

APPENDIX 4

Supplementary Synthetic Information Relevant to Chapter 3

A4.1 INTRODUCTION

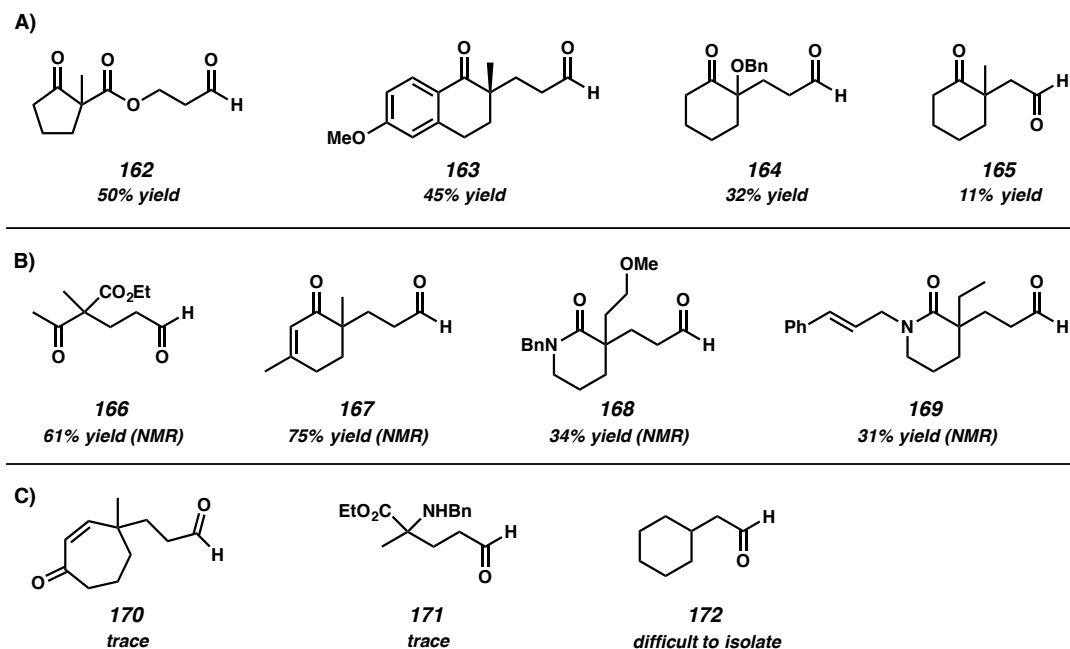
This section presents alkenes that were poor substrates for the nitrite-modified Tsuji–Wacker described in Chapter 3. These substrates were either unreactive, formed a complex mixture of products, generated only trace amounts of product, or supplied low yields of the desired aldehyde product.

A4.2 PRODUCTS FORMED IN LOW YIELD

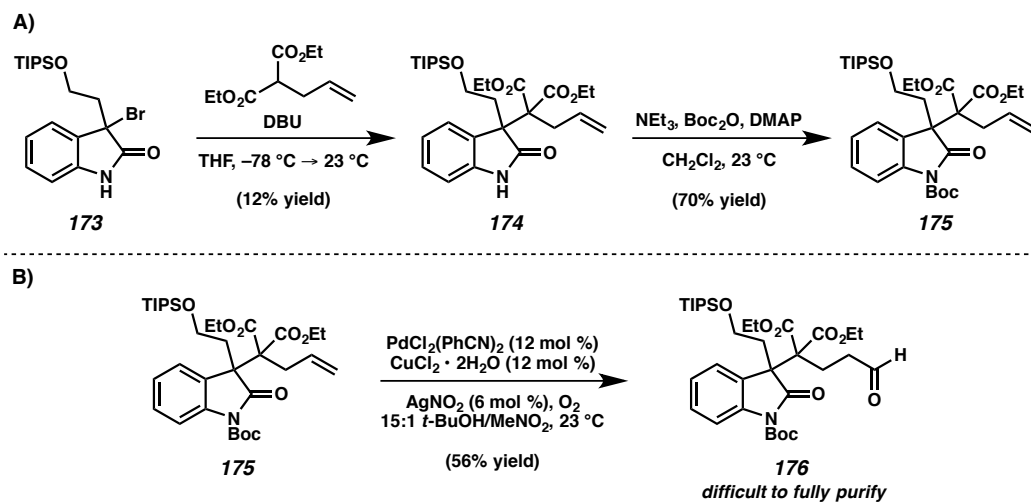
Some substrates underwent oxidation under nitrite-modified Tsuji–Wacker conditions but generated aldehyde product in low yield. For instance, aldehydes **162–165** (Figure A4.1A) were isolated in low yields. Certain aldehyde products were formed as inseparable mixtures with ketone side products (**166–167**, Figure A4.1B). Notably, lactam substrates generally produced low yields of aldehyde product that were often contaminated by ketone side-product (**168–169**). Aldehydes **170** and **171** were formed in trace amounts, and aldehyde **172** was observed in situ (via disappearance of substrate by

TLC) but was difficult to isolate (Figure A4.1C). Similarly, aldehyde **176** was generated readily from oxindole substrate **175** but contained inseparable impurities (Scheme A4.1).

Figure A4.1 Aldehyde products formed in low yield under nitrite-modified Tsuji–Wacker conditions

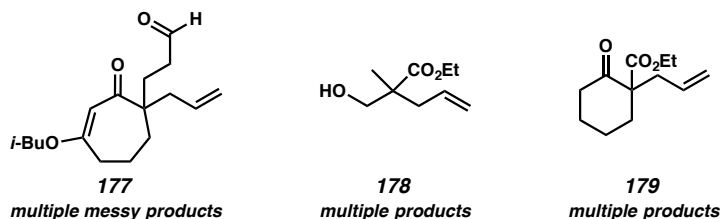


Scheme A4.1 A) Synthesis of oxindole substrate **175** and B) subsection of **175** to nitrite-modified Tsuji–Wacker conditions



A4.3 SUBSTRATES THAT FORM A COMPLEX MIXTURE OF PRODUCTS

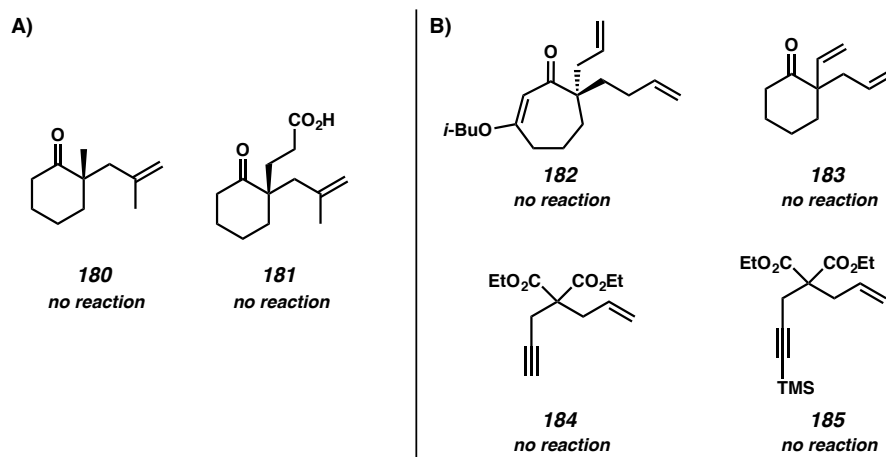
Figure A4.2 Substrates that form a mixture of inseparable products under nitrite-modified Tsuji–Wacker conditions



A4.4 UNREACTIVE SUBSTRATES

Some substrates were unreactive under the conditions for aldehyde-selective Tsuji–Wacker oxidation. These substrates include disubstituted olefins **180–181** (Figure A4.3A), dienes **182–183**, and enynes **184–185** (Figure A4.3B). We hypothesize that compounds **182–183** are unsuitable substrates for oxidation due to deactivation of the Pd catalyst through coordination to the second site of unsaturation in the substrate.

Figure A4.3 Substrates that do not react under nitrite-modified Tsuji–Wacker conditions



A4.5 FUTURE DIRECTIONS

These uncooperative substrates outline the limitations of the otherwise robust aldehyde-selective Tsuji–Wacker oxidation. A potential avenue for future exploration in this area is the addition of co-catalysts (i.e., Co) to pre-bind the alkyne moieties (e.g. in **184–185**) and thereby enable oxidation to proceed at the alkene. Issues in catalyst compatibility and side reactivity initiated by the co-catalyst may arise, however, and would need to be addressed.