Synthesis of Tetrasubstituted Benzotriazepinone Turn Mimics

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Abstract:

Benzotriazepines are a class of heterocycles that have exhibited binding affinity and activity at various receptors [1]. 1,3,5,8-Tetrasubstituted 1,3,4-benzotriazepin-2-ones have been shown to mimic both type I and I' β-turn conformations due in part to nitrogen pyramidalization and dynamic chirality [2]. Moreover, biological assessment of tetrasubstituted benzotriazepinones designed to mimic the peptide allosteric modulator Urocontrin have demonstrated ability to selectively enhance or diminish the activity of one of the two endogenous urotensin II receptor ligands without influence on the activity of its counterpart [3]. Our presentation focuses on the development of a modular strategy to prepare tetrasubstituted benzotriazepinones. Notably, photoreactive components are being introduced on the heterocycle structure with the goal of creating photoaffinity probes to label the binding site of the urotensin II receptor.

[1] Harvey, S.-M.; Wei, X.; Truong, D.; Lubell, W. D. Benzotriazepine Synthesis, Conformational Analysis, and Biological Properties. *Can. J. Chem.* **2024**, *102* (8), 469–498.

[2] Wei, X.; Douchez, A. and Lubell, W. D. 1,3,5,8-Tetrasubstituted 1,3,4-benzotriazepin-2-one scaffolds for β-turn mimicry without chiral carbons: synthesis and conformational analysis. *J. Org. Chem.* **2023**, *88* (7), 4633-48.

[3] Wei, X.; Diarra, S.; Douchez, A.; Cunico Dallagnol, J.C.; Hébert, T.E.; Chatenet, D.; Lubell, W.D. Urotensin II Receptor Modulation with 1, 3, 4-Benzotriazepin-2-one Tetrapeptide Mimics. *J. Med. Chem.* **2023**, *66* (20), 14241-14262.