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Ligand Effects in Diastereoselective Additions of Organocerium Reagents to Carbonyl Substrates**

Carmen Alcaraz and Ulrich Groth*

One of the most important contributions of lanthanide reagents to synthetic organic chemistry is the application of organocerium reagents in carbonyl addition reactions.^[1] Owing to their low basicity and high nucleophilicity, organocerium reagents afford much higher yields of addition products with highly enolizable substrates than the corresponding organolithium or organomagnesium reagents from which they can be generated in situ. Furthermore, the steric bulk of organocerium reagents should make them suitable candidates for achieving high diastereoselectivity in additions to carbonyl derivatives.^[2] The nature of the ligands determines the direction and extent of stereoselectivity in many carbonyl addition reactions,^[3] but the sense and magnitude of diastereoselectivity achievable in the addition of organocerium reagents to chiral carbonyl substrates has to date not been explored in a systematic fashion.

We report here on the synthesis of new alkoxy- and amidocerium compounds of the general formula $ClCe(OR)_2$, $Ce(OR)_3$, and $Ce(NR_2)_3$. Cerium(III) trialkoxides were prepared by ligand exchange reactions of the known $Ce(OiPr)_3^{[3c, 4]}$ with the appropriate alcohols^[5] [Eq. (a)]; cerium(III) chloride dialkoxides were obtained by reaction of the relevant cerium(III) trialkoxides with one equivalent of acetyl chloride^[6] [Eq. (b)]; amidocerium compounds were synthesized by reaction of the $CeCl_3$ ·THF complex with three equivalents of lithium amides^[7] [Eq. (c)]. All these alkoxy- and amidocerium compounds were



used without further purification; however, X-ray structures have not yet been obtained because of the low tendency of these compounds to form crystals.

For the addition reaction the cyclopentanone derivative *rac*-1 was used as a substrate since it is well known that diastereoselectivities in the addition of organometallic reagents to cyclopentanones are lower than that to cyclohexanones. The yields are also lower because of the high tendency of cyclopentanone derivatives to undergo enolization. The organocerium reagents

[*] Prof. Dr. U. Groth, Dr. C. Akaraz Fakultät für Chemie der Universität Universitätstrasse 10, D-78457 Konstanz (Germany) Fax: Int code + (7531)884155 e-mail: Ulrich.Groth@uni-konstanz.de

[**] Lanthanoids in Organic Synthesis, Part 2. This work was supported by the EU Commission, Directorate General XII, and the Fonds der Chemischen Industrie. C. A. thanks the EU Commission for a fellowship (Contract-No. ERBCHBI-CT94-1465). Part 1: Ref. [4b]. were formed in situ by treatment of the cerium compounds (see [Eqs. (a)-(c)]) with organolithium reagents at -78 °C for 1 h. Then 2-methyl-3-vinylcyclopentanone (*rac*-1)^[8] was added to afford the addition products *rac*-2 and *rac*-3. The results are



given in Table 1. The nature of these organocerium species is unknown and has proved resistant to study,^[9] but most probably organocerium species derived from cerium chloride dialkoxides are neutral species of the type $RCe(OR')_2$ and those derived from cerium trialkoxides are ate-complexes of the type $Li[CeR(OR')_3]$.

Table 1. Stereoselective additions of organocerium reagents to 2-methyl-3-vinyl-cyclopentanone (*rac*-1)[12].

Entry	Reagent	<i>de</i> [%][a]	Yield [%]	Enolization[%]
. 1	MeLi	10	65	22
2	MeLi/CeCl,	68	91	-
3	MeLi/Ce(NEt ₂) ₃	78	55	25
4	MeLi/Ce(NiPr2)3	79	50	36
5	MeLi/Ce(OiPr)3	83	95	-
6	MeLi/Ce(OiPr) ₃ [b]	86	93	-
7	MeLi/Ce(OiPr)3[c]	74	90	-
8	MeLi/ClCe(OtBu)2	77	85	-
9	MeLi/ClCe(OCHiPr2)2	87	89	-
10	nBuLi	49	56	36
11	nBuLi/ClCe(OCHiPr ₂) ₂	89	90	-
12	/BuLi	77	35	57
13	tBuLi/ClCe(OCHiPr2)2	90	80	-
14	PhLi	85	70	24
15	$PhLi/ClCe(OCHiPr_2)_2$	94	95	-

[a] Determined by GC analysis. [b] Addition at -98 °C. [c] In Et₂O.

Enolization of the starting ketone was only observed with organocerium reagents derived from cerium triamides (Table 1, entries 3 and 4). The ligands have a pronounced influence on the stereoselectivity of the addition reactions. As expected, increasing steric hindrance led to increased diastereoselectivity. Unfortunately, no addition took place with the sterically most demanding compounds Li[CeMe(OtBu)_3] and Li[CeMe(OCH*i*-Pr₂)_3]. Lowering the temperature (-98 °C) slighty improved the diastereoselectivity (entry 6) but carrying out the additions at -78 °C is more convenient. In Et₂O the diastereoselectivity obtained was lower than in THF (entry 7). The best results were achieved with RCe(OCH*i*Pr₂)₂ in THF. Its addition to the

cyclopentanone derivative *rac*-1 (entries 9, 11, 13 and 15) proceeds with good to very good diastereoselectivities (87-94% de), which are among the best reported for the addition of organometallic reagents to simple cyclopentanones.^[10, 11]

In order to establish the width of application of the new cerium derivatives in carbonyl addition reactions, the addition of organocerium reagents derived from $ClCe(OCHiPr_2)_2$ and $Ce(OCHiPr_2)_3$ to 2-methylcyclohexanone, 4-*tert*-butylcyclohexanone, and 2-phenylpropionaldehyde was investigated (Table 2).

Table 2. Stereoselective addition of organocerium reagents to selected carbonyl substrates.

Carbonyl derivative	Reagent	<i>de</i> [%][a]	Yield [%]
2-methylcyclohexanone	MeLi	63	74
2-methylcyclohexanone	MeCeCl ₂	88	89
2-methylcyclohexanone	$MeCe(OCHiPr_2)_2$	97	91
2-methylcyclohexanone	Li[CeMe(OCHiPr ₂) ₃]	-	-[b]
2-methylcyclohexanone	nBuLi	78	80
2-methylcyclohexanone	nBuCeCl ₂	94	92
2-methylcyclohexanone	nBuCe(OCHiPr,),	98	88
4-tert-butylcyclohexanone	MeLi	24	50
4-tert-butylcyclohexanone	MeCeCl,	36	93
4-tert-butylcyclohexanone	Li[CeMe(OCHiPr ₂) ₃]	68	88
2-phenylpropionaldehyde	MeLi	82	57
2-phenylpropionaldehyde	MeCeCl,	84	85
2-phenylpropionaldehyde	Li[CeMe(OCH <i>i</i> Pr ₂) ₃]	90	89

[a] Determined by GC analysis. [b] No addition took place, probably because of the bulky ligands.

As in the case of 2-methyl-3-vinylcyclopentanone (rac-1), no reaction took place in the addition of Li[MeCe(OCHiPr₂)₃] to 2-methylcyclohexanone. In contrast, the addition of MeCe- $(OCHiPr_2)_2$ and $nBuCe(OCHiPr_2)_2$ to 2-methylcyclohexanone gave the corresponding alcohols with diastereoselectivities of 97 and 98% de, by using the sterically less demanding organocerium compounds MeCeCl₂ and nBuCeCl₂ the selectivities dropped to 88 and 94% de, respectively. In the case of 4-tertbutylcyclohexanone and 2-phenylpropionaldehyde the addition reactions could be performed with the sterically most demanding compound Li[MeCe(OCHiPr₂)₃] and gave yields between 88 and 89%. With 4-tert-butylcyclohexanone an increase of diastereoselectivity from 36% (MeCeCl₂) to 68% de (Li[MeCe(OCHiPr₂)₃]) was established. The addition of Li[MeCe(OCHiPr₂)₃] to Cram's aldehyde (2-phenylpropionaldehyde) led to the corresponding alcohol with a diastereoselectivity of 90% de. In constrast the use of MeCeCl, (84% de) or MeLi (82% de) gave considerably lower selectivities. The application of these new organocerium reagents in natural product synthesis, for example for the enantioselective synthesis of the antifungal chokols,^[10, 13] is currently under investigation.

Experimental Section

All reactions were performed with rigorous exclusion of oxygen and water under a dry nitrogen atmosphere, using Schlenk, vacuum-line, and glovebox techniques. Preparation of cerium trialkoxides: To a solution of $Ce(OiPr)_3$ (6.0 mmol) in benzene (10 mL), the appropriate alcohol (20 mL) was added and the mixture was heated under reflux overnight. It was then cooled to room temperature and the solvent removed in vacuo (20 °C, 0.005 Torr) to afford the corresponding cerium trialkoxide in 90–95 % yield.

Preparation of cerium chloride dialkoxides: Acetyl chloride (2.0 mmol) was added to a solution of the appropriate cerium trialkoxide (2.0 mmol) in benzene (20 mL), and a pale brown solid precipitated immediately. The mixture was heated to reflux for 2 h, cooled to room temperature, and the solvent removed by cannula. The solid was dried in vacuo (20 °C, 0.005 Torr) to afford the cerium chloride dialkoxide in 80-90% yield.

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Carbonyl addition reactions: To a solution of the cerium compound (1.5 mmol) in THF (5 mL) cooled to -78 °C, methyllithium (1.2 mmol, 0.75 mL of a 1.6 N solution in diethyl ether) was added. After 1 h the appropriate carbonyl derivative (1.0 mmol) was added slowly and the mixture was stirred at -78 °C for 30 min. Then, a saturated aqueous NH₄Cl solution (10 mL) was added, solid material was removed through a short pad of Celite, the Celite was rinsed with diethyl ether, and the ethereal solution was dried with MgSO₄. The solvent was removed in vacuo and the residue purified by flash chromatography.

Received: May 5, 1997 [Z104221E] German version: Angew. Chem. 1997, 109, 2590–2592

Keywords: asymmetric synthesis \cdot cerium \cdot cycloalkanones ligand effects

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Template-Mediated Self Assembly of Six- and Eight-Membered Iron Coronates **

Rolf W. Saalfrank,* Ingo Bernt, Eveline Uller, and Frank Hampel

Dedicated to Professor Gottfried Huttner on the occasion of his 60th birthday

The "synthesis of properties"^[1] is a professed goal in supramolecular chemistry. There are a large number of naturally occurring iron oxide minerals with complex structures^[2] that serve as model compounds. Additionally, the iron-storage protein ferritin, which is the biological prototype of these inorganic systems,^[3, 4] has been investigated comprehensively. Furthermore, discrete clusters with up to nineteen oxygen-bridged iron atoms have been synthesized and unequivocally characterized.^[3] For better understanding of electron transfer processes and of magnetic properties of polynuclear iron,^[3, 5] manganese,^[6] and nickel complexes^[7] further studies on compounds of this type are necessary. The same is true for the recently described cyclic ferrocene heptamer^[8] and for metallacrown ethers with an enclosed cation^[9, 10] or anion.^[11] With respect to potential applications, iron(III) compounds certainly play a central role.

Our investigations have revealed that parallel to the family of classical crown ethers, cryptands, and their complexes there exists a class of topomerically analogous metallacrown ethers,^[10] metallacryptands,^[12, 13] and their inclusion compounds. In all these cases, bisbidentate ligands act as ditopic bridges. In addition we have studied the formation of one- (1D), two- (2D), and three-dimensional (3D) coordination polymers using coordinatively unsaturated, effectively linear bidentate dinitrile monomers.^[14] Through a combination of both methods, we planned to construct novel adamantanoid tetranuclear chelate complexes **1**. Following the strategy for the synthesis of the tetranuclear



chelate complexes $[M \subset Fe_4 L_6^1]^{[12b]}$ and of 1D coordination polymers $\frac{1}{\infty}[NaL^2(pmedta)]$ (pmedta = pentamethyldiethylenetriamine), $^{[14a]}$ this objective should be accomplished by reaction of four equivalents of a tripodal metal template and six equivalents of a α, ω -dinitrile. Evidently, 1,1,1-tris(diphenylphosphinomethyl)ethane (triphos) used by Huttner et al. $^{[15]}$ was better suited for this purpose than the ligands triethanolamine **2** and *N*-methyldiethanolamine (**6**) that we have used.

Contrary to what was expected, treatment of triethanolamine 2 with sodium hydride, iron(III) chloride, and fumaric acid dinitrile in THF afforded the yellow solid 3, in which the iron-toligand ratio was 1:1, instead of a tetranuclear chelate complex of type 1. However, even when no dinitrile was used the same result was obtained. Since the ¹H and ¹³C NMR spectra of product 3 do not allow an unequivocal characterization of its



molecular structure, we carried out an X-ray crystallographic structure analysis.^[16] According to this analysis, **3** is present in the crystal as a cyclic iron(\mathbf{m}) complex with a [12]metallacrown-6 structure, in which a sodium ion is encapsulated in the center, and chloride is the counterion (Figure 1). The six crystallo-

^[*] Prof. Dr. R. W. Saalfrank, Dipl.-Chem. I. Bernt, E. Uller, Dr. F. Hampel Institut für Organische Chemie der Universität Erlangen-Nürnberg Henkestrasse 42, D-91054 Erlangen (Germany) Fax: Int. code + (9131)85-6864 e-mail: saalfrnk@organik.uni-erlangen.de

^[**] Chelate complexes (metalla coronates), Part 9. This work was supported by the Deutsche Forschungsgemeinschaft, the Volkswagenstiftung and by the Fonds der Chemischen Industrie. We thank Prof. Dr. A. X. Trautwein and Dr. V. Schünemann, Universität Lübeck, for recording Mössbauer spectra. We also thank Prof. Dr. K.-P. Zeller, Universität Tübingen, and Prof. Dr. F. Vögtle, Universität Bonn, for recording numerous FAB-MS spectra. Part 8: Ref. [9].