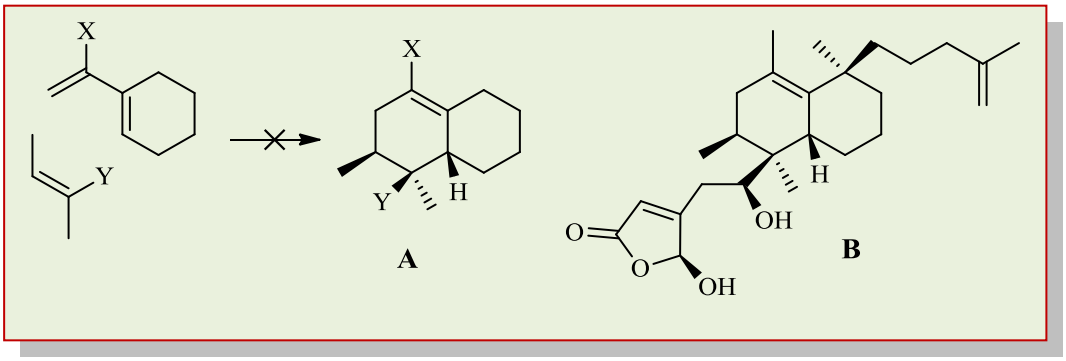
PROBLEM 1

[SUPPL Problem 1 # 1]

Arabic compound numbers in TAPSOC,
Roman numerals in Supplementary material

In Perspective

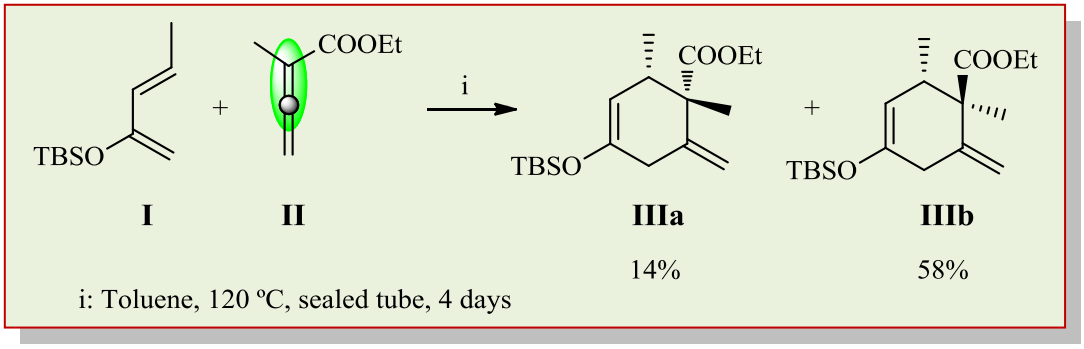
The reactions of Scheme 1.1 in your TAPSOC come from Prof. Michael E. Jung's laboratory in UCLA, as an effort to put together decalin derivative **A** by way of a Diels-Alder cycloaddition. However, this reaction would have to go regioselectively in the opposite direction of the classical reaction. This demands coaxing components to adopt a transition state in the less favorable *exo* mode. The long run aim was antitumoral dysidiollide (**B**), a phosphatase inhibitor. Compound **A** would incorporate three of the four stereogenic carbons in the decalin scaffold of **B**.



SCHEME SP1.1

How would this coaxing be achieved? Authors thought that a chromium carbene in the dienophile [Y = (OMe)C=Cr(CO)$_5$] would provide the desired stereoelectronic influence. Unfortunately, the cycloaddition never took place, giving only starting material. This carbene would be used later to construct the lactone appendage in **B**.

Failure to achieve the coveted cycloaddition led Jung and Nobuko Nishimura, an outstanding grad student [1], to probe properly substituted allenes such as **II**, as substitutes for dienophiles (Scheme SP1.2), landing on adducts **IIIa/b** and a cyclobutanol like **1** in your TAPSOC Scheme 1.1. Notice the greater reactivity of the C=C bond conjugated with the EWG. Some stereoselectivity was attained after long heating because of the thermal conversion of **1** into **IIIb**. This is part of this problem's mechanistic issues TAPSOC wants you to work out.



Ring opening with MeLi or NaH constitutes your mechanistic task. Pay particular attention to stereochemistry, considering the prevalence of *Z*- product **2**. Importantly, changing MeLi for LiHMDS (see glossary in your TAPSOC book) altered product distribution significantly (**2:3** jumped to 23:1).

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[1] Jung ME, Nishimura N. J. Am. Chem. Soc. 1999;212:3529-3530. DOI: 10.1021/ja9841660.