



PROBLEM 24

[SUPPL Problem 24 # 1]

Arabic compound numbers in TAPSOC,
Roman numerals in Supplementary material

In Perspective

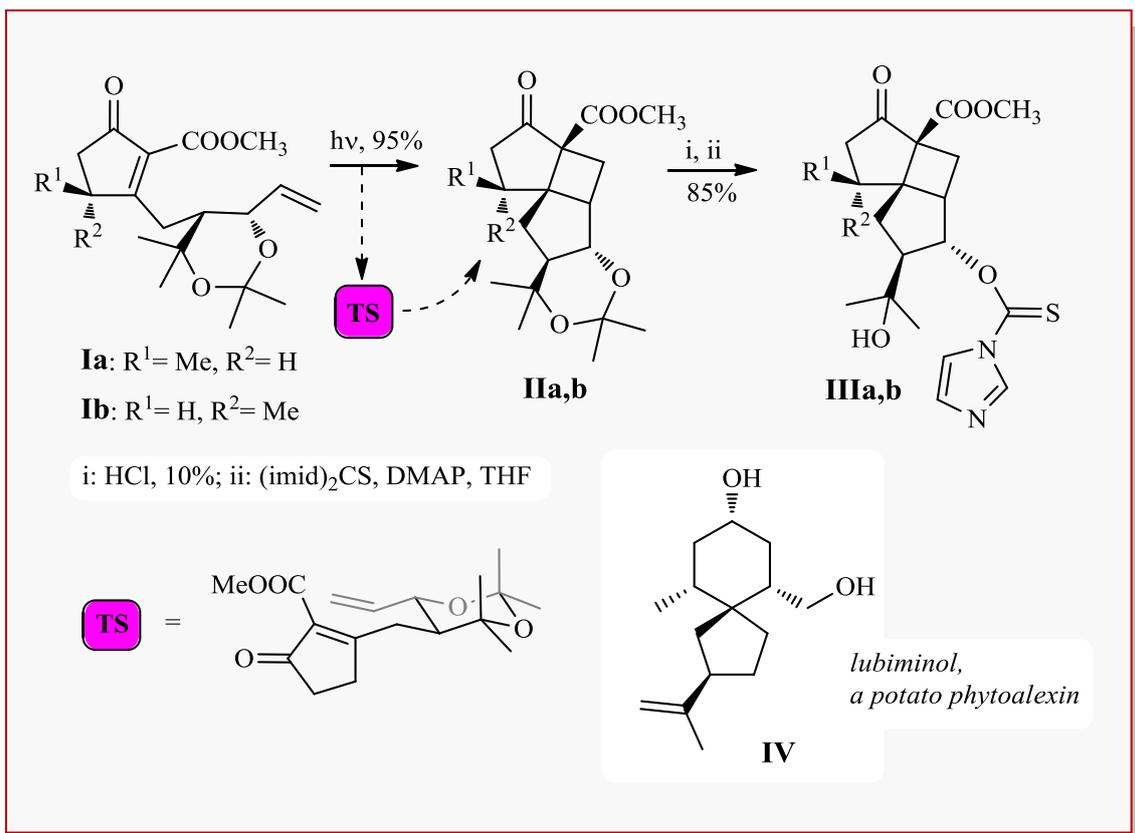
Reading published organic synthesis reports gives the impression that the increasingly sophisticated sequences run smoothly in the lab bench after much thought at the drawing board and planning. This is partly true, no doubt.

More often than not, however, reactions take an undesired and most frustrating turn after lengthy preparation of key precursors. These failures appear reflected in the final publication much less frequently than they occur; and certainly not in their real impact extent on people at the lab bench.

A most revealing article by professors Miguel Sierra and María de la Torre from Universidad Complutense and CSIC of Madrid underline this feature by showing a number of such abortive synthetic examples and how they were circumvented [1]. It was there that I found the source of the reactions in Scheme 24.1, in turn developed by professor Michael Crimmins and coworkers at the University of North Carolina. The reaction underwent an unexpected twist while attempting to build the typical spirobicyclic scaffold of (\pm)-lubiminol (**7**) (Scheme 24.2) in a stereoselective manner [read commentary below].

Lubiminol **IV** is a plant sesquiterpene with interesting bioactivities. When potato plants become infected with the fungus *Phytophthora infestans* (chiefly responsible for the Irish famine in 1845/49, and thus of the strong Irish culture in the Northeastern US) they respond by rapidly synthesizing specific organic metabolites to thwart the offense. These are called phytoalexins (allelochemicals produced upon microbial attack on plants). Lubiminol is one of these phytoalexins.

Lubiminol has a spirovetivane skeleton with four stereogenic centers including the spiro quaternary carbon [2]. Prof. Crimmins coped with the controlled construction of these asymmetric carbons through the previous acquisition of the cyclobutyl precursor by way of a photochemical [2+2] cycloaddition in ketoester **I** (scheme SP24.1.1). The correct configuration was obtained due to the preferred conformation of a chair-like transition state (TS).



SCHEME SP24.1.1

Because more simple models gave the anticipated spirobicyclic scaffold after exposure to TBTH and AIBN in up to 92% yield [3], the reaction was tested with a more complex precursor containing additional attributes of the final lubiminol (TAPSOC Scheme 24.1).

REFERENCES

- [1] Sierra MA, de la Torre MC. *Angew. Chem. Int. Ed.* 2000;39:1538-1559.
- [2] For a review on the stereospecific construction of quaternary centers, see: Fuji K. *Chem. Rev.* 1993;93:2037-2066.
- [3] Crimmins MT, Wang Z, McKerlie LA. *Tetrahedron Lett.* 1996;37:8703-8707.