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

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ABSTRACT

A one-pot transformation of amides, ureas, carbamates and sulfonamides into synthetically useful *N*-allenyl analogues using a ^{t}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.

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, Pellón[4] demonstrated that acridone (**5**) could be transformed into the *N*-allenyl analogue (**6**) by heating propargyl bromide (**2**) in an aqueous KOH/butanone solution in the presence of a phase-transfer catalyst, while in 2005, Plumet[5] demonstrated that lactams (**7**) could be transformed into their *N*-allenyl analogues (**8**) using THF/KOH at room temperature.

In continuation of our interest in allenamides[6] in Au-catalysed transformations,[7–12] we present a technically simple, yet robust 'one-pot' approach to synthesizing 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/^{t}BuOK was sufficient for full conversion into the *N*-allenyl carbamate **10** in an isolated yield of 68% (Scheme 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]

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 **11a–c** were converted in moderate to good yields under these DMSO/^{t}BuOK 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). Imidazolin-2-ones **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 (**5**) could be transformed into its *N*-allenyl analogue **19**, but its purification proved difficult and this is reflected in a poor overall isolated yield of only 12% (entry 11). Finally, imidazole (**20**) gave the desired *N*-allenyl analogue **21**[18] in a good yield of 54% (entry 12).

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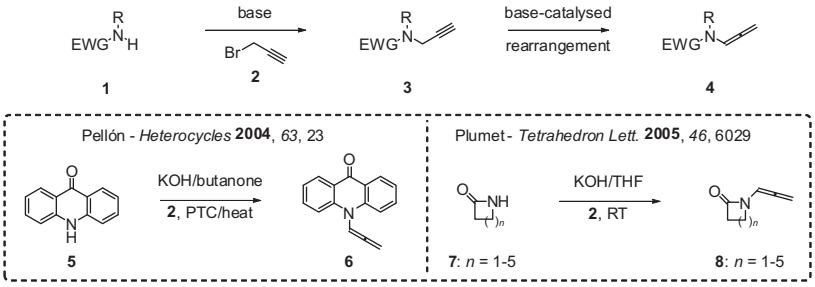
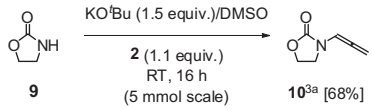


Scheme 1. Base-facilitated synthesis of *N*-allenyl analogues.



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

Table 1
Scope of the 'one-pot' synthesis of *N*-allenyl analogues[a]

Entry	Amide	*N*-Allenyl analogue	Yield[b] (%)
1	**9**	**10**[3a]	65
2	**11a**: n = 1	**12a**[3a]: n = 1	48
3	**11b**: n = 2	**12b**[3a]: n = 2	53
4	**11c**: n = 3	**12c**[3a]: n = 3	53
5	**13a**: R = Me	**14a**[3a]: R = Me	63
6	**13b**: R = H	**14b**[16]	23
7	**15a**: R = ^{i}Pr	**16a**[17]: R = ^{i}Pr	66
8	**15b**: R = Bn	**16b**[3a]: R = Bn	71
9	**15c**: R = 3,5-dimethoxybenzyl	**16c**: R = 3,5-dimethoxybenzyl	72
10	**17**	**18**[7e]	68
11	**5**	**19**[3a]	12
12	**20**	**21**[18]	54

[a] See Ref. 14 for a general method.
[b] Isolated yields.

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 ^{t}BuOK did effect conversion into the *N*-allenyl product, and that a fresh bottle of solid ^{t}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*-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.

Acknowledgment

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References and notes

1. For reviews on allenamides, see: (a) Lu, T.; Lu, Z.; Ma, Z.-X.; Zhang, Y.; Hsung, R. P. *Chem. Rev.* **2013**, *113*, 4862; (b) Wei, L.-L.; Xiong, H.; Hsung, R. P. *Acc. Chem. Res.* **2003**, *36*, 773; (c) Standen, P. E.; Kimber, M. C. *Curr. Opin. Drug Discovery Dev.* **2010**, *13*, 645; (d) De Agostino, A.; Prandi, C.; Tabasso, S.; Venturello, P. *Molecules* **2010**, *15*, 2667.
2. (a) Padwa, A.; Caruso, T.; Nahm, S.; Rodríguez, A. *J. Am. Chem. Soc.* **1982**, *104*, 2865; (b) Galons, H.; Bergerat, I.; Combet-Farnoux, C.; Miocque, M.; Decodts, G.; Bram, G. *J. Chem. Soc., Chem. Commun.* **1985**, 1730; (c) Radl, S.; Kovarova, L.; Holubek, J. *Collect. Czech. Chem. Commun.* **1991**, *56*, 439; (d) Phadtare, S.; Zemlicka, J. *J. Am. Chem. Soc.* **1989**, *111*, 5925; (e) Phadtare, S.; Zemlicka, J. *J. Org. Chem.* **1989**, *54*, 3675; (f) Jones, B. C. N. M.; Silverton, J. V.; Simons, C.; Megati, S.; Nishimura, H.; Maeda, Y.; Mitsuya, H.; Zemlicka, J. *J. Med. Chem.* **1995**, *38*, 1397.
3. For the current benchmark 'two-step' procedure, see: (a) Wei, L.-L.; Xiong, H.; Douglas, C. J.; Hsung, R. P. *Tetrahedron Lett.* **1999**, *40*, 6903; (b) Wei, L.-L.; Mulder, J. A.; Xiong, H.; Zificsak, C. A.; Douglas, C. J.; Hsung, R. P. *Tetrahedron* **2001**, *57*, 459; (c) Wei, L.-L.; Xiong, H.; Douglas, C. J.; Hsung, R. P. *Tetrahedron Lett.* **1999**, *40*, 6903; (d) Xiong, H.; Tracey, M. R.; Grebe, T. P.; Mulder, J. A.; Hsung, R. P.; Wipf, P.; Smotryski, J. *Org. Synth.* **2004**, *81*, 147.
4. Xuárez, L.; Pellón, R. F.; Fascio, M.; Montesano, V.; D'Accorso, N. *Heterocycles* **2004**, *63*, 23.
5. Fenández, I.; Monterde, M. I.; Plumet, J. *Tetrahedron Lett.* **2005**, *46*, 6029.
6. (a) Slater, N. H.; Brown, N. J.; Elsegood, M. R. J.; Kimber, M. C. *Org. Lett.* **2014**, *16*, 4606; (b) Singh, S.; Elsegood, M. R. J.; Kimber, M. C. *Synlett* **2012**, 565; (c) Hill, A. W.; Elsegood, M. R. J.; Kimber, M. C. *J. Org. Chem.* **2010**, *75*, 5406; (d) Kimber, M. C. *Org. Lett.* **2010**, *12*, 1128.
7. For a review of Au(I)-catalysed [2+2]- and [4+2]-cycloadditions, see: (a) Lopez, F.; Mascareñas, J. L. *Chem. Soc. Rev.* **2014**, *43*, 2904; for selected examples, see: (b) Lohse, A. G.; Hsung, R. P. *Org. Lett.* **2009**, *11*, 3430; (c) Li, X.-X.; Zhu, L.-L.; Zhou, W.; Chen, Z. *Org. Lett.* **2012**, *14*, 436; (d) Faustino, H.; Bernal, P.; Castedo, L.; López, F.; Mascareñas, J. L. *Adv. Synth. Catal.* **2012**, *354*, 1658; (e) Suárez-Pantiga, S.; Hernández-Díaz, C.; Piedrafita, M.; Rubio, E.; Gonzáleza, J. M. *Adv. Synth. Catal.* **2012**, *354*, 1651; (f) Faustino, H.; López, F.; Castedo, L.; Mascareñas, J. L. *Chem. Sci.* **2011**, *2*, 633; (g) Francos, J.; Grande-Carmona, F.; Faustino, H.; Iglesias-Sigüenza, J.; Díez, E.; Alonso, I.; Fernández, R.; Lassaletta, J. M.; López, F.; Mascareñas, J. L. *J. Am. Chem. Soc.* **2012**, *134*, 14322; (h) Montserrat, S.; Faustino, H.; Lledos, A.; Mascareñas, J. L.; Lopez, F.; Ujaque, G. *Chem. Eur. J.* **2013**, *19*, 15248; (i) Faustino, H.; Alonso, I.; Mascareñas, J. L.; Lopez, F. *Angew. Chem., Int. Ed.* **2013**, *52*, 6526.
8. For Au(I) hydroaminations, see: (a) Manzo, A. M.; Perboni, A. D.; Broggini, G.; Rigamonti, M. *Tetrahedron Lett.* **2009**, *50*, 4696; (b) Broggini, G.; Borsini, E.; Fasana, A.; Poli, G.; Liron, F. *Eur. J. Org. Chem.* **2012**, 3617.
9. For Au(I) hydroarylations, see: (a) Watanabe, T.; Oishi, S.; Fuji, N.; Ohno, H. *Org. Lett.* **2007**, *9*, 4821; (b) Pirovano, V.; Decataldo, L.; Rossi, E.; Vicente, R. *Chem. Commun.* **2013**, 3594; (c) Jia, M.; Cera, G.; Perrotta, D.; Monari, M.; Bandini, M. *Chem. Eur. J.* **2014**, *20*, 9875.
10. For Au(I) hydroalkoxylations, see: (a) Horino, Y.; Takata, Y.; Hashimoto, K.; Kuroda, S.; Kimurab, M.; Tamaru, Y. *Org. Biomol. Chem.* **2008**, *6*, 4105;

(b) González-Gómez, A.; Domínguez, G.; Pérez-Castells, J. *Eur. J. Org. Chem.* **2009**, 5057.
11. For Au(I) Nazarov type cyclisations, see: Ma, Z.-X.; He, S.; Song, W.; Hsung, R. P. *Org. Lett.* **2012**, *14*, 5736.
12. For Au(I) cyclopropanations, see: Sabbatani, J.; Huang, X.; Veiros, L. F.; Maulide, N. *Chem. Eur. J.* **2014**, *20*, 10636.
13. Heaney, H.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1973**, 499.
14. *Representative procedure*: To a solution of *N*-methyl *p*-toluenesulfonamide (**17**) (3.70 g, 20.00 mmol) in dry DMSO (40 mL) under an N_2 or Ar atmosphere was added ^{t}BuOK (3.36 g, 30.00 mmol) and the resulting solution stirred for 1 h. To this solution was added propargyl bromide (**2**) (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 N_2 or Ar. The mixture was then diluted with H_2O (100 mL) and the organic layer extracted with EtOAc (2 × 100 mL). The combined organic extracts were dried over Na_2SO_4, 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 CH_2Cl_2/petroleum ether giving the desired *N*-allenyl sulfonamide **18**[7e] as colourless plates (3.01 g, 68%); mp 82.0–82.5 °C; IR (CH_2Cl_2) ν_{max} 3030, 1598, 1448, 1357, 1157 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 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) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.5, 143.9, 133.7, 129.6, 127.5, 101.8, 87.8, 33.3, 21.7; MS-ESI found, $C_{11}H_{13}NO_2SNa$ found 246.0578, $[MNa]^+$ requires 246.0565.
15. The physical data for each known *N*-allenyl analogue **10**, **12a–c**, **14a**, **16b**, **16c**, **18**, **19** and **21** were in agreement with those previously reported.[3a,6c,7e,16]
16. Bis-*N*-allenyl urea **14b**; IR (CH_2Cl_2) ν_{max} 3025, 1755, 1520, 1145 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (t, *J* = 8.6 Hz, 2H), 5.39 (d, *J* = 6.8 Hz, 4H), 3.45 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.7, 153.6, 97.6, 87.6, 40.6; MS-ESI found, $C_9H_{10}N_2ONa$ found 185.0685, $[MNa]^+$ requires 185.0691.
17. *N*-Allenyl carbamate **16a**; $[\alpha]_D^{25}$ = 16.0 (*c* 1.00, $CHCl_3$); IR (CH_2Cl_2) ν_{max} 3019, 1750, 1516, 1408, 1140 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 155.5, 95.7, 87.6, 63.0, 58.9, 26.9, 17.6, 13.8; MS-ESI found, $C_9H_{13}NO_2Na$ found 190.0854, $[MNa]^+$ requires 190.0844.
18. Hubert, A. J.; Reimlinger, H. *J. Chem. Soc. C* **1968**, 606.