

S20-5 **Synthesis and Biological Evaluation of Novel Peripherally Selective Androgen Receptor Antagonists**

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It is well-established that androgens play a major role in the development and progression of prostate cancer. To identify novel androgen receptor antagonists, we conducted random screening of in-house compound library. Subsequent lead generation and optimization led to the discovery of (+)-(2*R*,5*S*)-4-[4-cyano-3-(trifluoromethyl)phenyl]-2,5-dimethyl-*N*-[6-(trifluoromethyl)pyridin-3-yl]piperazine-1-carboxamide (YM580). YM580 decreased the weight of rat ventral prostate in a dose-dependent manner, and induced the maximum antiandrogenic effect, comparable to that of surgical castration, without significantly affecting serum testosterone levels.