演習で学ぶ
有機反応機構

大学院入試から最先端まで

有機合成化学協会 編

化学同人

序　文

学协会の事业の一つとして．有機合成化學協会も以前から便覧や單行本などの出版事业を行ってきた．しかし，近年出版界を取り巻く事情も大きく変ゎった．そこで，本協会としこも新かに，時代に即応した出版活動を再出発させょぅということになり，2004年に出版委員会を新たに立ちあげ，少数の委员で今後の出版企画を検讨してきた．

現代の学问や研究の世界ではおびたガしいほどの研究情報が氾濫しており，それらを整理し绍介する各种の著作物が数多ぐ出版されている．しかし，ひと昔前に比べて出版事業を取り巻く状況ま大きく変貌している,情報は氾濫しているが．同時にコンピェーェタ技術が著しく発展したお陰で情報処理が簡単になり，とりわけコンビュ一タ検索により，新しい情報や必要なデ一タの入手が個人レベルでも格段に容易になつた．それによつて，今日では出版物の利用価値が相対的に減少していることは間違いない．

このような风潮のなかで，有机合成化学協会として出版事業を進めるからには，よほど特徴のあるものを指向しなければならない．本協会会員の多くの興味を引を，かつ有益な情報を提供しうる題目を選びだししかも一般の出版物とは一味違った，斬新な内容をもりた企画の提案である．このようなことを念頭において，出版委員会は努力を重ねている．

今回第一册目として東京大学大学院薬学系研究科の福山　透教授の研究室で企画編集された『演习で学ぞ有機反応機構——大学院入試武から最先端まで』を出版することになりか．福山研究室では多年にわたり，有機合成反応を理解し，反応機構を考える力の養成のために演習問題を数多く集めてこられた．本書は，それらを系統的にまとめて編集したもので，般の演習书とはかなり趣きの違ったユニ一クな内容になっている有機化学を専攻する学生に有機合成の面自きを会得きせ.また有機合成の研究者にも合成の実力をアマブさせるために大いに役立つものであり本協会の出版物，としてふさわしし‘ものキ考えている．

2005年7月

出版委員会委員長

辻 二郎

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まぇがき

医薬・农薬の開発から新素材の创製にいたるまで，有机合成化学の重要性は増大の途をたどっており，それにともなりて新反応や新化合物に関する論文が学術雑誌に汜濫している．19 世紀以来，連綿と情報を蓄積してきた「有机化学」という広大な海で，目指す目的地に達するためには優れた航海術を身につける必要がある．もちろん，さまざまな有機反応を一つ一つ覚ていくのは途方もなく时間がかかるし，非効率的である．

近年，計算化学の発展にょって，有機電子論に基づく形式的な反応機構解析の重要さが軽視視されるょうになった．しかし，電子論を習得することにょり，いろいろな反応を統一的に理解することが可能となり，反応経路の予測や，反応のデザィン，ひいては合成ル一トの設計に役立つことは明らかである．膨大な既知反応をただ丸暗記するだけでは何 も新しいことは生まれないが，その底流にとのょうな（形式的な）電子の流れがあるかを見きわめることが新しいアィデアの源泉となりうる．有机電子論，いわゆる Arrow-Pushing Mechanism では，主として活性反応種であるアニオン，カチオンやラジカルの安定性およひ生成・開裂する结合のエネルギ一などを考慮に人れながら，全体としてエネルギ一的に有利な生成物に導くょうな経路を考える学問である．初学者にとってとくに重要なのは，分子全体に目をくばり，決して省略することなく反応の各ステッブをノ一トに書いて．次に何が起こりうるかを注意深く考察することである．多くの有機化学教科書では，取録すべき概念や領域があまりにも多いためか，個々の反応についての解説には十分なスペ一スが割かれていないのが实情である．また，基本的な反応から高度な反応までのメカニズムを詳細に解説した演習書も少ない．

アメリカでは多くの大学の有機化学専攻の大学院生は Cumulative Examination というテストを毎月受験し，一定の合格数に達しなければ博士号の取得早資格が得られない．

試験には有機反応機構の問題が多く出題されるので，彼らは自主 にでも有機電子論を勉強せざるをえない仕組みになっている．一方，わが国では学部や大学院での専門教育が，アメリカの大学ほど厳しくは求められておらず，所属研究室に学生教育の大半の责任が委ねられている．てのょうな現状のもとで有機化学の力をつけるためには，講義ノ一ト，教科書，それに参考書も学习しつつ，演習书を自習していろいろな重要な反応の理解を徹底的に自分のものにするのが早道であると信ずる，

本書は初级問題(A)，中级問題(B)，上级問題(C)と解答编から構成されている《それぞれ A は基礎的で重要な反応问題，B は大学院人試レベルか，それょりやや难易度の高い問題 c は大学院から実社会の研究者レルの問題が集められている．

初学者は初级编の各問題が完全に自分のものになるまで何度も挑戦すべきであるし．簡単なステップを省略する癖のついた上级者には初级编も参考になると思う．また，20分考えてもわからないときにはさりさと降参して答えを見たほうがょいし，ゎからなかった問題は後目再挑戦して自分のものにすればぱ よい．そのために各問題 には三段阶のチュッソクボックスが用意されている．解答欄に書かれた反応機構は引用文献の著者が提示したものもあれぼ，福山研究室で考えたものもあり，両方併記の場合もある，

一般的に，有機反応では不安定な中間体の存在が確認できず，反応経路がブラックボックスのなかに人っていることが多い．したがって，真の反応機構は何かど悩むよりも．論理的に反応機構を考えられるようになることのほうが重要である．本書 の问題をすべて自分のものにすることができたなら．相当に有機化学の実力がつくことは疑いない．なお．解答欄のコメントは短い英語で書かれているが．初学者でもこの程度の英語ならさして負担 ならないことと，英語のほ うが簡潔に説明できるからということでごーi 承願いたい．

本考に劫載された問題の大部分は，当研究室のグル一プミ一ティングで出題されたり，スタッフが選んだものであるが，文部科学省特定領域研究「生体機能分子の創制」の計画班班員の方がたからご提供いただいた問題も合まれている．ここに感謝したい．また，本書は前々頁に示す当研究室のスタッフや院生が忙しい 究の合間をぬって執筆したものであるが，横島聡助手の献身的な努力なくしては完成しなかったことを特記 しておきたい．

最後に，本書の企画・製作にご助力いただいた化学同人編集部平 佑幸氏に深く感謝したい．

2005年7月　東京大学大学院薬学系所研究科

天然物合成化学排究室　福山　透

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問　題

■ 初级編

初级編ほ，有機化学の教科書で取ぇぁばちにているゐ基本的な反応中心に構成されていゑ

【例 題】2

問題数　78 題

■ 中级編

中级編ほ，大学院入試かゐ大学院修士課程のレバルた想定して構成ちぉているゐ

【例 題】20

問題数　128 題

■ 上级編

上级編ほ，歴史に有名な反応かち最新の論文まこ，手でたぇ十分な問題かち構成まれているゐ

【例 題】48

問題数　109 題

解　答

解答 初级編

解答 中级編

解答 上级編

【コラム】福山研のグループミーティング風景
　　　　　問題き解くコッ
【付　録】有機反応の反応機構を考ぇゐにって
　　　　　電気陰性度と酸性度定数
【索　引】和文索引ぉょび欧文索引

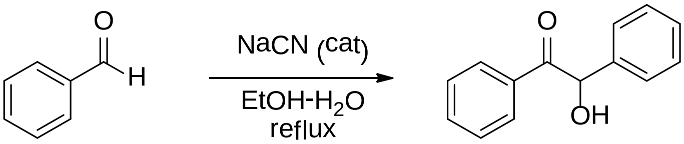
略語表

△	heat
Ac	acelyl
acac	acetylacetonate
AIBN	2,2''-azobisisobutyronitrile
aq	aqueous
Ar	aryl
Bn	benzyl
Boc	t-butoxycarbonyl
Bu	butyl
cat	catalytic amount
Cbz	benzyloxycarbonyl
CSA	10-camphorsulfonic acid
CSI	chlorosulfonyl isocyanate
Cy	cyclohexyl
DABCO	1,4-diazabicyclo[2.2.2]octane
dba	dibenzylidenacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
ICC	N.N'-dicyclohexylcarbodiimide
DDQ	2,3-dichloro-5.6-dicyano-1,4-benzo-quinone
DEAD	diethyl azodicarboxylate
DMAP	4-(dimethylamino)pyridine
DME	1,2-dimethoxyethane
DMF	N, N-dimethylformamide
DMSO	dimethyl sulfoxide
dppb	1,4-bis(diphenylphosphino)butane
DPPE	1,2-bis(diphenylphosphino)ethane
EDCI	1-ethyl-3-(3-dimethylaminopropyl carbodiimide
eq	equivalent
Et	ethyl
HMPA	hexamethylphosphoramide
hv	photoirradiation
i	iso
KHMDS	potassium hexamethyldisilazide
LDA	lithium diisopropylamide
liq	liquid
m	meta
mCPBA	m-chloroperbenzoic acid
Me	methyl
MEM	(2-methoxyethoxy)methyl
MOM	methoxymethyl
Ms	methanesulfonyl
MS	molecular sieves
n	normal
NBS	N-bromosuccinimide
NCS	N-chlorosuccinimide
NMM	N-methylmorphuline
NMO	N-methylmorpholine-N-oxide
Ns	o-nitrobenzenesulfonyl, nosyl
o	ortho
p	para
Ph	phenyl
Pr	propyl
rt	room temperature
s	secondary
SET	single electron transfer
t	tertiary
TBAF	tetra-n-butylammonium fluoride
TBS	t-butyldimethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
TfOH	trifluoromethanesullonic acid
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TMS	triraethylsilyl
tol	tolyl
TosMIC	p-toluenesulfonylmethyl isocyanide
Tr	triphenylmethyl, trityl
Ts	p-toluenesulfonyl, tosyl
TsOH	p-toluenestdfonic acid

問題　初级編

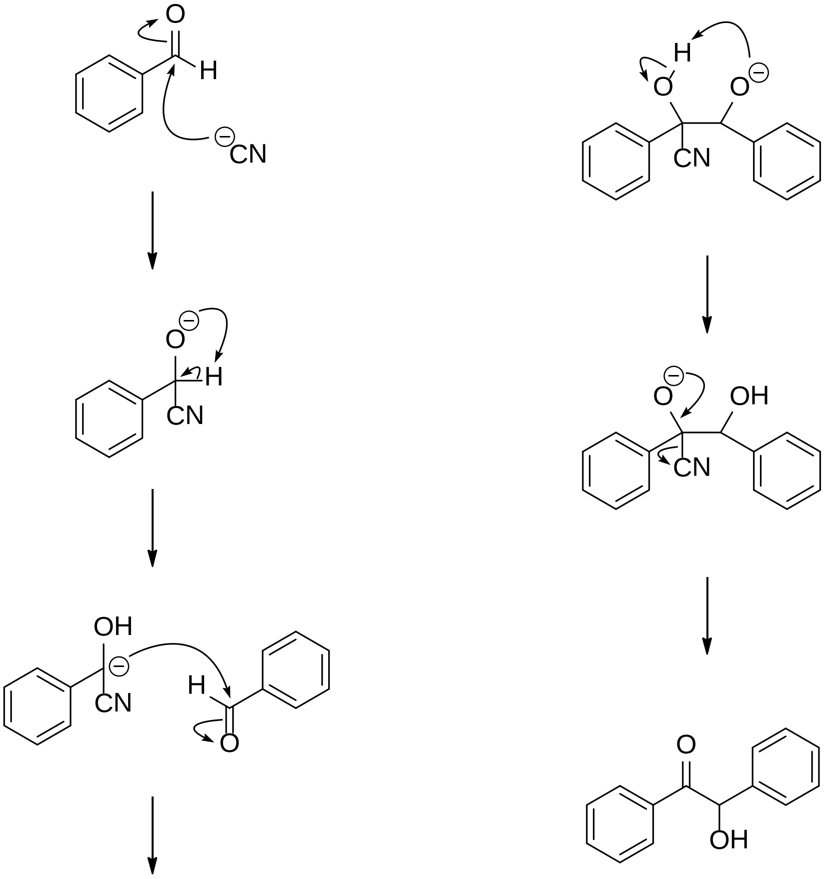
初级编は．有機化学の教科書で取りあげられている反応を中心に構成されている初学者は．教科書とともに．一問ずつ矢印を自らの手で描くことによって，有機反応の考え方の基礎を学んでほしいまた上级者にとっては，一見簡単そうに思える問題が多いかもしれないが，水素原子，電子などの細かなところまで一つ一つ丁寧に書いてみると，理解が不十分だった箇所が浮きぼりになると思うより難しい問題を解く前の準備運動として取り組んでほしい

例題 Provide reasonable arrow-push mechanisms for following recations



解答

benzoin condensation



Adams, R; Marvel, C. S. *Org. Synth., Coll*. Vol. Ⅰ **1941**, 94

问 题 Provide reasonable arrow-push mechanisms for following recations

Check Box

A001

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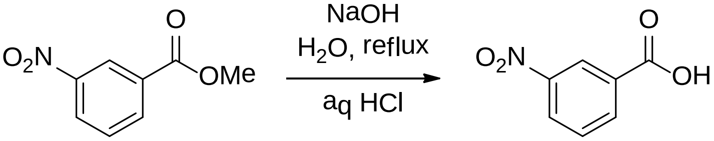

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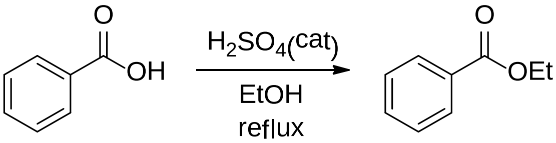

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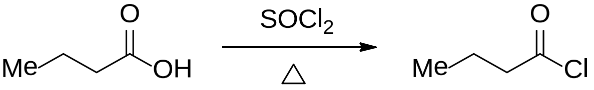

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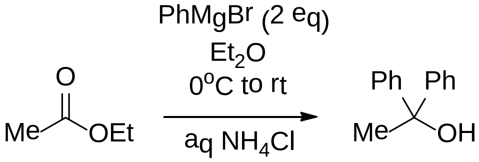

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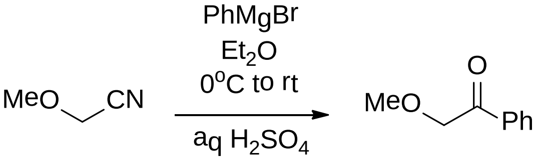

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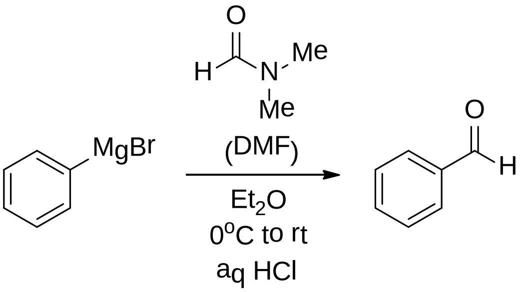

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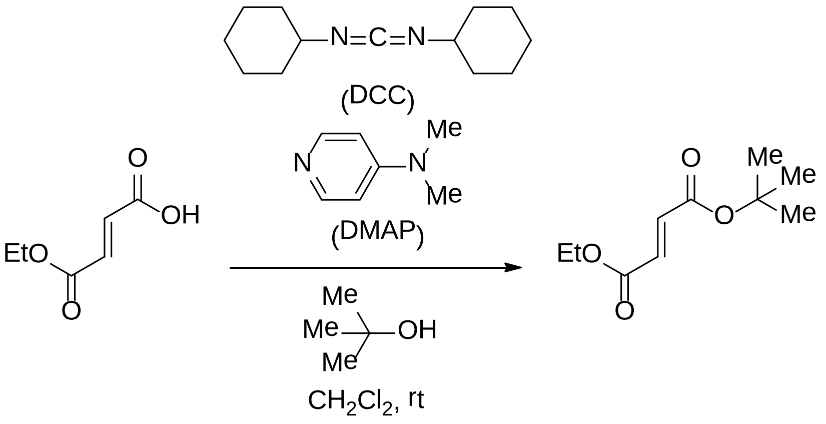

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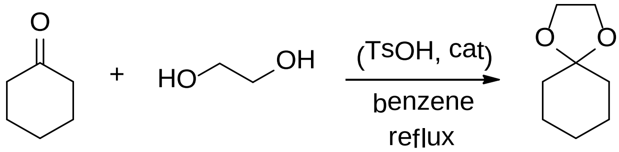

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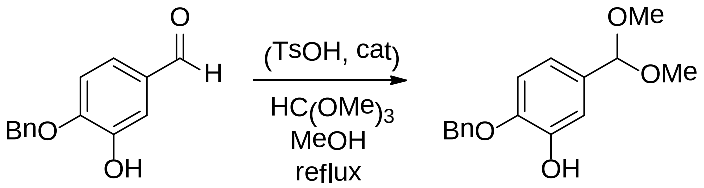

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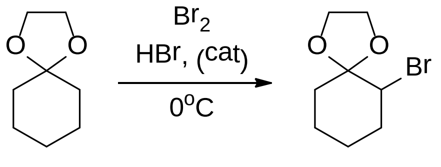

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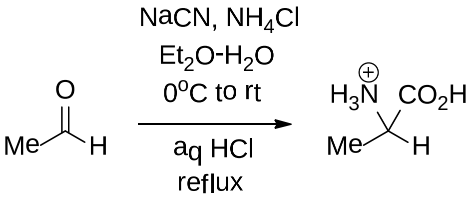

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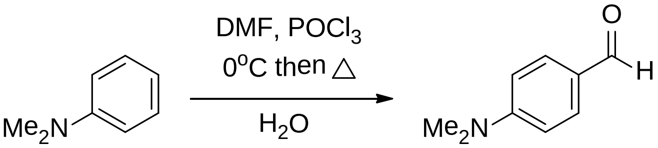

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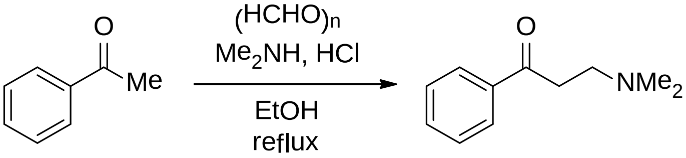

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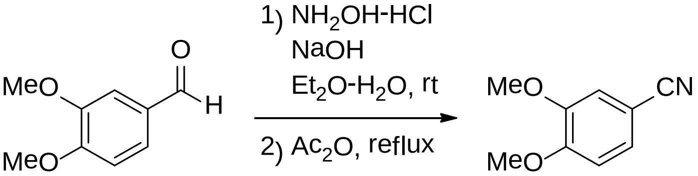

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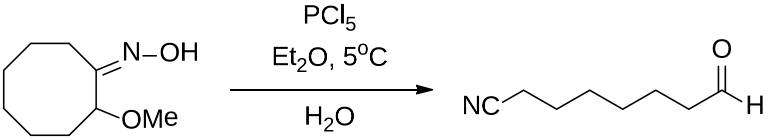

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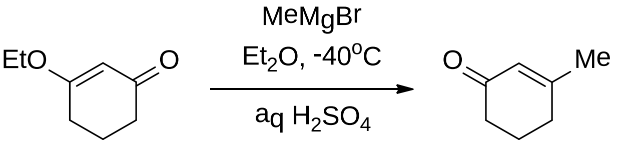

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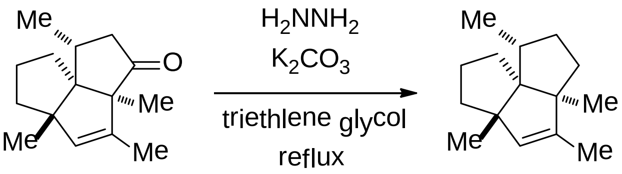

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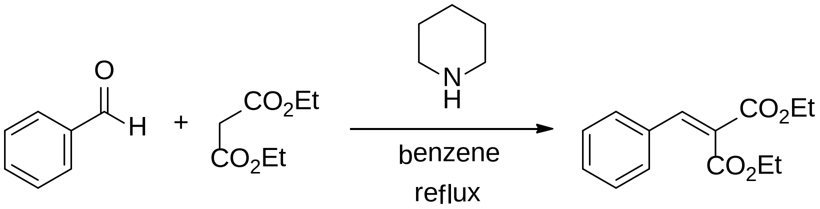

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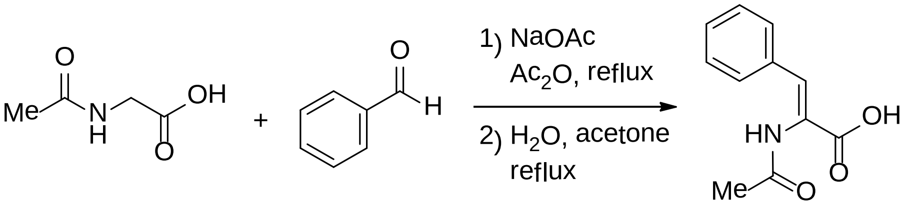

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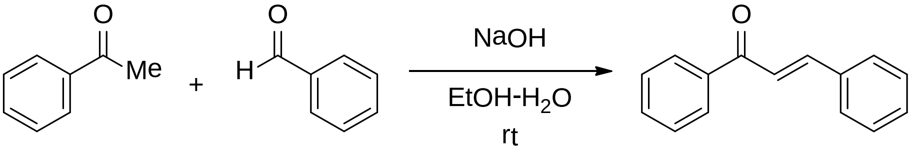

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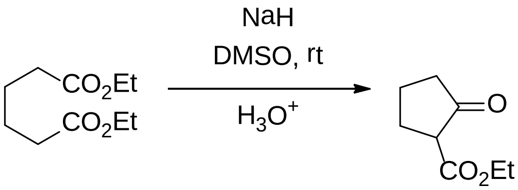

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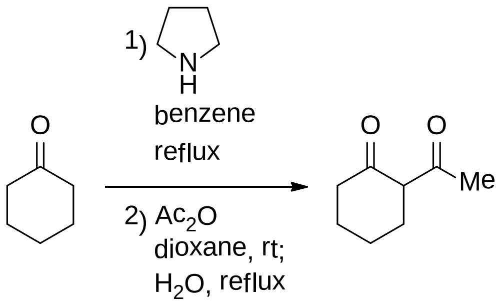

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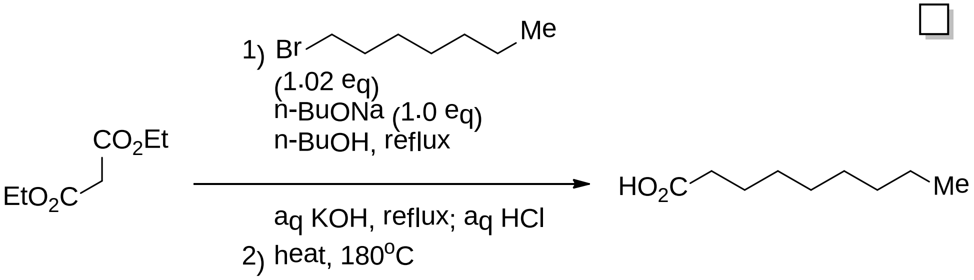

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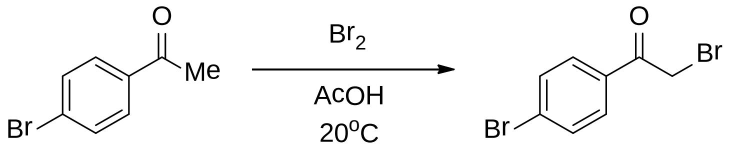

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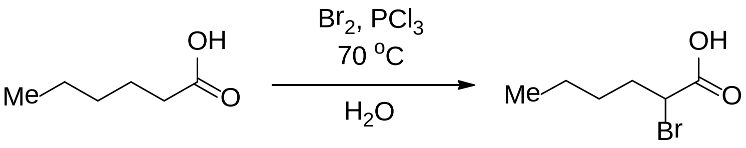

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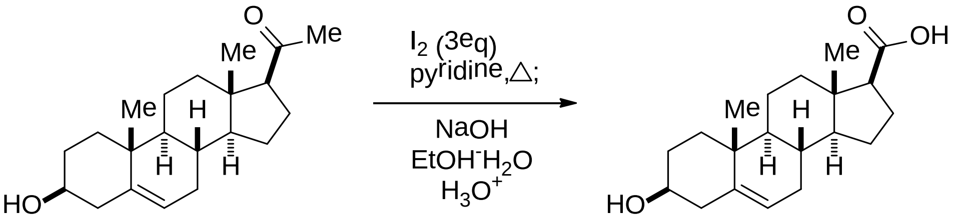

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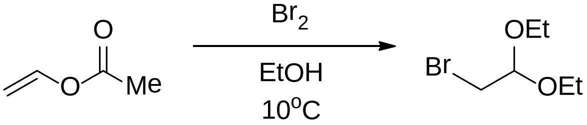

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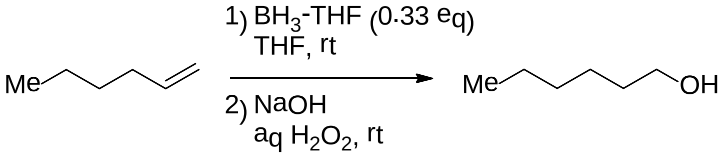

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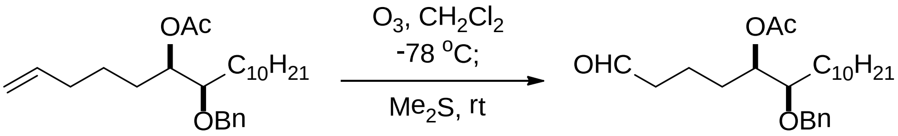

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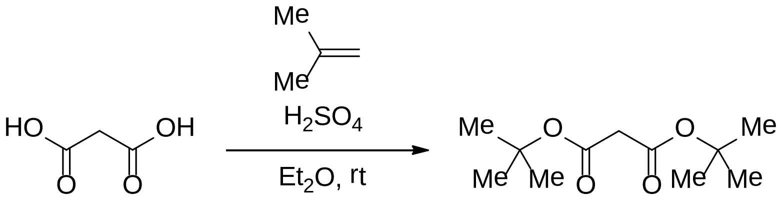

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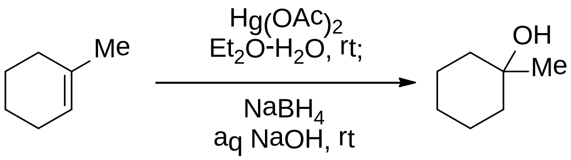

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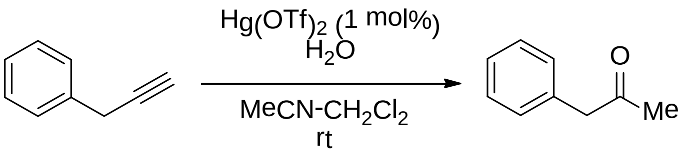

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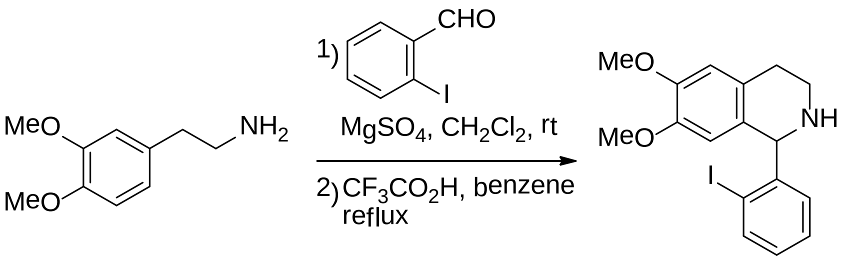

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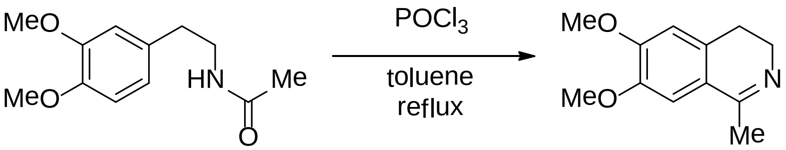

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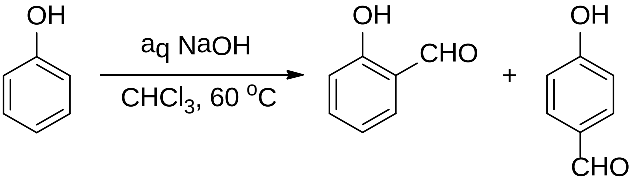

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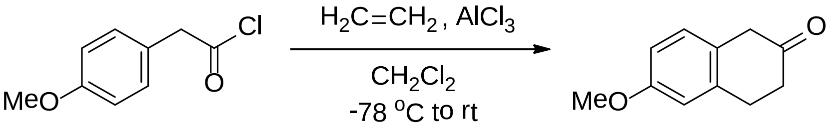

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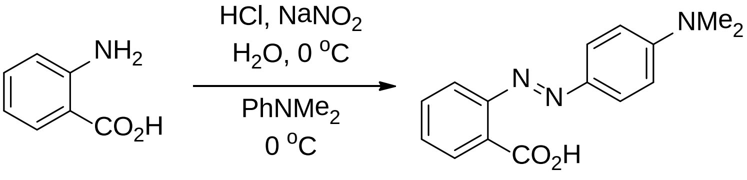

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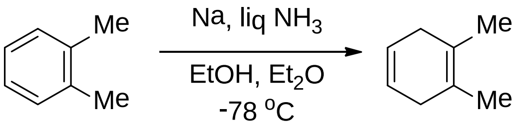

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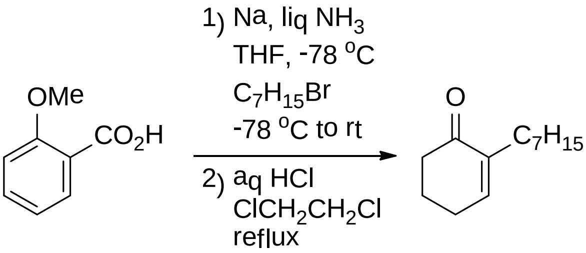

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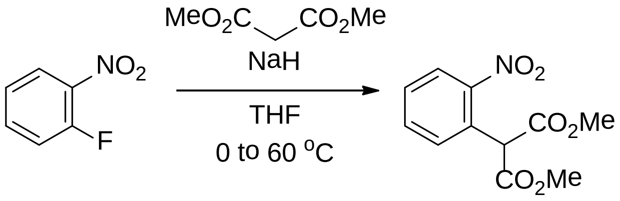

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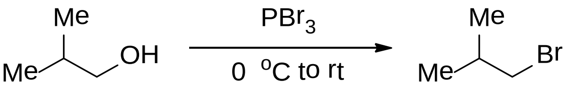

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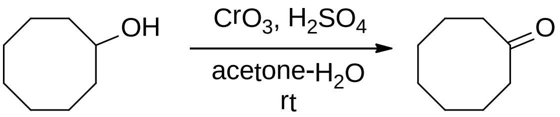

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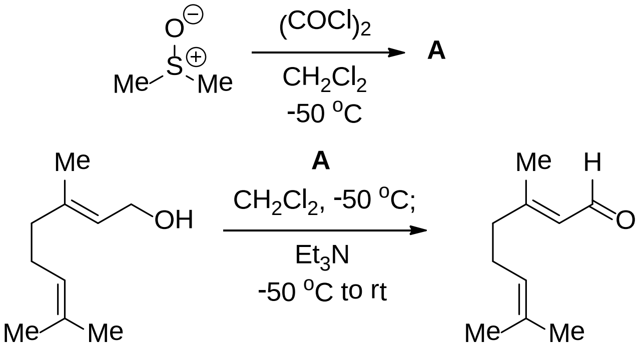

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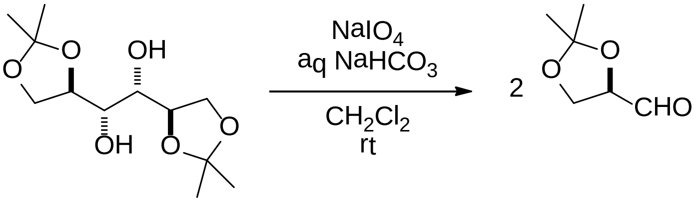

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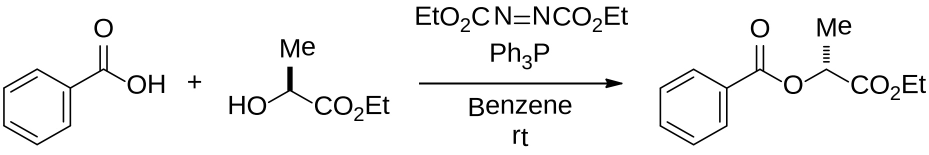

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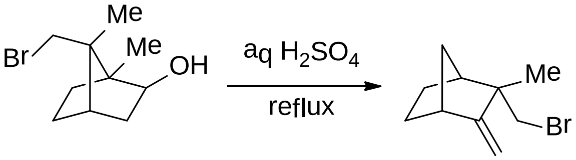

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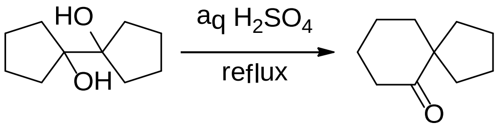

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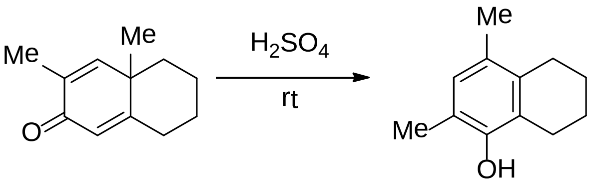

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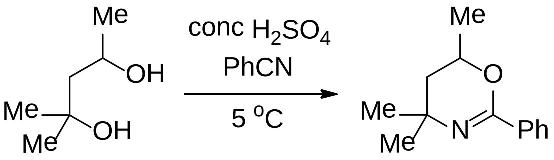

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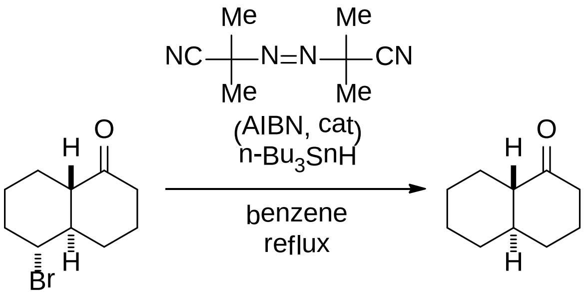

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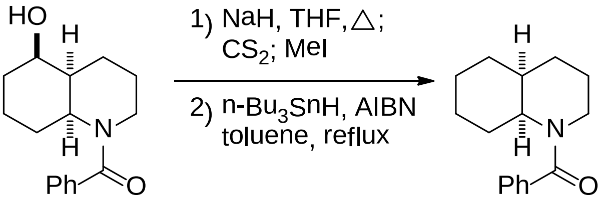

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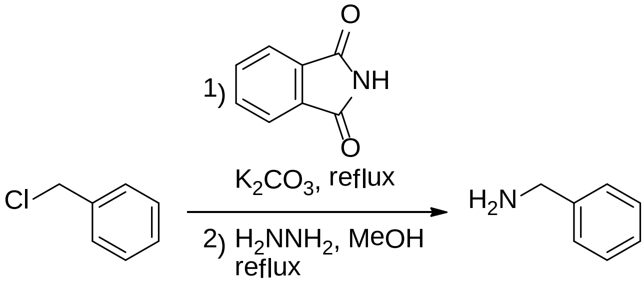

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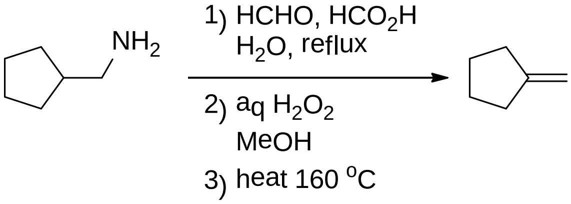

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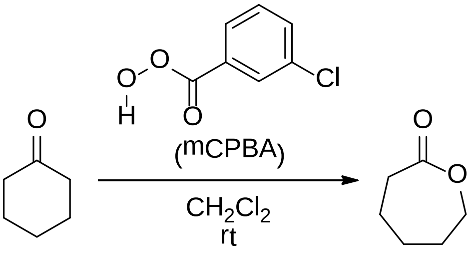

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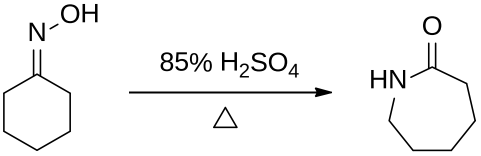

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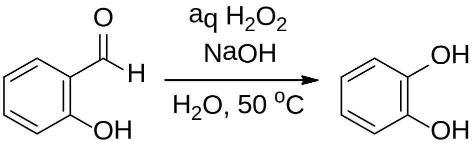

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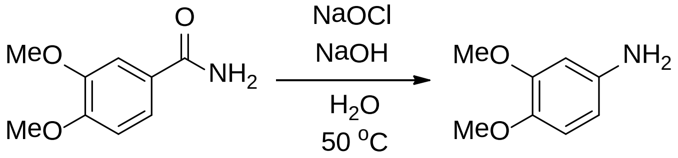

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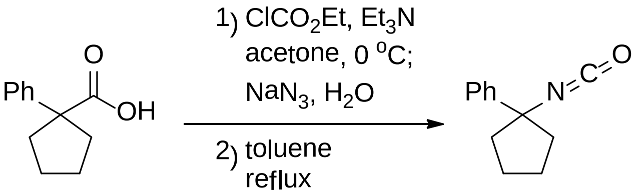

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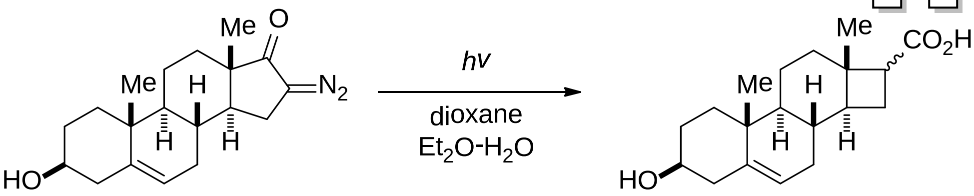

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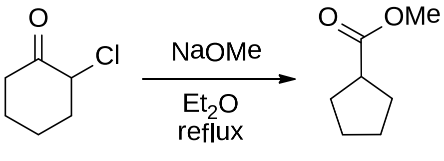

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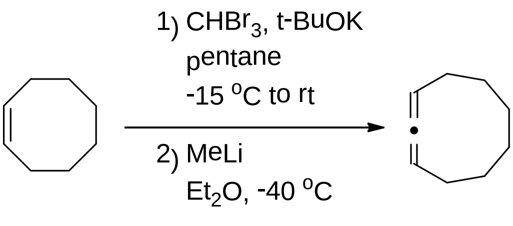

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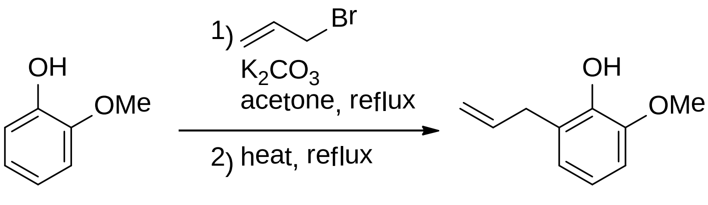

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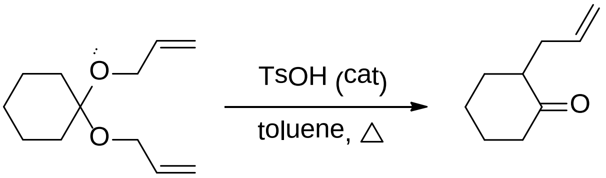

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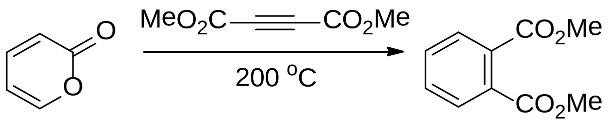

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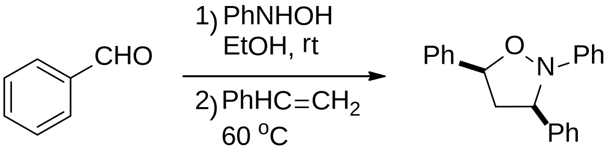

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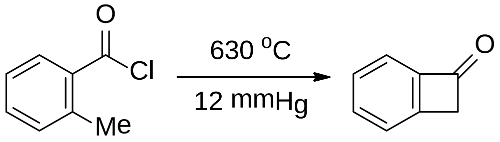

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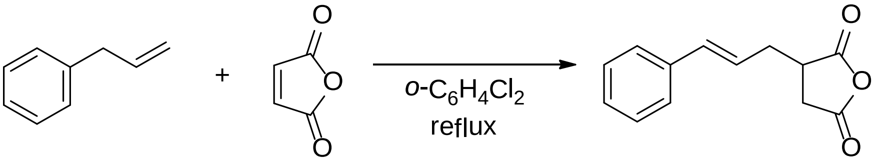

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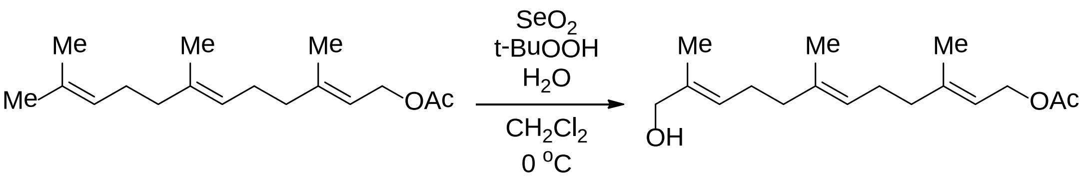

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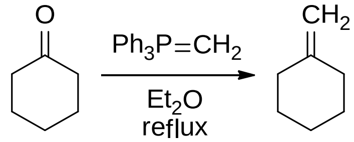

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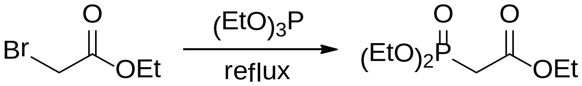

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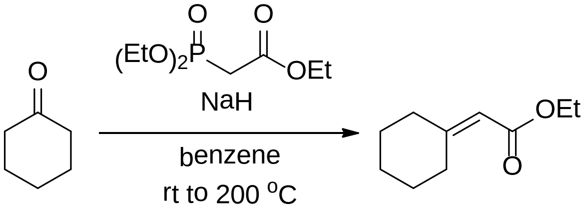

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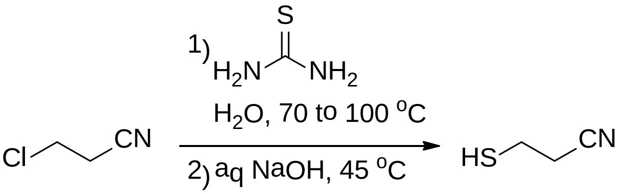

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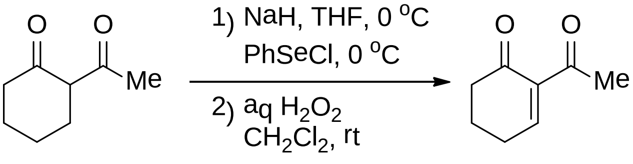

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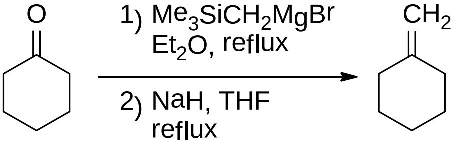

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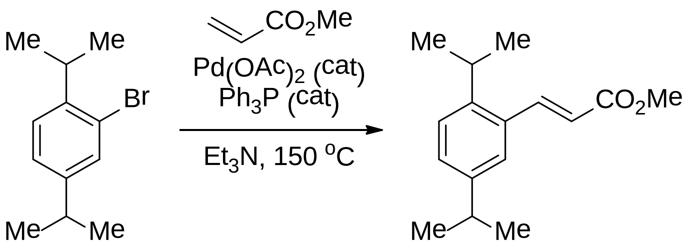

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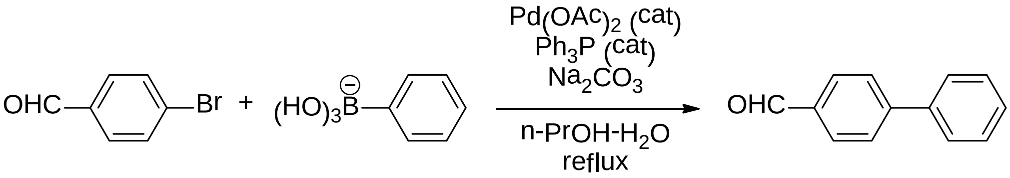

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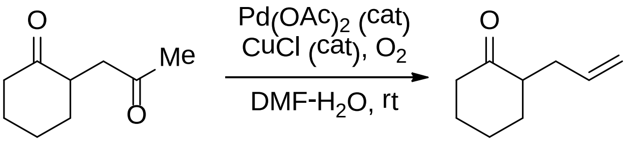

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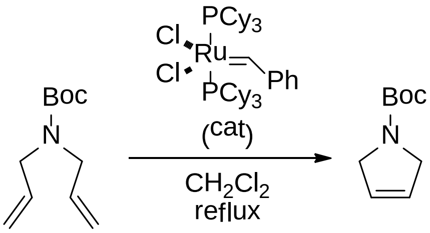


◆コラム①◆

福山研のグループミーティング風景

福山研究室では周に1回．グループミーティングの時間を使って反応機構の問題演習を行っている問題演習は，自分の頭で考え実際に手を動かして書くことになるので学生のトレ＊ニングとして非常に効果的であり，国内外の有機化学の研究室で実施しているところも少なくない参考までに当研究室での問題演習の様子を紹介したい．

まず問題は前の週にあらかじめ配られるこれを一週問かけて自力で解いてくるもちろん，分からない反応剤などについては参考書で調べてもよいことにしているが学生同士相談しないのが原則であるたまに出題ミスが発覚するが．その場合は速やかに全員に知らせる構造式や条件が间違っていれば当然解けるはすはなく．考える人の時間を無駄にするということで．出題は慎重になされる出題ミス 1 回につき100円の罰金を徴収するこの集まったお金は忘年会のときの酒代にし． 一年を振り返る

セミナー当日一问につき 4 人すつが当てられ黒板の前にでて解答を书く意気揚々と書きあげることができれ．ポよいが，解けなかった場合は黒板の前に立ち尽くすことになるそれも修行のうちであるそこで奮起し次回のやる気につなげてもらえればよいまたそのような経験をした問題ほど．強く記憶に残るようであるあまりにも解答が進まない場合や全員が思わぬ方向に進んでいる場合は出題者や上级生がヒントをだす

约 15~20 分で時間切れとしその後，出題者による解説を行う出題者は参考論文をもとに解説するが．反応機構が詳しく議論されていない場合や．論文に记されている反応機構とは別の可能性が考えられる問題もあるその時は．先生を含め全員で議論する必ずしも一つの答えに絞られるわけではないが，さまざまな可能性を考えることが勉強になる

問題はおもに学生が順番で出題することになっている．慣れない学生は＊つの問題を探すのに．出題の数週間前から大騒ぎである図書館で論文の山と格闘することになるが．せっかくよい问題が見つかったと思って先輩に見せても．にの問題はすでにだされた」にれでは問題にならない」など厳しい言葉が突きつけられるしかしこのプ D セスがまた重要な勉強の機会となる问題を見つけるためにはまず多くの論文を読まなくてはならすさらに内容もしっかり理解していはいと．簡単な「つまらない」問題しか見つけることができない慣れてくると．普段から論文をよく読み，その段階でいくつか問題をストックしておくようになるあまり長い間ストックしておくと別の人に出題されてしまい，悲しい目に遭うこともしばし｜ゴであるが

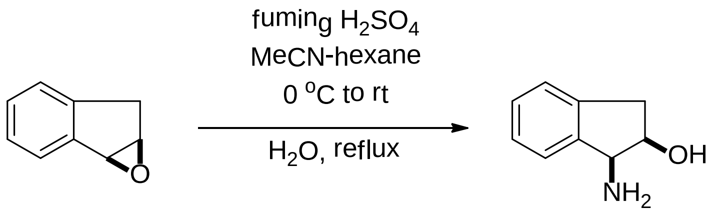
問題の解答は．グル＊プミ＊ティング後．担当の学生が清書し．研究室に保存しているまたその解答は问題と一緒に PDF ファイルとし．ホ＊ムペ＊ジで公開している諸般の事情で更新が遅れることもあるがぜひ参考にしていただきたい．

福山研究室 HP アドレス
http://www.f.u-tokyc.ac.jp/-fukuyama/index-l.htm

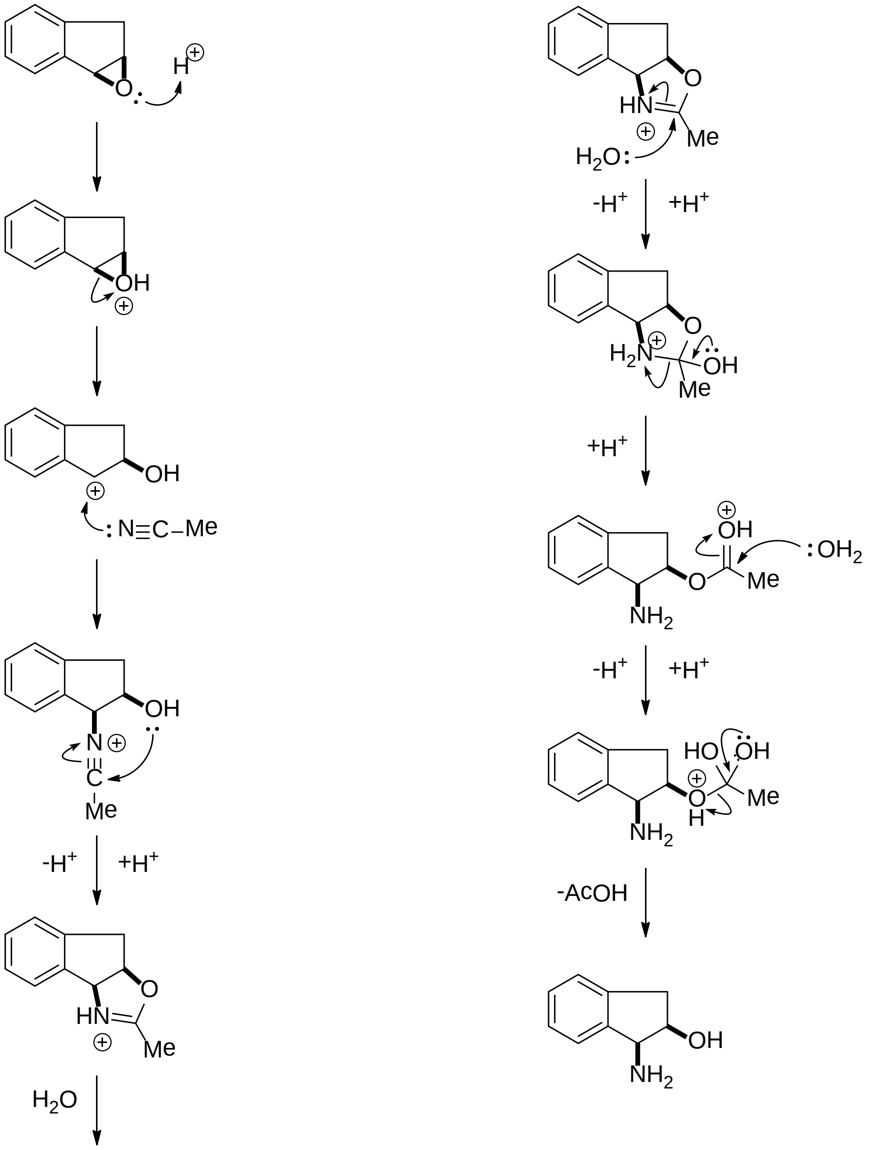
問題 中级編

中级编では．大学院入试から大学院修士课程のレベルを想定して問題を集めてあるまた反応機構の興味深い人名反応も数多く取りあげられており，合わせて学んでいってほしい前半は比較的基本的な问題．後半は発展的な问題を中心として，分野ことにまとめてある.後半は手応えを感じる问題もあるかもしれないが，有機合成化学の公式として，自在に反応機構が書けるようにがんばってほしい

例 题 Provide reasonable arrow-push mechanisms for following recations



解 答



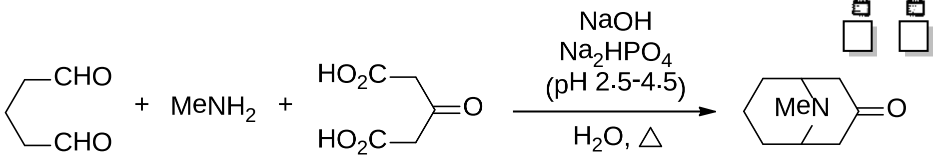
Jacobsen, E.N. *Org. Synth, Coll.* vol Ⅹ **2004**. 29

问 题 Provide reasonable arrow-push mechanisms for following recations

Check Box

B001

☐ ☐ ☐



B002

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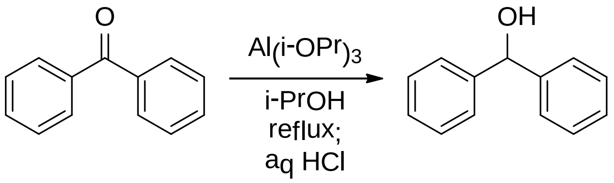

B003

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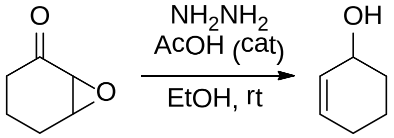

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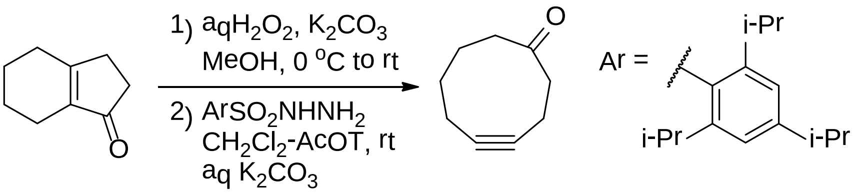

B005

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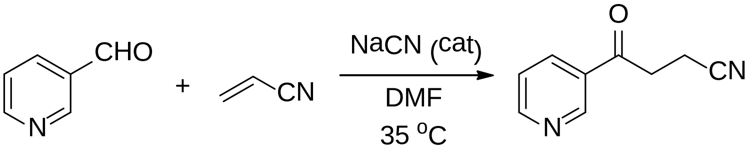

B006

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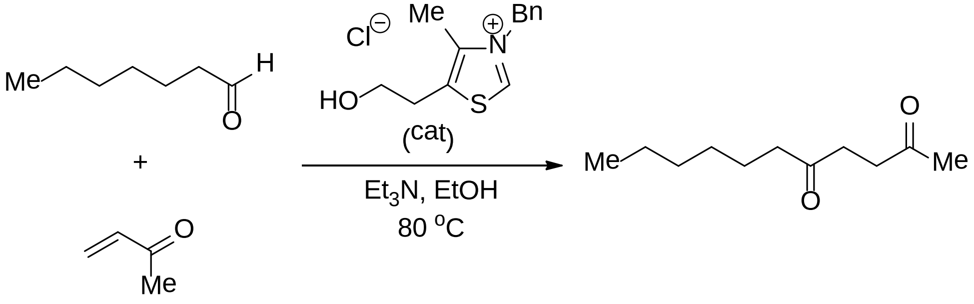
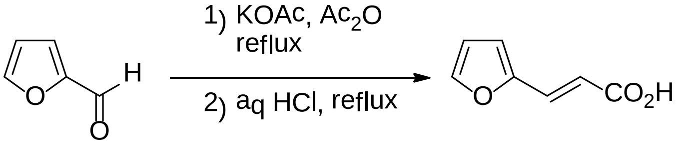
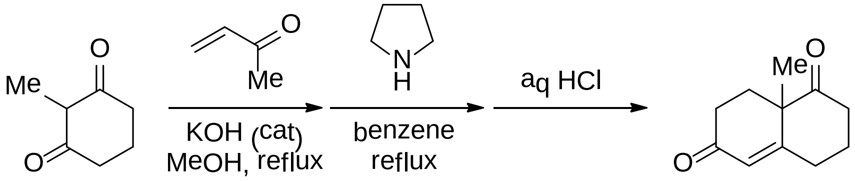


Check Box

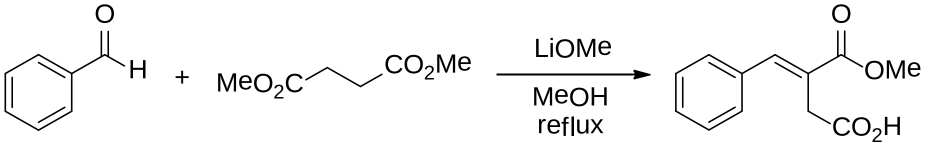
B007 ☐ ☐ ☐



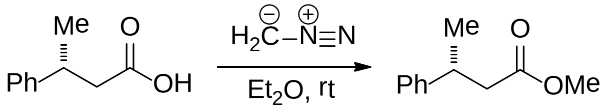
B008 ☐ ☐ ☐



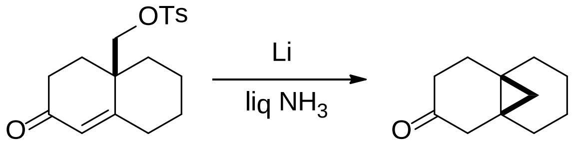
B009 ☐ ☐ ☐



B010 ☐ ☐ ☐



B011 ☐ ☐ ☐



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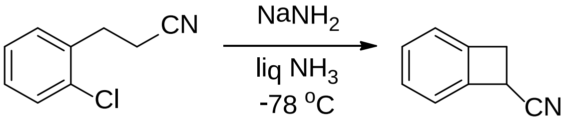

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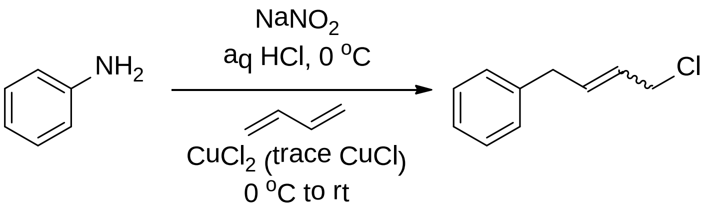
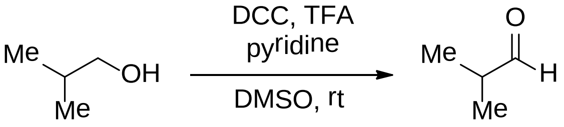
B013 ☐ ☐ ☐



B014 ☐ ☐ ☐



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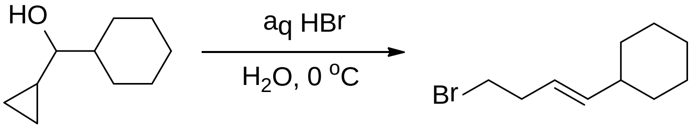

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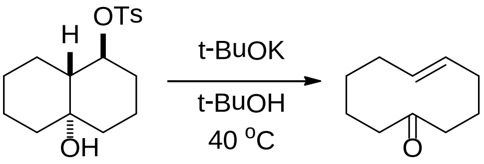

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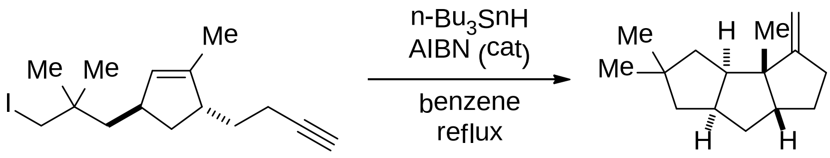

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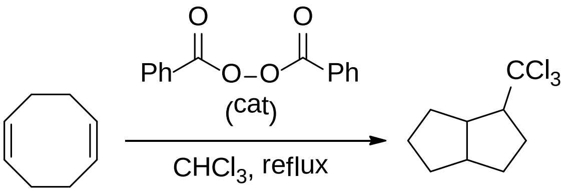

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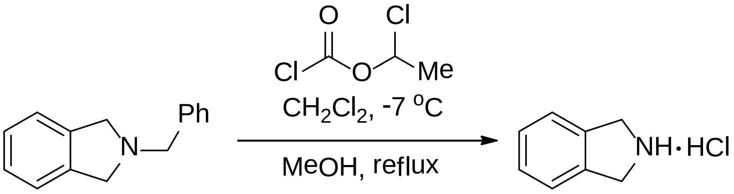
B019 ☐ ☐ ☐



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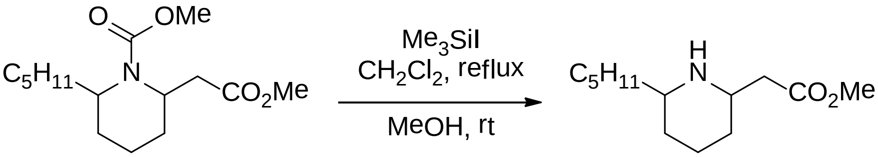

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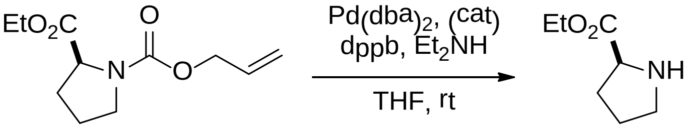

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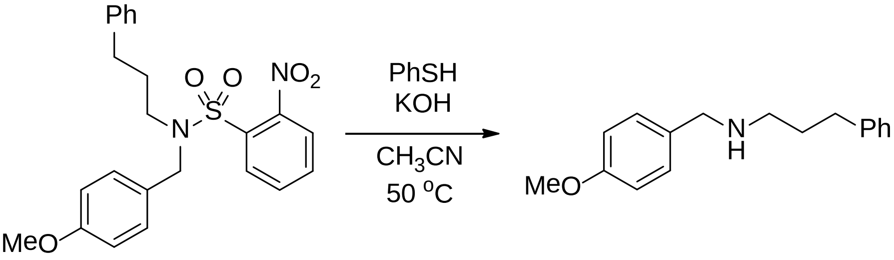

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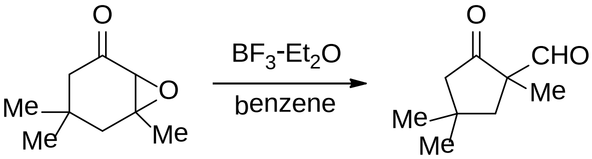

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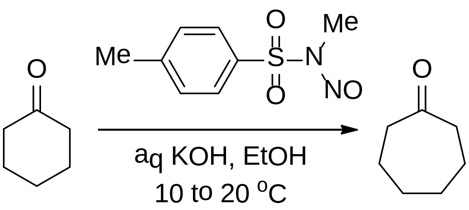

Check Box

B025

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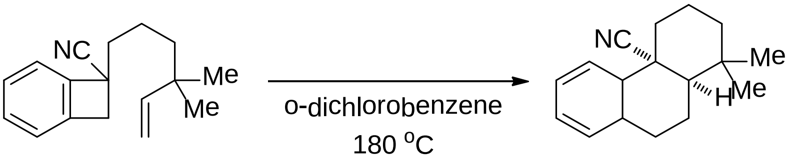

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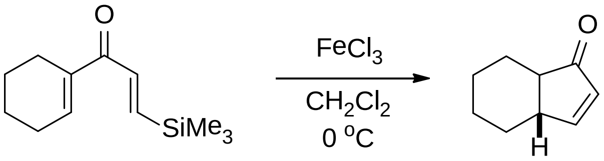

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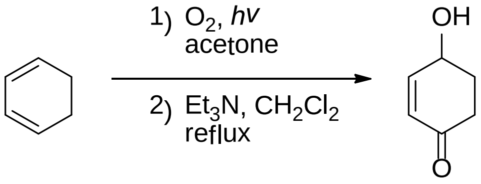

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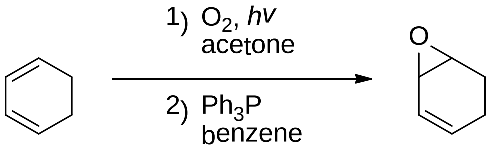

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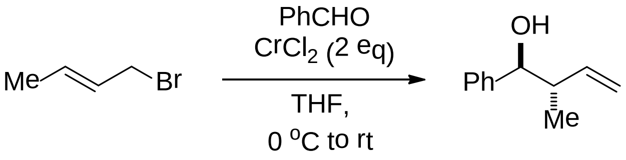

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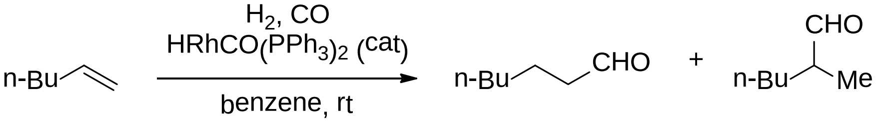

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B045

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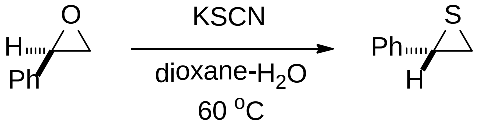

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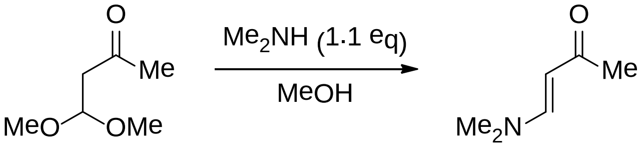

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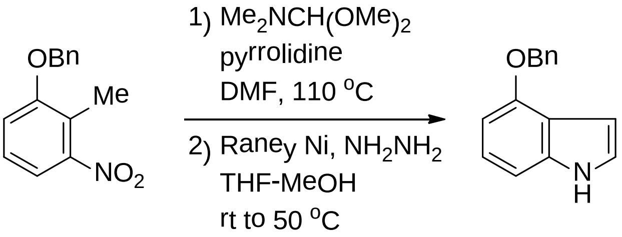

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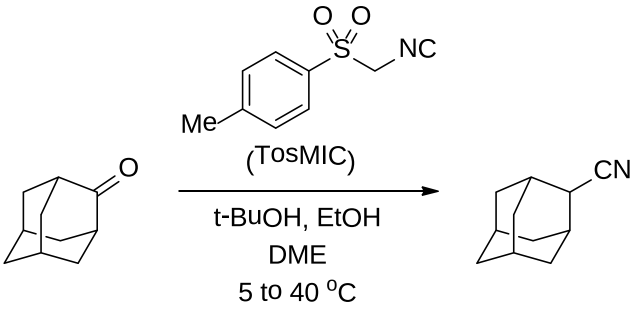

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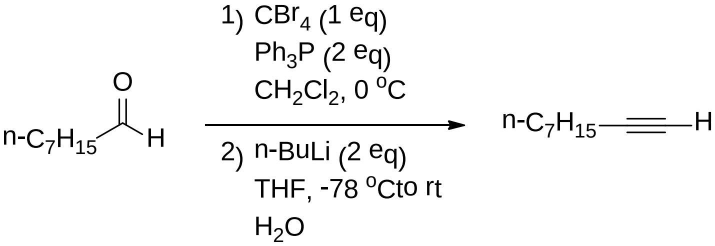

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B050

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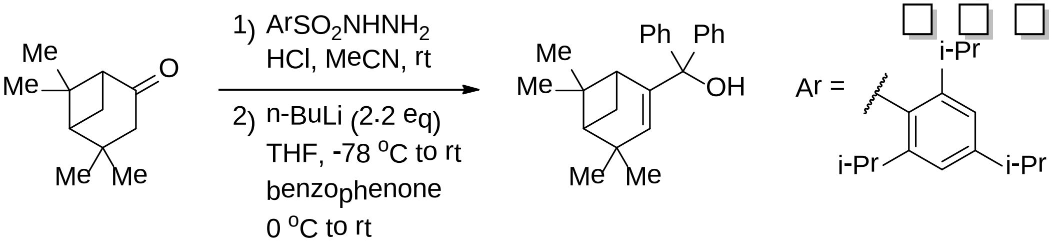

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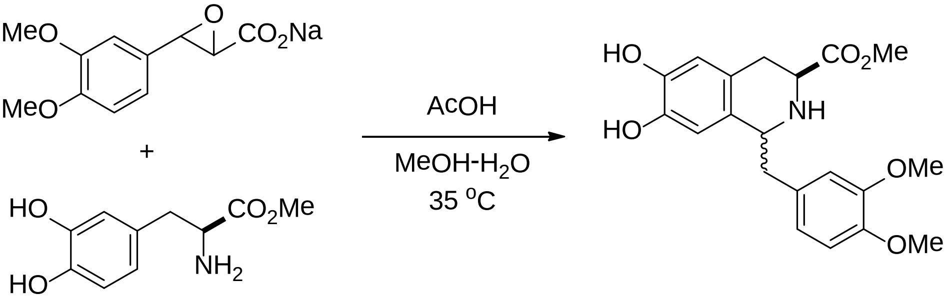

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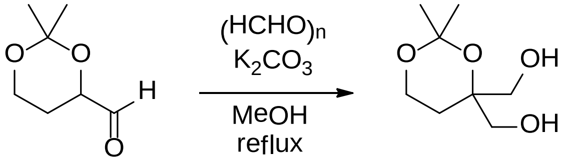

B053

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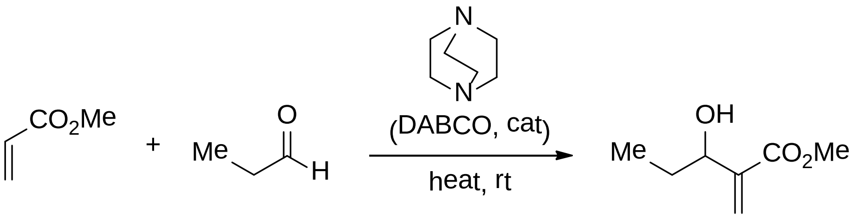

B054

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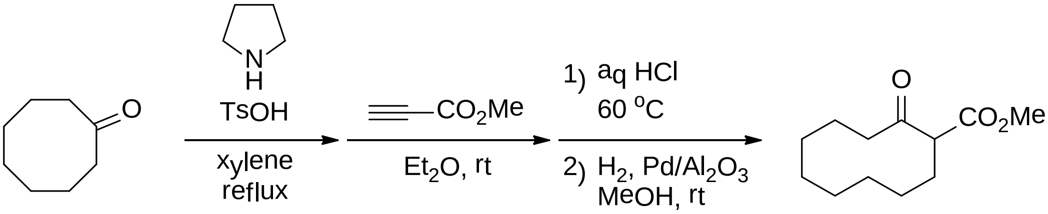

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B055

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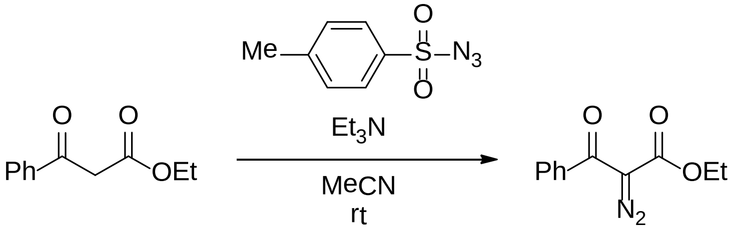

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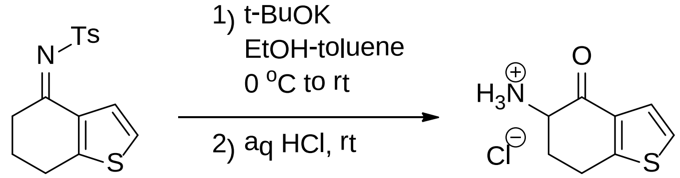

B057

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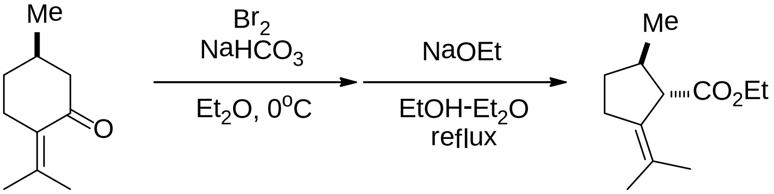

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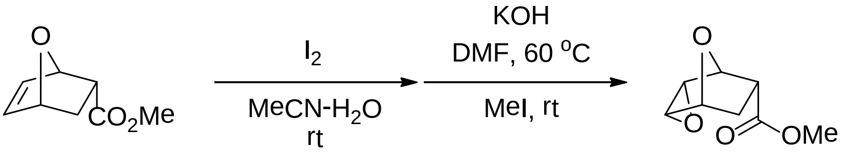

B059

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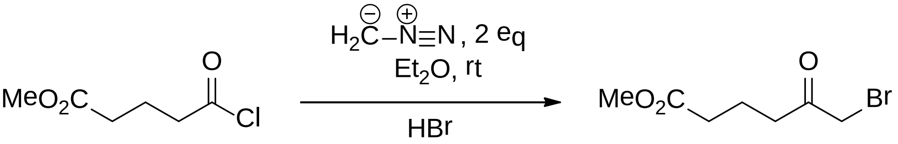

B060

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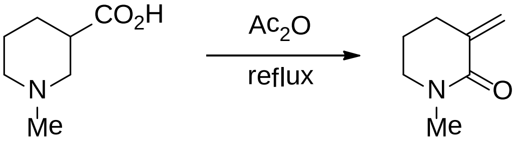

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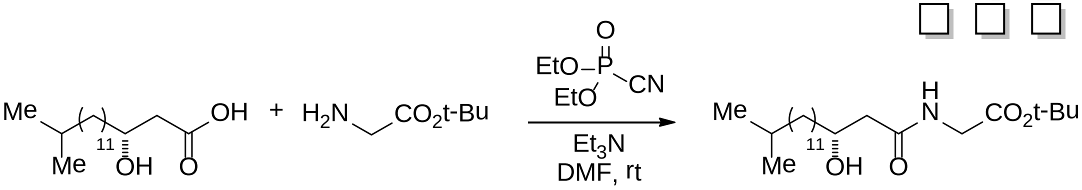
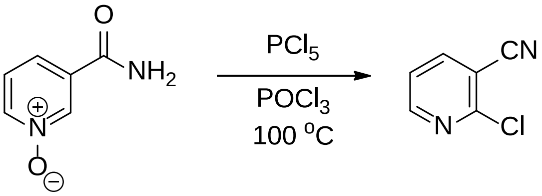
B061 ☐ ☐ ☐



B062 ☐ ☐ ☐



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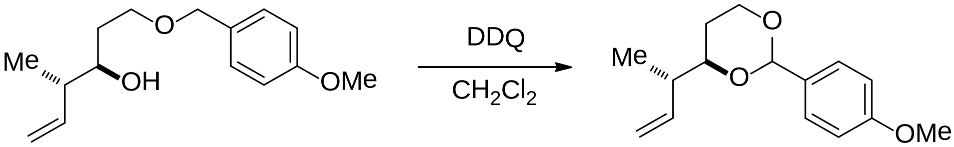
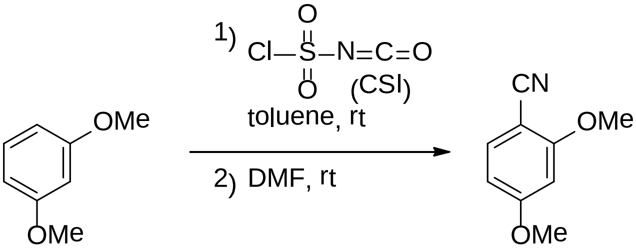


B064 ☐ ☐ ☐



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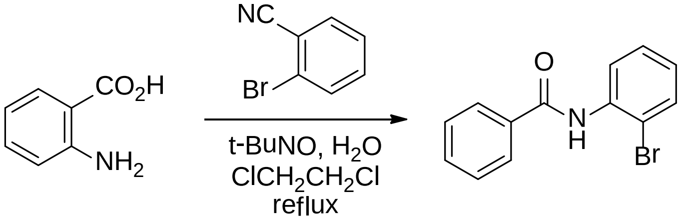

Check Box

B066

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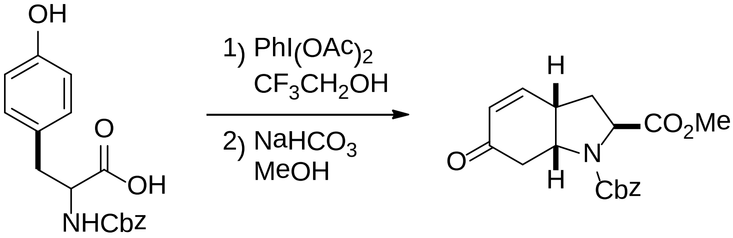

B067

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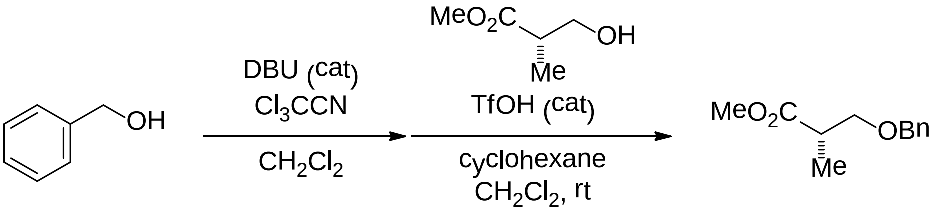

B068

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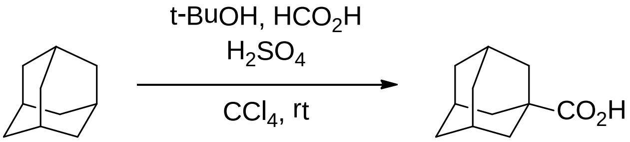

B069

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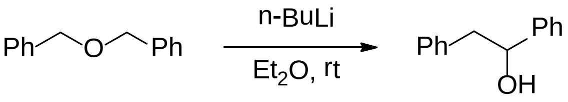

B070

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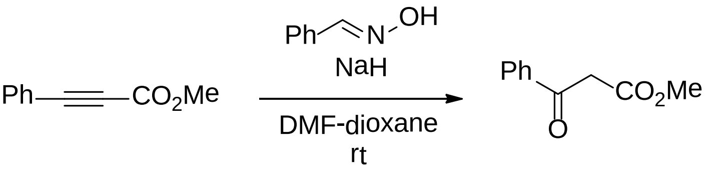
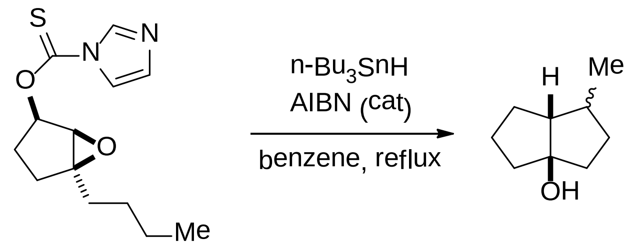


Check Box

☐ ☐ ☐

B071



B072

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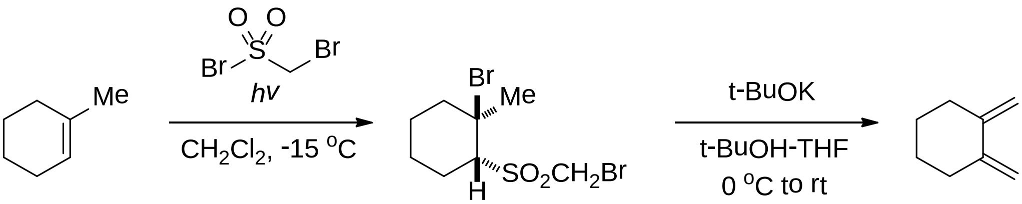

B073

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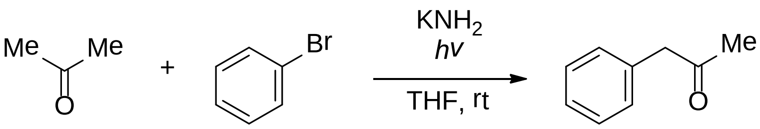

B074

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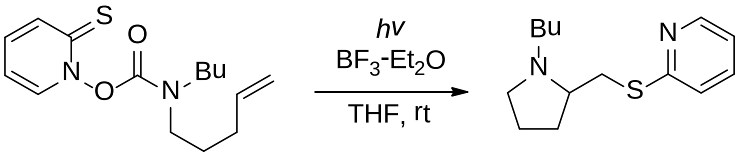

B075

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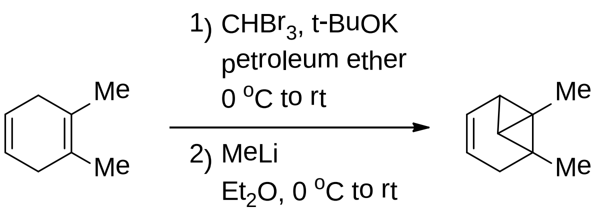
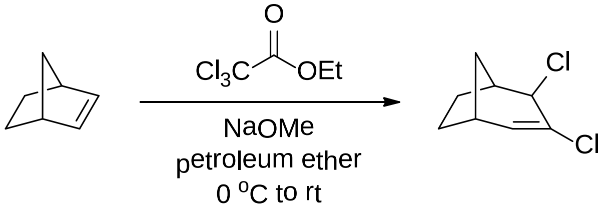


B076

Check Box

☐ ☐ ☐



B077

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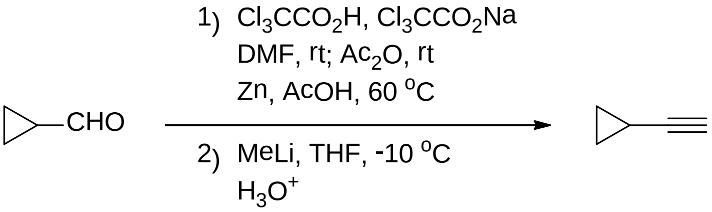

B078

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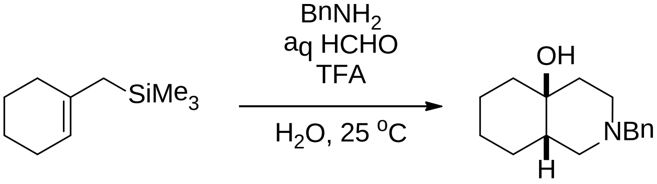
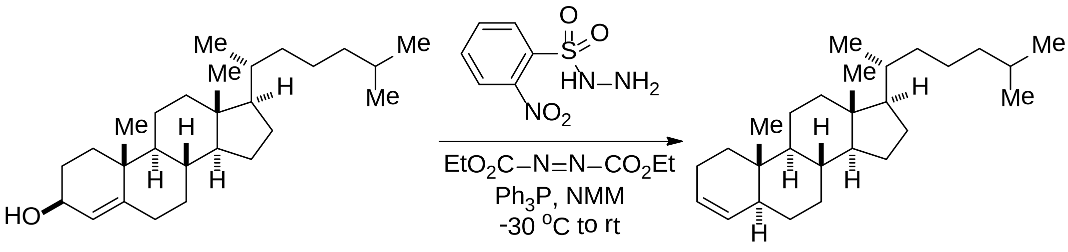


B079

☐ ☐ ☐



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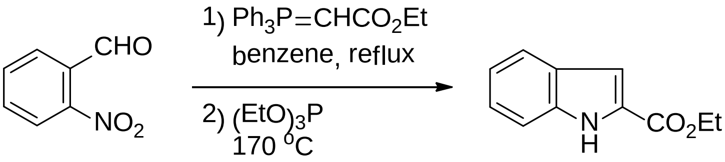

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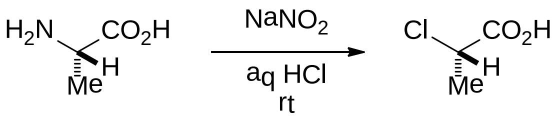

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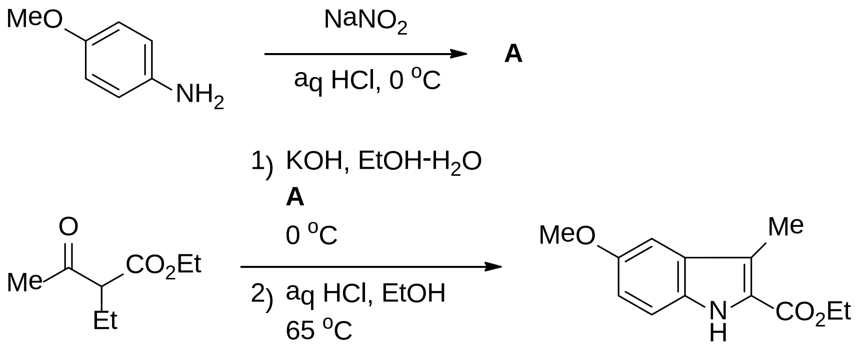

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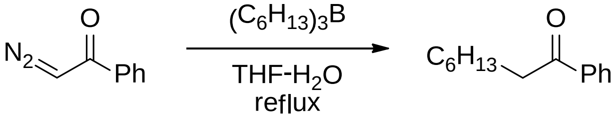

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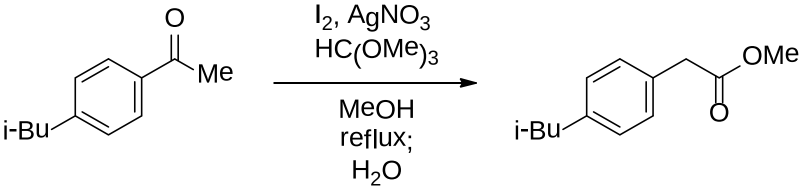

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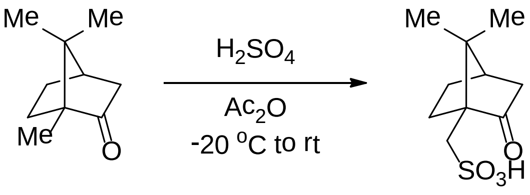

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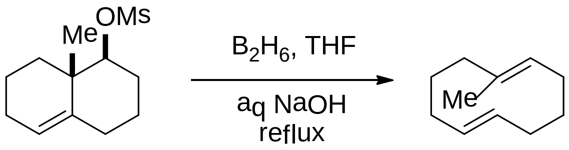

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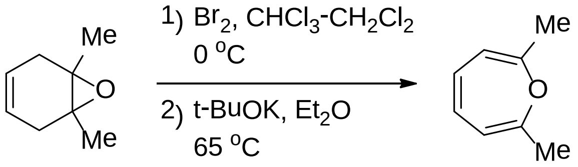

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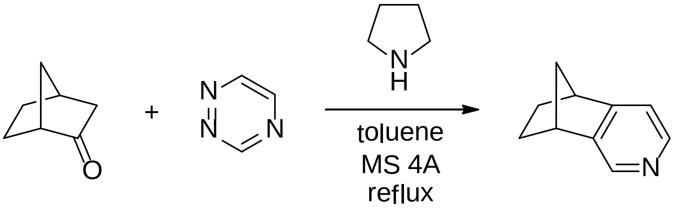

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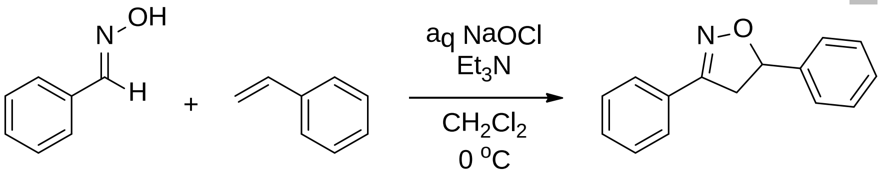

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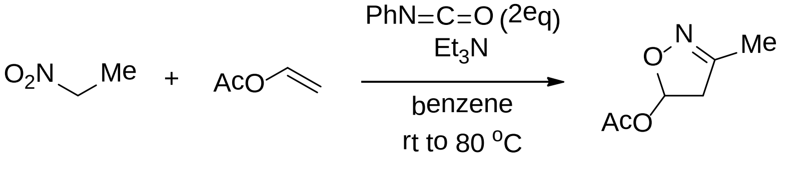

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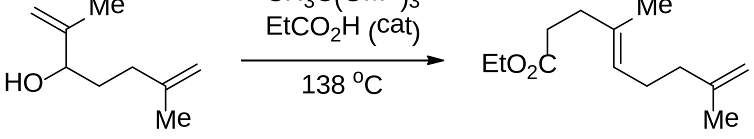

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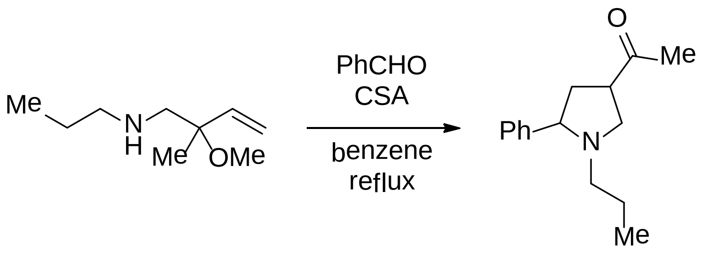

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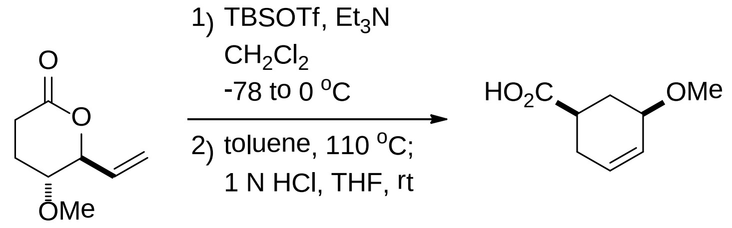

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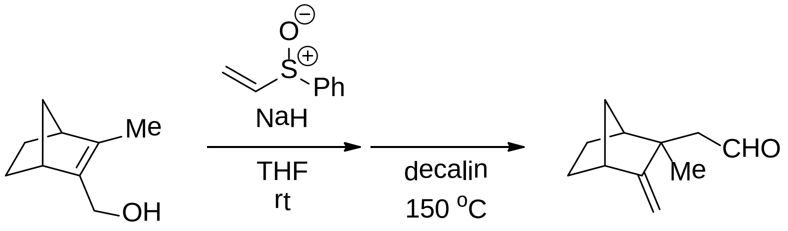

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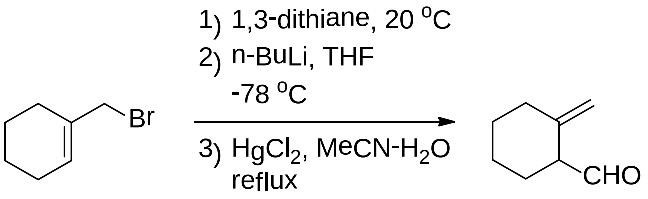

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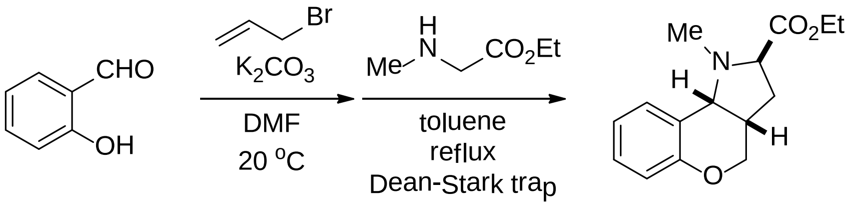

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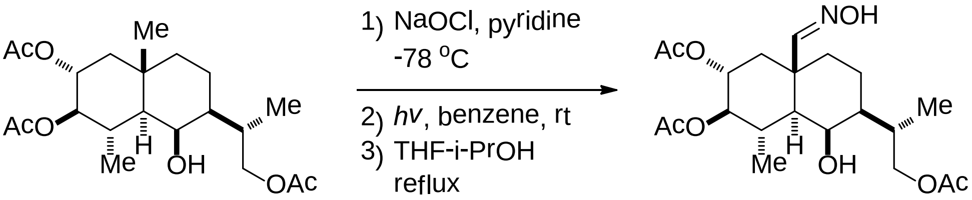

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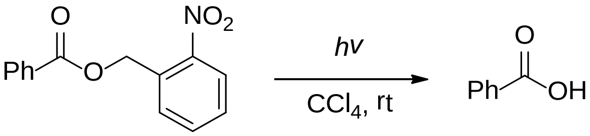

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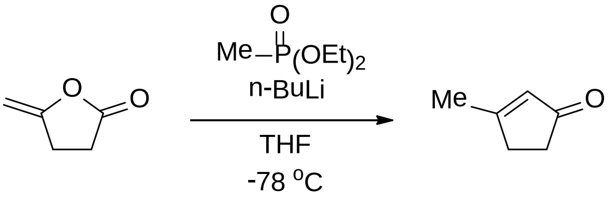

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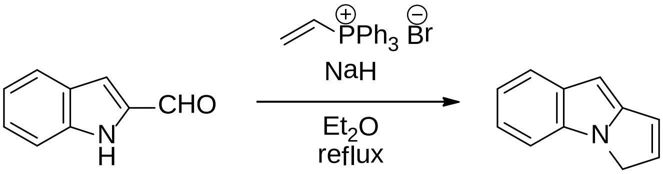

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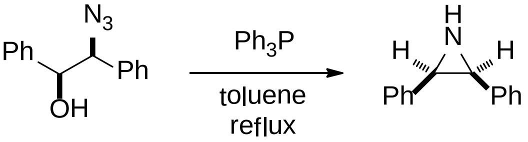

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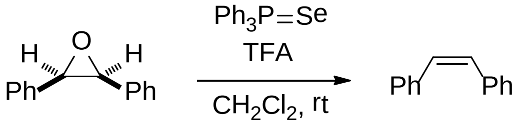

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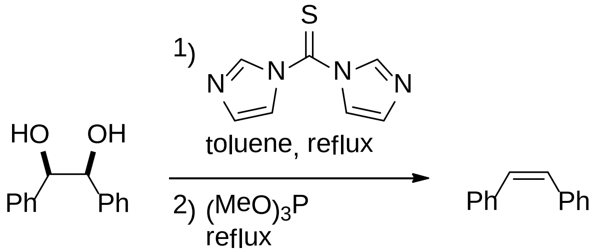

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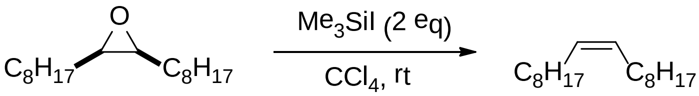

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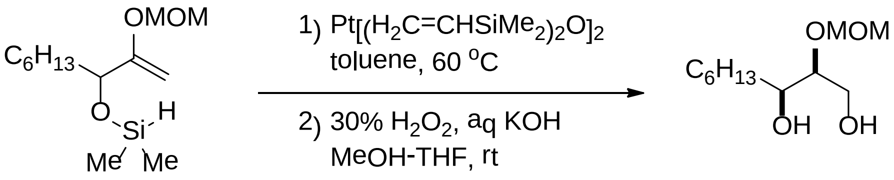

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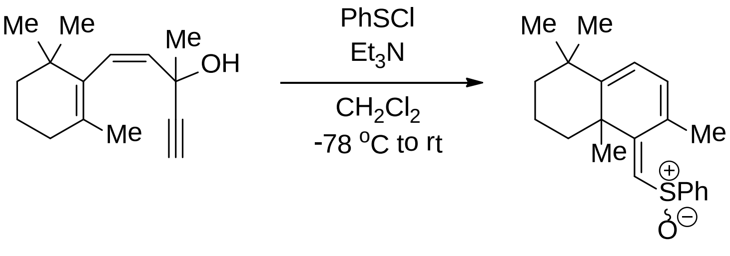

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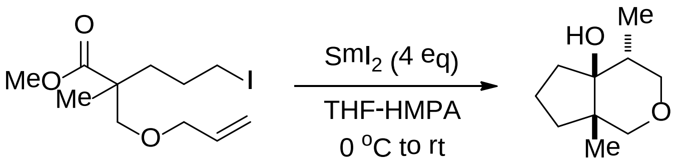

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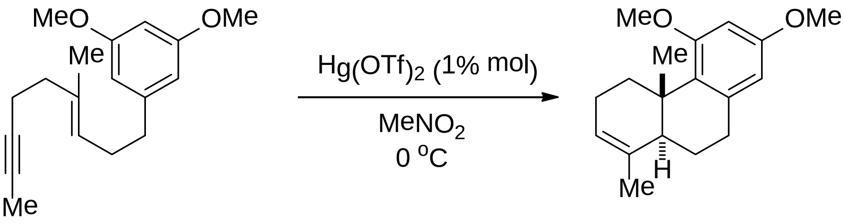

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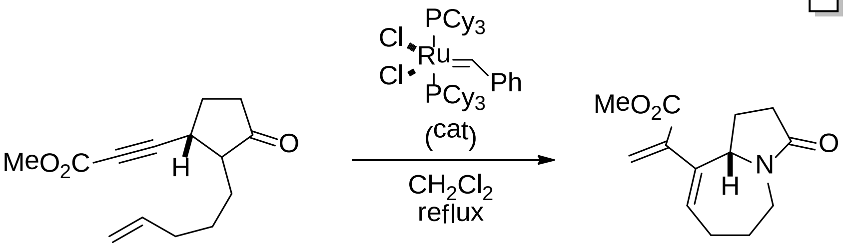

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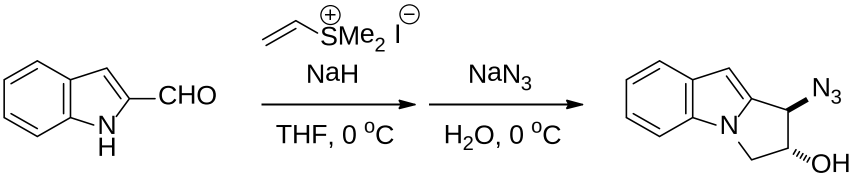

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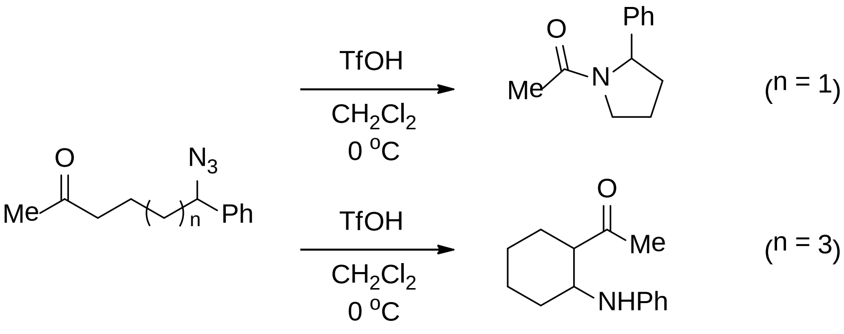

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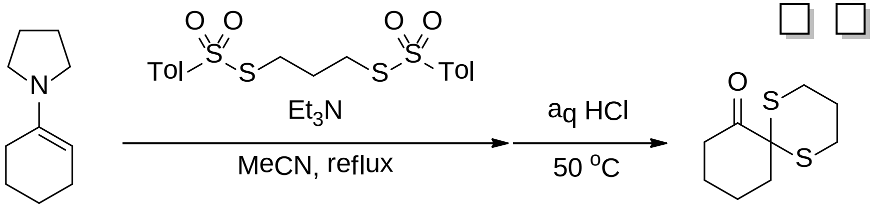

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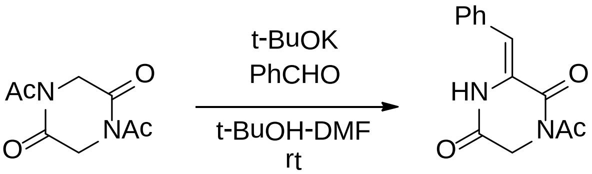

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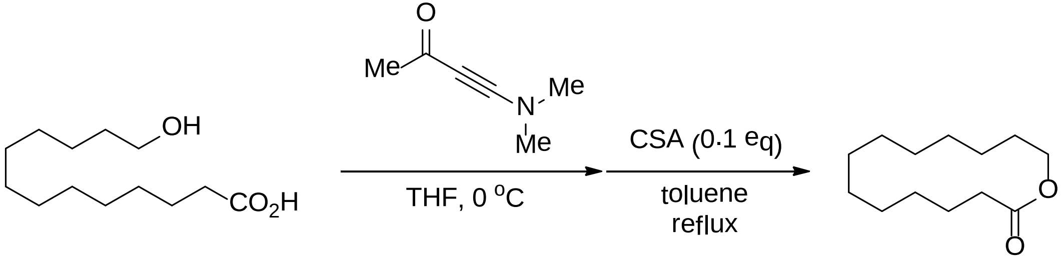

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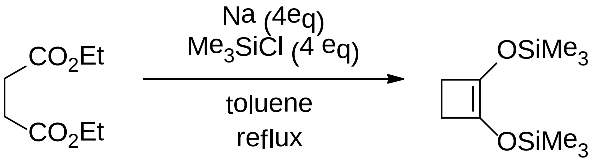

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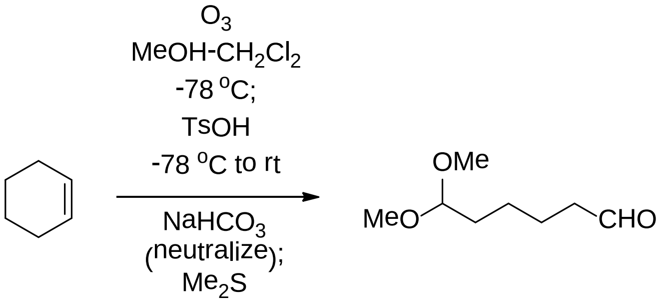

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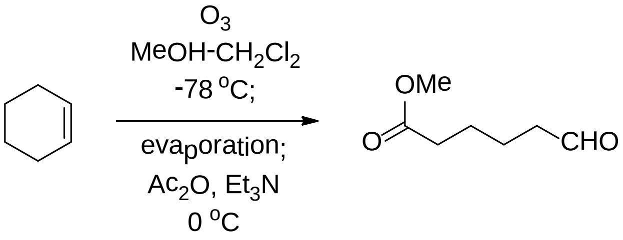

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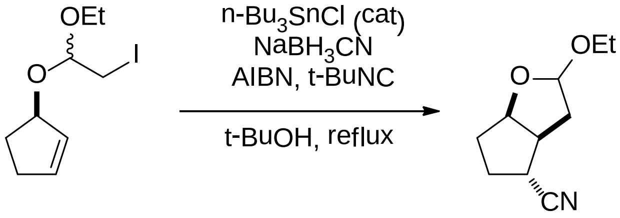

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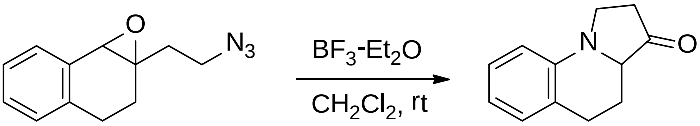

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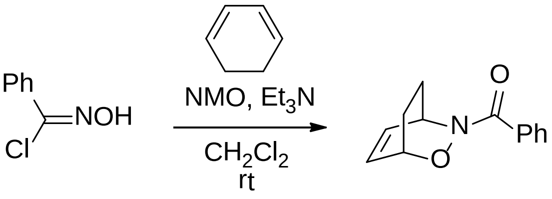

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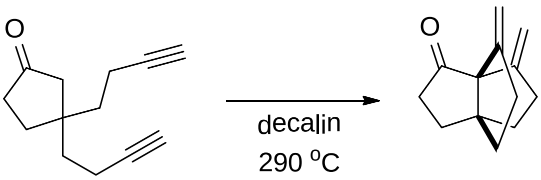

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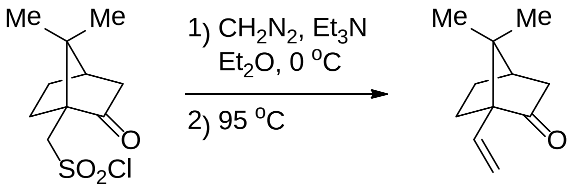

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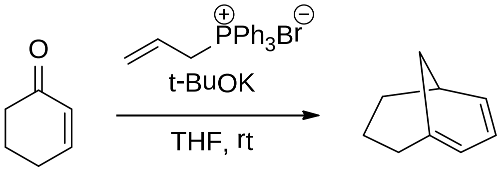

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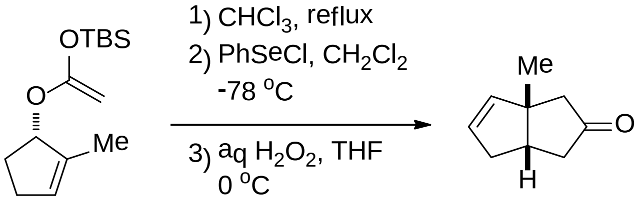

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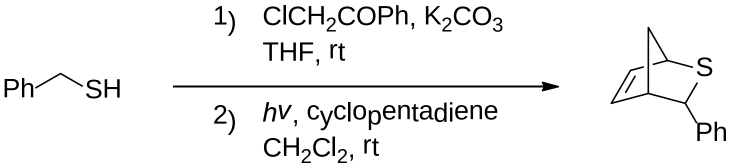

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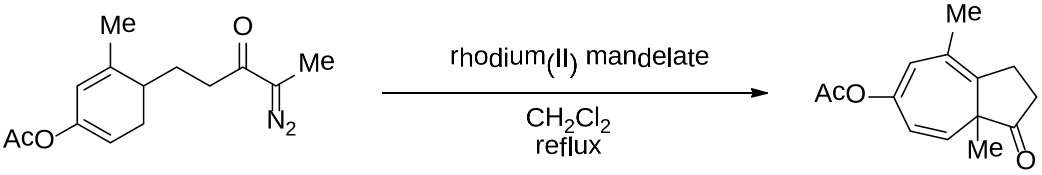

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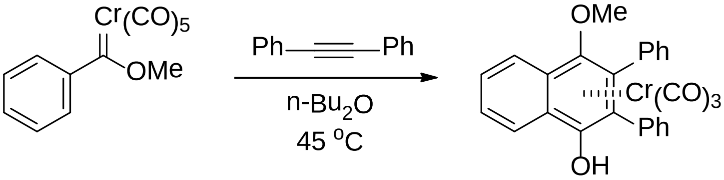

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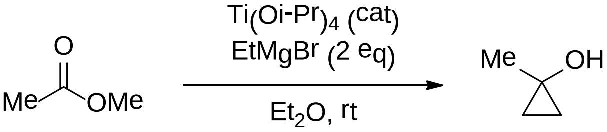


◆コラム②◆

問題き解くコッ

　反応機構の问題を解くにあたって付録にも述べたような基礎的な化学の知識が重要なことはもちろんであるがそれ以外にもちよっとした］ツがある

①構造式をしっかりと書くこと

　有機化学は構造式のおかげで比較的手軽に．あたかも目の前で起こっているかのことく紙の上に書き下すことが可能な学問であるそこで問題を解くにあたっては．ます頭のなかで考えたことをどんどん紙に書いてみる実際に構造を目にすることで次の一手が見えてくるものであるまた．構造はできるだけ丁寧に書くべきである分子が大きくなってくると構造式を省略して書きがちであるが． 実際の合成では分子全体を考えて反応条件を選択しなければならないので．つねに分子全体を見るトレーニングにもなる．

　中间体に関しても一つすつ丁寧に書くことをお薦めする頭のなかで反応機構を進めてしまい．実際に出発物と生成物のみしか書かない習慣が身についてしまうと．少し変わった反応が起こるときに．重要な分岐点となる中間体を見逃してしまうまた＊つの構造式で多くの矢印を書き反応を進めてしまうことも，同じ理由で危険をはらんでいる一つの中間体につき三つの矢印くらいが適当である．

②反応剤を知っておくこと

　まったく知らない反応剤が使われている場合，その問題を解くことは難しいので，反応剤についてはやはりある程度の知識が必要であるしかし辞書的ににの反応剤を使うとコレができる」というように結果だけを覚えるのではなく．ますはその反応機構（矢印）を書いてみることが重要である反応剤が反応機構で分類されていると．知らない反応剤にでくわしてもその働きを類推することができるようになる

　またわからない反応剤について調べた際には．目的の反応だけではなく． できるだけ視野を＊くもち．さまざまな使い方を勉強強る癖をつけておくと．日々の実験にもおおいに役立つ

③多くの可能性を考えること

　実際の反応機構は単純な一本道ではなくある分岐点ではいくつもの可能性が考えられるさまざまな局面でいかに多くの可能性を考えられるかが＊つの実力でありまたその多くの選択肢に対しどのように優先順位をつけて反応機構の考察を進めるかが重要である．分岐点での判断が不適切であるとわかった場合．そこに戻り次の可能性から考察を進める

の分子の構造を精査すること

　出発物と生成物のどことどこが対応しているかを分析することも．問題を解く重要なヒントになるまた生成物から条件を逆にたどっていき．中間体を予測するほうが簡単な場合もある

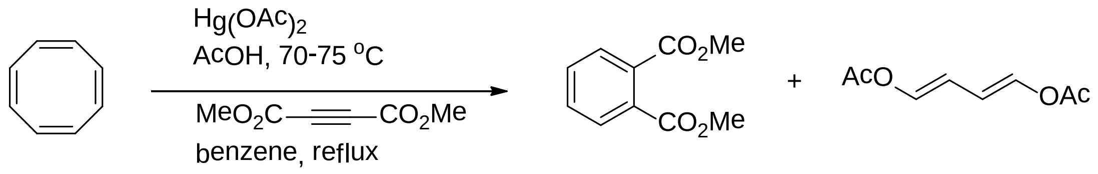
ノシ反応点からの数を数えてみよう

　問題を解いていて，ふと詰まることがあるそんなときは数を数えてみよう＊つの反応点から数えて．五つ目か六つ目の原子に＊＊する反＊点があれば． そこで分子内反応（分子内関与）が起こることが多い当研究室ではそのような問題で困っている学生がいると，「まだ幼稚園を卒業できないな」といわれてしまう幼稚園生でも数ぐらいは数えられると．

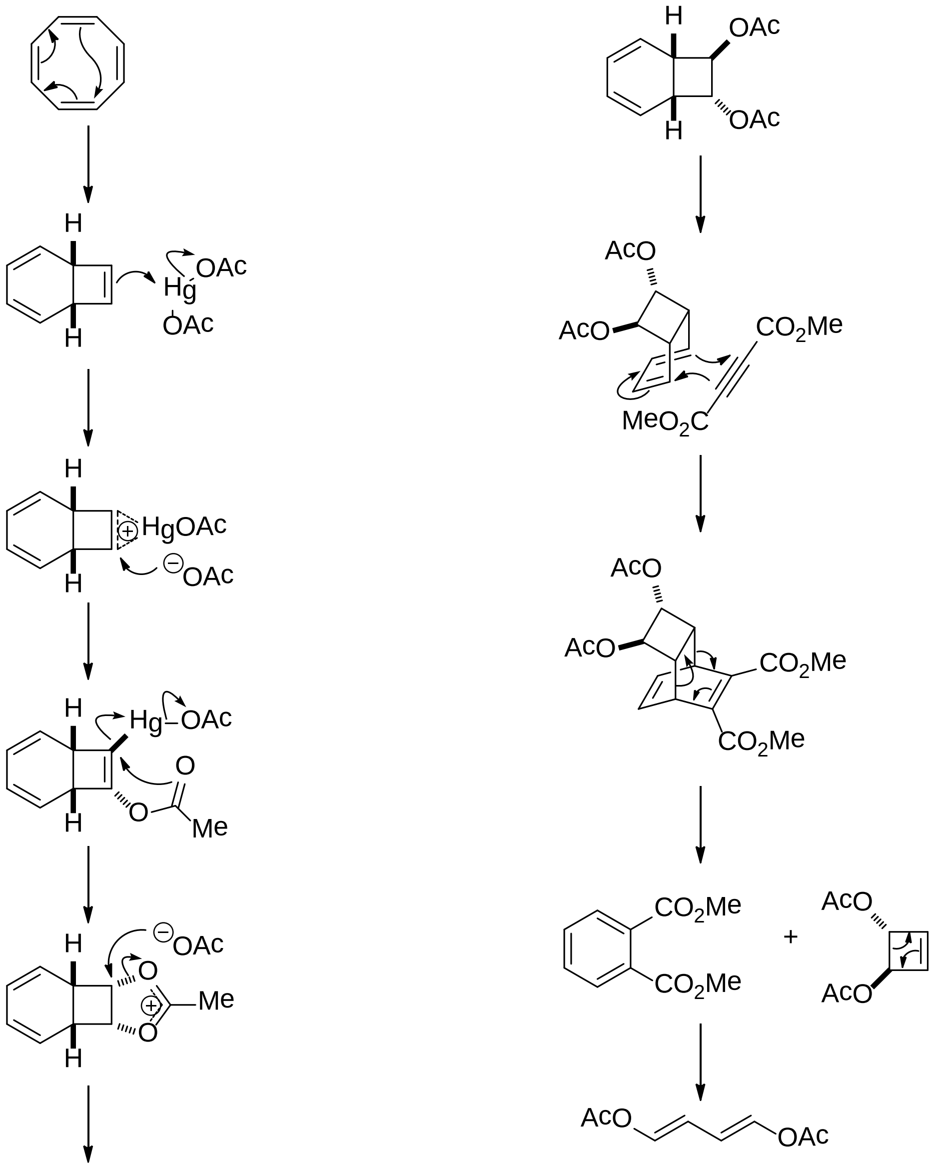
問題　上级編

上级编では，歴史的に有名な反応から最新の論文まで，手応え十分な問題を収載してある，しかしいすれも基本に忠実に解いていけば，解答に到達できるものばかりである．問題の順番は分野に関係なく完全にランダムに配置してあるが．おおよそ難易度順に配列してある．一つ一つ着実に，くじけることなく何度でも挑戦してほしい．

例 题 Provide reasonable arrow-push mechanisms for following recations



解 答



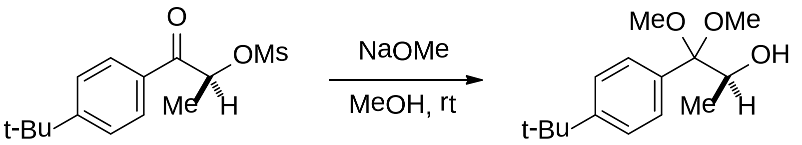
Noller, C. R;Dinsmore, R. *Org. Synth. Coll.* vol Ⅱ **1943**. 358

问 题 Provide reasonable arrow-push mechanisms for following recations

Check Box

C001

☐ ☐ ☐



C002

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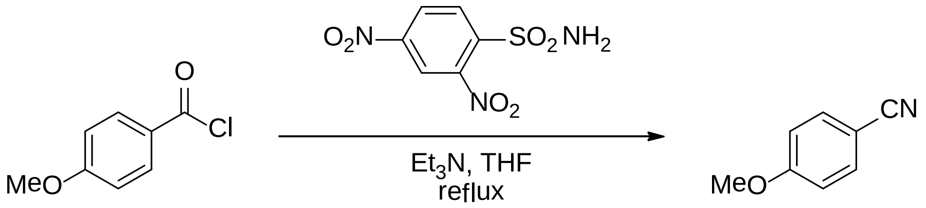

C003

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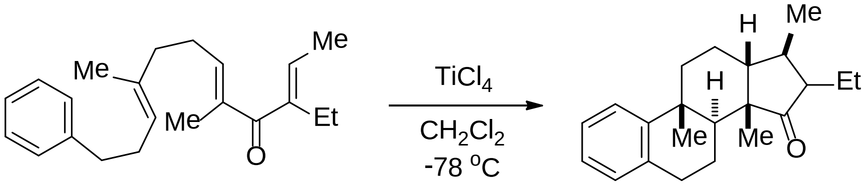

C004

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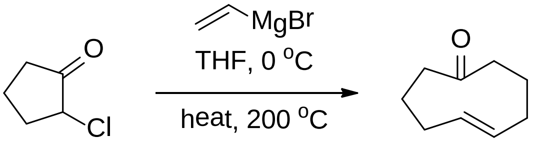

C005

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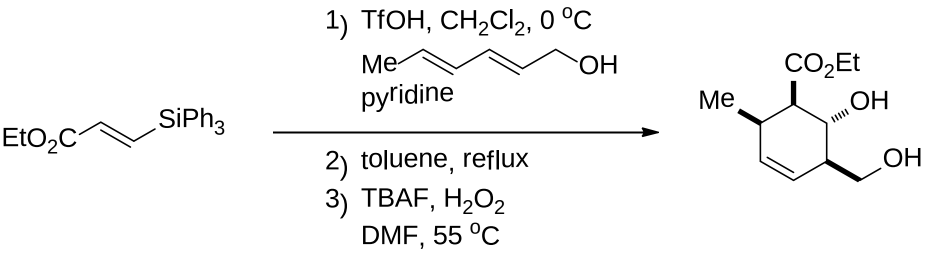

C006

Check Box

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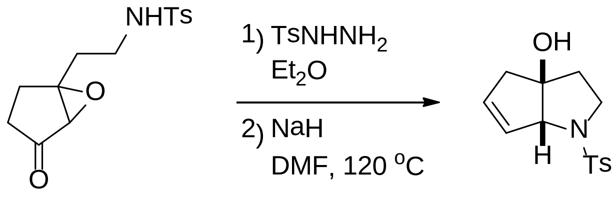

C007

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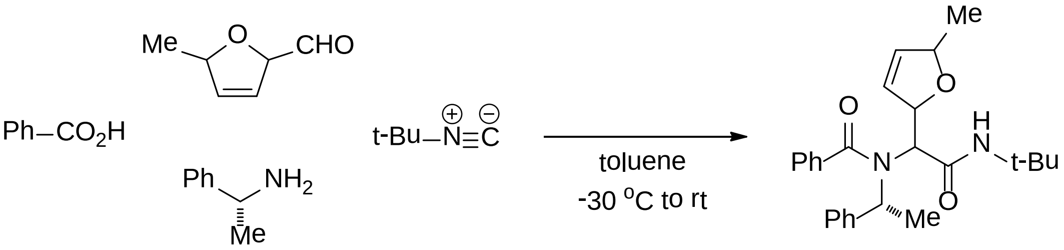

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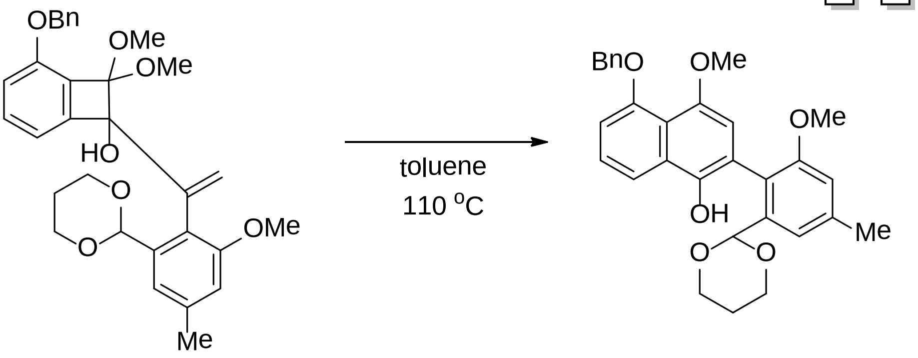

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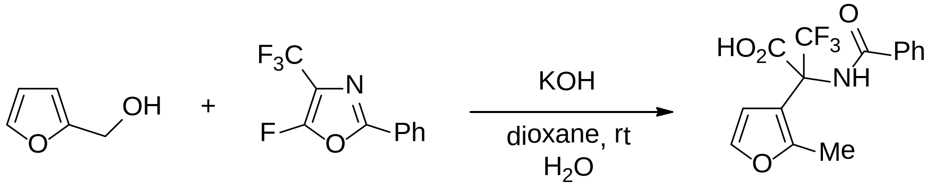

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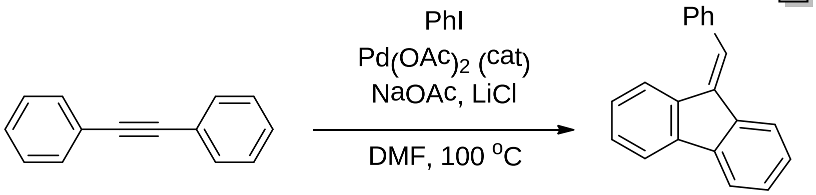

C011

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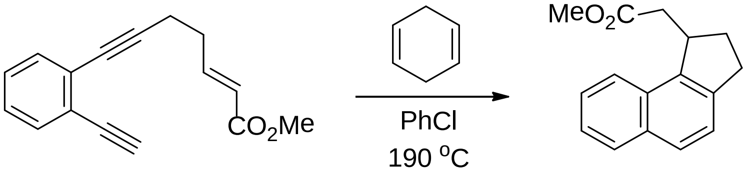

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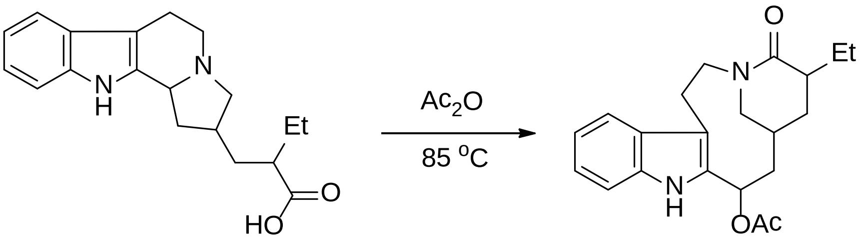

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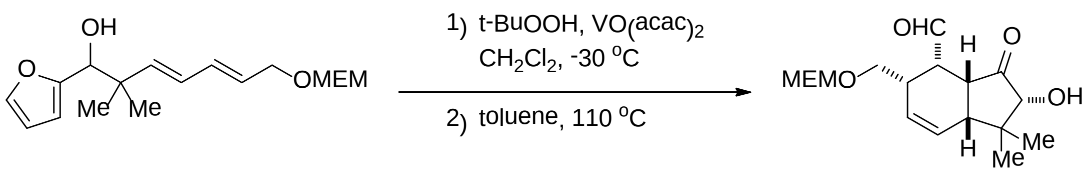

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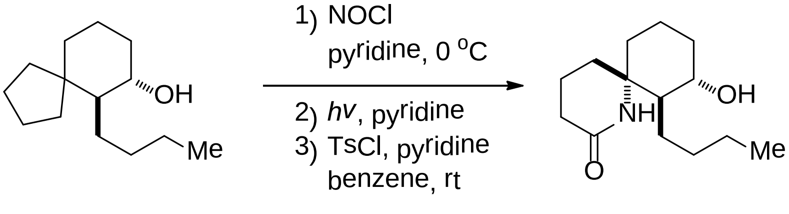

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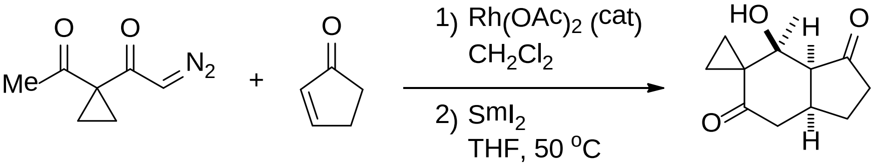

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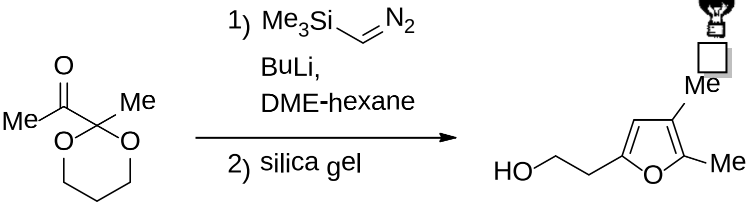

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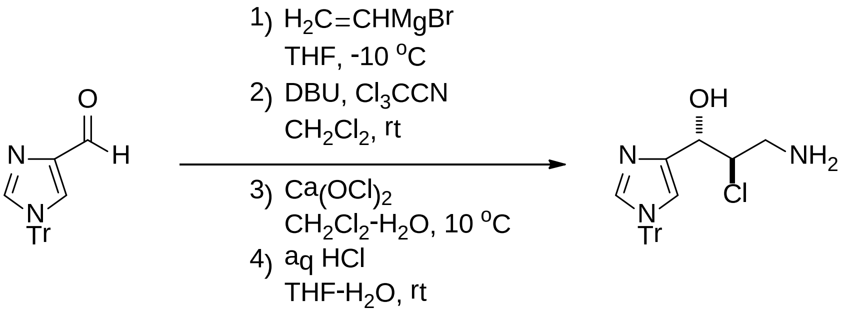

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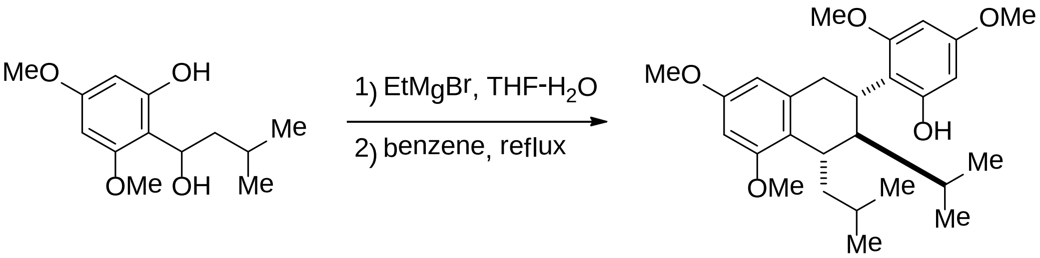

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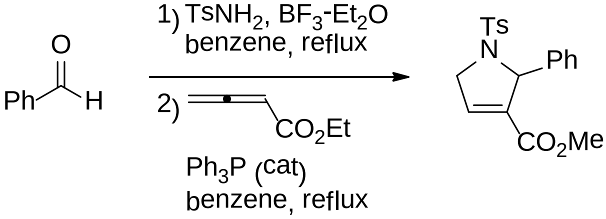

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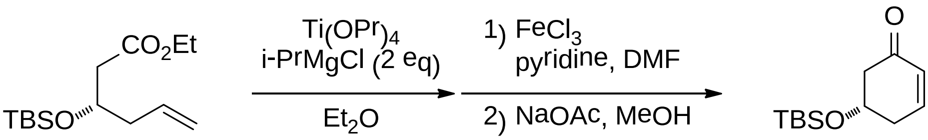

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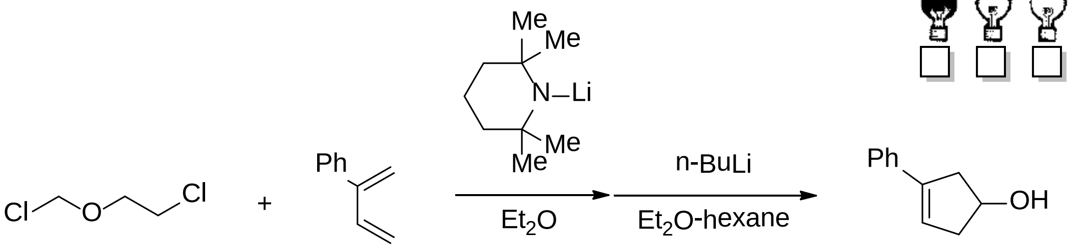

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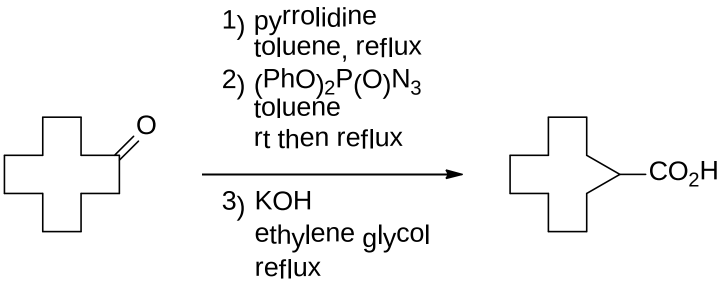

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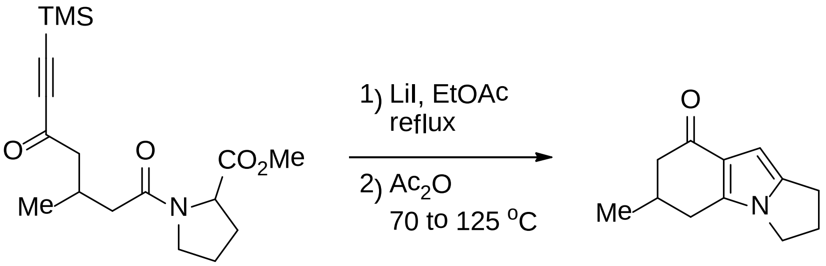

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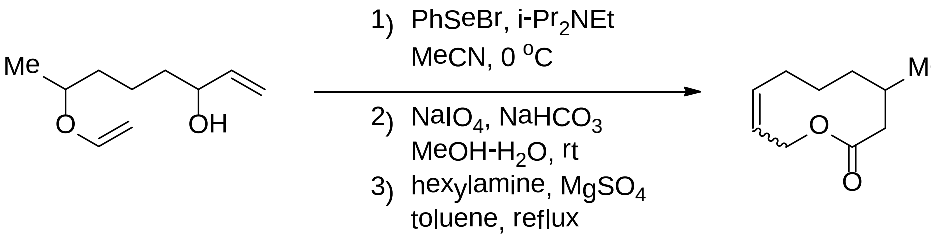

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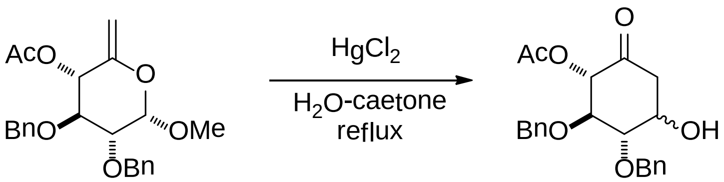

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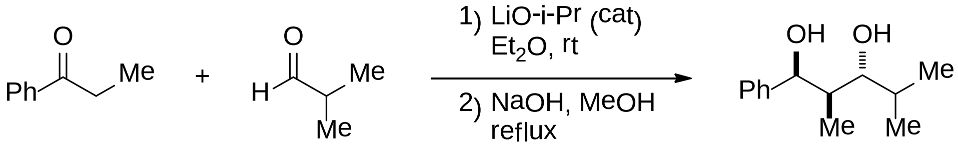

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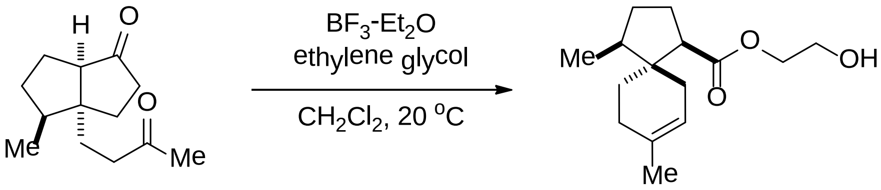

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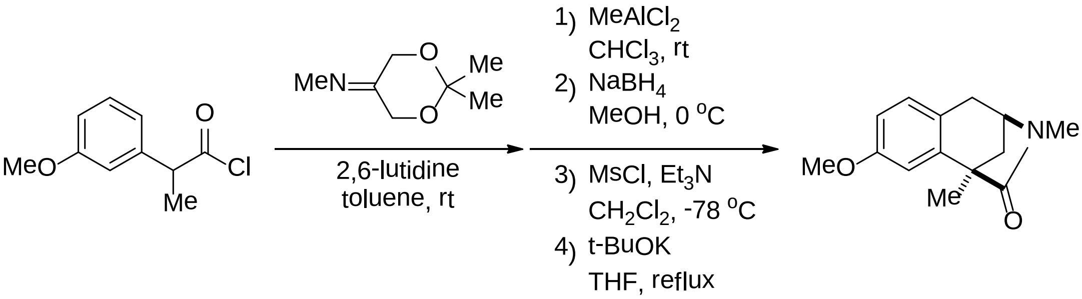

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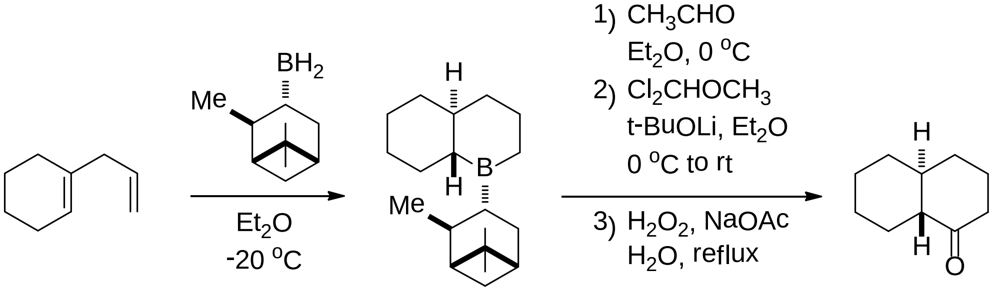

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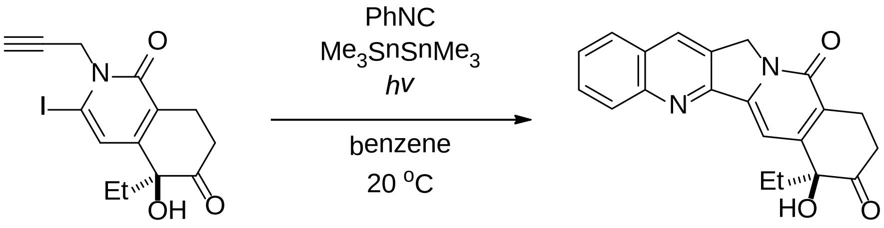

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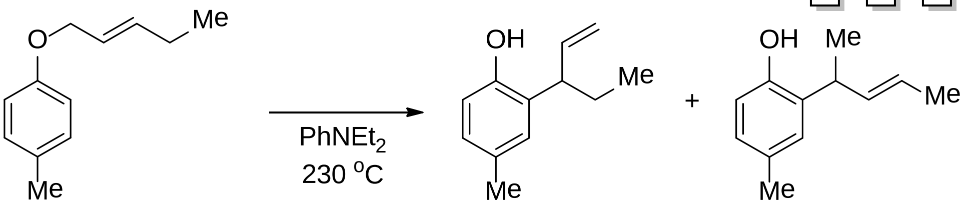

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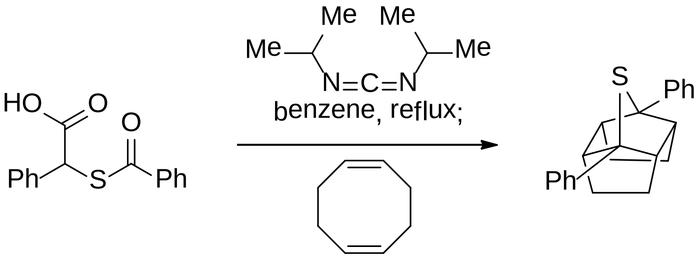

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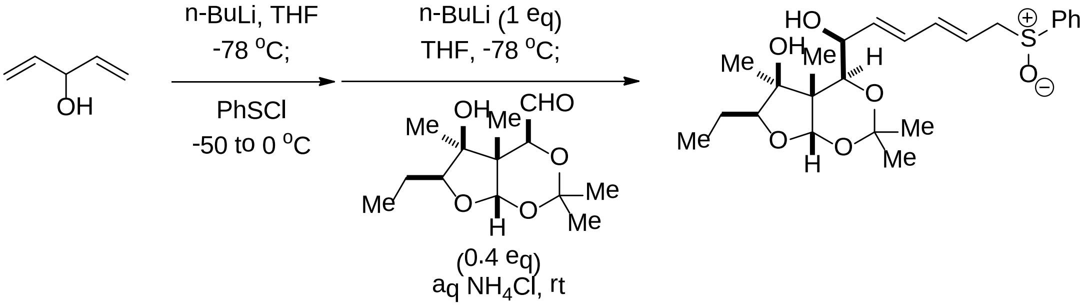

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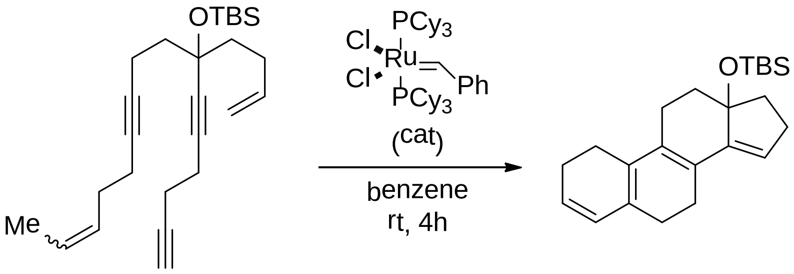

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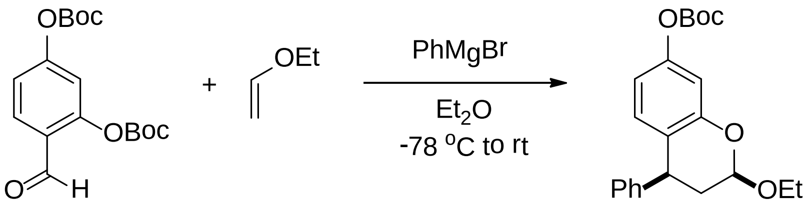

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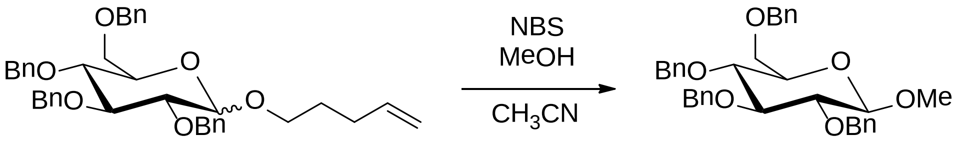

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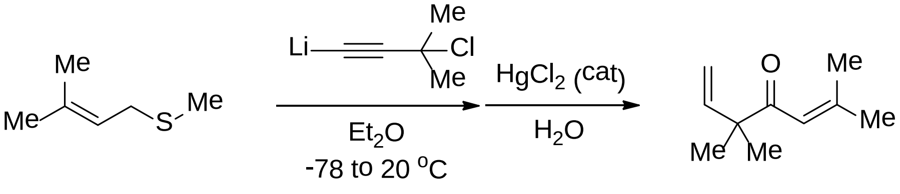

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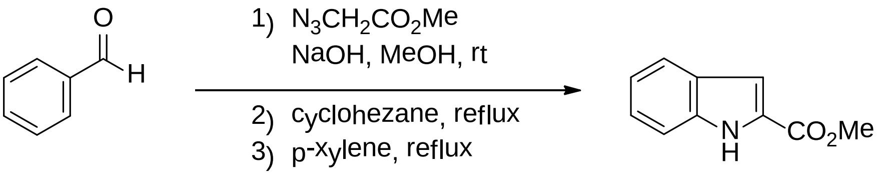

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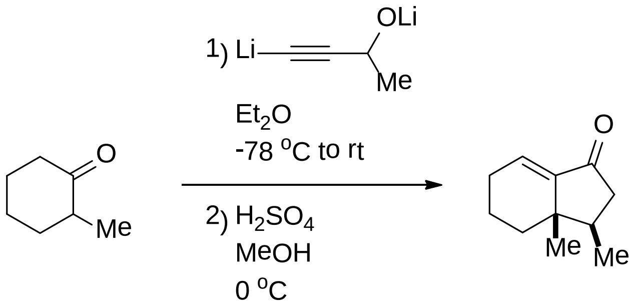

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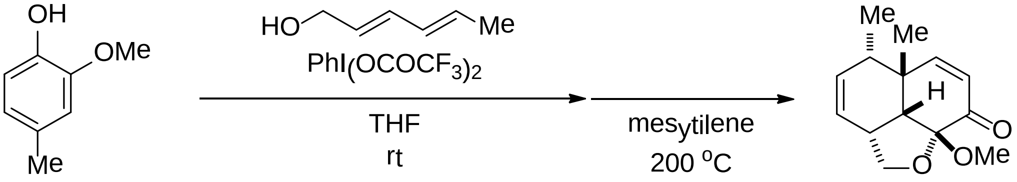

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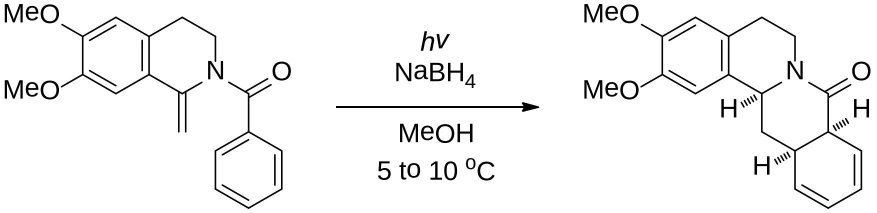

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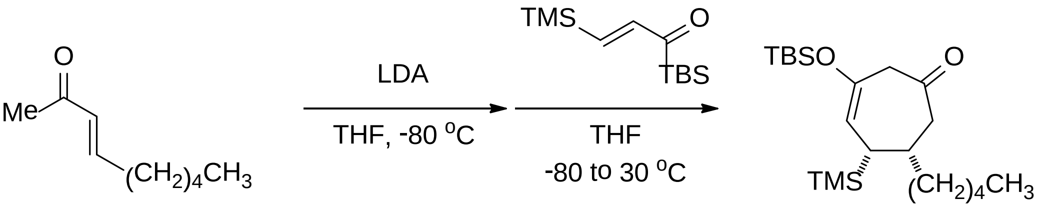

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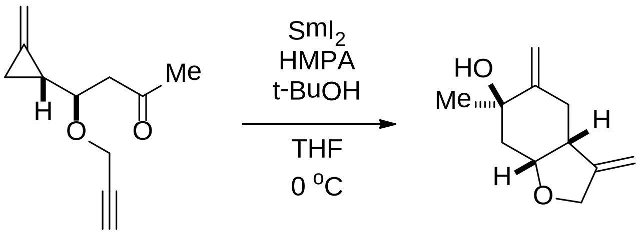

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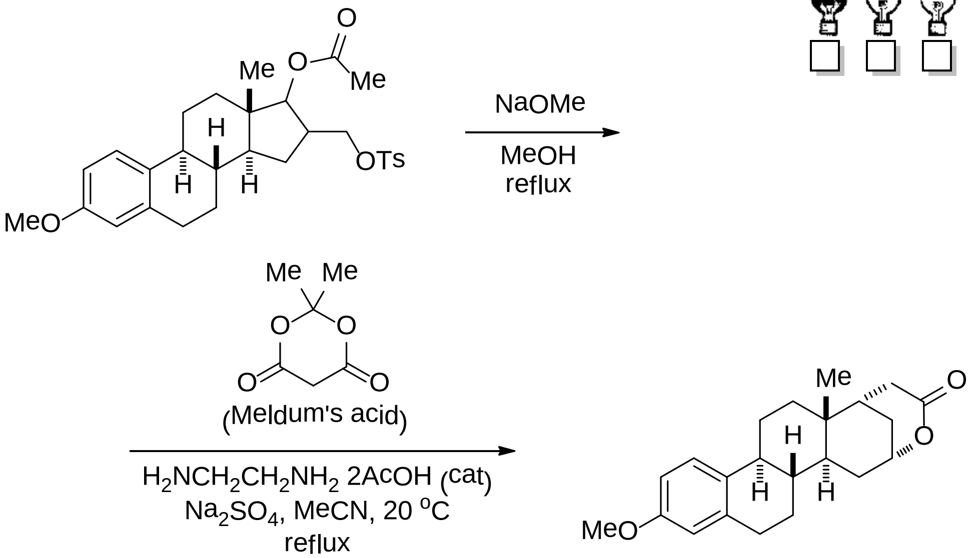

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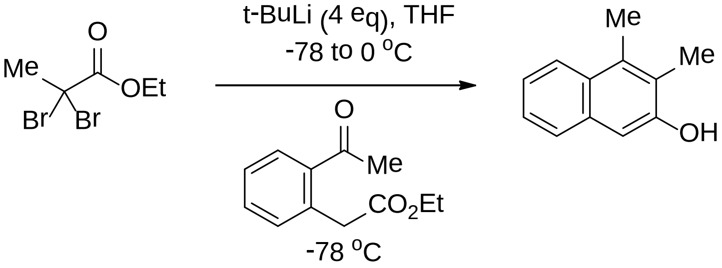

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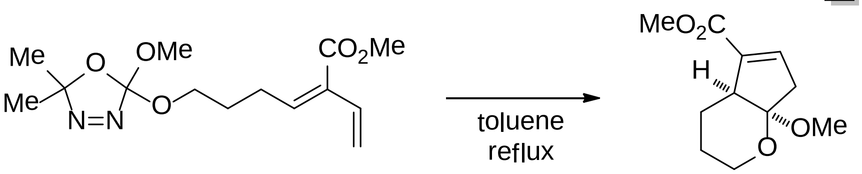

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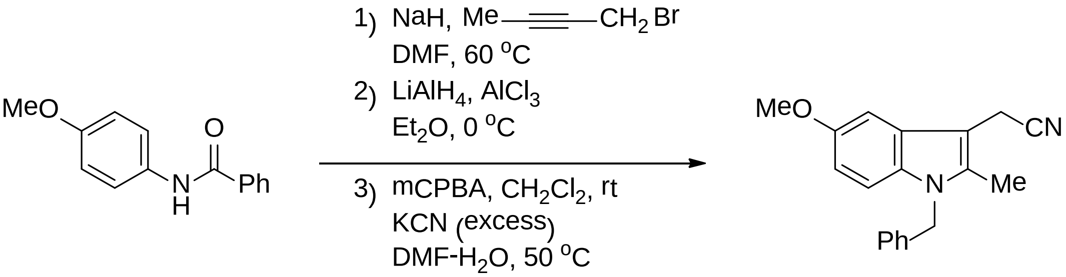

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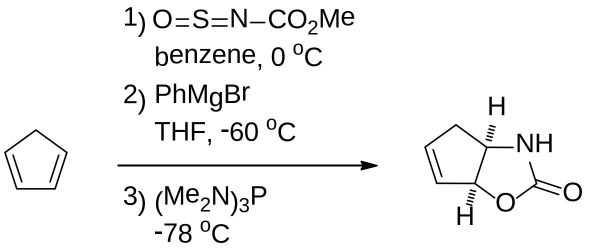

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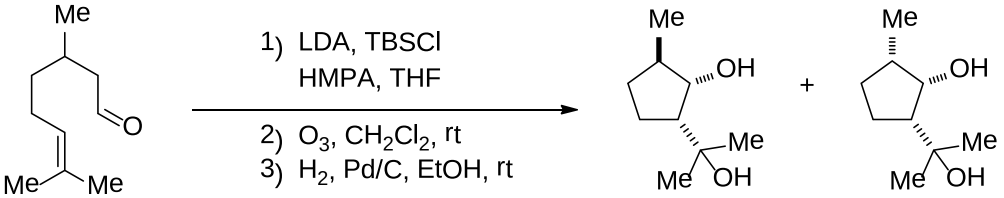

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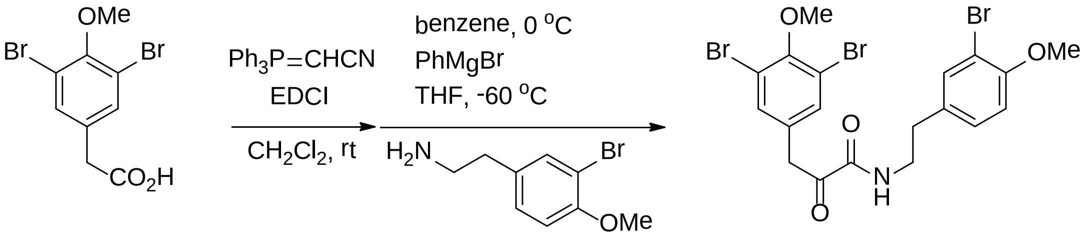

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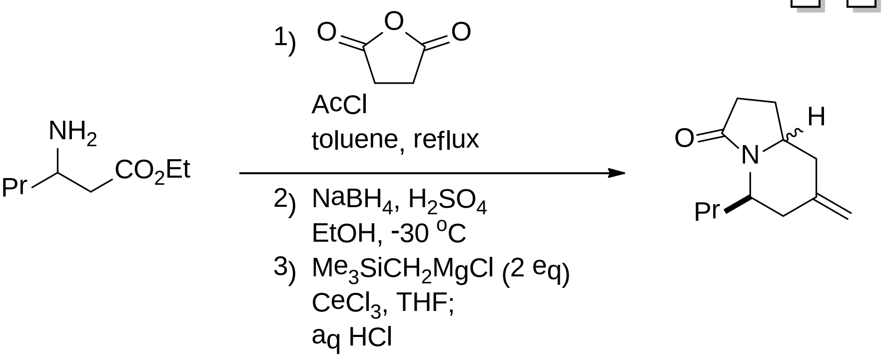

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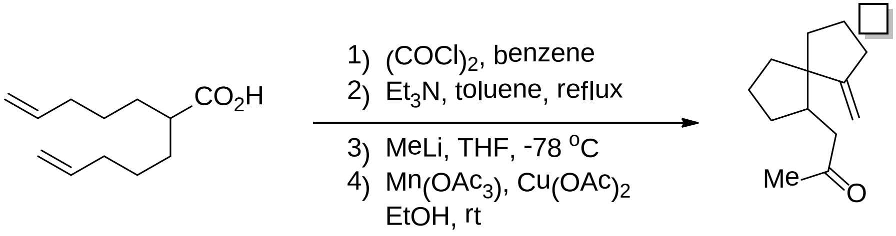

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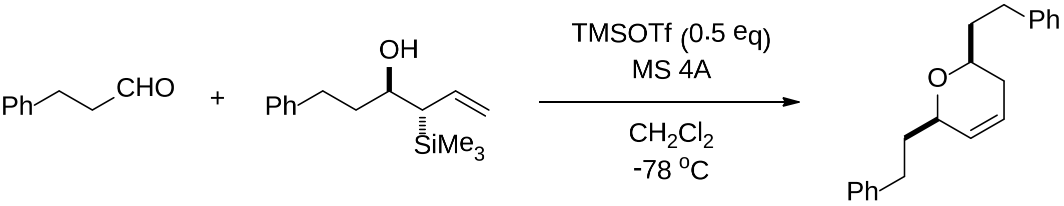

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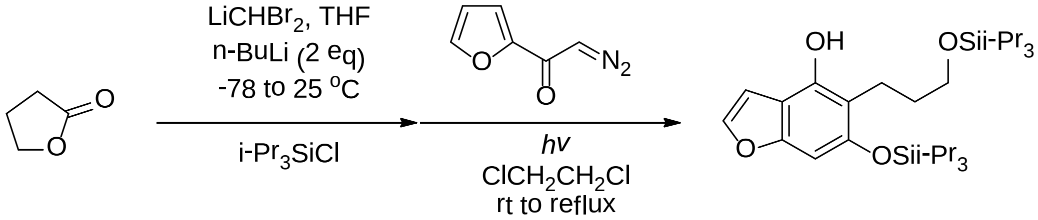

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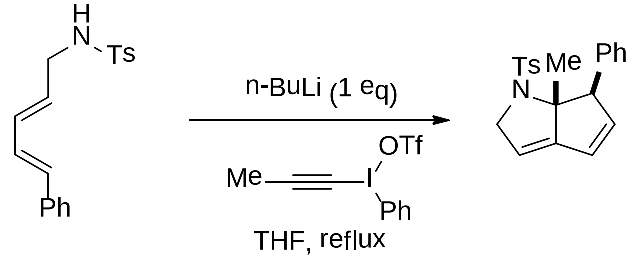

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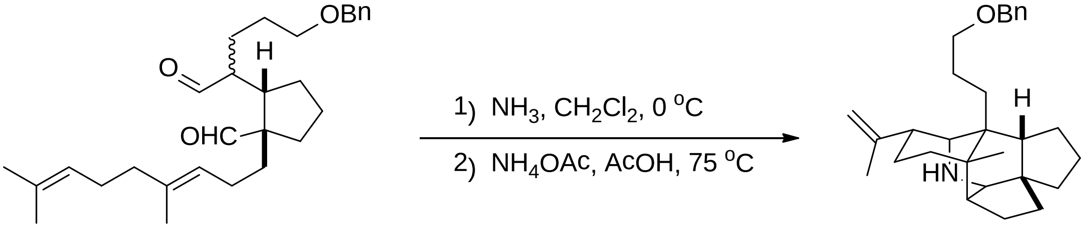

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C057

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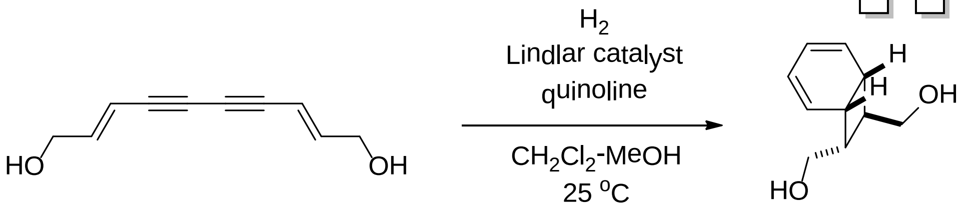

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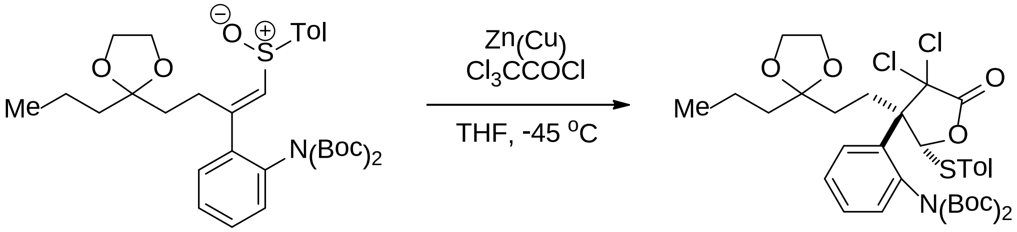

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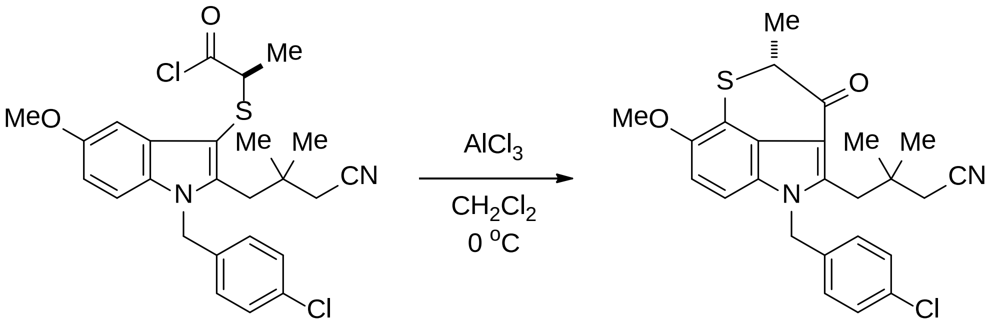

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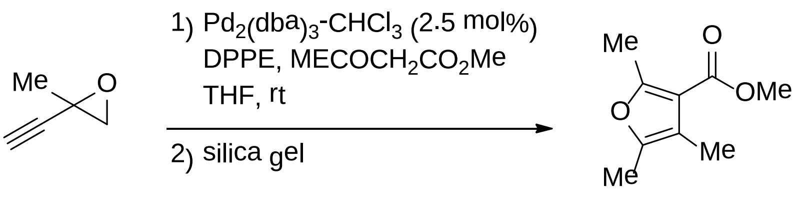

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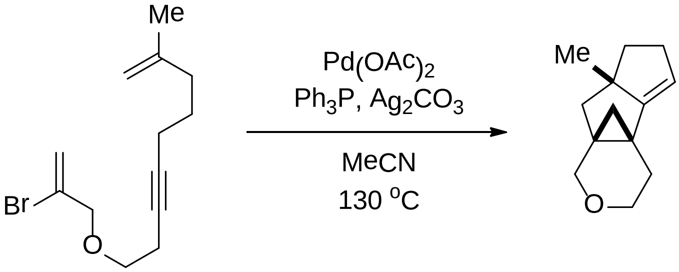

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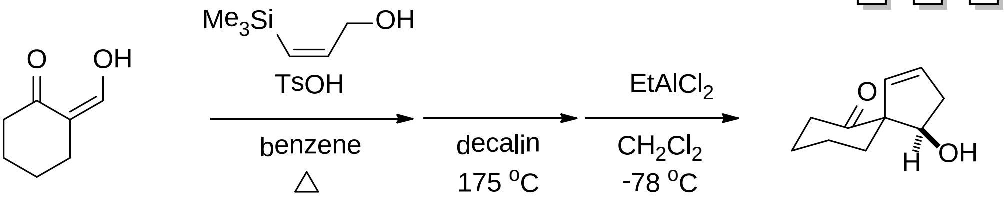

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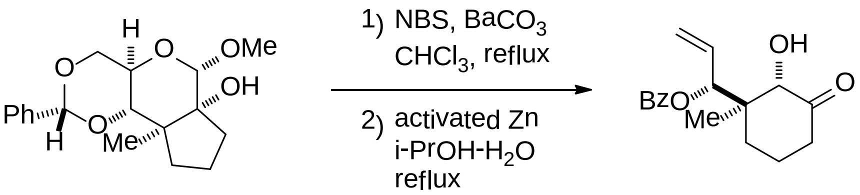

C064

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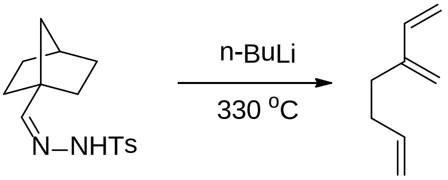

C065

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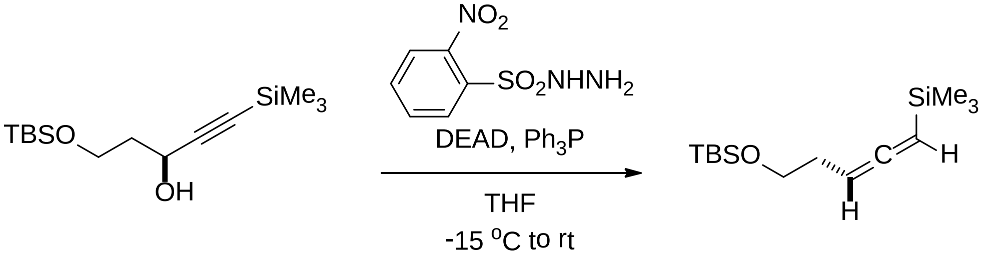

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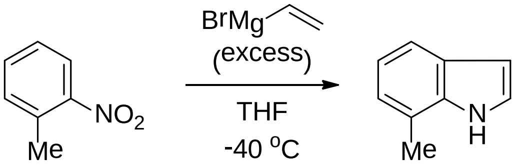

C067

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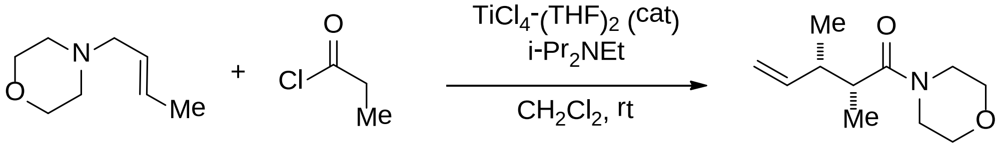

syn : anti = >99 : 1

C068

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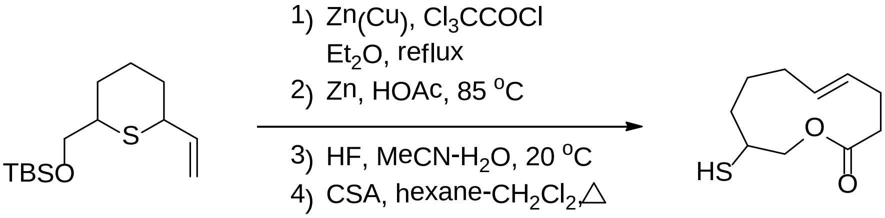

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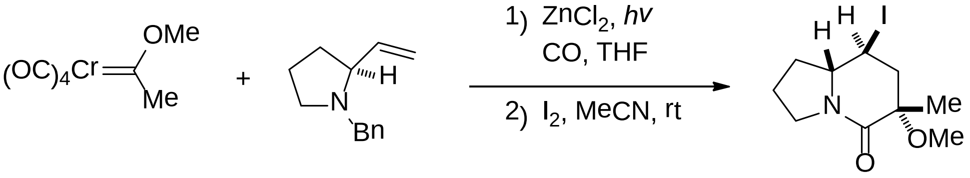

C070

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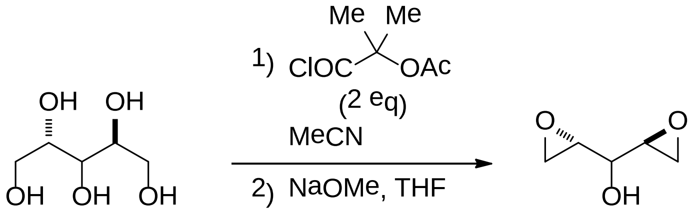

Check Box

C071

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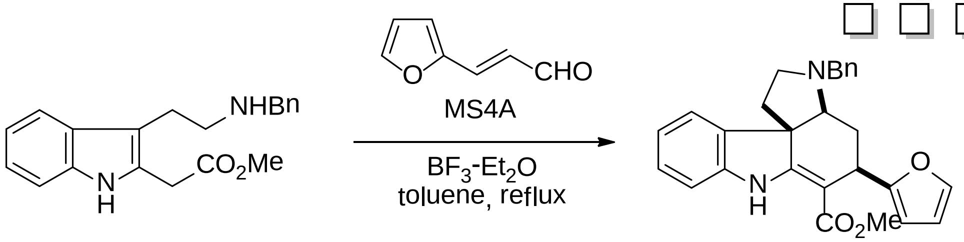

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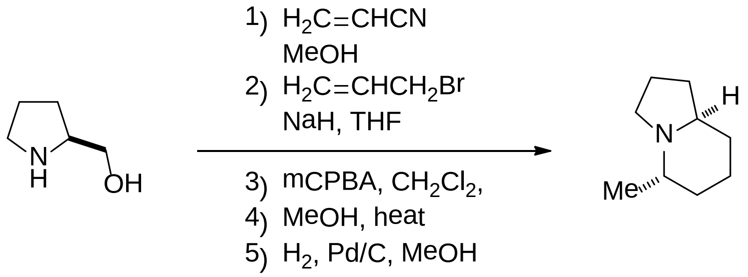

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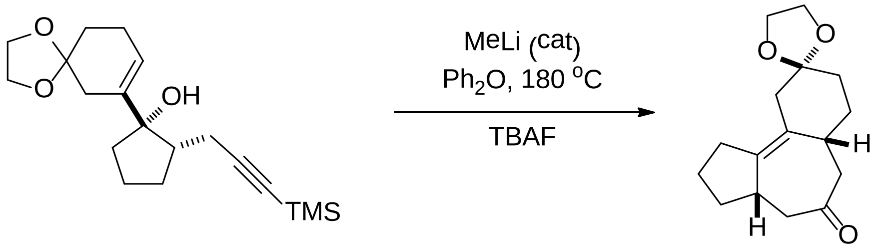

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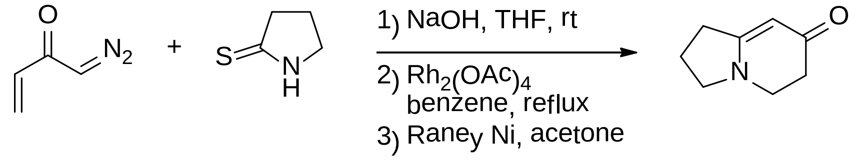

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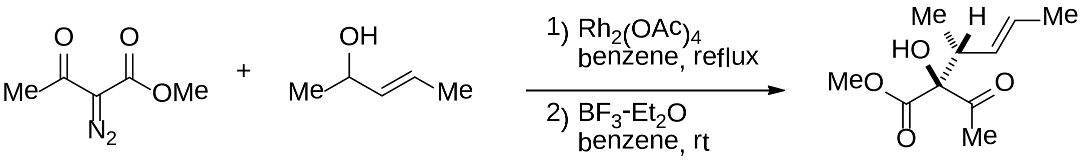

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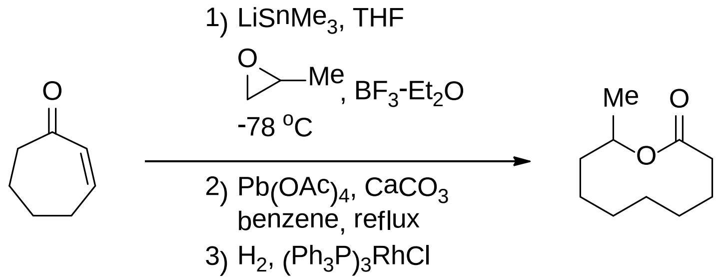

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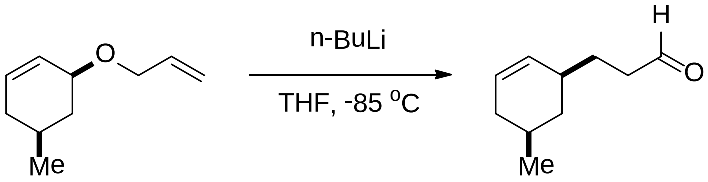

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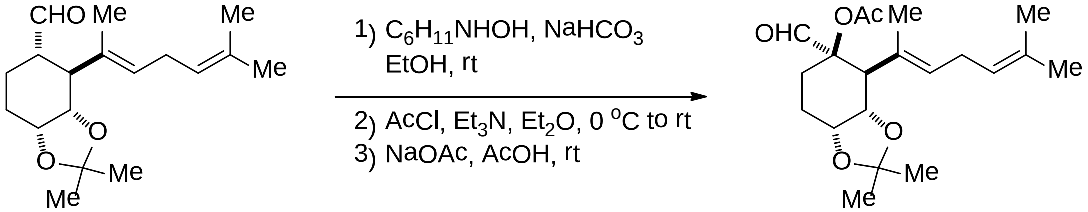

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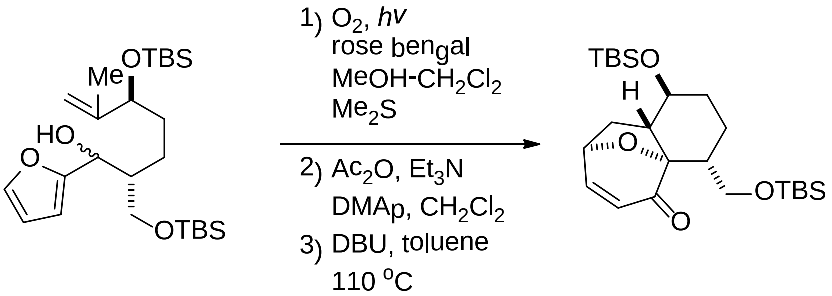

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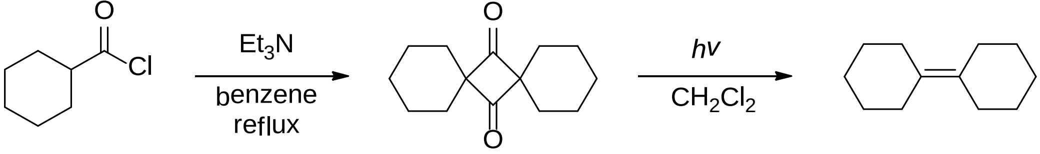

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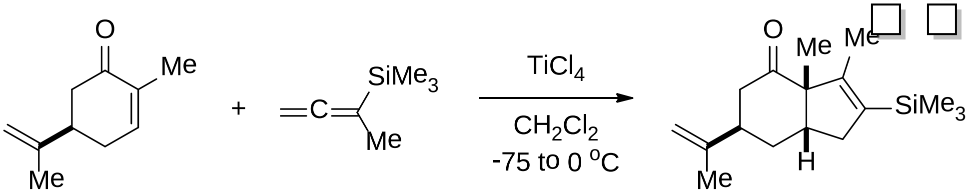

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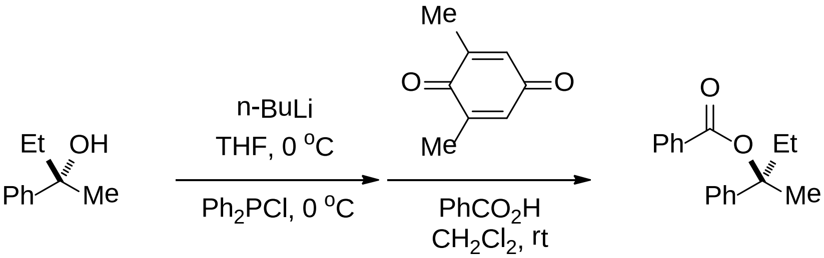

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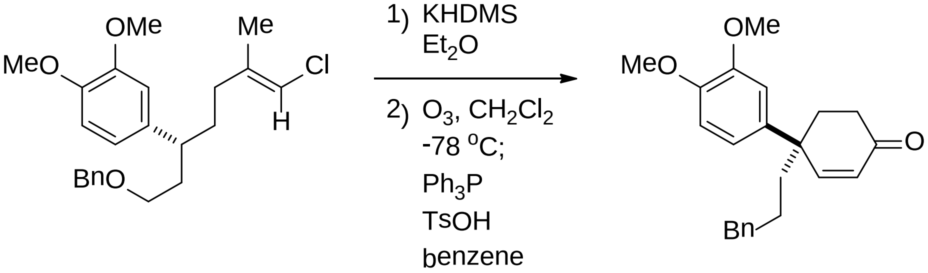

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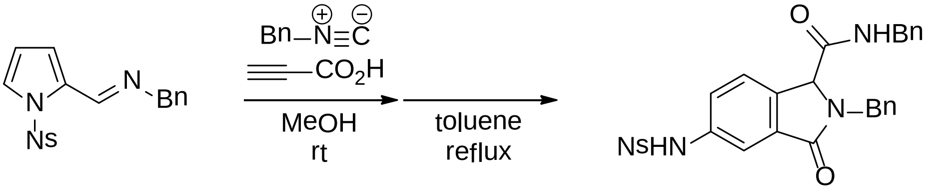

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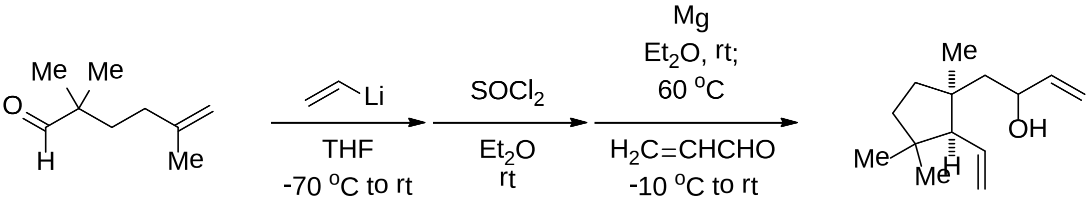

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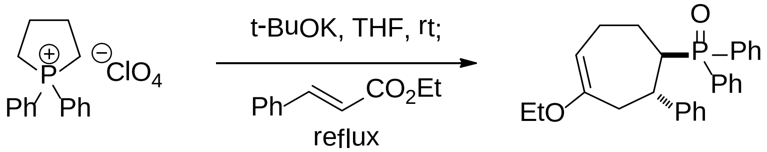

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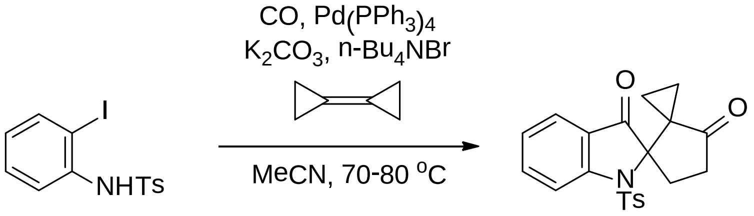

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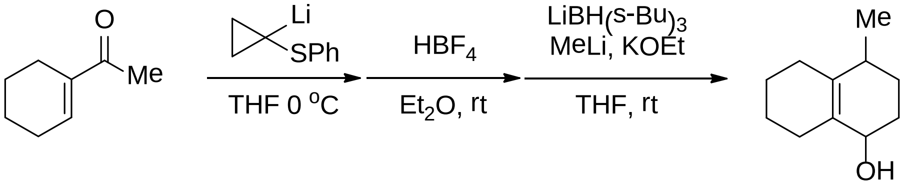

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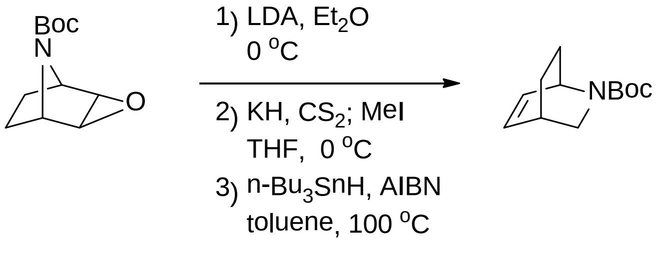

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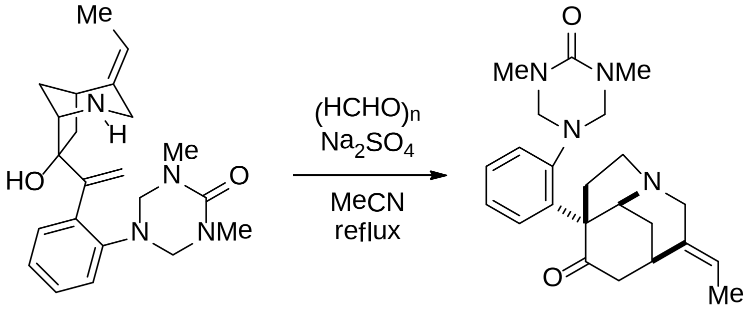

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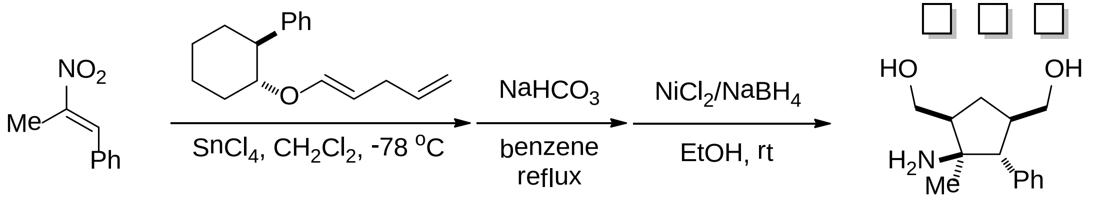

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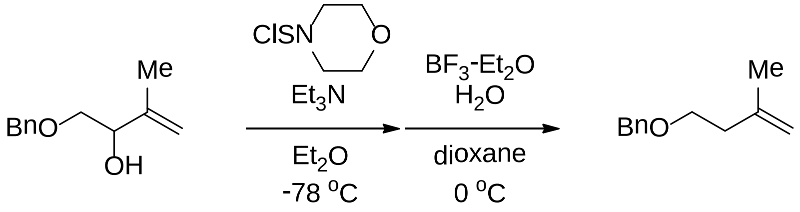

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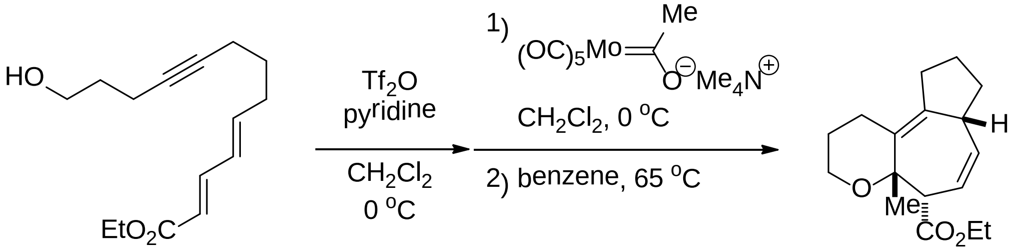

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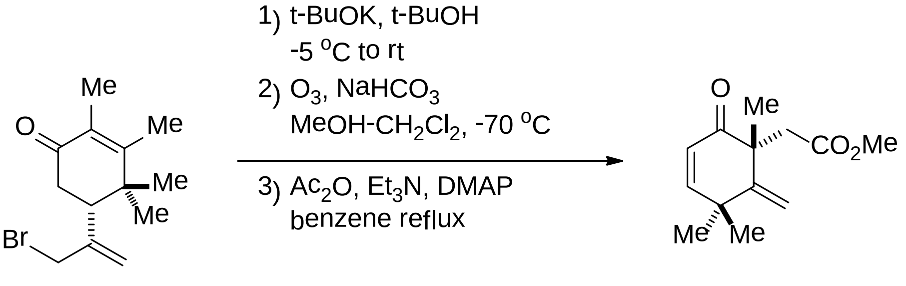

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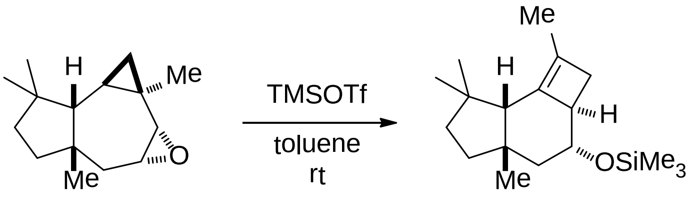

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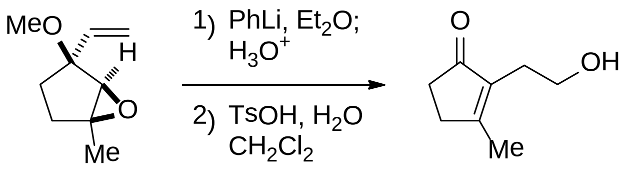

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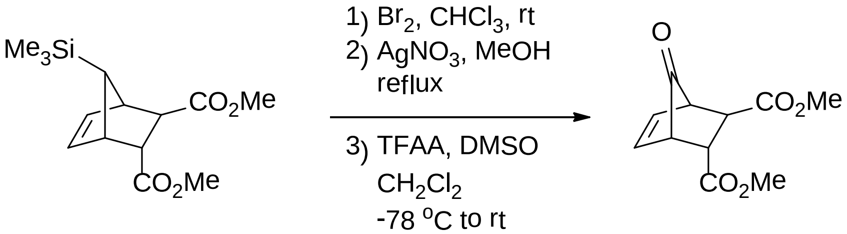

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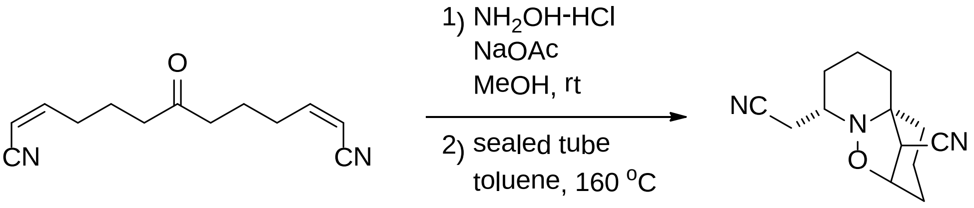

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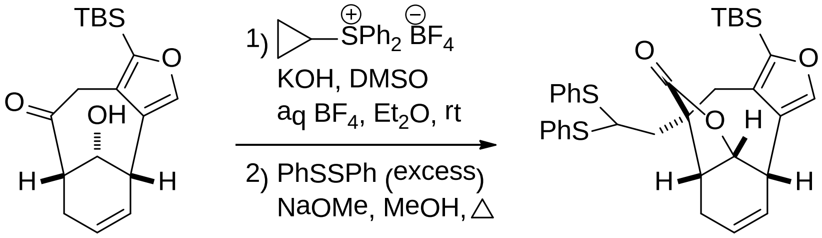

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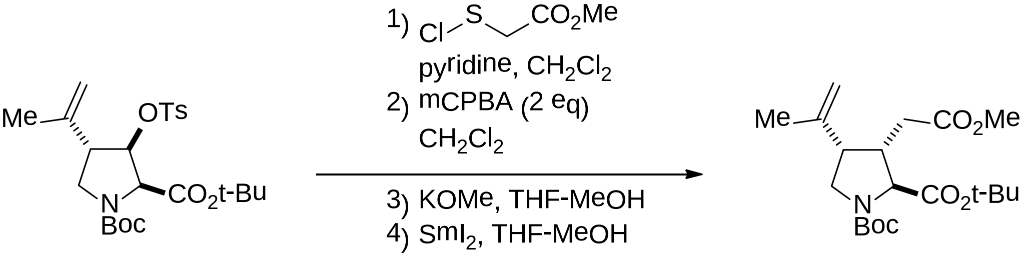

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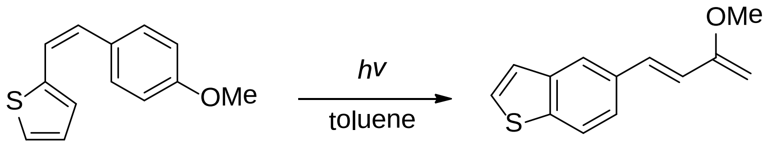

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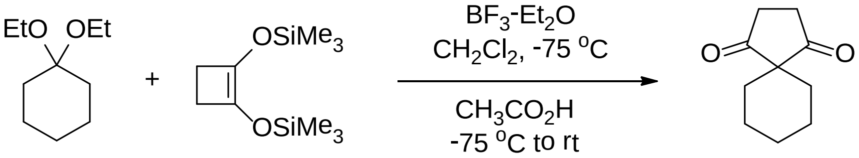

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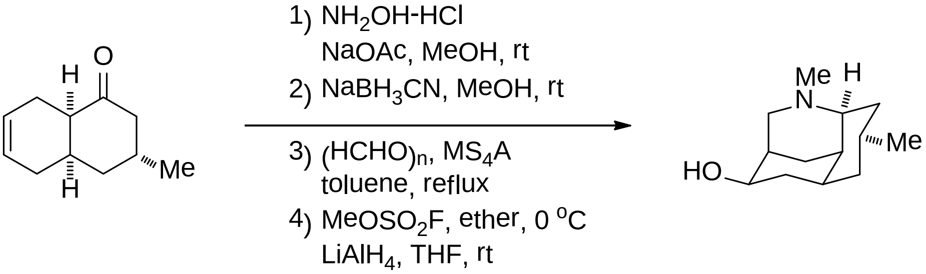

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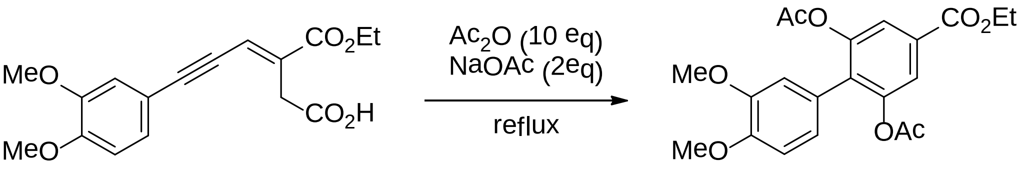

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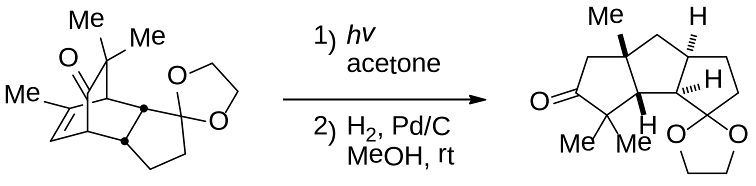

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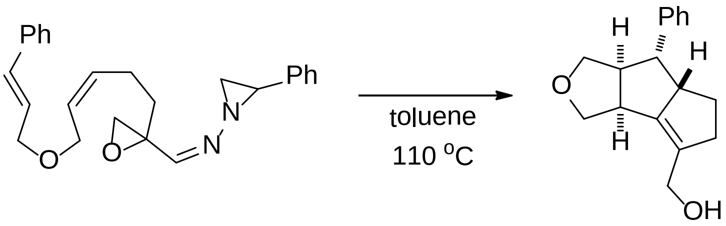

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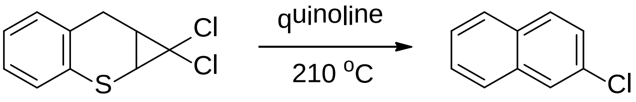

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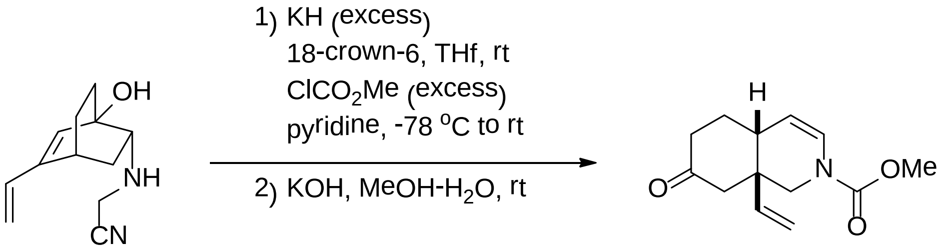

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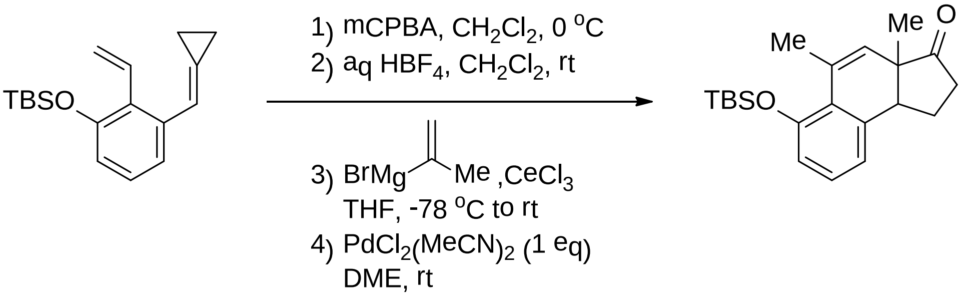
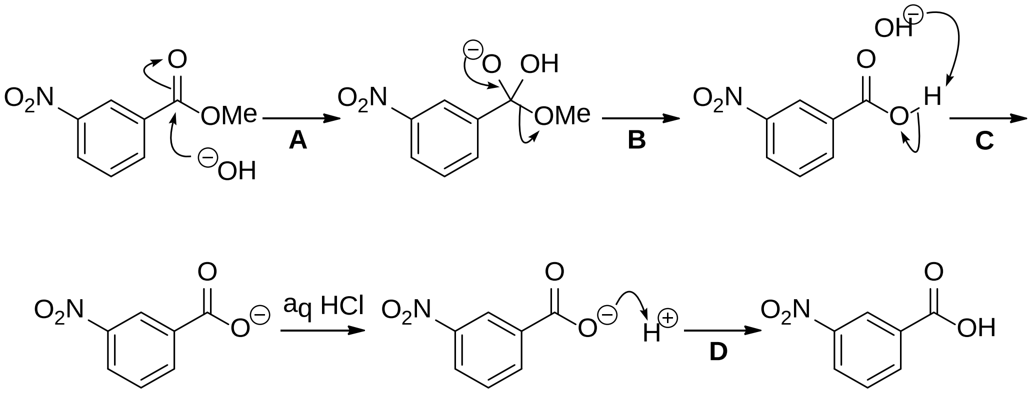


解答　初级編

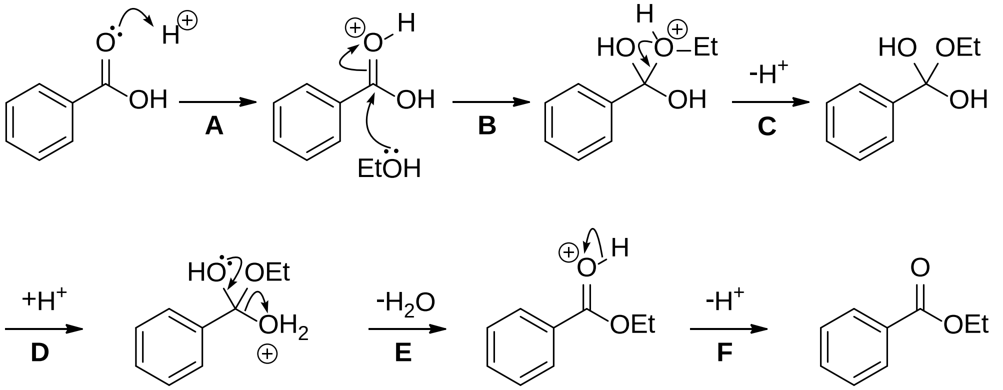
A001



Kamm, O.; Segur, J. B. *Org. Synth. Coll.* Vol. I **1941**, 391

A: Addition of hydroxide ion to the carbony group to form a tetrahedral intermediate. **B** : Elimination of methoxide ion helped by the oxygen lone pair. **C**: Deprotonation. pKa AcOH = 4.8, H_2O = 15.7. **D**: Protonation on work-up. pKa H_3O^+ = -1.7.

A002



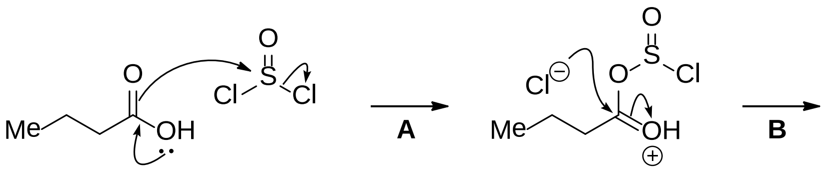
Fischer, E.; Speier, A. *Ber. Deut. Chem. Ges.* **1895**, 28, 3252

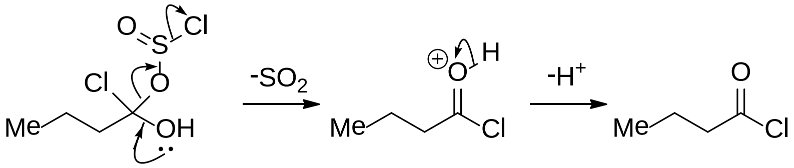
A: Activation of the carbonyl group by protonation. **B**: Addition of EtOH to the activated carbony group.

C: Deprotonation of the oxonium ion. **D**: Protonation makes a hydroxy group a good leaving group.

E: Elimination of water helped by the oxygen lone pair. **F**: Deprotonation

A003





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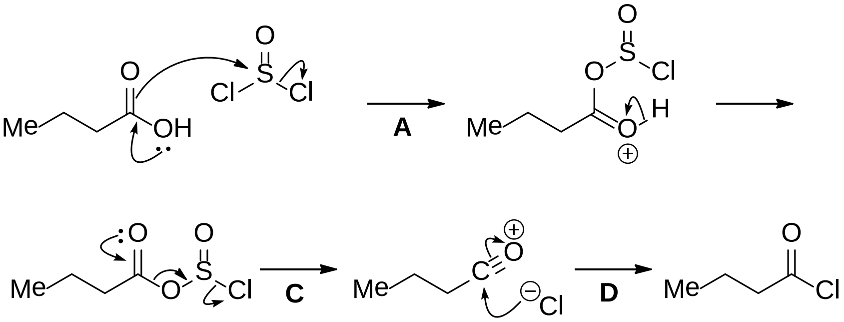
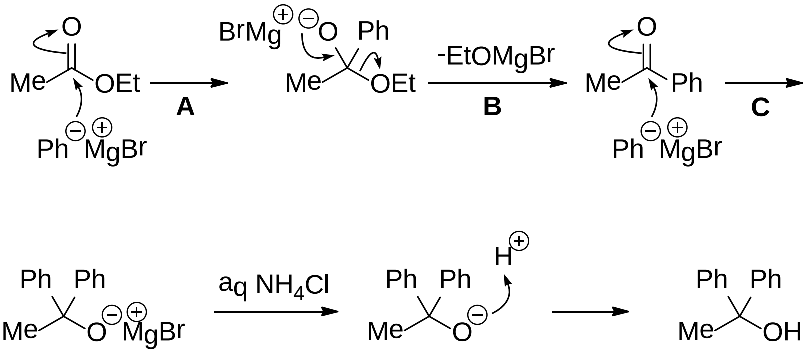


Helferich, B.; Schaefer, W. *Org. Synth., Coll* Vol I **1941**, 147.

A : Atack of a carboxylic acid to $SOCl_2$ forms a mixed anhydride. **B**: Addition of chloride ion to the carbonyl group to form a tetrahedral intermediate. **C**: Formation of an acylium ion. **D**: Addition of chloride ion to the acylium ion

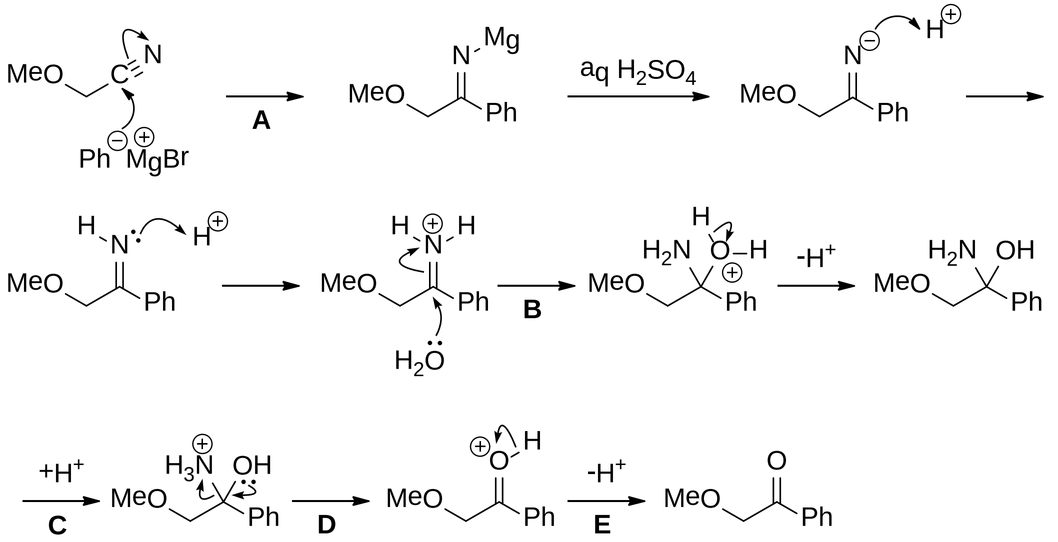
A004



Allen, C. F. H.; Converse, S. *Org. Synth., Coll*. Vol. I **1941**, 226.

A: Addition of PhMgBr to the carbonyl group of the ester to form a tetrahedral intermediate. **B**: Elimination of ethoxide ion to form a ketone. **C**: Addition of PhMgBr to the more reactive ketone to form a tertiary alkoxide.

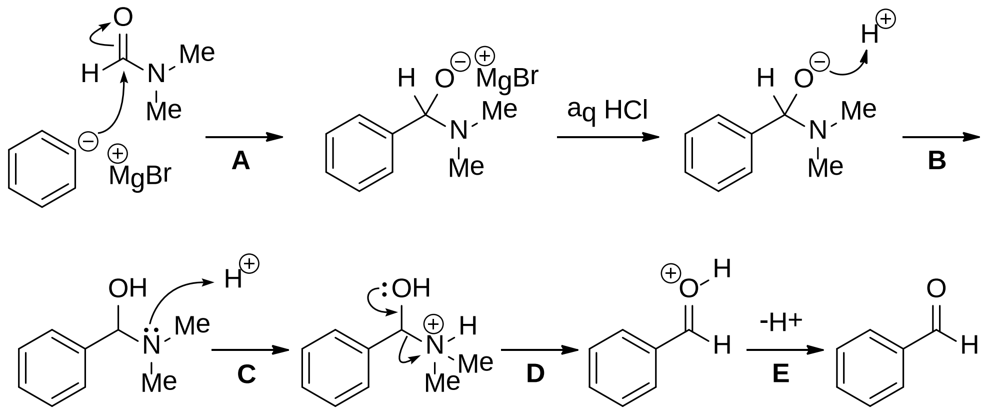
A005



Moffett, R. B.; Shriner, R. L *Org. Synth., Coll* Vol. III **1955**, 562.

A: Addition of PhMgBr to the nitrile forms an imine anion, **B**: Addition of water to the iminium ion gives a hemiaminal. **C**: Protonation occurs on a more basic amino group. pKa H_3O^+ = -1.7, $EtNH_3^+$ = 10.6. **D**: Elimination of ammonia helped by the oxygen lone pair. **E**: Deprotonation.

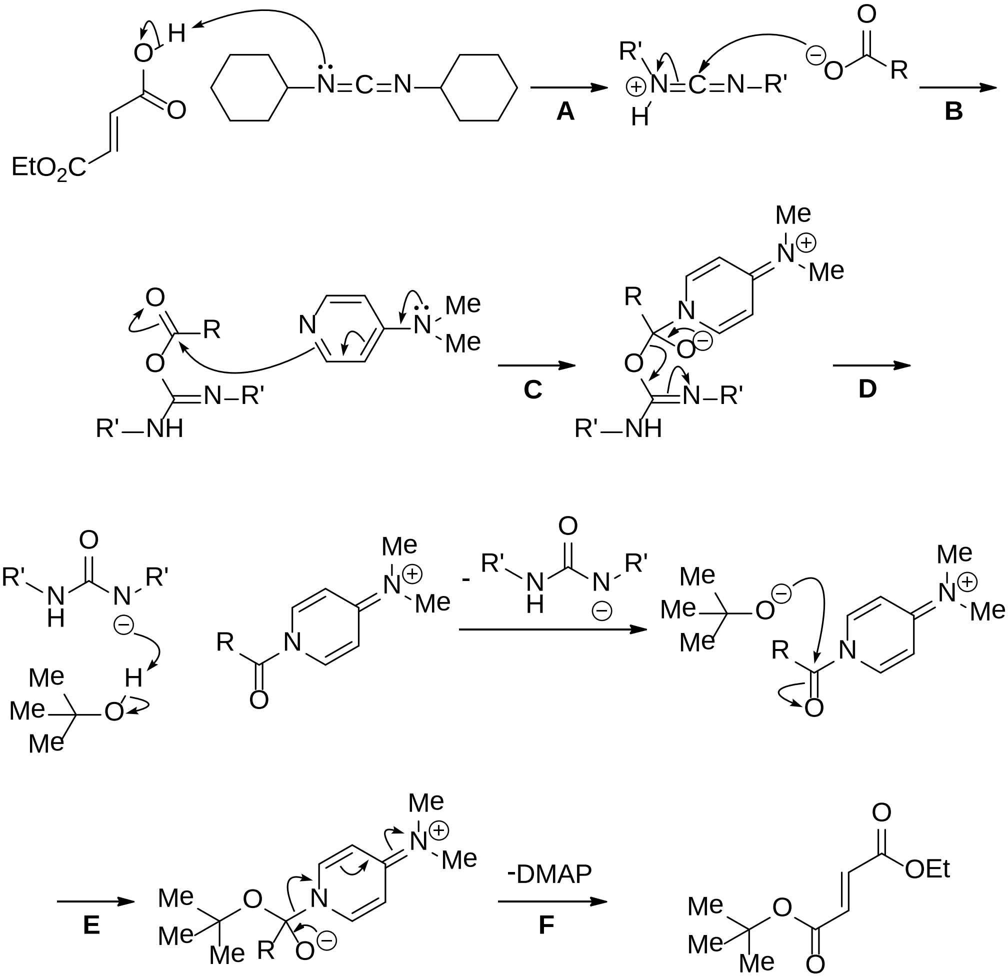
A006



Olah, G. A; Surya Prakash, G. K.; Arvanaghi, M. *Synthesis* **1984**, 228

A: Addition of PhMgBr to the carbonyl group. The resulting tetrahedral intermediate is relatively stable because the alkoxide anion cannot generate an amine anion (pKa i-PrOH = 17, Et_2NH = 36). **B**: Protonation on workup. **C**: Protonation of a more basic amino group. pKa H_3O^+ = -1.7, $EtNH_3^+$ = 10.6. **D**: Elimination of the amine helped by the oxygen lone pair **E**: Deprotonation.

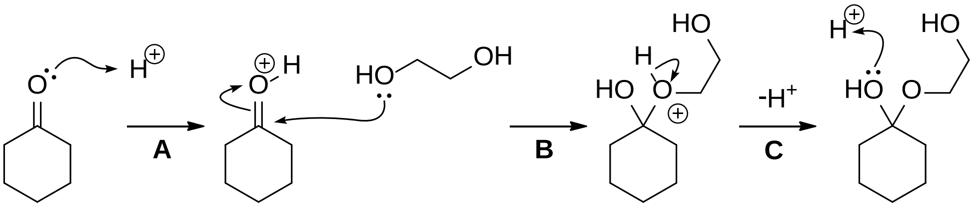
A007

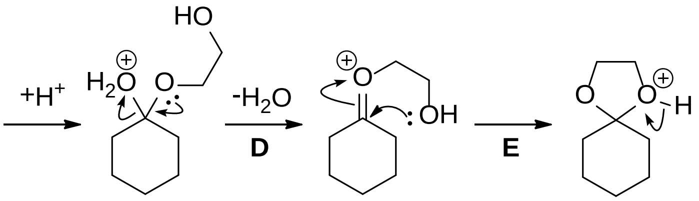


Neises, B.; Steglich, W. *Org. Synth.*, Coll. Vol. Ⅶ **1990**, 93.

A: Activation of DCC by protonation. **B**: Addition of the carboxylate to the protonated DCC. **C**: Addition of DMAP to the carbonyl group. **D**: Elimination of a urea anion which then abstracts a proton from an alcohol. **E**: Addition of the alkoxide anion to the carbonyl group to form a tetrahedral intermediate. **F**: Elimination of DMAP to form the product.

A008

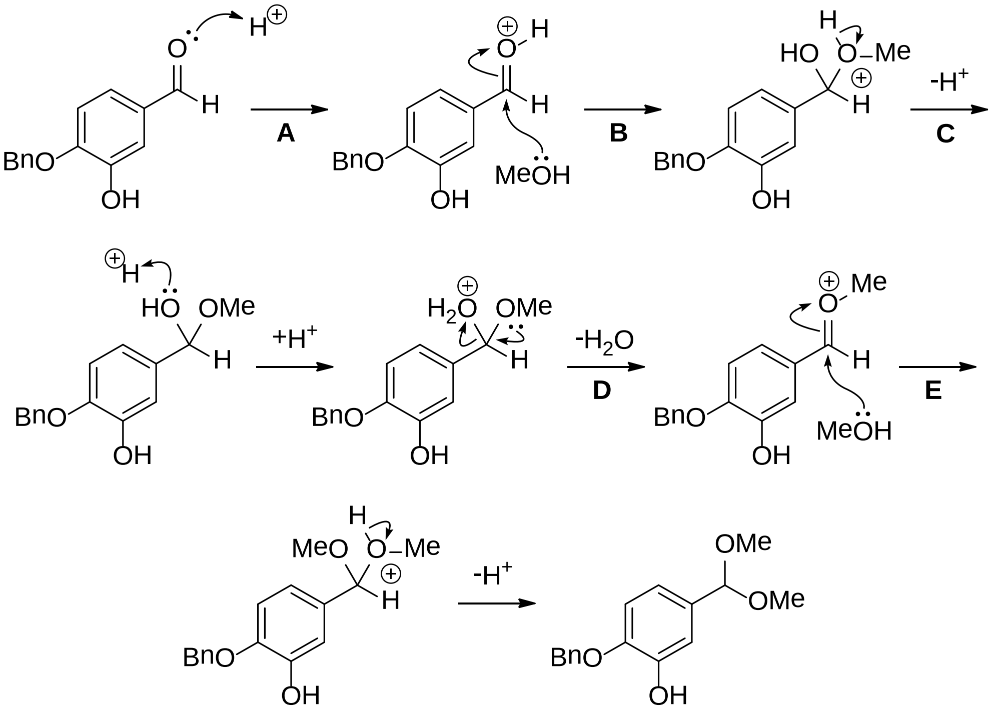


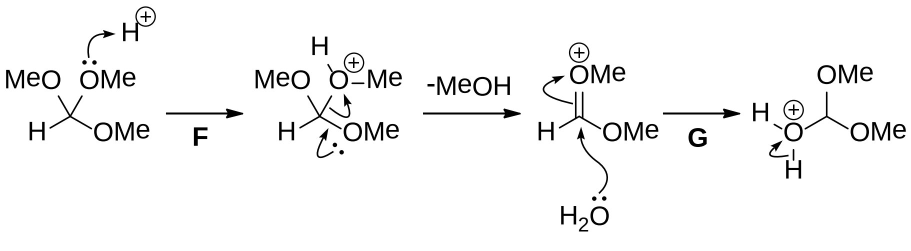


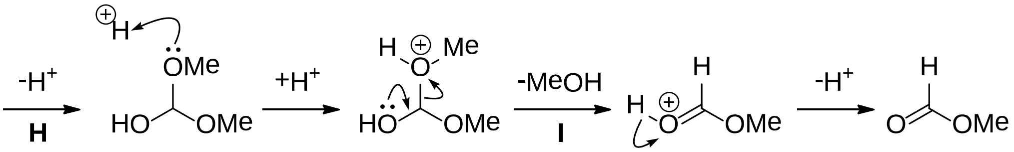
Daignault, R. A.; Eliel, E. L *Org. Synth., Coll* Vol. Ⅴ **1973**, 303.

A: Activation of the carbonyl group by protonation. **B**: Addition of ethylene glycol to the activated carbonyl group. **C**: Proton transfer. **D**: Elimination of water helped by the oxygen lone pair. **E**: Intramolecular addition of the second hydroxy group.

A009



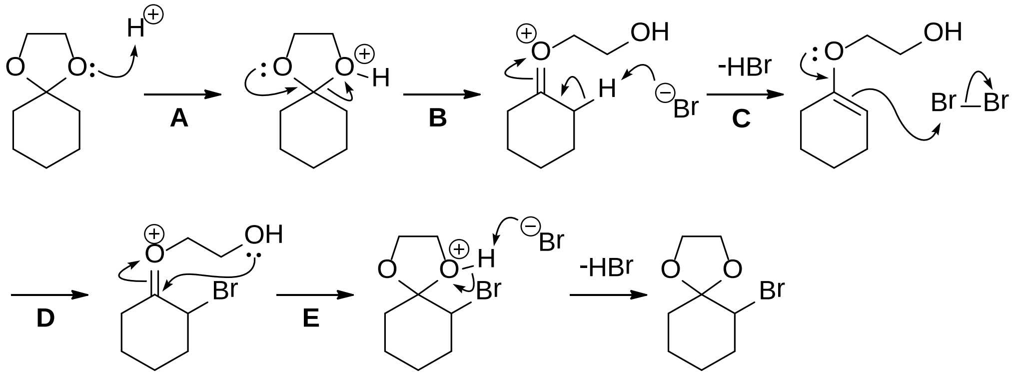




Baker, R.; Cooke, N. G.; Humphrey, G. R.; Wright, S. H. B.; Hirshfield, J. *J. Chem. Soc., Chem. Commun*. **1987**, 1102.

A: Activation of the carbonyl group by protonation. **B**: Addition of MeOH to the activated carbonyl group. C: Proton transfer. **D**: Elimination of water helped by the oxygen lone pair. **E**: Addition of MeOH and protonation to form a dimethyl acetal. **F**: Trimethyl orthoformate serves as a scavenger of water to let the equilibrium to the product side. Protonation followed by elimination of MeOH. **G**: Addition of water. **H**: Proton transfer. **I**: Elimination of MeOH followed by deprotonation to form HCO_2Me.

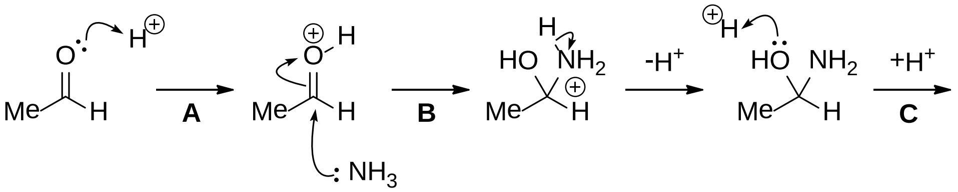
A010

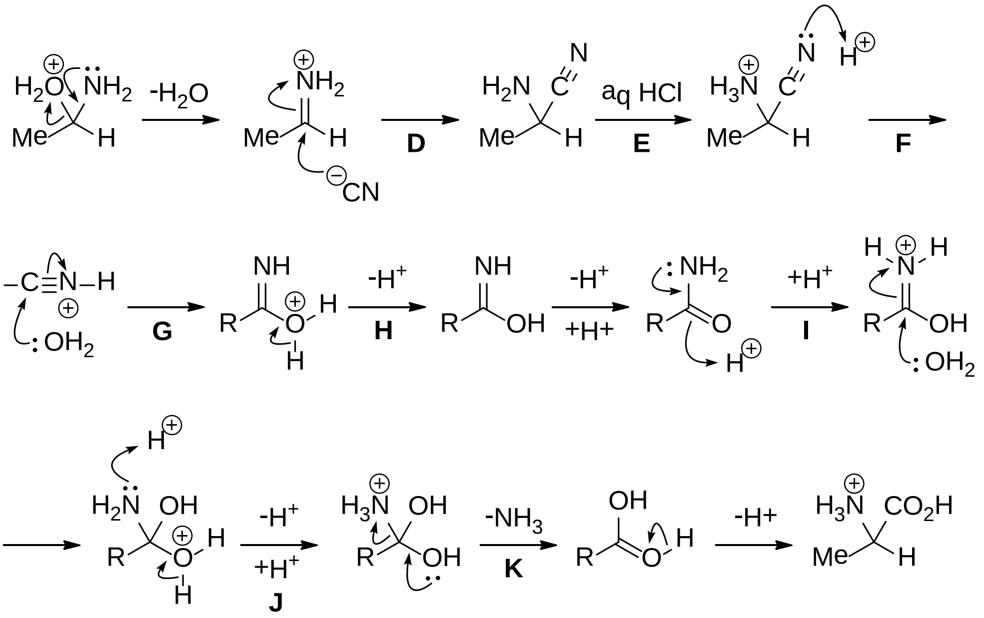


Aben, R. W. M.; Hanneman, E. J. M.; Scheeren, J. M. *Syn. Commun*. **1980**, 10, 821.

A: Protonation. **B**: Cleavage of the dioxolane ring helped by the oxygen lone pair. **C**: Deprotonation to form an enol ether. **D**: Bromination of the electron-rich enol ether. **E**: Intramolecular addition of the hydroxy group. Opening of the dioxolane ring of the product is more difficult because of the electron-withdrawing bromine atom.

A011

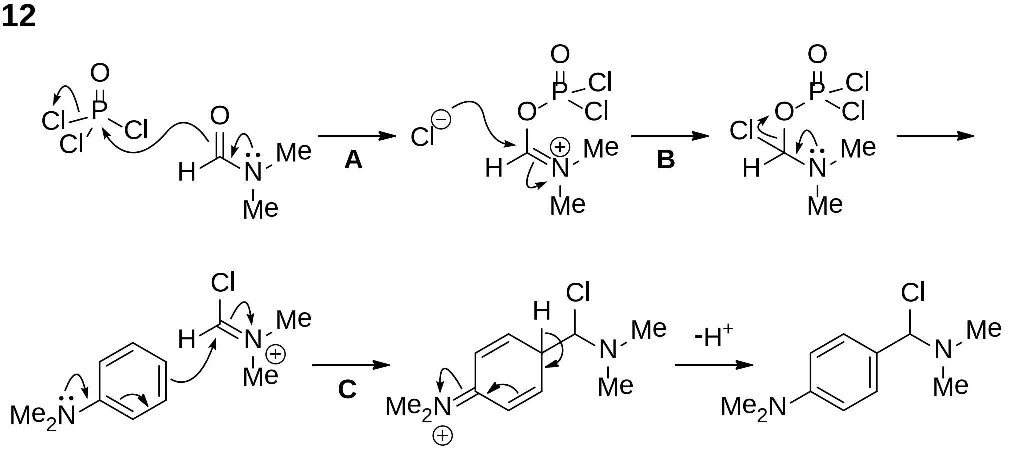


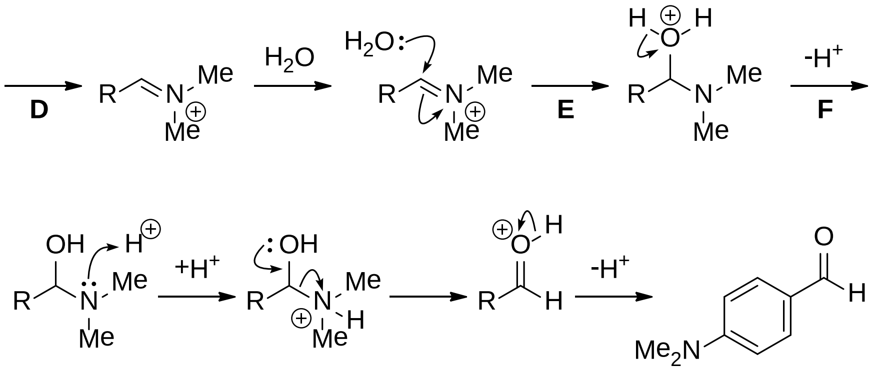


Kendall, E. C.; McKenzie, B F. *Org. Synth., Coll.* Vol. I **1941**, 21

Strecker amino acid synthesis, **A**: Protonation of the carbonyl group. **B**: Addition of NH_3 to the carbenyl group followed by deprotonation to form a hemiaminal. **C**: Protonation followed by elimination of water is helped by the nitrogen lone pair to form an iminium ion. **D**: Addition of a cyanide ion to form an aminonitrile. **E**: Acidic hydrolysis of the nitrile. The amino group is protonated throughout the reaction. **F**: Protonation of the nitrile to form a reactive nitrilium ion. **G**: Addition of water to the nitrilium ion. **H**: Deprotonation and tautemerization. **I**: Protonation of the resulting amide followed by addition of water. **J**: Proton transfer. **K**: Elimination of NH_3 followed by deprotonation to form the product.

A012

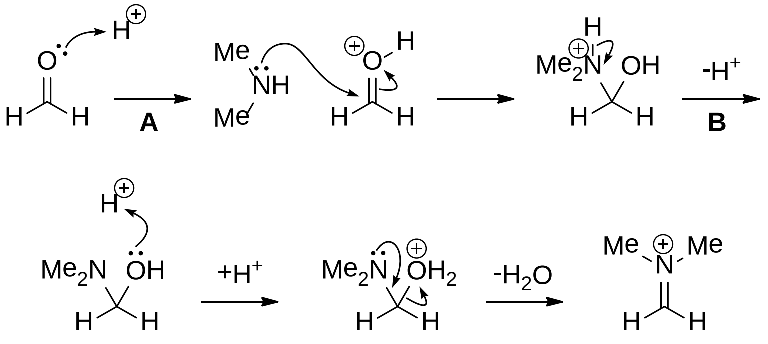


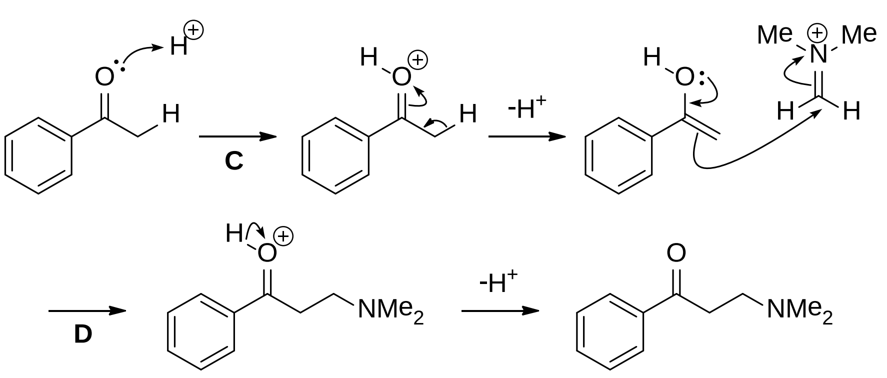


Campaigne, E.; Archer, W. L. *Org. Synth., Coll.* Vol. Ⅵ **1963**, 331

Vilsmeier reaction. **A**: The electron-rich oxygen of DMF attacks $POCl_3$ (oxygen of amides is generally more reactive toward electrophiles under neutral conditions). **B**: Addition of chloride ion followed by eation of a dichlorophosphate ion to form the Vilsmeier reagent. **C**: Addition of an electron-rich aromatic ring to Vilsmeier reagent followed by rearomatizatien **D**: Elimination of chloride ion helped by nitrogen lone pair leads to the formation of an iminium ion **E**: Addition of water to the iminium ion. F: Proton transfer followed by elimination of Me_2NH.

A013

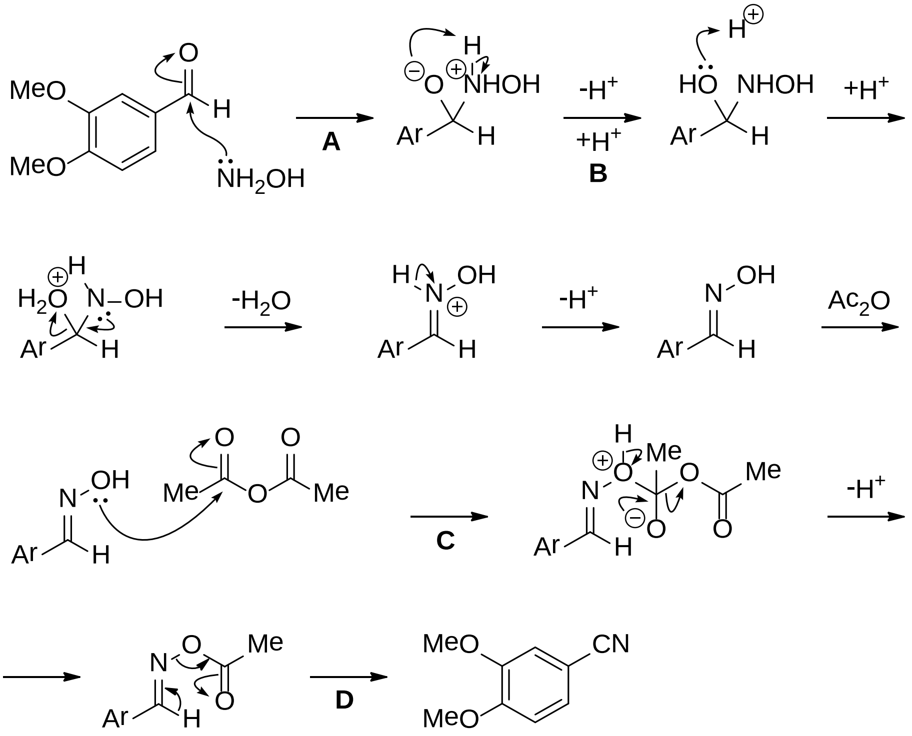




Maxwell, C. E. *Org Synth., Coll*. Vol. Ⅲ **1955**, 305.

Mannich reactien. A: Protonation of formaldehyde followed by addition of Me_2NH to the carbonyl group. B: Proton transfer followed by elimination of water to form an iminium ion. C: Tautomerization of the carbonyl goroup to form an enol. D: Attack of the electron-rich enol to the iminium ion.

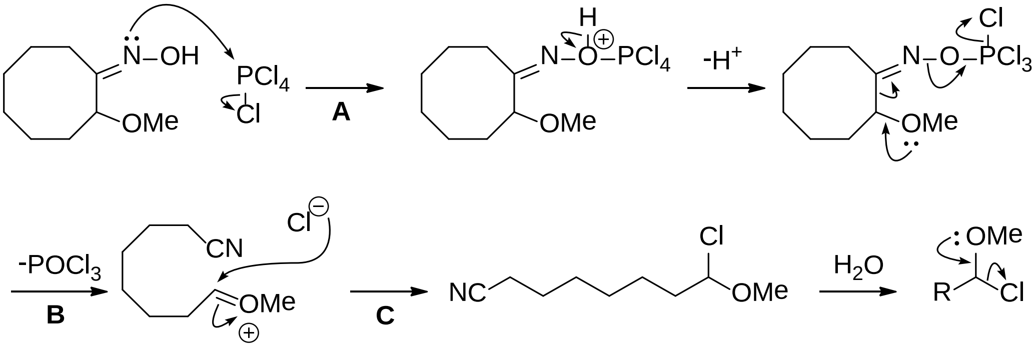
A014

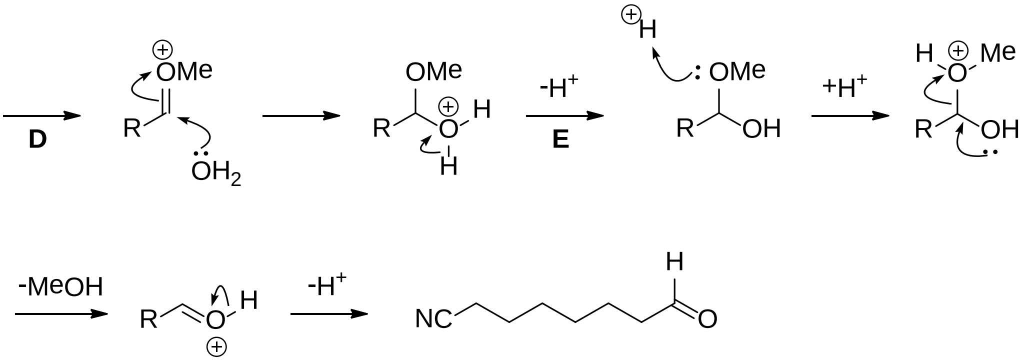


Buck, J. S,; Ide, W. S. *Org. Synth., Coll* Vol. II **1943**, 622

A: Addition of NH_2OH to the aldehyde. **B**: Proton transfer followed by elimination of water to form an oxime. **C**: Acetylation of the oxime. **D**: syn-Elimination of AcOH to form a nitrile.

A015

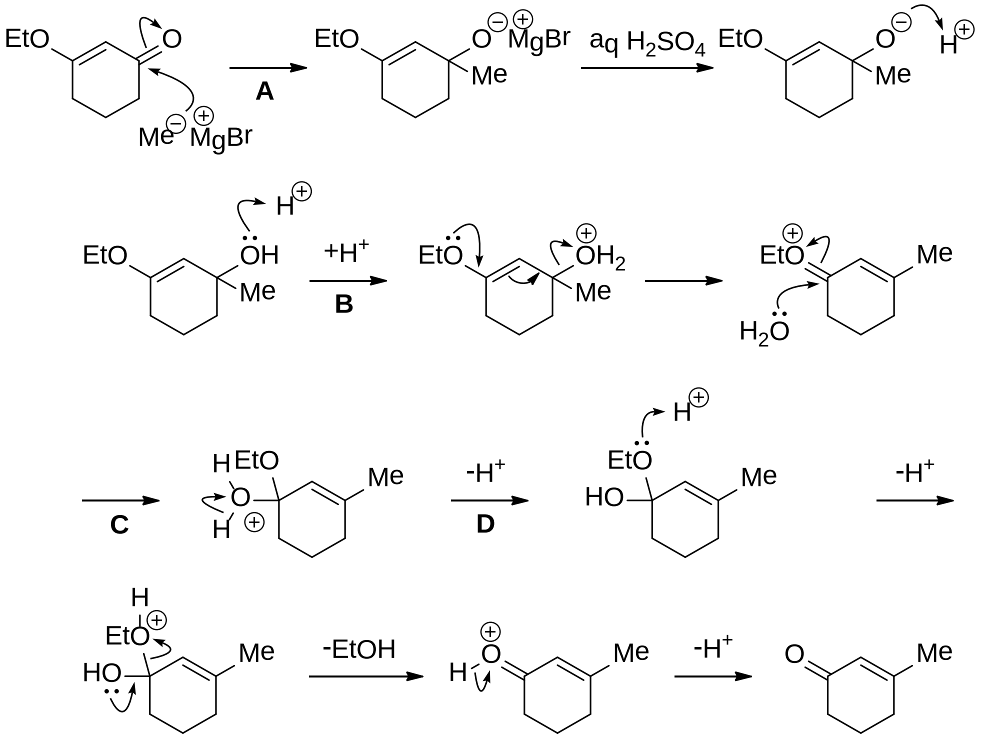




Ohno, M.; Naruse, N.; Terasawa, I. *Org. Synth., Coll.* Vol. V **1973**, 266

Beckmann fragmentation. **A**: Attack of the oxime to PCl$_5$. **B**: Elimination of POCl$_3$ is helped by the oxygen lone pair of the methoxy group, causing the cleavage of the C-C bond. **C**: Addition of chloride ion. **D**: Elimination of chloride ion followed by addition of water. **E**: Proton transfer followed by elimination of MeOH.

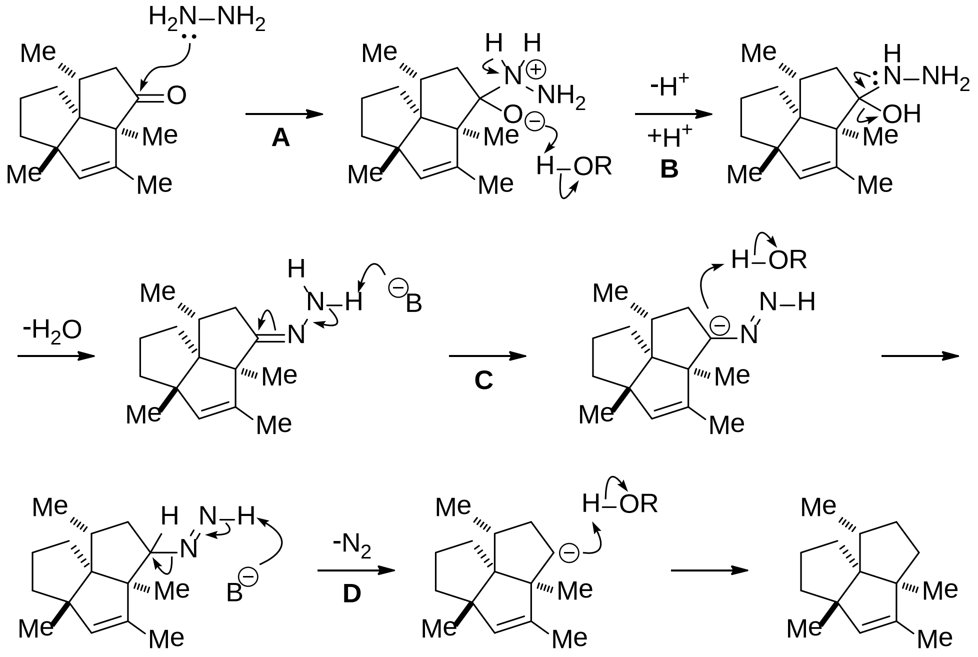
A016



Woods, G. F.; Griswold, P. H., Jr.; Armbrecht, B. H.; Blumenthal, D. I.' Plapinger, R
J. Am. Chem. Soc. **1949**, 71, 2028

A: 1,2-Addition of MeMgBr to the carbonyl group. **B**: Protonation followed by elimination of water helped by the oxygen lone pair of the ethoxy group. **C**: Addition of water. **D**: Proton transfer followed by elimination of EtOH.

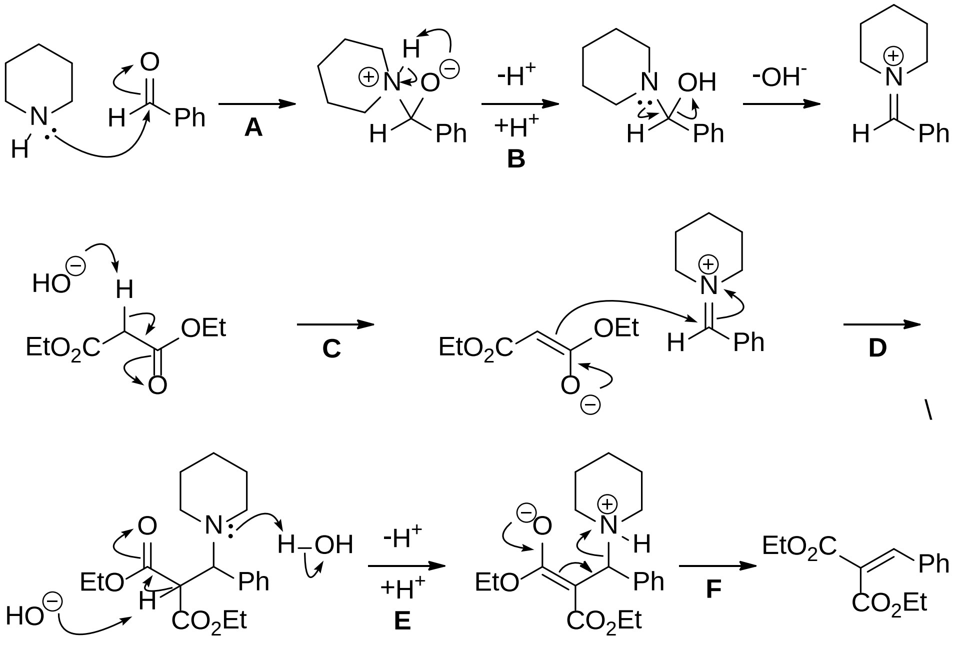
A017



Paquette, L. A.; Han, Y. K. *J. Org. Chem*. **1979**, 44, 4014.

Wolff-Kishner reduction **A**: Addition of H_2NNH_2 to the carbonyl group. **B**: Proton transfer followed by elimination of hydroxide ion to form a hydrazone. **C**: Deprotonation of the hydrazone. **D**: Elimination of N_2, an extremely good leaving group.

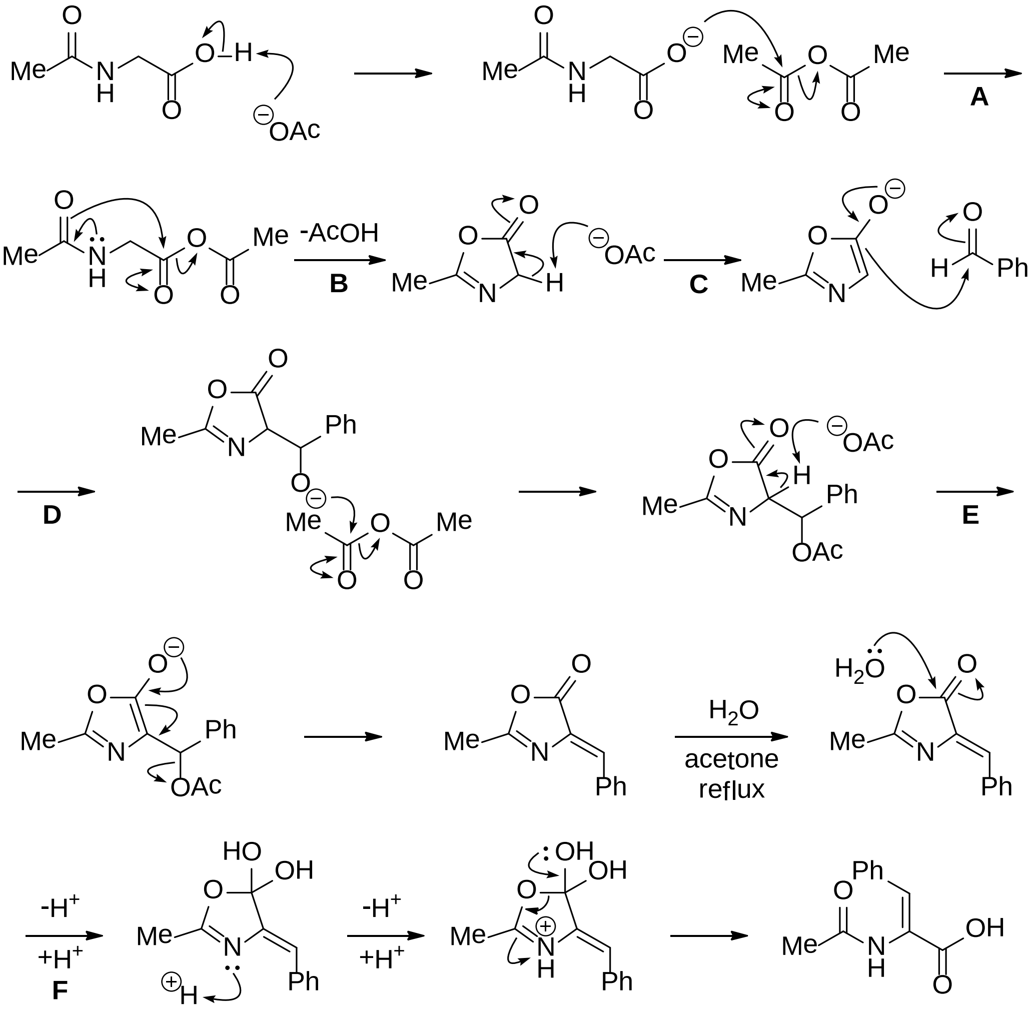
A018

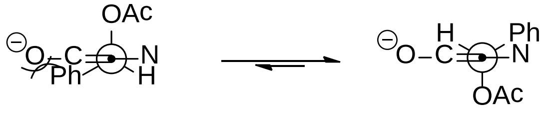


Allen, C. F. H.: Spangler, F. W. *Org. Synth., Coll*. Vol. III **1955**, 37

Knoevenagel condensation **A**: Addition of piperidine to the aldehyde. **B**: Proton transfer followed byelimination of hydroxide ion to form an iminium ion. **C**: Deprotonation of a malonate to form an enolate (pKa $RO_2CCH_2CO_2R$ = 13, H_2O = 15.7). **D**: Addition of the enelate to the iminium ion. **E**: Profonation of the amine and deprotonation of the malonate. **F**: Elimination of piperidine.

A019

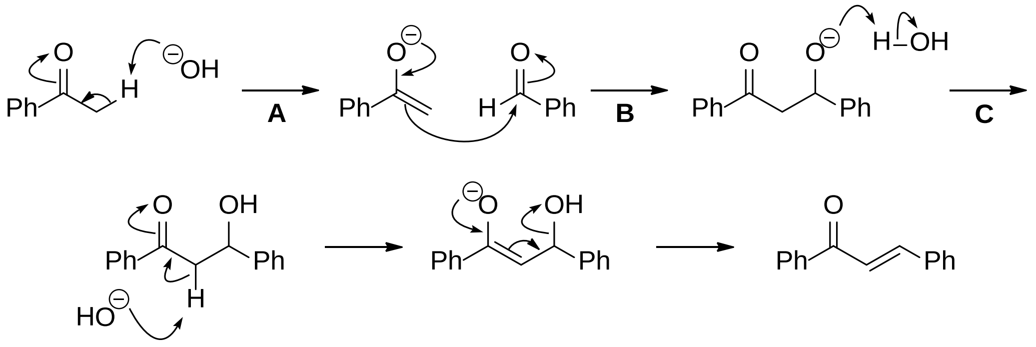


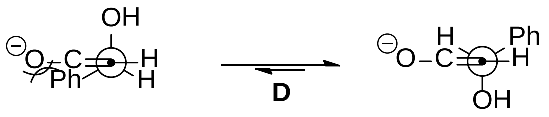


Herbst, R. M.; Shemin, D. *Org Synth., Coll*, Vol. Ⅱ **1943**, 1

A: formation of a mixed anhydride. **B**: Intramolecular attack of the amide oxygen to the mixed anhydride to form an azlactone. **C**: Facile deprotonation of the azlactone (aromatization). **D**: Addition the enolate to an aldehyde followed by acetylation. **E**: Deprotonation followed by elimination of an enolate anion. **F**: Hydrolysis of the azlactone

A020

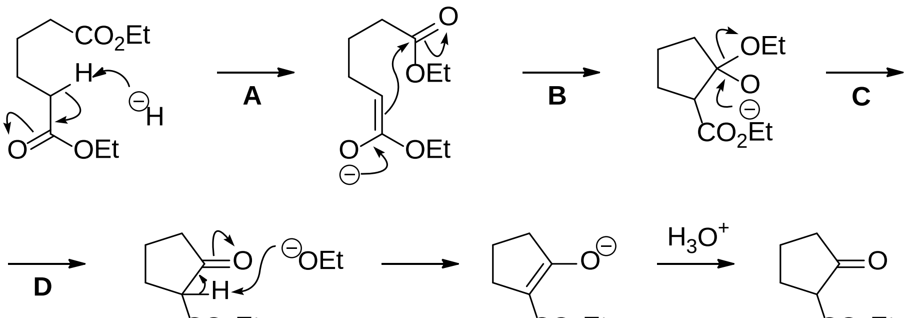




Kohler, E. P.; Chadwell, H. M. *Org. Synth., Coll* Vol. Ⅰ **1941**, 78

Aldol reaction. **A**: Deprotonation of the ketone to form an enolate. **B**: Attack of the enolate to an aldhyde **C**: Protonation and deprotonation followed by elimination of a hydroxy ion. **D**: Newman projection.

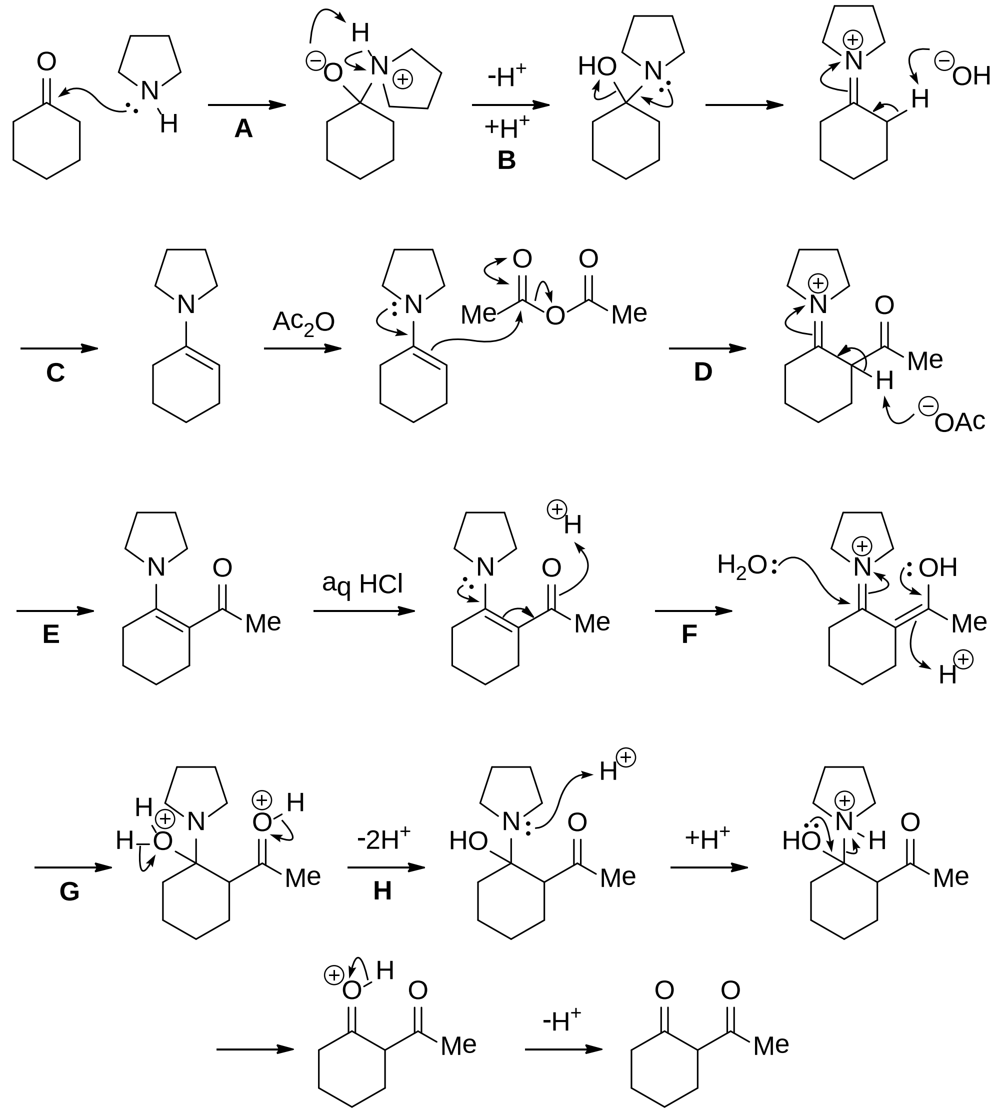
A021



Schaefer, J. P.; Bloomfield, J. J. *Org. React*. **1967**, 15 14

Dieckmann condensation. **A**: Deprotonation of the ester to form an enolate. **B**: Intramolecular addition of the enolate to the other ester, **C**: Elimination of ethoxide ion. **D**: pKa $RCOCH_2CO_2R$ = 18. EtOH = 16.

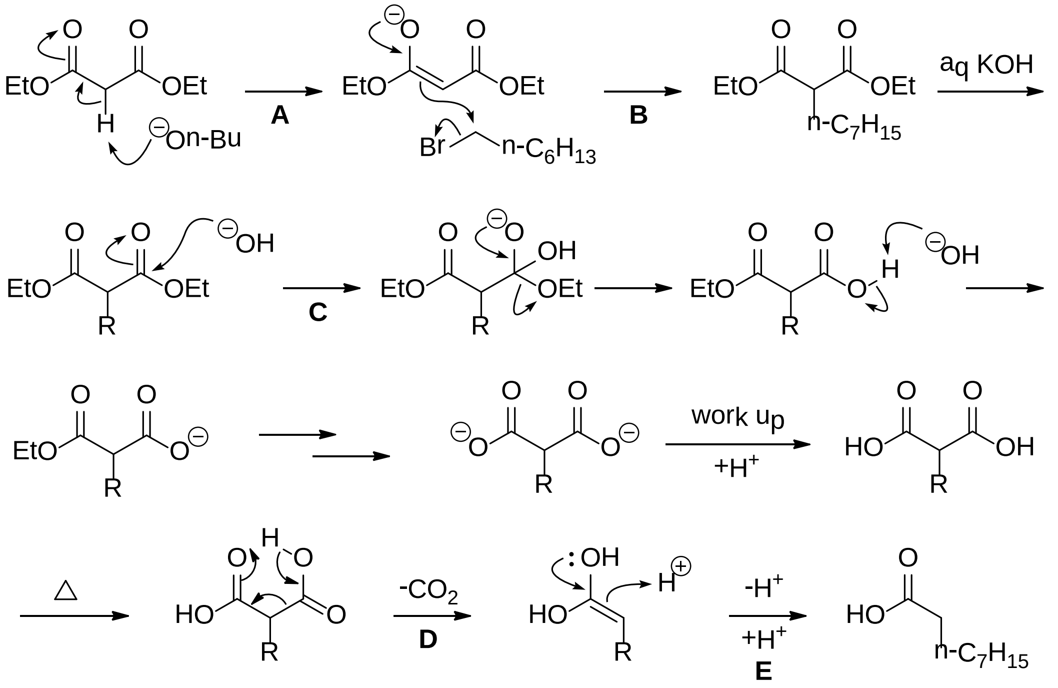
A022



Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R.
J. Am. Chem. Soc. **1963**, 85, 207.

Stork enamine reaction. **A**: Addition of pyrrolidine to the ketone. **B**: Proton transfer followed by elimination of hydroxide ion. **C**: Deprotonation to form an enamine. **D**: Attack of the enamine to acetic anhydride. **E**: Deprotonation to form a vinylogous amide. **F**: Protonation of the vinylogous amide. **G**: Addition of water to the resulting iminium ion. **H**: Proton transfer followed by elimination of pyrrolidine.

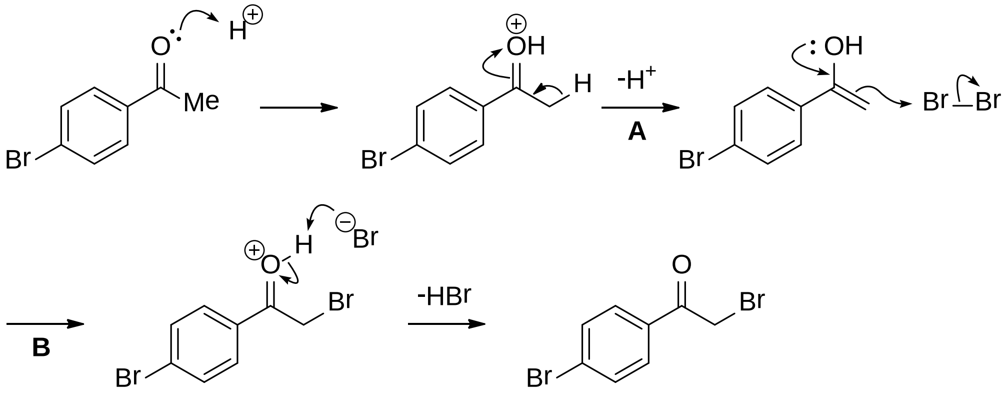
A023



Reid, E. E.; Ruhoff, J. R. *Org. Synth., Coll.* Vol. II **1943**, 474.

A: Deprotonation of the malonate to form an enolate (pKa ROH = 16, $RO_2CCH_2CO_2R$ = 13). **B**: Attack of the enolate to an alkyl bromide. **C**: Hydrolysis of the esters. **D**: Decarboxylation through a six-membered transition state. **E**: Tautomerization.

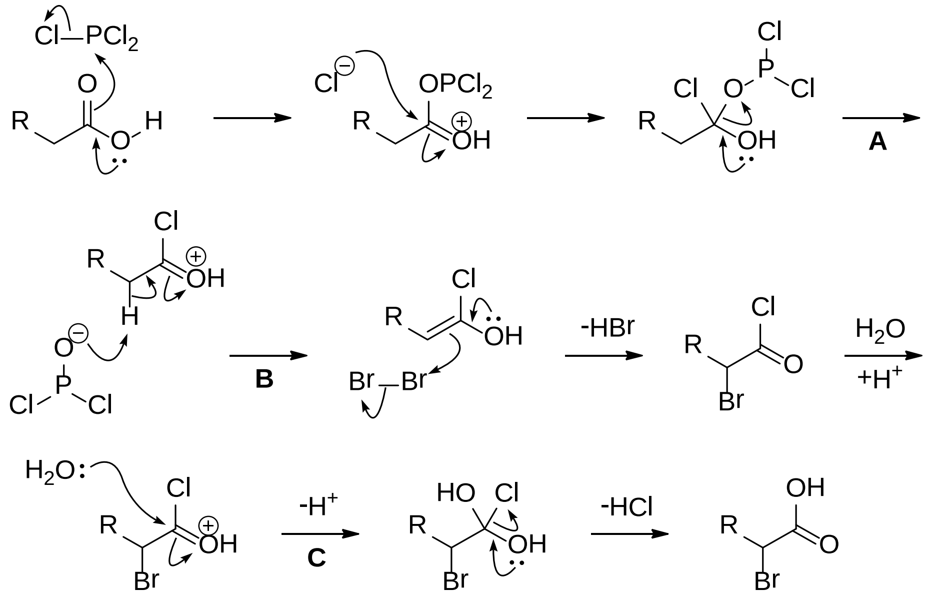
A024



Langley, W. D. *Org. Synth., Coll.* Vol. I **1941**, 127

A: Acid-catalyzed formation of an enol. **B**: Bromination of the electron-rich enol.

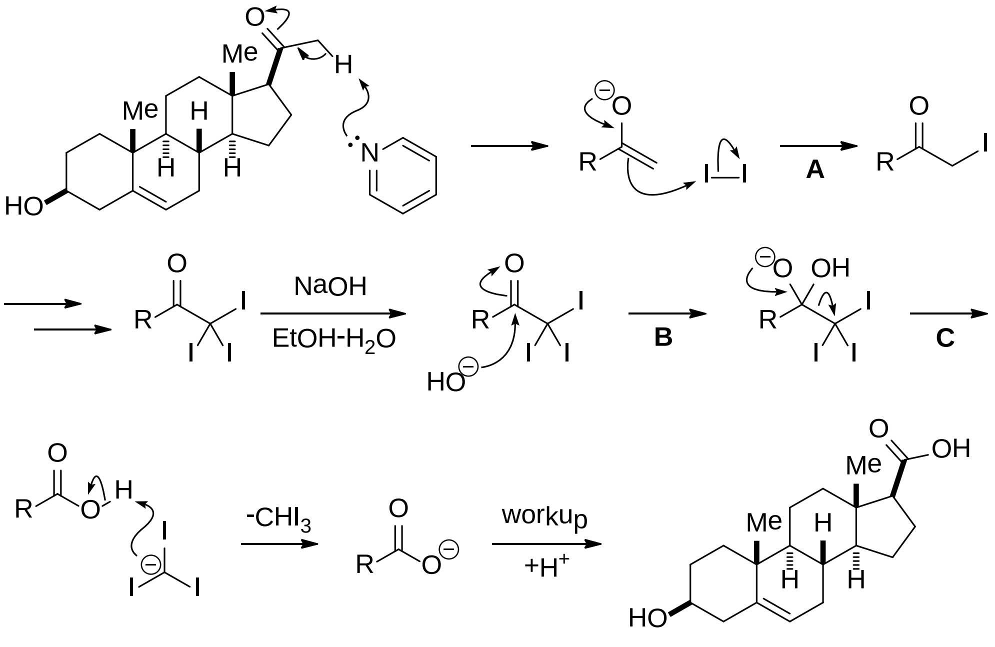
A025



Clarke, H. T.; Taylor, E. R. *Org. Synth., Coll.* Vol. Ⅰ **1941**, 115

Hell-Volhard-Zelinsky reactlon **A**: Formation of an acid chloride. **B**: pKa CH_3COCl = 16, CH_3CO_2R = 24. Formattion of an electron-rich enol followed by bromination. **C**: Hydrolysis of the acid chloride.

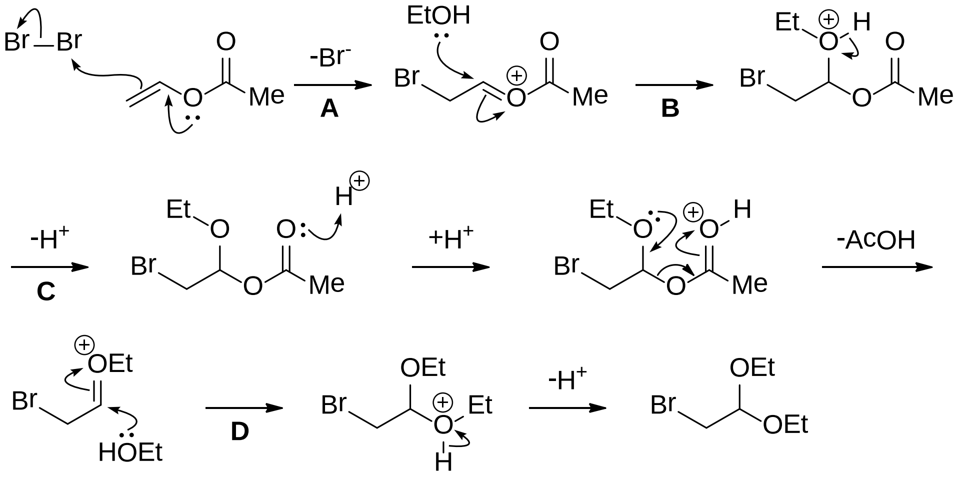
A026



Bergmann, E. D.; Rabinovitz, M.; Levinson, Z. H. *J. Am. Chem. Soc.* **1959**, 81, 1239.

Idioform reaction. **A**: Iodination of the α-position of the ketone. **B**: Addition of hydroxide ion. **C**: Elimination of an iodoform anion.

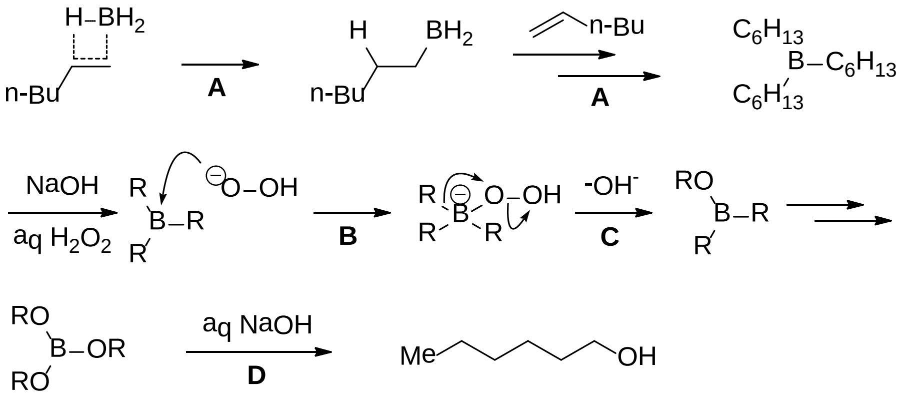
A027



McElvain, S. M.; Kundiger, D, *Org. Synth., Coll.* Vol. Ⅲ **1955**, 123

A: Bromination of the electron-rich enol ester. **B**: Addition of EtOH. **C**: Proton transfer followed by elimination of AcOH. **D**: Addition of EtOH.

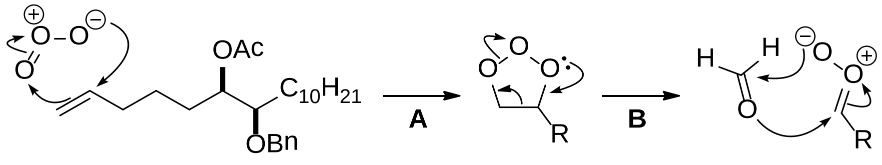
A028

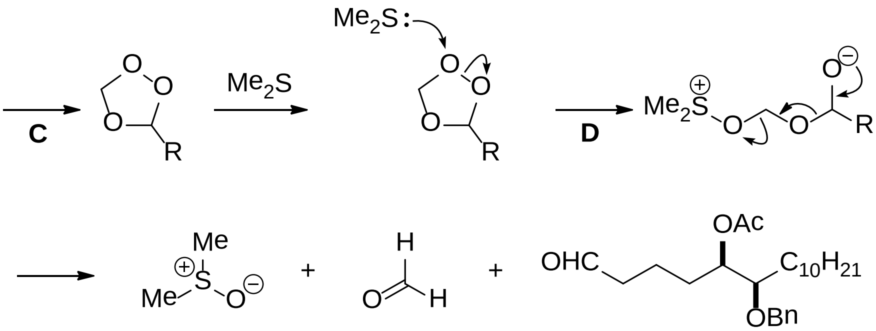


Kono, H.;Hooz, J *Org. Synth., Coll*, Vol, Ⅵ **1988**, 919

A: Hydroboration through a four-membered transition state. **B**: Attack of a hydroperoxide anion to the borane to form an ate complex, **C**: Migration of an alkyl group. **D**: Hydrolysis of the borate.

A029

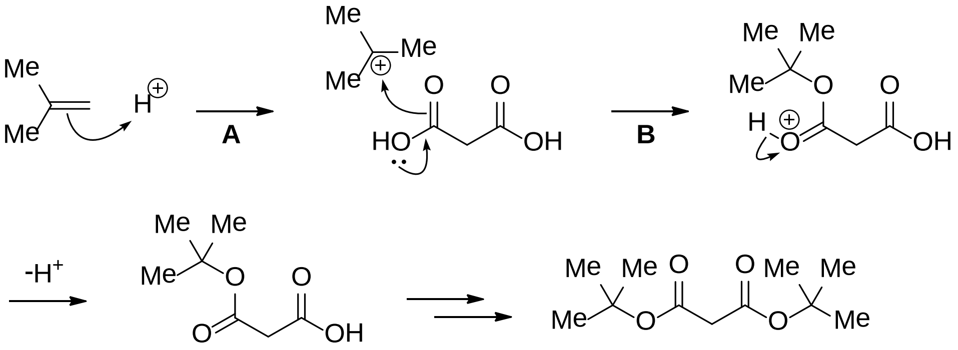




Ko, K.-Y.; Eliel, E. L. *J Org. Chem*. **1986**, 51, 5353

A: 1,3-Dipolar cycloaddition of ozone to the olefin. **B**: Heterolytic cleavage of the initial ozenide. **C**: Recombination of the resulting 1,3-dipole and the aldehyde to form an ozonide. **D**: Reductive cleavage of the O-O bond of the ozonide with Me_2S.

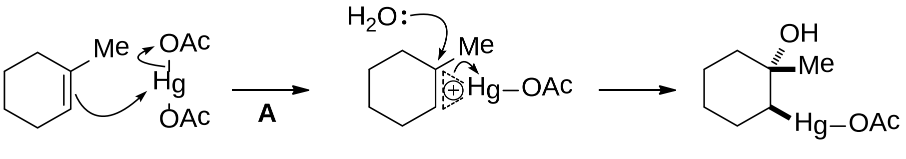
A030

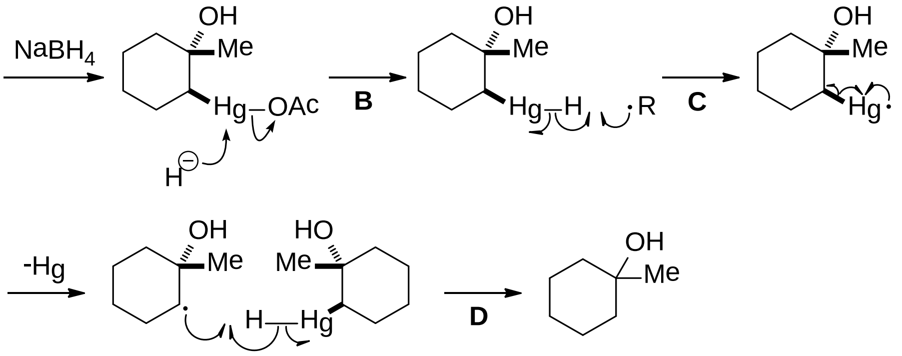


McCloskey, A. L.; Fonken, G. S.; Kluiber, R. W.; Johnson, W. S. *Org. Synth., Coll*. Vol. Ⅳ **1963**, 261.

A: Protonation of isobutylene to form a stable tertiary carbocation. **B**: Attack of a carboxylic acid to the esterication.

A031

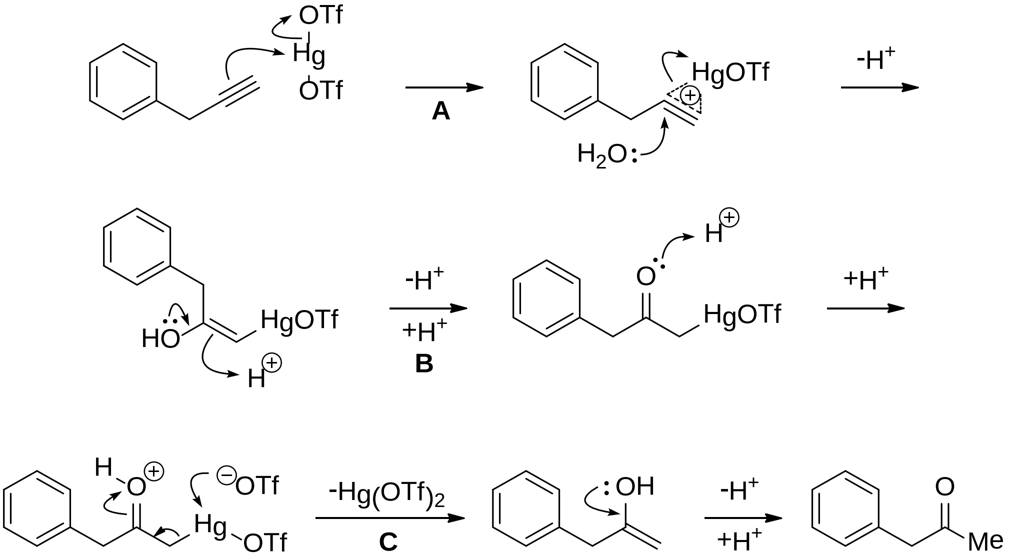




Jerkunica, J. M.; Traylor, T. G. *Org. Synth., Coll.* Vol. Ⅵ **1988**, 766.

A :Oxymercuration of the olefin. **B**: Reduction with $NaBH_4$ to form a Hg-H bond. **C**: Cleavage of the Hg-H bond followed by extrusion of Hg to form a secondary carbon radical. **D**: Abstraction of a Hydrogen atom.

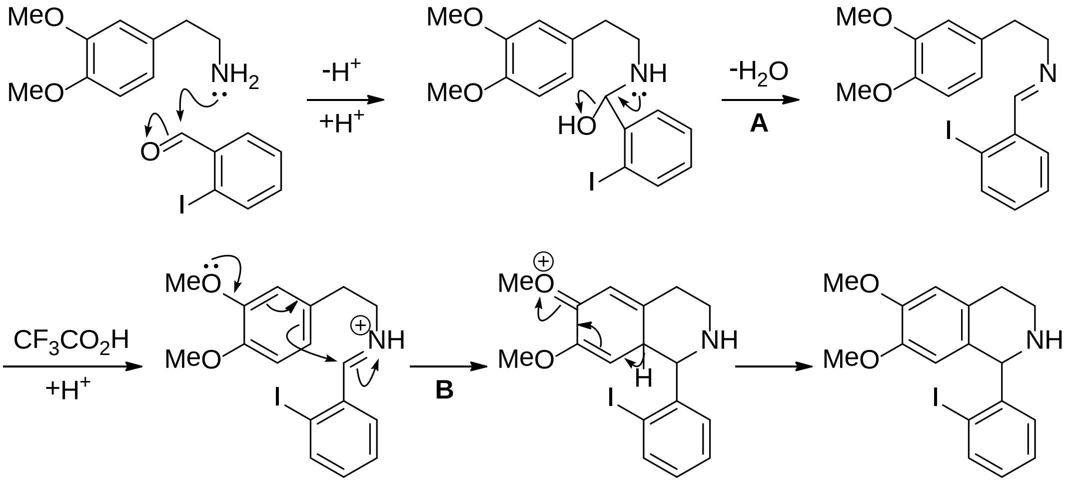
A032



Nishizawa, M.; Skwarczynski, M.; Imagawa, H.; Sugihara, T. *Chem. Lett.* 2002, 12.

A: Oxymercuration of the alkyne. **B**: Tautomerization of the enol. **C**: Demercuration to regenerate $Hg(OTf)_2$.

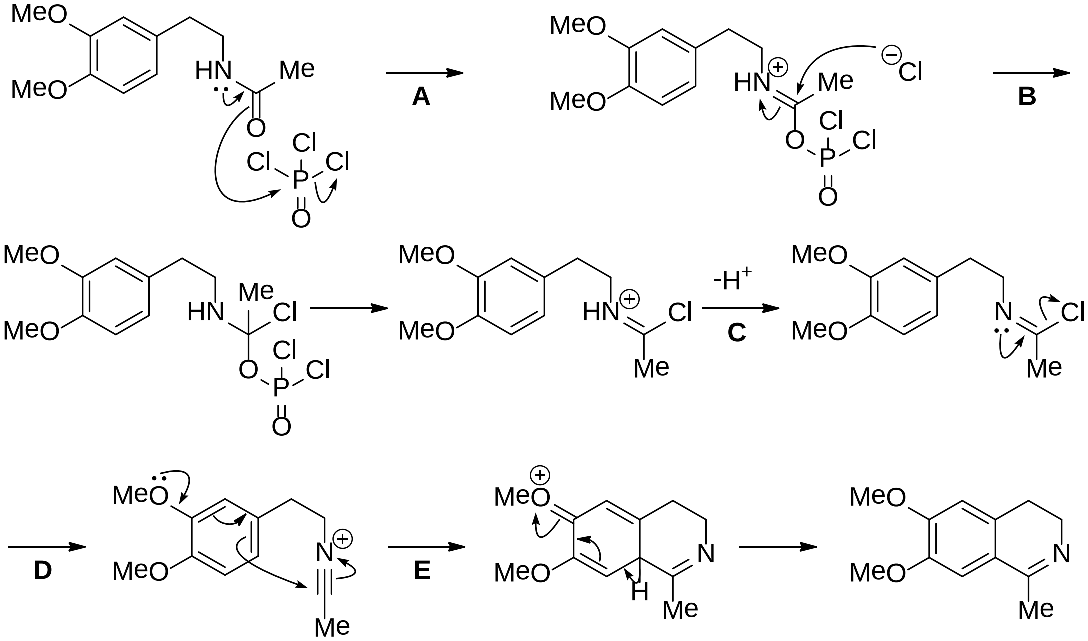
A033



Whaley, W. M.; Govindachari, T. R. *Org, React.* **1951**, 6, 151.

Pictet-Spengler reaction. **A**: Formation of an imine. **B**: Addition of an electron-rich aromatic ring to the iminium ion followed by aromatization.

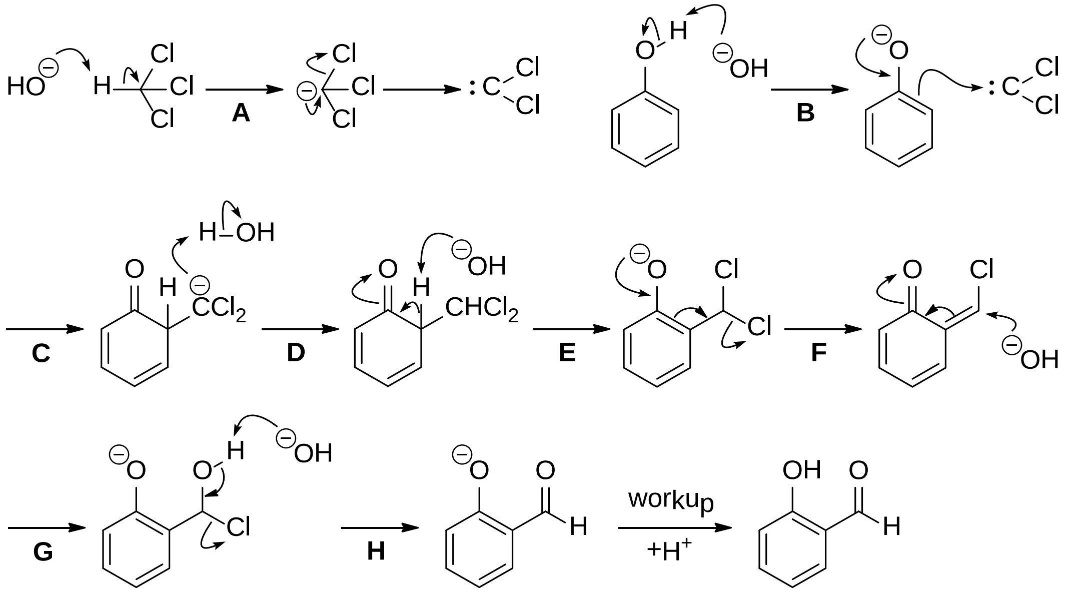
A034



Brossi, A: Dolan, L. A.; Teitel, S. *Org. Synth., Coll* Vol. Ⅵ **1988** 1

Bischler-Napieralski reaction. **A**: Attack of the oxygen atom of the amide to $POCl_3$. **B**: Addition of chloride ion followed by elimination of dichlorophosphate ion. **C**: Deprotonation. **D**: Elimination of chloride ion to form a nitrilium ion. **E**: Attack of an electron-rich aromatic ring to the nitrilium ion.

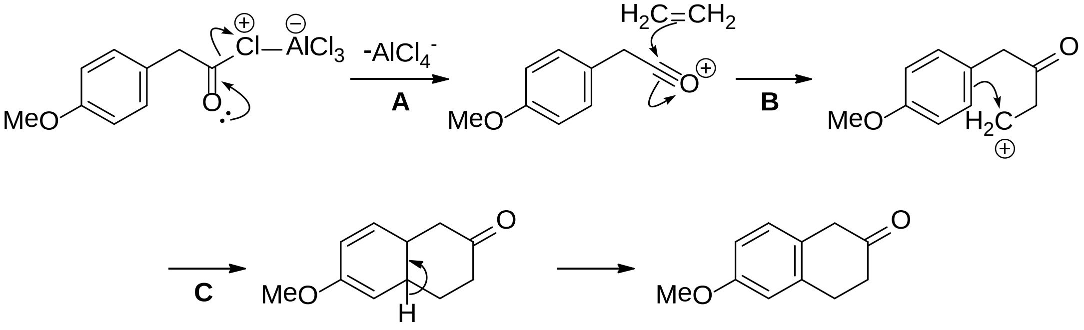
A035



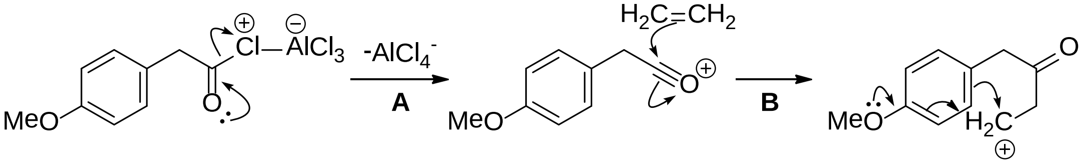
Wynberg, H.; Meijer, E. W. *Org. React.* **1982**, 28, 1.

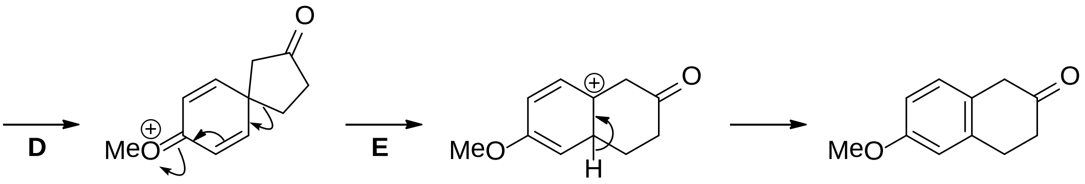
Reimer-Tiemann reaction. **A**: Deprotonation of $CHCl_3$ followed by α-elimination to form dichlorocarbene (pKa $CHCl_3$ = 13.6, H_2O = 15.7). **B**: Formation of phenoxide ion (pKa PhOH = 10). **C**: Attack of the phenoxide ion to dichlorocarbene. **D**: Protonation. **E**: Aromatization. **F**: Elimination of chloride ion helped by the oxygen lone pair of the phenoxide ion. **G**: Conjugate addition of hydroxide ion. **H**: Elimination of chloride ion.

A036



or

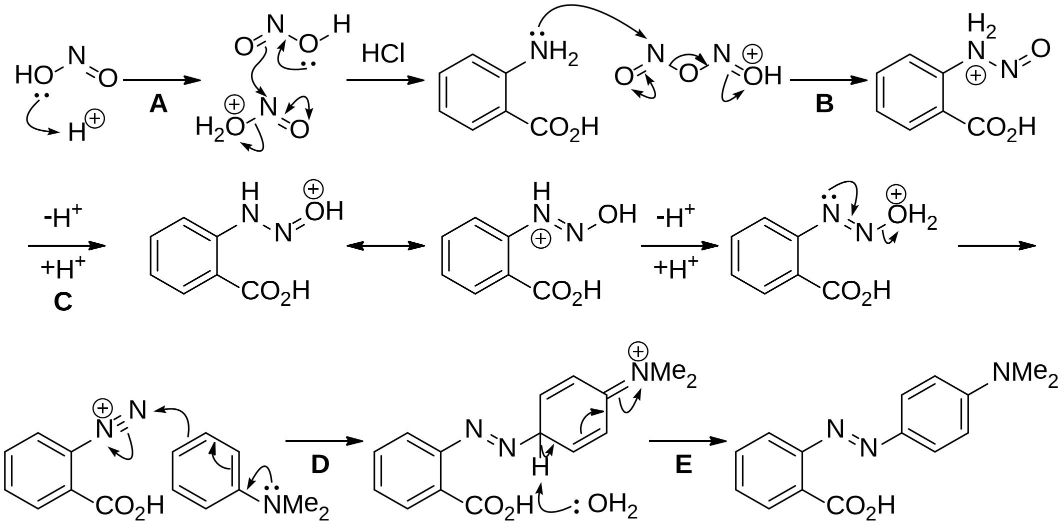




Sims, J. J.; Selman, L. H.; Cadogan, M. *Org. Synth, Coll.* Vol. Ⅵ **1988**, 744

Intramolecular Friedel-Crafts acylation. **A**: Formation of an acylium ion. **B**: Addition of ethylene to the aeylium ion. **C**: Attack of the aromatic ring to the resulting primary carbocatian. **D**: Attack of the aromatic ring at the para position of the methoxy group to the primary carbocation. **E**: 1,2-Alkyl shift.

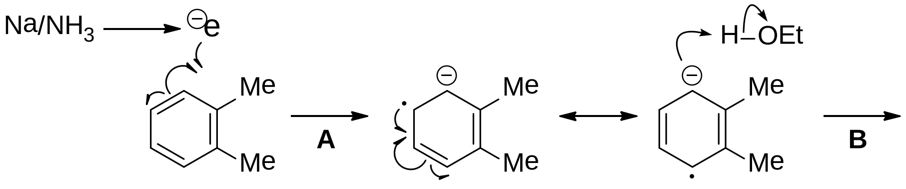
A037

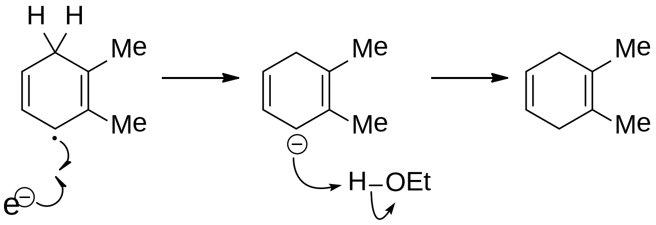


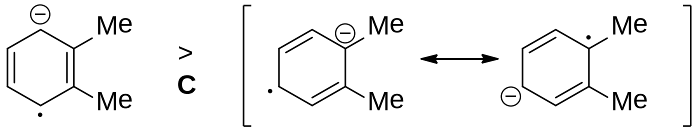
Clarke, H. T.; Kimer, W. R. *Org. Synth., Coll.* Vol. Ⅰ **1941**, 3. 4,

A: Formation of nitrous anhydride. **B**: Addition of the aniline to nitrous anhydride. **C**: Proton transfers fallowed by elimination of water to form a diazonium salt. **D**: Addition of electron-rich dimethylaniline to the diazonium salt. **E**: Aromatization.

A038



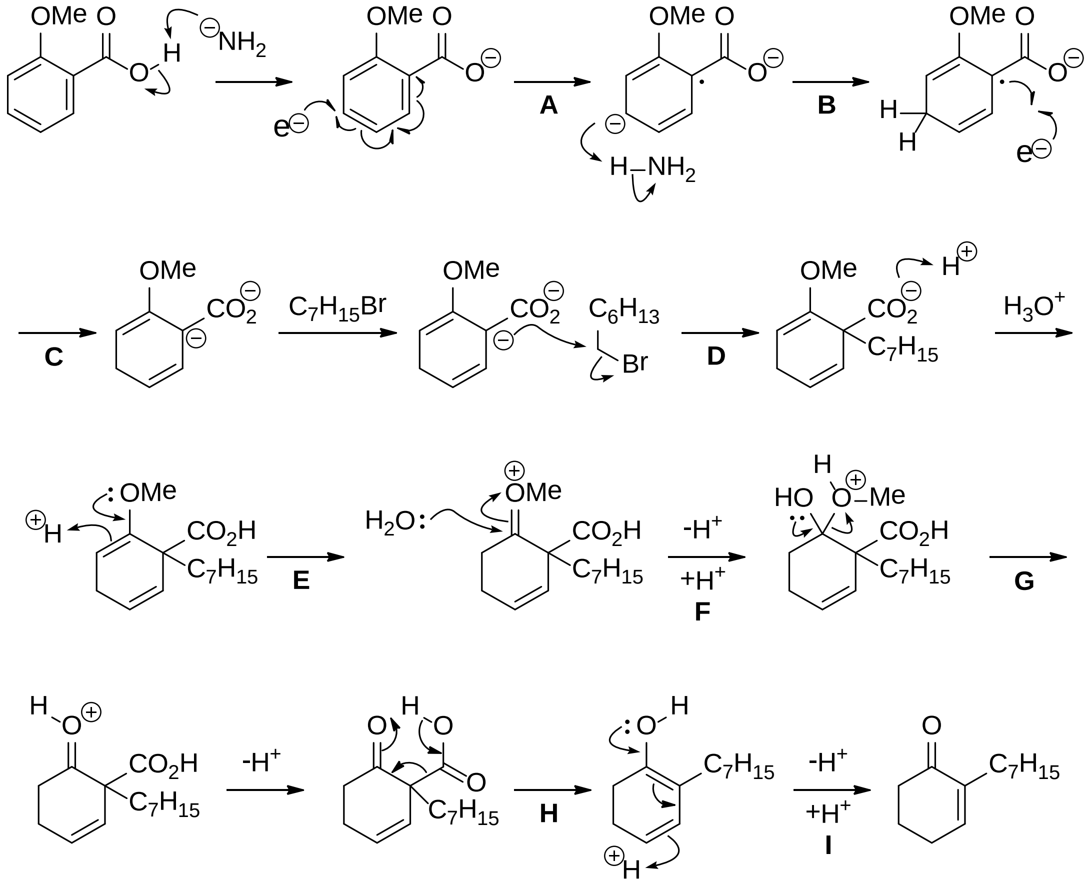




Paquette, L. A.; Barrett, J. H. Org. Synth., Coll. Vol. V **1973**, 467.

Birch reduction. **A**: Single electron transfer (SET) from Na to the aromatic ring to form a radical anion. **B**: Protonation. **C**: More substituted olefins are formed because alkyl groups destabilize a carbanion.

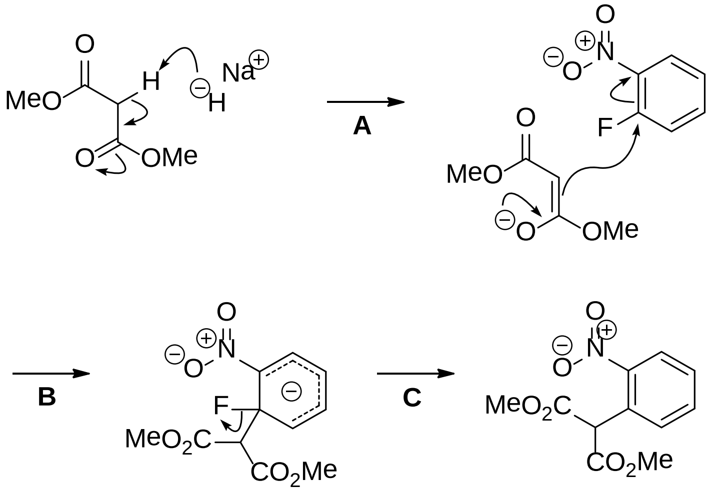
A039



Taber, D. F.; Gunn, B. P.; Chiu, I.-C. *Org. Synth., Coll* Vol. Ⅵ **1983**, 249.

Birch reduction **A**: Single electron transfer (SET) to form a radical stabilized by the carboxylate. **B**: Protonation of the radical anion, **C**: SET to form a dianion species. **D**: Alkylation of the dianionic species. **E**: Protonation of the electron-rich enol ether. **F**: Addition of water followed by proton transfer. G: Elimination of MeOH. H: Decarboxylation through a six-membered transition state. **I**: Tautomerization.

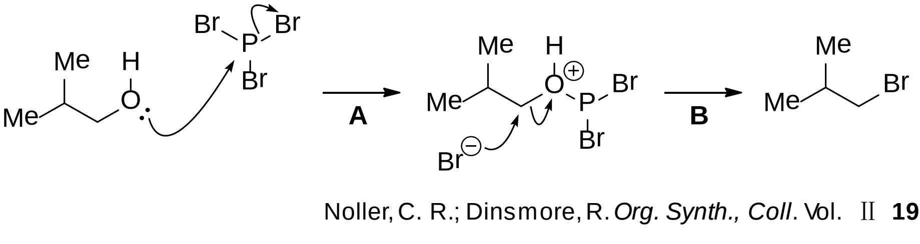
A040



Selvakumar, N.; Reddy, B. Y.; Azhagan, A. M.; Khera, M. K.; Babu, J. M.; Iqbal, J *Tetrahedron Lett.* **2003**, 44, 7065

A: Deprotonation of the malonate to form an enolate (pKa $RO_2CCH_2CO_2R$ = 13, H_2 = 35), **B**: Nucleophilic addition of the enolate to the electron-deficient aromatic ring. **C**: Elimination of fluoride ion.

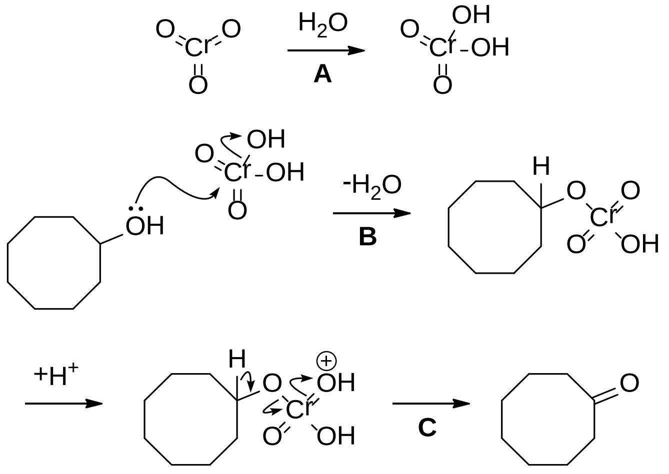
A041



Noller, C. R.; Dinsmore, R. *Org. Synth., Coll.* Vol. Ⅱ **1943**, 358

A: Attack of the alcohol to PBr_3. **B**: S_N2 reaction.

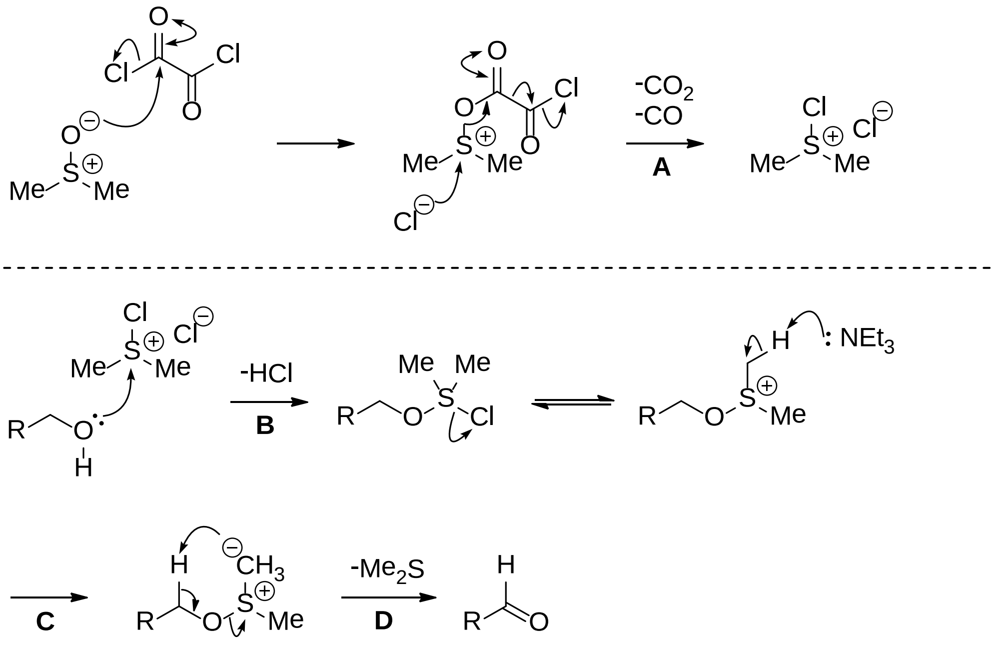
A042



Eisenbraun, E. J. *Org. Synth., Coll.* Vol. Ⅴ **1973**, 310.

Jones oxidation. **A**: Hydration of CrO_3. **B**:Attack of the alcohol to H_2CrO_4. **C**: Elimination of H_2CrO_3.

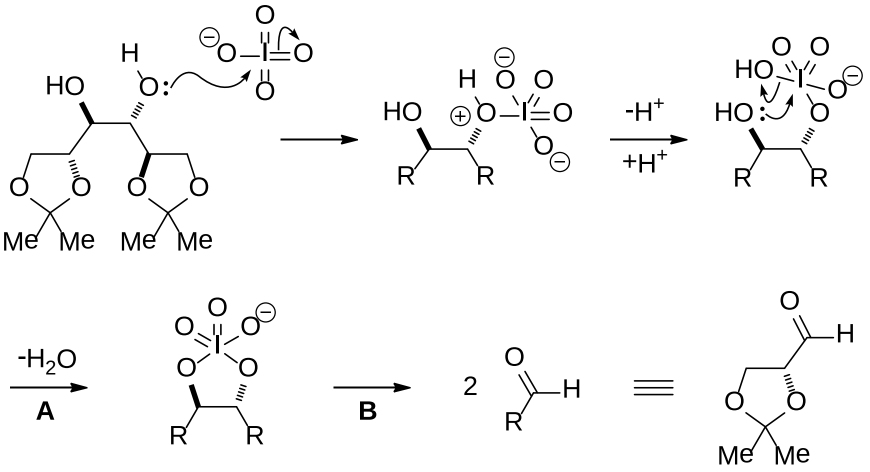
A043



LeopoLd, E. J. *Org. Synth., Coll.* Vol. Ⅶ **1990**, 258.

Swern Oxidation. **A**: Attack of DMSO to $(COCl)_2$ to form a chlorosulfonium ion with generation of CO and CO_2. **B**: Attack of an alcohol to the chlorosulfonium ion. **C**: Formation of a sulfur ylide. **D**: β-Elimination of Me_2S.

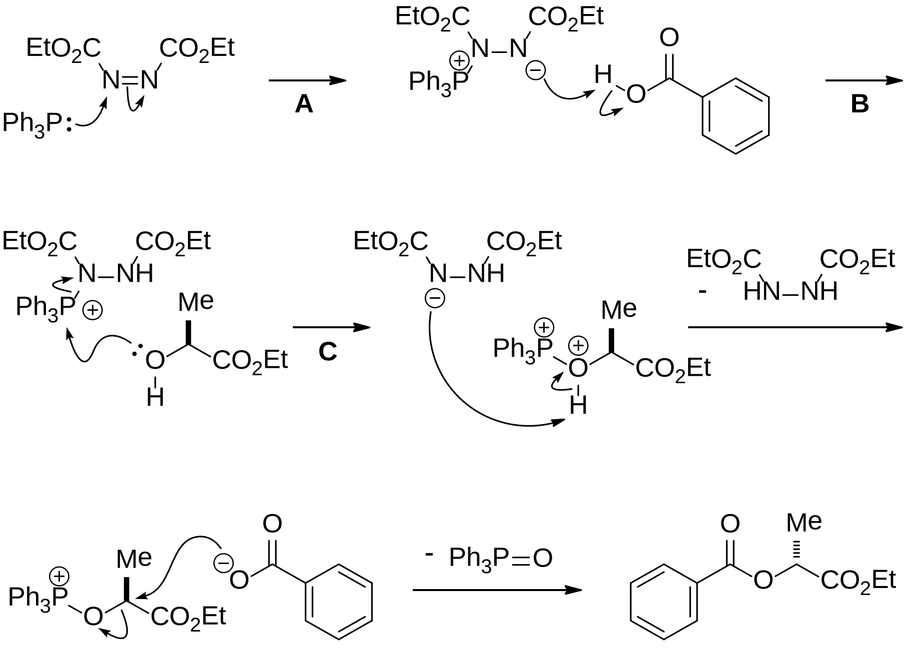
A044



Schmid, C. R.; Bryant, J. D. *Org. Synth., Coll.* Vol Ⅷ **1995**, 450

A: Formation of a cyclic intermediate. **B**: Cleavage of the C-C bond to form two molecules of the aldehyde,

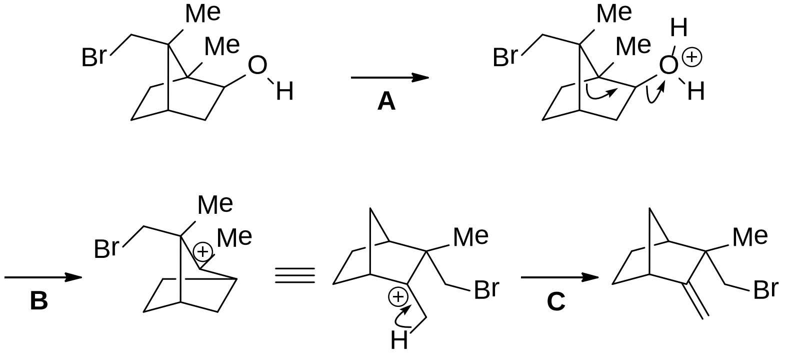
A045



Mitsunobu, O. *Synthesis* **1981** 1

Mitsunobu reaction. **A**: Conjugate addition of Ph_3P to DEAD to form a zwitter ion. **B**: Deprotonation to the most acidic proton in the reaction system. **C**: Attack of the alcohol to the activated reagent followed by deprotonation. **D**: Attack of the carboxylate with inversion of configuration.

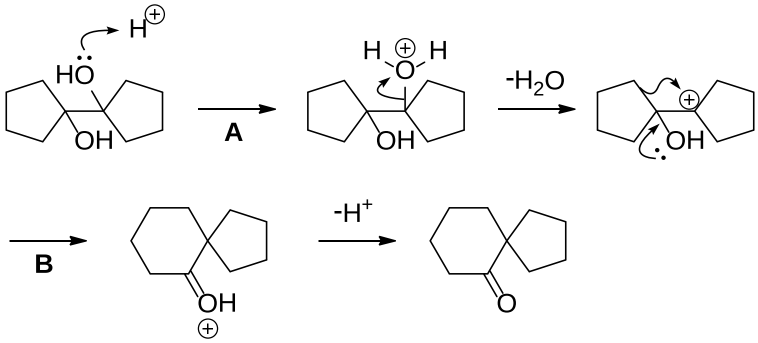
A046



Zhong, G.-F.; Schlosser, M. *Synlett*. **1994**, 173

Wanger-Meerwein rearrangement. **A**: Protonation of the alcohol. **B**: Elimination of water assisted by cleavage of the C-C bond to form a stable tertiary carbocation **C**: Deprotonation to form an olefin.

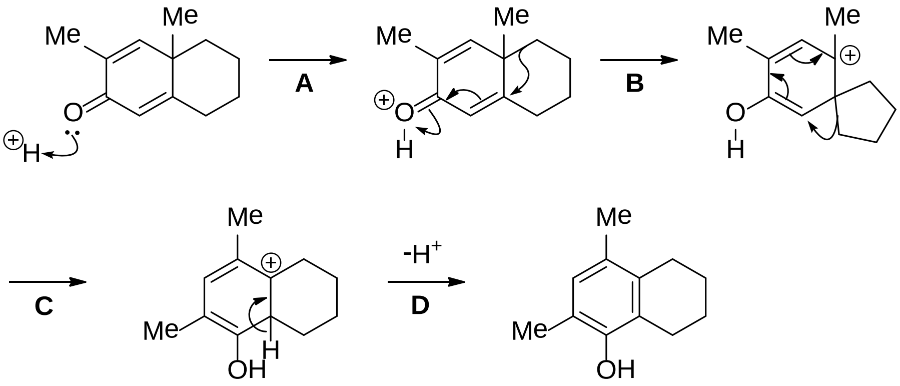
A047



Walter, C. R., Jr. *J. Am. Chem. Soc.* **1952**, 74, 5185.

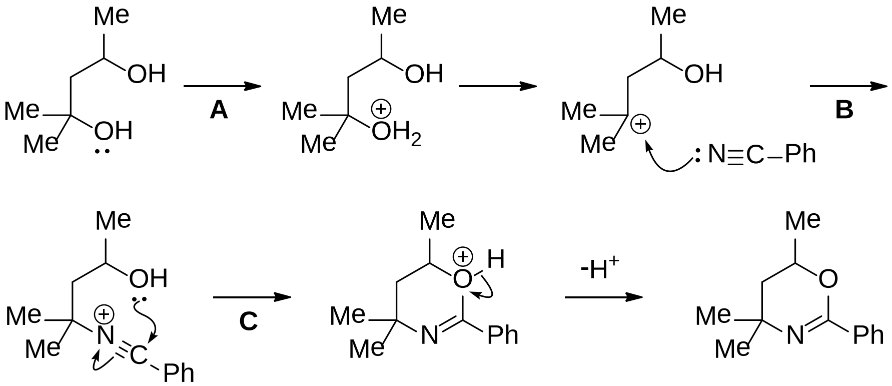
pinacol rearangement. **A**: Protonation of the alcohol followed by elimination of water to form a tertiary center. **B**: 1,2-Alkyl shift helped by the oxygen lone pair of the hydroxy group.

A048



Waring, A.J.; Zaidi, J. H.; Pilkington, J. W. *J. Chem. Soc., Perkin Trans.* I **1981**, 1454. Dienone-phenol rearrangement. **A**: Protonation of the ketone. **B**: 1,2-Alkyl shift to form a stable tertiary carbocation. **C**: 1,2-Alkyl shift to form a stable tertiary carbocation. **D**: Aromatization by deprotonation.

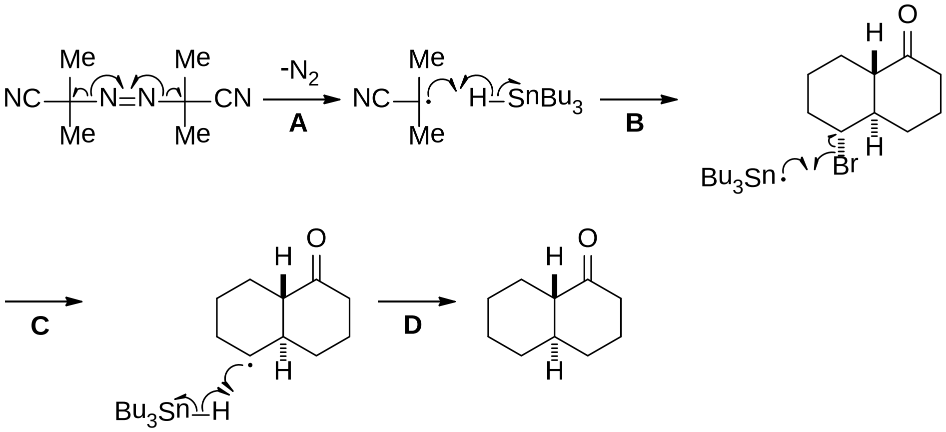
A049



Tillmanns, E.-J.; Ritter, J. J. *J. Org. Chem*. **1957**, 22, 839

Ritter reaction. **A**: Protonation of the tertiary alcohol followed by elimination of water to form a more stable tertiary carbocation. **B**: Attack of PhCN to the carbocation to form a nitrilium ion. **C** Intramolecular addition of the hydroxy group to the nitrilium ion.

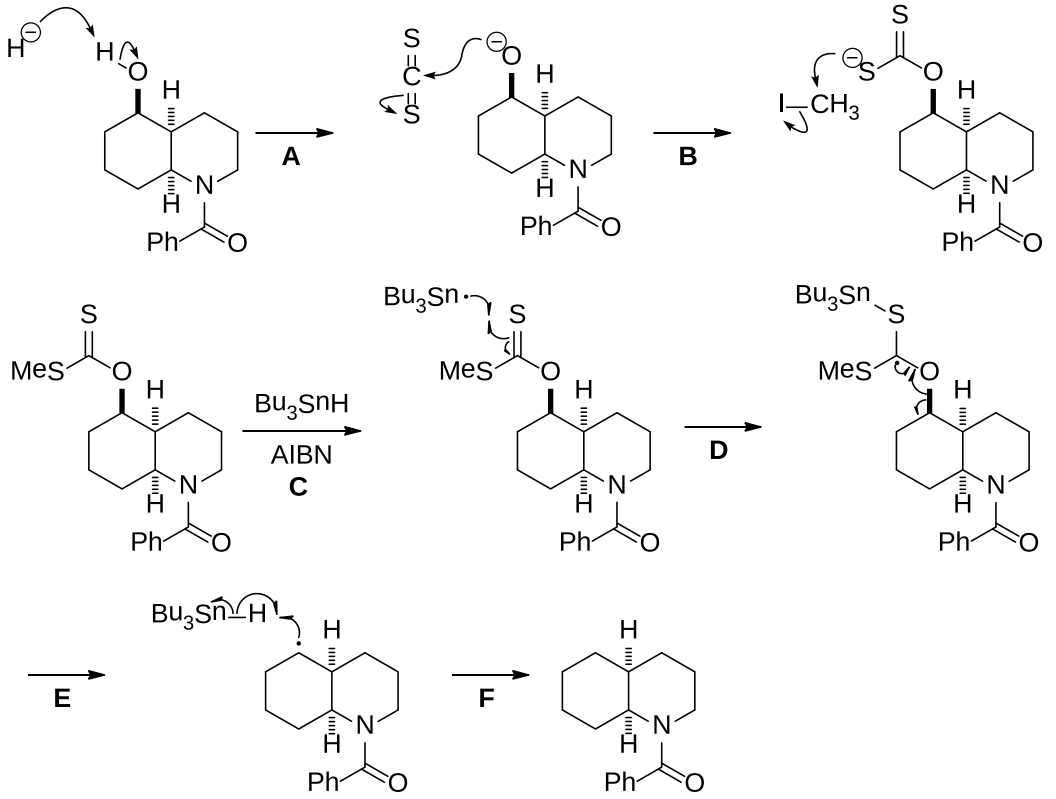
A050



Hamon, D. P. G.; Richards, K. R. *Aust. J. Chem*. **1953**, 36, 2243

A: Thermal decomposition of AIBN to give the stable tertiary radicals. **B**: Abstraction of a hydrogen atom from Bu_3SnH. **C**: The resulting tin radical reacts with a halide to form a carbon radical. **D**: Abstraction of a hydrogen atom from Bu_3SnH to continue the radical chain reaction.

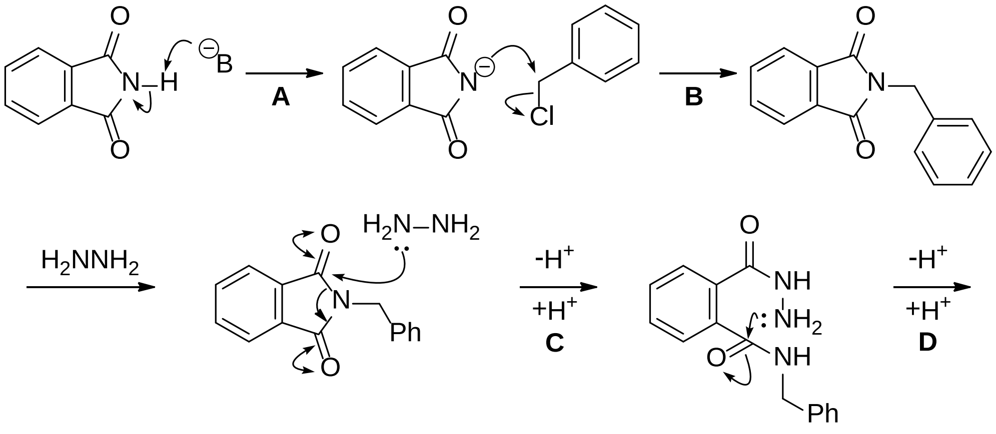
A051

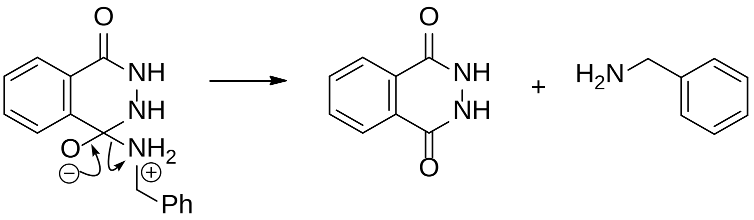


Comins, D, L.; Abdullah, A. H. *Tetrahedron Lett.* **1985**, 26, 43.

Barton-McCombie deoxygenation. **A**: Deprotonation of an alcohol. **B**: Addition of the alkoxide ion to CS_2 followed by methylation to form a xanthate. **C**: Generation of a tin radical. **D**: Attack of the radical to the sulfur atom of the xanthate to form a stable carbon radical. **E**: Cleavage of the C-O bond to form a secondary carbon radical. **F**: Abstraction of a hydrogen from Bu_3SnH.

A052

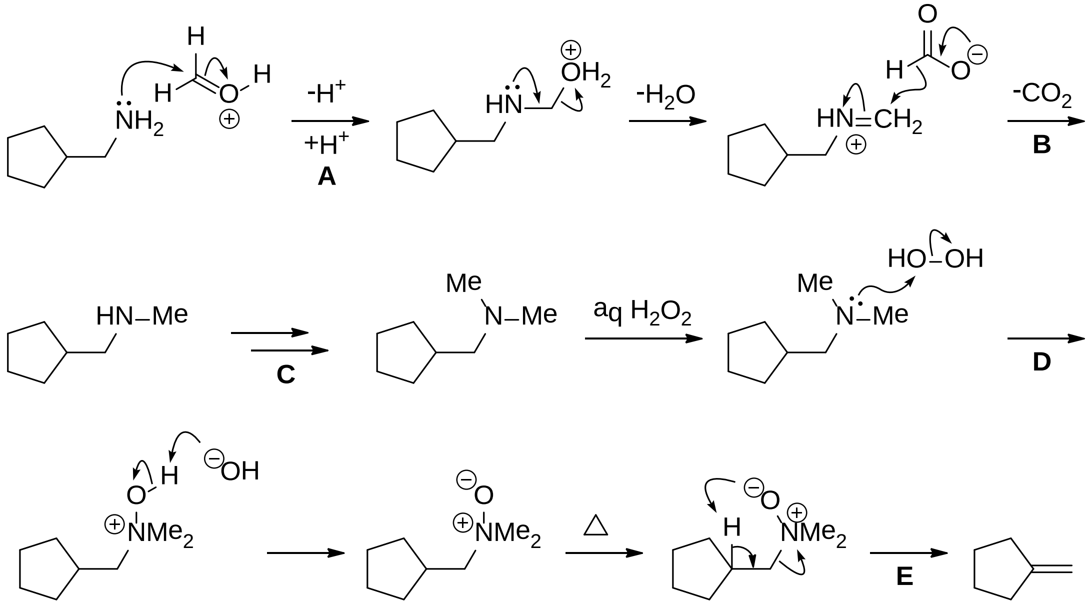




Manske, R. H. F. *Org. Synth., Coll.* Vol. II **1943**, 83.

Gabriel synthesis. **A**: pKa RCONHCOR = 9.6, HCO_3^- = 10.3. **B**: Afkylation, **C**: Addition of H_2NNH_2 to the imide to form a hydrazide. **D**: Intramolecular addition of the amino group of the hydrazide to the amide carbonyl to release benzylamine.

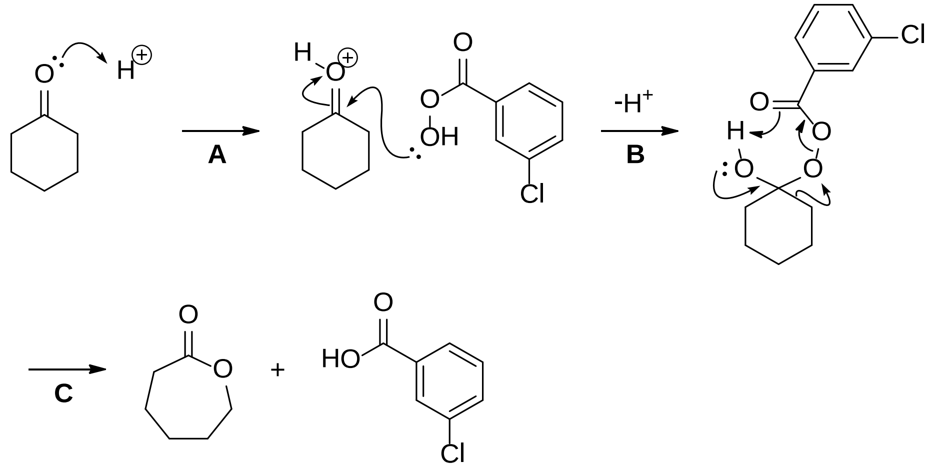
A053



Cope, A, C.; Bumgardner, C. L.; Schweizer. E. E. J. Am. Chem. Soc. **1957**, 79, 4729

Eschweiler-Clarke methylation (A-C)and Cope elimination (E). **A**: Addition of the amine to formaldehyde followed by dehydration to form an immium ion. **B**: Hydride transfer from a formate and to the iminium ion with generation of CO_2. **C**: Iteration of the same steps. **D**: Oxidation of the tertral amine to form an N-oxide. **E**: syn-Elimination.

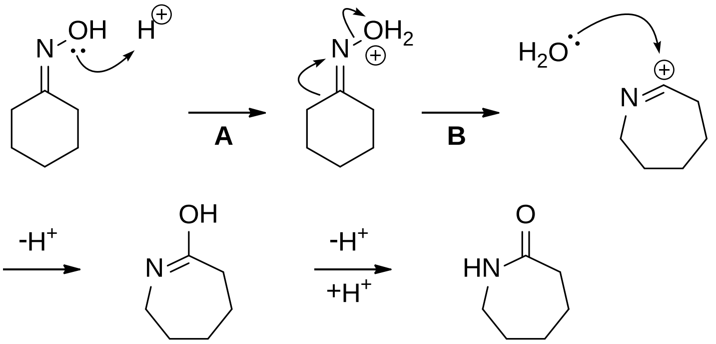
A054



Krow, G. R. *Org. React.* **1993**, 43, 251.

Baeyer-Villiger oxidation. **A**: Activation of the carbonyl group by protonation. **B**: Addition of mCPBA to the carbonyl group. **C**: 1,2-Alkyl shift helped by the oxygen tone-pair with cleavage of the peroxide to form a lactone.

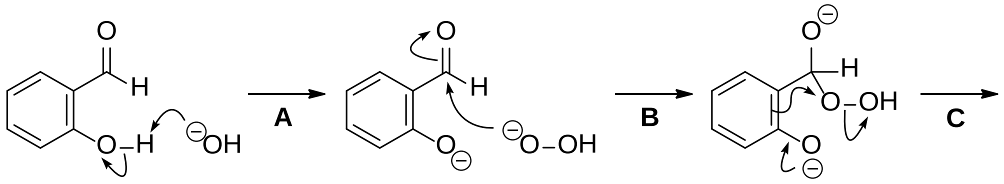
A055

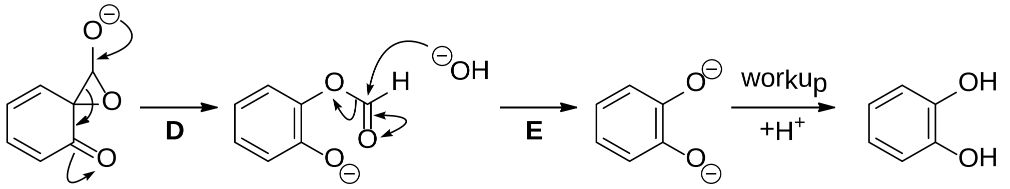


Eck, J. C.; Marvel, C. S. *Org. Synth., Coll.* Vol. II **1943**, 76.

Beckmann rearrangement. **A**: Protonation of the oxime. **B**: Migration of the alkyl substituent with simultaneous cleavage of the N-O bond.

A056

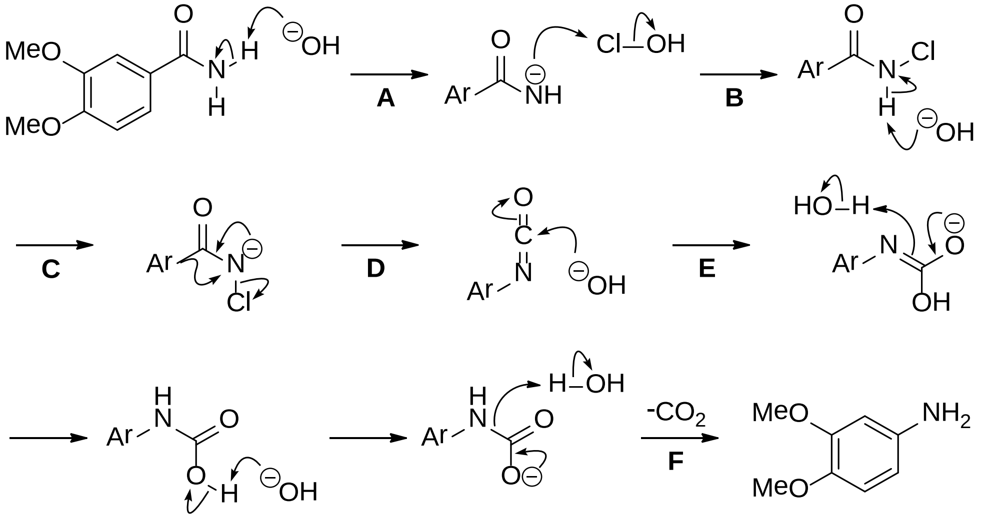




Dakin. H. D. *Org. Synth., Coll.* Vol. I **1941**, 149.

Dakin reaction. **A**: Deprotonation of the phenol (pKa PhOH = 10, H_2O = 15.7). **B**: Addition of hydroperoxide ion to the carbonyl group. **C**: Attack of the electron-rich aromatic ring to the peroxide oxygen with cleavage of the O-O bond to form an epoxide. **D**: Cleavage of the epoxide to restore the aromaticity, **E**: Hydrolysis of the resulting formate.

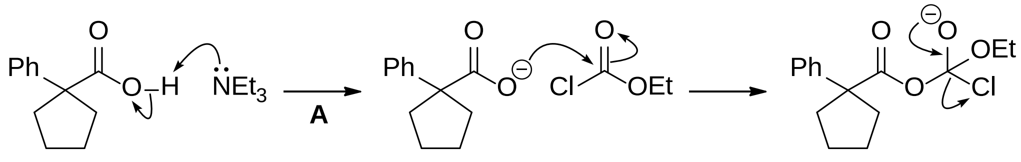
A057

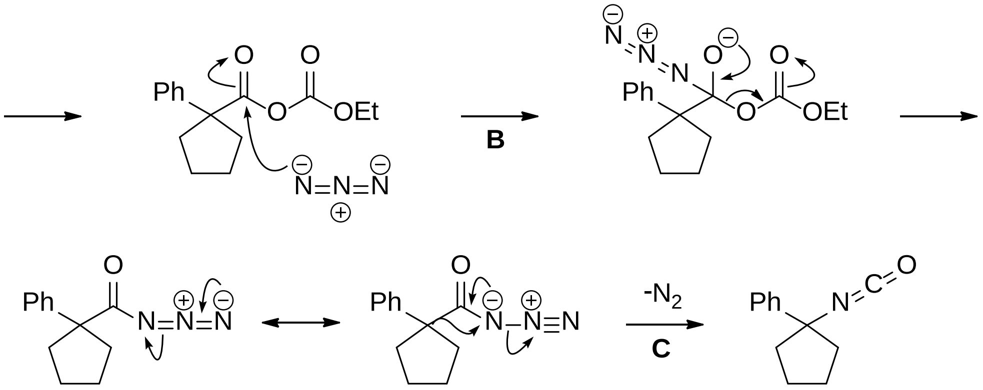


Buck. J. S.; Ide, W. S. *Org. Synth., Coll.* Vol. II **1943**, 44

Hofmann rearrangement. **A**: pKa $RCONH_2$ = 17, H_2O = 15.7. **B**: Chlorination of the amide anion. **C**: Deprotonation. **D**: The anion on the nitrogen atom induces migration of the aromatic ring with cleavage of the N-Cl bond to form an isocyanate. **E**: Addition of hydroxide ion to the isocyanate. **F**: Decarboxylation.

A058

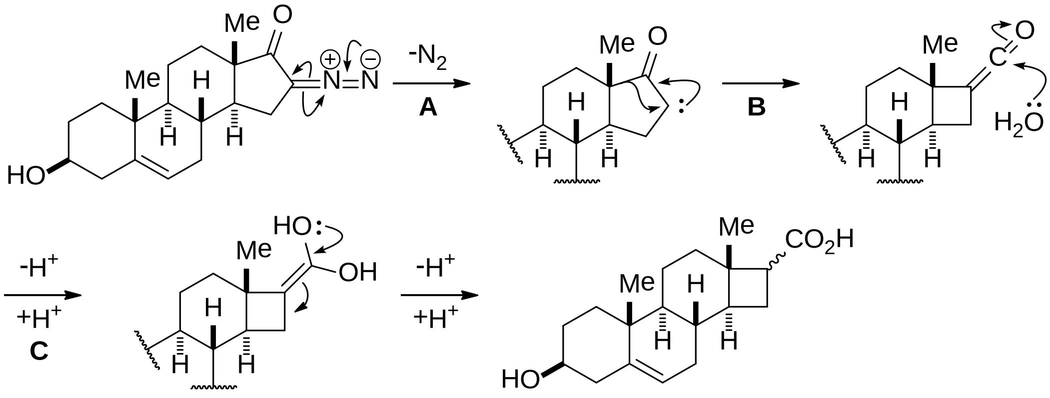




Kaiser, C.; Weinstock, J. *Org. Synth., Coll.* Vol Ⅵ **1988**, 910.

Curtius rearrangement. **A**: Formation of a mixed anhydride. **B**: Addition of azide ion to the mixed anhydride occurs at the more electron-deficient carbonyl group to form an acyl azide. **C**: Migration of the carbon atom to the nitrogen proceeds with retention of configuration as N$_2$, an extremely good leaving group, departs from the molecule.

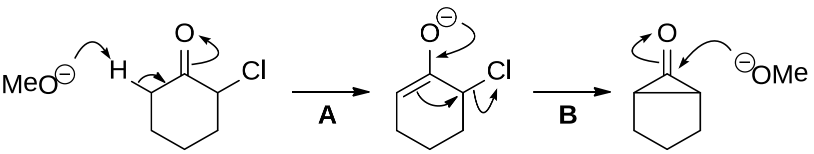
A059

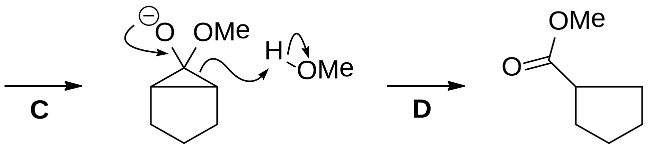


Wheeler, T. N.; Meinwald, J. *Org. Synth., Coll.* Vol. Ⅵ**1988**, 840.

Wolff rearrangement. **A**: Photo-induced generation of a carbene. **B**: Insertion of the carbene to the C-C bond results in a ring contraction to form a ketene. **C**: Addition of water to the ketene.

A060

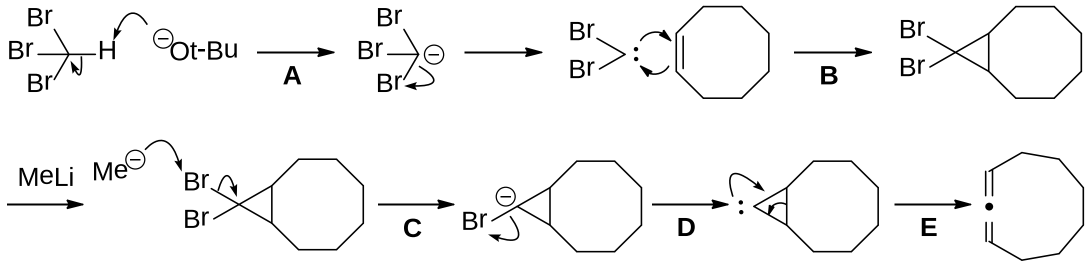




Goheen, D. W.; Vaughan, W. R. *Org. Synth., Coll.* Vol. Ⅳ **1963**, 594.

Favorskii rearrangement. **A**: Deprotonation to form an enolate. **B**: Formation of a cyclopropanone. **C**: Addition of methoxide ion to the carbonyl group. **D**: Cleavage of the cyclopropane ring with simultaneous protonation.

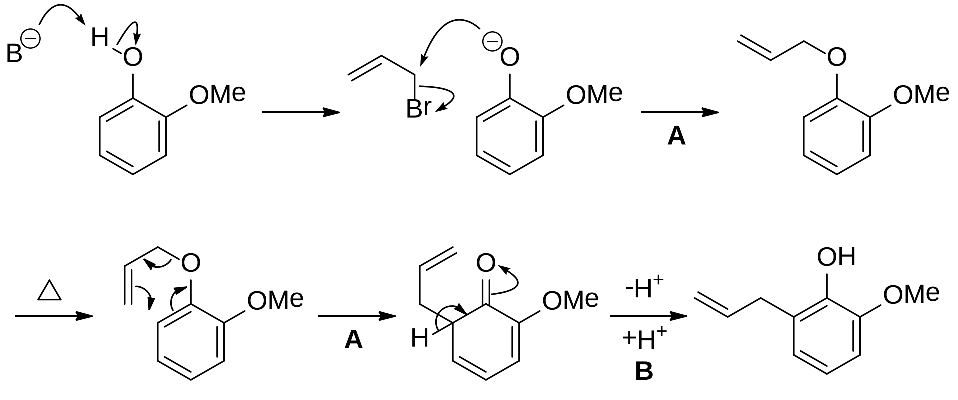
A061



Skattebel, L,; Solomon, S. *Org. Synth., Coll.* Vol. Ⅴ **1973**, 306,

A: Generation of a dibromocarbene via α-elimination of HBr, **B**: Insertion of the carbene to the olefin toform a cyclopropane. **C**: Halogen-lithium exchange. **D**: Generation of a carbene. **E**: Insertion of the carbene to the C-C bond to form an allene.

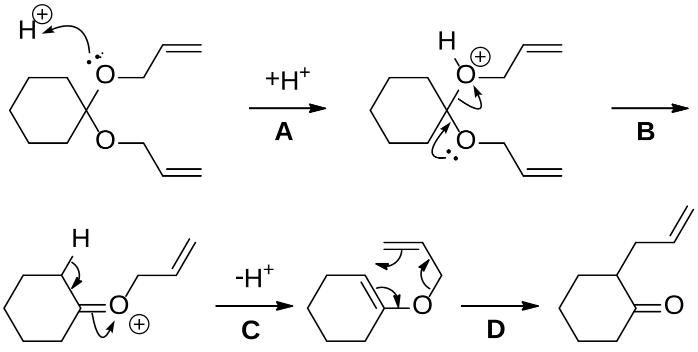
A062



Allen, C. F. H; Gates, J. W., Jr, *Org. Synth., Coll.* Vol. Ⅲ **1955**, 418

A: Allylation of the phenol. **B**: [3,3] Sigmatropic rearrangement (Claisen rearrangement). **C**: Aromatization.

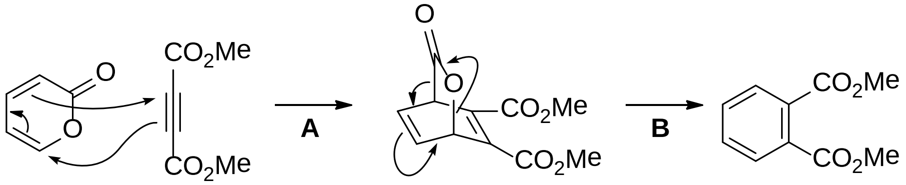
A063



Howard, W. L.; Lorette, N. B. *Org, Synth., Coll* Vol. Ⅴ **1973**.25

A: Protonation of an oxygen atom of the acetal. **B**: Elimination of allyl alcohol helped by the oxygen lone pair of the acetal. **C**: Deprotonation to form an enol ether. **D**: [3,3] Sigmatroplc rearrangement (Claisen rearrangement).

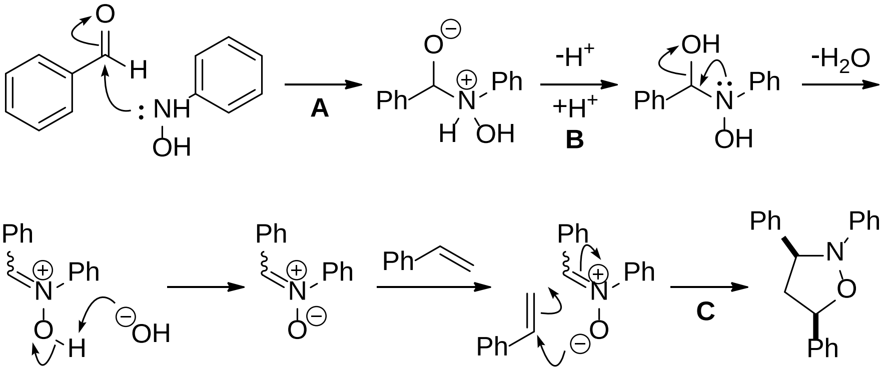
A064



Ziegler, T,; Layh, M.; Effenberger, F. *Chem. Ber.* **1987**, 120, 1347.

A: Diels-Alder reaction. **B**: Retro Diels-Alder reaction.

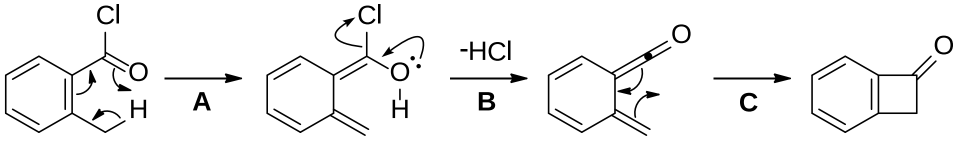
A065



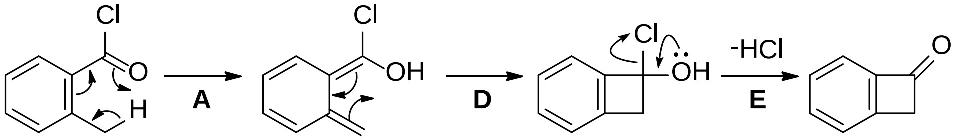
Brüning, I.; Grashey, R.; Hauck, H.; Huisgen, R.; Seidl, H, *Org. Synth., Coll*. Vol. Ⅴ **1973**, 1124

A: Addition of a hydroxylamine to the aldehyde. **B**: Proton transfer followed by elimination of water to form a nitrone **C**: 1,3-Dipolar cycloaddition of the nitrone to stvrene (electronically, [4+2] cycloaddition).

A066



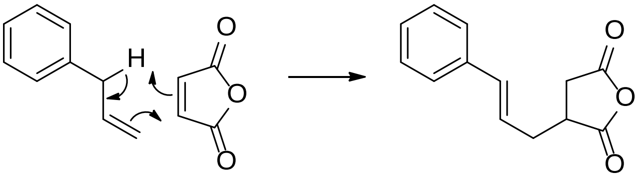
or



Schiess, P.; Barve, P. V.; Dussy, F E.; Pfiffner, A. *Org. Synth., Coll.* Vol. Ⅸ **1998**, 28.

A: Isoerization to form an o-quinodimethane. **B**: Elimination of HCl to form a ketene. **C**: 4e Elimination of hydrogen chloride to form a ketone.

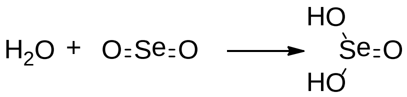
A067

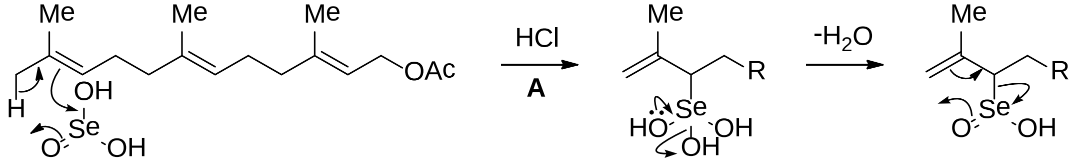


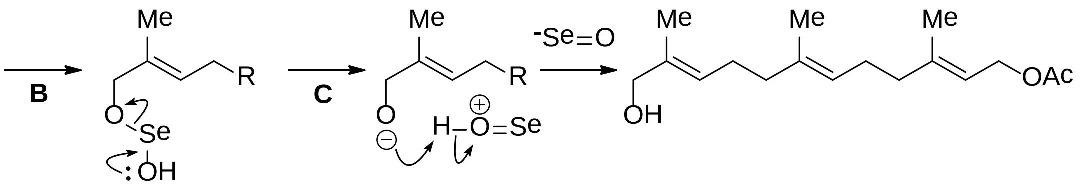
Rondestvedt, C. S., Jr. Org. Synth., Coll. Vol. /V 1963, 766

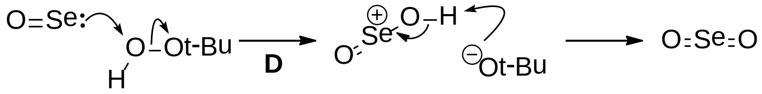
Ene reaction.

A068





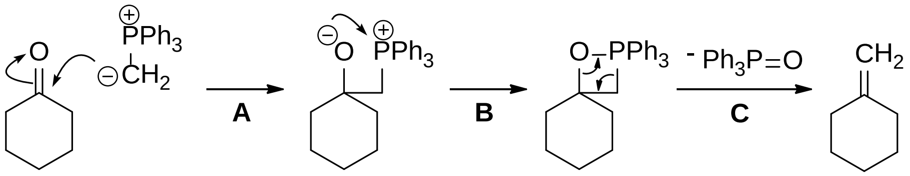




Umbreit, M. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, 99, 5526.

A: Ene reaction occurs on the least hindered olefin. **B**: [2,3] Sigmatropic rearrangement. **C**: Elimination of the alcohol. **D**: Oxidation of SeO with TBHP to regenerate SeO_2.

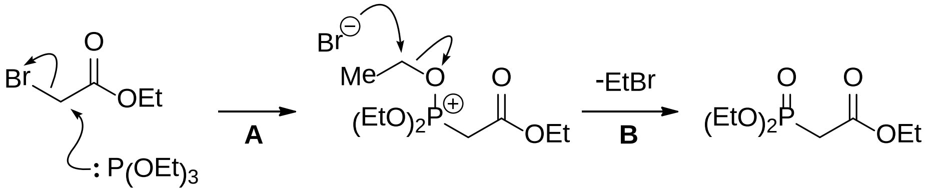
A069



Wittig, G.; Schoellkopf, U. Org. Synth., Coll. Vol. Ⅴ **1973**, 751.

Wittig reaction. **A**: Addition of the ylide to the carbonyl group to form a betaine. **B**: Attack of the alkoxide to the phosphonium cation to form an oxaphosphetane. **C**: Irreversible elimination of Ph_3PO.

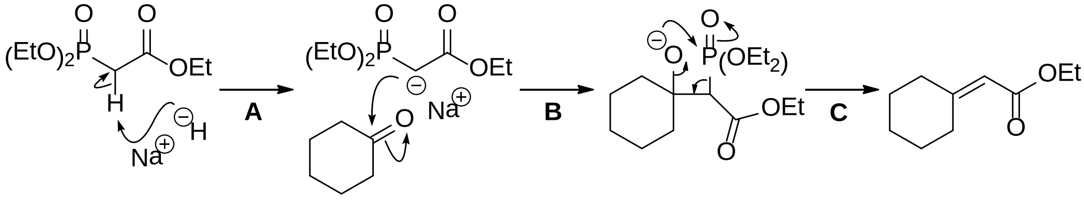
A070



van der Klei, A.; de Jong, R. L. P.; Lugtenburg, J.; Tielens, A. G. M. Eur. *J. Org. Chem*. **2002**, 3015.

Arbuzov reaction. **A**: Attack of $P(OEt)_3$ to the reactive bromoacetate to release bromide ion (S_N2 reaction). **B**: Attack of the resulting bromide ion to the ethyl group in an S_N2 fashion to form a phosphonate.

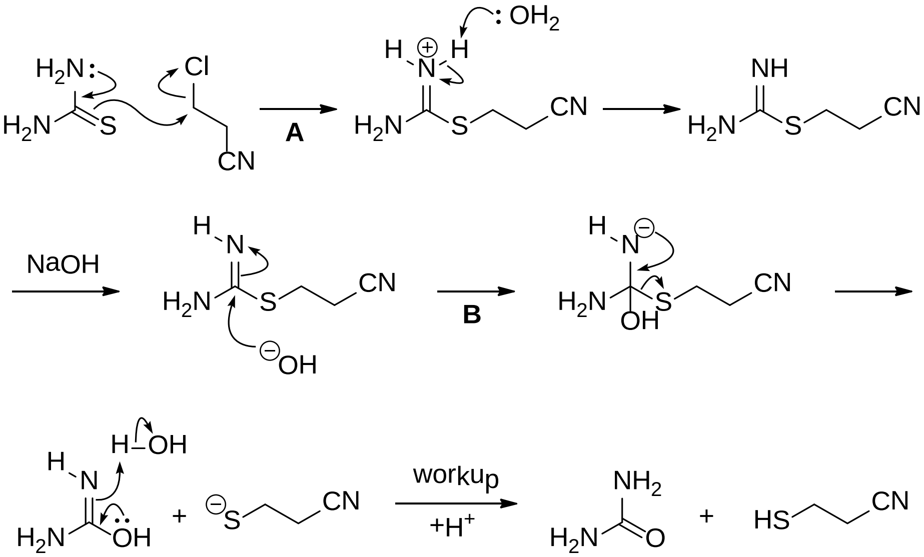
A071



Wadsworth, W. S., Jr.; Emmons, W. D. *Org. Synth., Coll.* Vol. Ⅴ **1973**, 547.

Horner-Wadsworth-Emmons reaction. **A**: Deprotonation of the phosphonate. **B**: Addition of the phosphonate ion to the ketone. **C**: Attack of the alkoxide to the phosphonate followed by elimination of a phosphate ion to form an olefin.

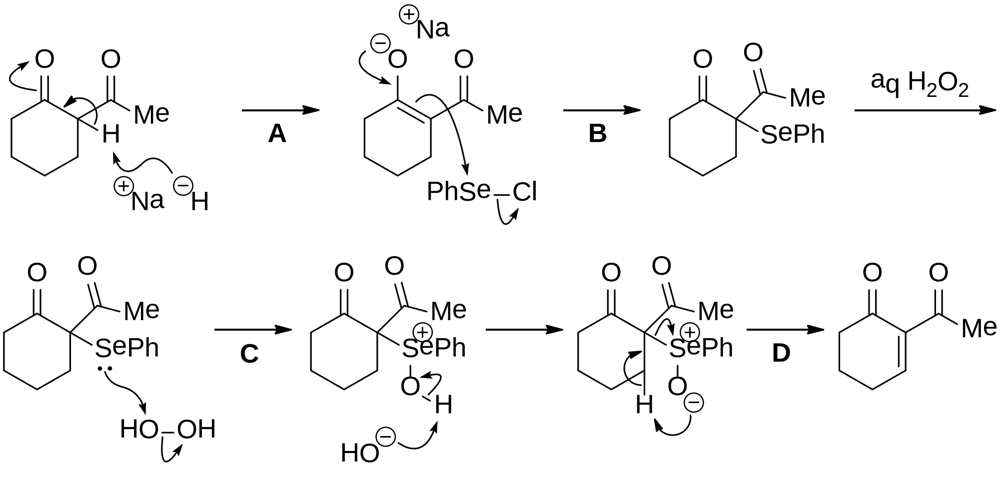
A072



Gerber, R, E.; Hasbun, C.; Dubenko, L. G.; King, M. F.; Bierer, D. E. *Org. Synth., Coll.* Vol. Ⅹ**2002**, 475

A: Attack of the more reactive sulfur atom of thiourea to the alkyl chloride to form an isothiourea (S_N2 reaction). **B**: Hydrolysis of the isothiourea.

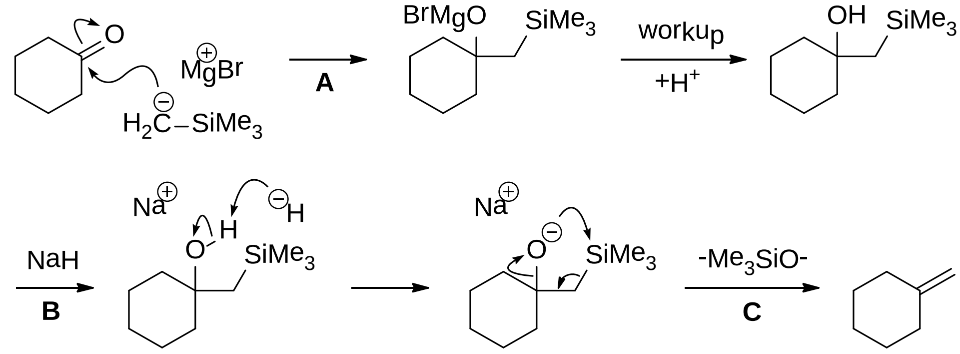
A073



Renga, J. M: Reich, H. J. *Org. Synth., Coll.* Vol. Ⅵ **1988**.23

A: Deprotonatien of the β-diketone (pKa $RCOCH_2COR$ = 9, H_2 = 35). **B**: Selenylation at the α-position. **C**: Oxidation of the selenide to form a selenoxide. **D**: β-Elimination.

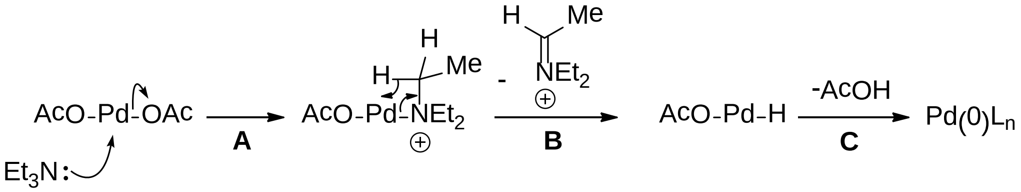
A074



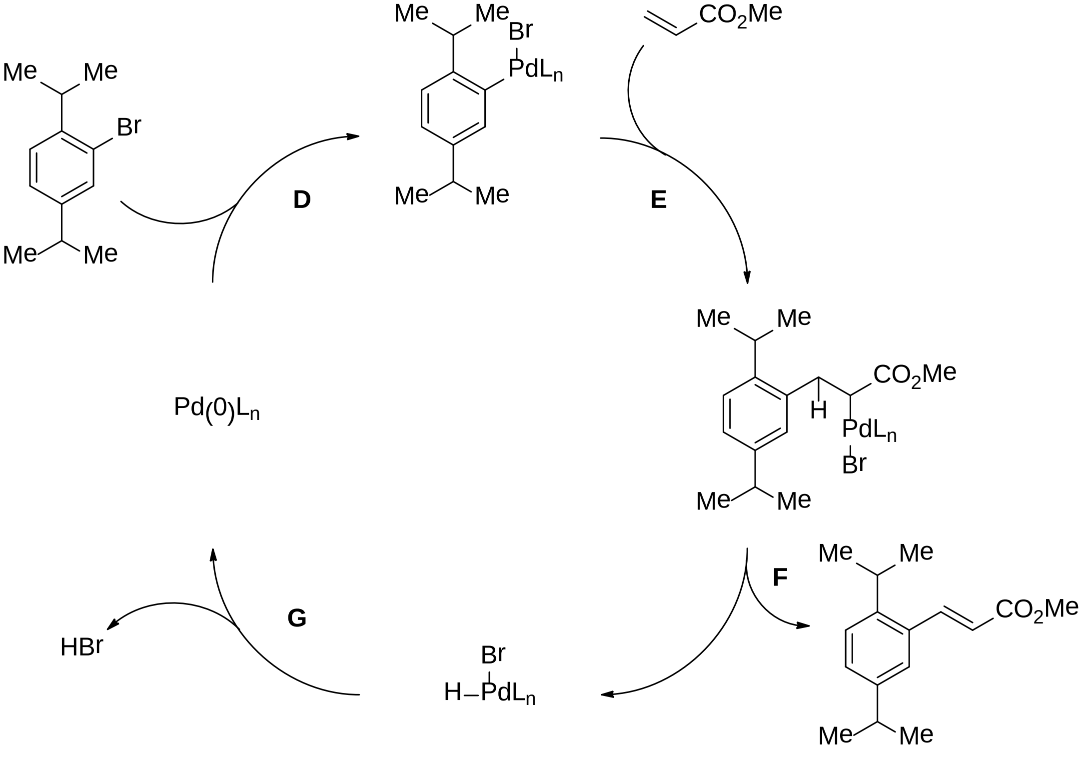
Ager, D. J. *Org. React.* **1990**, 38, 1.

Peterson olefination. **A**: Addition of Me3SiCH2MgBr to the ketone. **B**: Exchange of the counter cation from Mg to Na. **C**: Elimination of a silanol ion via a four-membered transition state.

A075



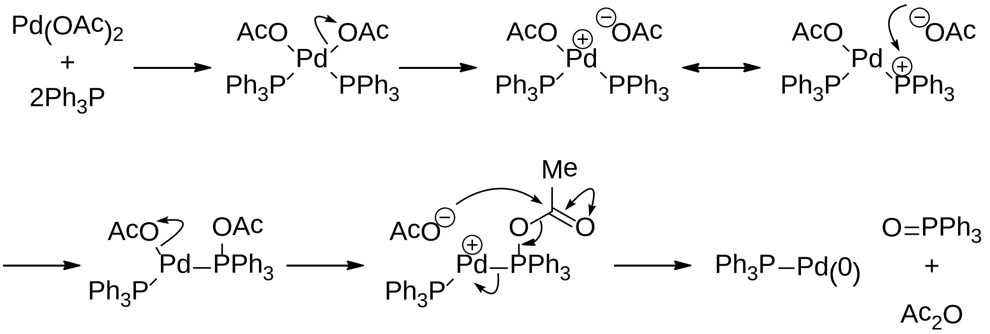
Reduction of Pd(OAc)$_2$ to Pd(0) using Et$_3$N. **A**: Ligand exchange. **B**: β-Elimination. **C**: Reductive elimination of AcOH.



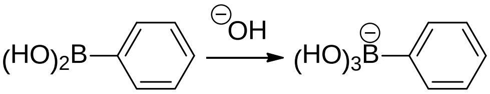
Patel, B. A.; Ziegler, C. B.; Cortese, N. A.; Plevyak, J. E.; Zebovitz, T. C.
Terpko, M.; Heck, R. F. *J. Org. Chem*. **1977**, 42, 3903.

Heck reaction. **D**: Oxidative addition. **E**: Carbopalladation. **F**: β-Elimination to form the product. **G**: Reductive elimination of HBr.

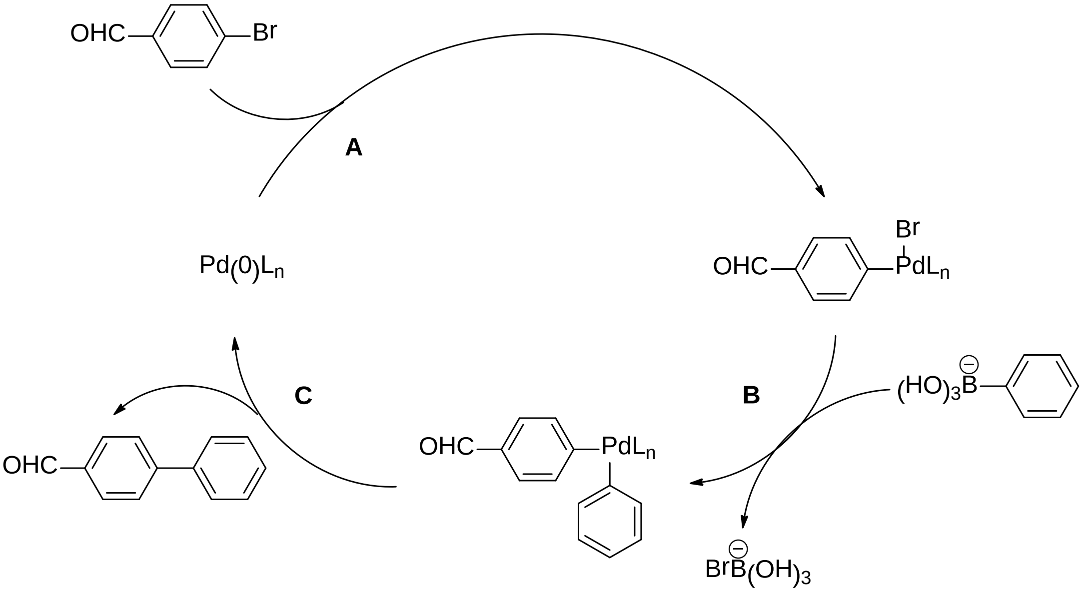
A076



Reduction of Pd(OAc)$_2$ to Pd(0) using Ph$_3$P.



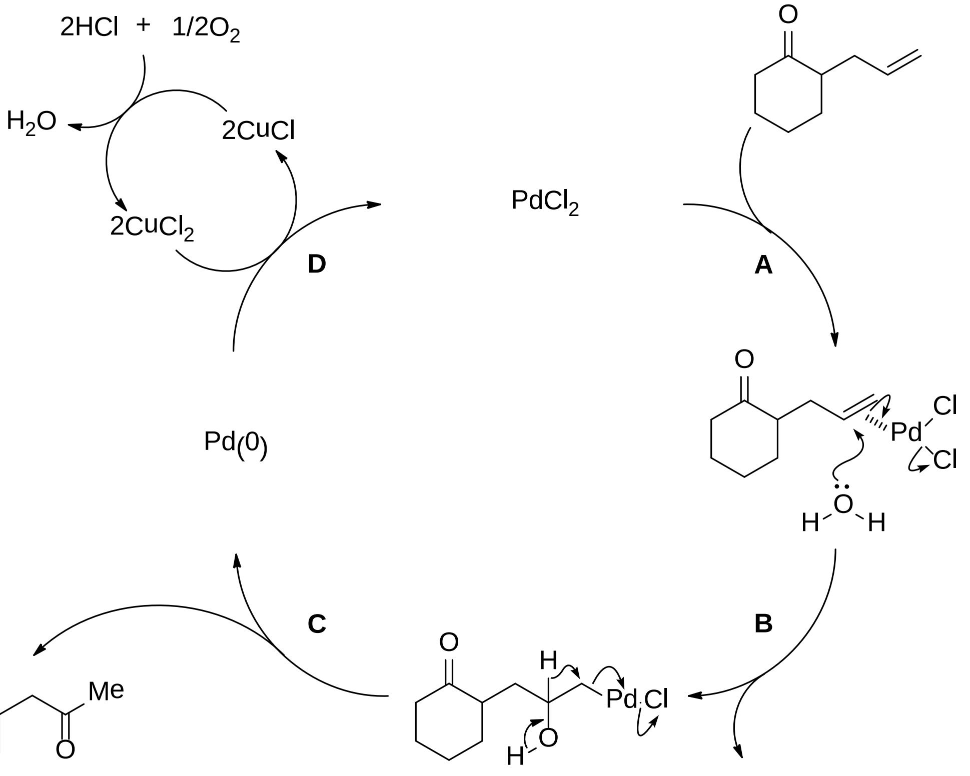
Activation of boronic acid,



Huff, B. E.; Koenig, T. M.; Mitchell, D.; Staszak, M. A. *Org. Synth., Coll* Vol. Ⅹ **2002**, 122

Suzuki-Miyaura coupling. **A**: Oxidative addition. **B**: Transmetallation. **C**: Reductive elimination.

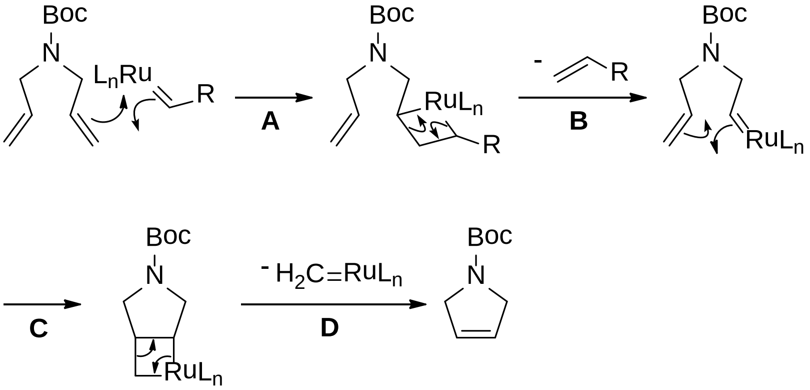
A077



Tsuji, J.; Shimizu, I.; Yamamoto, K. *Tetrahedron Lett.* **1976**, 34, 2975.

Wacker oxidation, **A**: Olefin complexation. **B**: Oxypalladation. **C**: Hydride shift. **D**: Oxidation of Pd(0) with $CuCl_2$ to regenerate $PdCl_2$. **E**: Oxidation of CuCl with O_2 to regenerate $CuCl_2$.

A078

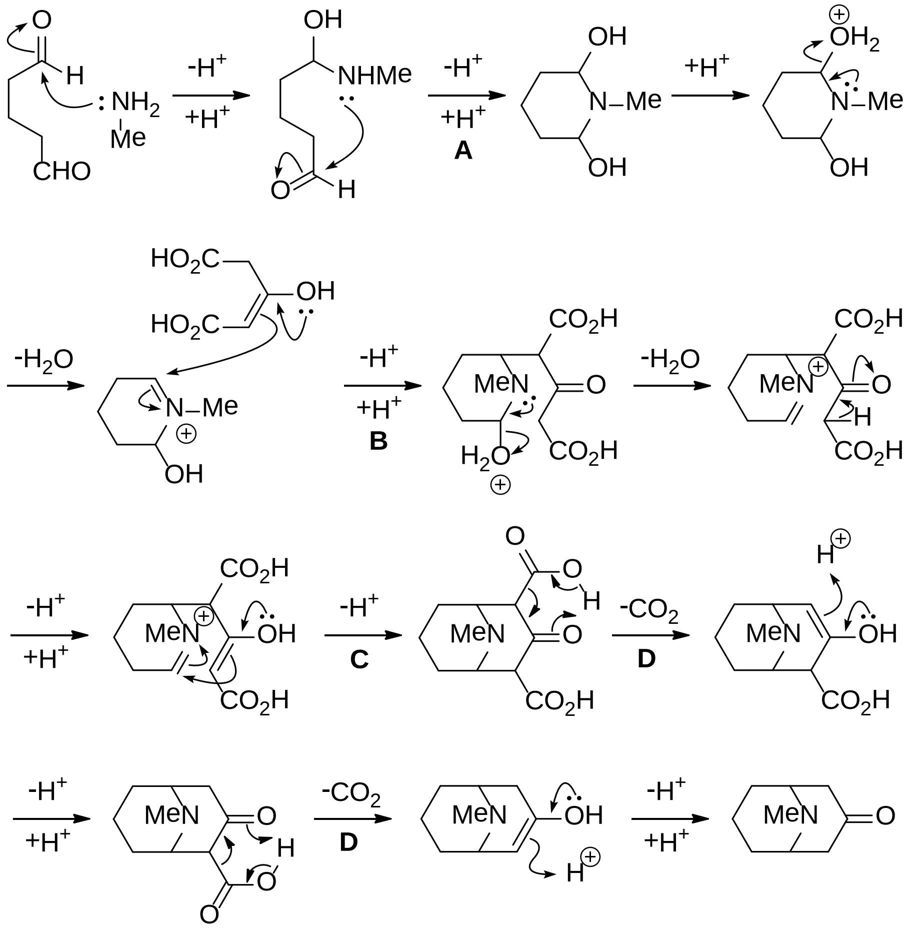


Ferguson, M. L.; O'Leary, D. J.; Grubbs, R. H. *Org. Synth.* **2002**, 80, 85.

Ring closing metathesis (RCM). **A**: Cycloaddition of a ruthenium carbene complex to the olefin to from a metallacyclobutane. **B**: Retro cycloaddition. **C**: Intramolecular cycloaddition of the ruthenium carbene complex. **D**: Retro cycloaddition to regenerate a ruthenium carbene complex.

解答 中级編

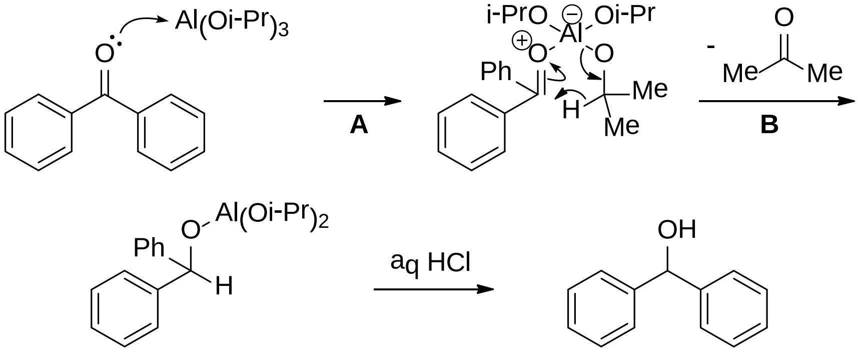
B001



Cope, A. C: Dryden, H. L.: Howell, C. F *Org. Synth., Coll.* Vol. Ⅳ **1963**, 816

Robinson-Schöpf reaction. **A**: Formation of a cyclic hemiaminal. **B**: Mannich reaction **C**: Intramolecular Mannich reaction. **D**: Decarboxylation through the six-membered transition state.

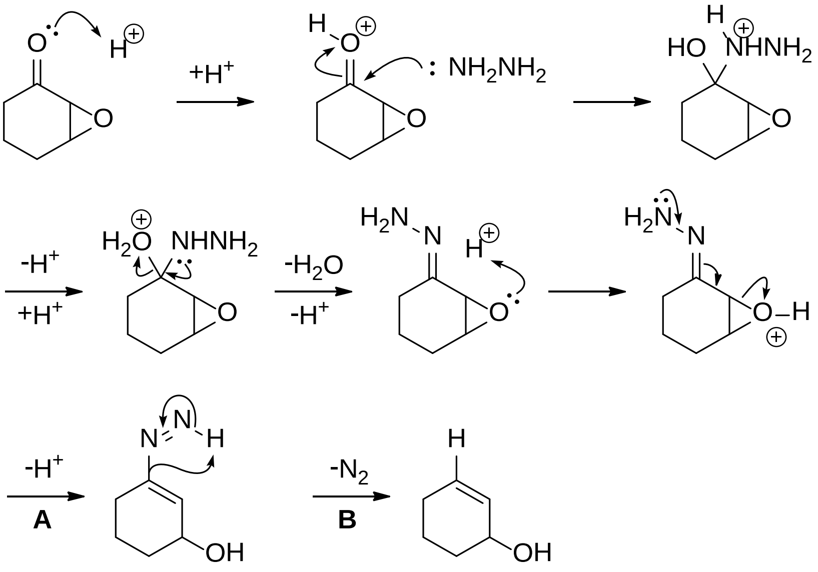
B002



Wilds, A. L. *Org. React.* **1944**, 2.

Meerwein-Ponndorf-Verley reduction. **A**: Formation of an ate complex. **B**: Hydride transfer via a six membered transition state with formation of acetone.

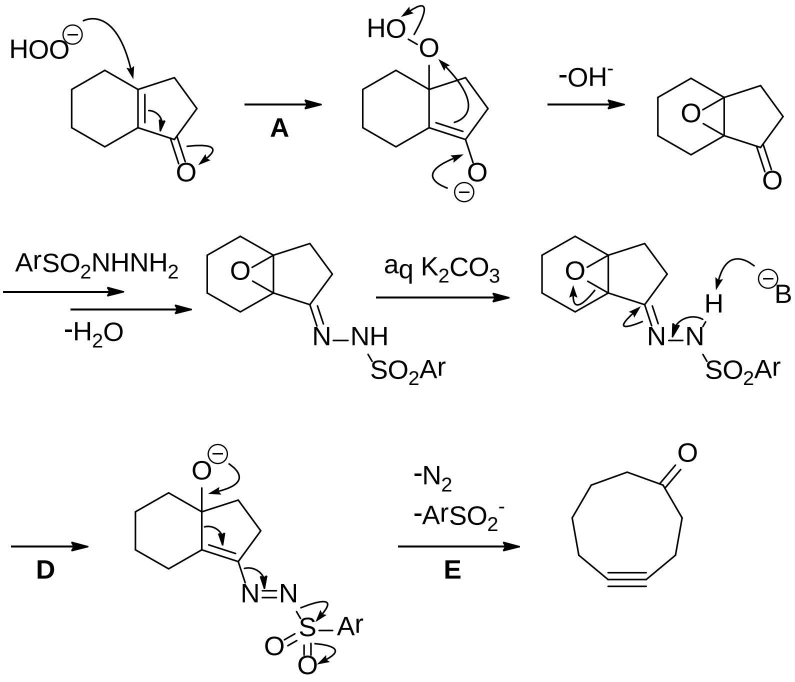
B003



Wharton, P. S.: Bohlen, D. H. *J. Org. Chem.* **1961**, 26, 3615.

Wharton rearrangement. **A**: Cleavage of the epoxide helped by the nitrogen lone pair of the hydrazone. **B**: Elimination of N_2 (an extremely good leaving group).

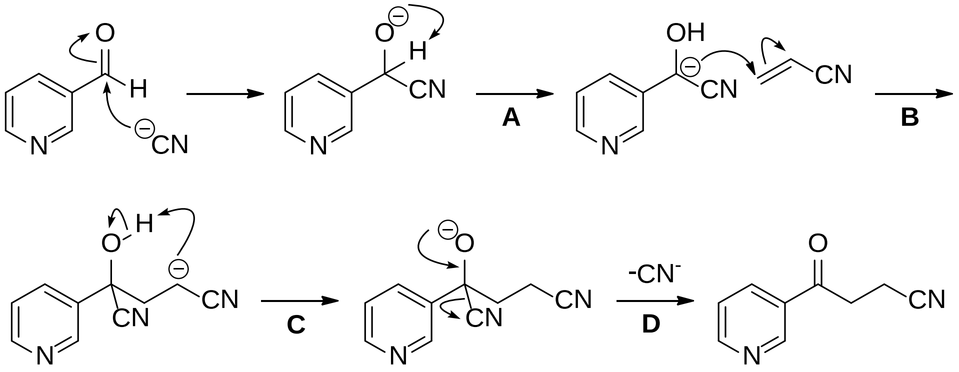
B004



Reese, C. B.; Sanders, H. P. *Synthesis* **1981**, 276.

Eschenmoser fragmentation. **A**: Michael addition. **B**: Formation of an epoxide (the O-O bond is activated). **C**: Formation of a hydrazone. **D**: pKa HCO_3^- = 10.3, $ArSO_2NH_2$ = 8.5. E: Fragmentation involving a loss of N2 and a sulfinate ion.

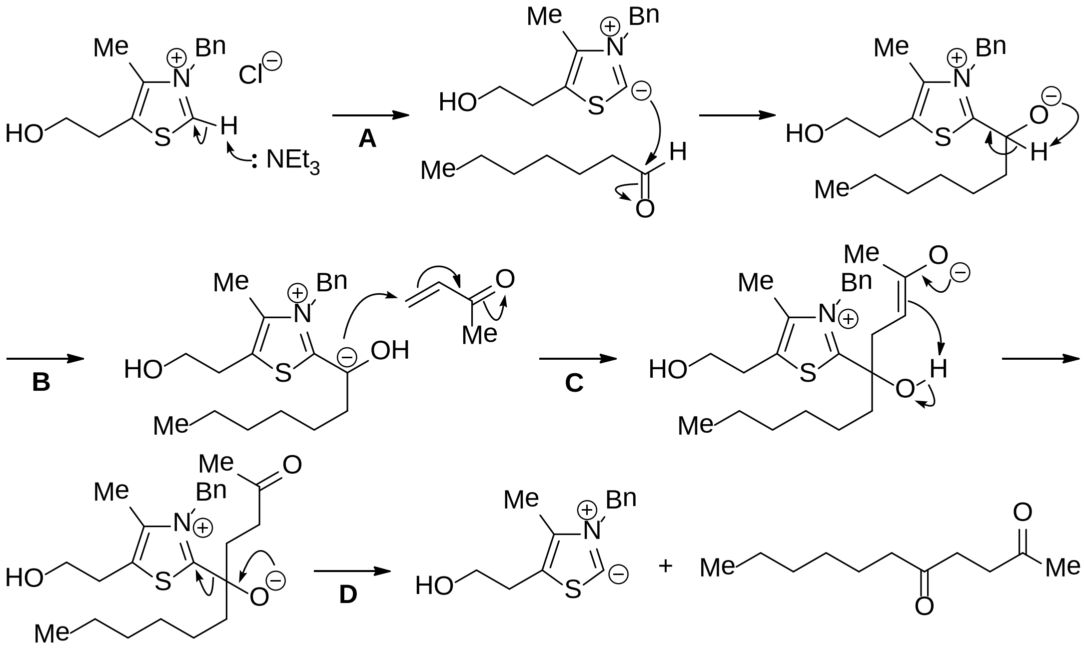
B005



Stetter, H.; Kuhlmann, H.; Lorenz, G. *Org. Synth., Coll* Vol. Ⅵ **1988**, 866

A: Formation of the less favored cyanohydrin carbanion. **B**: Michael addition. **C**: Regeneration of the cyanide ion (cyanohydrin is unstable under basic conditions).

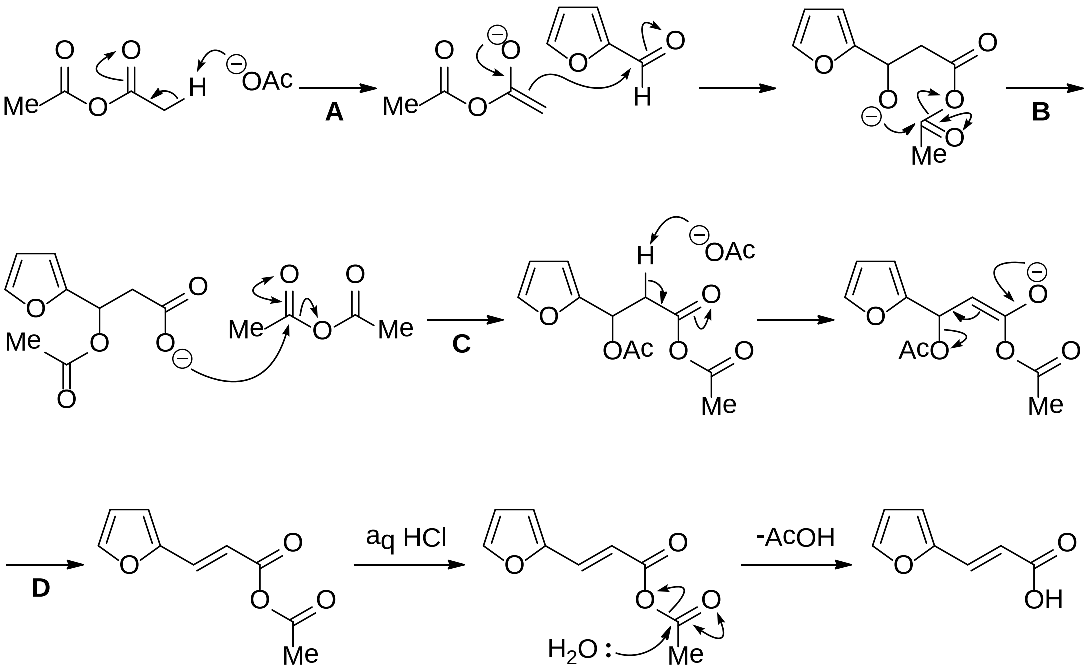
B006



Stetter, H.; Kuhlmann, H.; Haese, W. Org. Synth., Coll. Vol. Ⅷ 1993. 52

Stetter reaction. **A**: pKa thiazolinium ion = 10, $HNEt_3^+$ = 10.7. **B**: Generation of a stabilized carbanion (ref B005). **C**: Michael addition. **D**: Regeneration of the thiazolinium ion.

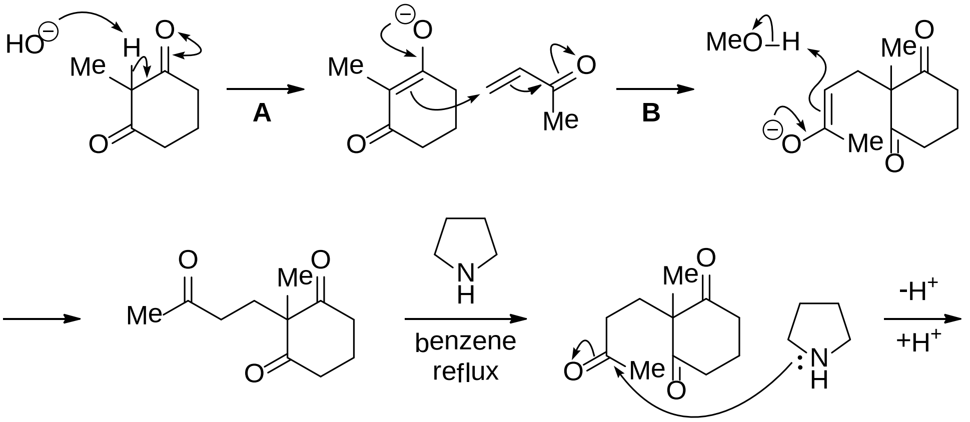
B007

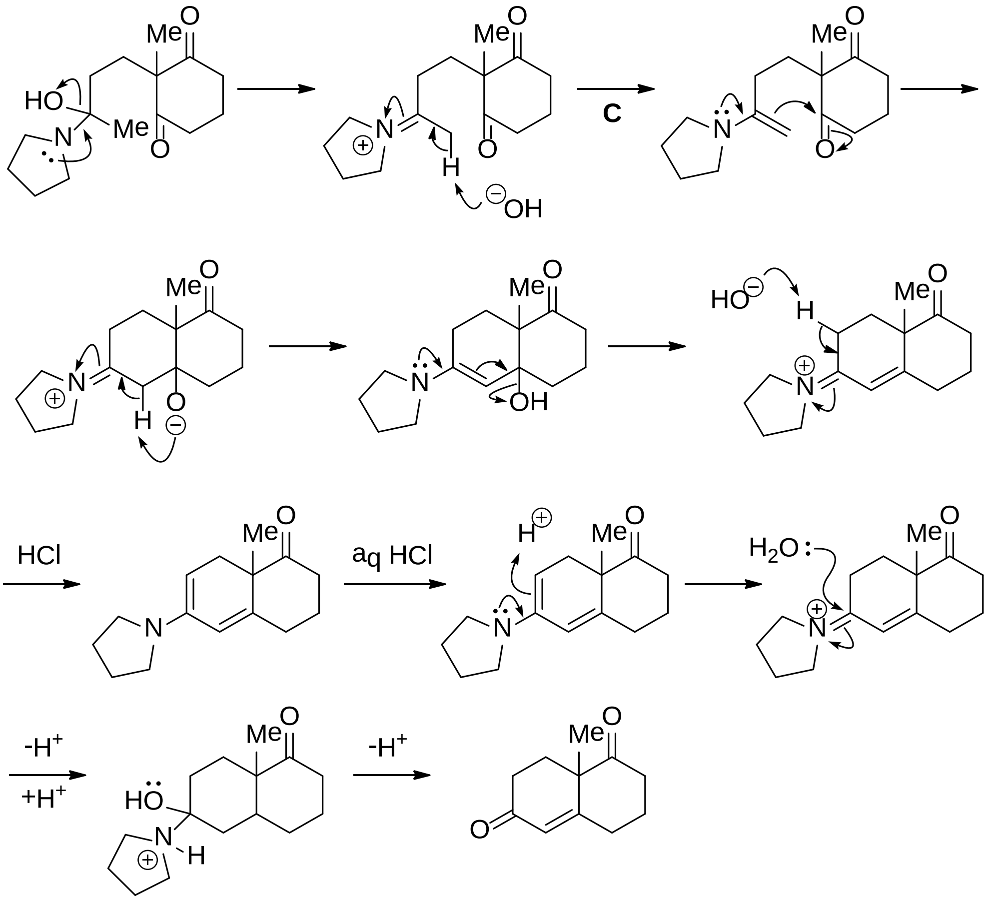


Rajagopalan, S.; Raman, P. V. A. *Org. Synth., Coll. Vol.* III **1955**, 425.

Perkin reaction. **A**: pKa $(CH_3CO)_2O$ = 13.5, AcOH = 4.8 (a small amount of the acetic anhydride anion can be formed). **B**: Intramolecular acyl transfer. **C**: Formation of a mixed anhydride. **D**: Base-catalyzed elimination of acetic acid.

B008

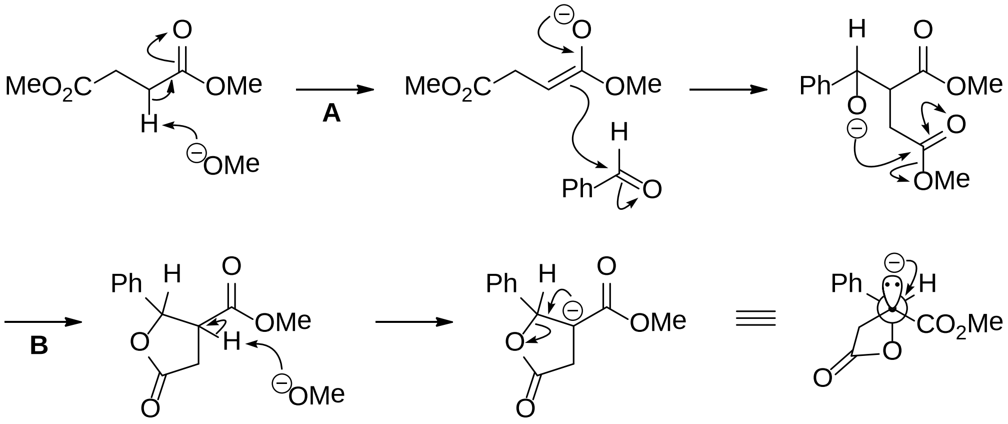


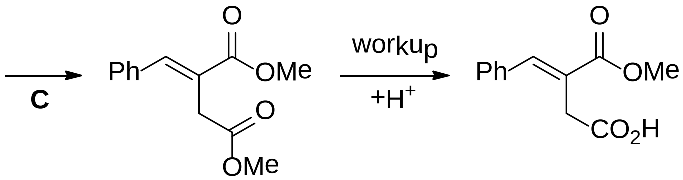


Ramachandran, S.; Newman, M. S. Org. Synth., *Coll. Vol.* V **1973**, 486

Robinson annulation. **A**: pKa RCOCH$_2$COR = 9, H_2O = 15.7. **B**: Michael addition. **C**: Formation of an enamine followed by an intramolecular addition to the ketone.

B009

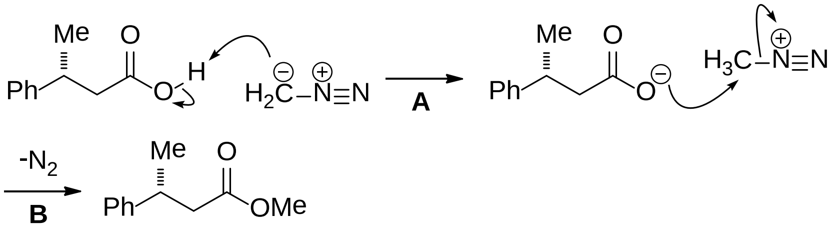




Johnson, W. S.; Daub, G. H. *Org. React.* **1951**. 6

Stobbe condensation. **A**: pKa CH_3CO_2R = 24, MeOH = 15.5. **B**: Formation of a five-membered lactone. **C**: Elimination of the carboxylate occurs by avoiding the steric repulsion between the phenyl and the methoxycarbonyl groups.

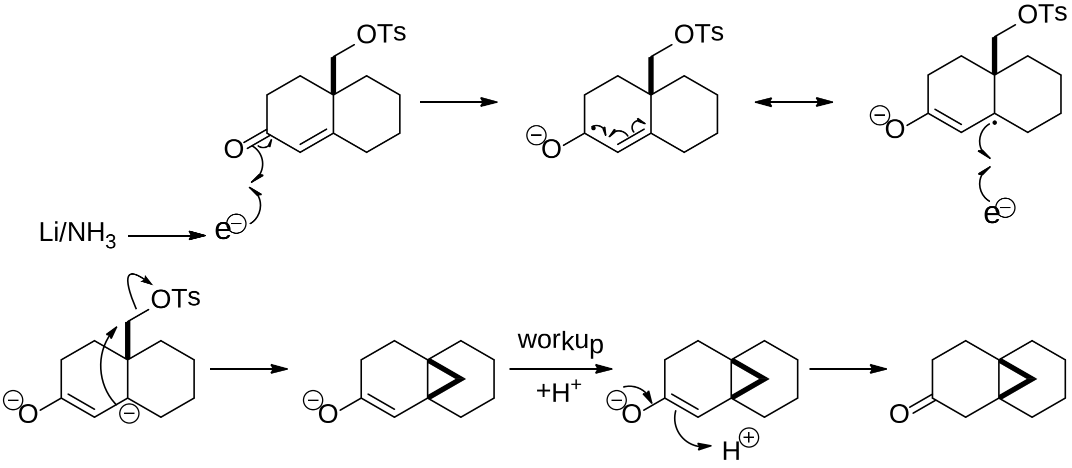
B010



Black, T. H. *Aldrichimica Acta* **1983**, 16, 3

A: pKa CH_3CO_2H = 4.8, CH_3N_2 = 10.2. **B**: The S_N2 reaction occurs in a solvent cage.

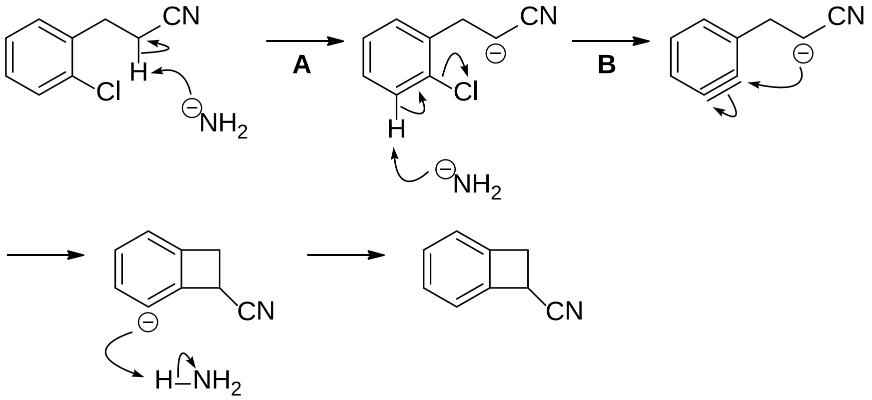
B011



Stork, G.; Tsuji, J. *J. Am. Chem. Soc.* **1961**, 83, 2783.

Two successive SET reactions followed by cyclopropane formation.

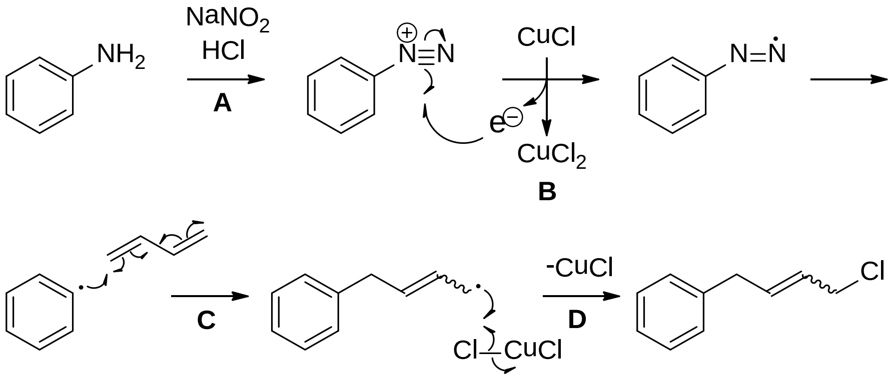
B012



Skorcz, J. A.; Kaminski, F. E. *Org. Synth., Coll.* Vol. Ⅴ **1973**.263

A: pKa CH_3CN = 25, NH_3 = 35. **B**: Formation of benzyne followed by an intramolecular nucleophilic addition.

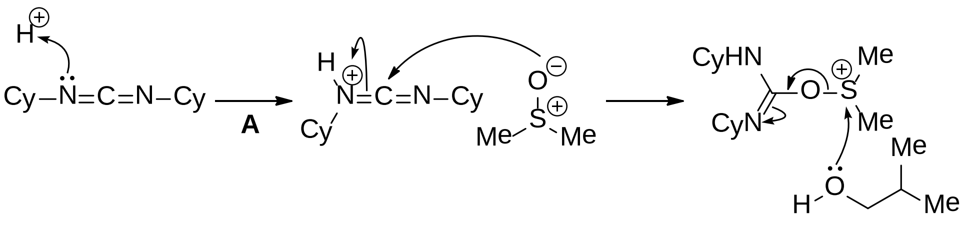
B013

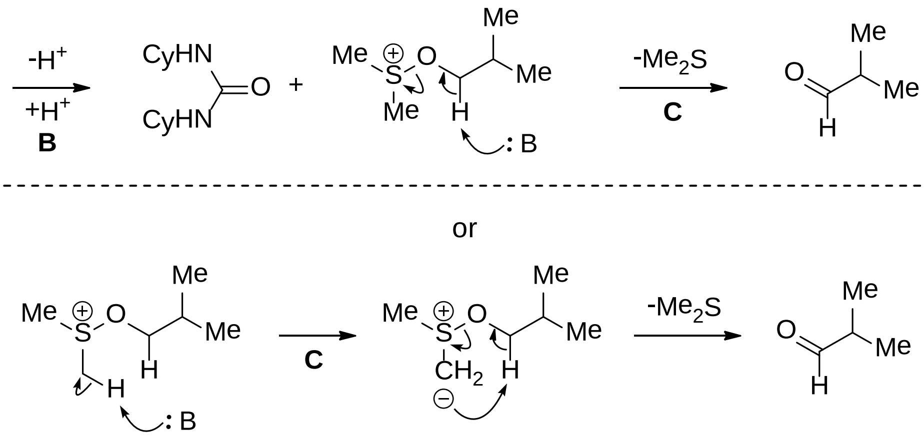


Ropp, G. A.; Coyner, E. C. *Org. Synth. Coll*, Vol. Ⅳ **1963**. 27

Meerwein arylation. **A**: Formation of a diazonium salt (ref A037). **B**: SET induces a loss of N_2 to form a phenyl radical. **C**: Addition of the phenyl radical to butadiene to form a stabilized radical. **D**: Recycle of CuCl to continue the radical chain reaction.

B014

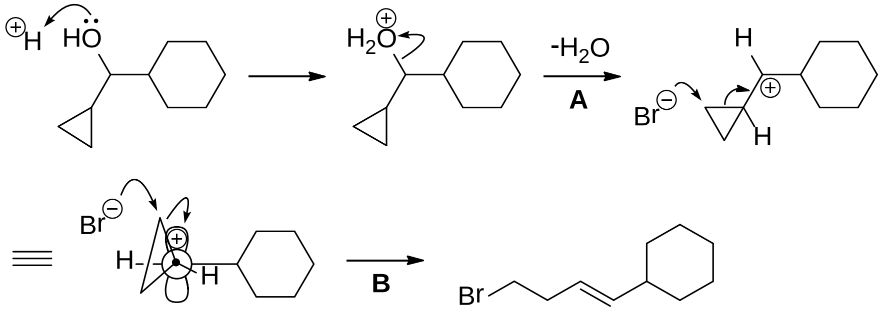




Tidwell, T. T. *Org. React.* **1990**, 39, 297.

Pfitzner-Moffatt oxidation. **A**: Activation of DCC by protonation. **B**: Nucleophilic substitution at the sulfur atom. **C**: β-Elimination of dimethyl sulfide might proceed either by 1) direct deprotonation with a base or 2) formation and collapse of a sulfur ylide.

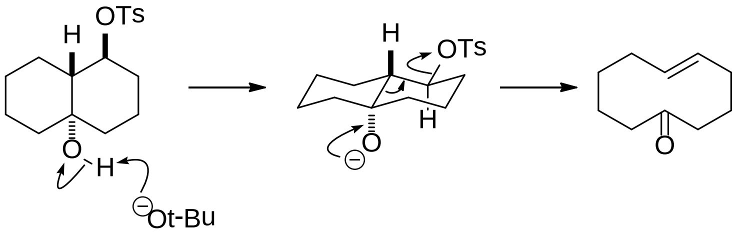
B015



Ferreri, C.; Ambrosone, M. *Syn. Commun.* **1995**, 25, 3351.

A: Generation of a carbocation stabilized by a cyclopropyl group. **B**: Cleavage of the cyclopropane ring occurs by avoiding the steric repulsion to form the trans-product.

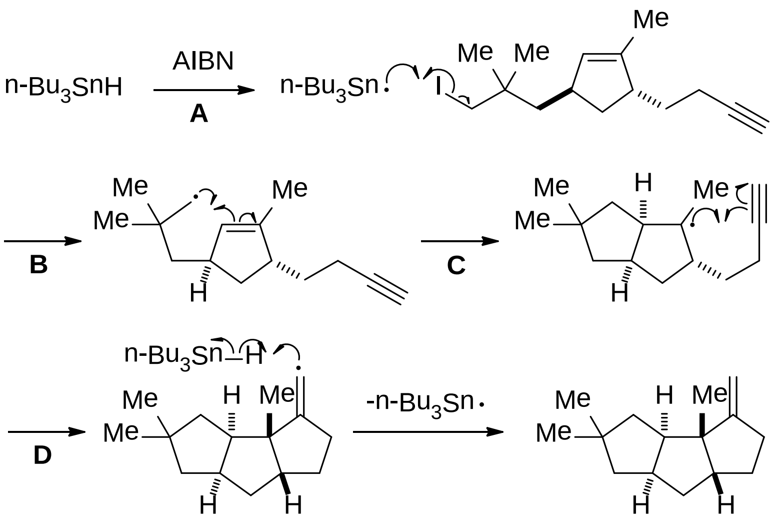
B016



Wharton, P. S.; Hiegel, G. A. *J. Org. Chem.* **1965**, 30, 3254.

Grob fragmentation. This Grob fragmentation can occur when the orbitals of the breaking C-C o-bond and C-OTs σ-bond overlap on the same plane (antiperiplanar interaction).

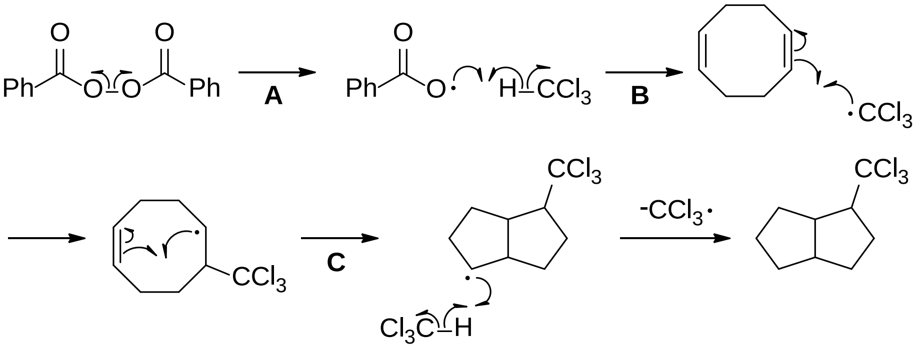
B017



Weinges, K.; Reichert, H.; Huber-Patz, U.; Irngartinger, H. *Liebigs Ann. Chem.* **1993**, 403.

A: Generation of a tin radical (ref A050). **B**: Attack on the iodide to initiate the radical chain reaction. **C**: 5-exo-trig Radical cyclization. **D**: 5-exo-dig Radical cyclization.

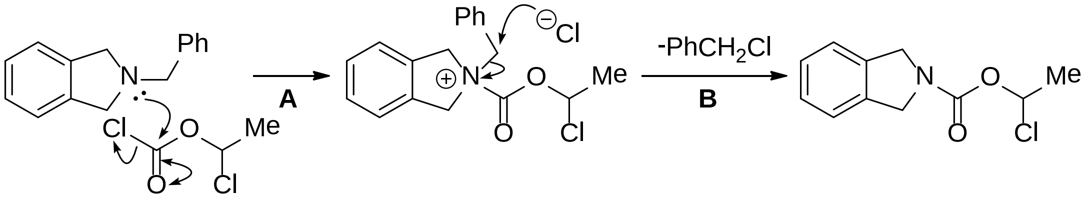
B018

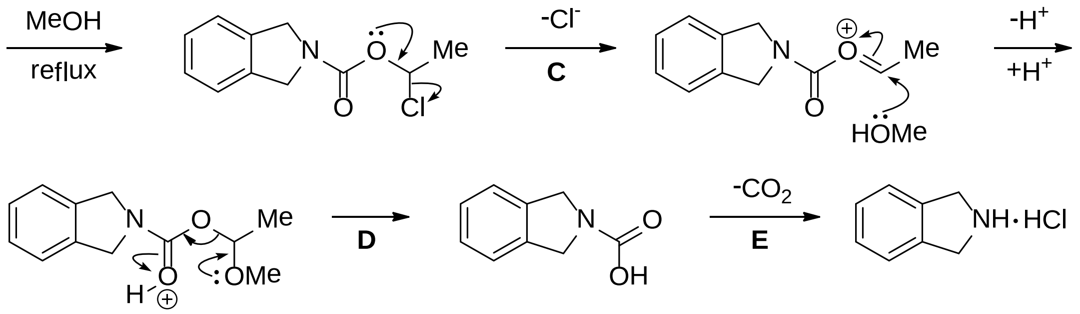


Dowbenko, R. *Org. Synth., Coll* Vol. Ⅴ **1973**, 93.

A: Homolytic cleavage of dibenzoyl peroxide. **B**: Generation of a trichloromethyl radical which then adds to 1,5-cyclooctadiene. **C**: Transannular radical cyclization.

B019

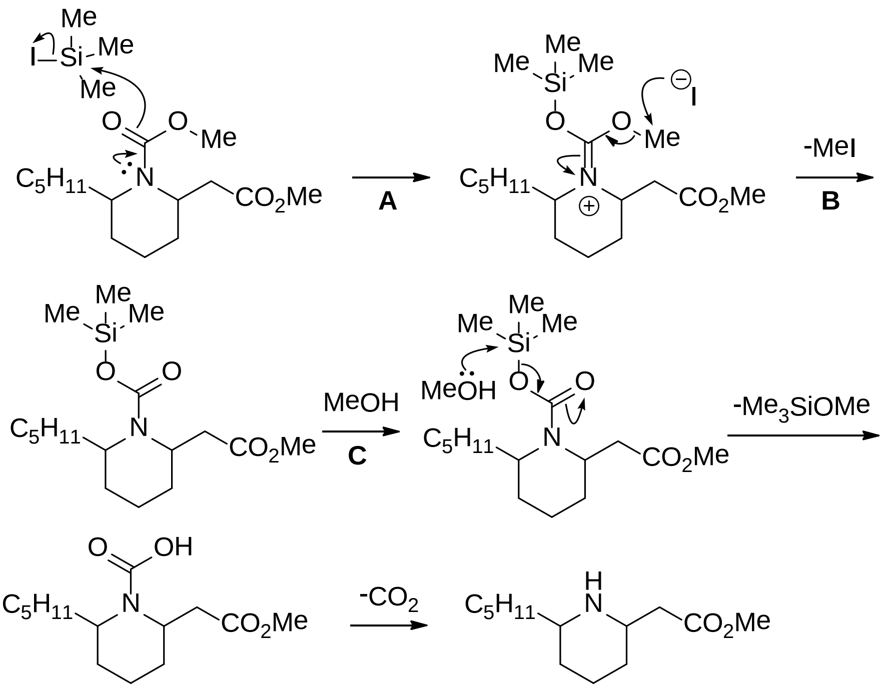




Yang, B. V.; O'Rourke, D.; Li, J. *Synlett.* **1993**, 195.

A: Acylation of a tertiary amine. **B**: Attack of chloride ion on the benzylic position. **C**: E1 elimination ofthe chloride followed by addition of methanol, **D**: Elimination of the carbamic acid helped by the oxygen lone pair of the methoxy group. **E**: Decarboxylation.

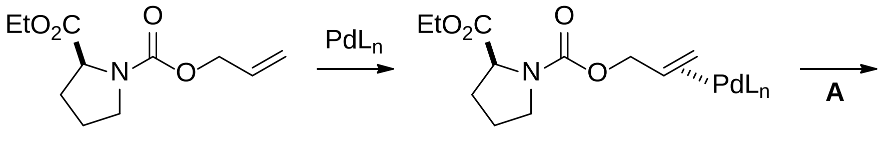
B020

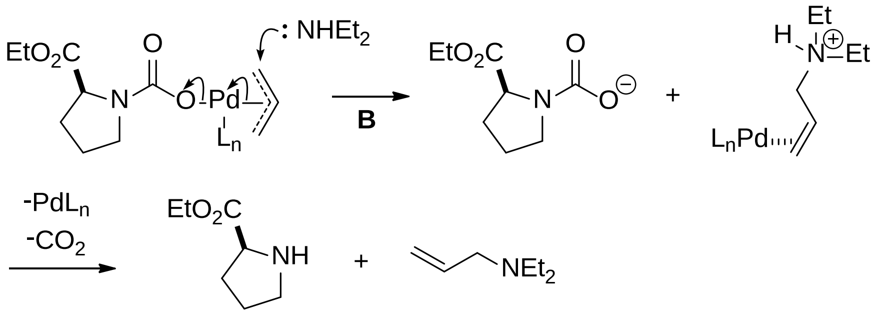


Laurent, P.; Braekman, J.-C.; Daloze, D. Eur. *J. Org. Chem.* **2000**, 2057.

A: Silylation of the electron-rich oxygen of the carbamate. **B**: Demethylation by S$_N$2 reaction. **C**: Methanolysis of the silyl carbamate.

B021

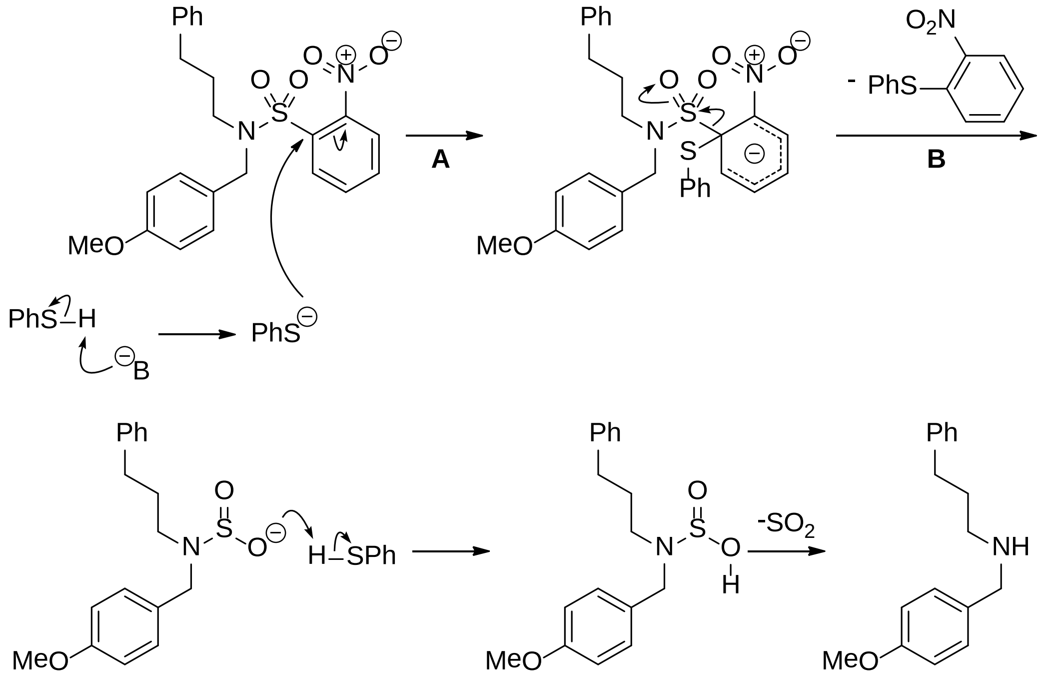




Genet, J. P.; Blart, E.; Savignac, M.; Lemeune, S.; Lemaire-Audoire, S.; Bernard, J. M. *Synlett* **1993**, 680.

A: Formation of a π-allylpalladium complex. **B**: Attack of Et_2NH to the π-allylcomplex.

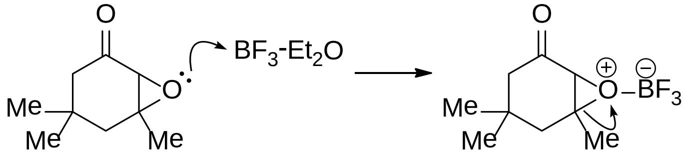
B022

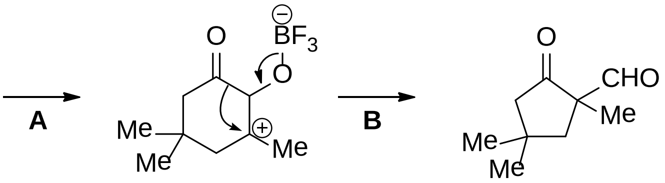


Kurosawa, W.; Kan, T.; Fukuyama, T. *Org. Synth., Coll.* Vol. X **2004**, 482.

A: Addition of a thiolate ion to the electron deficient aromatic ring to form a Meisenheimer complex. **B**: Elimination of an amidosulfurous acid anion which, upon protonation and extrusion of SO_2, gives an amine.

B023

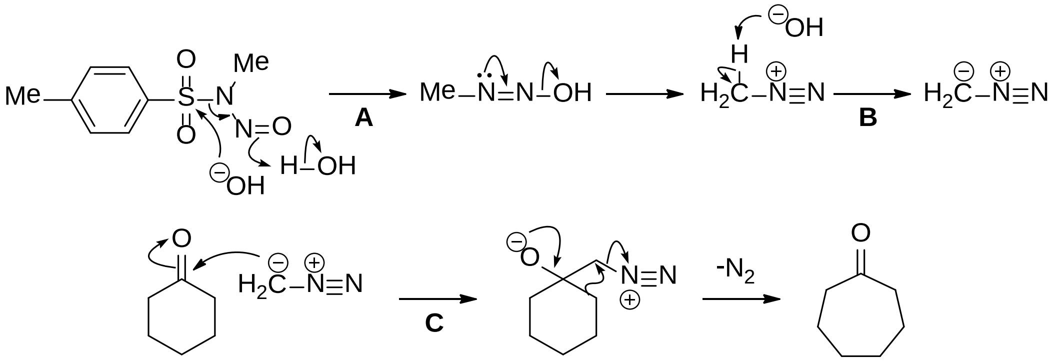




Ryerson, G. D.; Wasson, R. L.; House, H. O. *Org. Synth., Coll* Vol. Ⅳ **1963**, 957.

A: Cleavage of the epoxide to form the more stable tertiary carbecation (formation of a carbocation next to a carbonyl group is unusually difficult). **B**: Wagner-Meerwein-type rearrangement.

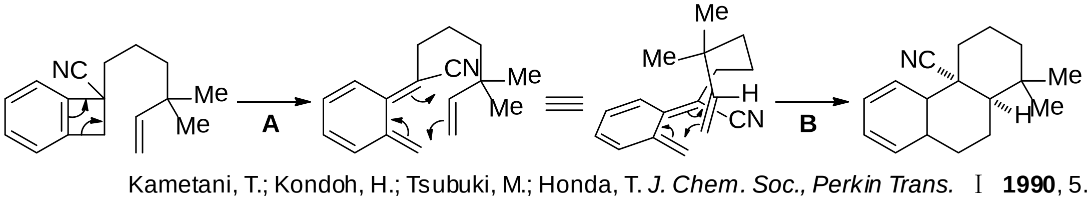
B024



de Boer, T. J.; Backer, H. J. *Org. Synth., Coll* Vol. Ⅳ **1963**, 225.

A: Hydrolysis of N-methyl-N-nitrososulfonamide. **B**: Formation of diazomethane. pKa CH_3N_2 = 10.2, H_2O = 15.7. **C**: Addition of diazomethane to a ketone followed by ring expansion (cf. Tiffeneau-Demjanov rearrangement).

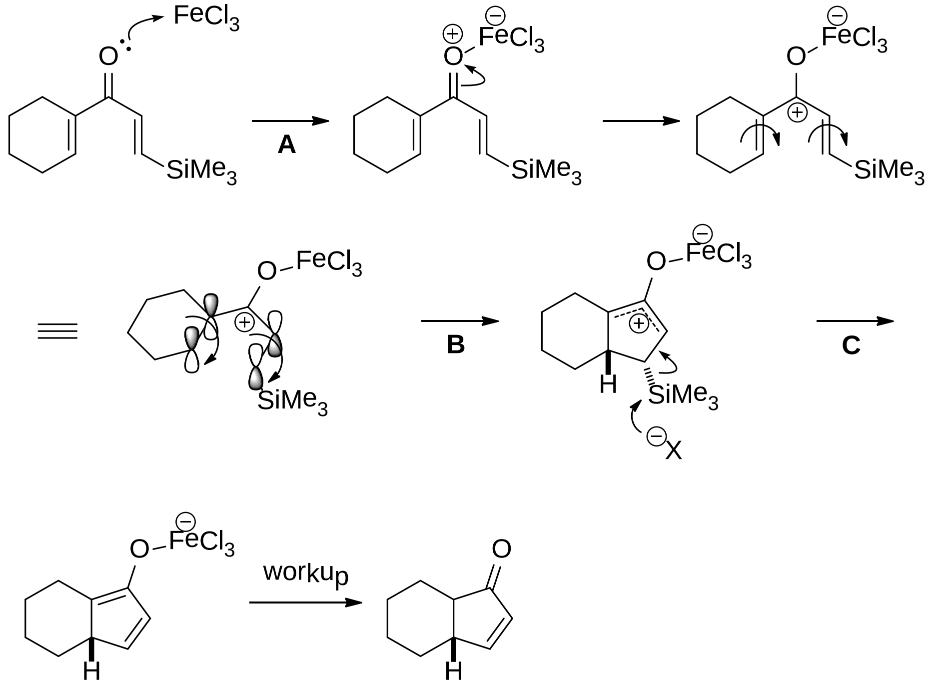
B025



Kametani, T.; Kondoh, H.; Tsubuki, M.; Honda, T. *J. Chem. Soc., Perkin Trans.* Ⅰ **1990**, 5.

A: 4e Conrotatory electrocyclic reaction to form an o-quinodimethane. **B**: Intramolecular Diels-Alder reaction.

B026

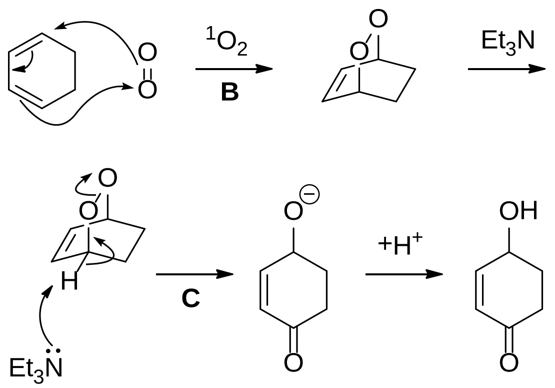


Jones, T. K.; Denmark, S. E. *Helv. Chim. Acta* 1983, 66, 2397.

Silicon-directed Nazarov reaction. **A**: Activation of the carbonyl group with $FeCl_3$, a Lewis acid. **B**: 4e Conrotatory electrocyclic reaction. **C**: Desilylation to form the olefin regioselectively.

B034

$$^3O_2 \xrightarrow[\textbf{A}]{h\nu} {}^1O_2$$

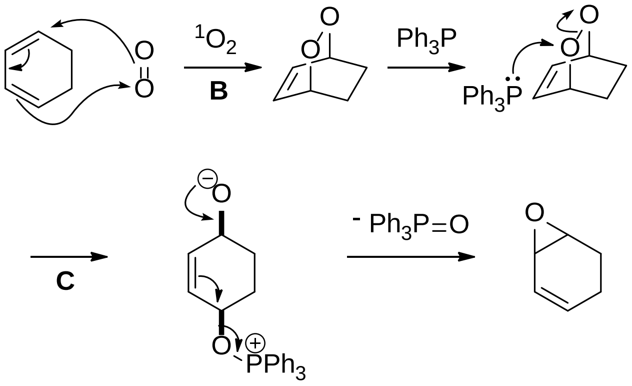


Balci, M. Chem. Rev. 1981, 81, 91.

A: Generation of singlet oxygen. B: Diels-Alder reaction. C: Base-induced cleavage of the endoperoxide.

B035

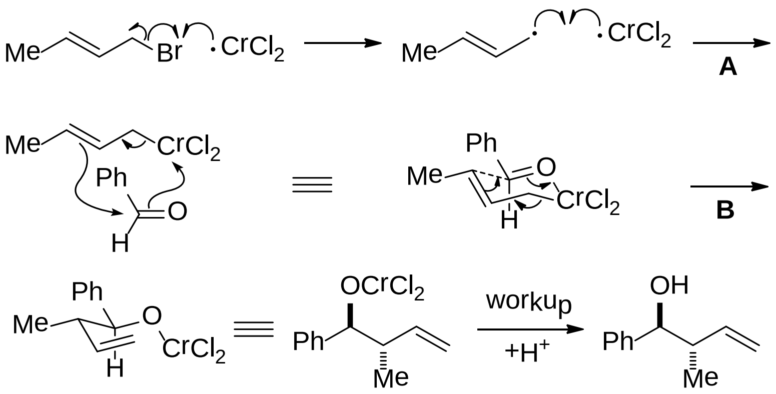
$$^{3}O_2 \xrightarrow[\textbf{A}]{h\nu} {}^{1}O_2$$



Balci, M. *Chem. Rev.* **1981**, 81, 91

A: Generation of singlet oxygen. **B**: Diels-Alder reaction. **C**: Reductive cleavage of the endoperoxide with triphenylphosphine. **D**: Formation of an epoxide via S_N2' reaction with elimination of triphenylphosphine oxide.

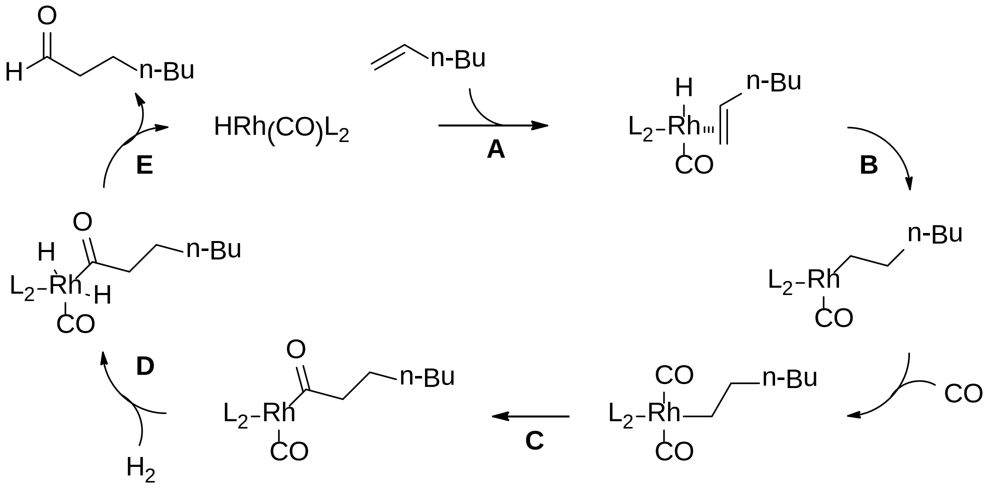
B041



Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. J. Am. Chem. Soc. **1977**, 99, 3179.

A: Since $CrCl_2$ is a single electron reductant, two molecules of $CrCl_2$ are needed to convert an alkyl bromide to the corresponding organochromium species. **B**: Addition to an aldehyde via a chair-like six-membered transition state.

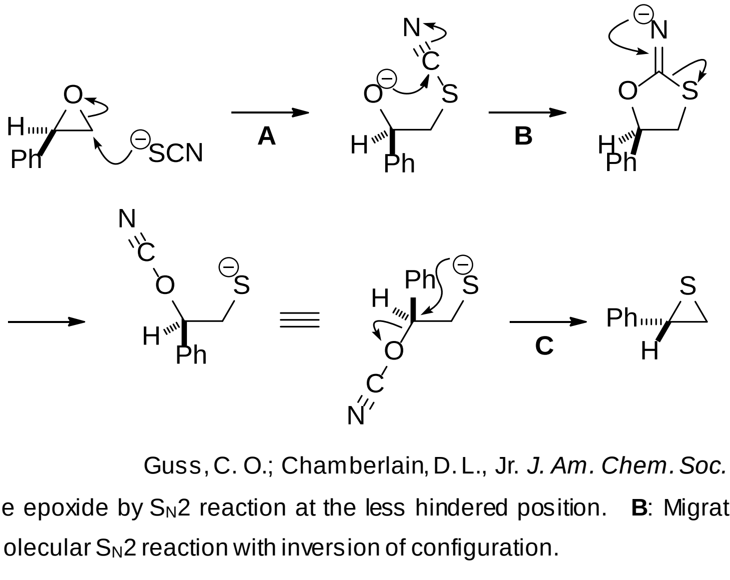
B042



Hallman, P. S.; McGarvey, B. R.; Wilkinson, G. *J. Chem. Soc. (A)* **1968**, 3143.

Hydroformylation. **A**: Complexation of the catalyst with an olefin. **B**: Hydrometallation. **C**: Insertion

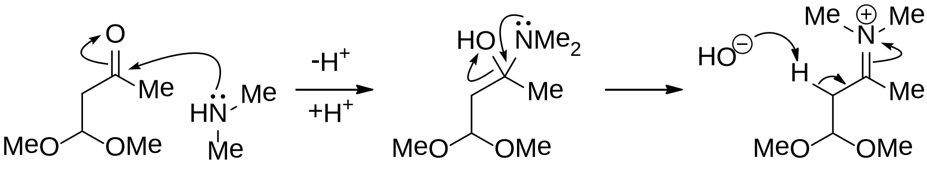
B045

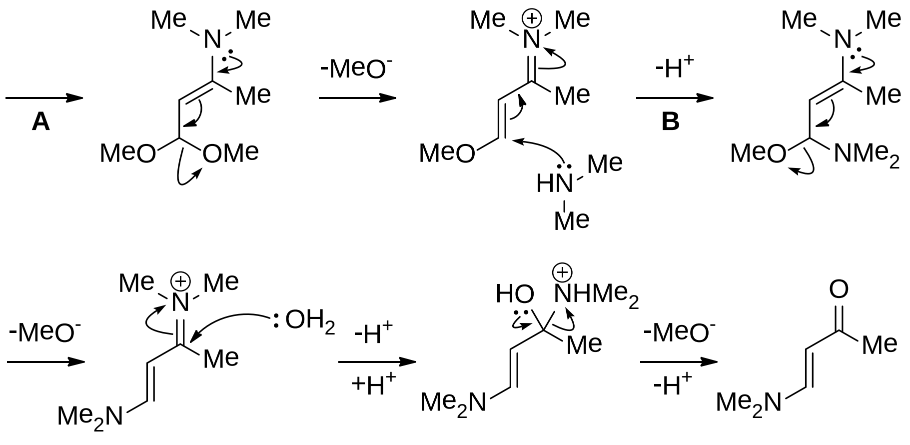


Guss, C. O.; Chamberlain, D. L., Jr. *J. Am. Chem. Soc.* **1952**, 74, 1342.

A: Cleavage of the epoxide by S_N2 reaction at the less hindered position. **B**: Migration of the cyano group. **C**: Intramolecular S_N2 reaction with inversion of configuration.

B046

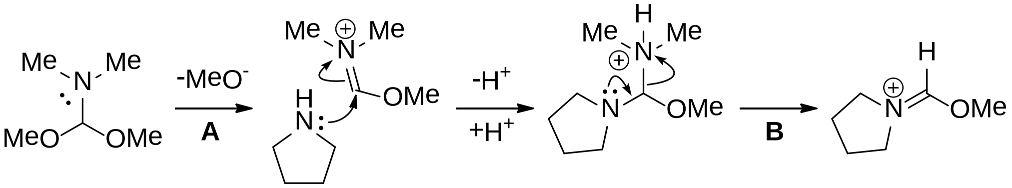


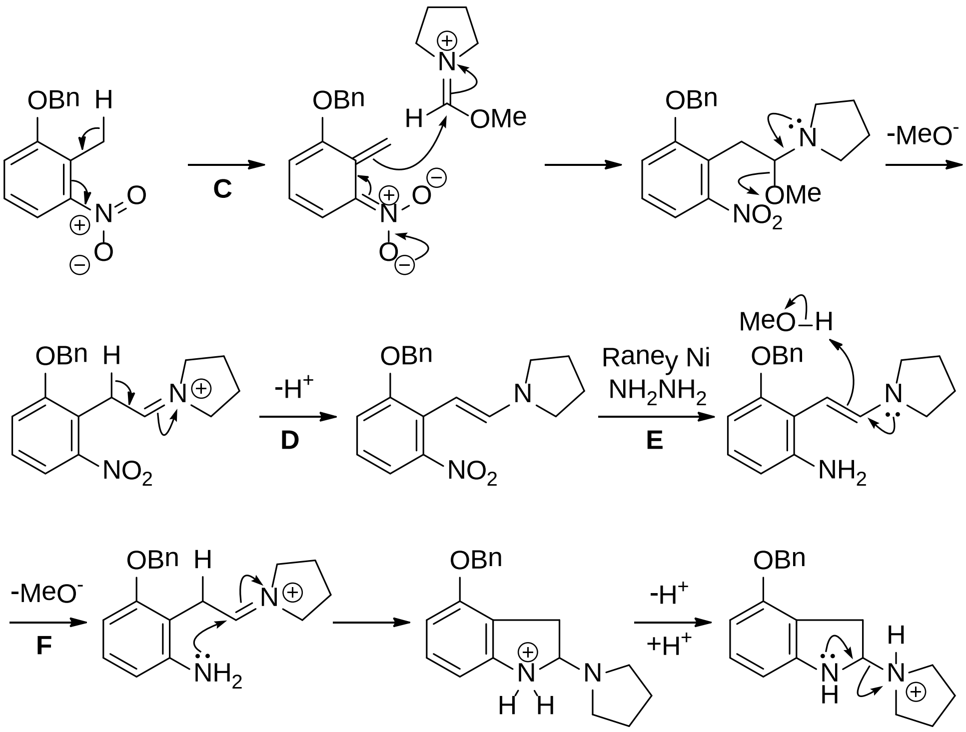


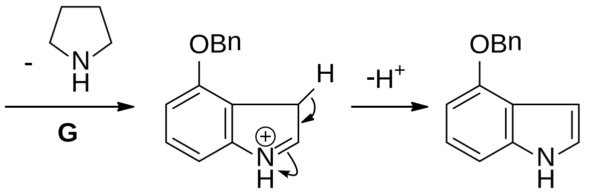
Kozmin, S. A.' He, S.; Rawal, V. H. *Org. Synth., Coll*. Vol. Ⅹ **2004**, 301.

A: Formation of an enamine to eliminate methoxide ion. **B**: Conjugate addition of dimethylamine to the α,β-unsaturated iminium ion.

B047



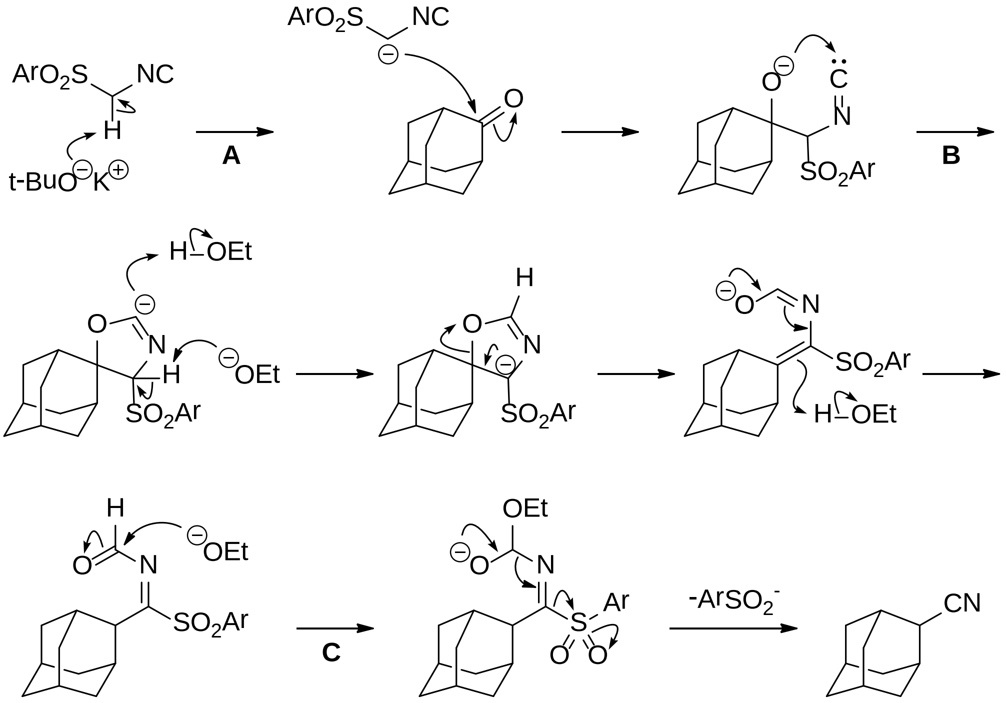




Batcho, A. D.; Leimgruber, W. *Org. Synth., Coll*. Vol. Ⅶ **1990**

Leimgruber-Batcho indole synthesis. **A**: Generation of an iminium ion under thermal conditions. **B**: Replacement of dimethylamine with pyrrolidine. **C**: Generation of a benzylic carbanion stabilized by o-nitro group. **D**: Formation of an enamine. **E**: Reduction of the nitro group. **F**: Protonation of the enamine to form the reactive iminium ion. **G**: Elimination of pyrrolidine helped by the nitrogen lone pair.

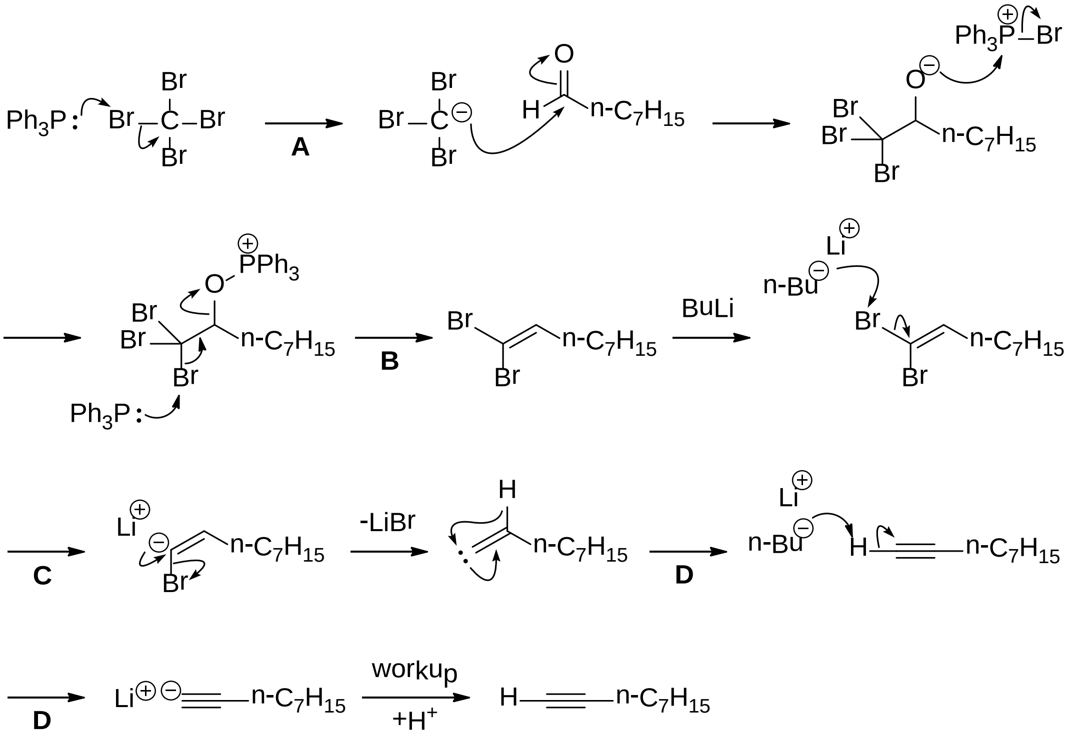
B048



Oldenziel, O. H.; Wildeman, J; van Leusen, A. M. *Org. Synth., Coll*. Vol Ⅵ **1988**, 41.

TosMIC (p-toluenesulfonylmethyl isocyanide). **A**: Deprotonation of an active methylene compound. **B**: Intramolecular addition to the isocyanide to form an oxazoline anion. **C**: Loss of the activated formyl group with a concomitant elimination of a toluenesulfinate ion (pKa $PhSO_2H$ = 1.5).

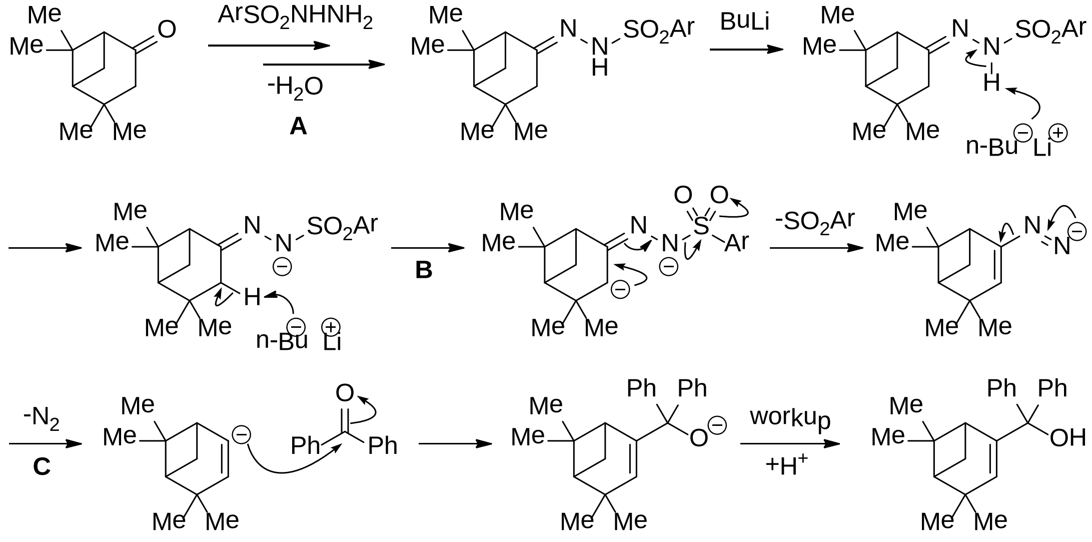
B049



Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 13, 3769

Corey-Fuchs reaction. **A**: Generation of a stable carbanion (cf. pKa $CHCl_3$ = 13.6). **B**: E2 elimination (triphenylphosphine oxide is an extremely good leaving group). **C**: Halogen-lithium exchange follow by α-elimination to generate an alkylidene carbene. **D**: C-H insertion of the carbene. **E**: pKa n-Bu^- = 50, RC≡CH = 25.

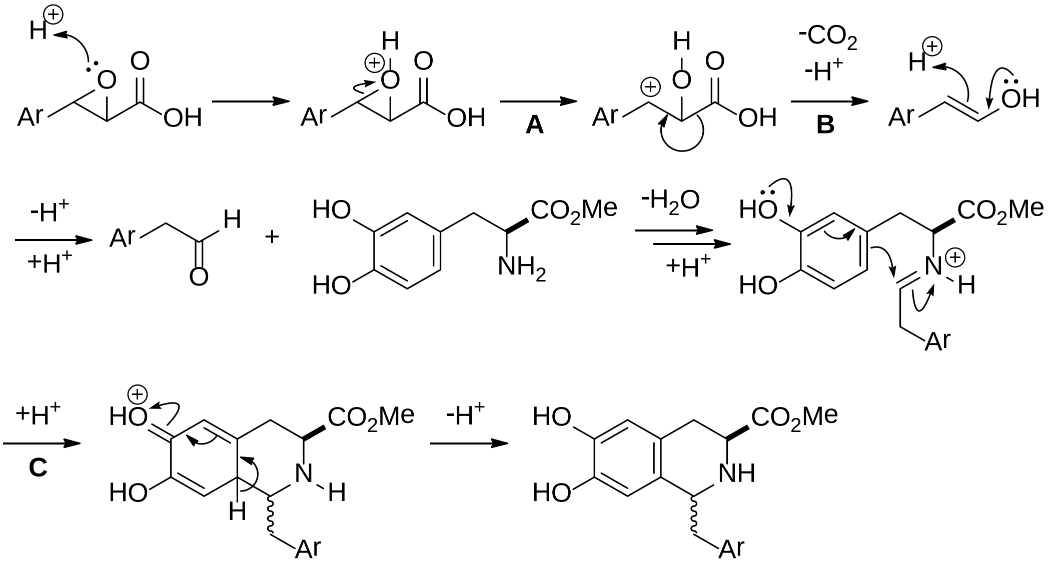
B050



Rupert, K. C.; Liu, C. C.; Nguyen, T. T.; Whitener, M. A.; Sowa, J. R.. J, *Organometallics* **2002**, 21,144

Shapiro reaction. **A**: Formation of a hydrazone. **B**: Deprotonation of the α-position of the hydrazone anion. **C**: Elimination of a sulfinate ion (pKa RSO_2H = 1.5). **D**: Loss of N_2 to form an alkenyl anion.

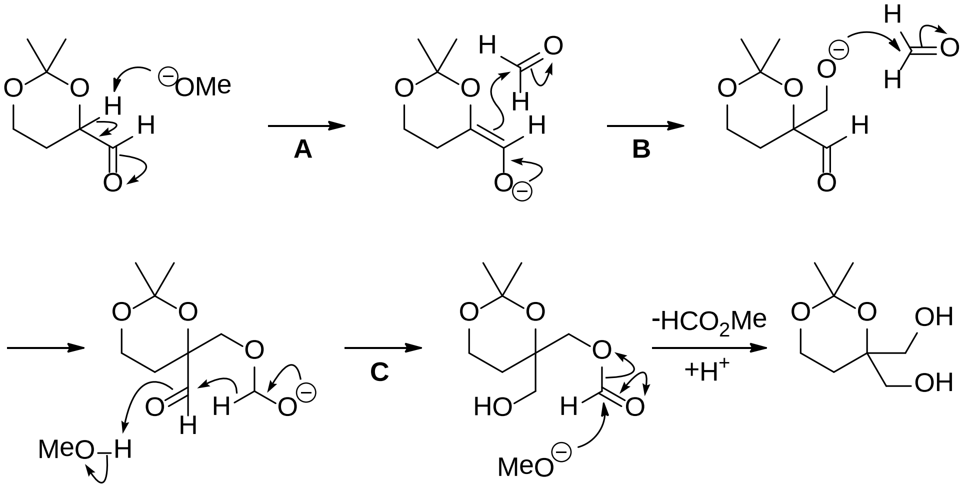
B051



Konda, M.; Shioiri, T.; Yamada, S. *Chem. Pharm. Bull.* **1975**, 23, 1025

A: Generation of a stabilized benzyl cation. **B**: Decarboxylation to form an enol, an aldehyde equivalent. **C**: Pictet-Spengler reaction (ref A033).

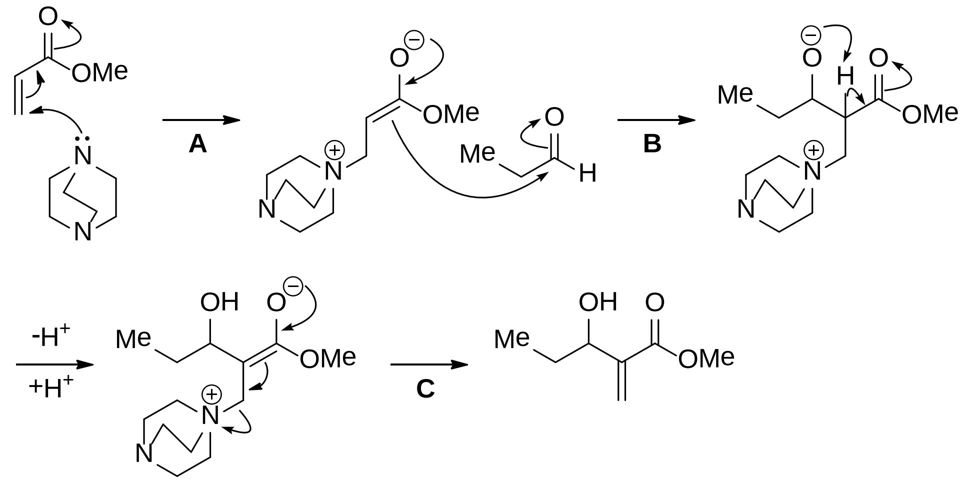
B052



Shimada, K.; Kaburagi, Y.; Fukuyama, T. *J. Am. Chem. Soc.* **2003**, 125, 4048.

A: pKa MeOH = 15.5, CH_3CHO = 16.7. **B**: Aldol reaction. **C**: Intramolecular hydride transfer (Cannizzaro-type reaction).

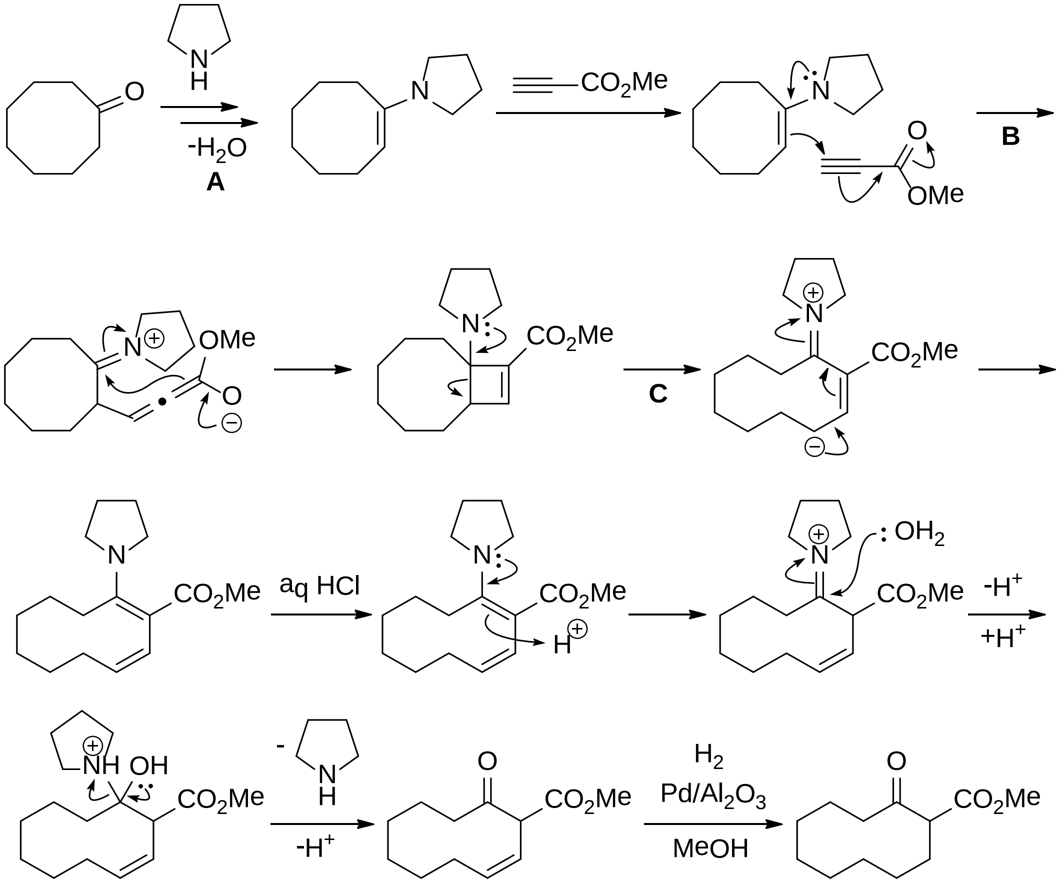
B053



Brown, J. M.; Evans, P. L.; James, A. P. *Org. Synth., Coll.* Vol. Ⅷ **1993**, 420.

Morita-Baylis-Hillman reaction. **A**: Michael addition of DABCO. **B**: Aldol reaction. **C**: Elimination of DABCO.

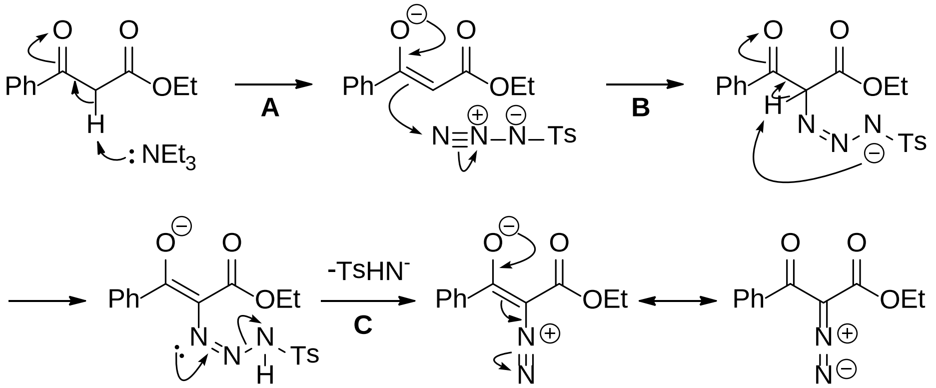
B054



Burpitt, R. D.; Thweatt, J. G. *Org. Synth., Coll.* Vol. V **1973**, 277.

A: Formation of an enamine. **B**: A stepwise formation of the four-membered ring by means of Michael addition. **C**: Cleavage of the cyclobutene to release the ring strain.

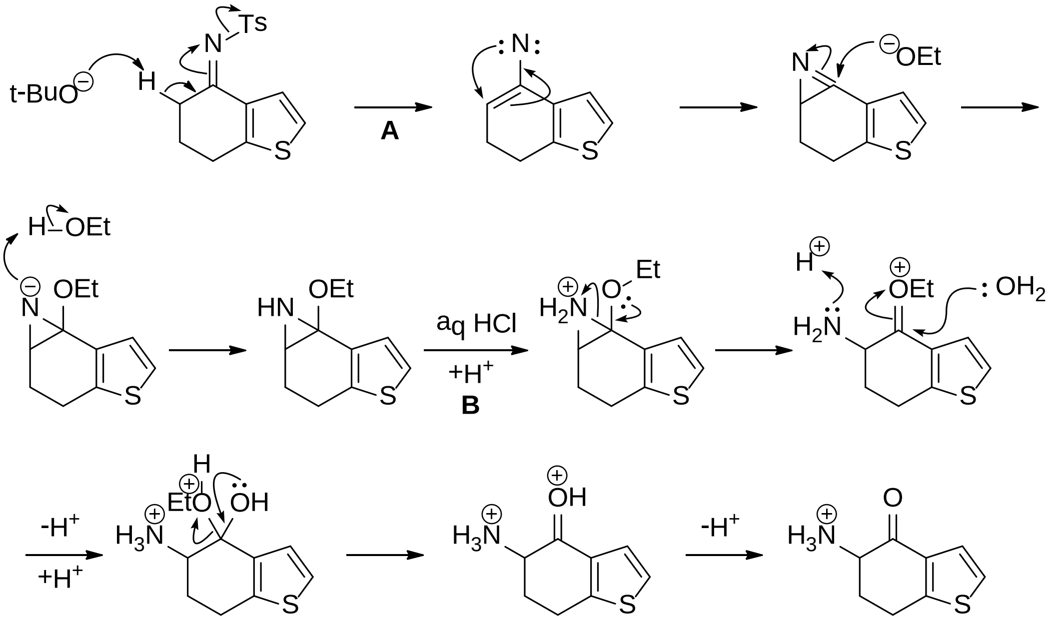
B055



Lall, M. S.; Ramtohul, Y. K.; James, M. N. G.; Vederas, J. C. *J. Org. Chem.* **2002**, 67, 1536.

Regiz Diazo transfer reaction. **A**: pKa $RCOCH_2CO_2R$ = 11, $HNEt_3^+$ = 10.7. **B**: Attack on the less hindered, electrophilic nitrogen. **C**: pKa $PhSO_2NH_2$ = 8.5:

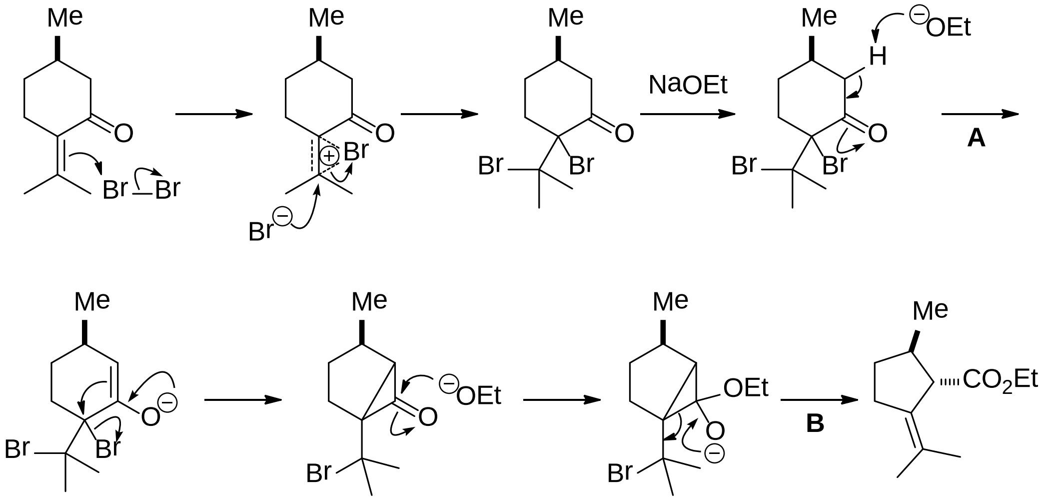
B056



Dijkstra, D.; Rodenhuis, N.; Vermeulen, E. S.; Pugsley, T. A.; Wise, L. D.; Wikstrm, H. V. *J. Med. Chem.* **2002**, 45, 3022.

Neber rearrangement. **A**: Generation of a nitrene to form the azirine, which then undergoes addition of ethanol. **B**: Acidic hydrolysis of the ethoxyaziridine.

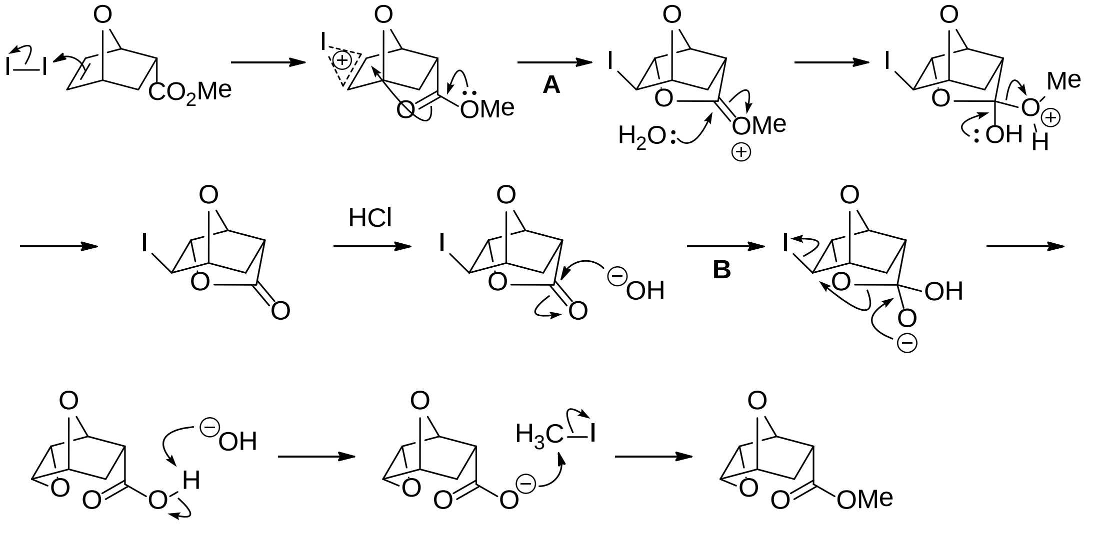
B057



Marx, J. N.; Norman, L. R. *J. Org. Chem.* **1975**, 40, 1602.

A: Favorskii rearrangement (ref A069). **B**: Cleavage of the strained cyclopropanone with a concurrent elimination of the bromide (formation of the thermodynamically more stable trans-ester).

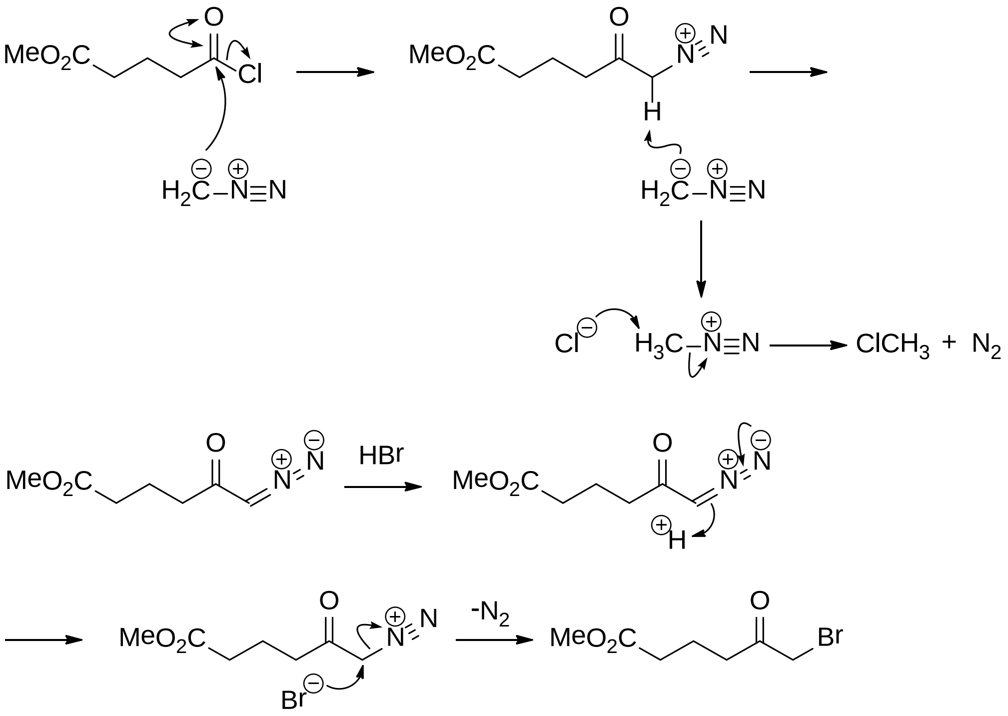
B058



Shoji, M.; Yamaguchi, J.; Kakeya, H.; Osada, H.; Hayashi, Y. *Angew. Chem. Int. Ed.* **2002**, 41,319;

A: Iodolactonization. **B**: Hydrolysis of the lactone followed by formation of the epoxide.

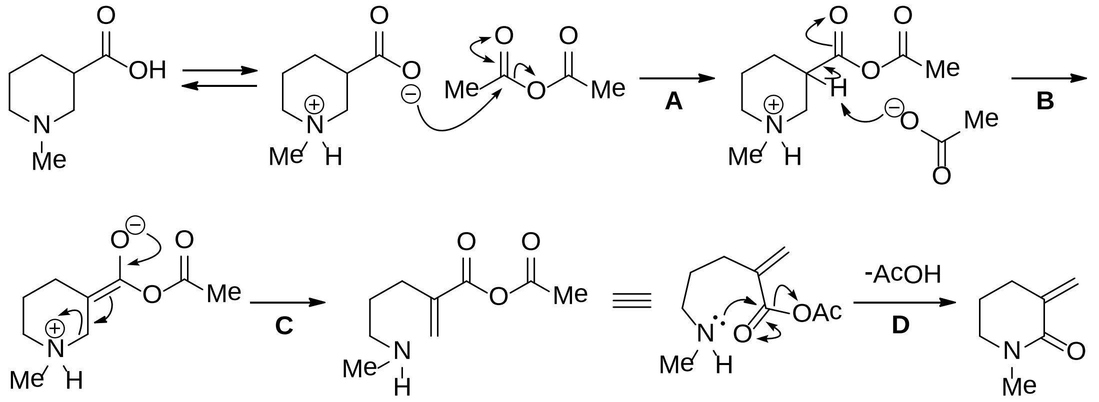
B059



Nair, V.; Jahnke, T. S. *Tetrahedron* **1987**, 43 4257.

Excess diazomethane is needed to scavenge HCl.

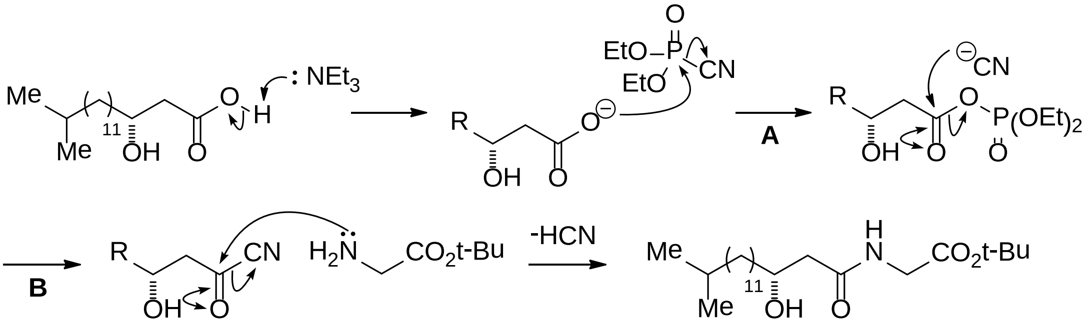
B060



Rueppel, M. L.; Rapoport, H. *J. Am. Chem. Soc.* **1978**, 92, 5781.

A: Formation of a mixed anhydride. **B**: pKa $(CH_3CO)_2O$ = 13.5. **C**: β-Elimination. **D**: Intramolecular acylation is faster than intermolecular one.

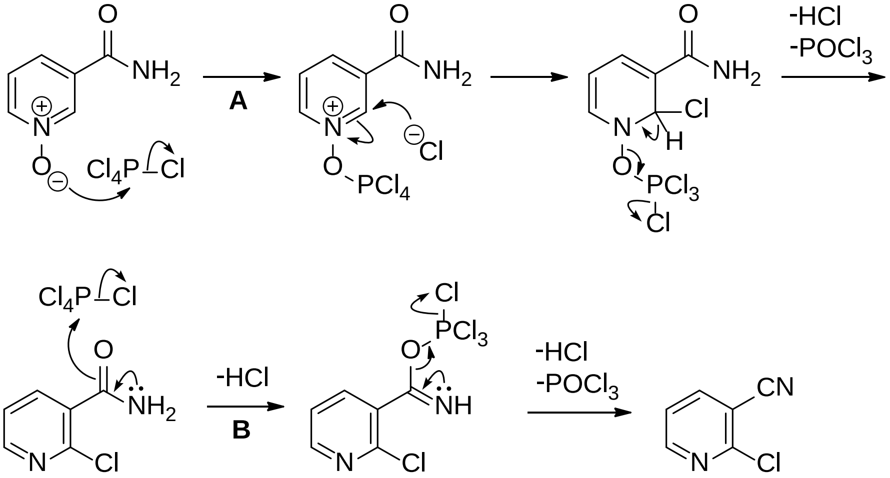
B061



Shioiri, T.; Terao, Y.; Irako, N.; Aoyama, T. *Tetrahedron* **1998**, 54, 15701.

A: Formation of a mixed anhydride. **B**: Formation of the reactive acyl cyanide.

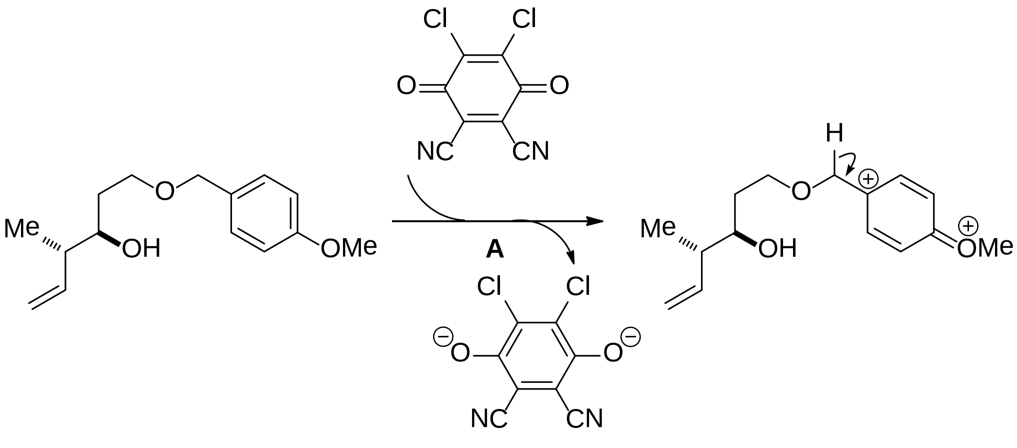
B062

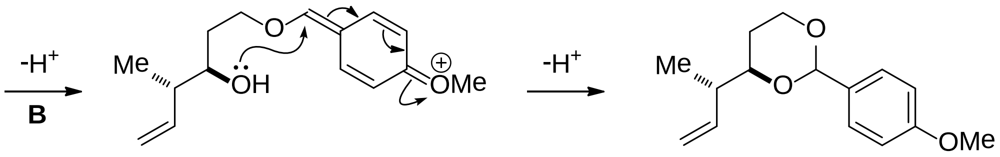


Taylor, E. C., Jr.; Crovetti, A. J. *Org. Synth., Coll.* Vol. Ⅳ **1963**, 166.

A: Activation of the N-oxide with PCl_5. **B**: Dehydration of the amide.

B063



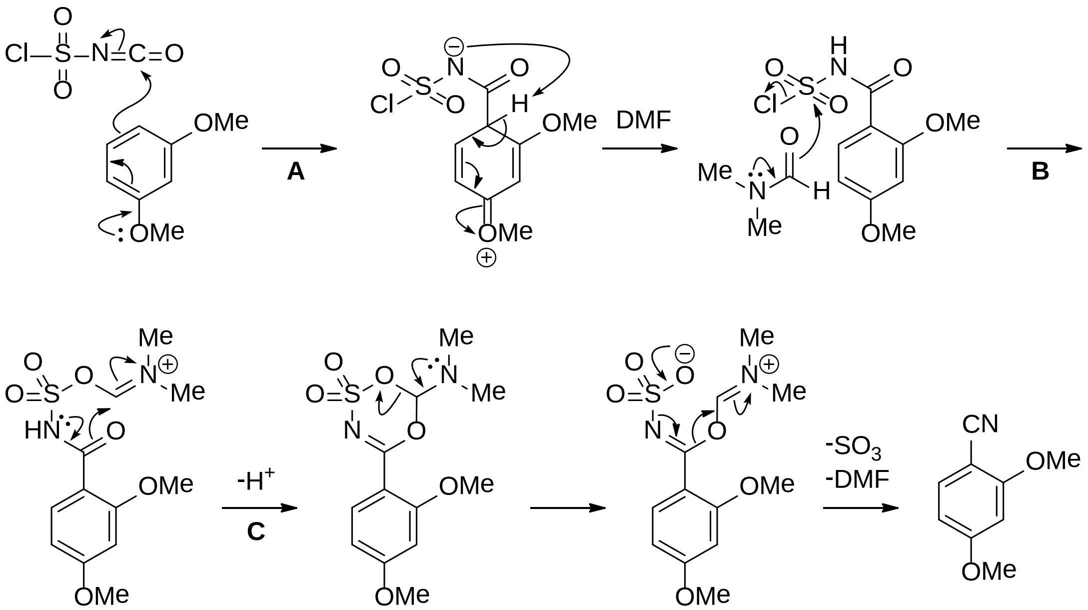


Crimmins, M. T.; Siliphaivanh, P. *Org. Lett.* **2003**, 5, 4641.

A: Transfer of two electrons from the starting material to DDQ by forming a charge-transfer complex.

B: Deprotonation to form a p-quinonemethide-type intermediate.

B064

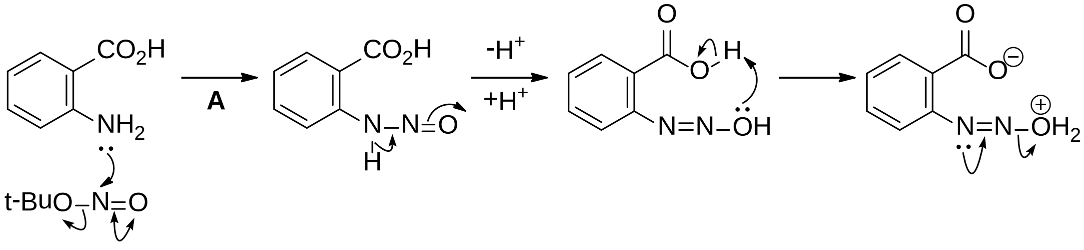


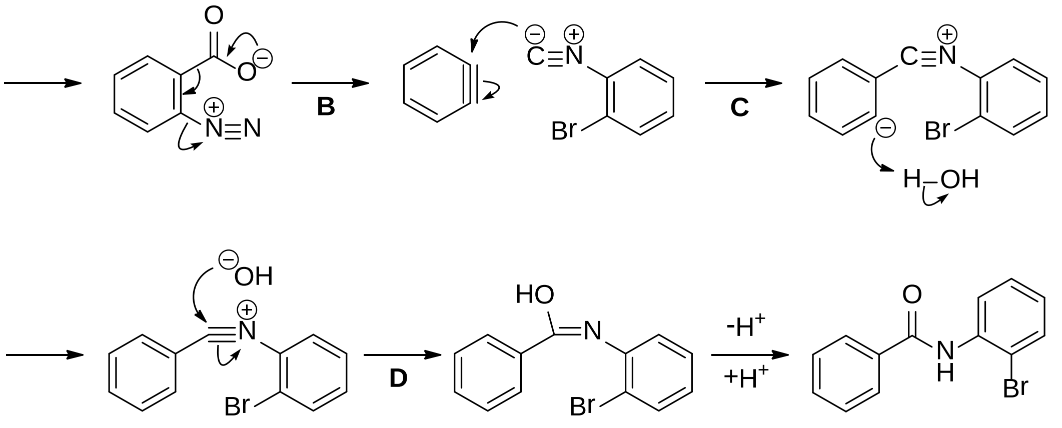
Lohaus, G. *Chem. Ber.* **1967**, 100, 2719.

A: Electrophilic substitution of an electron-rich aromatic compound. **B**: Attack on the oxygen of DMF.

C: Cyclization followed by fragmentation to form the nitrile.

B065

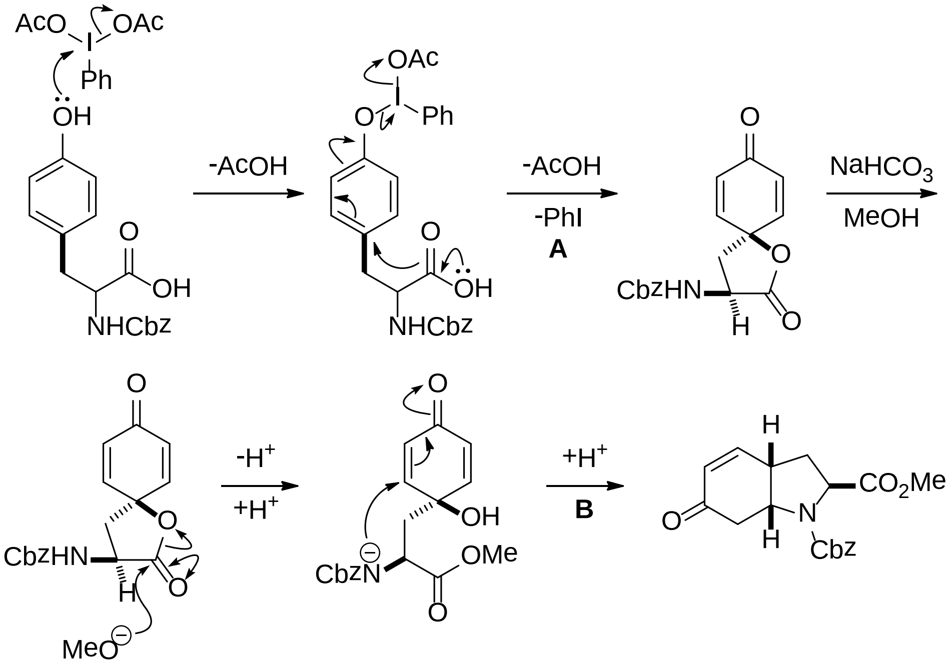




Rigby, J. H.; Laurent, S. *J. Org. Chem*. **1998**, 63, 6742.

A: Formation of a diazonium salt (ref A037). **B**: Formation of a benzyne with a loss of CO_2 and N_2.
C: Nucleophilic addition of the isocyanide. **D**: Addition of water to the nitrilium ion.

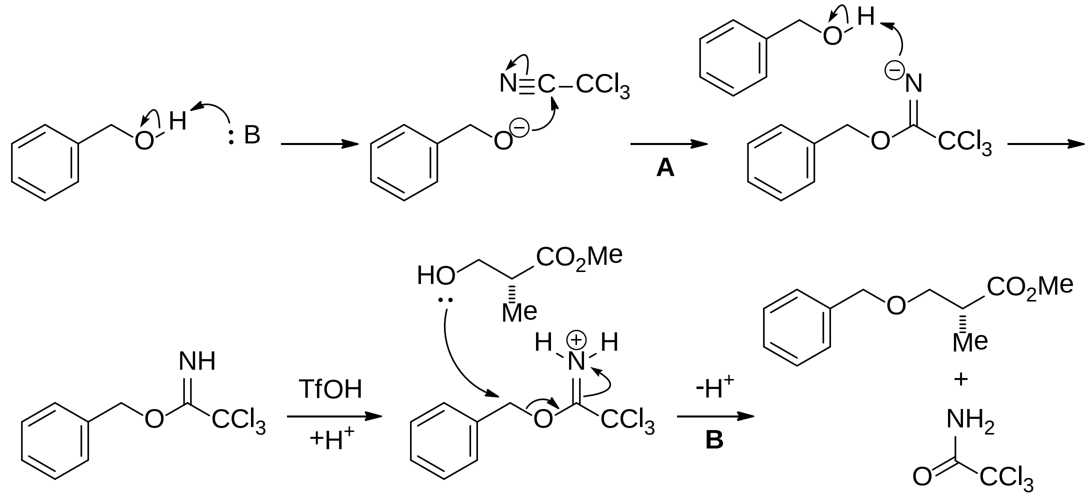
B066



Wipf, P.; Li, W. *J. Org. Chem*. **1999**, 64, 4576.

A: Oxidative lactonization of N-Cbz tyrosine. **B**: Intramolecular Michael addition to the cross-conjugated dienone.

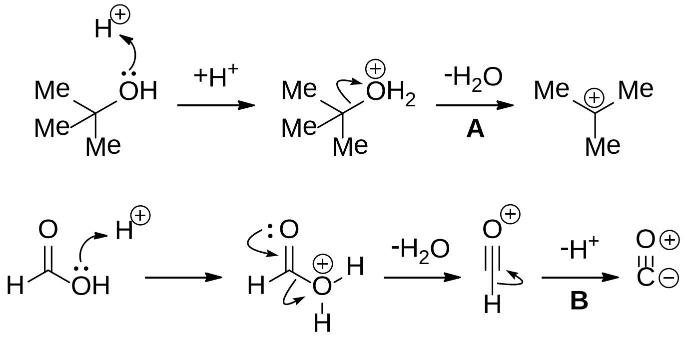
B067

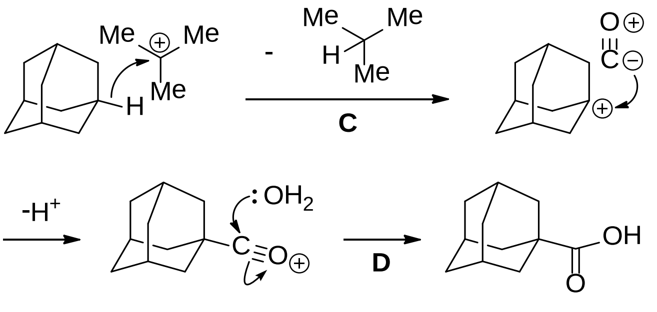


White, J. D.; Reddy, G. N.; Spessard, G. O. *J. Am. Chem. Soc.* **1988**, 110, 1624.

A: Addition of benzyl alcohol to electron-deficient Cl_3CCN with a help of catalytic amount of base. **B**: Ftherification of alcohols under acidic conditions.

B068

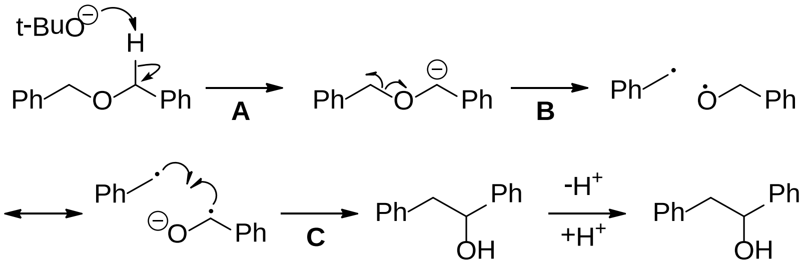




Koch, H.; Haaf, W. *Org. Synth., Coll.* Vol. V **1973**, 20.

A: Formation of a stable t-butyl cation. **B**: Generation of CO by dehydration of formic acid. **C**: Hydride abstraction from the bridgehead of adamantane. **D**: Addition of CO to form an acylium ion.

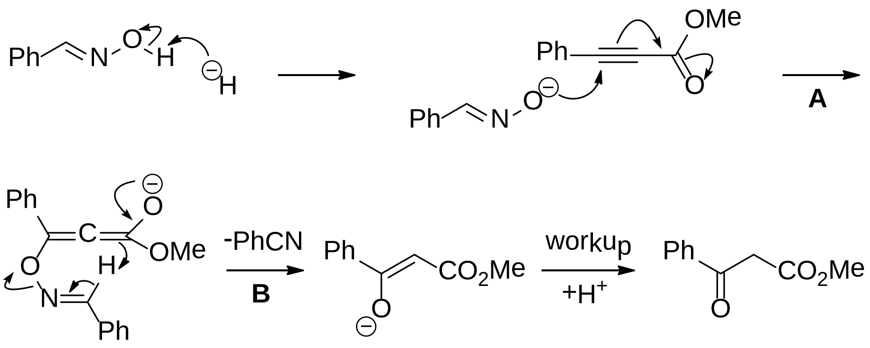
B069



Hauser, C. R.; Kantor, S. W. *J. Am. Chem. Soc.* **1951**, 73, 1437.

[1,2] Wittig rearrangement. **A**: pKa PhCH$_3$ = 41, n-BuH = 50. **B**: Homolytic cleavage to form a radical anion. **C**: A facile radical recombination in a solvent cage.

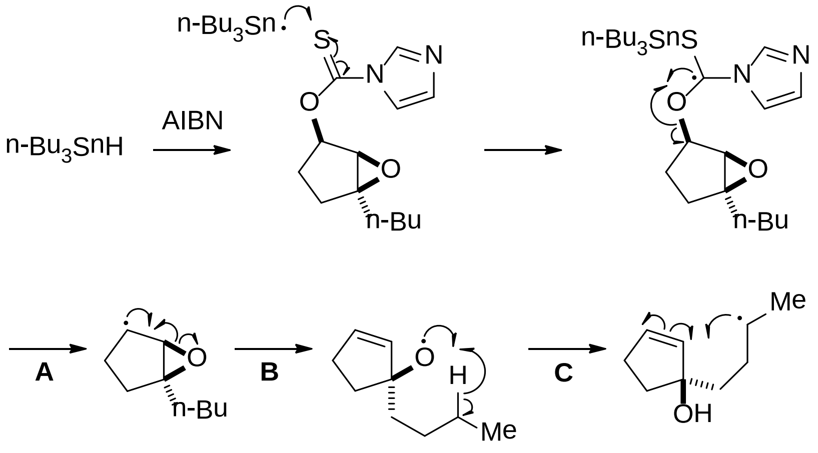
B070

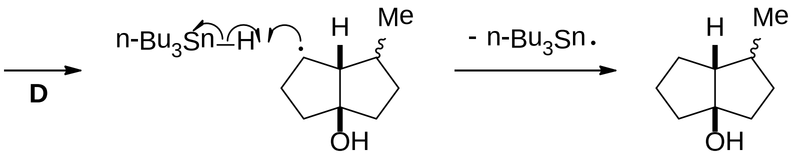


Gómez, V.; Perez-Medrano, A.; Muchowski, J. M. *J. Org. Chem.* **1994**, 59, 1219

A: Michael addition of an oxime anion. **B**: Intramolecular deprotonation to cause fragmentation.

B071

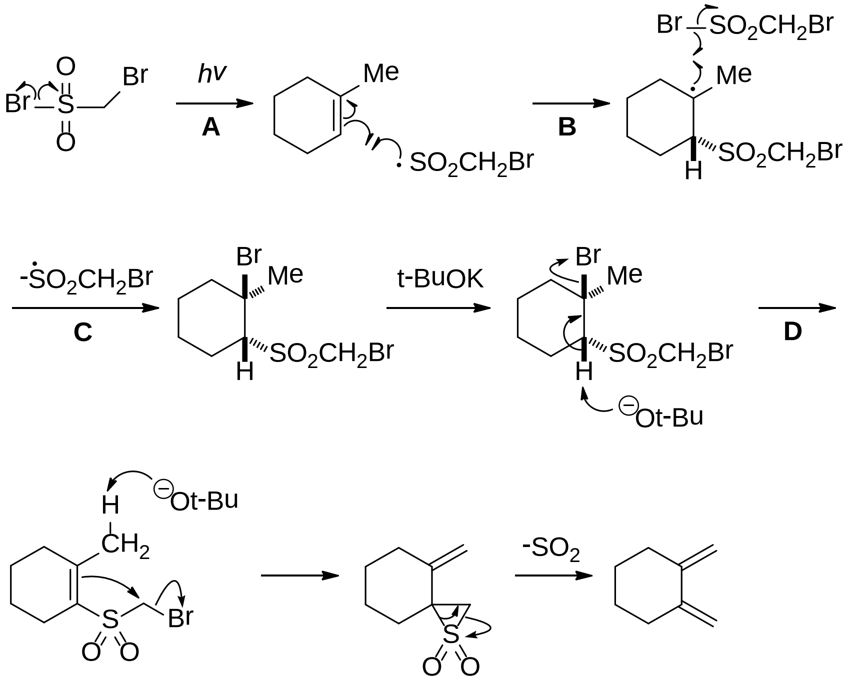




Rawal, V. H.; Newton, R. C.; Krishnamurthy, V. *J. Org. Chem*. **1990**, 55, 5181.

A: Barton-McCombie deoxygenation (ref A051). **B**: Cleavage of the strained epoxide ring. **C**: Intramolecular abstraction of a hydrogen via a six-membered transition state. **D**: 5-exo-trig Radical cyclization.

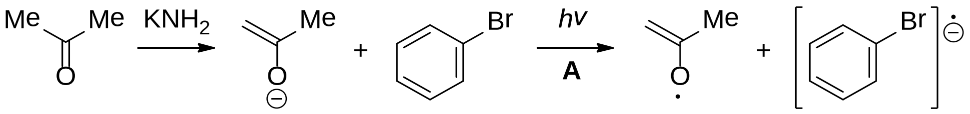
B072

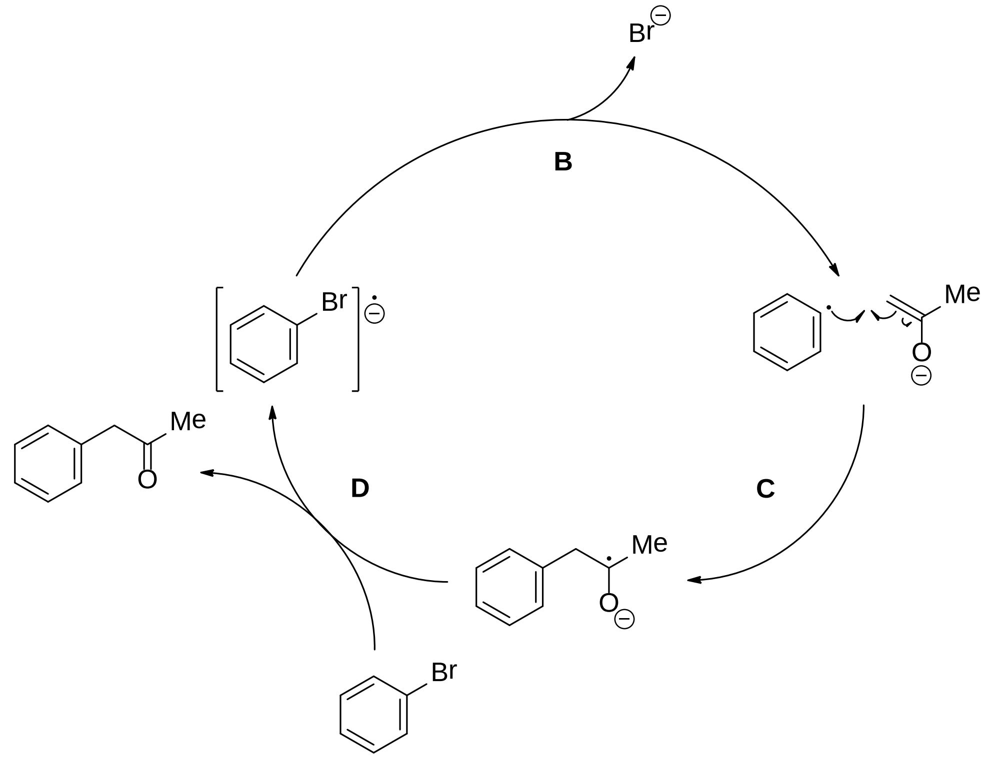


Block, E.; Aslam, M. *Org. Synth., Coll*. Vol. Ⅷ **1993**, 212.

A: Photo-induced homolytic cleavage to form a sulfinyl radical. **B**: Addition to the olefin to form a stable tertiary radical. **C**: Attack on the bromide of the reagent (radical chain reaction). **D**: Elimination of HBr followed by vinylogous Ramberg-Bäcklund reaction.

B073

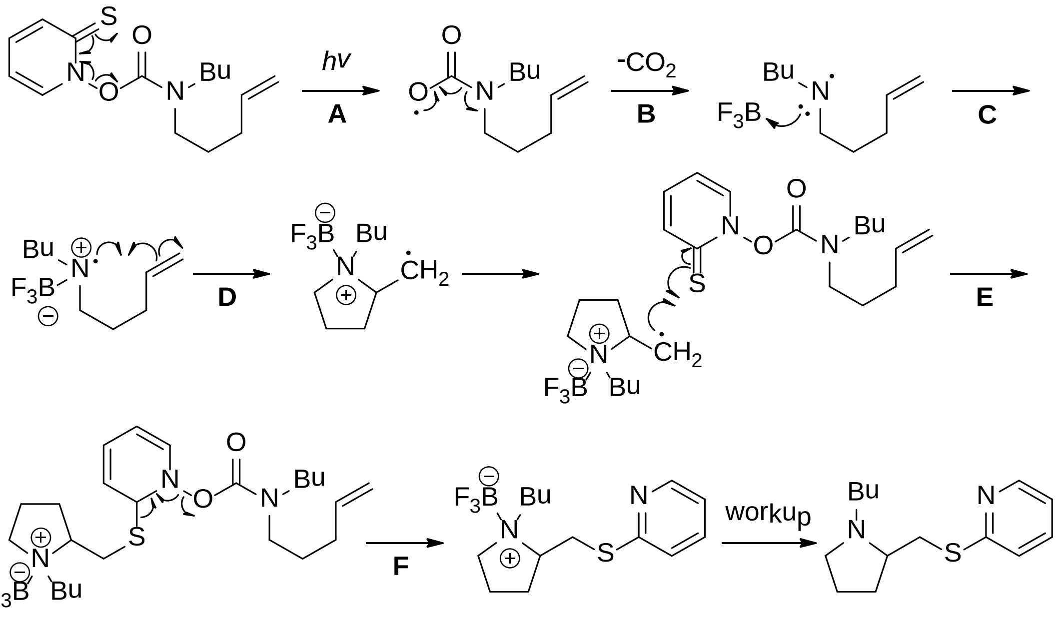




Rossi, R. A.; Bunnett, J. F. *J. Org. Chem.* **1973**, 38, 3020.

$S_{RN}1$ reaction. **A**: SET to bromobenzene to form a radical anion. **B**: Fragmentation of the radical anion to form a phenyl radical. **C**: Addition to enolate to form a radical anion. **D**: SET to continue the radical chain reaction.

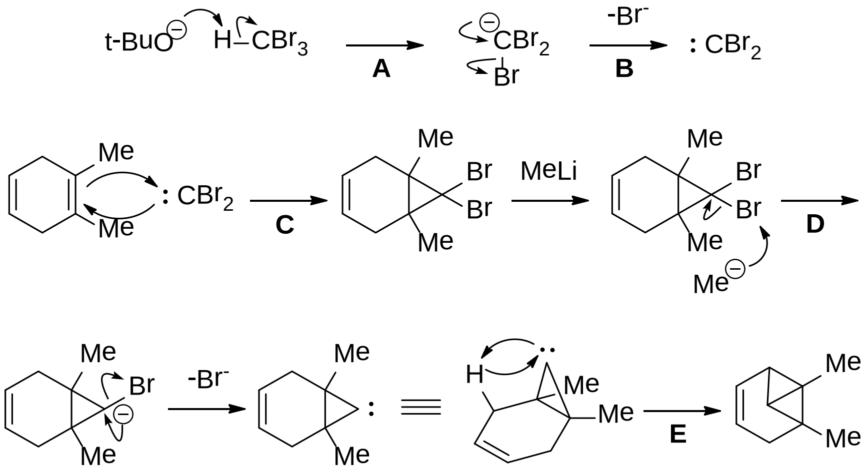
B074



Newcomb, M. Ha, C. *Tetrahedron Lett.* **1991**, 32, 6493.

A: Photo-induced homolytic cleavage. **B**: Decarboxylation to form an aminyl radical. **C**: Activation of the aminyl radical by Lewis acid. **D**: Kinetically favored 5-exo-trig radical cyclization. **E**: Group transfer reaction.

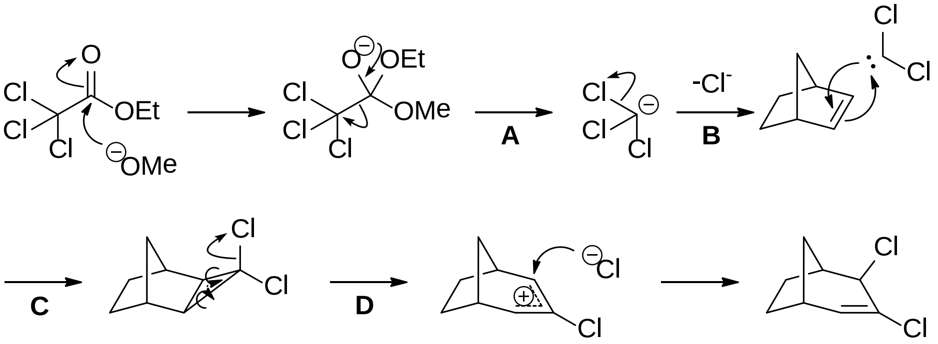
B075



Taylor, R. T.; Paquette, L. A. *Org. Synth., Coll.* Vol. Ⅷ **1990**, 200.

A: pKa $CHCl_3$ = 13.6. **B**: α-Elimination to form dibromocarbene. **C**: Cyclopropanation of the more electron-rich, tetrasubstituted olefin. **D**: Halogen-lithium exchange and subsequent α-elimination to form a carbene. **E**: C-H insertion of the carbene (the corresponding allene cannot be formed due to the excessive ring strain. ref A061).

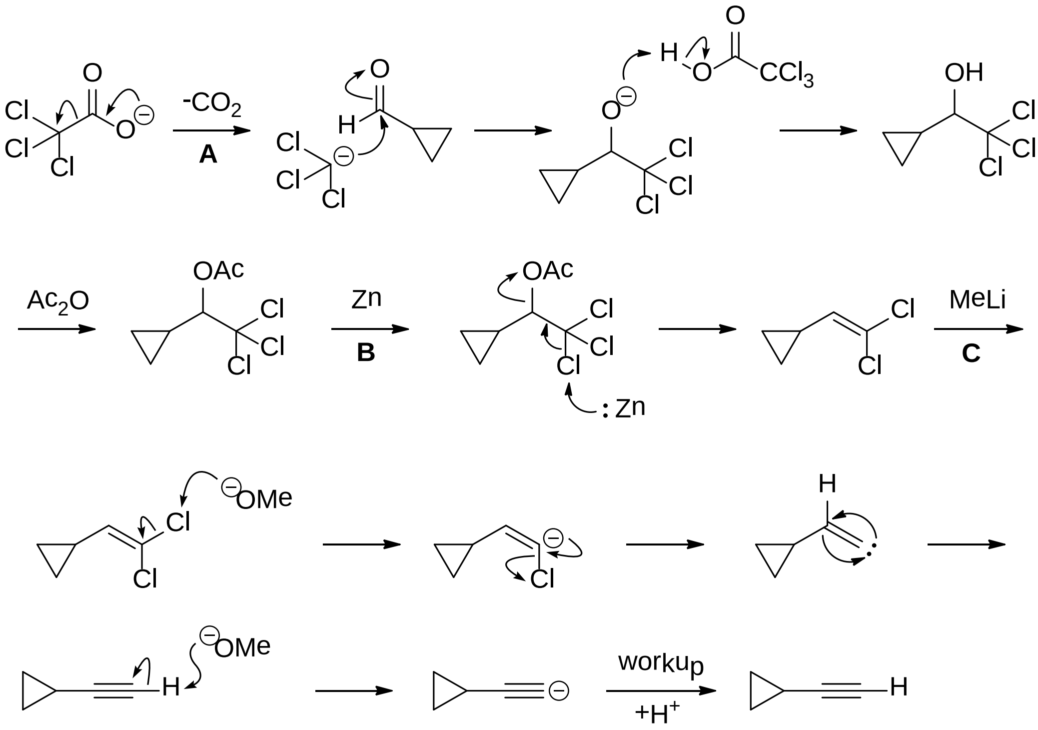
B076



Jefford, C. W.; Gunsher, J.; Hill, D. T.; Brun, P.; Gras, J. L.; Waegelt, B.
Org. Synth., Coll Vol. Ⅵ 1988, 142.

A: pKa $CHCl_3$ = 13.6. **B**: Generation of dichlorocarbene. **C**: Cyclopropanation from the sterically less hindered exo-side. **D**: 2e Disrotatory electrocyclic reaction to form an allyl cation.

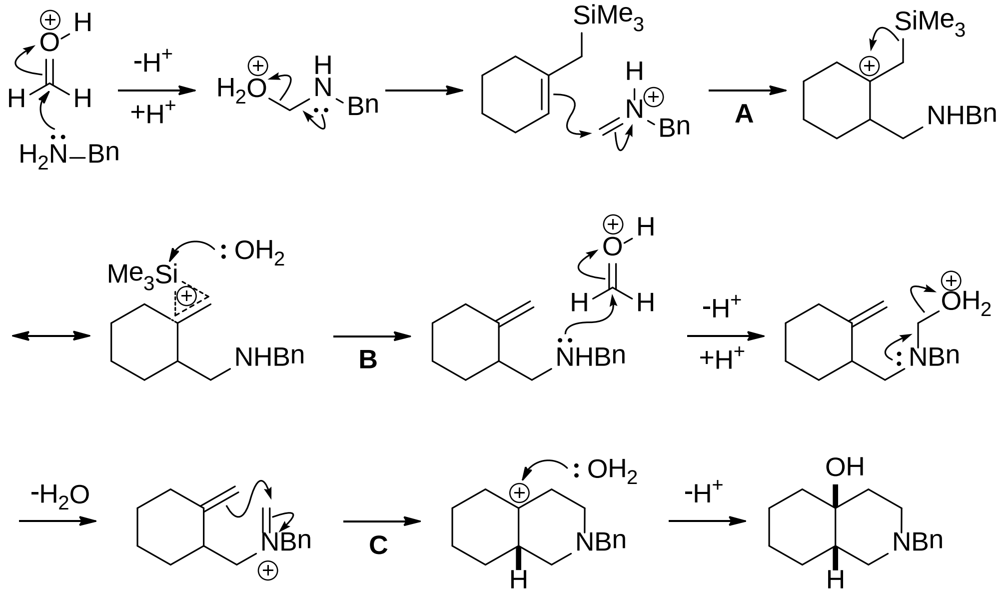
B077



Wang, Z.; Campagna, S.; Xu, G.; Pierce, M. E.; Fortunak, J. M.; Confalone, P. N.
Tetrahedron Lett. **2000**, 41, 4007.

A: pKa $CHCl_3$ = 13.6. **B**: Reduction with Zn to form a gem-dichloroolefin. **C**: Corey-Fuchs-type alkynylation (ref B049).

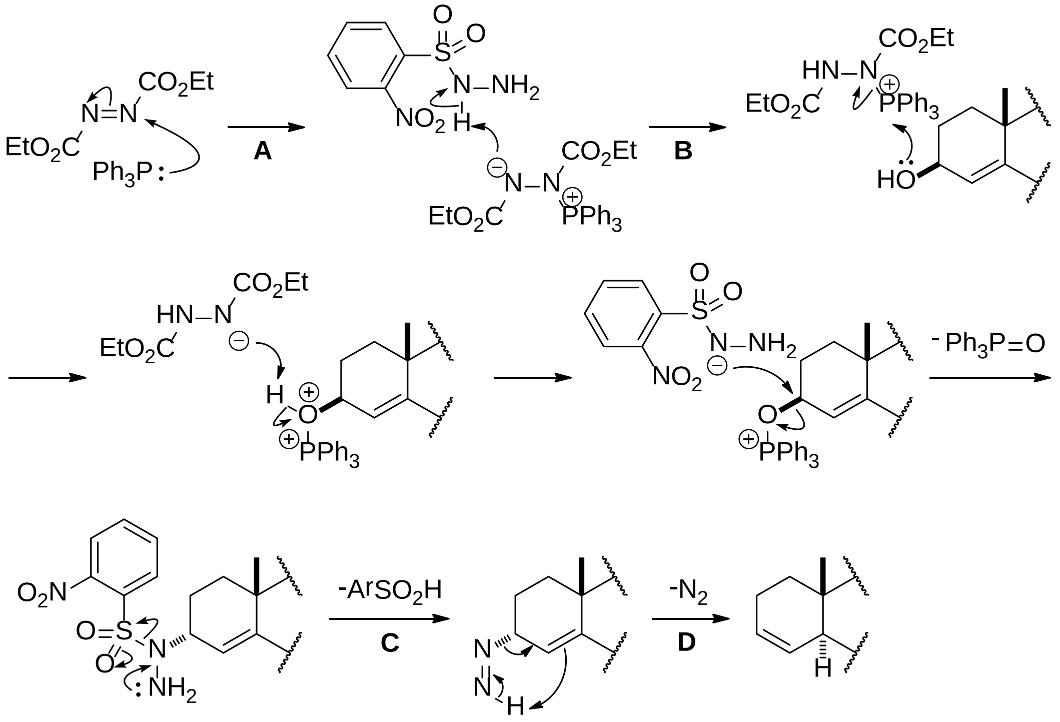
B078



Larsen, S. D.; Grieco, P. A.; Fobare, W. E *J. Am. Chem. Soc.* **1986**, 108, 3512.

A: Addition of an allylsilane to the iminium ion (a silyl group can stabilize the β-carbocation). **B**: Desilylation to form an olefin. **C**: Olefin-iminium ion cyclization to form a stable tertiary carbocation.

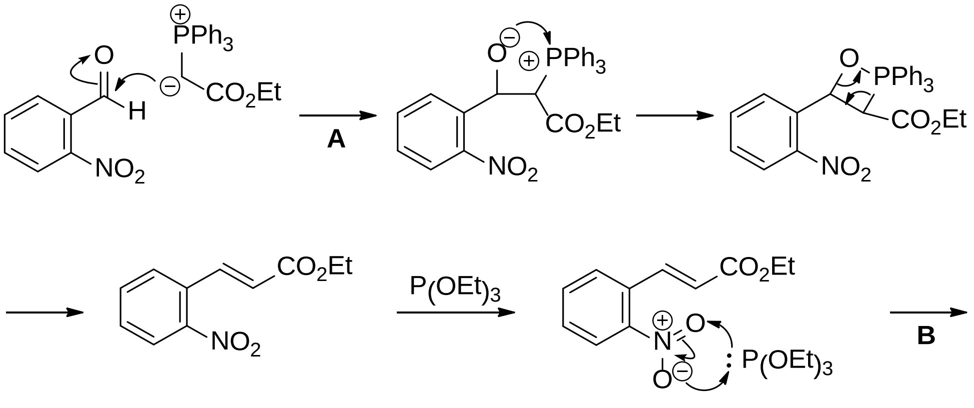
B079

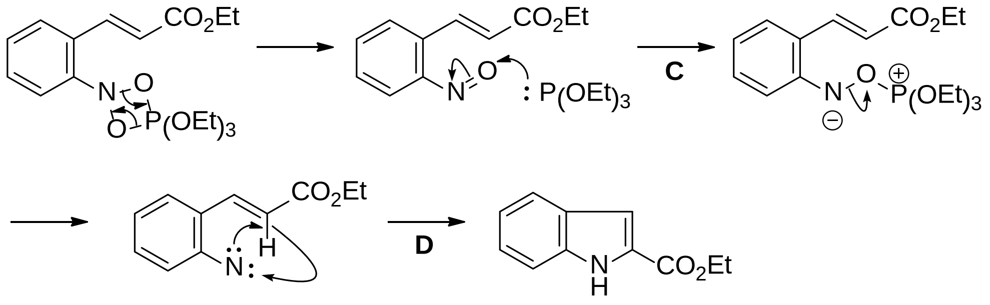


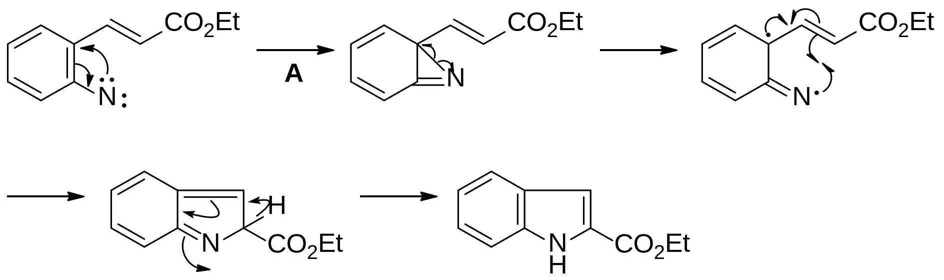
Myers, A. G.; Zheng, B. *Tetrahedron Lett.* **1996**, 37, 4841.

A: Mitsunobu reaction (ref A045). **B**: Deprotonation of the more acidic proton. **C**: Elimination of a sutfinate ion. **D**: Elimination of N_2 via a concerted mechanism.

B080



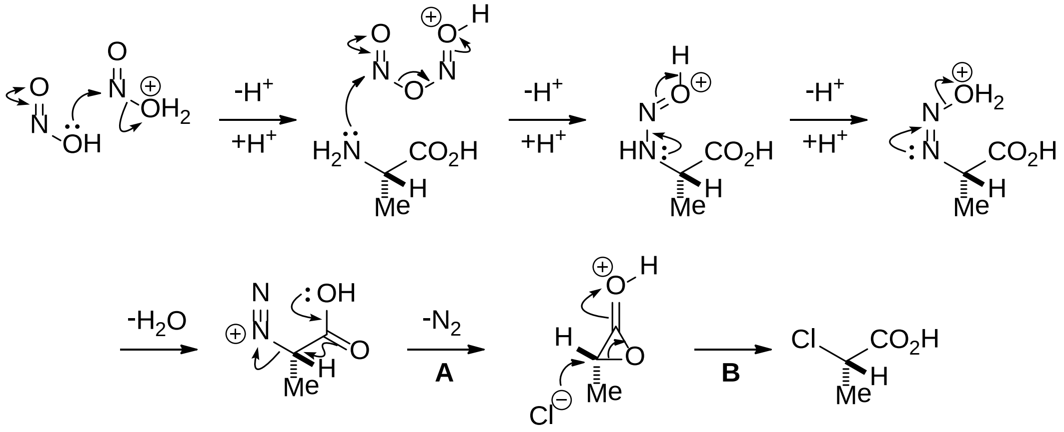




Mali, R. S.; Yadav, V. J. *Synthesis* **1984**, 862.

A: Wittig reaction. **B**: [4+2] Cheletropic reaction and elimination of a phosphate to form a nitroso intermediate. **C**: Deoxygenation of the nitroso compound to form a nitrene. **D**: Formation of the indole could be interpreted as a result of either 1) a direct C-H insertion or 2) formation of the azirine followed by homolytic cleavage and recombination of the resulting diradical.

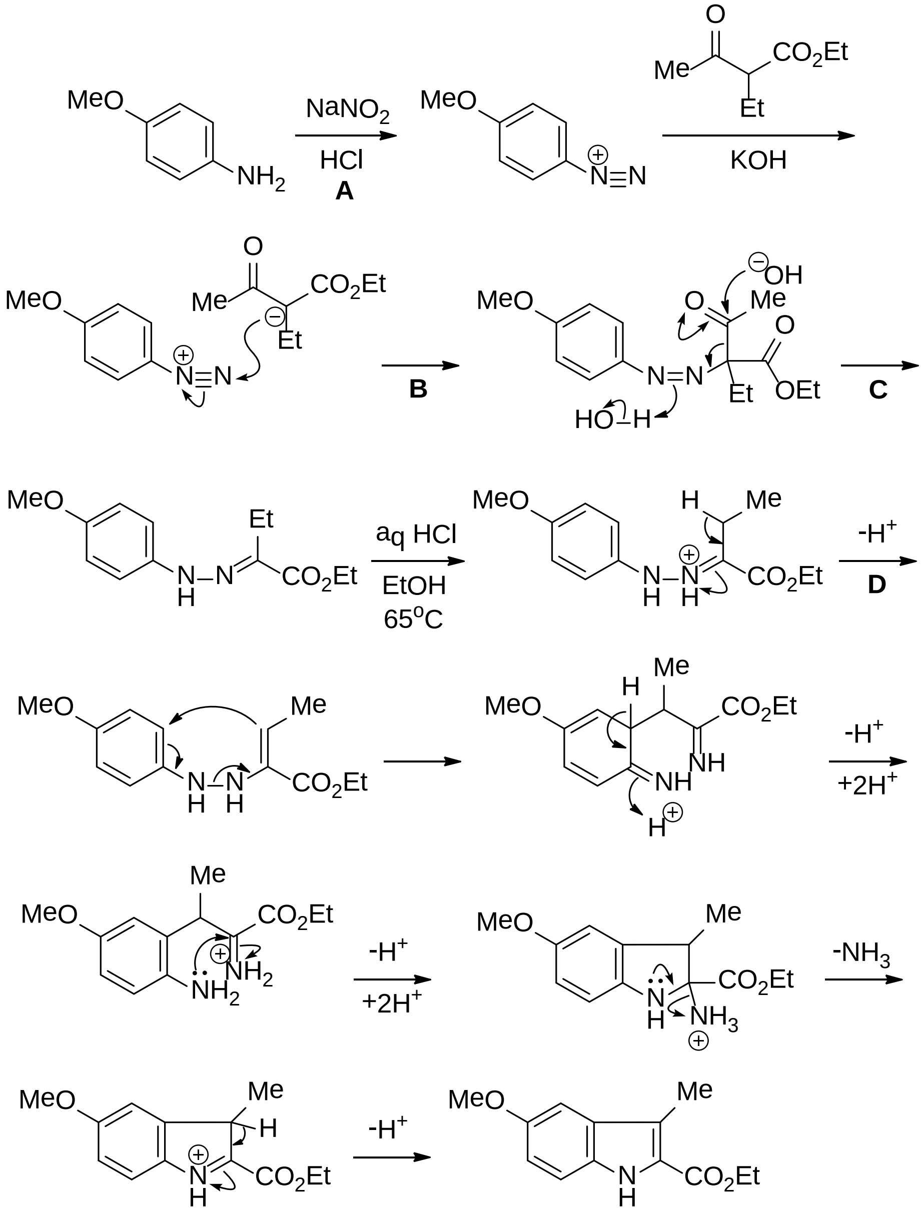
B081



Koppenhoefer, B.; Schurig, V. *Org. Synth., Coll.* Vol. Ⅷ **1993**. 119

A: Formation of a very reactive α-lactone via a diazonium salt. **B**: Cleavage of the α-lactone with chloride ion. The stereochemistry of the α-position is retained as a result of the double inversion.

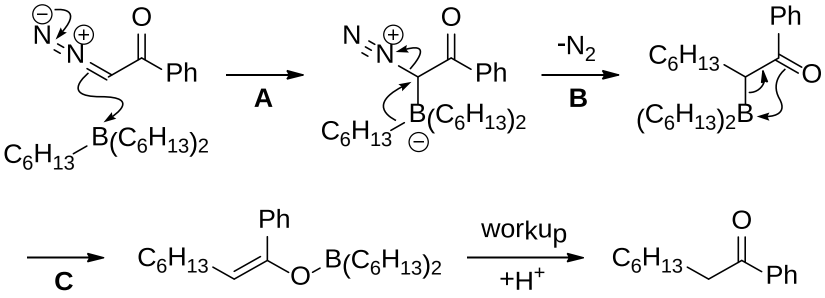
B082



Zhao, S.; Liao, X.; Wang, T.; Flippen-Anderson, J.; Cook, J. M.
J. Org. Chem. **2003**, 68, 6279.

Japp-Klingemann reaction and Fischer indole synthesis. **A**: Formation of a diazonium salt. **B**: Addition of the enolate to the diazonium salt. **C**: Ketone cleavage of β-ketoester to form a hydrazone. **D**: Fischer indole synthesis ref B031).

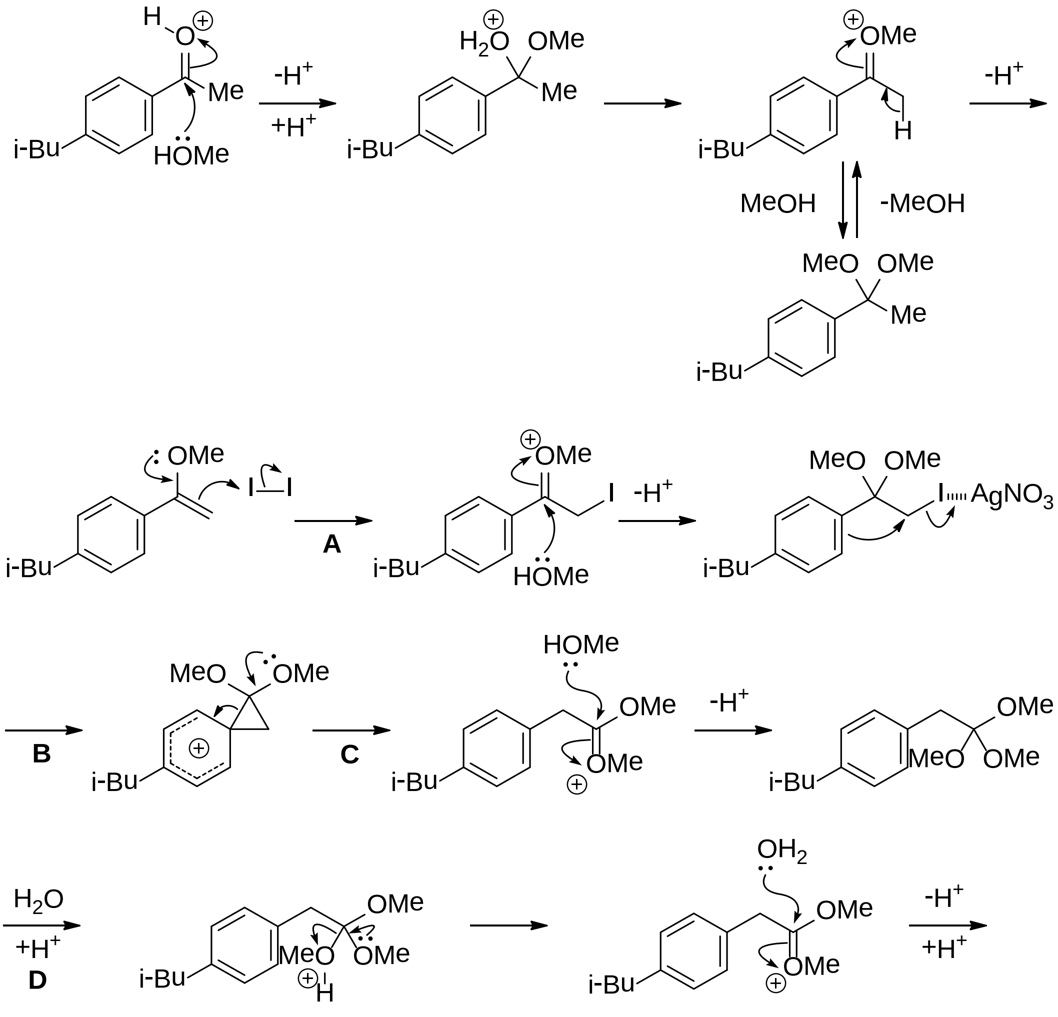
B083

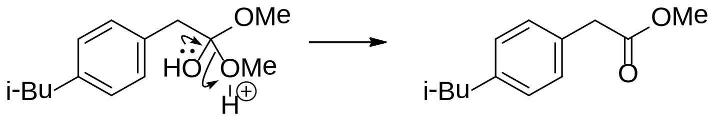


Kono, H.; Hooz, J. *Org. Synth., Coll.* Vol. Ⅵ **1988**, 919.

A: Attack of a diazoketone to B(n-hexyl)$_3$ to form an ate complex. **B**: Elimination of N_2 with a simultaneous migration of n-hexyl group. **C**: Formation of a boron enolate.

B084

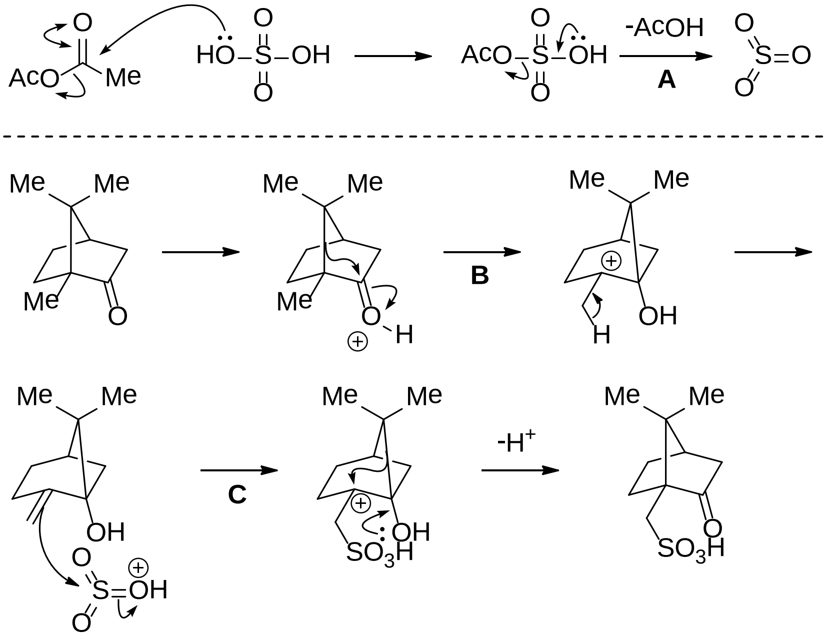




Oppolzer, W.; Rosset, S.; Brabander, J. D. *Tetrahedron Lett.* **1997**, 38, 1539.

A: Iodination of the enol ether with concomitant formation of a dimethyl acetal. **B**: Activation of the iodide with a silver ion to form a phenonium ion. **C**: Restoration of the aromaticity causes a cleavage of the electron-rich cyclopropane ring. **D**: The orthoester thus formed undergoes a facile hydrolysis to give the ester.

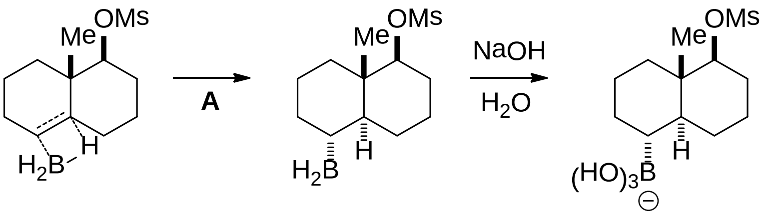
B085

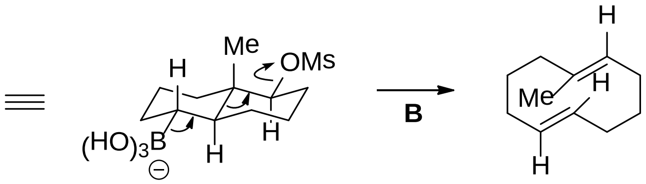


Bartlett, P. D.; Knox, L. H. *Org. Synth., Coll* Vol Ⅴ **1973**, 194.

A: Generation of SO_3. **B**: Wagner-Meerwein-type rearrangement. **C**: Sulfonation of the olefin to form a stable tertiary carbocation.

B086

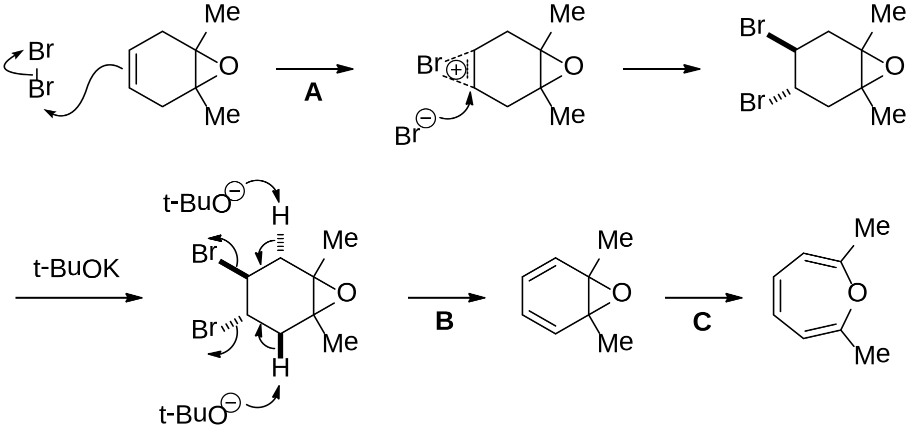




Marshall, J. A.; Bundy, G. L. *J. Am. Chem. Soc.* **1966**, 88, 4291.

A: Hydroboration from the less hindered side. **B**: Grob fragmentation ref B016).

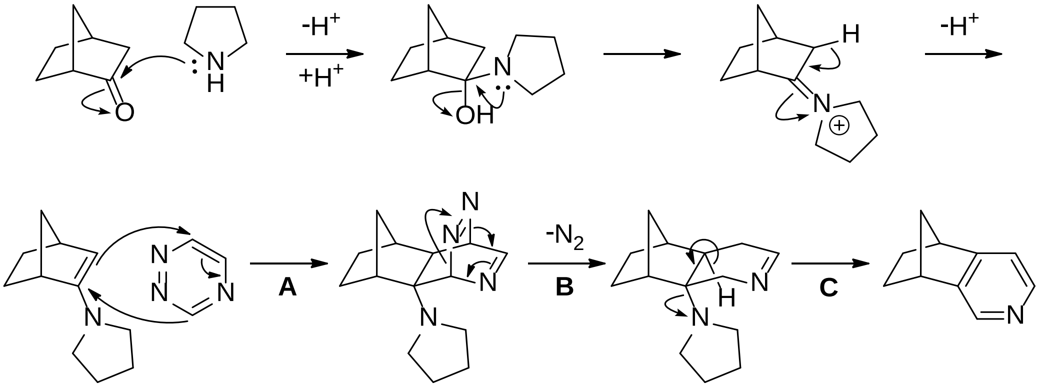
B087



Paquette, L. A.; Barrett, J. H. *Org. Synth., Coll.* Vol. V **1973**, 467.

A: Bromination of the olefin. **B**: Dehydrobromination to form a diene. **C**: 6e Disrotatory electrocyclic reaction (valence isomerism).

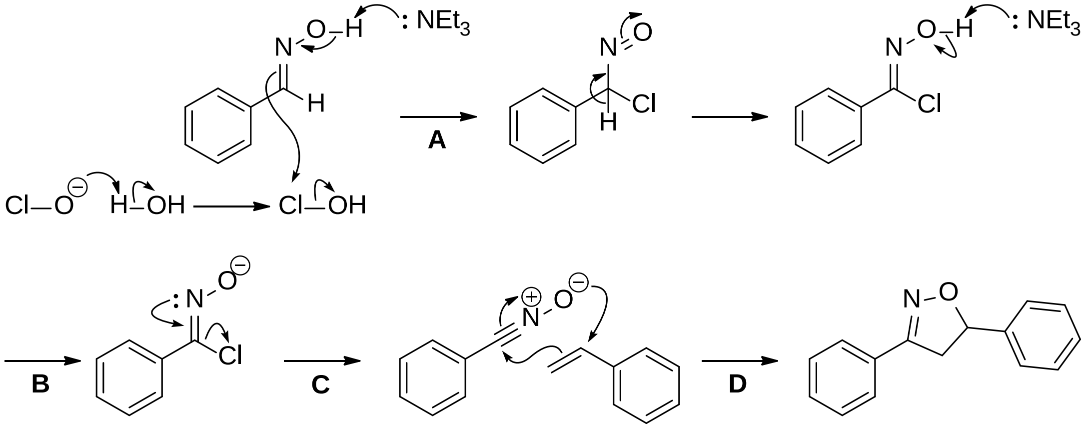
B088



Golka, A.; Keyte, P. J.; Paddon-Row, M. N. *Tetrahedron* **1992**, 48, 7663.

A: Inverse electron demand Diels-Alder reaction. **B**: Retro Diels-Alder reaction. **C**: Aromatization.

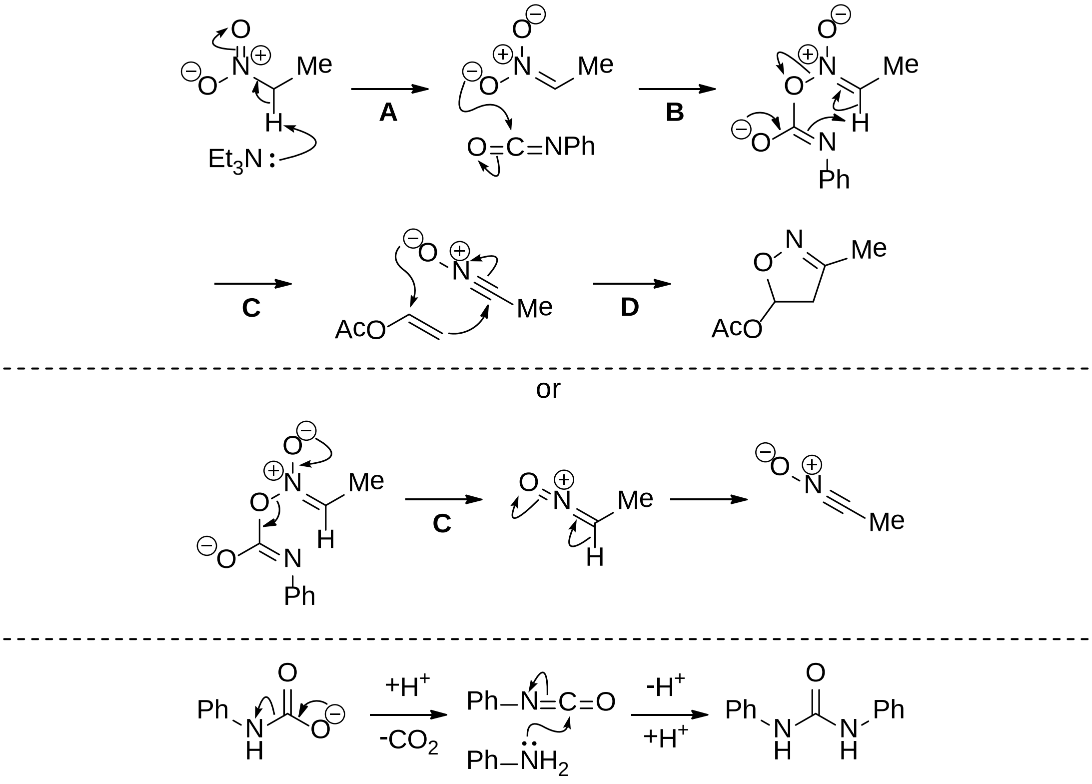
B089



Lee, G. A. *Synthesis* **1982**, 508.

A: Chlorination of an oxime. **B**: Elimination of chloride ion is facilitated by the formation of an oxime anion. **C**: Generation of a nitrile oxide. **D**: 1,3-Dipolar cycloaddition.

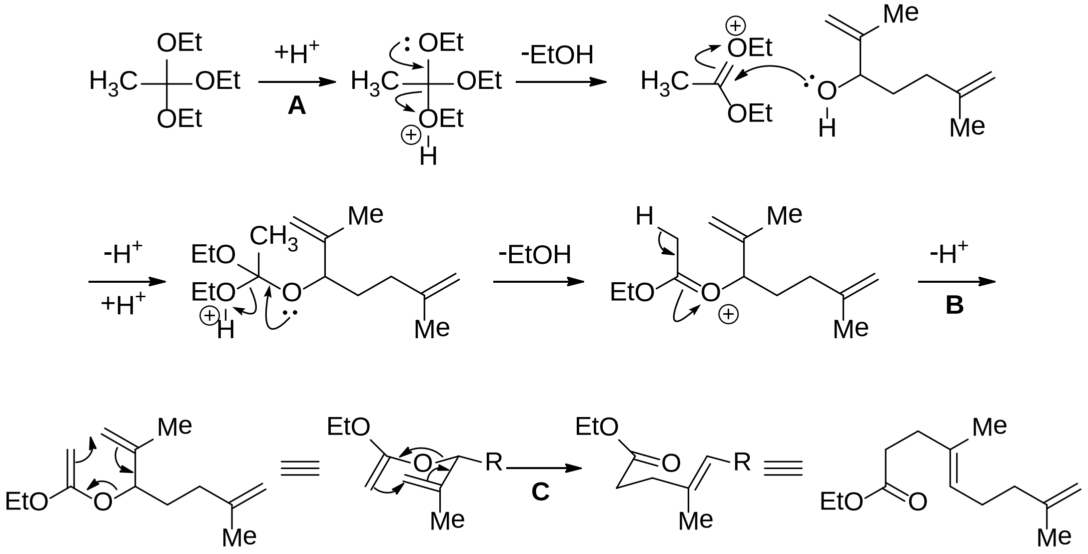
B090



Mukaiyama, T.; Hoshino, T. *J. Am. Chem. Soc.* **1960**, 82, 5339.

A: pKa CH_3NO_2 = 10.2, $HNEt_3^+$ = 10.7. **B**: Addition of the nitronate to PhNCO. **C**: Formation of the nitrile oxide might proceed either by 1) syn-elimination of the carbamate ion or 2) elimination of the carbamate ion followed by deprotonation. **D**: 1,3-Dipolar cycloaddition.

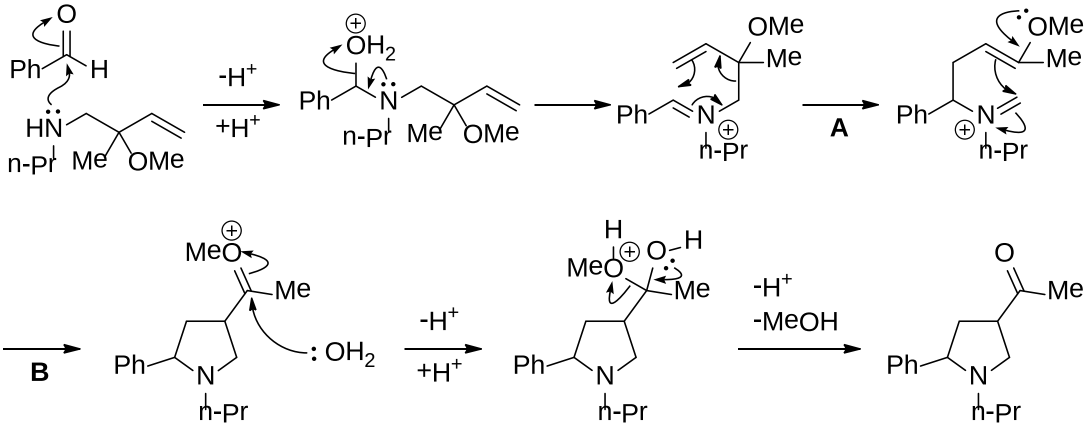
B091



Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J,; Li, T.-t.
J. Am. Chem. Soc. **1970**, 92, 741.

Claisen-Johnson rearrangement. **A**: Acid-catalyzed ether exchange of the orthoester. **B**: Formation of the mixed ketene acetal is effected by removal of ethanol from the reaction system by distillation. **C**: [3,3] Sigmatropic rearrangement via a chair-like transition state to form an (E)-olefin.

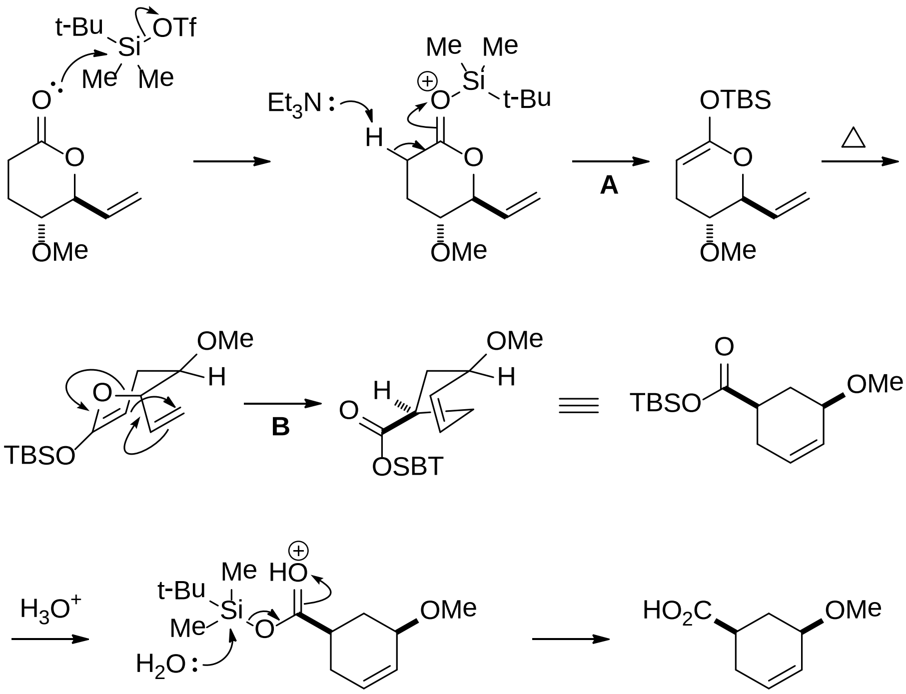
B092



Overman, L. E.; Kakimoto, M.; Okazaki, M. E.; Meier, G. P.
J. Am. Chem. Soc. **1983**, 105, 6622.

A: Aza-Cope rearrangement. **B**: Intramolecular Mannich reaction.

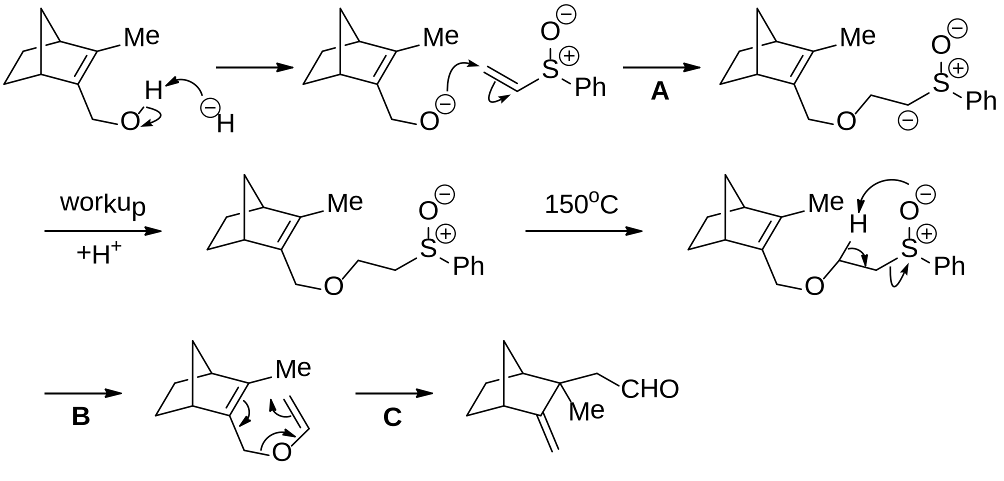
B093



Nakatsuka, M.; Ragan, J. A.; Sammakia, T.; Smith, D. B.; Uehling, D. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, 112, 5583.

Claisen-Ireland rearrangement. **A**: Formation of a ketene silyl acetal. **B**: [3,3] Sigmatropic rearrangement via a boat-like transition state.

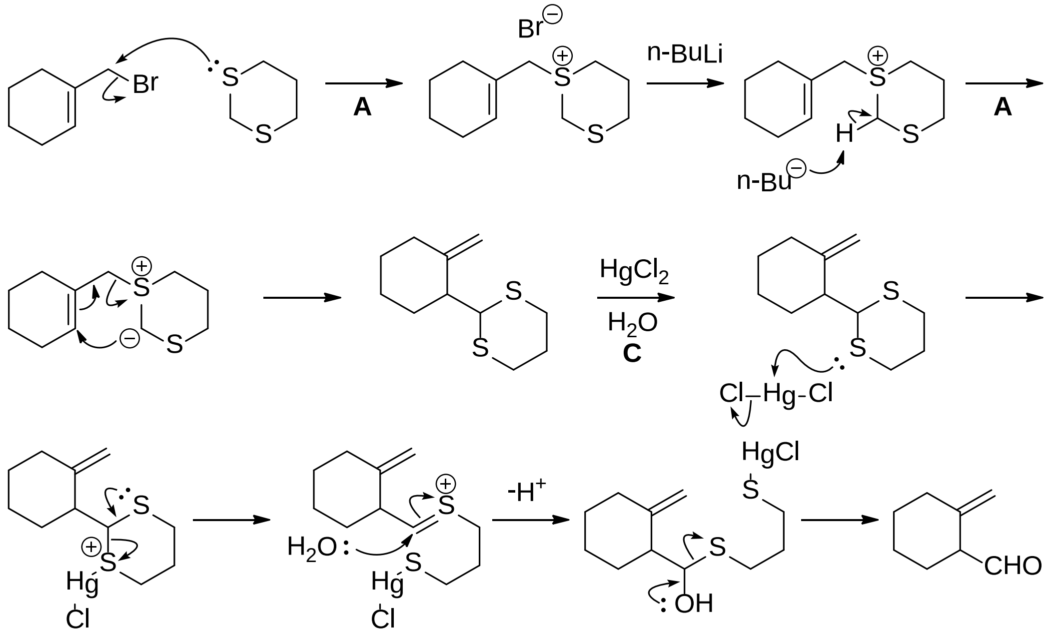
B094



Saito, M.; Kawamura, M.; Ogasawara, K. *Tetrahedron Lett.* **1995**, 36, 9003.

A: Conjugate addition to the vinyl sulfoxide. **B**: syn-Elimination. **C**: Claisen rearrangement.

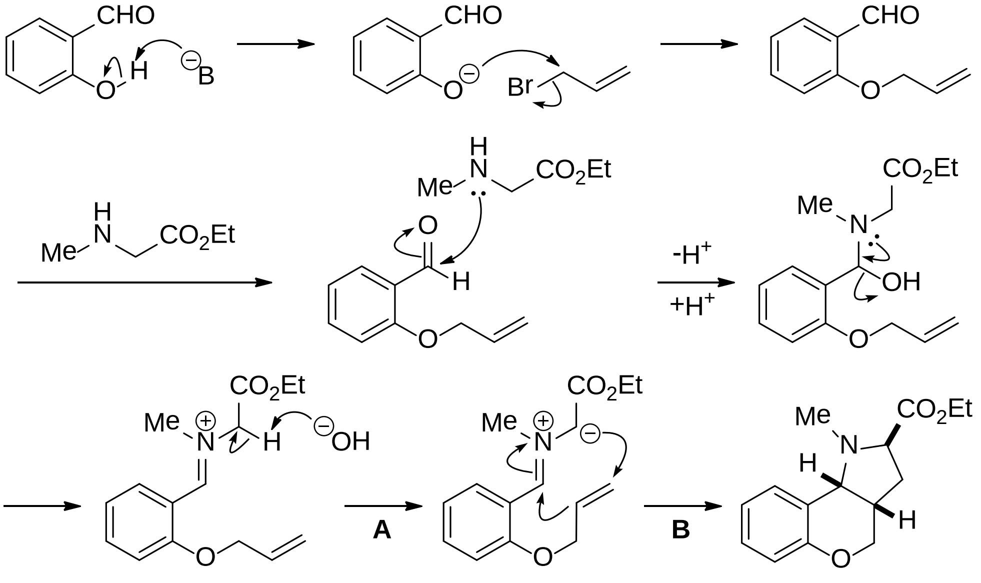
B095



Hunt, E.; Lythgoe, B. *J. Chem. Soc., Chem. Commun.* **1972**, 13, 757.

A: Formation of a sulfonium ion. **B**: Deprotonation to form a sulfur ylide, which undergoes [2,3] sigmatropic rearrangement. **C**: Hydrolysis of the thioacetal.

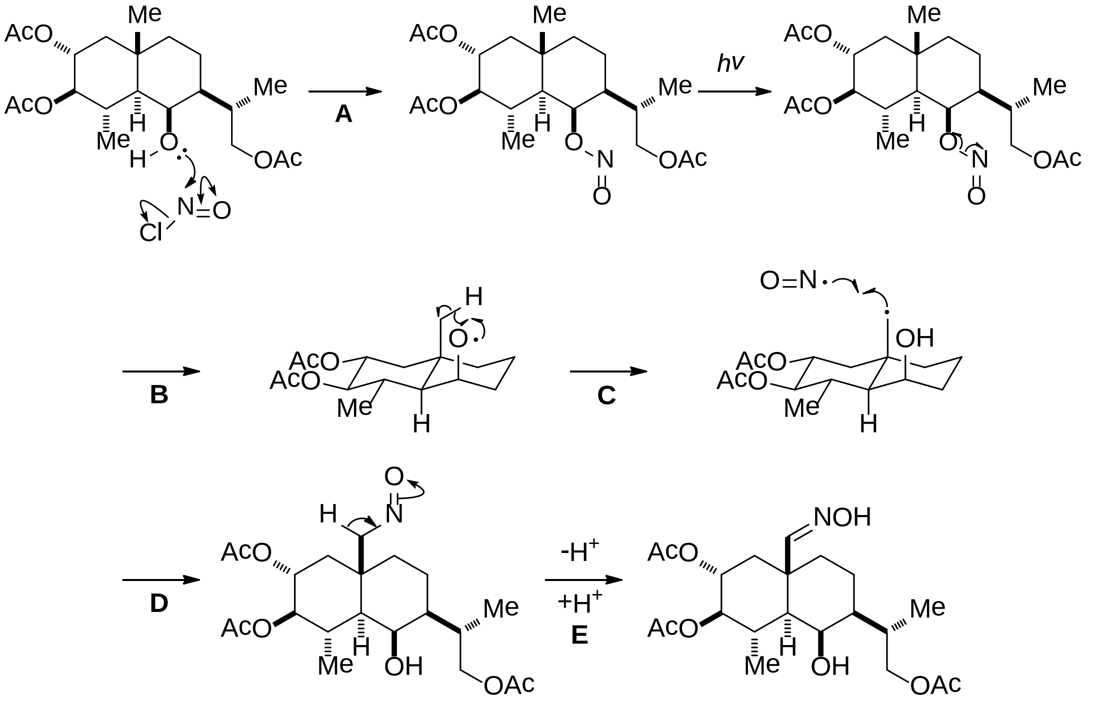
B096



Bashiardes, G.; Safir, I.; Mohamed, A. S.; Barbot, E; Laduranty, J. *Org. Lett.* **2003**, 5, 4915.

A: Formation of an azomethine ylide. **B**: Intramolecular 1,3-dipolar cycloaddition.

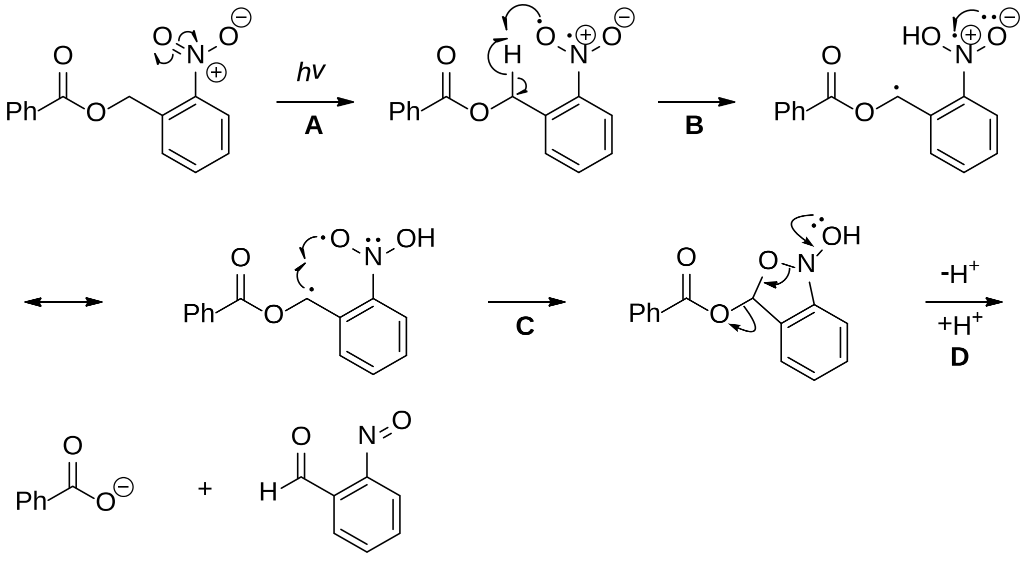
B097



Murai, A.; Nishizakura, K.; Katsui, N.; Masamune, T. *Tetrahedron Lett.* **1975**, 16, 4399.

Barton reaction. **A**: Formation of a nitrite. **B**: Homolytic cleavage. **C**: Abstraction of a hydrogen atom via a six-membered transition state. **D**: Recombination of ,NO with the resulting radical. **E**: Tautomerization.

B098

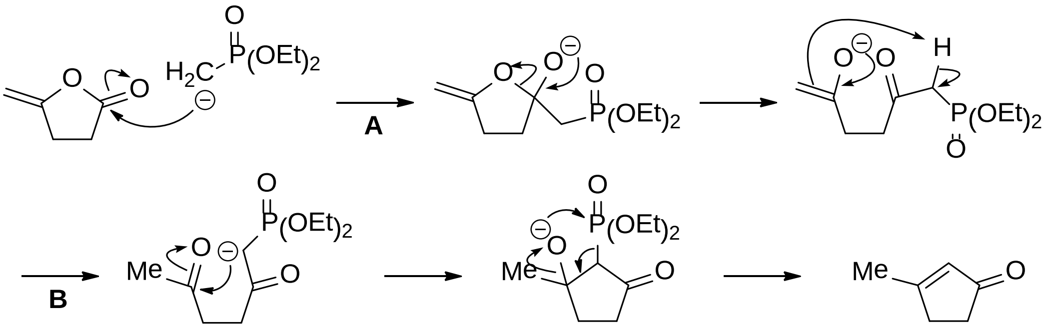


Barltrop, J. A.; Plant, P. J.; Schofield, P. *Chem. Commun.* **1996**, 822.

Photo-cleavable protecting group for acids. **A**: Photo-activated formation of a diradical. **B**:

Intramolecular abstraction of a hydrogen atom. **C**: Recombination of the diradical. **D**: Elimination of benzoic acid.

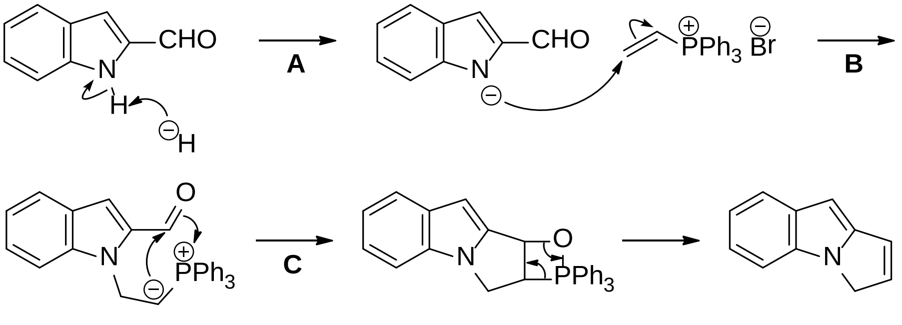
B099



Altenbach, H.-J.; Holzapfel, W.; Smerat, G.; Finkler, S. H. *Tetrahedron Lett.* **1985**, 26, 6329.

A: Addition to the reactive enol lactone. **B**: Intramolecular Horner-Wadsworth-Emmons reaction ref A071).

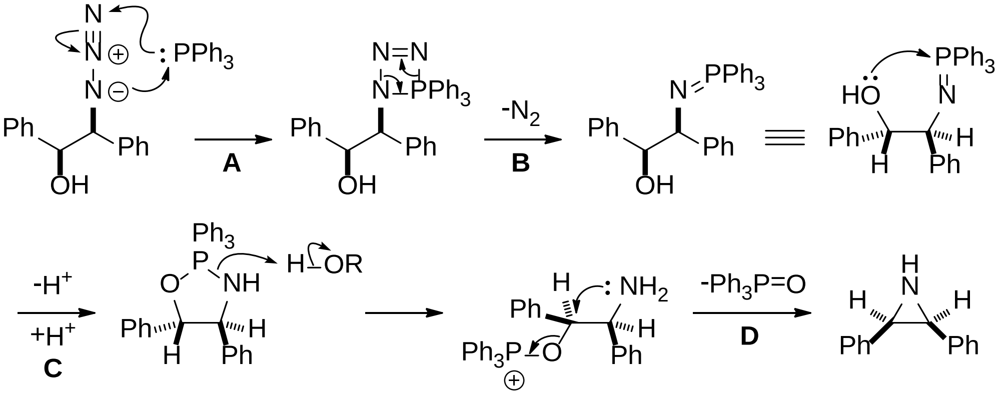
B100



Schweizer, E. E.; Light, K. K. *J. Org. Chem.* **1966**, 31, 870.

A: pKa of the parent indole NH = 17, H_2 = 35. **B**: Addition to the vinylphosphonium salt to form an ylide. **C**: Intramolecular Wittig reaction.

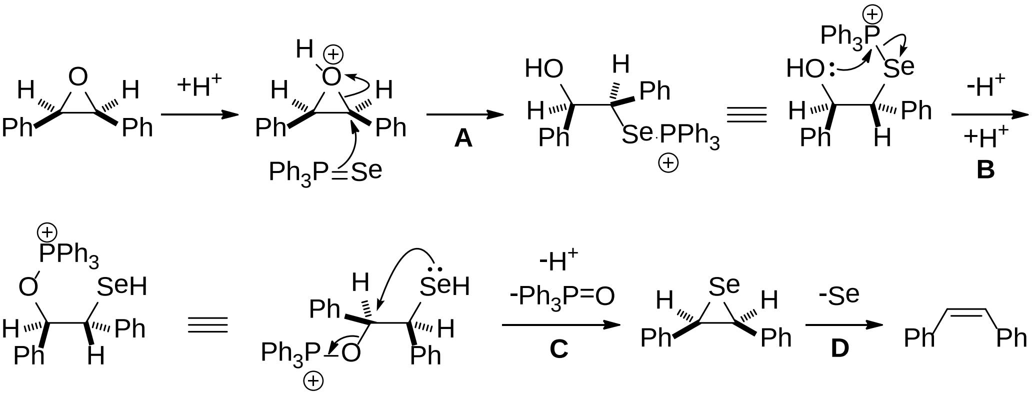
B101



Pöchlauer, P.; Müller, E. P.; Peringer, P. *Helv. Chim. Acta* **1984**, 67, 1238.

Staudinger reaction (A-B). **A**: Cheletropic reaction. **B**: Formation of an iminophosphorane. **C**: Migration of the phosphorus group. **D**: Intramolecular S_N2 reaction.

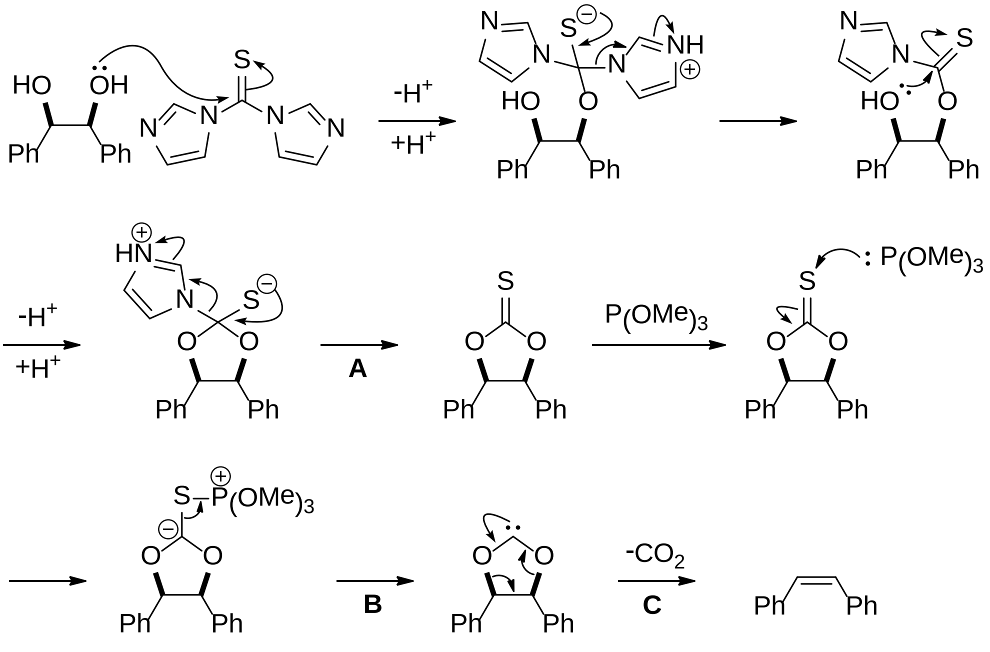
B102



Clive, D. L. J.; Denyer, C. V. *J. Chem. Soc., Chem. Commun.* **1973**, 253.

A: Acid-catalyzed cleavage of the epoxide with inversion of configuration. **B**: Migration of the phosphorus group. **C**: Intramotecular S_N2 reaction with inversion of configuration to form a cis-episelenide. **D**: Spontaneous extrusion of selenium.

B103



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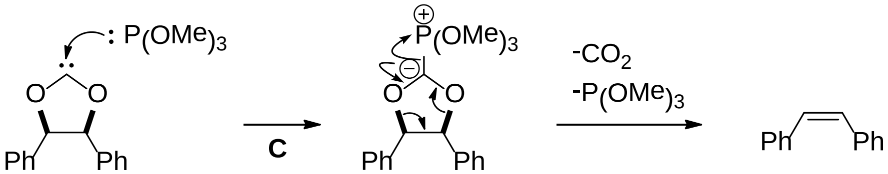
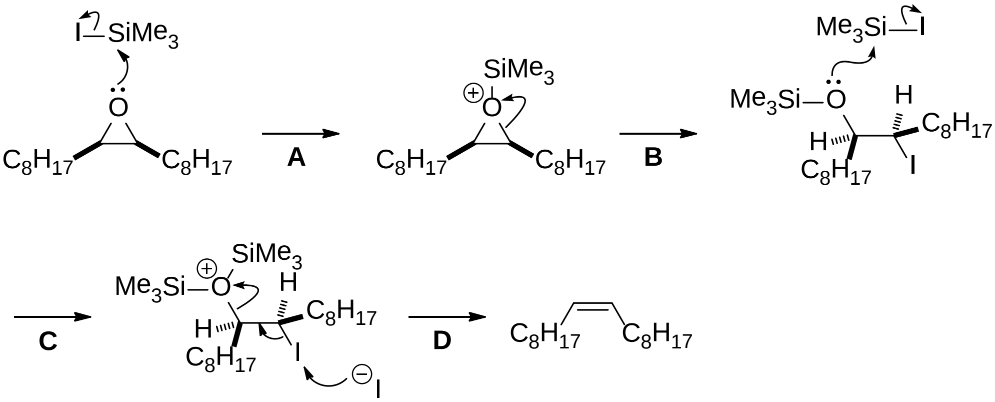


Corey, E. J.; Winter, R. A. E. *J. Am. Chem. Soc.* **1963**, 85, 2677.

Corey-Winter olefination. **A**: Formation of a thionocarbonate. **B**: Reductive desulfurization of the thionocarbonate to generate a carbene. **C**: The resulting carbene might undergo a direct fragmentation to form the cis-olefin. Alternatively, it would react with a phosphite to form an ylide, which then collapses to give the product.

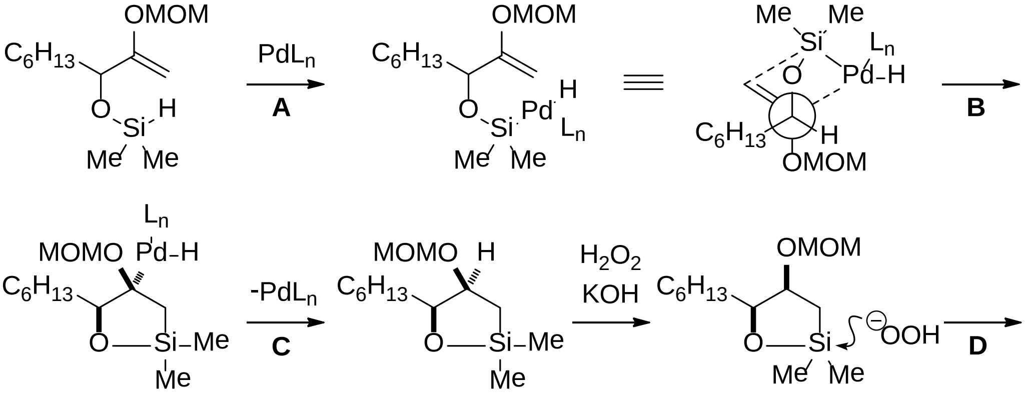
B104

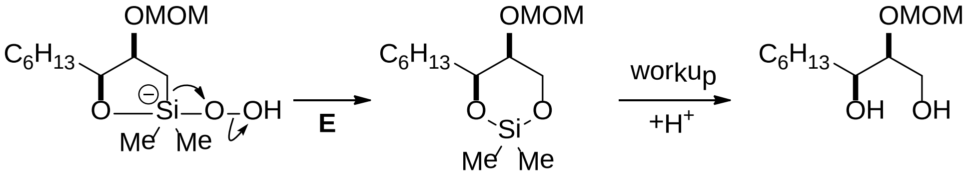


Denis, J. N.; Magnane, R.; Eenoo, M. V.; Krief, A. *Nouv. J. Chim.* **1979**, 3, 705.

A: Silylation of the epoxide. **B**: S_N2 reaction with inversion of configuration. **C**: Silylation of the silyl ether. **D**: E2 elimination.

B105

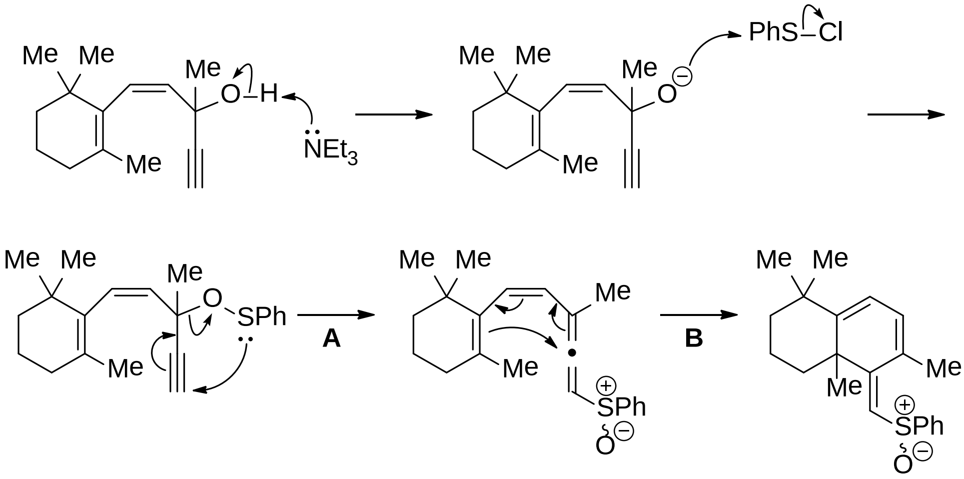




Tamao, K.; Nakagawa, Y.; Arai, H.; Higuchi, N.; Ito, Y. *J. Am. Chem. Soc.* **1988**, 110, 3712.

Tamao oxidation (D-E). **A**: Oxidative addition to the Si-H bond. **B**: Intramolecular diastereoselective silametallation to the olefin. **C**: Reductive elimination. **D**: Formation of a silicate ion. **E**: Migration of the Si-C bond.

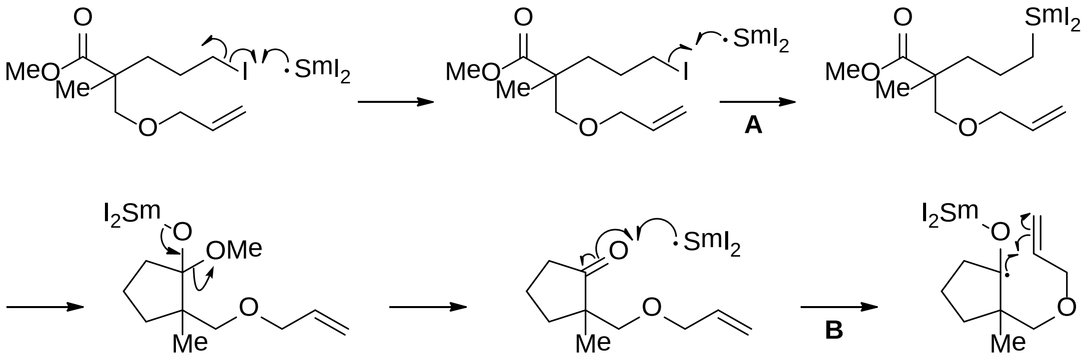
B106

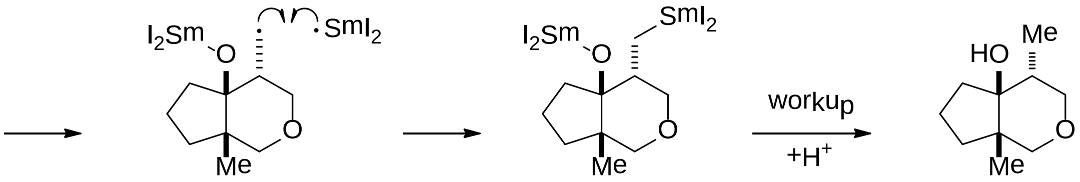


Okamura, W. H.; Peter, R.; Reischl, W. *J. Am. Chem. Soc.* **1985**, 107, 1034.

A: [2,3] Sigmatropic rearrangement of the propargyl sulfenate. **B**: 6e Disrotatory electrocyclic reaction.

B107

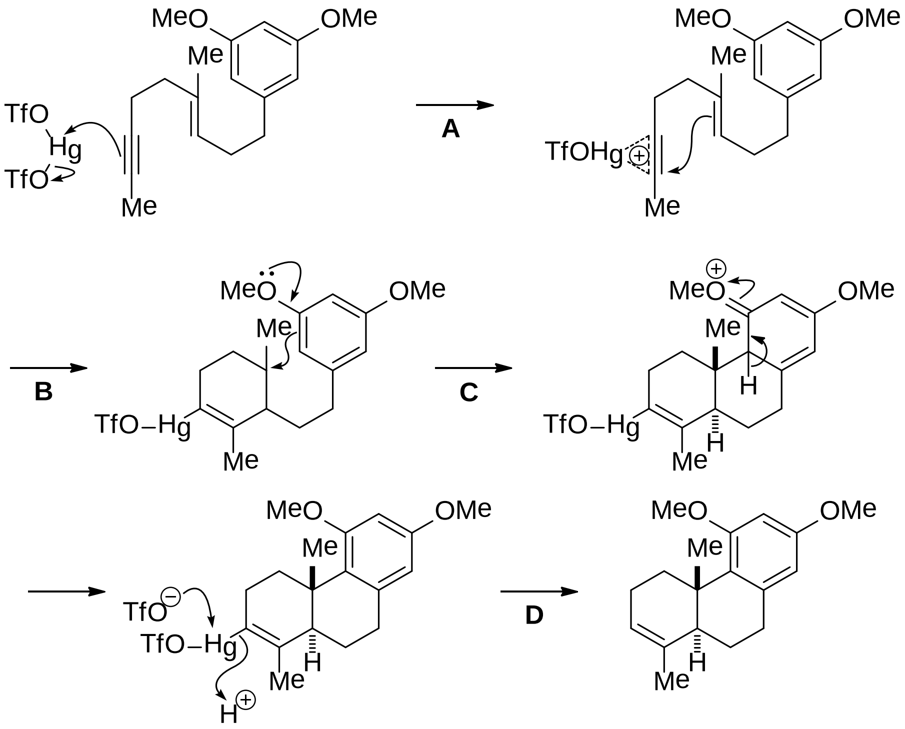




Molander, G. A.; Harris, C. R. *J. Org. Chem.* **1997**, 62, 2944

A: Since SmI_2 is a single electron reductant, two molecules of SmI_2 are needed to convert an alkyl iodide to the corresponding organosamarium species. **B**: SET to the ketone followed by radical cyclization.

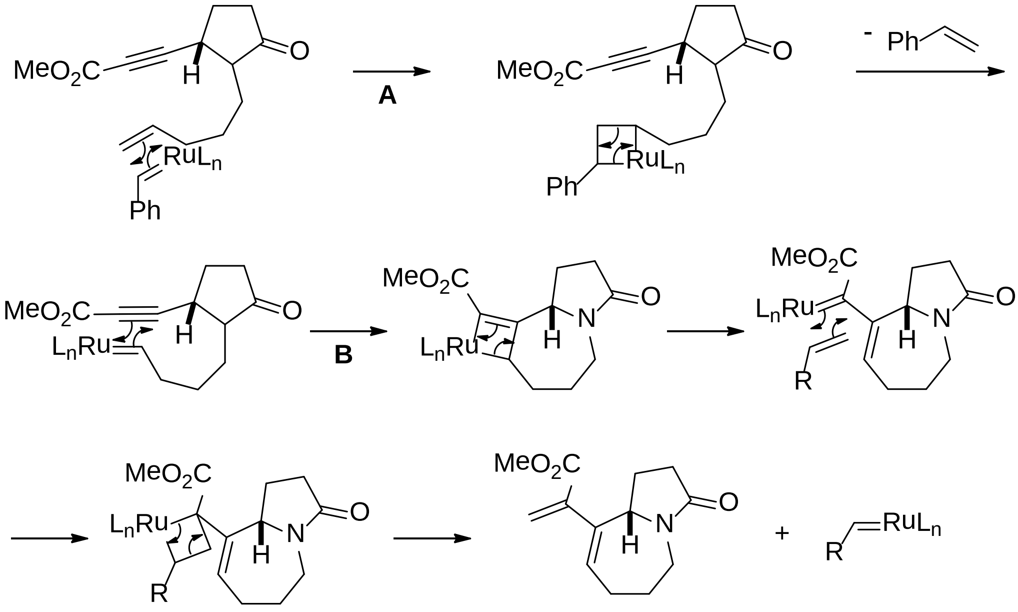
B108



Imagawa, H.; Iyenaga, T.; Nishizawa, M. *Org. Lett.* **2005**, 7, 451.

A: Coordination of $Hg(OTf)_2$ to the alkyne. **B**: 6-endo-dig cation cyclization to form a stable tertiarycarbocation. **C**: Attack of the electron-rich aromatic ring to the carbocation. **D**: Protonolysis of the C-Hg bond to regenerate the catalyst.

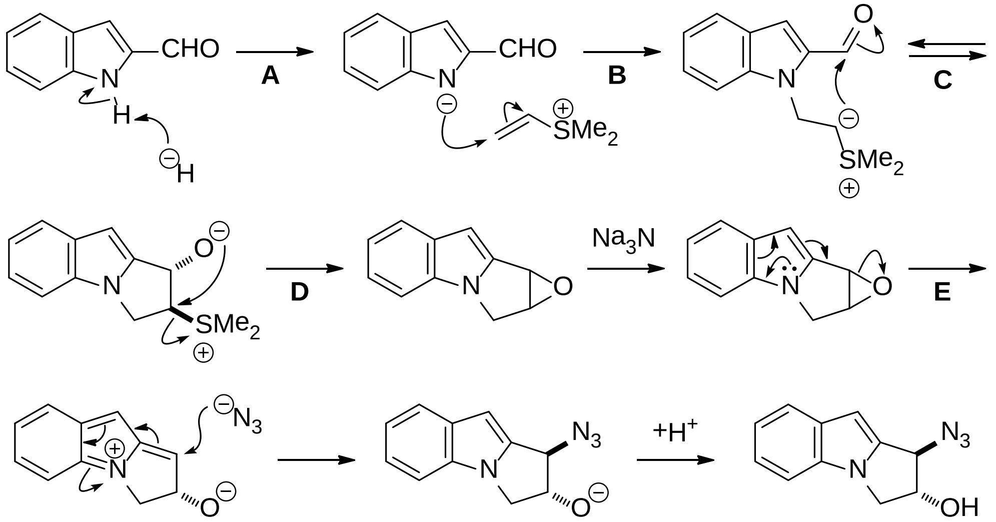
B109



Kinoshita, A.; Mori, M. *J. Org. Chem*. **1996**, 61, 8356.

Intramolecular enyne metathesis (ref A078). **A**: Intermolecular alkene metathesis. **B**: Intramolecular alkyne metathesis.

B110

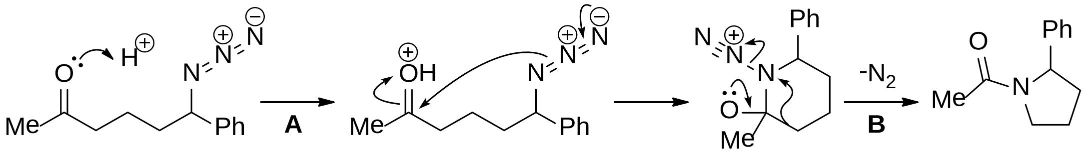


Wang, Y.; Zhang, W.; Colandrea, V. J.; Jimenez, L. S. *Tetrahedron* **1999**, 55, 10659.

A: pKa indole NH = 17, H_2 = 35. **B**: Addition of the vinylsulfonium salt to form an ylide. **C**: Intramolecular addition to the aldehyde (reversible). **D**: Intramolecular S_N2 reaction to form an epoxide. **E**: Cleavage of the epoxide helped by the indole nitrogen lone pair.

B111

n=1



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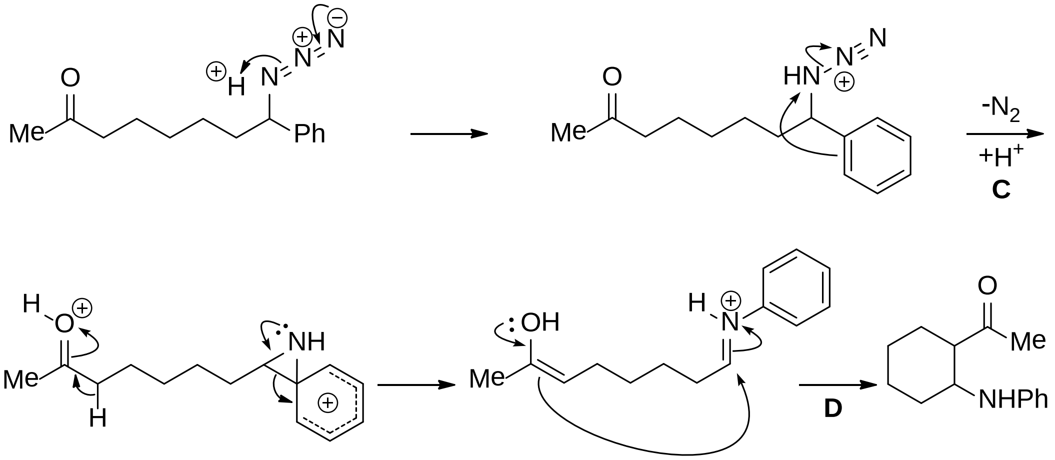
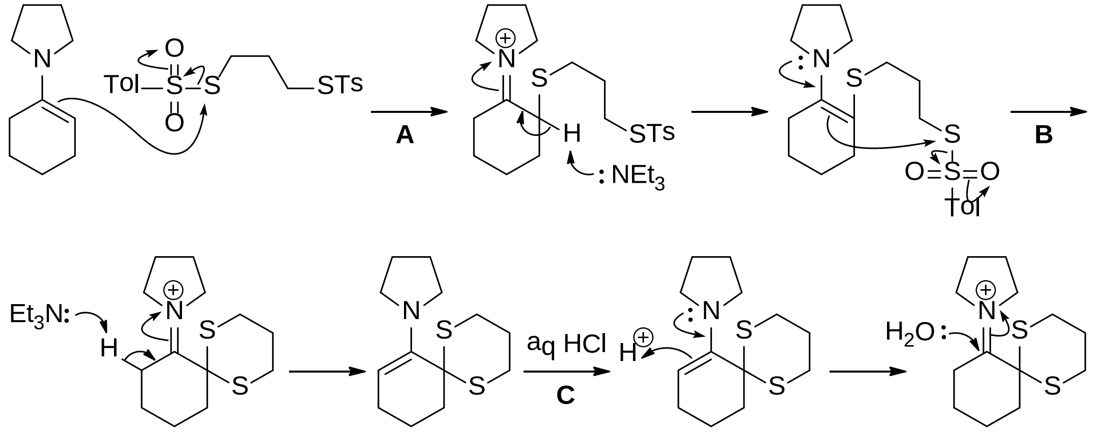
n=3

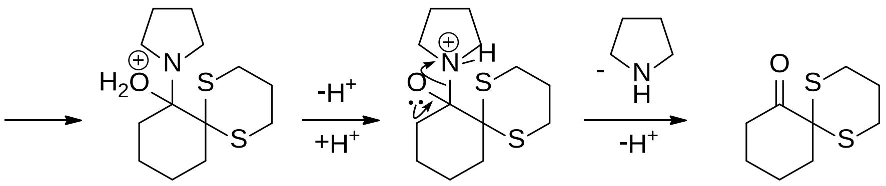


Wrobleski, A.; Aube, J. *J. Org. Chem.* **2001**, 66, 886.

Intramolecular Schmidt reaction. **A**: Activation of the carbonyl group by protonation followed by intramolecular addition of the azide (six-membered ring is easy to form). **B**: Ring contraction. **C**: The formation of a phenonium ion is preferred over the formation of the eight-membered ring. **D**: Intramolecular Mannich reaction.

B112

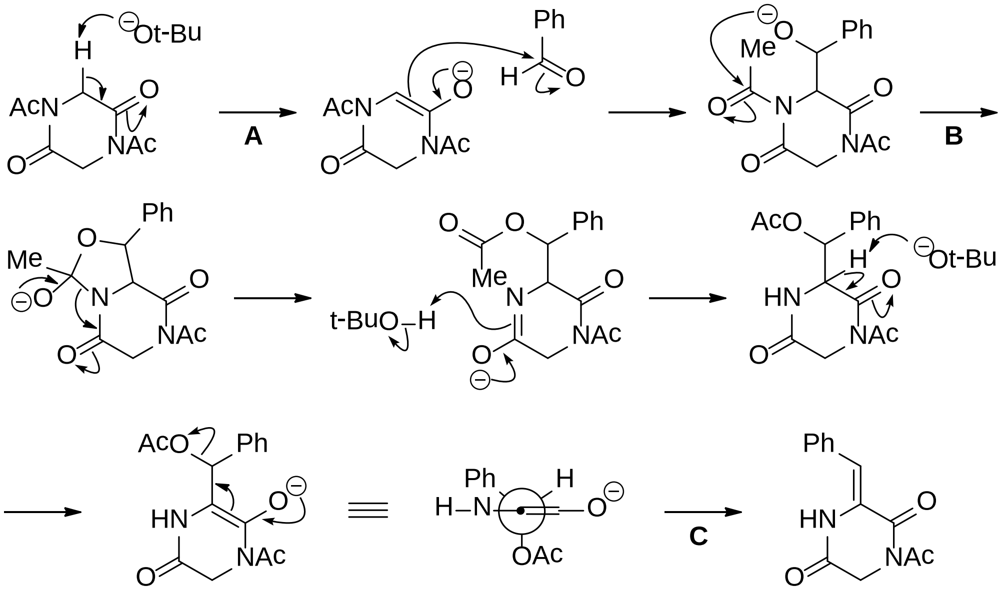




Woodward, R. B.; Pachter, I. J.; Scheinbaum, M. L. *Org. Synth., Coll.* Vol. Ⅵ **1988**, 1014.

A: pKa $PhSO_2H$ = 1.5. **B**: Formation of an easy to form six-membered ring. **C**: Hydrolysis of the enamine.

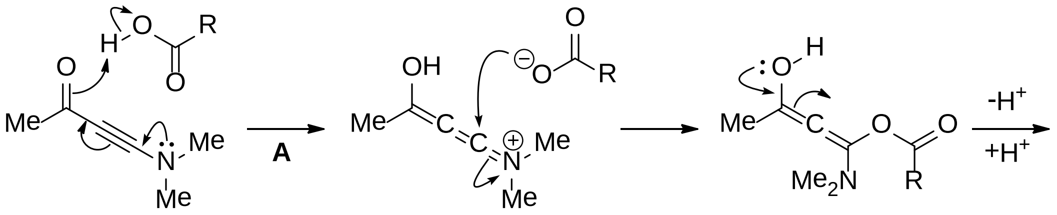
B113

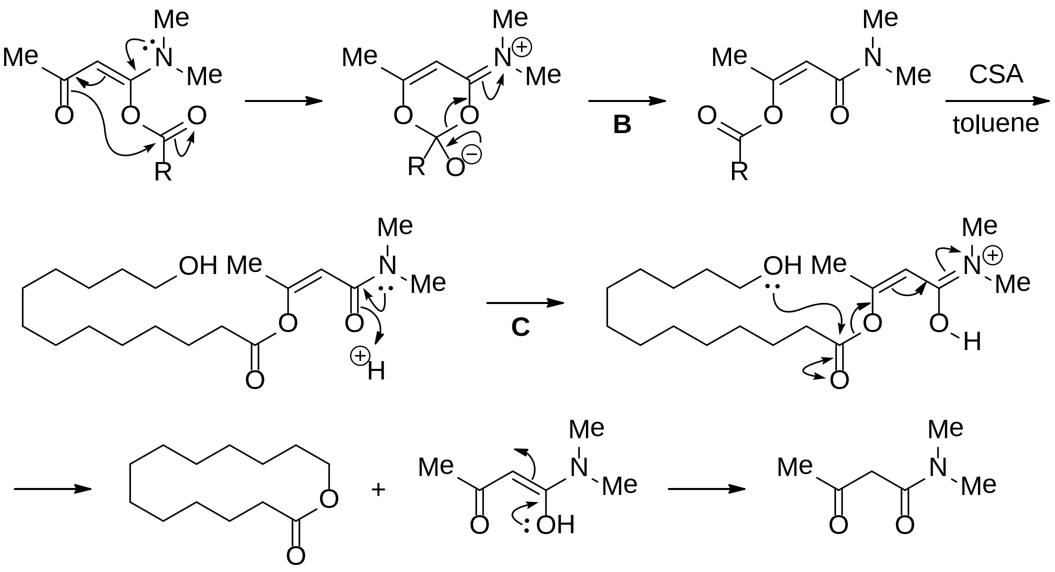


Gallina, C.; Liberatori, A. *Tetrahedron Lett.* **1973**, 1135.

A: Deprotonation of the α-position of an imide (more acidic than amides). **B**: Aldol reaction followed by an intramolecular acyl transfer via a five-membered ring transition state. **C**: Elimination of the acetoxy group.

B114

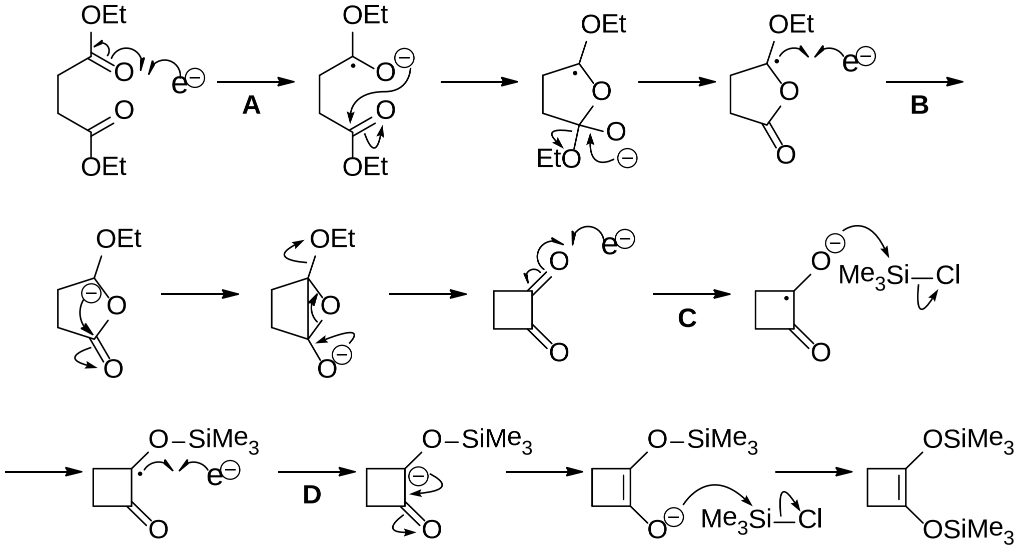




Gais, H. J. *Tetrahedron Lett.* **1984**, 25, 273.

A: Protonation of the carbonyl group followed by addition of the carboxylate to the iminium ion. **B**: Intramolecular acyl transfer to form a vinylogous anhydride. **C**: Activation of the vinylogous anhydride by protonation resulted in the formation of the macrocyclic lactone.

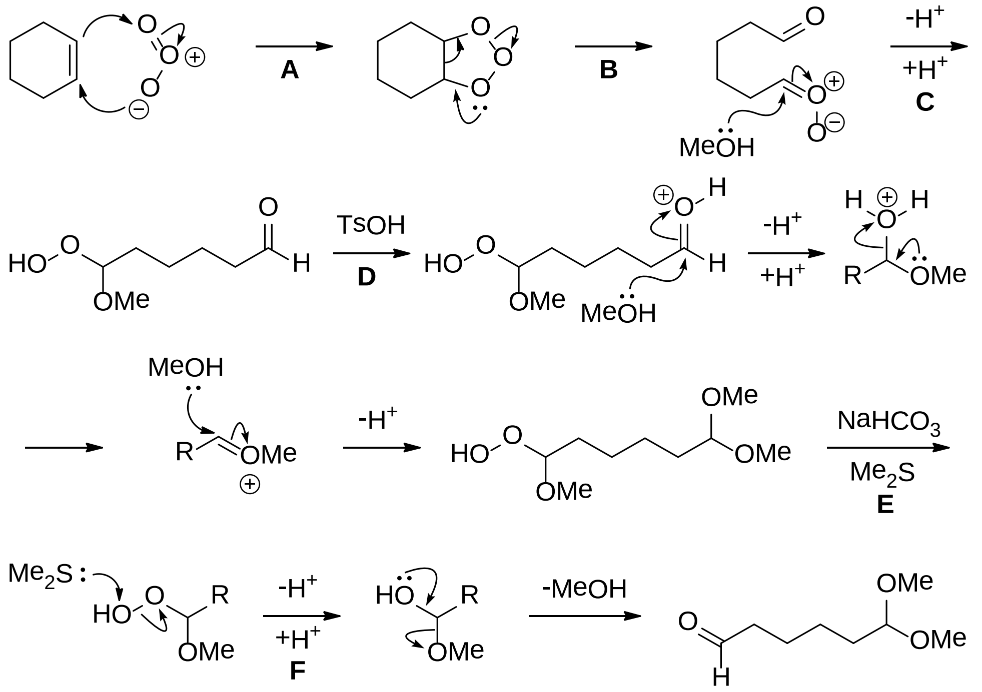
B115



Bloomfield, J. J.; Nelke, J. M. *Org. Synth., Coll* Vol. Ⅵ **1988**, 167.

Acyloin condensation. **A**: Single electron transfer (SET) to the carbonyl group followed by lactonization. **B**: SET followed by a ring contraction. **C**: SET followed by silylation. **D**: SET to form an enolate followed by silylation.

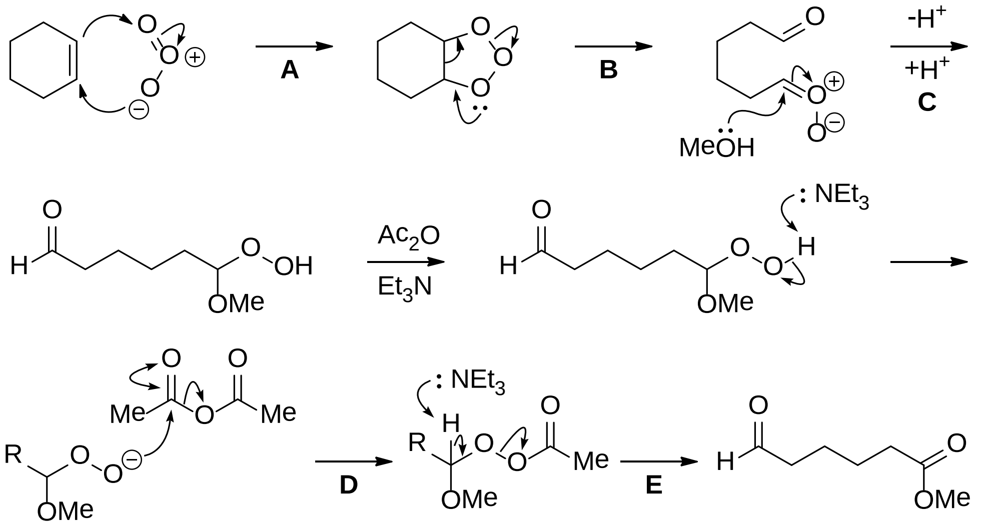
B116



Claus, R. E.; Schreiber, S. L. *Org. Synth., Coll* Vol. Ⅶ **1990**, 168.

A: 1,3-Dipolar cycloaddition of ozone to the olefin. **B**: Heterolytic cleavage of the initial ozonide. **C**: Trapping the dipole with methanol. **D**: Formation of a dimethyl acetal from the aldehyde (protonation of the less electron-dense hydroperoxy group is more difficult). **E**: Neutralization to kill TsOH. **F**: Reduction of the hydroperoxide with dimethyl sulfide.

B117



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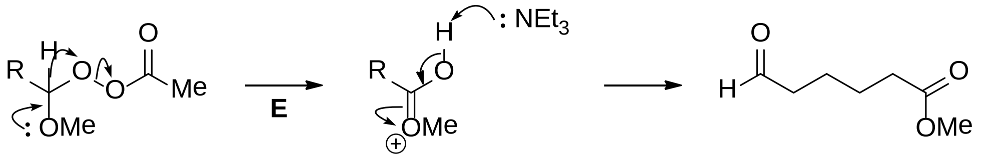
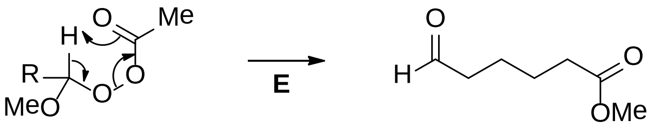
or



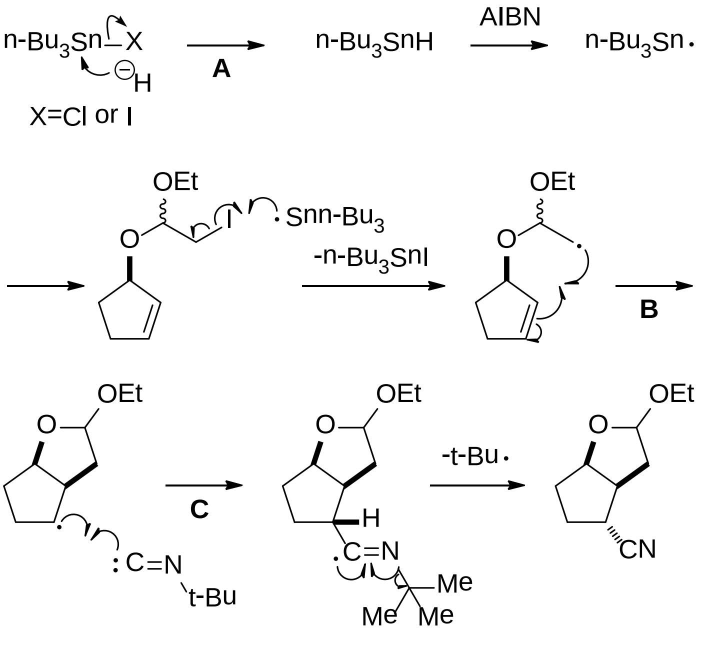
or



Claus, R. E.; Schreiber, S. L. *Org. Synth., Coll* VoL Ⅶ **1990**, 168

A: 1,3-Dipolar cycloaddition of ozone to the olefin. **B**: Heterolytic cleavage of the initial ozonide. **C**: Trapping the dipole with methanol. **D**: Acetylation. **E**: Elimination of acetic acid might proceed either by 1) deprotonation with triethylamine, 2) Baeyer-Villiger-type 1,2-hydride shift, or 3) thermal eliminatior via a six-membered transition state.

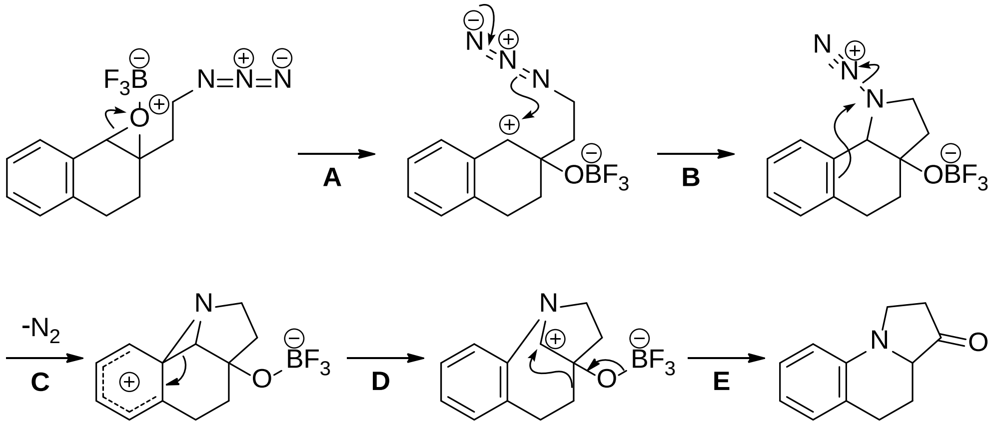
B118



Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, 108, 303.

A: Reduction of Bu_3SnX with $NaBH_3CN$ to form a low concentration of Bu_3SnH to avoid the premature reduction of the radical intermediates. **B**: 5-exo-trig Radical cyclization. **C**: Addition to the isocyanide followed by elimination of a stable t-butyl radical.

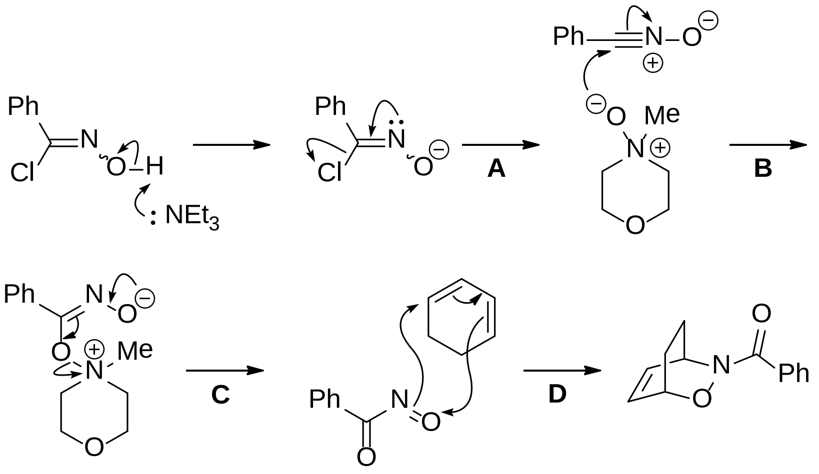
B119



Lang, S.; Kennedy, A. R.; Murphy, J. A.; Payne, A. H. *Org. Lett.* **2003**, 5, 3655.

A: Generation of a stable benzylic carbocation. **B**: Intramolecular attack of the azide. **C**: formation of an aziridine. **D**: Restoration of the aromaticity. **E**: 1,2-Alkyl shift.

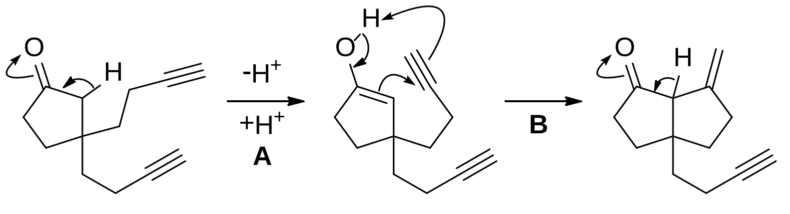
B120

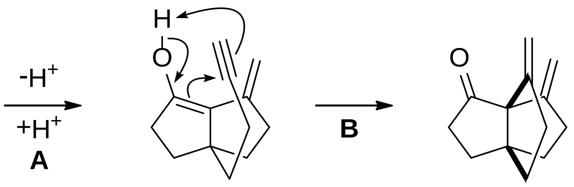


Quadrelli, P., Mella, M.; Invernizzi, A. G.; Caramella, P. *Tetrahedron* **1999**, 55, 10497.

A: Elimination of chloride ion is facilitated by the formation of an oxime anion. **B**: Addition of NMO to the nitrile oxide. **C**: Generation of an acylnitroso compound. **D**: Hetero-Diels-Alder reaction.

B121

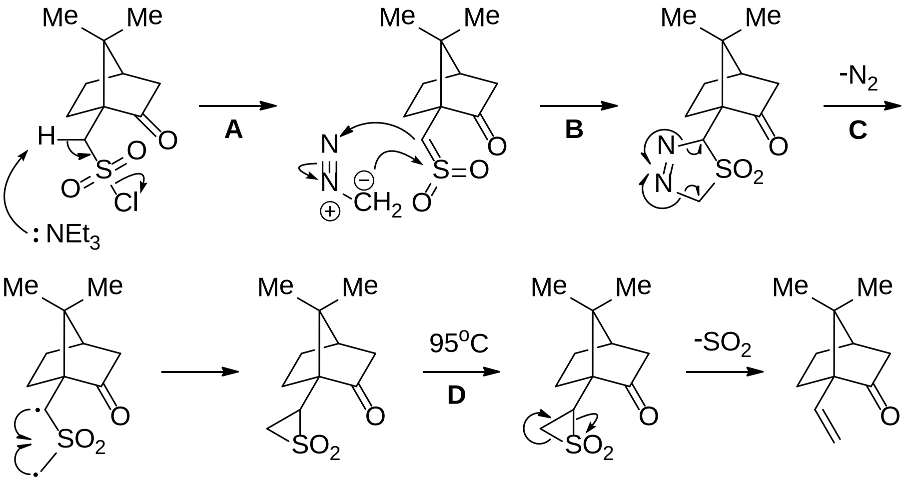




Drouin, J.; Leyendecker, F.; Conia, J., M. *Tetrahedron*. **1980**, 36, 1203.

A: Tautomerization. **B**: Oxy-ene reaction.

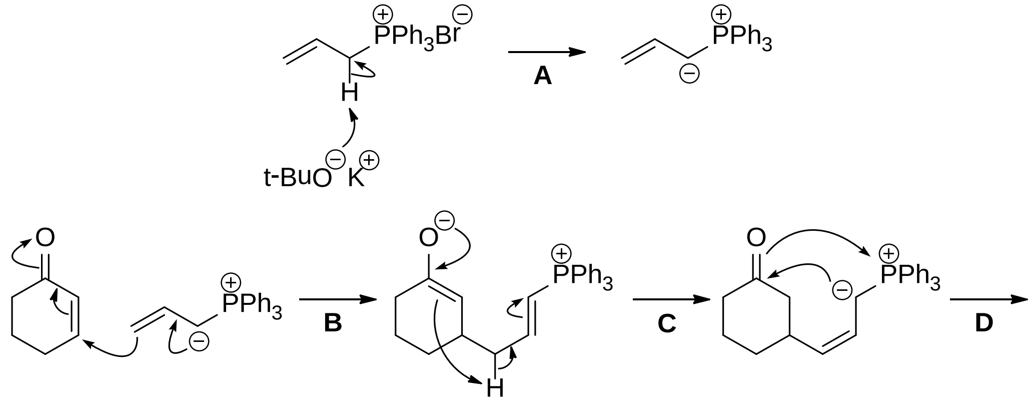
B122

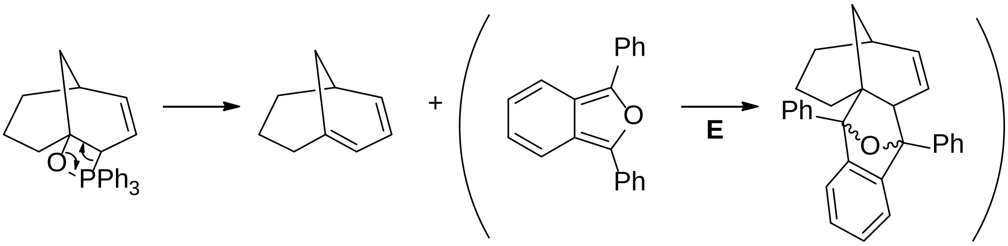


Fischer, N.; Opitz, G. *Org. Synth., Coll.* Vol. V **1973**, 877.

A: Generation of a sulfene. **B**: 1,3-Dipolar cycloaddition of diazomethane to the sulfene. **C**: Extrusion of N_2 to form an episulfone. **D**: Ramberg-Bäcklund reaction.

B123

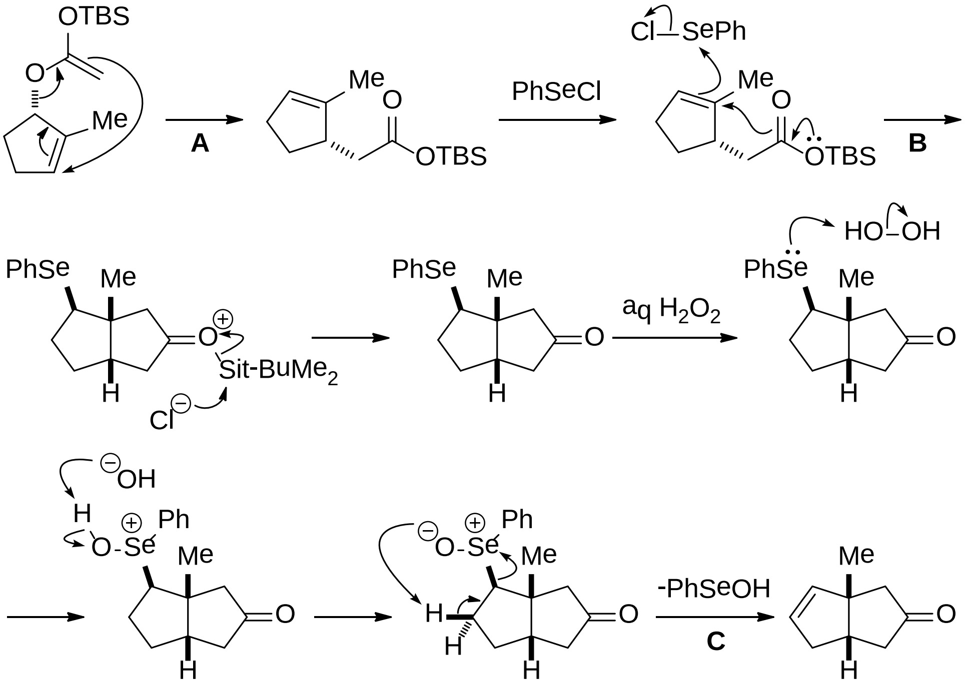




Dauben, W. G.; Ipaktschi, J. *J. Am. Chem. Soc.* **1973**, 95, 5088.

A: Generation of an ylide. **B**: Michael addition. **C**: Regeneration of a phosphorus ylide. **D**: Intramolecular Wittig reaction (irreversible). **E**: The unstable diene was trapped as the Diels-Alder product.

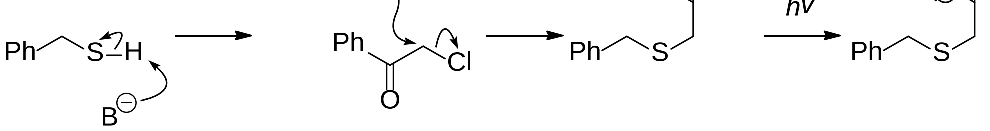
B124

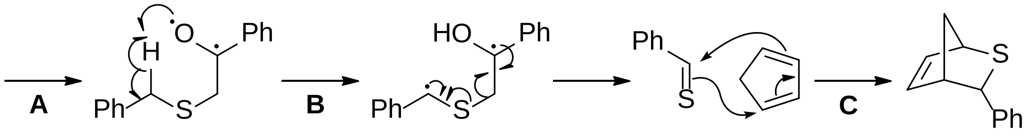


Curran, D. P.; Rakiewicz, D. M. *Tetrahedron* **1985**, 41, 3943,

A: Claisen-Ireland rearrangement. **B**: Selenolactonization. **C**: syn-Elimination of the selenoxide.

B125

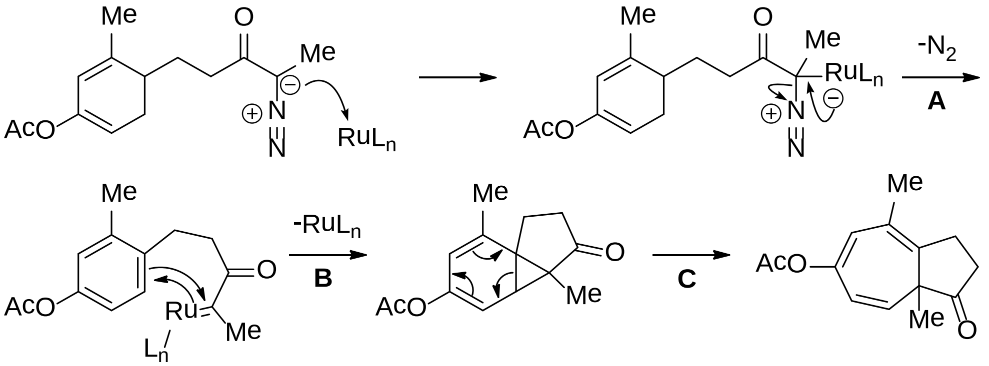




Vedejs, E.; Eberlein, T. H.; Mazur, D. J.; McClure, C. K.; Perry, D. A.; Ruggeri, R.; Schwartz, E.; Stults, J. S.; Varie, D. L.; Wilde, R. G.; Wittenberger, S. *J. Org. Chem*. **1986**, 51, 1556.

Norrish type II reaction. **A**: n-π* Transition. **B**: Intramolecular abstraction of a hydrogen atom followed by fragmentation to form a highly reactive thioaldehyde. **C**: Hetero-Diels-Alder reaction.

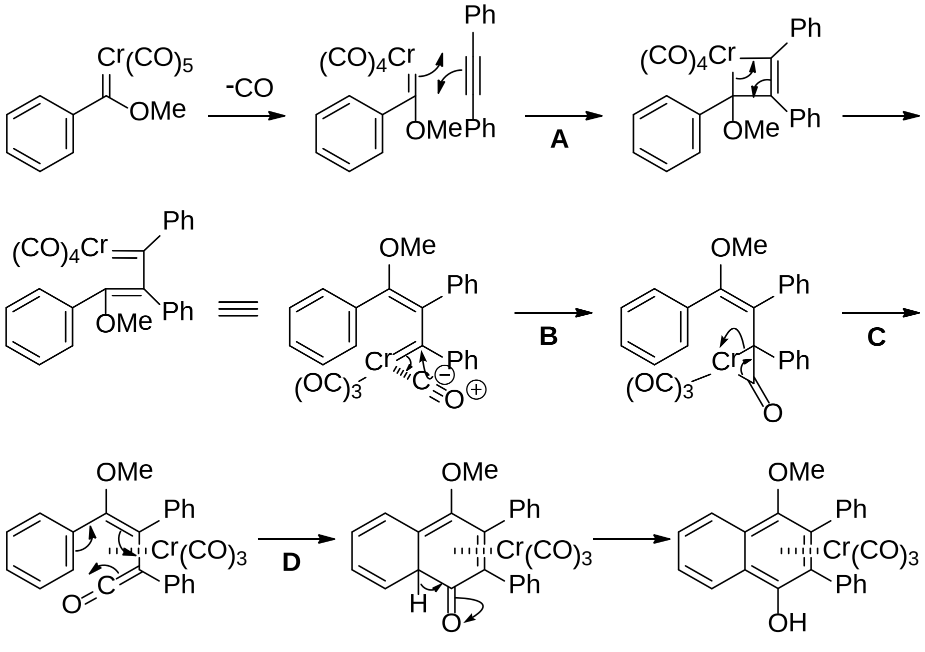
B126



Kennedy, M.; McKervey, M. A. *J. Chem. Soc., Perkin Trans.* I **1991**, 2565.

A: Formation of a rhodium carbene complex. **B**: Cyclopropanation of the aromatic ring. **C**: 6e Disrotatory electrocyclic reaction.

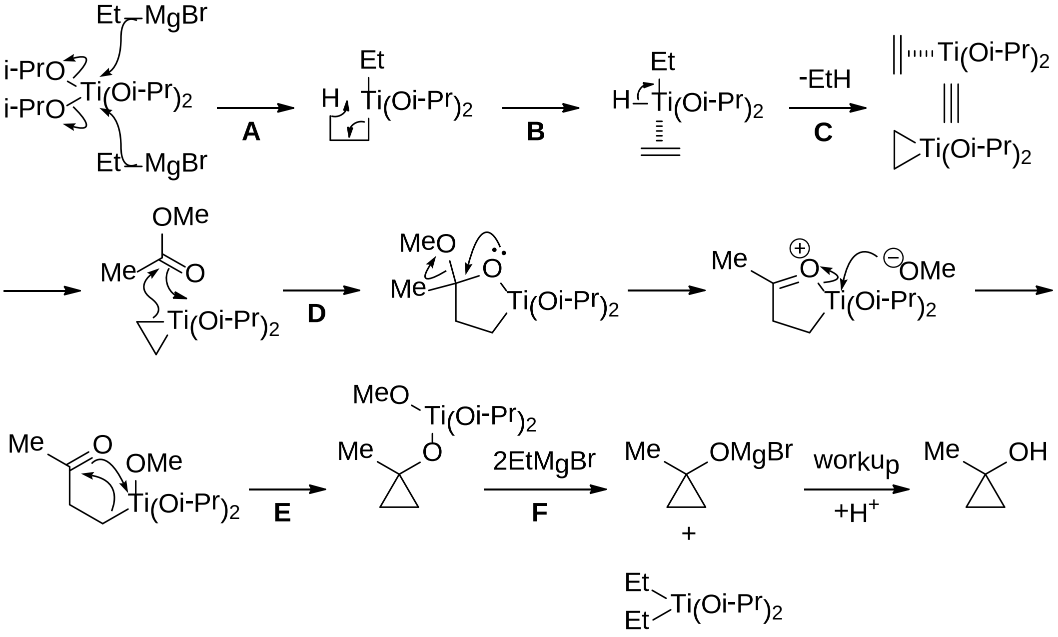
B127



Dötz, K. H. *Angew. Chem. Int. Ed. Engl.* **1975**, 14, 644.

Dötz reaction. **A**: Alkyne metathesis of Fischer carbene complex. **B**: Insertion of CO. **C**: Reductive elimination to form a ketene. **D**: 6e Electrocyclic reaction.

B128

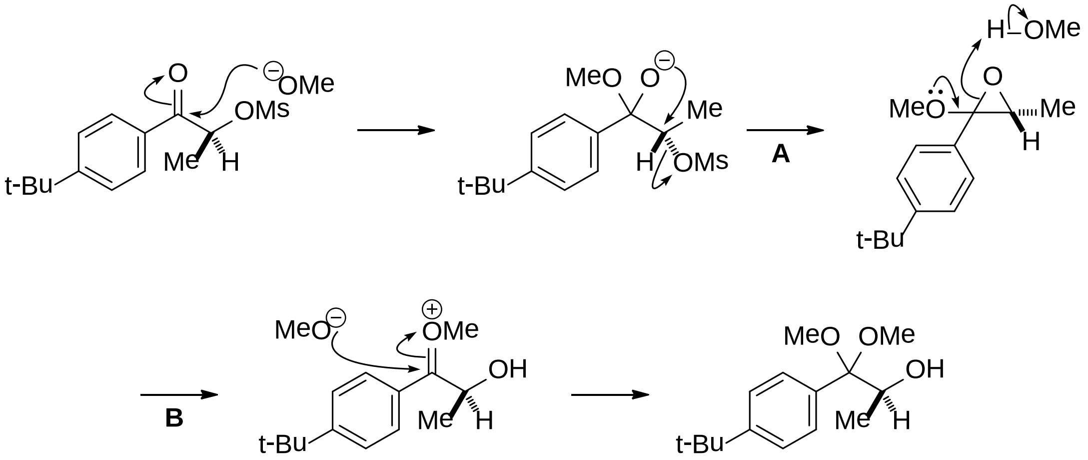


Kulinkovich, O. G.; Sviridov, S. V.; Vasilevski, D. A. *Synthesis* **1991**, 234.

Kulinkovich reaction. **A**: Substitution of the isopropoxide with EtMgBr. **B**: β-Elimination. **C**: Reductive elimination to form a titanium ethylene complex (or a titanocyclopropane). **D**: Carbotitanation. **E**.: Formation of a cyclopropane. **F**: Regeneration of the active reagent.

解答 上级編

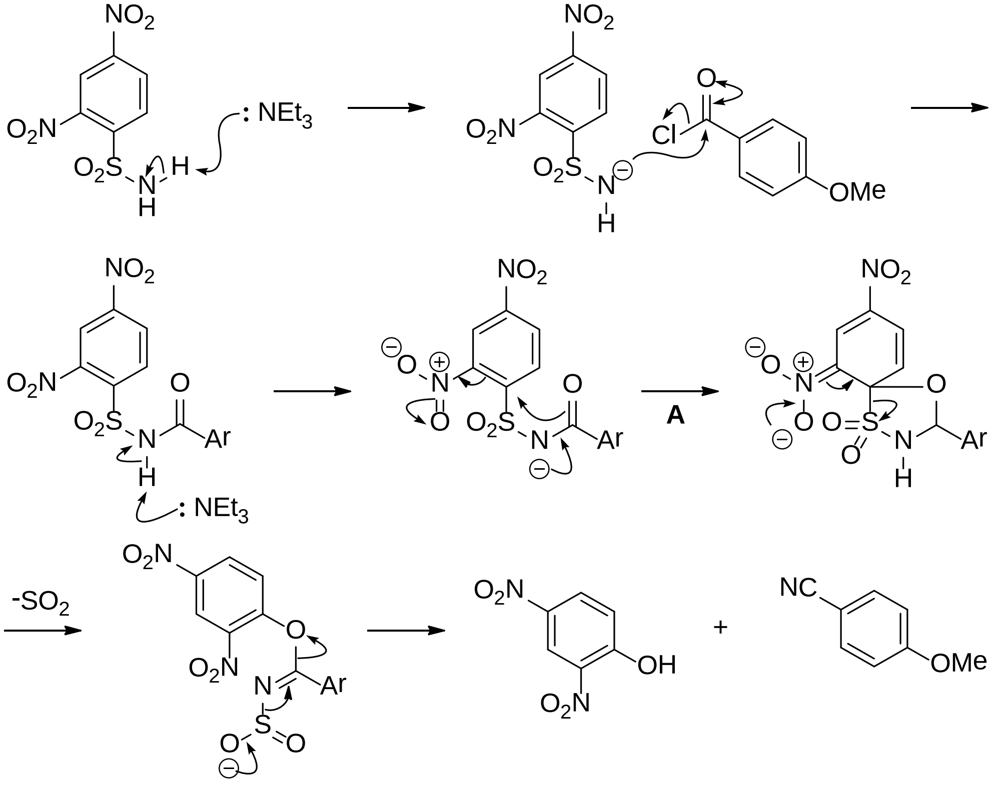
C001



Yamauchi, T.; Hattori, K.; Nakao, K.; Tamaki, K. *Bull. Chem. Soc. Jpn*. **1987**, 60, 4015.

A: Formation of an epoxide by intramolecular S_N2 reaction of a hemiacetal.   **B**: E1-like cleavage of the reactive epoxide.

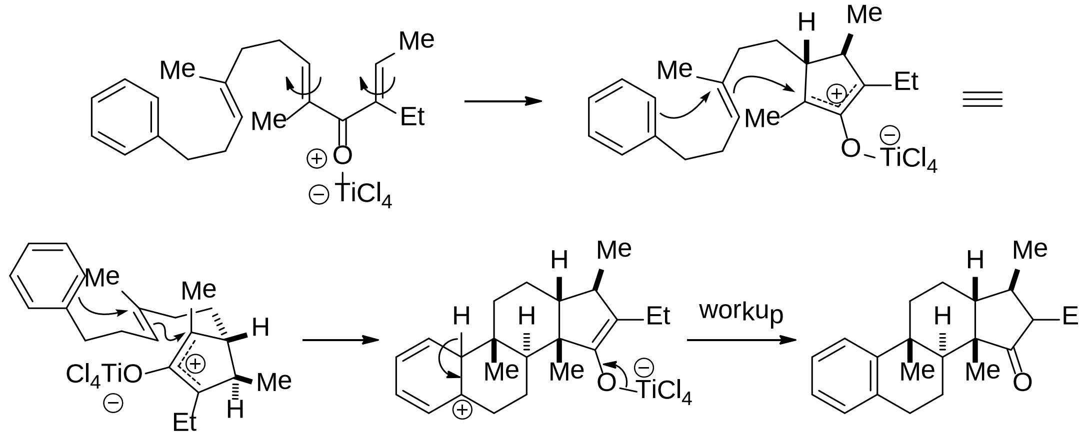
C002



Huber, V. J.; Bartsch, R. A. *Tetrahedron* **1998**, 54, 9281.

Smiles rearrangement.   **A**: Addition-elimination process via a Meisenheimer complex.

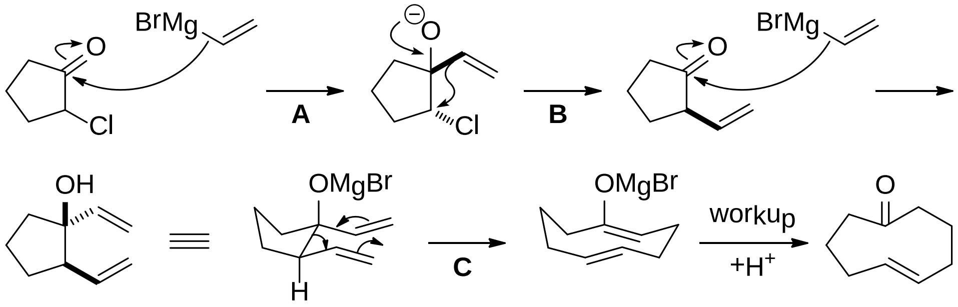
C003



Bender, J. A.; Arif, A. M.; West, E G. *J. Am. Chem. Soc.* **1999**, 121, 7443.

Cation-olefin cyclization initiated by Nazarov reaction (ref B026).

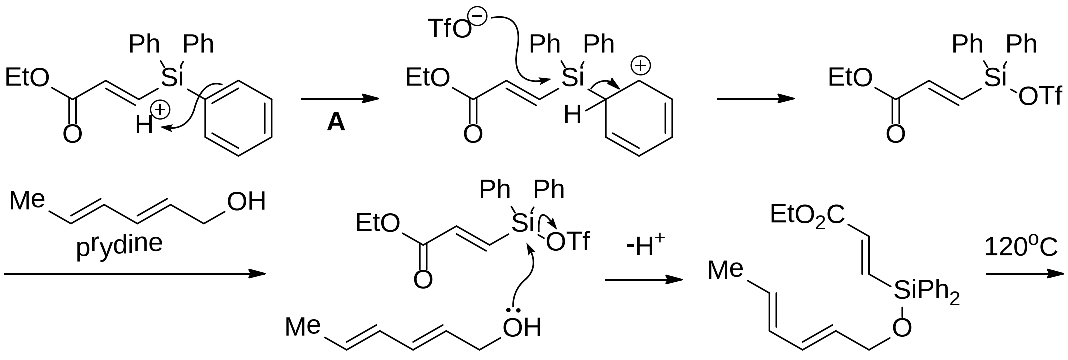
C004

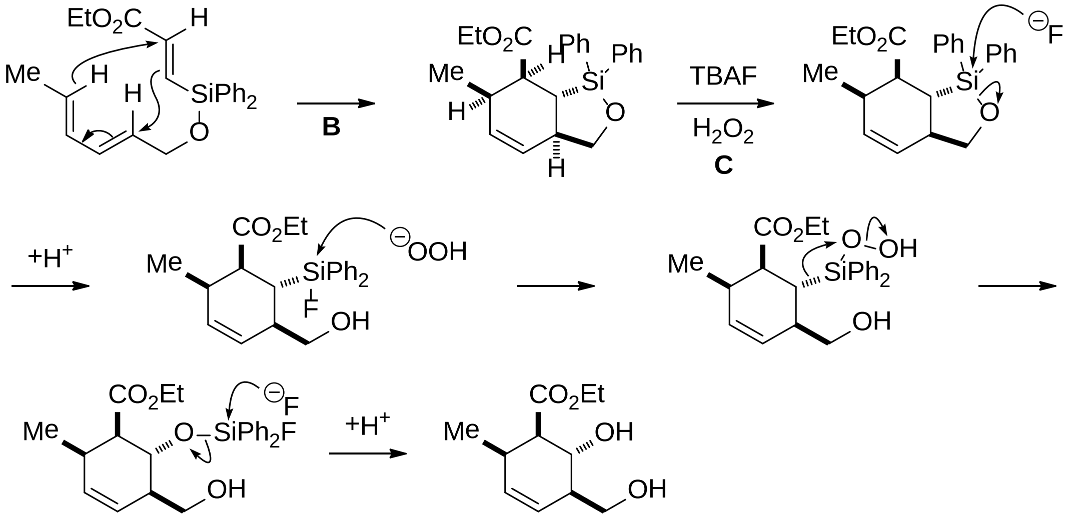


Kato, T.; Kondo, H. ; Nishino, M.; Tanaka, M.; Hata, G.; Miyake, A.
Bull. Chem. Soc. Jpn. **1980**, 53, 2958.

A: Addition of CH2=CHMgBr to the ketone from the opposite side of the α-substituent. **B**: 1,2-Alkenyl shift. **C**: Anion-accelerated oxy-Cope rearrangement via a chair-like transition state.

C005

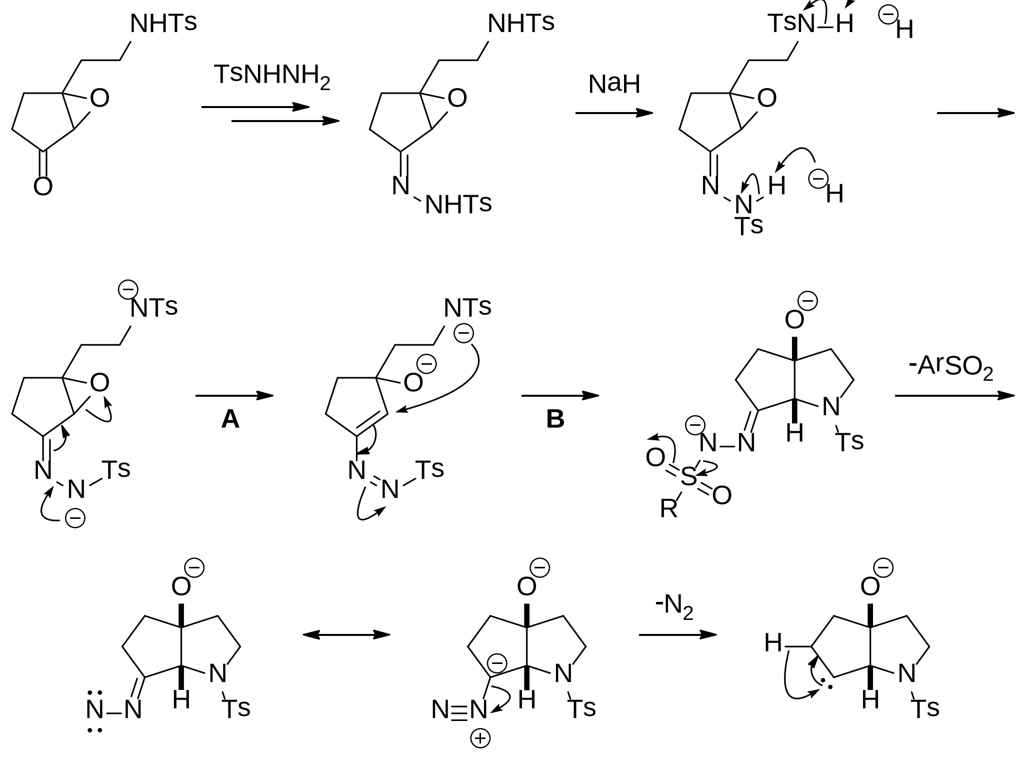


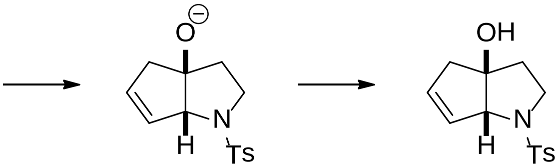


Sieburth, S. M.; Lang, J. *J. Org. Chem.* **1999**, 64, 1780.

A: Protodesilylation to form a silyl triflate. **B**: Intramolecular Diels-Alder reaction. **C**: Tamao-Fleming oxidation.

C006

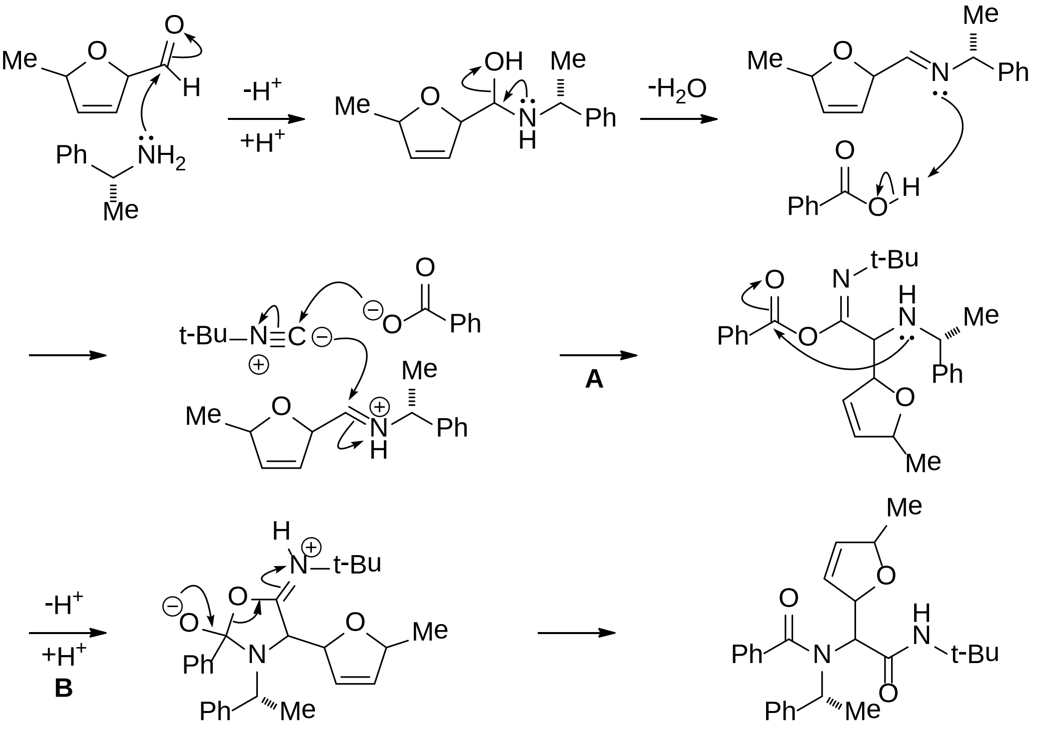




Kim, S. H.; Fuchs, P. L. *Tetrahedron Lett.* **1996**, 37, 2545.

A: Cleavage of the epoxide helped by the hydrazone anion. **B**: Conjugate addition of the sulfonamide anion.

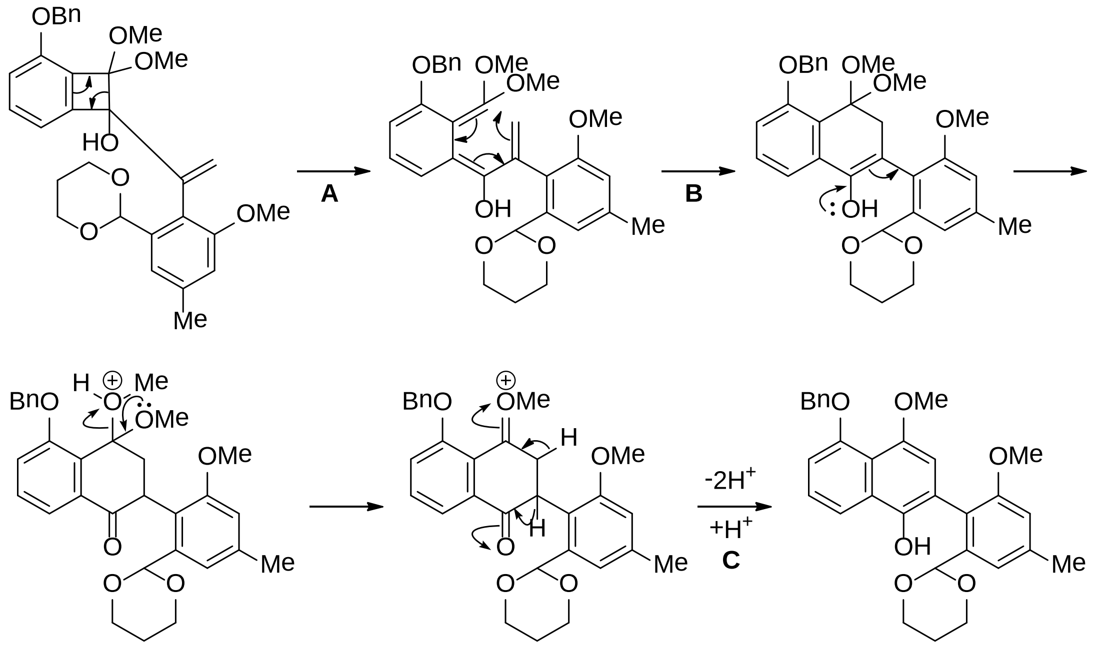
C007



Semple, J. E.; Wang, P. C.; Lysenko, Z.; Joullie, M. M.
J. Am. Chem. Soc. **1980**, 102, 7505.

Ugi reaction (four-component condensation, 4CC). **A**: Most likely, addition of the isocyanide to the iminium ion and addition of the benzoate ion to the ensuing nitrilium ion takes place simultaneously. **B**: Intramolecular acyl transfer reaction (the benzoyl group is activated).

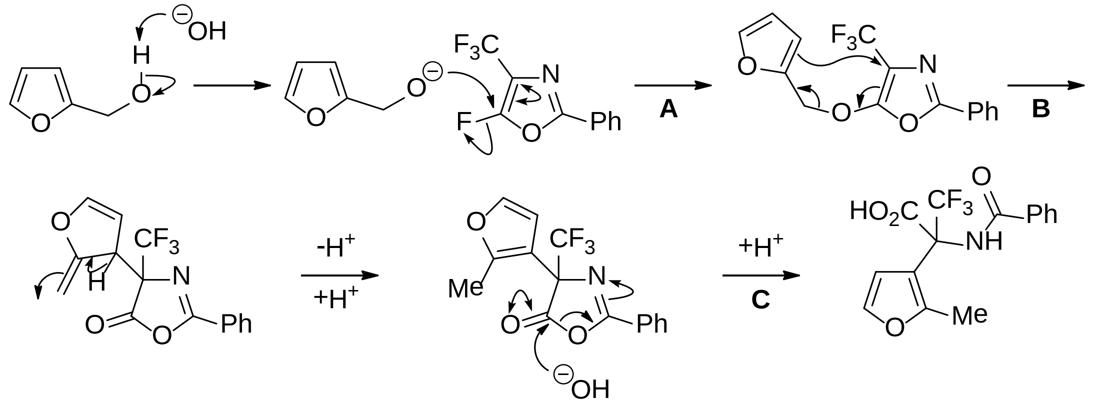
C008



Takemura, I.; Imura, K.; Matsumoto, T.; Suzuki, K. *Org. Lett.* **2004**, 6, 2503.

A: 4e Electrocyclic reaction. **B**: 6e Electrocyclic reaction. **C**: Aromatization.

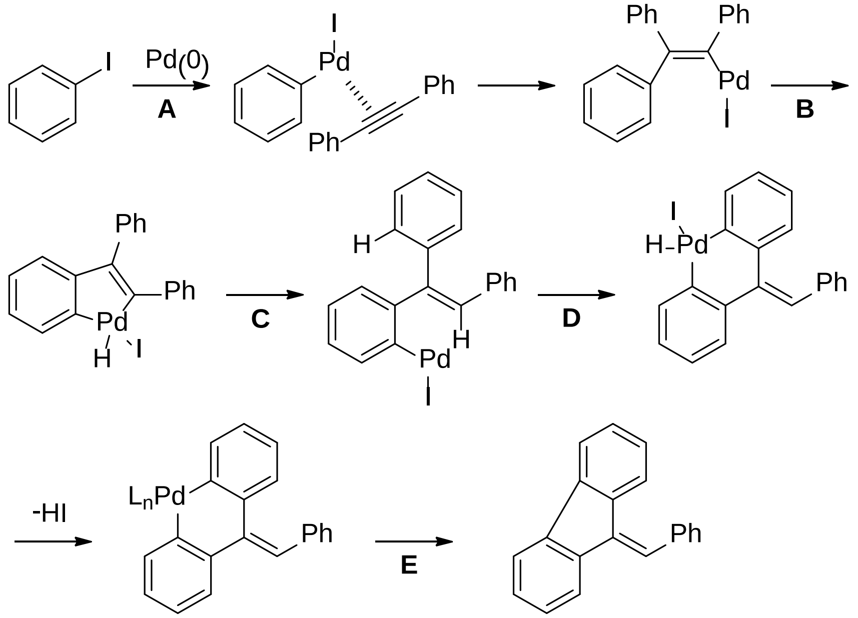
C009



Burger, K.; Gaa, K.; Geith, K.; Schierlinger, C. *Synthesis* **1989**, 850.

A: ipso-Substitution of the electron-deficient oxazole. **B**: Claisen rearrangement. **C**: Hydrolysis of the azlactone.

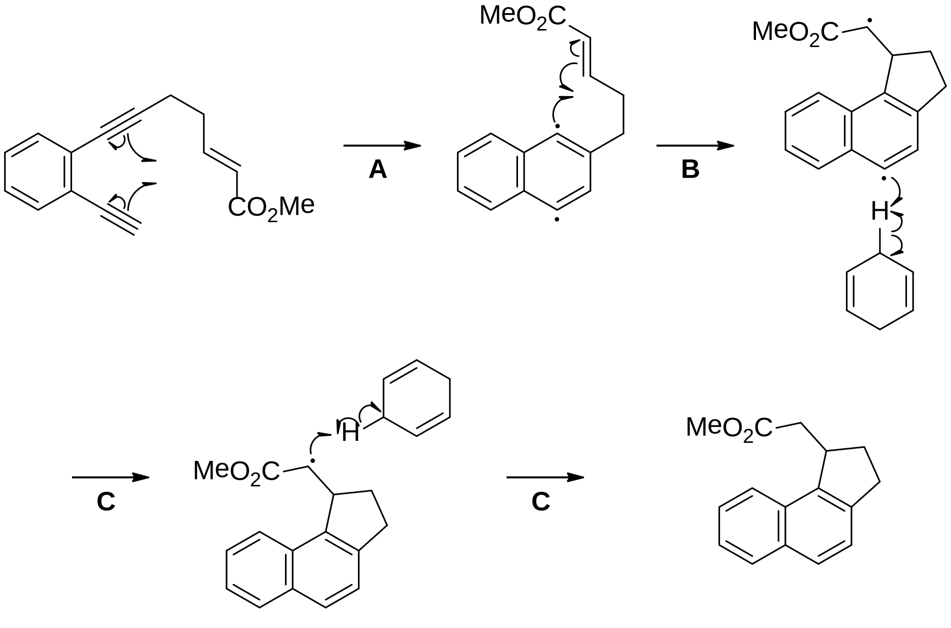
C010



Larock, R. C.; Tian, Q. *J. Org. Chem.* **2001**, 66, 7372.

A: Oxidative addition followed by carbopalladation to an alkyne. **B**: Oxidative addition to the aromatic C-H bond. **C**: Reductive elimination. **D**: Oxidative addition to another aromatic C-H bond. **E**: Reductive elimination to form the C-C bond.

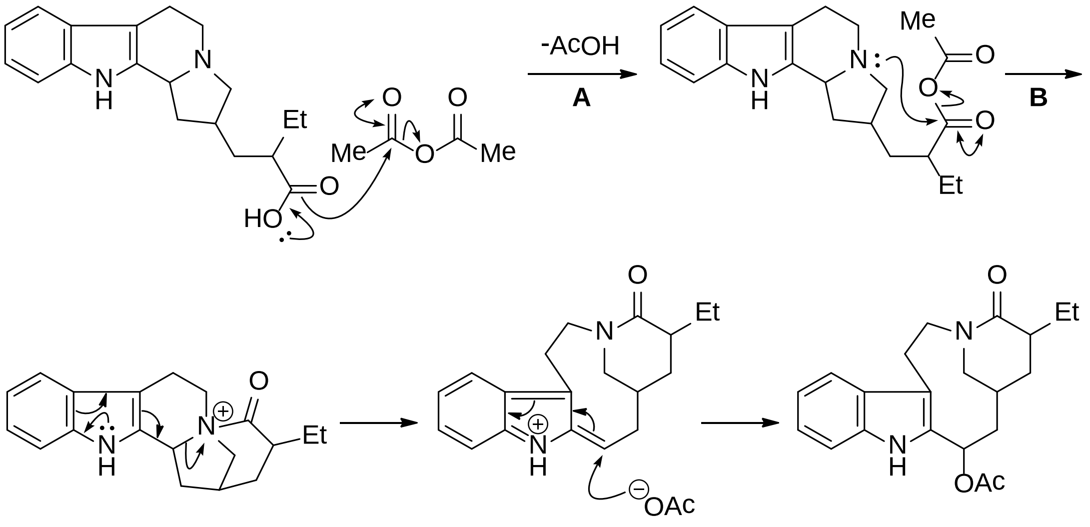
C011



Grissom, J. W.; Calkins, T. L.; Egan, M. *J. Am. Chem. Soc.* **1993**, 115, 11744.

Masamune-Bergman cyclization. **A**: Radical cyclization of an endiyne. **B**: Kinetically favored 5-exo-trig radical cyclization. **C**: Abstraction of a hydrogen atom from 1,4-cyclohexadiene.

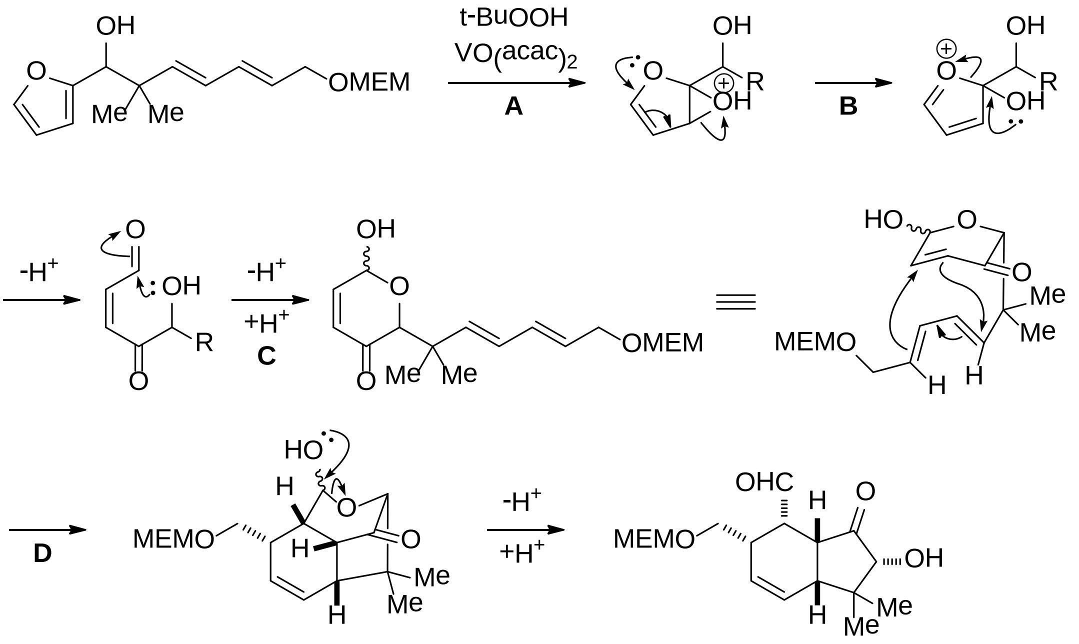
C012



Harley-Mason, J.; Atta-ur-Rahman *Tetrahedron* **1980**, 36, 1057.

A: Formation of a mixed anhydride. **B**: Acylation of the tertiary amine followed by cleavage of the C-N bond assisted by the nitrogen lone pair of the indole.

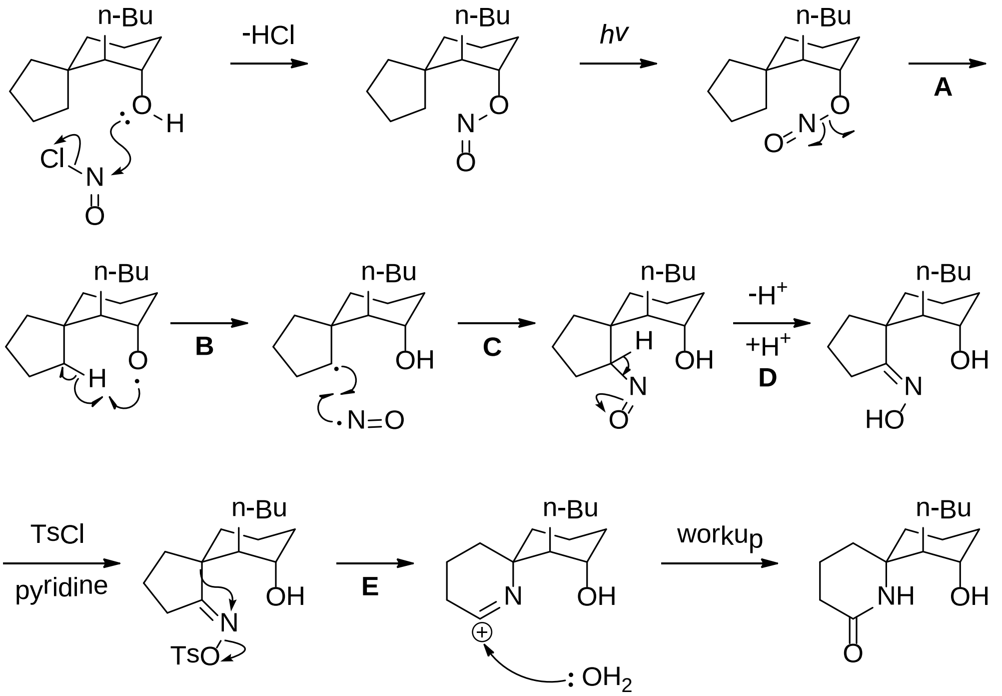
C013



Richter, E; Maichle-Mossmer, C.; Maier, M E. *Synlett*. **2002**, 1097.

Achmatowicz reaction (A-C). **A**: Epoxidation directed by the hydroxy group. **B**: Cleavage of theepoxide followed by the ring opening to form a cis-enal. **C**: Cyclization to form a lactol. **D**: Intramolecular Diels-Alder reaction.

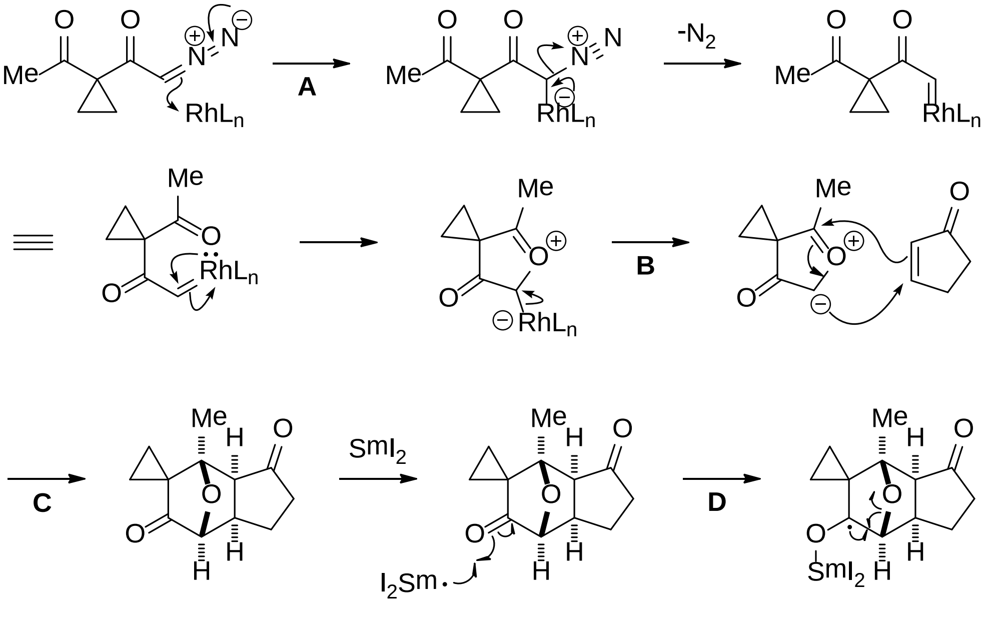
C014

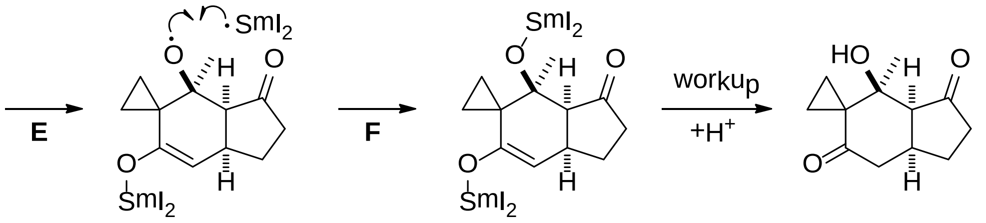


Corey, E. J.; Arnett, J. E; Widiger, G. N. *J. Am. Chem. Soc.* **1975**, 97, 430.

Barton reaction (A-D, ref 097). **A**: Photo-induced homolytic cleavage of the nitrite. **B**: Abstraction of a hydrogen atom via a six-membered transition state. **C**: Recombination of .NO with the resulting radical. **D**: Tautomerization to form an oxime. **E**: Beckmann rearrangement (ref A055).

C015

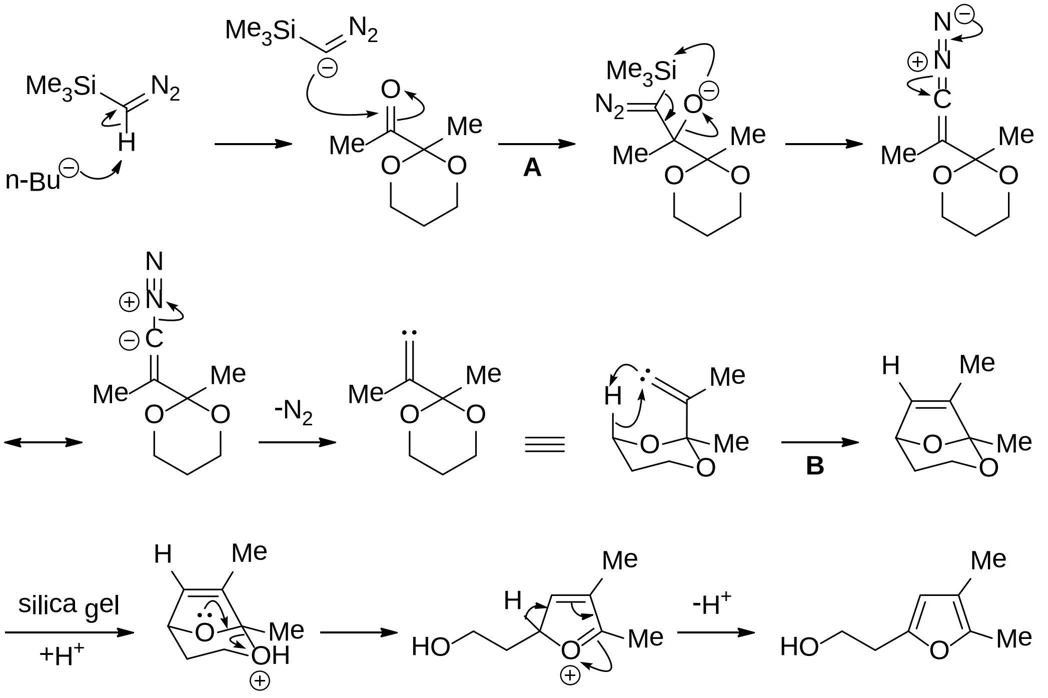




Padwa, A.; Sandanayaka, V. P.; Curtis, E. A.
J. Am. Chem. Soc. **1994**, 116, 2667.

A: Formation of a rhodium carbene complex. **B**: Formation of a carbonyl ylide. **C**: 1,3-Dipolar cycloaddition. **D**: SET to form a ketyl radical. **E**: Homolytic cleavage of the C-O bond. **F**: SET.

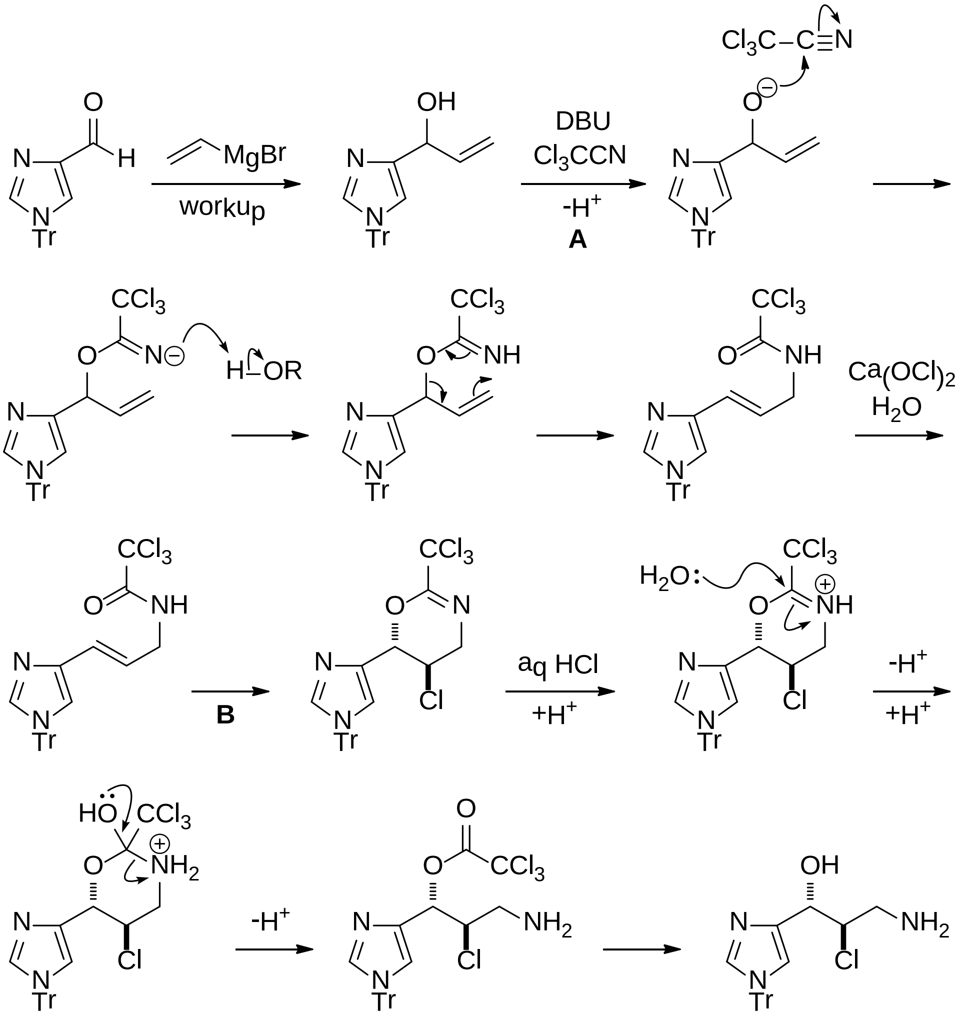
C016



Walker, L. F.; Connolly, S.; Wills, M.
Tetrahedron Lett., **1998**, 39, 5273.

A: Peterson olefination (ref A074) followed by elimination of N_2 to form an alkylidene carbene. **B**: C-H insertion.

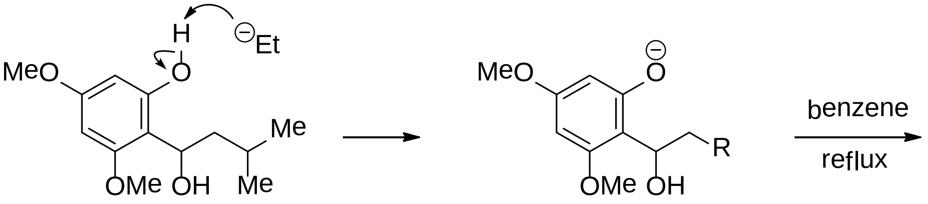
C017

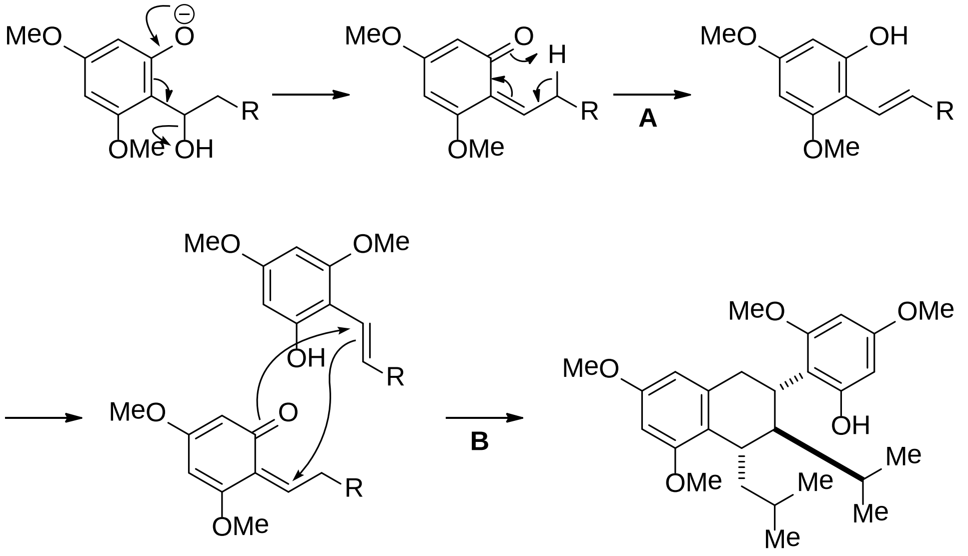


Commercon, A.; Ponsinet, G. *Tetrahedron Lett.* **1990**, 31, 3871.

A: Formation of a trichloroacetimidate followed by aza-Claisen rearrangement. **B**: While formation of five-membered rings is kinetically favored, activation by the imidazole ring directed the cyclization to form a six-membered ring.

C018

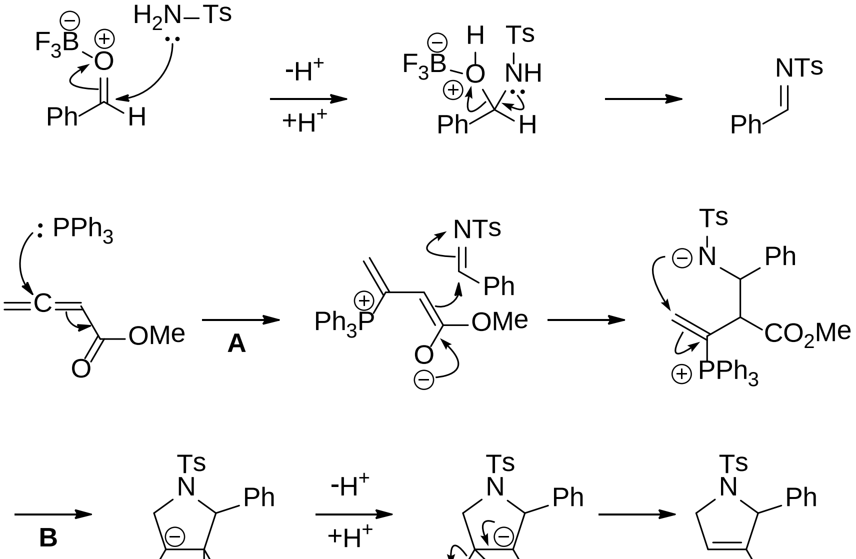




Tatsuta, K.; Tamura, T.; Mase, T. *Tetrahedron Lett.* **1999**, 40, 1925.

A: Restoration of the aromaticity. **B**: Hetero-Diels-Alder reaction.

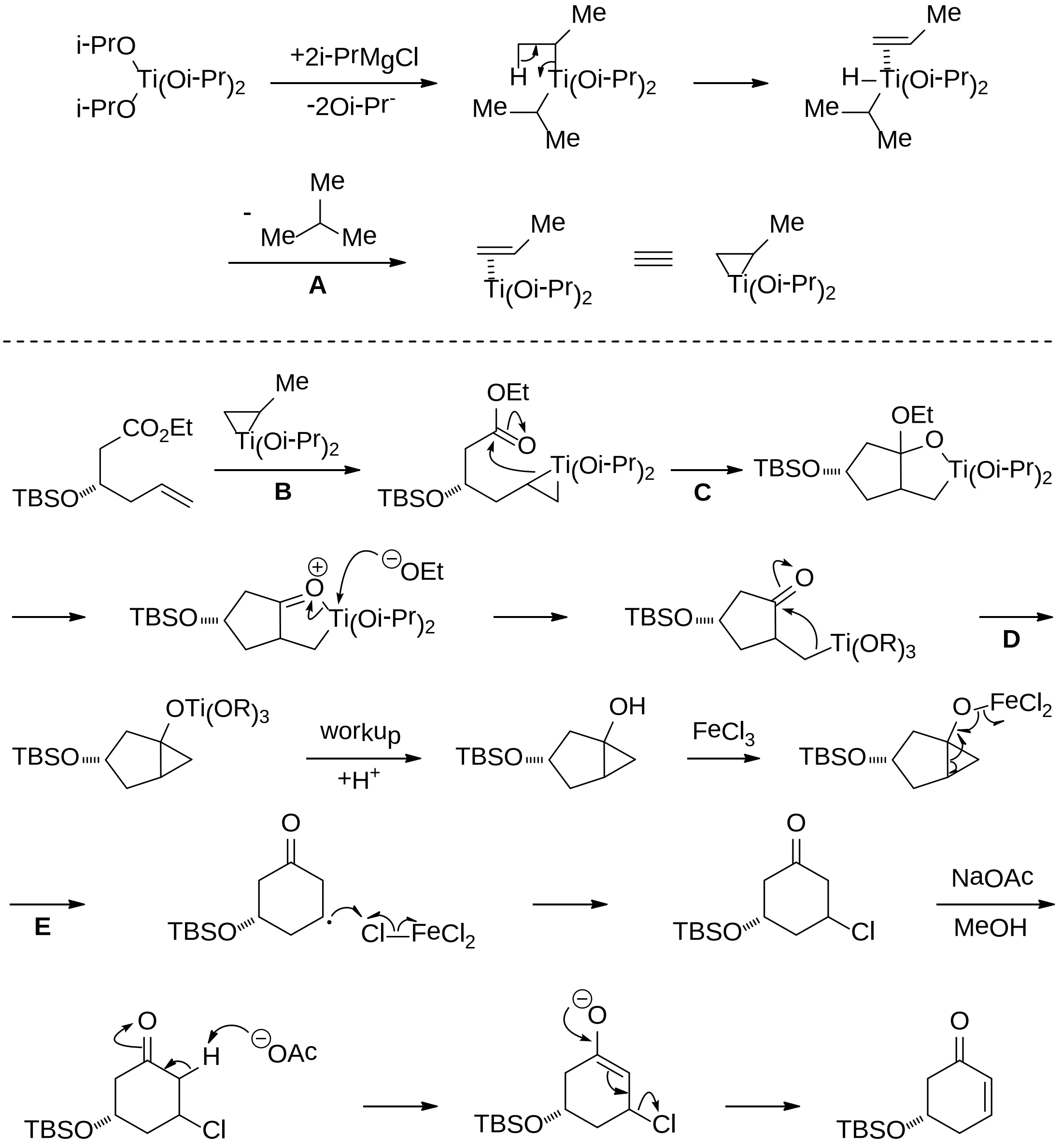
C019



Xu, Z.; Lu, X. *J. Org. Chem.* **1998**, 63, 5031.

A: Conjugate addition of Ph$_3$P to the allenyl ester to form an enolate. **B**: 5-endo-trig Cyclization to form an ylide. **C**: Proton transfer followed by elimination of Ph$_3$P.

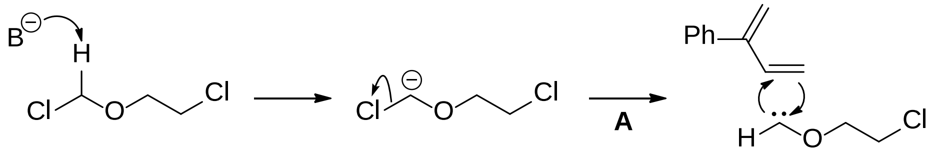
C020

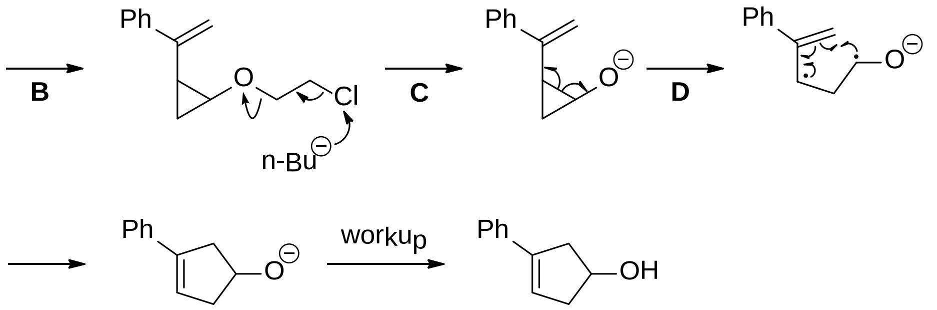


Hanazawa, T.; Okamoto, S.; Sato, F. *Tetrahedron Lett.* **2001**, 42, 5455.

A: Formation of a titanium-propylene complex or a titanacyclopropane derivative (ref B128). **B**: Olefin exchange. **C**: Intramolecular insertion of the carbonyl group to the titanium complex. **D**: Formation of a cyclopropane. **E**: Oxidative cleavage of the cyclopropane ring.

C021

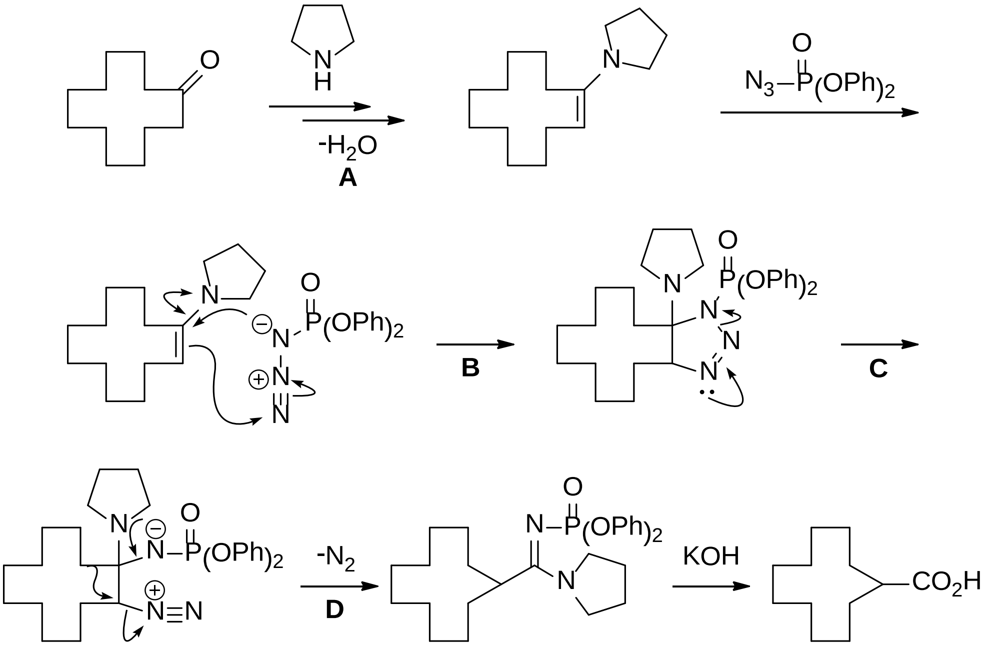




Danheiser, R. L.; Martinez-Davila, C.; Morin, J. M., Jr. *J. Org. Chem*. **1980**, 45, 1340.

A: α-Elimination to form a carbene. **B**: Cyclopropanation. **C**: β-Elimination to form a cyclopropanol anion. **D**: Anion-accelerated vinylcyclopropane rearrangement (homolytic cleavage followed by recombination of the diradical).

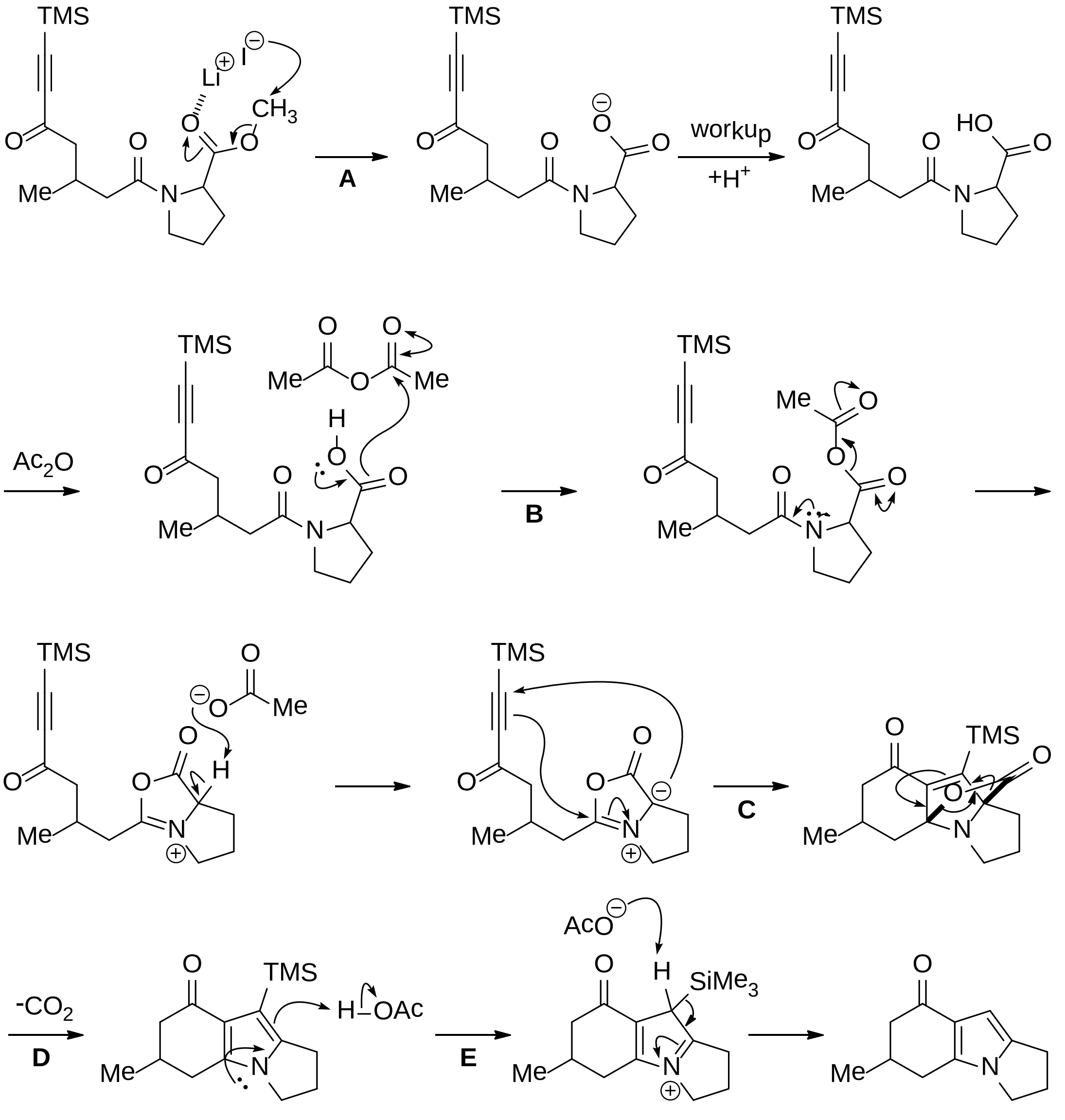
C022



Hamada, Y.; Shioiri, T. *Org. Synth., Coll*. Vol. Ⅶ **1990**, 207

A: Formation of an enamine. **B**: 1,3-Dipolar cycloaddition. **C**: Cleavage of the N-N bond. **D**: Tiffeneau-Demjanov-type ring contraction.

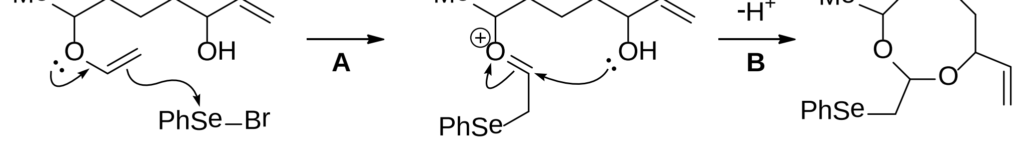
C023

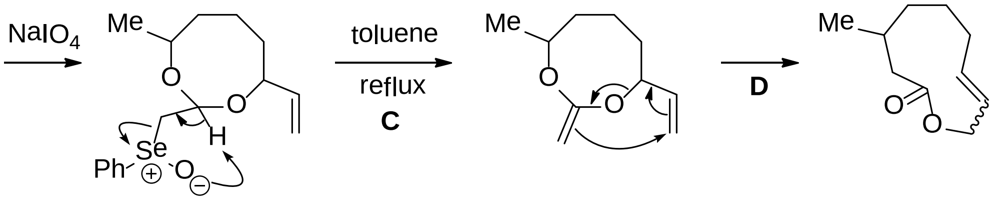


Nayyar, N. K.; Hutchison, D. R.; Martinelli, M. J. *J. Org. Chem.* **1997**, 62, 982.

A: Demethylation via an S$_N$2 process. **B**: Cyclization of the mixed anhydride followed by formation of a 1,3-dipole. **C**: Intramolecular 1,3-dipolar cycloaddition. **D**: Decarboxylation. **E**: Protodesilylation.

C024

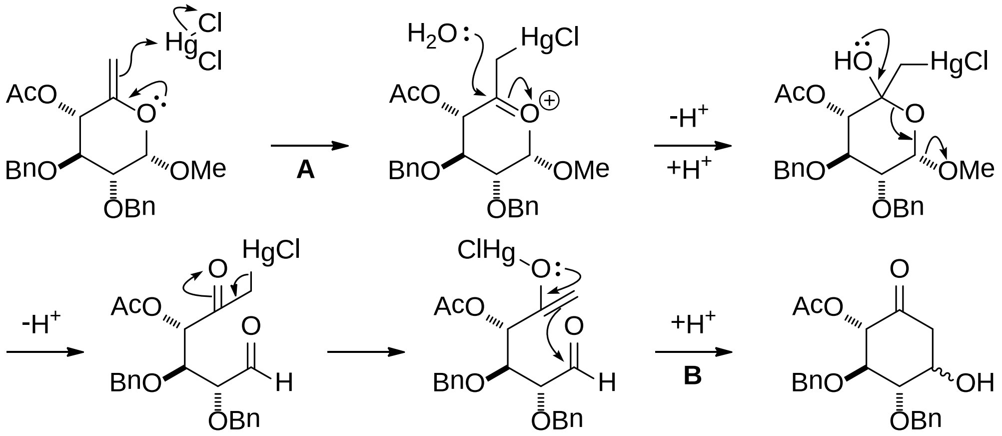




Petrzilka, M. Heir. *Chim. Acta* **1978**, 61, 3075.

A: Selenation of the electron-rich enol ether. **B**: Intramolecular acetal formation. **C**: β-Elimination of the selenoxide. **D**: Claisen rearrangement.

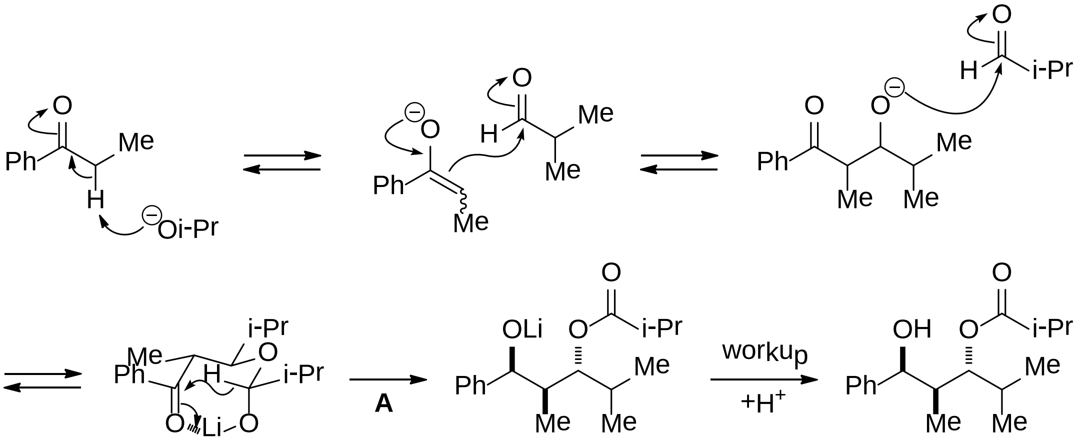
C025

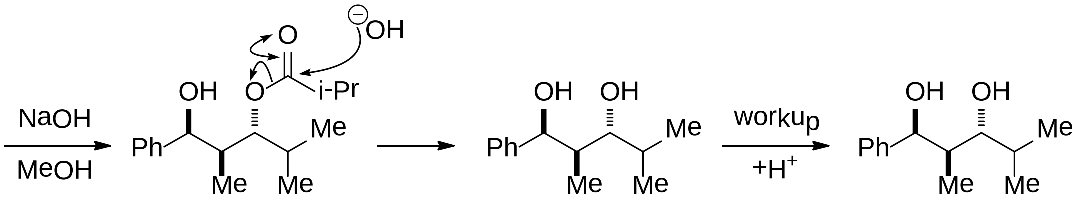


Chida, N.; Ohtsuka, M.; Nakazawa, K.; Ogawa, S.
J. Chem. Soc., Chem. Commun. **1989**, 436.

Ferrier rearrangement. **A**: Oxymercuration of enol ether. **B**: Intramolecular aldol reaction of the mercury enolate with the aldehyde.

C026

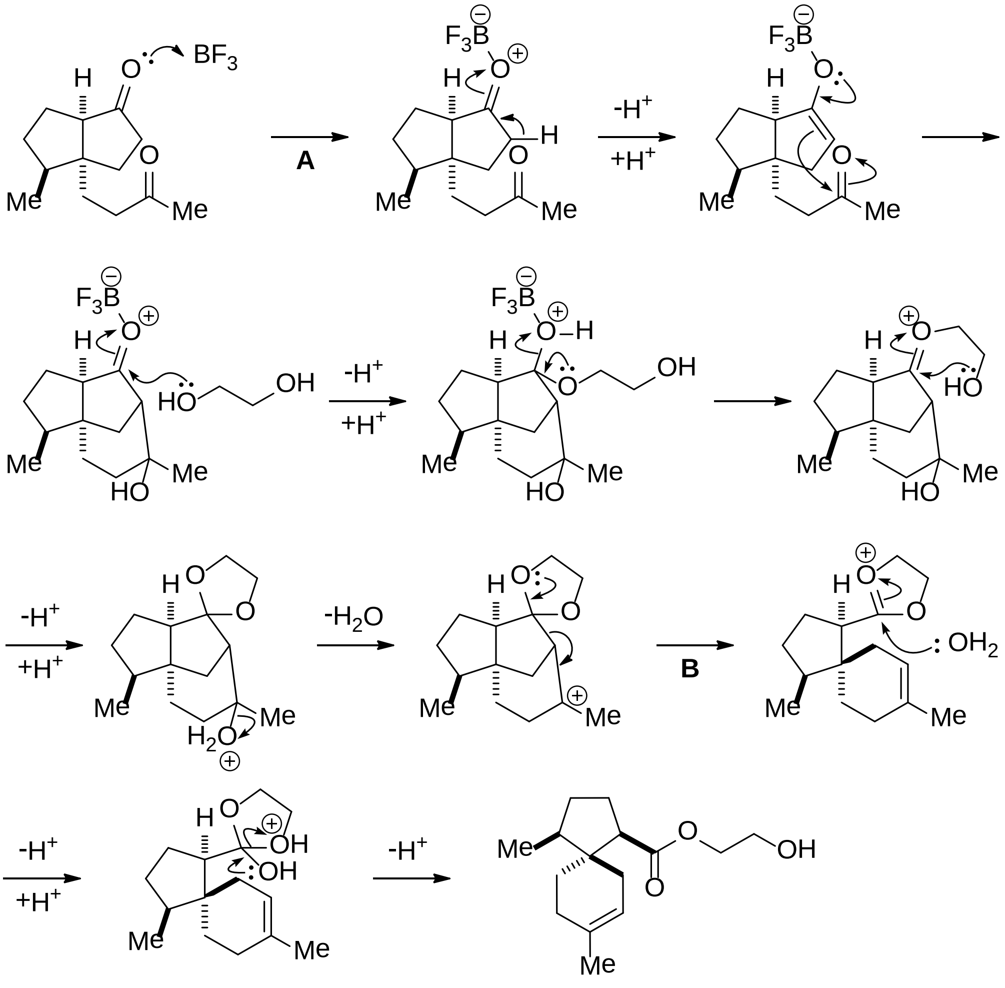




Mascarenhas, C. M.; Duffey, M. O.; Liu, S.-Y.; Morken, J. P. *Org. Lett*. **1999**, 1, 1427.

Tishchenko reaction. **A**: Intramolecular hydride transfer (Cannizzaro-type reaction) through a chair-like transition state.

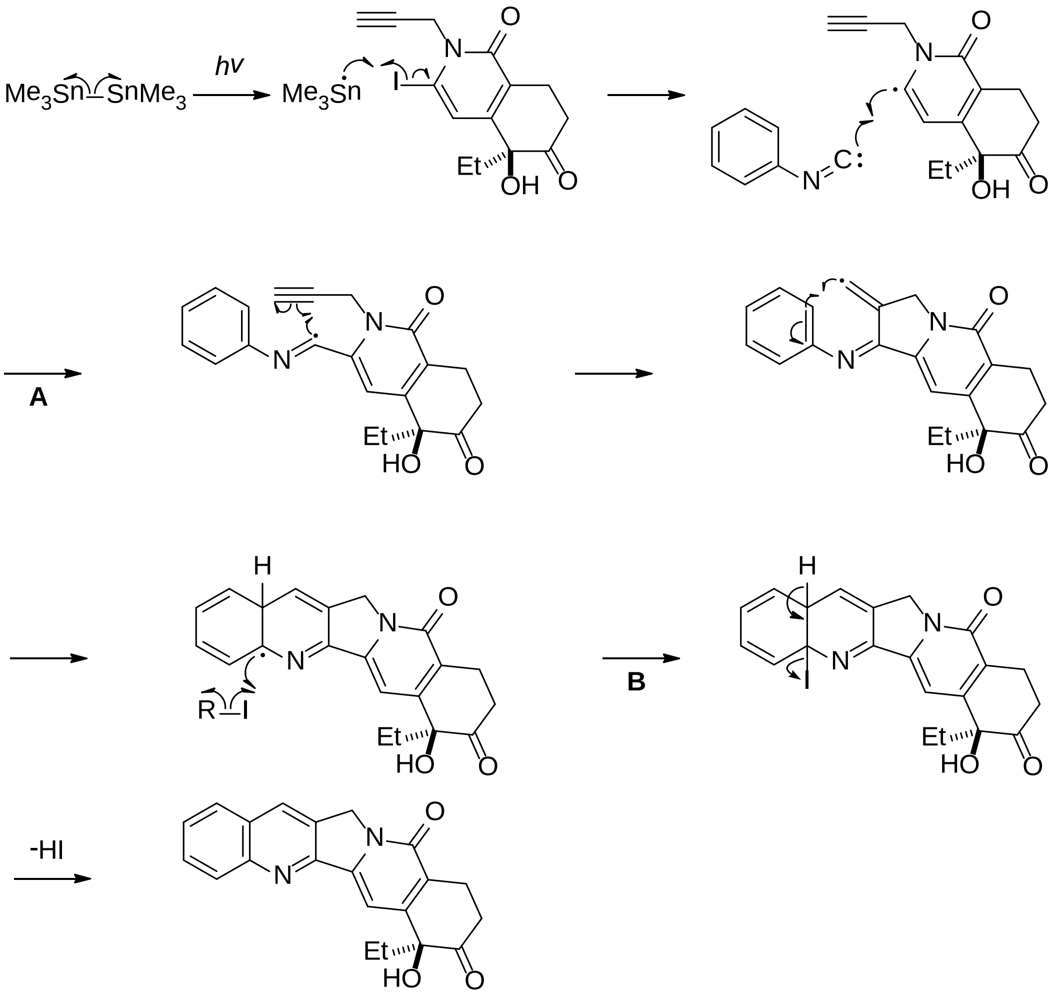
C027



Nagumo, S.; Suemune, H.; Sakai, K. *J. Chem. Soc., Chem. Commun*. **1990**, 1778.

A: Intramolecular acid-catalyzed aldol reaction. **B**: Grob-type fragmentation.

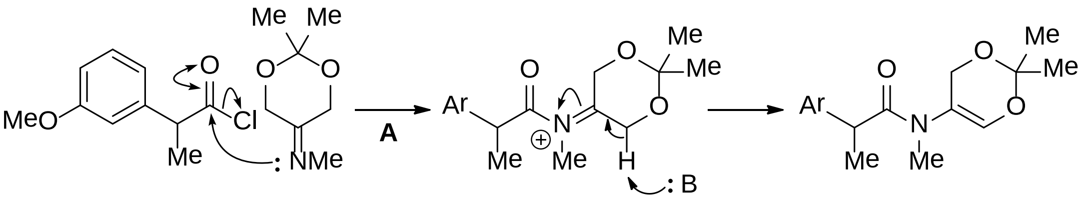
C028

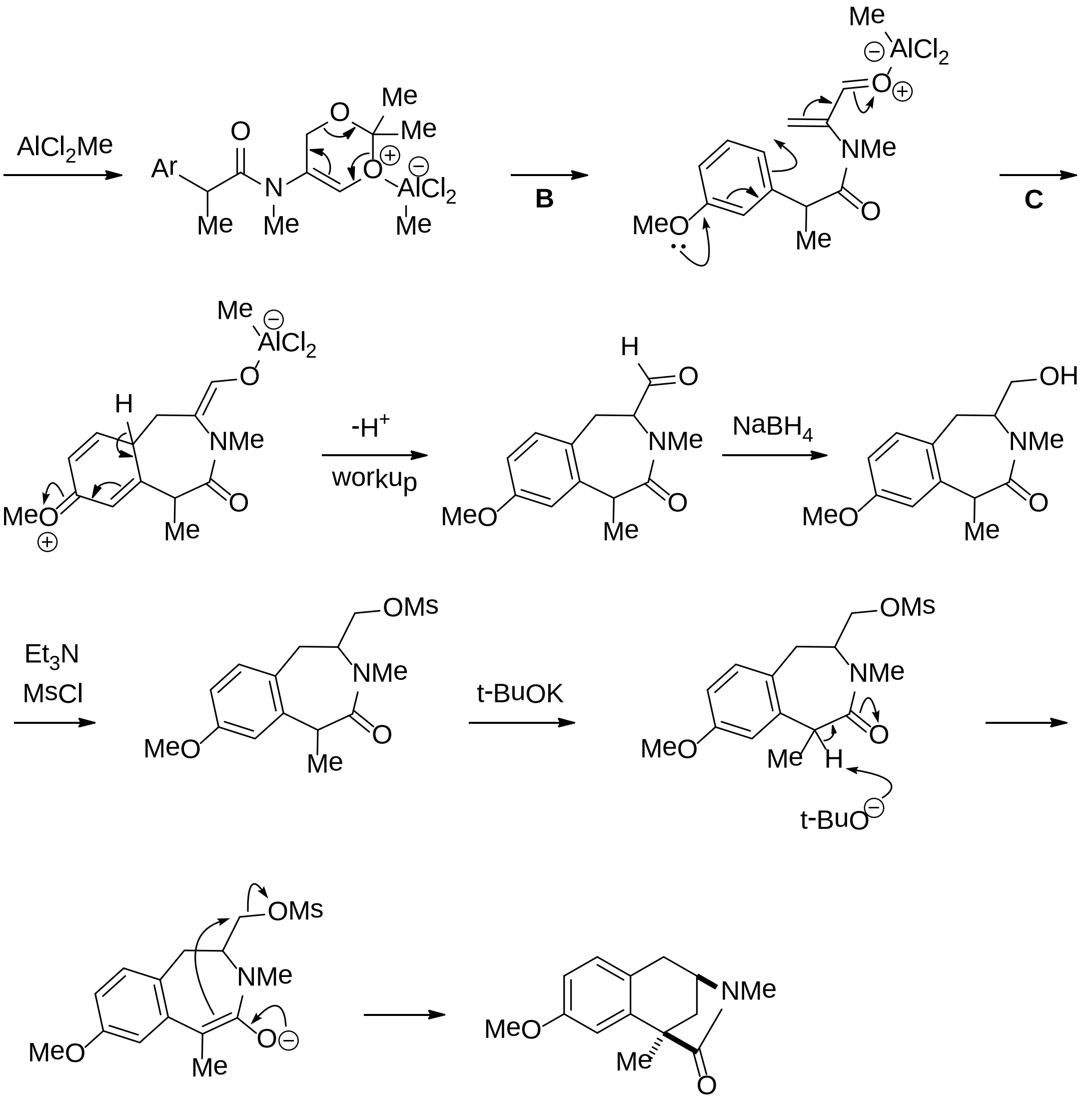


Curran, D. P.; Ko, S.-B.; Josien, H. *Angew. Chem. Int. Ed.* **1995**, 34, 2683.

A: Radical addition of an isocyanide to form an imidoyl radical. **B**: Atom transfer reaction.

C029

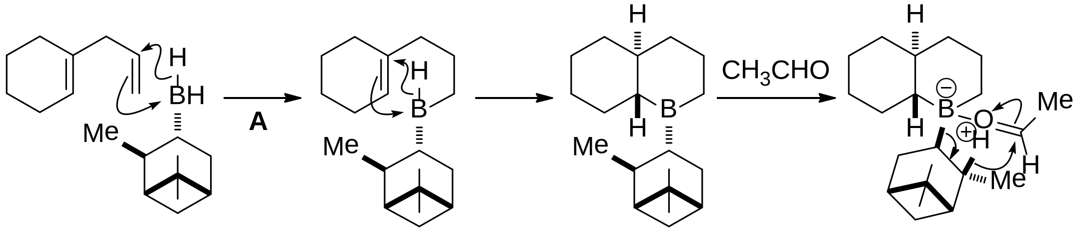


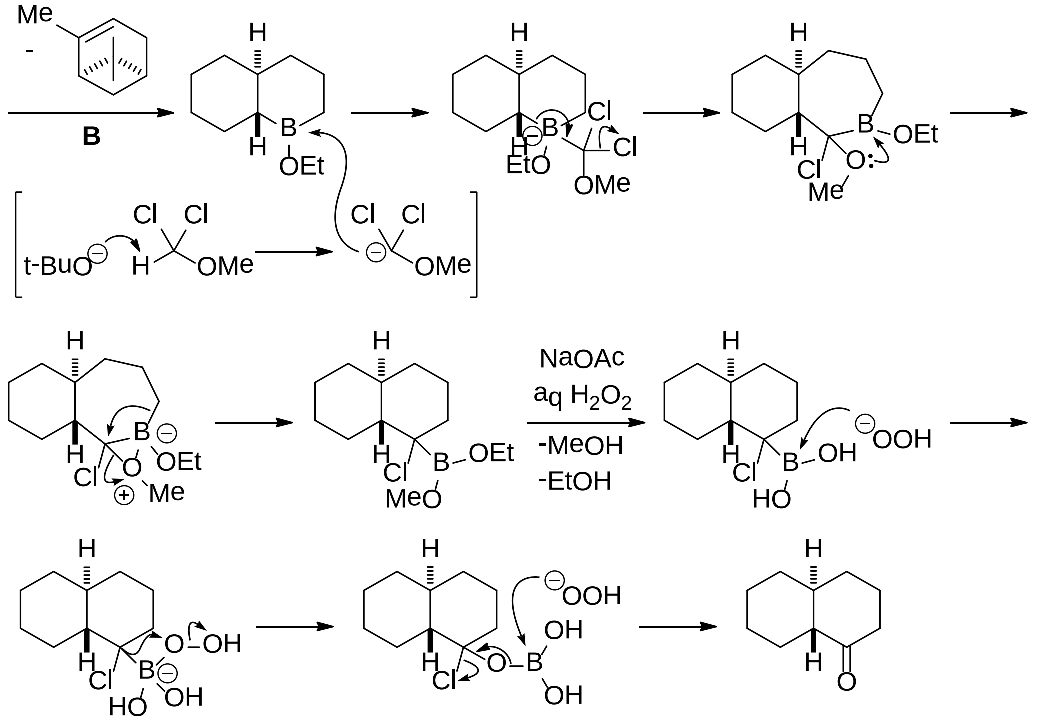


Fuchs, J. R.; Funk, R. L. *Org. Lett.*, **2001**, 3, 3923.

A: Acylation of the imine to form an enamide. **B**: Retro cycloaddition to form an (α-amidoacrolein. **C**: Intramolecular conjugate addition of the electron-rich aromatic ring to the amidoacrolein.

C030

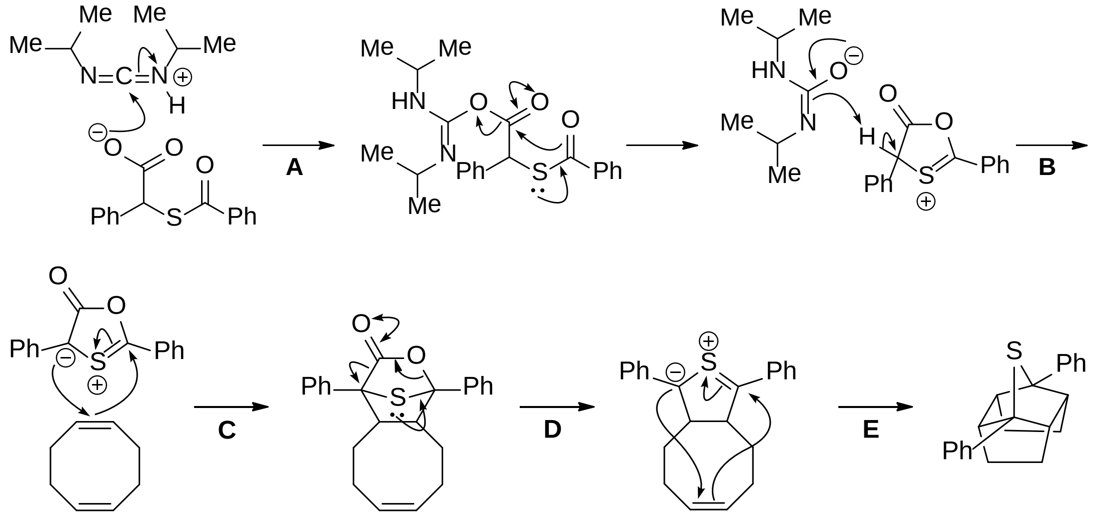




Brown, H. C.; Mahindroo, V. K.; Dhokte, U. P. *J. Org. Chem.* **1996**, 61, 1906.

A: Sequential hydroboration to form a trialkylborane. **B**: Hydride transfer via a six-membered transition state. See Meerwein-Ponndorf-Verley reduction (ref B002).

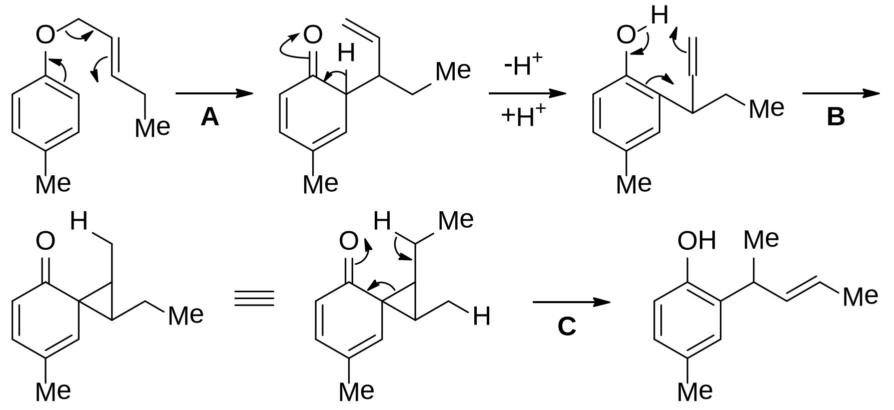
C031



Sponholtz III, W. R.; Trujillo, H. A.; Gribble, G. W. *Tetrahedron Lett.* **2000**, 41, 1687.

A: Activation of the carboxyl group as an O-acylisourea. **B**: Generation of a 1,3-dipole. **C**: 1,3-Dipolar cycloaddition. **D**: Decarboxylation to form a 1,3-dipole. **E**: Intramolecular 1,3-dipolar cycloaddition.

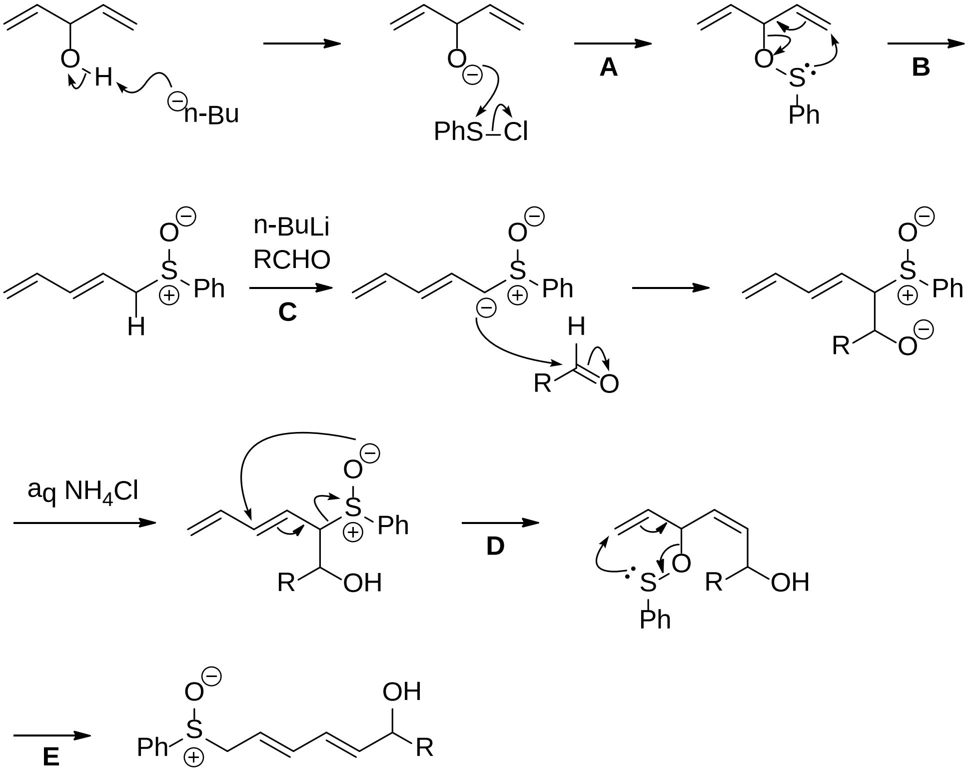
C032



Fukuyama, T.; Li, T.; Peng, G. *Tetrahedron Lett.* **1994**, 35, 2145.

Abnormal Claisen rearrangement. **A**: Claisen rearrangement followed by tautomerization. **B**: Intramolecular oxy-ene reaction to form a cyclopropane. **C**: Retro oxy-ene reaction.

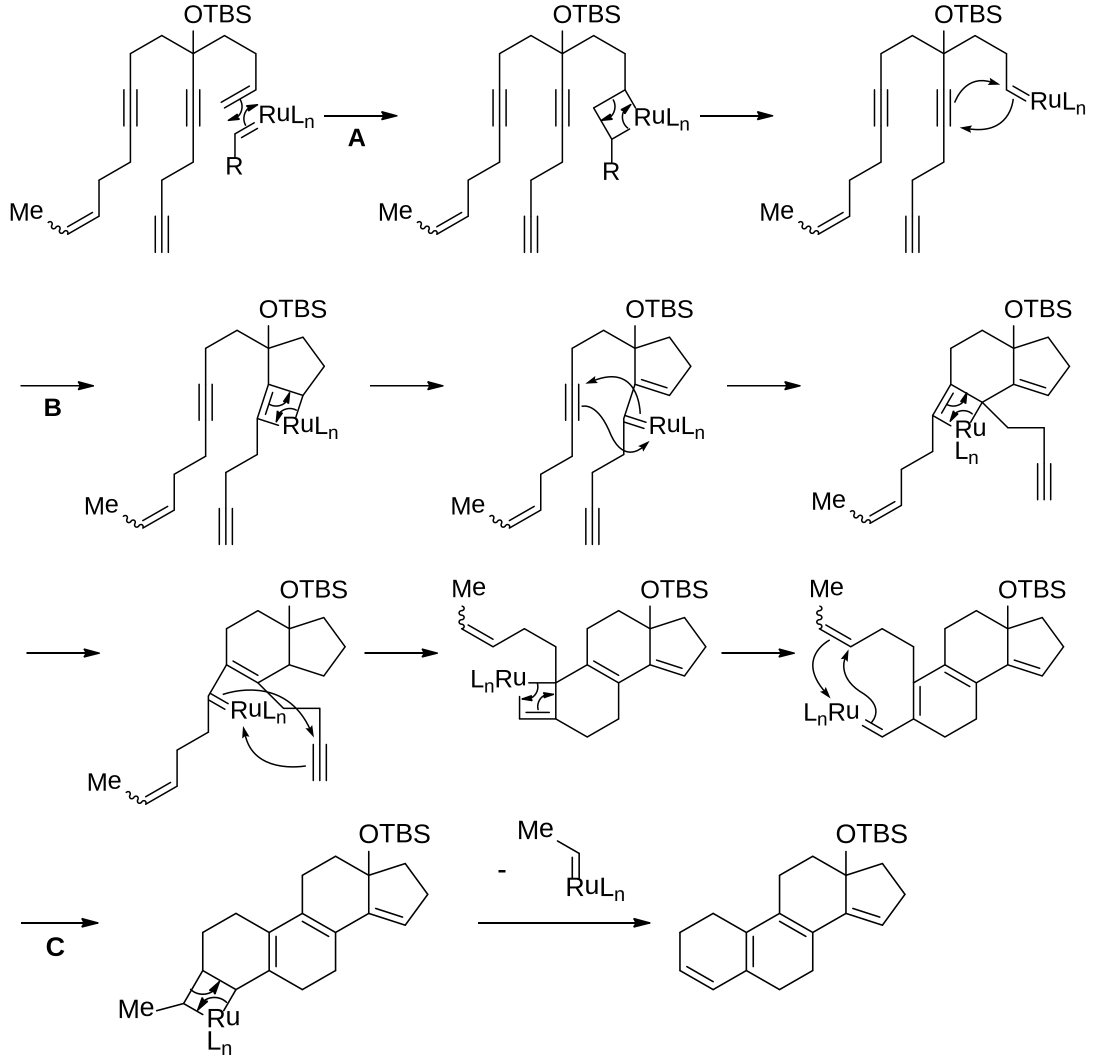
C033



Schreiber, S. L.; Satake, K. *J. Am. Chem. Soc.* **1984**, 106, 4186.

A: Formation of a sulfenate. **B**: [2,3] Sigmatropic rearrangement. **C**: Deprotonation followed by addition to the aldehyde (pKa DMSO = 35). **D**: [2,3] Sigmatropic rearrangement of the sulfoxide. **E**: [2,3] sigmatropic rearrangement of the sulfenate.

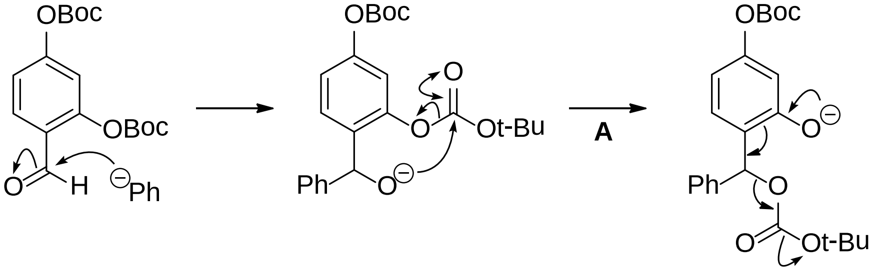
C034

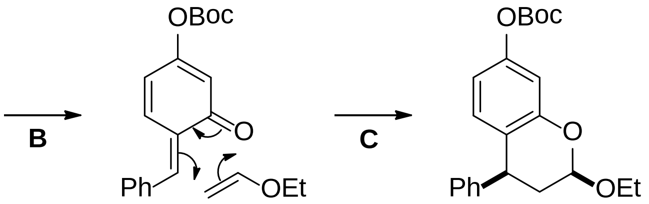


Zuercher, W. J.; Scholl, M.; Grubbs, R. H. *J. Org. Chem.* **1998**, 63, 4291.

Domino intramolecular enyne metathesis. **A**: Alkene metathesis at the terminal olefin. **B**: Sequential intramolecular alkyne metathesis to form a kinetically favored, six-membered intermediates. **C**: Intramolecular alkene metathesis.

C035



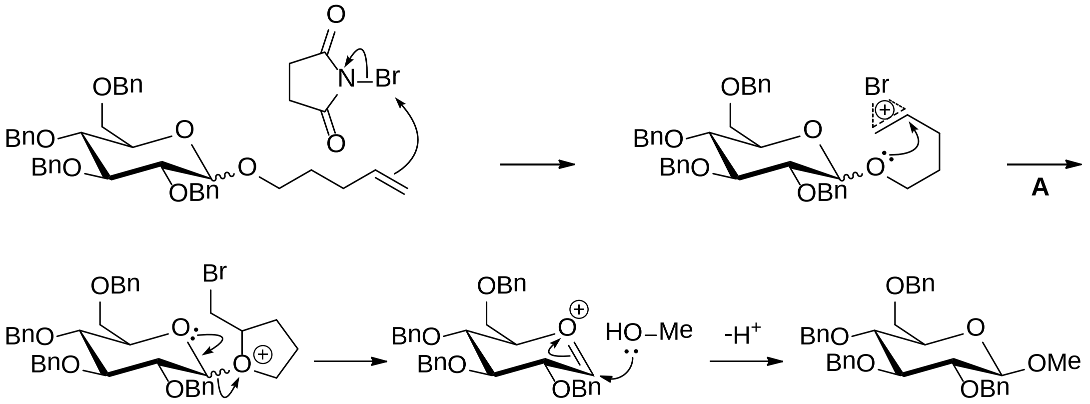


Jones, R. M.; Selenski, C.; Pettus, T. R. R. *J. Org. Chem.* **2002**, 67, 6911

A: Intramolecular acyl transfer (pKa PhOH = 10, t-BuOH = 19). **B**: Generation of o-quinonemethide

C: Hetero-Diels-Alder reaction to form an endo-adduct.

C036

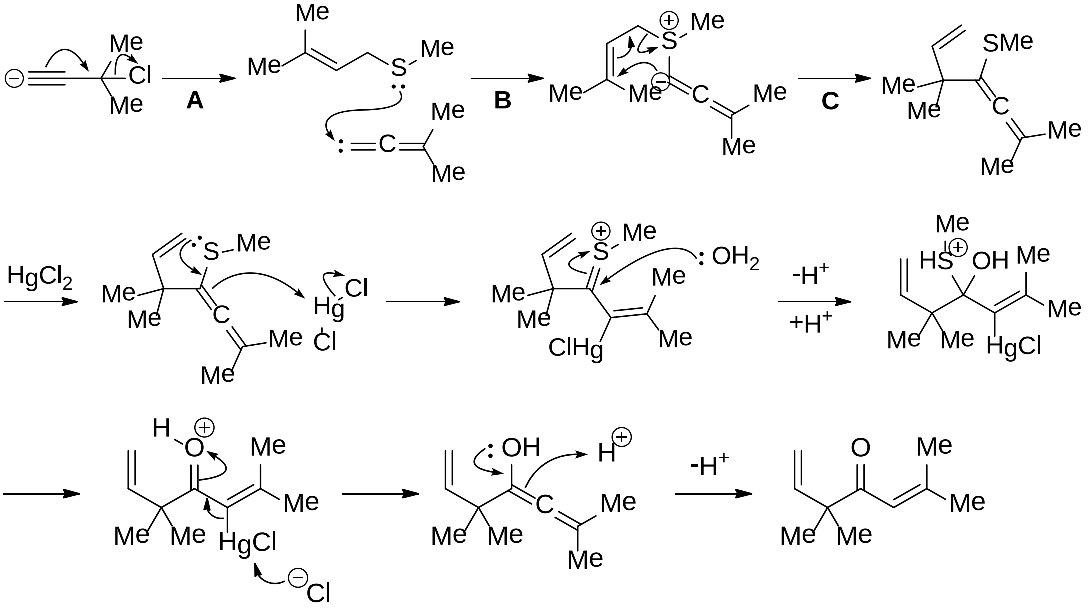


Fraser-Reid, B.; Konradsson, P.; Mootoo, D. R.; Udodong, U.

J. Chem. Soc., Chem. Commun. **1988**, 823.

A: Bromination of the olefin causes the formation of a five-membered oxonium ion.

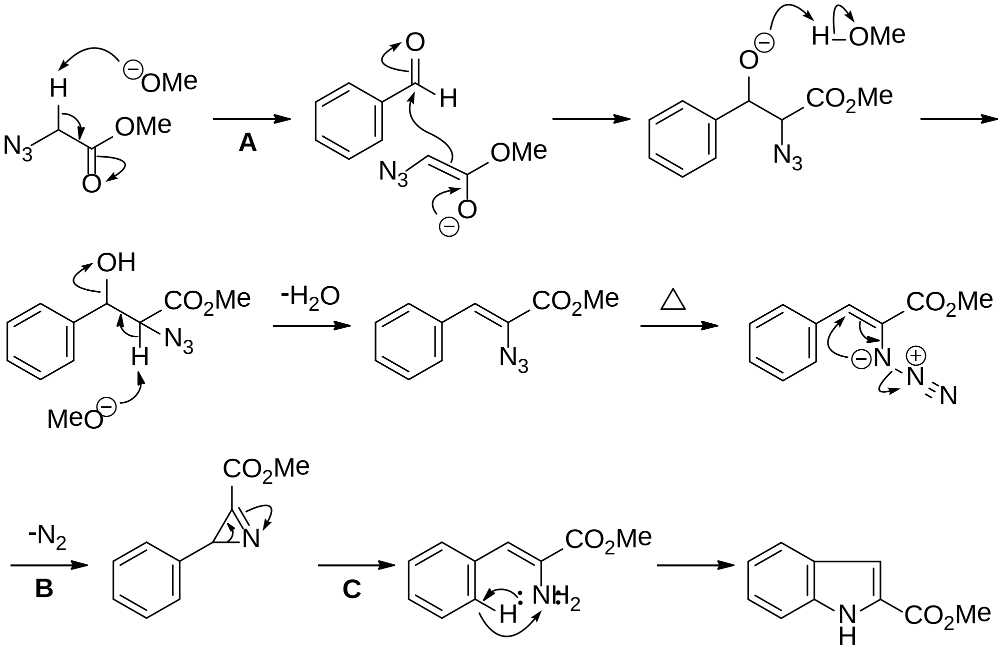
C037



Michelot, D.; Linstrumelle, G.; Julia, S. *J. Chem. Soc., Chem. Commun.* **1974**, 3, 10.

A: Generation of an alkylidene carbene. **B**: Formation of a sulfur ylide (carbene is electrophilic). **C**: [2,3] Sigmatropic rearrangement.

C038



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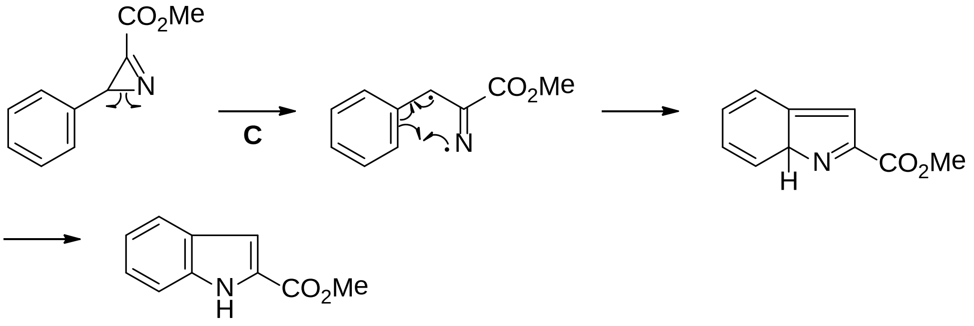
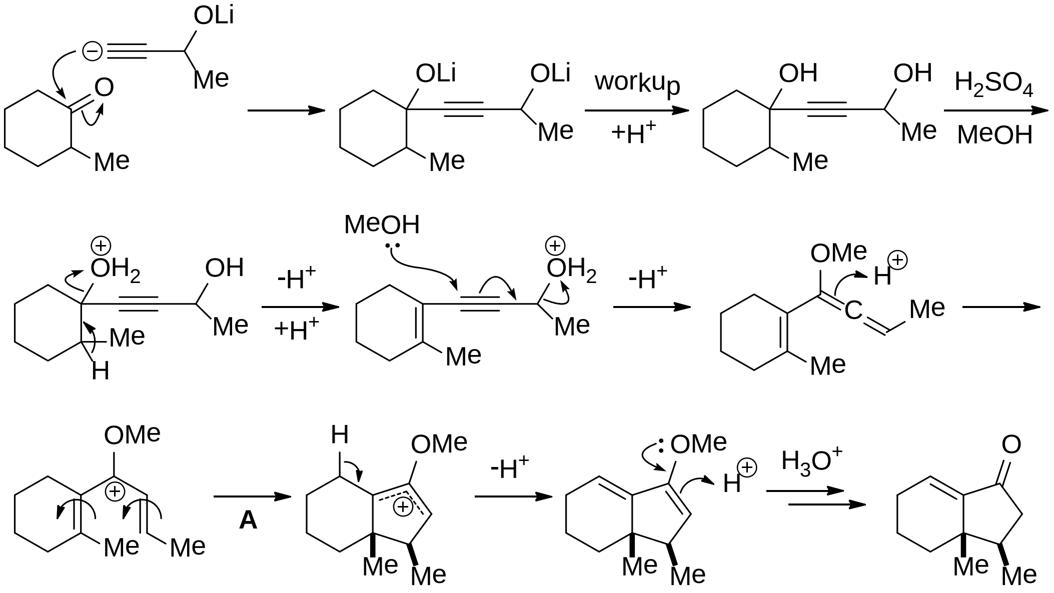
or



Knittel, D. *Synthesis* **1985**, 186.

A: Claisen-Schmidt reaction. **B**: Formation of an azirine. **C**: Cleavage of the azirine ring to form either 1) a nitrene which undergoes C-H insertion or 2) a diradical that recombines to form, upon aromatization.an indole.

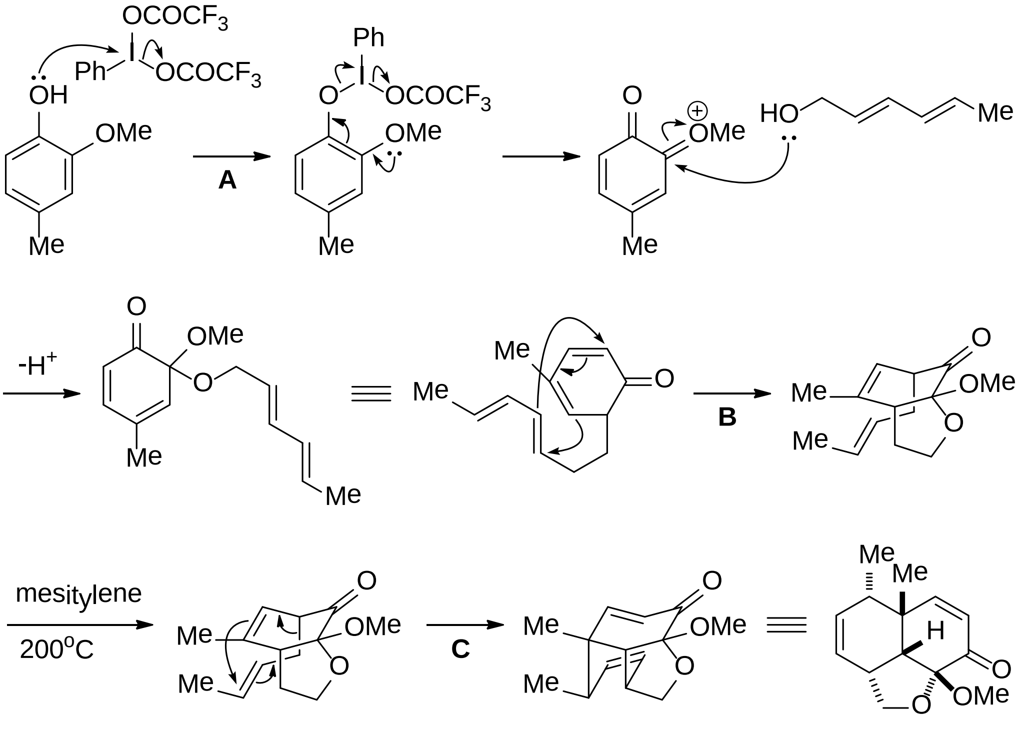
C039



Hiyama, T.; Shinoda, M.; Nozaki, H. *J. Am. Chem. Soc.* **1979**, 101, 1599.

A: Nazarov reaction (ref B026).

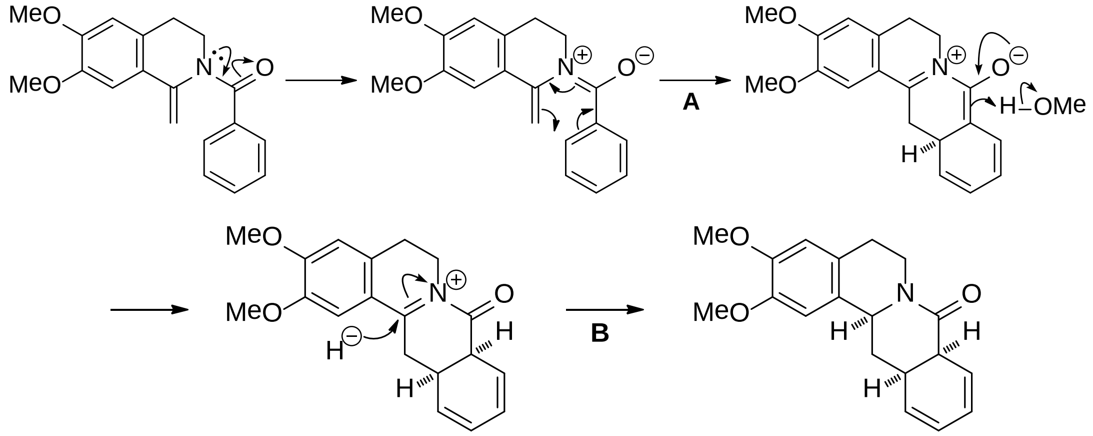
C040



Hsiu, P.-Y.; Liao, C.-C. *J. Chem. Soc., Chem. Commun.* **1997**, 1085.

A: Oxidation of the phenol to form a mixed o-quinone monoacetal. **B**: Intramolecular Diels-Alder reaction. **C**: Cope rearrangement.

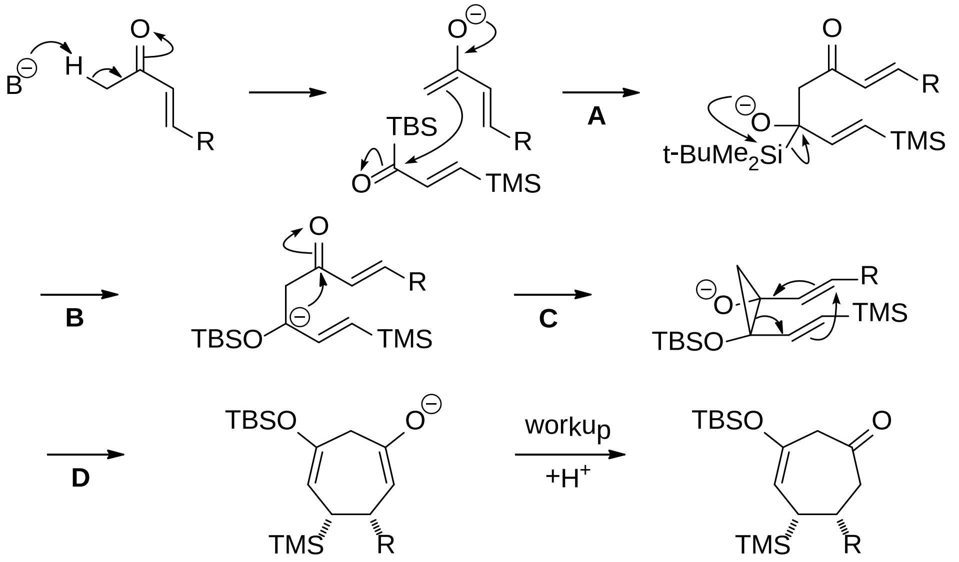
C041



Naito, T.; Tada, Y.; Nishiguchi, Y.; Ninomiya, I.
Heterocycles **1981**, 16, 1137.

A: 6e Electrocyclic reaction. **B**: Reduction of the acyliminium ion from the convex face.

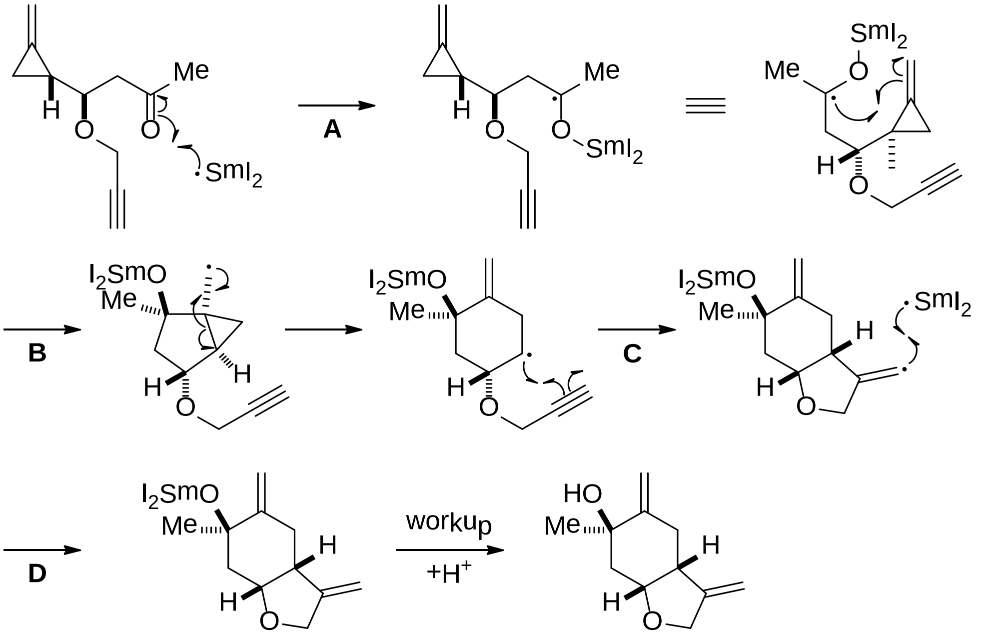
C042



Takeda, K.; Takeda, M.; Nakajima, A.; Yoshii, E.
J. Am. Chem. Soc. **1995**, 117, 6400.

A: 1,2-Addition of the enolate to the acylsilane. **B**: Brook rearrangement. **C**: Cyclopropanation. **D**: Anion-accelerated divinylcyctopropane rearrangement.

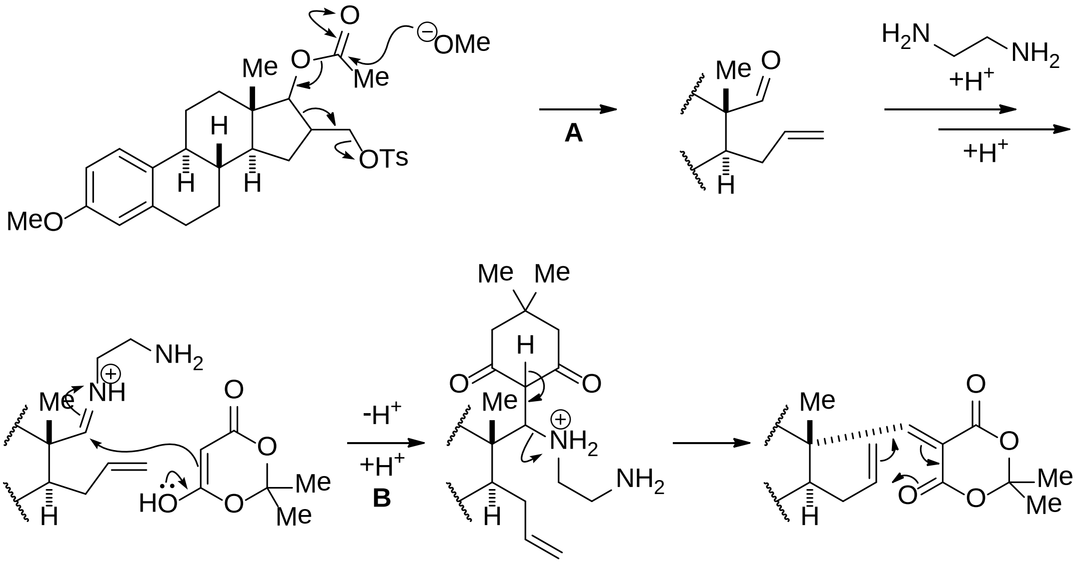
C043

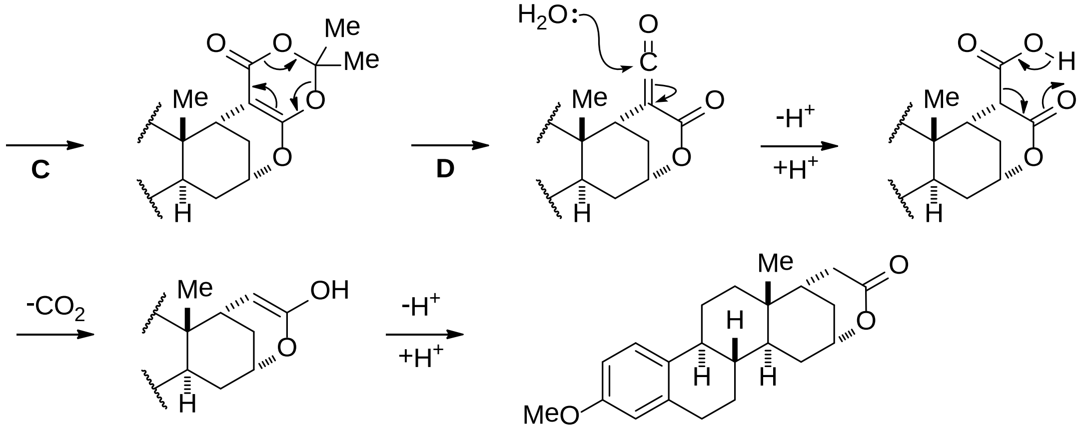


Boffey, R. J.; Santagostino, M.; Whittingham, W. G.; Kilburn, J. D.
Chem. Commun. **1998**, 1875.

A: SET. **B**: 5-exo-trig Radical cyclization to form a radical at a cyclopropylcarbinyl position which induces cleavage of the cyclopropane ring (cf. radical clock). **C**: 5-exo-dig Radical cyclization. **D**: SET.

C044

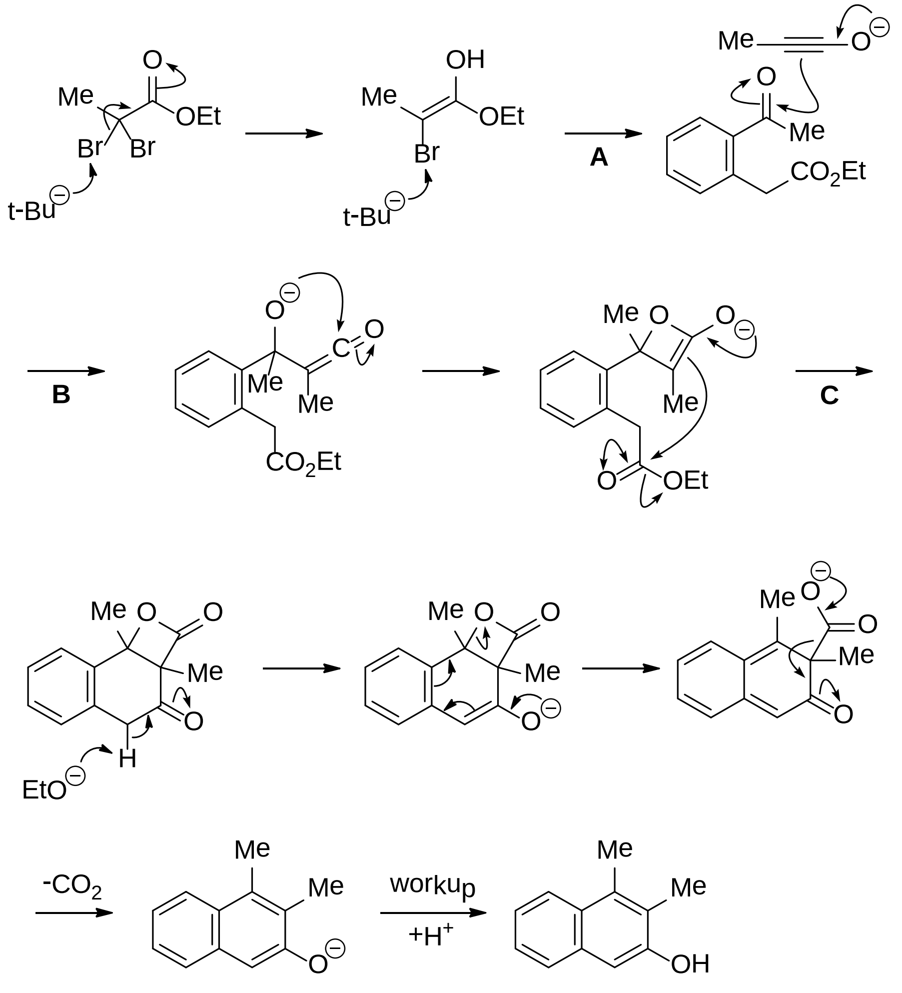




Tietze, L. F.; Wölfling, J.; Schneider, G. *Chem. Ber.* **1991**, 124, 591.

A: Grob-type fragmentation. **B**: Knoevenagel reaction (ref A018). **C**: Intramolecular hetero-Diels-Alder reaction. **D**: Retro Diels-Alder reaction to generate a highly reactive acylketene.

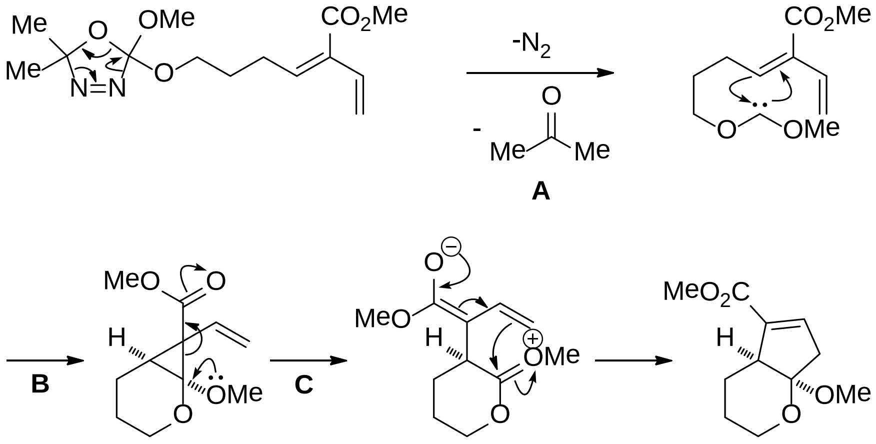
C045



Shindo, M.; Sato, Y.; Shishido, K. *J. Org. Chem*. **2001**, 66, 7818.

A: Formation of an ynolate. **B**: Addition of the ynolate to the ketone leads to the formation of a strained β-lactone enolate. **C**: Claisen condensation followed by aromatization with decarboxylation.

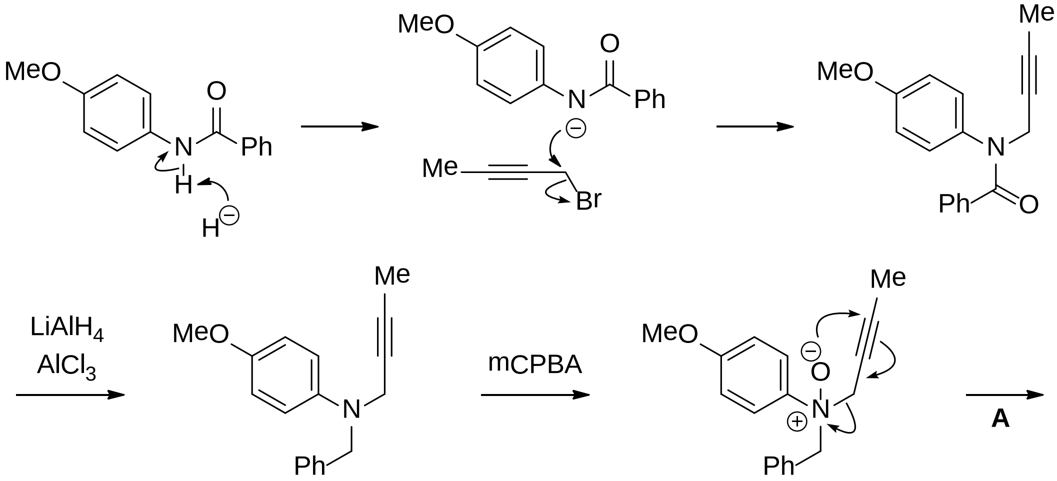
C046

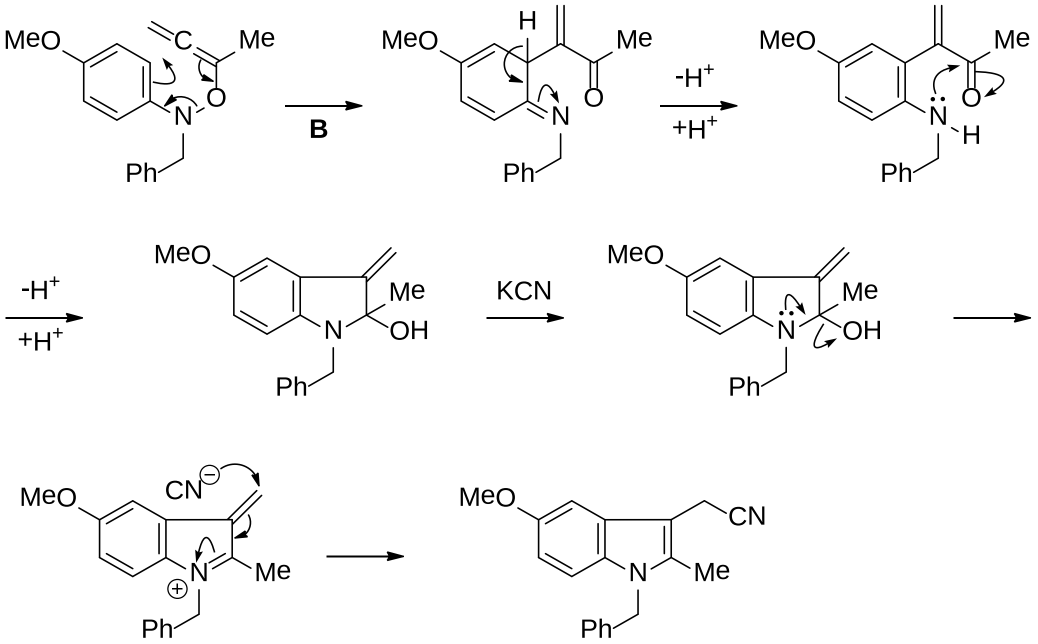


Spino, C.; Rezaei, H.; Dupont-Gaudet, K.; Belanger, F. *J. Am. Chem. Soc.* **2004**, 126, 9926.

A: Fragmentation to form a dialkoxycarbene. **B**: Cyclopropanation. **C**: Cleavage of the cyclopropane ring.

C047

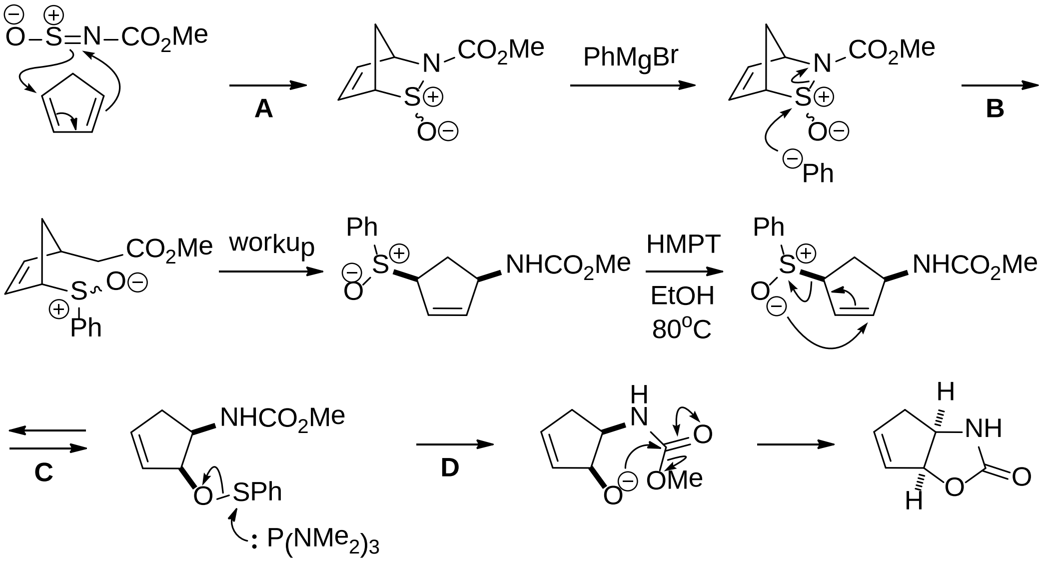




Makisumi, Y.; Takada, S. *Chem. Pharm. Bull.* **1976**, 24, 770.

A: [2,3] Sigmatropic rearrangement of the N-oxide. **B**: [3,3] Sigmatropic rearrangement.

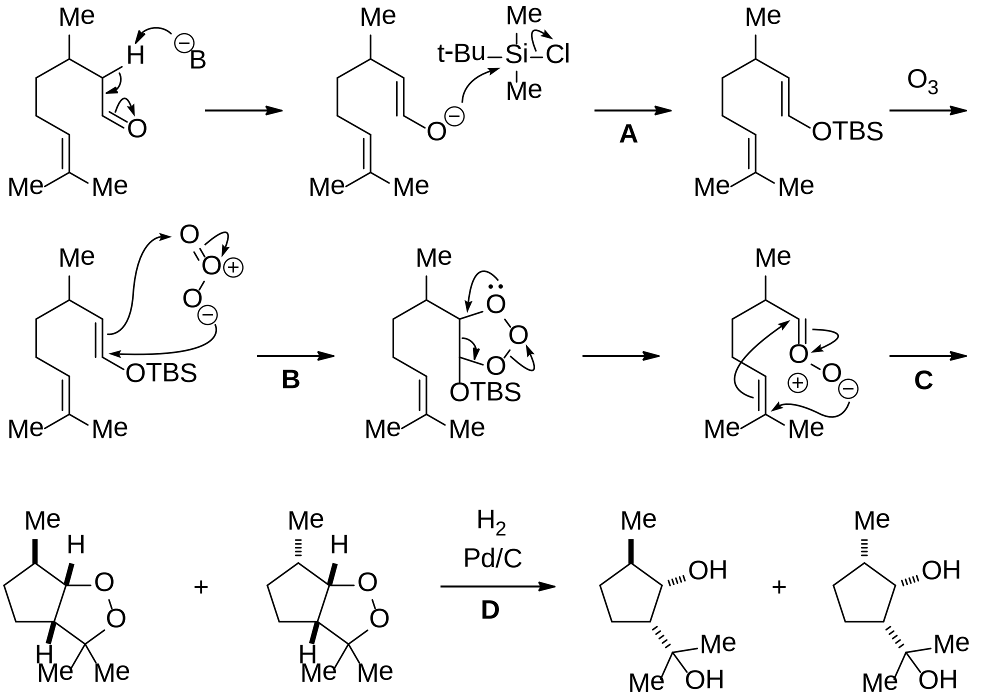
C048



Anderson, G. T.; Chase, C. E.; Koh, Y-H.; Seien, D.; Weinreb, S. M. *J. Org. Chem.* **1998**, 63, 7594.

A: Hetero-Diels-Alder reaction. **B**: Cleavage of the S-N bond by S$_N$2 attack of PhMgBr. **C**: [2,3] Sigmatropic rearrangement (reversible process). **D**: Irreversible cleavage of the S-O bond by attack of a thiophile (P(NMe$_2$)$_3$) generates an alkoxide ion which then cyclizes to give an oxazolidinone.

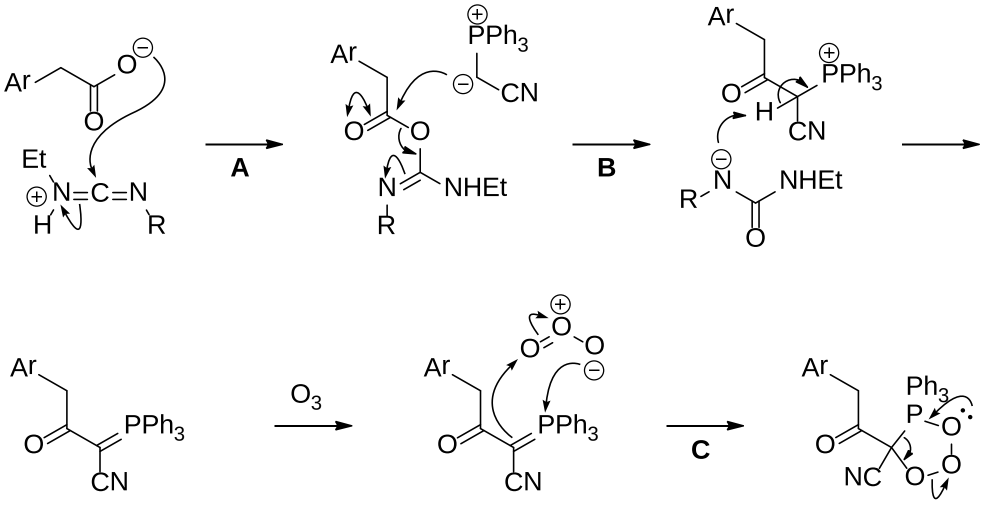
C049

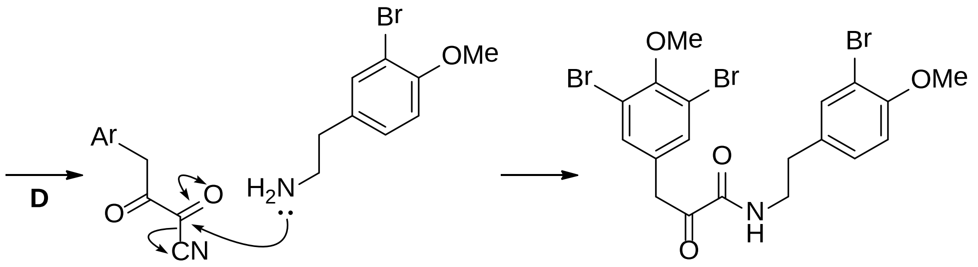


Casey, M.; Culshaw, A. J. *Synlett*

A: Formation of a silyl enol ether. **B**: 1,3-Dipolar cycloaddition of O_3 followed by cleavage of the ozonide to form a 1,3-dipole (carbonyl oxide). **C**: 1,3-Dipolar cycloaddition. **D**: Reductive cleavage of the O-O bond.

C050

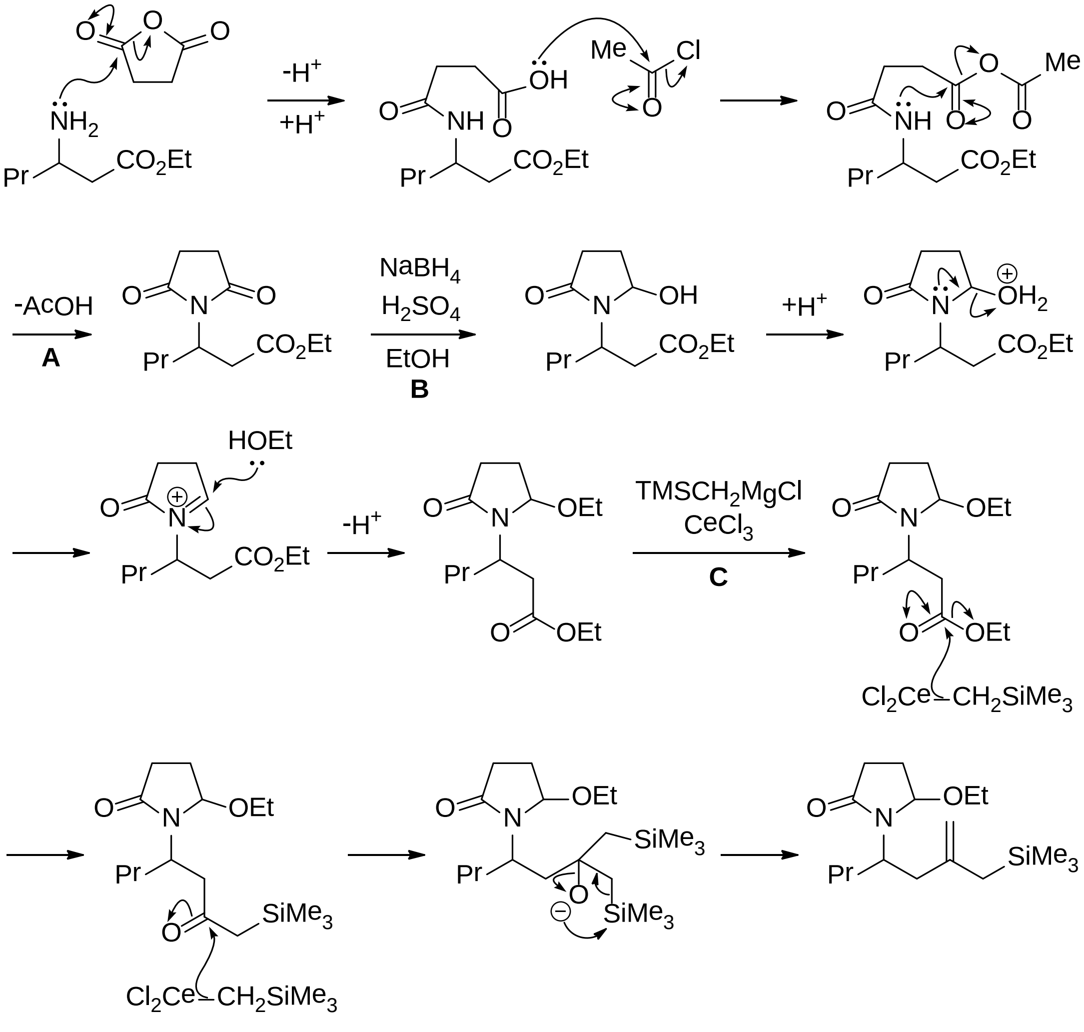


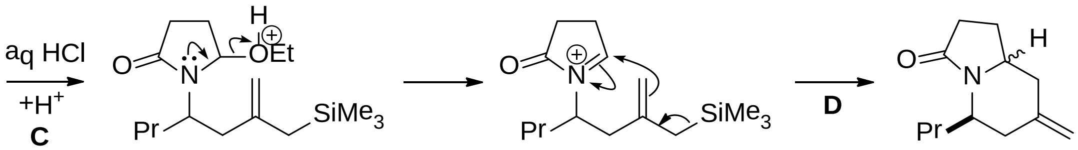


Wasserman, H. H.; Wang, J. *J. Org. Chem.* **1998**, 63, 5581.

A: Activation of the carboxylic acid as an O-acylisourea. **B**: Acylation of the stabilized ylide. **C**: 1,3-Dipolar cycloaddition of O_3 to the ylide. **D**: Fragmentation to generate an acyl cyanide.

C051

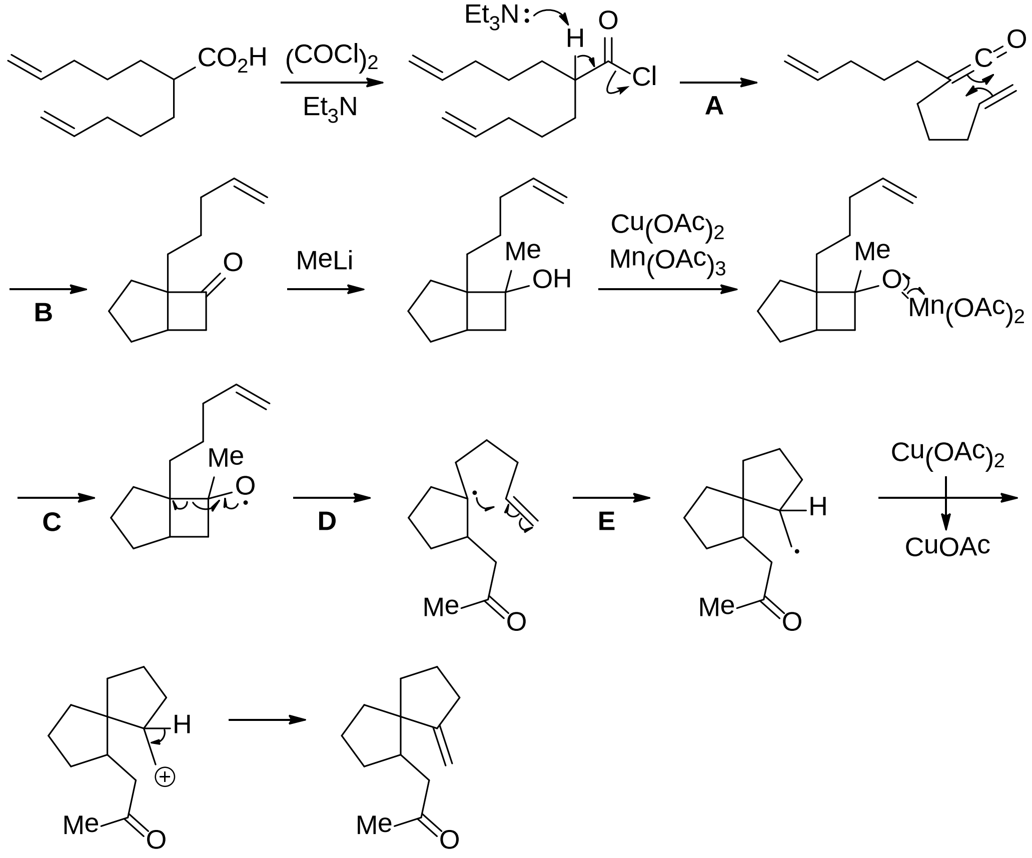




Chalard, E; Remuson, R.; Gelas-Mialhe Y.; Gramain J.-C.; Canet I.
Tetrahedron Lett. **1999**, 40, 1661.

A: Formation of a succinimide via a mixed anhydride. **B**: Partial reduction of the imide. **C**: Peterson olefination (ref A074) to form an allylsilane. **D**: Intramolecular addition of the allylsilane to the acyliminium ion.

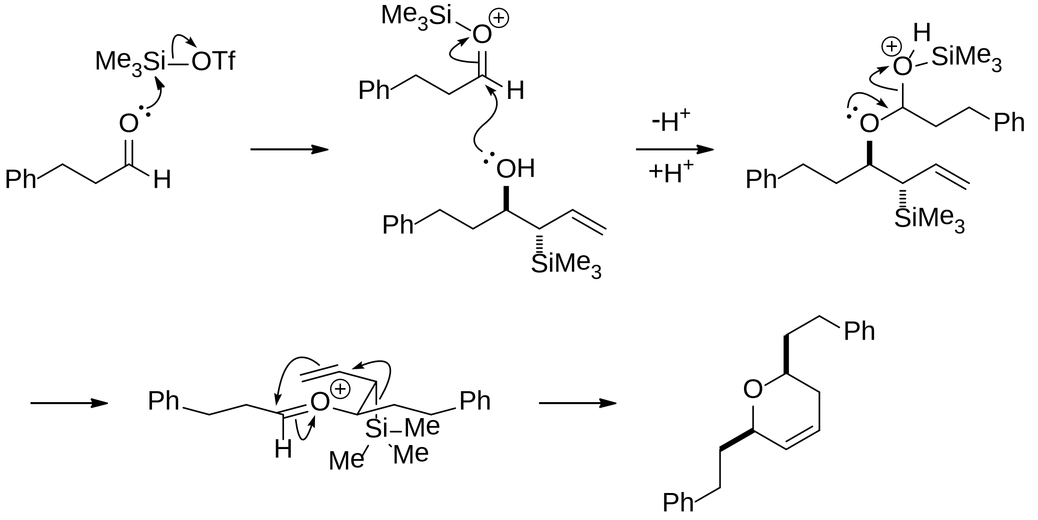
C052



Snider, B. B.; Vo, N. H.; Foxman, B. M. *J. Org. Chem.* **1993**, 58, 7228.

A: Formation of a ketene. **B**: Intramolecular [2+2] cycloaddition. **C**: Generation of an oxygen radical. **D**: Cleavage of the cyclobutane ring to form a stable tertiary carbon radical. **E**: 5-exo-trig Radical cyclization followed by oxidation with Cu(OAc)$_2$.

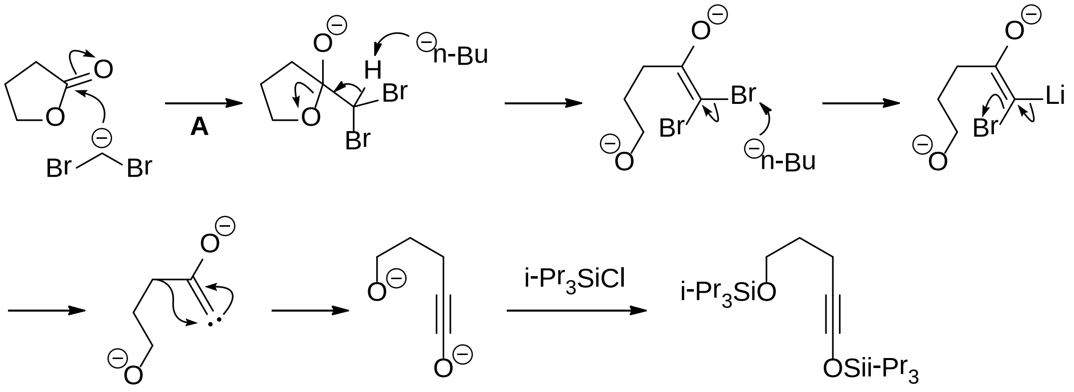
C053

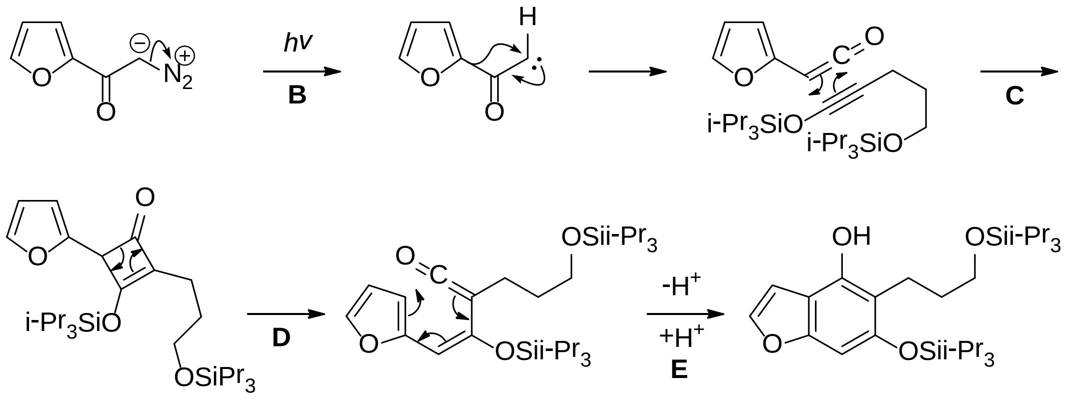


Roush, W. R.; Dilley, G. J. *Synlett.* **2001**, 955

Intramolecular Hosomi-Sakurai-type reaction.

C054

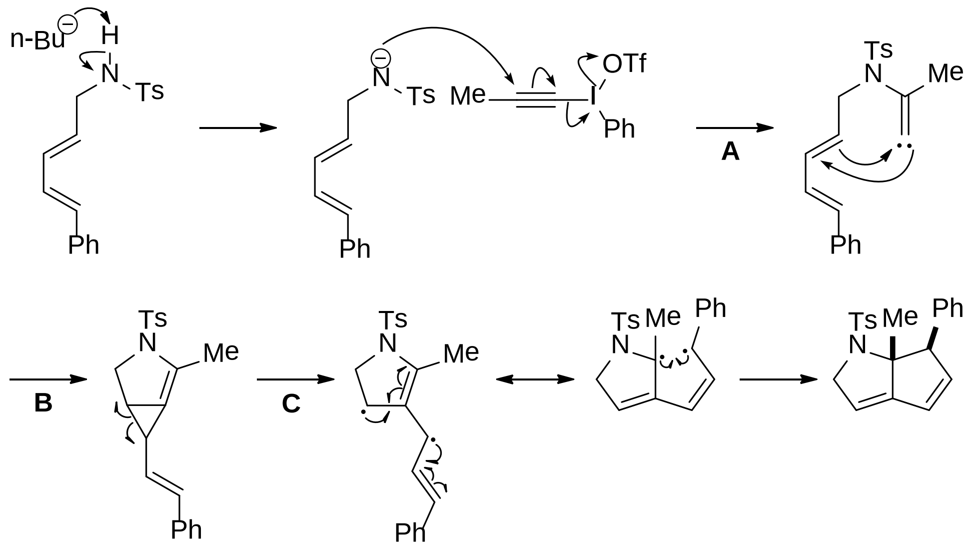




Danheiser, R. L.; Trova, M. P. *Synlett.* **1995**, 573.

A: Formation of an alkylidene carbene via α-elimination followed by insertion of the carbene into the C-C bond (Kowalski reaction). **B**: Wolff rearrangement. **C**: [2+2] Ketene cycloaddition. **D**: 4e Electrocyclic reaction. **E**: 6e Electrocyclic reaction followed by aromatization.

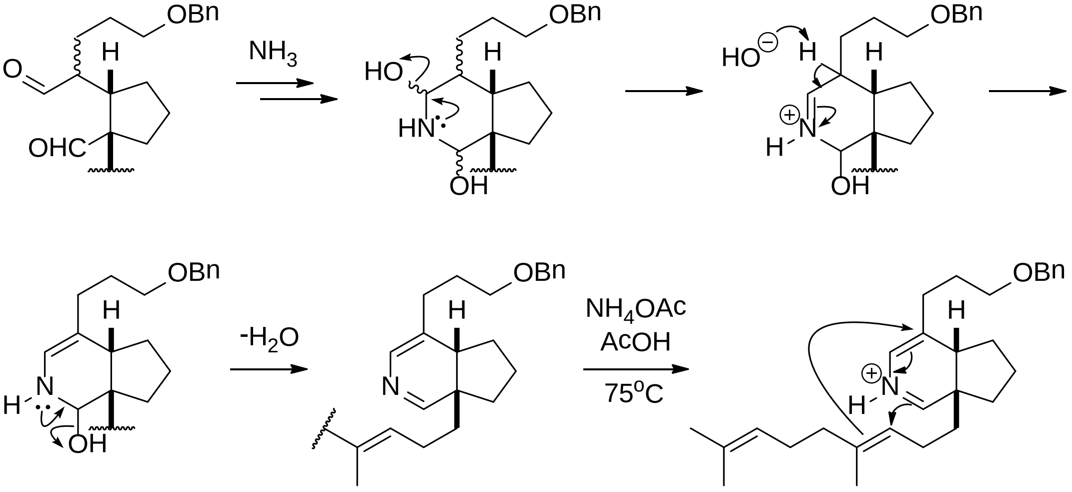
C055

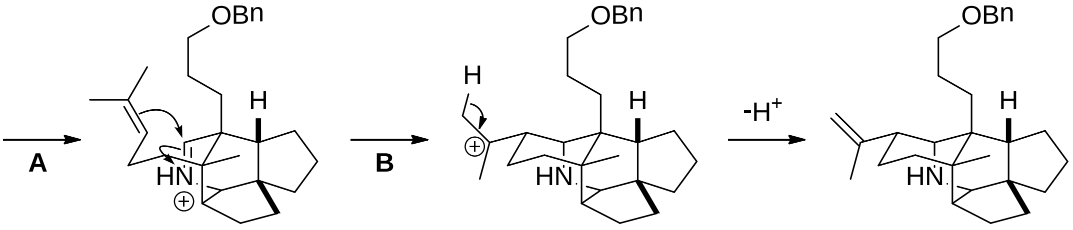


Feldman, K. S.; Mareska, D. A. *J. Org. Chem.* **1999**, 64, 5650.

A: Addition of a sulfonamide ion to the electron-deficient acetylene to form an alkylidene carbene. **B**: Cyclopropanation. **C**: Homolytic cleavage of the strained cyclopropylidene ring.

C056

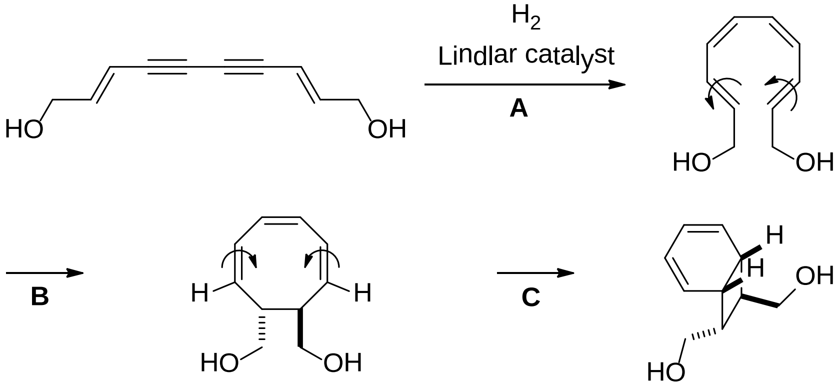




Heathcock, C. H.; Stafford, J. A. *J. Org. Chem.* **1992**, 57, 2566.

A: Aza-Diels-Alder reaction. **B**: Cation-olefin cyclization.

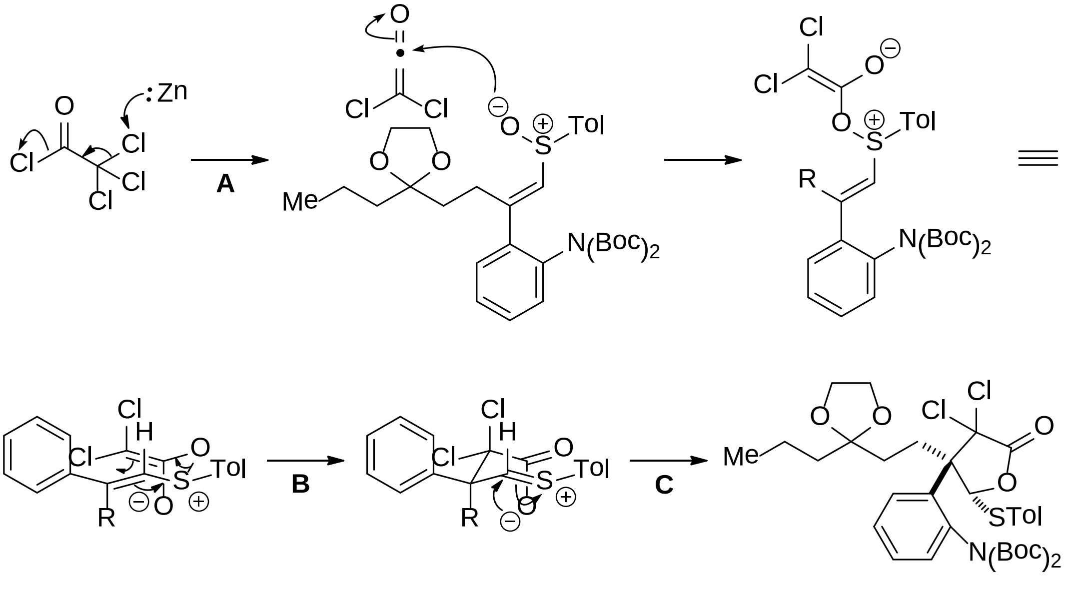
C057



Nicolaou, K. C.; Petasis, N. A.; Zipkin, R. E.; Uenishi, J.
J. Am. Chem. Soc. **1982**, 104, 5555.

A: Partial reduction of the alkynes to form a tetraene. **B**: 8e Conrotatory electrocyclic reaction. **C**: 6e Disrotatory electrocyclic reaction.

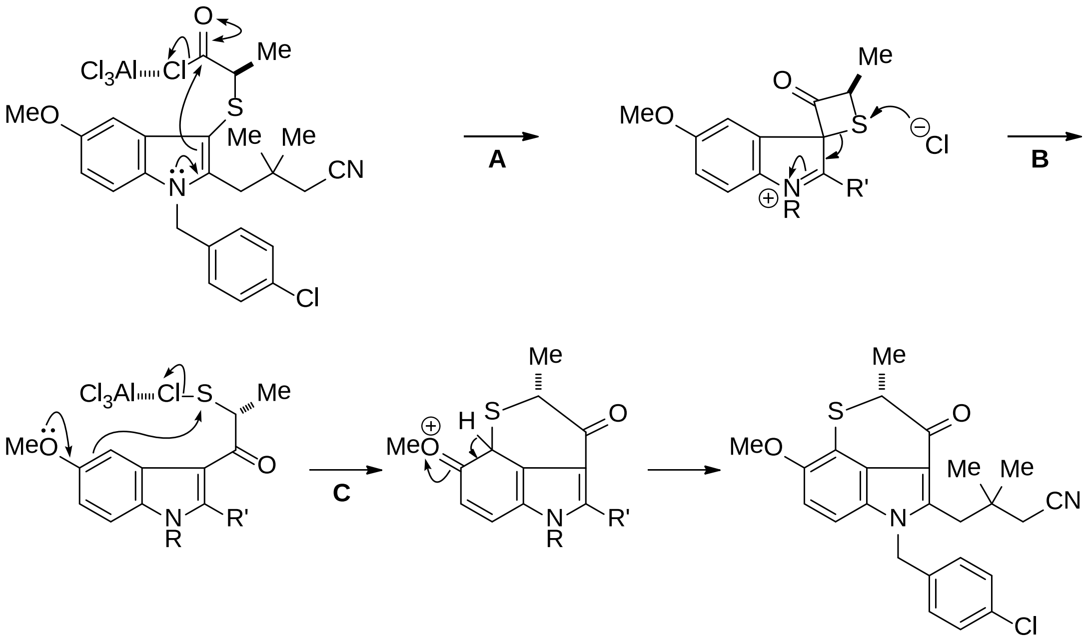
C058



Marino, J. P.; Rubio, M. B.; Cao, G.; de Dios, A.
J. Am. Chem. Soc. **2002**, 124, 13398.

A: Generation of dichloroketene. **B**: [3,3] Sigmatropic rearrangement. **C**: Cyclization of the carboxylate to the sulfenium ion.

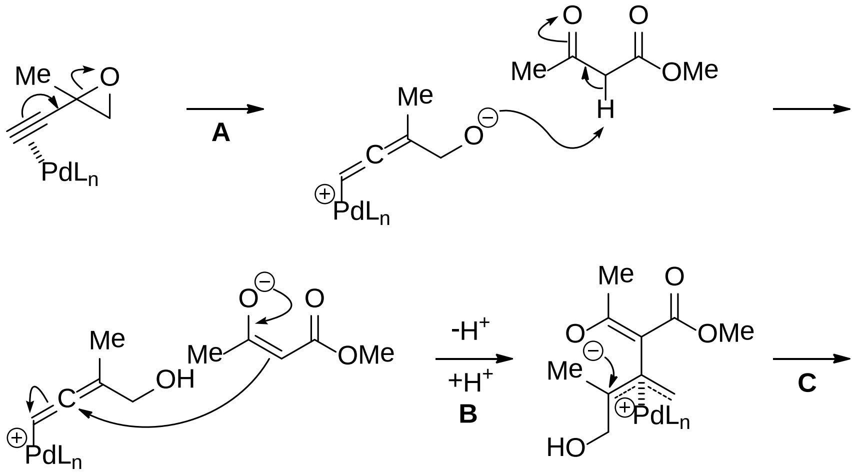
C059

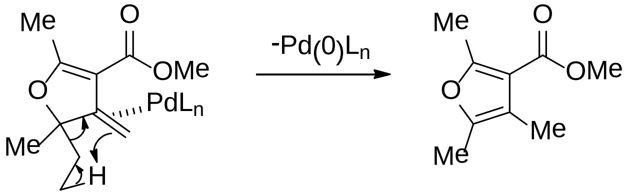


Chung, J. Y. L.; Reamer, R. A.; Reider, P. J. *Tetrahedron Lett.* **1992**, 33, 4717.

A: Friedel-Crafts acylation at the indole 3-position. **B**: Cleavage of the strained four-membered ring by chloride ion. **C**: Intramolecular electrophilic substitution by the resulting sulfenyl chloride.

C060

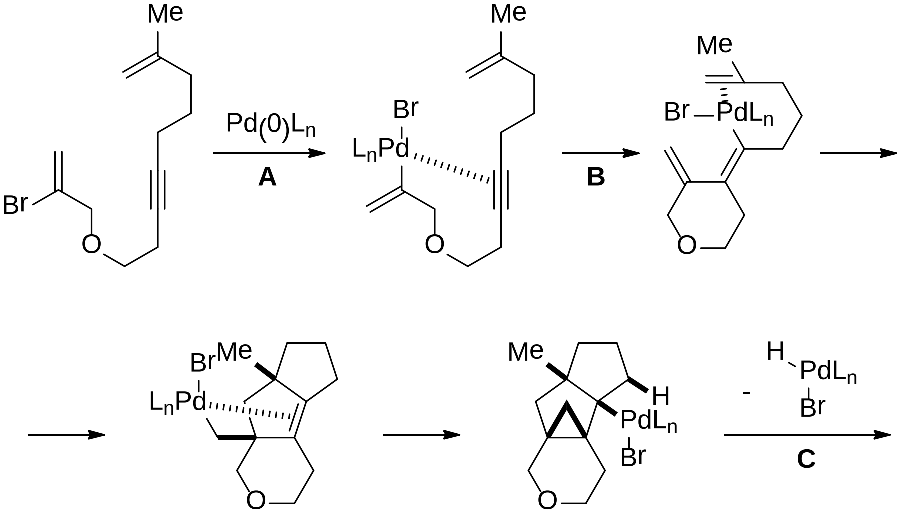




Minami, I.; Yuhara, M.; Tsuji, J. *Tetrahedron Lett.* **1987**, 28, 629.

A: Formation of an allenylpalladium species. **B**: Addition of the acetoacetate anion to generate a π-allylpalladium complex. **C**: Intramolecular nucleophilic attack to the π-allylpalladium complex.

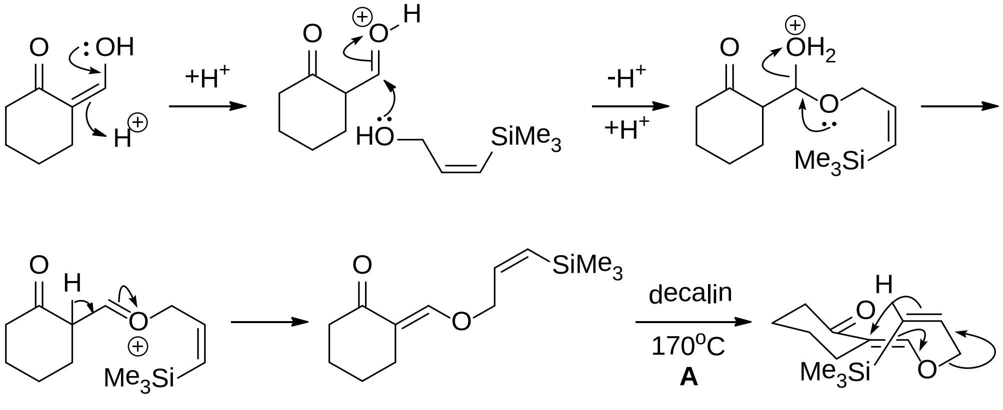
C061

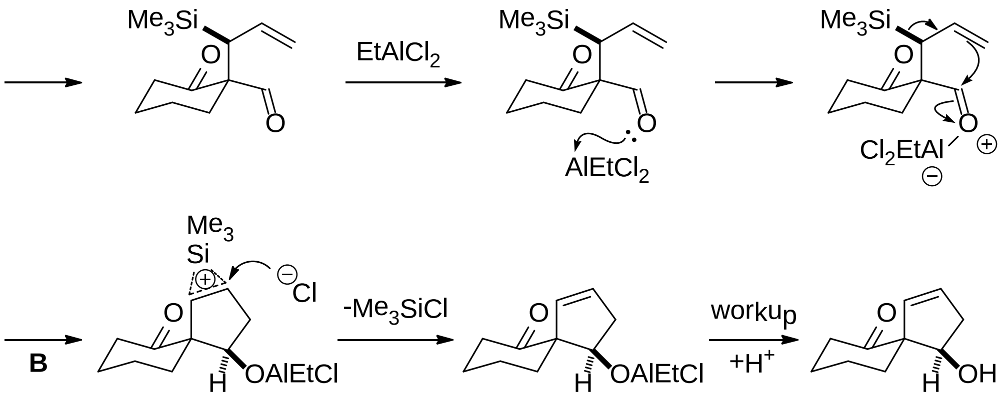


Meyer, R E.; Parsons, P. J.; de Meijere, A. *J. Org. Chem.* **1991**, 56, 6487.

A: Oxidative addition. **B**: Sequential intramolecular carbopalladation. **C**: β-Elimination.

C062

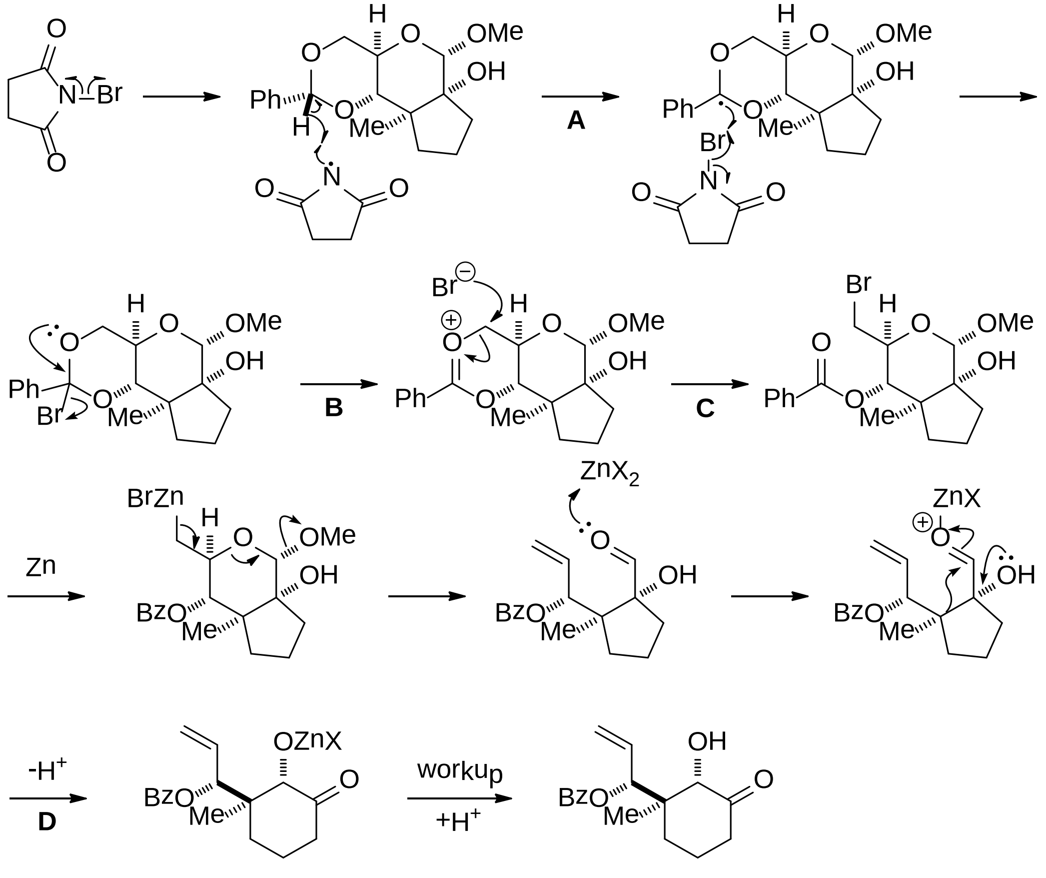




Paquette, L. A.; Ladouceur, G. *J. Org. Chem.* **1989**, 54, 4278.

A: Claisen rearrangement via a boat-like transition state. **B**: Intramolecular Hosomi-Sakurai reaction.

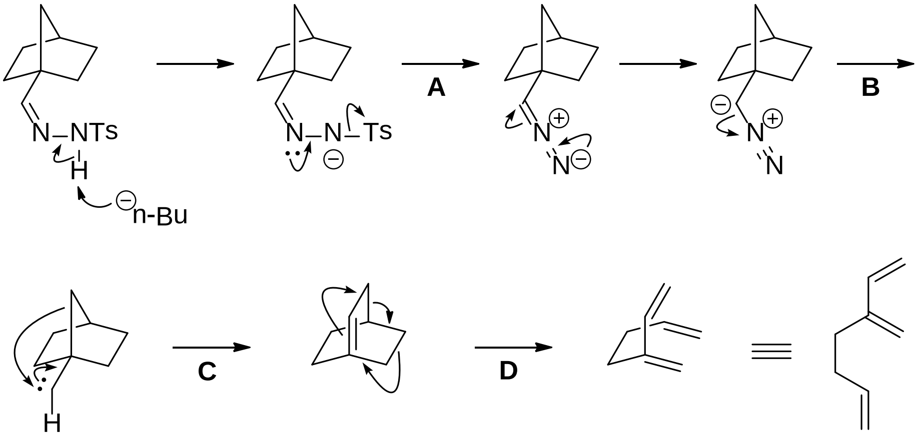
C063



Holt, D. J.; Barker, W. D.; Jenkins, P. R. *J. Org. Chem.* **2000**, 65, 482.

A: Radical bromination of the benzylic position. **B**: Formation of a stable carbocation. **C**: S_N2 reaction. **D**: 1,2-Alkyl shift.

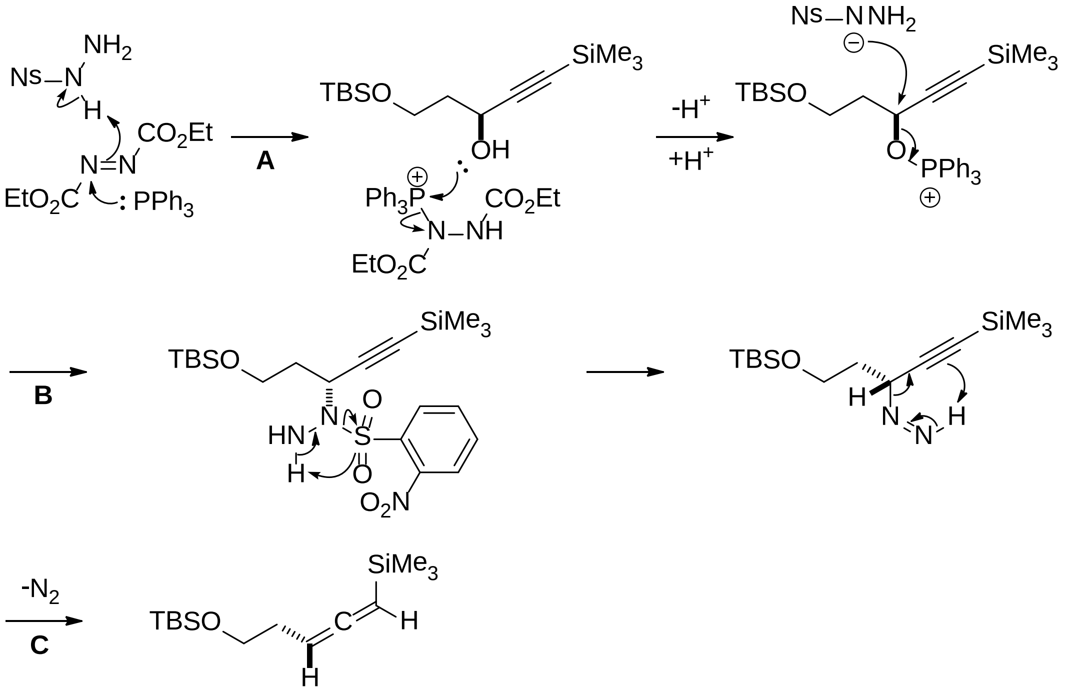
C064



Bian, N.; Jones, M., Jr. *Tetrahedron Lett.*, **1993**, 25, 3967.

A: Formation of a diazoalkane via α-elimination. **B**: Elimination of N_2 to form a carbene. **C**: Insertion of the carbene to the C-C bond. **D**: Retro Diels-Alder reaction.

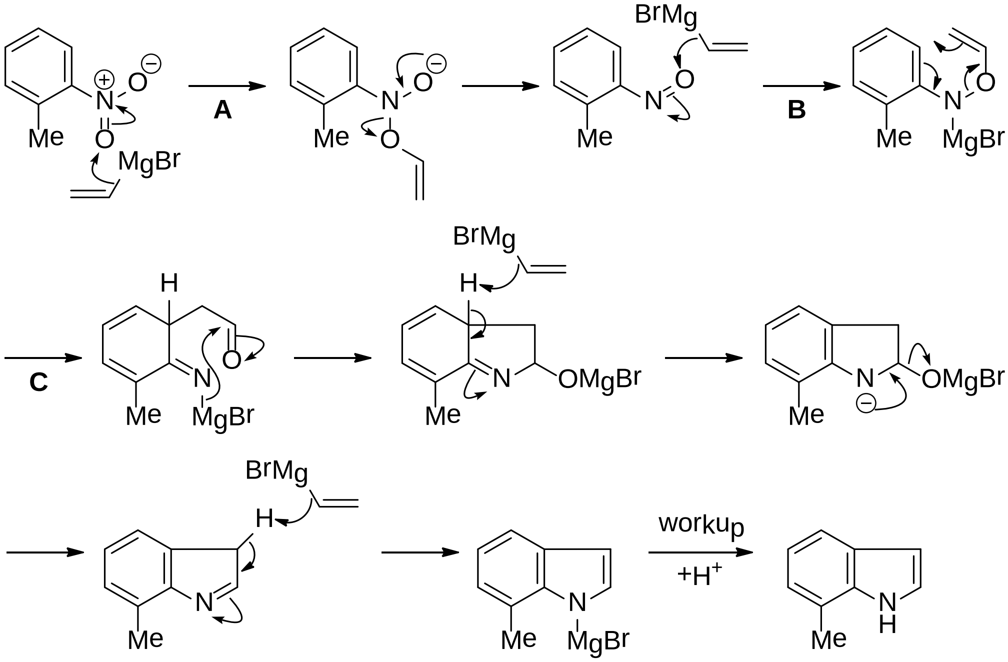
C065



Myers, A. G.; Zheng, B. *J. Am. Chem. Soc.* **1996**, 118, 4492.

A: Mitsunobu reaction (ref A045). **B**: Elimination of a sulfinic acid. **C**: Sigmatropic elimination of N_2 (stereospecific delivery of a hydride via a concerted mechanism).

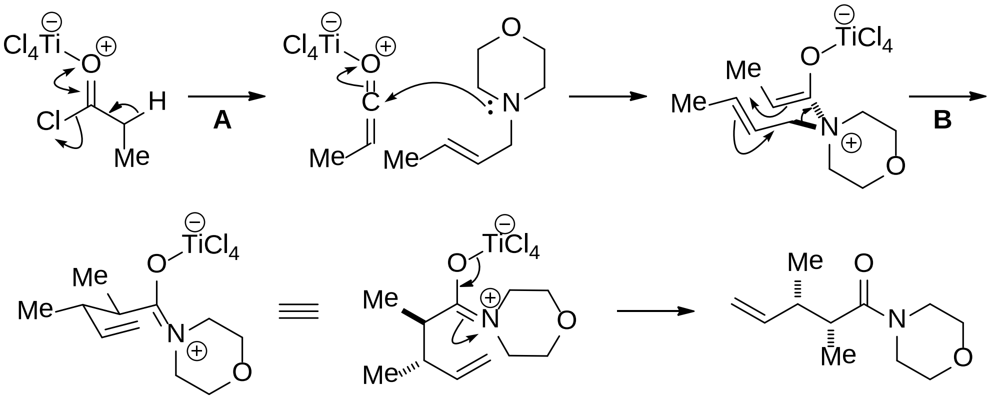
C066



Bosco, M.; Dalpozzo, R.; Bartoli, G.; Palmieri, G.; Petrini, M.
J. Chem. Soc., Perkin Trans. 2 **1991**, 657.

Bartoli indole synthesis. **A**: Reduction of the nitro group by means of addition of CH_2=CHMgBr and elimination of an enolate to form a nitroso compound. **B**: Addition of CH_2=CHMgBr to the nitroso group. **C**: [3,3] Sigmatropic rearrangement.

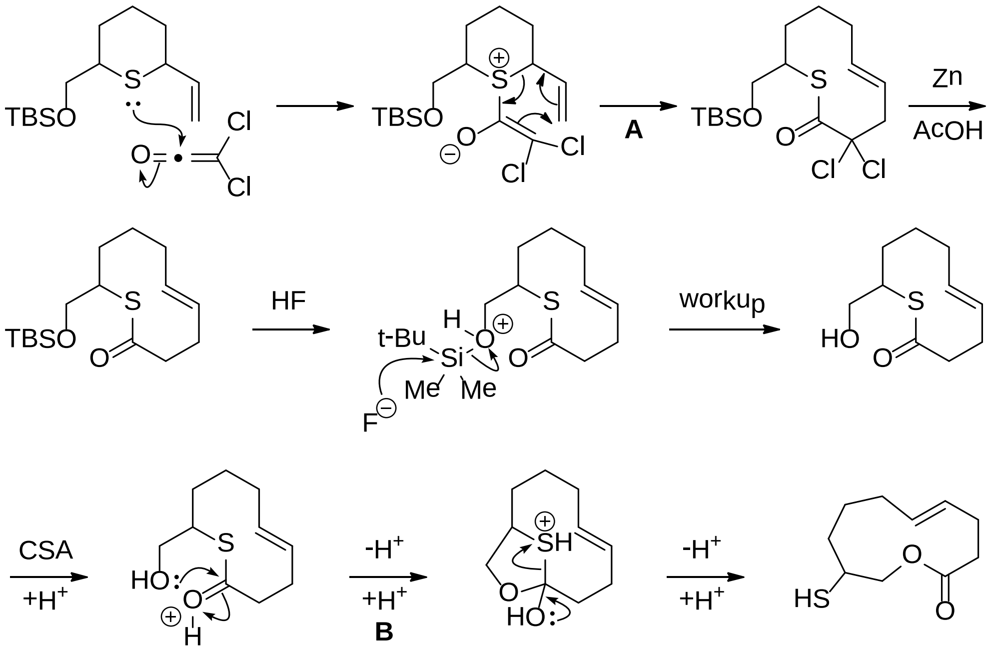
C067



Yoon, T. P.; Dong, V. M.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **1999**, 121, 9726.

A: Formation of a ketene. **B**: Aza-Claisen rearrangement through a chair-like transition state.

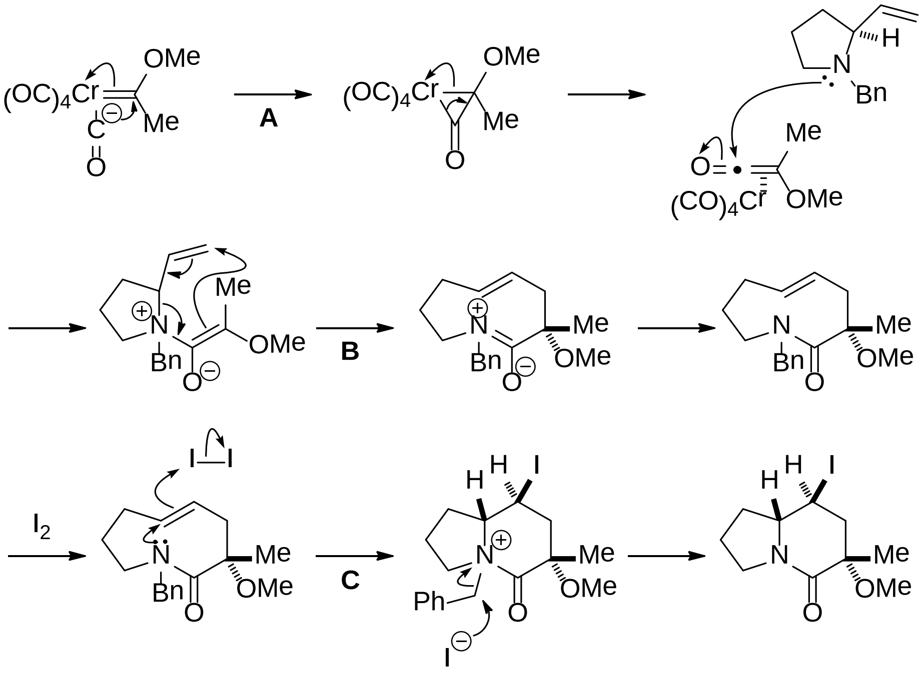
C068



Vedejs, E.; Buchanan, R. A. *J. Org. Chem*. **1984**, 49, 1840.

A: [3,3] Sigmatropic rearrangement. **B**: Intramolecular acyl transfer reaction.

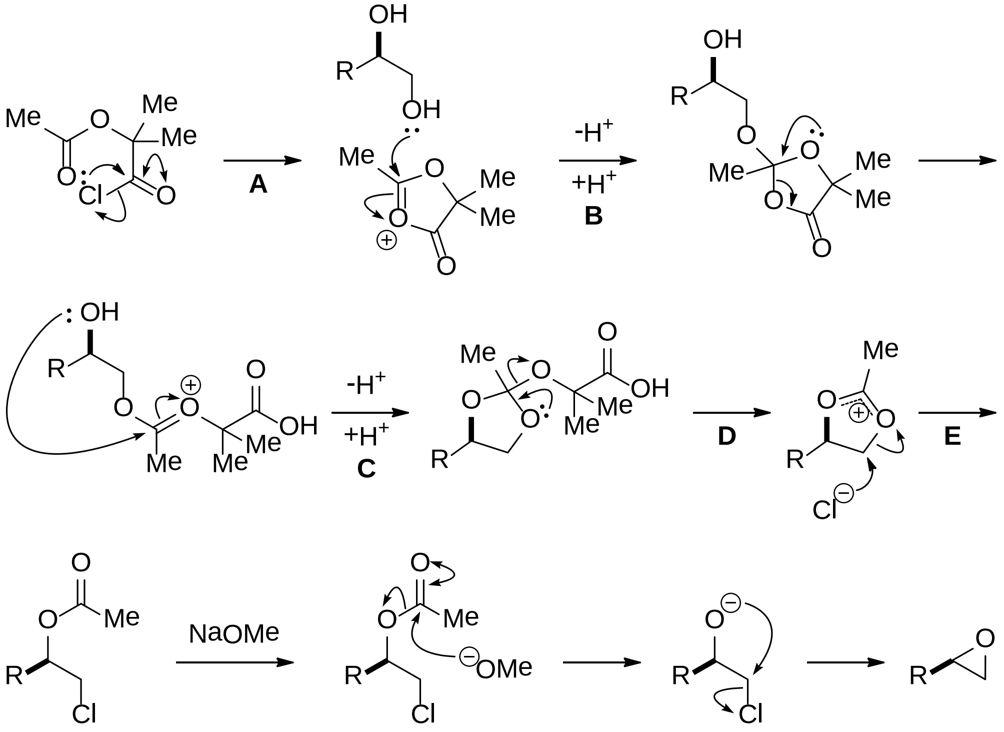
C069



eur, C. J.; Miller, M. W.; Hegedus, L. S. *J. Org. Chem.* **1996**, 61, 2871.

A: Photo-induced insertion of CO to form a ketene. **B**: Aza-Claisen rearrangement. **C**: Intramolecular iodoamidation followed by debenzylation in an S_N2 fashion.

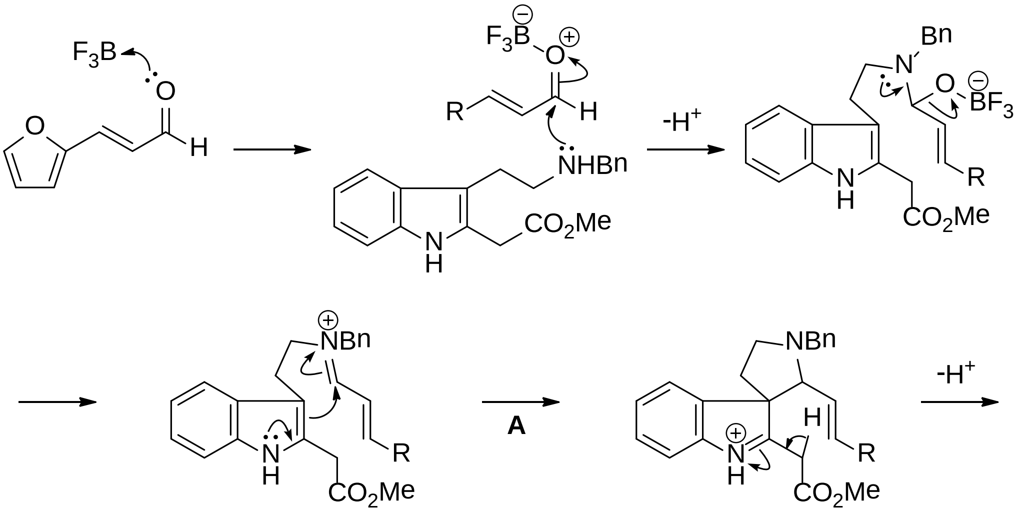
C070

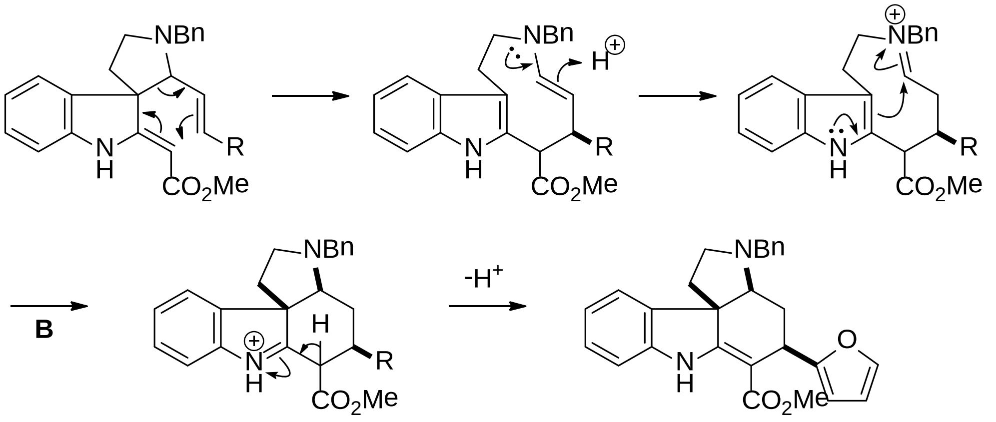


Schreiber, S. L.; Sammakia, T.; Uehling, D. E. *J. Org. Chem.*, **1989**, 54, 15.

A: Activation by cyclization. **B**: Formation of an orthoester followed by cleavage of the five-membered lactone. **C**: Intramolecular interception of the stable carbocation by the secondary alcohol. **D**: Cleavage of the resulting orthoester. **E**: S_N2 reaction at the less hindered carbon with chloride ion.

C071

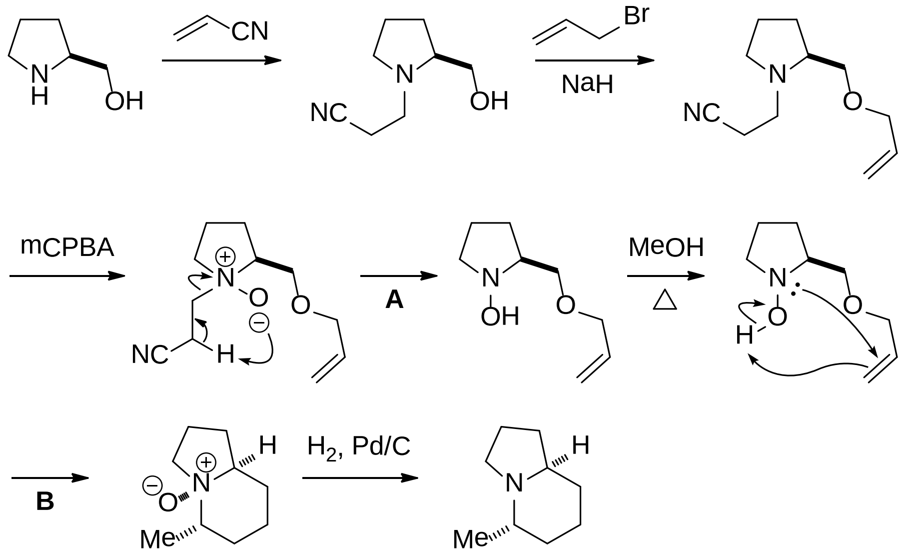




Parsons R. L.; Berk J. D.; Kuehne M. E. *J. Org. Chem*. **1993**, 58, 7482.

A: Mannich reaction followed by [3,3] sigmatropic rearrangement. **B**: Mannich reaction.

C072

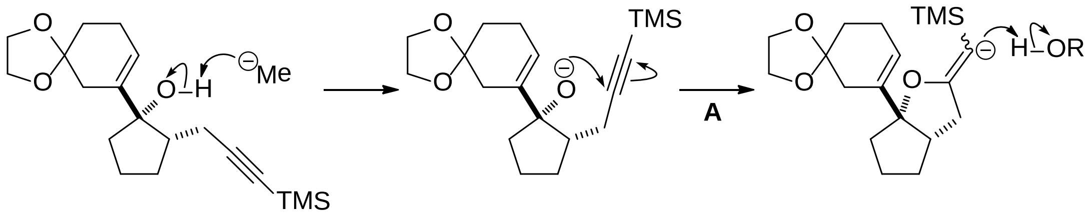


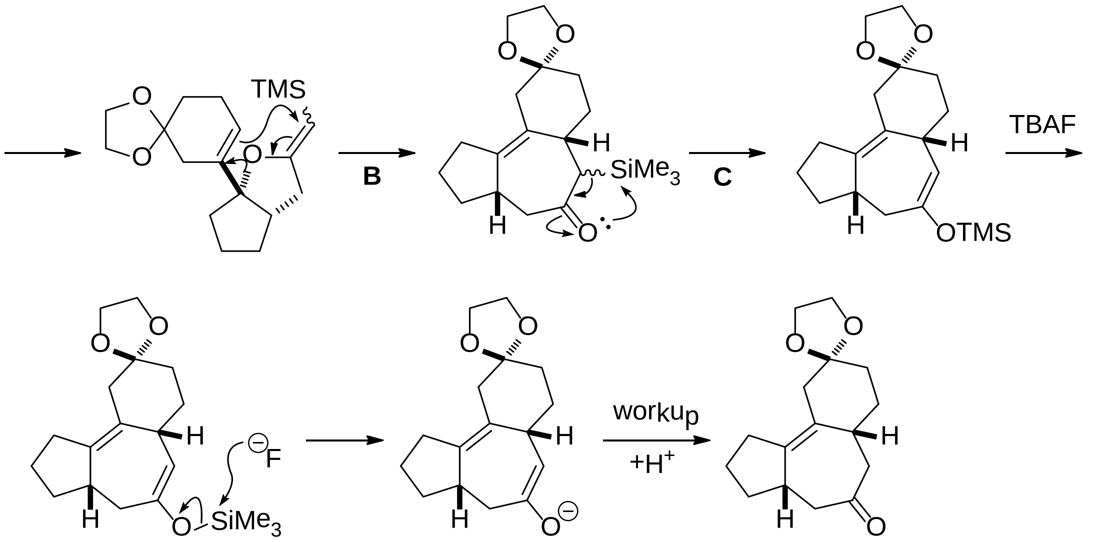
O'Neil, I. A.; Cleator, E.; Ramos, V. E.; Chorlton, A. P.; Tapolczay, D. J.

Tetrahedron Lett. **2004**, 45, 3655.

A: Cope elimination. **B**: Retro Cope elimination.

C073

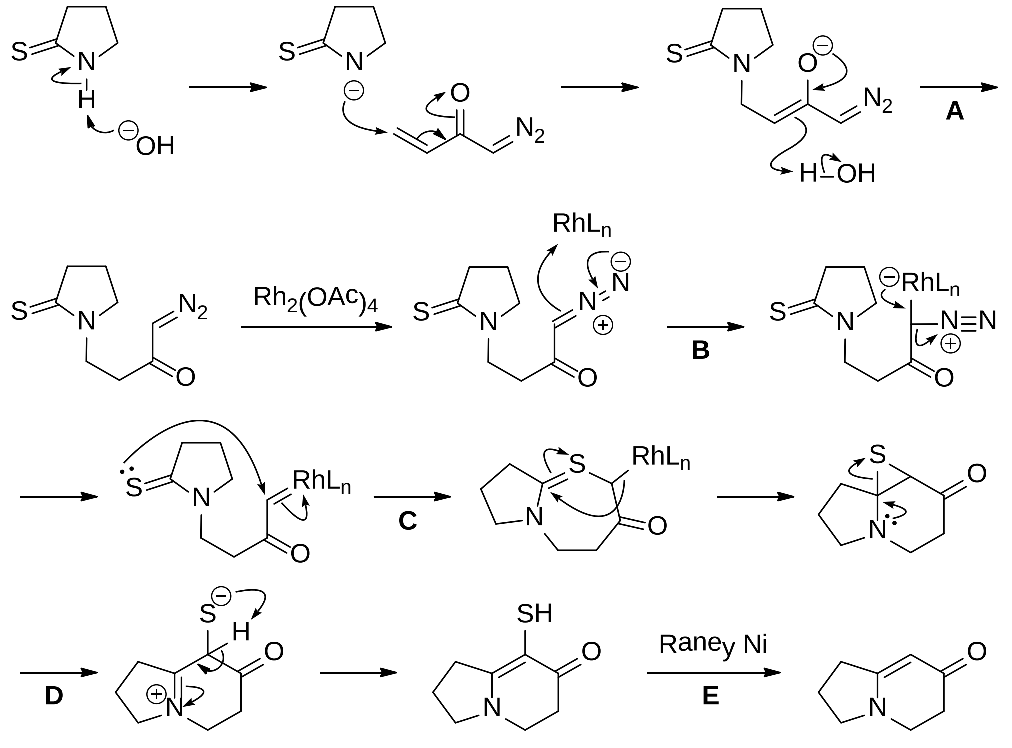




Ovaska, T. V.; Roses, J. B. *Org. Lett.* **2000**, 2, 2361.

A: 5-exo-dig Cyclization of the alkoxide ion. **B**: Claisen rearrangement. **C**: Migration of the silyl group to form a silyl enol ether.

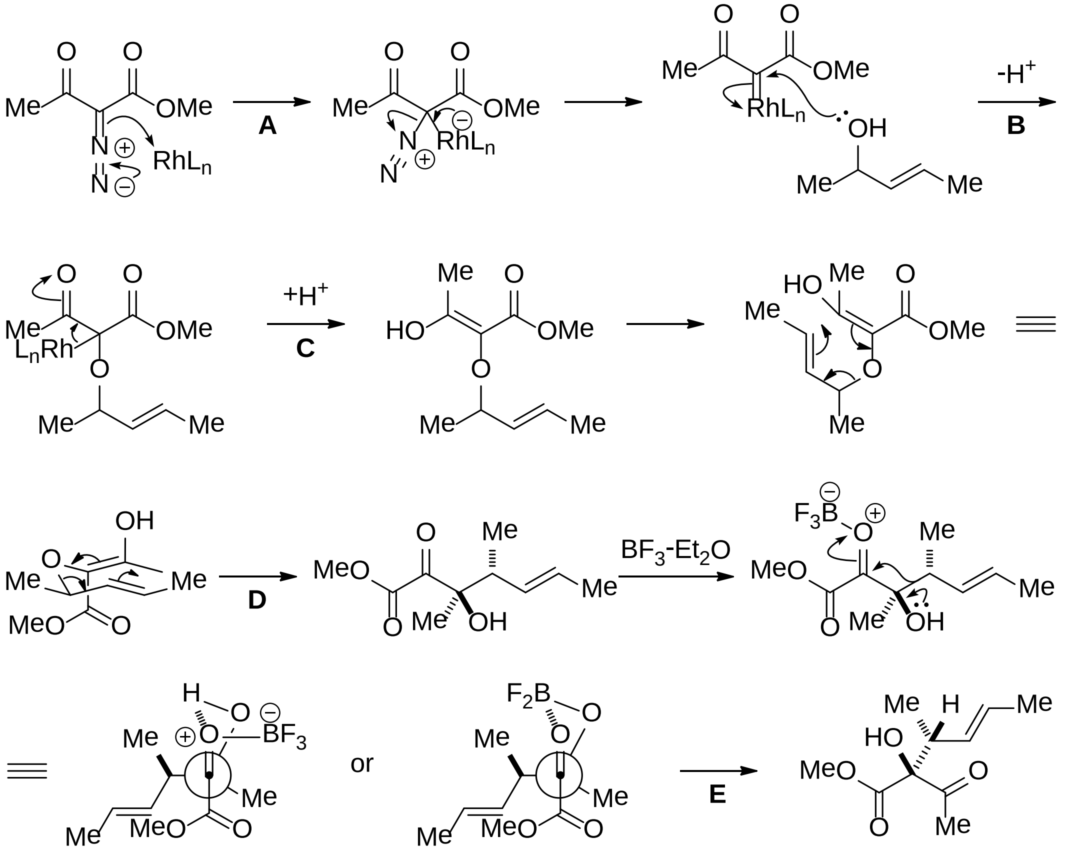
C074



Fang, F. G.; Prato, M.; Kim, G.; Danishefsky, S. J. *Tetrahedron Lett.* **1989**, 30, 3625.

A: Conjugate addition of a thiolactam anion. **B**: Formation of a rhodium carbene complex. **C**: Attack of the sulfur atom to the rhodium carbene complex followed by formation of a thiirane. **D**: Cleavage of the thiirane assisted by the nitrogen lone pair. **E**: Desulfurization.

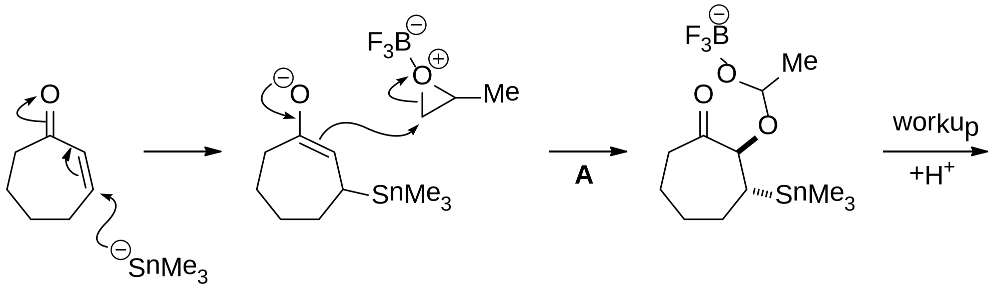
C075

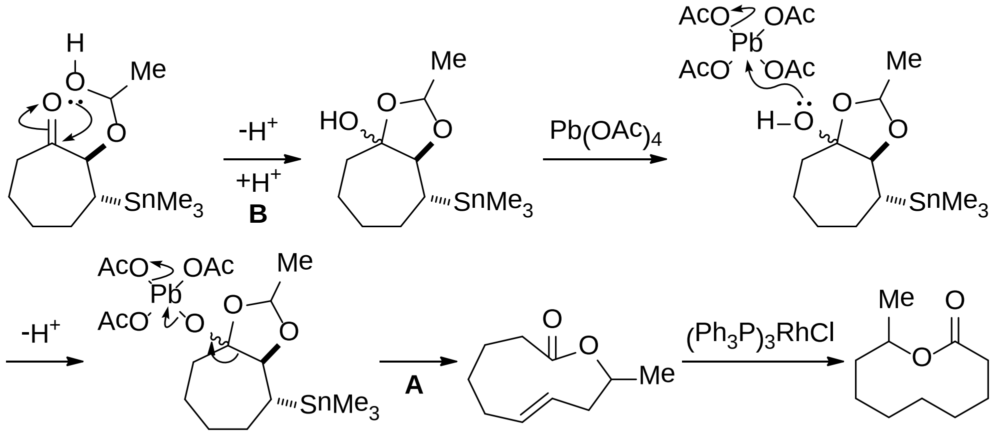


Drutu, I.; Krygowski, E. S.; Wood, J. L. *J. Org. Chem.* **2001**, 66, 7025.

A: Formation of a rhodium carbene complex. **B**: Addition of an alcohol to the carbene complex. **C**: Formation of an (Z)-enol. **D**: [3,3] Sigmatropic rearrangement via a chair-like transition state. **E**: 1,2-Migration through a synperiplanar transition state.

C076

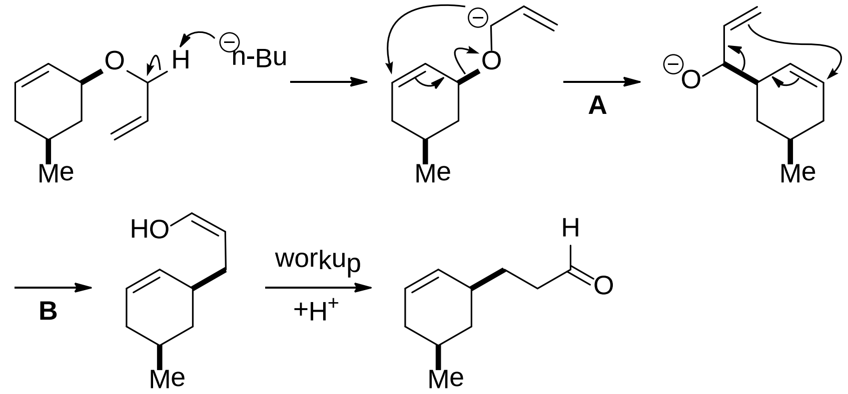




Posner, G. H.; Wang, Q.; Halford, B. A.; Elias, J. S.; Maxwell, J. P. *Tetrahedron Lett*. **2000**, 41, 9655.

A: Attack to the epoxide takes place from the less hindered side to form the trans-product. **B**: Formation of a hemiacetal. **C**: Oxidative fragmentation induced by $Pb(OAc)_4$.

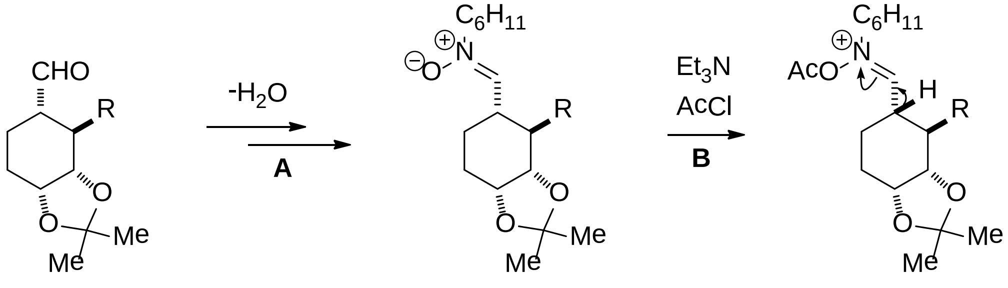
C077

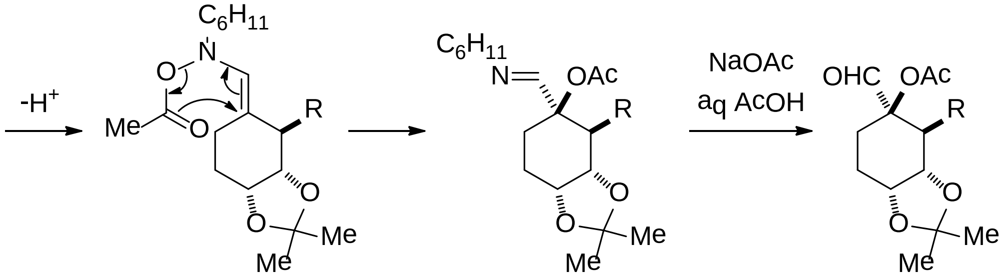


Sayo, N.; Kimura, Y.; Nakai, T. *Tetrahedron Lett*. **1982**, 23, 3931.

A: [2,3] Wittig rearrangement. **B**: Oxy-Cope rearrangement.

C078

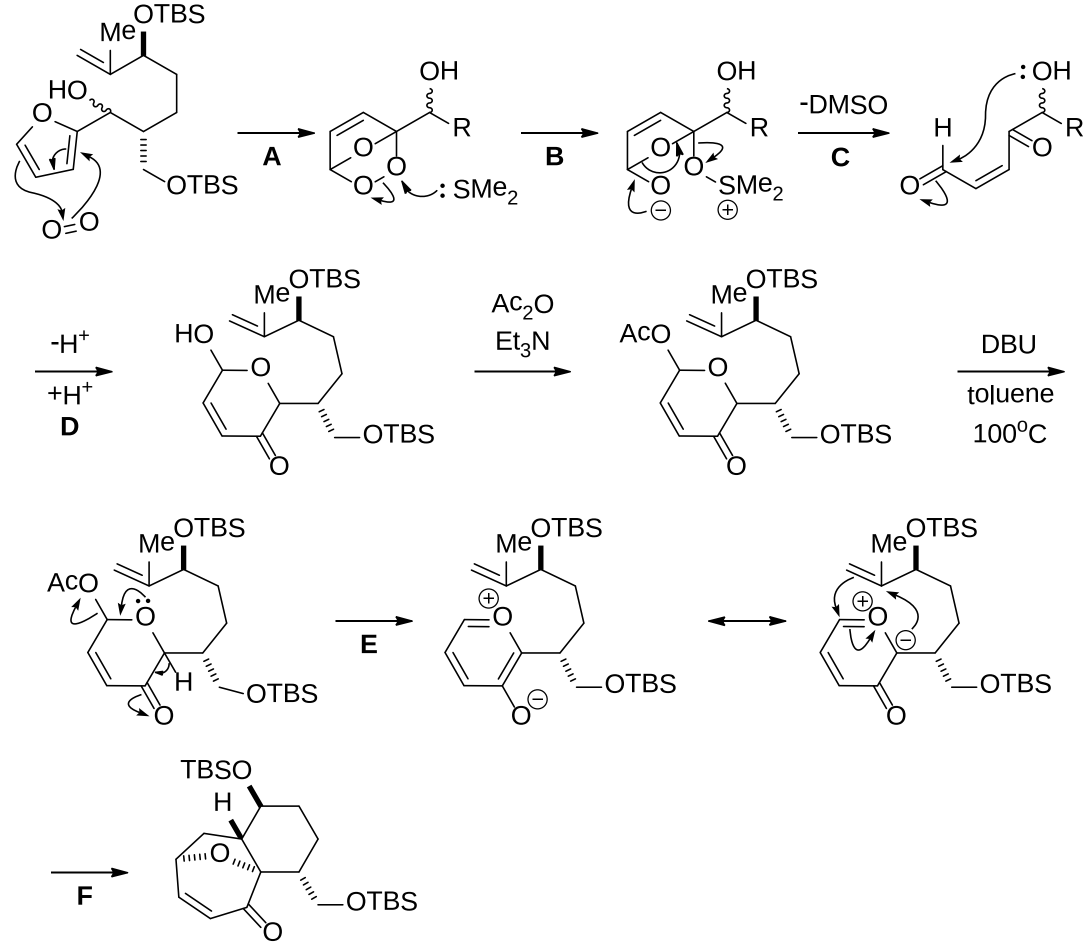




Vosburg, D. A.; Weiler, S.; Sorensen, E. J. *Angew. Chem. Int. Ed.* **1999**, 38, 971.

A: Formation of a nitrone. **B**: Acetylation followed by [3,3] sigmatropic rearrangement.

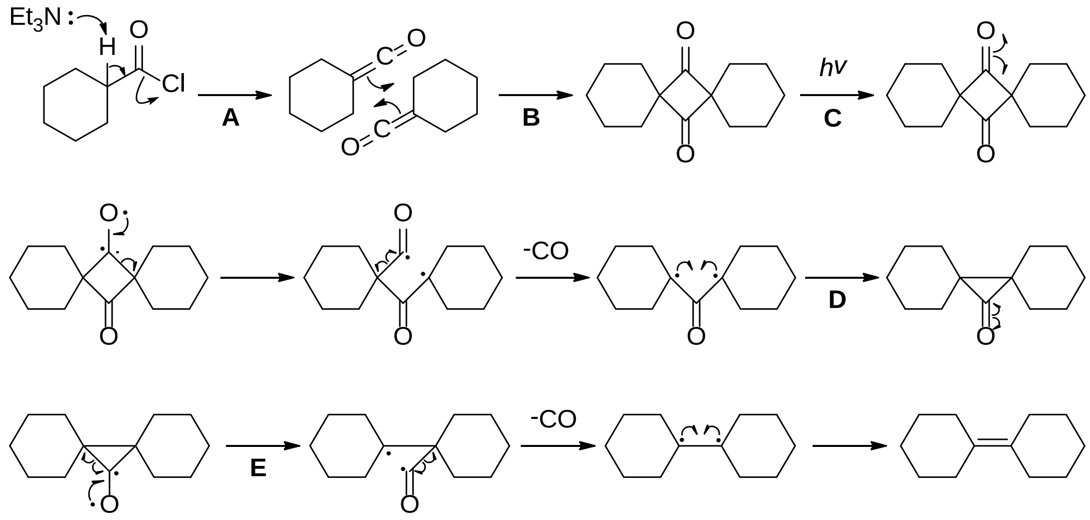
C079



Bauta, W. E.; Booth, J.; Bos, M. E.; DeLuca, M.; Diorazio, L.; Donohoe, T. J.; Frost, C.; Magnus, N.; Magnus, P.; Mendoza, J.; Pye, E; Tarrant, J. G.; Thom, S.; Ujjainwalla, F. *Tetahedron.* **1996**, 52, 14081.

Achmatowicz reaction (A-D). **A**: Diels-Alder reaction of singlet oxygen. **B**: Reductive cleavage of the endoperoxide with Me_2S. **C**: Elimination of DMSO to form cis-enal. **D**: Cyclization to form a lactol. **E**: Generation of a pyrylium ion (or a carbonyl ylide). **F**: 1,3-Dipolar cycloaddition.

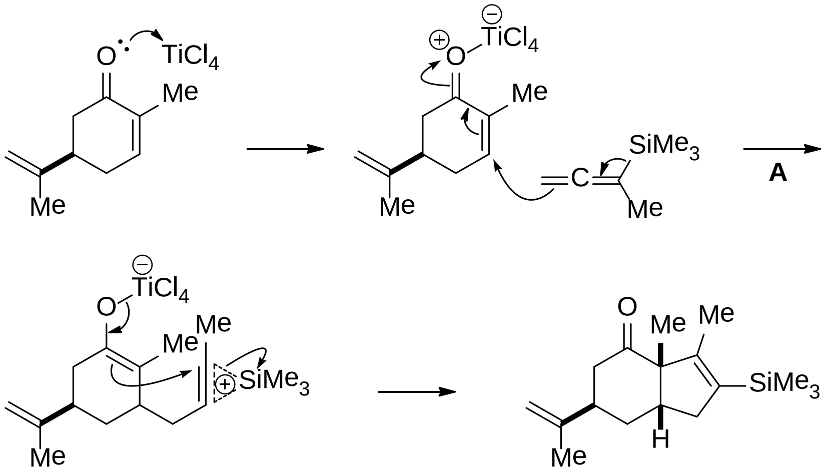
C080



Turro, N. J.; Leermakers, P. A. Vesley, G. E *Org. Synth., Coll.* Vol Ⅴ **1973**, 297

A: Formation of a ketene. **B**: [2+2] Head-to-tail dimerization of a hindered ketene. **C**: Norrish type I cleavage of the ketone followed by decarbonylation to form a diradical. **D**: Recombination of the diradical.

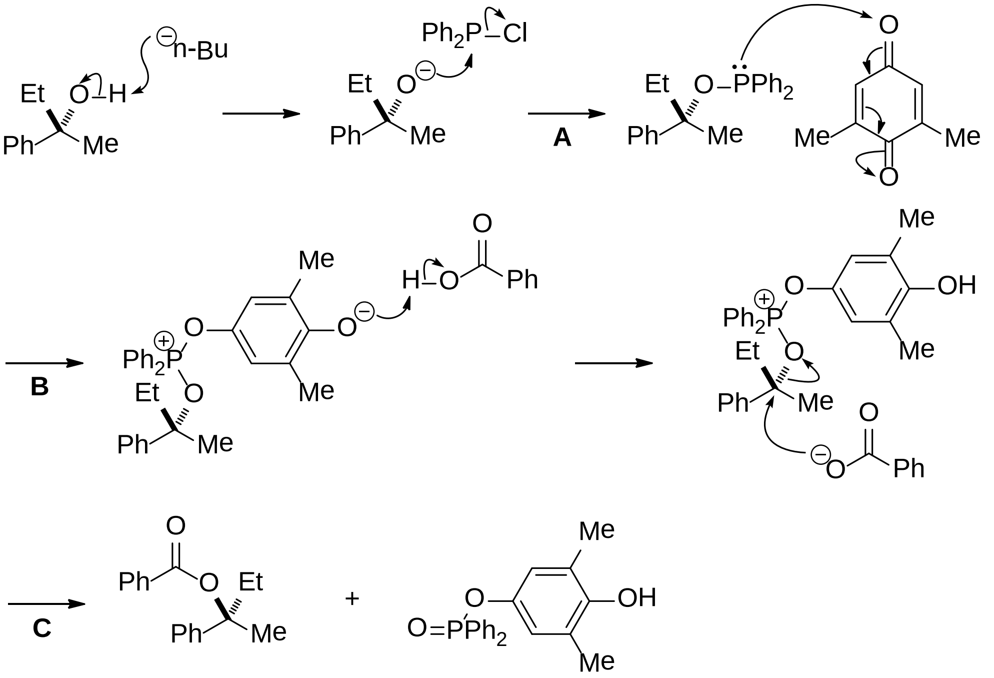
C081



Danheiser, R. L.; Fink, D. M.; Tsai, Y.-M. *Org. Synth., Coll.* Vol. Ⅷ **1993**, 347.

Danheiser annulation. **A**: Conjugate addition of the allenylsilane to form a carbocation stabilized by the silicon atom.

C082

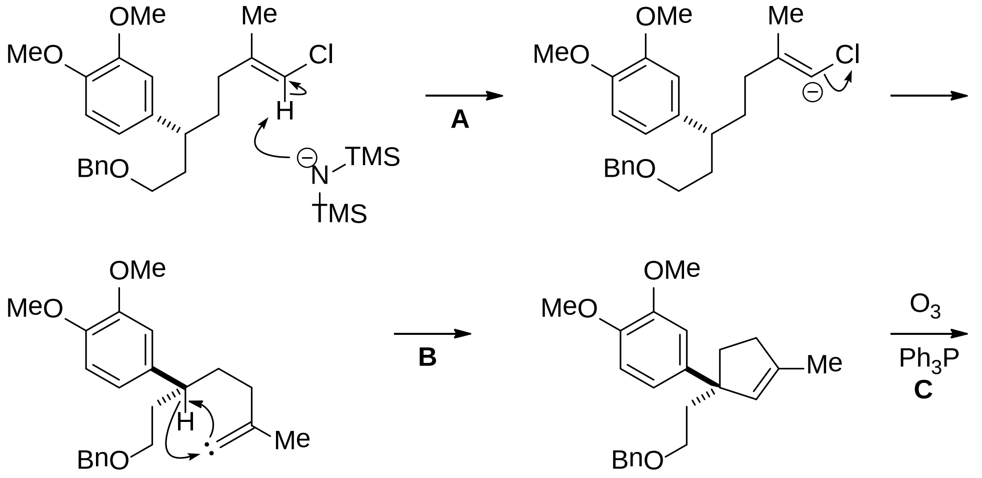


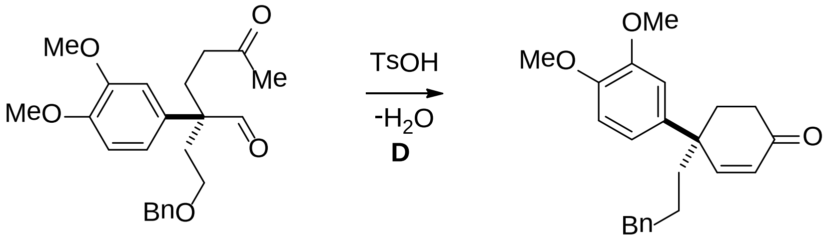
Mukaiyama, T.; Shintou, T.; Fukumoto, K. *J. Am. Chem. Soc.* **2003**, 125, 10538.

A: Formation of a phosphinite ester. **B**: Addition of the phosphinite to the electron-deficient quinone.

C: S_N2 reaction with inversion of configuration.

C083

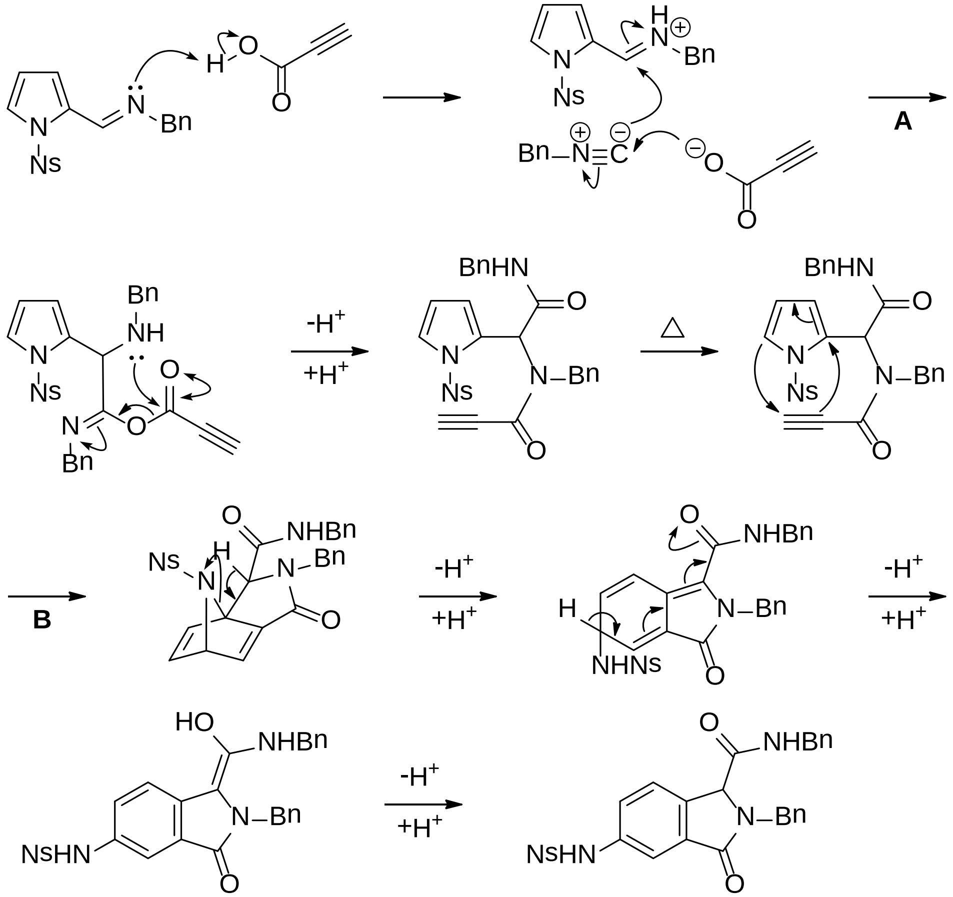




Taber, D. E; Neubert, T. D. *J. Org. Chem.* **2001**, 66, 143.

A: α-Elimination to form an alkylidene carbene. B: C-H insertion at the kinetically favored position. **C**: Ozonolysis. **D**: Intramolecular aldol reaction.

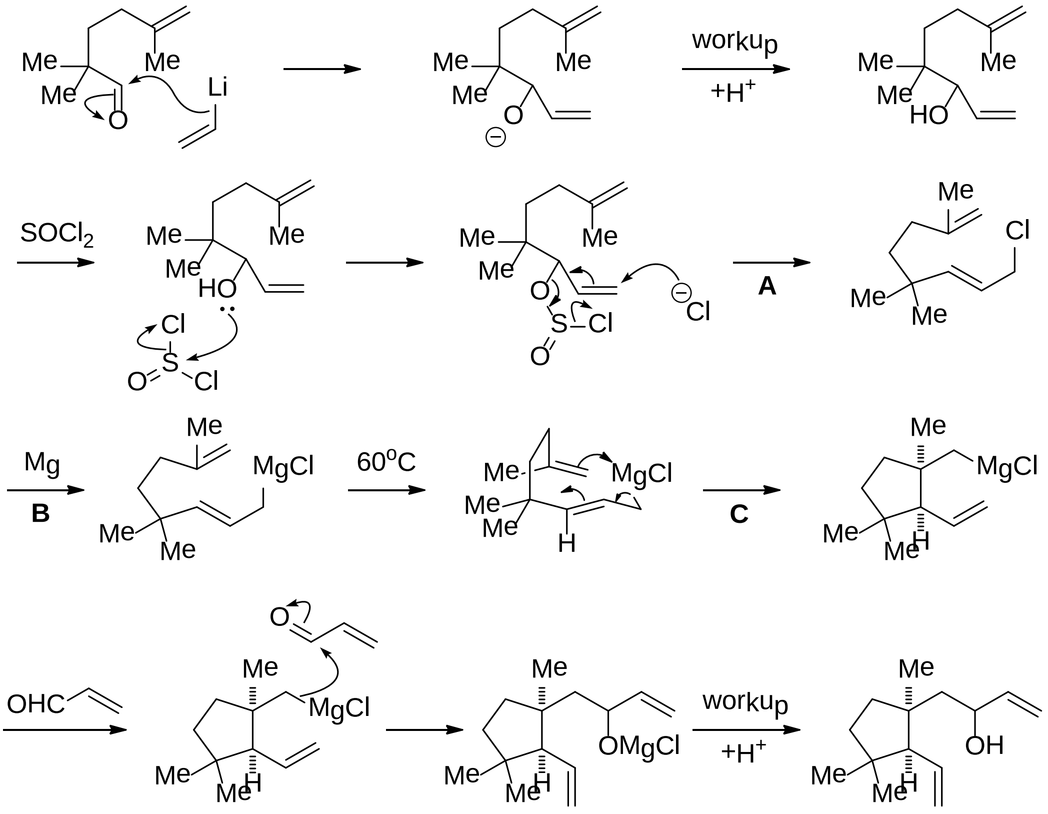
C084



Paulvannan, K. *J. Org. Chem.* **2004**, 69, 1207

A: Ugi reaction (ref C007). **B**: Intramolecular Diels-Alder reaction followed by β-elimination to release the ring strain.

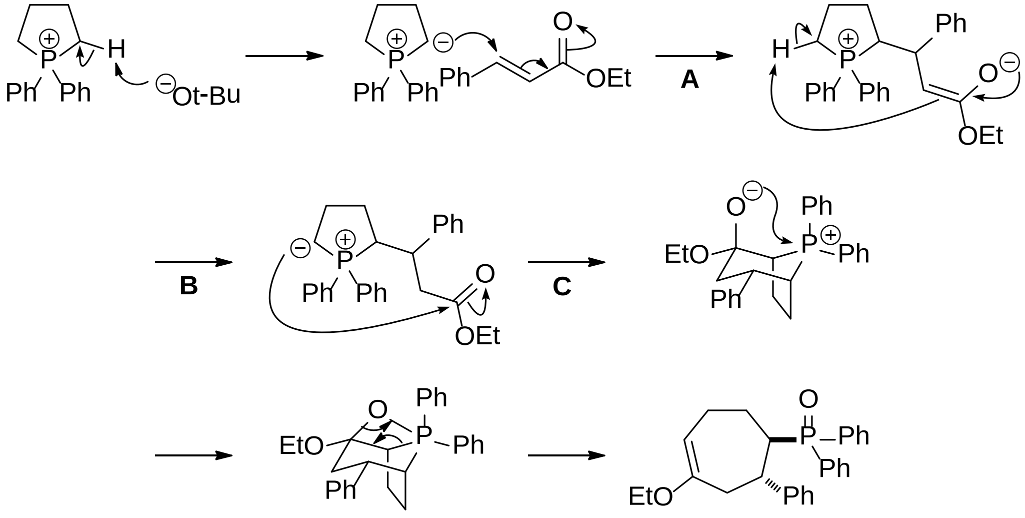
C085



Oppolzer, W.; Bättig, K. *Tetrahedron Lett.* **1982**, 23, 4669.

A: Formation of an allyl chloride via S_N2' reaction. **B**: Formation of a Grignard reagent. **C**: Magnesium-ene reaction through a chair-like conformation.

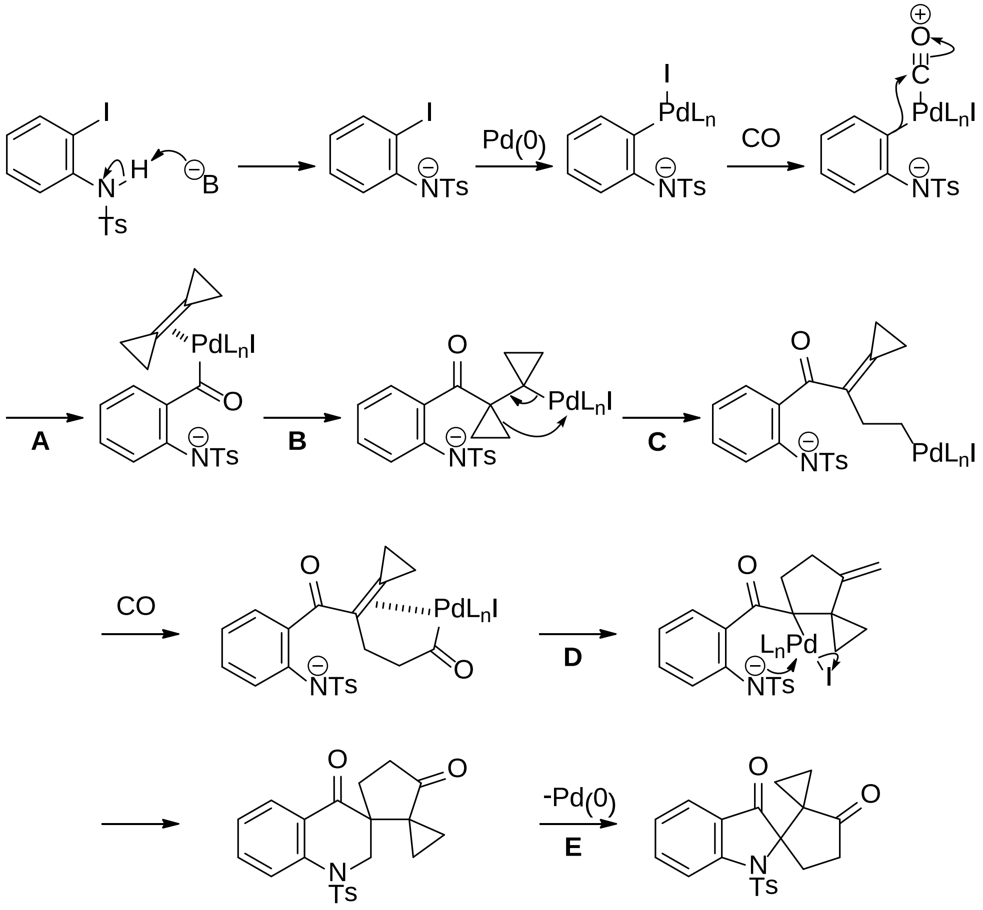
C086



Fujimoto, T.; Kodama, Y.; Yamamoto, I.; Kakehi, A. *J. Org. Chem.* **1997**, 62, 6627.

A: Conjugate addition of an ylide. **B**: Intramolecular proton transfer to generate an ylide. **C**: Intramolecular Wittig reaction.

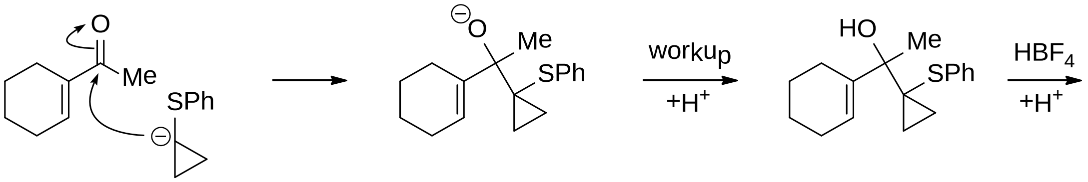
C087

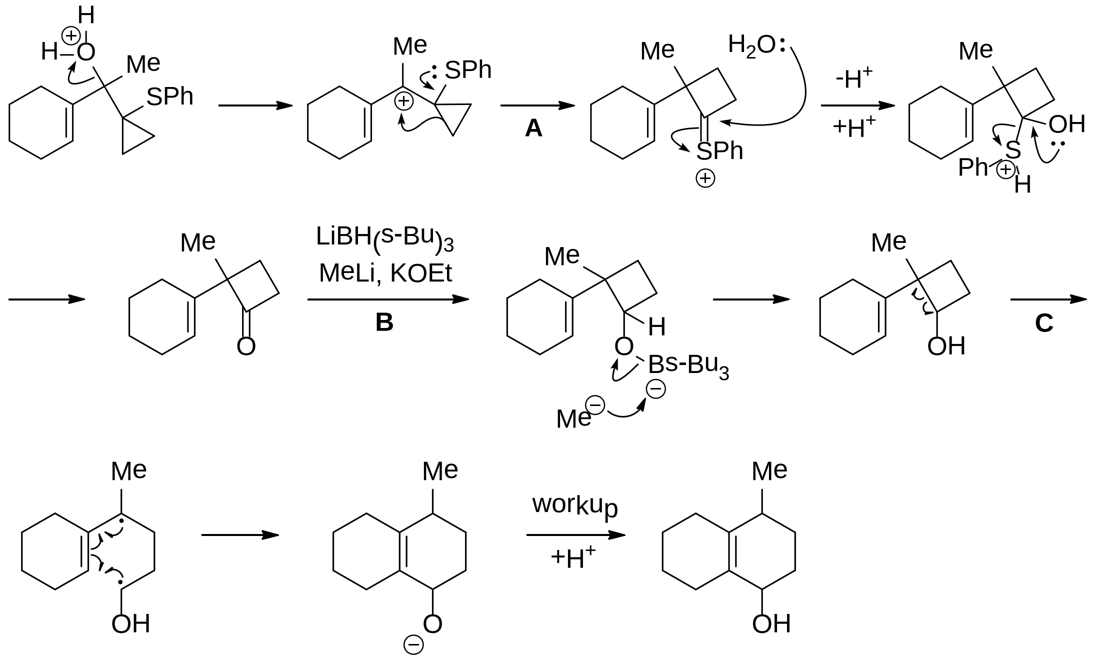


von Seebach, M.; Grigg, R.; de Meijere, A. Eur. *J. Org. Chem*. **2002**, 3268.

A: Pd-mediated carbonylation to form an acylpalladium species. **B**: Carbopalladation to a strained olefin. **C**: β-Carbon elimination. **D**: Intramolecular carbopalladation to the resulting strained olefin. **E**: Reductive elimination of the palladacycle.

C088

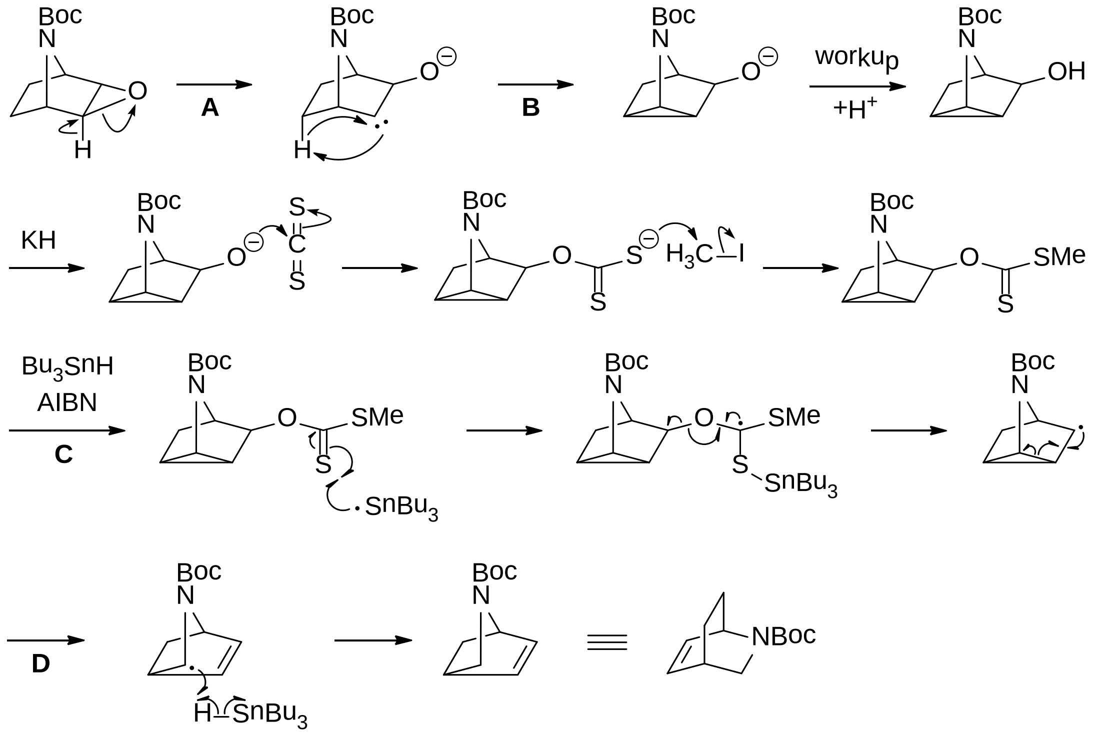




Danheiser, R. L.; Martinez-Davila, C.; Sard, H. *Tetrahedron*. **1981**, 37, 3943.

A: Pinacol-type rearrangement. **B**: Reduction of the ketone. **C**: Anion-accelerated vinylcyclobutane-cyclohexene rearrangement.

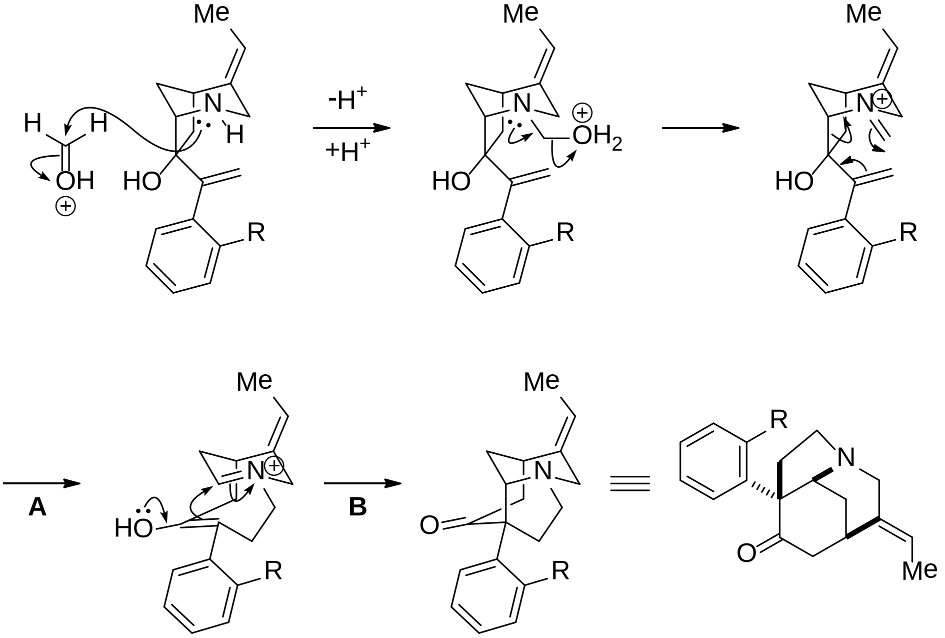
C089



Hodgson, D. M.; Maxwell, C. R.; Wisedale, R.; Matthews, I. R.;
Carpenter, K. J,; Dickenson, A. H.; Wonnacott, S.
J. Chem. Soc., Perkin Trans. 1 . **2001**, 3150.

A: α-Elimination of the epoxide to form a carbene. **B**: C-H insertion. **C**: Barton-McCombie deoxygenation of a xanthate (ref A051). **D**: Formation of a radical at a cyclopropylcarbinyl position induces cleavage of the cyclopropane ring (cf. radical clock).

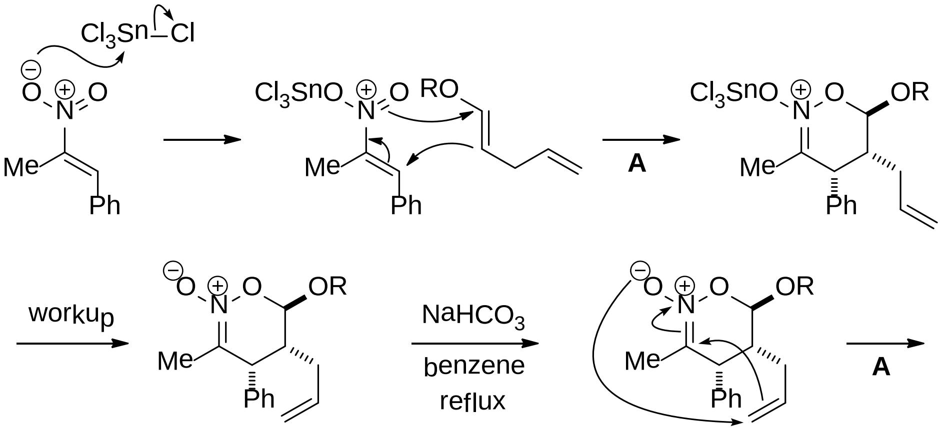
C090

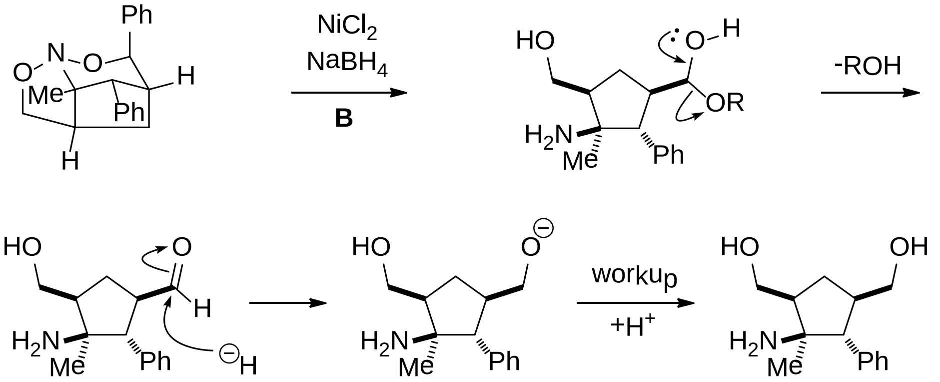


Angle, S. R.; Fevig, J. M.; Knight, S. D.; Marquis, R. W., Jr.; Overman, L. E
J. Am. Chem. Soc. **1993**, 115, 3966

A: Aza-Cope rearrangement. **B**: Mannich reaction.

C091

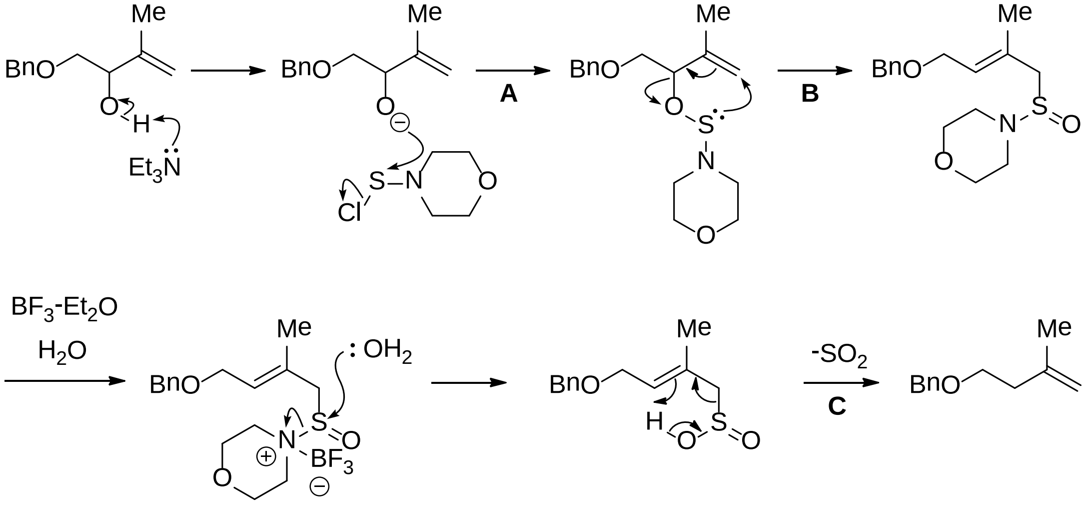




Denmark, S. E.; Dixon, J. A. *J. Org. Chem*. **1998**, 63, 6178.

A: Inverse electron demand hetero-Diels-Alder reaction. **B**: 1,3-Dipolar cycloaddition. **C**: Reductive cleavage of the N-O bonds.

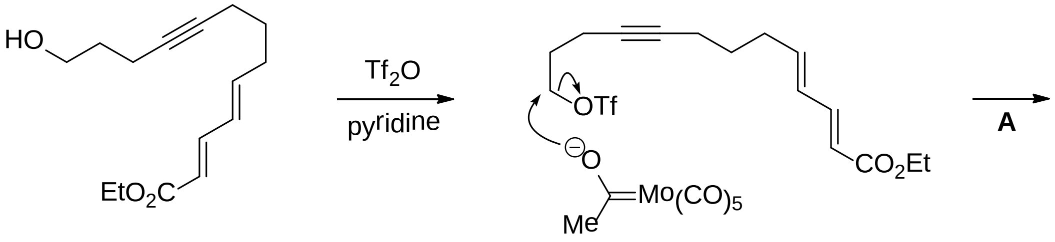
C092

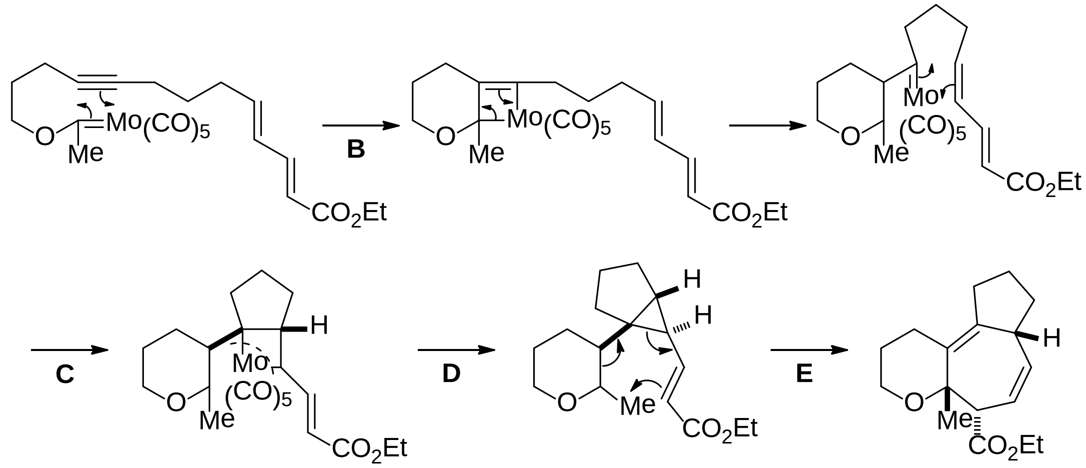


Baudin, J.-B.; Julia, S. A. *Tetrahedron Lett.* **1988**, 29, 3251.

A: Formation of a morpholinesulfenate. **B**: [2,3] Sigmatropic rearrangement. **C**: Extrusion of SO_2 through a six-membered transition state.

C093

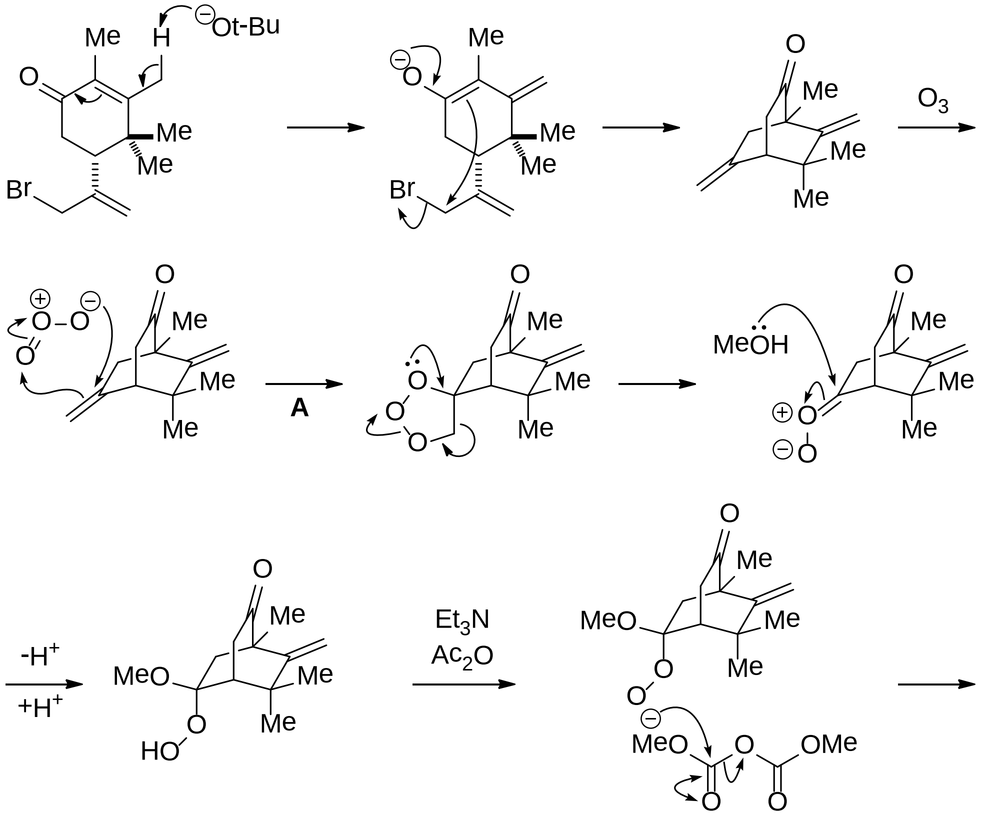


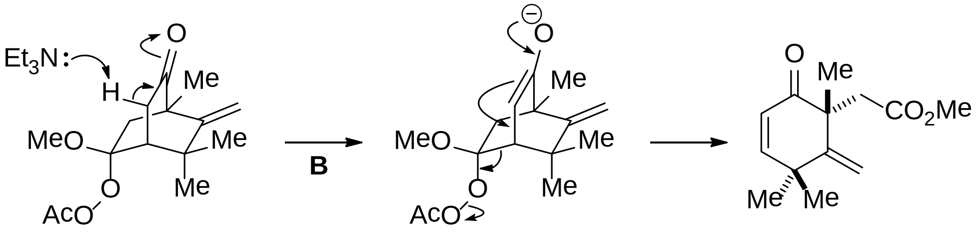


Harvey, D. E; Brown, M. F. *J. Org. Chem*. **1992**, 57, 5559.

A: Formation of a Fischer carbene complex. **B**: Intramolecular alkyne metathesis. **C**: Intramolecutar alkene metathesis. **D**: Reductive elimination to form a cyclopropane. **E**: Divinylcyclopropane rearrangement (ref A042) via a boat-like transition state.

C094

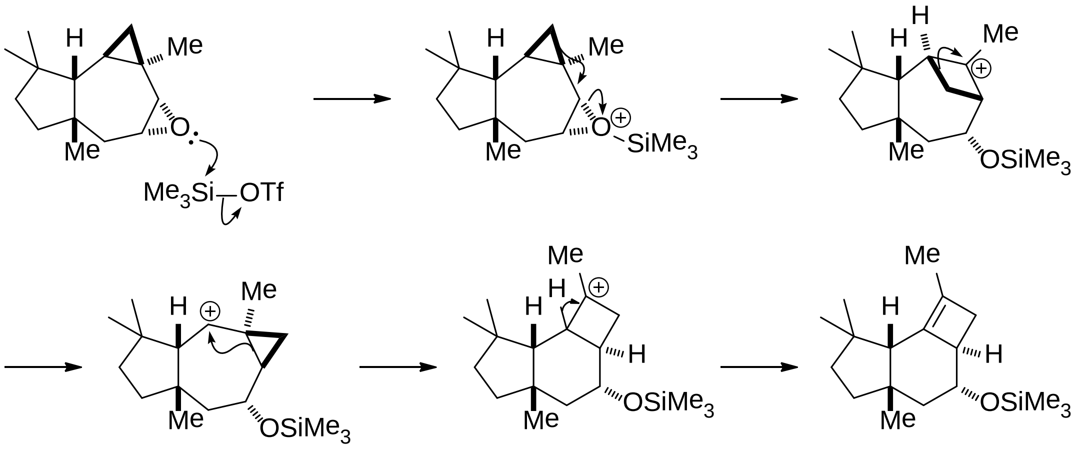




Srikrishna, A.; Anebouselvy, K.; Reddy, T. J. *Tetrahedron Lett.* **2000**, 41, 6643.

A: Ozonolysis of the less hindered olefin in MeOH to form a hydroperoxide (ref BI16, BI17). **B**: Grob-type fragmentation.

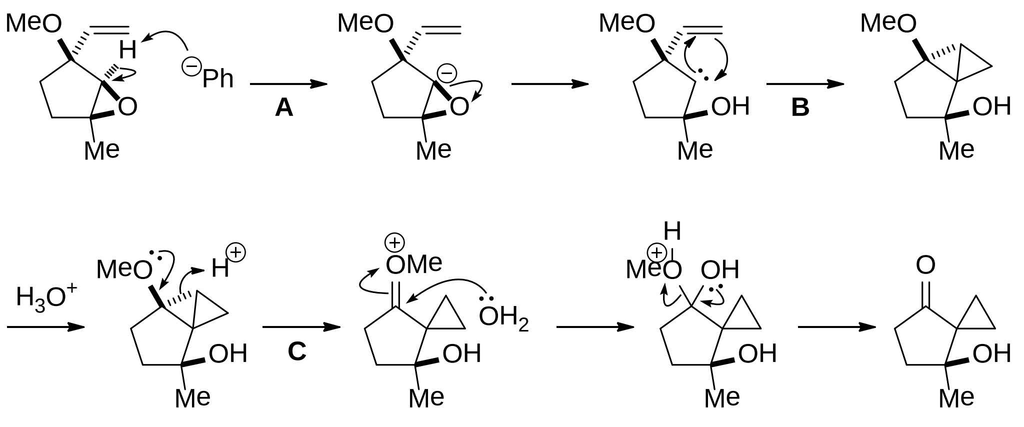
C095

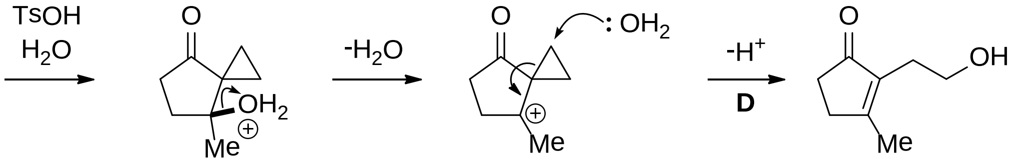


Fujita, T.; Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1982**, 23, 4091

Wagner-Meerwein rearrangements.

C096

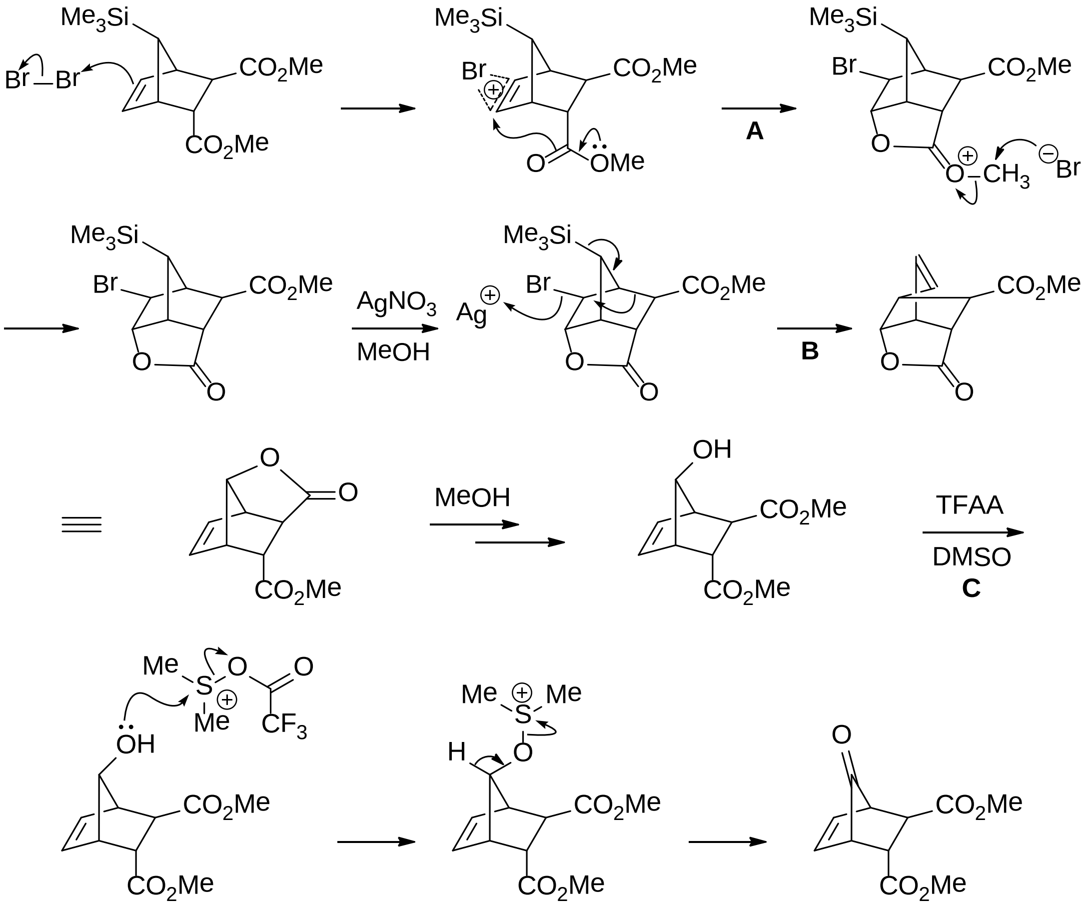




Dechoux, L.; Agami, C.; Doris, E.; Mioskowski, C. *Eur. J. Org. Chem*. **2001**, 4107.

A: α-Elimination of the epoxide to form a carbene. **B**: Cyclopropanation. **C**: Cleavage of the electron-rich cyclopropane ring. **D**: Cleavage of the cyclopropane ring.

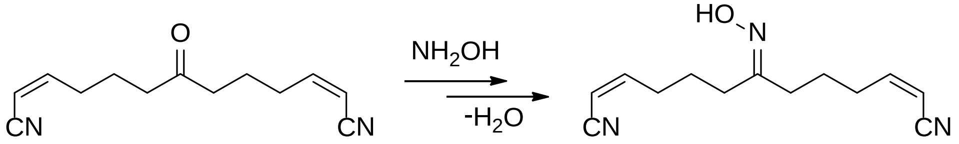
C097

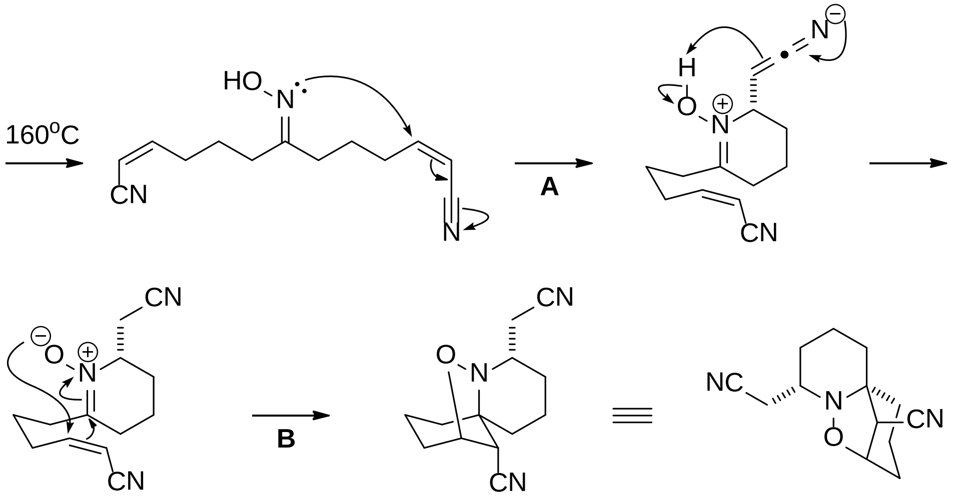


Fleming, I.; Michael, J. P. *J. Chem. Soc., Perkin Trans 1* .**1981**, 159.

A: Bromolactonization. **B**: Wagner-Meerwein rearrangement followed by desilylation. **C**: Swern oxidation.

C098



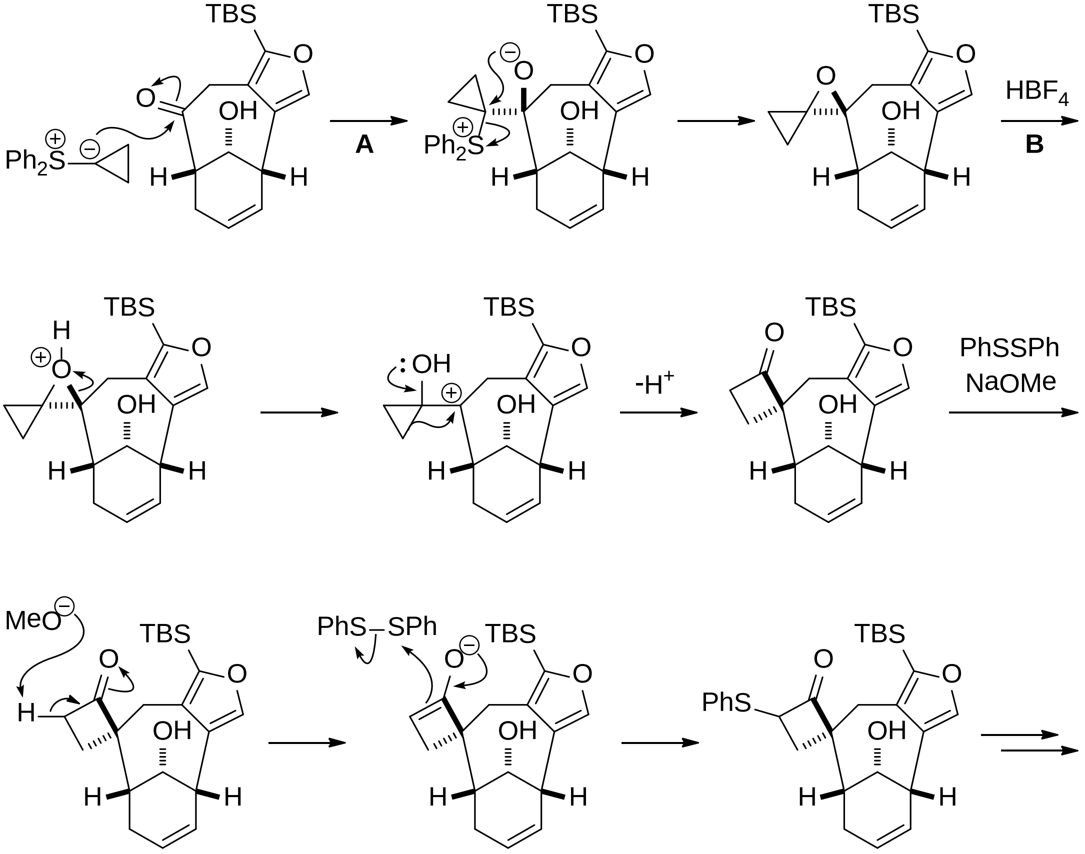


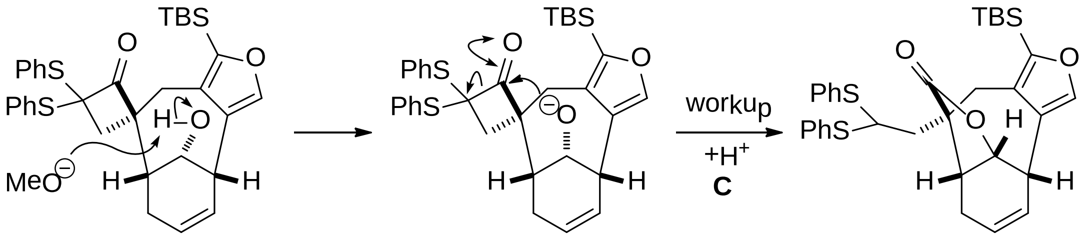
Stockman, R.A. *Tetrahedron Lett.* **2000**, 41, 9163.

A: Formation of a nitrone by intramolecular Michael addition of the oxime to the α,β-unsaturated nitrile.

B: Intramolecular 1,3-dipolar cycloaddition.

C099

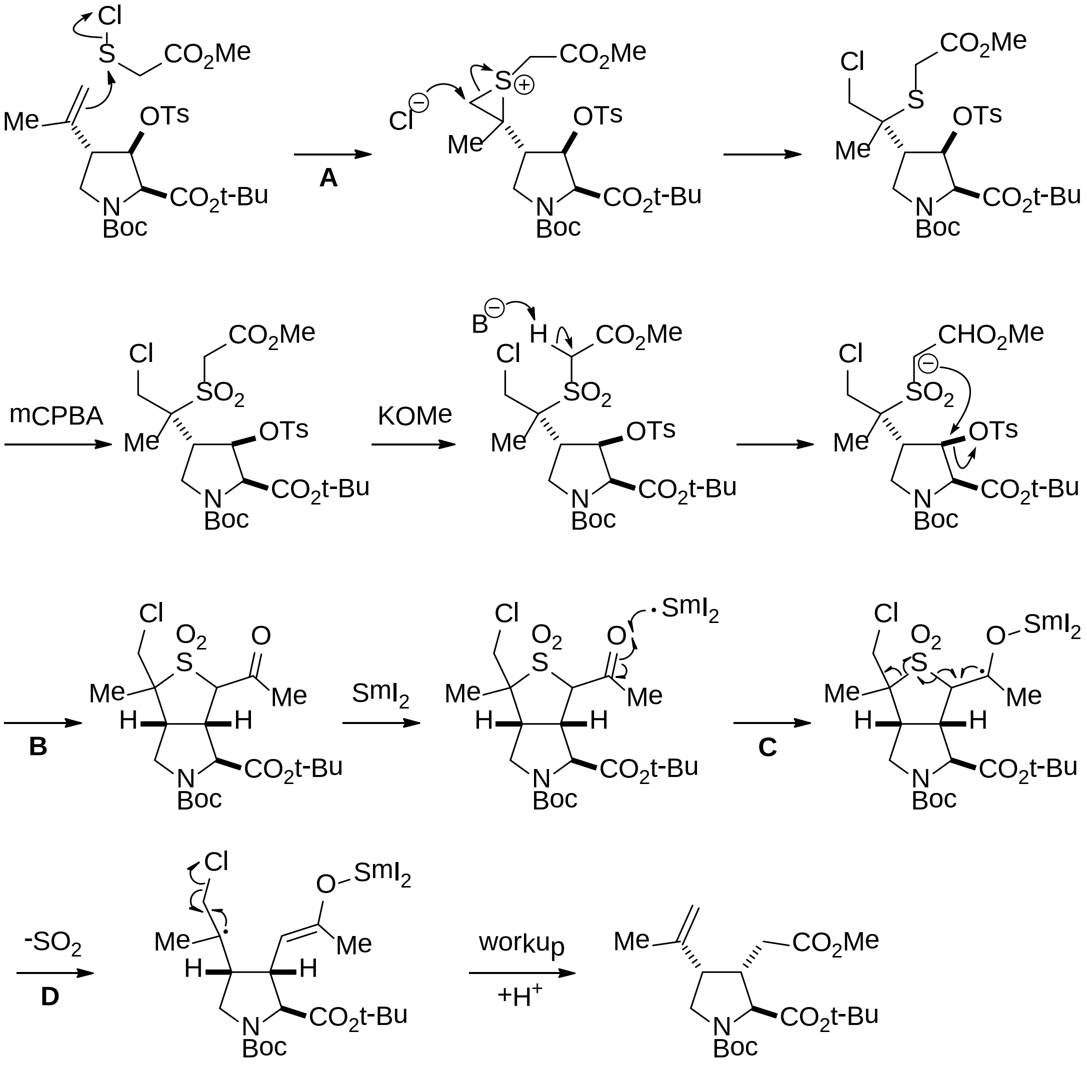




Kwon, O.; Su, D.-S.; Meng, D.; Deng, W.; D'Amico, D. C.; Danishefsky, S. J.
Angew. Chem. Int. Ed. **1998**, 37, 1880.

A: 1,2-Addition of the sulfur ylide followed by formation of an epoxide in an S_N2 fashion. **B**: Cleavage of the epoxide induces 1,2-migration to form a cyclobutanone via a stable tertiary carbocation. **C**: Ring opening of the cyclobutanone by the proximal alkoxide is facilitated by formation of the sulfur-stabilized carbanion.

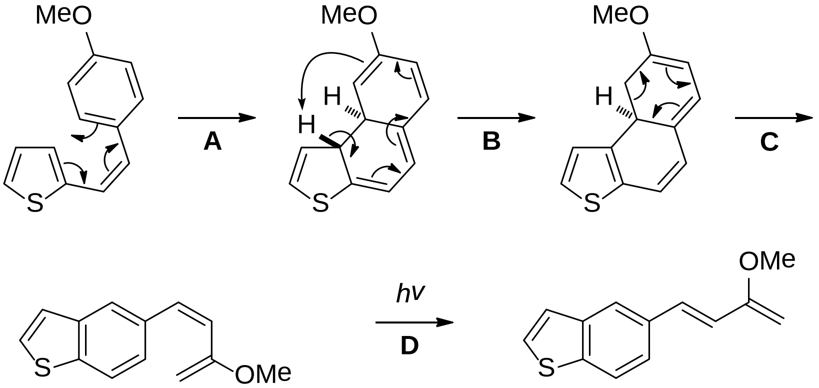
C100



Bachi, M. D.; Melman, A. *J. Org. Chem.* **1997**, 62, 1896.

A: Formation of an episulfonium salt followed by attack of chloride ion at the less hindered carbon. **B**: Cyclization proceeds by an S_N2 mechanism. **C**: SET. **D**: β-Cleavage followed by extrusion of SO_2 and elimination of a chloride radical.

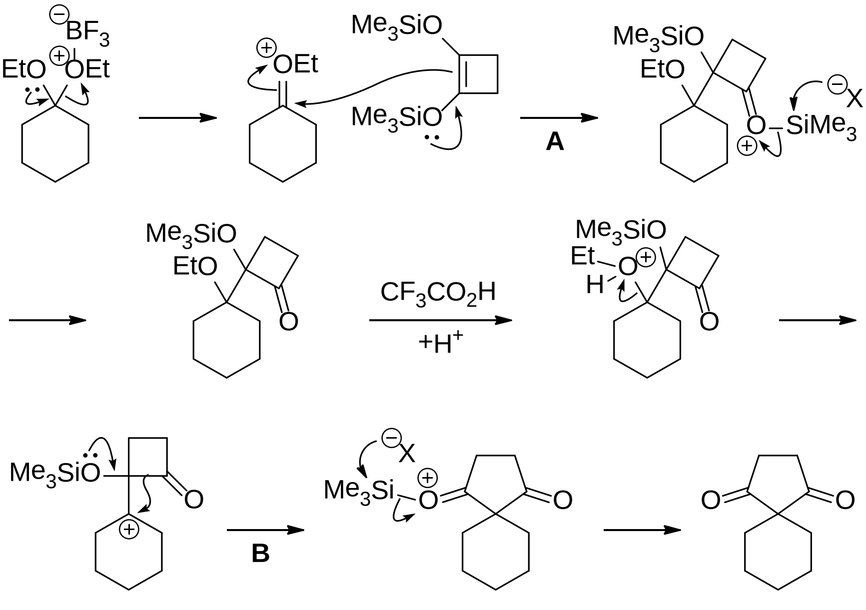
C101



Wu, J.-Y.; Ho, J.-H.; Shih, S.-M.; Hsieh, T.-L.; Ho, T.-I. *Org. Lett.* **1999**, 1, 1039.

A: Photo-induced 6e conrotatory etectrocyclic reaction. **B**: Thermally allowed suprafacial 1,9-hydrogen shift. **C**: 6e Electrocyclic reaction. **D**: Photoisomerization of the (Z)-olefin.

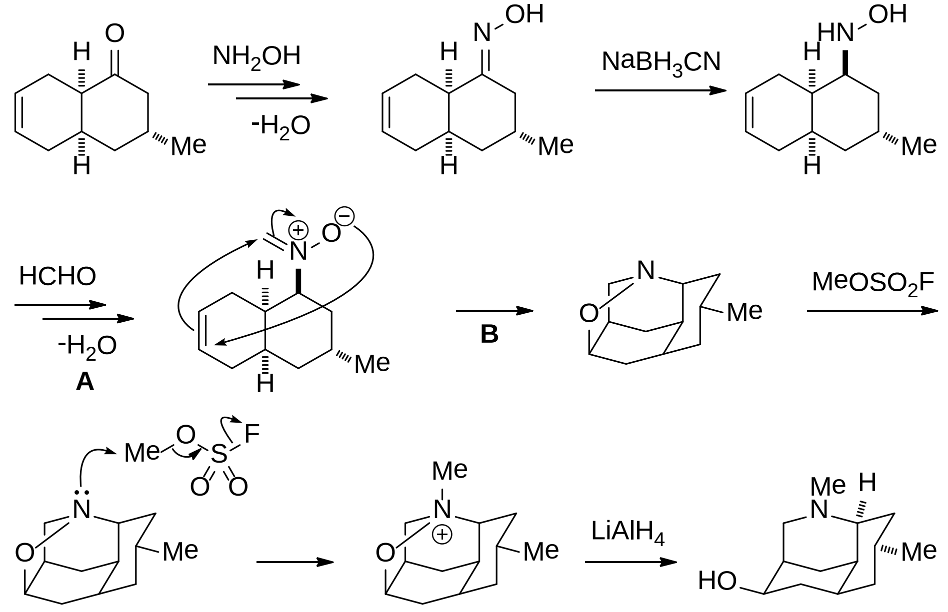
C102



Nakamura, E.; Kuwajima, I. *Org. Synth., Coll.* Vol. Ⅷ **1987**, 17.

A: Mukaiyama aldol reaction. **B**: Preferential migration of the carbonyl carbon (Pinacol rearrangement).

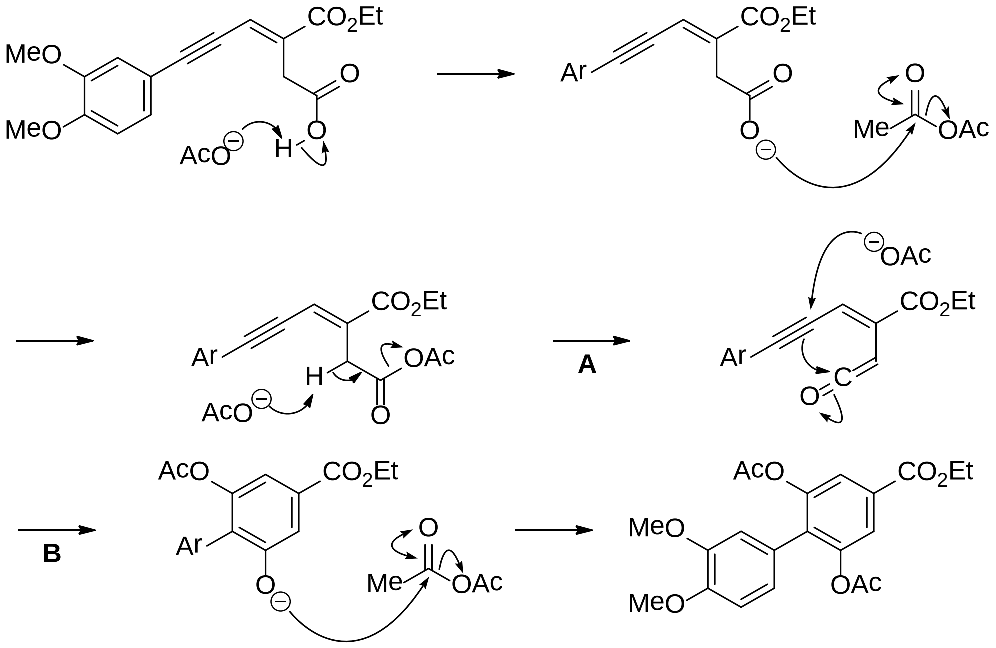
C103

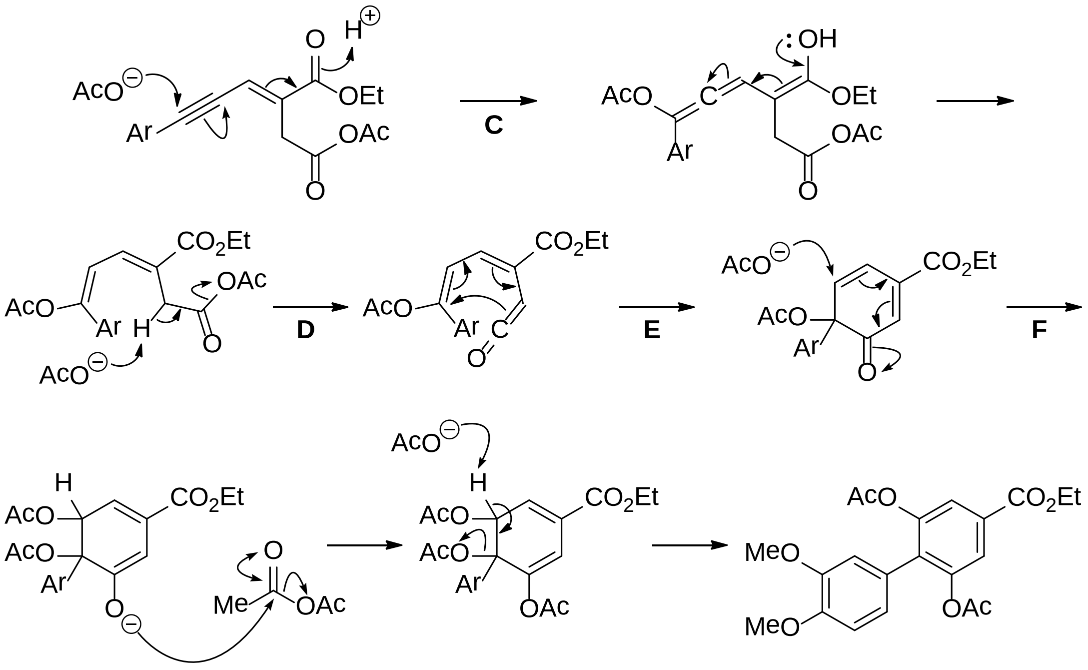


Oppolzer, W.; Petrzilka, M. *J. Am. Chem. Soc.* **1976**, 98, 6722.

A: Formation of a nitrone ref A065. **B**: 1,3-Dipolar cycloaddition.

C104

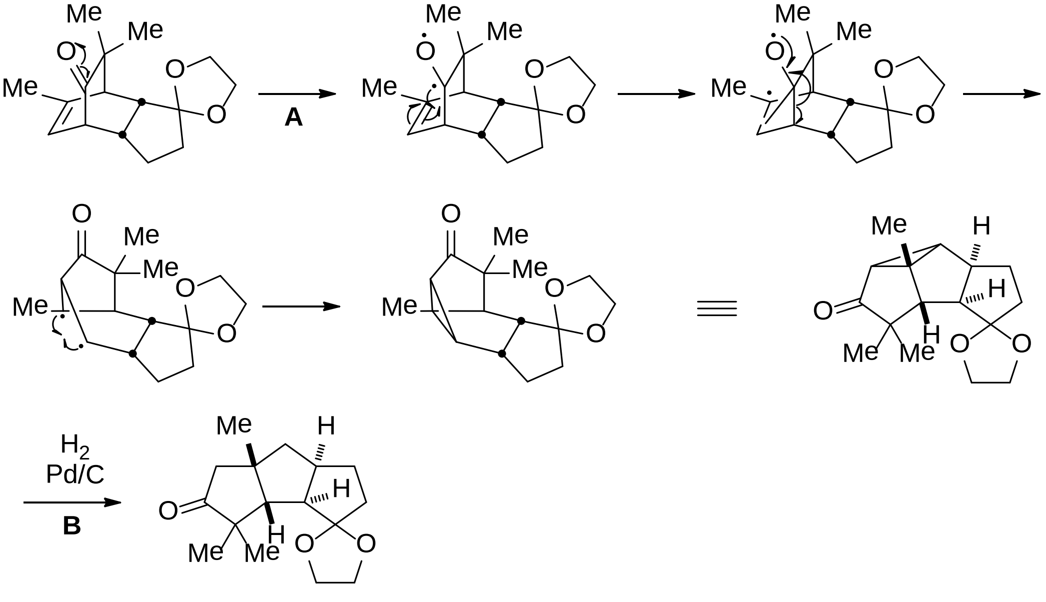




Serra, S.; Fuganti, C. *Synlett.* **2002**, 1661.

A: Generation of a ketene via a mixed anhydride. **B**: Benzannulation. **C**: Michael addition. **D**: Formation of a ketene. **E**: 6e Electrocyclic reaction. **F**: Michael addition.

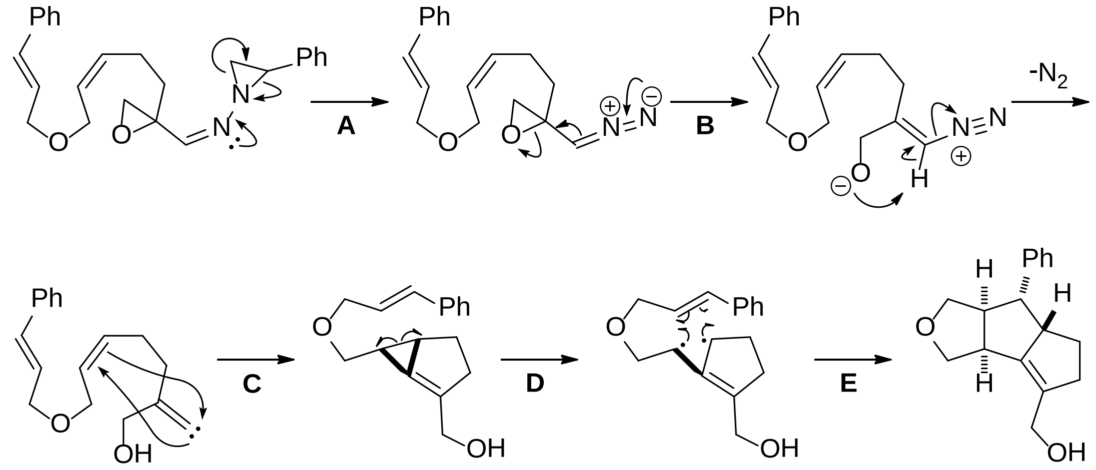
C105



Singh, V.; Prathap, S.; Porinchu, M. *J. Org. Chem.* **1998**, 63, 4011.

Oxa-di-π-methane rearrangement. **A**: n-π* Transition. **B**: Reductive cleavage of the cyclopropane ring.

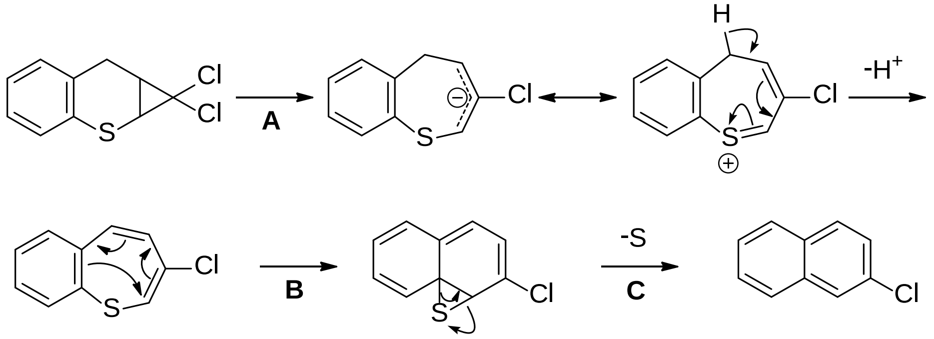
C106



Lee, H.-Y; Kim, Y. *J. Am. Chem. Soc.* **2003**, 125, 10157.

A: Thermal decomposition of an aziridinylimine to form a diazoalkane. **B**: Cleavage of the epoxide followed by elimination of N_2 to form an alkylidene carbene. **C**: Cyclopropanation. **D**: Homolytic cleavage of the strained cyclopropylidene ring to form a trimethylenemethane diradical. **E**: Radical addition.

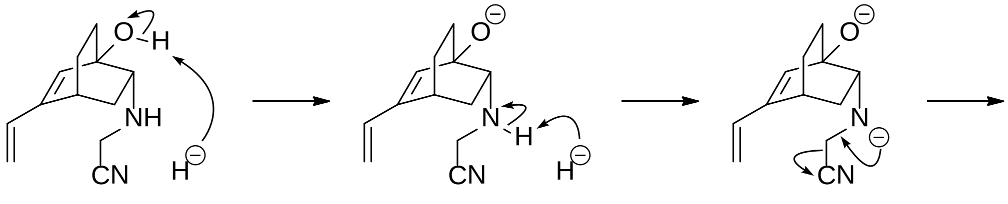
C107

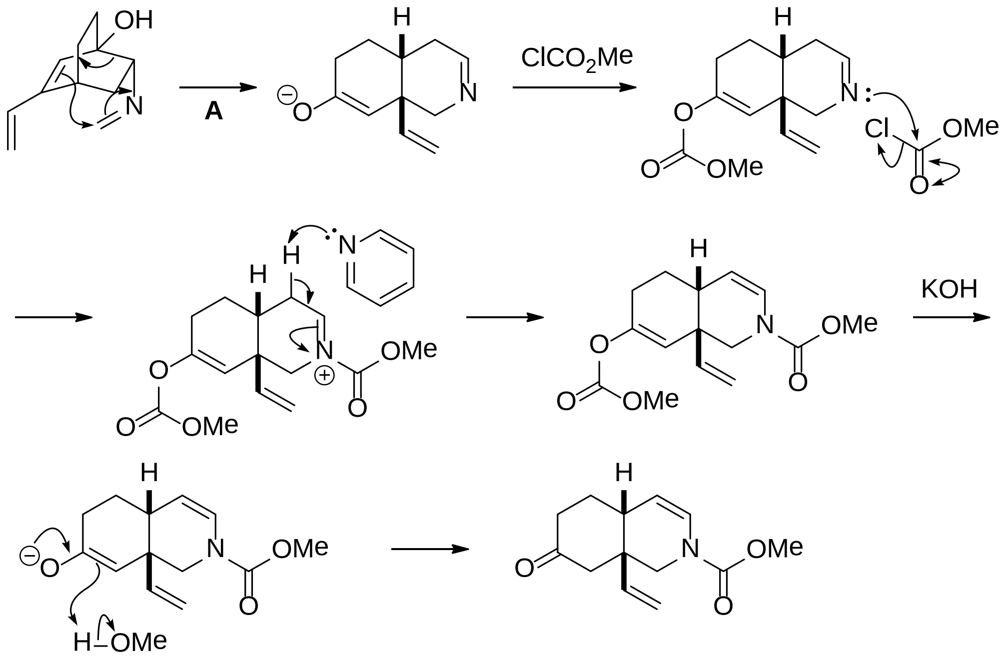


Parham, W. E.; Koncos, R. *J. Org. Chem.* **1961**, 83, 4034.

A: 2e Electrocyclic reaction. **B**: 6e Disrotatory electrocyclic reaction. **C**: Spontaneous loss of S.

C108

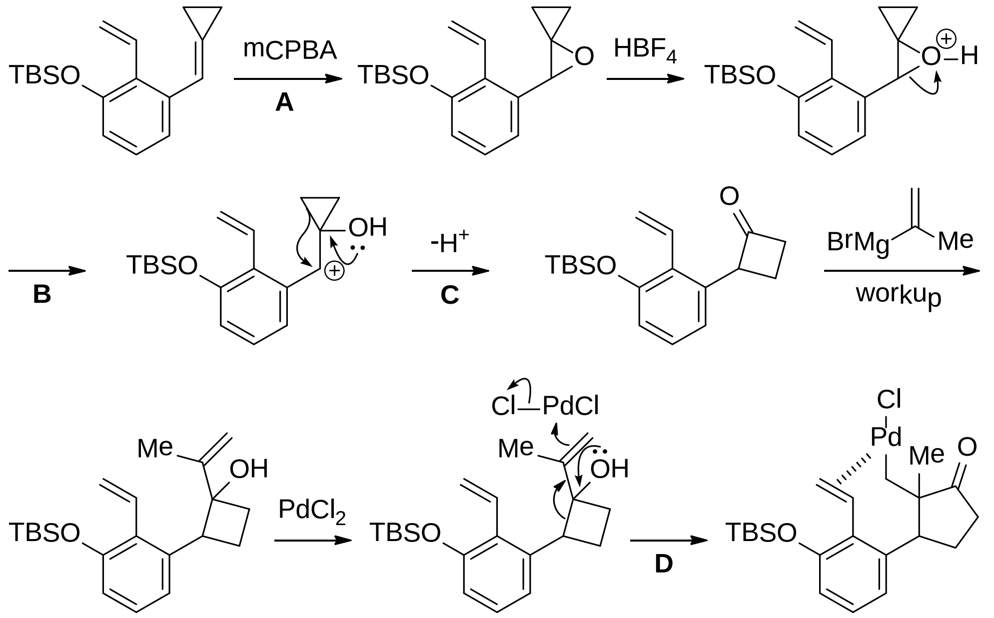


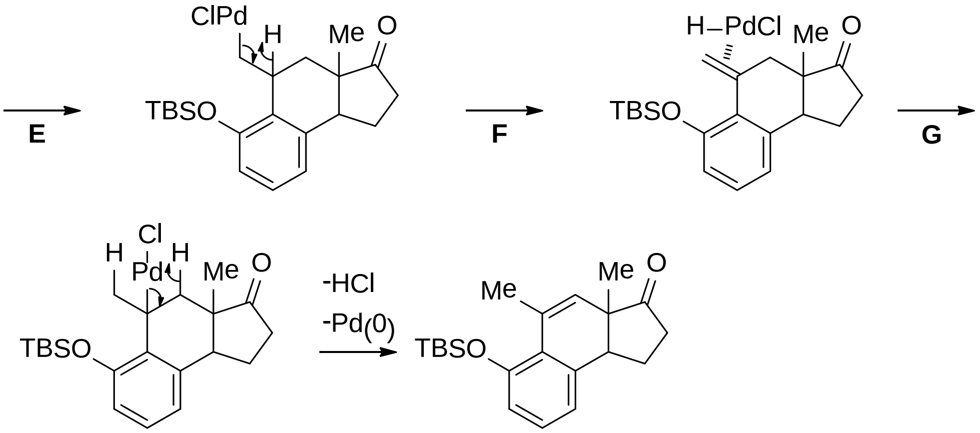


Earley, W. G.; Jacobsen, E. J.; Meier, G. P.; Oh, T.; Overman, L. E.
Tetrahedron Lett. **1988**, 29, 3781.

A: Anion-accelerated aza-Cope rearrangement.

C109





Nemoto, H.; Miyata, J,; Yoshida, M.; Raku, N.; Fukumoto, K. *J. Org. Chem*. **1997**, 62, 7850.

A: Epoxidation of the strained olefin. **B**: Cleavage of the epoxide to form a stable benzylic cation. **C**: 1,2-Migration to form a cyclobutanone (ref A099). **D**: Ring expansion reaction initiated by oxidation of the olefin with $PdCl_2$. **E**: Intramolecular carbopalladation. **F**: β-Elimination. **G**: Reversible hydropalladation and 6-elimination process to give the more stable endocyclic olefin.

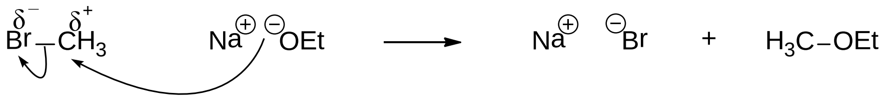
付　録

有机反応の反応機構を考えるにあたって

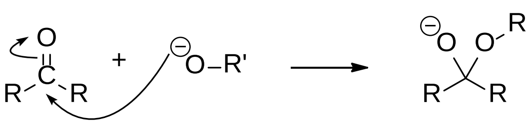
1．反応機構を考えるうえで重要な電気陰性度

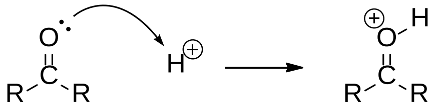
有机反応は，その反応様式によって極性反応，ラジカル反応，ペリ環状反応などに分類されるが，その多くの部分を占める極性反応においては，反応系中の電子の豊富な部位と，電子の不足な部位とが引き寄せ合い，結合の生成，切断が繰り返されながら反応が進行する．そこに介在しているのは電子であり，反応机构を考えるときに，それらの電子の动きを「曲がった矢印」を用いて表す．

電子は電子の豊富な部位から電子の不足な部位へと移動していく．そこで，どのように電子が動くかを考える＊つの手がかりとなるのが電気陰性度である．電気陰性度とは結合中の電子を引きつける固有の性質の尺度である．その値が大きいほど電子を引きつける力が強い（すなわち電気的に陰性になる）．たとえば臭化メチルを考えると，電子はより電気陰性度の大きい臭素原子上に引き寄せられ，炭素は部分的に正に荷電（δ^+）し，臭素原子ほ部分的に負に荷電（δ^-）することになる．この臭化メチルに＊し，ナトリウムエトキシド（NaOEt)を作用させると，負電荷をもっ酸素原子は，部分的な正電荷をもっ炭素原子に近づき，新たに酸素ー炭素结合が生成する．このとき臭化メチルの炭素ー臭素結合は切断され，その結合を形成していた電子対は臭素原子上に移動し，臭化物ィオンを生成する．



またカルポニル化合物の反応に関しては次のように考えることができる，カルボニル基はより電気陰性度の大きい酸素原子上に電子が引き寄せられ，炭素が δ^+，酸素が δ^- の部分的な電荷をもつ．カルボニル基に＊してアルコキシドのような電子を豊富にもつ求核基は，部分的な正電荷をもつ炭素原子に近づき，新たな結合を生成する．このとき炭素ー酸素三重结合を形成していたて电子は酸素原子上に移动する．一方，カルボニル化合物に対して塩酸のようなBrønsted酸を作用させると，正の電荷をもっプロトン（H^+）と，部分的な负電荷をもっ酸素原予の间で结合が生成してカチオンを生じる．このカチオンは，炭素ー酸素结合が大きく分極しており，求核基に対してより高い反応性をもつようになる．





このように化合物中の官能基の電荷を考え，最も反応性の高い部位どうしを反応させることが，反応機構を考える基本となる．

表①一般的な元素の電気陰性度

H						
2.1						
Li	Be	B	C	N	O	F
1.0	1.5	2.0	2.5	3.0	3.5	4.0
Na	Mg	Al	Si	P	S	Cl
0.9	1.2	1.5	1.8	2.1	2.5	3.0
K	Ca					Br
0.8	1.0					2.8
						I
						2.5

2. 酸解離定数 pKa から反応経路を予測

水溶液中で酸性化合物は次のように解離した状態にある．

$$\mathrm{HA} + \mathrm{H_2O} \rightleftharpoons \mathrm{A^-} + \mathrm{H_3O^+}$$

酸 HA に対してプロトンの解離した A$^-$を，HA の共役塩基とよぶ．このときその酸性度の目安として，酸解離定数がしばしば用いられる．希薄水溶液において，化合物の酸解離定数（PKa）は次のように定義される．

$$\mathrm{p}K_\mathrm{a} = -\log K_\mathrm{a} = \frac{\left[\mathrm{A^-}\right]\left[\mathrm{H_3O^+}\right]}{\left[\mathrm{HA}\right]}$$

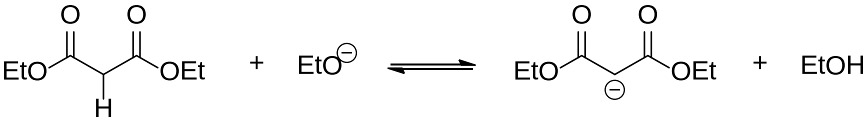
この定義によると，PK の値が小さいほどその酸性度は高くなる（平衡が右に偏る，プロトンを放出しやすい）．また塩基（B）の場合を考えると，その共役酸（HB$^+$）の pK$_a$ の値が大きいほど，その塩基性度は高くなる（平衡が左に偏る，プロトンを放しにくい）．

酸(HA)，塩基（酸 HB の共役塩基 B$^-$ ）が共存する場合，その平衡定数 K$_{eq}$ は酸，塩基それぞれの PK$_a$ を用いて次のように記述することができる．

$$\mathrm{HA} \quad + \quad \mathrm{B}^- \rightleftharpoons \mathrm{A}^- \quad + \quad \mathrm{HB}$$

$$\mathrm{p}K_{\mathrm{eq}} = -\log\frac{\left[\mathrm{A}^-\right]\left[\mathrm{HB}\right]}{\left[\mathrm{HA}\right]\left[\mathrm{B}^-\right]} = \mathrm{p}K_{\mathrm{a}}\left(\mathrm{HA}\right) - \mathrm{p}K_{\mathrm{a}}\left(\mathrm{HB}\right)$$

すなわち，二つの酸の PKa の差を計算することで，厳密には正確ではないが，溶液中での平衡状態を見積もることができる．たとえば，マロン酸ジエチル（$EtO_2CCH_2CO_2Et$; $pK_a = 13$)とナトリウムエトキシド(NaOEt,共役酸 EtOH 0) $pK_a = 16$)が共存するとき，その平衡状態はおおよそ次のように考えることができる．

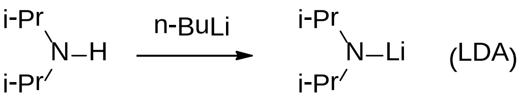


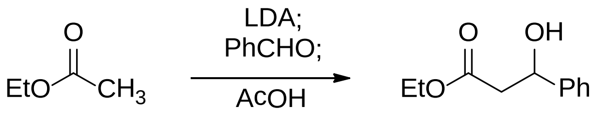
$$\mathrm{p}K_{\mathrm{eq}} = \mathrm{p}K_{\mathrm{a}}\left(\mathrm{malonate}\right) - \mathrm{p}K_{\mathrm{a}}\left(\mathrm{EtOH}\right) = 13 - 16 = \text{-}3$$

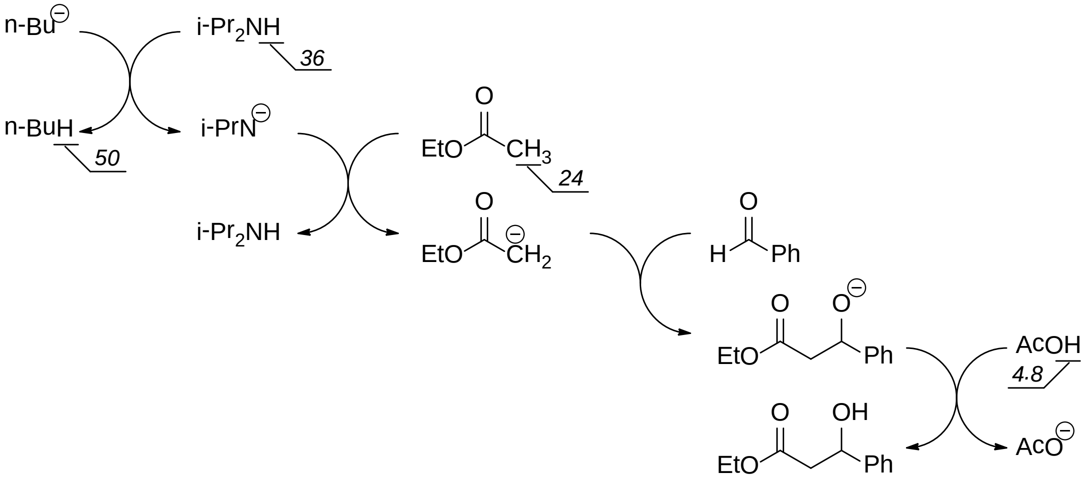
$$K_{\mathrm{eq}} = 10^3$$

K_{eq} より，この平衡はほとんど右側に偏っていることがわかる．化学的な見方をすると，弱酸であるマロン酸ジエチルは，強塩基であるナトリウムエトキシドにより，ほぼ完全に脱プロトン化されている，ということになる．

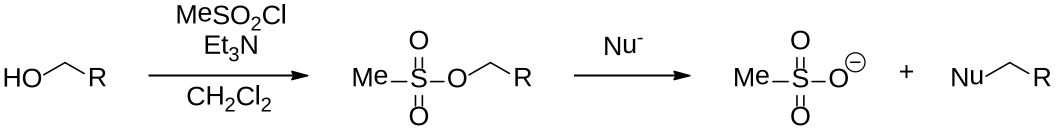
次に下のスキ＊ムのような反応を考えてみよう．リチウムジイソプロピルアミド(LDA）を用いたアルド＊ル反応の例である．n-ブチルリチウム（共役酸 n-ブタンの PK_a= 50）は，より PK_aの小さいジイソプロピルアミン（$pK_a = 36$）のプロトンを引き抜き，LDA を生成する．続いて LDA はエステルのα位のプロトン（$pK_a = 24$）を引き抜き，エステルのアニオンを生成する．このアニオンをベンズアルデヒドと反＊させると，縮合体を与えるが，生成物の共役酸の PKa はより小さいアルコ＊ル（$pK_a = 17$）となっている．後処理で酢酸（$pK_a = 4.8$）を加えると，アルコキシドがプロトン化され，生成物と酢酸アニオンを生じ反応が終 f する．以上のように，PK_a の高い试薬から順次低いものへど移り変わることにより，反応が門滑に進行している．





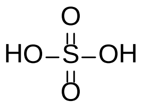
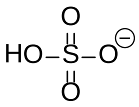
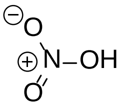
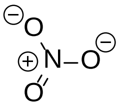
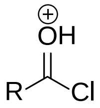
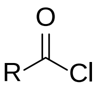
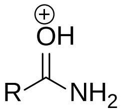
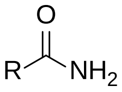
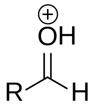
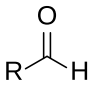
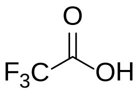
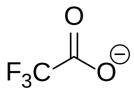
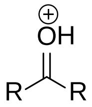
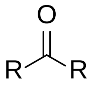
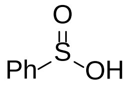
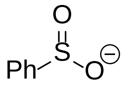
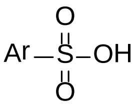
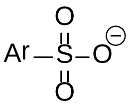
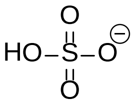
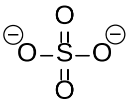
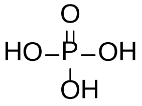
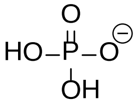
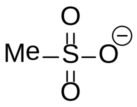
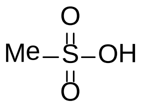
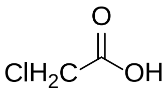
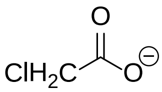
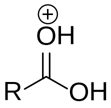
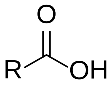
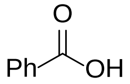
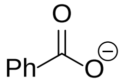
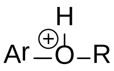
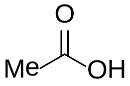
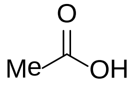
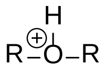
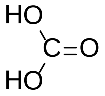
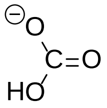
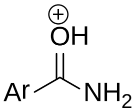
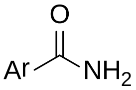


　また pK_a 値は，共役塩基の脱離能の目安にもなる．本質的に pK_a は酸解離反応の平衡状態を数値化したものなので直接的に脱離能を示すわけではないが，pK_a の値と脱離能の間には十分に相関がある.たとえばヒドロキシル基を足がかりこ置換反応を行う場合，通常ヒドロキシル基に求核基を作用させてもほとんど置換反応は進行しないが，メタンスルホニル基を作用させることにより，容易に求核基を導入できるようになる．これは水(pK_a = 15.7）とメタンスルホン酸（pK_a = -6）0) pK_a を比較すると理解することができる．



　実際にどのように反応が進行するかは pK_a だけではなくさまざまな要因で決まる，pK_a の大小に逆らって脱プロトン化が進行することもある.また上記酸解離定数の定義には，「希薄溶液中での水の濃度が一定である($[H_2O]$ ＝55.5M」という仮定が含まれているので，これまでの考察は実際の反応の状態を厳密には記述していない．しかし pKa の大小の比較から反応の结果を予測することは，反応機構を考えるうえで非常に有効な方法である．巻末におもな化合物の水溶液中での pK_a を表にまとめたので，ぜひ活用していただきたい．

表② 酸性度定数

pKa	酸	共役塩基	pKa	酸	共役塩基
−10	 $HO-SO_2-OH$	 $HO-SO_2-O^-$	−1.4		
−9			−0.5		
−8			0.5		
−7			1.5		
−6.5	 $Ar-SO_2-OH$	 $Ar-SO_2-O^-$	2.0	 $HO-SO_2-O^-$	 $^-O-SO_2-O^-$
−6.4	$ArOH_2^+$	ArOH	2.2	 $(HO)_3P{=}O$	 $(HO)_2P(=O)O^-$
−6	 $Me-SO_2-O^-$	 $Me-SO_2-OH$	2.9		
−6			4.2		
−6	 $Ar-\overset{+}{O}(H)-R$	Ar–O–R	4.8		
−3.5	 $R-\overset{+}{O}(H)-R$	R–O–R	6.4		
−2.4	$EtOH_2^+$	EtOH	10.0	PhOH	PhO^-
−1.7	H_3O^+	H_2O	11.6	HO–OH	$HO-O^-$
−1.5			12.2