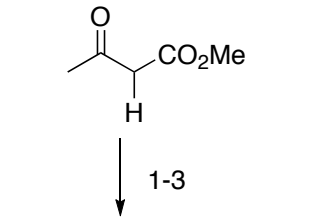
Intramolecular Photocycloaddtion-Cyclobutane Fragmentation: Total Synthesis of (±)-Silphinene

Michael T. Crimmins and S. Wayne Mascarella

JACS 1986, 108, 3435-3438



1) $CH(OMe)_3$, H_2SO_4
2) hv, NBS, $(PhCO_2)_2$, CCl_4, reflux
3) NaI

1) What is the pka of the indicated H?

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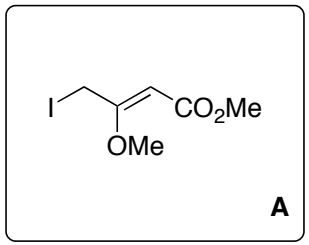
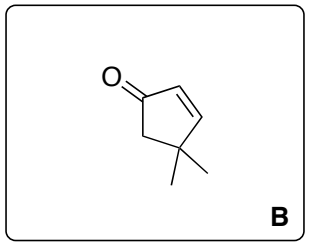


4) allyl alcohol, TsOH, p-cymene, reflux
5) $PdCl_2$, CuCl, O_2, DMF/H_2O
6) KOH 50 °C

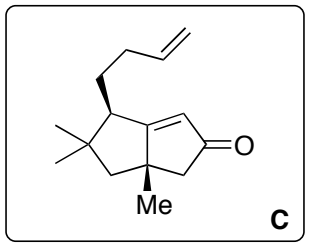
5) What is the name of this reaction and mechanism?

Wacker Oxidation, see below



B

7-13



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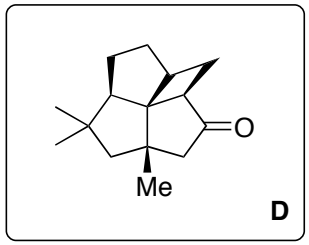

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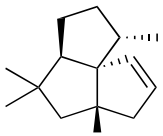
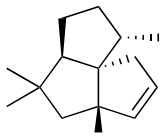
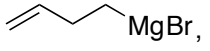
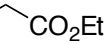


(±)-silphinene



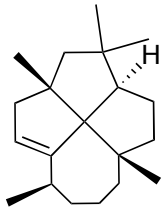
isosilphinene

7) Bu_3PCuI, THF,  , then **A,** HMPA
8) 30% $HClO_4$, CH_2Cl_2
9) NaOMe, MeOH, 0°C
10) Me_2CuLi, Et_2O, 0°C
11) LiCl, DMSO/H_2O, 145 °C to rt
12) ETSA, Bu_4NF, THF
13) Saegusa Oxidation

ETSA = TMS  CO_2Et

14) hv, rt

15) TMSCl, NaI, MeCN, 80 °C
16) Bu_3SnH, PhH, 90 °C
17) LDA, $(EtO)_2POCl$, tBuOH/THF, -78 °C
18) Li, $MeNH_2$, 40 °C



laurenene

12) Other alkyl amines tried gave inferior regioselectivity. Why might this combination lead to 96:4 isomer formation?

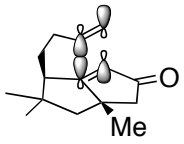
Authors declare this result surprising without much discussion. Cited paper briefly disscusses assymetric variations.
JACS 1976, 98, 2346

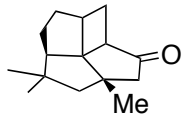
13) What conditions would you use to perform this transformation?

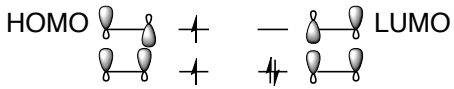
$Pd(OAc)_2$, p-benzoquinone, MeCN

14) Justify the stereochemistry of the resulting product using Woodward Hoffman rules.

4π Photochemical cycloaddition, suprafacial-suprafacial, newly formed bonds are on the same face

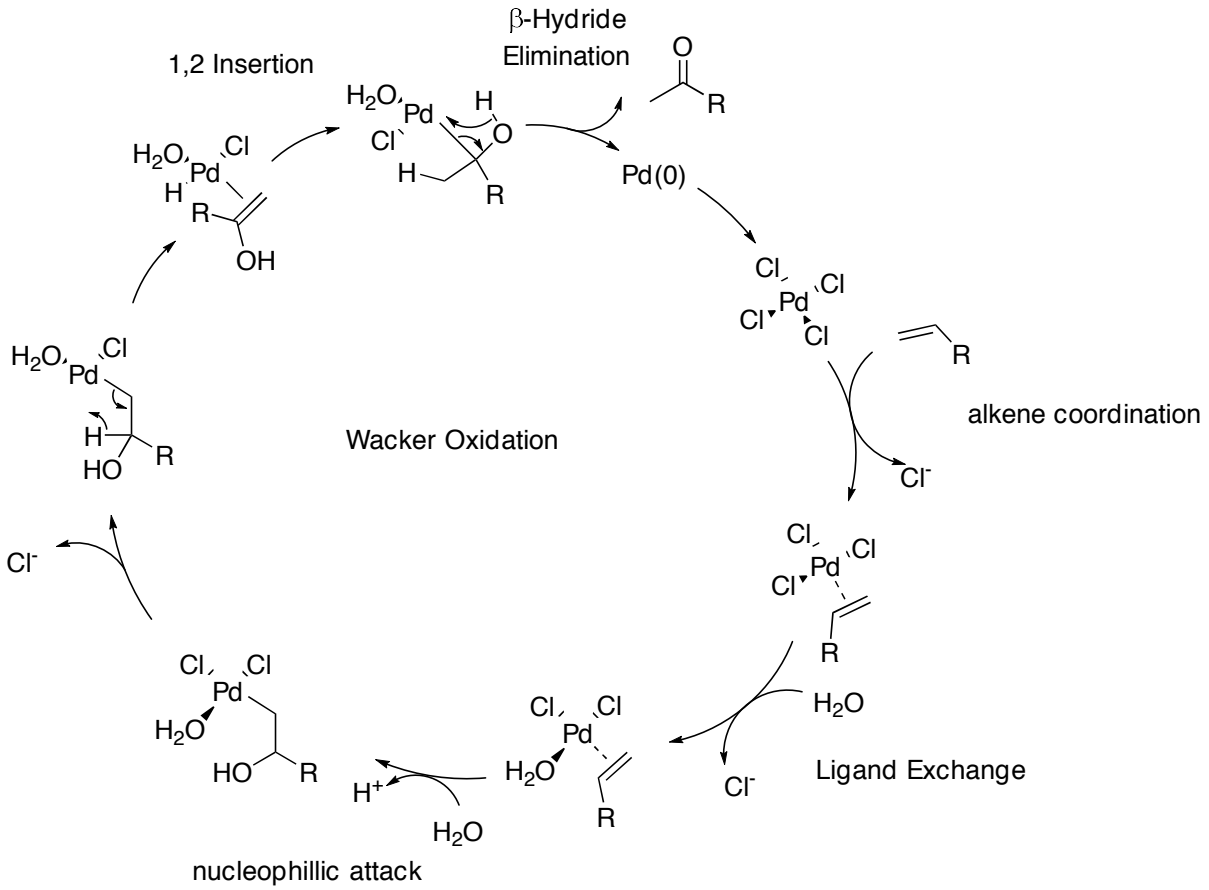






18) 4.5:1 regioselectivity, Can be separated using $AgNO_3$ impregnated silica

Bonus Question: The authors suggest a similar strategy can be used for the synthesis of laurenene. How?


β-Hydride
Elimination
1,2 Insertion
Pd(0)
alkene coordination
Wacker Oxidation
Ligand Exchange
nucleophillic attack