

MICROWAVE-ACCELERATED GLYCOSYLATIONS UNDER MILD CONDITIONS

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Glycosylation of alcohols often occur in the presence of a Lewis acid ‘promotor’ and often strong Lewis acids are used. However, there are several glycosylation methods for the synthesis of aryl glycosides, which do not require a Lewis acid ‘promotor’, e.g., by generation of a phenoxide nucleophile or by nucleophilic aromatic substitution [1]. Novel methods for glycosylation of aliphatic alcohols in the absence of strong Lewis acids, i.e. under mild conditions, holds great promise, e.g., for combinatorial chemistry and solid phase synthesis applications.

In a recent series of papers we have described a new, efficient method for glycosylation under strictly neutral, mildly basic, or very mildly acidic (LiClO₄) conditions [2, 3]. In this glycosylation technique, the anomeric leaving group on benzyl or benzoyl protected donors is methyl 3,5-dinitrosalicylate (DISAL) or its *para* regioisomer. The potential of DISAL glycosyl donors was demonstrated in their successful application to solid-phase oligosaccharide synthesis, solution synthesis of a hexasaccharide, intramolecular glycosylation, synthesis of glycosylated natural product analogues, and latest glycosylation with a range of protected glucosylamines. Microwave heating can dramatically increase reaction rates in organic chemistry [4]. Modern instruments allow precise control of temperature and pressure in sealed reaction tubes. We hypothesized that the very mild conditions of the DISAL methodology will make them compatible with promotion by precise microwave heating. Indeed, we were able to dramatically accelerate glycosylations with DISAL donors by microwave heating at 100 to 130 °C. We have investigated microwave glycosylation with several DISAL donors and compared them to other glycosyl donors, such as glycosyl bromides and trichloroacetimidates as well as thioglycosides. Microwave heating was also applied to glycosylation with a 4,6-benzylidene protected mannosyl DISAL donor in stereoselective glycosylations.

References

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