

MICROWAVE-ASSISTED SYNTHESIS OF SUBSTITUTED 2(1H)-QUINOLONES AS MAXI-K⁺ CHANNEL OPENERS

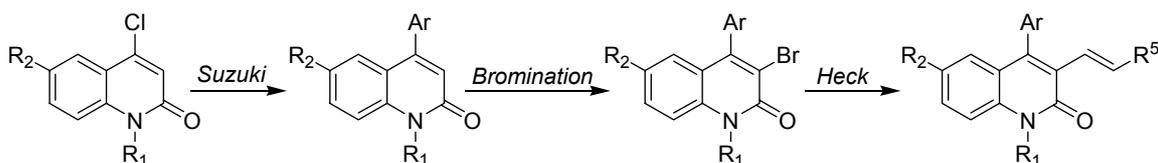
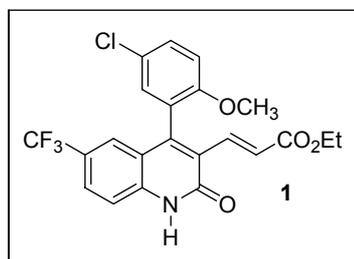
Toma Glasnov, Wolfgang Stadlbauer and C. Oliver Kappe*

Institute of Chemistry, Karl-Franzens-University Graz, Heinrichstrasse 28,
A-8010 Graz / Austria

Fax: +43-316-3809840; E-mail: oliver.kappe@uni-graz.at / www.maos.net

The erectile dysfunction is known as a persistent inability of a man to achieve and/or maintain erection sufficient for a satisfactory sexual performance. According recent studies more than 30 million man in the United States are affected. There are many different treatments but most widely used in the last years are such well-known drugs as Viagra®(Sildenafil) and its new analogs –Vardenafil and Tadalafil. In the recent few years some new chemical substances, known as maxi-K⁺ channel openers [1], have been studied by Bristol-Myers Squibb and reported as a potential new drug candidates, e.g. 2(1H) quinolone **1** [2].

Here we present a case study, involving a novel, stepwise, and diversity generating synthesis of some of these biologically active substituted quinolones, using a sequence of up to six microwave-assisted reaction [3] steps. Two of the key transformations involve rapid microwave-assisted Suzuki arylation on the C-4, and Heck olefination on the C-3 position. Scale-up and details of the reaction processing issues will be discussed.



- 1) Steers, W.D., *Rev.Urology*, **2002**, 4, 17-25
- 2) Hewawasam, P. et al., *J.Med.Chem.*, **2003**, 46, 2819-2822.
- 3) Kappe, C.O., *Angew.Chem.Int.Ed.*, **2004**, 43, in press.