

Snapshots of some topics of interest of recent notable advances in chemistry

# The Art of Problem Solving Strategies

## Table of contents

- 3 Snapshots of some topics of interest of recent notable advances in chemistry:
- 4 The art of problem solving strategies

# Snapshots of some topics of interest of recent notable advances in chemistry

*Atef S. Iskander*

*Managing Director / Founder*

# The Art of Problem Solving Strategies

Problem-solving strategies have emerged as an art of design. Design is characterized by developing new patterns to solve the scientific problem that transcends and transfigures conceptual boundaries. This snapshot presents a manifesto of some cursory examples of recent advances and selected topics across disciplines to highlight their power in solving problems.

**KEYWORDS:** Problem solving, Organic sensors, Hydrogen storage, Detection of tumor, Enantioselective cyclization, Sustainable synthesis.

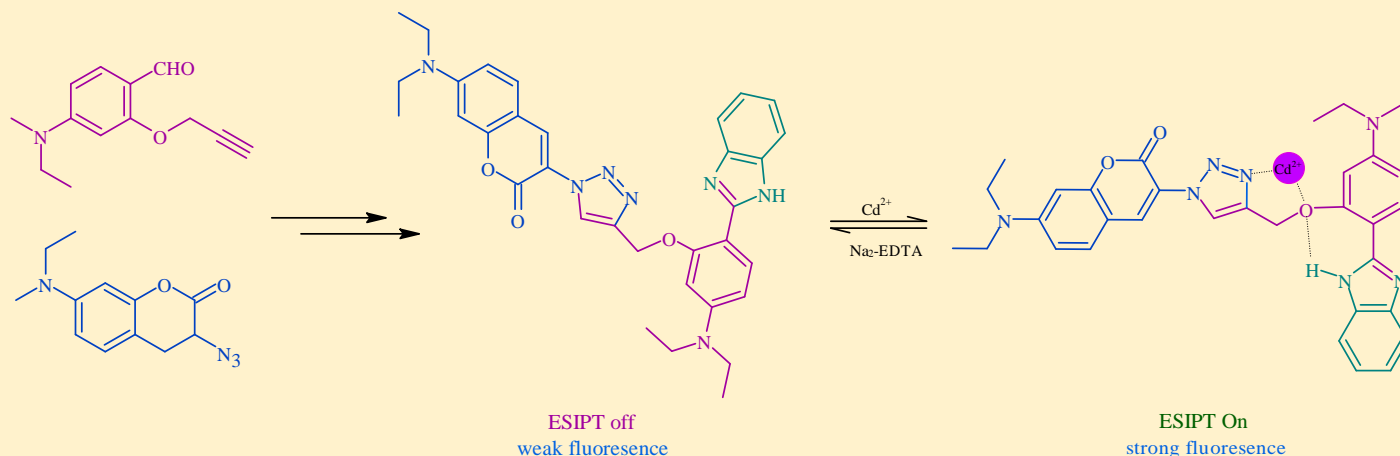
## Introduction

Scientific problem solving routinely is regarded as a design. Design is copious and being smeared as a viscous layer over the scientific problem, resulting in valuable constructive work. As such constructive work mobilizes the entire discipline toward strategies that offer greater wealth than existing alternatives. Wealthy strategies search for creative thinkers. Thinkers who favor creative thinking over analytical thinking to gain competitive advantage. Such a thought must emanate from a point of not knowing. Socrates, the Greek philosopher, is attributed to that: “The only true wisdom is in knowing you know nothing.” This notion resonates well with wealthy strategies that emanate from creative thinking.

The literature contains brilliant ideas that make it possible to stimulate researchers to develop a wealthy strategy resulting in excellent design that overcomes a wide range of technological bottlenecks that hinder the practical application of a variety of techniques at any appreciable scale. The published data is immensely valuable in enriching the understanding of the exact nature of the scientific problem and how to construct a strategy that paves the way for more ambitious and challenging solutions. A few cursory examples of recent advances in various disciplines are highlighted to underscore their power in problem solving.

## 1- Highly selective sensor toward Cd<sup>2+</sup> ions

An excited-state intramolecular proton transfer (ESIPT) strategy has been adapted to design a highly selective turn-on sensor for Cd<sup>2+</sup> ions *via* triazole-bridged coumarin-benzimidazole conjugated (Scheme 1).<sup>1</sup>



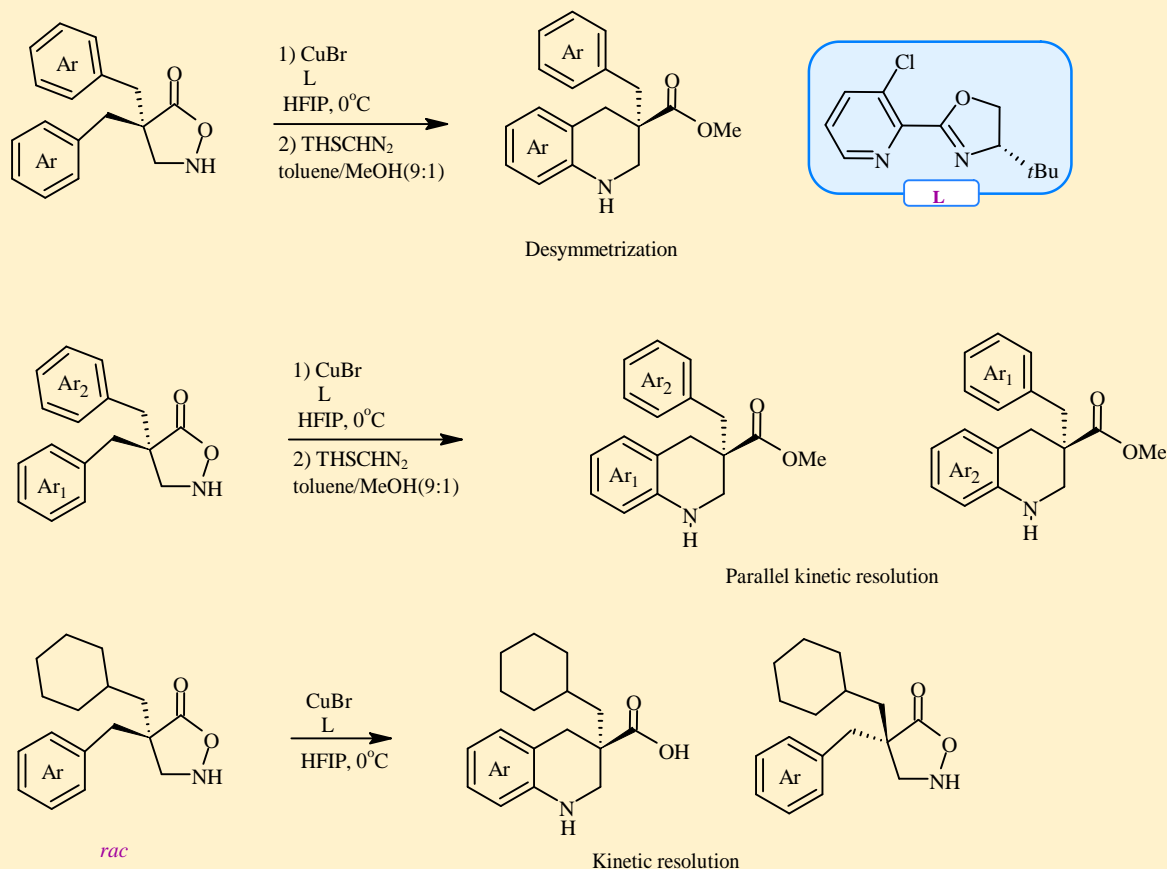
**Scheme 1.** ES IPT switching mechanism of triazole-bridged coumarin-benzimidazole conjugated in acidic media, and the proposed mode of its binding toward  $\text{Cd}^{2+}$ .

## 2- Enhancing hydrogen storage rates in palladium nanocubes

Nanomaterials have the potential to store and delivery energy in the form of electrochemical alloys due to their high surface-area-to-volume ratio. Electrochemical hydrogen absorption and desorption in shape-controlled palladium nanocubes does not occur uniformly across the entire nanoparticle surface, but selectively proceeds through high-activity sites at the corners and edges. Such abnormal linearly diffusive behavior hinders the hydrogen absorption rates and significantly reduces the nanoscaling advantage of the palladium dimensions. To solve this, a modification of the surface of palladium with an ultrathin platinum shell was performed, which almost removed the barrier for hydrogen absorption and allowed diffusion through the entire Pd/Pt surface.<sup>2</sup>

## 3- Enantioselective synthesis of $\beta$ -amino acids

In the context of the synthesis of nitrogen-containing chiral compounds based on catalytic asymmetric nitrene transfer as a synthetic strategy, a catalytic system has been designed which realizes asymmetric alkyl nitrene transfers beyond  $\text{C}(\text{sp}^3)\text{-H}$  insertion. Copper-catalyzed electrophilic amination of substituted isoxazolidin-5-ones was employed for the enantioselective synthesis of  $\beta$ -amino acids. The catalytic system promotes three classes of asymmetric transformations: desymmetrization, parallel kinetic resolution, and kinetic resolution, depending on the substrate structure. The ligand has a dramatic effect on the reaction outcome, and copper catalysis expands the repertoire of alkyl nitrene transfer and yields various cyclic and linear  $\beta$ -amino acids in their enantioenriched forms (Scheme 2).<sup>3</sup>



**Scheme 2.** Catalytic asymmetric desymmetrization, parallel kinetic resolution, and kinetic resolution.

#### 4- Design bispecific aptamer sensor for detection of malignant cells

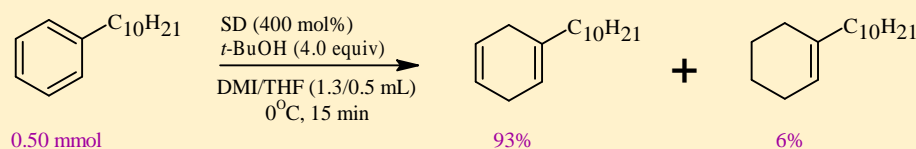
To overcome the hurdles in detecting malignant cells based on the elevated expression of cell surface markers, which many of them are also expressed in normal cells, a DNA aptamer-based bispecific system has been designed for precise recognition of a malignant cell based on the molecular signatures of the tumor microenvironment (TME).<sup>4</sup> The TME is characterized by abnormal fluctuations, including hypoxia, low extracellular pH (6.5 - 6.8) due to the upregulation of glycolysis, and the atypical expression of tumor-related enzymes. The extraordinary high level of the adenosine 5'- triphosphate (ATP) concentration within the TME than that of the typical cellular environment is regarded as a secondary biomarker to detect tumor cells.

In view of the TME's unique chemical signature, a bispecific sensor model has been designed, which takes advantage of the high concentration of ATP in the TME, and is termed ATP-regulated T cell sensor (ARTS) to detect tumor cells and their elevated protein expression specifically. The design of this sensor is based on one arm, *i.e.* ATP aptamer, toward a highly expressed tumor-related metabolite ATP and the other arm, an aptamer, against TCR-CD3 $\epsilon$  expressed on a T-cell lymphoma. Such design effectively combines two

molecular signatures related to a disease state, namely, altered ATP concentration in TME and an elevated expression of the cell surface marker TCR-CD3 $\epsilon$  in T-cells.

## 5- Towards sustainable organic synthesis

The Birch-types reduction of a variety of arenes under mild conditions was reported based on an approach that used sodium dispersion in paraffin oil (SD), in combination with environmentally benign 1,3-dimethyl-2-imidazolidinone (DMI) as an additive and *tert*-butanol as the proton donor, in a mixture of DMI and THF (Scheme 3).<sup>5</sup>



**Scheme 3.** Birch reduction of decylbenzene using SD and DMI.

## Conclusion

This snapshot presents a manifesto for scientific problem-solving strategies, focusing on understanding the little we know and recognizing that the unknown is a necessary condition for the construction of a problem-solving strategy. We need to focus on what we don't know. To design a strategy for a scientific problem, a series of approaches must be used, seeking the boundaries between different multimodals. The complex scientific problems must arise in a productive manner and confront what most researchers avoid.

## References

- 1) S. Mondal, S. Dey, *ACS Omega*, **2021**, *6*, 27936–27945.
- 2) L. J. T. Metzroth, E. M. Miller, A. G. Norman, S. Yazdi, G. M. Carroll, *Nano Lett.*, **2021**, *21*, 9131–9137.
- 3) R. K. Tak, H. Noda, M. Shibasaki, *Org. Lett.*, **2021**, *23*, 8617–8621.
- 4) N. Boykoff, L. Freage, J. Lenn, P. Mallikaratchy, *ACS Omega*, **2021**, *6*, 32563–3257.
- 5) S. Asako, I. Takahashi, T. Kurogi, Y. Murakami, L. Ilies, K. Takai, *Chem. Lett.*, **2022**, *51*, 38–40.