

AFRICA Application Note

Note Number : 4

Examples of AFRICA Chemistry

I Summary

This application note describes examples of some of the chemistry performed using the AFRICA system. This is not intended to be a detailed analysis of each reaction, more a demonstration of the range of reactions possible.

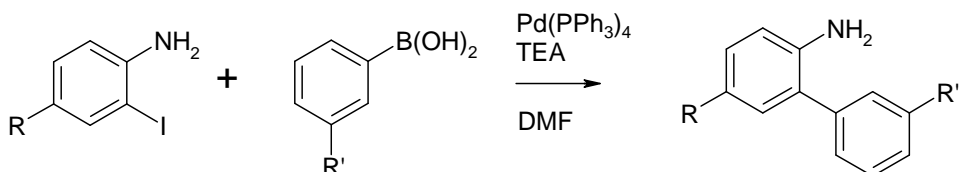
Note:

Much of the chemistry reported in this application note has been performed at customers' sites, often using commercially sensitive compounds. As such, the structures of some materials and the yields of some reactions have not been disclosed.

2 Reactions

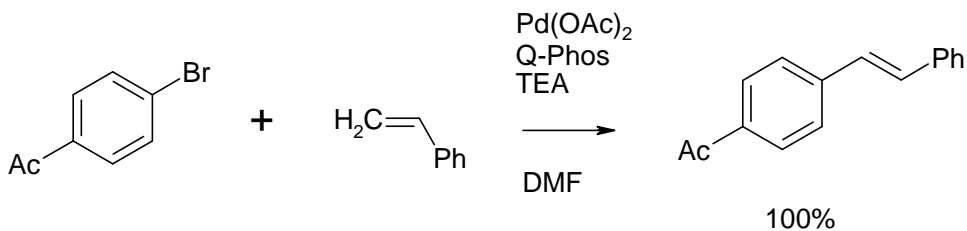
2.1 Homogeneous Catalysis

2.1.1 Suzuki Reaction



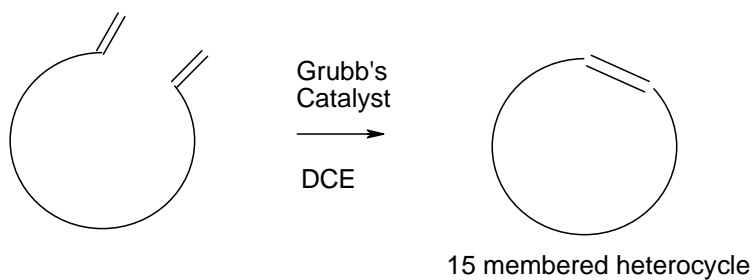
Keywords: Palladium catalysed cross coupling, Suzuki

2.1.2 Heck Reaction



Keywords: Palladium catalysed cross coupling, Heck

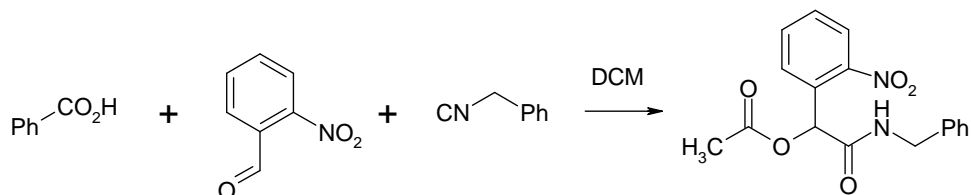
2.1.3 Grubbs Metathesis



Keywords: Ring closing metathesis, Grubbs

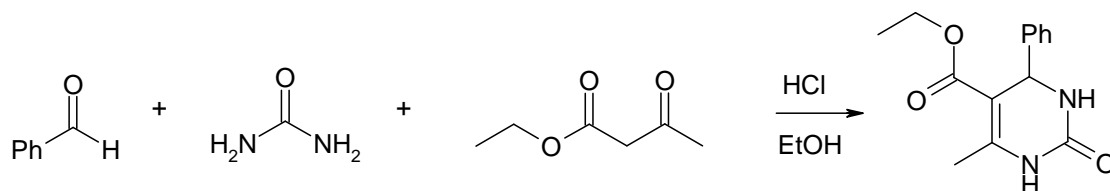
2.2 Multicomponent Reactions

2.2.1 Passerini 3CR



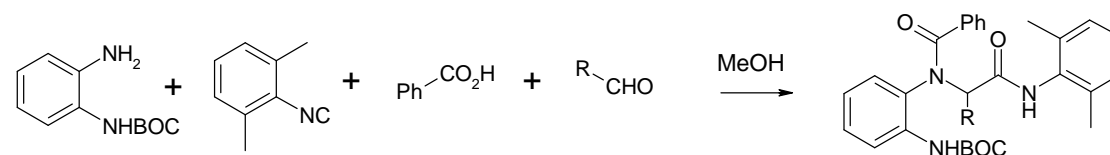
Keywords: Passerini, 3CR

2.2.2 Biginelli 3CR



Keywords: Biginelli, 3CR, heterocycle

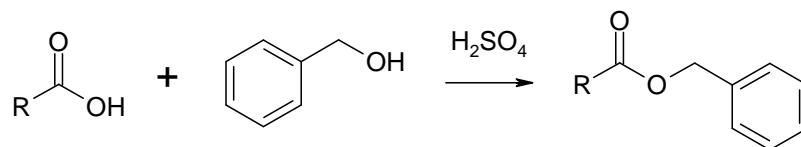
2.2.3 Ugi 4CR



Keywords: Ugi, 4CR, isonitrile

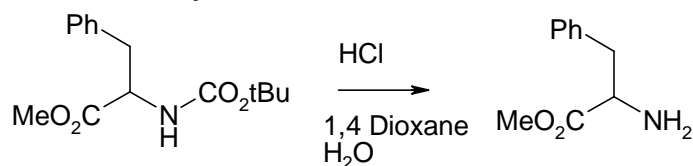
2.3 Protection/Deprotection Chemistry

2.3.1 Benzyl ester protection



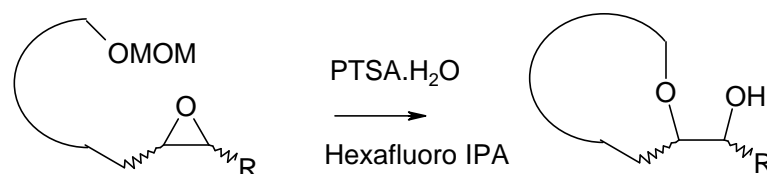
Keywords: Esterification, protection, sulphuric acid

2.3.2 BOC deprotection



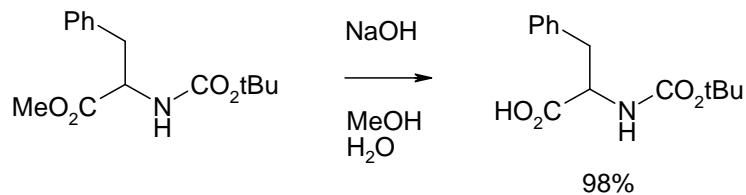
Keywords: BOC deprotection, protected phenyl alanine

2.3.3 MOM deprotection & intramolecular epoxide opening



Keywords: MOM ether, deprotection, epoxide opening

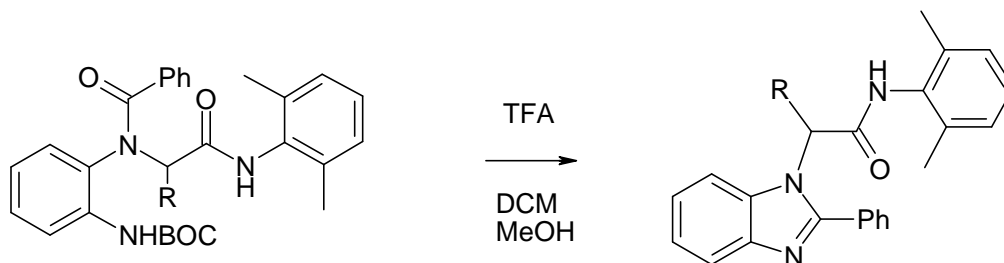
2.3.4 Ester saponification



Keywords: Saponification, hydrolysis

2.4 Ring Formations

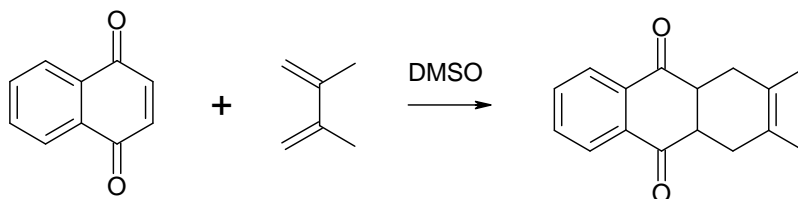
2.4.1 Benzimidazole formation



Keywords: BOC deprotection, benzimidazole formation, heterocycle, TFA (trifluoroacetic acid)

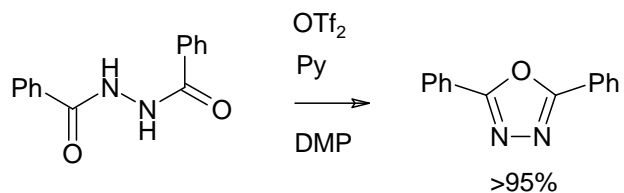
Note: Performed as continual 2 step flow process, starting material formed in situ as per 2.2.3

2.4.2 Diels Alder



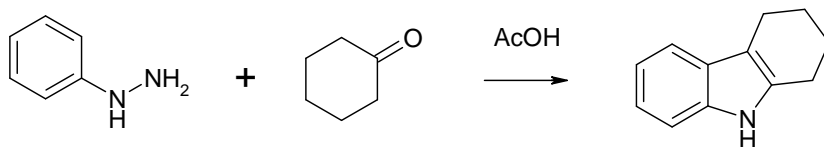
Keywords: Diels-Alder, 4+2 cycloaddition

2.4.3 1,3,4 oxadiazole formation



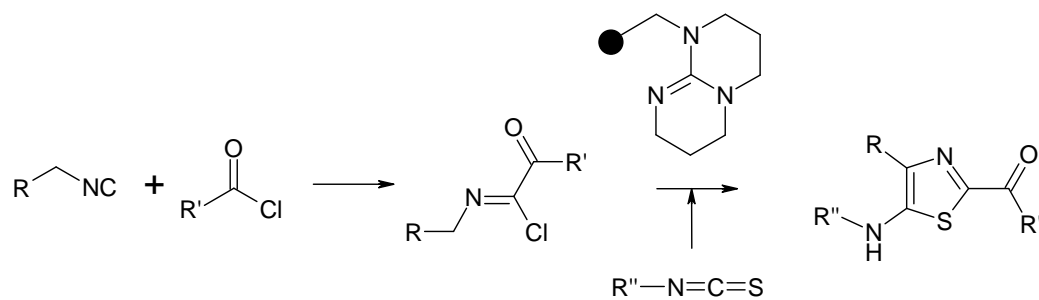
Keywords: 1,3,4 oxadiazole, hydrazide, triflic anhydride, heterocycle

2.4.4 Fischer indole synthesis



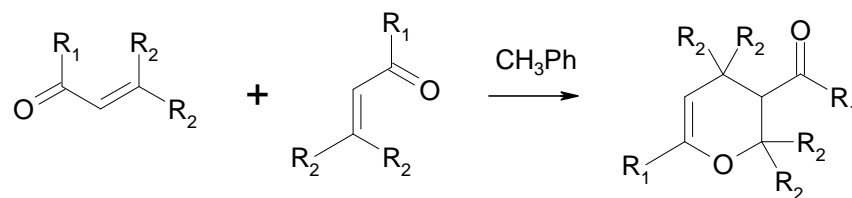
Keywords: Fischer indole synthesis, heterocycle

2.4.5 1,3 - Thiazole formation



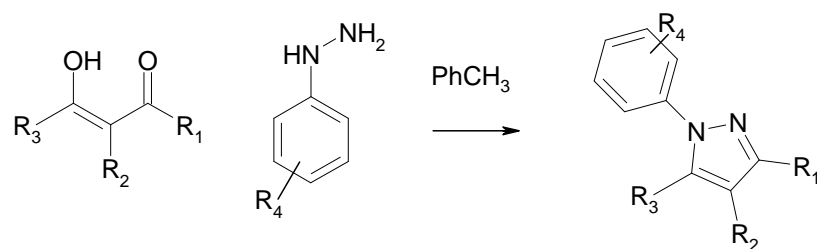
Keywords: University of Cambridge, heterocycle, solid phase synthesis, TBD polystyrene base

2.4.6 3,4-dihydropyran formation



Keywords: 3,4-dihydropyran, hetero Diels-Alder, heterocycle

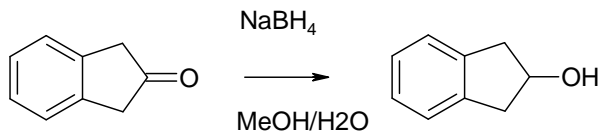
2.4.7 Pyrazole formation



Keywords: Pyrazole formation, heterocycle

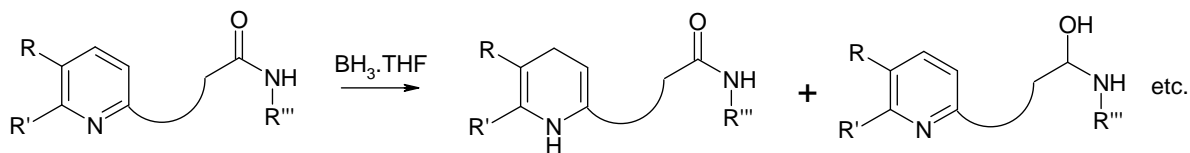
2.5 Oxidation and Reduction

2.5.1 Borohydride reduction



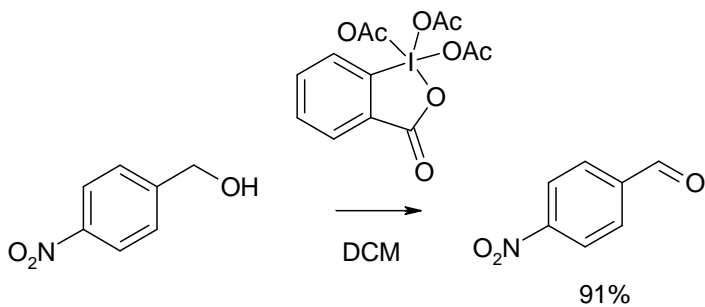
Keywords: Borohydride reduction

2.5.2 Borane reduction of a heterocycle



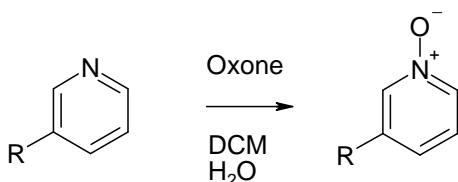
Keywords: Borane, heterocycle reduction, amide reduction

2.5.3 Dess-Martin alcohol oxidation



Keywords: Dess-Martin, alcohol, aldehyde, oxidation

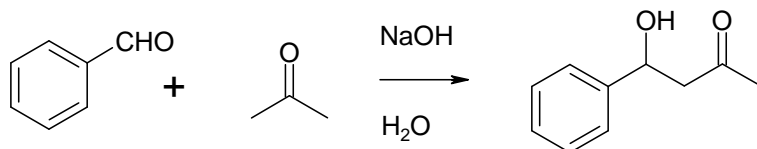
2.5.4 N-oxide formation



Keywords: N-oxide, Oxone®

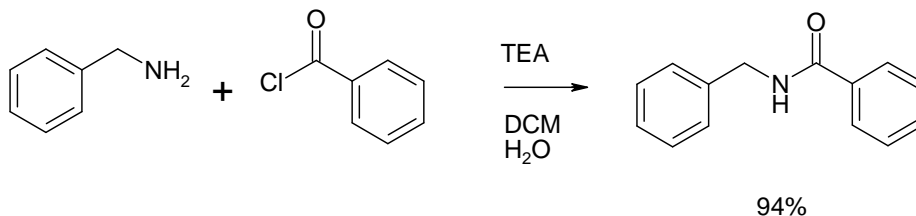
2.6 General Synthesis

2.6.1 Aldol reaction



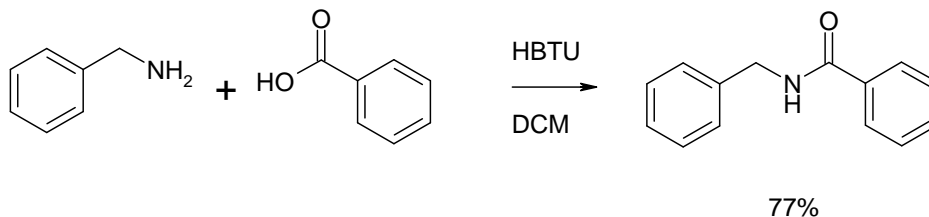
Keywords: Aldol, sodium hydroxide, aldehyde, ketone

2.6.2 Biphasic amide formation



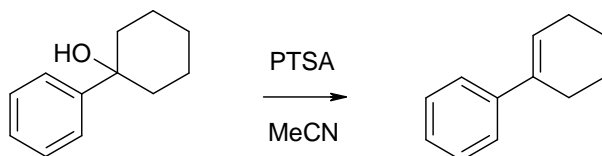
Keywords: Amide formation, biphasic

2.6.3 HBTU amide coupling



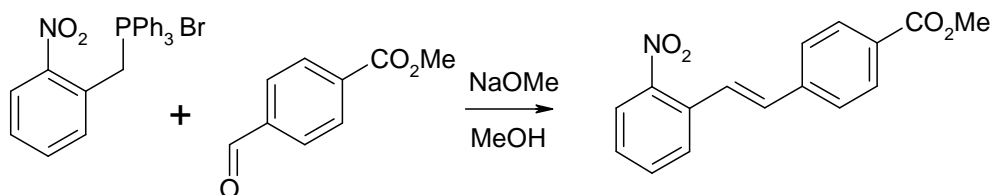
Keywords: HBTU, amide coupling

2.6.4 Elimination of alcohol to alkene



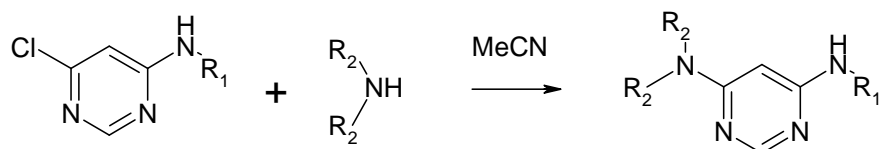
Keywords: Elimination, paratoluene sulphonic acid, alcohol, alkene

2.6.5 Wittig reaction



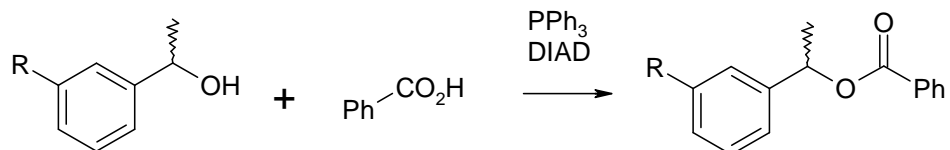
Keywords: Wittig, phosphonium salt, aldehyde, alkene, colour change

2.6.6 Nucleophilic aromatic substitution



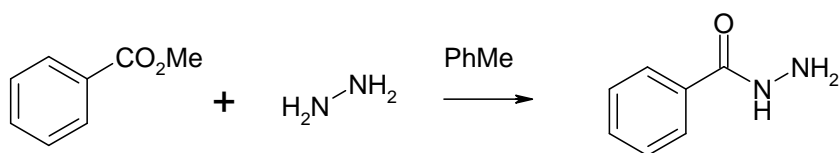
Keywords: Pyrimidine, S_NAr, nucleophilic aromatic substitution

2.6.7 Mitsunobu Reaction



Keywords: Mitsunobu, S_N2

2.6.8 Hydrazide formation



Keywords: Hydrazide, hydrazine