S31-2 Synthetic Study on (-)-Cercosporamide Derivatives as Novel Anti-diabetic Agents

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In our search for a novel anti-diabetic agent, (−)-Cercosporamide, which is known as an antifungal agent, showed a potent plasma glucose-lowering effect in hyperglycemic KK/Ta mice. We succeeded in modifying each of the functional groups of (−)-Cercosporamide and synthesized various derivatives. Compound A showed the most potent efficacy and safety among them. We found that compound A partially transactivated PPARγ. Although PPARγ full agonists such as Rosiglitazone have been clinically used and show beneficial effects, the use of these drugs has been limited because of their adverse effects, including edema, weight gain, and so on. Recently, it was proposed that a PPARγ partial agonist would be effective in improving insulin resistance without undesirable adverse effects. Accordingly, we embarked on a further investigation of (−)-Cercosporamide derivatives as PPARγ partial agonists and finally we acquired some promising compounds.