Supplementary Material

Materials and Methods

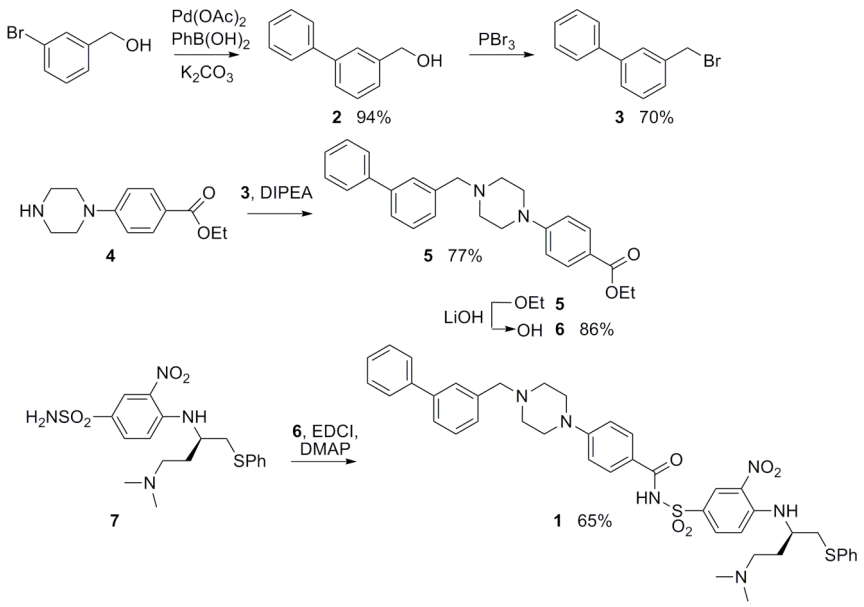
Synthesis of W1191542

The synthesis of **1** (Supp. Figure 1) was a variation of the route undertaken by Bruncko *et al.* (Bruncko et al., 2007). The key step in this approach exploited an EDCI coupling of the acid **6** and the sulfonamide **7**. The synthesis of the acid component **6** began with a Suzuki coupling of *m*-bromobenzyl alcohol with phenyl boronic acid to give the biaryl **2**. The biaryl **2** was brominated and subsequently utilised in the *N*-alkylation of the commercially available piperazine **4** to obtain **5**. Hydrolysis of the ester **5** afforded the acid **6**, which was employed in an EDCI coupling with the sulfonamide **7** (Wendt et al., 2006) to obtain **1** in an overall good yield.

Bruncko, M., Oost, T. K., Belli, B. A., Ding, H., Joseph, M. K., Kunzer, A. *et al*. Studies Leading to Potent, Dual Inhibitors of Bcl-2 and Bcl-xL. *J. Med. Chem.* (2007), **50**, 641-662.

Wendt, M. D., Wang, S., Kunzer, A., McClellan, W. J., Bruncko, M. *et al.* Discovery and Structure-Activity Relationship of Antagonists of B-Cell Lymphoma 2 Family Proteins with Chemopotentiation Activity in Vitro and in Vivo. *J. Med. Chem.* (2006), **49**, 1165-1181.

Supplementary Figure 1: Synthesis of W1191542



Supplementary Figure 2

Representative sensorgrams for direct binding assays performed on the Biacore S51 with ABT-737 (upper panel - injections of 270 nM, 90 nM, 30 nM, 10 nM and 3.3 nM) and W1191542 (lower panel – injections of 270 nM, 30 nM, 10 nM and 3.3 nM). The fine black line over each colored sensorgram is the fit (one-to-one binding with mass transport limitations) provided by the Biacore S51 Evaluation Version 1.2.1 data analysis software.