Organic chemistry with lanthanides

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Abstract. Lanthanides are briefly presented in an introductory section. The chemistry induced by divalent lanthanides, esssentially Sm(II) derivatives, is then discussed. Barbier type reaction and reduction of acid chlorides are mainly considered. Acid chlorides react with SmI_2 in various ways, giving rise to interesting organic chemistry.

INTRODUCTION

Lanthanides are members of a large family of elements (Figure 1), located between barium and hafnium in the 6th row of the periodic table. The name of rare earths covers lanthanides and some other elements (yttrium, scandium) usually mixed together in the ores. Lanthanides are no more considered as rare, since industrial processes allow to prepare them in high degree of purity. There is an increasing demand of some lanthanides for modern technology, Rhône-Poulenc Co. is the world leader for production of purified lanthanides. Cerium is the most abundant element in the lanthanide series, followed by lanthanum, neodynium and samarium. Thullium is the rarest lanthanide but it still remains four times more abundant than silver on the earth crust. Apart from cerium (ceric oxidations) lanthanides have been for a long time neglected by organic chemists. However in the last decade there has been a progressive change in that attitude, a recent review (ref.1) summarizes the use of lanthanides in organic synthesis.

Z	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71
Ln	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu

Figure 1 The Lanthanum Series

Several features concerning lanthanides (ref. 2) are of potential interest in organic chemistry:
Main oxidation state : + 3.
Oxidations possible by tetravalent lanthanides (mainly cerium).
Reductions possible by divalent lanthanides (Eu, Yb, Sm, Tm).
Rich coordination chemistry, with high coordination numbers.
Lewis acidity, especially for Ln(III) derivatives, with applications to catalysis .
Oxophilicity.
The 4-f orbitals do not much participate to bonding, most of Ln derivatives have a pronounced ionic character.

Redox chemistry with lanthanides involves monoelectronic transfers (Ce(IV) $\longrightarrow$ Ce(III), and Ln(II) $\longrightarrow$ Ln(III)). In the present article we wish to discuss the use of divalent lanthanides in organic chemistry (ref. 4) , and then to present some results we have recently obtained.

WHICH DIVALENT LANTHANIDE DERIVATIVES TO USE?

The standard redox potential values of couple Ln^{3+} / Ln^{2+} are:
Eu = -0.33 V, Yb = -1.35 V, Sm = -1.55 V, Tm = -2.1 V.

By looking to these values one can anticipate the decreasing order of reactivity towards organic compounds: Tm › Sm › Yb › Eu .

It is impossible to envisage using thullium, which is a very rare element. Some screenings on europium (II) showed that its reducing properties are not very promissing. The most attractive elements for organic chemists are samarium and ytterbium. We devised (ref. 7) a simple and smooth procedure to prepare diiodosamarium and diiodoytterbium:

$$Ln + ICH_2 CH_2I \text{ (in THF)} \longrightarrow LnI_2 + CH_2{=}CH_2 \text{ (Ln= Yb or Sm)}$$

These complexes are soluble in THF ($\leqslant$ 0.1 M). The solution can be stored for a long time under nitrogen. It soon appeared that diiodosamarium is the most interesting reagent (ref. 9), and it will be exclusively considered therein. THF solution of diiodosamarium is now commercially available (Alfa Co). Preparation of SmI_2 from samarium metal (powder or ingot, approximate price: 1 to 1.5 dollar/ g) does not present difficulties if performed under inert atmosphere. The deep green solution turns to yellow after the transformation Sm(II) $\longrightarrow$ Sm(III), giving an easy way to detect the end point of the reaction.

Diiodosamarium is a good starting material for the synthesis of other Sm(II) derivatives through exchange reactions (refs. 9, 10). For example $SmCp_2$ is easily obtained by addition of NaCp to a THF solution of SmI_2. $SmCp_2$, which is insoluble in THF, precipitates from the solution.

SUMMARY OF THE MAIN REACTIONS MEDIATED BY SmI_2

During several years we investigated the basic properties of diiodosamarium towards organic compounds (refs. 9, 11-16). Some reactions are indicated in Figure 2.
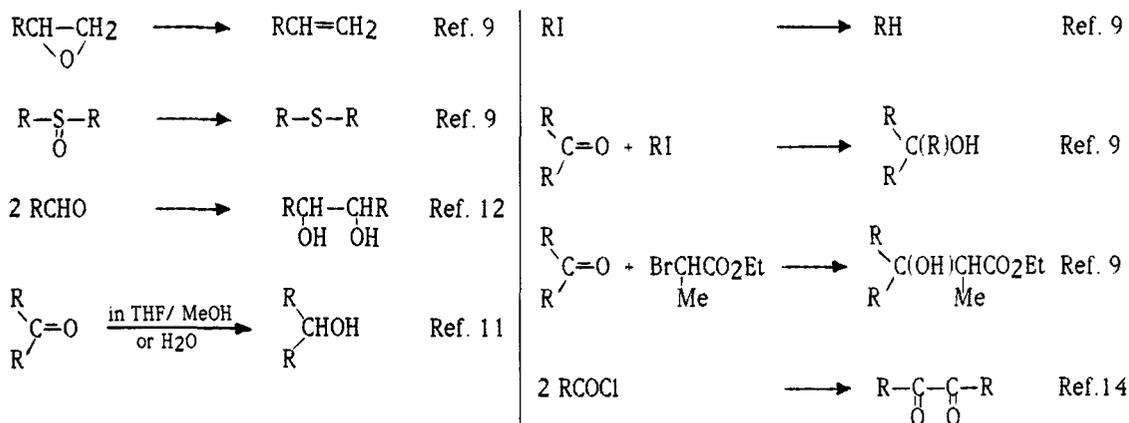

Figure 2

The particular case of C—C bond formation by the one pot reaction between aldehydes or ketones and organic halides was called Barbier reaction (the metal of the original Barbier reaction is replaced by SmI_2). The mechanism of the reaction has been discussed (ref. 12) and is believed to involve a radical in the initial stage :

$$RX + SmI_2 \longrightarrow R^{\bullet} + SmI_2 X$$

Ketones or aldehydes are also electron-acceptors *versus* SmI_2 , as evidenced by the pinacol formation :

$$\text{\Large$\diagdown$}C{=}O + SmI_2 \longrightarrow \text{\Large$\diagdown$}C{=}\overset{\overline{}}{O} \;\; \overset{+}{SmI_2} \longrightarrow \text{Pinacol}$$
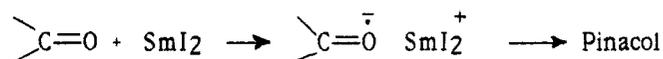
The C—C bond formation in the Barbier reaction is not fully elucidated. It could involve organometallic chemistry if the radical $R^{\bullet}$ is reduced by SmI_2 into $RSmI_2$. All attempts to prepare $RSmI_2$ from RX + SmI_2 failed (ref. 9), although such an organometallic species should be stable, since Grignard-like reagents have been prepared from the reaction of samarium metal on alkyl halides (ref. 12). Thus a radical coupling of $R^{\bullet}$ with a ketyl has been proposed. An alternative mechanism could be the direct addition of $R^{\bullet}$ on the carbonyl, followed by a fast reduction of the alkoxy radical.

The use of 6-bromohexenyl as the organic halide in the Barbier reaction with cyclohexanone mainly gave a cyclized product (ref. 12) :

This finding presumably involves a radical cyclization on the route leading to the product. The intramolecular Barbier reaction has been successfully achieved by Molander (ref. 18). Five and six-membered rings were obtained from various iodoketones and SmI_2 .

The coupling reaction (ref. 14) between acid chlorides leading to $\propto$-diketones is quite unusual. It has been discussed in the following way (ref. 15) :

The reaction involves the initial formation of an acyl radical which is believed to be reduced by SmI_2 into a diiodosamarium acyl complex. A mesomeric structure of alkoxycarbene can also be written, by analogy to a complex (t-BuCOLuCp_2$) prepared by Evans (ref. 19). We were unable to isolate the postulated samarium complex, but we devised experiments which can be interpretated as *in situ* trapping of the acylsamarium species by electrophiles (ref. 15). It involves the addition of a 1:1 mixture of an acid chloride and a ketone to a solution of SmI_2 in THF :

Various ketols have been obtained with isolated yields in the range of 50-70 % , after a few minutes at room temperature.

Diiodosamarium has been used since several years by many groups in Japan, USA or USSR for performing interesting chemistry. The main references till 1986 can be found in a review article (ref. 1).

NEW DEVELOPMENTS INVOLVING ACID CHLORIDES AND SmI₂

The reductive coupling between ketones and acid chlorides mediated by SmI_2 could be a useful way to introduce the side chain of corticosteroids, starting from a 17-ketosteroid:

This project needs to examine the reactivity at C_{17} and to establish the stereochemistry of reactions performed with SmI_2. Dehydroandrosterone (with protected OH) was taken as a model. Several reactions were successfully achieved in the presence of SmI_2 (Figure 3).
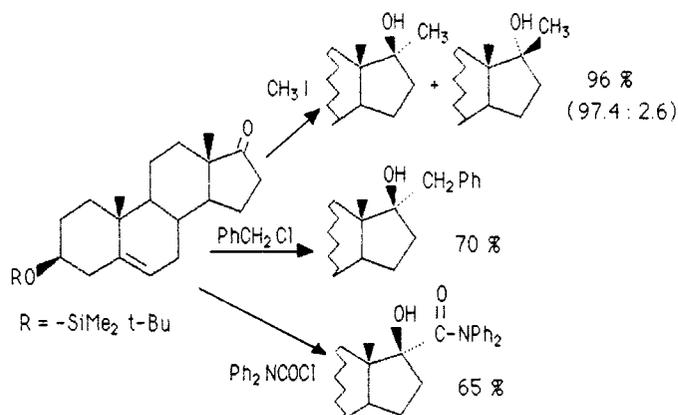

Figure 3 Reactions performed in THF at room temperature in the presence of 2 eq. of SmI_2

Barbier reaction with methyl iodide gave a tertiary alcohol attacking from usual α-side at C_{17} in a quantitative yield. The stereochemistry was established by comparison with an authentic sample. The 17 β OH / 17αOH ratio (97:3) is almost the same as that seen in the corresponding Grignard reaction performed with MeMgI. The reactions of $PhCH_2OCH_2COCl$ and $MeOCH_2COCl$ were then investigated on the same steroid. The structures of the isolated products were not the expected ones. The products are devoid of carbonyl group (Fig. 4). The reaction is quite general and
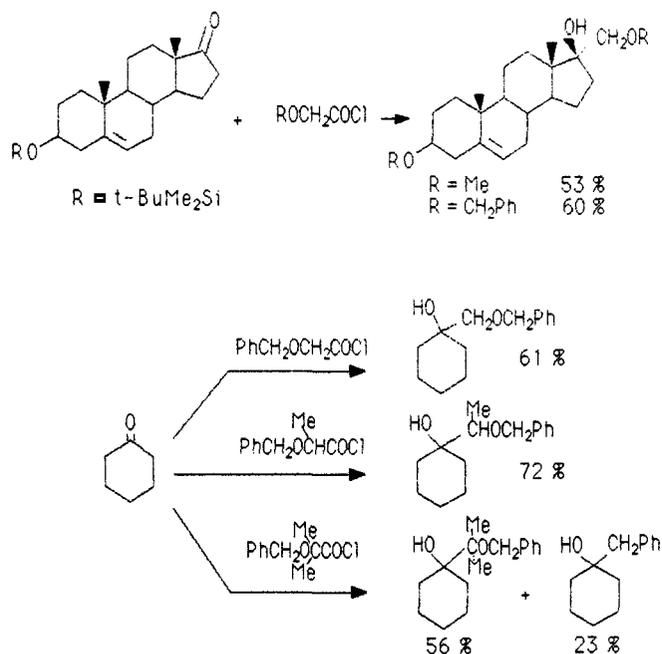

Figure 4

can give various kinds of glycol monoethers (ref. 20).The process is explained by a fast decarbonylation, presumably at the stage of the acyl radical :

$$ROCH_2COCl + SmI_2 \longrightarrow ROCH_2\overset{\bullet}{C}\text{-}O + SmI_2Cl$$
$$\downarrow$$
$$ROCH_2SmI_2 \longleftarrow ROCH_2{}^{\bullet} + CO$$
$$SmI_2$$
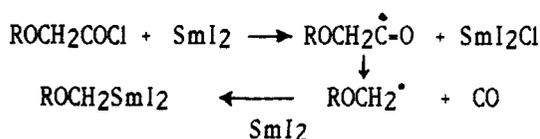
The driving force for the decarbonylation is the formation of a stabilized alkoxy radical. The initial formation of an acyl radical has been assumed in all the reactions involving an acid chloride and SmI_2 (ref. 15). It was interesting to try to trap intramolecularly such intermediates in a suitable model. For this purpose some salicylic acid derivatives were prepared (Fig. 5). The acid chlorides fastly react with SmI_2 to give products more complex than expected, since an additional cyclopropanol ring is formed (ref. 21). The yields in crude material are excellent, isolated yields in pure compounds are in the range of 50-60 % because of the instability of the products which partly decompose during the isolation procedure (flash-chromatography). Structures were established by spectroscopic methods (^{1} H and ^{13} C NMR, IR and MS). In the two first examples of Figure 5 only one stereoisomer is obtained, in the last case the product is a 10:1 mixture of *exo/endo* epimers.
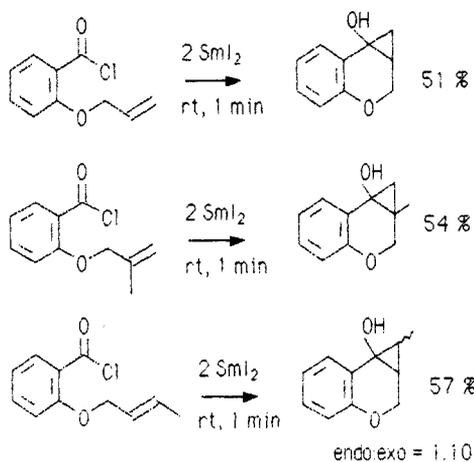
Figure 5 Cyclization in THF at room temperature in presence of 2 eq. of SmI_2
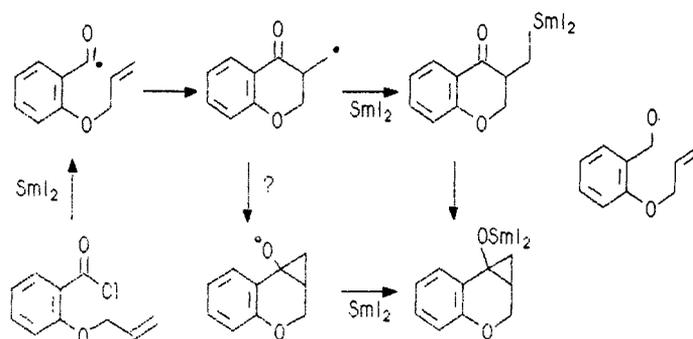
Figure 6 Tentative mechanism for cyclopropanol formation

The mechanism proposed for the reaction is indicated in Figure 6. The acyl radical has a high tendency to cyclize, as shown recently by Zard (ref. 22). It has been produced by the Barton method of photolysis of *S*-acyl xanthates (ref. 23). The last step of Figure 6, namely the intramolecular addition of an organosamarium species, is well supported by experiments of Imamoto et al.(ref. 24). These authors prepared cyclopropanols by treatment of iodomethylketones of type R-C(O)-CH(R)-CH_2I (*in situ* produced) by SmI_2 . The intramolecular carbene addition written in Figure 6 cannot fully be excluded but is unprecedented in lanthanide chemistry. More studies are needed to fully confirm mechanism of the reaction and to see the scope of this unusual transformation.

CHEMISTRY MEDIATED BY $SmCp_2$

There are evidences of a good stability of t-BuCOLuCp$_2$ (ref. 19). Cyclopentadienyl ligands should give an increased stability (by respect to iodide) to lanthanide complexes. Indeed we were able to produce at -20°C a stable acylsamarium complex from pivaloyl chloride and two equivalents of $SmCp_2$ (ref. 25). This complex, kept in THF solution at -20°C, further reacts with aldehydes to give α-ketols. This observation encouraged us to try to prepare organosamarium complexes from organic halides and $SmCp_2$, complexes that we did not previously obtain with SmI_2. We discovered that benzyl chloride as well as other benzylic halides reacts at room temperature with $SmCp_2$ (insoluble in THF), forming dark-brown solution of organosamarium complexes (ref. 26). These complexes are attacked by various electrophiles (D_2O, aldehydes, acid chlorides) to give the expected products. For example .
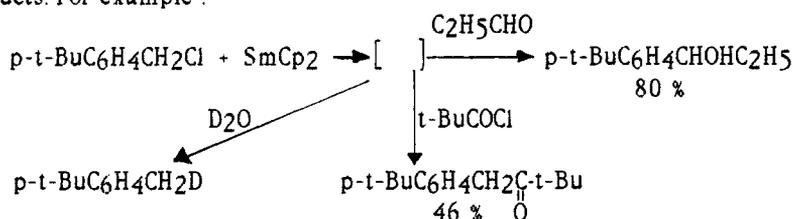
These observations are interesting, not only for synthetic applications in organic chemistry, but also for the possibility to develop a new route to organosamarium complexes with a carbon-samarium bond. Indeed organolanthanides have many unexpected properties, such as to promote CH activation of alkanes (ref. 27). Lanthanide hydrides ($(C_5Me_5)_2LnH$) are powerful homogeneous catalysts for hydrogenation of olefins (ref. 28), and can be formed by hydrogenation of the corresponding alkyllanthanides.

Dicyclopentadienylsamarium has been compared to SmI_2 in Barbier reactions (ref. 29). It gives much faster reactions than SmI_2 does.

CONCLUSION

Divalent lanthanides, especially diiodosamarium, are able to promote many types of organic reactions. Very often reactions are quite fast and selective. It is difficult to analyze the mechanistic details , because radical intermediates generate in the presence of an electron donor. Chemistry starting from acid chloride is quite unusual and deserves further investigation.

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