

**NAME REACTIONS
AND REAGENTS
IN ORGANIC SYNTHESIS**

Second Edition

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NAME REACTIONS AND REAGENTS IN ORGANIC SYNTHESIS

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 Favalaro.

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.

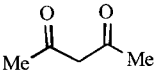
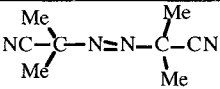
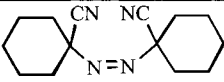
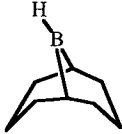
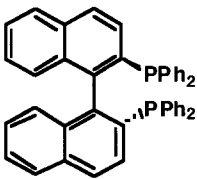
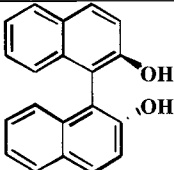
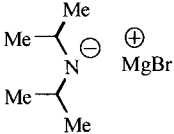
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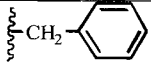
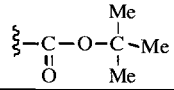
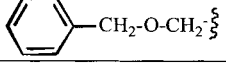
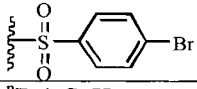
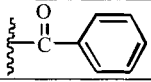
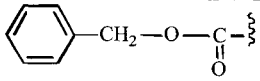
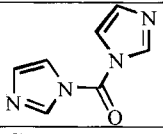
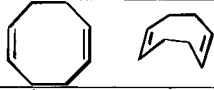
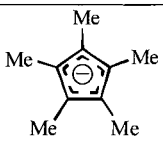
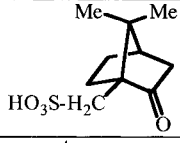
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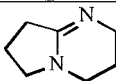
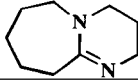
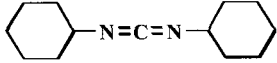
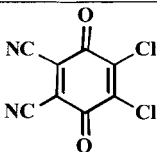
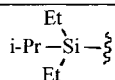
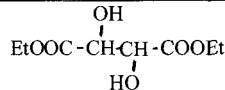
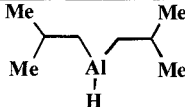
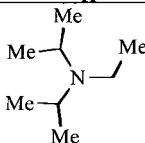
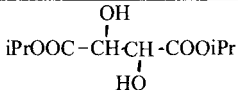
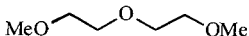
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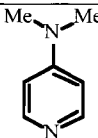
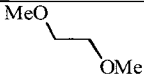
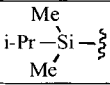
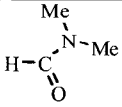
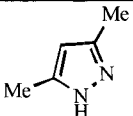
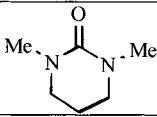
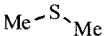
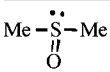
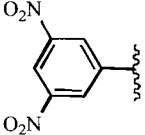
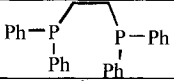
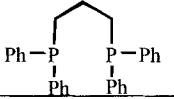
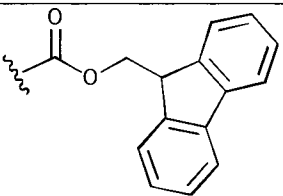
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ACRONYMS AND ABBREVIATIONS

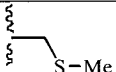
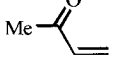
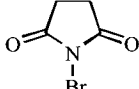
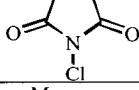
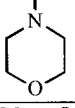
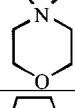
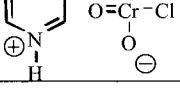
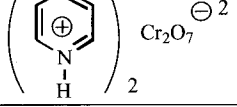
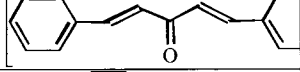
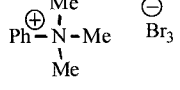
Acronym	Name	
Ac	Acetyl	
Acac	Acetylacetonate	
AcOH (HOAc)	Acetic acid	Me-COOH
AIBN	2,2'-Azobisisobutyronitrile	
ACN	1,1'-Azobis-1-cyclohexanenitrile	
<u>9-BBN</u>	9-Borobicyclo[3.3.1]nonane	
<u>BINAP</u>	2,2'-Bis(Diphenylphosphino)-1,1'-binaphthyl	
<u>BINOL</u>	1,1'-bi-2,2'-naphthol	
BITIP	Binol/Titanium isopropoxide	Ti(iPrO) ₄ / BINOL
<u>BMDA</u>	Bromomagnesium Diisopropylamide	
<u>BMS</u>	Borane Dimethylsulfide	BH ₃ -Me ₂ S

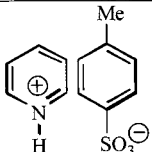
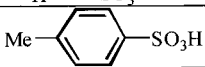
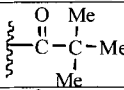
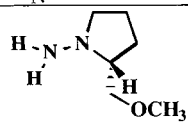
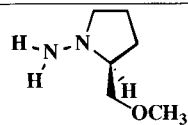
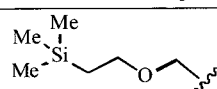
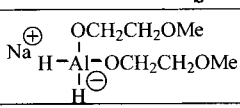
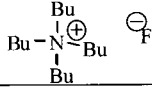
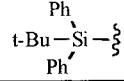
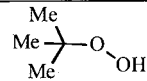
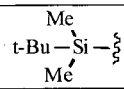
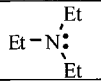
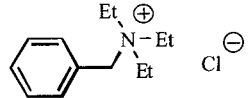
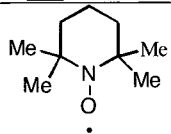
<u>BMS</u>	Borane Dimethylsulfide	$\text{BH}_3\text{-Me}_2\text{S}$
Bn-	Benzyl	
<u>Boc-</u> (t-Boc)	t-Butoxycarbonylchloride	
<u>BOM-</u>	Benzyloxymethyl-	
Bs	Brosylate	
<u>Bu3SnH</u>	tri- ⁿ butylstannane	$^n\text{Bu}_3\text{SnH}$
Bz	Benzoyl	
<u>CAN</u>	Ceric ammonium nitrate	$\text{Ce}(\text{NH}_4)_2(\text{NO}_3)_6$
<u>CAS</u>	Ceric ammonium sulfate	$\text{Ce}(\text{NH}_4)_4(\text{SO}_4)_4$
<u>Cbz-</u>	Carbobenzyloxy	
<u>CDI</u>	1,1'-Carbonyldiimidazole	
Cetyl	Hexadeca-	$\text{C}_{16}\text{H}_{33}\text{-}$
<u>cod</u>	Cyclooctadiene	
cp	Cyclopentadienyl	
cp*	Tetramethylcyclopentadienyl	
<u>CSA</u>	Camphorsulfonic Acid	
<u>DABCO</u> <u>TED</u>	1,4-Diazabicyclo[2.2.2]octane, TED, triethylenediamine	

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

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

HCTU	2-(6-Chloro-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate	
<u>HMPT</u> <u>HMPA</u>	Hexamethylphosphoric triamide	
HMTA	Hexamethylenetetramine	
HTIB	Hydroxy(tosyloxy)-iodobenzene	
Im	Imidazolyl	
<u>Icp₂BH</u>	Diisopinocampheylborane	
<u>LTA</u>	Lead tetraacetate	
<u>LTMP</u> <u>LiTMP</u>	Lithium 2,2,6,6-tetramethylpiperidine	
<u>MAD</u>	Methylaluminum bis(2,6-di-t-butyl-4-methylphenoxide)	
MCPBA	m-Chlorperoxybenzoic acid	
MeCN	Acetonitrile	
<u>MEM-</u>	2-Methoxyethoxymethyl	
Ms	Mesyl, Methanesulfonyl	

MTM	Methylthiomethyl	
MVK	Methyl Vinyl Ketone	
<u>NBS</u>	N-Bromosuccinimide	
<u>NCS</u>	N-Chlorosuccinimide	
<u>NMM</u>	4-Methylmorpholine	
<u>NMO</u>	N-Methylmorpholine-N-oxide	
NMP	N-Methylpyrrolidone	
PCC	Pyridinium chlorochromate Corey's Reagent	
PDC	Pyridinium dichromate	
<u>Pd(dba)₂</u>	Bis(dibenzylideneacetone)palladium (0)	
PMB	p-Methoxybenzyl	
PNB	para-Nitrobenzoyl	
<u>PPA</u>	Polyphosphoric Acid	Unspecified mixture with High concentration of P ₂ O ₅
<u>PTT</u> <u>(PTAB)</u>	Phenyltrimethylammonium tribromide Phenyltrimethylammonium perbromide	

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

TES	Triethylsilyl	
Tf	Triflate	
THF	Tetrahydrofuran	
THP	Tetrahydropyranyl	
TIPS	Triisopropylsilyl	
TMEDA	N,N,N',N'-Tetramethylethylenediamine	
<u>TPAP</u>	Tetra-n-Propylammonium Perruthenate	$\text{Pr}_4\text{N}^+\text{RuO}_4^-$
TPP	Triphenyl phosphine	
TMS	Trimethylsilyl	
<u>TMSOTf</u>	Trimethylsilyltrifluoromethanesulfonate	$\text{TMS}-\text{O}-\text{SO}_2\text{CF}_3$
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

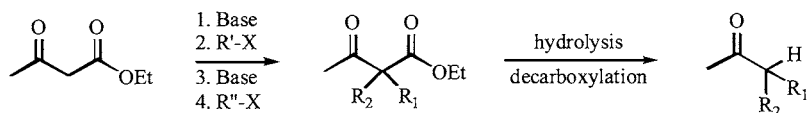
www.organic-chemistry.org/namedreactions/

<http://orgchem.chem.uconn.edu/namereact/named.html>

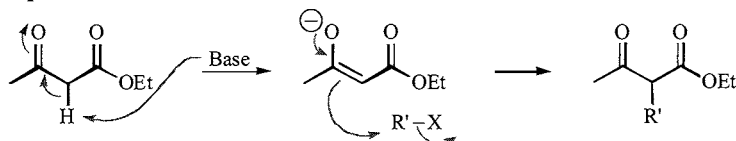
Some references are provided with a SciFinder (American Chemical Society) number so that one can access the abstract if needed.

Acetoacetic Ester Synthesis

The Reaction:

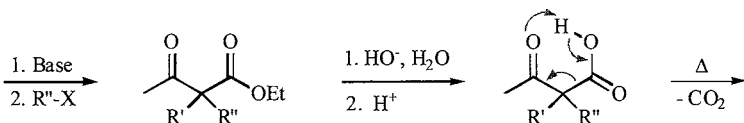


Proposed Mechanism:



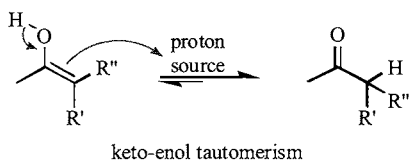
The methylene protons are the most acidic by influence from both carbonyls.

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



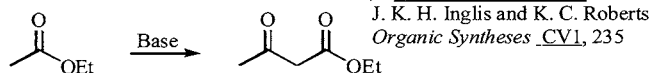
Alkylation can be done a second time (with a different R) if desired.

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



Notes:

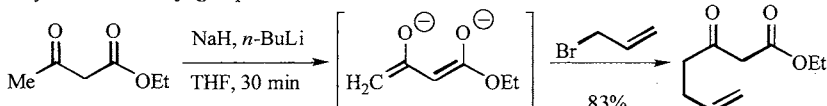
Acetoacetic Ester can be prepared by the condensation of ethyl acetate, called the **Acetoacetic Ester Condensation Reaction**, a **Claisen Condensation**:



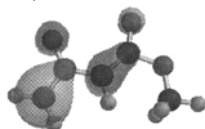
J. K. H. Inglis and K. C. Roberts
Organic Syntheses CV1, 235

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

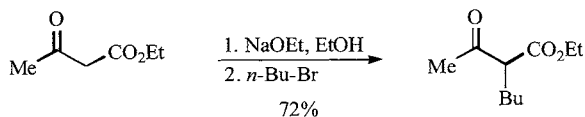
Weiler Modification: By using very strong bases, a dianion can be formed that will preferentially alkylate at the methyl group:



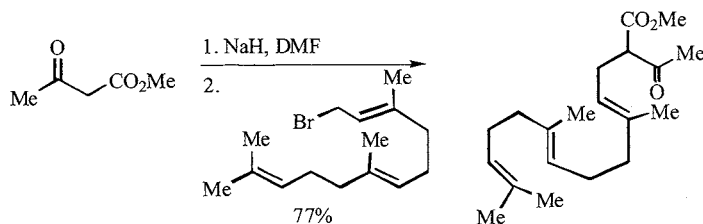
S. N. Huckin, L. Weiler *Journal of the American Chemical Society* **1974**, 96, 1082



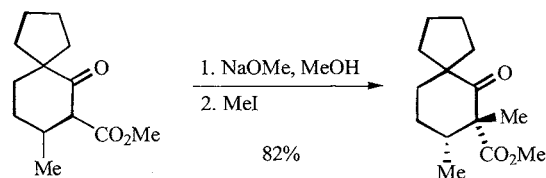
Simple AM1 calculation on Me ester shows the HOMO corresponding to the reactive intermediate

Examples:

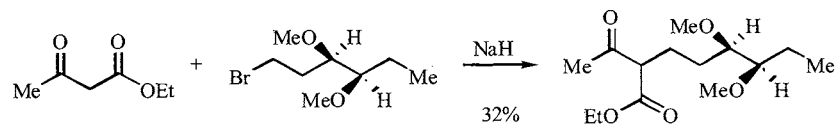
C. S. Marvel, F. D. Hager, *Organic Syntheses* **1941**, 1, 248



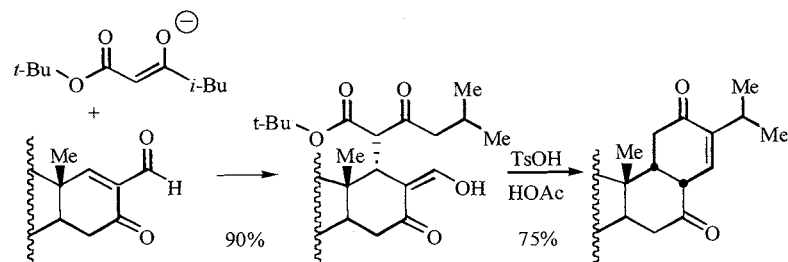
K. A. Parker, L. Resnick, *Journal of Organic Chemistry* **1995**, 60, 5726



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



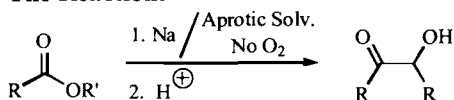
K. Mori, *Tetrahedron* **1974**, 30, 4223



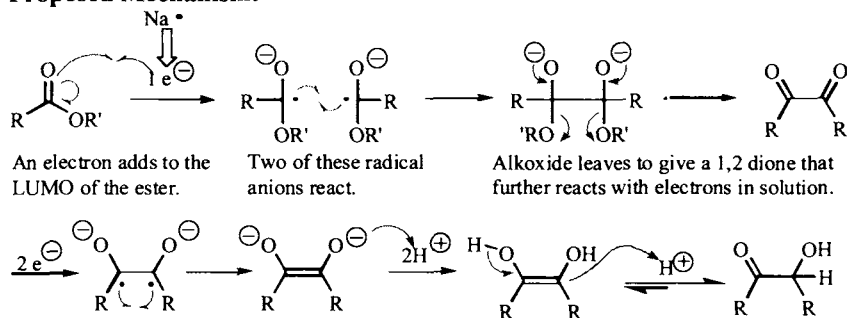
W. L. Meyer, M. J. Brannon, C. da G. Burgos, T. E. Goodwin, R. W. Howard, *Journal of Organic Chemistry* **1985**, 50, 438

Acyloin Condensation

The Reaction:



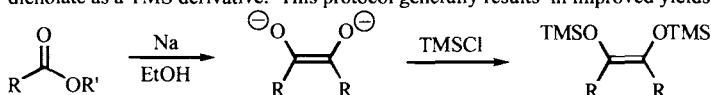
Proposed Mechanism:



Notes:

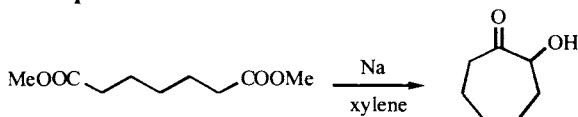
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 1562; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 1-3; S. M. McElvain, *Organic Reactions*, **4**, 4; J. P. Schaefer, J. J. Bloomfield,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

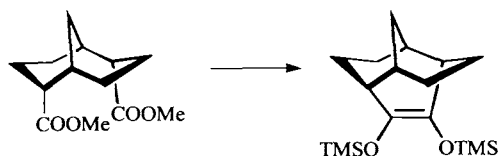


This reaction is better than either the **Dieckmann** or **Thorpe-Ziegler** reactions for preparing large rings.

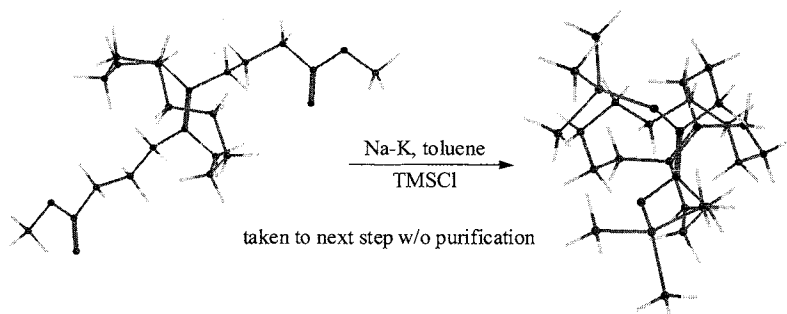
Examples:



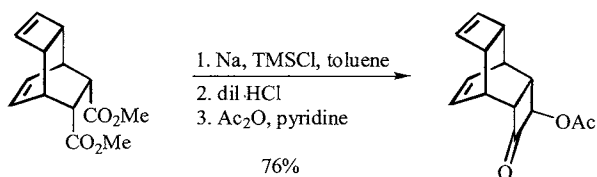
N. L. Allinger, *Organic Syntheses* **1963**, **4**, 840



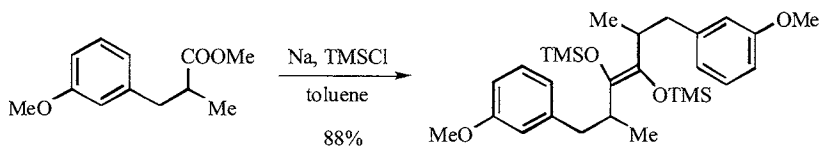
E. Butkus, A. Ilinskasa, S. Stoniusa, R. Rozenbergasa, M. urbanová, V. Setnikac, P. Bouc, K. Volkac, *Tetrahedron: Asymmetry* **2002**, **13**, 633



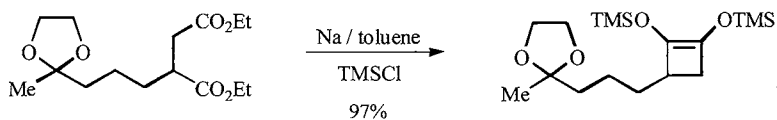
J. A. Marshall, J. C. Peterson, L. Lebioda, *Journal of the American Chemical Society* **1984**, 106, 6006



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



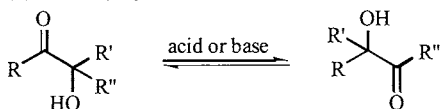
M. J. Meyers, J. Sun, K. E. Carlson, B. S. Katzenellenbogen, J. A. Katzenellenbogen, *Journal of Medicinal Chemistry* **1999**, 42, 2456



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

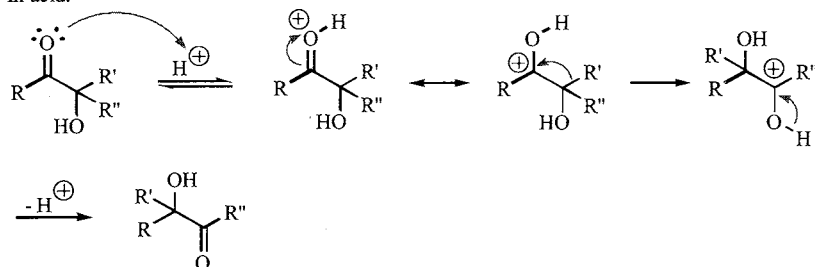
Acyloin Rearrangement

The Reaction:

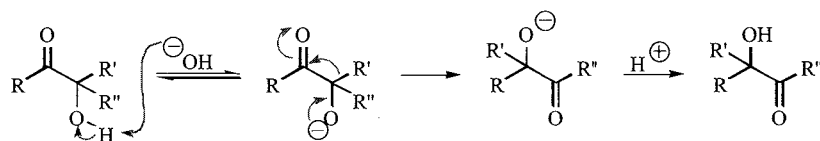


Proposed Mechanism:

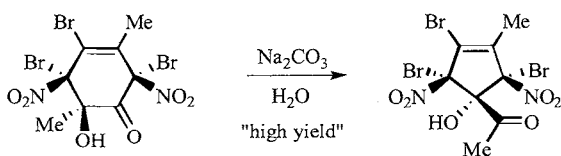
In acid:



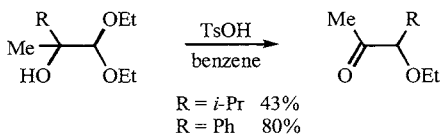
In base:



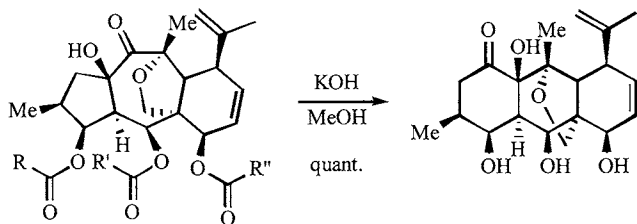
Examples:



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

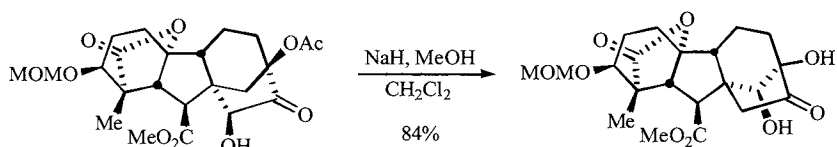


T. Sate, T. Nagata, K. Maeda, S. Ohtsuka, *Tetrahedron Letters* **1994**, 35, 5027



a mixture of acyl esters

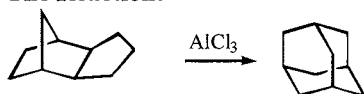
M. Rentzea, E. Hecker, *Tetrahedron Letters* **1982**, 23, 1785



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

Adamantane Rearrangement (Schleyer Adamantization)

The Reaction:



Proposed Mechanism:

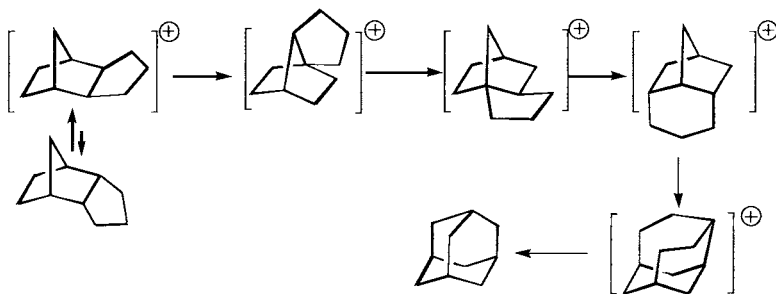
P. von R. Schleyer, P. Grubmeller, W. F. Maier, O. Vostrowsky, *Tetrahedron Letters* **1980**, 21, 921

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

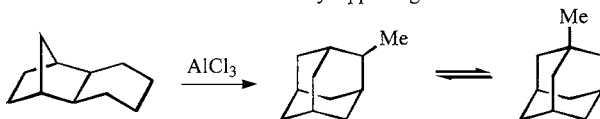
M. A. McKervey, *Tetrahedron* **1980**, 36, 971 provides a useful review:

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

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