128.6 (s), 127.6 (d), 127.0 (d), 126.9 (d), 126.6 (d), 124.6 (d), 122.8 (d), 121.7 (d), 119.4 (d), 117.1 (s), 115.4 (d), 103.8 (d), 83.8 (s), 49.4 (t), 28.2 (q), 21.6 (q); IR (neat): ν=3033, 2972, 2926, 1728, 1648, 1451, 1355, 1308, 1254,

1208, 1163, 1100, 1055, 1020, 946, 840, 814, 766 cm^{-1}; MS (EI), *m/z* (%): 502 (M^+, 5), 291 (21), 247 (20), 134 (32), 118 (22), 106 (22), 91 (100), 65 (27); Anal. Calcd. for $C_{29}H_{30}N_2O_4S$ (502.63): C, 69.30; H, 6.02; N, 5.57. Found: C, 68.91, H, 6.03, N, 5.43.

1-(4-Methylphenyl)sulphonyl-3-((*E*)-2-{benzyl[4-methylphenyl)sulphonyl]amino}ethenyl)-1*H*-indole (15b). Prepared according to the general procedure using **7** (64 mg, 0.22 mmol), **8** (0.27 mL of a 1 M solution in THF) and THF (2 mL). Thereafter NaOH (18 mg, 0.45 mmol), $Pd(PPh_3)_4$ (21 mg, 0.018 mmol), **14b** (59 mg, 0.15 mmol) and additional THF (3 mL) were added. The crude product was chromatographed on silica gel (hexanes:diethyl ether=19:1 (v/v)) to afford **15b** (59 mg, 71%) as colourless solid; mp 170–171°C; R_f 0.31 (hexanes:ethyl acetate=8:2 (v/v)). ^1H NMR (400 MHz): δ=7.95 (d, J=8.1 Hz, 1H), 7.74 (m, 2H), 7.73 (m, 2H), 7.52 (d, J=14.7 Hz, 1H), 7.44 (d, J=7.4 Hz, 1H), 7.18–7.38 (m, 12H), 5.66 (d, J=14.7 Hz, 1H), 4.66 (s, 2H), 2.42 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz): δ=144.9 (s), 144.2 (s), 135.8 (s), 135.3 (s), 135.2 (s), 135.1 (s), 130.0 (d), 129.9 (d), 128.9 (s), 128.7 (d), 127.6 (d), 127.4 (d), 127.0 (d), 126.9 (d), 126.8 (d), 124.9 (d), 123.4 (d), 121.7 (d), 119.9 (d), 119.0 (s), 113.7 (d), 102.6 (d), 49.5 (t), 21.53 (q), 21.51 (q); IR (neat): ν=3064, 2922, 1648, 1597, 1445, 1364, 1317, 1291, 1166, 1125, 1090, 1045, 978, 943, 837 cm^{-1}; MS (EI), *m/z* (%): 556 (M^+, 56), 401 (93), 246 (76), 155 (22), 91 (100), 44 (19); Anal. Calcd. for $C_{31}H_{28}N_2O_4S_2$ (556.70): C, 66.88; H, 5.07; N, 5.03. Found: C, 66.56, H, 4.91, N, 4.90.

***tert*-Butyl 3-((*E*)-2-{benzyl-[(4-methylphenyl)sulphonyl]-amino}ethenyl)-5-methoxy-1*H*-indole-1-carboxylate (15c).** Prepared according to the general procedure using **7** (132 mg, 0.46 mmol), **8** (0.56 mL of a 1 M solution in THF) and THF (2 mL). Thereafter NaOH (37 mg, 0.93 mmol), $Pd(PPh_3)_4$ (43 mg, 0.037 mmol), **14c** (115 mg, 0.31 mmol) and additional THF (5 mL) were added. The crude product was chromatographed on silica gel (hexanes:diethyl ether=19:1 (v/v)) to afford **15c** (122 mg, 74%) as colourless solid; mp 132–134°C; R_f 0.37 (hexanes:ethyl acetate=8:2 (v/v)). ^1H NMR (400 MHz): δ=7.74 (d, J=8.4 Hz, 2H), 7.47 (d, J=14.6 Hz, 1H), 7.25–7.41 (m, 9H), 6.90 (dd, J=8.9 Hz, J=2.4 Hz, 1H), 6.87 (d, J=2.4 Hz, 1H), 5.69 (d, J=14.6 Hz, 1H), 4.68 (s, 2H), 3.82 (s, 3H), 2.42 (s, 3H), 1.63 (s, 9H); ^{13}C NMR (100 MHz): δ=155.9 (s), 149.5 (s), 144.1 (s), 135.9 (s), 135.4 (s), 130.3 (s), 130.0 (d), 129.5 (s), 128.7 (d), 127.5 (d), 126.99 (d), 126.95 (d), 126.5 (d), 122.1 (d), 116.9 (s), 116.0 (d), 113.0 (d), 103.7 (d), 102.2 (d), 83.6 (s), 55.7 (q), 49.5 (t), 28.2 (q), 21.6 (q); IR (neat): ν=2979, 2927, 1728, 1652, 1478, 1452, 1390, 1369, 1349, 1338, 1318, 1304, 1273, 1212, 1161, 1092, 1018, 946, 836 cm^{-1}; MS (EI), *m/z* (%): 533 (M^+, 38), 448 (35), 447 (100), 445 (36), 357 (46), 356 (39), 343 (81), 342 (40), 329 (35), 328 (45); Anal. Calcd. for $C_{30}H_{32}N_2O_5S$ (532.66): C, 67.65; H, 6.06; N, 5.26. Found: C, 67.60, H, 6.07, N, 5.14.

1-(4-Methylphenyl)sulphonyl-3-((*E*)-2-{benzyl[4-methylphenyl)sulphonyl]amino}ethenyl)-5-methoxy-1*H*-indole (15d). Prepared according to the general procedure using **7** (130 mg, 0.46 mmol), **8** (0.55 mL of a 1 M solution in THF) and THF (2 mL). Thereafter NaOH (37 mg, 0.91 mmol), $Pd(PPh_3)_4$ (42 mg, 0.036 mmol), **14d** (130 mg, 0.30 mmol) and additional THF (5 mL) were added. The crude product was chromatographed on silica gel (hexanes:diethyl ether=19:1 (v/v)) to afford **15d** (149 mg, 84%) as colourless solid; mp 173–174°C; R_f 0.27 (hexanes:ethyl acetate=8:2 (v/v)). ^1H NMR (400 MHz): δ=7.83 (d, J=8.9 Hz, 1H), 7.74 (d, J=8.5 Hz, 2H), 7.69 (d, J=8.5 Hz, 2H), 7.43 (d, J=14.6 Hz, 1H), 7.16–7.36 (m, 10H), 6.89 (dd, J=8.9 Hz, J=2.3 Hz, 1H), 6.76 (d, J=2.3 Hz, 1H), 5.59 (d, J=14.6 Hz, 1H), 4.66 (s, 2H), 3.77 (s, 3H), 2.42 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz): δ=156.4 (s), 144.8 (s), 144.2 (s), 135.8 (s), 135.3 (s), 135.0 (s), 130.1 (s), 130.0 (d), 129.9 (s), 129.8 (d), 128.7 (d), 127.6 (d), 127.3 (d), 127.0 (d), 126.9 (d), 126.7 (d), 122.2 (d), 119.1 (s), 114.6 (d), 113.7 (d), 102.4 (d), 102.3 (d), 55.6 (q), 49.5 (t), 21.54 (q), 21.50 (q); IR (neat): ν=2924, 1651, 1597, 1495, 1473, 1454, 1363, 1214, 1166, 1122, 1090, 1038, 980, 944, 813 cm^{-1}; MS (EI), *m/z* (%): 586 (M^+, 9), 431 (15), 407 (10), 276 (36), 183 (13), 144 (15), 91 (100), 77 (11); Anal. Calcd. for $C_{32}H_{30}N_2O_5S_2$ (586.73): C, 65.51; H, 5.15; N, 4.77. Found: C, 65.49, H, 5.23, N, 4.67.

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References

1. (a) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147. (b) Suzuki, A. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998. (c) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. For the hydroboration of alkynes, see: (d) Brown, H. C. *Organic Syntheses via Boranes*; Wiley: New York, 1975. (e) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1971**, *93*, 1816. (f) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1972**, *94*, 4370. (g) Lane, C. F.; Kabalka, G. W. *Tetrahedron* **1976**, *32*, 981.

2. For representative examples of Suzuki–Miyaura cross-coupling reaction in the synthesis of natural products see: (a) Alvarez, R.; de Lera, A. R. *Tetrahedron: Asymmetry* **1998**, *9*, 3065. (b) White, J. D.; Kim, T.-S.; Nambu, M. *J. Am. Chem. Soc.* **1995**, *117*, 5612. (c) Cassani, G.; Massardo, P.; Piccardi, P. *Tetrahedron Lett.* **1983**, *24*, 2513. (d) Nicolaou, K. C.; Sorensen, E. J. *Classics in Total Synthesis*; VCH: Weinheim, 1996.

3. (a) Kamabuchi, A.; Moriya, T.; Miyaura, N.; Suzuki, A. *Synth. Commun.* **1993**, *23*, 2851. (b) Brown, H. C.; Ravindran, N.; Kulkarni, S. U. *J. Org. Chem.* **1980**, *45*, 384. (c) Brown, H. C.; Campbell, J. B., Jr. *J. Org. Chem.* **1980**, *45*, 389. (d) Brown, H. C.; Bhat, N. G.; Somayaji, V. *Organometallics* **1983**, *2*, 1311.

4. (a) Brown, H. C.; Blue, C. D.; Nelson, D. J.; Bhat, N. G. *J. Org. Chem.* **1989**, *54*, 6064. (b) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086.

5. (a) Zweifel, G.; Lewis, W.; On, H. P. *J. Am. Chem. Soc.* **1979**, *101*, 5101. (b) Fisher, R. P.; On, H. P.; Snow, J. T.; Zweifel, G. *Synthesis* **1982**, 127. (c) Masuda, Y.; Suyama, T.; Murata, M.; Watanabe, S. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2955.

6. (a) Brown, H. C.; Subrahmanyam, C.; Hamaoka, T.; Ravindran, N.; Bowman, D. H.; Misumi, S.; Unni, M. K.; Somayaji, V.; Bhat, N. G. *J. Org. Chem.* **1989**, *54*, 6068. (b) Brown, H. C.; Imai, T. *Organometallics* **1984**, *3*, 1392. (c) Campbell, J. B., Jr.; Molander, G. A. *J. Organomet. Chem.* **1978**, *156*, 71. (d) Brown, H. C.; Somayaji, V. *Synthesis* **1984**, 919.

7. (a) Hegedus, L. S.; Toro, J. L.; Miles, W. H.; Harrington, P. J. *J. Org. Chem.* **1987**, *52*, 3319. (b) Satoh, M.; Miyaura, N.; Suzuki, A. *Synthesis* **1987**, 373. (c) Miyaura, N.; Maeda, K.; Suginome, H.; Suzuki, A. *J. Org. Chem.* **1982**, *47*, 2117.

8. (a) Gridnev, I. D.; Miyaura, N.; Suzuki, A. *J. Org. Chem.* **1993**, *58*, 5351. (b) Gridnev, I. D.; Miyaura, N.; Suzuki, A. *Organometallics*, **1993**, *12*, 589; the direct hydroboration of 1-thio-1-alkynes is less regioselective and preferentially places the boron *alpha* to sulphur leading to regioisomeric analogues of the catalysed version: (c) Hoshi, M.; Masuda, Y.; Arase, A. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 447. (d) Gerard, J.; Bietlot, E.; Hevesi, L. *Tetrahedron Lett.* **1998**, *39*, 8735.

9. For reviews discussing the chemistry of ynamines, see: (a) Himbert, G. In *Methoden Org. Chem. (Houben-Weyl)*, 1993, Vol. E15, p 3267. (b) Collard-Motte, J.; Janousek, Z. *Top. Curr. Chem.* **1986**, *130*, 89. (c) Pitacco, G.; Valentin, E. In *The Chemistry of Amino, Nitroso and Nitro Compounds and their Derivatives, Supplement F, Part 1*; Patai, S., Ed.; Wiley: New York, 1982, p 624. (d) Ficini, J. *Tetrahedron* **1976**, *32*, 1449.

10. Witulski, B.; Stengel, T. *Angew. Chem.* **1998**, *110*, 495; *Angew. Chem. Int. Ed.* **1998**, *37*, 489.

11. Witulski, B.; Gößmann, M. *Chem. Commun.* **1999**, 1879.

12. (a) Witulski, B.; Stengel, T. *Angew. Chem.* **1999**, *111*, 2521; *Angew. Chem. Int. Ed.* **1999**, *38*, 2426. (b) Witulski, B.; Stengel, T.; Fernández-Hernández, J. M. *Chem. Commun.* **2000** (in press); for other recent examples on ynamide cycloadditions, see: (c) Rainier, J. D.; Imbriglio, E. *Org. Lett.* **1999**, *1*, 2037. (d) Hsung, R. P.; Zificsak, C. A.; Wie, L.-L.; Douglas, C. J.; Xiong, H.; Mulder, J. A. *Org. Lett.* **1999**, *1*, 1237.

13. (a) Toske, S. G.; Jensen, P. R.; Kauffman, C. A.; Fenical, W. *Tetrahedron* **1998**, *54*, 13459. (b) Umezawa, H.; Imoto, M.; Sawa, T.; Isshiki, K.; Matsuda, N.; Uchida, T.; Inuma, H.; Hamada, M.; Takeuchi, T. *J. Antibiot.* **1986**, *39*, 170. (c) Nakamura, H.; Iitaka, Y.; Imoto, M.; Isshiki, K.; Naganawa, H.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1986**, *39*, 314. (d) Okuma, K.; Anzai, K.; Suzuki, S. *J. Antibiot.* **1962**, *15A*, 115.

14. (a) Ziegenbein, W.; Franke, W. *Chem. Ber.* **1957**, *90*, 2291. (b) Harada, T.; Ohno, T.; Kobayashi, S.; Mukaiyama, T. *Synthesis* **1991**, 1216. (c) Brettle, R.; Shibib, S. M.; Wheeler, K. J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 831. (d) Redeker, U.; Engel, N.; Steglich, W. *Tetrahedron Lett.* **1981**, *22*, 4263. (e) Kuramochi, K.; Watanabe, H.; Kitahara, T. *Synlett* **2000**, 397. (f) Brettle, R.; Mosedale, A. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2185. (g) Laso, N. M.; Quiclet-Sire, B.; Zard, S. Z. *Tetrahedron Lett.* **1996**, *37*, 1605. (h) Meuzelaar, G.; Blom, A.; Maat, L.; Sheldon, R. A. *Eur. J. Org. Chem.* **1999**, 519.

15. Busacca, C. A.; Johnson, R. E.; Swestock, J. *J. Org. Chem.* **1993**, *58*, 3299.

16. Ogawa, T.; Kiji, T.; Hayami, K.; Suzuki, H. *Chem. Lett.* **1991**, 1443.

17. For the preparation of **5** and the discussion of the chemistry of alkynyliodonium salts, see: (a) Stang, P. J. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Eds.; VCH: Weinheim, 1995. (b) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123.

18. The hydroboration of the electron rich (*N*-methyl, *N*-phenyl)-1-alkynylamine failed under these conditions and gave only tarry decomposition products.

19. (a) Pindur, U.; Otto, C. *Tetrahedron* **1992**, *48*, 3515. (b) Pindur, U. *Heterocycles* **1988**, *27*, 1253. (c) Schlecht, M. F.; Giadinoto, S. *Heterocycles* **1987**, *25*, 485. (d) Akgün, E.; Pindur, U. *J. Heterocyclic Chem.* **1985**, *22*, 585.

20. **Crystal data for 15d:** STOE Imaging Plate Diffraction System, graphite monochromator, Mo K_α radiation (λ= 0.71073 Å), cell determination and refinement by STOE programmes Ver. 2.75, structure solution by direct methods (SHELXS-86)[21] and structure refinement by SHELXL-93,[22] hydrogen atoms were included in the refinement using riding models. $C_{32}H_{30}N_2O_5S_2$; M=586.70 g mol^{-1}; triclinic; space group $P\bar{1}$ (No. 2); lattice constants a=9.999(2), b=12.089(2), c=13.208(3) Å, α=88.19(3), β=87.94(3), g=68.49(3)°, V= 1484.1(5) Å^3; Z=2; $D_{cal.}$=1.313 Mg/m^3; μ=2.23 cm^{-1}; T= 293(2) K; crystal size 0.80×0.35×0.20 mm^3; $2.19 \leq \Theta \leq 26.20°$. 14688 reflections collected, 5429 independent reflections ($R_{int.}$=0.0433); 373 parameters; $w^{-1}=[\sigma^2(F_o^2)+ (0.0452P)^2]$ and $P=[(F_o^2)+2F_c^2]/3$; R^1=0.0387, wR^2=0.0933 for 2529 reflections with $I>2\sigma(I)$ and R^2=0.0760, wR^2=0.1102 for all data; residual electron density 264 e nm^{-3} and −230 e nm^{-3}, S=*GOF* (on F^2)=1.206. Crystallographic data of **15d** were deposited with the Cambridge Crystallographic Data Centre. CCDC reference number: 148382.

21. Sheldrick, G. M. SHELXS-86, Program for Crystal Structure Solution, University of Göttingen, 1990.

22. Sheldrick, G. M. SHELXL-93, Program for Crystal Structure Refinement, University of Göttingen, 1993.

23. (a) Ottoni, O.; Cruz, R.; Alves, R. *Tetrahedron* **1998**, *54*, 13915. (b) Kelly, T. A.; McNeil, D. W.; Rose, J. M.; David, E.; Shih, C.-K.; Grob, P. M. *J. Med. Chem.* **1997**, *40*, 2430. (c) Bocchi, V.; Palla, G. *Synthesis* **1982**, 1096.