

Modified Baylis-Hillman Reaction with Epoxides

By: Robert B. Login

Can the Baylis-Hillman reaction be modified to work with epoxides?

Several B-H reviews have appeared covering this reaction in very great detail. For example:

Tetrahedron, Vol. 52, No. 24, pp. 8001-8062, 1996

By: D. Basavaiah et. al.

Advances in the Baylis-Hillman Reaction-assisted Synthesis of Cyclic Frameworks

Vijay Singh and Sanjay Batra*

Tetrahedron 64 (2008) 4511-4574

Chem. Rev. 2003, 103, 811–891

Recent Advances in the Baylis–Hillman Reaction and Applications

Deevi Basavaiah,* Anumolu Jaganmohan Rao, and Tummanapalli Satyanarayana

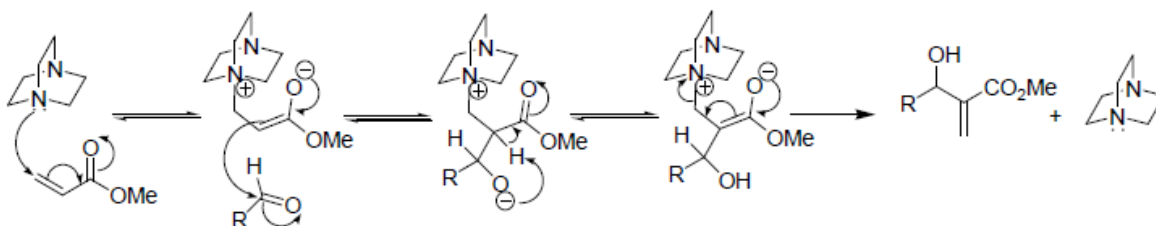
Chem. Rev. 2013, 113, 6659–6690

Recent Advances in Organocatalytic Asymmetric Morita–Baylis–Hillman/aza-Morita–Baylis–Hillman Reactions

Yin Wei and Min Shi*

If you review these references as I did you will find few if any mention of a reaction with epoxides.

To get a fix on the reason for this lets look at the mechanism:



Scheme 1

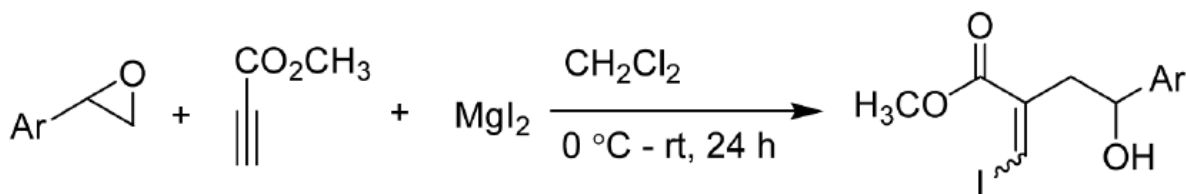
DABCO (other catalysts) adds to the vinyl EWG compounds like acrylate esters in a Michael reaction. Then the intermediate adds to an electrophile like a carbonyl then the intermediate falls apart to product and catalyst. The problem is that should an epoxide replace the carbonyl, DABCO would react with it to probably cause polymerization especially in the case of ethylene oxide. Also there would be no way that reaction could go by the above catalytic mechanism. However the following reference suggests a possible route to a modified B-H epoxide type reaction.

Org Lett. 2006 June 22; 8(13): 2771–2774. doi:10.1021/ol060828b.

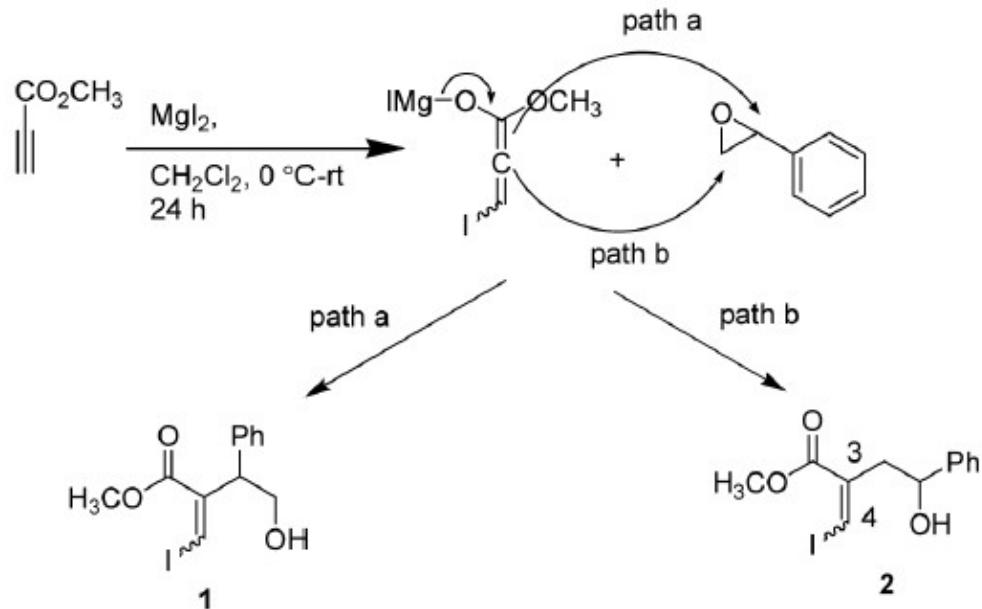
Novel Approach to Multifunctionalized Homoallylic Alcohols via Regioselective Ring Opening of Aryl Oxiranes with 3-Iodo Allenates

Adishesu Kattuboina, Parminder Kaur, Cody Timmons, and Guigen Li
 Department of Chemistry & Biochemistry, Texas Tech University, Lubbock, TX-79409-1061.

Abstract



yields up to 87%
 (Z:E) selectivity up to >20:1



Scheme 2.

Path b is prevalent.

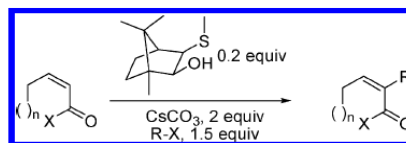
Admittedly, I do not have access to all the journals, but I can at least look at their published abstracts for example one of the few concerning epoxides (would like to see this one): [New directions for the Morita– Baylis–Hillman reaction; homologous aldol adducts via epoxide opening](#)

ME Krafft, JA Wright - Chemical communications, 2006 - pubs.rsc.org

In the presence of nucleophilic catalysts, epoxides have demonstrated variable stability and reactivity. An early communication reported that epoxides failed to yield recognizable products in the tertiary amine-catalyzed intermolecular MBH reaction with acrylates 8 whereas α,β - ...

Cited by 21 Related articles All 6 versions CiteSave

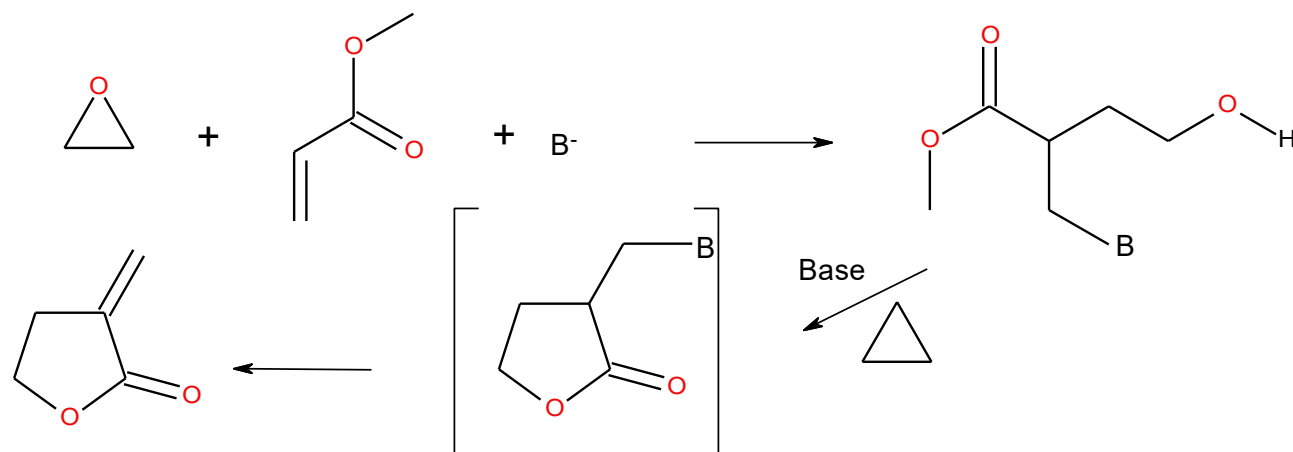
Org. Lett., Vol. 12, No. 10, 2010



A new Morita–Baylis–Hillman reaction methodology in which alkyl halides and epoxides act as electrophiles in their reaction with lactones and lactams is shown. Catalysis is efficiently performed by hydroxy sulfides under basic conditions. The procedure works efficiently with many alkyl halides but fails with aldehydes with which a conventional acid-catalyzed procedure is used.

The above catalyst gave a 65% yield with propylene oxide.

Besides the above references, and both of the above are very unsatisfying, I cannot find further reactions of the Baylis-Hillman type reaction with epoxides. However, let me propose the following preparation of alpha-methylene gamma butyrolactone (MBL):



B must have the ability to add by a Michael reaction without attacking the epoxide.

Acrylamide could be substituted for MA to afford the alpha-methylene gamma-butyrolactam monomer.

MBL has an extensive literature revolving around its ability to polymerize and copolymerize under free radical initiation very much like methyl methacrylate. Inclusion in polymers raises their T_g affording harder scratch resistant coatings. Assuming other epoxides might react, a wide variety of monomers would become available.

Patent references to MBL:

The apparently most economical(?) synthesis is with formaldehyde and butyrolactone. US 6,313,318 below claims this apparently simple process. It has to be conducted under high pressure in specialized equipment. Excess formaldehyde, I assume has to be recycled. All of this suggests high cost. My idea to use ethylene oxide could be more

economical? Please look at the patents that cited this patent:

<https://www.google.com/patents/US6232474#backward-citations>

US000315510D1

(12) **United States Patent**
Coulson et al.

(10) **Patent No.:** **US 6,313,318 B1**
(45) **Date of Patent:** ***Nov. 6, 2001**

(54) **PROCESS FOR THE PREPARATION OF α -METHYLENE LACTONES**

(75) Inventors: **Dale Robert Coulson; Leo E. Manzer,**
both of Wilmington; **Norman Herron,**
Newark, all of DE (US)

(73) Assignee: **E.I. du Pont de Nemours and Company,** Wilmington, DE (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **09/528,632**

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,166,357 11/1992 Orlek et al. 514/299

FOREIGN PATENT DOCUMENTS

0295553 A1 6/1988 (EP) .

0366304 A2 10/1989 (EP) .

10-120672 5/1998 (JP) .

10298172 11/1998 (JP) .

OTHER PUBLICATIONS

Watts et al., J. Chem. Soc. Chem. Comm. 27 (1970).

A. W. Murray et al., Synthesis, Jan. 1985, pp. 35-38.

J. MARTIN, A New Method for the Synthesis of α -M-ethylenebutyrolactones, Chemical Communications, 1970, 27, Dow Chemical Company, Eastern Research Laboratory, Wayland, Massachusetts.

Patented Jan. 6, 1953

2,624,723

UNITED STATES PATENT OFFICE

2,624,723

LACTONE DERIVATIVES AND METHOD OF MAKING

William J. McGraw, Morristown, N. J., assignor to Allied Chemical & Dye Corporation, New York, N. Y., a corporation of New York

US006388036B1

(12) **United States Patent**
Gridnev et al.

(10) **Patent No.:** **US 6,388,036 B1**
(45) **Date of Patent:** **May 14, 2002**

(54) **OLIGOMERIZATION, POLYMERIZATION AND COPOLYMERIZATION OF SUBSTITUTED AND UNSUBSTITUTED α -METHYLENE- γ -BUTYROLACTONES AND PRODUCTS THEREOF**

(52) **U.S. Cl.** 526/270; 526/172; 526/266; 526/268
(58) **Field of Search** 526/172, 266, 526/268, 270

(75) Inventors: **Alexei Alexeyevich Gridnev; Steven Dale Ittei**, both of Wilmington, DE (US)

(56) **References Cited**

FOREIGN PATENT DOCUMENTS

EP 0 722 960 A * 7/1996
JP 9012632 * 1/1997
JP 9012641 * 1/1997
WO 99/41218 * 8/1999

(73) Assignee: **E. I. du Pont de Nemours and Company**, Wilmington, DE (US)

US005880235A

United States Patent [19]
Schwind et al.

[11] **Patent Number:** **5,880,235**
[45] **Date of Patent:** **Mar. 9, 1999**

[54] **COPOLYMERS USEFUL FOR PRODUCING CAST GLASS AND THERMALLY DIMENSIONALLY STABLE MOLDING MATERIALS**

[56] **References Cited**

U.S. PATENT DOCUMENTS

2,624,723 1/1953 McGraw 260/88.3

(12) **United States Patent**
Pickett et al.

(10) **Patent No.:** **US 7,465,498 B2**
(45) **Date of Patent:** **Dec. 16, 2008**

(54) **TULIPALIN COPOLYMERS**

(75) Inventors: **James Edward Pickett**, Schenectady, NY (US); **Qing Ye**, Schenectady, NY (US)

(73) Assignee: **SABIC Innovative Plastics IP B.V.**, Bergen op Zoom (NL)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 216 days.

6,642,346 B2 11/2003 Brandenburg et al.
6,723,790 B2 * 4/2004 Brandenburg et al. 525/73
6,841,627 B2 * 1/2005 Brandenburg 525/386
6,899,995 B2 * 5/2005 Feiring et al. 430/272.1
7,166,416 B2 * 1/2007 Feiring et al. 430/272.1
2001/0025128 A1 * 9/2001 Gridnev 585/429
2002/0010312 A1 1/2002 Brandenburg et al.
2003/0130414 A1 7/2003 Brandenburg et al.
2003/0171522 A1 * 9/2003 Brandenburg 526/305
2004/0023157 A1 * 2/2004 Feiring et al. 430/272.1

(Continued)

FOREIGN PATENT DOCUMENTS

(21) Appl. No.: **11/289,928**

(22) Filed: **Nov. 30, 2005**

(65) **Prior Publication Data**
US 2007/0122625 A1 May 31, 2007

(51) **Int. Cl.**
B32B 27/08 (2006.01)

DE 19605154 * 8/1997
JP 09033736 A 7/1995
JP 09-012645 * 1/1997
JP 09012645 A 1/1997
WO WO 00/35960 * 6/2000
WO WO02/44845 S2 6/2002

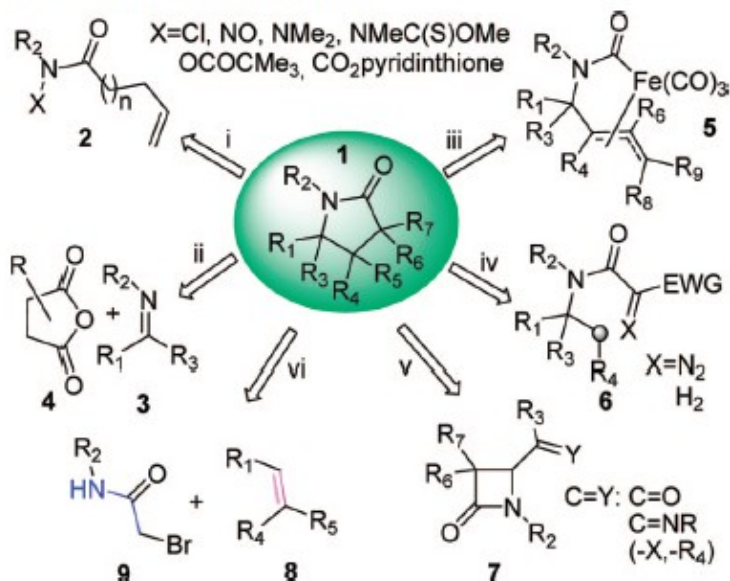
The above are a sampling of alpha-methylene-gamma-butyrolactone patents. Apparently DuPont failed to pay to keep their patent in force?

Alpha-methylene-gamma-butyrolactams (MBLA)

Comparing MBL to the corresponding lactam, one would expect a polymerizable monomer that would produce harder scratch resistant water soluble coatings because they would exhibit higher Tg's than PVP. PVP could be fine tuned to form harder and stiffer films by copolymerization with this monomer. Such copolymers could compete in hair fixatives at lower levels as compared to PVP.

As an aside, synthesis of various lactams themselves has been reviewed by S. Comesse et. al., JOC 2008, 73, 5566-5569. In that paper they present the following chart:

SCHEME 1. Representative Strategies Used for the Synthesis of γ -Lactam Skeletons



Please look at the references for the citations to each method (for convenience they appear below). Some of the synthesis procedures are more commercially conceivable than others and obviously a dedicated program would be required to perfect one or

another or even to invent a new approach. I show this chart as potential methods to prepare substituted derivatives that could be converted to the alpha methylene derivative.

There are patent references to MBLA that show that it can be radically polymerize by free radical initiation. I am not sure that commercial products resulted, but because the patents to Dupont (and there are several for MBL), one would think that this monomer would also be commercially available from them? If not, I suspect that commercial manufacture of the lactam monomers proved economically unacceptable. If true, then the point here is that an economical synthesis would lead to commercial success in my opinion because hair fixatives with higher Tg vs. PVP would have a niche. In general, the ability to control the Tg of copolymers must be of value.

(1) Fallis, A. G.; Brinza, I. M. *Tetrahedron* **1997**, *53*, 17543–17594.

(2) (a) Ng, P. Y.; Masse, C. E.; Shaw, J. T. *Org. Lett.* **2006**, *8*, 3999–4002.

Wei, J.; Shaw, J. T. *Org. Lett.* **2007**, *9*, 4077–4080. (c) Masse, C. E.; Ng, P. Y.; Fukase, Y.; Sanchez-Rosello, M.; Shaw, J. T. *J. Comb. Chem.* **2006**, *8*, 293–296. (d) Piwowarczyk, K.; Zawadzka, A.; Roszkowski, P.; Szawkało, J.; Leniewski, A.; Maurin, J. K.; Kranza, D.; Czarnockia, Z. *Tetrahedron: Asymmetry* **2008**, *19*, 309–317.

(3) Ley, S. V.; Cox, L. R.; Meek, G. *Chem. Rev.* **1996**, *96*, 423–442.

(4) For recent examples, see: (a) Choi, M. K.-W.; Yu, W.-Y.; Che, C.-M. *Org. Lett.* **2005**, *7*, 1081–1084. (b) Wee, A. G. H.; Duncan, S. C.; Fan, G.-J. *Tetrahedron: Asymmetry* **2006**, *17*, 297–307.

(5) Zhou, C.-Y.; Che, C.-M. *J. Am. Chem. Soc.* **2007**, *129*, 5828–5829.

(6) (a) Van Brabandt, W.; De Kimpe, N. *J. Org. Chem.* **2005**, *70*, 3369–3374. (b) Alcaide, B.; Almendros, P.; Cabrero, G.; Ruiz, M. P. *Org. Lett.* **2005**,

7, 3981–3984. (c) Park, J.-H.; Ha, J.-R.; Oh, S.-J.; Kim, J.-A.; Shin, D.-S.; Won, T.-J.; Lam, Y.-F.; Ahn, C. *Tetrahedron Lett.* **2005**, *46*, 1755–1757.

(7) Roberson, C. W.; Woerpel,

K. A. *J. Org. Chem.* **1999**, *64*, 1434–1435. (b) Romero, A.; Woerpel, K. A.

Org. Lett. **2006**, *8*, 2127–2130. (c) Sun, P.-P.; Chang, M.-Y.; Chiang, M. Y.;

Chang, N.-C. *Org. Lett.* **2003**, *5*, 1761–1763.

(8) Dong, C.; Mo, F.; Wang, J. *J. Org. Chem.* **2008**, *73*, 1971–1974,

references therein.

(12) **United States Patent**
Brandenburg et al.

(10) **Patent No.:** US 6,642,346 B2
(45) **Date of Patent:** Nov. 4, 2003

(54) COATING COMPOSITIONS CONTAINING
SUBSTITUTED AND UNSUBSTITUTED
EXOMETHYLENE LACTONE OR LACTAM
MONOMERS

4,728,543 A	3/1988	Kurauchi et al.	
4,943,614 A *	7/1990	Miyazaki et al.	525/117
5,166,357 A	11/1992	Orlek et al.	
5,244,696 A	9/1993	Hazan et al.	
5,880,235 A	3/1999	Schwind et al.	526/868

(75) Inventors: **Charles J. Brandenburg**, Wilmington, DE (US); **Randal D. King**, Kennett Square, PA (US); **Larry G. Oien**, Lapeer, MI (US); **Peter W. Uhlianuk**, Romeo, MI (US)

FOREIGN PATENT DOCUMENTS

JP	10120672	5/1998
JP	11279232	10/1999
WO	00/35960 A2	6/2000

United States Patent [19]
Song et al.

[11] **Patent Number:** 5,035,884
[45] **Date of Patent:** Jul. 30, 1991

[54] METHYLENE PYRROLIDONE
COPOLYMERS FOR CONTACT LENS AND
PHARMACEUTICAL PREPARATIONS

[58] **Field of Search** 351/160 R; 424/78, 80,
424/81, 430, 435, 436, 449; 523/108, 106, 111

[75] Inventors: **Suk-Zu Song**, Flanders; **Surendra C. Mehta**, Randolph; **Kuchi S. Murthy**, Morris Plains; **Russell U. Nesbitt**, Somerville; **Mahdi B. Fawzi**,

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,452,015	6/1969	Dillard	544/335
3,479,327	11/1969	Marijam	540/485
3,542,778	11/1970	Dillard	544/335

United States Patent [19]
Song et al.

[11] **Patent Number:** 4,931,519
[45] **Date of Patent:** Jun. 5, 1990

[54] COPOLYMERS FROM
N-ALKYL-3-ALKENYLENE-2-PYRROLI-
DONE

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,452,015	6/1969	Dillard	544/335
3,479,327	11/1969	Marijam	540/485
3,488,294	1/1970	Annand	526/258
3,542,778	11/1970	Dillard	544/335

[75] Inventors: **Suk-Zu Song**, Flanders; **Surendra C. Mehta**, Randolph; **Kuchi S. Murthy**, Morris Plains; **Russell U. Nesbitt**, Somerville; **Mahdi B. Fawzi**, Flanders, all of N.J.

FOREIGN PATENT DOCUMENTS

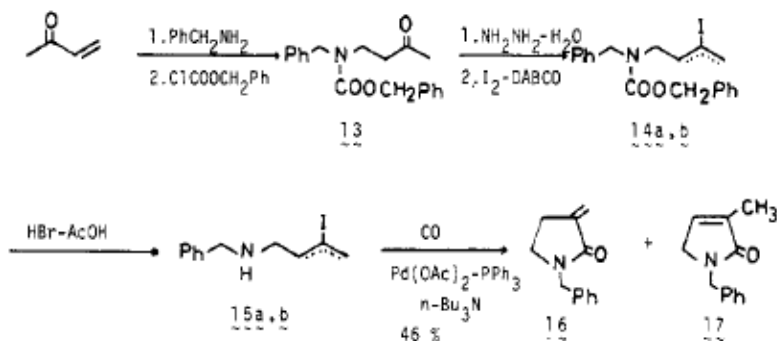
70/3307 5/1969 South Africa .

[73] Assignee: **Warner-Lambert Company**, Morris

The following are literature examples of the synthesis of these alpha-methylene lactams:

J. Org. Chem., Vol. 48, No. 22, 1983 4059

Scheme III



3376

J. Org. Chem. 1999, 64, 3376–3378

Indium-Promoted Preparation of α -Methylene- γ -butyrolactams from 2-(Bromomethyl)acrylic Acid and Aldimines[†]

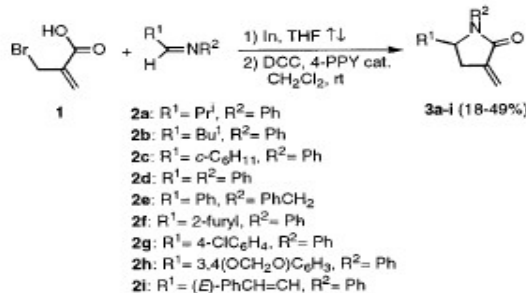
Prabir K. Choudhury, Francisco Foubelo, and Miguel Yus*

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, Apdo. 99, 03080 Alicante, Spain

Received November 24, 1998

α -Methylene- γ -butyrolactams¹ are interesting compounds from a biological point of view because they exhibit less cytotoxic activity than the corresponding

Scheme 1



Notes

Bull. Korean Chem. Soc. 2007, Vol. 28, No. 1 143

Synthesis of β,γ -Disubstituted α -Methylene- γ -butyrolactams Starting from the Baylis-Hillman Adducts

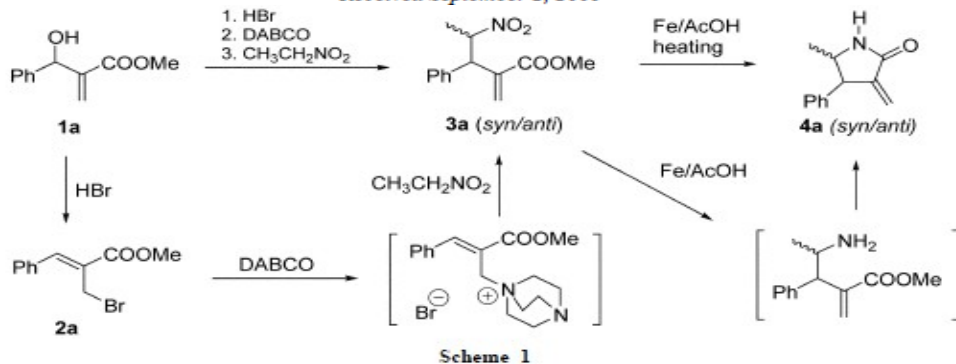
Ka Young Lee, Young Ju Lee,[†] and Jae Nyong Kim*

Department of Chemistry and Institute of Basic Science, Chonnam National University, Gwangju 500-757, Korea

*E-mail: kimjn@chonnam.ac.kr

[†]Korea Basic Science Institute, Gwangju Branch, Gwangju 500-757, Korea

Received September 2, 2006



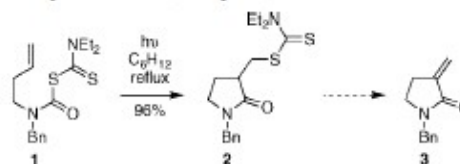
Thermal Elimination of Diethyldithiocarbamates and Application in the Synthesis of (\pm)-Ferrugine

Shamim Ahmed,[†] Luke A. Baker,[†] Richard S. Grainger,^{*†}
Paolo Innocenti,[‡] and Camilo E. Quevedo[‡]

School of Chemistry, University of Birmingham, Edgbaston,
Birmingham B15 2TT, U.K., and Department of Chemistry,
King's College London, Strand, London WC2R 2LS, U.K.

r.s.grainger@bham.ac.uk

SCHEME 1. Dithiocarbamate Group Transfer Carbamoyl Radical Cyclization and Proposed Elimination



SCHEME 2. Elimination of Dithiocarbamates under Basic and Thermal Conditions

Eur. J. Org. Chem. 2014, 1157–1162

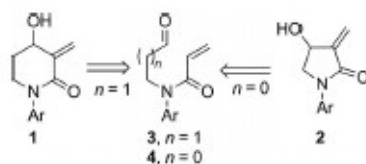
The Acrylamide Moiety as an Activated Alkene Component in the Intramolecular Baylis–Hillman Reaction: Facile Synthesis of Functionalized α -Methylene Lactam and Spirolactam Frameworks

Deevi Basavaiah,^{*[a]} Guddeti Chandrashekar Reddy,^[a] and Kishor Chandra Bharadwaj^[a]

Keywords: Baylis–Hillman reaction / Lactams / Nitrogen heterocycles / Spiro compounds

A facile strategy for the intramolecular Baylis–Hillman reaction by utilizing an acrylamide moiety as an activated alkene component was developed, which thus provides a conve-

nient protocol for obtaining five- and six-membered α -methylene lactam and spirolactam derivatives.



Scheme 1. Retrosynthetic strategy for α -methylene (γ - and δ -) lactam derivatives.

I hope this report is of value....thanks for reading! rloginconsulting.com