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

This item was submitted to Loughborough University’s Institutional Repository by the/an author.


Additional Information:

• NOTICE: this is the author's version of a work that was accepted for publication in Tetrahedron Letters. Changes resulting from the publishing process, such as peer review, editing, corrections, structural formatting, and other quality control mechanisms may not be reflected in this document. Changes may have been made to this work since it was submitted for publication. A definitive version was subsequently published in Tetrahedron Letters, vol 56, issue 2, January 2015, DOI: 10.1016/j.tetlet.2014.11.093.

Metadata Record: https://dspace.lboro.ac.uk/2134/16852

Version: Accepted for publication

Publisher: © Elsevier Ltd

Rights: This work is made available according to the conditions of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) licence. Full details of this licence are available at: https://creativecommons.org/licenses/by-nc-nd/4.0/

Please cite the published version.
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

EWG$_N$

\text{H}

R

\text{KO'Bu (1.5 equiv.), DMSO}

Br

(1.1 equiv.), RT, 16 h

12 examples
(20 mmol scale)

EWG$_N$

\text{H}

R

Leave this area blank for abstract info.
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

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Amide
Allenamide
Propargyl bromide
One-pot
Lactam

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 bench mark two-step approach.

2009 Elsevier Ltd. All rights reserved.

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 Pellöń demonstrated that acidones (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, Plumat 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.
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-allylen 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-allylen synthesis.a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amide</th>
<th>N-Alleny analogue</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>10a§</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>11a: n = 1</td>
<td>12a§: n = 1</td>
<td>48</td>
</tr>
<tr>
<td>3</td>
<td>11b: n = 2</td>
<td>12b§: n = 2</td>
<td>53</td>
</tr>
<tr>
<td>4</td>
<td>11c: n = 3</td>
<td>12c§: n = 3</td>
<td>53</td>
</tr>
<tr>
<td>5</td>
<td>13a: R = Me</td>
<td>14a§: R = Me</td>
<td>63</td>
</tr>
<tr>
<td>6</td>
<td>13b: R = H</td>
<td>14b§</td>
<td>23</td>
</tr>
<tr>
<td>7</td>
<td>15a: R = Pro</td>
<td>16a§: R = Pro</td>
<td>66</td>
</tr>
<tr>
<td>8</td>
<td>15b: R = Bn</td>
<td>16b§: R = Bn</td>
<td>71</td>
</tr>
<tr>
<td>9</td>
<td>15c: R = OMe</td>
<td>16c: R = OMe</td>
<td>72</td>
</tr>
<tr>
<td>10</td>
<td>17</td>
<td>18b§</td>
<td>68</td>
</tr>
<tr>
<td>11</td>
<td>19</td>
<td>20§</td>
<td>12</td>
</tr>
<tr>
<td>12</td>
<td>21</td>
<td>22§</td>
<td>54</td>
</tr>
</tbody>
</table>

aSee reference 14 for a general method. bIsolated yields.

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/ButOK conditions (entries 2–4), however, unlike the work of Plumet, the larger ring size did not result in diminished isolated yields of the alleneamide, as highlighted by 12c (entry 4). Midazolamines 13a and b were smoothly converted into their respective N-allylen ureas, with 14b being the first reported example of a bis-N-allylen urea to our knowledge (entries 5 and 6). All three chiral oxazolidinones 15a-c could be cleanly converted into N-allylen carbamates 16a-c (entries 7–9), and pleasingly N-methyl p-toluenesulfonamide (17) could be transformed into N-allylen sulfonamide 18 in a good yield of 68% (entry 10). The previous route to this commonly used N-allylen 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.76 Acridone (19) could be transformed into its N-allylen 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-allylen 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-allylen product, and that a fresh bottle of solid BuOK 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-allylen amides, ureas, carbamates and sulfonamides. The isolated yields for the synthesized N-allylen 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

We gratefully acknowledge financial support from the Department of Chemistry at Loughborough University.

References and notes


11. For Au(I) Nazarov type cyclisations, see: Ma, Z.; X.; He, S.; Song, W.; Huang, P. R. Org. Lett. 2012, 14, 5736.


14. Representative procedure: To a solution of the N-methyl p-toluenesulfonylanine (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:petroleum ether 1:1) to yield a pale yellow solid which was recrystallised from CH2Cl2/petroleum ether giving the desired N-allyl sulfonylaniline (18) as colourless plates (3.01 g, 68%); mp 82.0 – 82.5 °C; IR (CH2Cl2)υmax, 3030, 1598, 1448, 1357, 1157 cm−1; 1H (400 MHz, CDCl3) υ 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) υ 201.5, 143.9, 133.7, 129.6, 127.5, 101.8, 87.8, 33.3, 21.7; MS-ESI found, C19H16N2O2Na found 246.0578, [MNa]+ requires 246.0565.

15. The physical data for each known N-allylen analogue 10, 12a-e, 14a, 16b, 16c, 18, 20 and 22 was in agreement with that previously reported. 26

16. Bis-N-allylen urea 14b; IR (CH2Cl2)υmax, 3025, 1755, 1520, 1145 cm−1; 1H (400 MHz, CDCl3) υ 7.00 (t, J = 8.6 Hz, 2H), 5.39 (d, J = 6.8 Hz, 4H), 3.45 (s, 4H); 13C (100 MHz, CDCl3) υ 201.7, 153.6, 97.6, 87.6, 40.6; MS-ESI found, C17H16N2O2Na found 185.0685, [MNa]+ requires 185.0691.

17. N-Allylen carbamate 16a [δH]85 = 16.0 (c. 1.00, CHCl3); IR (CH2Cl2)υmax, 3019, 1750, 1516, 1408, 1140 cm−1; 1H (400 MHz, CDCl3) υ 6.86 (t, J = 6.4 Hz, 1H), 5.49 (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), 2.58 – 2.31 (m, 1H), 0.90 (d, J = 7.2 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H); 13C (100 MHz, CDCl3) υ 201.4, 155.5, 95.7, 87.6, 63.0, 58.9, 26.9, 17.6, 13.8; MS-ESI found, C17H15NO2Na found 190.0854, [MNa]+ requires 190.0844.