Iodonium-based Probes for the Activity-based Protein Profiling of Oxidoreductases

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An important challenge in activity-based protein profiling (ABPP) is expanding the pool of probe molecules to enzyme classes with more complex catalytic activities. Especially the enzyme class of oxidoreductases has not been yet covered with ABPP, with few exceptions such as Cyp450-enzymes[1] and monoaminooxidases (MAO)[2]. We sought to expand the tool box of ABPP by using aryliodonium compounds, which have previously been characterized as inhibitors of aldehyde dehydrogenase (ALDH2)[3] as a starting point to develop ABPP probes against oxidoreductases. The synthesis of the probes represented a considerable challenge, which required considerable optimization. With the probes in hand we could perform ABPP experiments confirming the suitability of the probes in the screening for oxidase activity.

[1] Wright AT, Cravatt BF, *Chem. Biol.* **2007**, *14*, 1043-1051.

[2] Krysiak JM, Kreuzer J, Macheroux P, Hermetter A, Sieber SA, Breinbauer R, *Angew. Chem. Int. Ed. Engl.* **2012**, *51*, 7035-7040.

[3] Neubauer R, Wölkart G, Opelt M, Schwarzenegger C, Hofinger M, Neubauer A, Kollau A, Schmidt K, Schrammel A, Mayer B, *Biochem. Pharmacol*. **2015**, *93*, 440-448.