27O-ISMS32 **Rapid and Efficient Synthesis of Deuterated Cyclobutane Derivatives Using Continuous Photo Flow Chemistry**

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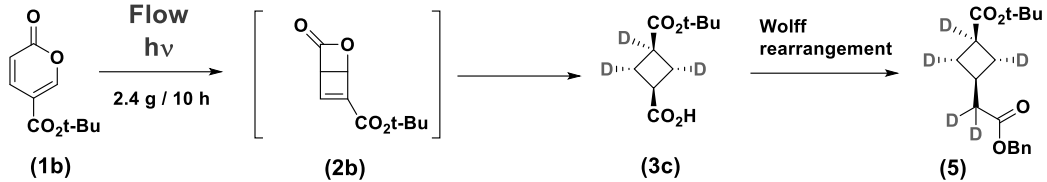
New deuterated cyclobutane derivatives, cis-3-(*tert*-butoxycarbonyl) -2,3,4-d_3-cyclo- butanecarboxylic acid **(3c)** and cis-3-((benzyloxycarbonyl)methyl-d_2)cyclobutane-1,2,4-d_3- carboxylic acid *tert*-butyl ester **(5)** were synthesized efficiently as building blocks useful for the preparation of corresponding deuterated drug candidates used as internal standard compounds in clinical pharmacokinetic studies by means of LC/MS/MS analyses.

Introduction of 3 deuterium atoms onto cyclobutane ring system has been achieved to afford **(3c)** by deuteration of **(2b)** which was prepared efficiently (3.6 g/10 h) using continuous photo flow chemistry reaction of **(1b)**. Homologation of **(3c)** using the Wolff rearrangement in the presence of benzylalkohol-O-d_1 led to formation of **(5)** successfully with excellent isotope purity. The relative configurations of 3 deuterium atoms onto cyclobutane ring system were revealed by means of NMR.



(1b) (2b) (3c) (5)