N,N'-Dicyclohexylurea - Effective Inhibitor of N-Acetyl-D-Glucosamine Glycosides Anomerisation

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It is well known that stereospecificity is an important problem in glycoside synthesis. Even the most stereospecific glycosidation methods not except an anomerisation process in presence of Brensted or Lewis acids owing to the second time anomerisation of primarily generated glycosides. Oxazoline and Helferich syntheses are the examples of such processes, where protonic and Lewis acids are used as catalyst or eliminated during a reaction. The rate of anomerisation process foremost depends from a strength of catalyst acid. For example, tert-butyl-2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside easily anomerizes in presence of HBr in chloroform solution at 50°C, but reaction do not take place in the same conditions using the same or even larger concentrations of HCL. So, when the presence of acid in a reaction mixture is unavoidable, the reagents for an acidity reduction should be used. We have found an urea derivatives as such reagents. The most effective of which is N,N'-dicyclohexyl urea (DCU), while widely used in glycoside synthesis tetramethylurea is not effective in this role. The use of DCU in many cases completely inhibited anomerisation process and lead to high glycoside yield.

For example glycosylation of benzyl- or tert-butyl alcohols with 2-methyl-(3,4,6-tri-O-acetyl-1,2-dideoxy-α-D-glucopyrano)-[2,1-d]-2-oxazoline hydrobromide or hydrochloride in CHCl$_3$ solution at 64°C lead to an anomeric mixtures containing up to 10% of 1,2-cis-glycoside, while anomeric glycosides were not detected in reaction products in presence of 0.2-0.5 equivalents DCU (per glycosilating reagent). More over, the yields of desired products are sufficiently increases from 55 to 68% (for tert-butylglycoside) and from 77 to 82% (for benzylglycoside).