A Convenient Synthesis of γ-Amino-Ynamides via Additions of Lithiated Ynamides to Aryl Imines; Observation of an Aza-Meyer–Schuster Rearrangement

Rui Qi,[a] Xiao-Na Wang,[b] Kyle A. DeKorver,*[c] Yu Tang,*[a] Chao-Chao Wang,[a] Qian Li,[a] Hui Li,[a] Ming-Can Lv,[a] Qing Yu,[a] Richard P. Hsung*[b]

[a] School of Pharmaceutical Science and Technology, and Tianjin Key Laboratory for Modern Drug Delivery & High-Efficiency, Tianjin University, Tianjin 300072, P. R. of China
E-mail: tangyu114@gmail.com

[b] Department of Chemistry and Division of Pharmaceutical Sciences, School of Pharmacy, University of Wisconsin–Madison, Madison, WI 53705, USA
E-mail: rhsung@wisc.edu

[c] Dow AgroSciences LLC, 9330 Zionsville Road, Indianapolis, IN 46268, USA
Fax +1(608)2625345; E-mail: kadekorver@dow.com

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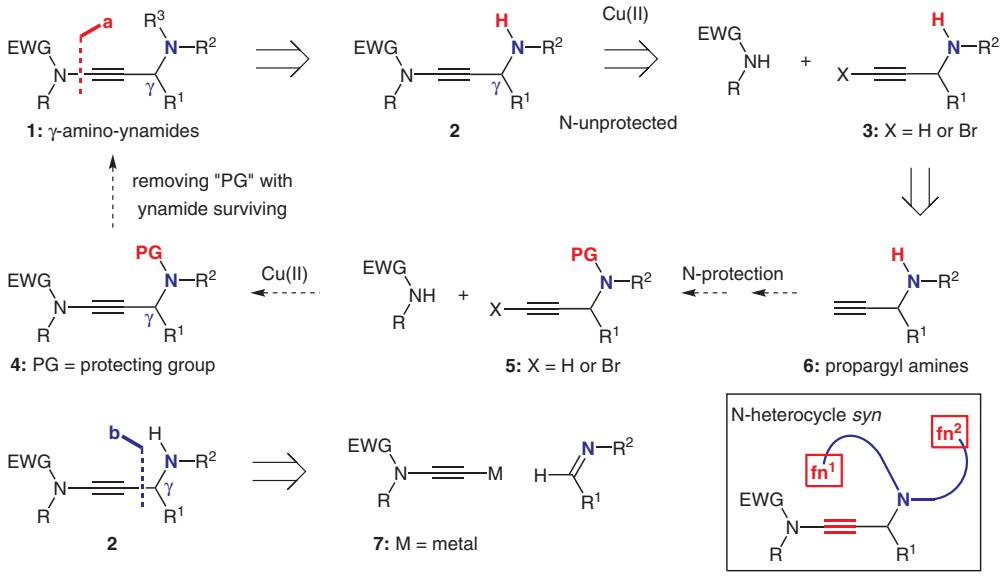
With the deepest respect and admiration, we dedicate this paper to Professor Scott E. Denmark on the very special occasion of his 60th birthday.

Abstract: Efforts in developing an expeditious and convenient method for synthesizing γ-amino-ynamides via nucleophilic addition of lithiated ynamides to aryl imines are described. This work also features an aza-variant of a Meyer–Schuster rearrangement of γ-amino-ynamides and their synthetic utility in intramolecular ketenimine [2+2] cycloadditions.

Key words: lithiated ynamides, γ-amino-ynamides, aryl imines, azetene, aza-Meyer–Schuster rearrangement

We have been involved with the chemistry of ynamides for the last 17 years, and this burgeoning field has attracted significant attention from the synthetic community.[1–4] Consequently, new and improved protocols for synthesizing ynamides[3] and their structural relatives[5,6] have continued to appear in the literature.[3e] Recently, when we employed γ-amino-ynamides **1** (see Scheme 1) to develop N-tethered intramolecular transformations for constructing N-heterocycles,[7] we recognized that this class of ynamides was not trivial to make.

The existing copper-catalyzed protocols,[1,2,5] albeit attractive, may not be suitable to couple directly amides with N-unprotected propargyl amines **3** (see retrosynthetic cleavage a).[8] On the other hand, with N-protected propargyl amines **5**, it would constitute an encumbered process, in addition to the fact that the penultimate deprotection step could still pose problems to the stability of the ynamides. The most direct access would be retrosynthetic pathway b,



Scheme 1 Possible approaches to γ-amino-ynamides; fn = functional group

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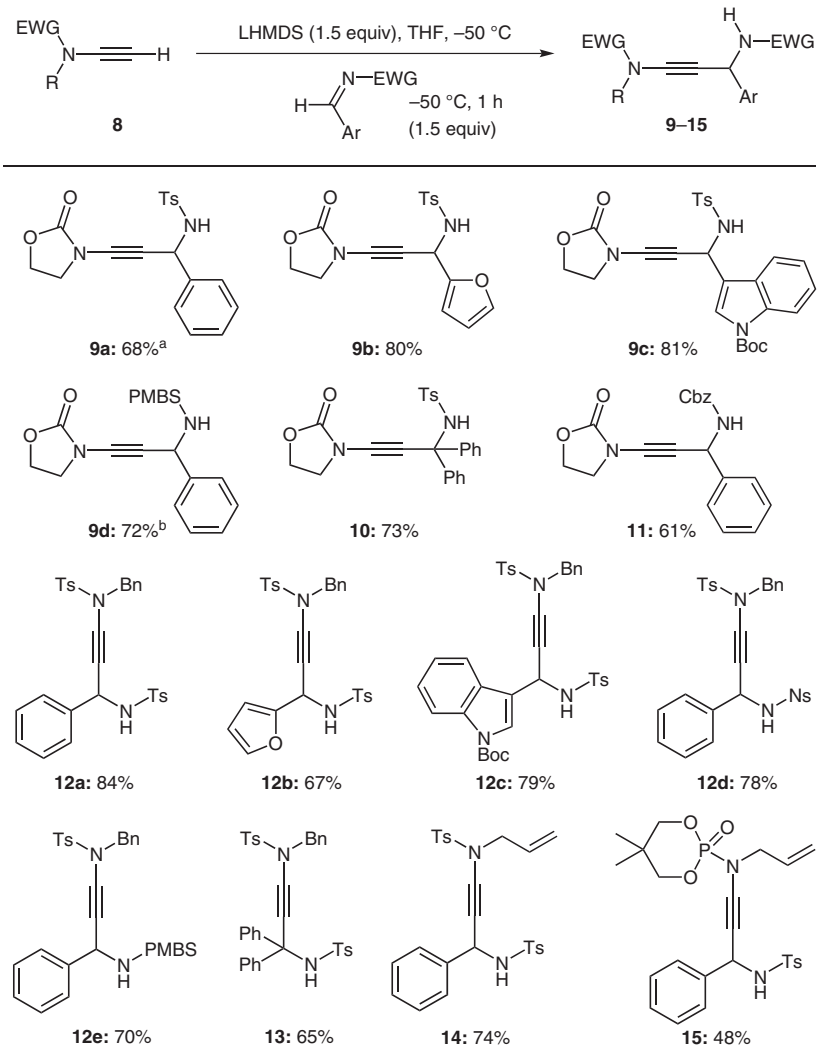
in which the metallated ynamide **7** could be added to a nitrogen source in the form of an imine. While metallated ynamides have been added to a number of electrophiles,[9] to the best of our knowledge, their addition to imines remains unreported.[1] Inspired by Poisson's recent account[10] on additions of lithiated ynol ethers to imines,[11] we explored this potentially expeditious method. We report here a general and convenient protocol for synthesizing γ-amino-ynamides.

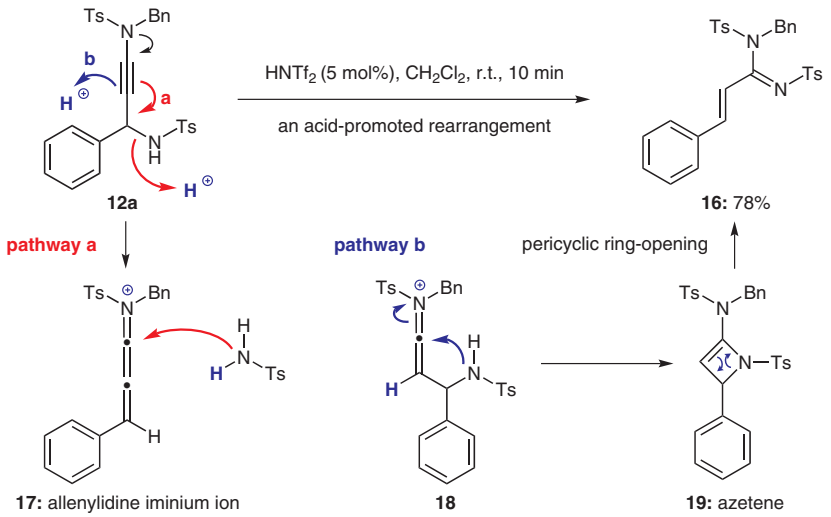
Deprotonation of ynamides **8** with lithium hexamethyldisilazide (LHMDS) (1.5 equiv) in tetrahydrofuran at –50 °C, followed by the addition of various imines, turned out to be a highly efficient protocol. A diverse array of *N*-sulfonyl or *N*-carbamoyl-γ-amino-ynamides **9**–**15** could be accessed in good yields through this simple method (Scheme 2). Examples of the ynamide precursors included: oxazolidinone-substituted (**9a**–**d**, **10** and **11**), sulfonyl-substituted (**12a**–**e**, **13** and **14**), or even phosphoryl-substituted[12] (**15**). Ketimines were also suitable substrates (**10** and **13**), while aldimines were represented by electron-withdrawing (**12d**) or -donating (**9d** and **12e**) sulfonyl systems.

What intrigued us was that some of these γ-amino-ynamides were not overtly stable to silica gel column chromatography, and appeared to rearrange cleanly into another compound, especially in the presence of acid. Upon further examination, we found that ynamide **12a** underwent rearrangement into α,β-unsaturated amidine **16** when treated with triflimide ($HNTf_2$) (5 mol%) at room temperature (Scheme 3). The assignment of amidine **16** was confirmed through its single crystal X-ray structure (Figure 1). Two possible mechanistic pathways can be proposed to account for this rearrangement. Pathway 'a' features an acid-promoted γ-elimination followed by reassociation of the departing amide with the allenylidine iminium ion **17**. Pathway 'b' favors an intramolecular non-dissociative possibility through pericyclic ring-opening of azetene intermediate **19**.[13]

To further delineate these two possibilities, we carried out the following crossover experiments (Scheme 4). After treating a mixture of γ-amino-ynamides **12a** and **12f** in a ratio of either 4:1 (reaction A), or 1:4 (reaction B) with *N*-phenyl-bis(trifluoromethanesulfonimide) (5 mol%), we examined closely the crude reaction mixture and all the



Scheme 2 Addition of lithiated ynamides to aryl imines. Yields are those of isolated products. PMBS = *p*-methoxybenzenesulfonyl.



Scheme 3 Acid-promoted rearrangement of ynamide **12a**

fractions resulting from purification of both reactions. We did not find possible crossover products **16af** and **16fa** in either reaction using ^{1}H NMR spectroscopy, and ynamides **12a** and **12f**, in both reactions, appeared to yield only their respective rearranged products **16a** and **16f**. The presence of products **16af** and **16fa** would have implied pathway a being operative.

To be more precise, we scanned the crude mixtures from incomplete reactions using LC–MS, and impressively, we did not find fractions with a mass that would correlate to either **16af** or **16fa** (see red arrows in Figure 2, which indicate where **16af** and **16fa** would be respectively, when co-injected with the crude mixtures from reactions A and B). It is noteworthy that rearrangement of ynamide **12a** appears to be much faster than that of **12f**. These results suggest the rearrangement occurs via pathway b involving the formation of azetene **19** and pericyclic ring-opening. Related ring-openings through oxetenes[14,15] are quite well known, and the current rearrangement essentially constitutes an aza-variant of the Meyer–Schuster rearrangement.[16]

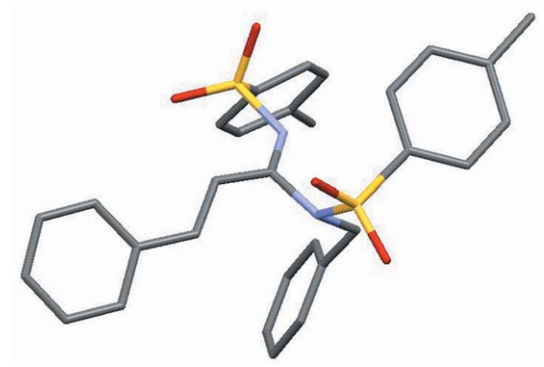
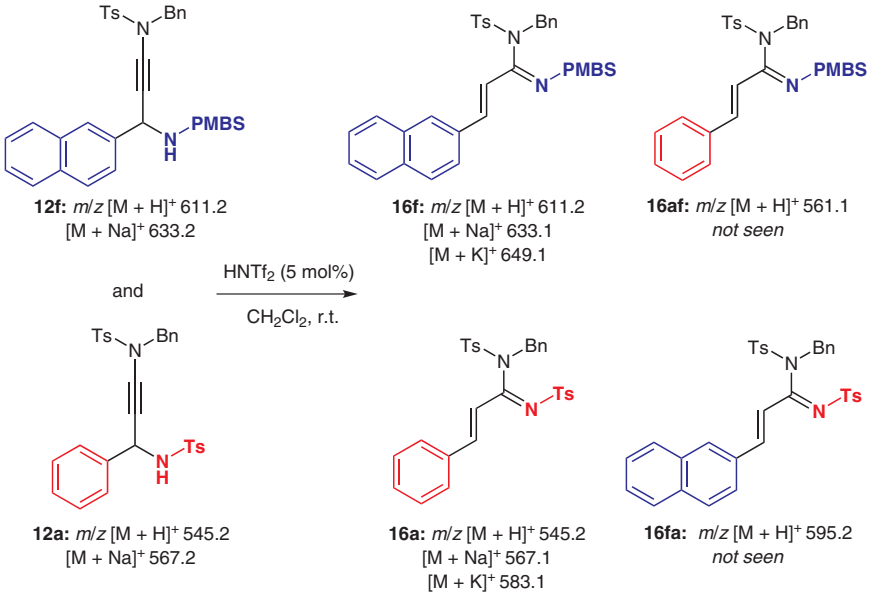
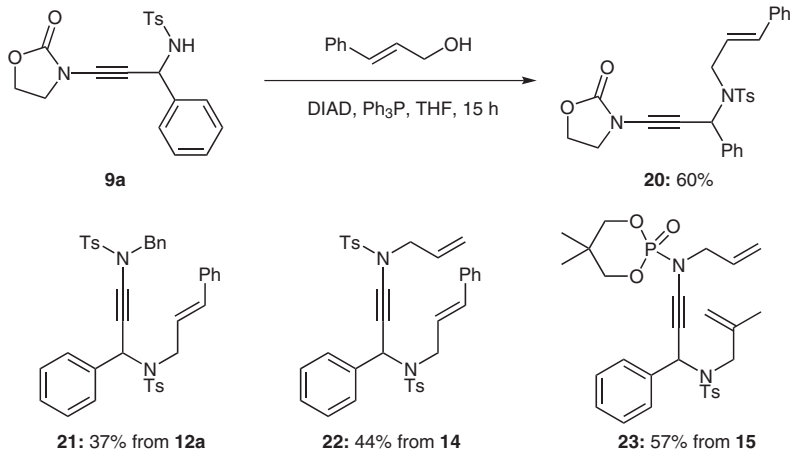


Figure 1 X-ray crystal structure of vinyl amidine **16** (ORTEP representation; CCDC 937489)



Scheme 4 A crossover experiment



Scheme 5 N-Allylations of γ-amino-ynamides

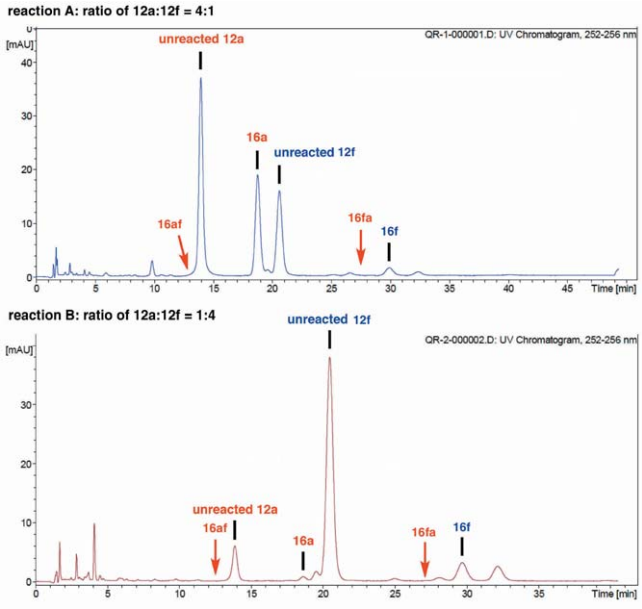
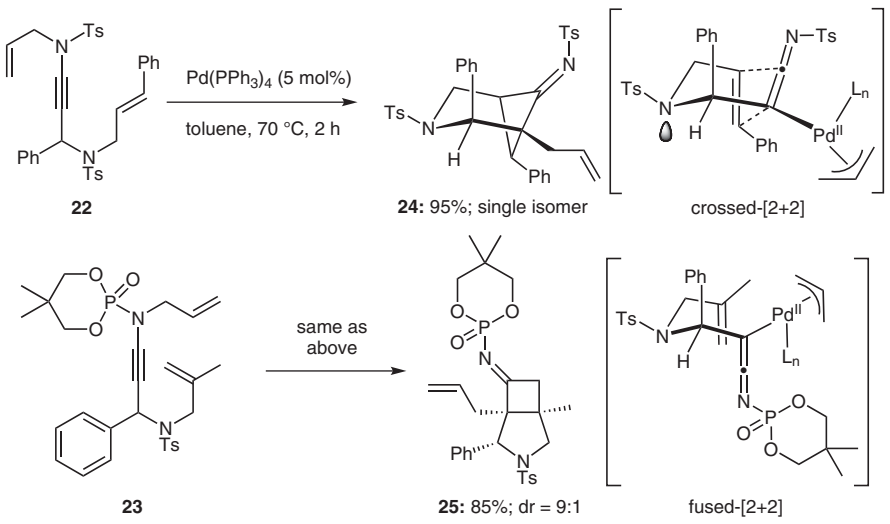


Figure 2 LC–MS traces from crossover experiments A and B

While this rearrangement is of interest both synthetically and mechanistically, and that this has become an ongoing project of another focus, we demonstrate here how these γ-amino-ynamides can be utilized in further transformations. As shown in Scheme 5, the γ-amino group in **9a** could be readily N-allylated using Mitsunobu conditions, leading to ynamide **20** in 60% yield. This N-allylation proved to be quite general for a number of γ-amino-ynamides such as **12a**, **14**, and **15** to give N-allylated products **21**–**23**, respectively. An immediate application of these products is in a palladium(0)-catalyzed aza-Claisen rearrangement[17–19] in tandem with ketenimine [2+2] cycloaddition,[20–23] leading to either a rare crossed cycloadduct **24** from ynamide **22**, or fused cycloadduct **25** derived from ynamide **23** in a highly stereoselective manner (Scheme 6).[7]

In conclusion, we have described herein our efforts in developing an expeditious and convenient method for synthesizing γ-amino-ynamides via nucleophilic addition of lithiated ynamides to aryl imines. In this study, we also uncovered an aza-variant of a Meyer–Schuster rearrange-



Scheme 6 Application of γ-amino-ynamides in [2+2] cycloadditions

ment of γ-amino-ynamides and demonstrated the usefulness of these γ-amino-ynamides in designing intramolecular transformations.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 600 MHz spectrometer at 25 °C. Chemical shift values are given in ppm and referenced to $SiMe_4$ as the internal standard (0.00 ppm). The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; qui, quintet; m, multiplet and dd, doublet of doublets. The coupling constants, *J*, are reported in hertz (Hz). IR spectra were recorded on a Bio Rad FTS-185 Fourier Transform infrared spectrophotometer. Mass spectra were obtained on an Agilent 6310 ion trap and HP5989A mass spectrometer. High-resolution mass spectrometry (HRMS) was conducted on a Bruker Micro Q-TOF spectrometer. Melting points were determined with a National Micro Melting point apparatus without corrections. Organic solutions were concentrated by rotary evaporation below 40 °C under vacuum. TLC plates were visualized by exposure to ultraviolet light.

Reagents and solvents were purchased as reagent grade and were used without further purification. Flash column chromatography was performed over silica gel 100–200 mesh and the eluent was a mixture of ethyl acetate and petroleum ether (PE).

γ-Amino-Ynamides; General Procedure

To a soln of the ynamide (0.1 M in freshly distilled THF) at –50 °C was added dropwise LHMDS (1.5 equiv, 1.0 M soln in THF) via a syringe. The mixture was allowed to stir at –50 °C for 1 h to ensure complete deprotonation. Next, a soln of the imine (1.5 equiv, 1.5 M in freshly distilled THF) was added over 10 min. After 1 h, H_2O (5 mL) was added and the mixture was allowed to warm to r.t., and then diluted with EtOAc. The organic phase was separated and the aq phase extracted twice with EtOAc. The combined organic phase was washed with sat. aq NaCl soln, dried over Na_2SO_4, and concentrated in vacuo. The crude residue was purified by silica gel flash column chromatography (gradient elution: EtOAc in PE) to give the corresponding γ-amino-ynamide.

4-Methyl-*N*-[3-(2-oxooxazolidin-3-yl)-1-phenylprop-2-yn-1-yl]benzenesulfonamide (9a)

Yield: 0.16 g (68%); white solid; mp 147–149 °C; R_f = 0.46 (hexanes–EtOAc, 2:3).

IR (KBr): 1415 (m), 1475 (m), 1492 (w), 1597 (w), 1761 (s), 1928 (w), 2268 (m), 2912 (w), 2972 (w), 3062 (w), 3086 (w), 3263 (br, s) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H), 3.64–3.73 (ddd, *J* = 8.4, 16.3, 22.7 Hz, 2 H), 4.39 (t, *J* = 8.0 Hz, 2 H), 4.92 (d, *J* = 8.4 Hz, 1 H), 5.48 (d, *J* = 8.4 Hz, 1 H), 7.29–7.34 (m, 5 H), 7.47 (d, *J* = 6.8 Hz, 2 H), 7.80 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.4, 46.7, 48.9, 64.0, 68.2, 77.0, 127.3, 127.6, 128.4, 128.9, 129.8, 138.80, 138.82, 143.1, 156.1.

MS (ESI): *m*/*z* (%) = 763 (100) [2 M + Na]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{18}N_2O_4SNa$: 393.0879; found: 393.0880.

***N*-[1-(Furan-2-yl)-3-(2-oxooxazolidin-3-yl)prop-2-yn-1-yl]-4-methylbenzenesulfonamide (9b)**

Yield: 0.18 g (80%); light yellow solid; mp 155–157 °C; R_f = 0.41 (hexanes–EtOAc, 2:3).

IR (KBr): 1373 (w), 1386 (w), 1423 (s), 1445 (w), 1477 (m), 1497 (w), 1597 (w), 1747 (s), 1984 (w), 2274 (m), 2860 (w), 2910 (w), 3205 (br, s) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.42 (s, 3 H), 3.73 (t, *J* = 8.0 Hz, 2 H), 4.39 (t, *J* = 8.0 Hz, 2 H), 5.16 (d, *J* = 8.0 Hz, 1 H), 5.52 (d, *J* = 8.0 Hz, 1 H), 6.26 (d, *J* = 3.2 Hz, 1 H), 6.36 (d, *J* = 3.2 Hz, 1 H), 7.28 (s, 1 H), 7.30 (d, *J* = 6.8 Hz, 2 H), 7.77 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.5, 43.7, 46.4, 63.1, 66.5, 75.3, 108.6, 110.5, 127.4, 129.5, 137.4, 143.1, 143.5, 149.2, 155.6.

MS (ESI): *m*/*z* (%) = 743 (100) [2 M + Na]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{16}N_2O_5SNa$: 383.0672; found: 383.0675.

3-[1-(4-Methylphenylsulfonamido)-3-(2-oxooxazolidin-3-yl)prop-2-yn-1-yl]-1-*tert*-butoxycarbonyl-1*H*-indole (9c)

Yield: 0.26 g (81%); white solid; mp 199–201 °C; R_f = 0.33 (hexanes–EtOAc, 2:3).

IR (KBr): 1367 (s), 1408 (m), 1435 (w), 1454 (m), 1478 (m), 1566 (w), 1598 (w), 1731 (s), 1782 (s), 2270 (w), 2355 (w), 2914 (w), 2986 (w), 3246 (br, s) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.66 (s, 9 H), 2.42 (s, 3 H), 3.59–3.71 (ddd, *J* = 8.4, 16.4, 24.4 Hz, 2 H), 4.38 (t, *J* = 8.0 Hz, 2 H), 4.93 (d, *J* = 8.8 Hz, 1 H), 5.59 (d, *J* = 8.8 Hz, 1 H), 7.21–7.24 (m, 3 H), 7.30–7.33 (t, *J* = 8.0 Hz, 1 H), 7.68 (d, *J* = 8.0 Hz, 1 H), 7.71 (s, 1 H), 7.80 (d, *J* = 8.0 Hz, 2 H), 8.10 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.4, 28.1, 42.0, 46.5, 64.1, 67.5, 76.0, 84.5, 115.2, 118.4, 120.5, 123.2, 125.0, 125.2, 127.4, 128.0, 129.7, 135.7, 138.6, 143.1, 149.3, 156.3.

MS (ESI): *m*/*z* (%) = 1041 (100) [2 M + Na]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{27}N_3O_6SNa$: 532.1513; found: 532.1516.

4-Methoxy-*N*-[3-(2-oxooxazolidin-3-yl)-1-phenylprop-2-yn-1-yl]benzenesulfonamide (9d)

Yield: 0.18 g (72%); white solid; mp 148–150 °C; R_f = 0.26 (hexanes–EtOAc, 2:3).

IR (KBr): 1421 (m), 1477 (m), 1499 (m), 1579 (m), 1596 (m), 1757 (s), 2260 (m), 2848 (w), 2916 (w), 2974 (w), 3010 (w), 3032 (w), 3080 (w), 3292 (br, s) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.66–3.70 (ddd, *J* = 9.2, 16.4, 24.8 Hz, 2 H), 3.88 (s, 3 H), 4.38 (t, *J* = 8.0 Hz, 2 H), 4.98 (d, *J* = 8.8 Hz, 1 H), 5.46 (d, *J* = 6.8 Hz, 1 H), 6.99 (d, *J* = 8.8 Hz, 2 H), 7.29–7.34 (m, 3 H), 7.48 (d, *J* = 8.0 Hz, 2 H), 7.85 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 46.5, 48.9, 56.1, 64.0, 68.4, 77.0, 114.5, 127.6, 128.3, 128.8, 129.4, 133.4, 138.9, 156.0, 162.6.

MS (ESI): *m*/*z* (%) = 795 (100) [2 M + Na]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{18}N_2O_5SNa$: 409.0829; found: 409.0828.

4-Methyl-*N*-[3-(2-oxooxazolidin-3-yl)-1,1-diphenylprop-2-yn-1-yl]benzenesulfonamide (10)

Yield: 0.15 g (73%); white solid; mp 183–185 °C; R_f = 0.30 (hexanes–EtOAc, 7:3).

IR (KBr): 1421 (m), 1449 (w), 1479 (w), 1599 (w), 1632 (w), 1767 (s), 2266 (m), 2320 (w), 2378 (w), 2878 (w), 2920 (w), 2938 (w), 3059 (w), 3165 (s), 3440 (br, s) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3 H), 3.78 (t, *J* = 8.0 Hz, 2 H), 4.40 (t, *J* = 8.0 Hz, 2 H), 5.38 (s, 1 H), 7.19 (d, *J* = 4.0 Hz, 2 H), 7.24–7.33 (m, 6 H), 7.50 (d, *J* = 8.0 Hz, 4 H), 7.61 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.4, 46.4, 62.7, 64.1, 70.5, 79.9, 127.2, 127.4, 127.8, 128.4, 129.3, 140.4, 142.6, 143.8, 156.1.

MS (ESI): *m*/*z* (%) = 915 (100) [2 M + Na]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{22}N_2O_4SNa$: 469.1192; found: 469.1192.

Benzyl 3-(2-Oxooxazolidin-3-yl)-1-phenylprop-2-yn-1-ylcarbamate (11)

Yield: 0.26 g (61%); white solid; mp 102–104 °C; R_f = 0.56 (hexanes–EtOAc, 2:3).

IR (KBr): 1377 (w), 1421 (m), 1454 (w), 1475 (w), 1493 (w), 1526 (s), 1687 (s), 1773 (s), 2262 (m), 2330 (w), 2360 (w), 2920 (w), 3033 (w), 3057 (w), 3309 (br, s) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.91 (t, *J* = 8.0 Hz, 2 H), 4.44 (t, *J* = 8.0 Hz, 2 H), 5.14 (dd, *J* = 12.0, 16.0 Hz, 2 H), 5.30 (d, *J* = 8.8 Hz, 1 H), 5.85 (d, *J* = 8.8 Hz, 1 H), 7.29–7.38 (m, 6 H), 7.52 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 46.5, 46.9, 64.1, 66.2, 69.6, 75.6, 127.3, 128.2, 128.27, 128.34, 128.8, 128.9, 137.3, 140.0, 155.9, 156.5.

MS (ESI): *m*/*z* (%) = 723 (38) $[2 M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{18}N_2O_4Na$: 373.1159; found: 373.1159.

_N_-Benzyl-4-methyl-_N_-[3-(4-methylphenylsulfonamido)-3-phenylprop-1-yn-1-yl]benzenesulfonamide (12a)

Yield: 0.61 g (84%); white solid; mp 158–160 °C; R_f = 0.28 (hexanes–EtOAc, 2:3).

IR (KBr): 1362 (s), 1400 (w), 1427 (m), 1450 (m), 1492 (m), 1597 (m), 1917 (w), 1964 (w), 2249 (m), 2367 (w), 2837 (w), 2871 (w), 2922 (w), 3070 (w), 3275 (br, s) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.37 (s, 3 H), 2.43 (s, 3 H), 4.29 (dd, *J* = 13.6, 20.8 Hz, 2 H), 4.72 (d, *J* = 8.4 Hz, 1 H), 5.34 (d, *J* = 8.4 Hz, 1 H), 7.12 (d, *J* = 6.8 Hz, 2 H), 7.18–7.20 (m, 5 H), 7.22–7.26 (m, 4 H), 7.29–7.33 (m, 3 H), 7.60 (d, *J* = 8.4 Hz, 2 H), 7.68 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.4, 21.6, 48.8, 55.2, 68.7, 79.4, 127.1, 127.6, 127.9, 128.3, 128.6, 128.73, 128.74, 128.9, 129.7, 130.5, 134.4, 135.2, 138.9, 139.2, 142.8, 145.4.

MS (ESI): *m*/*z* (%) = 1111 (100) $[2 M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{30}H_{28}N_2O_4S_2Na$: 567.1383; found: 567.1382.

_N_-Benzyl-_N_-[3-(furan-2-yl)-3-(4-methylphenylsulfonamido)prop-1-yn-1-yl]-4-methylbenzenesulfonamide (12b)

Yield: 0.35 g (67%); white solid; mp 116–117 °C; R_f = 0.20 (hexanes–EtOAc, 7:3).

IR (KBr): 1367 (s), 1420 (w), 1440 (m), 1498 (m), 1529 (w), 1660 (w), 1732 (w), 1801 (w), 1917 (w), 2247 (m), 2368 (w), 2723 (w), 2877 (w), 3032 (w), 3120 (br, s) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3 H), 2.42 (s, 3 H), 4.30 (dd, *J* = 14.0, 21.6 Hz, 2 H), 5.06 (d, *J* = 8.5 Hz, 1 H), 5.38 (d, *J* = 8.5 Hz, 1 H), 6.09 (d, *J* = 3.2 Hz, 1 H), 6.20 (t, *J* = 2.9 Hz, 1 H), 7.16 (m, 4 H), 7.26 (m, 6 H), 7.63 (d, *J* = 8.2 Hz, 2 H), 7.67 (d, *J* = 8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 21.7, 43.7, 55.2, 66.7, 78.9, 108.3, 110.4, 127.2, 127.7, 128.4, 128.6, 128.7, 129.6, 129.8, 134.1, 134.5, 137.4, 142.9, 143.5, 144.9, 149.8.

MS (ESI): *m*/*z* (%) = 1091 (100) $[2 M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{26}N_2O_5S_2Na$: 557.1175; found: 557.1175.

3-[3-(_N_-Benzyl-4-methylphenylsulfonamido)-1-(4-methylphenylsulfonamido)prop-2-yn-1-yl]-1-_tert_-butoxycarbonyl-1_H_-indole (12c)

Yield: 0.19 g (79%); white solid; mp 143–145 °C; R_f = 0.27 (hexanes–EtOAc, 4:1).

IR (KBr): 1082 (m), 1159 (s), 1370 (s), 1454 (m), 1597 (w), 1735 (s), 2254 (m), 2981 (w), 3252 (s) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.66 (s, 9 H), 2.30 (s, 3 H), 2.41 (s, 3 H), 4.17 (d, *J* = 14.4 Hz, 1 H), 4.37 (d, *J* = 14.4 Hz, 1 H), 5.03 (d, *J* = 8.8 Hz, 1 H), 5.60 (d, *J* = 8.4 Hz, 1 H), 7.06–7.11 (m, 4 H), 7.15–7.21 (m, 3 H), 7.23–7.27 (m, 3 H), 7.29–7.34 (m, 2 H), 7.55 (d, *J* = 4.4 Hz, 1 H), 7.60 (d, *J* = 8.0 Hz, 2 H), 7.64–7.66 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 21.6, 28.1, 42.7, 55.1, 67.7, 79.0, 84.0, 115.1, 117.5, 119.7, 122.8, 124.7, 124.9, 127.2, 127.4, 127.5, 128.3, 128.4, 128.5, 129.3, 129.7, 134.2, 134.6, 135.9, 137.2, 143.3, 144.7, 149.3.

MS (ESI): *m*/*z* (%) = 1389 (100) $[2 M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{37}H_{37}N_3O_6S_2Na$: 706.2016; found: 706.2016.

_N_-Benzyl-4-methyl-_N_-[3-(4-nitrophenylsulfonamido)-3-phenylprop-1-yn-1-yl]benzenesulfonamide (12d)

Yield: 0.16 g (78%); white solid; mp 141–143 °C; R_f = 0.38 (hexanes–EtOAc, 7:3).

IR (KBr): 1167 (s), 1348 (s), 1529 (s), 1597 (w), 2248 (m), 3275 (s) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 4.32 (s, 2 H), 5.33 (d, *J* = 8.0 Hz, 1 H), 5.47 (d, *J* = 8.0 Hz, 1 H), 7.15 (d, *J* = 6.8 Hz, 2 H), 7.20–7.27 (m, 6 H), 7.29–7.33 (m, 4 H), 7.64 (d, *J* = 8.4 Hz, 2 H), 7.90 (d, *J* = 8.8 Hz, 2 H), 8.15 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.6, 49.8, 55.0, 68.0, 80.4, 124.1, 127.2, 127.5, 128.2, 128.5, 128.6, 128.7, 129.9, 133.9, 134.3, 137.1, 145.0, 146.1, 149.8 (2 carbon signals missing due to overlap).

MS (ESI): *m*/*z* (%) = 1173 (100) $[2 M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{25}N_3O_6S_2Na$: 598.1077; found: 598.1057.

_N_-Benzyl-_N_-[3-(4-methoxyphenylsulfonamido)-3-phenylprop-1-yn-1-yl]-4-methylbenzenesulfonamide (12e)

Yield: 0.12 g (70%); white solid; mp 150–152 °C; R_f = 0.30 (hexanes–EtOAc, 7:3).

IR (KBr): 1367 (s), 1404 (w), 1435 (m), 1495 (s), 1579 (s), 1597 (s), 1801 (w), 1895 (w), 1951 (w), 1969 (w), 2032 (w), 2250 (s), 2585 (w), 2844 (w), 2947 (w), 3014 (w), 3032 (w), 3105 (w), 3226 (br, s) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 3.83 (s, 3 H), 4.34 (dd, *J* = 13.6, 24.4 Hz, 2 H), 4.85 (d, *J* = 8.4 Hz, 1 H), 5.35 (d, *J* = 8.4 Hz, 1 H), 6.89 (d, *J* = 8.8 Hz, 2 H), 7.15 (d, *J* = 6.4 Hz, 2 H), 7.20–7.33 (m, 10 H), 7.63 (d, *J* = 8.0 Hz, 2 H), 7.75 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 49.4, 55.1, 55.5, 68.5, 79.9, 114.1, 127.1, 127.6, 128.2, 128.4, 128.56, 128.58, 128.7, 129.3, 129.7, 131.9, 134.1, 134.5, 137.7, 144.8, 162.8.

MS (ESI): *m*/*z* (%) = 583 (100) $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{30}H_{28}N_2O_5S_2Na$: 583.1332; found: 583.1336.

_N_-Benzyl-_N_-[3-(4-methoxyphenylsulfonamido)-3-(naphthalen-2-yl)prop-1-yn-1-yl]-4-methylbenzenesulfonamide (12f)

Yield: 0.12 g (76%); white solid; mp 152–154 °C; R_f = 0.24 (hexanes–EtOAc, 7:3).

IR (KBr): 1360 (s), 1463 (w), 1496 (m), 1556 (s), 1576 (s), 1610 (s), 2830 (w), 3021 (w), 3445 (br, s) cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 2.37 (s, 3 H), 3.73 (s, 3 H), 4.35 (dd, *J* = 14.4, 36.6 Hz, 2 H), 5.00 (d, *J* = 8.0 Hz, 1 H), 5.48 (d, *J* = 8.1 Hz, 1 H), 6.77 (d, *J* = 5.6 Hz, 2 H), 7.14 (d, *J* = 4.4 Hz, 2 H), 7.17 (d, *J* = 5.2 Hz, 2 H), 7.24–7.30 (m, 4 H), 7.47 (s, 2 H), 7.60 (d, *J* = 5.2 Hz, 2 H), 7.69 (m, 5 H), 7.78 (d, *J* = 4.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 49.7, 55.2, 55.5, 68.6, 80.3, 114.1, 125.0, 126.2, 126.3, 126.4, 127.6, 127.6, 128.2, 128.4, 128.5, 128.6, 128.7, 129.4, 129.8, 131.9, 132.96, 133.02, 134.2, 134.5, 135.1, 144.8, 162.8.

MS (ESI): *m*/*z* (%) = 611 (100) $[M + H]^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{30}N_2O_5S_2Na$: 633.1488; found: 633.1487.

_N_-Benzyl-4-methyl-_N_-[3-(4-methylphenylsulfonamido)-3,3-diphenylprop-1-yn-1-yl]benzenesulfonamide (13)
Yield: 0.13 g (65%); white solid; mp 147–149 °C; R_f = 0.25 (hexanes–EtOAc, 10:3).

IR (KBr): 1367 (s), 1400 (m), 1438 (m), 1452 (s), 1493 (m), 1594 (m), 1649 (w), 1762 (w), 1803 (w), 1818 (w), 1936 (w), 2256 (s), 2322 (w), 2956 (w), 3034 (w), 3089 (w), 3208 (br, s) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3 H), 2.44 (s, 3 H), 4.35 (s, 2 H), 5.14 (s, 1 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 7.15–7.30 (m, 17 H), 7.39 (d, *J* = 8.0 Hz, 2 H), 7.71 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.4, 21.5, 54.8, 62.7, 71.3, 82.2, 127.0, 127.2, 127.7, 127.9, 128.2, 128.6, 128.8, 128.9, 129.2, 130.5, 134.5, 135.0, 140.4, 142.3, 143.6, 145.4.

MS (ESI): *m*/*z* (%) = 1263 (100) [2 M + Na]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{36}H_{32}N_2O_4S_2Na$: 643.1696; found: 643.1710.

_N_-Allyl-4-methyl-_N_-[3-(4-methylphenylsulfonamido)-3-phenylprop-1-yn-1-yl]benzenesulfonamide (14)
Yield: 0.31 g (74%); white solid; mp 123–124 °C; R_f = 0.22 (hexanes–EtOAc, 3:1).

IR (film): 1365 (s), 1597 (m), 1738 (m), 2248 (m), 2922 (m), 2961 (m) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 2.43 (s, 3 H), 3.72 (ddt, *J* = 1.2, 6.4, 14.8 Hz, 1 H), 3.78 (ddt, *J* = 1.2, 6.4, 14.8 Hz, 1 H), 4.98 (d, *J* = 8.4 Hz, 1 H), 5.10 (dq, *J* = 1.2, 16.8 Hz, 1 H), 5.12 (dq, *J* = 1.2, 10.4 Hz, 1 H), 5.41 (d, *J* = 8.4 Hz, 1 H), 5.52 (ddt, *J* = 6.4, 10.4, 16.8 Hz, 1 H), 7.22 (dd, *J* = 0.8, 8.4 Hz, 2 H), 7.26 (dd, *J* = 0.8, 8.4 Hz, 2 H), 7.28–7.34 (m, 3 H), 7.39–7.41 (m, 2 H), 7.63 (d, *J* = 8.4 Hz, 2 H), 7.71 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.6, 21.8, 49.6, 54.0, 68.1, 79.7, 120.1, 127.37, 127.39, 127.8, 128.4, 128.7, 129.7, 129.9, 130.7, 134.6, 137.7, 137.9, 143.5, 145.0.

MS (ESI): *m*/*z* (%) = 495 (100) [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{27}N_2O_4S_2$: 495.1407; found: 495.1427.

_N_-{3-[Allyl(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]-1-phenylprop-2-yn-1-yl}-4-methylbenzenesulfonamide (15)
Yield: 0.65 g (48%); white solid; mp 137–138 °C; R_f = 0.23 (hexanes–EtOAc, 1:1).

IR (film): 1273 (s), 1325 (s), 1454 (m), 2251 (m), 2888 (m), 2934 (m), 2968 (m), 3143 (br, m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.84 (s, 3 H), 1.01 (s, 3 H), 2.38 (s, 3 H), 3.60–3.69 (m, 2 H), 3.94–4.02 (m, 4 H), 5.15 (d, *J* = 9.5 Hz, 1 H), 5.18 (d, *J* = 16.0 Hz, 1 H), 5.35 (s, 1 H), 5.67–5.75 (m, 1 H), 6.22 (br s, 1 H), 7.20–7.26 (m, 5 H), 7.38–7.40 (m, 2 H), 7.73 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.4, 20.9, 21.2, 31.7 (d, *J* = 6.8 Hz), 49.1, 52.8 (d, *J* = 5.8 Hz), 62.6 (d, *J* = 5.8 Hz), 78.0 (d, *J* = 6.8 Hz), 81.5 (d, *J* = 4.8 Hz), 118.5, 126.0, 126.8 (d, *J* = 4.9 Hz), 127.7, 128.1, 129.1, 131.9, 137.6, 138.2, 142.8.

^{31}P NMR (202 MHz, $CDCl_3$): δ = –1.31.

MS (ESI): *m*/*z* (%) = 489 (100) [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{30}N_2O_5PS$: 489.1608; found: 489.1600.

γ-Amino-Ynamide Rearrangement; General Procedure
To a soln of the γ-amino-ynamide (0.05 M in anhyd CH_2Cl_2) was added $HNTf_2$ (0.05 equiv) at r.t. The resulting mixture was stirred at r.t. and the reaction progress was monitored using TLC analysis. When the starting material had been consumed completely, the mixture was quenched with Et_3N. Removal of the solvent in vacuo led to a crude residue that was purified using silica gel flash column chromatography (gradient elution: EtOAc in hexane).

(1_Z_,2_E_)-_N_-benzyl-_N_,_N′_-ditosylcinnamimidamide (16a)
Yield: 0.14 g (78%); white solid; mp 156–157 °C; R_f = 0.59 (hexanes–EtOAc, 7:3).

IR (KBr): 1346 (m), 1380 (w), 1399 (w), 1446 (w), 1495 (w), 1512 (w), 1558 (m), 1576 (m), 1612 (m), 1705 (m), 1747 (w), 2928 (w), 2964 (w), 3030 (w), 3064 (w), 3443 (br, s) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39 (s, 6 H), 4.93 (s, 2 H), 7.03–7.16 (m, 5 H), 7.18–7.24 (m, 6 H), 7.38–7.43 (m, 5 H), 7.46 (d, *J* = 8.4 Hz, 2 H), 7.51 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.5, 21.6, 52.0, 119.4, 127.0, 127.8, 128.2, 128.3, 128.4, 128.6, 128.9, 129.2, 129.6, 130.6, 134.3, 135.4, 135.7, 138.5, 143.1, 144.7, 145.0, 164.1.

MS (APCI): *m*/*z* (%) = 545 (100) [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{28}N_2O_4S_2Na$: 567.1383; found: 567.1384.

(1_Z_,2_E_)-_N_-Benzyl-_N′_-[(4-methoxyphenyl)sulfonyl]-3-(naphthalen-2-yl]-_N_-tosylacrylimidamide (16f)
Yield: 0.060 g (65%); yellow solid; mp 139–140 °C; R_f = 0.33 (hexanes–EtOAc, 7:3).

IR (KBr): 1364 (s), 1429 (m), 1454 (m), 1496 (s), 1557 (m), 1596 (s), 2252 (m), 2843 (w), 2914 (w), 3062 (w), 3219 (s) cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 3.80 (s, 3 H), 4.95 (s, 2 H), 6.81 (d, *J* = 12.0 Hz, 2 H), 7.14 (d, *J* = 12.0 Hz, 2 H), 7.20–7.26 (m, 7 H), 7.49–7.58 (m, 7 H), 7.80 (s, 1 H), 7.84 (t, *J* = 6.0 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.6, 52.1, 55.6, 100.0, 113.7, 119.5, 123.6, 126.8, 127.5, 127.8, 128.2, 128.4, 128.6, 128.7, 128.8, 129.1, 129.6, 130.5, 131.8, 133.2, 133.3, 134.4, 135.3, 135.8, 145.01, 145.02, 162.7, 164.0.

MS (ESI): *m*/*z* (%) = 611 (100) [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{30}N_2O_5S_2Na$: 633.1488; found: 633.1490.

(1_Z_,2_E_)-_N_-Benzyl-_N′_-[(4-methoxyphenyl)sulfonyl]-_N_-tosylcinnamimidamide (16af)
Yield: 0.24 g (72%); yellow solid; mp 149–151 °C; R_f = 0.39 (hexanes–EtOAc, 7:3).

IR (KBr): 1322 (m), 1361 (s), 1496 (m), 1556 (s), 1577 (s), 1595 (s), 1610 (s), 2841 (w), 2935 (w), 2960 (w), 3033 (w), 3062 (w) cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 3.82 (s, 3 H), 4.95 (s, 2 H), 6.81 (d, *J* = 8.5 Hz, 2 H), 7.02 (d, *J* = 16.2 Hz, 1 H), 7.11–7.14 (m, 3 H), 7.18–7.25 (m, 5 H), 7.38 (m, 5 H), 7.48 (d, *J* = 7.8 Hz, 2 H), 7.56 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.6, 52.0, 55.6, 113.7, 119.4, 127.8, 128.2, 128.29, 128.30, 128.6, 128.9, 129.1, 129.6, 130.6, 133.2, 134.3, 135.3, 135.7, 144.6, 145.0, 162.7, 164.0.

MS (ESI): *m*/*z* (%) = 561 (100) [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{28}N_2O_5S_2Na$: 583.1332; found: 583.1332.

(1_Z_,2_E_)-_N_-Benzyl-3-(naphthalen-2-yl)-_N_,_N′_-ditosylacrylimidamide (16fa)
Yield: 0.19 g (57%); yellow solid; mp 178–179 °C; R_f = 0.54 (hexanes–EtOAc, 7:3).

IR (KBr): 1361 (s), 1454 (w), 1496 (w), 1593 (m), 3028 (w), 3260 (w) cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.38 (s, 6 H), 4.95 (s, 2 H), 7.14 (d, *J* = 7.8 Hz, 2 H), 7.16 (d, *J* = 7.2 Hz, 2 H), 7.21–7.26 (m, 7 H), 7.48 (d, *J* = 8.4 Hz, 2 H), 7.52 (d, *J* = 7.8 Hz, 4 H), 7.57 (d, *J* = 8.4 Hz, 1 H), 7.80 (s, 1 H), 7.85 (m, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 21.5, 21.6, 52.1, 119.5, 123.6, 125.6, 126.8, 127.0, 127.5, 127.8, 128.2, 128.4, 128.6, 128.7, 128.8, 129.2, 129.6, 130.5, 131.8, 133.2, 134.4, 135.3, 135.7, 138.5, 143.1, 145.0, 145.2, 164.2.

MS (ESI): *m*/*z* (%) = 595 (100) $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{34}H_{30}N_2O_4S_2Na$: 617.1539; found: 617.1535.

N-Allylation; Typical Procedure

A flame-dried, screw-cap vial was charged with γ-amino-ynamide **14** (125.0 mg, 0.25 mmol), cinnamyl alcohol (36.9 mg, 0.275 mmol), PPh_3 (72.1 mg, 0.275 mmol) and THF (0.8 mL). The soln was stirred for 5 min at r.t., cooled to 0 °C and treated with diisopropyl azodicarboxylate (DIAD) (51.0 μL, 0.275 mmol) dropwise. The cooling bath was removed and the mixture was allowed to warm to r.t. The reaction progress was monitored using TLC, and when the starting material had been consumed (after 15 h), the solvent was removed in vacuo. The crude residue was purified by silica gel flash column chromatography [isocratic elution: hexanes–EtOAc, 4:1 containing 2% Et_3N (to buffer the silica gel)] to afford ynamide **22** as a mixture with DIAD-H_2 being the byproduct. Ynamide **22** (67.0 mg, 0.11 mmol, 44%) was recrystallized cleanly from the mixture using benzene–hexane.

***N*-Cinnamyl-4-methyl-*N*-[3-(2-oxooxazolidin-3-yl)-1-phenylprop-2-yn-1-yl]benzenesulfonamide (20)**

Yield: 0.18 g (60%); white solid; mp 129–130 °C; R_f = 0.22 (hexanes–EtOAc, 7:3).

IR (film): 1368 (w), 1417 (m), 1424 (m), 1441 (w), 1473 (m), 1493 (m), 1599 (w), 1789 (s), 2250 (m), 2924 (w), 2986 (w), 3038 (w), 3432 (br, s) cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.42 (s, 3 H), 3.56 (dq, *J* = 8.4, 26.4 Hz, 2 H), 3.81 (d, *J* = 6.6 Hz, 2 H), 4.29–4.33 (m, 2 H), 5.70 (dt, *J* = 6.6, 22.8 Hz, 1 H), 6.14 (d, *J* = 15.6 Hz, 1 H), 6.29 (s, 1 H), 7.02 (d, *J* = 7.2 Hz, 2 H), 7.15 (t, *J* = 7.2 Hz, 1 H), 7.20 (t, *J* = 7.2 Hz, 2 H), 7.24–7.26 (m, 1 H), 7.30–7.32 (m, 4 H), 7.59 (d, *J* = 7.8 Hz, 2 H), 7.85 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.5, 46.4, 47.4, 53.4, 63.0, 66.5, 78.4, 125.7, 126.3, 127.4, 127.9, 128.2, 128.3, 128.5, 129.6, 132.7, 136.2, 136.6, 136.9, 143.4, 155.7 (1 carbon signal missing due to overlap).

MS (APCI): *m*/*z* (%) = 487 (100) $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{26}N_2O_4SNa$: 509.1505; found: 509.1506.

(*E*)-*N*-Benzyl-*N*-[3-(*N*-cinnamyl-4-methylphenylsulfonamido)-3-phenylprop-1-yn-1-yl]-4-methylbenzenesulfonamide (21)

Yield: 0.17 g (37%); white solid; mp 125–126 °C; R_f = 0.54 (hexanes–EtOAc, 7:3).

IR (film): 1363 (m), 1399 (w), 1427 (w), 1454 (m), 1490 (m), 1592 (m), 2245 (m), 2857 (w), 2921 (w), 3028 (w), 3064 (w), 3438 (br, s) cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 2.33 (s, 3 H), 2.38 (s, 3 H), 3.56 (dd, *J* = 7.2, 15.0 Hz, 1 H), 3.72 (dd, *J* = 5.4, 15.0 Hz, 1 H), 4.36 (dd, *J* = 14.4, 39.0 Hz, 2 H), 5.51–5.56 (m, 1 H), 5.98 (d, *J* = 15.6 Hz, 1 H), 6.22 (s, 1 H), 6.90 (d, *J* = 6.0 Hz, 2 H), 7.10 (d, *J* = 7.2 Hz, 2 H), 7.16–7.23 (m, 12 H), 7.26–7.29 (m, 3 H), 7.64 (d, *J* = 8.4 Hz, 2 H), 7.75 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.5, 21.6, 47.4, 53.6, 55.2, 66.3, 81.6, 125.6, 126.4, 127.4, 127.7, 127.8, 128.0, 128.1, 128.3, 128.4, 128.5, 128.7, 129.7, 129.9, 132.4, 134.3, 134.7, 136.6, 136.96, 136.97, 143.4, 144.9 (1 carbon signal missing due to overlap).

MS (APCI): *m*/*z* (%) = 661 (100) $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{39}H_{36}N_2O_4S_2Na$: 683.2009; found: 683.2008.

(*E*)-*N*-Allyl-*N*-[3-(*N*-cinnamyl-4-methylphenylsulfonamido)-3-phenylprop-1-yn-1-yl]-4-methylbenzenesulfonamide (22)

Yield: 0.070 g (44%); white solid; mp 80–81 °C; R_f = 0.38 (hexanes–EtOAc, 2:1).

IR (film): 1365 (s), 1597 (m), 1738 (m), 2248 (m), 2922 (m), 2961 (m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.38 (s, 6 H), 3.77 (ddd, *J* = 1.0, 8.0, 15.5 Hz, 1 H), 3.82 (ddt, *J* = 1.5, 3.0, 6.0 Hz, 2 H), 3.88 (ddd, *J* = 1.0, 6.0, 15.5 Hz, 1 H), 5.108 (dq, *J* = 1.0, 11.0 Hz, 1 H), 5.115 (dq, *J* = 1.0, 17.5 Hz, 1 H), 5.53 (ddt, *J* = 6.0, 11.0, 17.5 Hz, 1 H), 5.60 (ddd, *J* = 6.0, 8.0, 16.0 Hz, 1 H), 6.13 (d, *J* = 16.0 Hz, 1 H), 6.26 (s, 1 H), 6.94 (dd, *J* = 1.5, 7.5 Hz, 2 H), 7.14–7.20 (m, 2 H), 7.22–7.30 (m, 7 H), 7.54 (dd, *J* = 1.0, 7.0 Hz, 2 H), 7.68 (d, *J* = 8.5 Hz, 2 H), 7.78 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.7, 21.8, 47.7, 53.7, 54.1, 65.9, 81.4, 120.0, 125.7, 126.5, 127.6, 127.8, 127.9, 128.28, 128.34, 128.4, 128.5, 129.8, 130.0, 130.9, 132.7, 134.9, 136.7, 137.1, 137.2, 143.5, 145.1.

MS (ESI): *m*/*z* (%) = 495 (60), 611 (30) $[M + H]^+$.[24]

***N*-{3-[Allyl(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]-1-phenylprop-2-yn-1-yl}-4-methyl-*N*-(2-methylallyl)benzenesulfonamide (23)**

Yield: 0.31 g (57%); colorless oil; R_f = 0.32 (Et_2O).

IR (film): 1281 (s), 1331 (s), 1453 (m), 2249 (m), 2891 (m), 2974 (m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.04 (s, 3 H), 1.08 (s, 3 H), 1.31 (s, 3 H), 2.44 (s, 3 H), 3.57–3.79 (m, 4 H), 4.01–4.09 (m, 2 H), 4.12–4.19 (m, 2 H), 4.57 (d, *J* = 47.0 Hz, 2 H), 5.20 (d, *J* = 10.0 Hz, 1 H), 5.21 (d, *J* = 17.0 Hz, 1 H), 5.72–5.78 (m, 1 H), 6.19 (d, *J* = 3.0 Hz, 1 H), 7.26–7.34 (m, 5 H), 7.52–7.54 (m, 2 H), 7.77 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.4, 21.1 (d, *J* = 2.4 Hz), 21.4, 32.1 (d, *J* = 6.8 Hz), 51.2, 53.0 (d, *J* = 5.8 Hz), 54.1 (d, *J* = 1.4 Hz), 59.5 (d, *J* = 5.8 Hz), 77.8 (d, *J* = 7.2 Hz), 77.9 (d, *J* = 6.7 Hz), 83.7 (d, *J* = 5.3 Hz), 113.8, 118.7, 127.7, 127.8, 127.9, 128.5, 129.4, 132.2 (d, *J* = 2.0 Hz), 136.1, 137.0 (d, *J* = 1.0 Hz), 140.9, 143.3.

^{31}P NMR (202 MHz, $CDCl_3$): δ = –0.75.

MS (APCI): *m*/*z* (%) = 543 (57) $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + NH_4]^+$ calcd for $C_{28}H_{39}N_3O_5PS$: 560.2343; found: 560.2337.

[2+2] Cycloaddition; Typical Procedure

To a flame-dried, screw-cap vial were added ynamide **23** [54.4 mg, 0.10 mmol, 0.1 M in toluene (1 mL)] and $Pd(PPh_3)_4$ (5.80 mg, 0.0050 mmol). The vial was sealed under N_2 and heated to 70 °C. After 2 h, TLC analysis showed complete consumption of the starting ynamide and the solvent was removed in vacuo. The crude residue was purified through silica gel flash column chromatography (isocratic elution: hexanes–EtOAc, 1:1) to afford cycloadduct **25** (46.3 mg, 0.085 mmol) in 85% yield.

(*E*)-*N*-[(1*R*,2*R*,5*S*)-1-Allyl-2,7-diphenyl-3-tosyl-3-azabicyclo[3.1.1]heptan-6-ylidene]-4-methylbenzenesulfonamide (24)

Yield: 0.060 g (95%); white solid; mp 114–115 °C; R_f = 0.40 (hexanes–EtOAc, 2:1).

IR (film): 1327 (s), 1453 (m), 1597 (m), 1660 (s), 1727 (m), 2852 (m), 2930 (m), 3032 (w) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.76 (dd, *J* = 9.0, 15.5 Hz, 1 H), 1.84 (ddt, *J* = 2.0, 5.0, 15.5 Hz, 1 H), 2.37 (s, 3 H), 2.45 (s, 3 H), 3.62 (s, 1 H), 4.206 (s, 1 H), 4.212 (d, *J* = 15.5 Hz, 1 H), 4.62 (dd,

J = 5.5, 11.0 Hz, 1 H), 4.76 (dd, J = 1.0, 17.0 Hz, 1 H), 5.07 (d, J = 10.0 Hz, 1 H), 5.48 (dddd, J = 5.0, 9.0, 10.0, 17.0 Hz, 1 H), 5.72 (s, 1 H), 6.88 (d, J = 7.0 Hz, 2 H), 7.03 (t, J = 8.0 Hz, 2 H), 7.07–7.09 (m, 4 H), 7.16 (t, J = 7.5 Hz, 1 H), 7.21–7.23 (m, 5 H), 7.33 (d, J = 8.0 Hz, 2 H), 7.83 (d, J = 8.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 21.8, 30.7, 45.9, 53.1, 54.0, 66.1, 72.2, 120.1, 127.0, 127.7, 127.8, 127.9, 128.1, 128.5, 128.6, 128.9, 129.5, 129.8, 130.8, 136.2, 136.4, 136.6, 137.0, 143.3, 144.7, 193.5.

MS (ESI): m/z (%) = 611 (100) $[M + H]^+$.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{35}H_{35}N_2O_4S_2$: 611.2038; found: 611.2047.

2-{(*E*)-[(1*R*,4*R*,5*S*)-5-Allyl-1-methyl-4-phenyl-3-tosyl-3-azabicyclo[3.2.0]heptan-6-ylidene]amino}-5,5-dimethyl-1,3,2-dioxaphosphinane 2-Oxide (25)

Yield: 0.050 g (85%); colorless oil; R_f = 0.15 (hexanes–EtOAc, 1:1).

IR (film): 1287 (s), 1340 (s), 1702 (s), 2879 (m), 2933 (m), 2966 (m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.95 (s, 3 H), 1.37 (s, 3 H), 1.45 (s, 3 H), 2.02–2.06 (m, 1 H), 2.13–2.18 (m, 1 H), 2.29 (s, 3 H), 3.28 (t, J = 2.5 Hz, 2 H), 3.38 (d, J = 10.5 Hz, 1 H), 3.83 (d, J = 10.5 Hz, 1 H), 3.98 (dd, J = 10.5, 21.0 Hz, 2 H), 4.39 (dd, J = 4.0, 10.0 Hz, 2 H), 4.59 (dd, J = 1.5, 17.0 Hz, 1 H), 4.90 (dd, J = 1.0, 10.0 Hz, 1 H), 5.24 (s, 1 H), 5.65–5.73 (m, 1 H), 6.95 (t, J = 8.0 Hz, 4 H), 7.10–7.15 (m, 4 H), 7.21 (d, J = 7.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.8, 20.3, 21.4, 22.2, 32.4 (d, J = 6.2 Hz), 32.5, 43.6, 53.2 (d, J = 16.2 Hz), 59.8, 70.4 (d, J = 27.4 Hz), 71.6 (d, J = 2.4 Hz), 77.8 (d, J = 7.2 Hz), 78.2 (d, J = 6.7 Hz), 118.7, 126.8, 128.0, 128.3, 128.8, 129.0, 131.7, 135.4, 135.7, 142.7, 200.4 (d, J = 9.6 Hz).

^{31}P NMR (202 MHz, $CDCl_3$): δ = –3.02.

MS (APCI): m/z (%) = 543 (100) $[M + H]^+$.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{28}H_{36}N_2O_5PS$: 543.2078; found: 543.2062.

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