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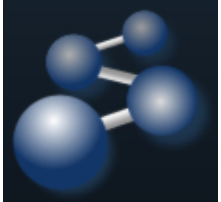

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Aiming for the Ideal Synthesis

In the 20th century the art and science of complex natural product total synthesis defined the frontiers of organic chemistry. Throughout these decades fundamental insights into reactivity and selectivity principles were achieved by these numerous synthetic endeavors. The capability and power of organic synthesis has thus experienced a dramatic increase putting today's synthetic chemists in the position to construct molecules of more or less any degree of structural complexity. The perception defining "art" in organic synthesis has therefore changed with time and in our opinion is described best by Hendrickson when he addressed the "ideal synthesis" as one which: "…creates a complex molecule… in a sequence of only construction reactions involving no intermediary refunctionalizations, and leading directly to the target, not only its skeleton but also its correctly placed functionality" (Hendrickson, J.B. J. Am. Chem. Soc. 1975, 97, 5784).

This prescient statement truly encompasses and epitomizes the "economies" of synthesis design many years before ideas of atom, step, and redox-economy were formally galvanized. Now, in 2010, the field has reached an awe-inspiring level, with many proclaiming that synthesis has matured. But before one declares the science of synthesis an endeavor in engineering, one only needs to reflect on the inspiring ease with which Nature crafts large quantities of her most complex molecules (e.g. vancomycin and taxol). Total synthesis in this century must therefore be keenly aware of this ultimate challenge – to be able to provide large quantities of complex natural products with a minimum amount of labor and material expenses. The natural consequence of pursuing such a goal is to embrace the Hendrickson dictum (vide supra). Pursuing synthesis in such a way forces the practitioner into the role of an inventor. It naturally also leads to explorations into biology since multiple collaborations can be forged with ample materials.

Representative Publications:

Newhouse, T.; Baran, P.S.; Hoffmann, R.W. The Economies of Synthesis, Chem. Soc. Rev. 2009, 39, 3010–3021.
Chen, K.; Baran, P.S. Total synthesis of eudesmane terpenes by site-selective C–H oxidations, Nature, 2009, 459, 824-828.
Burns, N.Z.; Baran, P.S.; Hoffmann, R.W. Redox Economy in Organic Synthesis, Angew. Chem. Int. Ed., 2009, 48, 2854 - 2867.
Shenvi, R.A.; O'Malley, D.P.; Baran, P.S. Chemoselectivity: The Mother of Invention in Total Synthesis, Acc. Chem. Res., 2009, 42, 530–541.

Baran, P.S.;Maimone, T. J.; Richter, J. M. Total synthesis of marine natural products without using protecting groups, Nature, 2007, 446, 404-408.
Young, I.S.; Baran, P.S. Protecting-group-free synthesis as an opportunity for invention, Nature Chemistry, 2009, 1, 193 - 205.

(For more information, see our publications page)