Iodocyclocarbamation Reaction of N-Allenylmethyl-N-arylcarbamates

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Introduction

5-Substituted-3-aryl-2-oxazolidinones can be considered privileged chemical structures1,2 because of the wide range of therapeutic activity profiles they often exhibit. 5-(Iodomethyl)-3-aryl-2-oxazolidinones would appear to be especially desirable synthetic intermediates because of their potential applicability to the preparation of a variety of these pharmaceutical substances.

The synthesis of oxazolidinone rings via the iodocyclocarbamation reaction is known in the literature,3,4 but there are few references to the synthesis of 5-(iodomethyl)-3-aryl-2-oxazolidinones, one exception being the indole derivatives described by Brickner and co-workers.5,6

The focus of this summer project was to see if an N-allenylmethyl nitrogen substituent, in lieu of the usual N-allyl moiety, would allow facile access to oxazolidinones bearing a vinyl iodide side chain at the C-5 position.

Retrosynthetic Analysis

The initially targeted 5-substituted oxazolidinone 1 was envisioned as arising from an iodocyclocarbamation reaction of N-allenylmethylcarbamate 2. Compound 2 could be obtained by Crabbé homologation6 of the propargyl derivative 3, which would be readily available via N-alkylation of carbamate 4 with propargyl bromide. Alternatively, 4 could be directly alkylated with 4-bromo-1,2-butanediene.6

Preparation of the N-Allenylmethylcarbamate

DMF was the preferred solvent for all N-alkylation reactions. In accord with the literature,7 Cuprous iodide and dicyclohexylamine were the best additives for the Crabbé homologation. In cases where sodium hydride failed as a base for these N-alkylations, we found that cesium carbonate was a superior replacement. Finally, while 4-bromo-1,2-butadiene was an effective alkylation agent, its preparation was lengthy and difficult.8

1H NMR of Iodocyclocarbamation Product

Conclusions

• N-Allenylmethylcarbamates were readily prepared, either by N-propargylation followed by Crabbé homologation, or by direct alkylation, using 4-bromo-1,2-butadiene.
• The sp carbon of allene 2 was observed at δ 208.85 ppm in the 1H NMR spectrum.
• The iodocyclocarbamation reaction of allene derivative 2 afforded a 72% isolated yield of the targeted oxazolidinone vinyl iodide 1 but complete conversion has not been realized.

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References