

Automated Click Chemistry – Synthesis of a Triazole Library

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Introduction

PharmBioTec's department of Drug Discovery focuses on the synthesis of small, drug-like molecules for a broad range of therapeutic targets. Usually a large number of compounds is needed to identify active species, or to improve the activity/pharmacokinetic profile of an initial hit. Instead of employing time and labor-intensive bench work, PharmBioTec has chosen another path, that of automation. Towards this end PharmBioTec has acquired the most flexible platform for organic synthesis on the market: Chemspeed's ISYNTH. This modular robotic platform enables library synthesis and work-up in easy to use disposable reactors. It is suited for low and high temperatures, for handling liquids / solids and working under inert or reactive gas pressure atmosphere.

Objectives

- Synthesize a library of 32 triazoles in a fully automated protocol, including work-up and sampling, starting from commercially available boronic acids and alkynes
- Compare yields obtained in the manual and automated procedures

Experimental Set-up

ISYNTH, a software-driven robotic platform containing:

- Solid Dispensing Unit
- 4-Channel Liquid Handling Unit
- 20 mL Disposable Glass Reactors
- Phase-separation cartridges for automated work-up



Workflow



Results

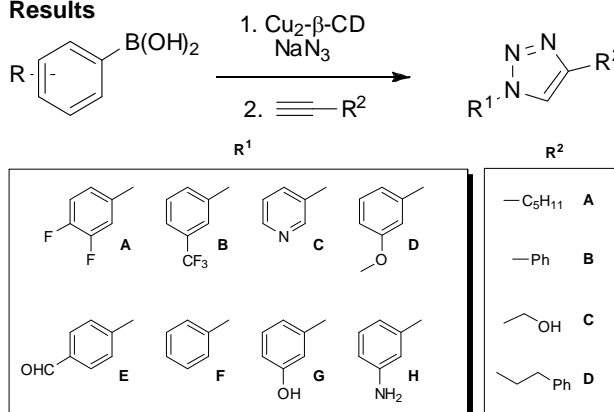
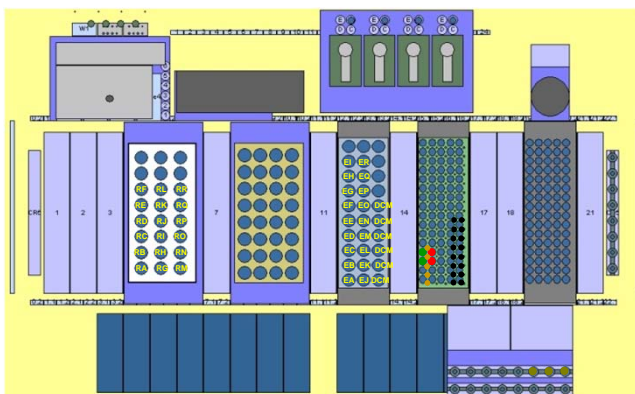


Figure 1 – Overview of prepared compounds

All reaction steps, including work-up, were performed in the ISYNTH platform.



A: RA-RR (Reaction-Zone)

B: EA-ER (Extraction-Zone)

C: DCM

Cu-CD-Complex, Sodium Azide, Alkynes, HPLC-Samples, MgSO₄

Figure 2 – Schematic layout of the experiment, showing storage positions of raw materials and reaction wells.

Crude products were purified by preparative HPLC if their purity was below 95%. The average yields obtained were above 30% and comparable to manual procedure [1].

Conclusions

A library of 32 triazoles was synthesized on the ISYNTH platform, with an average purity of 96% (after HPLC). Generation of such libraries is achieved in the same time as it takes for a single compound manually.

Reference

[1] Kaboudin, B.; Abedi, Y.; Yokomatsu, T. *Org. Biomol. Chem.* **2012**, *10*, 4543–4548