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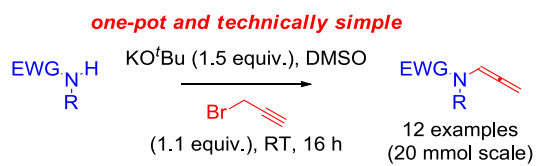
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Graphical Abstract

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A simple one-pot preparation of *N*-allenyl amides, ureas, carbamates and sulfonamides using a DMSO/^tBuOK protocol

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ABSTRACT

A one-pot transformation of amides, ureas, carbamates and sulfonamides into synthetically useful *N*-allenyl analogues using a ^tBuOK/DMSO protocol is reported. The procedure is experimentally simple and robust, and provides *N*-allenyl analogues, commonly used within the literature, in yields comparable to the bench mark two-step approach.

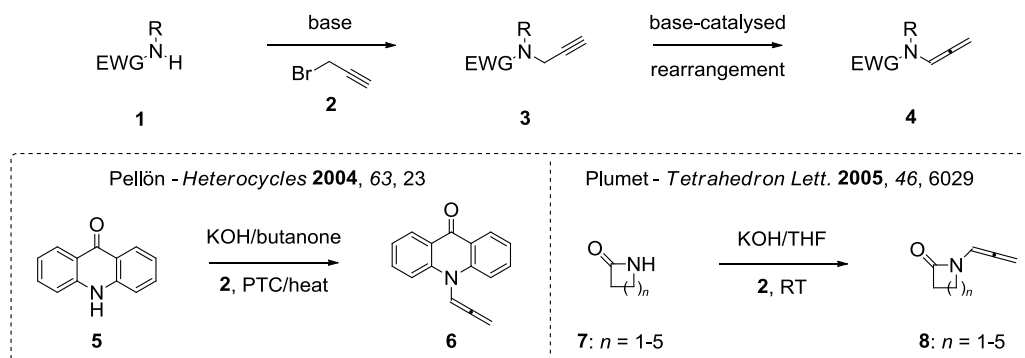
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N-Allenyl amides (allenamides), of the general structure **4**, have become an increasingly widespread and valuable synthon, with the number of reports of their use increasing yearly (Scheme 1).¹ While synthetic approaches to these substrates have been well documented,^{1a} it is the base catalysed rearrangement of propargyl amides that has presented itself as the stand-alone method of choice for their synthesis.^{2,3} However, one of the drawbacks of this method is the reliance on the formation and isolation of the propargyl amide (**3**), which is in turn derived from an amide (**1**) and propargyl bromide (**2**) under basic conditions.

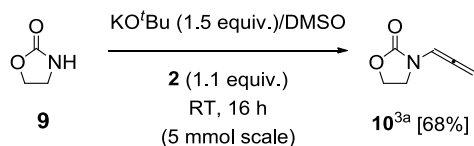
To date, there have been two reports of the direct conversion of amides into allenamides of the type **4** using this base-mediated approach. In 2004 Pellön⁴ demonstrated that acridones (**5**) could

be transformed into their *N*-allenyl analogues (**6**) by heating propargyl bromide (**2**) in an aqueous KOH aqueous/butanone solution in the presence of a phase-transfer catalyst, while in 2005, Plumet⁵ demonstrated that lactams (**7**) could be transformed to their *N*-allenyl analogues (**8**) using THF/KOH at room temperature.

In continuation of our interest in allenamides⁶ in Au-catalysed transformations,⁷⁻¹² we present a technically simple, yet robust 'one-pot' approach to synthesising these valuable building blocks using an adapted protocol of Heaney and Ley.¹³ We reported in 2010^{6c} that treatment of 2-oxazolidinone (**9**) and excess propargyl bromide (**2**) with a mixture of DMSO/^tBuOK was sufficient for full conversion into the *N*-allenyl carbamate **10** in an isolated yield of 68% (Scheme 2).



Scheme 1. Base-facilitated synthesis of *N*-allenyl analogues.



Scheme 2. One-pot synthesis of **10** from **9** and **2**.

Herein, we demonstrate the generality of this procedure for the synthesis of a selection of *N*-allenyl amides, ureas, carbamates and sulfonamides that have been used extensively in the literature, and importantly, on an appreciable scale (20 mmol) (Table 1).¹⁴⁻¹⁷

Table 1. Scope of the ‘one-pot’ *N*-allenyl synthesis.^a

Entry	Amide	<i>N</i> -Allenyl analogue	Yield [%] ^b
1			65
2			48
3	11b : <i>n</i> = 2	12b ^{3a} : <i>n</i> = 2	53
4	11c : <i>n</i> = 3	12c ^{3a} : <i>n</i> = 3	53
5			63
6	13b : R = H		23
7			66
8	15b : R = Bn	16b ^{3a} : R = Bn	71
9			72
10			68
11			12
12			54

^aSee reference 14 for a general method. ^bIsolated yields.

Firstly, the synthesis of **10** could be confidently scaled up to 20 mmol with no discernable decrease in the isolated yield (entry 1). Using this procedure,¹⁴ the cyclic lactams **12a-c** were converted in moderate to good yields under these DMSO/^tBuOK conditions (entries 2–4), however, unlike the work of Plumet, the larger ring size did not result in diminished isolated yields of the allenamide, as highlighted by **12c** (entry 4). Imidazolines **13a** and **b** were smoothly converted into their respective *N*-allenyl ureas, with **14b** being the first reported example of a bis-*N*-allenyl urea to our knowledge (entries 5 and 6). All three chiral oxazolidinones **15a-c** could be cleanly converted into *N*-allenyl carbamates **16a-c** (entries 7–9), and pleasingly *N*-methyl *p*-toluenesulfonamide (**17**) could be transformed into *N*-allenyl sulfonamide **18** in a good yield of 68% (entry 10). The previous route to this commonly used *N*-allenyl sulfonamide **18** relied on sulfonamide formation on *N*-methylpropargyl amine, and as such, this new approach represents a significantly cheaper, and technically easier method for its synthesis.^{7e} Acridone (**19**) could be transformed into its *N*-allenyl analogue **20**, but its purification proved difficult and this is reflected in a poor overall isolated yield of only 12% (entry 11). Finally, imidazole (**21**) gave the desired *N*-allenyl analogue **22** in good yield of 54% (entry 12).

Some technical observations on this procedure deserve comment; (a) we found the use of dry DMSO to be vital to this ‘one-pot’ approach; (b) the quality of the ^tBuOK did effect conversion into the *N*-allenyl product, and that a fresh bottle of solid ^tBuOK gave superior yields; and (c) slow dropwise addition of propargyl bromide is necessary for adequate temperature control of the reaction mixture.

In conclusion, we have developed a convenient, scalable (20 mmol) and robust ‘one-pot’ method for the synthesis of *N*-allenyl amides, ureas, carbamates and sulfonamides. The isolated yields for the synthesized *N*-allenyl analogues shown in table 1 are on par with the benchmark procedure of Hsung,³ and furthermore, this procedure is experimentally simple. We therefore envisage this ‘one-pot’ approach being attractive in instances when synthesizing these building blocks on large scale is required.

Acknowledgments

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- Representative procedure: To a solution of the *N*-methyl *p*-toluenesulfonamide (**17**) (3.70 g, 20.00 mmol) in dry DMSO (40 mL) under an N₂ or Ar atmosphere was added ^tBuOK (3.36 g, 30.00 mmol) and the resulting solution stirred for 1 h. To this solution was added propargyl bromide (2.50 ml, 80% soln. in toluene, 22.00 mmol) dropwise over 40 min with care! After the addition was complete the mixture was stirred at room temperature overnight under N₂ or Ar. The mixture was then diluted with H₂O (100 mL) and the organic layer extracted with EtOAc (2 x 100 mL). The combined organic extracts were dried over Na₂SO₄, filtered and the solvent removed under vacuum. The crude reaction product was then purified by filtration through a pad of silica (EtOAc:petroleum ether / 1:1) to yield a pale yellow solid which was recrystallised from CH₂Cl₂/petroleum ether giving the desired *N*-allenyl sulfonamide **18**^{7e} as colourless plates (3.01 g, 68%); mp 82.0 – 82.5 °C; IR (CH₂Cl₂) ν_{\max} 3030, 1598, 1448, 1357, 1157 cm⁻¹; ¹H (400 MHz, CDCl₃) δ 7.67 – 7.64 (m, 2H), 7.31 – 7.28 (m, 2H), 6.87 (t, *J* = 6.4 Hz, 1H), 5.27 (d, *J* = 6.4 Hz, 2H), 2.69 (s, 3H), 2.41 (s, 3H); ¹³C (100 MHz, CDCl₃) δ 201.5, 143.9, 133.7, 129.6, 127.5, 101.8, 87.8, 33.3, 21.7; MS-ESI found, C₁₁H₁₃NO₂SNa found 246.0578, [MNa]⁺ requires 246.0565.
- The physical data for each known *N*-allenyl analogue **10**, **12a-c**, **14a**, **16b**, **16c**, **18**, **20** and **22** was in agreement with that previously reported.^{3a, 6c, 7e, 16}
- Bis-*N*-allenyl urea **14b**; IR (CH₂Cl₂) ν_{\max} 3025, 1755, 1520, 1145 cm⁻¹; ¹H (400 MHz, CDCl₃) δ 7.00 (t, *J* = 8.6 Hz, 2H), 5.39 (d, *J* = 6.8 Hz, 4H), 3.45 (s, 4H); ¹³C (100 MHz, CDCl₃) δ 201.7, 153.6, 97.6, 87.6, 40.6; MS-ESI found, C₉H₁₀N₂O₂Na found 185.0685, [MNa]⁺ requires 185.0691.
- N*-Allenyl carbamate **16a**; [α]_D²⁵ = 16.0 (c 1.00, CHCl₃); IR (CH₂Cl₂) ν_{\max} 3019, 1750, 1516, 1408, 1140 cm⁻¹; ¹H (400 MHz, CDCl₃) δ 6.86 (t, *J* = 6.4 Hz, 1H), 5.45 (dd, *J* = 6.4, 10.0 Hz, 1H), 5.39 (dd, *J* = 6.4, 10.0 Hz, 1H), 4.30 (t, *J* = 8.8 Hz, 1H), 4.22 (dd, *J* = 4.4, 9.2 Hz, 1H), 3.87 (dt, *J* = 4.0, 8.8 Hz, 1H), 2.38 – 2.31 (m, 1H), 0.90 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ¹³C (100 MHz, CDCl₃) δ 201.4, 155.5, 95.7, 87.6, 63.0, 58.9, 26.9, 17.6, 13.8; MS-ESI found, C₉H₁₃NO₂Na found 190.0854, [MNa]⁺ requires 190.0844.
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