From Limestone to Catalysis: Application of Calcium Compounds as Homogeneous Catalysts

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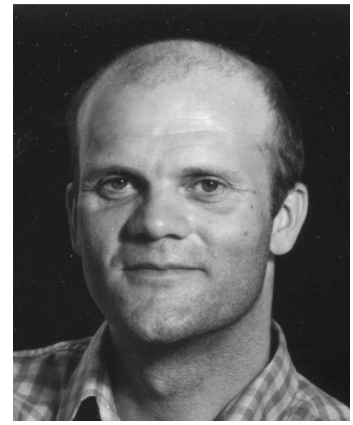

Sjoerd Harder, born in The Netherlands, obtained his Ph.D. degree in experimental organolithium chemistry under the supervision of Lambert Brandsma (1990, Utrecht) and was awarded the H. J. Backer prize in organic chemistry for this contribution. After postdoc work in theoretical organic chemistry with Paul R. von Schleyer (1991, Erlangen), he moved to the group of Andrew Streitwieser (1992, Berkeley) to work on superbases. His third postdoc stay in the group of Hans Brintzinger (1993, Konstanz) was extended, and he received his habilitation on investigations of group 1 sandwich complexes (lithocene, sodocene, and cesocene) in 1998. He intensified his work on the heavier group 2 metals (Ca, Sr, Ba) and cooperated in a BASF project on highly reactive alkaline-earth metal benzyl complexes for styrene polymerization. In 2004 he became a professor of Inorganic Chemistry at the University of Duisburg-Essen. Since 2010 he has held the chair of inorganic chemistry at the University of Groningen. His current research interests include catalysis with early main group organometallics, hydrogen elimination in metal amidoborane complexes, multimetallic catalysts, lanthanide chemistry (catalysis and luminescence), and Cp^{BIG} chemistry, *i.e.* chemistry with superbulky cyclopentadienyl ligands.

1. Introduction and Scope

Organometallic chemistry is generally considered the key to homogeneous catalysis, which, although a century old, is still today a very dynamic discipline.[1] The past decade has seen two Nobel prizes related to organometallics and its application in catalysis (2001: Knowles, Noyori, and Sharpless; 2005: Chauvin, Grubbs, and Schrock).

Transition metal chemistry forms the heart of catalysis. The availability of d-orbitals allows for fast and reversible changes in the metal's oxidation states, a prerequisite in many catalytic cycles. They are also responsible for activation of a large variety of strong bonds, including H—H, C═O, C═C, and C≡C. Participation of partially filled d-orbitals, however, is not a requirement for catalytic conversions. Early d^0-species are among the most active transition metal catalysts,[2] and also lanthanide chemistry has made an important contribution to the field.[3] In the latter case, processes are controlled by metal Lewis-acidity, ligand-basicity, and steric and electronic factors, rather than by redox processes and/or orbital overlap.

Main group organometallic chemistry has never been recognized for its catalytic potential. Examples are mainly limited to Lewis-acidic catalysis with late main group elements such as Al, B, or Sn.[4] The highly basic features of the early main group metal complexes (group 1 and 2), however, are less exploited and are only beginning to gain momentum. Early main group metal complexes show typical organolanthanide-like reaction behavior, such as σ-bond metathesis and addition to saturated bonds. As these reactions are also the basis for lanthanide catalysis, it is not surprising that this compound class can be exploited in catalytic reactions. It is the author's personal view that the strength of organocalcium reagents in catalysis is related to the position of Ca in the periodic table (Scheme 1). Being a

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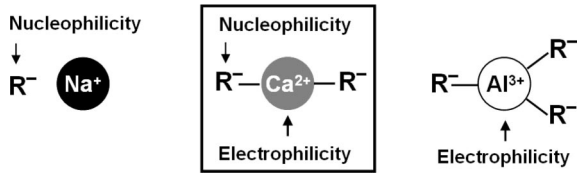
Scheme 1. Organocalcium Reagents Can Be Considered Intermediate between Group 1 and Group 3 Reagents



group 2 metal, its compounds combine nucleophilic reactivity, typical for group 1 reagents, with a significant dose of metal Lewis-acidity, typical for group 3 reagents. The latter Lewis-acidity is important for substrate binding and activation. This is nicely illustrated by the fact that lanthanide(III) catalysts can activate isolated C═C bonds for polymerization, hydrogenation, or hydrosilylation whereas lanthanide(II) catalysts are restricted to conversions of slightly activated (conjugated) C═C bonds. Apart from redox behavior, lanthanide(II) and calcium chemistry can be astoundingly similar (the close similarity of ytterbium(II) and calcium chemistry is discussed in depth at the end of this mansucript).

Among the many good arguments to develop a calcium based homogeneous catalysis, three motives should be underscored in particular:

(i) Organocalcium mediated reactions are interesting from an academic point of view. Prior to the systematic use of the more reactive heavier alkaline-earth metal complexes in catalysis, not much was known on their chemistry, and information on metal−carbon σ-bonded species was especially scarce.[5] Development of Ca-mediated reactions goes hand in hand with an explosive growth of fundamental calcium chemistry.

(ii) The most active transition metal catalysts are those based on the platinum group metals (PGM: Ru, Os, Rh, Ir, Pd, and Pt). The current trend in transition metal catalysis is the move to cheaper alternatives. This goal has been described by Bullock, briefly and clearly, as the quest for "cheap metals for noble tasks", and it especially relates to transition metals such as Fe, Co, and Ni.[6] Calcium, being the fifth most frequent element in the earth's crust (3.4 wt %),[7] is in this respect an extremely attractive element with effectively endless supplies and worldwide accessibility. Its straightforward isolation and reduction makes it also one of the cheapest metals.

(iii) Last but not least, calcium is the biocompatible metal *per se* and well-represented in the human body. Therefore, Ca-mediated synthesis does not only fit the current trend to develop chemistry based on less poisonous compounds[8] but also would be very advantageous in the development of biocompatible polymers suitable for internal medical application or as biodegradable materials (see section 3.1).

The scope of this review is limited to catalytic conversions which are mediated by calcium complexes. In some cases, we extend this chemistry with relevant examples of similar strontium or barium catalysts and discuss trends related to metal size. Occasionally also alkali metal based catalysts are the subject of this paper. It is by no means attempted to give a complete review of group 1 metals in catalysis, but merely comparisons with calcium catalyzed reactions are made. This allows conclusions regarding the influence of the metal and could answer the important question whether reactions should be rather classified as base-catalyzed (irrespective of the metal) or organocalcium catalyzed (in which case the metal choice is relevant). Although this review will deal mainly with cases in which the calcium (pre)catalysts are well-defined and understood, important catalytic conversions in which the calcium species are less or undefined will also be treated. Mechanistic investigations are plagued by the fact that early main group organometallics can be highly dynamic in solution. The reader is warned that the reaction mechanisms presented here are catalytic cycles that have been proposed on the basis of observations. In some cases these cycles are well-understood and intermediates have been structurally characterized; in other cases experimental evidence is hardly available and mechanisms are based on analogy with lanthanide chemistry.

This is the first extensive review article that covers all aspects of Ca-mediated reactions up to the year 2010.[9]

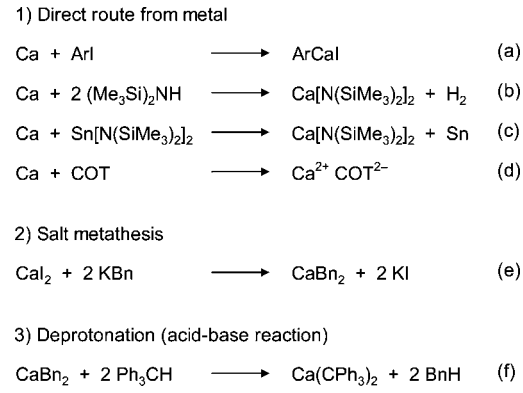
2. Organocalcium Chemistry and Catalysts

Within the discipline of organometallic chemistry, the chemistry of calcium can be regarded as a "sleeping beauty". A hundred years after Victor Grignard's breakthrough in organomagnesium chemistry,[10] activities in organocalcium chemistry finally started to grow rapidly. Its longstanding merely dormant existence can be attributed to several factors. The general thought that calcium chemistry is similar to magnesium chemistry is not only misleading but certainly impeded its development. The increasing electropositivity down the group of alkaline-earth metals is responsible for an increasing metal−carbon bond polarity. The ionicity of the metal−carbon bond has been quantified by charge analyses in simple Me_2M species. The following bond ionicities were calculated: Be−C, 74%; Mg−C, 77%; Ca−C, 87%; Sr−C, 91%; and Ba−C, 94%.[11] The concomitant increase in metal−carbon bond length and, therefore, decrease in metal−carbon bond strength is responsible for the sharp increase in reactivity down the group. Therefore, Grignard-like routes to the heavier alkaline-earth metal analogues have been plagued by decomposition through Wurtz-coupling and ether cleavage. Only very recently, have the first well-defined arylcalcium "Grignard's" been prepared.[12] The synthetic route is so far limited to aryl groups, which are much less sensitive to Wurtz-coupling than alkyl halide substrates. Highly reactive arylcalcium "Grignard's" cleave ethers at −35 °C. This demonstrates the enormous difference in reactivity with the closely related organomagnesium complexes, which are often prepared in refluxing ether solvents.

Apart from their much higher reactivity, syntheses of heavier alkaline-earth metal complexes are also hindered by their generally poor solubility. Their considerable ionic radii (Ca^{2+}, 1.00 Å; Sr^{2+}, 1.18 Å; and Ba^{2+}, 1.35 Å)[13] already indicate that coordinative saturation is increasingly difficult, and this often results in insoluble coordination polymers. Use of large and/or multidentate ligands can circumvent this solubility issue.

In many catalytic schemes, calcium alkoxide or amide complexes are sufficiently reactive to promote the desired conversion. In other cases, more potent carbanions are needed, and for these purposes, synthetic routes to benzylcalcium complexes have been developed (see section 3.2): they are highly reactive but do not react with ether solvents. Another group of stabilized alkylcalcium reagents is based on the famous "big R" ligand $(Me_3Si)_2HC^-$, a carbanion electronically and sterically stabilized by Me_3Si-substitution. Lappert et al. reported the first landmark synthesis of a σ-bonded alkylcalcium

Scheme 2. Exemplary Synthetic Routes toward Organocalcium Reagents (COT = Cyclooctatetraene, Bn = Benzyl)



complex, $[(Me_3Si)_2HC]_2Ca\cdot(dioxane)_2$,[5a] using metal-vapor-synthesis, and recently, Hill et al. showed that its THF adduct is also accessible through a standard "wet" chemistry method.[14] Hanusa et al. reported the structure of bis(1,3-Me_3Si-allyl)calcium$\cdot(THF)_2$ whereas Okuda et al. presented a synthetic procedure to the THF-free simple bis(allyl)calcium.[15]

Nowadays organocalcium compounds and related alkoxides or amides can be prepared by several synthetic routes. As this area has been reviewed thoroughly,[16] the historical development and extensive discussion of organocalcium chemistry will not be part of this work, but merely a short summary of synthetic methods is given (Scheme 2).

The first group of methods (a−d) makes convenient use of calcium metal (which in some cases needs to be activated), but substrate choice is limited. The second type of synthetic route, the salt metathesis (e), can be applied in general and works most efficiently with CaI_2 as the calcium species and an organopotassium precursor (formation of the highly insoluble KI is the driving force for this reaction). Ether solvents are generally a prerequisite for this method. As coordinated ether ligands are not always easy to remove and can react with the more reactive organocalcium species (ether cleavage), this method has its restrictrions. In the third method (f), calcium compounds are conveniently prepared by deprotonation of a substrate with a strong organocalcium base such as dibenzylcalcium. This reaction is limited to substrates with pK_a values <35 but generates toluene as a byproduct that is easy to remove.

Syntheses of stable heteroleptic calcium complexes, i.e. compounds with two different ligands at the metal (L^1-Ca-L^2), pose another problem. As the ligand−metal bond becomes progressively weaker along the row Mg > Ca > Sr > Ba, ligand exchange processes may impede syntheses of heavier alkaline-earth metal complexes. Control of these so-called Schlenk equilibria, first described by Schlenk for the exchange of ligands between a heteroleptic Grignard reagent RMgX and homoleptic R_2Mg/MgX_2 species,[17] is a great challenge in organocalcium chemistry. Although homoleptic organocalcium species can also be active as (pre)catalysts, there are two cases in which it is absolutely essential to use heteroleptic catalysts such as LCaR (in which L is usually a large stabilizing but passive spectator ligand and R represents the active group responsible for catalytic reactivity). In the first case, spectator ligand L is used to solubilize the LCaR catalyst and any ligand exchange could lead to precipitation of insoluble, but catalytically active, R_2Ca. In the second case, the spectator ligand L influences either the activity or selectivity of the catalyst; for example, the stability of an enantioselective catalyst such as L*CaR (in which L* is a chiral enantiopure ligand) is a prerequisite for chiral induction.

Hanusa et al. made considerable contributions to an understanding of Schlenk equilibria in organocalcium chemistry.[18] Many heteroleptic calcium complexes crystallize as such but, when dissolved, are in Schlenk equilibrium with homoleptic species. The stability of heteroleptic calcium complexes may depend strongly on temperature, concentration, presence of polar (co)solvents, ligand bulk, and also, as shown by Chisholm,[19] ligand denticity. Despite many follow-up studies,[20] it is even today generally not predictable whether a targeted heteroleptic calcium complex will be stable toward ligand exchange. Recently, Gauvin and Harder et al. introduced a surefire concept to prevent ligand distribution by fixation of the CaR unit on a solid silica support with isolated siloxide units: (≡SiO)CaR.[21] The observation that such materials do not leach R_2Ca indicates that ligand exchange likely proceeds through an associative mechanism.

In order to give the reader an idea which calcium complexes have been used so far in catalysis, compounds **1**−**25** have been summarized in Scheme 3. This scheme also contains the abbreviations for commonly encountered ligands and formulas for Li, K, Mg, Sr, Ba, and Yb species relevant to this work. The review is arranged according to reaction type.

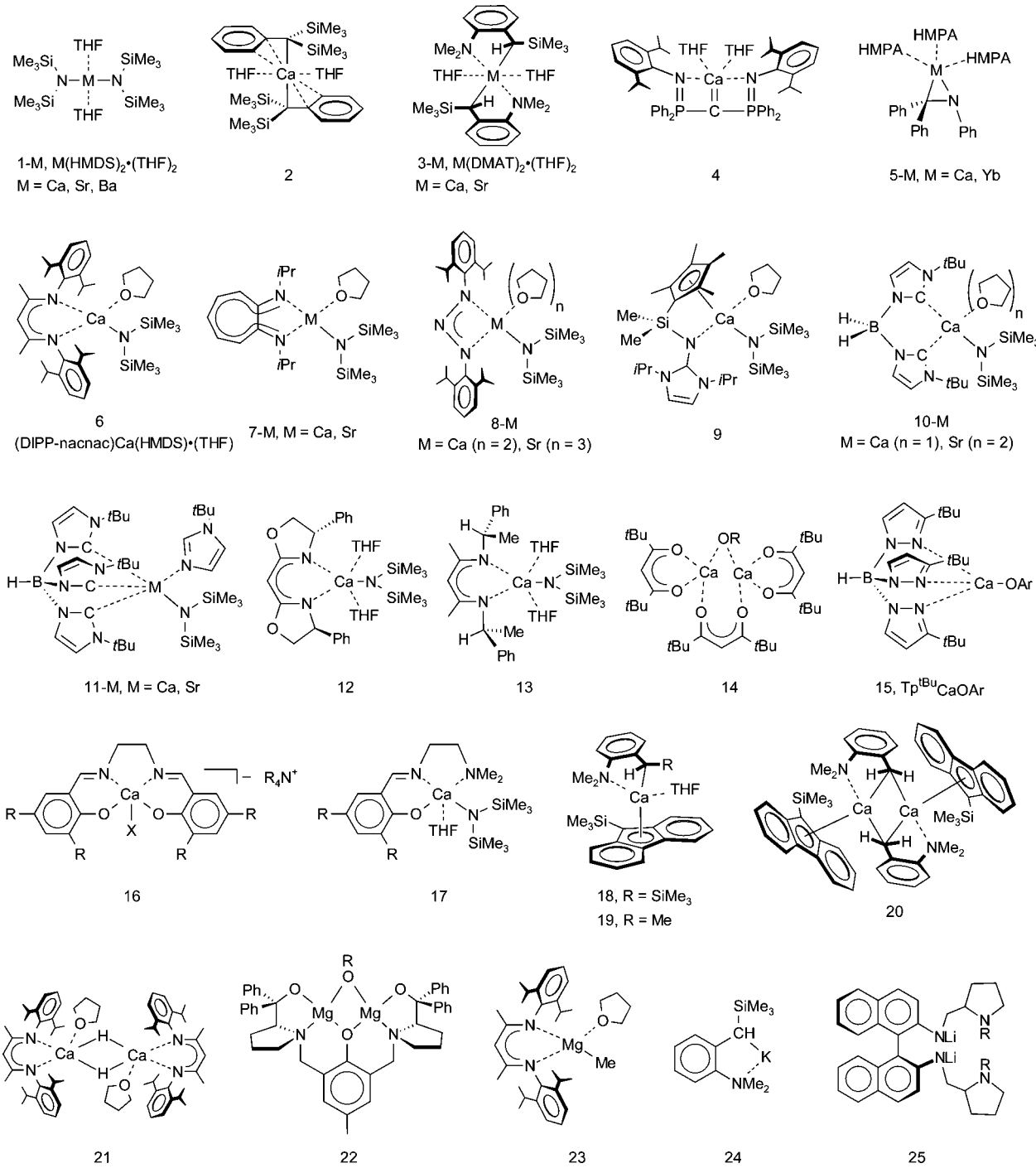
3. Polymerization Catalysis

Group 1 organometallic compounds have a rich history as initiators in living anionic polymerization[22] of moderately activated alkenes such as styrene, butadiene, or isoprene. It is therefore surprising that little is known of the use of the heavier group 2 organometallics in anionic polymerization. This is not due to their lack of reactivity but likely inherent to poor accessibility, poor solubility, and poor understanding of their structures and chemistry. The past decade, however, has seen rapid progress in the use of well-defined organocalcium complexes as polymerization catalysts. This development is paralleled by an increased understanding of synthetic routes and structures of such complexes. Here, the latest development of well-defined organocalcium catalysts in the polymerization of activated alkenes and polar monomers is reviewed.

3.1. Polymerization of Polar Monomers

As the world will run out of fossil fuels at some stage,[23] polymers based on alkenes slowly will have to be replaced by materials produced from renewable feedstocks. Environmental issues also increase the demand for biodegradable materials.[24] Polyoxygenates could likely represent a new generation of polymers fulfilling these requirements.[25−29] The ring-opening of cyclic ethers is generally catalyzed by complexes based on early transition metals (including lanthanides) as well as early and late main-group metals. Biodegradable polymers are used in medical applications such as sutures, screws for bone fixation, drug delivery systems, and tissue engineering.[30] Therefore, polymerization catalysts based on the biocompatible metal Ca are currently receiving an increasing interest. Calcium alkoxide species play a central role in catalytic cycles (Scheme 4) for polymerization of cyclic esters such as lactides (LA),

Scheme 3. Overview of Common Calcium and Other Group 1 and 2 Complexes Discussed in This Paper

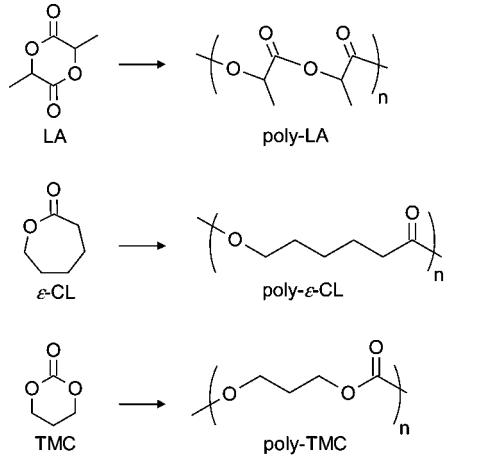


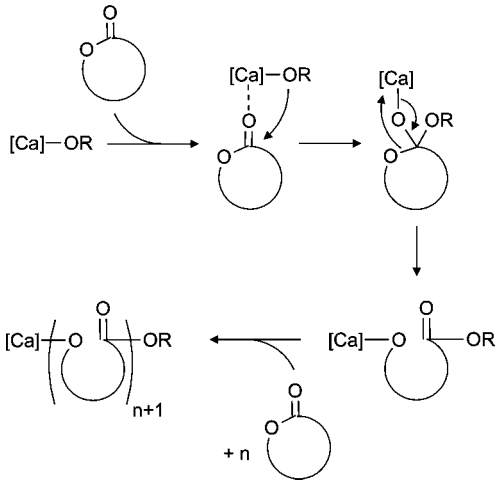
ε-caprolactone (ε-CL), and trimethylene carbonate (TMC), thus also giving research on well-defined Ca-alkoxide complexes an impetus.

Westerhausen and Feijen found that the homoleptic complex $Ca(HMDS)_2 \cdot (THF)_2$ (**1-Ca**) is fast in ε-CL polymerization but slow in the polymerization of L-lactide (L-LA).[31a−c] However, addition of alcohols (i.e., the *in situ* generation of a calcium-alkoxide functionality) led to a more controlled living L-LA polymerization and gave products of controlled molecular weight, of low polydispersity (PDI = 1.03), and with tailored end-functionalities. Westerhausen and Feijen also introduced the heteroleptic calcium complex **14** as an efficient catalyst for ε-CL and L-LA polymerization.[31d,e] Noteworthy is the exclusive formation of isotactic polylactide. This indicates that there is no base-catalyzed epimerization of the chiral carbon center, as can be observed in early main group metal mediated lactide polymerizations.[32]

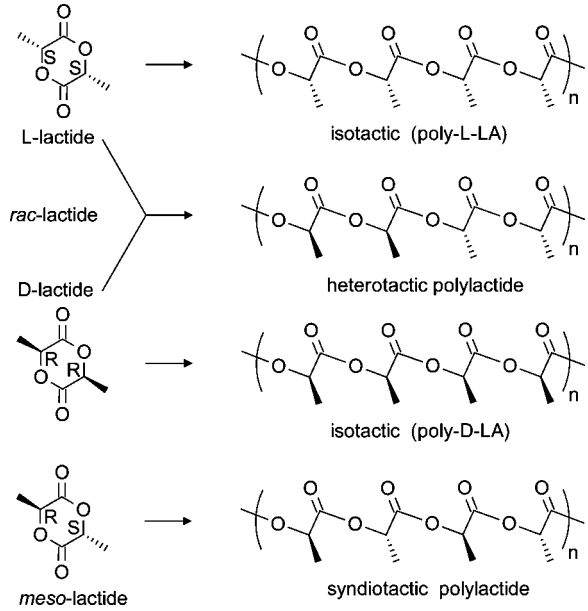
The stereoregularity of polylactides has a tremendous effect on the rates of their biological degradation as well as on mechanical and physical properties.[24,33] Although isotactic polylactide is easily accessible by homopolymerization of either D- or L-lactide, syntheses of syndiotactic or heterotactic polylactides involve stereocontrolled polymerization of *meso*-lactide or *rac*-lactide (a 1/1 mixture of D- and L-lactide), respectively (Scheme 5). Coates milestone zinc catalyst[27] (DIPP-nacnac)ZnO*i*Pr (DIPP-nacnac = CH{(CMe)(2,6-$iPr_2C_6H_3N$)}$_2$) gave a high degree of chain-end controlled stereoselectivity in lactide polymerization and allowed for the synthesis of heterotactic polylactide from *rac*-lactide.[34] The comparable Mg complex (DIPP-nacnac)MgO*i*Pr gave

Scheme 4. General Scheme for the Ca-Mediated Ring-Opening Polymerization of Cyclic Esters: Lactides (LA), ε-Caprolactone (ε-CL), and Trimethylenecarbonate (TMC)





Scheme 5. Stereochemistry of the Lactide to Polylactide Conversion



extremely fast *rac*-lactide polymerization; however, the polylactide obtained is purely atactic.[34] Chisholm et al. could show that choice of solvent is critical for the stereoselectivity. Whereas polymerization of *rac*-lactide by (DIPP-nacnac)-MgO*t*Bu in weakly polar solvents (CH_2Cl_2 or benzene) gave a mainly atactic polymer, ring-opening polymerization in THF showed a stereoselectivity comparable to that of the Zn-catalyst.[35c] Gibson et al. investigated the detailed intricacies of this observed selectivity by calculation.[36a] This group also reported on Mg catalysts with asymmetric nacnac ligands that contain pendant chelating arms. These complexes did not show increased stereocontrol; instead, evidence for increased transesterification was found, i.e. chain transfer by inter- or intramolecular alkoxide/ester attack ("backbiting").[36]

The group of Chisholm reported extensive studies on the development of single-site catalysts LMOR with group 2 metals (Mg and Ca) and compared these with the Zn analogues.[35] Competition experiments of the precursor amides (DIPP-nacnac)Ca(HMDS)·(THF) (**6**), (DIPP-nacnac)Mg(HMDS), and (DIPP-nacnac)Zn(HMDS) with a stoichiometric amount of L-LA showed, as expected, the reactivity order Ca > Mg > Zn.[35e] Lactide polymerization using excess L-LA, however, was found to be much faster with the Mg instead of the Ca catalyst. The unusually slow polymerization rate for the Ca catalyst either is explained by aggregation of the Ca species to a larger multinuclear cluster or is due to ligand scrambling, resulting in ill-defined or insoluble catalytically active species.[35e−g] These observations suggested that the β-diketiminate ligand DIPP-nacnac is not bulky enough and that extra denticity is needed to confer single-site living polymerization. The calcium complex Tp^{tBu}CaOAr (**15**) is an extremely fast and efficient catalyst for lactide polymerization.[35e] Apparently, the bulky tridentate scorpionate ligand prevents aggregation of the catalytically active Ca species. Polymerization of *rac*-LA gave a high degree of heterotactic polylactide. The latter stereocontrol is extremely sensitive to ligand bulk: a scorpionate ligand with slightly smaller substituents, Tp^{iPr}, gave mainly atactic polymer.[35e] Lactide polymerization with Tp^{tBu}CaOAr (**15**) is not living (M_n = 37.8 kg·mol^{-1}, PDI = 1.74).[35f] This is likely due to the loose bond between the scorpionate ligand and Ca. Introduction of Lewis-base sidearms did not improve this kinetic lability.[35g] Chisholm also reported chiral enantiopure scorpionate complexes of Mg which polymerize *rac*-lactide with a slight enantioselectivity.[35b]

Darensbourg et al. recently introduced calcium catalysts based on Schiff base ligands (salen) and investigated their use in the polymerization of cyclic esters extensively.[37] Polymerizations are initiated either by a salen−Ca complex with a $R_4N^+X^-$ cocatalyst (**16**, X = Cl, Br, N_3)[37a] or by well-defined single-site catalysts (**17**).[37b,c] The latter calcium single-site catalysts showed excellent activities for the ring-opening polymerization of LA and TMC. Kinetic experiments indicate that polymerizations are first order in both [monomer] and [catalyst]. The high level of polymerization control was demonstrated by the linear relationship between M_n and monomer conversion as well as by the narrow molecular weight distribution in some of the polymers (PDI ≈ 1.02−1.05). Tacticity control could only be achieved at lower temperatures. The quasi-living character of the polymerization reaction allowed for the synthesis of diblock copolymers of TMC and LA. The latter are less brittle than pure poly-LA and represent valuable thermoplastic elastomers for biomedical application.[38] Other work on lactide

polymerization with calcium catalysts based on Schiff base-like ligands or phenoxy ligands has been presented by the groups of Bochmann, Lin, and Carpentier.[39]

Although Ca-mediated polymerization is mainly focused on the cyclic monomers LA, ε-CL, and TMC, early results on methylmethacrylate (MMA) polymerization by organocalcium compounds should be mentioned: addition of Cp_2Ca to MMA gave poly-MMA of high syndiotacticity (92% *rr*).[40] However, the calcium catalysts used in these investigations were by no means well-defined complexes, and this claim could not be reproduced. It was found that Cp_2Ca and the more soluble Cp^*_2Ca gave atactic poly-MMA.[40b] Gibson et al. recently introduced a well-defined (DIPP-nacnac)Mg(enolate) complex and demonstrated its excellent syndioselectivity in MMA polymerization ($rr = 96\%$).[41]

Commercially available calcium acetylacetonate, $Ca(acac)_2$, has been successfully applied in glycolide polymerization and was also found to be very effective in glycolide/ε-CL copolymerization. High yields and molecular weights indicate a low contribution of "backbiting" side reactions.[42]

All calcium catalysts discussed here are not active in the ring-opening polymerization of epoxides. This is nicely demonstrated by a crystal structure of $Tp^{tBu}CaOAr\cdot(PO)$ in which propylene oxide (PO) coordinates to Ca^{2+} as a neutral ligand.[35e] The inactivity of calcium complexes in epoxide homopolymerization strongly contrasts with the industrial use of the Ca-based Union-Carbide catalyst for this conversion.[43] As the exact nature and the mechanism of operation of this heterogeneous catalyst are not clear, we will not further discuss this catalytic system.

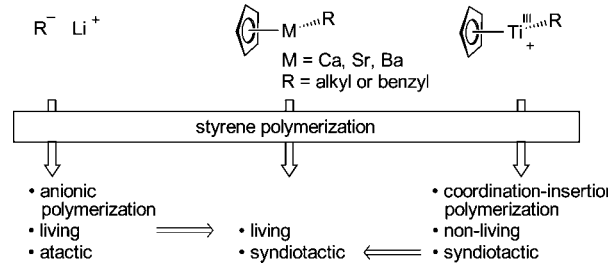
The Ca (and Mg) catalysts described above are also not active in the copolymerization of cyclohexene oxide (CHO) and CO_2. Since there is strong evidence for a bimetallic mechanism for this particular polymerization,[27] Harder et al. developed a series of bridged Mg and Ca amides.[44] However, also these bimetallic complexes showed no evidence for efficient CHO/CO_2 polymerization. Hitherto, the bimetallic magnesium complex (**22**) represents the only example of a group 2 catalyst active in CHO/CO_2 copolymerization which can even be performed even at the low CO_2 pressure of 1 bar.[45]

3.2. Polymerization of Activated (Conjugated) Alkenes

Anionic polymerization of activated alkenes, such as styrene, butadiene, or isoprene, is classically initiated by catalytic amounts of alkyllithium reagents. However, it was already found at an early stage that addition of group 2 alkoxides influences the microstructure of the polymer.[46] A mixed organolithium/calcium alkoxide initiator gave in the polymerization of styrene and butadiene a highly random copolymer with mainly *trans*-linkages (arising from *trans*-selective 1,4-butadiene insertion).[46e] This styrene−butadiene copolymer can be utilized in tire tread rubbers that exhibit improved wear-characteristics. Alkene polymerizations with heavier homometallic alkaline-earth metal catalysts are rare,[47] and also in these cases only activated (conjugated) alkene monomers could be used. The organometallic group 2 species used in these studies were prepared *in situ* and were by no means characterized.

In the middle 1990s the groups of Brintzinger, Harder, and Knoll (BASF) teamed up to develop synthetic routes toward well-defined organometallic complexes of the heaviest alkaline-earth metals (Ca, Sr, Ba).[48] The idea was to introduce discrete alkaline-earth single-site catalysts in which one of the ligands is a passive "spectator" (e.g., Cp) whereas the other is a highly reactive alkyl that can initiate styrene polymerization (Scheme 6). Such a species can be seen as a "cross-breed" of highly ionic organolithium compounds, which are known to produce atactic polystyrene (PS) by a living anionic polymerization,[49] and a cationic half-sandwich complex of Ti^{III}, which was shown to give highly syndiotactic PS ($r > 99\%$) by a chain-end controlled coordination−insertion mechanism.[50] The group 2 "cross-breed" could combine the advantages of living polymerization (heavier alkaline-earth metal compounds display a high degree of ionic character) with those of a syndiospecific polymerization (ionic bonds to the 2+ alkaline-earth metal cation are substantially stronger than those to Li^+, and a coordination−insertion mechanism might be feasible). This would allow controlled styrene homopolymerization to syndiotactic PS (*s*-PS), a material with unique properties.[51] More important, its living character would enable the syntheses of block-copolymers containing crystalline *s*-PS blocks.

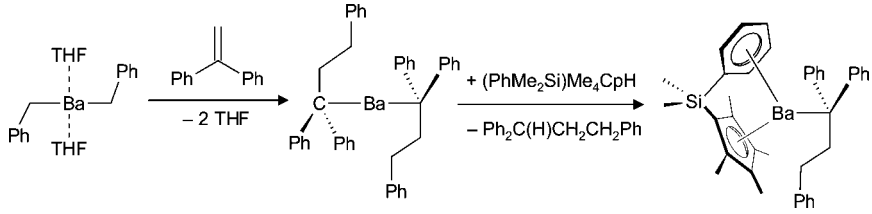
Scheme 6. Concept for Combined Living and Stereoselective Styrene Polymerization



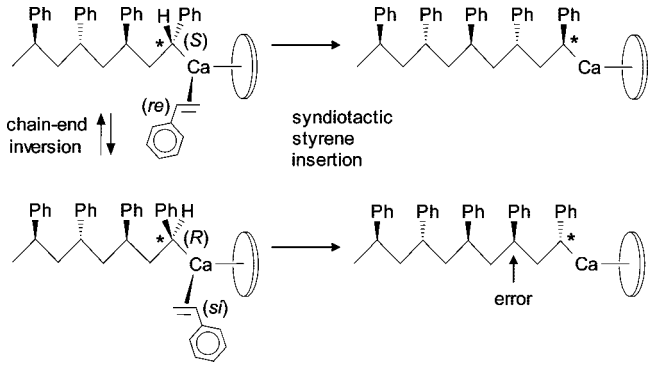
As Ba^{2+} is a large cation (ionic radius: 1.34 Å) that allows for precoordination of large alkene monomers such as styrene, the first efforts focused on the syntheses of highly reactive organobarium complexes. A convenient route for the synthesis of dibenzylbarium was developed and, in order to increase its solubility, this reagent was further reacted with 1,1-diphenylethylene.[52] Subsequent reaction with the substituted cyclopentadiene $(PhMe_2Si)Me_4CpH$ (Cp′H) gave the expected single-site catalyst (Scheme 7). The resulting heteroleptic benzylbarium complex was highly dynamic and not stable toward ligand exchange. The Schlenk equilibrium, however, could be manipulated: addition of Cp'_2Ba drives the equilibrium to the heteroleptic side and only the polymerization-active species $Cp'BaC(Ph)_2CH_2CH_2Ph$ and excess of polymerization-inactive Cp'_2Ba were present. Although this mixture was highly active in styrene polymerization, only atactic PS was obtained.[52]

As benzylbarium complexes are extremely sensitive and show a high kinetic lability toward ligand exchange, this research was directed toward more docile benzylcalcium complexes.[53] The first well-defined dibenzylcalcium complex (**2**) was extensively stabilized by Me_3Si substitutents at the benzylic carbon and did not initiate the polymerization of styrene.[53a] Reducing Me_3Si-substitution and introducing an intramolecular chelating Me_2N-substituent gave the well-defined dibenzylcalcium complex (**3-Ca**), which was shown to be an active but somewhat slow initiator for styrene polymerization with two propagating chains per Ca center (slight tailing in the low molecular weight range is due to a low initiation/propagation ratio).[53b] This homoleptic dibenzylcalcium complex is an excellent precursor for the heteroleptic catalyst **18**, which in aromatic solvents is stable

Scheme 7. Synthesis of a Heteroleptic Barium Alkyl Complex for Styrene Polymerization

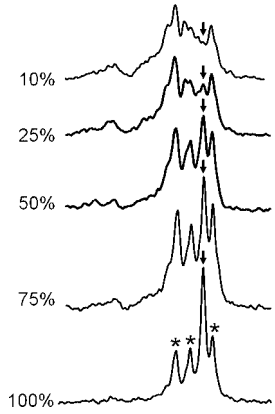


Scheme 8. Chain-End Controlled Syndiotactic Styrene Polymerization (The Chiral Chain-End Determines the Stereoselectivity of Monomer Coordination, *re* or *si*)[a]



[a] The ratio between insertion and inversion rates determines the stereoregularity of the obtained polystyrene.

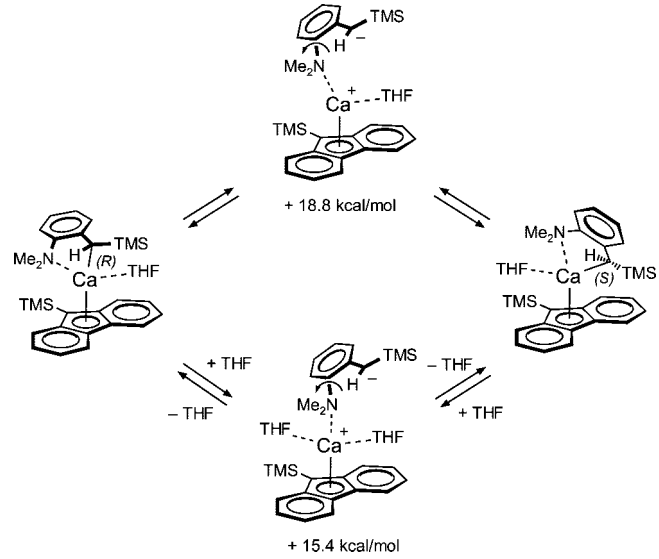
Scheme 9. Effect of Styrene Concentration (wt %) on Syndioselectivity[a]



[a] Shown are the ^{13}C NMR signals for the C_{ipso} in the Ph substituents of the polymer. The arrow indicates the syndiotactic heptade *rrrrrr* (145.5 ppm). A single error insertion gives rise to three new signals *mrrrrr*, *rmrrrr*, and *rrmrrr* in a 1/1/1 ratio (designated by a * at 145.4, 145.6, and 145.7 ppm).

toward ligand exchange (the Schlenk equilibrium is completely at the heteroleptic side).[53c] Styrene polymerization with **18** in an apolar medium (cyclohexane) gave a slightly syndiotactically enriched PS. It was suspected that the anticipated chain-end controlled syndioselectivity for styrene insertion might have been nullified by inversion of the chiral chain-end. This would give rise to a single stereoerror (Scheme 8). A similar inversion of the chiral benzylic carbon atom in **18** was demonstrated by VT-NMR in C_6D_6 ($\Delta G^{\ddagger}$ = 18.8 kcal/mol).[53c] In this case, the ratio between chain-end inversion and styrene insertion should be controllable by the styrene concentration. Indeed, an increase in the styrene concentration had a dramatic effect on the syndioselectivity (Scheme 9),[53c] as did lowering of the polymerization temperature. ^{13}C NMR analysis of the PS microstructures showed that hitherto reported pentade/hexade assignments of signals

Scheme 10. Inversion of Chirality at the Benzylic Carbon in 18 Is Accelerated by Addition of THF ($\Delta G^{\ddagger}$ Values Have Been Determined by VT-NMR)[53e]



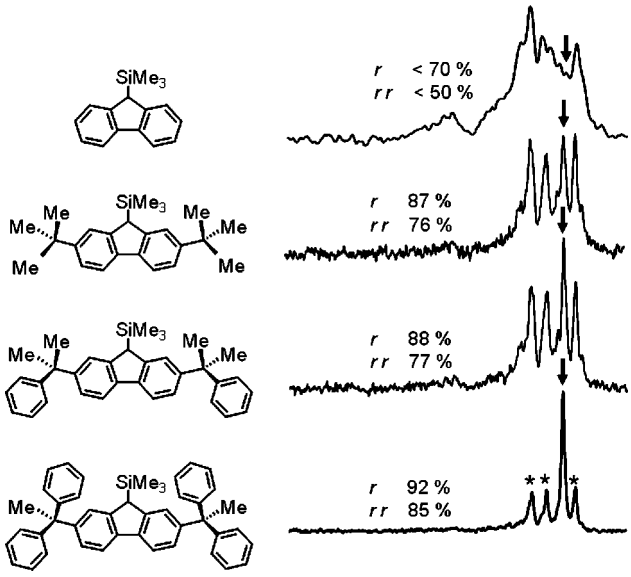
were wrong, and a new heptade/hexade assignment was introduced.[53d] Polymerization in pure styrene at −20 °C gave a syndiotactic polymer that follows Bernoullian statistics with $r = 92\%$ and $rr = 85\%$.[53d] Stereoerrors ($m = 8\%$) arise from inversion of the metal-bound chain-end.

The addition of only a few equivalents of THF to a solution of **18** in benzene lowers the barrier for inversion of the chiral carbon from 18.8 to 15.4 kcal/mol (Scheme 10). The presence of THF could therefore substantially influence the syndioselectivity of styrene polymerization.[53e] Styrene polymerization with the dimeric THF-free benzylcalcium initiator **20**, however, did not improve syndioselectivity, and no difference was found in polymers obtained with THF/Ca ratios of 1/1 or 0/1. Addition of a few equivalents of THF during polymerization, however, dramatically decreased the syndiotacticity of the polymer obtained.[53e] This confirms the working theory that excess polar solvent lowers the stereoselectivity of Ca-mediated styrene polymerization (likely by acceleration of chain-end inversion).

Since the initiator **20** is more reactive than the α-Me_3Si-stabilized benzylcalcium complex **18**, faster initiation and narrower molecular weight distribution were observed. The even more reactive α-Me-substituted benzylcalcium complex **19** also shows fast initiation but can be disadvantageous due to possible decomposition by intramolecular deprotonation of the spectator ligand.[53f]

The syndioselectivity of Ca-mediated styrene polymerization can also be controlled by the spectator ligand. As stereocontrol is steered by communication of the chiral chain-end with the precoordinated styrene monomer (Scheme 8), it was reasoned that increasing the bulk of the 9-Me_3Si-fluorenyl ligand in **18** could improve communication and

Scheme 11. Effect of Steric Bulk in the 2- and 7-Positions of the Fluorenyl Ligand in 18 on the Syndioselectivity of Styrene Polymerization (10% Styrene in Cyclohexane, 50 °C)[a]



[a] See Scheme 9 for signal assignments.

thus stereoselectivity. Use of the hypersilyl-substituted spectator ligand $(Me_3Si)_3Si$-fluorenyl did not give the expected improvement in stereoselectivity.[53g] This is likely due to steric blockage of the metal center, resulting in a ten times slower observed rate of insertion (the ratio between the rates for insertion and inversion determines the stereoselectivity). A benzylcalcium complex with a fluorenyl spectator ligand containing an intramolecularly coordinating pendant amino arm, 9-$Me_2NCH_2CH_2$-fluorenyl, was not active at all in styrene polymerization.[53h] This shows that free coordination sites at the metal are important and is indirect evidence for a coordination−insertion mechanism. This observation also suggests that large bulky substituents in the direct vicinity of the metal will always retard the insertion step, thus allowing for racemization of the chain-end by inversion. For these reasons, the steric bulk of the fluorenyl ligand was increased in the remote positions 2 and 7.[53h] Gradually increasing the size of the substituents in these positions resulted in an increasing control of syndioselectivity (Scheme 11). The most syndiotactic polymer was obtained with the most bulky calcium initiator at −20 °C ($r = 95\%$, $rr = 90\%$). These new initiators allow for syndioselective styrene polymerization not only in neat styrene but also under diluted conditions. More important, the dramatic effect of the ligand on stereoselectivity shows that heteroleptic benzylcalcium complexes function as single-site catalysts in which monomer precoordination and stereoselective insertion are key steps.

In addition to well-defined benzylcalcium complexes, strontium complexes have also been shown to polymerize styrene in a living syndioselective fashion.[53g,i] Polymerization with the more ionic Sr initiators is faster but also less selective than that with Ca initiators. This is likely due to the more ionic and weaker Sr−C bond that causes fast chain-end inversion (a change to Ba initiators gave an even more atactic polymer).[52] Styrene polymerization with a mixture of Ca and Sr initiators (20 °C) gave a bimodal distribution of chain lengths. This indicates that chain-transfer processes between metals are slow at room temperature. However, polymers obtained at 50 °C show a monomodal molecular weight distribution, suggesting that at higher temperature chain-transfer becomes an issue.[53i] The heavier alkaline-earth metal complexes were also tested in isoprene polymerization. There is evidence for living polymerization with a high content of 1,2- and 3,4-insertions, and styrene/isoprene block-copolymers could be obtained.[53i] Okuda et al. recently introduced bis(allyl)calcium as an active initiator for butadiene polymerization and obtained narrow molecular weights (PDI = 1.15, 1,2/1,4-ratio = 0.92, 1,4-cis/1,4-trans ratio = 0.81).[15b]

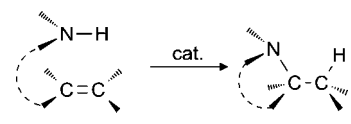
Successful use of organocalcium species as initiators for syndioselective and living styrene polymerization can be attributed to the right balance of Lewis-basic and Lewis-acidic properties (Scheme 1). Equally reactive organolithium compounds are efficient initiators for styrene polymerization, but the significantly lower Lewis-acidity of the Li^+ cation results in very loose bonding of the chain-end, which translates to faster chain-end inversion ($\Delta G^{\ddagger}$ for inversion of the benzylic carbon in chiral benzyllithium complexes is ca. 9 kcal/mol).[54] Organomagnesium complexes would be more Lewis-acidic than calcium compounds; however, they are less ionic and do not polymerize styrene.

4. Hydroamination and Hydrophosphination

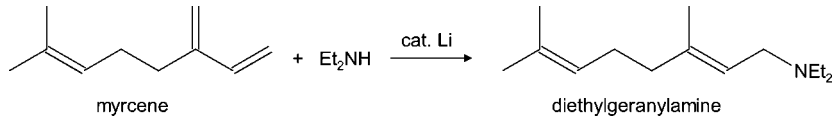
As nitrogen containing compounds represent important synthetic targets in industry, there is significant interest in the development of efficient synthetic protocols.[55] The highly atom-efficient hydroamination, defined as the addition of a polar N−H bond to a multiple bond, is therefore an area of considerable research activity.[56] Although the focus is mainly on C=C and C≡C containing substrates, C=O and C=N functionalities have been hydroaminated. The hydroamination of alkenes, which can either proceed inter- or intramolecularly (Scheme 12), is a thermodynamically allowed exothermic reaction. However, on account of repulsive interaction between the amine lone pair and the electron-density in the unsatured bond, it is kinetically unfavorable. This explains the need for a catalytic procedure, and catalysts based on metals throughout the periodic table have been reported. These include not only the early and late transition metals,[57] but also lanthanide[58] catalysts are highly efficient. This reaction can also be accelerated substantially by addition of catalytic amounts of acid[59] or base.[60] Most noteworthy, it has been known for nearly 60 years that simple addition of alkali metals catalyzes the hydroamination of conjugated alkenes.[61] This particular reaction is the first step in the Takasago process, a large industrial scale synthesis of (−)-menthol from natural myrcene (Scheme 13).[62] In addition, commercially available *n*BuLi was shown to be an effective catalyst for the intramolecular hydroamination of aminoalkenes (among which also are secondary aminoalkenes).[60b] Lithium amide species are the catalytic key intermediates in these conversions.

Recently, well-defined calcium amide complexes were found to be active in the intramolecular hydroamination of aminoalkenes and the intermolecular hydroamination of

Scheme 12. Catalytic Inter- or Intramolecular Hydroamination of an Alkene



Scheme 13. Industrial Application of a Lithium Amide Catalyzed Intermolecular Hydroamination



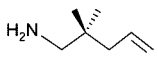
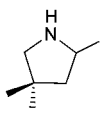
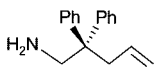
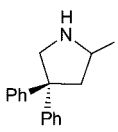
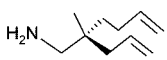
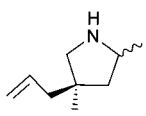
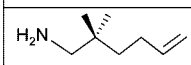
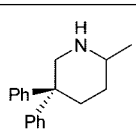
activated C═C bonds, carbodiimides, and isocyanates. As amines are isolobal to phoshines, this concept could also be extended to intermolecular hydrophosphination.

4.1. Intramolecular Hydroamination of Aminoalkenes

Recently, Hill et al. introduced the first well-defined calcium amide complex **6**, which was originally developed by Chisholm as a lactide polymerization catalyst,[19] as a catalyst for the intramolecular hydroamination of aminoalkenes (Table 1).[63] These initial results have been extended in later years by the groups of Hill,[64] Roesky,[58l,65] Tamm,[58l] and Harder.[66] For example, alternative ligand systems have been introduced: **7-M**,[65a] **10-M**,[64d] **11**,[64e] **8-Ca**,[64a] and **9**.[58l] Although the simple homoleptic complex $Ca(HMDS)_2 \cdot (THF)_2$ (**1-Ca**) was found not to be catalytically active,[63] it was shown by Harder et al. that it is an efficient catalyst for certain aminoalkene substrates (see section 4.2).[66] Apart from Ca catalysts, also Mg (**23**)[64c] and Sr complexes (**7-Sr**,[65b] **8-Sr**,[64a] **10-Sr**,[64d] and **11-Sr**[64d]) have been found to be catalytically active. The proposed mechanism (Scheme 14), which is similar to that observed in the lanthanide-mediated ring closure of aminoalkenes,[58] is supported by several observations.[64c]

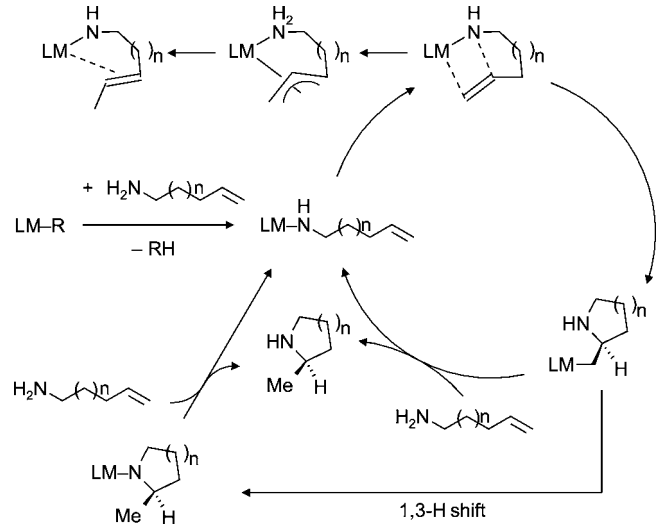
The first step in the mechanism is a σ-bond metathesis between the organometallic reagent LMR and the primary amine (L represents an unreactive spectator ligand and R the reactive functionality). Depending on the nature of the metal and the basicity of the anion R^-, this step is generally fast. For the calcium amide catalyst **6**, this was shown to be an equilibrium (the acidity of $(Me_3Si)_2NH$ is comparable to that of primary amines); however, in case carbanions are used, this is a fast irreversible step.[64c]

Table 1. Intramolecular Hydroamination of Aminoalkenes with Catalyst 6 (10 mol %, C_6D_6)[63]

Susbstrate	Product(s)	T (°C)	t (h)	Conv. (%)
		25	0.25	>99
		25	0.25	>99
		25	0.25	>99
		60	6	86[a]

[a] Ring closure of large 6-membered rings needs more forcing conditions: 20 mol % catalyst was used.

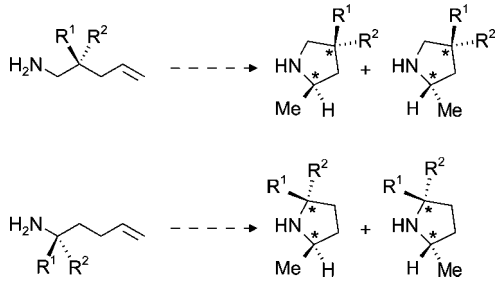
Scheme 14. Catalytic Cycle for the Intramolecular Hydroamination of Aminoalkenes and Possible Side-Reactions



The second step involves intramolecular nucleophilic attack of the metal amide on the alkene functionality. This rate-determining step involves a highly ordered metallacyclic transition state. As not even the much more reactive benzylcalcium complexes show addition to isolated (nonactivated) C═C bonds, this particular reaction is only enabled on account of its intramolecular character, which minimizes entropy loss. The amide/alkene addition is also regioselective, and only the more stable primary alkylmetal intermediates are formed. The unusual conversion of an amide to a highly energetic unstabilized alkylcalcium complex (a species which hitherto has never been prepared!) can only be understood by thermodynamic gain obtained from breaking a C═C bond and making a C—C and a C—N bond. The intermediacy of an unstabilized primary alkylcalcium complex has been proven by *D*-labeling studies: aminoalkenes containing the ND_2 fragment react to cyclic products that contain a CH_2D ring substituent.[64c] Generally proposed cycles show that monodeuteration originates from intermolecular deuteration of the highly reactive primary alkylmetal species with the amine substrate. Alternatively, an intramolecular 1,3-H shift cannot be excluded and should be considered in the overall mechanism (Scheme 14). Although the *D*-labeling studies cannot discriminate between inter- or intramolecular deuteration, entropy advantage and frequent occurrence of 1,3-H shifts are in favor of the intermolecular route. Examples of the proposed intermediate, a cyclic secondary metal amide, have indeed been isolated from stoichiometric reactions.[64c,58h] A rare, but occasionally observed, side-reaction is alkene isomerization. This can be envisioned by intramolecular deprotonation at the allylic position and subsequent protonation at the terminal carbon nucleus (Scheme 14).

For Ca-mediated intramolecular hydroamination of aminoalkenes, the following general conclusions can be drawn: (i) Consistent with Baldwin's guidelines for ring formation,[67]

Scheme 15. Intramolecular Hydroamination, Giving Diastereomeric Products



conversion rates increase with decreasing ring size 7 < 6 < 5 (more forcing reaction conditions are needed for formation of the larger rings). (ii) Substituents on the aminoalkene skeleton have a drastic influence on the conversion rates. Substitution at the terminal alkene carbon results in complete inactivity, whereas a substituent on the internal alkene carbon is allowed. Large geminal substituents R in the alkane bridge ($H_2C{=}CHCH_2CR_2CH_2NH_2$) increase the conversion rate by the Thorpe−Ingold effect:[68] a wide R−C−R angle leads to C−C−C angle compression in the ring to be formed. Two different substituents in the alkane bridge give rise to diastereomeric products (Scheme 15). Large diastereomeric excess (up to 98% *de*) is only observed when the two different substituents R^1 and R^2 are in α-N position close to the nucleophilic center.[64c] (iii) The effects of the metal are not clear-cut. Comparison of similar catalysts such as **6** (Ca) and **23** (Mg) led to the conlusion that conversion rates for the more ionic calcium catalyst are substantially higher (circa three times).[64c] Going to the even larger and more electropositive metal Sr gave in some cases an increase in the reaction rate[64d,e] but also has been reported to slow down conversion.[64a,65b] These seemingly contradicting observations could be understood by assuming that for the heavier alkaline-earth metal catalysts Schlenk equilibria are an issue. This would result in rather insoluble homoleptic intermediates which, after precipitation, would be deactivated. As there is generally no information on the position of the Schlenk equilibria for short-living reaction intermediates, it is too early to draw definite conclusions on the effect of the metal.

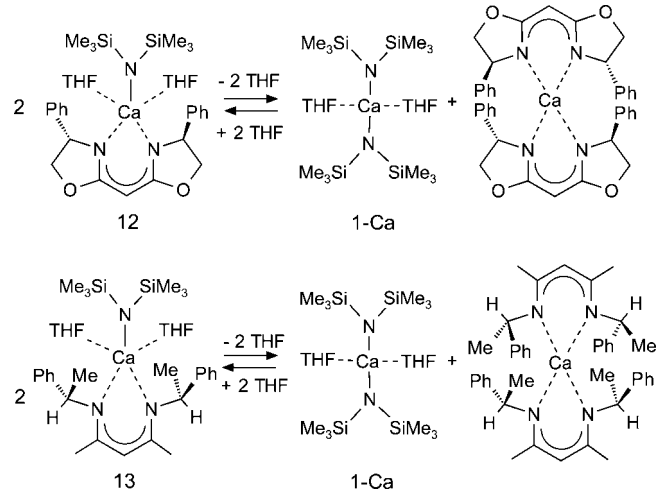
Although Mg catalysts are in general less productive than catalysts with its heavier congeners (Ca, Sr), they have a clear advantage. They are more robust, and even at higher temperatures no ligand exchange and formation of inactive homoleptic metal species is observed. This enables also at higher temperatures an efficient conversion.

Finally, it should be mentioned that recently also a well-defined lithium amide complex (**25**) has been developed for the intramolecular alkene hydroamination.[60e] As catalyst **25** is chiral and enantiopure, enantioselective ring closure was observed.

4.2. Enantioselective Intramolecular Hydroamination of Aminoalkenes

The lithium amide catalyst **25** is chiral and gave good enantioselectivities for ring closure (up to 75% *ee*).[60e] In Ca-mediated styrene polymerization, high syndioselectivities are obtained by an efficient chain-end stereocontrolled alkene insertion step (see section 3.2). Therefore, the question arose whether calcium catalysts with chiral enantiopure spectator ligands could induce the formation of enantiopure products. This approach gave good enantioselectivities in lanthanide-catalyzed alkene hydroamination.[58b,j]

Scheme 16. The First Chiral Heteroleptic Calcium Amide Complexes and Their Schlenk Equilibria



To this purpose, the first enantiopure calcium amide complexes have been prepared: a *bis*-oxazolide (BOX) calcium amide complex (**12**) and a β-diketiminate calcium amide complex (**13**).[66] Although a crystal structure could be obtained for **12**, both **12** and **13** are in solution in equilibrium with their homoleptic counterparts (Scheme 16). This Schlenk equilibrium is dynamic and can be steered to the heteroleptic side by addition of catalytically unactive homoleptic calcium complexes $(BOX)_2Ca$ and (β-diketiminate)$_2$Ca, respectively.

Use of such enantiopure mixtures as catalysts in the intramolecular hydroamination of alkenes was disappointing. Only for $H_2C{=}CHCH_2CPh_2CH_2NH_2$, a substrate activated by the Thorpe−Ingold effect, was efficient conversion found. The extremely low enantioselectivities (5−10% *ee*) are likely caused by the fact that the Schlenk equilibrium for the desired catalytic species, L*CaN(H)$CH_2CPh_2CH_2CH{=}CH_2$, is largely toward the homoleptic side. This would explain the lack of stereocontrol and was confirmed by stoichiometric experiments. It also explains why the catalyst mixtures only showed activity for the substrate $H_2C{=}CHCH_2CPh_2CH_2NH_2$. It was found that this is the only substrate that also shows an efficient conversion with the homoleptic achiral catalyst $Ca(HMDS)_2{\cdot}(THF)_2$ (**1-Ca**): 5 mol % catalyst gave at 20 °C after one hour full conversion.[66]

Therefore, development of chiral ligands that prevent ligand exchange by the Schlenk equilibrium remains a challenging future goal. It is anticipitated that such a goal is more easily achieved in magnesium chemistry. Future research should therefore be directed toward more robust heteroleptic enantiopure magnesium catalysts.

4.3. Intermolecular Hydrophosphination and Hydroamination of Activated Alkenes

The atom-efficient hydrophosphination of alkenes[56a,69] is an attractive synthetic method for the syntheses of a variety of phosphines that are important ligands in transition metal catalysis. Various methods that involve radical[70] or transition metal[71] catalysts have been described. The groups of Casey and Knochel could show that this reaction is even catalyzed by commercially available *t*BuOK.[72] In analogy to the Ca-mediated intramolecular hydroamination of aminoalkenes, Hill et al. developed a procedure for alkene hydrophosphination.[73] The proposed catalytic cycle (Scheme 17) is similar

Scheme 17. Catalytic Cycle for the Intermolecular Hydrophosphination of Activated Alkenes (e.g. Styrene)

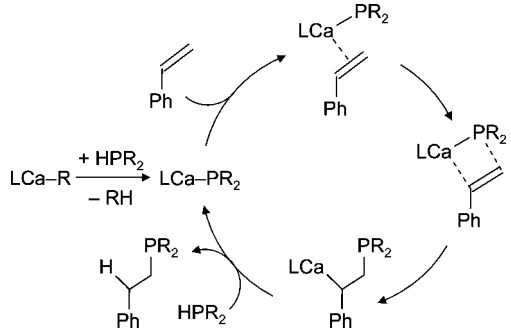
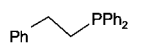
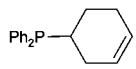
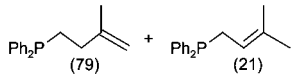
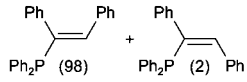


Table 2. Intermolecular Hydrophosphination of Activated Alkenes with Catalyst 6 (10 mol %, C_6D_6)[73]

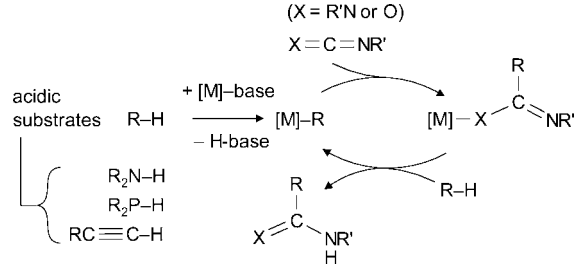
Susbstrate	Product(s)	T (°C)	t (h)	Conv. (%)
PhCH=CH$_2$		75	20	95
Cyclohexadiene		75	24	78
isoprene	 (79) (21)	25	24	95
Ph-C≡C-Ph	 (98) (2)	75	13	94[a]

[a] 20 mol % catalyst was used.

to that for the intramolecular alkene hydroamination (Scheme 14); however, there is an important difference: addition of the calcium phosphide to the C=C double bond is not intramolecular. As the phosphide/alkene addition lacks the entropic support of chelation, only activated alkene substrates or an internal acetelyne could be converted to phosphines (Table 2). More sterically hindered alkenes such as α-Me-styrene or stilbene did not undergo hydrophosphination. The high regioselectivity in the phosphination of styrene, i.e. exclusive 2,1-addition, originates from the preferred formation of a stabilized benzylcalcium intermediate (1,2-addition would give the much more reactive and less stable alkylcalcium intermediate $LCaCH_2CH(Ph)PR_2$). Hydrophosphination of an internal alkyne gave predominantly *syn*-addition (Table 2). It is essential that a heteroleptic calcium catalyst is used (**6**). The resting state in the cycle is (DIPP-nacnac)$CaPR_2$, a complex that could be isolated and is catalytically active itself. Conversion with the homoleptic $Ca(HMDS)_2 \cdot (THF)_2$ catalyst is much slower, presumably on account of the observed precipitation of insoluble $Ca(PR_2)_2$. The latter homoleptic calcium phosphide complex, however, is active in the catalytic hydrophosphination of alkynes.[74]

Hill and Barret et al. recently extended this concept to the intermolecular hydroamination of *para*-substituted styrenes, in which case homoleptic catalysts could be used: $M(HMDS)_2 \cdot (THF)_2$.[75] The following conclusions can be drawn: (i) primary amines react faster than secondary amines, (ii) electron-poor C=C bonds react faster than electron-rich bonds, (iii) the exclusive preference for 2,1-insertion is explained by the stability of benzylic intermediates, and (iv) catalyst efficiency follows the order Sr > Ca > Ba or Mg. This order is in agreement with *ab initio* calculations on model systems.[75]

Scheme 18. Generalized Cycle for the Base Catalyzed Addition of Acidic Substrates to Carbodiimides (X = NR′) or Isocyanates (X = O)



4.4. Hydroamination and Hydrophosphination of Activated C=N Bonds

Substituted guanidines are useful building blocks for many biologically relevant compounds[76] and can be used as ligands in organometallic chemistry.[77] Although they can be advantageously obtained by stoichiometric nucleophilic addition of various amides to extremely electrophilic carbodiimides, catalytic conversions reduce cost and simplify workup procedures. The catalytic addition of amines to substituted carbodiimides can generally be accomplished with early transition metal catalysts (group 3−5).[78] Richeson et al. introduced a catalytic scheme for the hydroamination of carbodiimides with the readily available Li(HMDS) (also *n*BuLi or heavier metal amides Na(HMDS) and K(HMDS) are efficient catalysts).[79] Under mild conditions, a large variety of guanidines could be obtained and intermediates in the catalytic cycle were isolated and characterized by X-ray diffraction. In addition, the Li-catalyzed addition of terminal acetylenes to carbodiimides gave propiolamidines according to the same scheme (a general catalytic cycle is shown in Scheme 18).[79] Hou et al. recently described the alkali metal catalyzed hydrophosphination of carbodiimides.[80] Base catalyzed addition of relative acidic substrates ($pK_a \approx$ 15−30) to carbodiimides is likely a general method.

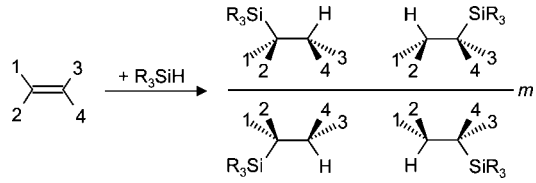
Following these examples, Hill et al. could show that the hydroamination of carbodiimides can be catalyzed by the homoleptic heavier alkaline-earth metal amides $M(HMDS)_2 \cdot (THF)_2$ (**1-M**; M = Ca, Sr, and Ba).[81] Isolated intermediates show that the deprotonaned guanidine product is a ligand for the catalysts itself. In analogy, the same group reported on the Ca-mediated acetylenation of carbodiimides.[82] The groups of Hill and Westerhausen extended this concept further with the Ca-mediated hydrophoshination of carbodiimides.[83]

Addition of amines to the C=N bond in isocyanates gives biologically important urea products. While for some amines this reaction is readily achievable under uncatalyzed conditions, its catalyzed form is much faster and does not require elevated temperatures. Hill et al. showed that homoleptic heavier alkaline-earth metal amides $M(HMDS)_2 \cdot (THF)_2$ (**1-M**; M = Ca, Sr, and Ba) are also catalysts for the addition of Ph_2NH to either adamantyl- or arylisocyanates.[84] The general catalytic cycle, shown in Scheme 18, applies. It should be mentioned that the addition of Ph_2NH to adamantylisocyanate is even faster with the simple Li(HMDS) as a catalyst.[85]

5. Hydrosilylation

Hydrosilylation is describing the addition of a polar Si−H bond to a multiple bond, in particular a C=C, C=O, or C=N

Scheme 19. Hydrosilylation of Substituted Alkenes

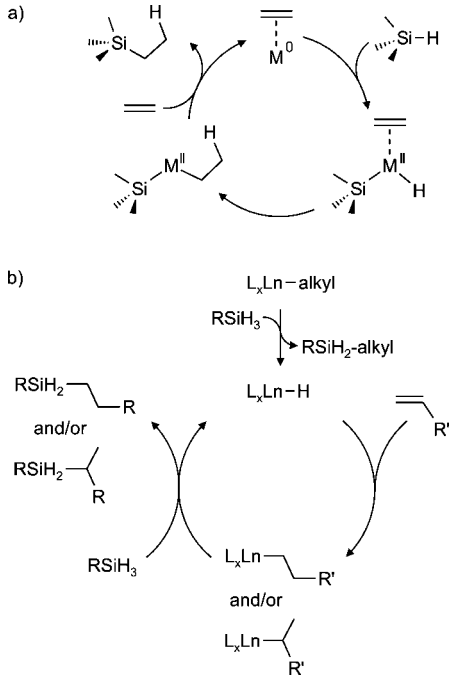


unsaturated moiety. This highly atom-efficient key transformation is of great importance to the silicon industry and in organic synthesis, dendrimer, or polymer chemistry.[86] For the hydrosilylation of substituted double bonds, control of regio- and/or stereoselectivity is an issue that makes this conversion particularly challenging (Scheme 19). Recently well-defined early main group metal catalysts have been introduced for this reaction. As the proposed mechanisms for hydrosilylation of C═C or C═O bonds differ substantially, we discuss these separately.

5.1. Alkene Hydrosilylation

There are numerous methods to initiate alkene hydrosilylation. Classical thermal and radical-initiated reactions often lead to oligomers, especially when readily polymerizable alkenes (e.g., styrenes) are used.[87] The use of transition metal catalysts is already known since Speier's breakthrough discovery of highly active $H_2PtCl_6 \cdot 6H_2O/i$PrOH,[88] a catalyst which was later replaced by the even more active and selective Karstedt catalyst also based on Pt.[89] Since then, many transition metal complexes have been introduced. The first mechanistic studies led to the proposal of the Chalk−Harrod mechanism (Scheme 20a),[90] a cycle that involves the catalytic activation of the Si−H bond by oxidative addition to the metal. To date, a variety of mechanistic proposals are known. Some of these catalytic cycles propose metal silylene intermediates: M═Si(R)R′.[91]

Scheme 20. (a) The Classical Chalk−Harrod Mechanism for Alkene Hydrosilylation. (b) The Hydride Cycle for Organolanthanide Catalyzed Reactions (Ln = Lanthanide Metal)[a]



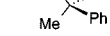
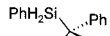
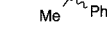
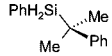
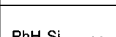
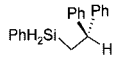
[a] The regioselectivity is determined in the addition step.

Despite the high activity of Pt^0 catalysts, side reactions such as alkene isomerization, hydrogenation, and in some cases poor regiochemistry are still an issue. Especially formation of colloidal Pt is thought to be responsible for these undesired byproduct.[92] More recently, lanthanide-based catalysts have been developed.[93] These catalysts show in some cases poor regioselectivity; however, they also feature several advantages, including (i) tunability of the regiochemistry by metal-size and ligand choice and (ii) enantioselective hydrosilylation. Hydrosilylation with such d^0-catalysts proceeds through a different mechanism (Scheme 20b). Reaction of an alkyllanthanide functionality with a silane results in formation of a lanthanide hydride complex. The latter intermediate, which is the true catalytically active species, can add to an unsaturated bond, thus giving a new alkyllanthanide complex (this step decides on regioselectivity). Subsequent reaction of the alkyllanthanide intermediate with silane gives the product and regenerates the lanthanide hydride catalyst. This simple "hydride cycle" does not involve oxidation state changes of the metal but is solely based on addition and σ-bond metathesis reactions, typical for polar organometallic compounds. This led us to assume that early main group organometallics could also be catalysts in the alkene hydrosilylation.

Alkene hydrosilylation catalyzed by $LiAlH_4$ has been described but requires highly active SiH_4 and high pressures, resulting in multiple hydrosilylation.[94] Other representative catalysts from the main group elements are the Lewis acids $AlCl_3$ and $B(C_6F_5)_3$;[95] however, in these cases the hydrosilylation mechanism is based on formation of a carbenium cation. Harder et al. introduced the first well-defined early main group metal catalysts for the hydrosilylation of alkenes.[96] The expectation that organocalcium catalysts could promote the alkene hydrosilylation through an analogue pathway as described for the organolanthanide catalysts (Scheme 20b) was initially met by several doubts. (i) The catalytically active species is a metal hydride complex, which at that time never had been observed in calcium chemistry. It was also questionable whether it could be prepared from a calcium precatalyst and a silane. (ii) As Schlenk equilibria pose a larger problem for the heavier alkaline-earth metal complexes, ligand exchange reactions could result in precipitation of the catalytically active species: $2LCaH \rightarrow L_2Ca + CaH_2\downarrow$. (iii) Organocalcium reagents only add to activated double bonds as in styrene or butadiene. Anticipating that a possible calcium hydride does not react with an isolated C═C bond would limit the substrates to those containing conjugated double bonds. In this case alkene polymerization could be a problematic side-reaction.

It was found that calcium hydride complexes indeed could be obtained by reaction of the calcium benzyl (or amide) functionality with $PhSiH_3$. Heteroleptic calcium hydride complexes LCaH are in general not stable toward ligand exchange; however, in one case a stable dimer with bridging hydride ions could be characterized (**21**).[97] This β-diketiminate complex dissolves well in aromatic solvents and is even at 100 °C stable toward decomposition into insoluble CaH_2. Complex **21**, as well as *in situ* prepared calcium hydride species, indeed does not react with unactivated alkenes.[96] Activation by conjugation with another double bond is a prerequisite. In order to prevent alkene polymerization, 1,1-diphenylethylene was used as a substrate (DPE is an activated alkene that in the presence of a strong base does not polymerize for steric reasons). Interestingly, it was found

Table 3. Hydrosilylation of Alkenes with $PhSiH_3$ (50 °C)[96]

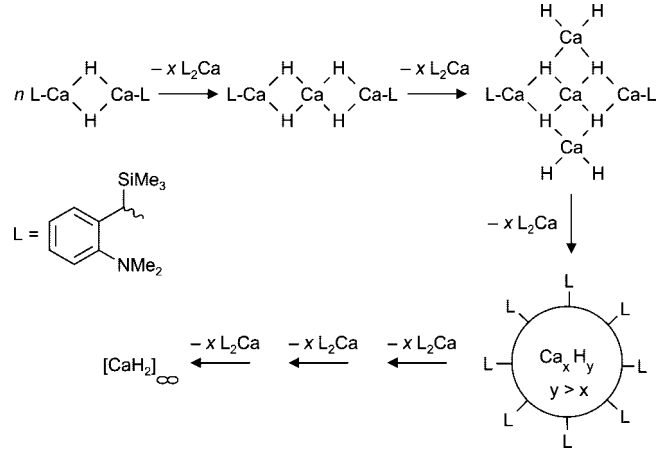
Entry	alkene	catalyst (mol %)	solvent	product	time (hr)	conversion (%)
1	$Ph_2C{=}CH_2$	**18** (5)	none		16	10
2	$Ph_2C{=}CH_2$	**3-Ca** (2.5)	none		16	>98
3[a]	$Ph(H)C{=}CH_2$	**3-Ca** (2.5)	none		<0.1	>98
4	$Ph(Me)C{=}CH_2$	**3-Ca** (2.5)	none		24	20
5	$Ph(Me)C{=}CH_2$	**3-Sr** (2.5)	none		2.5	>98
6	$Ph_2C{=}CH_2$	K(DMAT) **24** (5)	none		2	>98
7	$Ph_2C{=}CH_2$	**3-Ca** (2.5)	THF		3	>98
8	$Ph_2C{=}CH_2$	**3-Sr** (2.5)	THF		2	>98

[a] Reaction at 20 °C.

that the homoleptic dibenzylcalcium complex **3-Ca**, $Ca(DMAT)_2\cdot(THF)_2$, is a more efficient catalyst in alkene hydrosilylation than the heteroleptic benzylcalcium complex **18** (cf. Table 3, entries 1 and 2). Also, it was observed that hydrosilylation of readily polymerizable alkenes such as styrene is an extremely fast and clean conversion already at room temperature (Table 3, entry 3). The lack of even oligomeric byproduct indicates that alkene hydrosilylation is considerably faster than alkene polymerization. Similar observations have been made for the hydrosilylation of cyclohexadiene and isoprene. The substrate α-methylstyrene only gave a very slow and incomplete conversion (Table 3, entry 4). Use of a similar organostrontium catalyst (**3-Sr**), however, led to a considerable acceleration of this, and other catalytic hydrosilylation reactions (Table 3, entry 5). Interestingly, the similar benzyl potassium complex K(DMAT), **24**, is also catalytically active in the hydrosilylation of DPE (Table 3, entry 6),; however, with other substrates it mainly led to alkene polymerization.

As the homoleptic benzylcalcium complexes are much better catalysts than heteroleptic calcium complexes, the question arises: what is (or are) the catalytically active species, heteroleptic RCaH or "molecular CaH_2"? It is feasible that *in situ* formed CaH_2 reacts so fast with the substrate that precipitation of $[CaH_2]_\infty$ is prevented. It is also possible that *in situ* generated CaH_2 aggregates to $[CaH_2]_n$ oligomers, that are still sufficiently reactive for reaction with alkenes. However, freshly ground commercially available CaH_2 was found not to be active as a hydrosilylation catalyst. Experimental observations hint to the possible existence of larger hydride-rich clusters which are stabilized by carbanions

Scheme 21. Possible Transformation of a Dimeric Calcium Hydride Complex in Larger Hydride-Rich Clusters That via Intermediate CaH_2 Nanoparticles Eventually Turns into a Saltlike Precipitate of $[CaH_2]_\infty$[a]



[a] For clarity this representation has been simplified and only a four-coordinate Ca^{2+} ion is shown (the coordination number of Ca in CaH_2 is 6).

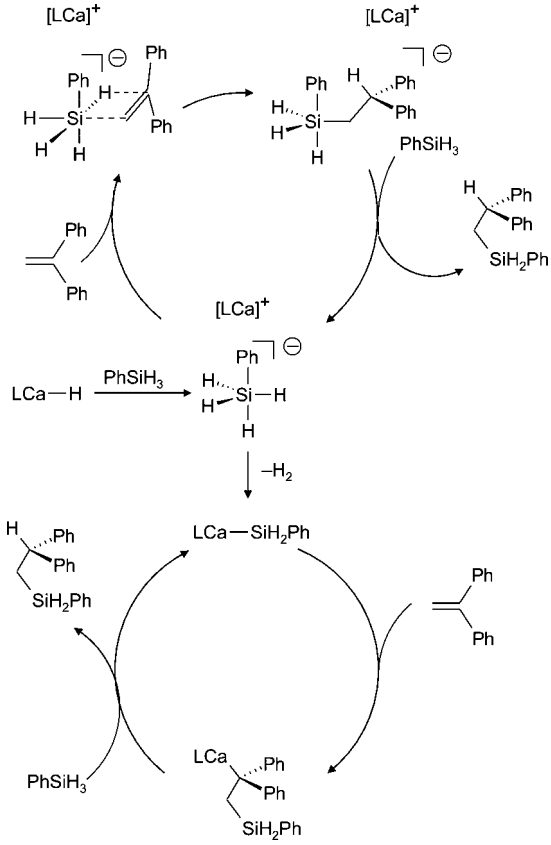
in the outer-shell (Scheme 21). Reaction of $Ca(DMAT)_2\cdot(THF)_2$ with 1 equiv of $PhSiH_3$ in benzene gave clean conversion to $PhH_2Si(DMAT)$ and presumably Ca(DMAT)(H). Stepwise concentration of this solution repeatedly only led to precipitation of crystalline $Ca(DMAT)_2\cdot(THF)_2$. The remaining clear mother liquor vigorously reacted with methanol to give H_2. This indicates the presence of hydride-rich nanosized clusters: $[Ca(DMAT)_{<1}(H)_{>1}]_n$. Although hydride-rich calcium clusters have never been structurally characterized, analogy to magnesium hydride chemistry[98] enforces their possible existence.

It should be noted that, in contrast to transition or lanthanide metal mediated alkene hydrosilylation, alkaline-earth metal catalysts exclusively give one regioisomer as the product: the silyl group is always bound to the benzylic or allylic carbon atoms. This can be explained by assuming a catalytic cycle similar to that proposed for lanthanide catalysts (Scheme 20b). As organometallic compounds of the heavier group 2 metals are highly ionic, the intermediates in the catalytic cycle always represent the most stable carbanion, i.e. a benzyl or allyl anion. The observation that a similar organopotassium catalyst **24** in the hydrosilylation of DPE exclusively gave the regioisomer with a silyl substituent at the terminal carbon should therefore be regarded as highly unexpected (Table 3, entry 6). Interestingly, under very polar conditions (in THF), also calcium and strontium catalysts gave exclusively the other regioisomer (Table 3, entries 7−8) whereas somewhat less polar conditions (Et_2O) gave a mixture of isomers. It was therefore proposed that, dependent on the polarity of the catalyst or solvent, different reaction mechanisms operate.

A possible explanation for switching the regioselectivity by polarity could be the formation of an ion-pair that contains the anion $PhSiH_4^-$; that is, the metal hydride catalyst does not react with the alkene substrate but with $PhSiH_3$ (Scheme 22). Formation of such hypervalent anions is well-documented in Si-chemistry,[99] and this proposed intermediate finds precedence in the crystal structure of $[K^+\cdot(18\text{-crown-}6)][Ph_3SiH_2^-]$.[100]

After formation of the anion $PhSiH_4^-$, there are two scenarios. This hypervalent anion is the catalytically active

Scheme 22. Proposed Formation of the Hypervalent Species $PhSiH_4^-$, Which May Act as a Catalyst by Concerted Addition to $Ph_2C{=}CH_2$ (top) or Can Eliminate H_2 To Give a Silanide Catalyst



species and adds to the C=C double bond in a concerted reaction. As this mechanism is reminiscent of alkene hydroboration, similar rules apply for its regioselectivity: the steric bulk of the two phenyl substituents directs hydride attack toward the most substituted alkene carbon (Scheme 22, top). Another possible cycle involves a silanide ion that originates from the decomposition: $PhSiH_4^- \rightarrow PhSiH_2^- + H_2$.[99a] The silanide anion could act as a catalytically active species in a similar way as the hydride, which would result in a reversed addition (Scheme 22, bottom). The K(DMAT)-mediated addition of a silane to a C=C double bond constrained in a cycle proceeds with exclusive *trans*-selectivity.[96] This shows that under polar conditions a nonconcerted (multistep) mechanism is operative and is an indication for the "silanide cycle" (Scheme 22, bottom). The possibility of metal-silanide intermediates in transition metal catalyzed alkene hydrosilylation has been proposed earlier.[101]

In summary, benzyl complexes of the group 2 metals Ca and Sr are very effective catalysts for hydrosilylation of conjugated double bonds. The more polar Sr catalysts show the highest activities. The alkene hydrosilylation is much faster than the alkene polymerization: no oligomeric or polymeric side-products have been observed. Although an analogue benzyl potassium catalyst can be used in the hydrosilylation of DPE, other substrates gave alkene polymerization. This underscores the importance of the metal in the mechanism. The catalytic reactions are in all cases initiated by formation of a highly reactive metal-hydride, which adds either to an alkene or to the silane, depending on the polarity of the metal-hydride bond or solvent. In some cases the regiochemistry of the hydrosilylation can be completely controlled either by the polarity of the solvent or by metal choice. The latter feature makes these early main group metal catalysts unique in hydrosilylation catalysis.

5.2. Ketone Hydrosilylation

Catalytic hydrosilylation of ketones, i.e. the formal addition of a silane R_3SiH to a ketone $R'_2C{=}O$ to give $R_3SiOCHR'_2$, is a convenient one-step procedure for preparation of protected alcohols.[102] Catalysts are generally based on the transition metals, but also catalysts that contain Sn,[103] Cu,[104] and Zn[105] have been reported. Also strong Lewis acids, such as $B(C_6F_5)_3$,[106] or alkali metal alkoxides[107] catalyze this reaction.

Harder et al. recently showed that the calcium hydride complex **21** catalyzes the hydrosilylation of various ketones.[108] Unexpectedly, the Ca-mediated addition of $PhSiH_3$ to a ketone $R_2C{=}O$ always gave the bis-alkoxysilane $PhHSi(OCHR_2)_2$ as the major product, even when an excess of $PhSiH_3$ was used. Table 4 summarizes the hydrosilylation of a variety of ketones using calcium catalyst **21** and the optimal silane ketone ratio of 1:2.

Although **21** reacts smoothly with a variety of ketones, it is unlikely that the hydrosilylation of ketones proceeds through addition of the calcium hydride functionality to a ketone (Scheme 23, top) for several reasons. (i) Reaction of **21** with stoichiometric amounts of α-hydrogen containing ketones such as PhC(O)Me, cyclohexanone, and $PhCH_2C(O)CH_2Ph$ is not very selective and gave, apart from addition, significant deprotonation (enolization) as a side-reaction.[108] The hydrosilylation products, however, contain at most minor amounts of enoxy-substituents. (ii) It is questionable whether the conversion of an alkoxide into a hydride, the last step along this route, will proceed. Whereas the calcium amide functionality readily reacts with $PhSiH_3$ to a calcium hydride, stoichiometric reaction of several calcium alkoxide complexes with $PhSiH_3$ failed to give hydrides.

A more likely scenario is a catalytic cycle that involves the hypervalent species $[PhSiH_4^-][(DIPP\text{-}nacnac)Ca^+]$ (Scheme 23, bottom). Concerted addition of the ketone would result in a similar intermediate as proposed in the top cycle. Therefore it is possible that in the first step the top cycle is operative. This would explain the minor amounts of enoxy functionalities in the product of entry 3 (Table 4). A similar mechanism was proposed for the sodium alkoxide catalyzed hydrosilylation of ketones.[107] Also in the latter, strong preference for the formation of the *bis*-alkoxysilane $PhHSi(OCHR_2)_2$ was observed. This is likely due to the high reactivity of the anion $[PhSiH_3(OCR^1R^2)^-]$ toward ketones. The alkoxy substituent renders the Si center much more Lewis acidic than that in $[PhSiH_4^-]$, thus promoting a double hydrosilylation. Triple hydrosilylation is hardly observed on account of steric strain.

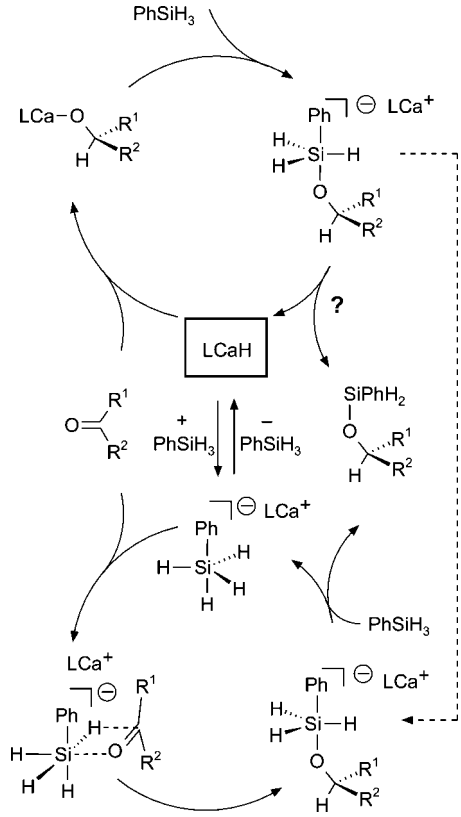
In conclusion, the Ca-mediated hydrosilylation of ketones gives bis-alkoxysilane $PhHSi(OCHR_2)_2$ products in good

Table 4. Hydrosilylation of Ketones with $PhSiH_3$ (1.25 mol % catalyst 21, benzene, 50 °C)[108]

entry	ketone	time (h)	$PhHSi(OR)_2$ (%)	alkoxy/enoxy
1	PhC(O)Ph	15	96	
2	PhC(O)Me	34	95	100/0
3	cyclohexanone	3	91	96/4
4	$PhCH_2C(O)CH_2Ph$[a]	34	96	100/0
5	adamantone[b]	0.2	95	100/0

[a] 5 mol % catalyst was used. [b] Reaction at 20 °C.

Scheme 23. Possible Mechanisms for the Catalytic Hydrosilylation of Ketone $R^1R^2C{=}O$ with $PhSiH_3$ Using a Calcium Hydride Catalyst (LCaH)



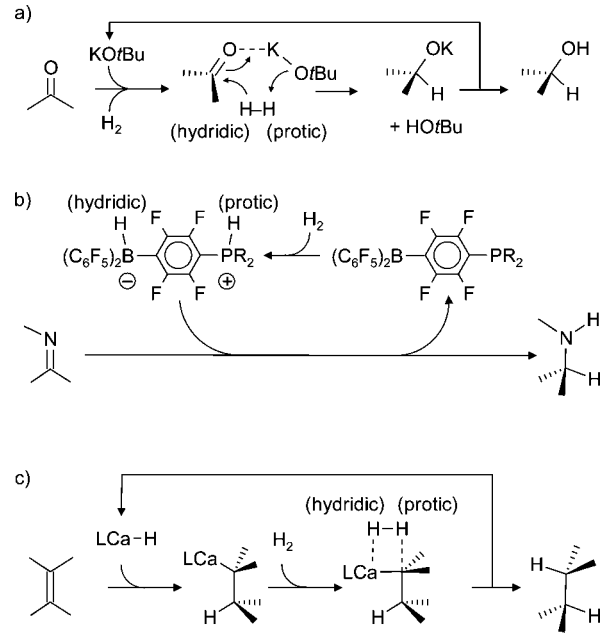
yield and selectivity. Enolization of the ketone functionality is generally not an issue. The proposed cycle for catalytic hydrosilylation of ketones differs from that proposed for the Ca-mediated hydrosilylation of alkenes. It contains the solvent-separated-ion-pair $[PhSiH_4^-][LCa^+]$, and therefore, the metal only plays a minimal role. As similar results can be obtained using sodium alkoxide catalysts,[107] the role of calcium is merely that of a countercation.

6. Alkene Hydrogenation

The catalytic hydrogenation of unsaturated compounds represents one of the earliest examples in heterogeneous as well as homogeneous catalysis.[109] On account of its high industrial potential, this particular conversion is even nowadays intensively investigated.[110] Whereas traditional homogeneous hydrogenation catalysts are based on precious metals (Pt, Pd, Rh), there is an increase in research efforts to find cheaper alternatives.[6] New generation catalysts for hydrogenation cleave molecular hydrogen heterolytically in a hydridic (H^-) and protic (H^+) functionality. So-called ionic hydrogenation catalysts incorporate both functionalities: e.g. −OH and M−H (M = Fe or Ru).[111]

Recently, Berkessel et al. reported the first nontransition metal catalyst for the hydrogenation of ketones exemplified by the simple reagent KO*t*Bu (Scheme 24a).[26,112] Moreover, Stephan et al. introduced the first metal-free systems for activation of hydrogen.[113] These so-called "frustrated Lewis-pairs" have been shown to be catalytically active in the hydrogenation of imines or ketones (Scheme 24b).[114] Both reactions are based on the heterolytic rupture of H_2 (protic/hydridic) and subsequent reduction of the unsaturated bond by combined electrophilic and nucleophilic attack. Nontransition metal catalysts for alkene hydrogenation are hardly known. Catalysts such as NaH, KH, MgH_2, or $LiAlH_4$ need forcing conditions (150−225 °C, 60−100 bar H_2) and gave predominantly oligomeric or polymeric products.[115] Considering the fact that soluble calcium hydride complexes were successfully applied in alkene hydrosilylation, Harder et al. posed the question whether these complexes could also be catalysts for alkene hydrogenation.[116]

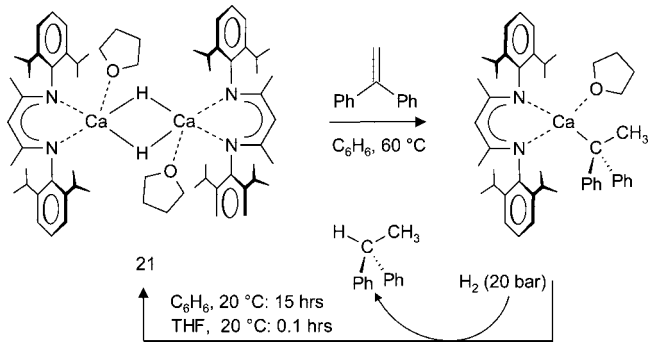
Scheme 24. Catalytic Hydrogenation of (a) Ketones by KO*t*Bu, (b) Imines by a "Frustrated Lewis Pair", and (c) Alkenes by a Calcium Hydride Complex



A tentative mechanism for this conversion is shown in Scheme 24c. The first step, addition of a calcium hydride complex to an alkene, has been verified by stoichiometric reactions.[117] It works efficiently only for conjugated alkenes, e.g. styrene or butadiene, thus giving benzylic or allylic calcium intermediates. The second step, protonation of the organocalcium species by molecular hydrogen, is the critical step in the mechanism and also follows the heterolytic protocol (protic-hydridic). This σ-bond metathesis step should be sufficiently fast to compete with a most likely side reaction: alkene polymerization (conjugated alkenes are prone to polymerization). Although alkyllanthanides react extremely fast with H_2,[118] this reaction was unprecedented in calcium chemistry. However, there are rare examples in lithium chemistry: pressurizing *t*BuLi with H_2 (200 bar) gave an active form of LiH.[119] Polar (co)solvents such as TMEDA or THF accelerate this conversion considerably, and *n*BuLi in THF reacts with H_2 already at 1 bar.[120] This protonation reaction can be considered as an acid−base reaction, and its feasibility is strongly dependent on the basicity of the carbanion. As the pK_a value of H_2 is relatively high (≈35),[121] it was questionable whether resonance-stabilized benzylic and allylic calcium reagents react with H_2 to give a calcium hydride functionality.

Stoichiometric addition of the calcium hydride complex **21** to 1,1-diphenylethylene (DPE) smoothly gave the expected benzylic complex (Scheme 25), which was fully characterized by a crystal structure determination.[116] The benzylic intermediate could indeed be protonated by H_2 under relatively mild conditions (20 bar, 20 °C) to give **21** and hydrogenated DPE. Although this second step took overnight

Scheme 25. Stoichiometric Addition of Calcium Hydride Complex 21 to DPE and Subsequent Protonation of the Intermediate by H_2 (Polar Solvents Accelerate the Last Step)



to complete in benzene, in THF completeness was reached within 5 min. This cycle was also operative under catalytic conditions. The homoleptic dibenzylcalcium catalyst **3-Ca** was equally active as heteroleptic **21** (Table 5, entry 1−2). Polar solvents significantly accelerate the reaction but also gave small amounts of dimeric byproduct (1,1,3,3-tetraphenylbutane; entry 3). This demonstrates that under polar conditions oligomerization side reactions become an issue. It was found that the analogue Sr catalyst **3-Sr** works equally well. Hydrogenation of DPE was even catalyzed by the K complex K(DMAT) (**24**, entry 4), but a much higher H_2 pressure of 100 bar was essential. The fact that even KH can be used as a catalyst underscores the role of metal hydrides as intermediates. Other conjugated alkenes were successfully hydrogenated (entries 5−8). These less sterically hindered substrates were found to be sensitive toward oligomerization, and under polar conditions (THF) only oligomerization was observed. Likewise, a highly polar K catalyst in an apolar solvent (benzene) gave major alkene oligomerization. Use of K catalysts in alkene hydrogenation is therefore limited to sterically hindered alkenes that are insensitive toward polymerization (DPE or 1-phenylcyclohexene; entry 8).

The following conclusions have been drawn: (i) Benzylcalcium as well as strontium complexes represent the first nontransition metal catalysts for alkene hydrogenation. (ii) Although the method is limited to conjugated alkenes, this might be advantageous in selective hydrogenation; *cf.* cyclohexadiene is exclusively hydrogenated to cyclohexene. (iii) Metal hydride species play a key role in the mechanism. (iv) Polar conditions accelerated conversions but gave oligomeric products for substrates sensitive toward polymerization. (v) Although in some cases benzylpotassium species can be used as the catalyst, a much higher H_2 pressure was needed and sterically less-hindered alkenes gave major oligomerization. The fine balance between alkene hydrogenation and oligomerization can be controlled by choice of metal and solvent. The benzylcalcium and strontium catalysts are in this respect unique.

7. Aldol-, Mannich-, and Michael-Type Reactions

As aldol-, Mannich-, and Michael-type of reactions can be base-catalyzed, it is not unexpected that calcium complexes are catalytically active. In fact, $Ca(OH)_2$ is used as a catalyst in the large scale production of pentaerythrit, $C(CH_2OH)_4$, and catalyzes the first step: cross-aldol coupling of acetaldehyde with 3 equiv of formaldehyde gives $HC(O)C(CH_2OH)_3$. The advantage of using homogeneous calcium complexes rather than cheap technical bases is the possibility to control the dia- and/or enantioselectivities. In most of these reactions the catalytically active calcium species are poorly defined and usually prepared *in situ*. The sometimes very high obtained selectivities, however, deserve a brief overview of this field, which was recently highlighted.[122]

7.1. Enantio- and Diastereoselective Conversions

Noyori and Shibasaki introduced the first chiral group 2 metal alkoxide catalysts for the asymmetric cross-aldol coupling of acetophenone and a variety of aldehydes (Scheme 26).[123,124] These group 2 catalysts show very high activities, and products could be isolated in good isolated yields. Moreover, high enantioselectivities up to 91% *ee* have been realized. The catalysts in these conversions are prepared *in situ* (Scheme 26) and have not been characterized. However, as an excess of chiral protic ligand is essential for effective conversion, it is likely that oligomeric species with remaining OH-acidity are involved. Mass spectrometry studies on catalyst solutions confirm the oligomeric nature of these catalytic mixtures. In view of the fact that a significant chiral amplification has been found,[123] supports the idea that aggregated species play an important role. Protonation and deprotonation of the chiral ligand are essential steps in the proposed mechanism (Scheme 27).[124] Also, the asymmetric

Scheme 26. Enantioselective Cross-Aldol Reaction

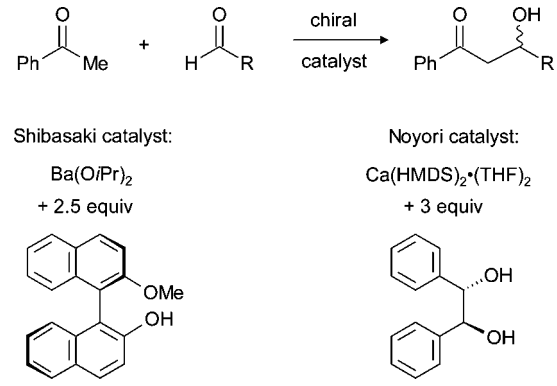
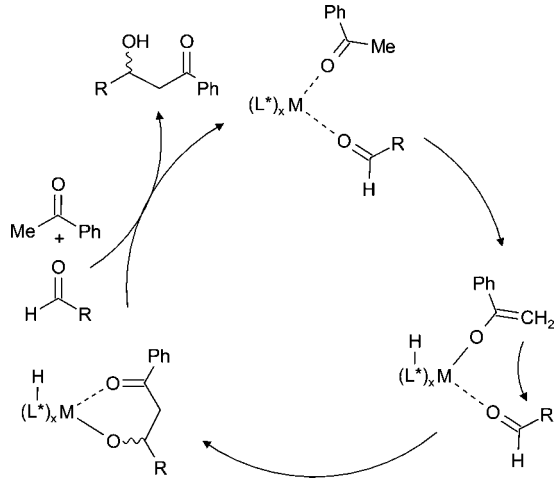


Table 5. Hydrogenation of Conjugated Alkenes with Various Catalysts[116]

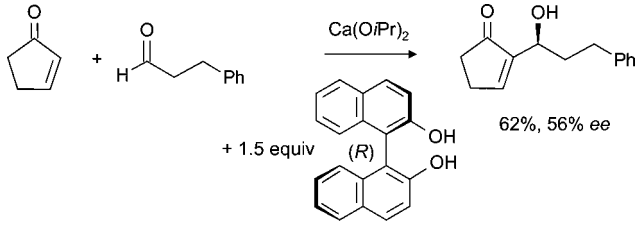
entry	alkene	catalyst (mol %)	solvent	T (°C)	P (bar)	t (h)	conv (%)	products
1	$Ph_2C{=}CH_2$	**21** (5)	C_6H_6	60	20	17	49	Ph_2CHCH_3
2	$Ph_2C{=}CH_2$	**3-Ca** (2.5)	C_6H_6	60	20	17	41	Ph_2CHCH_3
3	$Ph_2C{=}CH_2$	**3-Ca** (2.5)	THF	20	20	3.5	94	92% Ph_2CHCH_3, 8% dimer[a]
4	$Ph_2C{=}CH_2$	K(DMAT), **24** (5)	THF	20	100	13	>99	97% Ph_2CHCH_3, 3% dimer[a]
5	$Ph(H)C{=}CH_2$	**3-Ca** (2.5)	C_6H_6	20	20	15	>99	85% $PhCH_2CH_3$, 15% oligomers[b]
6	$Ph(Me)C{=}CH_2$	**21** (5)	C_6H_6	60	20	25	60	$PhCH(CH_3)_2$
7	cyclohexadiene	**3-Ca** (2.5)	C_6H_6	20	20	22	96	cyclohexene + traces of dimer
8	1-Ph-cyclohexadiene	K(DMAT), **24** (5)	THF	60	100	18	>99	1-Ph-cyclohexane + traces of dimer

[a] 1,1,3,3-Tetraphenylbutane. [b] Oligomers mainly consist of dimers and traces of trimers and tetramers.

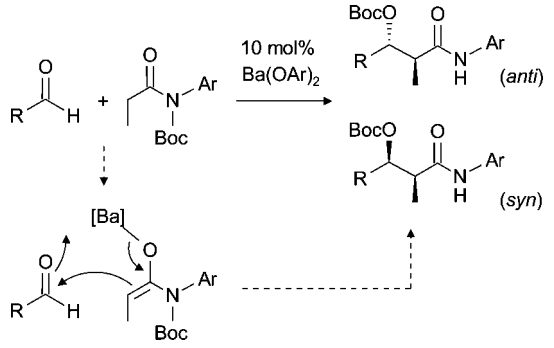
Scheme 27. Proposed Mechanism for the Asymmetric Aldol Reaction (the Chiral Ligand L* Serves as a Proton Reservoir)



Scheme 28. Ca-Mediated Asymmetric Baylis−Hillman Reaction



Scheme 29. Amide/Aldehyde Aldol Coupling (with Concomitant Intramolecular Boc-Transfer)

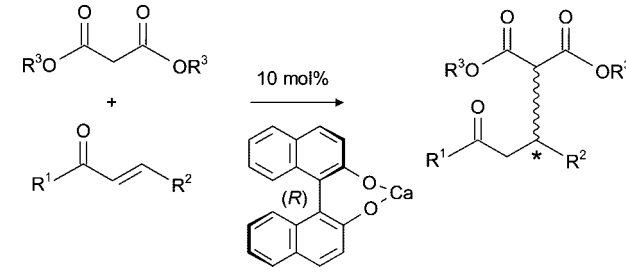


Baylis−Hillman reaction (Scheme 28) is catalyzed by a mixture of $Ca(OiPr)_2$ and an excess of a chiral binaphtol.[125]

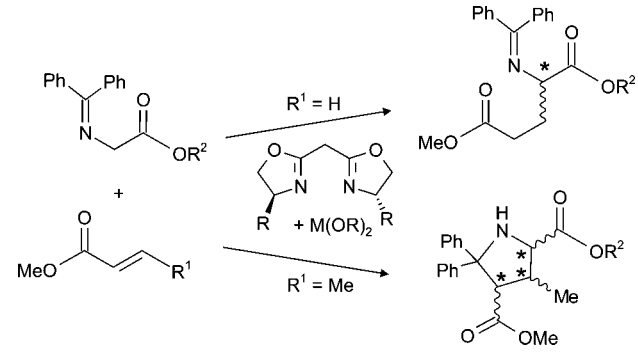
Kobayashi et al. showed that simple group 2 metal alkoxides are very effective catalysts for the amide/aldehyde aldol coupling (Scheme 29).[126] Whereas lanthanide alkoxides were essentially not active, the activity of the group 2 catalysts increased along the series Mg < Ca < Sr < Ba. Barium-phenolate catalysts were found to be especially active. Substituents in the *ortho*-position, e.g. $(2,6\text{-}Me_2\text{-}C_6H_3O)_2Ba$, steer this coupling reaction toward an unprecented diastereoselectivity for the *anti*-product (98% *anti*). Catalysts have been prepared *in situ* and were not characterized. The first step in the assumed mechanism is proposed to be formation of a barium enolate (Scheme 29).

Kobayashi et al. also described the very similar direct-type catalytic Mannich reaction between an amide and an activated imine (*cf.* Scheme 29 with Ph(H)C═NR instead of aldehyde).[127] Similar to what is shown for the amide/aldehyde aldol coupling, these conversions gave high product yields and have a strong preference for the *anti*-product.

Scheme 30. Asymmetric Michael Addition with Chiral (*R*)-(+)-BINOL-Ca



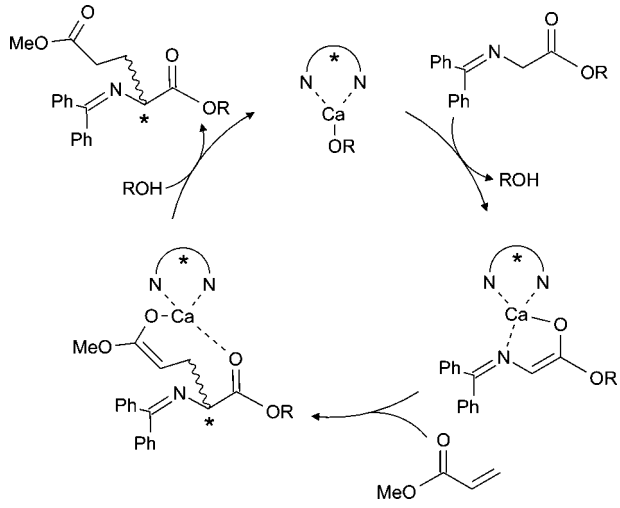
Scheme 31. Asymmetric 1,4-Addition of α-Amino Acid Derivatives to Enones Which, Dependent on the R^1 Substituent in the Enone, Can Be Followed by a [3 + 2] Cycloaddition



Kumaraswamy et al. introduced the calcium-BINOL system as a catalyst for the asymmetric Michael addition (Scheme 30) and found good isolated yields (up to 90%), combined with a significant enantioselectivity (up to 88% *ee*).[128] The same authors extended this work[129] and varied substituents in the chiral BINOL ligand. The octahydro-BINOL ligand, a hydrogenated form of BINOL, improved the enantioselectivity significantly. In all cases, the catalysts were made *in situ* by reaction of the dipotassium salt of the chiral BINOL ligand with excess of $CaCl_2$. These calcium salts have not been further characterized (attempts to obtain suitable crystals for a structural characterization of the catalyst failed).[129]

Susbequently, enantioselective 1,4-addition of enolates to enones was further developed by Kobayashi et al.[130] The 1,4-addition of α-amino acid derivatives to enones (Scheme 31) with several alkaline-earth metal catalysts was investigated. Catalyst were made *in situ* by addition of 1 equiv of a chiral bis(oxazoline) ligand (BOX) to a homoleptic metal alkoxide, $M(OR)_2$. While Mg alkoxides were not active at all, the activities for the heavier alkaline-earth metal catalysts increased along the row Ca < Sr < Ba. Depending on substrate and BOX ligand, high enantioselectivities up to 94% *ee* could be obtained. Interestingly, slight changes in the enone substrate (R^1 = Me instead of H) gave rise to a subsequent ring closure. The latter [3 + 2] cycloaddition proceeds with extremely high diastereo- and enantioselectivity (up to 99% *ee*). Also for these conversions, the catalysts have not been investigated in detail. It is assumed that the methylene unit bridging the oxazaline rings of the BOX ligand is singly deprotonated by the calcium base. This would give a chiral heteroleptic calcium alkoxide, (BOX)CaOR, similar to **12**. Indeed, a mixture of $Ca(OR)_2$ and a BOX ligand with a bridging CMe_2 unit did not show catalytic activity, implying that the acidic CH_2 bridge is essential. A ^1H NMR study on a catalyst mixture, however, hints to an

Scheme 32. Proposed Mechanism for the Asymmetric 1,4-Addition of α-Amino Acid Derivatives to Enones Catalyzed by Chiral (BOX)CaOR



acid−base equilibrium between BOX-H + $Ca(OR)_2$ and (BOX)CaOR + ROH. Independently, Harder et al. demonstrated that the same reaction with a more basic calcium amide complex exclusively gave the heteroleptic calcium amide complex **12**, which was fully characterized by a single crystal structure determination.[66] Based on the assumption that the catalytically active species is (BOX)CaOR, a tentative mechanism has been proposed (Scheme 32). A similar protocol has been proposed for the addition of sulfonylimidates to imines.[131] Interestingly, the choice of the group 2 metal has large consequences for the diastereoselectivity of such conversions, thus implying that the metal plays a role in the mechanisms.

7.2. Remarks on Stereoselective Induction

The group 2 metal mediated conversions described in section 7.1 show excellent enantio- and diastereoselectivities. Although in all cases catalysts have been prepared *in situ* and were not further characterized, speculative reaction mechanisms and modes of stereoselective induction have been proposed.

On the other hand, the first enantiopure chiral calcium amide complexes **12** and **13** gave no, or at most very poor, enantioselectivities in hydroamination or hydrosilylation reactions.[66] It could be demonstrated that this is due to ligand distribution reactions (Schlenk equilibria) that strongly favor the homoleptic Ca species, thus undermining the concept of enantioselective catalysis by a chiral catalyst such as L^*CaNR_2 (see section 4.2).

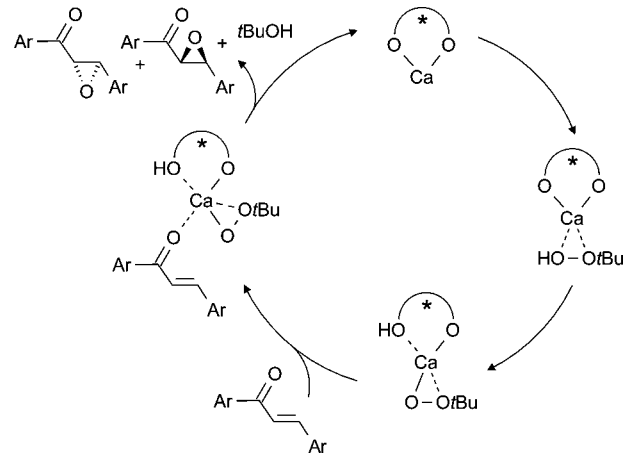
The observation that the asymmetric 1,4-addition to enones and or imines with a similar BOX catalyst proceeds with excellent stereoselectivities (up to 99% *ee*) implies that either (i) for this particular case Schlenk equilibria must be fully at the heteroleptic side or (ii) homoleptic species are completely inactive. Closer inspection of the mechanism (Scheme 32) shows that the heteroleptic Ca alkoxide species involved in the enantioselective step is stabilized by chelation through the imine arm. As Hill et al. showed that intramolecular chelation inhibits ligand exchange and is an important contribution to the stability of heteroleptic Ca complexes,[20a] it is likely that this is a prerequisite in Ca-mediated enantioselective catalysis. This would explain the very poor chiral induction of **12** and **13** in hydroamination and hydrosilylation catalysis, both reactions with intermediates that are not stabilized through intramolecular chelation. The idea that stabilization of the chiral heteroleptic intermediate by intramolecular chelating substituents plays an important role in stereocontrol should give impetus to future plans in this area.

8. Miscellaneous Conversions

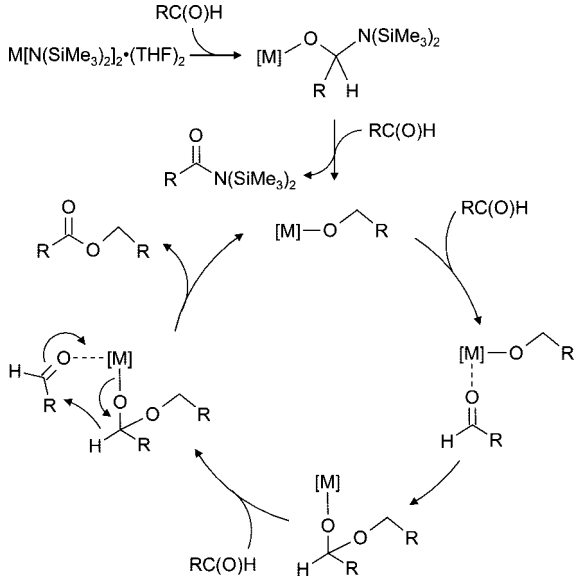
The stoichiometric epoxidation of the C═C double bond in chalcones by *t*BuOOLi proceeds rapidly and in high yield. This formed the basis for the asymmetric catalytic epoxidation of chalcones by *t*BuOOH with a mixture of $(n\text{Bu})_2\text{Mg}$ and enantiopure diethyltartrate as the catalyst. Jackson et al. obtained enantioselectivities up to 94% *ee*.[132] Kumaraswamy et al. introduced BINOL-Ca for the epoxidation of chalcones and reported selectivities up to 80% *ee*.[133] Although the catalyst is prepared *in situ* and has not been characterized further, the authors suggest that it is likely a trimeric or tetrameric cluster. For the sake of clarity, they presented a tentative simplified mechanism based on monomeric BINOL-Ca (Scheme 33). As in the asymmetric Michael addition (Scheme 32), protonation/deprotonation of the BINOL ligand are essential steps in the catalytic cycle. This work was extended by a survey for ligand substituent effects, and the methodology was successful in the Ca-mediated enantioselective synthesis of (*S*)-(+)-fenopren (84% *ee*), an anti-inflammatory agent only active in its *S*-form.[134]

Heavier alkaline-earth amides have been recently introduced by Hill et al.[135] as catalysts in the Tischtschenko reaction,[136a,b] i.e. the dimerization of aldehydes to the corresponding carboxylic ester: $2RC(O)H \rightarrow RC(O)OCH_2R$. The latter reaction is generally mediated by Al-alkoxides[136] or by transition metal[137] and lanthanide[138] catalysts. In addition it is also catalyzed by the simple Lewis acid $B(OH)_3$, albeit under forcing conditions.[139] The heteroleptic calcium complex **6** was found to be a very active catalyst for benzaldehyde dimerization to benzylbenzoate.[135] However, the β-diketiminate ligand in **6** was not supported during catalysis and was transformed into its protonated form. For this reason, the homoleptic alkaline-earth amides $M(HMDS)_2 \cdot (THF)_2$ (**1-M**, M = Ca, Sr, Ba) were tested as potential catalysts. Their activity decreased with metal size (Ca > Sr > Ba), a trend which is opposite to that observed for homoleptic lanthanide catalysts $Ln(HMDS)_3$ (Ln = Sc, Y, La), where the most active catalyst was based on the largest metal La. The low activity for the Ba catalyst might

Scheme 33. Asymmetric Epoxidation of Chalcones by Chiral BINOL-Ca (Shown for Simplicity as a Monomer)



Scheme 34. Proposed Mechanism for the Tischtschenko Reaction, 2RC(O)H → RC(O)OCH$_2$R, Catalyzed by Alkaline-Earth Metal Amide Complexes (in Analogy to the Cycle for Organolanthanide Catalysts)[138a]

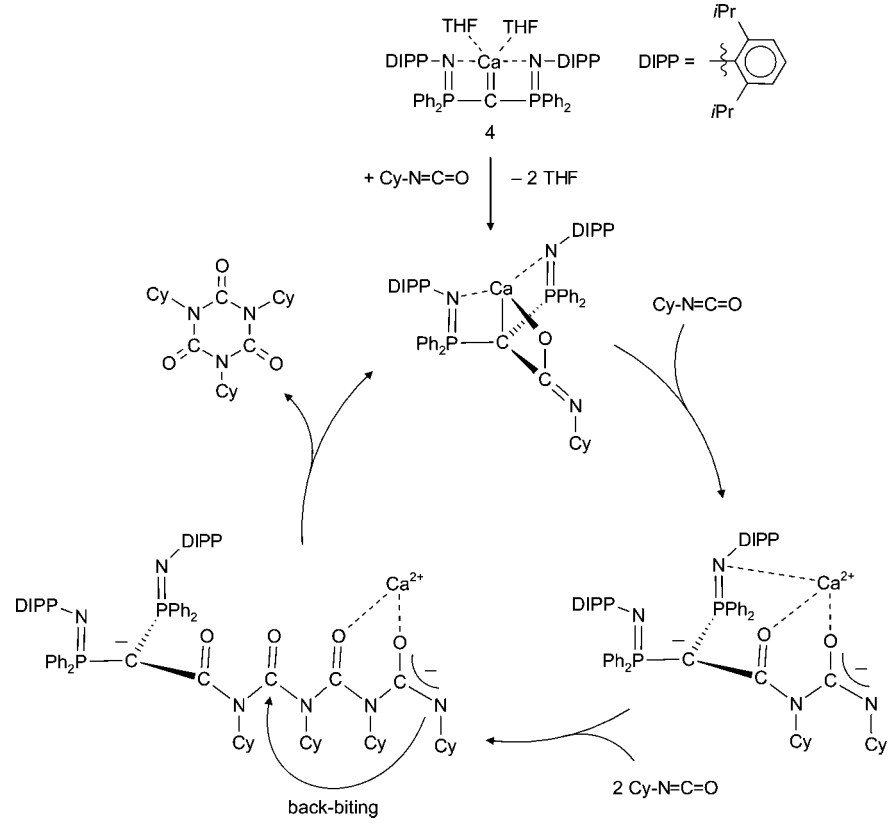


be explained by the poor solubility of Ba-alkoxides (an intermediate in the catalytic cycle). It could be shown that catalytic activity was not due to formation of insoluble alkaline-earth oxides (CaO, SrO, or BaO), which are known to be heterogeneous catalysts for the same reaction.[140] The alkaline-earth metal mediated Tischtschenko coupling likely proceeds through a mechanism similar to that introduced for the lanthanide catalyzed reaction (Scheme 34).[138a] The metal amide is converted to a metal alkoxide which is the actual catalyst. This proceeds likely by a Meerwein−Pondorf−Verley-type reduction, and a similar hydrogen transfer process also plays a role in a later step in the cycle. The calcium amide precatalyst could also be used in the polymerization of the dialdehyde terephtaldicarboxaldehyde to the corresponding polyester.[135]

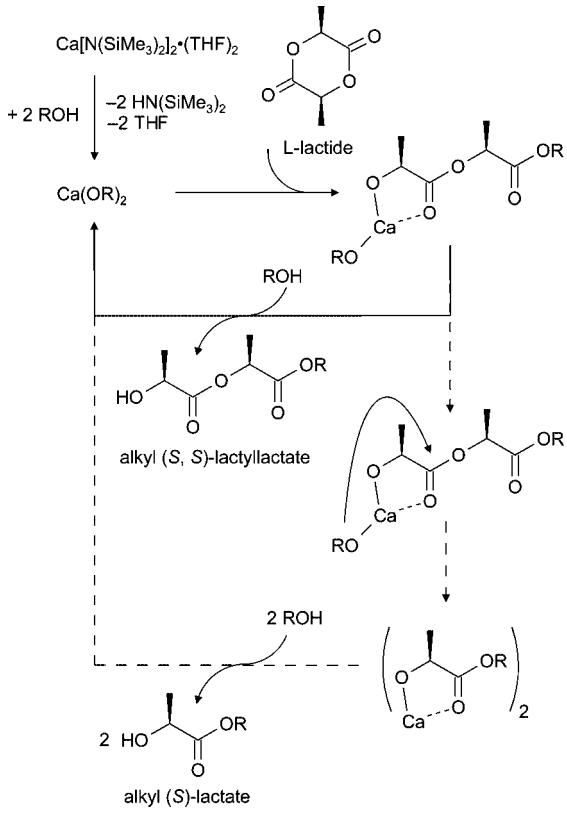
Harder et al. recently published the first calcium carbene complexes R$_2$C═Ca (**4**).[141] These compounds possess a formal double bond between Ca and carbon but should be considered to have significant methandiide character R$_2$C^{2-} Ca^{2+}. Addition of an excess of cyclohexylisocyanate resulted in catalytic trimerization (Scheme 35). The first step in the reaction is a [2 + 2]-cycloaddition of the Ca═C bond and the C═O bond in the isocyanate. Proof for this mechanism has been found in the crystal structures of intermediates after single and double isocyanate insertions.[136] Insertion of two further equivalents of cyclohexylisocyanate results in a short polymer chain which, after intramolecular nucleophilic attack of a C═O functionality ("backbiting"), eliminates the trimer. Cyclohexylisocyanate trimerization is extremely slow (5 mol % catalyst, 80% conversion after one week at 50 °C). This allowed for the isolation and structural characterization of the first two intermediates. Smooth conversion, however, is observed in the trimerization of phenylisocyanate (1 mol % **4**, 90% conversion after 3 h at 20 °C).[141b]

An interesting application of a calcium amide mediated alcoholysis of L-lactide was recently reported by Phomphrai et al.[142] Reaction of this cyclic ester with catalytic amounts of Ca(HMDS)$_2$•(THF)$_2$ in an alkyl alcohol gives either an alkyl lactyllactate or an alkyl lactate (Scheme 36). The selectivity of this reaction is dependent on the catalyst concentration (and reaction times). The first step in the reaction is ring-opening of L-lactide (similar to the case of Ca-mediated L-lactide polymerization; see section 3.1). The product reacts at low catalyst concentration (1 mol %)

Scheme 35. Trimerization of Cyclohexylisocyanate by a Calcium Carbene Complex (4)



Scheme 36. Ca-Mediated Alcoholysis of L-Lactide in an Alkyl Alcohol Gives Either Alkyl (*S*,*S*)-Lactyllactate or Alkyl (*S*)-Lactate

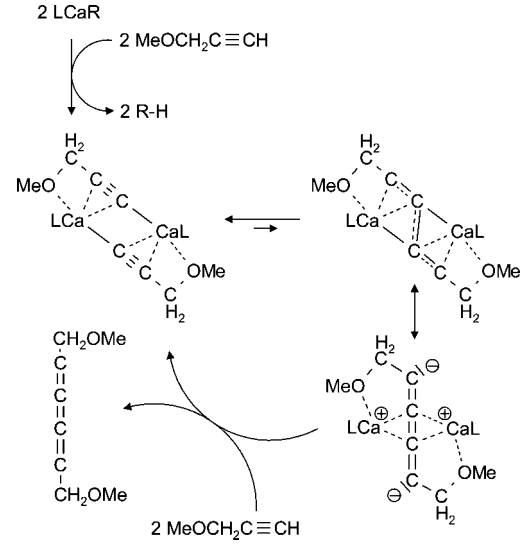


immediately with excess alcohol to give an alkyl lactyllactate. At high catalyst concentration (5 mol %), however, further degradation to an alkyl lactate is observed. In all cases, there is no epimerization of the chiral carbon centers and products with exclusive *S*-chirality are obtained.

$Ca[OCH(CF_3)_2]_2$ was recently used as a catalyst in the Pictet−Spengler reaction.[143] It combines high yields with high regioselectivity and provides a mild alternative to the traditional Brønsted acids employed in this reaction.

Hill et al. recently reported on an unexpected C−C coupling of terminal alkynes.[144] During their investigations on the Ca-mediated addition of $MeOCH_2C{\equiv}CH$ to carbodiimides (see 4.4), $MeOCH_2C{=}C{=}C{=}CCH_2OMe$ was isolated as an unanticipated byproduct. Stoichiometric reaction of calcium catalyst **6** with 2 equiv of the alkyne gave only the corresponding butatriene as product. The first step in the reaction is formation of a heteroleptic alkynide complex (Scheme 37) which could be isolated and was found to be dimeric. The alkynide anions bridge asymmetrically between the Ca centers with a Ca−C σ-bond and a side-on Ca−C π-bond. Bonding is completed by the chelating action of the propargyl ether group. The next step, coupling of two carbanionic centers, seems less straightforward. It should be mentioned, however, that Teuben et al. reported evidence for a similar equilibrium in lanthanide chemistry: dimeric $[Cp^*_2La(\mu\text{-}C{\equiv}CMe)]_2$ is in equilibrium with the C−C coupled species which was characterized by X-ray diffraction.[145] The second equivalent of alkyne can cleave off the 2-fold deprotonated butatriene to give the product and catalyst. The mechanism for this C−C coupling requires a dimeric state. It is therefore noteworthy that the same reaction in THF, in which monomeric structures are likely, hardly proceeds. The stoichiometric alkyne dimerization is limited

Scheme 37. Proposed Mechanism for the Ca-Mediated Coupling of 3-Methoxypropyne



to alkynes with a potentially coordinating ether functionality. Therefore, asymmetric (σ, π)-alkynide bridging seems essential for this C−C coupling process.

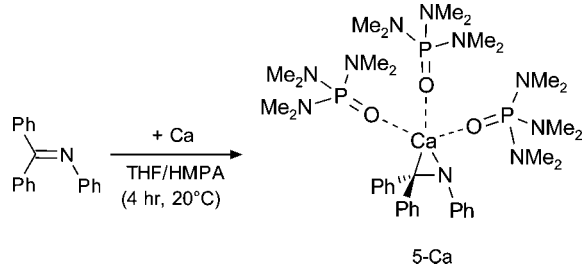
Although this reaction worked under stoichiometric conditions, a catalytic conversion could not be observed. It was suspected that the acidic alkyne protonated the β-diketiminate ligand in **6** and would give insoluble homoleptic $Ca(C{\equiv}CCH_2OMe)_2$. The triazenide complex **8-Ca**, which is less prone to spectator ligand protolysis, could be used as a catalyst (6.25 mol %, 75 °C, 91% conversion after 48 h). As **8-Ca** is sensitive to ligand distribution, the exact nature of the catalyst is not clear.[144]

9. Analogies between Yb^{2+} and Ca^{2+} Chemistry

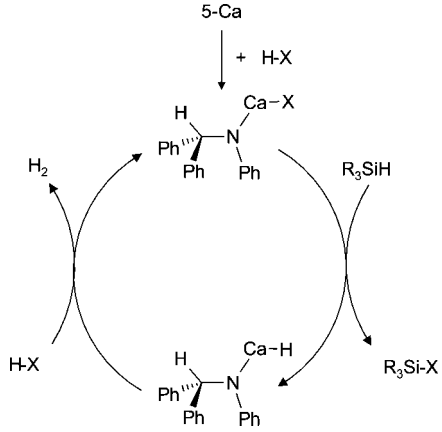
Although the chemical behavior of heavier alkaline-earth metal complexes has often been compared to that of the lanthanide (Ln) metal complexes in their most common +3 oxidation state, there are in particular parallels with Ln^{2+} metal complexes.[146] This is due to the very limited radial extension of the f orbitals. Therefore, lanthanide chemistry is, just like heavier alkaline-earth metal chemistry, simplified to a level of ionic bonding in which structures and reactivities are governed by electrostatic and steric factors. As the ionic radii for Ca^{2+} and Yb^{2+} are very similar (Ca^{2+}, 1.00 Å; Yb^{2+}, 1.02 Å),[13] there is a striking similarity in their crystal structures,[146f−h,147] IR spectra,[146a] NMR spectra,[147] gas phase behaviors,[148] and reactivities.[146g,h] The same relationship exists between the pairs Eu^{2+}/Sr^{2+} and Sm^{2+}/Sr^{2+}, which also have similar ionic radii (Sm^{2+}, 1.22 Å; Eu^{2+}, 1.17 Å; Sr^{2+}, 1.18 Å).[13]

Similarities between the chemistry of Yb^{2+} and Ca^{2+} can also be advantageously used in catalysis. Takaki et al. extensively explored the use of the Yb(II) complex **5-Yb** in catalysis. This azametallacyclopropane is a versatile and easily accessible catalyst for a large number of catalytic conversions, such as the alkyne-isomerization,[144] dehydrogenative silylation of terminal alkynes[150] and amines,[151] hydrosilylation of imines[151] and olefins,[152] dehydrogenative polymerization of $PhSiH_3$,[153] and intermolecular hydrophosphination of alkynes.[154] The impressive scope of this simple catalyst has been reviewed recently.[153] As the proposed mechanisms for these conversions do not involve a change

Scheme 38. Synthesis of the Azametallacyclopropane 5-Ca



Scheme 39. Proposed Mechanism for the Catalytic Dehydrogenative Silylation of Terminal Alkynes (H-X = HC≡CR) and Amines (H-X = HNR_2); HMPA Ligands Not Shown



in the metal oxidation state, a similar Ca catalyst could have the same high catalytic potential.

Harder et al. prepared the Ca-analogue **5-Ca** according to the same convenient one-pot procedure (Scheme 38) and could obtain the product in the form of large dark-red crystals.[155] The crystal structure of **5-Ca** is isomorpous to that of **5-Yb**. The calcium complex was shown to be similarly catalytically active in the dehydrogenative silylation of terminal alkynes and amines, two reactions that had no precedence in Ca-mediated syntheses. The proposed mechanism for these conversions equals that proposed earlier by Takaki and is based on the fact that the aryl substituent on the N atom of the catalyst has a large effect on catalyst activities (Scheme 39). It is therefore suggested that the $Ph_2C(Ar)N^{2-}$ ligand in **5-Ca** is protonated to give $Ph_2HC(Ar)N^{-}$, which acts as a spectator ligand in the active catalyst. Like **5-Yb**, **5-Ca** was also active in the isomerization of terminal alkynes to internal alkynes. In all cases, very similar activities and selectivities were found. This is indirect proof of the fact that the true catalyst in reactions catalyzed by **5-Yb** is an Yb(II) species. The observation that **5-Yb** is only active for hydrosilylation of conjugated alkenes[152] underscores this argument. Close similarities in structures and catalytic behavior of these Ca and Yb catalysts implicate that all other conversions described for **5-Yb**[153] might run equally well with **5-Ca**. The latter calcium catalyst represents a much cheaper alternative to the well-studied Yb catalyst (1 mol Ca = € 10; 1 mol Yb = € 2637).[156] Moreover, it is prepared in crystalline purity in one step directly from calcium metal and commercially available precursors. It was found that the very polar, but carcinogenic, cosolvent HMPA is in some cases essential for an efficient conversion. It is likely that such cosolvents keep the intermediate calcium hydride species in solution. This demonstrates the importance of solvent effects in Ca-mediated reactions and should stimulate further research on the use of highly polar, less poisonous, cosolvents.

Apart from astounding similarities in Ca and Yb chemistry, also remarkable differences have been observed.[147] As dicussed in section 3.2, the heteroleptic benzyl calcium complex **18** is an initiator for the syndioselective polymerization of styrene (up to $r = 92\%$ and $rr = 85\%$) whereas the homoleptic dibenzyl calcium complex **3-Ca** gave a predominantly atactic polymer. The Yb analogue of heteroleptic **18**, however, gave polystyrene of much lower syndiotacticity. Even more surprising was the observation that the homoleptic Yb-analogue of **3-Ca** gave a polystyrene of considerable syndiotacticity (up to $r = 93\%$ and $rr = 86\%$). As polymerizations can be monitored by ^{1}H NMR, the diamagnetic +2 oxidation state was largely maintained during the reaction. Although not fully understood, these differences in selectivity are likely due to very small differences in metal−ligand bonding.[147]

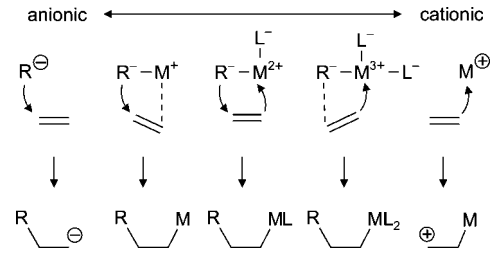
10. Conclusions and Perspectives

The current review shows that calcium chemistry, which once was merely a laboratory curiosity, has grown in a rather short time to an area of increasing activity. This development is, as demonstrated here, partly driven by its advantageous application in catalysis. Organocalcium compounds have been shown to catalyze reactions such as alkene hydrosilylation and hydrogenation, conversions that one immediately relates to transition metal catalysis. It should be recognized that many of the processes that can be mediated by organolanthanide catalysts likely can be accomplished with an organocalcium complex. Despite this similarity to lanthanide catalysis, which is based on a similar protocol for bond breaking and making, there are also distinctive differences. Whereas Ln(III) catalysts are able to activate isolated C═C bonds, calcium reagents only react with slightly activated (conjugated) double bonds (at least in intermolecular reactions). This substrate restriction can also be seen as an advantage: only one of the double bonds in a conjugated system is selectively functionalized.

As Ln(II) reagents also only react with conjugated double bonds, the activation of isolated C═C bonds by Ln(III) complexes must be sought in the much higher Lewis acidity of the Ln(III) nucleus. The addition of polar organometallic species to double bonds can be classified according to a scale in which pure anionic and pure cationic addition are the extremes (Scheme 40). Apparently, activation of isolated alkenes only takes place at the cationic end of the scale. This explains the superiority of lanthanide and group 4 (Ti, Zr, Hf) catalysts in olefin polymerization.

The introduction of this scale poses the important question: are organocalcium mediated processes merely base-catalyzed

Scheme 40. Scale for Nucleophilic/Electrophilic Addition to the C═C Double Bond



or does the metal play a crucial role? In some of the cases, group 1 metal based catalysts also gave satisfying conversion rates: e.g. intramolecular alkene hydroamination, intermolecular hydroamination, and hydrophosphination of activated C═N bonds or ketone hydrosilylation. In other cases, however, the choice of a group 2 metal is vital to successful conversion. For example, metal choice can be a decisive factor for the well-controlled production of polymers from polar monomers (section 3.1). Also in alkene polymerization, metal choice affects the stereoregularity of the polymers to a great extent (section 3.2). Styrene polymerization with group 1 metal species should be considered as largely anionic polymerization (with a small influence of the metal) and gives atactic polystyrene. In contrast, the bond between the polymer chain-end and a group 2 metal is much stronger; thus, a more coordination−insertion type of mechanism is operative. In the latter case, it could also be shown that stereocontrol can be steered by subtle changes in the bulk of the spectator ligand. Therefore, such systems show great similarity to single-site transition metal catalysts. Also, reactions that involve addition to conjugated C═C bonds (alkene hydrosilylation and hydrogenation) are sensitive to metal choice. In these examples, exchange of the calcium metal for a group 1 metal often results in acceleration of the polymerization side-reaction. Moreover, in alkene hydrosilylation, metal choice has been shown to have a drastic influence on regioselectivity. Also in the highly enantioselective aldol-, Mannich, and Michael-type reactions (section 7.1), group 2 metals are superior to group 1 metals. In these cases, ionically bound chiral spectator ligands are essential for chiral induction.

Although the past decade has seen major advances in Ca-mediated syntheses, this discipline is still very young. From the results shown here, many ideas for future explorations can be deduced. Apart from application of calcium based catalysts in new reactions, the following focus points could be envisioned:

(i) As most of the organocalcium catalysts (here defined as species with a Ca−C bond) are sensitive toward hydrolysis, there are stringent requirements on water content in the used solvents. Also, there is not a high tolerance for functional groups such as OH, NH, and CX (X = halogen) or reactive unsaturated bonds. Calcium alkoxide complexes, however, show a much higher tolerance to hydrolysis and functional groups and should have a bright future for use in more practical applications.

(ii) As kinetic data for catalytic experiments are generally lacking, there is very little experimental evidence for the proposed mechanisms. Gathering kinetic data is severely hindered by the sensitivity of the catalyst toward hydrolysis (which would give hydroxide incorporation and cluster formation), ligand exchange by the Schlenk equilibrium, and solubility issues. These factors lead to uncertainties relating to the structure and composition of active species and/or its concentration. Theoretical calculations, however, could provide important insights into the proposed mechanisms.

(iii) The design of ligands that prevent Schlenk equilibria is highly desirable for those cases in which the stability of a heteroleptic calcium complex is essential to activity and/or selectivity of the catalyst.

(iv) Hitherto, there are only a few examples of enantio- or diastereoselective Ca-mediated processes. In most of these cases, the structures or composition of the catalysts is unknown. A full understanding of catalyst structures and factors controlling these reactions is desirable for future development. Also, new chiral ligands which steer the Schlenk equilibrium to the heteroleptic side should be developed.

(v) Solvent effects largely influence the structures and reactivities of polar early main group metal complexes. Although this review describes a few examples of solvent effects in Ca-mediated reactions, a fundamental study of this aspect is highly desirable and could contribute to further development of the field.

I would like to end this review article with a personal note. Once, after giving a lecture on calcium complexes in catalysis for an audience more inclined to organic chemistry, I got the compliment "it was very nice to see your recent contributions to organocatalysis". After remarking that the work presented should be considered as organometallic catalysis and that the metal calcium is crucial in many of the cases, I got the reply "but calcium is not a real metal". This demonstrates how much the chemical community is focused on transition metal catalysis. Hopefully, this review contributes to acceptance and further development of this field in homogeneous catalysis.

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