



## PROBLEM 19

### [SUPPL Problem 19 # 1]

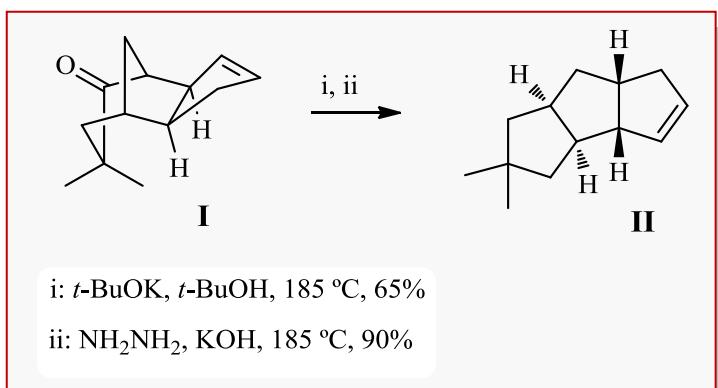
Arabic compound numbers in TAPSOC,  
Roman numerals in Supplementary material

#### In Perspective

Professor J. B. Stothers and Mr Cheng, his assistant at the time, at the University of Western Ontario, Canada, studied in detail this reaction as part of their quest to explore the limits of enolate formation. Presumably inactive protons were abstracted by strong base (bridgehead,  $\beta$  or  $\gamma$  protons) when ordinary  $\alpha$  protons were absent.

It is for you to determine whether anything of the sort actually occurred in this particular reaction.

In fact, the subject of homoenolates was being pursued since the early 60's by other mainstream research groups [1-4]. From these early explorations in highly rigid ketone scaffolds, only a few research groups managed to find synthetic applications. Scheme SP19.1.1, a case in point, portrays the synthesis of the hirsutene skeleton, a compound with a long held interest among synthetic chemists [5]. Try to solve the mechanism now before checking out the answer in Scheme SP19.1.2 on next page.



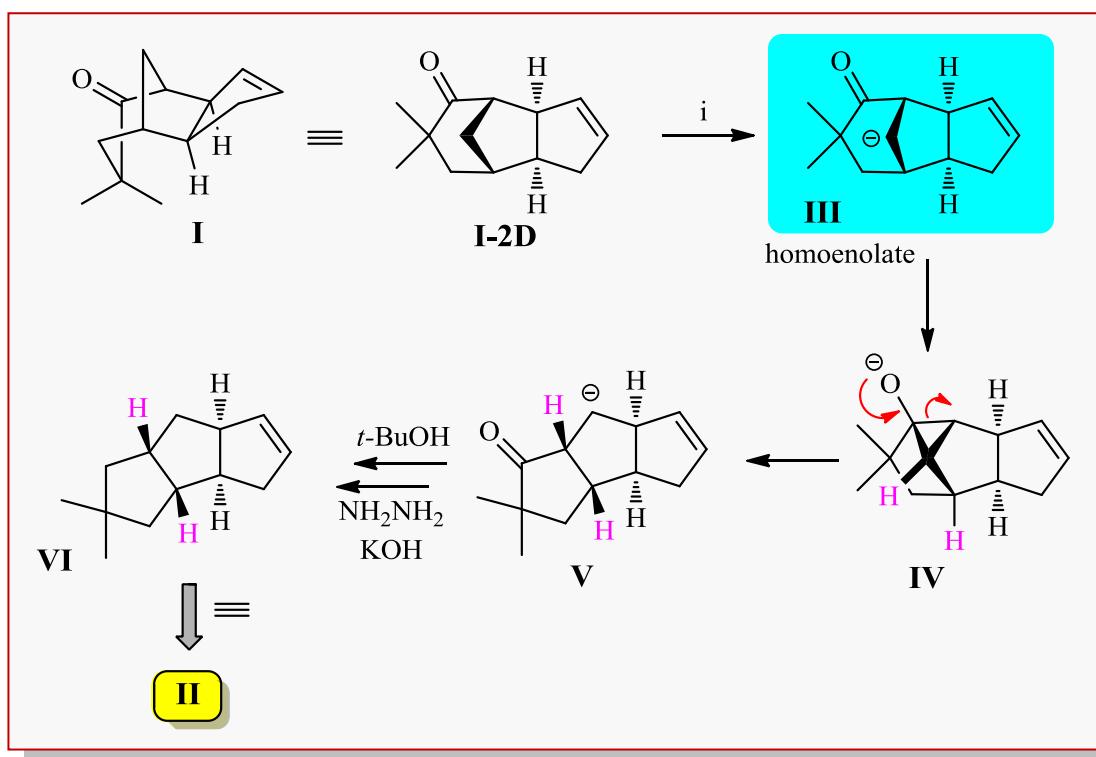
SCHEME SP18.2.1

Solution:

You probably adopted the following strategy:

- 1) Portray both **I** and **II** in the same visual code, 2D for example
- 2) Label a few carbon atoms at key sites where you suspect, at first sight, bonding changes occur.
- 3) Identify the bonding change: only one C-C bond breaks, only one new C-C bond is created. When you do, then the necessity of a homoenolate becomes obvious.
- 4) Realize that the hydrazine-KOH treatment, (condition ii) is simply a Wolff-Kishner reduction of the ketone that governed the first step. By including this reaction in Scheme SP19.1.1 and thus erasing the site of this ketone in the primary product, the mechanism became a little more difficult and interesting.

Scheme SP19.1.2 portrays the **I** → **II** chemistry



SCHEME SP19.1.2

## REFERENCES

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- [1] Howe R, Winstein S. J. Am. Chem. Soc. 1965;87:915-916.
- [2] Fukunaga T J. Am. Chem. Soc. 1965;87:916-917.
- [3] Johnson AL, Petersen NO, Rampersad MB, Stothers JB. Can. J. Chem. 1974;52:4143-4145.
- [4] Nickon A, Lambert JL, Oliver JE, Covey DF, Morgan J. J. Am. Chem. Soc. 1976;98:2593-2599.
- [5] Dawson BA, Ghosh AK, Jurlina JL, Stothers JB. J. Chem. Soc. Chem. Commun. 1983;204-205.