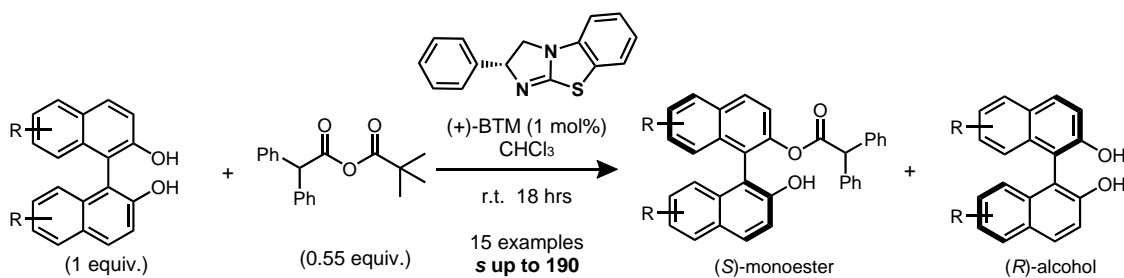


# ISOTHIUREA-CATALYSED REGIOSELECTIVE ACYLATIVE KINETIC RESOLUTION OF AXIALLY CHIRAL BIARYL DIOLS

Shen Qu, Mark. D. Greenhalgh and Andrew. D. Smith

EaStCHEM School of Chemistry, University of St Andrews, Fife, KY16 9ST, UK

While kinetic resolution (KR) processes of alcohols bearing point chirality has been widely explored, the acylative KR of alcohols bearing axial chirality remains surprisingly underdeveloped, with only 2 methods of organocatalytic acylative KR of biaryl alcohols reported to date.<sup>[1,2]</sup> To address this limitation, we have developed an operationally-simple isothiurea-catalysed acylative kinetic resolution of unprotected 1,1'-biaryl-2,2'-diol derivatives that provides access to axially-chiral biaryl diols in highly enantioenriched form (*s* values up to 190).<sup>[3]</sup> Following extensive reaction optimization, investigation of reaction scope and limitations provided three key observations: i) the diol motif of the substrate was essential for obtaining good conversion and high *s* values; ii) the use of an stable  $\alpha,\alpha$ -disubstituted mixed anhydride (2,2'-diphenylacetic pivalic anhydride) was critical to minimize diacylation and give high selectivity; iii) The presence of substituents in the 3,3'-positions of the diol hindered effective acylation. This observation led to the first highly regioselective acylative kinetic resolution of unsymmetrically-substituted biaryl diol substrates.



[1] G. Ma, J. Deng, M. P. Sibi, *Angew. Chem. Int. Ed.*, **2014**, 53, 11818-11821

[2] S. Lu, S. B. Poh, Y. Zhao, *Angew. Chem. Int. Ed.*, **2014**, 53, 11041-11045

[3] S. Qu, M. D. Greenhalgh, A. D. Smith, *Chem. Eur. J.*, **2019**, 25, 2816-2823