

Introduction to ACS Catalysis Virtual Special Issue on Cascade Catalysis



Cascade Catalysis

This virtual special issue of ACS Catalysis on Cascade Catalysis (<http://pubs.acs.org/page/accacs/vi/cascade.html>) includes studies that cover different recent approaches in cascade catalysis, including established and emerging methodologies.

A cascade reaction is, in a broad and general definition, the combination of various chemical steps in one pot without isolating the intermediates. For a catalytic cascade, a catalyst is required for at least one step during the sequence of transformations. Cascade reactions are valuable because they avoid the need for purification of the intermediates and circumvent time-consuming protection/deprotection steps and functional group interconversions. Furthermore, they are extremely useful when the sequence involves unstable intermediates that might be trapped in situ and used in the next step. Consequently, the cascade approach allows increasing the efficiency of organic synthesis by saving operational work-up steps, thereby improving the atom economy and ideally increasing the yield of the overall transformation compared with a classical sequence of single-step transformations. Cascades are an emerging technology in organic chemistry, introducing elegance and efficiency to synthetic strategies.

The definition of cascade reactions is rather broad because of the general types of transformations that fall under this category, including single catalysts triggering domino reactions as well as combinations of various steps catalyzed by different catalysts. Furthermore, diverse terms are used in different disciplines (chemistry, biology, biotechnology) to describe the same type of transformations.

Classification of Cascades. (1) Mode of operation. One parameter used to divide the cascades is whether the reactions are performed operationally in a sequential fashion in one pot without isolating the intermediates or whether all reagents are present from the start. In the first case, a reaction step of the cascade is finished before the reagents/catalyst(s) for the next transformation are added or the conditions are adapted. In the second case, one can distinguish between cascades requiring exclusively one catalyst triggering mostly a spontaneous domino

sequence, whereas another group of cascades requires a catalyst, reagent, or both for each transformation of the cascade.

Consequently, in the overview below, we will group the cascades of this virtual special issue according to the mode of operation in (i) cascades that are run sequentially, (ii) domino cascades, and (iii) relay cascade reactions in which numerous reactions are run in one pot and employ different catalysts that have different roles for each step (in biocatalysis often also referred to as simultaneous cascade).

(2) Number of reaction steps. Another parameter to describe a cascade is the number of reaction steps or the number of catalysts employed.

(3) Type of catalyst. The type of catalyst—(organo)metal-, organo-, or biocatalyst—may provide a special challenge if these catalysts should be employed simultaneously because of the moderate compatibility of these types of catalysts and reaction media. Although enzymes/biocatalysts can be more easily combined in a simultaneous cascade, because of their natural aqueous environment, the reaction conditions for the other two types of catalysts are often divergent. Nevertheless, combinations of different types of catalysts have been described and can also be found in this virtual special issue (e.g., for organocatalyst with Au, see D. J. Dixon, <http://pubs.acs.org/doi/abs/10.1021/cs401008v>); or for organo- with biocatalysis, see H. Gröger; <http://pubs.acs.org/doi/abs/10.1021/cs4010387>). A special case might be cooperative catalysis in which two catalysts are required to achieve the best results, as exemplified by a palladium and a gold catalyst in a cross-coupling reaction (Suzanne A. Blum; <http://pubs.acs.org/doi/abs/10.1021/cs400641k>).

In this virtual special issue, the Viewpoint, the Reviews, and the Perspectives provide an excellent overview of the state of the art and also show possible trends and techniques for the future. The Perspective focuses on heterogeneous catalysis in

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cascades (Avelino Corma; <http://pubs.acs.org/doi/abs/10.1021/cs401052k>), and one Review focuses on a single type of biocatalyst in various cascades—namely, ω -transaminases to access amines (Wolfgang Kroutil; <http://pubs.acs.org/doi/abs/10.1021/cs400930v>)—and another Review deals with organocatalysis for the synthesis of spirooxindoles (Carlos F. Barbas, III; <http://pubs.acs.org/doi/abs/10.1021/cs401172r>). Another Review concerns the Lewis acid-catalyzed cascade rearrangement of propargylic alcohols (Ping Lu, Yanguang Wang; <http://pubs.acs.org/doi/abs/10.1021/cs400922y>). Both the Review on carbene migration initiated by transition-metal catalysis (Jianbo Wang; <http://pubs.acs.org/doi/abs/10.1021/cs4006666>) and the Perspective on cascades involving radicals (Corey R. J. Stephenson; <http://pubs.acs.org/doi/abs/10.1021/cs400995r>) concentrate on the reactive species involved during the cascade.

The effect of catalyst organization is reviewed for metallic nanoparticles supported on various biomolecule-derived supports (Jose M. Palomo; <http://pubs.acs.org/doi/abs/10.1021/cs401005y>) as well as for nanostructured enzyme cascade reactions to promote substrate channeling along the cascade (Ian Wheeldon and Kumar; <http://pubs.acs.org/doi/abs/10.1021/cs401009z>).

The Letters and Research Articles can be classified according to the mode of operation:

(1) Sequential cascades: The first step needs to be finished before the second step is started by the addition of another catalyst or reagent or changing the reaction conditions.

Several contributions nicely demonstrate the numerous possibilities for performing such cascades; for instance, two metal catalysts employed in two sequential steps (Pd for isomerization, Rh for hydroformylation, Joost N. H. Reek; <http://pubs.acs.org/doi/abs/10.1021/cs400872a>) or a metal-catalyzed step (Pd, Stille-type coupling) followed by a chemical carboxylation (Bruce A. Arndtsen; <http://pubs.acs.org/doi/abs/10.1021/cs401164z>). An organocatalytic step may be followed by either gold catalysis (Darren J. Dixon; <http://pubs.acs.org/doi/abs/10.1021/cs401008v>) or biocatalytic reduction (alcohol dehydrogenase) of a ketone functionality (Harald Gröger; <http://pubs.acs.org/doi/abs/10.1021/cs4010387>). In a final example, both sequential steps were catalyzed by biocatalysts (enoate reductase, alcohol dehydrogenase) and an additional enzyme for recycling the cofactor (Jörg Pietruszka; <http://pubs.acs.org/doi/abs/10.1021/cs5000262>).

(2) Domino cascades. These involve one catalyst initiating the formation of a reactive intermediate or transforming an unstable intermediate.

Some examples in this virtual special issue again show various options for cascade design, such as a Pd-catalyzed cross-coupling reaction followed by ring closure of the reactive intermediate (Bert U. W. Maes, Romano V. A. Orru, and Eelco Ruijter; <http://pubs.acs.org/doi/abs/10.1021/cs400926z>) or Pt(II)-initiated multistep asymmetric cycloisomerization (Michel R. Gagné; <http://pubs.acs.org/doi/abs/10.1021/cs401190c>). Organocatalysts were used to trigger a cascade by use of a *N*-heterocyclic carbene (Xuegong She; <http://pubs.acs.org/doi/abs/10.1021/cs400602v>) or a chiral spirocyclic SPINOL–phosphoric acid, respectively (Xufeng Lin; <http://pubs.acs.org/doi/abs/10.1021/cs400591u>). Iodide also proved to be suitable to trigger a formal [3 + 3] cycloaddition (Shun-Jun Ji; <http://pubs.acs.org/doi/abs/10.1021/cs400904t>). To complete the spectrum, one example uses a biocatalyst for ketone reduction, followed by a spontaneous cyclization (Vicente Gotor; <http://pubs.acs.org/doi/abs/10.1021/cs4010024>).

(3) Relay cascades. These require that all reaction steps run separately, such that each step could also be performed independently. Each step might be catalyzed by a different catalyst.

Such contributions in this virtual special issue cover a bifunctional organometallic catalyst bearing an acidic and a basic functionality (Hexing Li; <http://pubs.acs.org/doi/abs/10.1021/cs400761r>), a cascade involving one metal catalyst (tetrapropylammonium perruthenate for two convergent oxidation steps) and one organocatalyst (for two subsequent reactions, domino catalysis; Magnus Rueping; <http://pubs.acs.org/doi/abs/10.1021/cs401176s>), as well as a two-step cascade using tin-containing β -zeolites combining Brønsted and Lewis acid catalysts (James A. Dumesic; <http://pubs.acs.org/doi/abs/10.1021/cs400593p>). Interestingly, the starting material for the last example was obtained by an enzyme cascade from glucose. An example involving the use of a biocatalyst combines the enzyme-catalyzed selective oxidation with a chemical non-stereospecific reduction for deracemization (Nicholas J. Turner; <http://pubs.acs.org/doi/abs/10.1021/cs400724g>). An additional four examples involve exclusively enzyme-catalyzed reaction steps with up to five biocatalysts. For instance, three different enzymes immobilized on a carrier convert CO₂ to methanol (Zhongyi Jiang; <http://pubs.acs.org/doi/abs/10.1021/cs401096c>) or a three-enzyme cascade effects sucrose oxidation in a biofuel cell (Shelley D. Minter; <http://pubs.acs.org/doi/abs/10.1021/cs4003832>). Five biocatalysts were required to transform sucrose to synthetic amylose (Y.-H. Percival Zhang; <http://pubs.acs.org/doi/abs/10.1021/cs400961a>). By coproducing two recombinant enzymes in one cell (monooxygenase and epoxide hydrolase), only one catalyst production procedure is required, making this a very attractive approach (Zhi Li; <http://pubs.acs.org/doi/abs/10.1021/cs400992z>).

Cascade reactions have gained attention in recent years as useful tools for the efficient construction of complex molecular structures, which can be easily accessed from simple and readily available starting materials. Investigating the potential of cascade reactions is a current hot topic for identifying the full spectrum of possible transformations and catalyst combinations that are easily applicable, from a practical point of view, to the synthesis of sophisticated molecules. A vision for the future is to have a modular system for total synthesis, whereby a module represents a cascade transformation. Thus, a total synthesis may not be seen as a sequence of various reaction steps, but as a sequence of modules. For instance, a significant part of the synthetic route may be achieved by using enzymatic cascades for providing the starting material (starting from natural resources), followed by the subsequent module(s) involving organo-, metal, or biocatalysis or combinations thereof.

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Notes

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