100 Years after Grignard: Where Does the Organometallic Chemistry of the Heavy Alkaline Earth Metals Stand Today?

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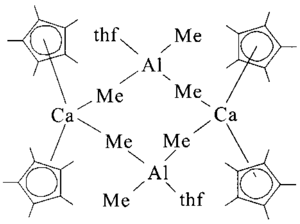
The preparation of the alkylmagnesium halides by the direct synthesis from magnesium and haloalkanes 100 years ago[1] led to a vast development of organometallic chemistry. Since then these Grignard compounds have been shown to be widely applicable as readily available metalation and metathesis reagents in organic and inorganic chemistry. Even geminal bismagnesiated alkanes have been isolated and structurally characterized.[2] Although interest in corresponding compounds of the heavier alkaline earth metals has risen in the past few years,[3] great difficulties are associated with their direct synthesis. On the one hand, the metals calcium, strontium, and barium are rather inert; on the other hand, the organometallic derivatives are extremely reactive. The high reactivity often leads to ether cleavage reactions; however, in apolar solvents, the organometallic compounds of the heavy alkaline earth metals are often insoluble. Consequently, two different synthetic strategies were developed in the last few years, namely the activation of the metals as well as the reduction of the reactivity of the organometallic reagent by steric shielding with bulky substituents and/or by shielding of the metals with multidentate Lewis bases.

Interest in the organometallic compounds of the heavier alkaline earth metals has increased recently not least due to the fact that an intermediate position between the derivatives of the alkali metals and of the metals of the scandium group is expected. Calculations showed already that monomeric dimethylstrontium and -barium should be bent,[4] whereas dimethylcalcium is expected to be linear similar to the monomeric fluorides[5] (Table 1). Also for the dimeric coligand-free alkaline earth metal dihydrides, uncommon structures of the bicyclic type $HM(\mu\text{-}H)_3M$ for calcium and strontium as well as tricyclic $Ba(\mu\text{-}H)_4Ba$ were predicted[6] as a consequence of a small but structure-determining influence of the d orbitals.

Table 1. Calculated structural parameters of monomeric alkaline earth metal difluorides, -hydrides, and -methanides of calcium, strontium, and barium of the type R-M-R.

M	R	M–R [pm]	R-M-R [°]	Ref.
Ca	F	205	180	[5]
	H	206	180	[6b]
	Me	249	180	[4]
Sr	F	219	144	[5]
	H	220	140	[6b]
	Me	262	131	[4]
Ba	F	233	126	[5]
	H	231	119	[6b]
	Me	276	116	[4]

Although numerous examples of alkaline earth metallocenes[7] and molecules with π-bonded anionic ligands are known,[8] organocalcium chemistry has still only developed slowly since the report of the bis(1,4-dioxane) complex of bis[bis(trimethylsilyl)methyl]calcium (**1**), the first structurally characterized representative, by Lappert and co-workers.[9] The Ca–C bond lengths of 248.3 pm lie in the region predicted by calculations. Whereas this research group chose the cocondensation of calcium with chlorobis(trimethylsilyl)methane to activate the metal, a few years later the synthesis of bis[tris(trimethylsilyl)methyl]calcium (**2**) (Ca–C 245.9 pm, C-Ca-C 149.7°), which surprisingly is bent at the metal atom, succeeded from the metathesis reaction of the corresponding coligand-free potassium derivative and calcium diiodide.[10] This reaction was performed in benzene because the high reactivity of the organocalcium compound led to ether cleavage reactions. It was impossible to develop a chemistry based on **2** for the same reason.



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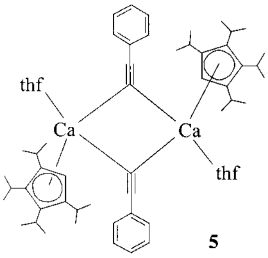
The reaction of decamethylcalcocene with trialkylalane in THF gave the loose adduct **3**,[11] whereas the use of calcium bis[bis(trimethylsilyl)amide] led to the elimination of dialkylaluminum amide and to the formation of dimeric bis(trimethylsilyl)amidocalcium tetrakis(trimethylsilylmethyl)alanate (**4**).[12] The alanate anions bind as bidentate ligands with Ca–C bond lengths of 263.8 and 267.8 pm. However, the elimination of another molecule of $(Me_3Si)_2NAl(CH_2SiMe_3)_2$ and the formation of dialkylcalcium starting from **4** failed.

The pK_a values of the acids determine the equilibrium of metalation reactions. Since alkaline earth metal bis[bis(trimethylsilyl)amides] are soluble in common organic solvents and are commonly employed as soluble starting compounds, more H-acidic hydrocarbons such as cyclopentadienes or phenylacetylene are necessary. This route was used by Burkey and Hanusa[13] to prepare dimeric tetraisopropylcyclopentadienylcalcium phenylacetylide **5**. The bridging phenylacetylide ligands display Ca–C distances of 252.1 and 255.1 pm.



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Molecules with Sr–C and Ba–C σ bonds have not been investigated as extensively. Carbene adducts of barium bis[bis(trimethylsilyl)amide] dissociate in solution;[14] however, those

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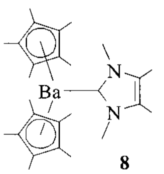

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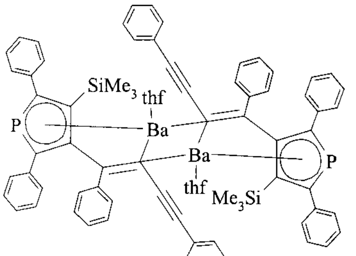
of decamethylcalcocene (**6**), -strontocene (**7**), and -barocene (**8**) have been structurally characterized (Ca–C 256.2, Sr–C 285.4 and 286.8, Ba–C 295.1 pm).[15] The addition of diphenylbutadiyne to barium bis[bis(trimethylsilyl)phosphanide] yielded dimeric and intramolecularly shielded alkenylbarium phospholide **9** with an unsymmetric Ba_2C_2 cycle with Ba–C bond lengths of 288.1 and 307.1 pm.[16] By shielding of the alkaline earth metal with crown ethers, Ruhlandt-Senge and co-workers[17] succeeded in isolating crystalline triphenylsilylacetylides of calcium (**10**), strontium (**11**), and barium (**12**) with bent $M-C\equiv C$ fragments and mean Ca–C, Sr–C, and Ba–C bond lengths of 254, 272, and 285 pm, respectively. The similar acidity of acetylenes (pK_a values at 29) and of triphenylmethane (p$K_a = 30$) also suggest their metalation; however, surprisingly the dependency on the metalating reagent was observed. Only the use of the recently published bis(tetrahydrofuran)dibenzylbarium[18] (**13**) allowed the synthesis of the crown ether complex of bis(triphenylmethyl)barium (**14**), although as a solvent-separated ion pair ([18]C-6 = [18]crown-6; hmpt = hexamethylphosphoric acid triamide).[19]



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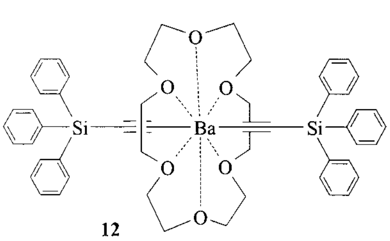

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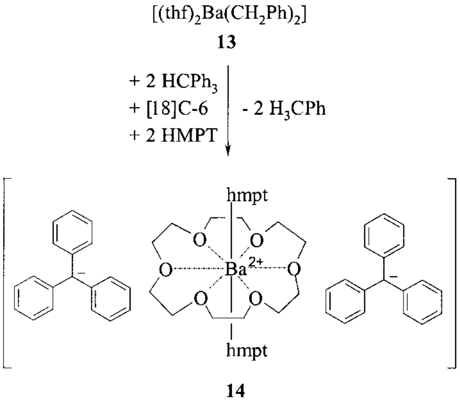
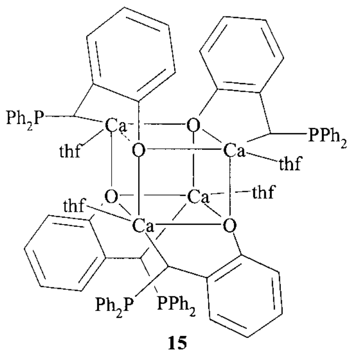


Other metalating reagents such as barium bis[bis(trimethylsilyl)amide] did not lead to this product, but allowed the isolation of the crystalline ether cleavage product which was already described earlier.[20] With the intention of binding soft carbanions to the heavy alkaline earth metals and of avoiding ether cleavage reactions, substituted dibenzylcalcium[21] and -barium[22] have attracted more interest over the last few years. The alkaline earth metal cations avoid the formation of σ bonds, but prefer η^3 coordination to the π system of the carbanion. An interesting exception is compound **15** with a Ca_4O_4 heterocubane moiety, which is available in rather poor yield from the ether cleavage reaction of calcium diiodide with (2-methoxyphenyl)(di-*p*-tolylphosphanyl)methyllithium. The calcium atoms reside in a distorted octahedral environment; the Ca–C bond lengths are 259.1 pm.[23]



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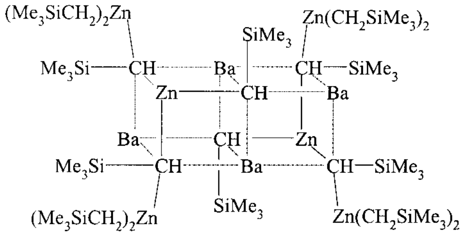
The transmetalation of bis(trimethylsilylmethyl)zinc with distilled barium gave barium bis[tris(trimethylsilylmethyl)zincate] (**16**) in good yield, whereas the Ba-C-Zn bridges can be regarded as three-center, two-electron bonds (Ba–C 302.8 and 305.5 pm). Depending on the solvent, toluene or tetrahydrofuran molecules complete the coordination sphere of the soft metal center.[24] The transmetalation under application of ultrasound leads to the metalation of the methylene groups and to the formation of the centrosymmetric cage compound $[Ba_4Zn_6(CH_2SiMe_3)_8(CHSiMe_3)_6]$ (**17**).[25] In this $Ba_4Zn_2C_6$ double cube the carbon atoms show a distorted octahedral coordination sphere. Compounds with bonds between the heavy alkaline earth metals and heavy tetrels are gaining interest, as shown for example, for the structurally characterized stannanides of barium.[26]



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The structural characterization of unsubstituted dialkylstrontium and -barium compounds are still to be achieved. The increasing knowledge about the synthetic strategies and the structures of these compounds is expected to be accompanied by an increase in the use of such compounds for industrial applications mainly as anionic polymerization catalysts, as has already been proven for selected derivatives.[8d, 27] However, we are still at the beginning of a vastly developing chemistry of the heavy homologous Grignard reagents.

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The Light Shall Show the Way—Or: The Conformational Changes of the Retinal Chromophore in Rhodopsin upon Light Activation

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The Visual Pigment Rhodopsin—A Paradigm for the G-Protein-Coupled Receptors (GPCRs)

Only a few molecules can be considered as biochemical "classics" which have also made their way as distinctive examples into biochemistry textbooks. Amongst these is the archetype of visual pigments, bovine rhodopsin.[1] The strong scientific interest in understanding the structure and function of rhodopsin is not only a consequence of its fascinating conversion of absorbed light into a biological signal, but is also a consequence of the fact that it serves as a paradigm for a large and continuously growing number of other receptors with seven transmembrane α-helices. Common to all these membrane-intrinsic receptors is their capability to respond to external stimuli such as other sensory (olfactory and gustatory), hormone-mediated, or neurotransmitter-mediated signals, and to mediate the signal by activating a heterotrimeric G-protein in the interior of the cell.[2]

Scientific investigation of visual pigments started more than a century ago with work by pioneers such as W. Kühne, who demonstrated image formation on the retina-embedded "Sehpurpur"[3] when illuminated patterns were exposed to the eye. Since then, many multidisciplinary approaches have been used to understand the function of visual proteins, and have included the efforts of pharmacologists, biologists, biophysicists, medicians, neurologists, and even theoreticians. *Chemists* became involved in visual research through the identification of the vitamin A aldehyde retinal as the chromophoric principle of visual proteins by George Wald

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