NAME REACTIONS AND REAGENTS IN ORGANIC SYNTHESIS

Second Edition

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Second Edition

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Preface

It has been a long haul. The start for this revision came almost the same way that the original edition started. For the first edition it was Mike Ellerd, then an undergraduate at Montana State, who organized my crude Name Reaction handouts so well that others encouraged the conversion into a book. At Colby College, Frank Favaloro did the same thing, making "study sheets" and adding to the list of Name Reactions. He graduated in 1996 and I started reformatting and expanding. With encouragement from Darla Henderson, this became a project. By then Frank had finished graduate school and was enthusiastic about participating. I had also retired from formal teaching and found much more time for creative work. The three of us started to work in earnest!

This edition differs substantially from the first by the inclusion of many modern Name Reactions instead of sticking exclusively with the old, tried and true. There are many reactions not covered; indeed, we ultimately eliminated those that had little contemporary use. We generally applied a "rule of thumb" that a newer name had to be cited by multiple authors. Therefore there are some relatively new protocols that have not stood the test of time; however the breadth of recent use warranted inclusion. As for reagents, we have focused on both Name Reagents and those whose acronyms are often used in place of the actual name. We have noted the common use of these forms in current literature.

First and foremost, this is a book to be used. Feel free to write in the text . . . use any available blank space to add your own notes. Transform this into ***your*** book of Name Reactions! It is intended to serve as a starting point. Within a two page format for reactions and one page for reagents, the reader will find a basic, generalized definition / formula, a mechanism that conveys a possible course from starting material to product, notes which describe a few of the major highlights of the reaction or which points the reader to related reactions (by name or similarity) and recent examples of use. We have tried to convey the current mechanistic thinking with special care to show intermediate steps, point out proton exchanges, and sometimes suggest transition states, but without going through kinetics, isotope effects, etc.

Wherever appropriate, we have included references to selected secondary sources. They contain more detailed discussions on the topics introduced in this book. In all cases, we recommend use of the primary literature. The examples in the following pages are but a small taste of the detail, variation, scope and experimental detail available. Our choices reflect our personal interests; there is no "better or worse" implied! We tried to use current examples from journals that seem to be most commonly accessible, both in paper form and electronically, to student and professional alike. When recent references were difficult to come by, we made use of the abstracts and reaction-search engine of *SciFinder* (American Chemical Society). In these cases, we supplied a number [AN year: XXXX] that will allow ready access to the abstract. To the authors of the works we have chosen to describe, we hold the most sincere gratitude and we hope we have faithfully represented your work.

Colby College
Waterville, ME
Feb 1, 2005

ACKNOWLEDGMENTS

As always, completion of a project requires more than just the work of the authors. Without the consideration, support and patience of spouses: Margaret (Brad), Mary (Mike) and Michelle (Frank), this probably could not have been completed.

Special thanks goes to the chemistry community for their endless development of new methods for creating C-C and C-heteroatom bonds. It has been an enlightening experience to chronicle the explosion of new "named" reactions and protocols. We have not lost view of the obvious new participation of the world chemical community.

Each of us can thank mentors and special people that have given us encouragement:

Brad:
I still owe much to my formal mentors:
Richard F. Smith who first provided the excitement of chemistry, A.Paul Krapcho, graduate mentor and friend, and the late Henry Rapoport, postdoctoral advisor.

I thank my colleagues from Colby College, Dasan Thamattoor and Jeff Katz, for their help in reading parts of this manuscript. And, of course my former graduate and undergraduate students . . . two of the latter are now coauthors, who were the reason for my continued interest in the academic life. Special thanks goes to Prof.Tom Poon (Claremont McKenna, Pitzer, & Scripps Colleges) for a great two years as a Dreyfus Fellow with me at Colby. He taught me much, and worked closely with Frank Favaloro.

I would like to thank several Colby staff that made my working easier: Susan W. Cole of the Science Library could always be depended on to solve any library problem that developed in the absolutely great electronic resources of Colby College, and patiently put up with my many requests, piled up books and journals and general use of the library. The Colby College ITS staff was extremely good-natured and helpful for computer questions. Their help was greatly appreciated.

Mike:
My appreciation goes out to all of my professors at Montana State, who,years ago sparked my interest in chemistry, and to those who still today keep that interest very much alive.

Frank:
I would like to thank all of those who not only taught me organic chemistry, but also to be excited for the art it contains: Gordon W. Gribble, Tadashi Honda, Thomas Spencer, Peter Jacobi, David Lemal, Thomas Poon, Philip Previte and, most importantly, Brad Mundy. Thank you to the many friends and co-workers who provided support, advice and the occasional reference: Erin Pelkey, Janeta Popovici-Müller, Tara Kishbaugh, Jeanese Badenock, Alison Rinderspacher and Chaoyang Dai.

Of course a project with a publisher requires interaction. Darla Henderson, Amy Byers, Camille Carter and Dean Gonzalez were the people who kept the ball rolling and the project in focus.

Colby College
Waterville, ME

Feb 1, 2005

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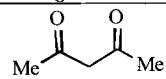
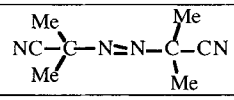
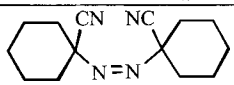
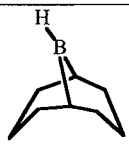
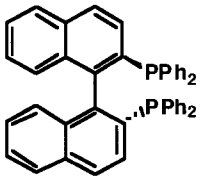
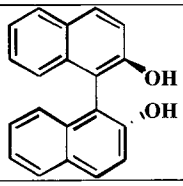
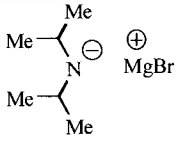
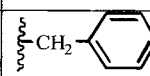
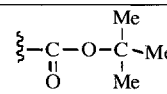
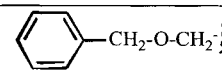
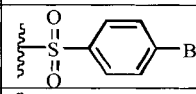
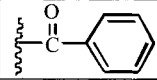
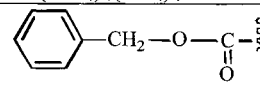
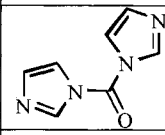
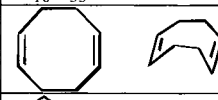
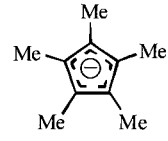
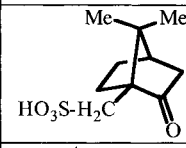
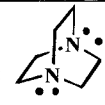
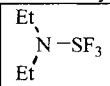
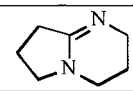
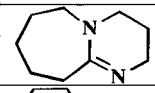
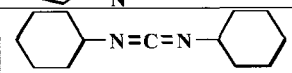
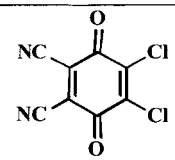
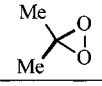
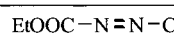
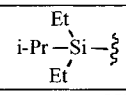
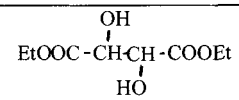
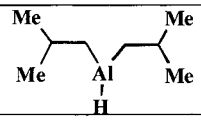
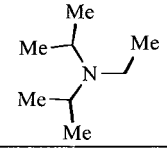
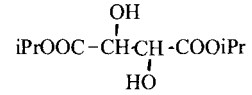
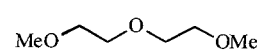
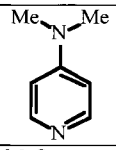
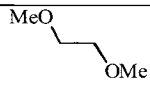
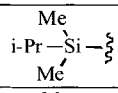
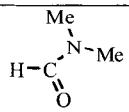
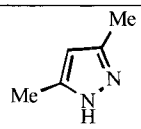
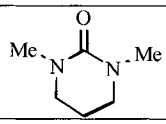
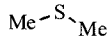
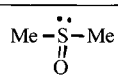
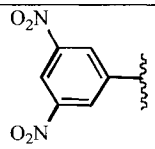
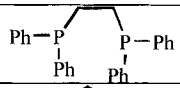
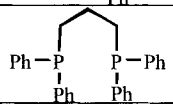
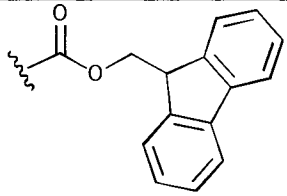
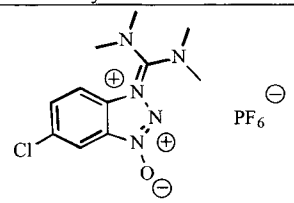
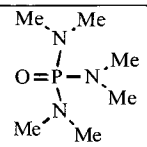
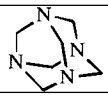
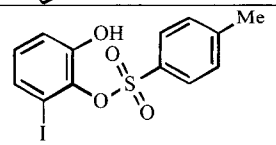
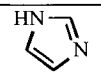
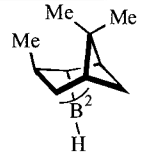
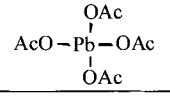
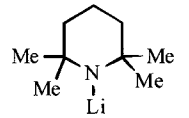
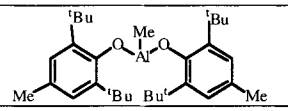
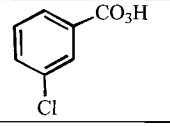
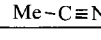
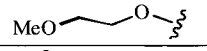
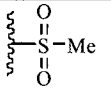
ACRONYMS AND ABBREVIATIONS

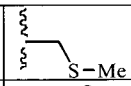
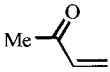
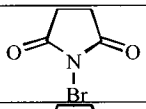
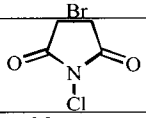
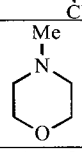
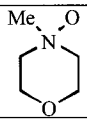
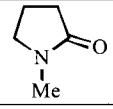
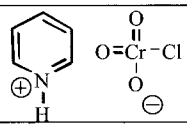
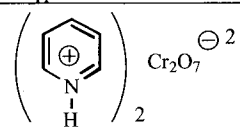
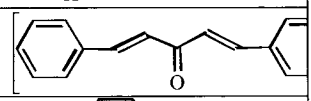
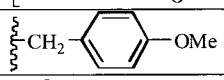
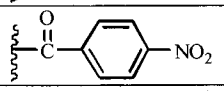
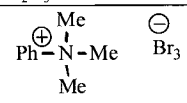
Acronym	Name	
Ac	Acetyl	
Acac	Acetylacetonate	
AcOH (HOAc)	Acetic acid	Me-COOH
AIBN	2,2'-Azobisisobutyronitrile	
ACN	1,1'-Azobis-1-cyclohexanenitrile	
9-BBN	9-Borobicyclo[3.3.1]nonane	
BINAP	2,2'-Bis(Diphenylphosphino)-1,1'-binaphththyl	
BINOL	1,1'-bi-2,2'-naphthol	
BITIP	Binol/Titanium isopropoxide	$Ti(iPrO)_4$ / BINOL
BMDA	Bromomagnesium Diisopropylamide	
BMS	Borane Dimethylsulfide	BH_3-Me_2S

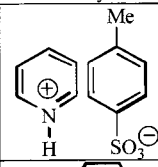
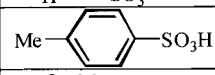
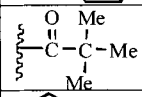
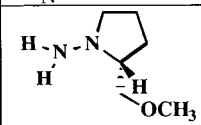
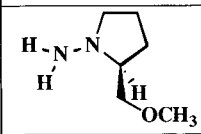
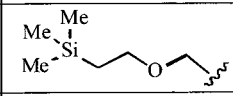
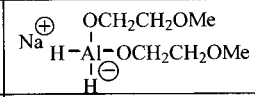
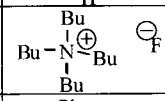
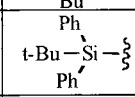
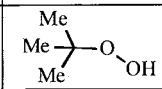
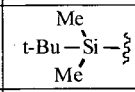
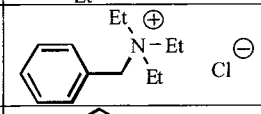
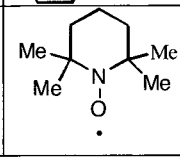
BMS	Borane Dimethylsulfide	BH_3-Me_2S
Bn-	Benzyl	
Boc- (t-Boc)	t-Butoxycarbonylchloride	
BOM-	Benzyloxymethyl-	
Bs	Brosylate	
Bu_3SnH	tri-^{n}butylstannane	$^nBu)_3SnH$
Bz	Benzoyl	
CAN	Ceric ammonium nitrate	$Ce(NH_4)_2(NO_3)_6$
CAS	Ceric ammonium sulfate	$Ce(NH_4)_4(SO_4)_4$
Cbz-	Carbobenzyloxy	
CDI	1,1'-Carbonyldiimidazole	
Cetyl	Hexadeca-	$C_{16}H_{33}$-
cod	Cyclooctadiene	
cp	Cyclopentadienyl	
cp*	Tetramethylcyclopentadienyl	
CSA	Camphorsulfonic Acid	
DABCO ***TED***	1,4-Diazabicylo[2.2.2]octane, TED, triethylenediamine	

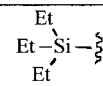
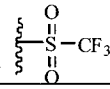
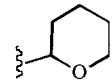
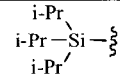
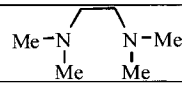
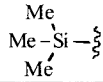
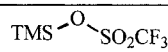
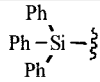
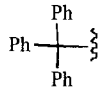
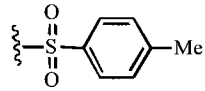
DAST	Diethylamino)sulfur trifluoride	
DBN	1,5-Diazabicyclo[4.3.0]non-5-ene	
DBU	1,5-Diazabicyclo[5.4.0]undec-7-ene	
DCC	Dicyclohexylcarbodiimide	
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone	
DDO	Dimethyldioxirane	
DEAD	Diethyl Azodicarboxylate	
DEIPS	Diethylisopropylsilyl	
DET	Dietkyl tartrate	 in R-, S, and meso forms
DIBAL ***DIBAL-H***	Disobutylaluminum hydride	
DIEA ***DIPEA***	Diisopropylethylamine ***Hunig's base***	
DIPT	Diisopropyl tartrate	 in R-, S, and meso forms
Diglyme	Diethylene glycol dimethyl ether	

DMAP	4-(Dimethylamino)pyridine	
DME	1,2-Dimethoxyethane Glyme	
DMIPS	Dimethylisopropylsilyl	
DMF	Dimethylformamide	
DMP	Dimethylpyrazole	
DMPU	N,N'-Dimethylpropyleneurea	
DMS	Dimethylsulfide	
DMSO	Dimethylsulfoxide	
DNP	2,4-dinitrophenyl	
dppe	1,2-Bis(diphenylphosphino)ethane (DIPHOS)	
dppp	1,2-Bis(diphenylphosphino)propane	
ee	enantiomeric excess = % major enantiomer - % minor enantiomer	
Fmoc	9-Fluorenylmethoxycarbonyl	

HCTU	2-(6-Chloro-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate	
HMPT ***HMPA***	Hexamethylphosphoric triamide	
HMTA	Hexamethylenetetramine	
HTIB	Hydroxy(tosyloxy)-iodobenzene	
Im	Imidazoyl	
Icp_2BH	Diisopinocampheylborane	
LTA	Lead tetraacetate	
LTMP ***LiTMP***	Lithium 2,2,6,6-tetramethylpiperidide	
MAD	Methylaluminum bis(2,6-di-t-butyl-4-methylphenoxide)	
MCPBA	m-Chlorperoxybenzoic acid	
MeCN	Acetonitrile	
MEM-	2-Methoxyethoxymethyl	
Ms	Mesyl , Methanesulfonyl	

MTM	Methylthiomethyl	
MVK	Methyl Vinyl Ketone	
NBS	N-Bromosuccinimide	
NCS	N-Chlorosuccinimide	
NMM	4-Methylmorpholine	
NMO	N-Methylmorpoline-N-oxide	
NMP	N-Methylpyrrolidone	
PCC	Pyridinium chlorochromate Corey's Reagent	
PDC	Pyridinium dichromate	
$Pd(dba)_2$	Bis(dibenzylideneacetone)palladium (0)	
PMB	p-Methoxybenzyl	
PNB	para-Nitrobenzoyl	
PPA	Polyphosphoric Acid	Unspecified mixture with High concentration of P_2O_5
PTT ***(PTAB)***	Phenyltrimethylammonium tribromide Phenyltrimethylammonium perbromide	

PPTS	Pyridinium para-toluenesulfonate	
PTSA	p-Toluenesulfonic acid; Tosic acid	
Pv	Pivaloyl	
Py	Pyridine	
RAMP	(R)-1-Amino-2- Methoxymethylpyrrolidine	
SAMP	(S)-1-Amino-2- Methoxymethylpyrrolidine Ender's Reagent	
SEM	2-Trimethylsilylethoxy-methoxy	
SMEAH	Sodium Bis(2- methoxyethoxy)aluminum Hydride	
TBAF	Tetrabutylammonium fluoride	
TBDPS	*tert*-Butyldiphenylsilyl	
TBHP	*t*-Butyl hydroperoxide	
TBS TBDMS	*tert*-Butyldimethylsilyl	
TEA	Triethylamine	
TEBA ***TEBAC***	Benzyltriethylammonium chloride	
TEMPO	2,2,6,6-Tetramethylpiperidin-1-oxyl	

TES	Triethylsilyl	
Tf	Triflate	
THF	Tetrahydrofuran	
THP	Tetrahydropyranyl	
TIPS	Triisopropylsilyl	
TMEDA	N,N,N',N'- Tetramethylethylenediamine	
TPAP	Tetra-n-Propylammonium Perruthenate	$Pr_4N^+RuO_4^-$
TPP	Triphenyl phosphine	
TMS	Trimethylsilyl	
TMSOTf	Trimethylsilyltrifluoro- methanesulfonate	
TPS	Triphenylsilyl	
Trt	Trityl	
Ts- Tos-	Tosyl p-toluenesulfonyl	

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NAME REACTIONS

In this section we provide a summary of Name Reactions. The format is slightly modified from our previous book, but maintains the essential features:

Reaction:

Summary reaction.

Proposed Mechanism:

Currently accepted mechanisms. We have tried to be complete in showing steps, intermediates and the necessary curly arrow notations.

Notes:

Additional comments and references from key sources.

Examples:

Current examples if possible.

When a term is underlined, (for example, ***Aldol Condensation***) it means that the concept can be found under an independent heading in the book.

General Bibliography:

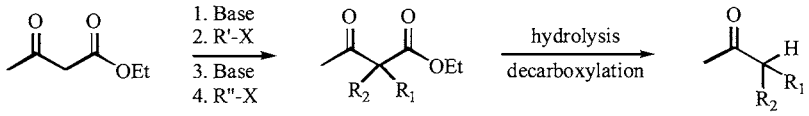
B. P. Mundy, M. G. Ellerd, *Name Reactions and Reagents in Organic Synthesis*, John Wiley and sons, Inc., New York, 1988;
M. B. Smith, J. March in *March's Advanced Organic Chemistry,* 5th ed., John Wiley and Sons, Inc., New York, 2001;
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998;
V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002;
J. J. Li, *Name Reactions*, Springer, Berlin, 2002;
Comprehensive Organic Synthesis, B. M. Trost, editor-in-chief, Pergamon Press, Oxford, 1991;
M. B. East, D. J. Ager, *Desk Reference for Organic Chemists*, Krieger Publishing Company, Malabar, FL, 1995;
M. Orchin, F. Kaplan, R. S. Macomber, R. M. Wilson, H. Zimmer, *The Vocabulary of Organic Chemistry,* John Wiley and Sons, Inc., New York, 1980;
A. Hassner, C. Stumer, *Organic Syntheses Based on Name Reactions and Unnamed Reactions*, Pergamon, Oxford, 1994;
The Merck Index, Merck & CO., Inc., Whitehouse Station, N. J. (now in the 13th Edition) Each edition has an updated list of Named Reactions.
See also: http://themerckindex.cambridgesoft.com/TheMerckIndex/NameReactions/TOC.asp

Other URL's to Name Reaction Websites:
www.monomerchem.com/display4.html
www.chempensoftware.com/organicreactions.htm
www.organic-chemistry.org/namedreactions/
http://orgchem.chem.uconn.edu/namereact/named.html

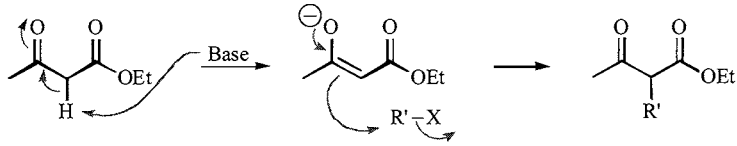
Some references are provided with a SciFinder (American Chemical Society) number so that one can access the abstract if needed.

Acetoacetic Ester Synthesis

The Reaction:

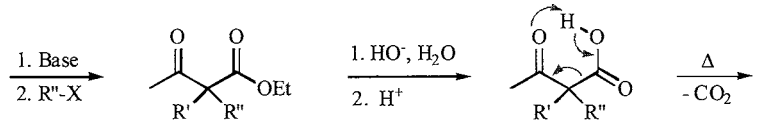


Proposed Mechanism:



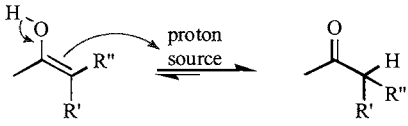
The methylene protons are the most acidic by influence from both carbonyls.

X can be Cl, Br, I, OTs, etc.



Alkylation can be done a second time (with a different R) if desired.

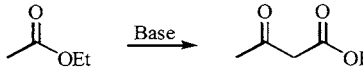
Ester hydrolysis/saponification, then with heat, the β-keto acid decarboxylates to give an enol.



keto-enol tautomerism

Notes:

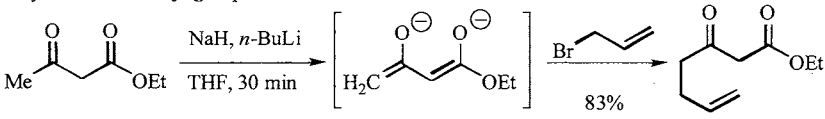
Acetoacetic Ester can be prepared by the condensation of ethyl acetate, called the ***Acetoacetic Ester Condensation Reaction***, a ***Claisen Condensation***:



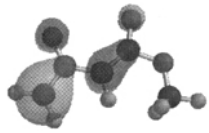
J. K. H. Inglis and K. C. Roberts *Organic Syntheses* CV1, 235

See M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 549; and C. R. Hauser, B. E. Hudson, Jr., *Organic Reactions* **1**, 9

Weiler Modification: By using very strong bases, a dianion can be formed that will preferentially alkylate at the methyl group:

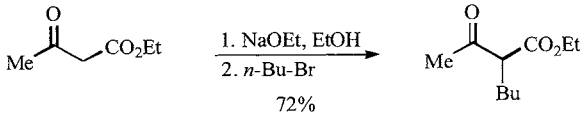


S. N. Huckin, L. Weiler *Journal of the American Chemical Society* **1974**, 96, 1082

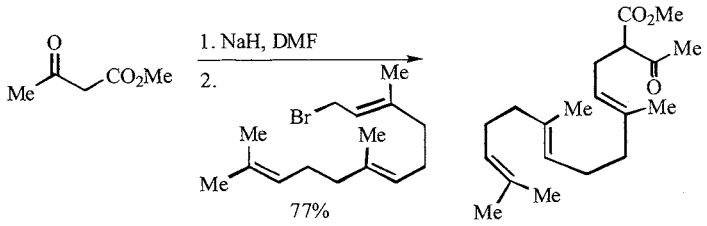


Simple AM1 calculation on Me ester shows the *HOMO* corresponding to the reactive intermediate

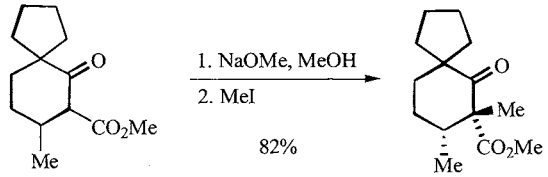
Examples:



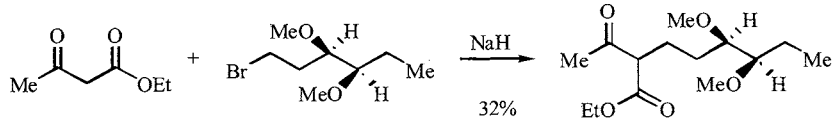
C. S. Marvel, F. D. Hager, *Organic Syntheses* **1941**, 1, 248



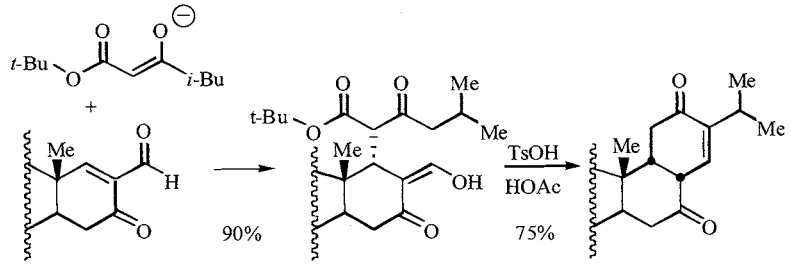
K. A. Parker, L. Resnick, *Journal of Organic Chemistry* **1995**, 60, 5726



Y.-Q. Lu, C.-J. Li, *Tetrahedron Letters* **1996**, 37, 471



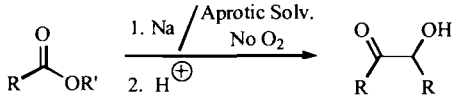
K. Mori, *Tetrahedron* **1974**, 30, 4223



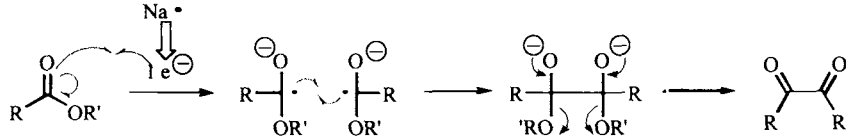
W. L. Meyer, M. J. Brannon, C. da G. Burgos, T. E. Goodwin, R. W. Howard, *Journal of Organic Chemistry* **1985**, 50, 438

Acyloin Condensation

The Reaction:



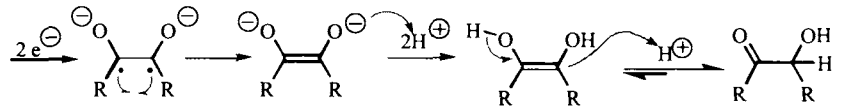
Proposed Mechanism:



An electron adds to the LUMO of the ester.

Two of these radical anions react.

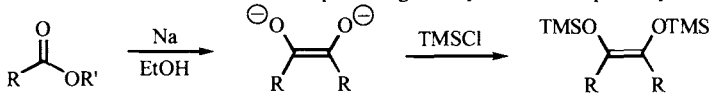
Alkoxide leaves to give a 1,2 dione that further reacts with electrons in solution.



Notes:

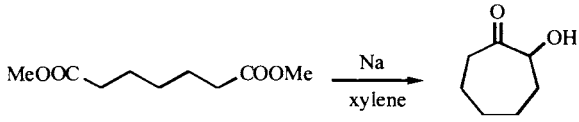
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 1562; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 1-3; S. M. McElvain, *Organic Reactions*, **4**, 4; J. P. Schaefer, J. J. Bloomfield, *Organic Reactions*, **4**, 15; J. J. Bloomsfield, J. M. Owsley, J. M. Nelke, *Organic Reactions* **23**, 2

The ***Rühlmann modification (Bouveault-Blanc Condensation or Rühlmann Reaction)*** traps the dienolate as a TMS derivative. This protocol generally results in improved yields.

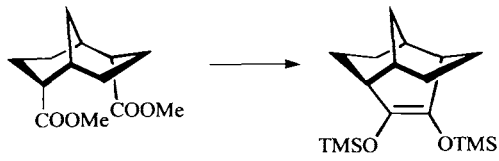


This reaction is better than either the ***Dieckmann*** or ***Thorpe-Zeigler*** reactions for preparing large rings.

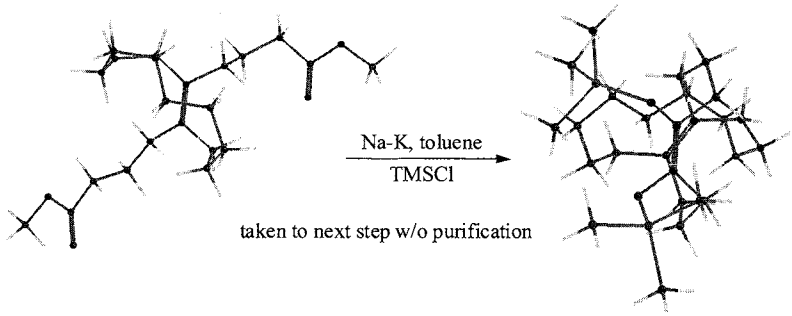
Examples:



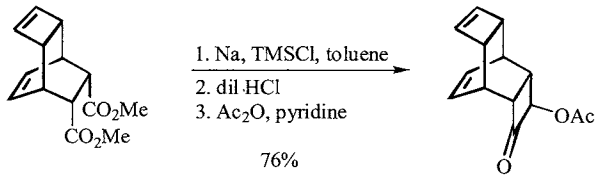
N. L. Allinger, *Organic Syntheses* **1963**, 4, 840



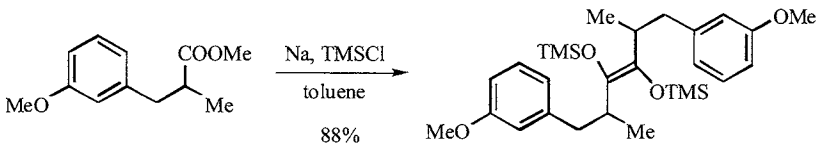
E. Butkus, A. Ilinskasa, S. Stoniusa, R. Rozenbergasa, M. urbanováb, V. Setnikac, P. Bouc, K. Volkac, *Tetrahedron: Asymmetry* **2002**, 13, 633



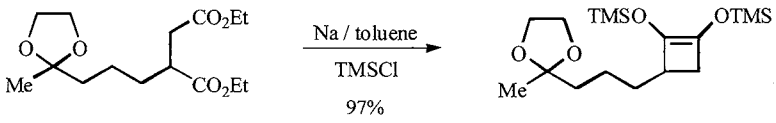
J. A. Marshall, J. C. Peterson, L. Lebioda, *Journal of the American Chemical Society* **1984**, 106, 6006



G. Mehta, R. Vidya, *Journal of Organic Chemistry* **2001**, 66, 6913



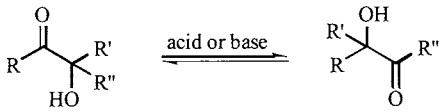
M. J. Meyers, J. Sun, K. E. Carlson, B. S. Katzenellenbogen, J. A. Katzenellenbogen, *Journal of Medicinal Chemistry* **1999**, 42, 2456



A. N. Blanchard, D. J. Burnell, *Tetrahedron Letters* **2001**, 42, 4779

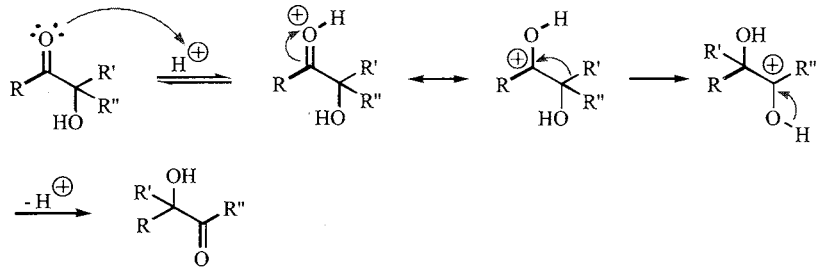
Acyloin Rearrangement

The Reaction:

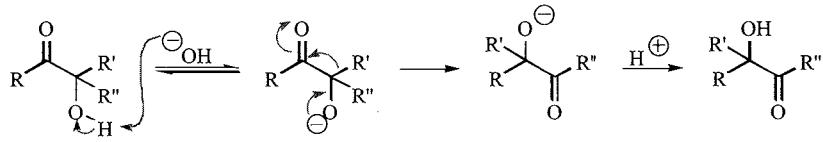


Proposed Mechanism:

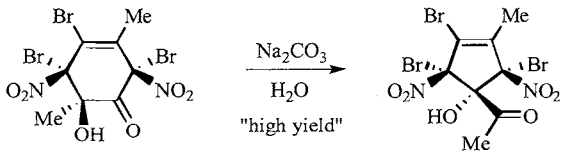
In acid:



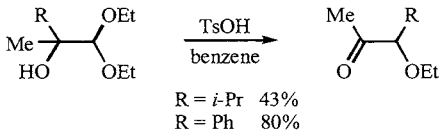
In base:



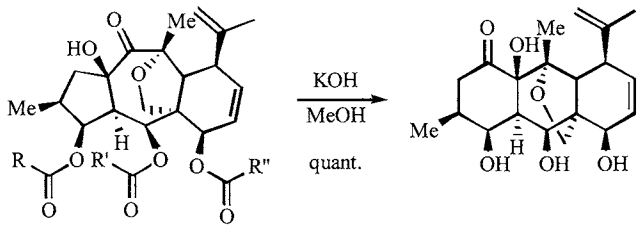
Examples:



P. A. Bates, E. J. Ditzel, M. P. Hartshorn, H. T. Ing, K. E. Richards, W. T. Robinson, *Tetrahedron Letters* **1981**, 22, 2325

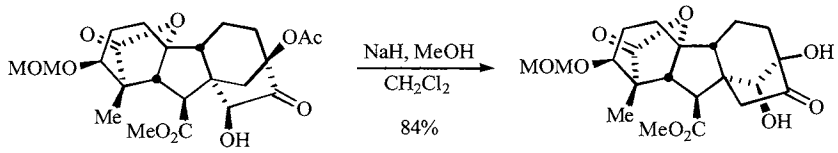


T. Sate, T. Nagata, K. Maeda, S. Ohtsuka, *Tetrahedron Letters* **1994**, 35, 5027



a mixture of acyl esters

M. Rentzea, E. Hecker, *Tetrahedron Letters* **1982**, 23, 1785



J. Liu, L. N. Mander, A. C. Willis, *Tetrahedron* **1998**, 54, 11637

Adamantane Rearrangement (Schleyer Adamantization)

The Reaction:

Proposed Mechanism:

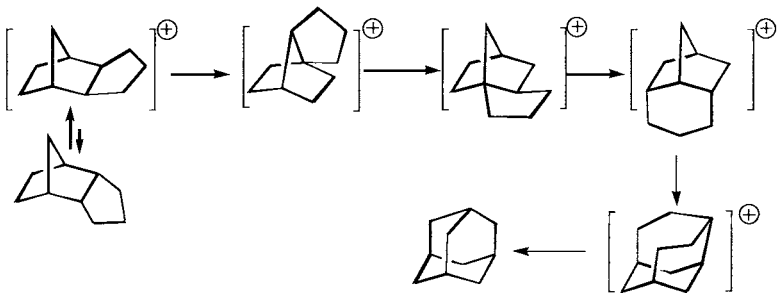
P. von R. Schleyer, P. Grubmcller, W. F. Maier, O. Vostrowsky, *Tetrahedron Letters* **1980**, 21, 921

M. Farcasiu, E. W. Hagaman, E. Wenkert, P. von R. Schleyer *Tetrahedron Letters* **1981**, 22, 1501

E. M. Engler, M. Farcasiu, A. Sevin, J. M. Cense, P. V. R. Schleyer, *Journal of the American Chemical Society* **1973**, 95, 5769

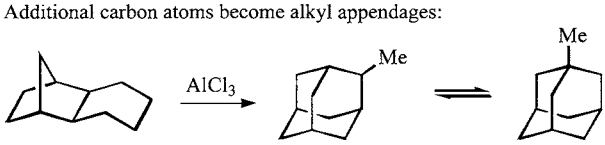
M. A. McKervey, *Tetrahedron* **1980**, 36, 971 provides a useful review:

This reaction consists of a series of deprotonations, protonations, hydride transfers and ***Wagner-Meerwein rearrangements***. There are postulated to be 2897 possible routes between starting material and product! A few of the steps have been tested experimentally; most of the data are computational. The following structural features seem to be supported:



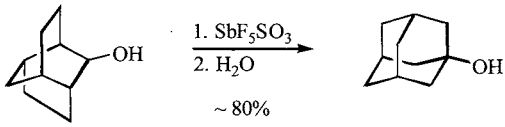
Notes:

Tricyclic molecules having 10 carbon atoms are converted to adamantane with Lewis acids. Additional carbon atoms become alkyl appendages:



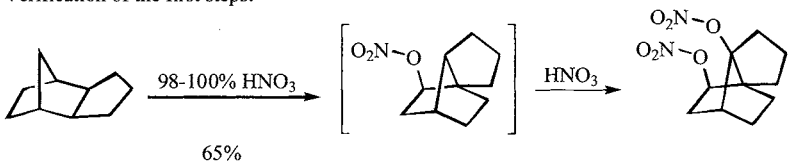
M. A. McKervey, *Tetrahedron* **1980**, 36, 971

Examples:



H. W. Whitlock, Jr., M. W. Siefken, *Journal of the American Chemical Society* **1968**, 90, 4929

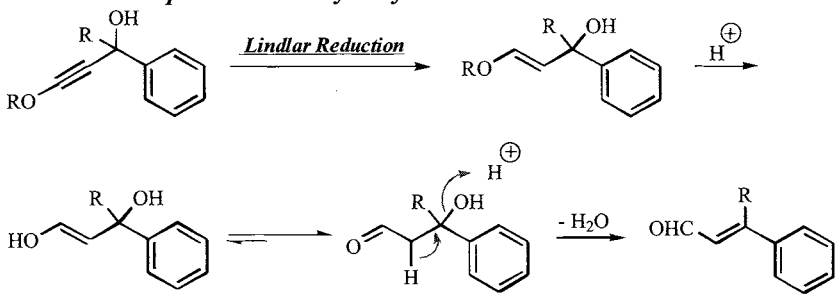
Verification of the first steps:



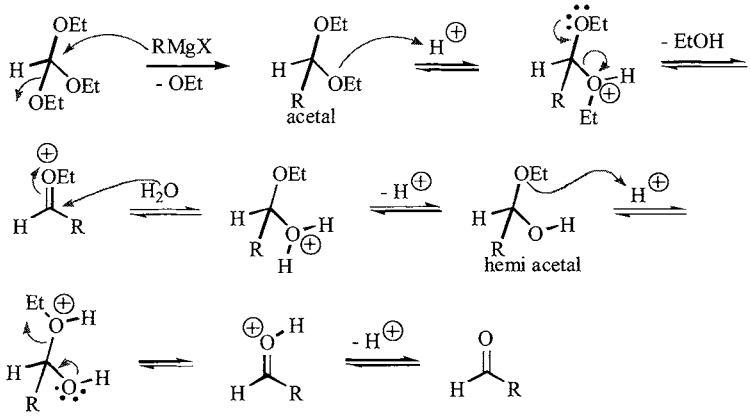
P. A. Krasutsky, I. R. Likhotvorik, A. L. Litvyn, A. G. Yurchenko, D. Van Engen *Tetrahedron Letters* **1990**, 31, 3973

Aldehyde Syntheses

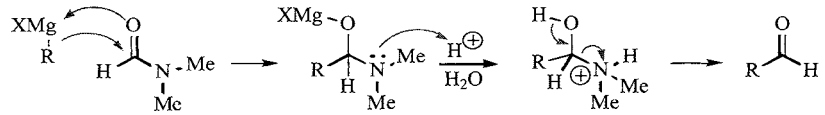
Arens-van Dorp Cinnamaldehyde Synthesis



Bodroux-Chichibabin Aldehyde Synthesis

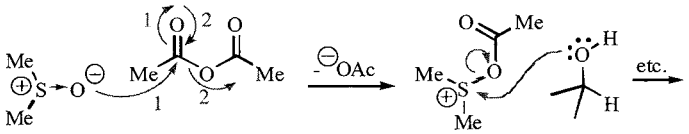


Bouveault Aldehyde Synthesis

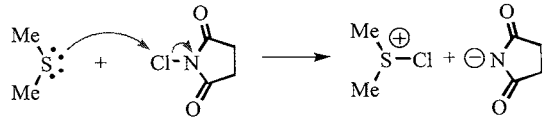


DMSO-based Oxidations

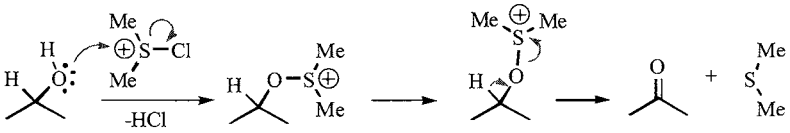
Albright-Goldman Oxidation / Albright-Goldman Reagent



Corey-Kim Oxidation / Corey-Kim Reagent

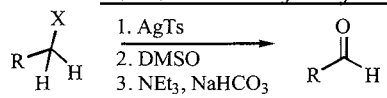


NCS
N-ChloroSuccinimide



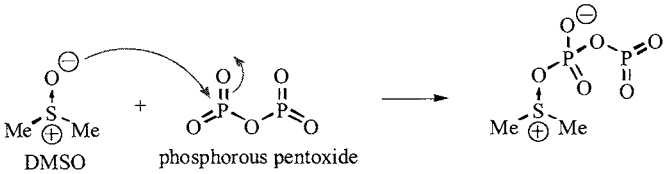
Scavanged by NR_3

Kornblum Aldehyde Synthesis

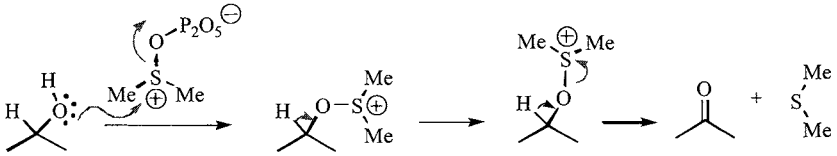


X = I, Br, OTs

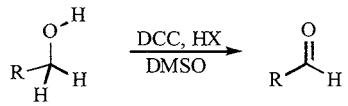
Onodera Oxidation



DMSO phosphorous pentoxide

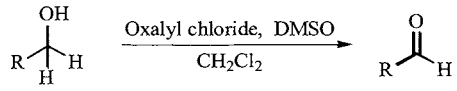


Pfitzner-Moffatt Oxidation



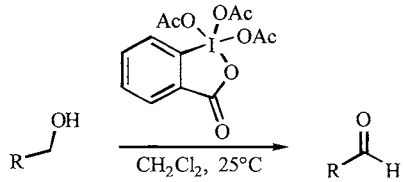
also for ketones

Swern Oxidation



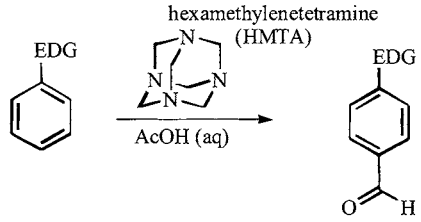
also for ketones

Dess-Martin Oxidation

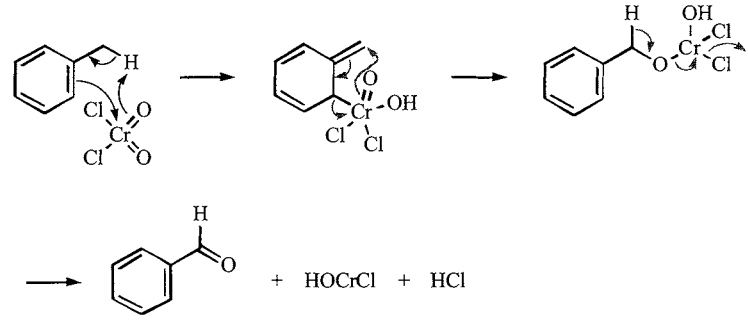


also for ketones

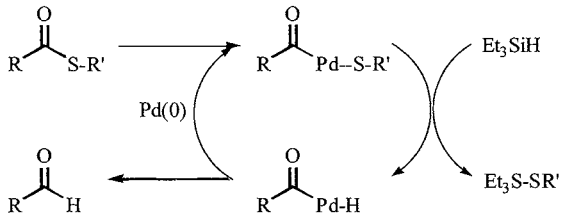
Duff Reaction



Étard Reaction

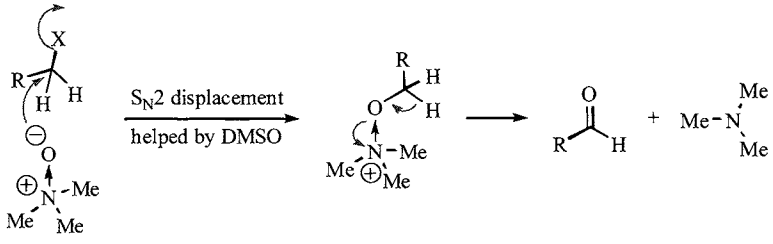


Fukuyama Reduction

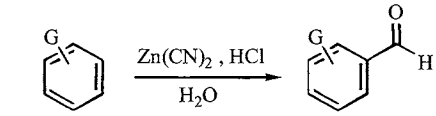


M. Kimura, M. Seki, *Tetrahedron Letters* **2004**, 45, 3219

Ganem Oxidation



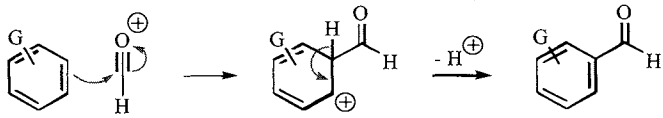
Gattermann Reaction (Gatterman Aldehyde Synthesis) / Gattermann Reagent



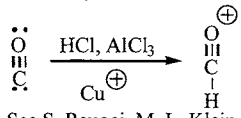
G = alkyl, OR

Gatterman-Koch Reaction (see under Gatterman Reaction)

There seems to be agreement that the product-forming part of the mechanism is:

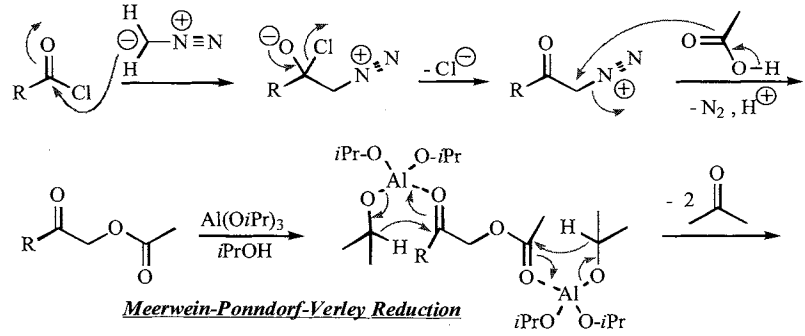


However, the details of the formation of the formyl cation seem to be less assured.

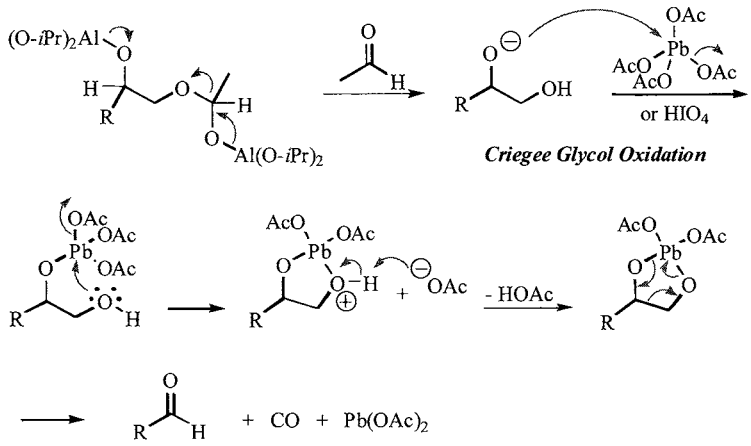


See S. Raugei, M. L. Klein, *Journal of Physical Chemistry B*, **2001**, 105, 8213 for pertinent references to experiment, and their computational study of the formyl cation.

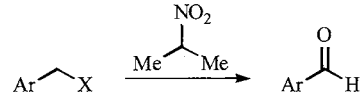
Grundmann Aldehyde Synthesis



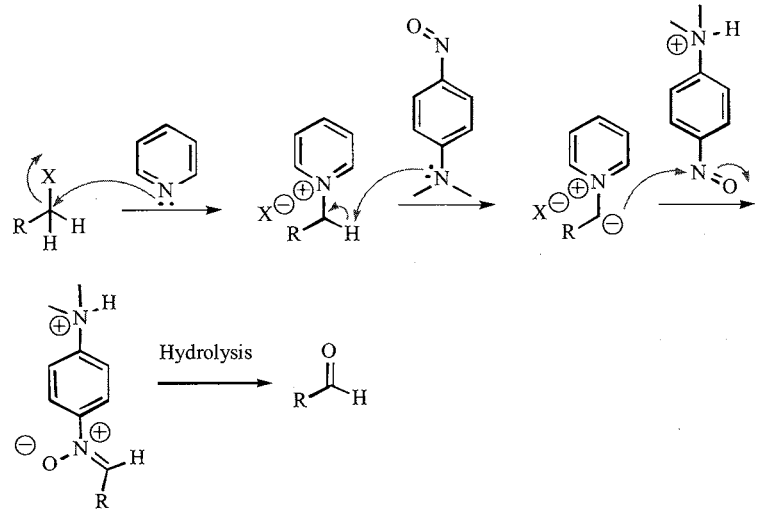
Meerwein-Ponndorf-Verley Reduction



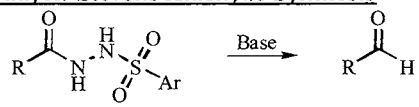
Hass-Bender Reaction



Kröhnke Aldehyde Synthesis

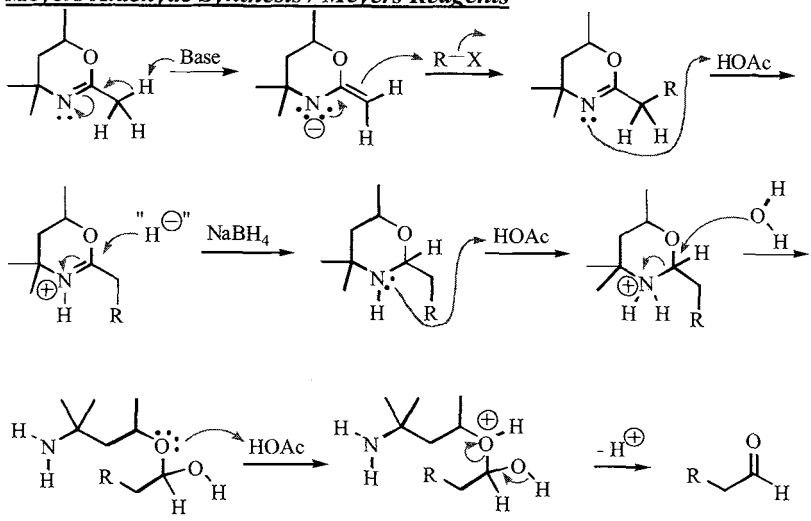


McFadyen-Stevens Aldehyde Synthesis

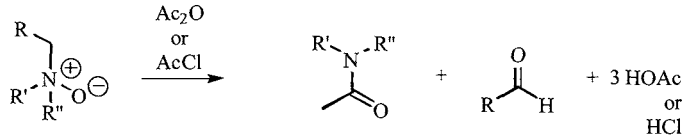


R = Ar or alkyl with no α-protons

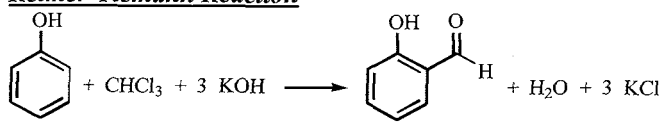
Meyers Aldehyde Synthesis / Meyers Reagents



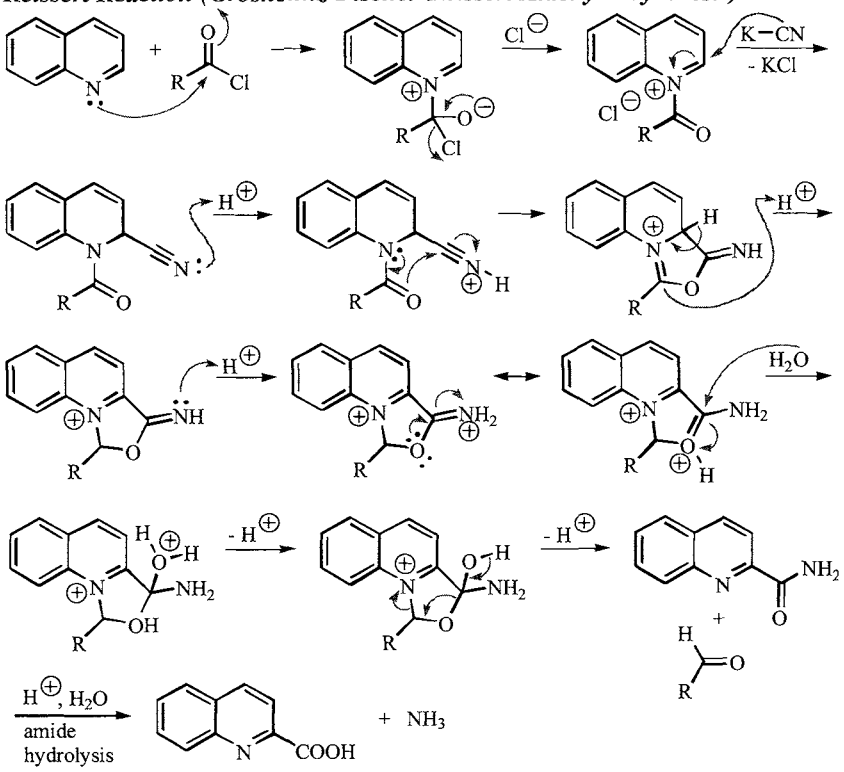
Polonovski Reaction



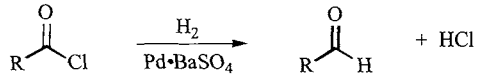
Reimer-Tiemann Reaction



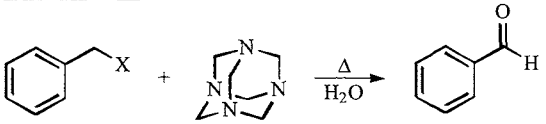
Reissert Reaction (Grosheintz-Fischer-Reissert Aldehyde Synthesis)



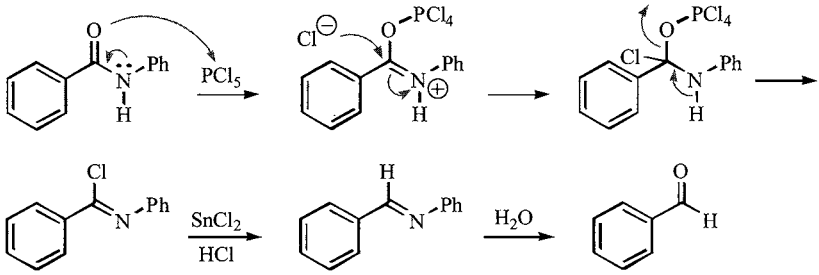
Rosenmund Reduction



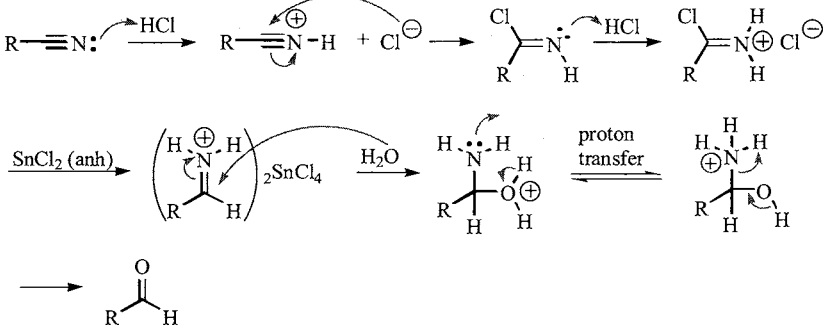
Sommelet Reaction



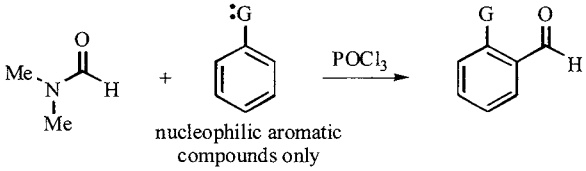
Sonn-Muller Method



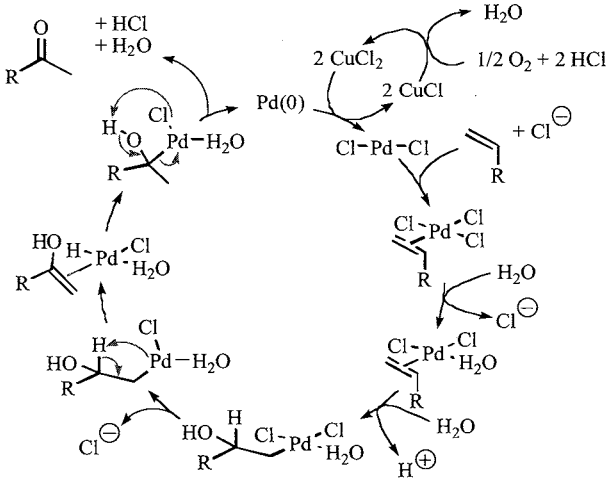
Stephen Reduction (Stephen Aldehyde Synthesis)



Vilsmeier-Haack Reaction

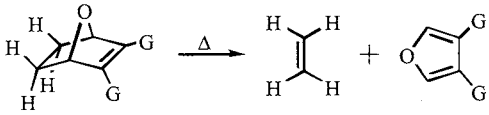


Wacker Oxidation Reaction

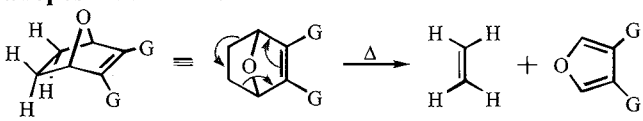


Alder-Rickert Reaction

The Reaction:



Proposed Mechanism:

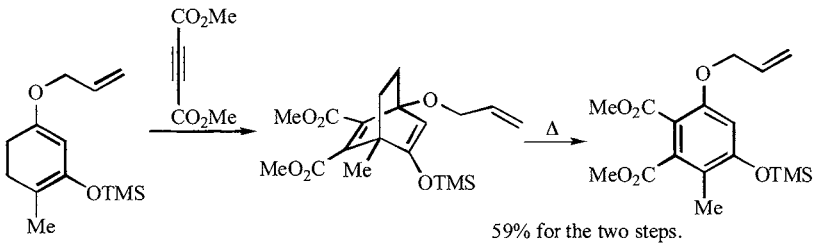


This reaction is a reverse ***Diels-Alder Reaction***. The orbital considerations controlling the "backward: reaction are the same as the "forward" reaction.

Notes:

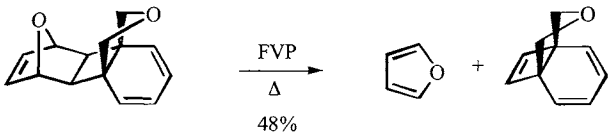
It seems accepted that almost any "***retro-Diels-Alder***" reaction can be included in the grouping, "***Alder-Rickert Reaction***".

Examples:

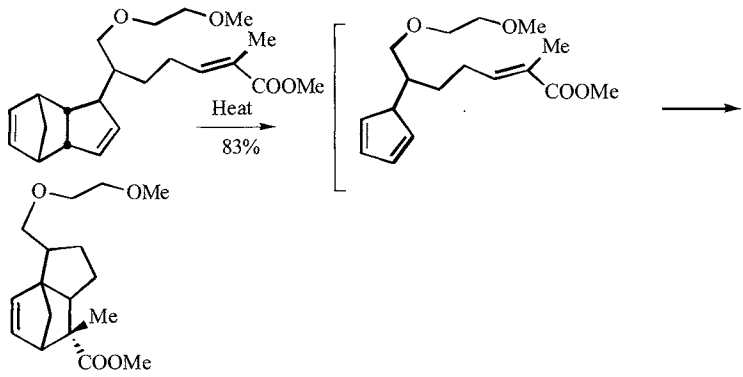


59% for the two steps.

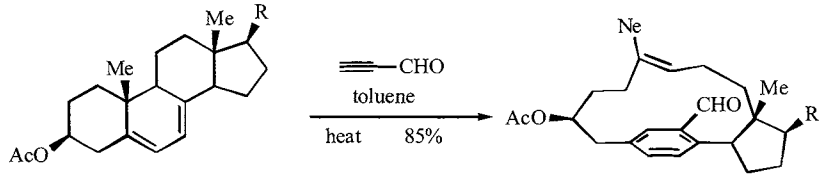
J. W. Patterson, *Tetrahedron* **1993**, 49, 4789



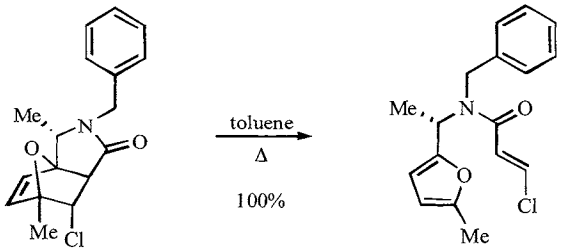
R. N Warrener, J.-M. Wang, K. D. V. Weerasuria, R. A. Russell, *Tetrahedron Letters* **1990**, 31, 7069



D. W. Landry, *Tetrahedron* **1983**, 39, 2761



D. Schomburg, M. Thielmann, E. Winterfeldt, *Tetrahedron Letters* **1985**, 26, 1705



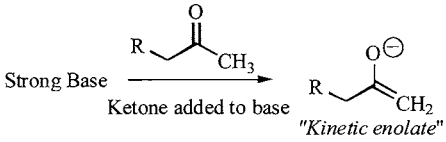
M. E. Jung, L. J. Street, *Journal of the American Chemical Society* **1984**, 106, 8327

Aldol Type Reactions

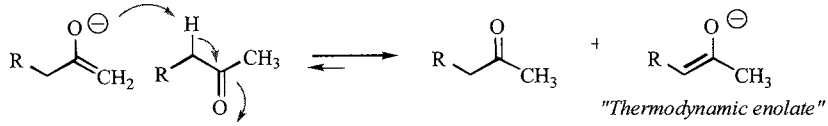
The Reaction:

This reaction has become an extremely important tool in the reaction toolbox of organic chemists. Because of the variety of approaches to the aldol products, this summary section is prepared.

Most synthetically useful approaches use a preformed enolate as one of the reactants.

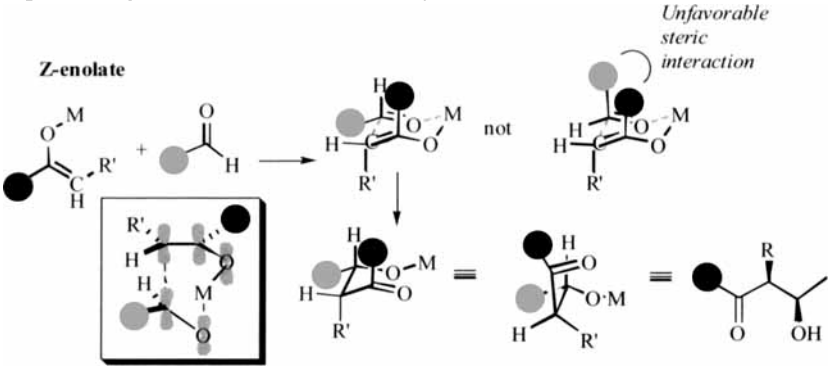


With a weaker base and / or slow addition of base to the ketone, an equilibrium will be established and a *"thermodynamic enolate"* will predominate.



The most useful approach is when the enolate can be trapped and used in a configurationally stable form.

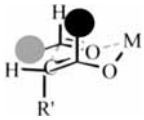
A generic analysis of enolate addition to an aldehyde:



A similar exercise can be provided for the *E*-enolate.

Zimmerman-Traxler model

An analysis of the steric effects in a chair-transition state for the reaction:

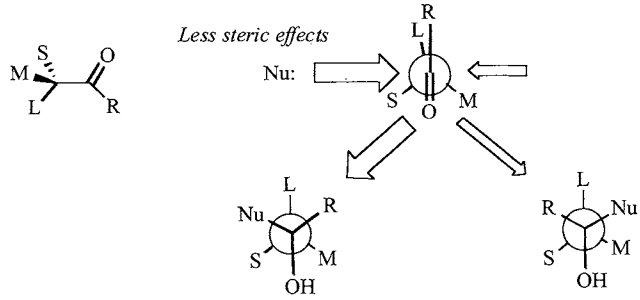


A ***directed aldol reaction*** requires that one partner provides a preformed enolate (or chemically equivalent reactive species) and is then added to the second carbonyl-containing molecule.

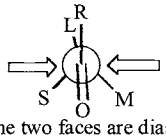
When one of the reactants is chiral, asymmetric induction can provide enantioselective products:

Cram's Rule and Related Views on Asymmetric Induction

This rule was developed to rationalize the steric course of addition to carbonyl compounds.[1] The conformations of the molecules are shown in their ***Newman structures***, and a preferred conformation is selected in which the *largest group,* **L**, is situated *anti* to the carbonyl oxygen. This conformation assumes a model having a *large* oxygen, sometimes referred to as the "big O" model.[2] Examination of steric hindrance to nucleophile trajectory determined the major product.[3] We might point out, at the start, that Reetz has recently reported that "how" the reaction is carried out; for example "slow" vs. "fast" mixing, can dramatically alter product ratios.[4]



In cases where the alpha-carbon is chiral, attack at the carbonyl carbon introduces a new stereogenic center. The two carbonyl faces are *diastereotopic* and attack at the *re* and *se* faces are different



The two faces are diastereotopic

A modification of the ***Cram model***, in which the medium sized group, **M**, eclipsed the carbonyl oxygen, was developed by Karabatsos[5]; however, it generally predicted the same product as the ***Cram model***. In this model, which assumes two major conformations, the major product is that which is derived from attack at the less hindered side of the more stable conformer.

---

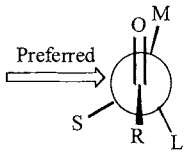
1. a. See J. D. Morrison, H. S. Mosher, *Asymmetric Organic Reactions*, Prentice-Hall, Englewood Cliffs, 1971, Chapter 3, for a somewhat dated, but excellent account of this concept.
b Cram's first work, (D. J. Cram, F. A. Abd Elhafez, *Journal of the American Chemical Society* **1952**, 74, 5828) set the stage for intense studies that have spanned 50 years.

2. The original thought included the notion that there was a large steric bulk associated with the oxygen by nature of metal complexing.

3. Application of the ***Curtin-Hammett Principle*** would suggest that the different ground state conformers have minimal influence on the product composition. It is the difference in activation energies for the two different isomers that controls the reaction, and the diastereomeric transition states would be attained from either ground state conformation.

4. M. T. Reetz, S. Stanchev, H. Haning, *Tetrahedron* **1992**, 48, 6813

5. a G. J. Karabatsos *Journal of the American Chemical Society* **1967**, 89, 1367;
b. G. J. Karabatsos, D. J. Fenoglio, *Topics in Stereochemistry* **1970**, 5, 167

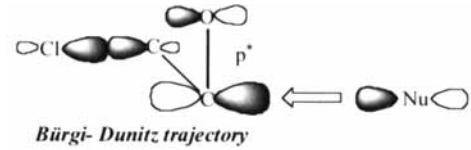


Felkin–Cherest-Anh Rule

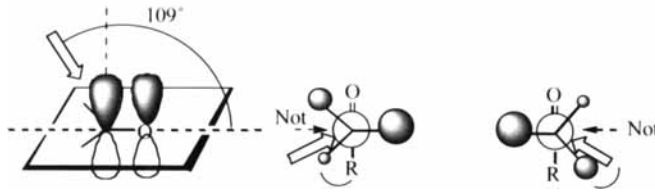
Like ***Cram's Rule***, the ***Felkin-Cherest-Anh model***, developed by Felkin and coworkers[6], is an attempt to understand and predict the stereochemistry of addition to a carbonyl group. This model requires a "small O" interpretation in which the largest group is oriented *anti* to the attacking nucleophile's trajectory. One should note that the ***Felkin-Cherest-Anh model*** neglects the interaction of the carbonyl oxygen. In this approach, the *R/S* or *R/M* interactions dominate.

This is the important interaction that must be minimized. Note that in this approach the carbonyl substituent plays an important role.

Calculations in this model are based on an orbital interaction as described below. It should also be noted that the trajectory of delivery of nucleophile to the carbonyl carbon is defined by an angle of about 109°.



Bürgi- Dunitz trajectory

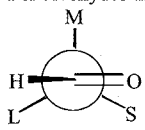


Preferred conformation. Less interaction between the small group and the R-group. We also note that this model "feels" the influence of increasing size of R.

We see in this coformer an increased interaction between the medium group and R. Also, there is more interaction with the nucleophile.

This model often leads to the same conclusions obtained from the other models. It does, however, recognize the nonpassive role of the **R**-group in ketones. In this model one would predict an *increase* of stereodifferentiation as the size of **R-** increases. This has been found experimentally.

For aldehydes the transition state model will be:



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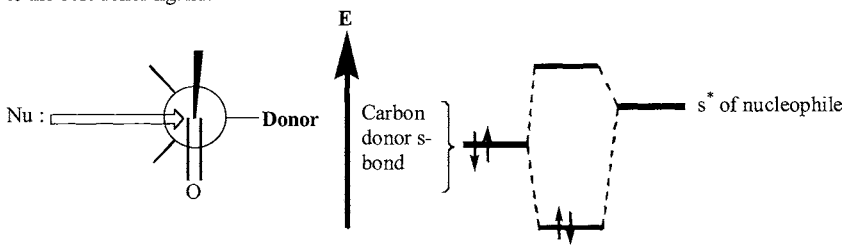
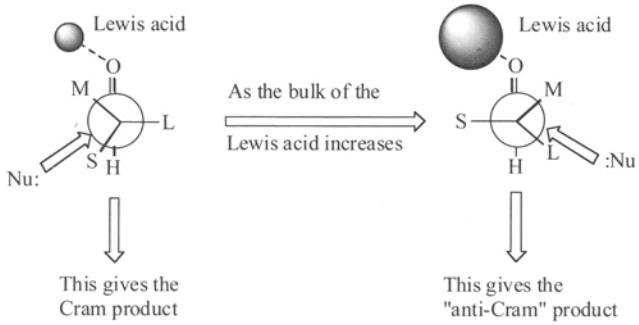
6. M. Cherest, H. Felkin, N. Prudent, *Tetrahedron Letters*, **1968**, 9, 2199

A useful orbital approach by Cieplak[7] has suggested that the nucleophile will attack the carbonyl *anti* to the best donor ligand.



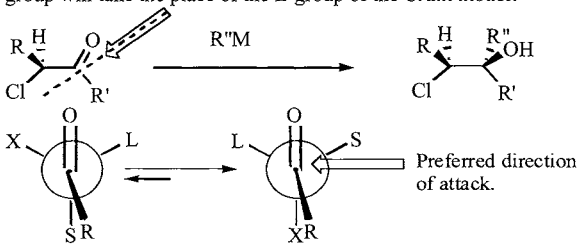
Cases for Modification of the Models

Sometimes the Lewis acid that coordinates with the carbonyl oxygen is sufficiently bulky that it seriously influences the stereochemistry of attack. Sometimes these reaction products, which seem opposite of the expected ***Cram Rule*** analysis, are termed ***"anti-Cram" products***. Compare the "normal" situation with the influence of a sterically bulky Lewis acid:



Dipolar Model

There is evidence to suggest that competing dipole effects will alter the preferred conformation. Thus, for example, halogens will prefer a conformation in which the dipoles are *anti* to one another. This is often described as the ***Cornforth model.***[8] In this model the highly polarized group will take the place of the L-group of the ***Cram model.***



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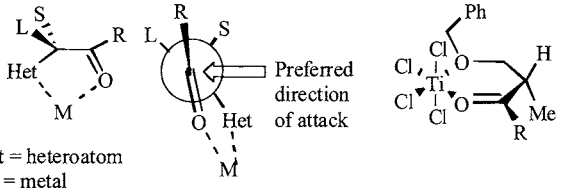
7. a. A. S. Cieplak, B. D. Yait, C. R. Johnson, *Journal of the American Chemical Society* **1989** 111, 8447

b. A. S. Cieplak, *Journal of the American Chemical Society* **1981**, 103, 4548

8. J. W. Cornforth, R. H. Cornforth, K. K. Methew, *Journal of the Chemical Society* **1959**, 112

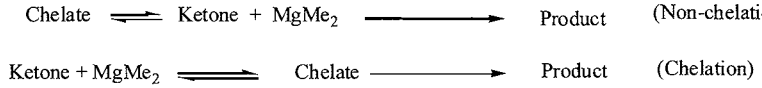
Chelation Control[9]

Neighboring heteroatoms can provide a site for complexing.



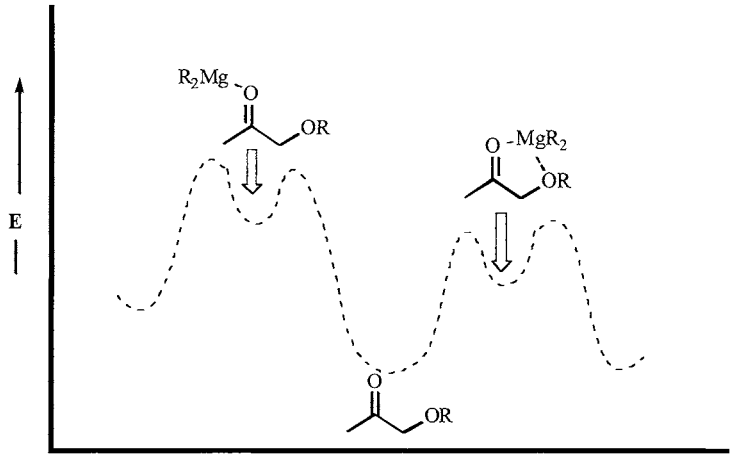
Het = heteroatom
M = metal

Product stereochemistries can be greatly influenced by these chelation control effects. This was first observed by Cram.[10] There are many controversies about this topic, and the issue remains a topic of investigative interest.[11] Without kinetic data, it has been suggested that it is impossible to distinguish the following two mechanistic types:[12]



Rate enhancement should be a requirement for chelation control because if chelation is the source of stereoselectivity it necessarily follows that the chelation transition state should be of a lower energy pathway.[13]

These concepts are seen on the energy diagram below. It should be noted that an interesting conclusion from this analysis is that *increased selectivity* is associated with *increased reactivity*. This might be considered to run counter to a number of other analyses of reactivity and selectivity.



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9. M. T. Reetz, *Accounts of Chemical Research* **1993**, 26, 462

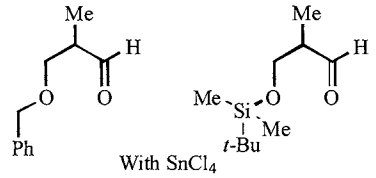
10. D. J. Cram, K. R. Kopecky, *Journal of the American Chemical Society* **1959**, 81, 2748

11. a. W. C. Still, J. H. McDonald, *Tetrahedron Letters*, **1984**, 1031
    b. M. T. Reetz, *Angewandte Chemie, International Edition in English*, **1984**, 23, 556
    c. G. E. Keck, D. E. Abbott, *Tetrahedron Letters* **1984**, 25, 1883
    d. S. V. Frye, E. L. Eliel, *Journal of the American Chemical Society* **1988**, 110, 484

12. J. Laemmle, E. C. Ashby, H. M. Neumann, *Journal of the American Chemical Society* **1971**, 93, 5120

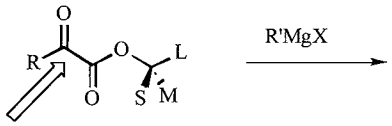
13. X. Chen, E. R. Hortelano, E. L. Eliel, S. V. Frye *Journal of the American Chemical Society* **1992**, 114, 1778

The *a priori* prediction of which functional groups will provide complexation are not always obvious. Keck[14] demonstrated some dramatic differences in oxygen chelation resulting from minor differences in substitution.



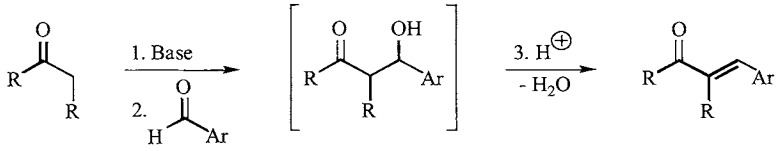
Stong chelate *No chelate*

A potentially useful extension of the ***Cram's rule*** is the asymmetric induction provided by a remote ester (***Prelog's rule***):

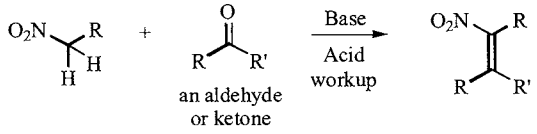


Reactions based on the Aldol Reaction:

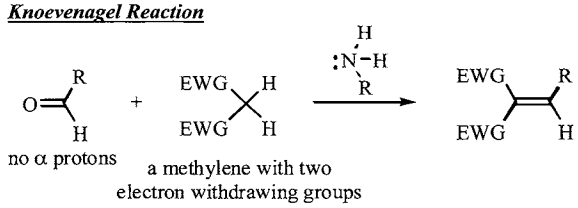
Claisen-Schmidt:



Henry Reaction



Knoevenagel Reaction

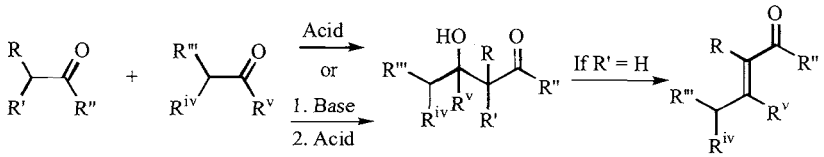


---

14. G. E. Keck, S. Castellino, *Tetrahedron Letters* **1987**, 28, 281

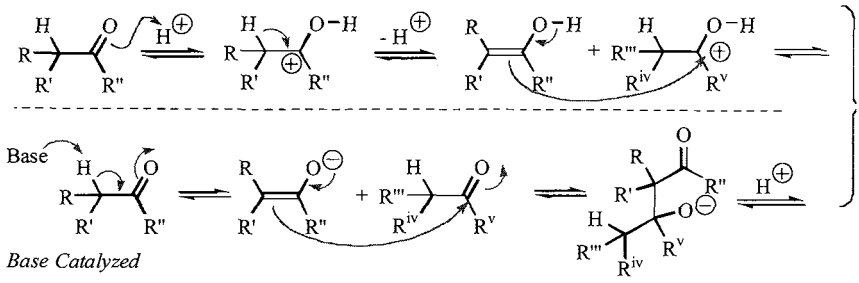
Aldol Condensation

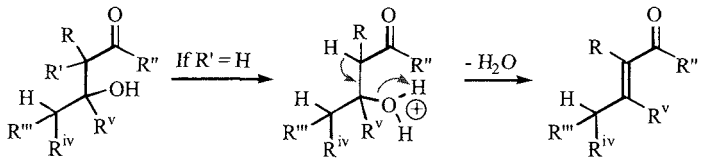
The Reaction:



Proposed Mechanism:

Acid Catalyzed



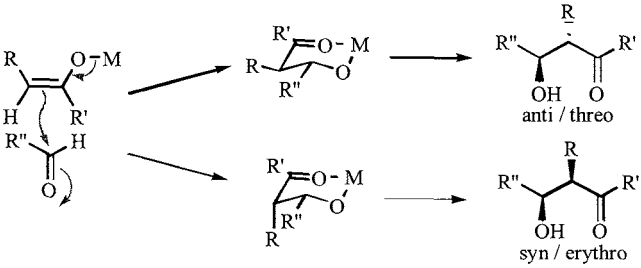


If R' = H, dehydration is possible to give the α, β unsaturated ketone.

Dehydration is often irreversible and a driving force.

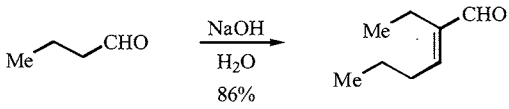
Notes:

If the starting materials are not the same, the reaction is known as a ***"mixed" aldol condensation.***

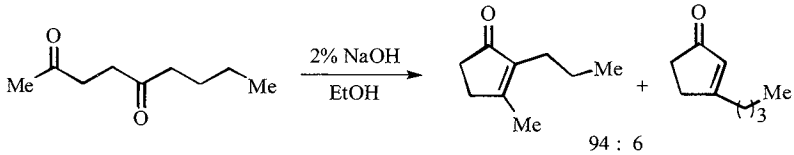


M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1218-1213; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 4-10; A. T. Nielsen, W. J. Houlihan, *Organic Reactions* **16** (full volume); T. Mukaiyama, *Organic Reactions*, **28**, 3; C. J. Cowden, I. Patterson, *Organic Reactions* **51**, 1.

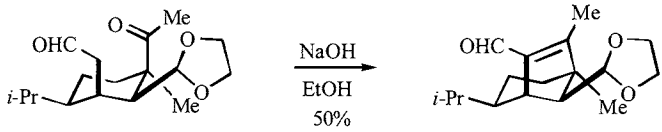
Examples:



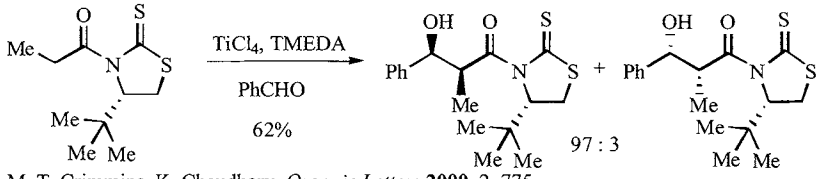
M. Haussermann, *Helvetica Chimica Acta* **1951**, 34, 1482 (Reported in A. T. Nielsen, W. J. Houlihan, *Organic Reactions* **16,** page 8).



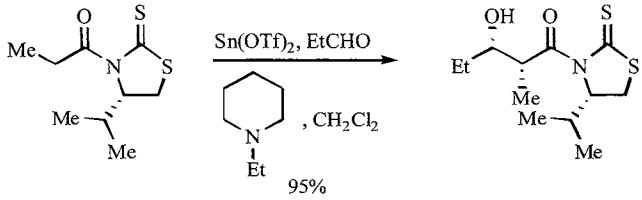
P. M. McCurry, Jr., R. K. Singh, *Journal of Organic Chemistry* **1974**, 39, 2316



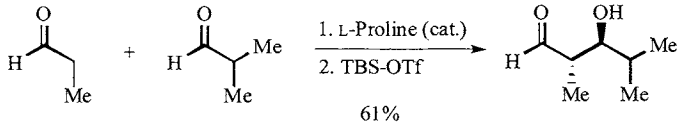
E. J. Corey, S. Nozoe, *Journal of the American Chemical Society* **1965**, 87, 5728



M. T. Crimmins, K. Chaudhary, *Organic Letters* **2000**, 2, 775



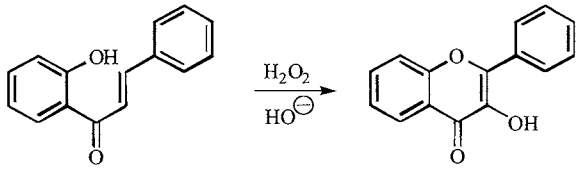
D. Zuev, L. A. Paquette, *Organic Letters* **2000**, 2, 679



P. M. Pihko, A. Erkkila, *Tetrahedron Letters* **2003**, 44, 7607

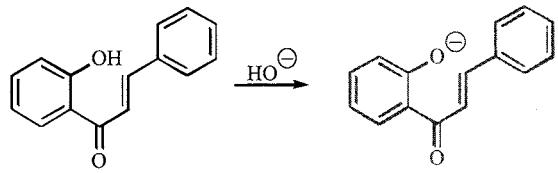
Algar-Flynn-Oyamada Reaction

The Reaction:

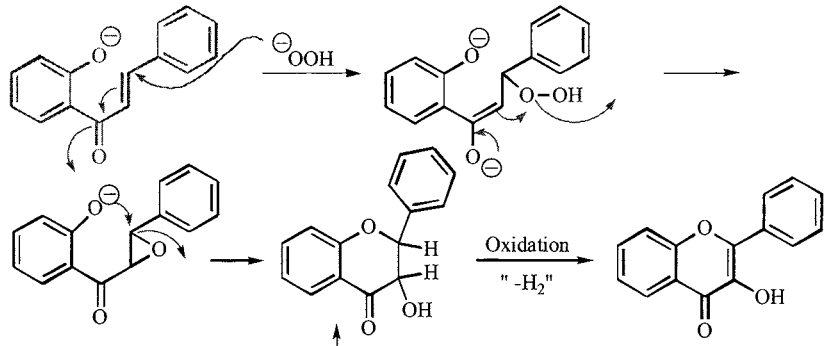


Proposed Mechanism:

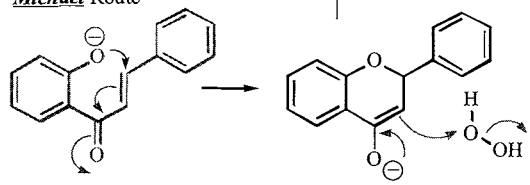
$H_2O_2 + HO^{\ominus} \longrightarrow {}^{\ominus}OOH + H_2O$



Enone Epoxidation Route:



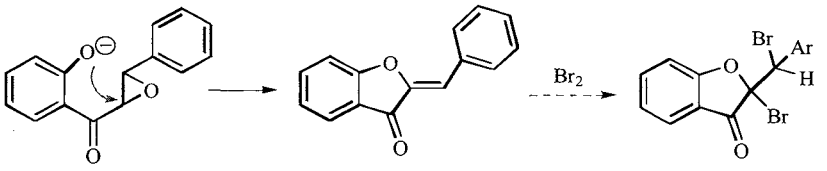
Michael Route



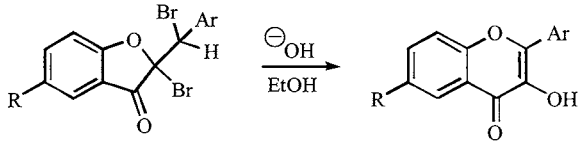
T. M. Gormley, W. I. O'Sullivan, *Tetrahedron* **1973**, 29, 369
See: M. Bennett, A. J. Burke, W. I. O'Sullivan, *Tetrahedron* **1996**, 52, 7178 for a detailed analysis of the role of the epoxide intermediate.

Notes:

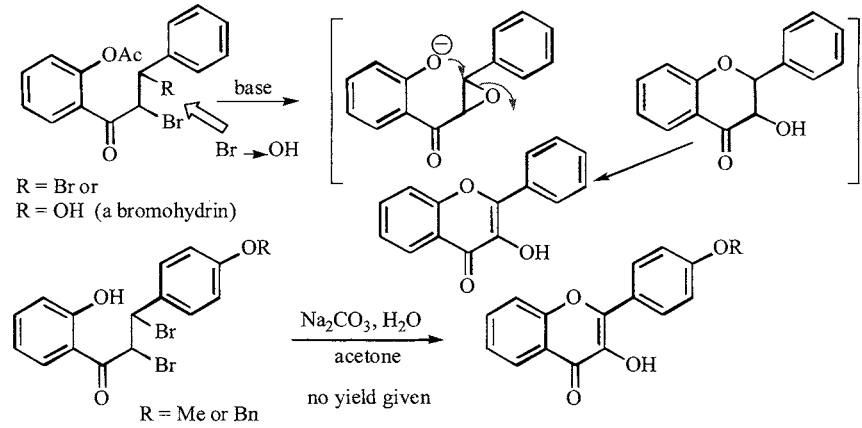
Sometimes an "arone" can be formed.



Auwers Synthesis



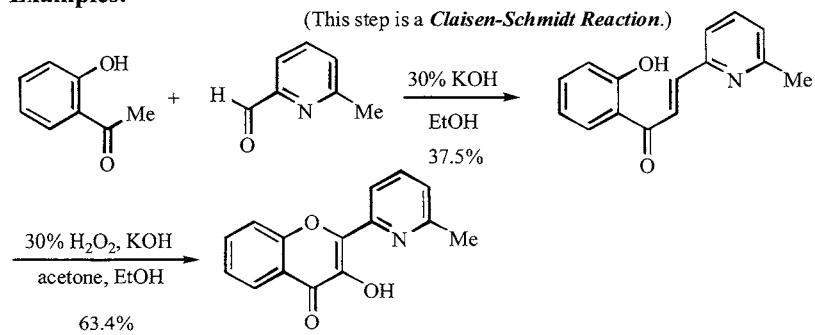
The Rasoda Reaction:



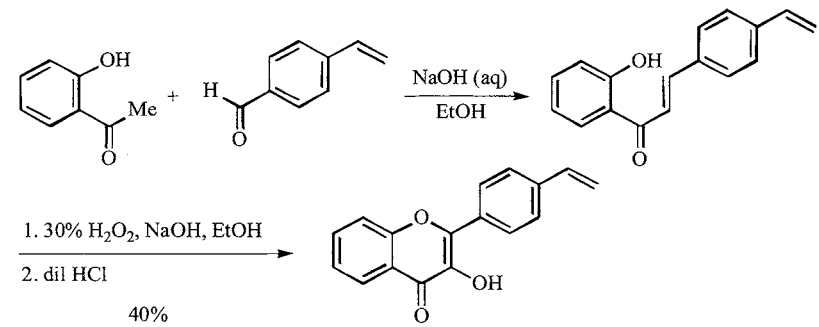
M. G. Marathey, *Journal of Organic Chemistry* **1955**, 20, 563

Examples:

(This step is a ***Claisen-Schmidt Reaction***.)



K. B. Raut, S. H. Wender, *Journal of Organic Chemistry* **1960**, 25, 50



J. R. Dharia, K. F. Johnson, J. B. Schlenof, *Macromolecules* **1994**, 27, 5167

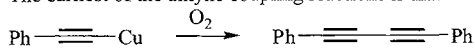
Alkyne Coupling

The Reaction:

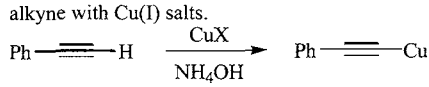
General Discussion:

See P. Siemsen, R. C. Livingston, F. Diederich, *Angewandte Chemie International Edition in English* **2000**, 39, 2632 and K. Sonogashira, *Comprehensive Organic Synthesis*, Vol 3, Chapter 2.5

The earliest of the alkyne coupling reactions is that of Glaser, who had noted:

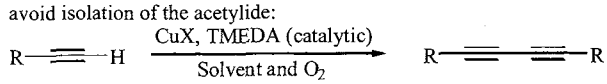


In much of the early work, the copper acetylides were prepared from the reaction of a terminal alkyne with Cu(I) salts.



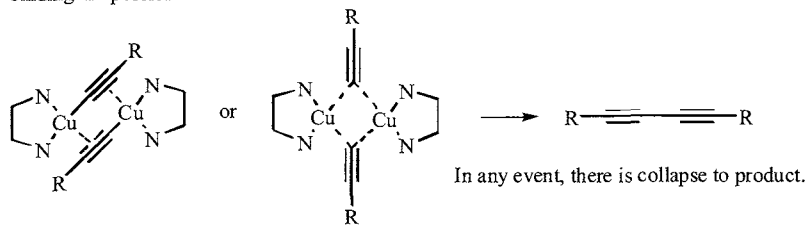
The reaction was of limited use due to the explosive nature of copper acetylides.

In the ***Hay modification*** of the ***Glaser reaction***, it was noted that the reaction could be modified to avoid isolation of the acetylide:



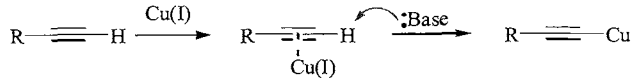
A. S. Hay, *Journal of Organic Chemistry* **1962**, 27, 3320

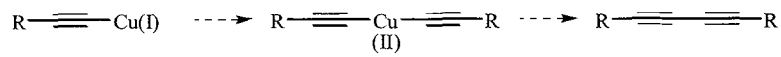
In this process the TMEDA-Cu complex readily binds to the alkyne. Various interpretations of the binding are possible:



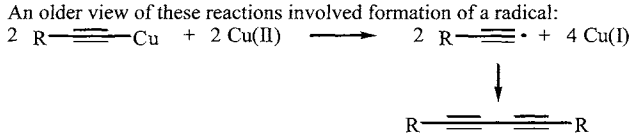
In any event, there is collapse to product.

There is evidence that the role of oxidant is to convert Cu(I) to Cu(II). It may be:





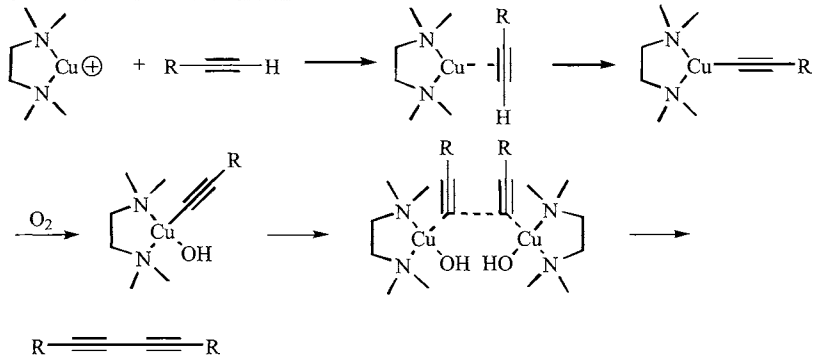
An older view of these reactions involved formation of a radical:



This would require that hetero-coupling of two different alkynes give a statistical product mix. This is not observed.

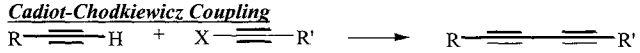
A computational study of the ***Glaser reaction*** provides additional mechanistic insight.
L. Fomina, B. Vazquez, E. Tkatchouk, S. Fomine, *Tetrahedron* **2002**, 58, 6741

Selected intermediates are shown:

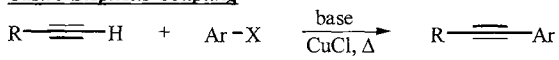


There is much to learn about the details of these reactions. In different sections the following reactions will be described:

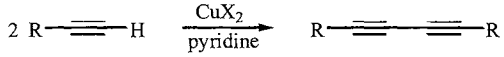
Cadiot-Chodkiewicz Coupling



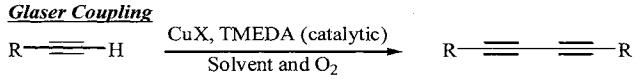
Castro-Stephens Coupling



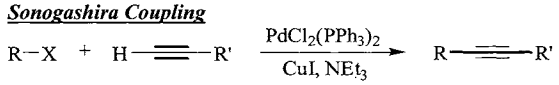
Eglinton Reaction



Glaser Coupling

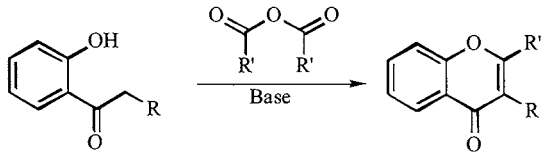


Sonogashira Coupling

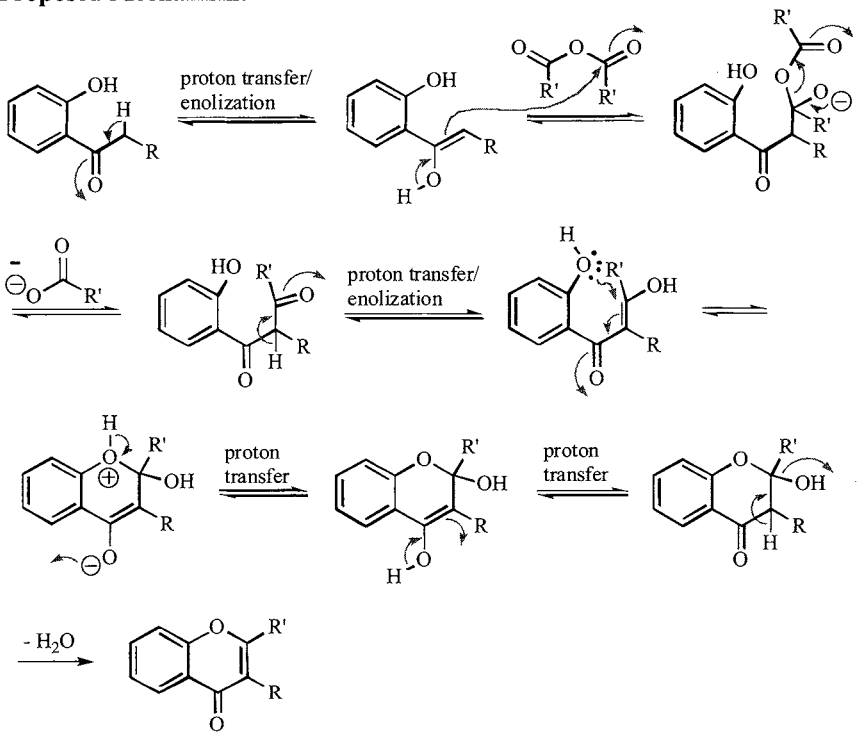


Allan-Robinson Reaction

The Reaction:



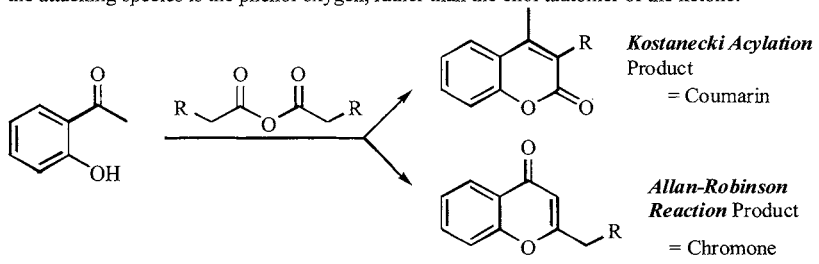
Proposed Mechanism:



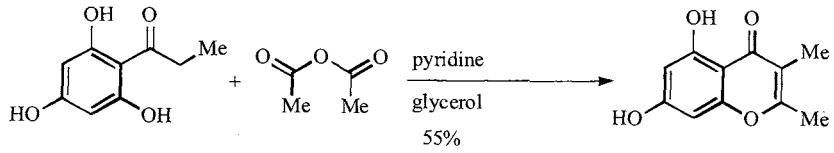
Notes:

The rate determining step is dependent on both the concentration of enolacetate and acetate ion. T. Szell, D. M. Zorandy, K. Menyharth, *Tetrahedron* **1969**, 25, 715

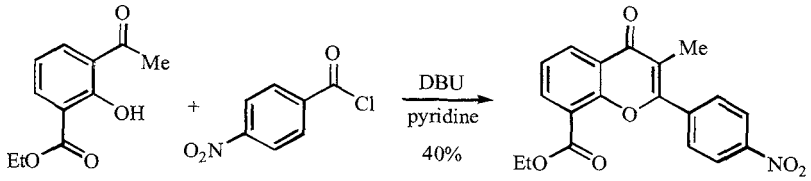
In the related ***Kostanecki Reaction***, the same reagents give a different product. In that case, the attacking species is the phenol oxygen, rather than the enol tautomer of the ketone.



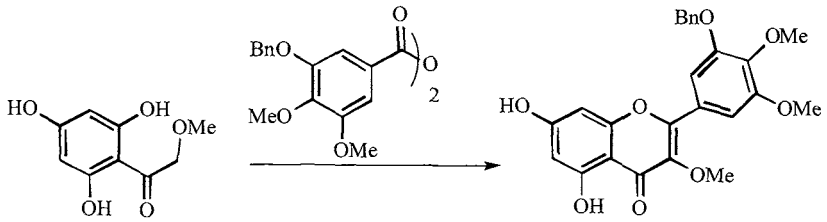
Examples:



T. Szell, *Journal of the Chemical Society*, C, **1967**, 2041 (AN 1968:2779)



C. Riva, C. De Toma, L. Donadel, C. Boi, R. Pennini, G. Motta, A. Leosardi, *Synthesis* **1997**, 195



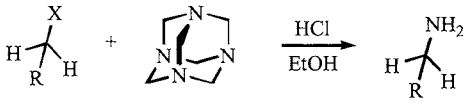
No yield given, product synthesis to confirm structure of an isolated compound.

G. Berti, O. Liv, D. Segnini, I. Cavero, *Tetrahedron* **1967**, 23, 2295

Amine Preparations

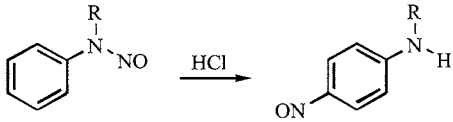
See R. E. Gawley, *Organic Reactions* **1988**, 35, 1

Delépine Reaction



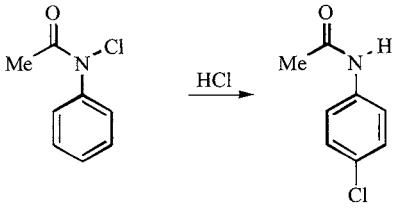
Fischer-Hepp and Related Rearrangements

Fischer-Hepp Rearrangement

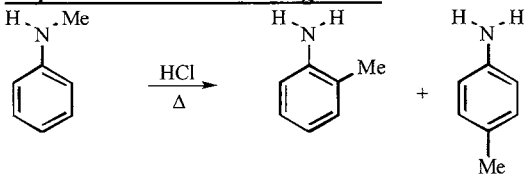


HCl is the preferred acid.

Orton Rearrangement

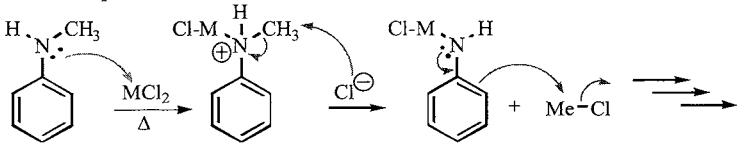


Hofmann-Martius Rearrangement



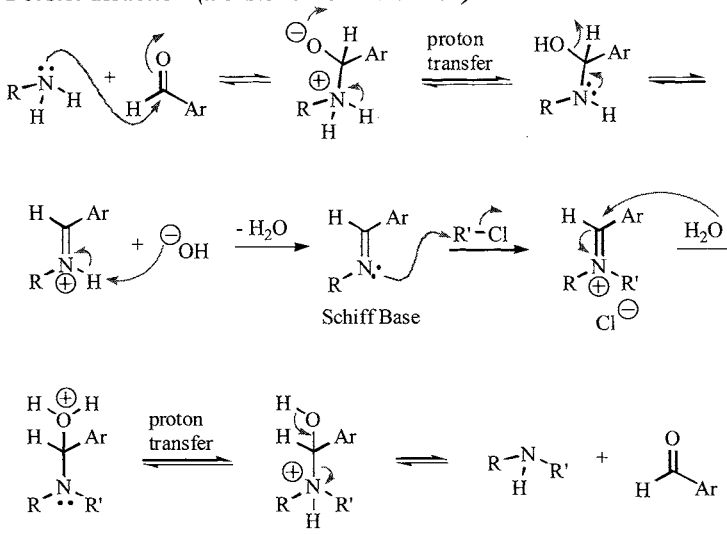
Reilly-Hickinbottom Rearrangement

Similar to ***Hoffmann-Martius Rearrangement*** except that it uses Lewis acids and the amine rather than protic acid and the amine salt.

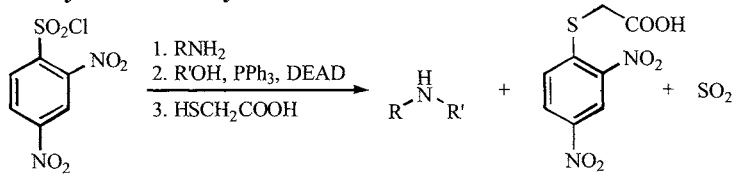


M = Co, Cd, Zn

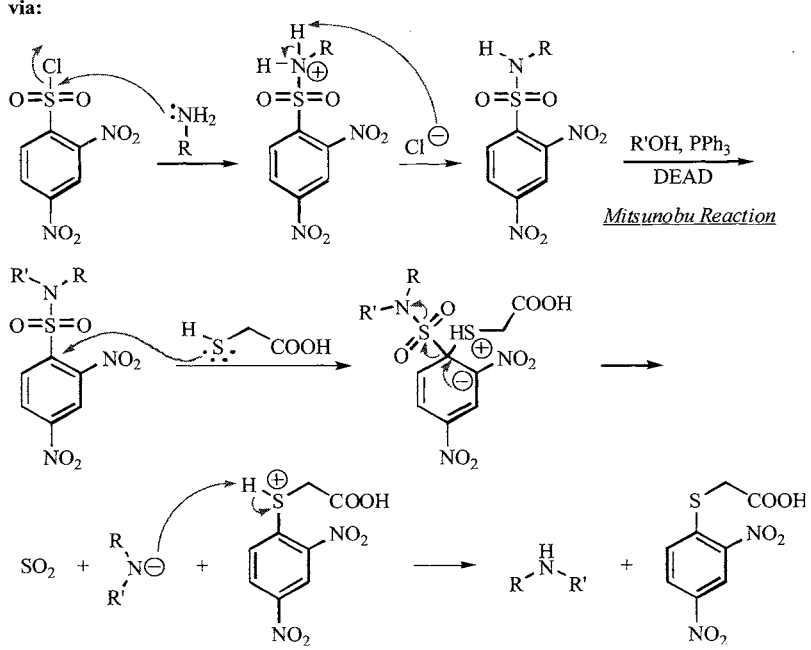
Forster Reaction (Forster-Decker Method)



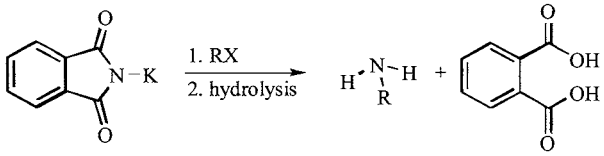
Fukuyama Amine Synthesis



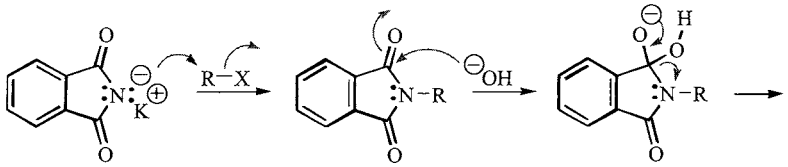
via:

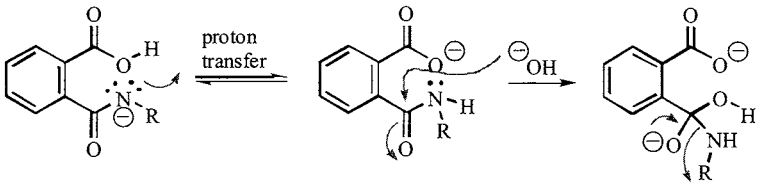


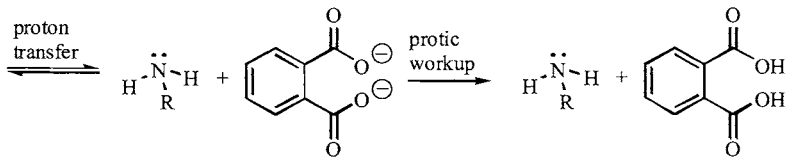
Gabriel Synthesis



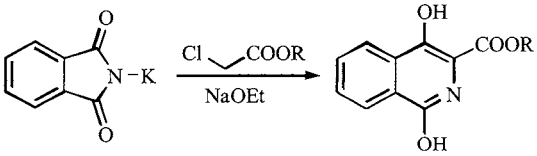
via:



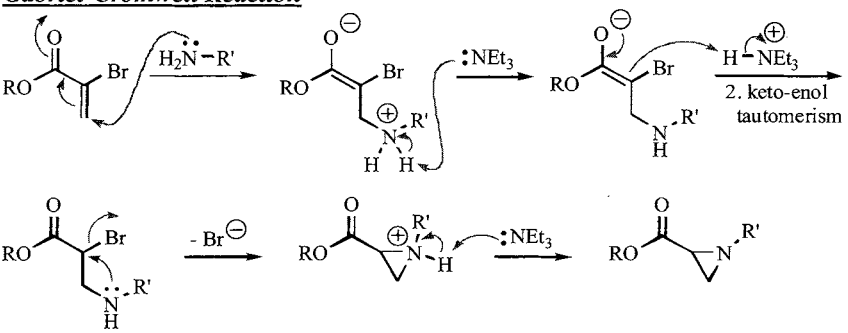




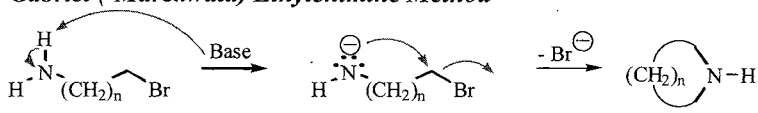
Gabriel-Colman Rearrangement



Gabriel-Cromwell Reaction

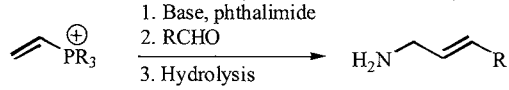


Gabriel (-Marckwald) Ethylenimine Method

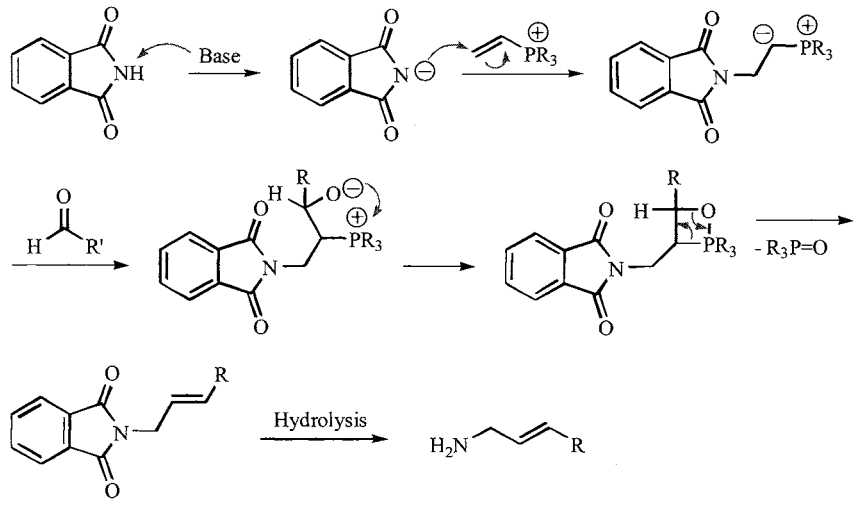


Schweizer Allyl Amine Synthesis

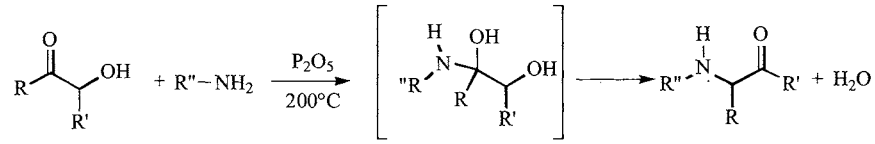
A combination of ***Gabriel*** and ***Wittig*** chemistry



via:

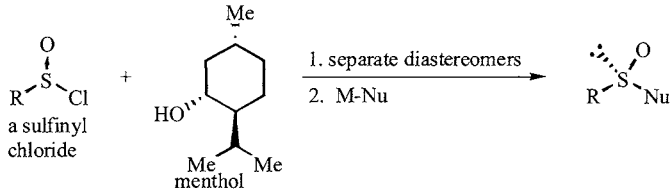


Voight Amination / Reaction

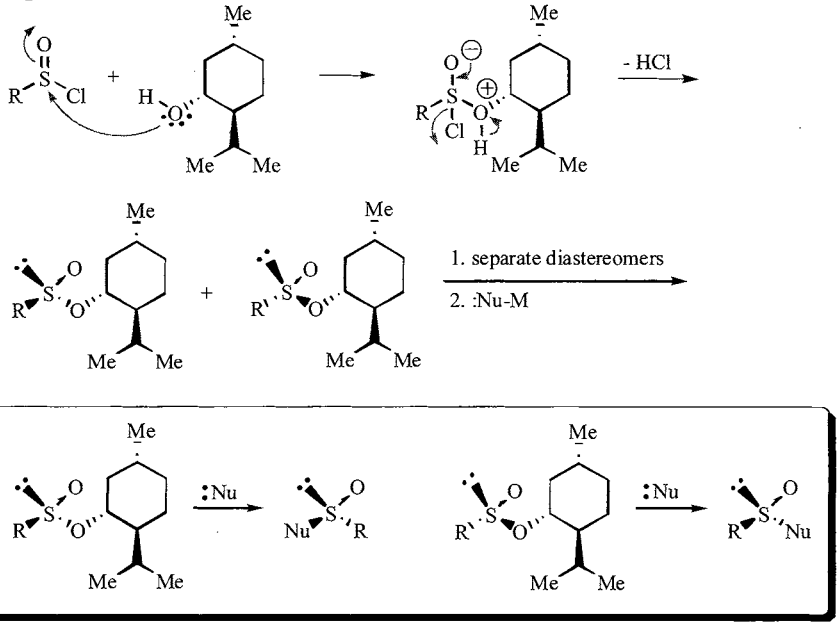


Andersen Sulfoxide Synthesis

The Reaction:



Proposed Mechanism:

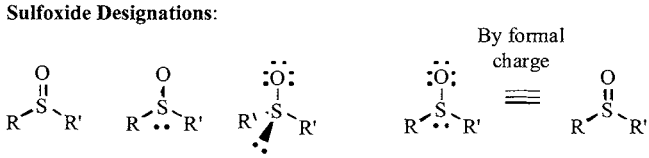


K. K. Andersen, *Tetrahedron Letters* **1962**, 3, 93

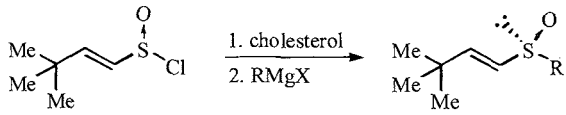
Notes:

Other chiral auxiliaries have been used besides menthol.

Sulfoxide Designations:

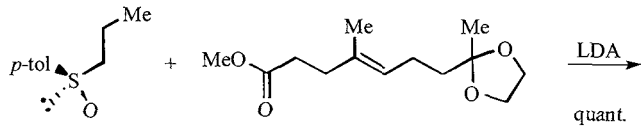


Examples:

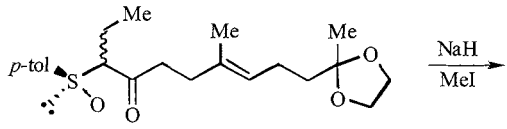


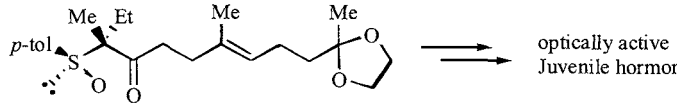
R = *n*-Bu: yield = 61%, 83% ee
R = Ph-CH_2: yield = 78%, 91% ee

R. R. Strickler, A. L. Schwan, *Tetrahedron: Asymmetry* **1999**, 10, 4065



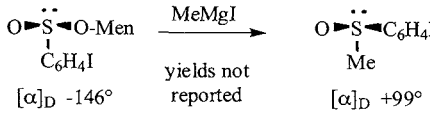
quant.
50:50 mixture





9:1 diastereoselectivity

H. Kosugi, O. Kanno, H. Uda, *Tetrahedron: Asymmetry* **1994**, 5, 1139

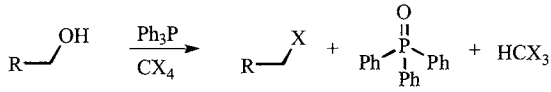


$[\alpha]_D$ -146° $[\alpha]_D$ +99°

P. Bickart, M. Axelrod, J. Jacobs, K. Mislow, *Journal of the American Chemical Society* **1967**, 89, 697

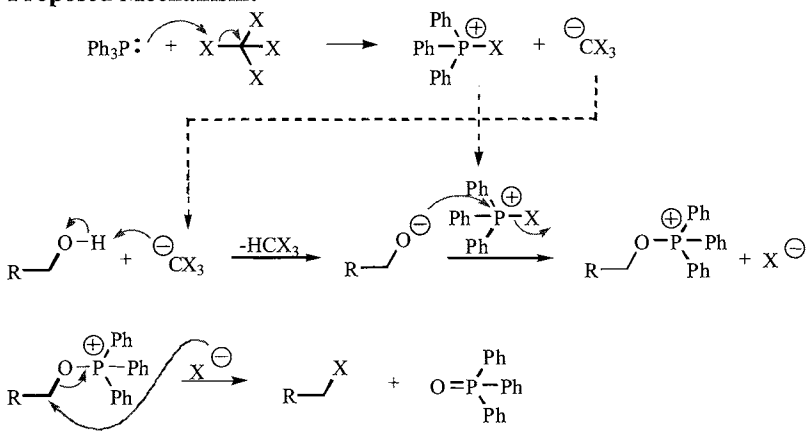
Appel Reaction

The Reaction:



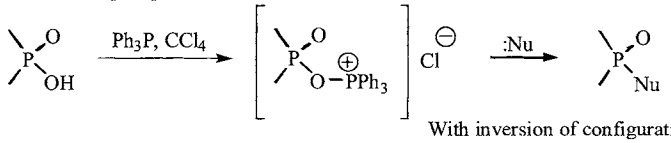
X = Cl or Br

Proposed Mechanism:



Notes:

There are two processes called the ***Appel Reaction***. Although similar, the second is concerned with reactions of phosphorous:

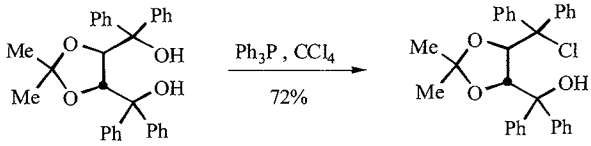


With inversion of configuration around P.:

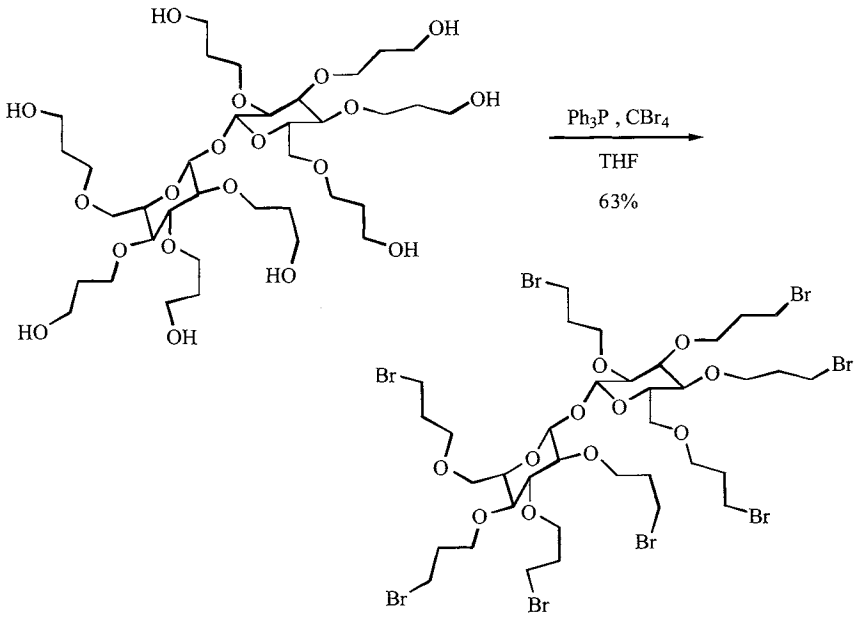
J. Baraniak, W. J. Stec, *Tetrahedron Letters* **1985**, 26, 4379

See also: J. Beres, W. G. Bentrude, L. Parkanji, A. Kalman, A. E. Sopchik, *Journal of Organic Chemistry* **1985**, 50, 1271

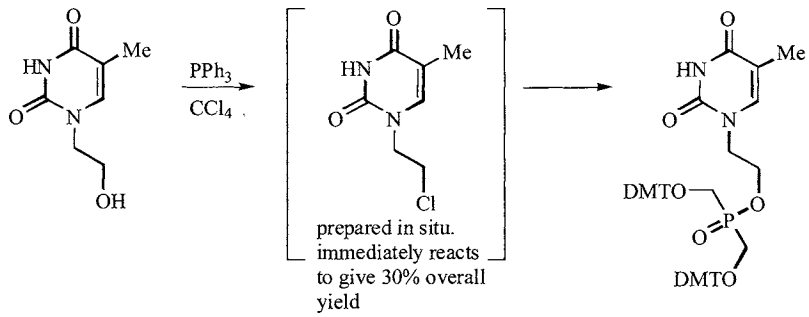
Examples:



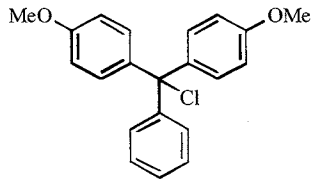
D. Seebach, A. Pichota, A. K. Beck, A. B. Pinkerton, T. Litz, J. Karjalainen, V. Gramlich, *Organic Letters* **1999**, 1, 55



M. Dubber, T. K. Lindhorst, *Organic Letters* **2001**, 3, 4019



ODMT (ODMTr) is the 4,4'-dimethoxytrityl group, a common –OH protecting group for the carbohydrate moieties in syntheses of polynucleotides.

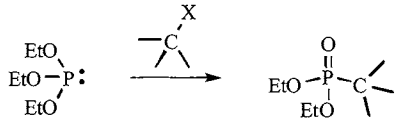


4,4'-dimethoxytrityl chloride [40615-36-9]

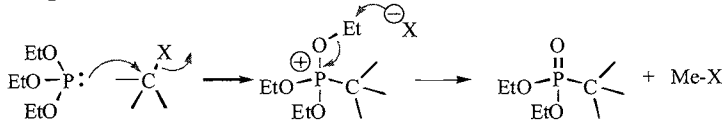
B. Nawrot, O. Michalak, M. Nowak, A. Okruszek, M. Dera, W. J. Stee, *Tetrahedron Letters* **2002**, 43, 5397

Arbuzov Reaction (Michaelis-Arbuzov Reaction)

The Reaction:



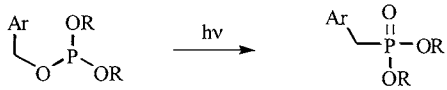
Proposed Mechanism:



Notes:

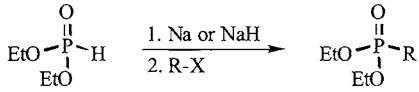
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, p. 12.; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1234.

The Photo-Arbuzov Reaction:

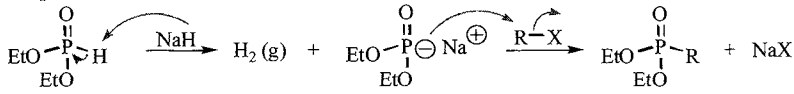


Michaelis-Becker Reaction (Michaelis Reaction)

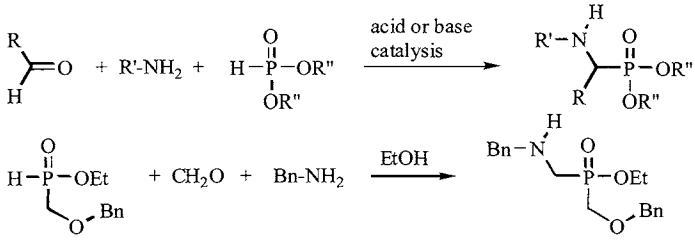
The Reaction:



Proposed Mechanism:

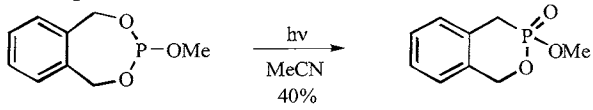


Kabachnik-Fields Reaction

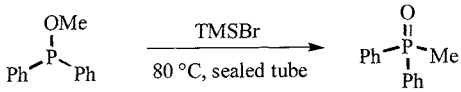


H.-J. Cristan, A. Herve, D. Virieux, *Tetrahedron* **2004**, 60, 877

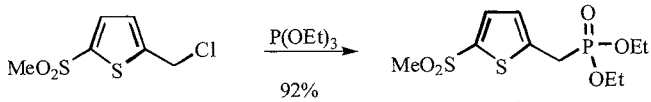
Examples:



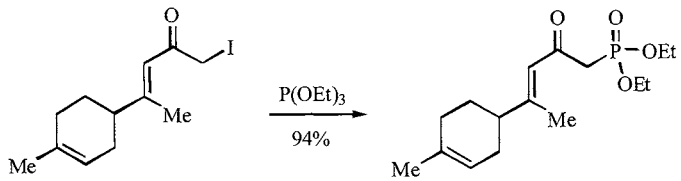
M. S. Landis, N. J. Turro, W. Bhanthumnavin, W. G. Bentrude, *Journal of Organometallic Chemistry* **2002**, 646, 239



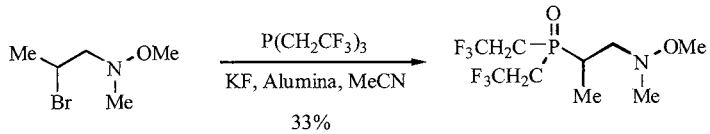
P.-Y. Renard, P. Vayron, C. Mioskowski, *Organic Letters* **2003**, 5, 1661



S.-S Chou, D.-J. Sun, J.-Y. Huang, P.-K. Yang, H.-C. Lin, *Tetrahedron Letters* **1996**, 37, 7279

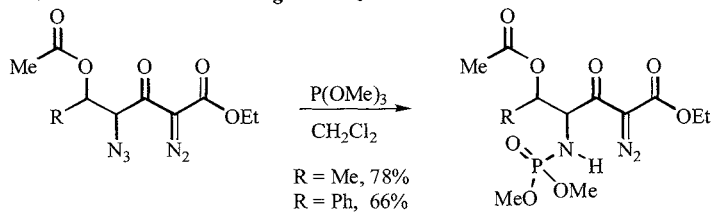


R. W. Driesen, M. Blouin, *Journal of Organic Chemistry* **1996**, 61, 7202

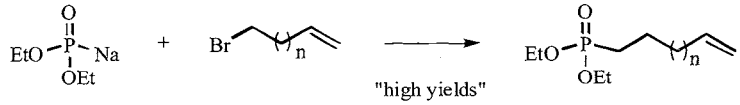


S. Fortin, F. Dupont, P. Deslongchamps, *Journal of Organic Chemistry* **2002**, 67, 5437

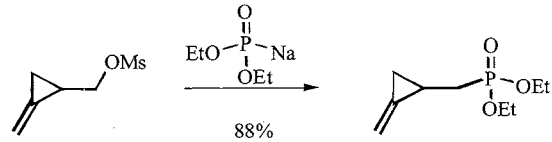
Described as a tandem ***Staudinger-Arbuzov Reaction***:



M. M. Sá, G. P. Silveira, A. J. Bortoluzzi, A. Padwa, *Tetrahedron* **2003**, 59, 5441



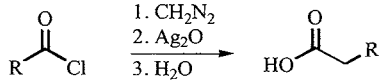
I. Pergament, M. Srebnik, *Organic Letters* **2001**, 3, 217



H.-P. Guan, Y.-L. Qui, M. B. Ksebati, E. A. Kern, J. Zemlicka, *Tetrahedron* **2002**, 58, 6047

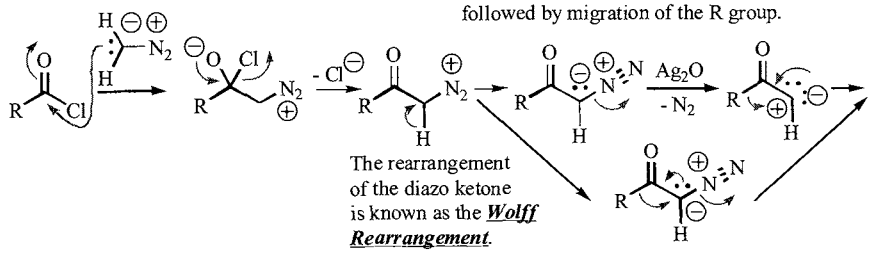
Arndt-Eistert Homologation Reaction

The Reaction:



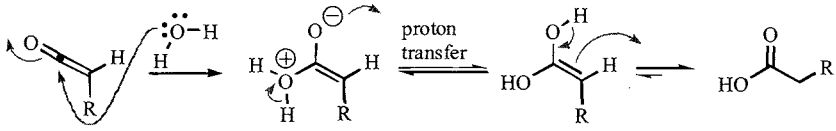
Proposed Mechanism:

Elimination of nitrogen gives a carbene, followed by migration of the R group.



The rearrangement of the diazo ketone is known as the ***Wolff Rearrangement***.

Alternatively, R migration and N_2 elimination may be concerted, avoiding the formation of a carbene.



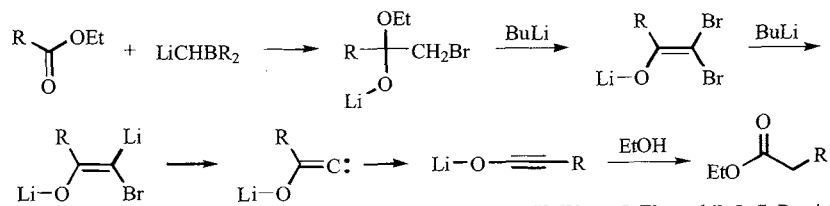
keto-enol tautomerism

Notes:

See: *Diazomethane*

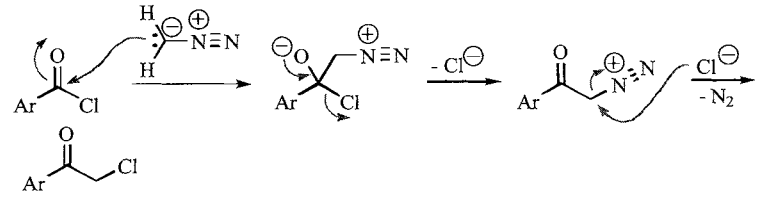
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1405-1407; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 13-15; W. E. Bachmann, W. S. Struve, *Organic Reactions* **1**, 2

The ***Kowalski Ester Homologation*** provides a similar conversion (C. Kowalski, M. S. Haque, *Journal of Organic Chemistry* **1985**, 50, 5140)

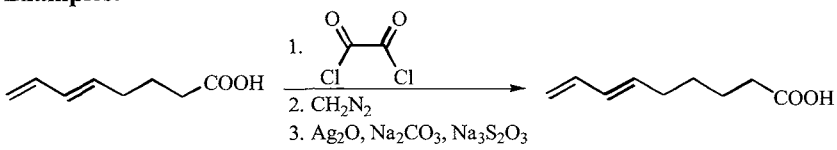


See also: P. Chen, P. T. W. Cheng, S. H. Spergel, R. Zahler, X. Wang, J. Thottathil, J. C. Barrish, R. P. Polniaszek, *Tetrahedron Letters* **1997**, 38, 3175

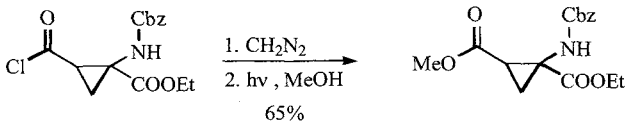
Nierenstein Reaction



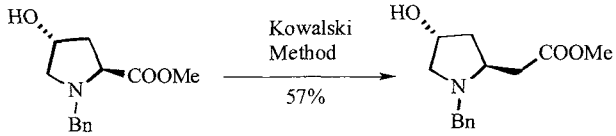
Examples:



T. Hudlicky, J. P. Sheth, *Tetrahedron Letters* **1979**, 29, 2667

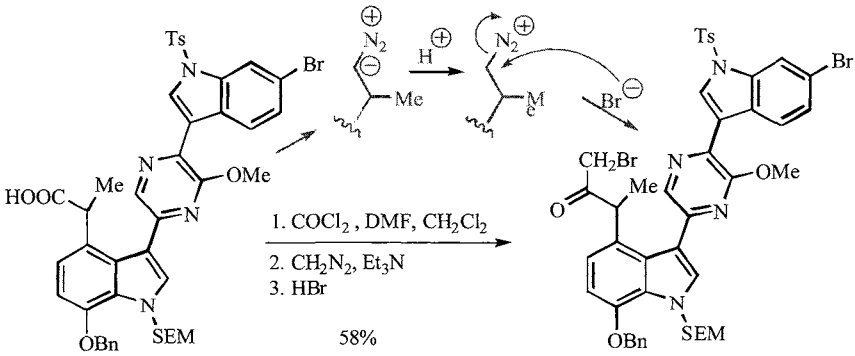


J. M. Jimenez, R. M. Ortuno, *Tetrahedron: Asymmetry* **1996**, 7, 3203

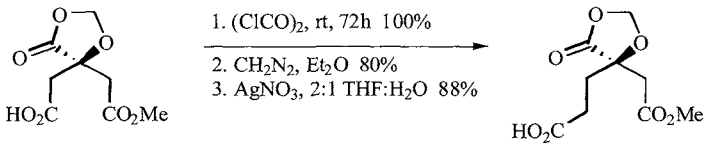


A number of examples to show that this method is more mild than the ***Arndt-Eistert*** reaction

D. Gray, C. Concello', T. Gallagher, *Journal of Organikc Chemistry* **2004**, 69, 4849



N. J. Garg, R. Sarpong, B. M. Stoltz, *Journal of the American Chemical Society* **2002**, 124, 13179

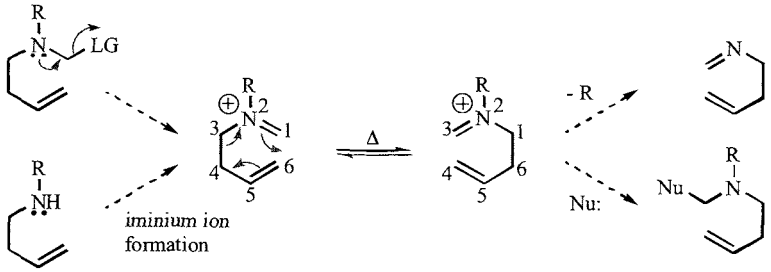


R. A. Ancliff, A. T. Russell, A. J. Sanderson *Tetrahedron: Asymmetry* **1997**, 8, 3379

Aza-Cope Rearrangement

The Reaction:

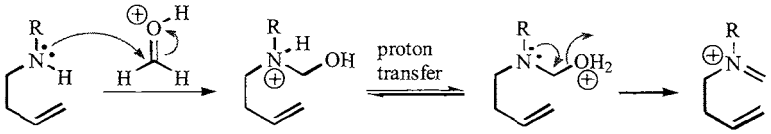
Proposed Mechanism:



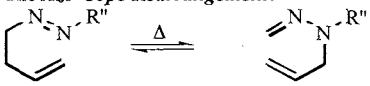
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1445.

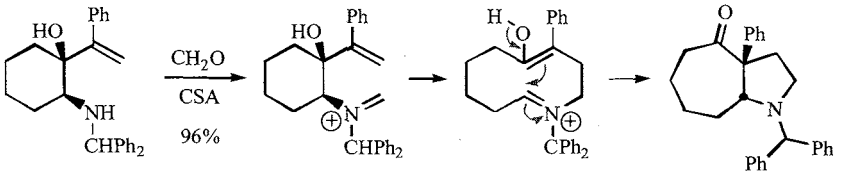
iminium ion formation



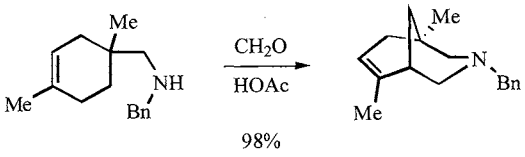
The ***Azo-Cope Rearrangement***:



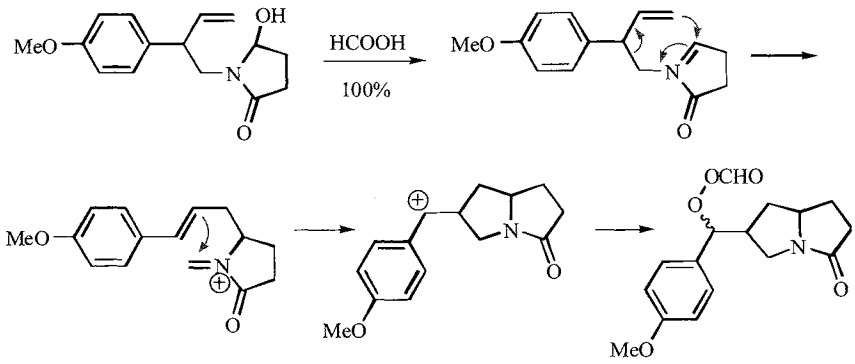
Examples:



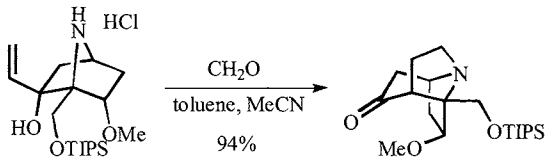
L. E. Overman, E. J. Jacobsen, R. J. Doedens, *Journal of Organic Chemistry* **1983**, 48, 3393



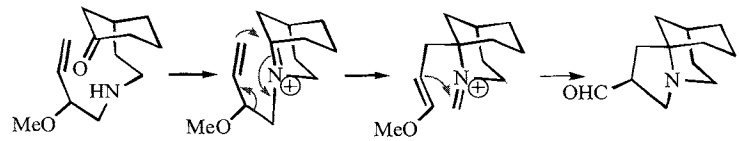
K. Shishido, K. Hiroya, K. Fukumoto, T. Kametani, *Tetrahedron Letters* **1986**, 27, 1167



H. Ent, H. De Koning, W. N. Speckamp *Journal of Organic Chemistry* **1986**, 51, 1687



M. Bruggemann, A. I. McDonald, L. E. Overman, M. D. Rosen, L. Schwink, J. P. Scott, *Journal of the American Chemical Society* **2003**, 125, 15284

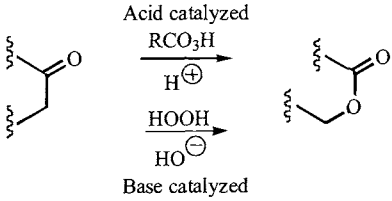


No yield given for this step, catalyzed by tosic acid in benzene.

K. M. Brummond, J. Lu, *Organic Letters* **2001**, 3, 1347

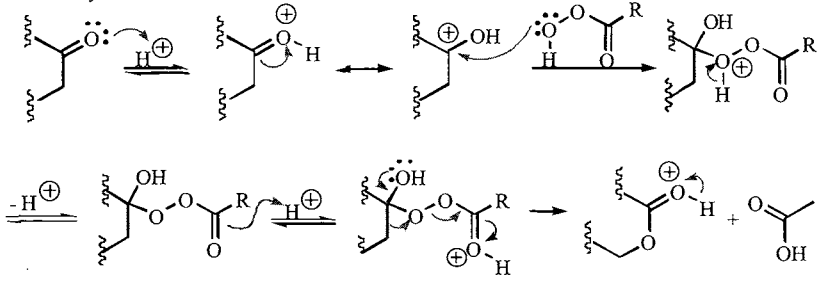
Baeyer-Villiger Reaction

The Reaction:

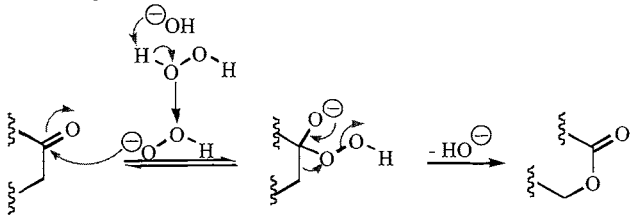


Proposed Mechanism:

Acid catalyzed:



Base catalyzed:

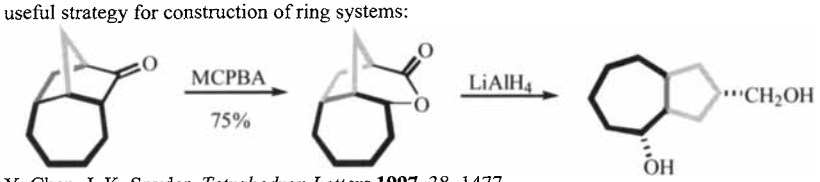


Notes:

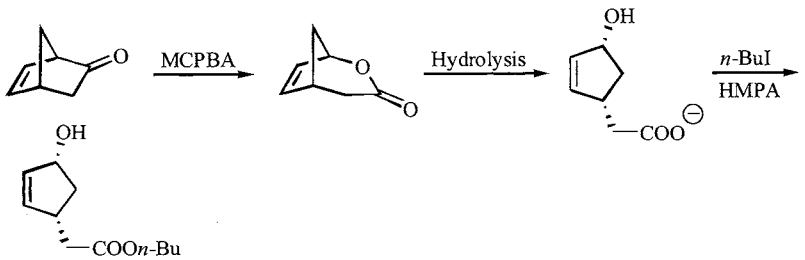
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1417-1418; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 16-19; C. H. Hassall, *Organic Reactions* **9**, 3; G. R. Krow, *Organic Reactions* **43**, 3.

Migratory Apptitude: 3° > 2°> Ph-CH_2-> Ph- > 1°> Me > H

Hydrolysis or reduction of the lactone ring provided by reaction with cyclic ketones provides a useful strategy for construction of ring systems:



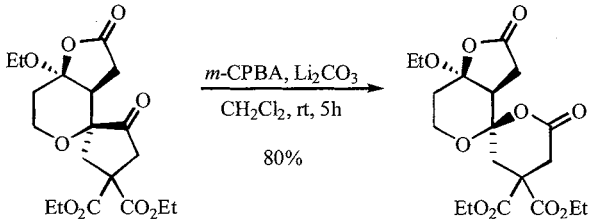
Y. Chen, J. K. Snyder, *Tetrahedron Letters* **1997**, 38, 1477



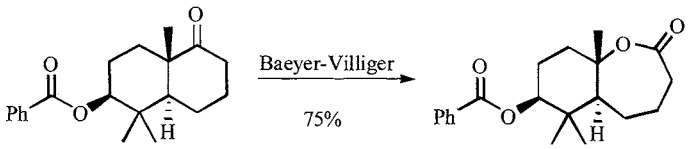
A. E. Greene, C. Le Drian, P. Crabbe, *Journal of the American Chemical Society* **1980**, 102, 7584

Examples:

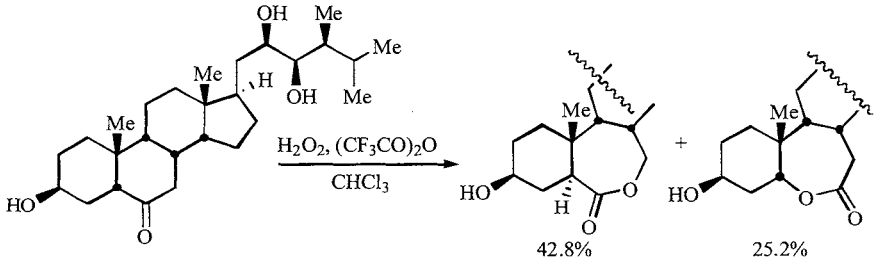
Note the retention of stereochemistry after the oxygen insertion. This is a general observation.



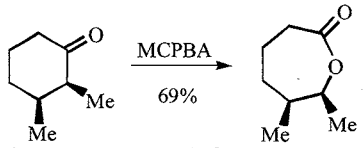
N. Haddad, Z. Abramovich, I. Ruhman *Tetrahedron Letters* **1996**, 37, 3521



F. W. J. Demnitz, R. A. Parhael, *Synthesis* **1996**, 11, 1305



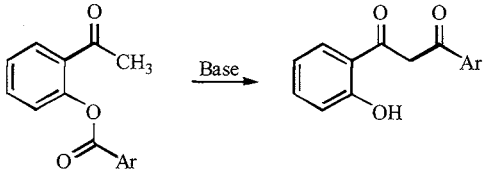
B. Voigt, J. Schmidt, G. Adam, *Tetrahedron* **1996**, 52, 1997



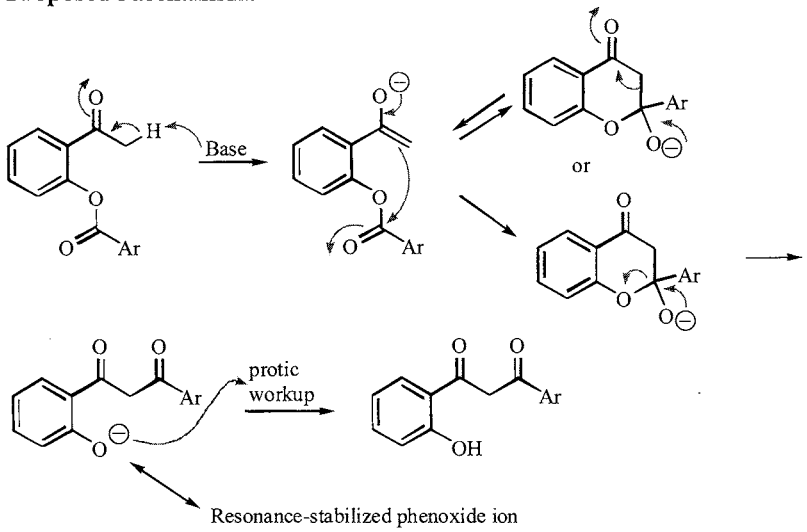
G. Magnusson, *Tetrahedron Letters* **1977**, 18, 2713

Baker-Venkataraman Rearrangement

The Reaction:



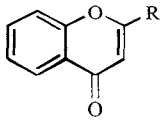
Proposed Mechanism:



See: T. Szell, G. Balaspiri, T. Balaspiri, *Tetrahedron* **1969**, 25, 707

Notes:

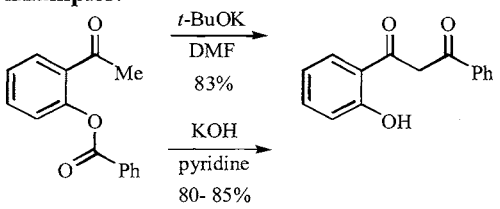
These β-diketones are useful intermediates for the synthesis of flavones and chromones:



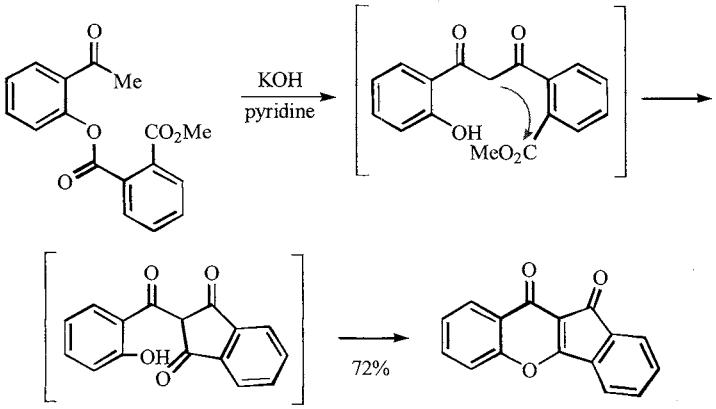
R = Ph: Flavone; R = Me: Chromone

V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, pp. 277-278

Examples:

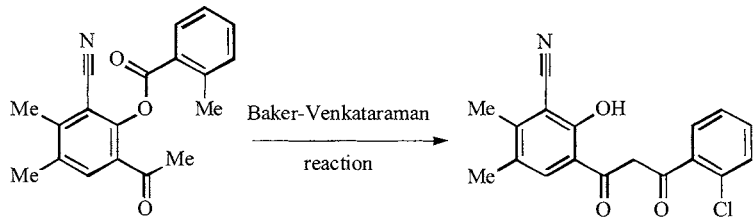


A. Nishinaga, H. Ando, K. Maruyama, T. Mashino, *Synthesis* **1992**, 839
T. S. Wheeler, *Organic Syntheses*, CV4, 478

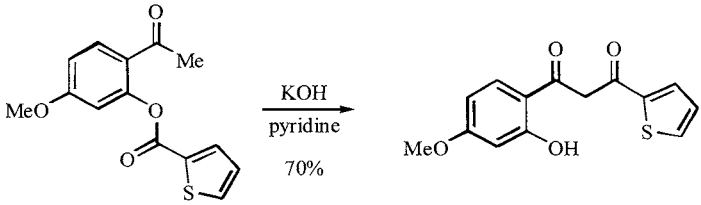


A ring closure that is often associated with the reaction is called the ***Baker-Venkataraman Reaction***.

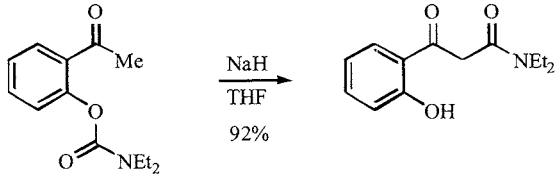
N. Thasana, S. Ruchirawat, *Tetrahedron Letters* **2002**, 43, 4515



S. J. Cutler, F. M. El-Kabbani, C. Keane, S. L. Fisher-Shore, C. D. Blanton, *Heterocycles* 1990, 31, 651 (AN 1990:552089)



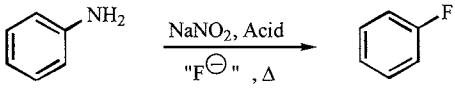
P. F. Devitt, A. Timoney, M. A. Vickars, *Journal of Organic Chemistry* **1961**, 26, 4941



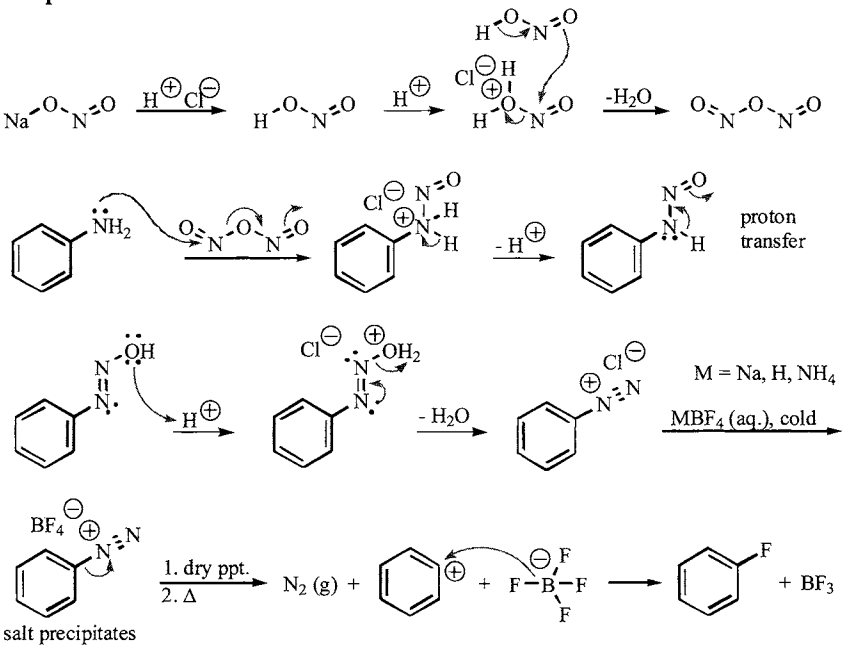
A. V. Kalinin, A. J. M. da Silva, C. C. Lopes, R. S. C. Lopes, V. Snieckus *Tetrahedron Letters* **1998**, 39, 4995

Balz-Schiemann Reaction (Schiemann Reaction)

The Reaction:

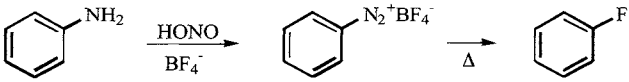


Proposed Mechanism:



Notes:

The original work:



G. Balz, G. Schiemann,*Berichte der Deutschen Chemischen Gesellschaft* **1927**, 60, 1186

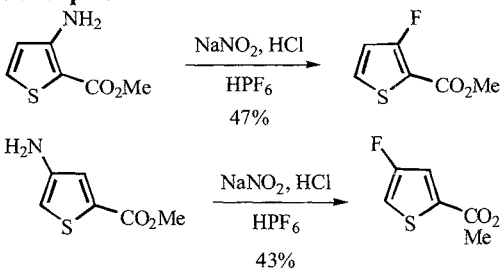
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 237-238; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 875; A. Roe, *Organic Reactions* 5, 4

Reaction is often incorporated into the ***Sandmeyer Reactions*** series,

Procedural improvement to avoid isolation of the (toxic) intermediate:
D. J. Milner, P. G. McMunn, J. S. Moilliet, *Journal of Fluorine Chemistry* **1992**, 58, 317 and D. J. Milner, *Journal of Fluorine Chemistry* **1991**, 54, 382

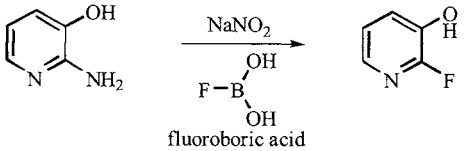
Reaction improvement by using ionic liquid salts:
K. K. Laali, V. J. Gettwert, *Journal of Fluorine Chemistry* **2001**, 107, 31

Examples:

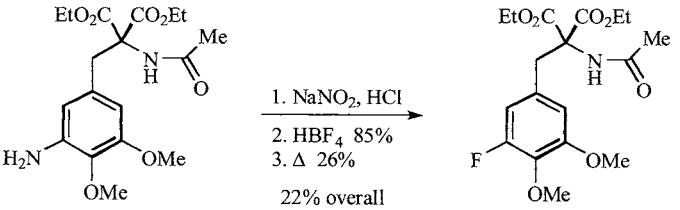


A. Kiryanov, A. Seed, P. Sampson, *Tetrahedron Letters* **2001**, 42, 8797

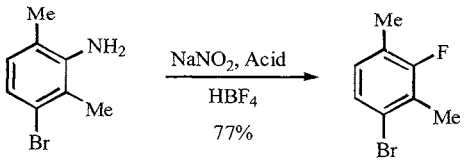
A modified ***Balz-Schiemann Reaction***:



F. Dolle, L. Dolci, H. Valette, F. Hinnen, F. Vaufrey, H. Guenther, C. Fuseau, C. Coulon, M. Buttalender, C. Crouzel *Journal of Medicinal Chemistry* **1999**, 42, 2251



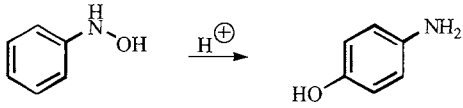
M. Argentini, C. Wiese, R. Weinreich, *Journal of Fluorine Chemistry* **1994**, 68, 141



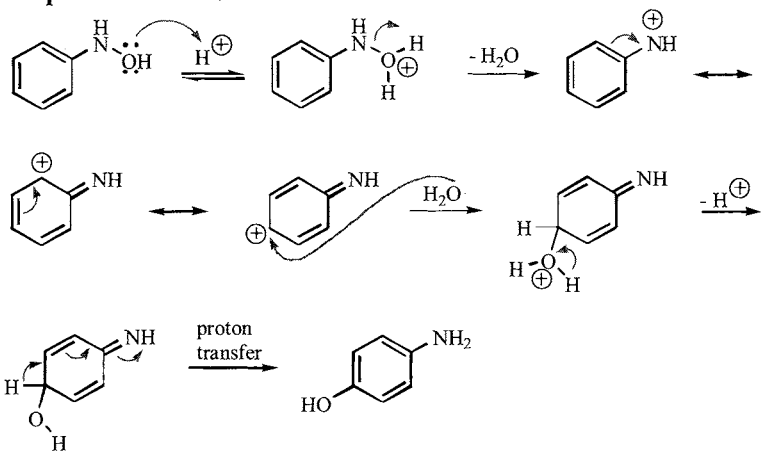
H. Hart, J. F. Janssen, *Journal of Organic Chemistry* **1970**, 35, 3637

Bamberger Rearrangement

The Reaction:



Proposed Mechanism:

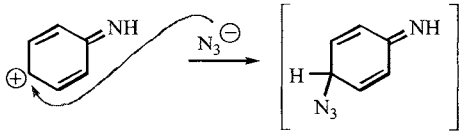


See discussion in: N. Haga, Y. Endo, K.-i. Kataoka, K. Yamaguchi, K. Shudo, *Journal of the American Chemical Society* **1992**, 114, 9795

Notes:

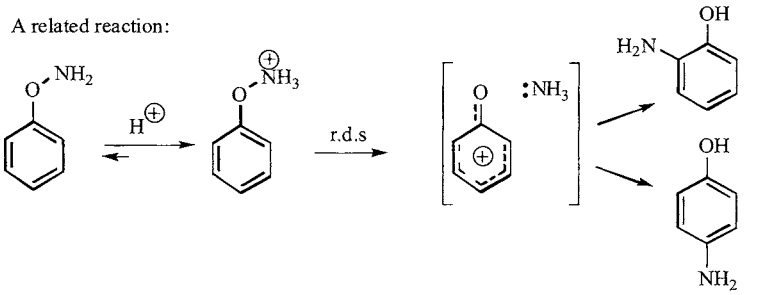
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 878; V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, p. 449

By addition of azide ion to the reaction, the intermediate can be competitively trapped:



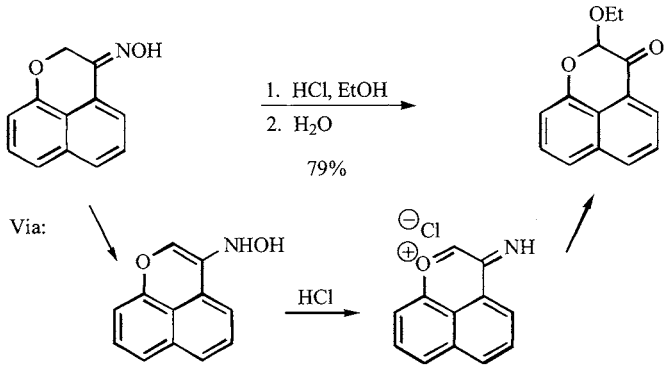
J. C. Fishbein, R. A. McClelland, *Journal of the American Chemical Society* **1987**, 109, 2824

A related reaction:

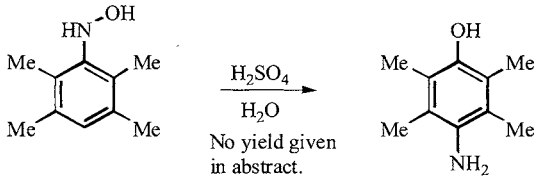


N. Haga, Y. Endo, K.-i. Kataoka, K. Yamaguchi, K. Shudo, *Journal of the American Chemical Society* **1992**, 114, 9795

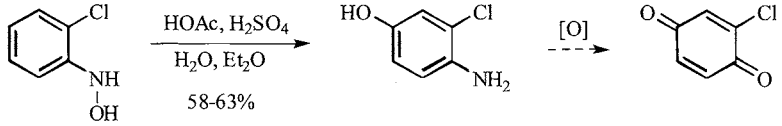
Examples:



J. C. Jardy, M. Venet, *Tetrahedron Letters* **1982**, 23, 1255



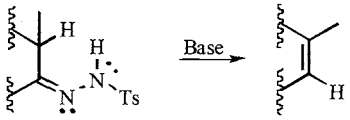
G. G. Barclay, J. P. Candlin, W. Lawrie, P. L. Paulson, *Journal of Chemical Research Synopses* **1992**, 245



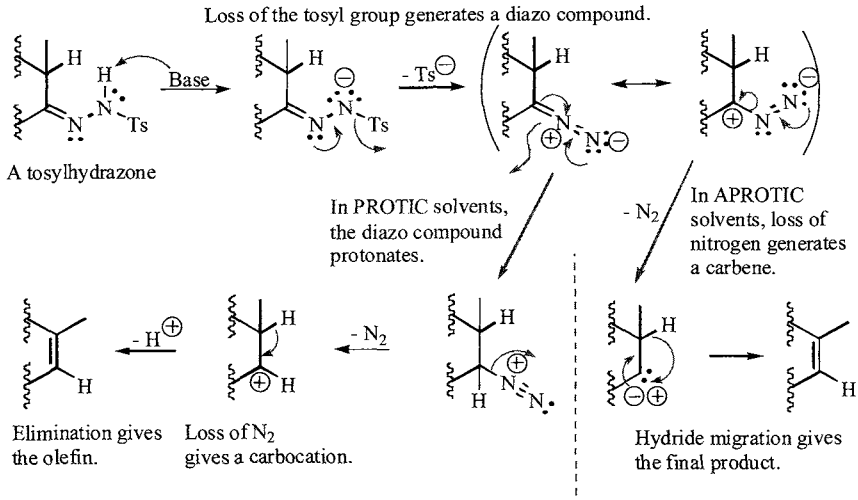
R. E. Harman, *Organic Syntheses* CV4, 148

Bamford-Stevens Reaction

The Reaction:



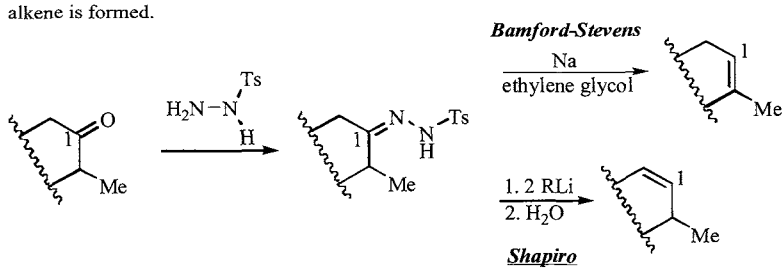
Proposed Mechanism:



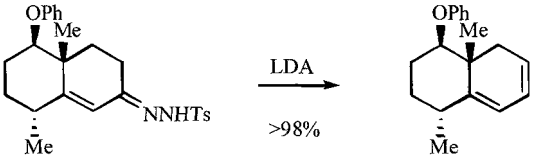
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1335; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 19-22; R. H. Shapiro, *Organic Reactions* **23**, 3

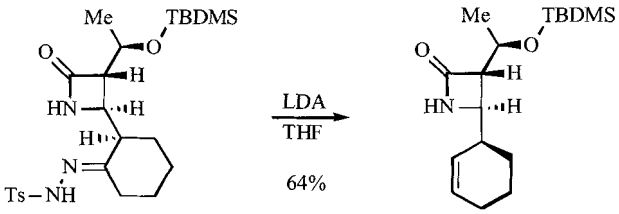
In the related ***Shapiro reaction***, two equivalents of an alkyl lithium are used and the less substituted alkene is formed.



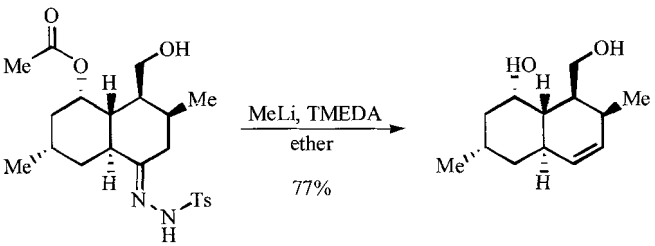
Examples:



P. A. Grieco, T. Oguri, C.-L. J. Wang, E. Williams, *Journal of Organic Chem*istry **1977**, 42, 4113

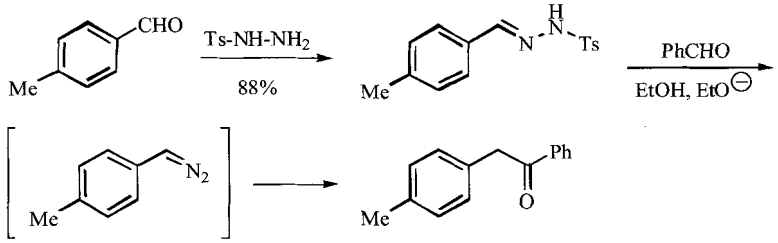


C. Marchioro, G. Pentassuglia, A. Perboni, D. Donati, *Journal of the Chemical Society Perkin Transactions 1* **1997**, 463



S. J Hecker, C. H. Heathcock, *Journal of the American Chemical Society* **1986**, 108, 4586

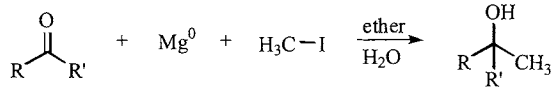
A general method for the homologation of aldehydes to benzylic ketones makes use of the ***Bamford-Stevens*** approach, via intermediate aryldiazomethanes:

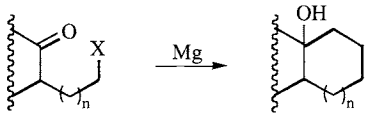


S. R. Angle, M. L. Neitzel, *Journal of Organic Chemistry* **2000**, 65, 6458

Barbier (Coupling) Reaction

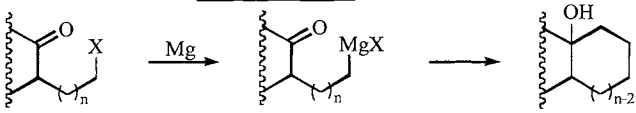
The Reaction:





Proposed Mechanism:

Resembles an internal ***Grignard reaction***:



Notes:

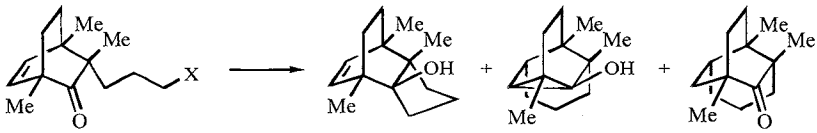
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1205

This reaction was used before it was noted that adding the halide to magnesium prior to the addition the carbonyl gave a better reaction. See the ***Grignard Reaction***.

Other metals may be used.

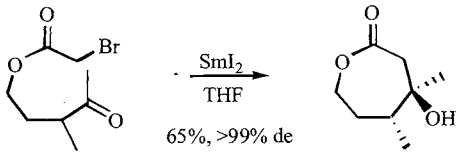
A variety of reactions of a carbonyl and an organohalogen compound are classified as ***Barbier and Barbier-type***.

Examples:



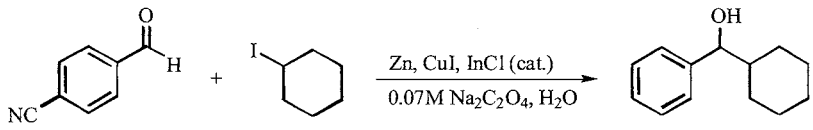
X	Conditions	Ratio
Br	Li powder, ultrasound, Et_2O	34 50 -
Br	Mg turning, $HgCl_2$, ultrasound, THF	10 12 37
I	BuLi, THF	71 - -

W. Zhang, P. Dowd, *Tetrahedron Letters* **1993**, 34, 2095

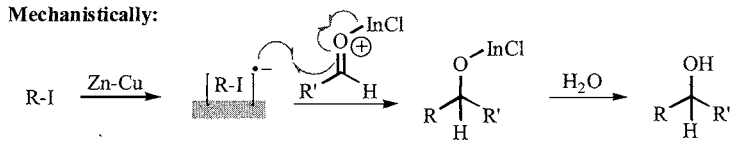


C. A. Molander, J. B. Etter, L. S. Harring, P.-J. Thorel, *Journal of the American Chemical Society* **1991**, 113, 3889

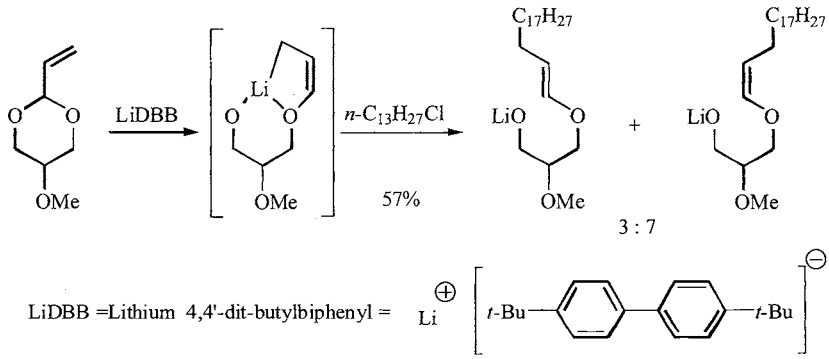
For a review of diiodosamarium chemistry (including ***Barbier Reactions***) see:
H. Kagan, *Tetrahedron* **2003**, 59, 10351



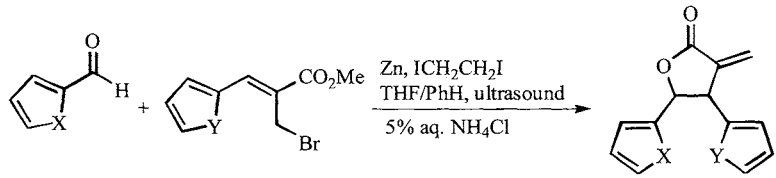
Mechanistically:



C. C. K. Keh, C. Wei, C.-J, Li, *Journal of the American Chemical Society* **2003**, 125, 4062



J. Shin, O. Gerasimov, D. H. Thompson, *Journal of Organic Chemistry* **2002**, 67, 6503

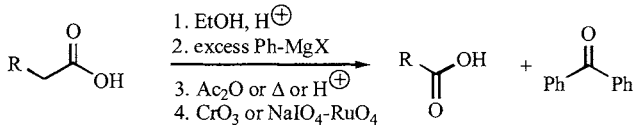


X = O, Y = S 68% (cis/trans = 95/5) X = S, Y = S 72% (cis/trans = 95/5)
X = O, Y = O 71% (cis/trans = 56/44) X = S, Y = O 43% (cis/trans = 52/48)

A. S.-Y. Lee, Y.-T. Chang, S.-H. Wang, S.-F. Chu, *Tetrahedron Letters* **2002**, 43, 8489

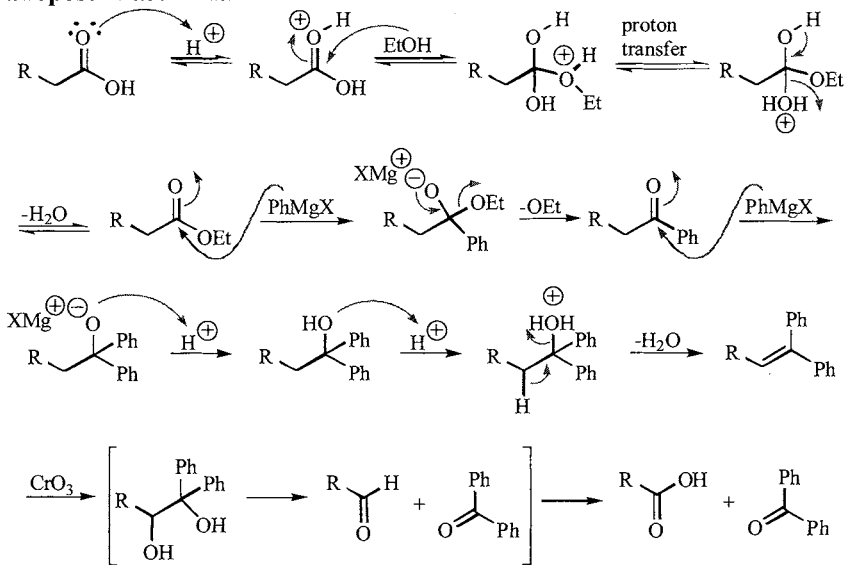
Barbier-Wieland Degradation (Barbier-Locquin Degradation)

The Reaction:



A procedure for decreasing a chain length by one carbon.

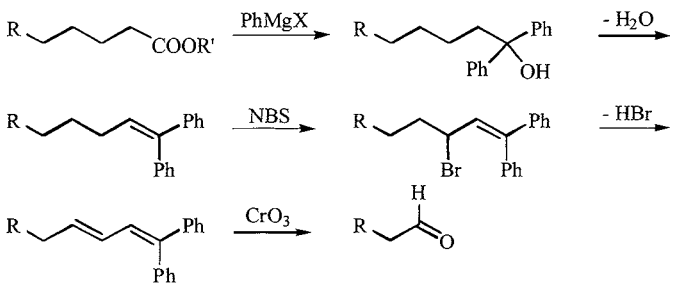
Proposed Mechanism:



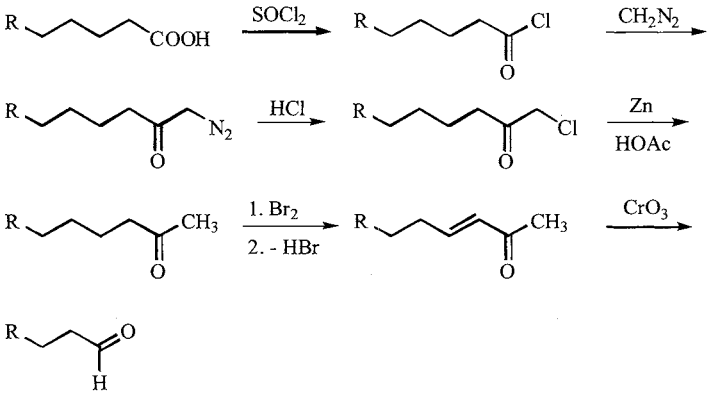
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1526.

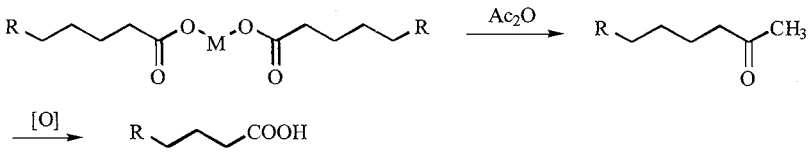
A variation of this procedure, the ***Meystre-Miescher-Wettstein Degradation (Miescher Degradation)*** removes three carbons from the chain:



Gallagher-Hollander Degradation

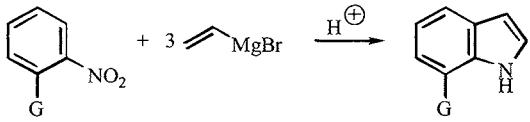


Krafft Degradation

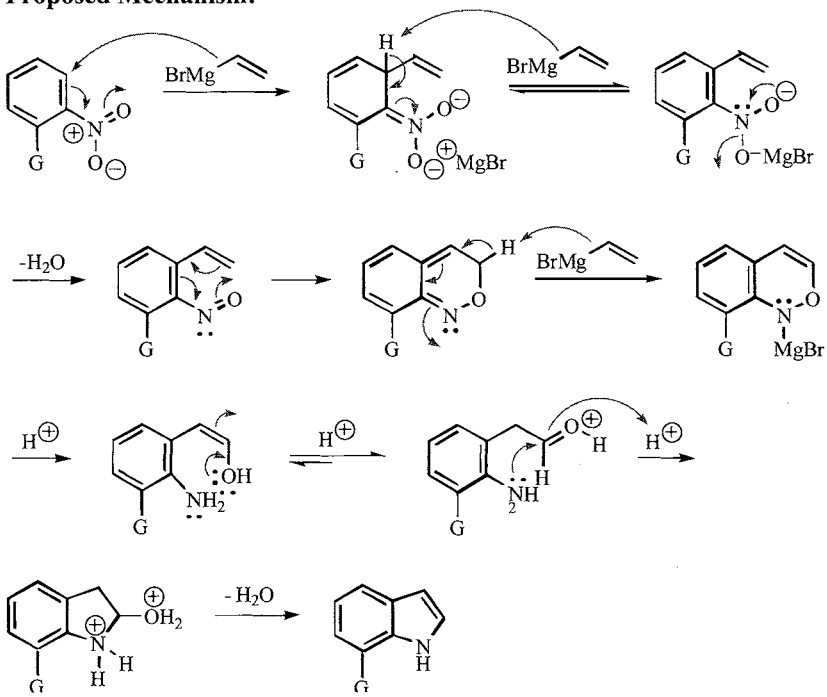


Bartoli Indole Synthesis

The Reaction:



Proposed Mechanism:

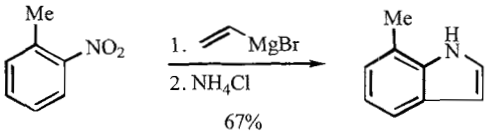


Notes:

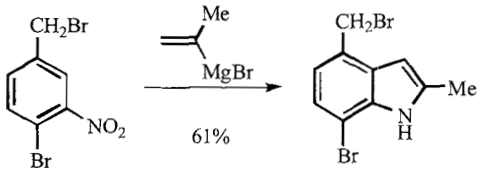
G. Bartoli, G. Palmieri, M. Bosco, R. Dalpozzo, *Tetrahedron Letters* **1989**, 30, 2129;
G. Bartoli, M. Bosco, R. Dalpozzo, *Tetrahedron Letters* **1985**, 26, 115

The reaction works only with the ortho position of the nitrobenzene occupied.

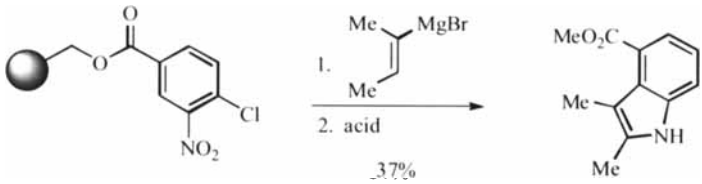
Examples:



G. Bartoli, G. Palmieri, M. Bosco, R. Dalpozzo, *Tetrahedron Letters* **1989**, 30, 2129



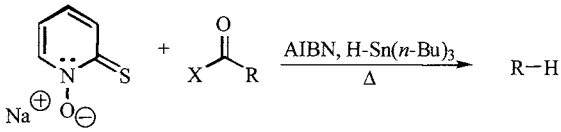
A. Dobbs, *Journal of Organic Chemistry* **2001**, 66, 638



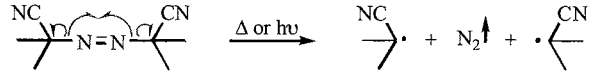
K. Knepper, S. Brase, *Organic Letters* **2003**, 5, 2829

Barton Decarboxylation

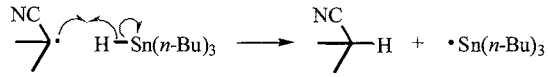
The Reaction:



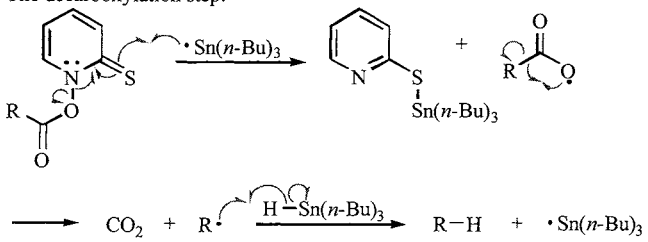
Proposed Mechanism:



AIBN = Azo-*bis*-isobutyronitrile

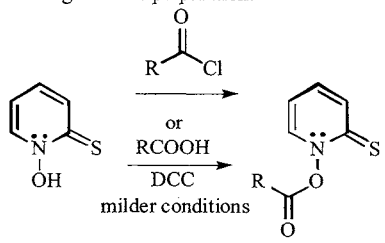


The decarboxylation step:

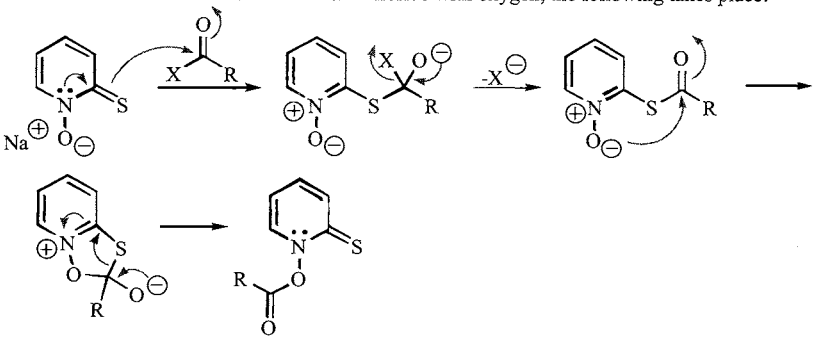


Notes:

Starting material preparation:

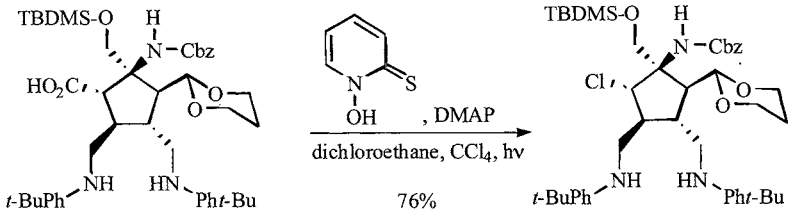


Rather than direct reaction of the the acid chloride with oxygen, the following takes place:

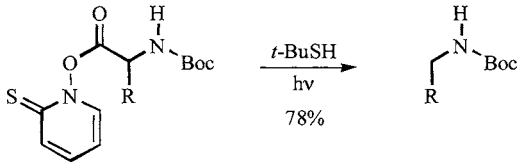


D. Crich *Aldrichimica Acta* **1987**, 20, 35

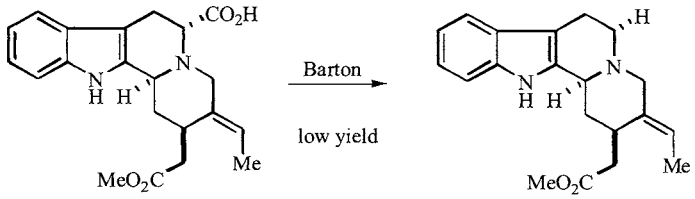
Examples:



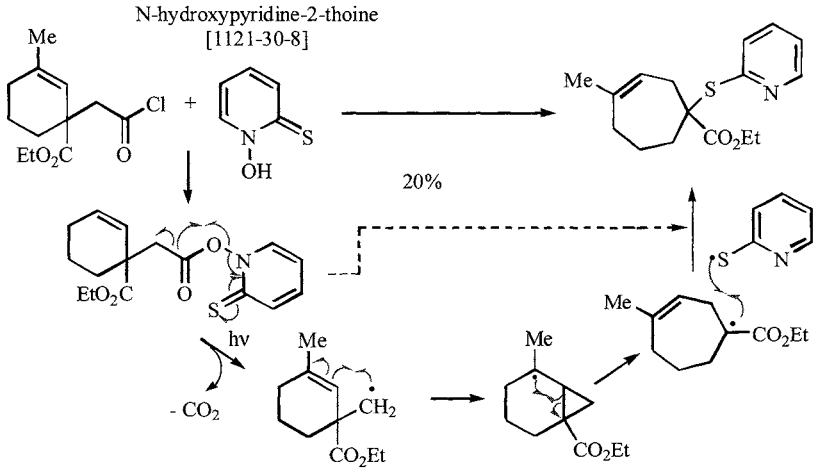
J. T. Starr, G. Koch, E. M. Carreira, *Journal of the American Chemical Society* **2000**, 122, 8793



D. H. R. Barton, Y. Herve, P. Potier, J. Thierry, *Tetrahedron*, **1988**, 44, 5479



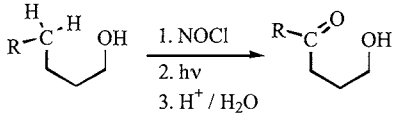
S. F. Martin, K. X. Chen, C. T. Eary, *Organic Letters* **1999**, 1, 79



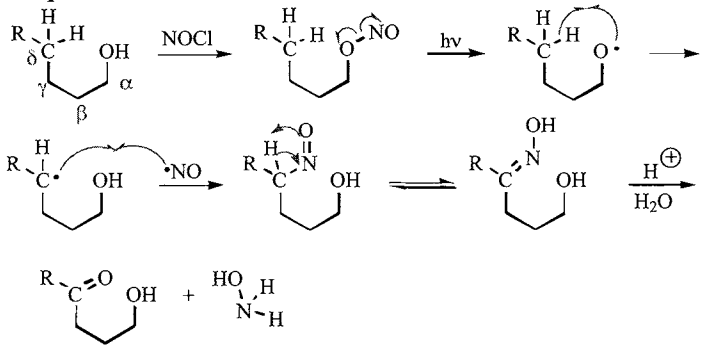
E. Bacque, F. Pautrat, S. Z. Zand, *Organic Letters* **2003**, 5, 325

Barton Reaction (Barton Nitrite Photolysis Reaction)

The Reaction:

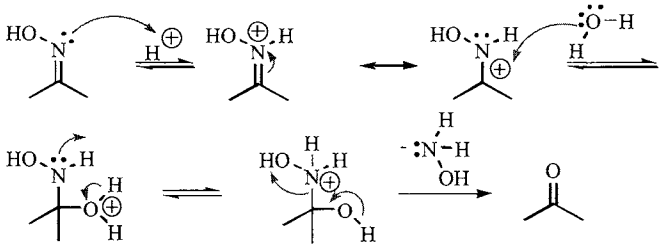


Proposed Mechanism:



Notes:

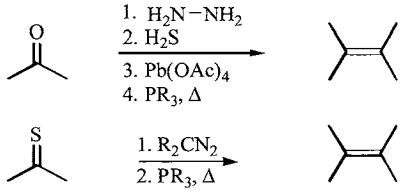
Hydrolysis mechanism



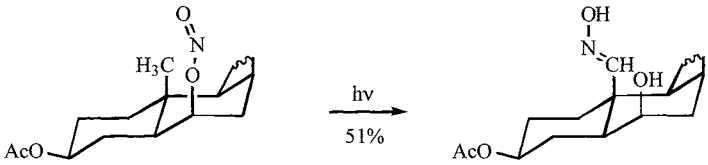
This reaction is a useful method for functionalizing a remote position (the δ–position).

Also by Barton is the

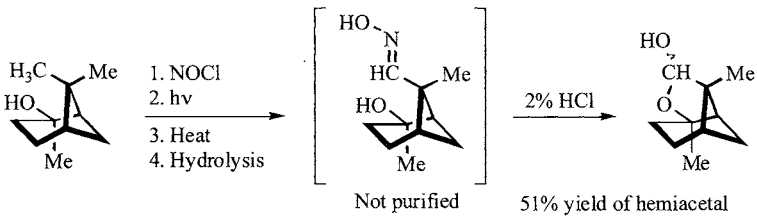
Barton-Kellogg Reaction (Barton Olefin Synthesis)



Examples:



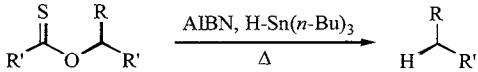
D. H. R. Barton, I. M. Beaton, L. E. Geller, M. M. Pechet, *Journal of the American Chemical Society* **1960**, 82, 2640



P. D. Hobbs, P. D. Magnus *Journal of the American Chemical Society* **1976**, 98, 4594

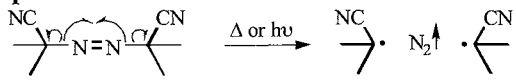
Barton-McCombie Reaction (Barton-Deoxygenation)

The Reaction:

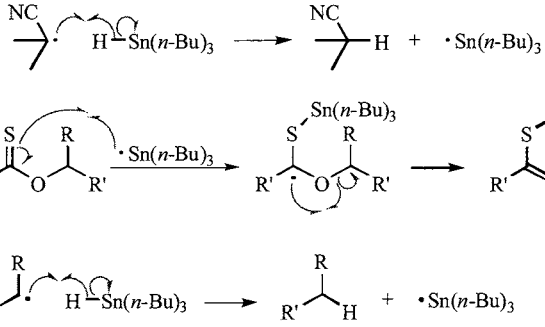


R' = H, CH_3, SCH_3 (= xanthate, see ***Chugaev Reaction***), Ph, OPh, imidazolyl

Proposed Mechanism:



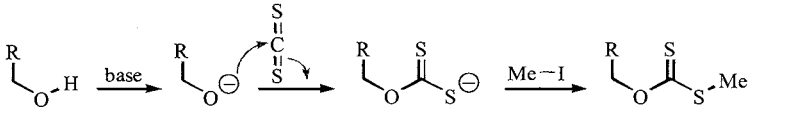
AIBN = Azo-*bis*-isobutyronitrile



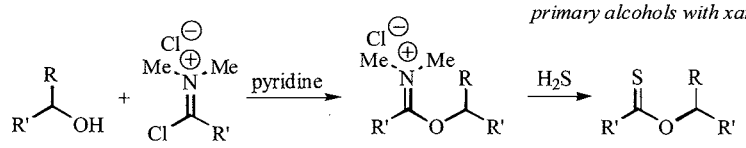
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 527.
For a discussion of mechanism: D. Crich, *Tetrahedron Letters* **1988**, 29, 5805

Depending on the substrate, different thiocarbonyl compounds have been used:

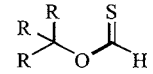


primary alcohols with xanthates



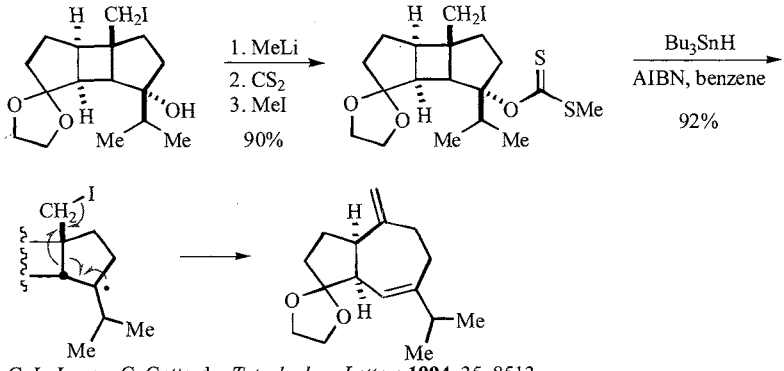
imidoyl chloride methochloride
(from phosgene and an amide)

secondary alcohols with thiocarbonyl esters

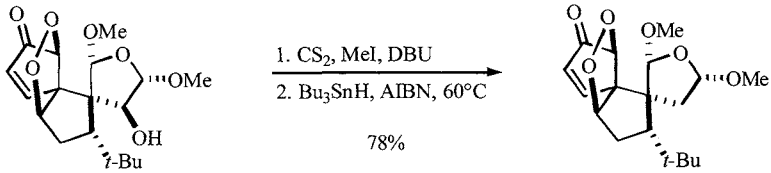


tertiary alcohols with thioformates

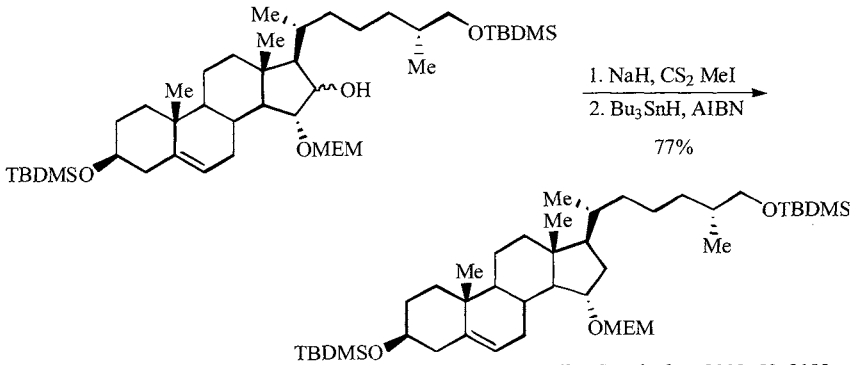
Examples:



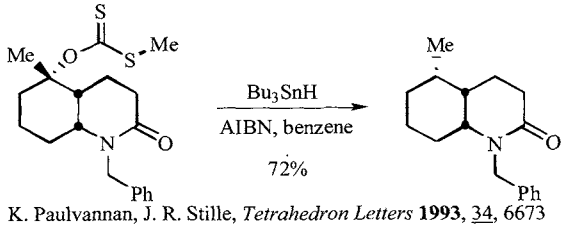
G. L. Lange, C. Gottardo, *Tetrahedron Letters* **1994**, 35, 8513



M. T. Crimmins, J. M. Pace, P. G. Nantermet, A. S. Kim-Meade, J. B. Thomas, S. H. Watterson, A. S. Wagman, *Journal of the American Chemical Society* **1999**, 121, 10249



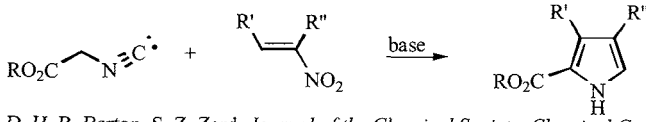
J. R. Williams, D. Chai, J. D. Bloxton, II, H. Gong, W. R. Solvibile, *Tetrahedron* **2003**, 59, 3183



K. Paulvannan, J. R. Stille, *Tetrahedron Letters* **1993**, 34, 6673

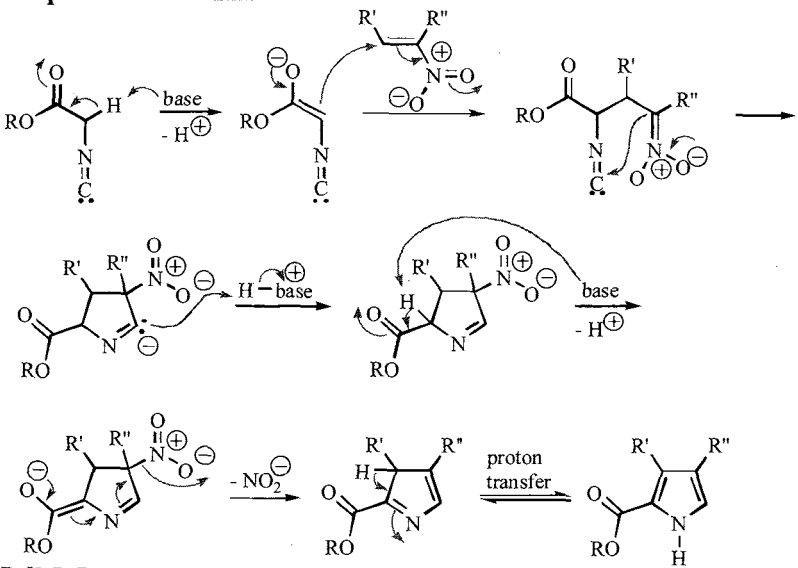
Barton-Zard Pyrrole Synthesis

The Reaction:



D. H. R. Barton, S. Z. Zard, *Journal of the Chemical Society, Chemical Communications* **1985**, 1098
D. H. R. Barton, J. Kervagoret, S. Zard, *Tetrahedron* **1990**, 46, 7587

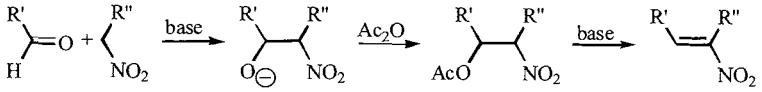
Proposed Mechanism:



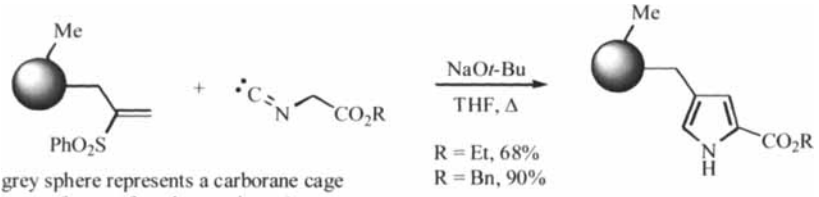
D. H. R. Barton, J. Kervagoret, S. Zard, *Tetrahedron* **1990**, 46, 7587

Notes:

One possible starting material preparation: A ***Henry Reaction*** followed by trapping with Ac_2O and elimination of the resultant acetate.

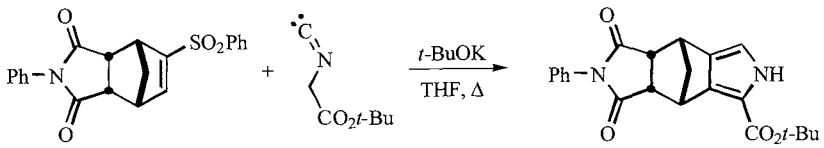


Examples:



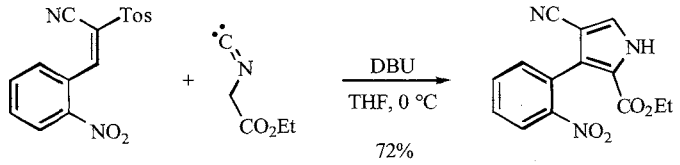
grey sphere represents a carborane cage
(see reference for a better picture)

S. Chayer, L. Jaquinod, K. M. Smith, M. G. H. Vicente *Tetrahedron Letters* **2001**, 42, 7759

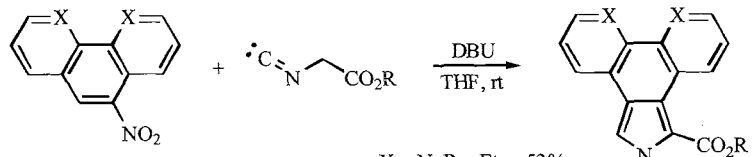


part of a 7 step procedure of overall 32% yield

D. Lee, T. M. Swager *Journal of the American Chemical Society* **2003**, 125, 6870

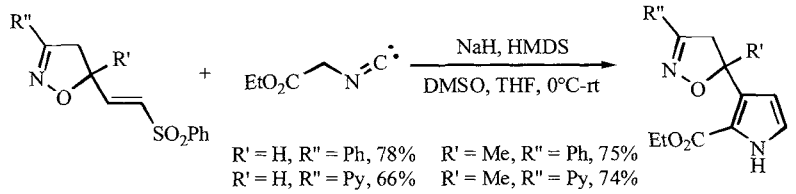


J. Bergman, S. Rehn *Tetrahedron* **2002**, 58, 9179



X = CH, R = Et, 86% X = N, R = Et, 53%
X = CH, R = *t*-Bu, 65% X = N, R = *t*-Bu, 83%
X = N, R = Bz, 73% (refluxing THF / *i*-PrOH)

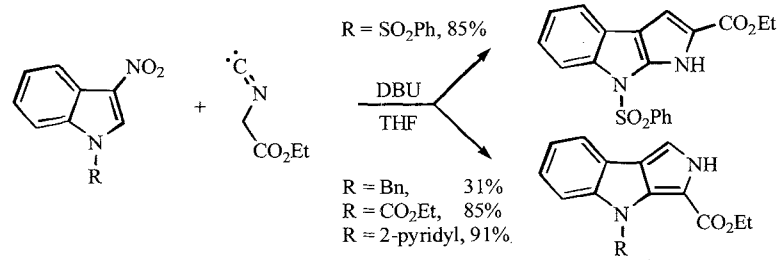
T. D. Lash, B. H. Novak, Y. Lin *Tetrahedron Letters* **1994**, 35, 2493



R' = H, R" = Ph, 78% R' = Me, R" = Ph, 75%
R' = H, R" = Py, 66% R' = Me, R" = Py, 74%

S. H. Hwang, M. J. Kurth *Tetrahedron Letters* **2002**, 43, 53

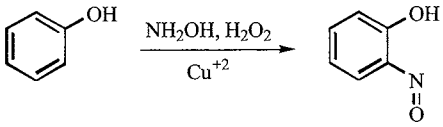
A rearranged / abnormal ***Barton-Zard Pyrrole*** product is observed when the protecting group on nitrogen is phenyl sulfonyl. However, when R = Bn, CO_2Et or 2-pyridyl, the expected pyrrolo[3,4,*b*]indole is obtained.



E. T. Pelkey, L. Chang, G. W. Gribble *Chemical Communications* **1996**, 1909
E. T. Pelkey, G. W. Gribble *Chemical Communications* **1997**, 1873

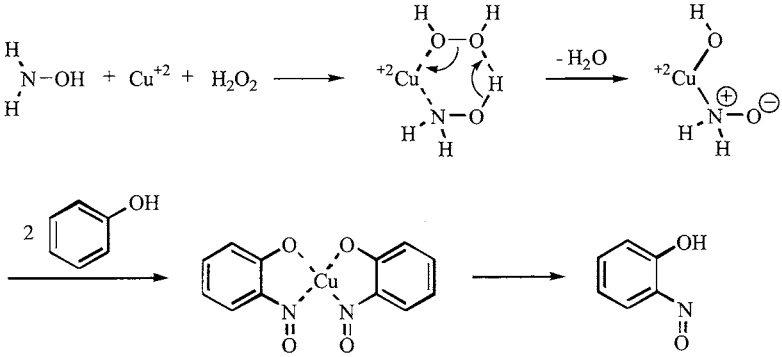
Baudisch Reaction

The Reaction:



Proposed Mechanism:

There is much not known about the details of this reaction.



Notes:

For studies on the mechanism: See K. Maruyama, I. Tanimoto, R. Goto, *Tetrahedron Letters* **1966**, 47, 5889