This article was downloaded by: [Michigan State University] On: 28 December 2014, At: 17:44 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/lsyc20

Cerium(III) Amide Enolate. Addition of Propionamide to Conjugated Enones

Xiao Shang ^a & Hsing-Jang Liu ^a ^a Department of Chemistry, University of Alberta, Edmonton, Alberta, T6G 2G2, Canada Published online: 23 Sep 2006.

To cite this article: Xiao Shang & Hsing-Jang Liu (1995) Cerium(III) Amide Enolate. Addition of Propionamide to Conjugated Enones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 25:14, 2155-2159, DOI: <u>10.1080/00397919508015896</u>

To link to this article: http://dx.doi.org/10.1080/00397919508015896

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages,

and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

CERIUM(III) AMIDE ENOLATE. ADDITION OF PROPIONAMIDE TO CONJUGATED ENONES

Xiao Shang and Hsing-Jang Liu*

Department of Chemistry, University of Alberta Edmonton, Alberta, Canada T6G 2G2

Abstract: The cerium(III) enolate of propionamide 1 was found to undergo preferential 1,2-addition with most of the sterically hindered conjugated enones studied. The effects of HMPA and 12crown-4 on the regioselectivity were also investigated.

Organocerium reagents have been shown to be higher yielding and more regioselective in addition reactions with aldehydes, ketones and conjugated enones than the corresponding lithium and Grignard reagents.¹ Recent studies carried out in our laboratory have demonstrated that the cerium(III) enolates derived from esters,² nitriles³ and amides⁴ add efficiently to sterically hindered aldehydes and ketones as well as the highly enolizable ones to give products in

Copyright © 1995 by Marcel Dekker, Inc.

^{*} To whom correspondence should be addressed.



Scheme 1

greater yields than those obtained using the corresponding lithium enolates.

Recently, Heathcock *et al.* carried out an extensive investigation on the addition of lithium enolates of several amides to α,β -unsaturated ketones.⁵ It was observed that, in general, reactions involving sterically hindered reactants gave predominantly 1,4adducts. In light of our previous findings that the cerium(III) enolates of esters and nitriles add to conjugated enones exclusively in a 1,2-fashion, we have undertaken a study on the addition of cerium(III) propionamide enolate to a number of selected enones with the intention of improving 1,2-selectivity.

The cerium(III) enolate of propionamide 1 was prepared by sequential treatment of the amide with lithium diisopropylamide and anhydrous CeCl₃ in THF (Scheme 1), as described previously.⁴ Addition of cyclohexyl propenyl ketone 2 and work-up of the reaction after 7 h at -78 °C with EtOAc extraction gave a mixture of

Entry	Enone	Time (h)	Yield (%)	1,2/1,4 <i>a</i>
1	c-C ₆ H ₁₁	7	76	80 : 20
	2			
2	2	4.5	94	28 : 72 ^b
3	2	8	68	71 : 2 9 ¢
4	2	20	73	43 : 57ª
5	Ph h	4	30	69 : 31
6	3 o p-BrC ₆ H ₄	0.6	90	65 : 35
	4			
7	4	10	100	52 : 48
8	i-Pr	1	33	80 : 20
	5			
9	5	3.5	34	$55:45^{b}$
10	o t-Bu	1.6	81	<5 : 95
	6			

 Table 1: Addition of the cerium(III) enolate of propionamide 1

 to conjugated enones

a Ratios were determined based on isolated products.

b HMPA (5 eq) was added before transmetallation.

c 12-Crown-4 (2 eq) was added before transmetallation.

d 12-Crown-4 (2.6 eq) was added before transmetallation.

1,2- and 1,4-addition products in 76% yield and in a ratio of 4:1. This ratio represents a considerable improvement in 1,2-selectivity over the result obtained using the corresponding lithim enolate. In that case, a 2:3 ratio in favor of the 1,4-adduct was observed. In order to further improve the 1,2-selectivity, cation-chelating agents, such as HMPA and 12-crown-4 were applied. Neither of these reagents, however, was found to enhance the desired selectivity. In fact, both reagents, HMPA in particular, appear to have an adverse effect, in agreement with the solvent effects observed previously for conjugated additions.⁷ We have also examined several other hindered enones 3-6, which were shown to give mainly 1,4-addition products upon treatment with the lithium amide enolates.⁵ An examination of the results compiled in Table 1 reveals that, in most cases, 1,2-addition occurred preferentially with the cerium(III) enolate. The only exception was trans-2,2-dimethyl-4-hexen-3-one (6). In this case, the cerium enolate showed little improvement over the lithium reagent,⁵ and the 1,4-adducts were formed virtually exclusively, apparently due to the high degree of steric congestion of the carbonyl. It has been noted previously that the 1,2- and 1,4selectivity with lithium amide enolates are temperature and time dependent. With higher temperature and longer reaction time, an increasing amount of the 1,4-adduct is usually formed.⁵ This was also noted in the present study. Prolonged treatment of enone 4 resulted in the increased production of the 1,4-adducts at the expense of the 1,2-adducts.

In conclusion, we have demonstrated the use of cerium enolates to facilitate the 1,2-addition of amides to conjugated enones.

Acknowledgments:

We are grateful to the Natural Sciences and Engineering Research Council of Canada and the University of Alberta for financial support, and to the Government of the Province of Alberta for scholarship to XS.

References and Notes

- 1. Imamoto, T. Pure & Appl. Chem., 1990, 62, 747 and references cited therein.
- 2. Liu, H.J. and Zhu, B.Y. Can. J. Chem., 1991, 69, 2008.
- 3. Liu, H.J. and Al-said, N.H. Tetrahedron Lett., 1991, 32, 5473.
- 4. Shang, X. and Liu, H.J. Synth. Commun., 1994, 24, 2485.
- Oare, D.A., Henderson, M.A., Sanner, M.A., and Heathcock, C.H. J. Org. Chem., 1990, 55, 132.
- 6. Two diastereomers were formed.
- Perlmutter, P., Conjugate Addition Reactions in Organic Synthesis, Pergamon, Oxford, 1992, p. 8.

(Received in the USA 01 December 1994)