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CO-Driven Sulfoximinocarbonylation of Aryl Halides via Continuous Flow

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Carbonylation reactions play a crucial role in organic and industrial chemistry, enabling the introduction of carbonyl groups into organic substrates using carbon monoxide (CO). [1] While CO is cost-effective and atom-efficient reagent, its toxicity and high-pressure handling present significant challenges in traditional batch processes. In recent years, flow chemistry has revolutionized these transformations, offering enhanced efficiency, safety, and precise control of reaction parameters. [2, 3]

Sulfoximines are valuable scaffold in pharmaceutical, agricultural, and organic chemistry as chiral auxiliaries and intermediates. [4] Despite their synthetic potential, previous approaches often rely on toxic reagents, excessive oxidants, and tedious purification steps, leading to low conversions and undesirable by-products. [5]

Here, we report a continuous flow protocol for the *N*-arylation of different functionalized aryl halides with sulfoximines under CO pressure using a palladium-based catalyst, a base, and a ligand (Figure 1). Comprehensive screening of organic bases in batch mode allowed to identify optimal conditions, which were then translated into a flow system operating at 80 °C and 6 bar for 40 minutes. This innovative strategy provides rapid reactions, high selectivity, and good to excellent yields (up to 90%) across a small library, demonstrating the advantages of continuous flow technology in carbonylation chemistry.

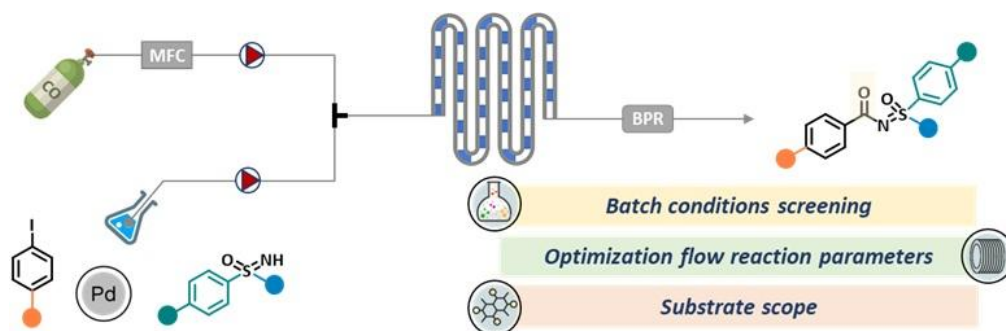


Figure 1: Batch screening, flow set-up optimization, and substrate scope for sulfoximinocarbonylation between substituted aryl iodides and sulfoximines.

References

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- [4] Guo, S.-R., Kumar, P. S., Yuan, Y.-Q., Yang, M.-H., Palladium catalyzed arylation of NH-sulfoximines with aryl halides using chloroform as the CO precursor, Tetrahedron Lett. 58 (2017) 2681–2684.
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