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Synthesis of ynamides from formamides

David Brückner*

Fachbereich Chemie, Philipps-Universität Marburg, Hans-Meerwein-Strasse, D-35032 Marburg, Germany

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Abstract—*N*-Formyl-tosylamides can be efficiently converted to *N*-ethynyl-tosylamides in two steps via the corresponding dichlorovinylamides.

1. Introduction

The chemistry of ynamines has been studied extensively in the past.[1] However, their sensitivity and difficulties in their preparation prevented broader application in synthetic chemistry so far.[2] Ynamides,[3] however, are electron deficient and hence possess a significantly higher stability, which makes them valuable synthetic building blocks.[4,5] In recent years, the chemistry of ynamides has attracted many chemists resulting in a multitude of publications demonstrating the synthetic potential of ynamides for various applications such as cycloadditions[6,7] and cycloisomerizations,[8] transition metal-catalyzed coupling reactions,[9,10] radical cyclizations,[11] ring-closing metatheses,[12,13] acid-catalyzed hydroarylations,[14] hydrohalogenations,[15] carbometallations[16] and rearrangement reactions.[17,18]

Among the practical and commonly used syntheses of ynamides[4] are the reaction of a deprotonated amide with a hypervalent iodine salt,[6,19] N-alkynylation of amides by alkynyl bromides,[20] and the base-catalyzed isomerization of propargyl amides.[12,21]

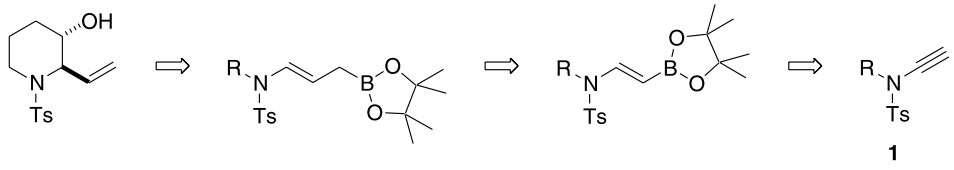
We report here the synthesis of *N*-ethynyl-tosylamides **1** from formamides in two steps employing cheap, readily available reagents, which might be advantageous to larger scales. Since our first publication[22] this method has already been utilized by other groups.[8,10,13,18,23]

2. Results and discussion

In the course of our research into intramolecular allylborations aiming at the stereoselective formation of substituted piperidine rings,[24] we envisaged to start the synthesis of the mandatory allylboronic ester from an ynamide **1** (see Scheme 1). At that time we thought of trying to synthesize the desired ynamides in a novel manner.

Inspired by the well-known conversion of aldehydes to alkynes developed by Corey and Fuchs[25] we planned to transfer this method to the conversion of formamides **3** to ynamides **1** (see Scheme 2).

As only a few *N*-formyl-tosylamides **3** had been described before,[26,27] we explored new and general methods to synthesize these mixed imides. Two strategies proved to be successful: formylation of substituted tosylamides **4** and alkylation of *N*-formyl-toluenesulfonamide[26] (**6**), respectively (Scheme 3 and Table 1).[28]



Scheme 1. Retrosynthetic path from allylboronic esters to ynamides.

Keywords: Ynamides; Formamides; Alkenation; Enamides; Mixed imides.
* Present address: Bayer HealthCare AG, Aprather Weg, 42096 Wuppertal, Germany. Tel.: +49 202 368512; e-mail: david.brueckner@bayerhealthcare.com

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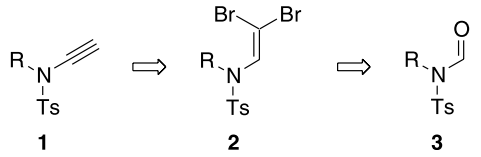
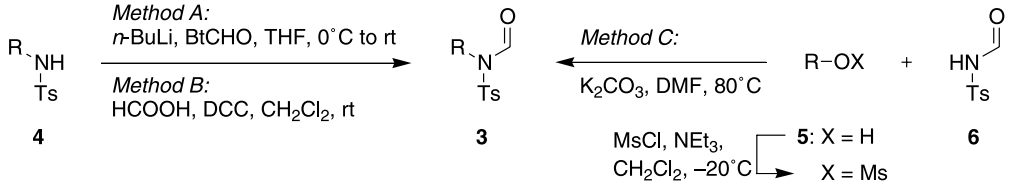


Scheme 2. Synthetic plan towards ynamides.

formic acid in the presence of dicyclohexylcarbodiimide[30] provided the *N*-formylated tosylamide **3f** in excellent yield (Scheme 3, Method B). Preparation of formamides **3** directly from an alcohol is also possible as shown in entry 4 (Table 1). Here, alkylation of **6** with the mesylate generated from alcohol **5d** afforded formamide **3d** in moderate yield (Scheme 3, Method C).[31]



Scheme 3. Different preparations of *N*-formyl-tosylamides **3**.

Table 1. Preparation of *N*-formyl-tosylamides **3**

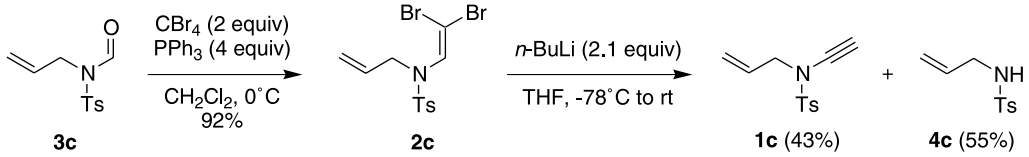
Entry	R	Method	3	Yield (%)[a]
1	*n*-Bu	A	**a**	95
2	*i*-Pr	A	**b**	85
3	$-CH_2CH_2=CH_2$	A	**c**	93
4	$-CH_2C(CH_3)=CH_2$	C	**d**	49
5	Bn	A	**e**	90
6	Ph	B	**f**	99

[a] Isolated yield of analytically pure product.

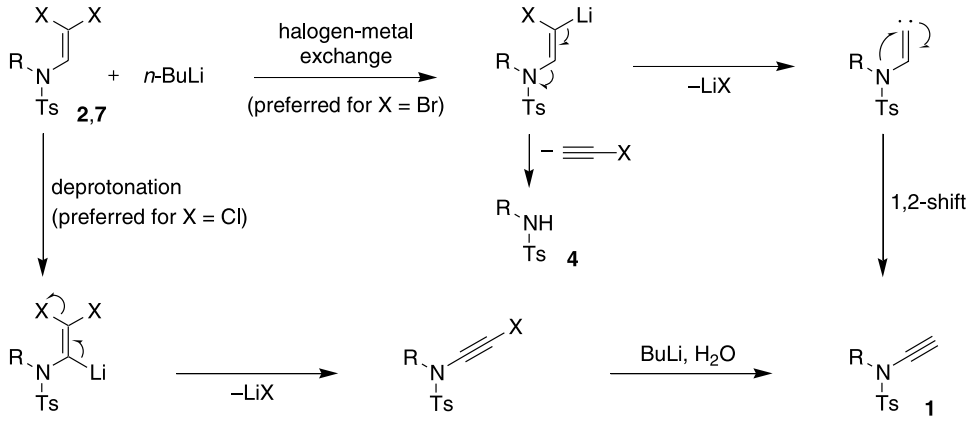
Formylation of **4a–c,e** succeeded with high yields by deprotonating the amide with *n*-butyllithium in THF followed by treatment with formylbenzotriazole (BtCHO),[29] which is easy to prepare and to handle (Scheme 3, Method A). In the case of phenyl toluenesulfonamide **4f** (Table 1, entry 6) this method gave unsatisfactory conversion (53%), possibly because of its lower nucleophilicity. Here, reaction with

The required formamides in hand, we applied the protocol for dibromomethylenation described by Corey and Fuchs.[25] Reaction of **3c** with triphenylphosphine and CBr_4 afforded the dibromoenamide **2c** in very good yield. However, the following step—treatment with *n*-butyllithium—resulted in a mixture of the desired ynamide **1c** and tosylamide **4c** (see Scheme 4).

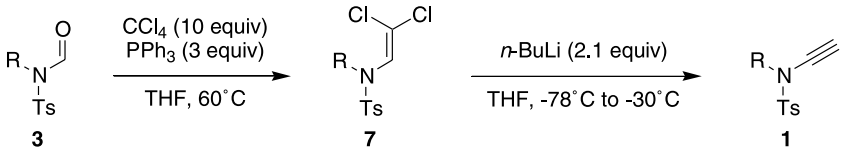
A possible explanation of this result is given in Scheme 5. The initial bromo–lithium exchange is followed by two competing eliminations, that of lithiumbromide or of bromoacetylene, respectively, resulting in a mixture of **1** and **4** (in which the *E*/*Z*-selectivity of the bromo–lithium exchange certainly will have an impact on the **1**:**4**-ratio). But a second reaction sequence is conceivable as well. If the initial step is a deprotonation, an elimination of lithium halogenide should follow leading to the triple bond. A cleavage of the C–N bond appears to be unlikely here. We hoped to promote the second pathway by switching



Scheme 4. Synthesis of ynamides via dibromovinylamides.



Scheme 5. Proposed mechanism of the reaction of dihalovinylamides with *n*-BuLi.



Scheme 6. Synthesis of ynamides via dichlorovinylamides.

from bromine to chlorine as the chlorine-lithium exchange is significantly slower.

The dichloromethylenation of esters and lactones to 2,2-dichlorovinylethers is a well-studied reaction,[32] however, the corresponding conversion of formamides to dichlorovinylamines had not been described yet. Nevertheless, treatment of formamides **3** with triphenylphosphine (3 equiv) and excess tetrachloromethane (10 equiv, slow addition) in tetrahydrofuran at 60 °C proceeded very well and lead to the dichlorovinylamides **7a–f** in excellent yields (Scheme 6 and Table 2). Subsequent dehalogenation of **7** with *n*-butyllithium (2.1 equiv) in tetrahydrofuran at −78 °C and quenching at −30 °C with methanol afforded the desired ynamides **1a–f** in very good yields (Table 2). Formation of undesired tosylamides **4** was not observed supporting the proposed reaction mechanism (Scheme 5). *N*-Ethynyl-tosylamides **1** are nearly colorless crystalline solids that can be purified by chromatography on aluminum oxide or silica gel (the latter can slightly diminish the yield). As shown in Table 2, both steps gave good to excellent yields for a variety of substituents with diverse steric demands and electronic properties.

Table 2. Conversion of formamides to dichlorovinylamides **7** and ynamides **1**

Entry	3	R	7	Yield (%)[a]	1	Yield (%)[a]
1	**a**	*n*-Bu	**a**	99	**a**	86
2	**b**	*i*-Pr	**b**	96	**b**	93
3	**c**	$-CH_2CH_2{=}CH_2$	**c**	97	**c**	81
4	**d**	$-CH_2C(CH_3){=}CH_2$	**d**	97	**d**	95
5	**e**	Bn	**e**	96	**e**	80
6	**f**	Ph	**f**	81	**f**	97

[a] Isolated yield of analytically pure product.

This procedure may also be applied to the synthesis of ynolethers[22] serving as an alternative to Greene's one-pot synthesis.[33]

3. Conclusion

A facile, reliable and high-yielding procedure for the preparation of *N*-ethynyl-tosylamides has been developed that employs non-expensive, readily available starting materials allowing for easy scale up.

4. Experimental

4.1. General

All reactions were carried out under an argon atmosphere. All starting materials were purchased from commercial sources and used without further purification. Solvents were dried prior to use by standard methods. Boiling range of petroleum ether (PE): 40–60 °C. All temperatures quoted are uncorrected. ^{1}H and ^{13}C NMR spectra were acquired on Bruker ARX-200 and AC-300 spectrometers. Flash chromatography was performed on silica gel Si60 (40–60 μm; E. Merck KGaA, Darmstadt).

4.2. Syntheses of formamides 3

4.2.1. *N*-Formyl-*N*-isopropyl-4-methyl-benzenesulfonamide (3b) (representative procedure for the formylation of tosylamides 4, Method A). A solution of **4b** (213 mg, 1 mmol) in THF (5 mL) at 0 °C was treated with *n*-BuLi (670 μL, 1.64 M in hexane, 1.1 mmol). After 5 min, a solution of formylbenzotriazole (177 mg, 1.2 mmol) in THF (2 mL) was added and the mixture stirred for 2 h at rt. Dilution with *tert*-butyl methyl ether (TBME, 20 mL) and workup with satd $NaHCO_3$ (15 mL) followed by flash chromatography on silica gel (pentane/TBME 5:1) afforded formamide **3b** (205 mg, 85%) as a colorless crystalline solid. R_f 0.52 (PE/EtOAc 5:1); mp 38–39 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.26$ (d, $J=6.9$ Hz, 6H), 2.47 (s, 3H), 4.11 (septd, $J=6.9$, 1.3 Hz, 1H), 7.36–7.42 (m, 2H), 7.74–7.79 (m, 2H), 9.11 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) $\delta=19.5$, 21.6, 50.0, 127.4 (2C), 130.2 (2C), 135.6, 143.2, 161.6. Anal. Calcd for $C_{11}H_{15}NO_3S$: C 54.75, H 6.27, N 5.80; Found: C 54.82, H 6.11, N 5.92.

4.2.2. *N*-Butyl-*N*-formyl-4-methyl-benzenesulfonamide (3a). According to Method A starting from compound **4a**, yield 95% (1 mmol scale, 241 mg), colorless oil. R_f 0.31 (PE/EtOAc 5:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=0.86$ (t, $J=7.3$ Hz, 3H), 1.18–1.37 (m, 2H), 1.45–1.57 (m, 2H), 2.46 (s, 3H), 3.38–3.45 (m, 2H), 7.35–7.40 (m, 2H), 7.71–7.77 (m, 2H), 9.09 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) $\delta=13.9$, 20.3, 22.0, 30.7, 43.0, 127.8 (2C), 130.6 (2C), 135.6, 145.8, 161.7. Anal. Calcd for $C_{12}H_{17}NO_3S$: C 56.45, H 6.71, N 5.49; Found: C 56.39, H 6.73, N 5.70.

4.2.3. *N*-Allyl-*N*-formyl-4-methyl-benzenesulfonamide (3c). According to Method A starting from compound **4c**, yield 93% (0.74 mmol scale, 165 mg), colorless crystalline solid. R_f 0.26 (PE/EtOAc 5:1); mp 43 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=2.46$ (s, 3H), 4.11 (dt, $J=6.0$, 1.3 Hz, 2H), 5.08 (dq, $J=10.2$, 1.0 Hz, 1H), 5.15 (dq, $J=17.2$, 1.0 Hz, 1H), 5.60 (ddt, $J=17.0$, 10.3, 6.0 Hz, 1H), 7.36 (d, $J=8.1$ Hz, 2H), 7.74 (d, $J=8.3$ Hz, 2H), 9.11 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) $\delta=21.6$, 44.6, 119.0, 127.5 (2C), 130.2 (2C), 130.7, 135.2, 145.5, 160.9. Anal. Calcd for $C_{11}H_{13}NO_3S$: C 55.21, H 5.48, N 5.85; Found: C 55.06, H 5.21, N 5.81.

4.2.4. *N*-Benzyl-*N*-formyl-4-methyl-benzenesulfonamide (3e). According to Method A starting from compound **4e**, yield 90% (2 mmol scale, 518 mg), colorless crystalline solid. R_f 0.38 (PE/EtOAc 5:1); mp 95–96 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.40 (s, 3H), 4.72 (s, 2H), 7.17–7.20 (m, 5H), 7.20–7.25 (m, 2H), 7.53–7.59 (m, 2H), 9.19 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=21.6, 45.7, 127.3, 127.7, 128.36, 128.42, 130.0, 134.6, 135.3, 145.2, 161.5. Anal. Calcd for $C_{15}H_{15}NO_3S$: C 62.26, H 5.23, N 4.84; Found: C 62.16, H 5.28, N 4.90.

4.2.5. *N*-Formyl-*N*-phenyl-4-methyl-benzenesulfonamide (3f) (Method B). Tosylamide **4f** (247 mg, 1 mmol) was dissolved in CH_2Cl_2 (1 mL) and treated successively with formic acid (75 μL, 2 mmol) and DCC (516 mg, 2.5 mmol). The temperature rose to 40 °C. The mixture was stirred for 24 h, diluted with CH_2Cl_2 (10 mL) and filtered over a short pad of Celite. After removal of the solvent the residue was purified by flash chromatography on silica gel (pentane/TBME 4:1) to give formamide **3f** (274 mg, 99%) as colorless crystals. R_f 0.60 (CH_2Cl_2+2% acetone); mp 117–118 °C (lit.[27] mp 133 °C); ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.45 (s, 3H), 6.90–6.95 (m, 2H), 7.27–7.45 (m, 5H), 7.54–7.59 (m, 2H), 9.32 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=21.7, 128.0 (2C), 129.4 (2C), 129.86, 129.88 (2C), 130.0 (2C), 132.0, 134.2, 145.7, 161.1. Anal. Calcd for $C_{14}H_{13}NO_3S$: C 61.07, H 4.76, N 5.09; Found: C 60.96, H 4.89, N 5.20.

4.2.6. *N*-Formyl-*N*-(2-methyl-allyl)-4-methyl-benzenesulfonamide (3d) (Method C). A solution of 2-methyl-allylalcohol (**5d**) (505 μL, 6 mmol) and triethylamine (1.25 mL, 9 mmol) in CH_2Cl_2 (20 mL) was cooled to −20 °C. Methanesulfonyl chloride (604 μL, 7.8 mmol) was added and the mixture stirred for 1.5 h. Dilution with diethylether (20 mL) and aqueous workup with satd NH_4Cl (20 mL) furnished the crude mesylate, which was dissolved in DMF (3 mL). *N*-Formyltoluenesulfonamide[26] (**6**) (598 mg, 3 mmol) and K_2CO_3 (622 mg, 4.5 mmol) were added and the mixture heated to 80 °C for 14 h. Workup with TBME (3×20 mL) and satd $NaHCO_3$ (20 mL) followed by flash chromatography on silica gel (pentane/TBME 6:1) furnished formamide **3d** (370 mg, 49%) as a colorless crystalline solid. R_f 0.31 (PE/EtOAc 5:1); mp 49 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.55 (s, 3H), 2.46 (s, 3H), 4.08 (s, 2H), 4.77–4.79 (m, 1H), 4.80–4.83 (m, 1H), 7.33–7.35 (m, 2H), 7.35–7.38 (m, 2H), 9.17 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=19.8, 21.6, 47.5, 113.5, 127.6 (2C), 130.1 (2C), 135.1, 138.2, 145.5, 161.2. Anal. Calcd for $C_{12}H_{15}NO_3S$: C 56.90, H 5.97, N 5.53; Found: C 57.05, H 6.14, N 5.75.

4.2.7. *N*-Formyltoluenesulfonamide (6).[26] Toluenesulfonyl amide (8.56 g, 50 mmol) was added to a solution of sodium methylate (1.50 g, 65 mmol) in methanol (100 mL). The solution was warmed to 40 °C for 30 min before ethyl formate (20.2 mL, 250 mmol) was added dropwise. Stirring at 40 °C was continued overnight. Subsequently, the mixture was acidified (pH 3–4) with 2 M HCl, solvents removed in vacuo, the residue taken up in water (50 mL), and the acidified (2 M HCl) mixture extracted with MTBE (5×50 mL). To remove not converted starting material, the crude product was dissolved in MTBE (50 mL) and thoroughly washed with satd $NaHCO_3$ (100 mL). The aqueous phase was acidified (2 M HCl) and extracted with MTBE (4×50 mL) to give **6** (8.7 g, 87%) as a colorless crystalline solid. R_f 0.20 (CH_2Cl_2/MTBE 5:1); mp 102–103 °C (MTBE); ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.46 (s, 3H), 7.37 (m, 2H), 7.80 (m, 2H), 8.50 (br s, 1H), 8.65 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=21.6, 127.0, 130.2, 136.1, 145.6, 162.0.

4.3. Syntheses of dihaloenamides 2 and 7

4.3.1. *N*-Allyl-*N*-(2,2-dibromovinyl)-4-methyl-benzenesulfonamide (2c). A solution of PPh_3 (6.03 g, 23 mmol) in CH_2Cl_2 (15 mL) was cooled to 0 °C and CBr_4 (3.81 g, 11.5 mmol) was added. After 1 h formamide **3c** (1.38 g, 5.75 mmol) dissolved in CH_2Cl_2 (8 mL) was added. Stirring was continued for 3 h at 0 °C and 4 h at rt. PE (25 mL) was added and the mixture was filtered, the solid residue dissolved in CH_2Cl_2 (15 mL) and precipitated by addition of pentane (15 mL). Filtration–dissolution–precipitation was repeated once more. The combined filtrates were concentrated and the crude product was purified by flash chromatography on silica gel (pentane/TBME 8:1) to give dibromovinylamide **2c** (2.10 g, 92%) as a colorless crystalline solid. R_f 0.30 (PE/EtOAc 5:1); mp 100 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=2.42 (s, 3H), 3.98 (dt, J=6.3, 1.3 Hz, 2H), 5.10–5.23 (m, 2H), 5.69 (ddt, J=16.9, 10.2, 6.5 Hz, 1H), 6.68 (s, 1H), 7.31 (m, 2H), 7.69 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ=21.6, 51.8, 95.7, 119.5, 127.4 (2C), 129.9 (2C), 131.3, 131.8, 135.6, 144.2. Anal. Calcd for $C_{12}H_{13}Br_2NO_2S$: C 36.48, H 3.32, N 3.54; Found: C 36.50, H 3.46, N 3.41.

4.3.2. *N*-(2,2-Dichlorovinyl)-*N*-isopropyl-4-methyl-benzenesulfonamide (7b) (representative procedure for the dichloromethylenation of formamides 3). Formamide **3b** (172 mg, 0.71 mmol) and PPh_3 (559 mg, 2.13 mmol) were dissolved in THF (7 mL). CCl_4 (687 μL, 7.1 mmol) was added via syringe over a period of 6 h at 60 °C. After stirring for an additional hour, the mixture was diluted with TBME (15 mL). Aqueous workup with satd $NaHCO_3$ (15 mL) afforded after flash chromatography on silica gel (pentane/TBME 6:1) dichlorovinylamide **7b** (210 mg, 96%) as a pale yellow crystalline solid. R_f 0.62 (PE/EtOAc 5:1); mp 86–87 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.02 (d, J=6.7 Hz, 6H), 2.43 (s, 3H), 4.21 (sept, J=6.7 Hz, 1H), 6.08 (s, 1H), 7.30–7.33 (m, 2H), 7.70–7.74 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=20.3, 21.5, 52.5, 121.0 (*C*=CCl_2), 127.3 (2C), 129.7 (2C), 132.7 (C=*C*Cl_2), 136.7, 143.8. Anal. Calcd for $C_{12}H_{15}NO_2SCl_2$: C 46.76, H 4.91, N 4.54; Found: C 46.77, H 4.95, N 4.53.

4.3.3. *N*-Butyl-*N*-(2,2-dichlorovinyl)-4-methyl-benzenesulfonamide (7a). As described for compound **7b** starting from compound **3a**, yield 99% (1.46 mmol scale, 464 mg), yellowish crystalline solid. R_f 0.43 (PE/EtOAc 5:1); mp 66 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.90 (t, J=7.1 Hz, 3H), 1.42 (m, 4H), 2.43 (s, 3H), 3.31 (t, J=7.1 Hz, 2H), 6.26 (s, 1H), 7.32 (d, J=8.1 Hz, 2H), 7.68 (d, J=8.1 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ=13.6, 19.7, 21.5, 30.4, 48.9, 124.4, 124.9, 127.2, 129.8, 135.5, 144.0. Anal. Calcd for $C_{13}H_{17}Cl_2NO_2S$: C 48.45, H 5.32, N 4.35; Found: C 48.64, H 5.43, N 4.52.

4.3.4. *N*-Allyl-*N*-(2,2-dichlorovinyl)-4-methyl-benzenesulfonamide (7c). As described for compound **7b** starting from compound **3c**, yield 97% (3.93 mmol scale, 1.17 g), colorless crystalline solid. R_f 0.41 (PE/EtOAc 5:1); mp 90 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H), 4.00 (d, J=6.3 Hz, 2H), 5.15 (dq, J=10.0, 1.0 Hz, 1H), 5.18 (dq, J=17.1, 1.2 Hz, 1H), 5.68 (ddt, J=17.0, 10.2, 6.3 Hz, 1H), 6.31 (s, 1H), 7.32 (d, J=8.1 Hz, 2H), 7.69 (d, J=8.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=21.6, 51.7, 119.4, 124.3, 124.8, 127.4 (2C), 129.9 (2C), 131.9, 135.7, 144.2. Anal. Calcd for $C_{12}H_{13}Cl_2NO_2S$: C 47.07, H 4.28, N 4.57; Found: C 47.01, H 4.27, N 4.42.

4.3.5. *N*-(2,2-Dichlorovinyl)-*N*-(2-methyl-allyl)-4-methyl-benzenesulfonamide (7d). As described for compound **7b** starting from compound **3d**, yield 97% (1.13 mmol scale, 350 mg), colorless crystalline solid. R_f 0.43 (PE/EtOAc 5:1); mp 84 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.76 (s, 3H), 2.44 (s, 3H), 3.88 (s, 2H), 4.84–4.87 (m, 1H), 4.90–4.93 (m, 1H), 6.20 (s, 1H), 7.31–7.36 (m, 2H), 7.67–7.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=19.8, 21.5, 55.2, 115.1, 124.7, 125.2, 127.2 (2C), 129.8 (2C), 135.4, 139.4, 144.2. Anal. Calcd for $C_{13}H_{15}Cl_2NO_2S$: C 48.76, H 4.72, N 4.37; Found: C 48.95, H 4.89, N 4.23.

4.3.6. *N*-(2,2-Dichlorovinyl)-*N*-benzyl-4-methyl-benzenesulfonamide (7e). As described for compound **7b** starting from compound **3e**, yield 96% (1.76 mmol scale, 600 mg), colorless crystalline solid. R_f 0.40 (PE/EtOAc 5:1); mp 126 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=2.43 (s, 3H), 4.53 (s, 2H), 6.21 (s, 1H), 7.28 (m, 5H), 7.34 (d, J=8.3 Hz, 2H), 7.72 (d, J=8.3 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ=21.5, 52.6, 124.7, 125.6, 127.2, 127.9, 128.3, 128.5, 129.8, 135.0, 135.6, 144.2. Anal. Calcd for $C_{16}H_{15}Cl_2NO_2S$: C 53.94, H 4.24, N 3.93; Found: C 53.83, H 4.12, N 3.87.

4.3.7. *N*-(2,2-Dichlorovinyl)-*N*-phenyl-4-methyl-benzenesulfonamide (7f). As described for compound **7b** starting from compound **3f**, yield 81% (1 mmol scale, 276 mg), colorless crystalline solid. Mp 115–116 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=2.43 (s, 3H), 6.97 (s, 1H), 7.06 (m, 2H), 7.28 (m, 5H), 7.47 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ=21.6, 118.2, 126.2, 127.7, 128.0, 128.3, 128.9, 129.6, 134.1, 138.2, 144.6. Anal. Calcd for $C_{15}H_{13}Cl_2NO_2S$: C 52.64, H 3.83, N 4.09; Found: C 52.83, H 3.93, N 3.95.

4.4. Syntheses of ynamides 1

4.4.1. *N*-Ethynyl-*N*-isopropyl-4-methyl-benzenesulfonamide (1b) (representative procedure for the synthesis of ynamides 1). A solution of dichlorovinylamide **7b** (205 mg, 0.66 mmol) in THF (3.3 mL) was cooled to −78 °C and treated with *n*-BuLi (0.96 mL, 1.53 M in hexane, 1.46 mmol). The mixture was warmed to −30 °C within 2 h and then MeOH (135 μL) was added. Dilution with TBME (10 mL) and workup using satd $NaHCO_3$ (5 mL) gave a yellow crude product, which was purified by flash chromatography on basic alox (pentane/TBME 6:1) to yield the desired ynamide **1b** (146 mg, 93%) as a pale yellow crystalline solid. R_f 0.58 (PE/EtOAc 5:1); mp 95–97 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.11 (d, J=6.6 Hz, 6H), 2.45 (s, 3H), 2.80 (s, 1H), 4.13 (sept, J=6.6 Hz, 1H), 7.32–7.37 (m, 2H), 7.79–7.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=20.4, 21.5, 52.0, 61.0 (C≡*C*H), 72.9 (*C*≡CH), 127.3 (2C), 129.7 (2C), 135.9, 144.5. Anal. Calcd for $C_{12}H_{15}NO_2S$: C 60.73, H 6.37, N 5.90; Found: C 60.88, H 6.48, N 5.99.

4.4.2. *N*-Butyl-*N*-ethynyl-4-methyl-benzenesulfonamide (1a). As described for compound **1b** starting from compound **7a**, yield 86% (1.18 mmol scale, 255 mg), yellow oil. R_f 0.41 (PE/EtOAc 5:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.83 (t, J=7.3 Hz, 3H), 1.21–1.51 (m, 4H), 2.37 (s, 3H), 2.65 (s, 1H), 3.22 (t, J=7.2 Hz, 2H), 7.28 (d, J=8.0 Hz, 2H), 7.72 (d, J=8.0 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ=13.5, 19.4, 21.6, 29.6, 50.9, 58.9, 76.4, 127.6, 129.7, 134.6, 144.6.

4.4.3. *N*-Allyl-*N*-ethynyl-4-methyl-benzenesulfonamide (1c). As described for compound **1b** starting from compound **7c**, yield 81% (3.78 mmol scale, 721 mg), colorless crystalline solid. R_f 0.25 (PE/EtOAc 5:1); mp 68–70 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=2.37 (s, 3H), 2.65 (s, 1H), 3.88 (dt, J=6.2, 1.2 Hz, 2H), 5.11–5.24 (m, 2H), 5.66 (ddt, J=17.1, 10.1, 6.3 Hz, 1H), 7.29 (m, 2H), 7.74 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ=21.5, 53.9, 59.2, 75.8, 120.0, 127.7 (2C), 129.7 (2C), 130.5, 134.6, 144.8. Anal. Calcd for $C_{12}H_{13}NO_2S$: C 61.25, H 5.57, N 5.95; Found: C 61.35, H 5.41, N 5.89.

4.4.4. *N*-Ethynyl-*N*-(2-methyl-allyl)-4-methyl-benzenesulfonamide (1d). As described for compound **1b** starting from compound **7d**, yield 95% (1.09 mmol scale, 257 mg), colorless crystalline solid. R_f 0.34 (PE/EtOAc 5:1); mp 69 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.72 (s, 3H), 2.46 (s, 3H), 2.71 (s, 1H), 3.86 (s, 2H), 4.91–4.94 (m, 1H), 4.95–4.98 (m, 1H), 7.33–7.38 (m, 2H), 7.79–7.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=19.5, 21.6, 57.5, 59.0, 75.8, 115.8, 127.7 (2C), 129.7 (2C), 134.5, 138.4, 144.7. Anal. Calcd for $C_{13}H_{15}NO_2S$: C 62.62, H 6.06, N 5.62; Found: C 62.32, H 5.90, N 5.77.

4.4.5. *N*-Benzyl-*N*-ethynyl-4-methyl-benzenesulfonamide (1e). As described for compound **1b** starting from compound **7e**, yield 80% (1.61 mmol scale, 367 mg), colorless crystalline solid. R_f 0.34 (PE/EtOAc 5:1); mp 102–103 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.44 (s, 3H), 2.67 (s, 1H), 4.49 (s, 2H), 7.27–7.35 (m, 7H), 7.73–7.79 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=21.6, 55.2, 59.6, 76.2, 127.6, 128.3, 128.5, 128.6, 129.7, 134.2, 134.6, 144.7. Anal. Calcd for $C_{16}H_{15}NO_2S$: C 67.34, H 5.30, N 4.91; Found: C 67.02, H 5.32, N 5.06.

4.4.6. *N*-Ethynyl-*N*-phenyl-4-methyl-benzenesulfonamide (1f). As described for compound **1b** starting from compound **7f**, yield 97% (1.52 mmol scale, 401 mg), pale yellow crystalline solid. R_f 0.30 (PE/EtOAc 5:1); mp 86–87 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=2.44 (s, 3H), 2.84 (s, 1H), 7.21–7.37 (m, 7H), 7.54–7.62 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ=21.6, 58.9, 76.4, 126.1, 128.1, 128.3, 129.0, 129.5, 132.7, 138.1, 145.1. Anal. Calcd for $C_{15}H_{13}NO_2S$: C 66.40, H 4.83, N 5.16; Found: C 66.25, H 4.61, N 5.07.

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