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A simple one-pot preparation of $N$-allenyl amides, ureas, carbamates and sulfonamides using a DMSO/\text{BuOK} protocol

Thomas W. Bousfield, Marc C. Kimber*

one-pot and technically simple

\[
\text{EWG}_N^\text{H} \quad \text{KO}^\text{Bu} \quad \text{Br} \quad \text{EWG}_N^\text{R}
\]

(1.1 equiv.), RT, 16 h

12 examples (20 mmol scale)
A simple one-pot preparation of $N$-allenyl amides, ureas, carbamates and sulfonamides using a DMSO/BuOK protocol

Thomas W. Bousfield, Marc C. Kimber*

Department of Chemistry, Loughborough University, Leicestershire, LE11 3TU, UK; Tel: ++44 (0) 01509 22 2570.
E-mail: M.C.Kimber@lboro.ac.uk

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ABSTRACT

A one-pot transformation of amides, ureas, carbamates and sulfonamides into synthetically useful $N$-allenyl analogues using a BuOK/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 benchmark 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). While synthetic approaches to these substrates have been well documented, it is the base catalysed rearrangement of propargyl amides that has presented itself as the stand-alone method of choice for their synthesis. 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 Pellón 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, Plumet 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 allenamides in Au-catalysed transformations, we present a technically simple, yet robust ‘one-pot’ approach to synthesising these valuable building blocks using an adapted protocol of Heaney and Ley. We reported in 2010 that treatment of 2-oxazolidinone (9) and excess propargyl bromide (2) with a mixture of DMSO/BuOK 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.
Tetrahedron

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, the cyclic lactams 12a–c were converted in moderate to good yields under these DMSO/BuOK conditions (entries 2–4), however, unlike the work of Plumat, 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. 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 BuOK did effect conversion into the N-allenyl product, and that a fresh bottle of solid BuOK gave superior yields; and (c) slow dropping 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, 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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References and notes


14. Representative procedure: To a solution of the N-methyl p-toluenesulphonamide (17) (3.70 g, 20.00 mmol) in dry DMSO (40 mL) under an N₂ or Ar atmosphere was added BuOK (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:pentane ether / 1:1) to yield a pale yellow solid which was recrystallised from CHCl₃/pentane ether giving the desired N-allyl sulphonamide 18 as colourless plates (3.01 g, 68%); mp 82.0 – 82.5 °C; IR (CHCl₃) νmax 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); νC (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, C₉H₉NO₂Na found 246.0578, [MNa]⁺ requires 246.0565.

15. The physical data for each known N-allyl analogue 10, 12a-c, 14a, 16b, 16c, 18, 20 and 22 was in agreement with that previously reported. 

16. Bis-N-allyl urea 14b: IR (CHCl₃) νmax 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); ¹C (100 MHz, CDCl₃) δ 201.7, 153.6, 97.6, 87.6, 40.6; MS-ESI found, C₁₀H₁₆N₂Na found 185.0685, [MNa]⁺ requires 185.0691.

17. N-Allenyl carbamate 16a: [α]D²⁵ = 16.0 (c 1.00, CHCl₃); IR (CHCl₃) νmax 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 (dt, J = 7.2 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H); ¹C (100 MHz, CDCl₃) δ 201.4, 152.4, 95.7, 87.6, 63.0, 58.9, 26.9, 17.6, 13.8; MS-ESI found, C₁₀H₁₄NO₂Na found 190.0854, [MNa]⁺ requires 190.0844.