



PROBLEM 20

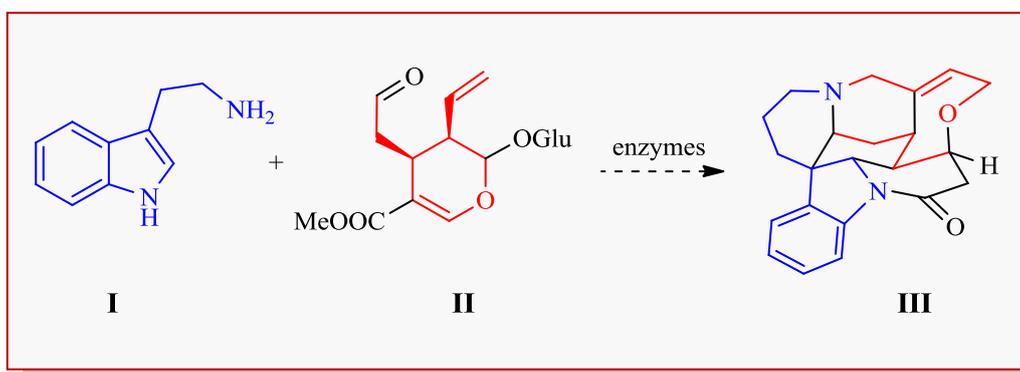
[SUPPL Problem 20 # 1]

Arabic compound numbers in TAPSOC,
Roman numerals in Supplementary material

In Perspective

Compound **3** (in TAPSOC Scheme 20.1) was discovered by chance in professor Keith Jones's laboratory at Kingston University (UK) as a by-product of a reaction originally designed to build the pentacyclic core of strychnine (**III**) shown below [1].

The complex structure is built along a biocatalytic conveyor belt within parenchymal cells of plants of the South American *Strychnos* genus to thwart biotic ecological challenges. Tryptamine (**I**) and secologanin (**II**) are the building blocks in the plant.



SCHEME SP20.1.1

The synthesis of complex structures from the same starting materials found in living organisms has inspired chemists to follow the same path in the laboratory. One recent piece of research explores the organocatalysis cascade approach to gain access to more than one complex alkaloid scaffold [2].

The synthesis of strychnine and related alkaloids possessing most challenging structures has been pursued from an endless string of approaches that continues to be unabated to this day [2,3].

Some of you may perhaps consider **1** → **2** as too simple to really deserve much attention. It may hold clues, however, that could help in understanding the more demanding mechanism of **1** → **3**. Additionally, authors [1] do not specify the stereochemistry of products, meaning that they are diastereomeric mixtures. The paucity of data in this concern does not help to devise an unambiguous mechanism but, at the same time, confers more flexibility to design our strategy.

In fact, the stereochemical game involved in the synthesis of **2** is far more complicated than is apparent. In order to show the truth of this assert let me invite you to predict which diastereomers of **2** would be expected to prevail.

REFERENCES

- [1] Cannon JS, Overman LE. “Is there no end to the total synthesis of strychnine? Lessons learned in strategy and tactics in total synthesis”. *Angew. Chem. Int. Ed.* 2012;51:4288-4311.
- [2] Jones SB, Simmons B, Mastraccio A, MacMilland DWC. *Nature* 2011;475:183-188.
- [3] Curran DP, Shen W. *J. Am. Chem. Soc.* 1993;115:6051-6059.