

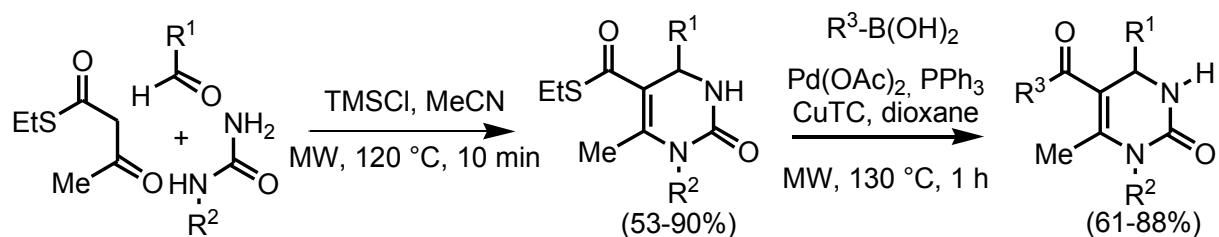
SYNTHESIS OF HETEROCYCLIC COMPOUND LIBRARIES BY AUTOMATED SEQUENTIAL AND PARALLEL MICROWAVE SYNTHESIS

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Transition metal-catalyzed carbon-carbon bond forming reactions are one of the most important methods in organic synthesis. In the fast growing field of Pd-catalyzed cross coupling reactions, recently Liebeskind and co-workers developed a novel carbon-carbon bond forming protocol, involving Pd(0)-catalyzed, Cu(I) carboxylate mediated coupling of thiol esters or thioethers under base free conditions [1].

In continuation of our interest in the generation of diversely substituted and novel types of privileged scaffolds of the 3,4-dihydropyrimidin-2-one type [2], we applied the Liebeskind-Srogl cross-coupling protocol for the efficient synthesis of 5-aryl-dihydropyrimidinones. Using automated sequential microwave synthesis involving robotic vial handling in single mode cavities [3] a library of 30 different 5-aryl-dihydropyrimidinones was prepared. Nearly identical yields were obtained when a sub set of 16 ketones was prepared in a single microwave irradiation experiment using a 48 vessel rotor system contained in a multimode microwave reactor [4].



References

- [1] Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc.* **2000**, *122*, 11260.
Liebeskind, L. S.; Srogl, J. *Org. Lett.* **2002**, *4*, 979.
- [2] For reviews on DHPMs, see: Kappe, C. O. *Tetrahedron*, **1993**, *49*, 6937. Kappe, C. O. *Acc. Chem. Res.* **2000**, *33*, 879. Kappe, C. O. *Eur. J. Med. Chem.* **2000**, *35*, 1043. Kappe, C. O.; Stadler, A. *Org. React.* **2004**, *63*, 1.
- [3] Stadler, A.; Kappe, C. O. *J. Comb. Chem.* **2001**, *3*, 624.
- [4] For recent reviews on microwave synthesis, see: Kappe, C. O. *Angew. Chem. Int. Ed.* **2004**, *43*, 6250. Kappe, C. O.; Dallinger, D. *Nature Rev. Drug Discov.*, **2006**, *5*, 51.