



# A NEW HIGHLY EFFICIENT STRATEGY FOR GENERATION OF INDAN SCAFFOLDS VIA A ONE-POT ANNULATION REACTION

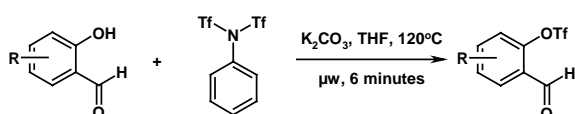
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## Introduction

In lead identification processes there is an increasing need for new, rigid and densely functionalised, organic scaffolds of relatively small size. We wanted to investigate a new efficient route to indan scaffolds, catalysed by palladium. Aryl triflates are useful starting materials in many types of palladium-catalysed coupling-reactions. Automated and focused microwave flash-heating has recently been proven to increase the preparative efficiency and to dramatically reduce reaction times in several different fields of organic chemistry. In addition, we therefore decided to undertake a study of microwave-promoted high-speed triflation of phenols.

## Triflation of salicylic aldehydes



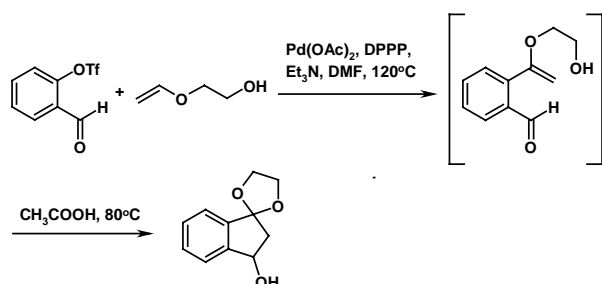
Eight different salicylic aldehydes were investigated. Complete conversions and high yields were achieved after only 6 minutes of microwave irradiation.

Product	Yield*	Product	Yield*
	78 %		70 %
	73 %		50 %
	67 %		66 %
	87 %		69 %

\*Isolated yields after flash chromatography and/or recrystallisation. (>95 % pure)

## Generation of indan scaffolds

Palladium-catalysed reactions of the triflated salicylic aldehydes with ethylene glycol vinyl ether provided, in a one-step annulation reaction, a direct entry to protected hydroxy indanones.



## Reaction path

The reaction proceeds through two steps: The vinyl ether is arylated internally through a bidentate ligand controlled Heck reaction. Subsequent ring closure is thereafter triggered by addition of acid to the reaction mixture.

## Results (four examples):

Product	Yield*
	60 %
	50 %
	24 %
	38 %

\*Isolated yields after dry-flash. (>95 % pure)

## Summary

We have developed a new rapid and robust method for the generation of aryl triflates and an efficient synthetic route from salicylic aldehydes to indan scaffolds. The annulation reaction is foreseen to permit selective functionalisations at both of the oxygen carrying carbons.

## Acknowledgement

We would like to thank The Swedish Research Council for Engineering Sciences (TFR) for financial support, and Personal Chemistry AB for access to the Smith Synthesizer™.

