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Editorial

The Impact of Process Chemists and Engineers on Green Chemistry

Process chemists and engineers in industry generally feel that green chemistry is an academic pursuit − until green chemistry considerations can lower the cost of goods. As Canales Clariond said, "The world doesn't move because of idealism... It moves because of economic incentives."[1] The pharmaceutical industry is striving to become more cost competitive through process intensification and other efforts,[2] and minimizing waste and negative environmental impacts are now serious considerations even at the stage of early route selection.[3] As the world sees increases in the cost of waste disposal and the price of petrochemicals, green chemistry considerations come to the forefront.[4]

The biggest economic impact of green chemistry for multistep syntheses will be effected now by following the first principle: prevent waste, do not reduce waste just at the end of the pipeline.[5] For example, in 2002 Pfizer received a Presidential Green Chemistry Challenge Award[6] for simplifying the process to make sertraline from a racemic starting material, eliminating four solvents and one reagent, almost doubling the manufacturing yield, and reducing process waste cost by over $100,000/year.[7] However, Pfizer's preferred route to sertraline probably includes resolution of the starting material by simulated moving bed chromatography, an approach that further reduces costs by eliminating the processing used to make the undesired enantiomer of sertraline.[8] Merck developed a cost-effective, waste-minimizing route to Aprepitant using crystallization-induced asymmetric transformation (CIAT), with the undesired diastereomers being converted in situ to the desired intermediates.[6,9] Merck also developed an asymmetric hydrogenation of an unprotected enamine to manufacture sitagliptin, saving two steps.[6,10] Lonza designed and implemented a manufacturing route to niacinamide beginning with an inexpensive byproduct of a nylon-6 precursor.[11] Codexis directed the evolution of three enzymes for the efficient preparation of a chiral precusor to atorvastatin calcium using an inexpensive achiral starting material.[6] In what is perhaps the ultimate approach to an active pharmaceutical ingredient (API), paclitaxel is produced directly from plant cell fermentation for Bristol-Myers Squibb, eliminating six intermediates.[6] In all these award-winning approaches the benefits were realized by judicious route selection.

As responsible process chemists and engineers, we should minimize waste, and there are many ways to do that. Achieving higher yields reduces the environmental quotient (EQ) of waste production.[12] Processing using fewer unit operations and under more concentrated conditions can markedly reduce waste,[13] cycle times, and labor costs. But the biggest impacts on the cost of goods (COG) and the environment will be in designing routes that require fewer steps. With consistently high yields, fewer steps require smaller quantities of starting materials, solvents, and reagents and less labor; less waste and reduced costs for waste disposal also result. To reduce the number of steps new reactions and new technologies are important,

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(13) Thanks to Trevor Laird for emphasizing this important point.

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especially enzymes,[14] and we should review and consider older approaches. To apply green chemistry principles across the life cycle of our compounds we must continue to support new synthetic initiatives and encourage bright, unbiased researchers recently from academia to invent new approaches to existing compounds. We can also provide feedback to drug discovery: Have we selected the most potent or bioavailable compound or the compound that can be prepared in the fewest steps? Is the chiral center of the prodrug really necessary? But the biggest impact we can probably have is through designing and redesigning routes to lower the COG, by selecting different starting materials. By taking care of the COG we will also take care of our environment.

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