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A mild and efficient method for the synthesis of vinylogous carbamates from alkyl azides☆

D. Srinivasa Reddy,* Trideep V. Rajale, K. Shivakumar and Javed Iqbal

Discovery Research, Dr. Reddy's Laboratories Ltd, Bollaram Road, Miyapur, Hyderabad 500 049, India

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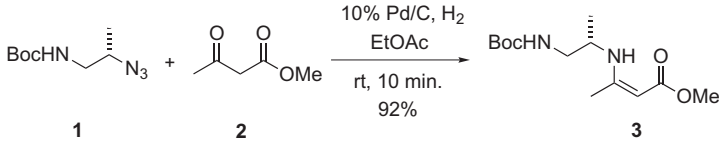
Abstract—A mild and efficient one-pot method for the synthesis of vinylogous carbamates is reported starting from alkyl azides under a hydrogen atmosphere using 10% Pd/C. The resulting products are useful intermediates for the synthesis of heterocyclic compounds, natural products, and in peptidomimetics.

Vinylogous carbamates also known as enaminoesters are versatile building blocks in the synthesis of various heterocycles,[1] natural products[2] and are often endowed with useful pharmacological properties.[3] Recent reports show that these compounds are useful in peptidomimetics[4] and also in the preparation of β-amino acids.[5] Vinylogous carbamates are generally prepared by condensation of amines with β-ketoesters, with azeotropic removal of water, use expensive reagents, and some of these suffer from incomplete reaction, long reaction times, and the use of hazardous solvents.[6] In this Letter, we describe the synthesis of various vinylogous carbamates starting from alkyl azides and β-ketoesters in a one-pot procedure.

During the synthesis of aza-cyclic peptides for β-turn mimics in the laboratory of Professor Aubé, one of us (D.S.R.) observed that hydrogenation of the alkyl azide **1** in the presence of methyl acetoacetate **2** furnished the vinylogous carbamate **3** in high yield (Scheme 1).[7] No aqueous work-up was needed, the catalyst was simply filtered off, and on evaporation of all volatiles the product **3** was obtained in high yield. This method has not previously been documented.[8] Hence, we decided to generalize this simple and efficient procedure to access other useful vinylogous carbamates.

A variety of alkyl azides were treated with methyl acetoacetate **2** in the presence of 10% Pd/C under hydrogen to furnish the corresponding vinylogous carbamates in high yields and these are summarized in Table 1.[9] It is noteworthy that in all cases we did not observe any significant amounts of over reduced products or the intermediate amines. Although a competitive debenzylation would be possible under these reaction conditions, reactions involving benzyl azides (entries 5–7, Table 1) did not undergo loss of the benzyl group, the corresponding vinylogous carbamates being obtained in good yields. In all cases the products were isolated as mixtures of *Z*,*E*-isomers. In general the isomers were not separable.



1 2 3

Scheme 1.

Keywords: Alkyl azide; Enaminone; Hydrogenation.
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* Corresponding author. Tel.: +91 40 2304 5439; fax: +91 40 2304 5438; e-mail: dsreddy@drreddys.com

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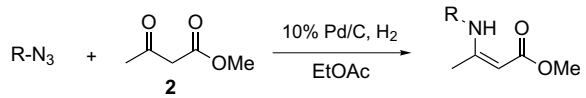
Table 1.



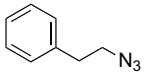
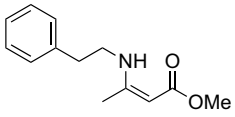
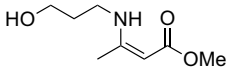
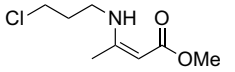
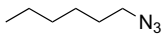
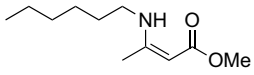
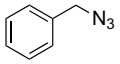
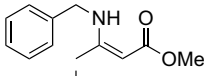
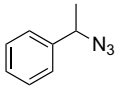
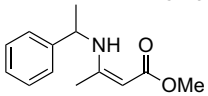
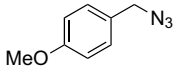
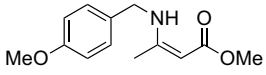
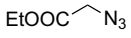
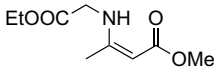
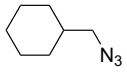
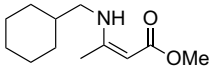
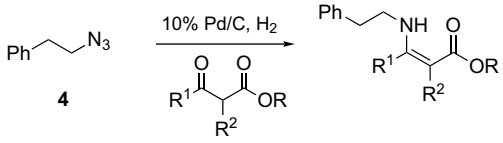
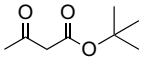
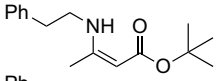
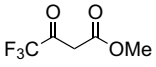
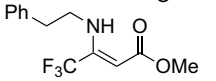
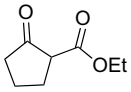
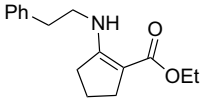
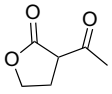
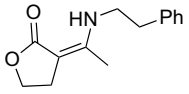
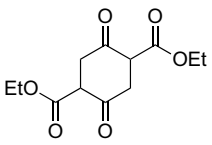
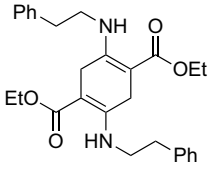
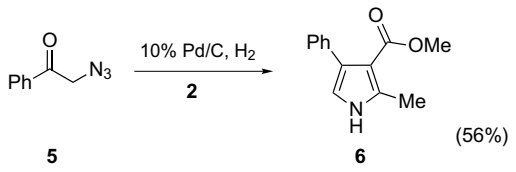
Entry	Azide	Product	Yield (%)
1			100
2			84
3			82
4			64
5			75
6			67
7			71
8			55
9			48

Table 2.



Entry	Keto ester	Product	Yield (%)
1			60
2			62
3			67
4			66
5			45



Scheme 2.

Products with *Z* double bond geometry were favoured over the *E*-isomers. It is postulated that intramolecular hydrogen bonding could be responsible for the observed equilibrium shift toward *Z*-isomers.[10] In Table 2, we have summarized the results obtained from the reaction of phenethyl azide **4** with different β-ketoesters.[11]

Interestingly, trisubstituted pyrrole **6**[12] was isolated in moderate yield when we reacted α-azido acetophenone **5** with methyl acetoacetate under the same reaction conditions (Scheme 2).[13] Although we do not have support for the mechanism, we believe that formation of the pyrrole involves the vinylogous carbamate as an intermediate.

In short, we have developed a simple and environmentally friendly procedure for the synthesis of vinylogous carbamates starting from alkyl azides and β-ketoesters using 10% Pd/C catalyst and hydrogen. In one example, we also showed that one can access trisubstituted pyrroles starting from β-ketoesters and α-azido ketones in a one-pot procedure. New applications of these important vinylogous carbamates in the synthesis of natural products and heterocycles will be the subject of future work from our laboratory.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.12.047.

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9. To a solution of alkyl azide (1 equiv) and methyl acetoacetate (2 equiv) in EtOAc was added a catalytic amount of 10% Pd/C (~10% weight) and the reaction mixture was stirred under hydrogen (balloon) at room temperature. After 0.5–2 h, the catalyst was filtered off and the residue obtained after the removal of all volatiles, passed through a small silica gel plug to furnish the desired products as a *Z*:*E* mixture.
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13. This reaction was not optimised.