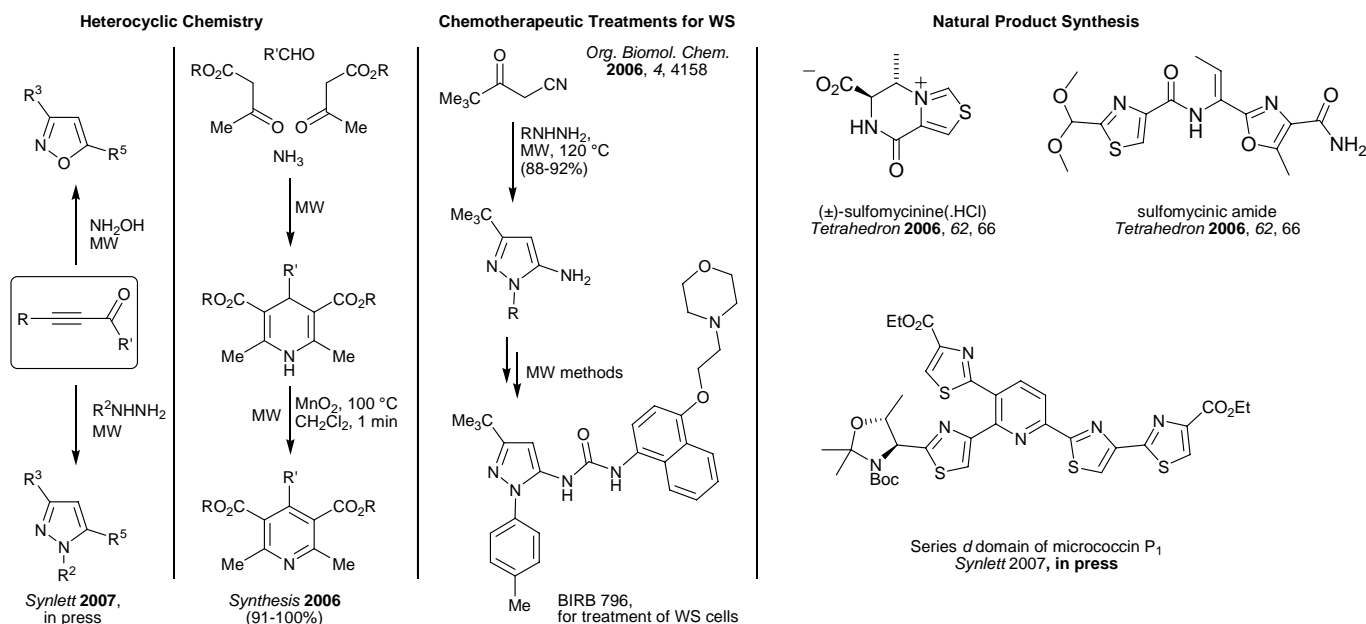


8.2 Dr Mark C Bagley, School of Chemistry, Cardiff University

Advantages of microwave-mediated synthesis and its application to the study of Werner Syndrome

Within our group, with the help of the Centre, we have established many new findings in heterocyclic chemistry, natural product synthesis and chemical biology (**Scheme 1**). We have shown that microwave irradiation can improve many processes in heterocyclic chemistry, in terms of facility, efficiency and product yield, over traditional conductive heating methods (*Top. Heterocycl. Chem.* 2006). The synthesis of simple but heavily functionalized heteroaromatic targets, including pyridines (*Synthesis* 2006) and pyrazoles (*Synlett* 2007), have all been improved under microwave irradiation. Related methodology has been applied in the synthesis of key fragments of the thiopeptide antibiotics, including the sulfomycin degradation products sulfomycinine and sulfomycinic amide (*Tetrahedron* 2006) and the central heterocyclic domain of micrococcin P₁ (*Synlett* 2007).



Scheme 1. Microwave irradiation improves the speed and/or efficiency of many different processes in heterocyclic chemistry, in this years work within the group

We have applied our success in microwave-mediated methodology to the study of Werner Syndrome (WS), a rare human genetic disease that shows accelerated ageing and an increased cancer incidence, and is interesting for the insights that it gives into both processes. A key feature of WS is that cells from these individuals show a much-reduced cellular lifespan in the laboratory as a consequence of replicative senescence. This is a key area of interest within cancer research because of its potential as a tumour suppressor mechanism. In order to determine the role of the p38 stress signalling pathway in the accelerated senescence of WS cells we have prepared small molecule p38 α inhibitors, such as BIRB 796, using novel methodology and are now in the process of testing these inhibitors to see if they can rescue the features of accelerated ageing.