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Conversions of sulfone-containing vinyl azides to vinyl triazoles and enamides☆

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ABSTRACT

Reported is the efficient conversion of four 3-sulfonyl prop-1-enyl azides into seven 3-sulfonyl prop-1-enyl triazoles. Results demonstrate that the stereochemical integrity of the alkene was maintained during this process. The conversion of (*Z*)-((3-azidoallyl)sulfonyl)benzene into the corresponding *Z*-enamides proved more challenging and only modest yields of (*Z*)-*N*-(3-(phenylsulfonyl)prop-1-en-1-yl) acetamide and benzamide were obtained using Williams' thioacid method. Attempts to form these compounds using Staudinger ligation-type reactions proved unsuccessful.

1. Introduction

Sulfones represent a useful functional group which are frequently used in the construction of more complex compounds [1,2] and the varied chemistry sulfones impart have led to them being referred to as chemical chameleons [3] and pluripotent groups [4]. Representative uses of the sulfone group include: α-sulfonyl alkylation, reductive or more traditional sulfinate elimination, the Julia olefination (including its variants) [5] and the Ramberg-Bäcklund reaction [6]. Unsaturated sulfones also offer useful synthetic possibilities. α,β-Unsaturated sulfones (e.g. **1**, Scheme 1), also known as vinyl sulfones, undergo conjugate addition reactions with a range of soft and hard nucleophiles and also engage in cycloaddition chemistries [7]. In addition, compounds of the type **1** can be effectively isomerised into their β,γ-unsaturated counterpart, **3**, on treatment with base (Scheme 1) [8].

In the forward sense (**1** to **3**) this isomerisation reaction serves to "de-conjugate" the alkene from the electron withdrawing group and this process is not limited to sulfones [9–13]. Numerous examples demonstrate that if an *E*-alkene (e.g. **1**) is used, synthetically useful levels of *Z*-selectivity for the new alkene (*Z*-**3**) may be obtained - although it should be mentioned that this does depend on the substituents present and the reaction conditions employed. An interesting tandem variant of the general process outlined in Scheme 1 has been reported where, from intermediate **2**, a Ramberg-Bäcklund reaction can take place [14].

In relation to this process we have recently studied this type of transformation and have found that the reaction is particularly facile and selective when the γ-substituent is an azido goup [15]. For instance, four differently substituted *E*-allylic bromides, **4**–**7** were converted, *via* a two-step one-pot process, into their vinyl azides **8**–**11**. Apart from its convenience the one-pot process circumvented isolation of the intermediate azido vinyl sulfone which, in the case of **12**, proved not to be bench stable. Examples where R = H gave good to excellent levels of *Z*-selectivity in the formation of the new vinyl azide (i.e. compounds **8**–**10**). In the case of R = Me a reversal in stereochemical outcome was observed in the formation of predominantly *E*-**11**. On the basis of experimental and computational results it is believed that these isomerisation reactions operate under kinetic control and that the selectivity observed stems from a favoured vinyl sulfone conformer [15].

Because vinyl azides are synthetically useful groups [16] this indirect, stereocontrolled, method to form the sulfone functionalised the vinyl azides is of interest. In this current work reactivity of

☆ This article is dedicated to Prof. Richard Taylor on the year of his 71st birthday in acknowledgement for his many contributions to the area of synthetic organic chemistry and with personal thanks for the knowledge he imparted.

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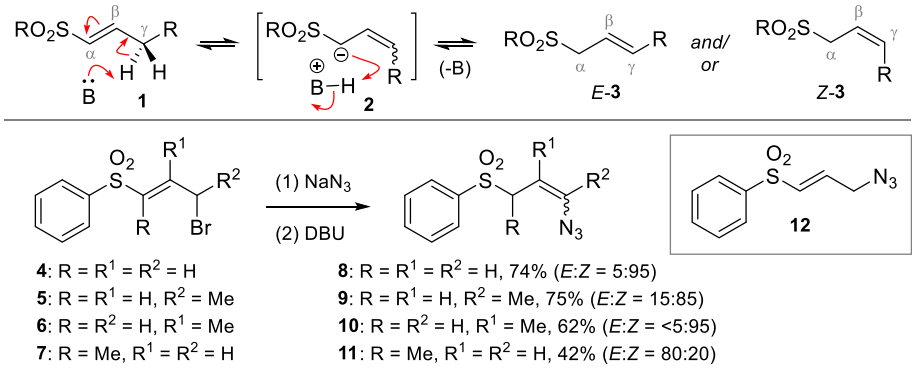
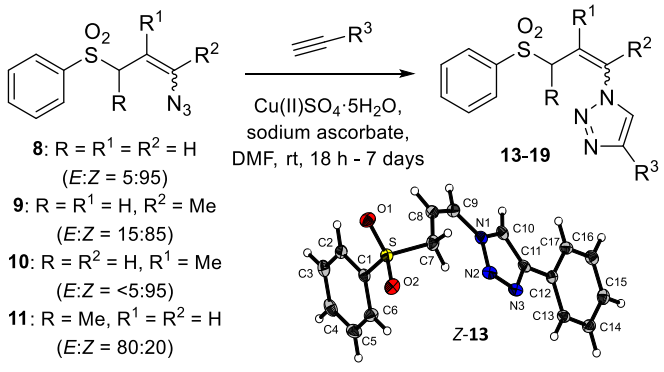


Scheme 1. The isomerisation of substituted vinyl and allyl sulfones and the formation of vinyl azides **8**–**11** from vinyl sulfones **4**–**7** (B = base; DBU = 1,8-diazobicyclo[5.4.0]undec-7-ene).

these sulfone containing vinyl azides has been explored. Namely, the copper promoted azide-alkyne click reaction of vinyl azides **8** to **11** is reported and preliminary work investigating the conversion of vinyl azides into enamides is also described.

2. Results and discussion

Compounds **8** to **11** were accessed according to our previously published procedure [15] and their copper promoted azide-alkyne click (CuAAC) chemistry was considered [17]. As shown in Scheme 2, firstly azide **8** was reacted with several terminal alkynes, using typical reaction conditions [18]. Use of phenyl acetylene, oct-1-yne and methyl propiolate gave the expected triazoles, **13**–**15** in good yields (Scheme 2, Entries 1–3). It should be noted that no changes in alkene geometry were observed in these reactions [19] and in the case of *Z*-**13** a single crystal X-ray structure was obtained [20]. Use of trimethylsilyl acetylene gave a moderate yield of triazole *Z*-**16** in which the trimethylsilyl group had been lost [21]. No alternative products were detected. Use of the more robust, and bulky triisopropylsilyl acetylene led only to the recovery of *Z*-**8** under the same reaction conditions. Next the isomeric methyl substituted vinyl azides, **9**, **10** and **11** were reacted similarly with phenyl acetylene. In each case the adducts, **17**–**19**, were isolated in good yields and the balance of alkene isomers in these adducts matched those found in the vinyl azide starting materials (Entries 5–7).



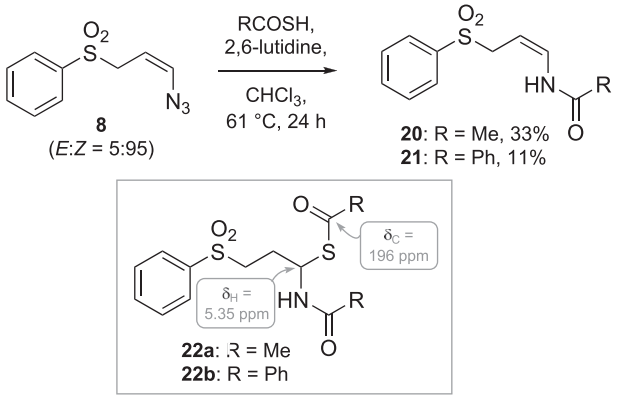
Entry	Compound	Yield[a] (*E*:*Z*)[b]
1	**13**: R = R^1 = R^2 = H, R^3 = Ph	79% (<5:95)
2	**14**: R = R^1 = R^2 = H, R^3 = *n*-Hex	65% (<5:95)
3	**15**: R = R^1 = R^2 = H, R^3 = CO_2Me	69% (<5:95)
4	**16**: R = R^1 = R^2 = H, R^3 = H	46%[c] (5:95)
5	**17**: R = R^1 = H, R^2 = Me, R^3 = Ph	75% (20:80)
6	**18**: R = R^2 = H, R^1 = Me, R^3 = Ph	81% (<5:95)
7	**19**: R = Me, R^1 = R^2 = H, R^3 = Ph	86% (80:20)

[a]Yield after purification by flash column chromatography; [b]Ratio determined for purified material by ^{1}H-NMR spectroscopy; [c]From ethynyltrimethylsilane

Scheme 2. Use of vinyl azides **8**–**11** in the CuAAC reaction to form vinyl triazoles **13**–**19**. Single crystal X-ray structure of *Z*-**13** (thermal ellipsoids shown on the 50% probability level) [20].

The conversion of sulfonyl containing *Z*-vinyl azide **8** into the corresponding enamide was subsequently considered. Enamides represent an interesting functional group and are present in a variety of natural products of both structural and biological interest [22]. For instance, pamerolide A, crocacin A, TMC-95 A, the members of the ceanothine family and salicylihalamide A all contain a stereodefined enamide with a 1,2-disubstitution pattern on the carbon-carbon double bond. As outlined in Scheme 3, using Williams' method [23] **8** (*E*:*Z* = 5:95) was converted into *N*-acetyl *Z*-enamide **20** using thioacetic acid and lutidine. Although the reaction did not proceed to completion *Z*-**20** was successfully isolated in 33% yield. Unlike the CuAAC reactions (Scheme 2) in this reaction some alkene isomerisation was observed and the small amounts of the minor *E*-isomer was formed, which was chromatographically separable from the major *Z*-isomer. Starting material (**8**) was additionally recovered (25%) and trace amounts of a material tentatively assigned to mixed *N*,*S*-acetal (**22**), resulting from the reaction of **20** with thioacetic acid, was also detected.

Unfortunately, attempts to use thiobenzoic acid in the reaction were more disappointing. Although the reaction did work the conversion and consequent yields of the *N*-benzoyl enamide **21**



Scheme 3. Conversion of vinyl azides **8** into *Z*-enamides **20** and **21**.

were poorer than in the case of thioacetic acid, although 39% of unreacted *Z*-**8** was recovered. Compound **22** (R = Me and Ph) proved to have similar polarity to the *E*-enamides **20** and **21** but could be clearly detected by diagnostic NMR spectroscopic signals and mass spectrometry (see SI).

Staudinger-functionalisation chemistry was also briefly investigated as a potential means to directly convert a vinyl azide into an enamide [24]. Using either 2-(diphenylphosphaneyl)phenyl acetate [25] or *S*-[(diphenylphosphaneyl)methyl]ethanethioate [26] evolution of gaseous nitrogen was detected, however, in both cases no **20** was isolated.

In order to further explore the preparation of sulfonyl containing enamides the synthesis of **21** was also considered using an alternative route (Scheme 4). Hippuric acid was converted in 70% to known Weinreb amide **23** using a carbodiimide coupling [27]. Thereafter, a reduction-Horner-Wadsworth-Emmons sequence give **25** in a poor overall yield as a single geometrical isomer. Nevertheless, from **25**, compound **21** can be accessed *via* the vinyl sulfone to allyl sulfone transposition outlined in general terms in Scheme 1. It should be noted that, in contrast to the azide-based route, following this isomerisation method **21** is formed as a mixture of stereoisomers within which the *E*-isomer predominates.

3. Conclusion

In conclusion, described is the use of a series of sulfonyl substituted vinyl azides (**8**–**11**) in CuAAC reactions in order to prepare novel sulfonyl functionalised 1-vinyl substituted 1,2,3-triazoles (**13**–**19**). These were isolated in reasonable to good yields. In all cases the stereochemistry of the initial double bond was maintained in the formation of **13**–**19**. A preliminary study of the reactivity of the azido group in **8** under conditions aimed at converting it into an amido group was studied. This type of Staudinger-functionalisation chemistry was also briefly investigated and using thioacid conditions the *Z*-vinyl azide could be converted into the corresponding *Z*-enamide (although the conversion was poor).

4. Experimental section

4.1. General directions

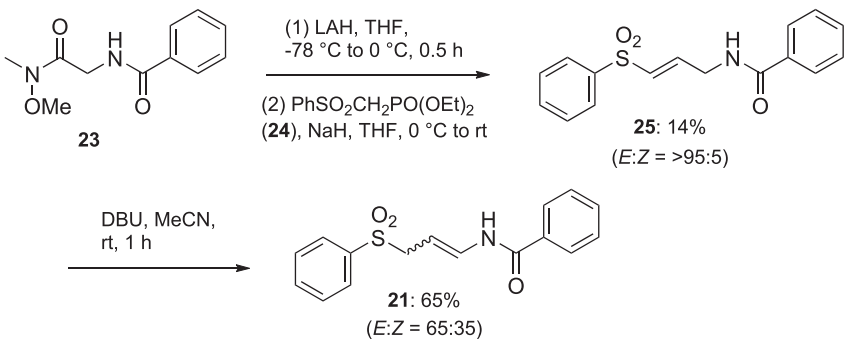
Reagents from commercial suppliers were used without further purification. ^{1}H, ^{1}H-decoupled ^{13}C NMR spectra were recorded on Varian Unity 300, 400 and 500 MHz spectrometers and coupling constants (*J*) are quoted in Hertz. All values are reported in ppm and were referenced to either tetramethylsilane, or residual protonated chloroform. Assignment was aided by two-dimensional NMR experiments (g-COSY and HSCQ). High resolution mass spectra were carried out with a Waters/Micromass LCT ESI mass spectrometer under electrospray ionisation conditions (ESI) and a time-of-flight (TOF) analyser. Infrared spectra were recorded on a Bruker Alpha FTIR spectrometer. Melting points were recorded on a Gallenkamp electrothermal melting point apparatus and are uncorrected. Thin-layer chromatography was performed on silica coated aluminium sheets and compounds were visualised with UV light and aqueous potassium permanganate, followed by heating. Merck silica gel (0.040–0.063 mm) was used for flash column chromatography. Compounds **8**–**11** and **24** were prepared according to procedures previously described in the literature [15].

4.2. (Z)-4-Phenyl-1-[3-(phenylsulfonyl)prop-1-en-1-yl]-1H-1,2,3-triazole **13**

Sodium ascorbate (71 mg, 0.36 mmol, 0.8 equiv.) was added to a stirred solution of vinyl azide **8** (100 mg, 0.45 mmol, 1.0 equiv.), phenylacetylene (50 mg, 0.49 mmol, 1.1 equiv.) and $CuSO_4 \cdot 5H_2O$ (34 mg, 0.13 mmol, 0.3 equiv.) in DMF (4 mL). This mixture was stirred at room temperature for 18 h. Solvent was removed *in vacuo*, the residue was re-dissolved in EtOAc (20 mL) and washed with water (20 mL). The aqueous layer was back extracted with EtOAc (2 x 20 mL) and the combined organic layers were washed with brine (60 mL), dried over $MgSO_4$ and solvent was removed *in vacuo* to give crude product. Purification by column chromatography (*c*-Hex:EtOAc, 2:1) yielded triazole **13** (115 mg, 79%) as a white crystalline solid. X-Ray quality crystals were grown from the slow infusion of pentane into a saturated solution of **13** in DCM. M.p. = 153–155 °C (DCM). R_f = 0.25 (*c*-Hex:EtOAc, 2:1). IR (neat): 3091, 3050, 1730, 1582, 1560, 1361,1238, 1150, 1071, 1018 cm^{-1}. HRMS (ES^+) $C_{17}H_{16}N_3O_2S$ (MH^+) calcd. 326.0977; found 326.0963.^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.62 (dd, *J* = 8.0, 1.5 Hz, 2H, CH_2), 5.76 (dt, *J* = 9.5, 8.0 Hz, 1H, CH), 7.05 (dt, *J* = 9.5, 1.5 Hz, 1H, CH), 7.34–7.40 (m, 1H, ArH), 7.41–7.52 (m, 4H, ArH), 7.54–7.60 (m, 1H, ArH), 7.69 (s, 1H, CH), 7.76–7.80 (m, 2H, ArH), 7.89–7.93 (m, 2H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.0 (CH_2), 111.1 (CH), 120.2 (CH), 125.8 (CH), 127.1 (CH), 128.3 (CH), 128.7 (CH), 129.0 (CH), 129.1 (CH), 129.5 (C), 133.9 (CH), 138.4 (C), 147.2 (C) ppm.

4.3. (Z)-4-Hexyl-1-[3-(phenylsulfonyl)prop-1-en-1-yl]-1H-1,2,3-triazole **14**

In a procedure identical to triazole **52** above (but with stirring for 18 h), azide **8** (203 mg, 0.91 mmol, 1.0 equiv.), 1-octyne (110 mg, 1.00 mmol, 1.1 equiv.), $CuSO_4 \cdot 5H_2O$ (68 mg, 0.27 mmol, 0.3 equiv.)



Scheme 4. Synthesis of enamide **21** from hippuric acid.

and sodium ascorbate (145 mg, 0.73 mmol, 0.8 equiv.) were stirred at room temperature in DMF (10 mL) for 18 h. The mixture was worked-up as described above and was further purified by column chromatography (*c*-Hex:EtOAc, 2:1) which yielded triazole **14** (197 mg, 65%) as a white crystalline solid. M.p. = 88–90 °C. R_f = 0.30 (*c*-Hex:EtOAc, 2:1). IR (neat): 3075, 3014, 2923, 2878, 1583, 1379, 1246, 1151, 1086, 954 cm^{-1}. HRMS (ES^+): $C_{17}H_{24}N_3O_2S$ (MH^+) calcd. 334.1589; found 334.1599.^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, J = 7.0 Hz, 3H, CH_3), 1.25–1.39 (m, 6H, CH_2), 1.63 (p, J = 7.5 Hz, 2H, CH_2), 2.67 (t, J = 7.5 Hz, 2H, CH_2), 4.59 (dd, J = 8.0, 1.5 Hz, 2H, CH_2), 5.66 (dt, J = 9.5, 8.0 Hz, 1H, CH), 6.96 (dt, J = 9.5, 1.5 Hz, 1H, CH), 7.22 (s, 1H, CH), 7.47–7.53 (m, 2H, ArH), 7.56–7.62 (m, 1H, ArH), 7.87–7.93 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.5 (CH_2), 25.6 (CH_2), 28.8 (CH_2), 29.2 (CH_2), 31.5 (CH_2), 55.0 (CH_2), 110.0 (CH), 121.5 (CH), 127.2 (CH), 128.3 (CH), 129.0 (CH), 133.8 (CH), 138.5 (C), 147.9 (C).

4.4. Methyl (Z)-1-[3-(phenylsulfonyl)prop-1-en-1-yl]-1H-1,2,3-triazole-4-carboxylate **15**

In a procedure identical to that described above for the synthesis of triazole **13**, azide **8** (178 mg, 0.79 mmol, 1.0 equiv.), methyl propiolate (74 mg, 0.88 mmol, 1.1 equiv.), $CuSO_4 \cdot 5H_2O$ (60 mg, 0.24 mmol, 0.3 equiv.) and sodium ascorbate (130 mg, 0.64 mmol, 0.8 equiv.) in DMF (10 mL) were stirred at room temperature for 3.5 h. After work-up as described the crude reaction product was purified by flash column chromatography (*c*-Hex:EtOAc, 1:1) which yielded triazole **15** (170 mg, 69%) as a white crystalline solid. M.p. = 123–125 °C. R_f = 0.30 (*c*-Hex:EtOAc, 1:1). IR (neat): 3099, 3062, 1713, 1584, 1346, 1264, 1243, 1156, 1073, 1032 cm^{-1}. HRMS (ES^+): $C_{14}H_{13}N_3O_4S$ (MH^+) calcd. 308.0705; found 308.0695.^{1}H NMR (400 MHz)): δ = 3.97 (s, 3H, CH_3), 4.53 (dd, J = 8.0, 1.5 Hz, 2H, CH_2), 5.88 (dt, J = 9.0, 8.0 Hz, 1H, CH), 7.04 (dt, J = 9.0, 1.5 Hz, 1H, CH), 7.48–7.54 (m, 2H, ArH), 7.58–7.64 (m, 1H, ArH), 7.87–7.93 (m, 2H, ArH). ^{13}C NMR (100 MHz): δ = 52.6 (CH_3), 55.0 (CH_2), 113.6 (CH), 126.9 (CH), 128.2 (CH), 128.4 (CH), 129.4 (CH), 134.2 (CH), 138.4 (C), 139.6 (C), 160.6 (C) ppm.

4.5. (Z)-1-[3-(Phenylsulfonyl)prop-1-en-1-yl]-1H-1,2,3-triazole **16**

Azide **8** (55 mg, 0.25 mmol, 1.0 equiv.), ethynyltrimethylsilane (27 mg, 0.27 mmol, 1.1 equiv.), $CuSO_4 \cdot 5H_2O$ (18 mg, 0.07 mmol, 0.3 equiv.) and sodium ascorbate (40 mg, 0.19 mmol, 0.8 equiv.) were stirred at room temperature in DMF (4 mL) for 7 days. Work-up as described above followed by purification by column chromatography (*c*-Hex:EtOAc, 1:1) yielded triazole **16** (23 mg, 36%, 46% based on recovered starting material) as a white crystalline solid. M.p. = 140–142 °C. R_f = 0.25 (*c*-Hex:EtOAc, 1:1). IR (neat): 3116, 3057, 3020, 1734, 1583, 1390, 1237, 1152, 1074, 1014 cm^{-1}. HRMS (ES^+): $C_{11}H_{12}N_3O_2S$ (MH^+) calcd. 250.0650; found 250.0640.^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.58 (dd, J = 8.0, 1.5 Hz, 2H, CH_2), 5.73 (dt, J = 9.5, 8.0 Hz, 1H, CH), 7.04 (dt, J = 9.5, 1.5 Hz, 1H, CH), 7.46–7.52 (m, 2H, ArH), 7.55 (d, J = 1.0 Hz, 1H, CH), 7.56–7.62 (m, 1H, ArH), 7.64 (d, J = 1.0 Hz, 1H, CH), 7.86–7.91 (m, 2H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.1 (CH_2), 111.1 (CH), 124.7 (CH), 127.2 (CH), 128.4 (CH), 129.2 (CH), 133.4 (CH), 134.1 (CH), 138.6 (C) ppm.

4.6. (E/Z)-4-phenyl-1-[4-(phenylsulfonyl)but-2-en-2-yl]-1H-1,2,3-triazole **17**

As described above, azide **9** (77 mg, 0.325 mmol, 1.0 equiv.), phenylacetylene (36 mg, 0.36 mmol, 1.1 equiv.), $CuSO_4 \cdot 5H_2O$ (24 mg, 0.10 mmol, 0.3 equiv.) and sodium ascorbate (51 mg, 0.26 mmol, 0.8 equiv.) in DMF (5 mL) were stirred at room temperature for 24 h. At this stage some **17** was evident by TLC so phenylacetylene (36 mg, 0.36 mmol, 1.1 equiv.) was added and stirring maintained for 16 h. Work-up as described and purification by column chromatography (*c*-Hex:EtOAc, 1:1) yielded triazole **17** (83 mg, 75%) as a white solid with an *E:Z* ratio of 20:80. R_f = 0.25 (*c*-Hex:EtOAc, 2:1). IR (neat): 3139, 3056, 2926, 1684, 1387, 1212, 995, 777, 686, 431 cm^{-1}. HRMS (ES^+): $C_{18}H_{18}N_3O_2S$ (MH^+) calcd. 340.1120; found 340.1129.^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.11 (s, 0.6H, CH_3),* 2.31 (s, 2.4H, CH_3),† 4.01 (d, J = 8.5 Hz, 0.4H, CH_2),* 4.09–4.17 (m, 1.6H, CH_2),† 5.69 (td, J = 8.0, 1.25 Hz, 0.8H, CH),† 6.06 (td, J = 8.5, 1.0 Hz, 0.2H, CH),* 7.32–7.39 (m, 1H, ArH), 7.40–7.50 (m, 3.4H, ArH), 7.52–7.62 (m, 1H, ArH), 7.64 (t, J = 8.0 Hz, 0.2H, ArH),* 7.69 (s, 0.8H, ArH),† 7.77–7.86 (m, 4H, ArH), 7.81 (d, J = 8.0 Hz, 0.4H, ArH),* 7.95 (s, 0.2H, ArH)* ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (CH_3), 22.8 (CH_3), 55.2 (CH_2), 55.4 (CH_2), 106.5 (CH), 111.0 (CH), 117.1 (CH), 119.4 (CH), 125.8 (CH), 125.9 (CH), 128.2 (CH), 128.5 (CH), 128.6 (CH), 129.0 (CH), 129.1 (CH), 129.4 (CH), 129.6 (CH), 129.9 (C), 130.0 (C), 134.0 (CH), 134.3 (CH), 138.2 (C), 138.3 (C), 138.6 (C), 139.7 (C), 147.4 (C), 150.0 (C) ppm. *Denotes signals for ***E*-17**; †Denotes signals for ***Z*-17**.

4.7. (Z)-1-[2-methyl-3-(phenylsulfonyl)prop-1-en-1-yl]-4-phenyl-1H-1,2,3-triazole **18**

In an identical procedure to that described above, azide **10** (75 mg, 0.32 mmol, 1.0 equiv.), phenylacetylene (36 mg, 0.36 mmol, 1.1 equiv.), $CuSO_4 \cdot 5H_2O$ (24 mg, 0.10 mmol, 0.3 equiv.) and sodium ascorbate (50 mg, 0.25 mmol, 0.8 equiv.) were stirring at room temperature in DMF (5 mL) for 21 h. Work-up and purification by column chromatography (*c*-Hex:EtOAc, 2:1) yielded triazole **18** (87 mg, 81%) as a white crystalline solid. M.p. = 141–142 °C. R_f = 0.25 (*c*-Hex:EtOAc, 2:1). IR (neat): 2995, 2926, 1678, 1368, 1260, 1146, 1018, 854, 593 cm^{-1}. HRMS (ES^+): $C_{18}H_{18}N_3O_2S$ (MH^+) calcd. 340.1120; found 340.1136.^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.21 (d, J = 1.5 Hz, 3H, CH_3), 4.46 (s, 2H, CH_2), 6.90 (d, J = 1.5 Hz, 1H), 7.34–7.52 (m, 6H, ArH, CH), 7.73–7.81 (m, 5H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.1 (CH_3), 58.6 (CH_2), 120.4 (CH), 124.5 (CH), 124.9 (C), 125.8 (CH), 128.3 (CH), 128.6 (CH), 129.1 (CH), 129.3 (CH), 129.9 (C), 133.8 (CH), 138.7 (C), 147.2 (C) ppm.

4.8. (E/Z)-4-phenyl-1-[3-(phenylsulfonyl)but-1-en-1-yl]-1H-1,2,3-triazole **19**

In an identical procedure to that described above for the synthesis of triazole **13**, azide **11** (46 mg, 0.19 mmol, 1.0 equiv.), phenylacetylene (19 mg, 0.21 mmol, 1.1 equiv.), $CuSO_4 \cdot 5H_2O$ (13 mg, 0.06 mmol, 0.3 equiv.) and sodium ascorbate (31 mg, 0.16 mmol, 0.8 equiv.) were stirred in DMF (4 mL) at room temperature for 16 h. TLC analysis indicated **11** remained, therefore, phenylacetylene (19 mg, 0.21 mmol, 1.1 equiv.) was added and stirring maintained for a further 8 h. Work-up and purification by column chromatography (*c*-Hex:EtOAc, 1:1) yielded triazole **19** (57 mg, 86%) as a white crystalline solid in an *E:Z* ratio of 80:20. M.p. = 137–140 °C.

R_f = 0.25 (*c*-Hex:EtOAc, 2:1). IR (neat): 3135, 2988, 2934, 1669, 1285, 1258, 1084, 1000, 940, 687 cm^{-1}. HRMS (ES^+): $C_{18}H_{18}N_3O_2S$ (MH^+) calcd. 340.1120; found 340.1136.^{1}H NMR (400 MHz, $CDCl_3$): ***E*-19**: δ = 1.55–1.62 (m, 3H, CH_3), 3.87–3.96 (m, 1H, CH), 6.23 (dd, *J* = 14.5, 8.5 Hz, 1H, CH), 7.15 (dd, *J* = 14.5, 1.0 Hz, 1H, CH), 7.35–7.40 (m, 1H, ArH), 7.42–7.49 (m, 2H, ArH), 7.52–7.60 (m, 2H, ArH), 7.65–7.71 (m, 1H, ArH), 7.82–7.91 (m, 4H, ArH), 7.97 (s, 1H, CH). ***Z*-19**: δ = 1.55–1.62 (m, 3H, CH_3), 5.16–5.29 (m, 1H, CH), 5.60 (dd, *J* = 10.5, 9.5 Hz, 1H, CH), 6.95 (dd, *J* = 9.5, 0.5 Hz, 1H, CH), 7.35–7.40 (m, 1H, ArH), 7.42–7.49 (m, 2H, ArH), 7.52–7.60 (m, 2H, ArH), 7.64 (s, 1H, CH), 7.65–7.71 (m, 1H, ArH), 7.82–7.91 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8 (CH_3), 13.9 (CH_3), 58.7 (CH), 61.5 (CH), 114.5 (CH), 116.7 (CH), 118.7 (CH), 120.40 (CH), 125.9 (CH), 125.9 (CH), 126.0 (CH),128.8 (CH), 128.9 (CH), 129.1 (CH), 129.1 (CH), 129.1 (CH), 129.2 (CH) 129.4 (CH), 129.4 (CH), 129.8 (CH), 133.9 (CH), 134.4 (CH), 136.5 (C), 137.4 (C), 148.4 (C) ppm.

4.9. (Z)-N-[3-(Phenylsulfonyl)prop-1-en-1-yl]acetamide **20**

To a stirred solution of vinyl azide **8** (224 mg, 1.00 mmol, 1.0 equiv.) in $CHCl_3$ (1 mL) at room temperature, was added thioacetic acid (176 mg, 2.31 mmol, 2.3 equiv.) and 2,6-lutidine (247 mg, 2.31 mmol, 2.3 equiv.) sequentially by syringe. The mixture was heated to reflux for 48 h, cooled to room temperature and solvent was removed *in vacuo* to afford a crude residue. The residue was purified by column chromatography (gradient elution; *c*-Hex:-EtOAc, 6:1 to EtOAc) affording starting material **8** (56 mg, 25%, *E*:*Z*; 5:95) and *Z*-enamide **20** (79 mg, 33%) as a white crystalline solid. M.p. = 117–119 °C. R_f = 0.40 (EtOAc). IR (neat): 3345, 3207, 1679, 1652, 1583, 1366, 1122, 998, 727, 521 cm^{-1}. HRMS (ES^+): $C_{11}H_{13}NO_3NaS$ (MNa^+) calcd. 262.0514; found 262.0525.^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.08 (s, 3H, CH_3), 3.90–3.93 (m, 2H, CH_2), 4.45 (app. q, *J* = 8.5 Hz, 1H, CH), 6.97–7.05 (m, 1H, CH), 7.54–7.60 (m, 2H, ArH), 7.64–7.71 (m, 1H, ArH), 7.86–7.91 (m, 2H, ArH), 8.47 (d, *J* = 10.0 Hz, 1H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4 (CH_3), 54.6 (CH_2), 95.1 (CH), 128.5 (CH), 129.4 (CH), 130.2 (CH), 134.3 (CH), 138.0 (C), 168.6 (C) ppm. Further elution gave a mixture of *E*-**20** and **22** (R = Me) (25 mg).

4.10. (Z)-N-[3-(Phenylsulfonyl)prop-1-en-1-yl]benzamide **21**

In an identical procedure to that described above, vinyl azide **8** (201 mg, 0.90 mmol, 1.0 equiv.), 2,6-lutidine (222 mg, 2.07 mmol, 2.3 equiv.) and thiobenzoic acid (286 mg, 2.07 mmol, 2.3 equiv.) were heated to reflux for 48 h in $CHCl_3$ (1 mL). Purification by column chromatography using gradient elution (*c*-Hex:EtOAc, 6:1 to 1:1) gave starting material **8** (78 mg, 39%, *E*:*Z*; 5:95) and **21** with a co-running contaminant. Additional purification of the latter fraction by column chromatography (DCM) afforded **21** (30 mg, 11%–18% based on RSM) as a white crystalline solid. M.p. = 86–88 °C. R_f = 0.50 (*c*-Hex:EtOAc, 1:1). IR (neat): 3401, 2899, 1651, 1383, 1130, 1080, 999, 797, 688, 525 cm^{-1}. HRMS (ES^+): $C_{16}H_{16}NO_3S$ (MH^+) calcd. 302.0851; found 302.0846.^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.96–3.99 (m, 2H, CH_2), 4.59 (q, *J* = 8.0 Hz, 1H, CH), 7.22–7.30 (m, 1H, CH), 7.47–7.53 (m, 2H, ArH), 7.55–7.62 (m, 3H, ArH), 7.66–7.72 (m, 1H, ArH), 7.90–7.94 (m, 2H, ArH), 7.95–8.00 (m, 2H, ArH), 9.49 (d, *J* = 9.5 Hz, 1H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.1 (CH_2), 96.1 (CH), 127.7 (CH), 128.6 (CH), 129.0 (CH), 129.5 (CH), 131.2 (CH), 132.6 (CH), 132.8 (C), 134.4 (CH), 137.9 (C), 165.2 (C) ppm.

4.11. N-{2-[Methoxy(methyl)amino]-2-oxoethyl}benzamide **23**

To a stirred solution of hippuric acid (1.29 g, 7.20 mmol, 1.0 equiv.) in $CHCl_3$ (35 mL), was added EDCI·HCl (1.66 g, 8.64 mmol, 1.2 equiv.), *N*,*O*-dimethylhydroxylamine hydrochloride (0.84 g, 8.62 mmol, 1.2 equiv.) and diisopropylethylamine (1.15 mL, 8.64 mmol, 1.2 equiv.) was added last (*note: exotherm!*). The resulting solution was stirred at room temperature for 27 h and quenched with 1 M HCl (30 mL), the organic layer was washed with brine (30 mL), dried over $MgSO_4$, filtered and solvent was removed *in vacuo*. Purification by flash column chromatography (*c*-Hex:-EtOAc, 2:1) afforded Weinreb amide **23** (1.12 g, 70%) as a colourless crystalline solid. R_f = 0.20 (*c*-Hex:EtOAc, 1:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.22 (s, 3H, CH_3), 3.74 (s, 3H, CH_3), 4.36 (d, *J* = 3.5 Hz, 2H, CH_2), 7.11 (bs, 1H, NH), 7.38–7.44 (m, 2H, ArH), 7.44–7.50 (m, 1H, ArH), 7.79–7.84 (m, 2H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.5 (CH_3), 41.3 (CH_2), 61.7 (CH_3), 127.1 (CH), 128.6 (CH), 131.7 (CH), 134.0 (C), 167.4 (C), 169.8 (C) ppm. *Data are consistent with that reported in the literature.* [27].

4.12. (E)-N-[3-(Phenylsulfonyl)allyl]benzamide **25**

Weinreb amide **23** (246 mg, 1.12 mmol, 1.0 equiv.) was added dropwise as a solution in THF (3 mL) to a flame dried flask containing $LiAlH_4$ (44 mg, 1.16 mmol, 1.04 equiv.) in THF (3 mL) at −78 °C. The mixture was warmed to 0 °C (ice-water bath). After 20 min, the solution was again cooled to −78 °C and aq. sat. NH_4Cl (10 mL) was added. The mixture was allowed warm to room temperature, diluted with H_2O (10 mL) and extracted with EtOAc (3 x 10 mL). Combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4, filtered and solvent was removed *in vacuo* to afford crude aldehyde. This was then dissolved in THF (6 mL) and added to 0 °C solution of phosphonate **24** (324 mg, 1.11 mmol, 1.0 equiv.) and 60% NaH (40 mg, 1.00 mmol, 0.9 equiv.) in THF (6 mL) which had been stirred at this temperature for 0.5 h. The mixture was stirred and gradually warmed to room temperature over 16 h H_2O (10 mL) was added and the organics were extracted with EtOAc (3 x 10 mL). Combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, filtered and solvent was removed *in vacuo*. Purification by column chromatography afforded vinyl sulfone **25** (40 mg, 14%) as a viscous colourless oil. R_f = 0.25 (*c*-Hex:EtOAc, 2:1). IR (neat): 3334, 3058, 2919, 1643, 1528, 1141, 999, 710, 559, 533 cm^{-1}. HRMS (ES^+): $C_{16}H_{16}NO_3S$ (MH^+) calcd. 302.0851; found 302.0857.^{1}H NMR (400 MHz, $CDCl_3$): 4.28 (ddd, *J* = 6.5, 4.5, 2.0 Hz, 2H, CH_2), 6.48 (dt, *J* = 15.0, 2.0 Hz, 1H, CH), 6.98 (bs, 1H, NH), 7.02 (dt, *J* = 15.0, 4.5 Hz, 1H, CH), 7.35–7.41 (m, 2H, ArH), 7.45–7.54 (m, 3H, ArH), 7.58–7.63 (m, 1H, ArH), 7.76–7.80 (m, 2H, ArH), 7.81–7.86 (m, 2H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 39.9 (CH_2), 127.2 (CH), 127.8 (CH), 128.7 (CH), 129.5 (CH), 131.0 (CH), 132.0 (CH), 133.6 (C), 133.7 (CH), 139.9 (C), 143.3 (CH), 167.6 (C) ppm.

4.13. (E/Z)-N-[3-(Phenylsulfonyl)prop-1-en-1-yl]benzamide **21**

To a stirred solution of vinyl sulfone **25** (34 mg, 0.11 mmol, 1.0 equiv.) in MeCN (1 mL), was added DBU (9 mg, 0.06 mmol, 0.5 equiv.). The mixture was quenched by addition of 1 M HCl (2 mL) after 1 h and subsequently diluted with H_2O (2 mL) and extracted with EtOAc (3 x 3 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and solvent was removed *in vacuo* to give (*E*/*Z*)-**21** (22 mg, 65%) as an off-white solid in an *E*:*Z* ratio of 65:35.^{1}H NMR (400 MHz, DMSO-d_6):*δ = 4.10–4.17 (m, 2H, CH_2), 5.32 (dt, *J* = 14.0, 8.0 Hz, 1H, CH), 6.99–7.05 (m, 1H, CH), 7.47–7.53 (m, 2H, ArH), 7.55–7.77 (m, 5H, ArH), 7.85–7.92 (m, 3H, ArH), 10.50 (d, *J* = 10 Hz, 1H, NH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6):*δ = 56.9 (CH_2), 98.7 (CH), 127.7 (CH), 128.0 (CH), 128.6 (CH), 129.4 (CH), 131.6 (CH), 132.2 (CH), 133.0 (C), 133.8 (CH), 138.9 (C), 164.0 (C) *Data for *E*-isomer only, for *Z*-**21** data see above.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2021.131933.

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