

*Development of Total Synthesis Strategies and Application to Phenylspirodrimanes*

**Abstract:** Natural products play an important role in drug discovery and serve as one major source of bioactive compounds. With the development of cheminformatics, the chemical space of natural products has been navigated and it provides a larger area of developing novel drug candidates. However, the synthetic challenge arising from their structural complexities impede deep studies of their application in pharmacotherapy. In addition, the feasibility of structural modification of natural products raises a demand to develop synthetic strategies enabling diversification of the targets. We have explored the chemical space of phenylspirodrimane, a secondary metabolite from *Stachybotrys*, in silico and enumerated possible derivatives by coupling with commercially available aryl bromide. Our synthetic strategy is aiming to access the chemical space of phenylspirodrimane physically and employs the cross-coupling between drimane moiety and aryl halide as the key step. Meanwhile, the available synthetic routes are analyzed by cheminformatics tools to help the design of new synthetic strategies.