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Selective hydrogenation of nitro groups to amines using a heterogeneous biocatalyst

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PURPOSE OF THE ABSTRACT
This study describes the development of a heterogeneous biocatalyst for the reduction of aryl nitro compounds to corresponding amines.

Aryl amines are important molecules often present in pharmaceuticals[1] and used as synthons in azo dyes, which have applications such as pigments and food additives.[2] To prepare these compounds, the amine functional group is often installed into an aromatic molecule ?masked' as a nitro group, which is reduced at a later stage to provide the desired amine.[3,4] These organic nitro chemicals are prepared through well-established and efficient, albeit often hazardous methods,[5,6] and recent efforts have lowered the associated risks through process engineering (e.g., in flow).[7]

There are many methods to reduce the nitro product to provide the corresponding amine. Precious metal (Pd, Pt, Au, Ag)[8-11] and base metal (Ni, Mn, Cu)[12-14] catalysts have been used with hydrogen gas, however, they are not general in terms of chemoselectivity and functional group tolerance. Moreover, the amine product can sometimes poison the catalyst, adding further complexity to metal-catalysed strategies. Conversely, biocatalytic nitro reductions are gentle alternatives to metal-based ones. For instance, nitroreductases, which have been engineered to facilitate process intensification and widen substrate scope with demonstrated chemoselectivity, operate under mild reaction conditions.[15-16] However, when used for amine synthesis, nitroreductases rely on 3 or more equivalents of a reducing agent, typically in the form of cofactors NAD(P)H, which in turn are commonly re-generated from their oxidised form using 3 or more equivalents of glucose.

To overcome the limitations of the existing approaches, we have developed a heterogeneous hydrogenation biocatalyst that enables the reduction of nitroaromatic compounds to the corresponding amines (Fig. 1). The biocatalyst is easily accessible, stable and selective, and can be handled similarly to typical hydrogenation catalysts (e.g., Pd/C) but avoids using toxic metals that are often not functional group tolerant. Moreover, it opens up an opportunity to translate the nitro reduction process into a continuous flow reactor.

FIGURES

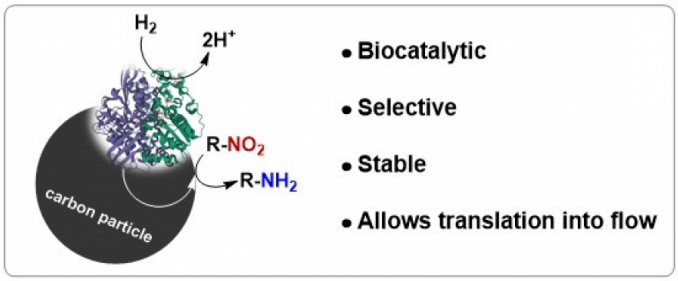

FIGURE 1

Figure 1.

Novel heterogeneous hydrogenation biocatalyst for selective reduction of aromatic nitro compounds to corresponding amines.

FIGURE 2

KEYWORDS

nitro reduction | biocatalysis | aryl amines

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