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

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To cite this article: Xiao Shang & Hsing-Jang Liu (1994) Cerium(III) Amide Enolate. Addition to Aldehydes and Ketones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 24:17, 2485-2489, DOI: 10.1080/00397919408010557

To link to this article: http://dx.doi.org/10.1080/00397919408010557

SYNTHETIC COMMUNICATIONS, 24(17), 2485-2489 (1994)

CERIUM(III) AMIDE ENOLATE.
ADDITION TO ALDEHYDES AND KETONES

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Abstract: The cerium(III) amide enolates, prepared *in situ* from the corresponding lithium enolates and anhydrous $CeCl_3$, *were found to* undergo facile additions to ketones and aldehydes. Yields of the adducts are superior to those obtained using the lithium enolates.

Organocerium reagents have been shown to react with carbonyl compounds better than their lithium counterparts and the corresponding Grignard reagents.[1] Recent work carried out in our laboratory has demonstrated that the cerium(III) enolates of esters and nitriles add efficiently to sterically hindered ketones as well as the highly enolizable ones to give products in greater yields than those obtained using lithium enolates.[2,3] In continuation of our studies in this area, we have investigated the formation of cerium(III) enolates of amides via transmetallation and their addition to aldehydes and ketones. Preliminary results are described herein.

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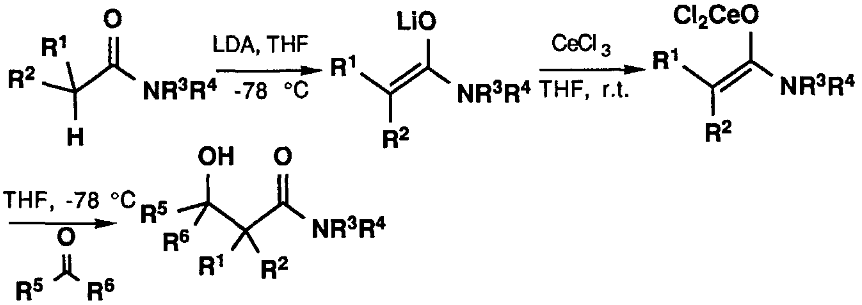
The transmetallation process used to generate the cerium amide enolates was carried out in the following manner (**Scheme 1**). An amide was treated with 1.1 equiv. of lithium diisopropylamide in THF at -78 °C for 1 h. The lithium enolate thus formed was transferred *via* a canula to a suspension of anhydrous $CeCl_3$ in THF. The resulting mixture, which was usually colored (from pink to brown, depending on the structure of the amide), was stirred at room temperature for at least 1h before a THF solution of the carbonyl compound was introduced *via* a canula at -78 °C.

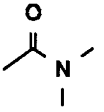
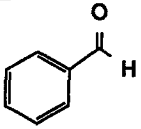
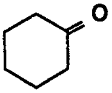
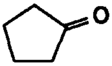
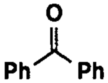
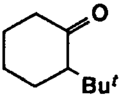
The addition reaction of the cerium enolate and the carbonyl compound was usually carried out at -78 °C and monitored by thin layer chromatography. After completion, the reaction mixture was allowed to warm up to room temperature and quenched with a saturated aqueous solution of KH_2PO_4. The resulting solution was extracted with ether and the combined extracts were washed with saturated aqueous solution of $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4 and concentrated. The crude product mixture was purified by flash chromatography on silica gel. The pure product(s) thus isolated was characterized by spectroscopic methods and elemental analysis.

The cerium(III) enolates of *N,N*-dimethylacetamide, *N,N*-dimethylpropionamide and *N,N*-dimethylisobutyramide with an increasing number of α-substituents were prepared and their reactivity examined using a variety of aldehydes and ketones. Results are compiled in the Table which also contains some results obtained using the corresponding lithium enolates for comparison. An examination of the Table reveals that, in general, better yields of the expected adducts were

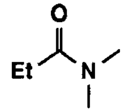
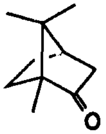
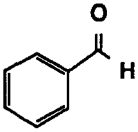
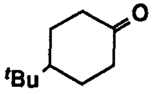
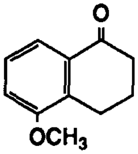
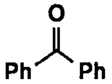
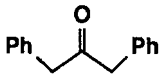
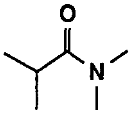
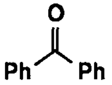
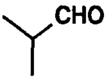


Scheme 1

Table. Addition of cerium and lithium amide enolates to carbonyl compounds

Entry	Amide	Substrate	%Yield (Ce)	Time & Temperature	%Yield (Li)
1			99	-78 °C, 60 min	68 [a]
2	"		89	-78 °C, 20 min	86 [a]
3	"		86	-78 °C, 30 min	-
4	"		92	-78 °C, 60 min	93 [a]
5	"		96 [b]	-78°C, 3 h	-
6	"		98 [c]	-78 °C, 3 h	93 [c]

(continued)

7			94 (95:5)[d]	-78 °C, 8 h	57 (90:10)
8	"		90 (53:47)[d]	-78 °C, 20 min	-
9	"		98 (97:3)[d]	-78 °C, 40 min	-
10	"		98 (85:15)[d]	-78 °C, 40 min	-
11	"		97	-78 °C, 40 min	86 [a]
12	"		92	-78 °C, 40 min	82
13			0	-78 °C, 20 h	0 [a]
14	"		51	-78 °C, 20 h	47

[a]Results were taken from ref. 4. [b]Only a single diastereomer was formed. Its stereochemistry remains to be determined. [c]A single stereoisomer with an *exo*-OH group was formed. [d]Two diastereomers were formed in the indicated ratio.

obtained with the cerium enolates. This improvement over the lithium enolates is especially profound with aldehydes (Entry 1), the sterically hindered ketones (Entries 6, 7 and 11) and compounds with greater acidity (Entry 12). This finding could be attributed to the high nucleophilicity and low basicity generally associated with organocerium(III) compounds. It should also be noted that neither the cerium enolate nor the lithium enolate derived from *N,N*-dimethylisobutyramide was found to undergo addition with carbonyl compounds efficiently (Entries 13 and 14), apparently due to the steric congestion.

Acknowledgment:

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 a scholarship to X.S.

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(Received in the USA 08 February 1994)