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## LANTHANIDES IN ORGANIC SYNTHESIS

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## 1. INTRODUCTION

Lanthanides are elements which were discovered between 1850(Ce) and 1945(Pm). The preparation of pure derivatives was not an easy task because in the ores the lanthanides are mixed together along with yttrium and thorium. The name "rare earths" applies to the lanthanides, yttrium and scandium.

Modern technology allows a clean separation of the lanthanides from each other. The yearly world production of lanthanides (mainly as oxides) can be estimated as 40,000 tons. Molycorp is the largest producer of lanthanides (as mixtures), while Rhone-Poulenc is the world leader in separated rare earths. Ore deposits are located in several countries ; the most important reserves are in China. The main uses of lanthanides are in ceramics and glasses (additives and dyes), metallurgy, electronics (magnetic or luminescence materials) and petrochemicals (catalytic cracking or oxidation catalyzed by lanthanide oxides). Apart from ceric oxidations the use of lanthanide derivatives in organic synthesis has developed only recently. Organolanthanide chemistry and structural investigations of molecular species are also in rapid evolution[1] allowing for a better understanding of the organic reactions induced by lanthanides. The 15 elements from lanthanum to lutetium constitute a unique family of closely related elements (the difference lying in the number of 4f electrons) from which can be expected reagents or catalysts with "tunable" chemical properties.

In this review we present the uses of lanthanides in organic synthesis by considering successively the lanthanides in an increasing state of oxidation: metals, Ln(II), Ln(III), Ln(IV). The main oxidation state is +3, hence, Ln(IV) compounds are powerful oxidants,[2] while divalent lanthanides are one-electron donors.[3] The chemistry of lanthanides is also characterized by the hardness of the metal centre. Lanthanide ions are usually considered as hard acids in the HSAB classification of Pearson, being located between Sr(II) and Ti(IV). However, some Ln(III) and Ln(II) complexes are able to coordinate strongly to phosphines.[4] Ln(IV), Ln(III) and Ln(II) derivatives undoubtedly are Lewis acids, as deduced from their chemical behaviour, but their properties are closely related to the nature of the ligands around the metal centre. Another characteristic feature of lanthanides is their strong affinity for oxygen. The oxophilicity of 4f-elements is difficult to quantify (for an indirect measure derived from the gas-phase dissociation of the diatomic species Ln(O), (see Ref. 5 and references quoted therein). Oxophilicity is a property which can be helpful for the activation of oxygenated organic functions.

For about a decade there has been an increasing interest of organic chemists in the lanthanides. Organic chemistry first benefited from the wide use of nmr shift reagents, but catalysts and reagents based on lanthanide derivatives are being investigated more and more, allowing interesting discoveries. Only a few reviews are available on the chemistry induced by lanthanides. Catalytic properties of lanthanide salts were reviewed as early as 1959.[6] The industrial applications of lanthanide oxides as catalysts are described in Ref. 7. The only review on ceric oxidations can be found in Ref. 2. In 1983–84 a review appeared on preparations of divalent lanthanides and their use in organic chemistry,[3] and one on applications of lanthanides [except Ln(IV)] in organic chemistry.[8] In 1985 a brief survey on use of lanthanides in organic synthesis appeared.[9] The same year a review on 4f-elements in organic synthesis[5] was published.

## 2. LANTHANIDE METALS

Most of the lanthanide metals are commercially available as ingots or powder. The cheapest metals are lanthanum ($823/kg), cerium ($637/kg), samarium ($1595/kg), neodymium ($1295/kg), praseodymium ($1954/kg). These prices apply to ingots of 99.9% purity (Aldrich catalog, 1985–86). Only a few attempts have been made to check the properties of these metals towards organic compounds.

### 2.1. *Alloys*

Lanthanide metals give intermetallic compounds with various metals (Ni, Co, Mg, etc.) which behave in presence of molecular hydrogen as a "hydrogen sponge." One of these hydride alloys was recently used as a reagent for the reduction of alkenes, alkynes and aldehydes.[10] $LaNi_5H_6$ exhibits a reactivity pattern (Table 1) different from standard hydrogenation catalysts (e.g. Raney nickel, Pd, Rh) in that it is not poisoned by thiophene. $SmMg_3$ reacts with anthracene dissolved in THF to give a complex which absorbs hydrogen and then catalyzes the hydrogenation of ethylene.[11]

### 2.2. *Vapours*

Vaporization of Sm or Yb onto a THF matrix gives small metallic particles. Vaporized Sm is a good catalyst for the hydrogenation of olefins but not of alkynes.[12] It also catalyzes the rapid transformation of methylacetylene into allene at 0°.

### 2.3. *Reactions in liquid ammonia*

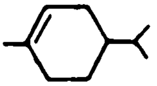
Europium and ytterbium metal dissolve in liquid ammonia to give blue solutions containing ammoniated electrons [and Eu(II) or Yb(II) ions]. They are the only lanthanide metals to do so. Ytterbium was used by White and Larson[13] for the reduction of aromatic systems in a Birch-type reaction (Table 2). Carbon-carbon double bonds of conjugated ketones are also reduced in liquid $NH_3$/EtOH solution. In absence of ethanol the formation of pinacols is observed.

Many Yb(II) complexes can be generated from liquid ammonia solutions of Yb by the addition of various organic substrates (cyclopentadiene, cyclooctatetraene, acetylenes, etc.). This point is beyond the scope of the present review, for more details see Refs. 1, 3.

### 2.4. *Reactions in organic solvents*

Barbier-like reactions have been observed between organic iodides and ketones using Yb or Sm suspended in THF (see part II—Table 6).[36] Cerium mediated Barbier-type and Reformatsky-type

Table 1. Reduction by $LaNi_5H_6$[10]

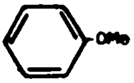
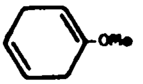
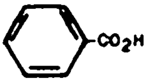
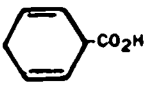
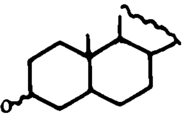
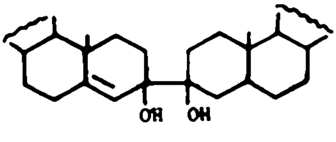
| Compound | Product[a] | Isolated yield (%) |
|---|---|---|
| $n$-$C_{10}H_{21}CH{=}CH_2$ | $n$-$C_{12}H_{26}$ | 86 |
| Limonene |  | 88 |
| $Ph{-}C{\equiv}C{-}Ph$ | $PhCH_2CH_2Ph$ | 96 |
| $Me_2C{=}CH(CH_2)_2C(Me){=}CHCHO$ | $Me_2C{=}CH(CH_2)_2CH(Me)CH_2CHO$ | 89 |
| $n$-$C_{11}H_{23}CHO$ | $n$-$C_{11}H_{23}CH_2OH$ | 98 |
| $n$-$C_6H_{13}COMe$ | $n$-$C_6H_{13}CH(OH)Me$ | 91 |
| $PhCH{=}NC_6H_{11}$ | $PhCH_2NHC_6H_{11}$ | 97 |
| $p$-$NO_2C_6H_4CO_2Et$ | $p$-$NH_2C_6H_4CO_2Et$ | 97 |
| Sulfoxides, sulfones, oximes | no reaction | |

[a] Reaction in THF-MeOH (2 : 3) from 0° to room temperature.

reactions were recently investigated by Imamoto *et al.*[14] Most of the experiments were performed in THF with cerium amalgam or with cerium turnings in presence of a catalytic amount of mercury(II) chloride. Many allyl or propargyl halides and carbonyl compounds smoothly lead to homoallylic alcohols (Table 3), while β-hydroxyesters are obtained in good yields from α-bromo- and α-iodoesters (Table 4). The reaction of ethyl iodoacetate and 2-furaldehyde proceeds even at −70°. The mechanism of these reactions was not investigated. This method is promising, since it uses a metal which is available as the ingot at moderate price.

Various metals used as powder (Ce, La, Nd, Sm) were recently found to give an organolanthanide when attacked by ethyl-2-bromopropionate in THF.[15] The reagent (of hypothetical structure A) readily reacts at room temperature with ketones to lead to γ-lactones with yields in the range of 60–70% (pinacols are the by-products).

Table 2. Reduction by ytterbium in liquid ammonia[13]

| Compound | Product[a] | Yield (%) |
|---|---|---|
|  |  | 80 |
|  |  | 56 |
| $Ph{-}C{\equiv}C{-}Ph$ | E-$PhCH{=}CHPh$ | 75 |
| Cholestenone |  | 80[b] |
| Cholestenone |  | "Major product" |

[a] Reactions performed in presence of EtOH, except for the last entry.
[b] After $CrO_3$ oxidation of the crude alcohol.

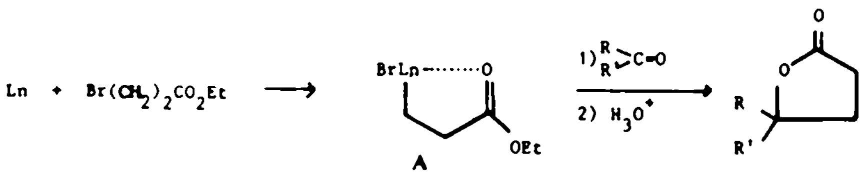
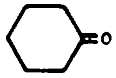
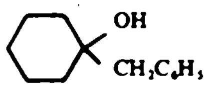


Table 3. Cerium amalgam mediated synthesis of homoallylic alcohols[14]

| Halide | Carbonyl compound | Product[a] | Isolated yield (%) |
|---|---|---|---|
| $CH_2{=}CH{-}CH_2I$ | $p$-$BrC_6H_4COCH_3$ | $p$-$BrC_6H_4C(OH)(CH_3)CH_2CH{=}CH_2$ | 95 |
| $C_6H_5CH_2I$ | $C_6H_5COCH_3$ | $C_6H_5C(OH)(CH_3)CH_2C_6H_5$ | 84 |
| $C_6H_5CH_2I$ |  |  | 59 |
| $CH_2{=}C(CH_3)CH_2I$ |  |  | 59 |
| $CH_2{=}C(Me)CH_2I$ | $MeCO{-}C_6H_4{-}(CH_2)_2COOMe$ | $CH_2{=}C(Me)CH_2C(OH)(Me){-}C_6H_4(CH_2)_2{-}COOMe$ | 89 |
| $HC{\equiv}CCH_2I$ | $p$-$ClC_6H_4CHO$ | $p$-$ClC_6H_4CHOHCH_2C{\equiv}CH$ | 65 |
| | | $p$-$ClC_6H_4CHOHCH{=}C{=}CH_2$ | 27 |
| $CH_2{=}CHCH_2Br$ | 2-acetylnaphthalene | $C_{10}H_7{-}C(OH)(CH_3)CH_2CH{=}CH_2$ | 71 |
| $CH_2{=}CHCH_2Br$ | $p$-$CH_3O{-}C_6H_4COCH_3$ | $p$-$CH_3O{-}C_6H_4C(OH)(CH_3)CH_2CH_2CH{=}CH_2$ | 85 |

[a] Reactions were performed in THF from 0° to room temperature for iodides, and at room temperature for bromides.

Table 4. Reformatsky reaction using cerium metal[14]

| α – Halo ester | Carbonyl compound | Temperature (°C) | β – Hydroxyester yield (%) |
|---|---|---|---|
| $ICH_2COOEt$ | $n$-$C_5H_{11}CHO$ | 0 | 63 |
| $ICH_2COOEt$ | 2-furaldehyde | −70 | 76 |
| $ICH_2COOEt$ | $C_6H_5CHO$ | 0 | 81 |
| $ICH_2COOEt$ | cyclododecanone | 0 | 75 |
| $ICH_2COOEt$ | $p$-$NO_2C_6H_4COCH_3$ | −40 | 74 |
| $BrCH_2COOEt$ | $C_6H_5COCH_3$ | r.t. | 60 |

## 3. LANTHANIDES(II)

### 3.1. *Introduction*

The dipositive oxidation state is unusual for the lanthanides. The divalent state is easily attained only with europium ($Eu^{2+} = 4f^7$), samarium ($Sm^{2+} = 4f^6$) and ytterbium ($Yb^{2+} = 4f^{14}$), which are characterized by half-filled, nearly half-filled or filled 4f subshells, respectively. The $E^0_{aq}$ values ($Ln^{3+}/Ln^{2+}$) are $-0.35$ V, $-1.15$ V and $-1.55$ V for europium, ytterbium and samarium, respectively.[3] Divalent europium salts are quite stable in water, whereas $Sm^{2+}$ and $Yb^{2+}$ reduce water rapidly. The $E^0_{aq}$ values provide qualitative information on the relative reducing properties of $Ln^{2+}$ versus organic compounds. On this basis it is predicted that the reactivity sequence will be: Sm(II) > Yb(II) > Eu(II). Indeed, the most interesting reactions arise from $Sm^{2+}$ derivatives which are also prepared from the cheapest of the three lanthanides.

### 3.2. *Preparation of Ln(II) derivatives*

A set of convenient methods are now available for the preparation of many Ln(II) complexes, only a few of which will be presented here. (For a review covering Yb(II) and Sm(II) preparations, see Ref. 3.)

$EuCl_2$ is easily obtained by reduction of $EuCl_3$ with amalgamated zinc in acidic medium. $SmI_2$ and $YbI_2$, which are soluble in THF, are easily prepared by reaction (1):

$$Ln + ICH_2CH_2I \rightarrow LnI_2 + CH_2{=}CH_2 \qquad (1)$$

(Sm or Yb ingots or powder)

The procedure is quite simple, and is detailed in various papers.[16-20,49] $SmI_2$ and $YbI_2$ solutions (0.1 M) can be stored under nitrogen for a long period of time. They are convenient starting material for the preparation of more sophisticated complexes thanks to the methathesis reaction (2).

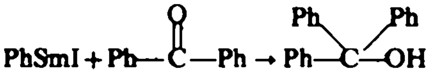
$$LnI_2+2\,NaA \rightarrow LnA_2+2\,NaI \qquad (2)$$

For example, by this method $SmCp_2$ (insoluble in THF)[17] is easily available.

Most of the organic transformations have been realized with Sm(II) (namely $SmI_2$), the best electron donor in the series Eu(II), Yb(II), Sm(II). Yb(II) is sometimes useful, whereas Eu(II) seems quite unreactive except in a few cases.

### 3.3. *C—C bond formation mediated by Ln(II) derivatives*

3.3.1. *Ln(II) organometallics*. D. F. Evans *et al.*[21,22] were the first to prepare and study Grignard analogues based on Eu(II), Yb(II) and Sm(II). The most conveniently obtained are RYbI species (from Yb and RI). They are soluble in THF and their solutions react as typical Grignard reagents :

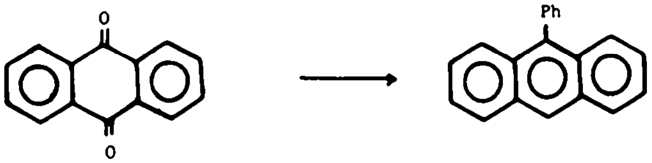


$$PhSmI+Ph\text{—}\overset{\displaystyle O}{\overset{\|}{C}}\text{—}Ph \rightarrow Ph\text{—}\overset{Ph\quad Ph}{C}\text{—}OH \qquad (72\%)$$

$$PhYbI+ClSi(CH_3)_2Ph \rightarrow PhSi(CH_3)_3 \qquad (73\%)$$

$$PhYbI+PhN{=}C{=}O \rightarrow PhCONHPh \qquad (52\%)$$

More recently, reactions of the "RYbI" reagent were reinvestigated by Fujiwara *et al.*[23,26] PhYbI (prepared from Yb and PhI at 30° in THF) reacts with allyl bromide or iodide at room temperature in moderate yield (30%).[26] The coupling reaction with either *cis* or *trans*-styryl bromide catalyzed by CuBr occurs with retention of configuration at the vinylic center. PhYbI reacts with ketones, aldehydes, esters and nitriles leading to alcohols and ketones.[23,25] An unusual selectivity towards ester functions compared to ketones was found. This is a reversed trend compared to Grignard reagents. It is also interesting to note that ketones are formed from the esters as well as from benzoyl chloride.[24] PhYbI and MeYbI react with $\alpha,\beta$-unsaturated carbonyl compounds (acrolein, chalcone, 2-cyclohexen-1-one . . .) to give exclusively 1,2-addition.[25] The same behaviour was observed by Beletskaya *et al.*[27] for the reaction of PhLnI (Ln = Eu, Yb, Sm) with chalcone, yields being in the range of 55 to 80%. These authors have also investigated the addition of PhLnI to carbonyl compounds;[28] the best results are obtained with PhYbI. It is interesting to note that deoxygenation was observed by the action of an excess of the organolanthanide reagent on the intermediate carbinolate.[29,30] Thus, anthraquinone reacts with four equivalents of PhYbI to give 60% of 9-phenylanthracene as the only product.



Aromatic substitution on hexafluorobenzene occurs readily in THF at 30° with better selectivity and yields than the Grignard or organolithium reagents:[31]

$$PhYbI+C_6F_6 \rightarrow YbFI+C_6F_5Ph \qquad (70\%)$$

Deacon *et al.*[31-33] prepared diorganoytterbium *in situ* from organomercury compounds in THF. They found that these react at room temperature in THF with aromatic and aliphatic aldehydes and ketones. Addition to the carbonyl group occurs to give alcohols with yields in the range of 40–80%.

Divalent organolanthanides [especially Yb(II) and Sm(II)] are interesting species because of their dual reactivity either as Grignard-like reagents or one-electron donors (Ln(II) → Ln(III) + $e^-$). Most of their properties seem to be related to a Grignard-type behaviour (with some special specificities which need to be further explored). However, their reducing character appears in some reactions. Thus, $YbR_2$ reacts with benzophenone with the formation of benzophenone pinacol.[32] PhYbI and $PhCH_2Br$ in presence of CuBr as catalyst gives dibenzyl instead of the expected diphenylmethane.[26] Carboxylation of $(C_6F_5)_2Yb$ furnished a mixture of $C_6F_5CO_2H$ and o-H—$C_6F_4CO_2H$.[33]

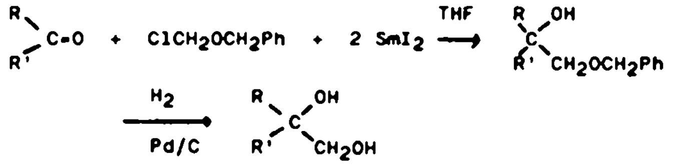
3.3.2. *Barbier-like reactions.* The first evidence of the possibility of using Ln(II) species as a soluble electron-donor in a Barbier-like reaction came from $SmI_2$ chemistry, as described by Namy, Girard and Kagan:[16]

$$RX + R'C(=O)R' + 2\,SmI_2 \longrightarrow R\text{-}C(R')(R')\text{-}OSmI_2 \xrightarrow{H^+} R\text{-}C(R')(R')\text{-}OH$$

This reaction was found to be of wide generality and its scope and mechanism was studied.[16,18-20] This one-pot reaction is especially easy to realize because of the accessibility of $SmI_2$ and the stability of its THF solutions when protected from oxygen.[17,18,20] Representative results are listed in Table 5. The reaction proceeds at room temperature or at the reflux temperature of THF according to the structure of the reactants. A catalytic amount of $FeCl_3$ strongly accelerates the reaction (entry 3). $SmI_2$ does not allow clean condensation between alkyl halides and aldehydes. A mixture of products arise from Meerwein–Ponndorf–Verley–Oppenauer reactions which occur between the intermediate alcoholate and aldehyde.[16,35] Unfortunately, unsymmetrically substituted allylic halides do not react regiospecifically (entry 15). However, allyl and benzyl halides give good reactions with aldehydes. Ester groups are compatible with the reaction (entries 9, 10). Selective reactions are possible when unsymmetric dihalides are used (entries 6, 8). The mechanism of the Barbier-like reaction has been investigated, electron-transfer reactions with radical intermediates are likely.[34]

Molander and Etter[36] were able to prepare bicyclic alcohols through the cyclization of 2-(n-haloalkyl)cycloalkanones (n = 3, 4) mediated by low valent lanthanides, mainly $SmI_2$, $YbI_2$, Sm or Yb (Table 6). The selectivity observed with ytterbium with respect to samarium was ascribed to differences in size (Ln—O bond) and solvation. The reaction occurs under kinetic control since experiments showed the absence of epimerisation.

The Barbier reaction mediated by $SmI_2$ was used by Imamoto *et al.*[37] for the hydroxymethylation of carbonyl compounds:



$$RR'C{=}O + ClCH_2OCH_2Ph + 2\,SmI_2 \xrightarrow{THF} RR'C(OH)CH_2OCH_2Ph \qquad (A)$$

$$\xrightarrow[Pd/C]{H_2} RR'C(OH)CH_2OH \qquad (B)$$

Table 5. Barbier reaction using $SmI_2$[16,18-20]

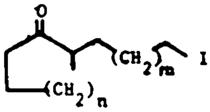
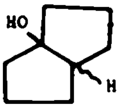
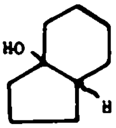
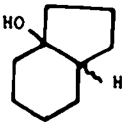
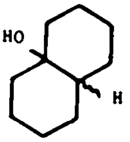
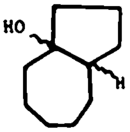
| Entry | Carbonyl compound | RX | Conditions[a] | Products | Yield (%) |
|---|---|---|---|---|---|
| 1 | 2-octanone | $CH_3I$ | 25°, 1 h | n-$C_7H_{15}$—$C(OH)(CH_3)_2$ | 95 |
| 2 | 2-octanone | n-BuI | 65°, 8 h | 5-methylundecan-5-ol | 76 |
| 3 | 2-octanone | n-BuI | 25°, 3 h[b] | 5-methylundecan-5-ol | 73 |
| 4 | 2-octanone | n-BuI | 65°, 12 h[c] | 5-methylundecan-5-ol | 97 |
| 5 | 2-octanone | n-BuOTs | 65°, 12 h | 5-methylundecan-5-ol | 49 |
| 6 | 2-octanone | $I(CH_2)_6Cl$ | 65°, 1 day | 1-chloro-7-methyltridecan-7-ol | 74 |
| 7 | Cyclohexanone | allyl bromide | 25°, 20 min | 1-allylcyclohexanol | 69 |
| 8 | 2-octanone | 1,3-dichloro-propene | 25°, 20 days | 1-chloro-4-methyl-1-decen-4-ol | 84 |
| 9 | Cyclohexanone | ethyl bromo-propionate | 25°, 10 min | ethyl 2-(1-hydroxycyclohexyl)propionate | 51 |
| 10 | 2-octanone | $TsO(CH_2)_9CO_2Me$ | 65°, 10 h[d] | methyl 11-hydroxyl-11-methylheptodecanoate | 63 |
| 11 | 2-octanone | allyl bromide | 25°, 10 min | n-$C_7H_{15}$—CHOH—$CH_2$—CH=$CH_2$ | 53 |
| 12 | 2-octanone | benzyl bromide | 25°, 3 min | n-$C_7H_{15}$—$CHOHCH_2Ph$ | 86 |
| 13 | Isobutyraldehyde | benzyl bromide | 25°, 3 min | i-Pr—CHOH—$CH_2Ph$ | 87 |
| 14 | Pivaldehyde | allyl iodide | 25°, 5 min | t-BuCHOH—$CH_2$—CH=$CH_2$ | 78 |
| 15 | 2-octanone | cinnamyl chloride | 25°, 40 min | 1-phenyl-4-methyl-1-decen-4-ol<br>3-phenyl-4-methyl-1-decen-4-ol | 50<br>35 |

[a] Stoichiometry [C=O]/[$SmI_2$]/[RX] = 1:1:2 unless otherwise stated. For more details see the experimental section of refs 16–20.

[b] In presence of 0.1 mol eq of $FeCl_3$.

[c] Stoichiometry [C=O]/[$SmI_2$]/RX = 1:3:3.

Table 6. Barbier cyclization methodology involving lanthanides[37]

| Reactant[a] | Product yield (%) | Cis/trans ratio | Ln agent |
|---|---|---|---|
|  | | | |
| n = 1 m = 1 |  60 | 99.5:0.5 | [b] |
| n = 1 m = 2 |  67 | 18:1 | [b] |
| n = 2 m = 1 |  75 | 1.3:1 | [b] |
| n = 2 m = 2 |  75 | 1.5:1 | [b] |
| n = 3 m = 1 |  85 | 2.0:1 | [b] |
| n = 3 m = 1 | 77 | 3.1:1 | [c] |
| n = 3 m = 1 | 59 | 6.9:1 | [d] |
| n = 3 m = 1 | 71 | 4.1:1 | Sm |
| n = 3 m = 1 | 77 | 6.7:1 | Yb |

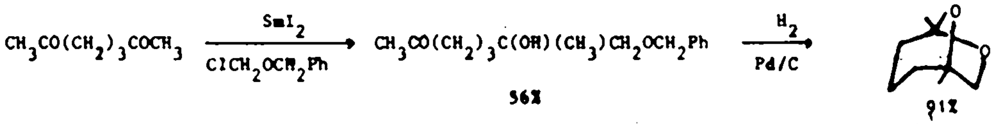
[a] Reaction in THF at room temperature.

[b] 2 mol eq $SmI_2$, catalytic $Fe(PhCOCHCOPh)_3$.

[c] 2 mol eq $SmI_2$.

[d] 2 mol eq $YbI_2$, catalytic $Fe(PhCOCHCOPh)_3$.

Carbinol A was isolated in good yields from ketones; the reaction proceeds in a few hours at room temperature. This method allowed a short synthesis of frontalin:

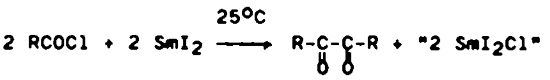


The reaction with aldehydes does not result in the formation of carbinol A because of the fast pinacol formation induced by $SmI_2$ (see Table 4). This side-reaction could be suppressed by the addition of tetraethyleneglycol dimethyl ether or dibenzyl ether (1 mol equiv. with respect to $SmI_2$) which acts as a complexing agent of $SmI_2$. Thus, A(R = H, R′ = $PhCH_2CH_2$) was isolated in 60% yield.

3.3.3. *Pinacol formation.* $SmI_2$ is an excellent reagent for the formation of pinacols from aldehydes in aprotic THF solutions. Aromatic aldehydes usually give high yields of pinacols at room temperature after one minute. Aliphatic aldehydes lead to pinacols after a few hours, while aliphatic ketones require a day.[18,38]

3.3.4. *Coupling reactions of allylic and benzylic halides.* Benzyl halides are rapidly transformed into 1,2-diphenylethane in presence of one equivalent of $SmI_2$.[20] Cinnamyl halides or unsymmetrical allylic halides also lead to coupling, but without enough regioselectivity to give a useful synthetic process. It is interesting to note that in presence of aldehydes or ketones the dimerization is completely suppressed in favor of the Barbier reaction.[19,20] Alkyl halides RX upon heating in the presence of $SmI_2$ in THF are reduced to alkanes RH to the exclusion of coupled products R-R.

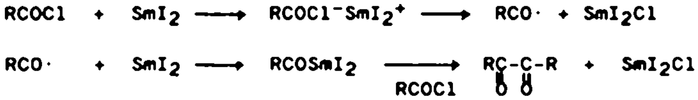
3.3.5. *Acid chlorides.* Surprisingly, acid chlorides in presence of one or two equivalents of samarium diiodide in THF do not lead to reduction products such as aldehydes or primary alcohols. In all cases which were investigated[39,40] the following transformation was observed:



$$2\ RCOCl + 2\ SmI_2 \xrightarrow{25^{\circ}C} R-\underset{O}{\underset{\|}{C}}-\underset{O}{\underset{\|}{C}}-R + \text{"}2\ SmI_2Cl\text{"}$$

The reaction is very fast with aromatic acid chlorides and requires only a few minutes. Isolated yields are 78%, 69% and 72% for R = phenyl, *p*-methoxyphenyl and *p*-chlorophenyl, respectively. The end-point of the reaction is indicated by the disappearance of the blue-green color of $SmI_2$. Yields are lower with aliphatic acid chlorides. Thus, for R = $n\text{-}C_8H_{17}$ diketone was isolated in 50% yield after a reaction time of 10 min. When R = *t*-Bu an α-ketol was isolated (46%) instead of the α-diketone.

The mechanism of this unusual reaction is believed[39] to be as follows:

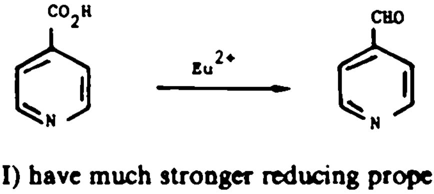


$$RCOCl + SmI_2 \longrightarrow RCOCl^{-}SmI_2^{+} \longrightarrow RCO\cdot + SmI_2Cl$$
$$RCO\cdot + SmI_2 \longrightarrow RCOSmI_2 \xrightarrow[RCOCl]{} R\underset{O}{\underset{\|}{C}}-\underset{O}{\underset{\|}{C}}-R + SmI_2Cl$$

The acylsamarium intermediate could not be isolated but was trapped by other electrophiles besides RCOCl.[39] This gave a method to prepare α-ketols from an equimolar mixture of an acid chloride and an aldehyde or ketone. This mixture in THF is poured into a THF solution of $SmI_2$ at room temperature. Under these conditions, the acyl anion species is formed and trapped by the carbonyl compound. Some examples are given in Table 7. There are as yet no examples of intramolecular reactions of acid chlorides mediated by $SmI_2$; it was found that $SmI_2$ is ineffective in cyclizing dodecandioyl dichloride.[41]

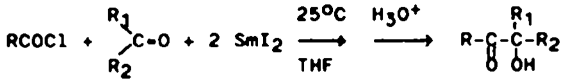
### 3.4. *Reduction by Ln(II) derivatives*

3.4.1. *Carbonyl groups.* One of the early attempts[42] to use divalent lanthanides was the reduction of *isonicotinic acid* by Eu(II) salts:



Samarium(II) and ytterbium(II) have much stronger reducing properties than europium(II). THF solutions of $SmI_2$ in presence of methanol have reducing properties towards *aldehydes*.[16,20] $SmI_2$ often gives quantitative reductions of aldehydes to alcohols at room temperature, while $YbI_2$ is quite inefficient. Under the same conditions ketones are reduced much more slowly. The mechanism of carbonyl reduction by $SmI_2$ has been discussed.[34] The initial formation of a ketyl radical $R(R')C{=}O^{\dot{-}}$ was proposed. In the absence of methanol, there is a dimerization to the pinacol (see Table 4). Protonation by methanol gives the hydroxy-radical ($R(R')\dot{C}{-}OH$) which is further reduced

Table 7.[39]



$$RCOCl + R_1R_2C{=}O + 2\ SmI_2 \xrightarrow[THF]{25^{\circ}C} \xrightarrow{H_3O^+} R{-}C({=}O){-}C(R_1)(R_2){-}OH$$

| R | $R_1$ | $R_2$ | Reaction time | Yield (%) |
|---|---|---|---|---|
| Ph | Ph | H | 0.5 min | 86 |
| $t$-Bu | Et | H | 4 min | 64 |
| $t$-Bu | Et | Et | 3 min | 83 |
| $n$-$C_8H_{17}$ | Et | H | 1.5 min | 63 |
| $Ph_2N$ | $n$-$C_7H_{15}$ | H | 40 min | 67 |

by $SmI_2$ to the carbanion $R(R')\bar{C}$—OH which is subsequently protonated. A minor pathway involves H abstraction from THF or $CH_3OD$ by the hydroxyalkyl radical. This was supported by the use of MeOD which gives 90% RCHDOH and 10% $RCH_2OH$ from RCHO. $SmI_2$ or $YbI_2$ solutions do not reduce esters or acids.

3.4.2. *Conjugated C=C double bonds*. Cinnamic acid and its ethyl ester are reduced at room temperature in excellent yields:[20]

$$C_6H_5CH{=}CH{-}CO_2R + 2\ LnI_2 + 2\ MeHO \rightarrow C_6H_5{-}CH_2CH_2CO_2R$$

R = H or Et 98%

Ln = Yb or Sm

Apart from this special case there is no other report of reductions of C=C double bonds of conjugated acids or esters. Hydrogenolysis was observed[43] in the following example:

$$CH_3CH(OH)CH{=}C(Me)CO_2Et + 2\ SmI_2 \rightarrow CH_3CH{=}CH{-}CH(Me)CO_2Et \quad (90\%)$$

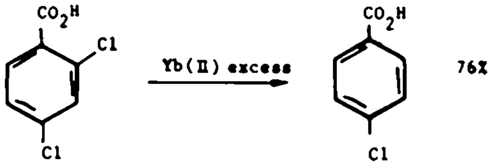
In conjugated aldehydes and ketones there is competition between C=C and C=O reductions.[20]

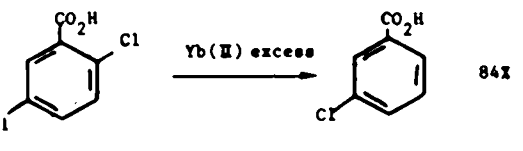
3.4.3. *Organic halides*. THF solutions of $SmI_2$ are moderately reactive at room temperature towards primary and secondary alkyl halides RX. However RX is completely transformed into the alkane RH after reflux for several hours[20] with the total absence of coupling product R-R. As predicted from redox potentials the reactivity decreases in the following order: RI > RBr > RCl. Phenyl and vinyl halides are unreactive, except for 1-iodo naphthalene which is reduced to naphthalene.[18] Allylic or benzylic halides give a coupling reaction exclusively (see above).

The reduction of RX is initiated by a one-electron transfer from $SmI_2$ giving $R^{\cdot}$ (perhaps through $RX^{\cdot}$). The organic radical $R^{\cdot}$ can either (R = alkyl) abstract hydrogen from THF to give RH or dimerize to R-R (when R = allyl or benzyl). The competitive reduction of $R^{\cdot}$ by $SmI_2$ to the organometallic species $RSmI_2$ generally does not occur. Hydrogenolysis by $D_2O$ after the disappearance of $SmI_2$ only gives RH, the hydrogen coming from a THF molecule which is presumably coordinated to a samarium atom.[34]

The reaction of $YbI_2$ with $IC_5Me_5$ produces $YbI_3$. The fate of the organic moiety was not studied.[44] Trace amounts of LiI catalyze the reaction, presumably via the formation of $YbI_3$ and an inner sphere electron transfer.

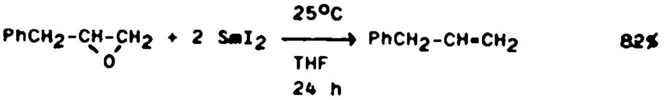
Selective removal of ortho halogens in halogenobenzoic acids was obtained by using an excess of $(C_6F_5)_2Yb$ in THF.[45] The reaction is especially facile with polyhalosubstituted benzoic acids:





A mechanism was proposed which involves transient formation of a carboxylate Yb(II) complex $(C_6F_5)YbO-\underset{\underset{O}{\|}}{C}-Ar$ by protolysis. Electron transfer to the ortho halogen via a six-membered transition state, followed by hydrogen capture from THF by the ortho aryl-radical is then postulated. $YbI_2$ transforms $C_6F_5CO_2H$ into a mixture of 2,3,4,5- and 2,3,5,6-tetrafluorobenzoic acids.[33]

3.4.4. *Deoxygenation reactions*. $SmI_2$ in THF deoxygenates *epoxides* smoothly:[20]

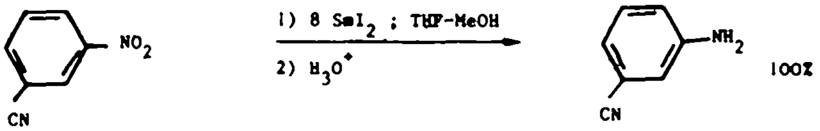


$$PhCH_2-\underset{\diagdown O \diagup}{CH-CH_2} + 2\ SmI_2 \xrightarrow[\text{THF, 24 h}]{25°C} PhCH_2-CH=CH_2 \quad 82\%$$

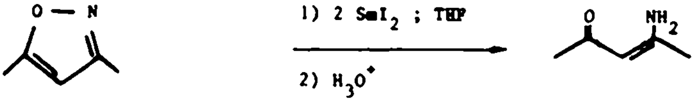
$Sm(C_5Me_5)_2$ (two equivalents) was transformed by reaction with epoxypropane into the complex $(C_5Me_5)_2Sm-O-Sm(C_5Me_5)_2$ whose structure was established by X-ray crystallography.[47] By analogy, when $SmI_2$ is used to remove an oxygen atom, the formation of a complex $I_2SmOSmI_2$ can be postulated. This species later disproportionates into $SmI_3$ (which usually precipitates) and a soluble species "SmIO" whose exact structure was not established.

Sulfoxides are transformed into sulfides; for example Ph—SO—Ph is reduced to Ph—S—Ph (90%) by $SmI_2$ after 2 hours at 65° in THF.[20]

3.4.5. *Reactions of nitrogen compounds*. Little information is currently available. Several imines and oximes were reduced by $SmI_2$ in THF containing methanol.[18] Both aromatic and aliphatic nitriles are unreactive towards $SmI_2$. Nitroaromatics are rapidly reduced to amines, allowing some selective reductions:[20]

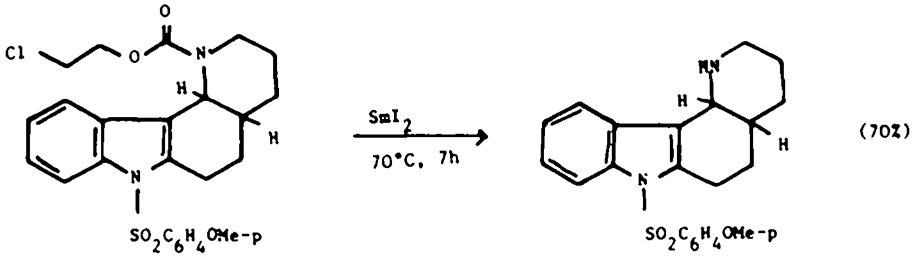


Natale studied[48] the cleavage of the N—O bond of isoxazoles by $SmI_2$:

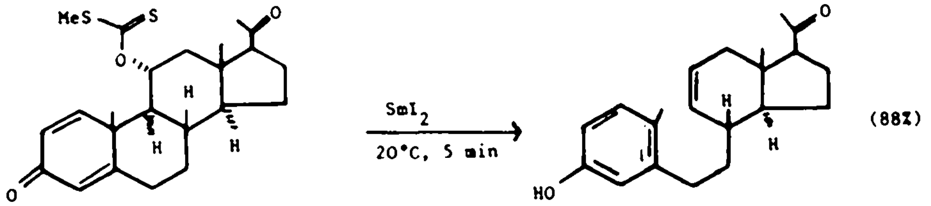


The isoxazole ring can be considered as a protected form of a 1,3-diketone.

3.4.6. *Fragmentation reactions*. Magnus *et al.*[42,51] used the strong electron-donor properties of $SmI_2$ for selective cleavage of a 2-chloroethyl carbamate where many other reducing agents had failed (Zn/AcOH, $CrCl_2$/HCl, $Bu_3SnH$/AIBN . . .):

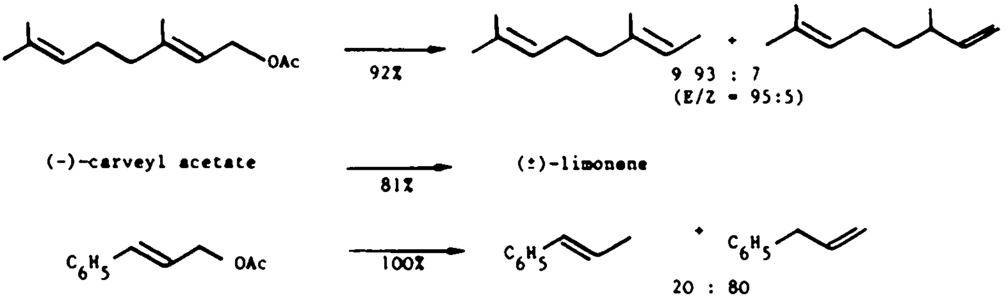


The same authors obtained a very clean fragmentation of an 11-steroidal xanthate into a 9,10-seco-steroid whereas $Bu_3SnH$/AIBN or $Li/NH_3$ gave a mixture of products:

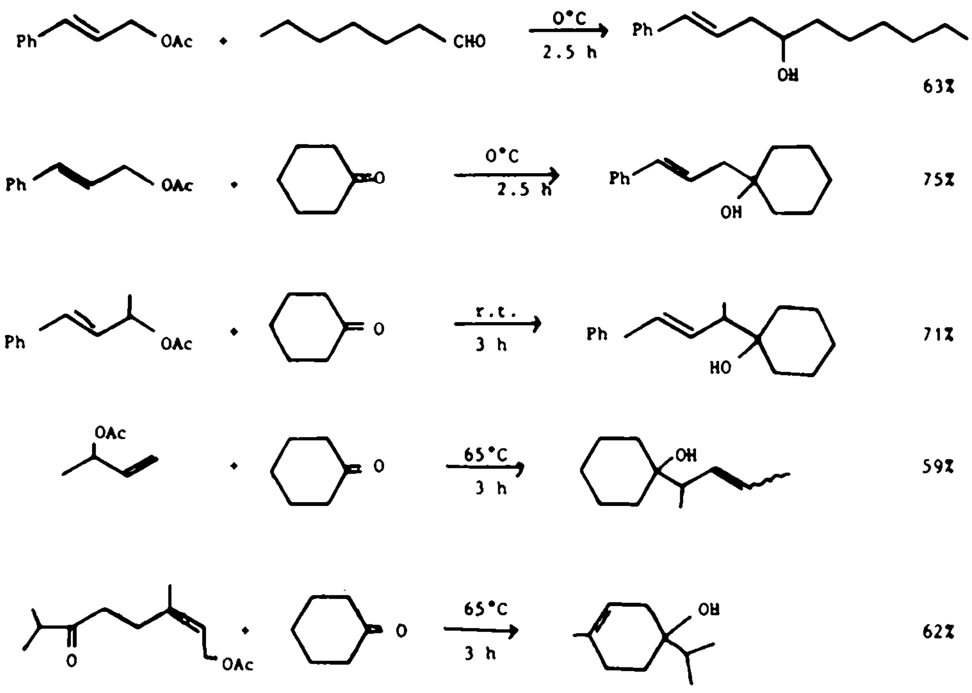


The success of this fragmentation was ascribed to the ability of $SmI_2$ to rapidly give two one-electron transfers to the xanthate moiety, avoiding accumulation of a radical intermediate.

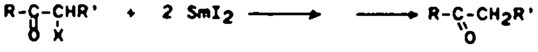
3.4.7. *Allylic acetates.* Allylic acetates were recently reduced efficiently to alkenes by Inanaga *et al.*[52] with 2 eq of $SmI_2$ and 1 eq of isopropanol in THF at room temperature, in the presence of a catalytic amount of a palladium (O) complex.



Allylic acetates are coupled with carbonyl compounds by 2 eq. of $SmI_2$ in THF in the presence of 1% mol eq. of $Pd(PPh_3)_4$[53] to give homoallylic alcohols, the overall process being similar to a Barbier-like reaction. The Pd(O) catalyst could be replaced by the combination $NiCl_2/PPh_3$ (1 : 2). Some examples using a Pd(O) catalyst are indicated below:

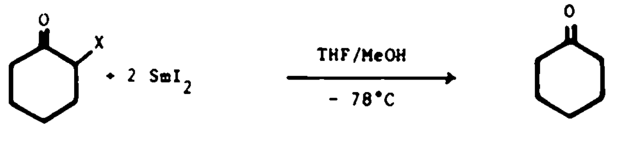


3.4.8. *α-Hetero substituted ketones.* Recently it was found that $SmI_2$ is the reagent of choice for the reduction of α-hetero substituted ketones to ketones:[54,55]

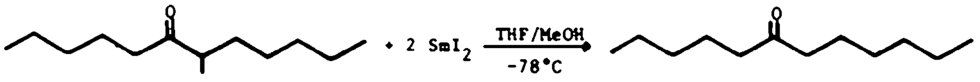


$$\mathrm{R{-}\underset{\displaystyle\overset{\|}{O}}{C}{-}\underset{\displaystyle X}{\underset{|}{CHR'}}} \quad + \quad 2\ \mathrm{SmI_2} \longrightarrow \quad \longrightarrow \mathrm{R{-}\underset{\displaystyle\overset{\|}{O}}{C}{-}CH_2R'}$$

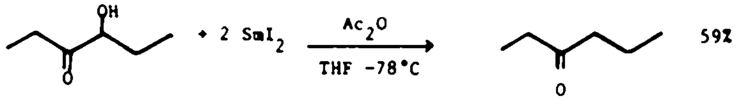
The reaction was studied in details by Molander and Hahn.[54] Experiments were performed in a THF/MeOH mixture (2 : 1) at −78°, which gave almost instantaneous reductions when X = OAc, OSiMe$_3$, OCOCH$_2$Ph, OTs, Cl, SPh, SO$_2$Ph, HgCl. Only α-hydroxyketones provided low yields. Improvement was obtained by adding a solution of the α-hydroxyketone and acetic anhydride in THF to SmI$_2$, without isolation of the α-acetoxy ketone. Some examples are indicated below:

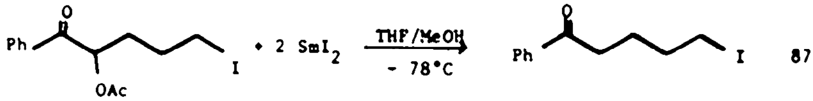


| X | Yield (%) |
|---|---|
| Cl | 100 |
| SPh | 76 |
| SO$_2$Ph | 88 |
| HgCl | 94 |

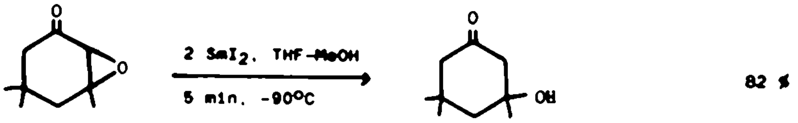


| X | Yield (%) |
|---|---|
| AOc | 75 |
| OSiMe$_3$ | 98 |
| OTs | 94 |

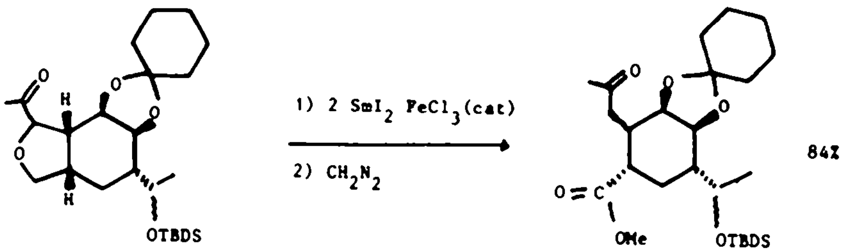




Similar procedures applied to α,β-epoxyketones result in formation of β-hydroxyketones:[46]

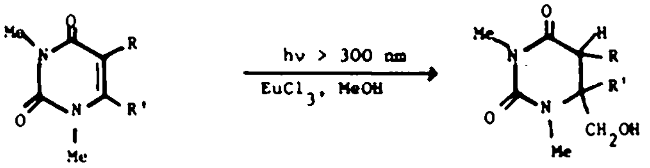


The reduction is operative on complex molecules; thus, White *et al.*[55] succeeded in the following transformation:

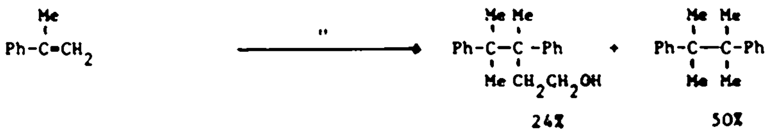


It is interesting to note that the authors tried many reductive systems all which gave low yields or cleavage of the silyl ether. By contrast, the SmI$_2$ reduction in presence of catalytic amounts of ferric chloride gave an excellent yield after 25 min. at room temperature in THF.

3.4.9. *Hydroxymethylation induced by a photoredox Eu(III)/Eu(II) system in methanol.* Irradiation of a methanol solution of EuCl$_3$ (λ > 300 nm) induces the following overall reactions using 0.1 mol eq. of EuCl$_3$ with respect to the organic substrates:[56,57]



R = R' = H 90%
R = Me ; R' = H 80%
R = F ; R' = H 50%



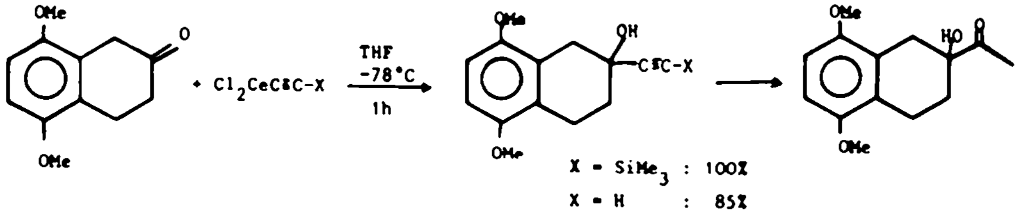
## 4. LANTHANIDES (III)

### 4.1. *Introduction*

Many of the applications of lanthanides to organic chemistry deal with trivalent lanthanides, the trivalent state being the most common oxidation state. The low price of many trivalent salts allows their use in stoichiometric reactions. Moreover, the Lewis acid and coordinating properties of trivalent lanthanides often lead to interesting catalysts.

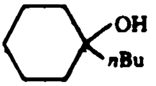
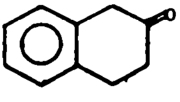
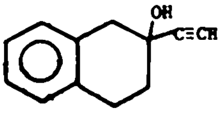
### 4.2. *Stoichiometric reactions*

4.2.1. *Grignard-like reactions of organolanthanides.* Trivalent organolanthanides have been prepared from the metals (cerium or lanthanum) and organic iodides,[21,22] whereas europium, ytterbium and samarium metals forms divalent species. These Ln(III) organometallics were studied briefly as Grignard-like reagents. Thus, cerium reacts with iodobenzene in THF at room temperature to give a mixture of organometallic species (presumably $R_3Ce$, $R_2CeI$ and $RCeI_2$) which react with benzophenone. Triphenylmethanol was isolated in 45% yield. More recently, organocerium reagents were studied extensively by Imamoto *et al.*[14] As previously discussed Barbier-type or Reformatsky-type reactions gave excellent results using cerium metal or cerium amalgam (see Tables 3 and 4). Another approach to organocerium reagents is the transmetallation between organolithium compounds and anhydrous $CeI_3$ or $CeCl_3$. The organocerium(III) reagents react cleanly in THF at −78 to −65° with a variety of carbonyl compounds (Table 8). There is a preference for 1,2-addition to enones. A detailed comparison with Grignard reagents on selected compounds showed higher reactivity and better selectivity for 1,2-additions to enones.[58] The most interesting feature is the low basicity of the reagents, which allows additions to ketones which are very prone to enolization[59] (see entries 8–10, Table 8). This last characteristic was useful at some stage of the total synthesis of several natural products. Thus, Terashima *et al.*[60] found that 2-trimethylsilylethynylcerium(III) reagents react efficiently with 1,2,3,4-tetrahydronaphthalen-2-one derivatives which are further transformed into synthetic intermediates for natural and unnatural anthracyclinones, for example:



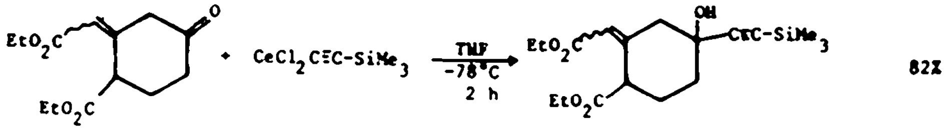
X = SiMe$_3$ : 100%
X = H : 85%

Table 8. Addition of organocerium reagents to aldehydes and ketones

| Entry | Reagent | Carbonyl compound | Product[a] | Yield (%)[c] |
|---|---|---|---|---|
| 1 | $n$-BuLi—$CeI_3$ |  $PhC(=O)CH_3$ | $PhC(OH)(CH_3)n$Bu | 98 |
| 2 | $n$-BuLi—$CeI_3$ | cyclohexanone |  | 95 |
| 3 | $n$-BuLi—$CeI_3$ | $PhCH_2CH_2CHO$ | $PhCH_2CH_2CHOH$ $n$-Bu | 92 |
| 4 | $sec$-BuLi—$CeI_3$ | $PhCOCH_3$ | $PhC(OH)CH_3$ $sec$-Bu | 98 |
| 5 | $n$-BuLi—$CeCl_3$ | $p$-$IC_6H_4COCH_3$ | $p$-$IC_6H_4C(OH)(CH_3)$ $n$-Bu | 93 |
| 6 | $n$-BuLi—$CeCl_3$ | $PhCH{=}CH{-}CHO$ | $PhCH{=}CH{-}CHOH$ $n$-Bu[b] | 96 |
| 7 | $n$-BuLi—$CeCl_3$ | $PhCH{=}CH{-}COCH_3$ | $PhCH{=}CHCOH(CH_3)$ $n$-Bu | 95 |
| 8 | $HC{\equiv}CLi$—$CeCl_3$ |  |  | 89 |
| 9 | $t$-BuLi—$CeCl_3$ | $(PhCH_2)_2CO$ | $(PhCH_2)_2C(OH)$ $t$-Bu | 65 |
| 10 | $PhC{\equiv}CLi$—$CeCl_3$ | $CH_3COCH_2Br$ | $CH_3C(OH)(CH_2Br)C{\equiv}CPh$ | 95 |

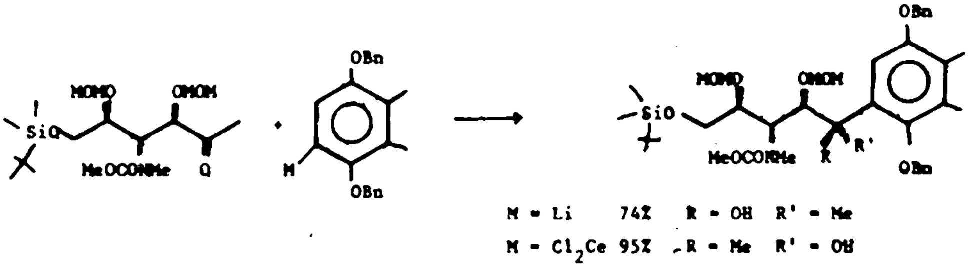
[a] Reaction performed at −75°, 3 h, unless stated otherwise.
[b] −73°, 1 h.
[c] Isolated yield.

The acetylenic reagents were prepared from $CeCl_3$ and $LiC{\equiv}C{-}X$. Tamura *et al.*[61] used $Cl_2CeC{\equiv}C{-}SiMe_3$ in an early step of the total synthesis of 11-deoxyanthracyclinones:

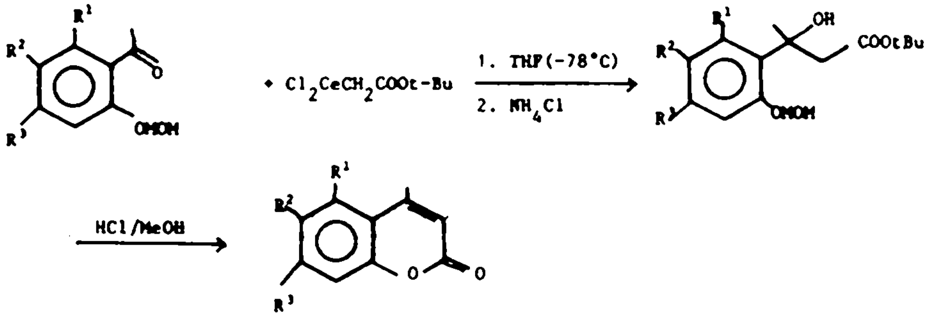


The use of the lithium reagent instead of the cerium(III) reagent gave only an 11% yield, the main reaction being the enolization of the ketone.

It is interesting to note that organocerium and organolithium reagents do not necessarily give the same stereochemistry of addition to a carbonyl group which is part of a chiral molecule. Thus, Terashima *et al.*[62] discovered that nucleophilic addition of related aryllithium and arylcerium compounds to a chiral open-chain ketone occurs in the opposite manner. This ketone is a key intermediate in the total synthesis of the DEF-ring system of nogalamycin. The aryllithium reagent gave the desired stereochemistry, while the arylcerium reagent gave the unnatural epimer. These results were rationalized by assuming a strong intramolecular coordination between cerium and the adjacent benzyl ether, whereas lithium prefers to coordinate to a THF molecule.



Cerium analogues of the Reformatsky reagent were found useful where the Reformatsky reaction failed, as in the case of protected ortho-hydroxyacetophenones.[63] Substituted coumarins were obtained in excellent yields.



Kauffman *et al.*[64] investigated the behaviour of "$X_2LnR$" reagents prepared *in situ*, for their selectivity in competitive experiments in THF on equimolar amounts of heptanal and diethylketone. The selectivity in favor of attack on aldehydes is good with $Cl_2LaMe$ (11.5 : 1) but drops from cerium to samarium ($Cl_2CeMe$ 3.8 : 1; $Cl_2SmMe$ 2.1 : 1).

Well-characterized permethylated anionic complexes of most of the lanthanides could be synthesized[65] in the presence of tmeda by the following route:

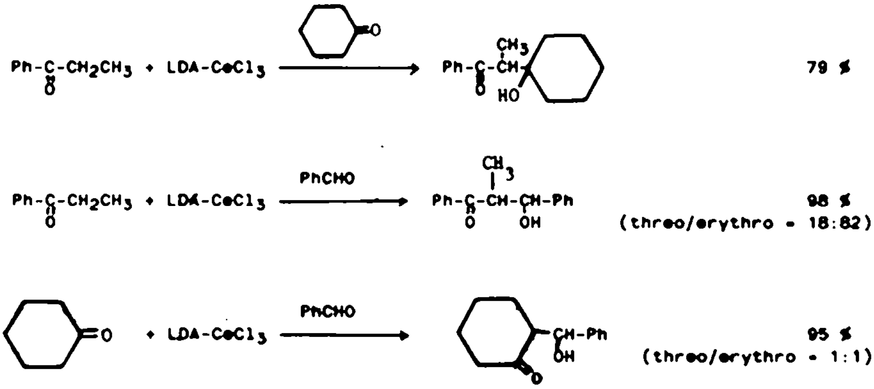
$$LnCl_3 + 6\,MeLi + 3\,tmeda \xrightarrow{Et_2O} Li(tmeda)_3Ln(Me)_6 + 3\,LiCl$$

These complexes react with α,β-unsaturated aldehydes or ketones, mainly by 1,2-addition.[66]

A new route to organolanthanides was devised by Wayda, Bertz *et al.*[67] Organolithium or Grignard reagents are treated with $Ln(O\text{-}iPr_3)$ or $Ln(N(SiMe_3)_2)_3$ (with Ln = Sm mainly) under an inert atmosphere at −78° in ether. These organometallics were used at room temperature in the opening of various epoxides and compared to organocopper and organoaluminum reagents. Chemical yields are excellent in the alkylation of epoxides, the regioselectivity of the reaction parallels that observed with trialkylaluminum in the case of styrene epoxide. Butadiene monoepoxide gives the following results:

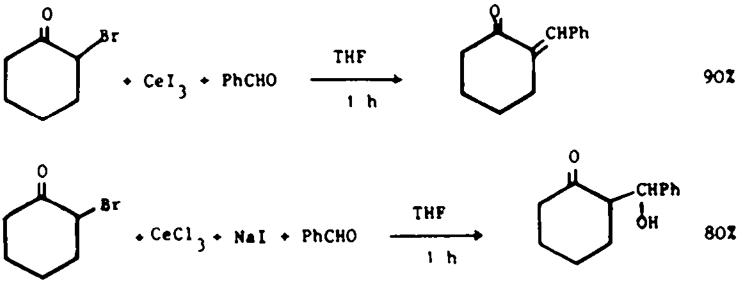
Preliminary results indicate that these reagents lead only to 1,2-addition to cyclohex-2-en-1-one.

4.2.2. *Aldol condensations*. Crossed-aldol reactions are useful transformations which have been performed in various ways. An additional method via cerium enolates was described by Imamoto *et al.*[68] It is based on the preparation of lithium enolates from ketones with LDA or LBTMSA (lithium bis-trimethylsilylamide) followed by transmetallation by treatment with anhydrous CeCl$_3$ at −78°. The cerium enolate reacts with aldehydes and ketones at −78° with in several hours. Aldols are isolated in better yields than with the lithium enolates under the same experimental conditions. Some examples are indicated below:



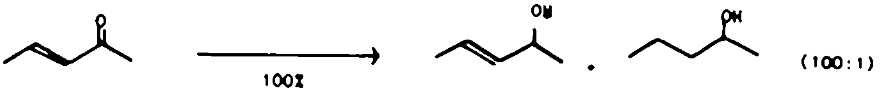
Stereoselectivity with cerium enolates is the same as with lithium enolates. The authors assumed that the cerium enolates react via the well-recognized six-membered transition state of lithium enolates. Cerium(III) should chelate more tightly to the intermediate aldol than the lithium ion, suppressing retro-aldol and cross-enolization reactions.

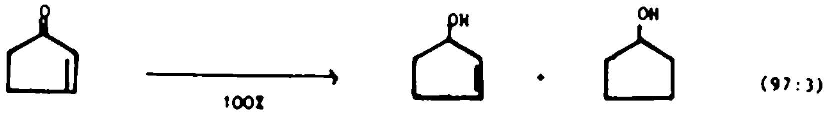
Ho *et al.*[69] studied the dehalogenation of α-haloketones into ketones by Ce(III) sulfate and NaI in aqueous THF; the same reaction was also observed by the action of NaI alone.[70] The ketone is formed by protonation of an intermediate enolate. Fukuzawa *et al.*[71] modified the procedure with Ce(III)/NaI by working in dry THF, with the aim of trapping the intermediate cerium enolate with an aldehyde. When equimolar amounts of α-haloketone, aldehyde and CeI$_3$ in THF were stirred at room temperature for an hour, a good yield of conjugated ketone was obtained. If CeI$_3$ is replaced by CeCl$_3$/NaI (1 : 3) the aldol is isolated.

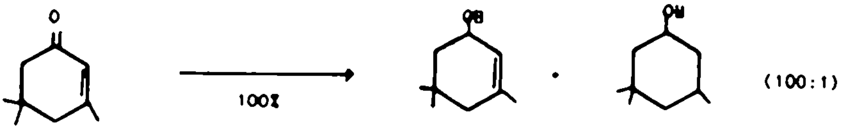


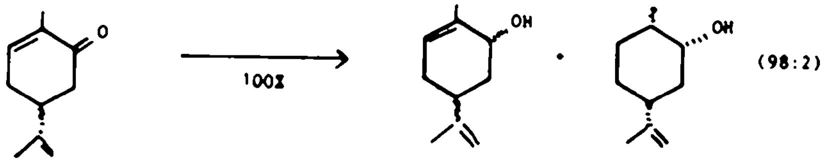
It was demonstrated that β-ketoalcohols can be converted into α,β-unsaturated ketones by CeI$_3$ in THF. This indicates that in the absence of NaI, CeI$_3$ works as a dehydrating agent.

4.2.3. *Reductions in presence of cerium trichloride* (a) *Conjugated α-enones*. In 1978 Luche[72,73] reported that conjugated ketones are cleanly reduced to allylic alcohols with sodium borohydride (1 mol eq.) in methanol in the presence of 1 mol eq. of LnCl$_3$, nH$_2$O. Among the various lanthanide trihalides, CeCl$_3$, 6 H$_2$O was selected as giving the best results. The reactions are conducted at room temperature, without special exclusion of air and moisture; good yields of products are obtained within 5 min. Some examples are indicated below:

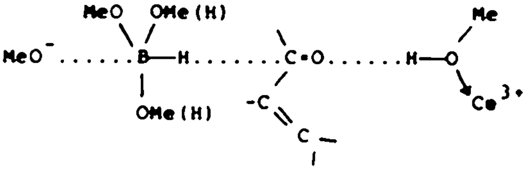




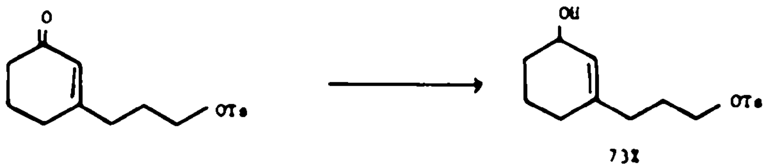




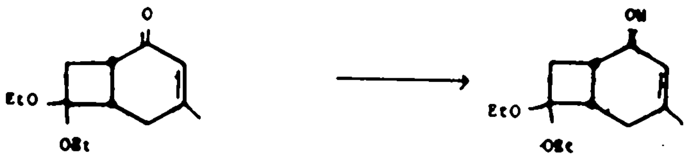
The mechanism of the reduction was studied.[74] It was demonstrated that there is no intervention of a cerium borohydride. Cerium trichloride enhances the acidity of methanol (through complexation) and induces its reaction with $NaBH_4$ giving $BH_{4-n}(OCH_3)_n$-species. $CeCl_3$ meanwhile interacts with the carbonyl group. The following transition state for the hydride transfer was proposed by the authors:[74]



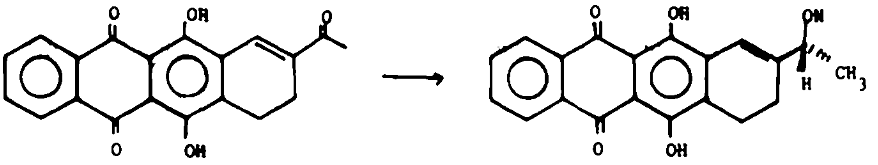
The Luche reagent is now widely used in synthetic organic chemistry for the preparation of allylic alcohols. The procedure allows work on functionalized molecules with a high degree of selectivity (esters, tosylates, sulfides and amides are compatible functional groups). Some examples are listed below using $CeCl_3$-$NaBH_4$/MeOH as indicated above (for additional examples see Refs. 5 and 8).



ref. 75

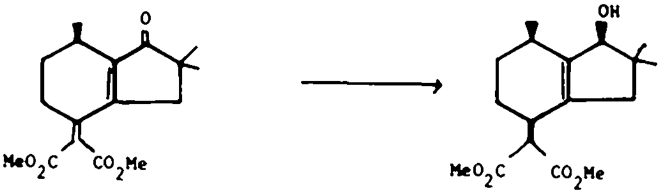


ref. 76



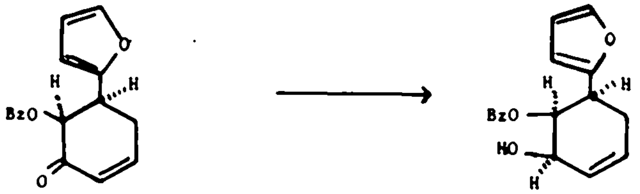
88%

ref. 77



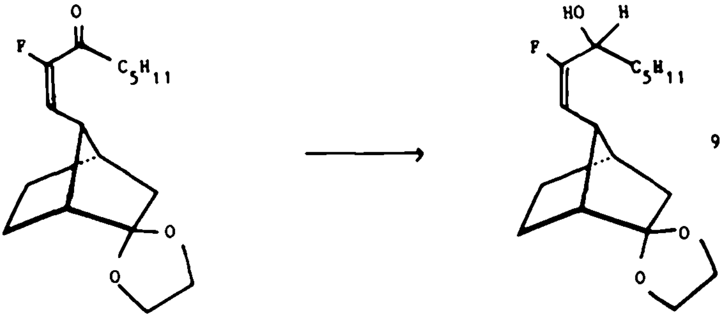
91%

ref. 78



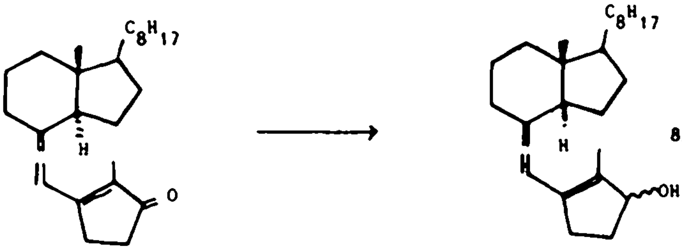
90%

ref. 80



95%

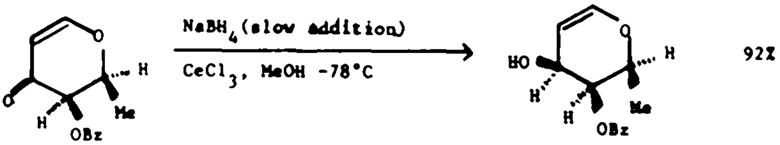
ref. 81



85%

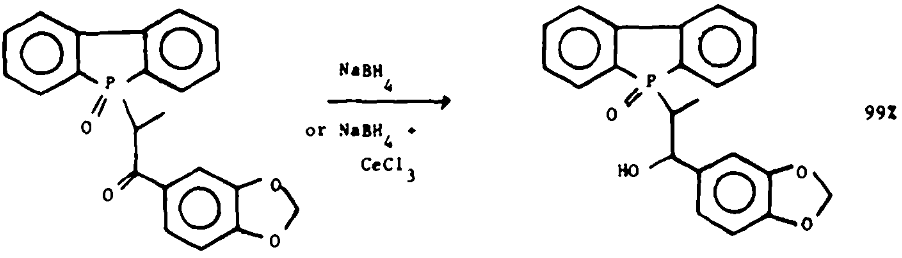
ref. 82

The Luche reagent sometimes gives good stereoselectivity in the reduction of chiral enones. Danishefsky *et al.*[83] modified the procedure by working at −78° in order to increase the stereoselectivity:



92%

This procedure was applied recently by Warren and Elliott[84] to reverse the stereoselectivity of reduction of a saturated ketone bearing a phosphine oxide functionality in $\beta$ position:



NaBH$_4$ : Threo/erythro 85:15

NaBH$_4$ + CeCl$_3$ : threo/erythro 15:85

The influence of CeCl$_3$ was ascribed to a chelate effect of carbonyl and P=O groups on Ce$^{3+}$.

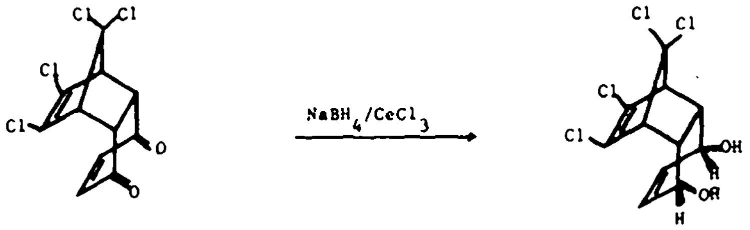
(b) The transformation of *cinnamoyl chloride* into cinnamyl alcohols was performed in good yields in acetonitrile by NaBH$_4$ (1 mol eq.) and anhydrous CeCl$_3$ (0.1 mol eq.) after 5 min.:[85]

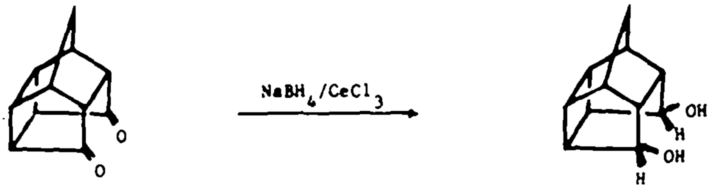
$$\text{ArCH{=}CHCOCl} + \text{NaBH}_4 \xrightarrow[\text{CH}_3\text{CN}]{\text{CeCl}_3} \text{ArCH{=}CHCH}_2\text{OH}$$

75–80%

It is interesting to point out that here CeCl$_3$ is used in catalytic amounts.

A facile stereoselective reduction of enediones and cage diketones using NaBH$_4$–CeCl$_3$ in methanol at 0° was recently reported by Marchand *et al.* Some typical examples are indicated below:





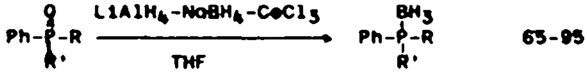
When the cage diketone was reduced by NaBH$_4$ alone a mixture of stereoisomeric diols was obtained.[86]

(c) *Reduction of organic halides and phosphines oxides with LiAlH$_4$–CeCl$_3$.* Imamoto *et al.*[87] found that anhydrous CeCl$_3$ (15 mol eq.) and LAH (4.5 mol eq.) in THF or DME at reflux is able to reduce many organic halides (including fluorides), as well as phosphine oxides, after reaction times of a few hours:

| | |
|---|---|
| $CH_3(CH_2)_{11}F \rightarrow C_{12}H_{26}$ | 90% |
| 1-fluoronaphthalene → naphthalene | 94% |
| $Ph_3PO \rightarrow Ph_3P$ | 95% |
| $Ph_2P(O)CH_3 \rightarrow Ph_2PCH_3$ | 98% |

Unfortunately this process gives racemization at phosphorus when the starting material is an optically active phosphine with an asymmetric phosphorus site.

Cerium trichloride was also used by Imamoto *et al.*[88] in an efficient one-pot preparation of phosphine-boranes from phosphine oxides:



$$\mathrm{Ph{-}P(O)(R')R} \xrightarrow[\text{THF}]{\text{LiAlH}_4\text{-NaBH}_4\text{-CeCl}_3} \mathrm{Ph{-}P(BH_3)(R')R} \qquad 65\text{-}95\ \%$$

This reaction works at room temperature only in presence of $CeCl_3$ which was assumed to play a dual role: activation of the phosphine oxide by coordination so that the deoxygenation with LAH proceeds readily and activation of $NaBH_4$ for the transfer of $BH_3$.

## 4.3. *Catalytic reactions*

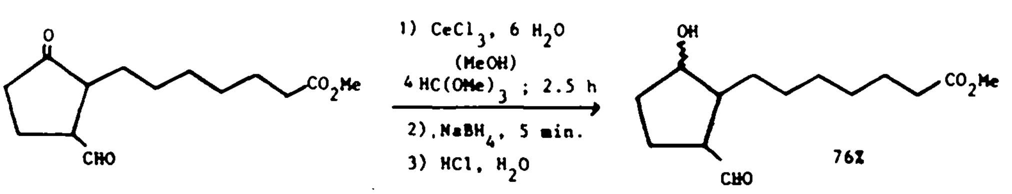
It was recognized early that Lewis acidity is associated with many lanthanide derivatives, especially the trihalides. Lewis acidity, electrophilicity and oxophilicity are some of the properties which provide the driving forces for various catalytic processes. in some of these the lanthanide derivative is used in stoichiometric amount, but, in principle, can be recovered unchanged. However, in many cases the reaction is truly catalytic with respect to the lanthanide. The main reactions will be successively presented according to the structure of the lanthanide compounds: purely inorganic salts (trihalides, perchlorates, . . .), alcoholates, carboxylates, $\beta$-diketonates and cyclopentadienyl complexes.

4.3.1. *Acetal formation.* As early as 1922 Adkins and Nissen[89] compared $CeCl_3$ to other metal halides as a catalyst in the reaction of acetaldehyde and ethanol for the synthesis of the corresponding acetal. $CeCl_3$ was found to be less efficient than calcium chloride. Recently Luche and Gemal[90] found that rare earth chlorides are highly efficient catalysts for acetal formation from aldehydes. In a typical procedure: an aldehyde is dissolved in a methanolic solution of $LnCl_3$ (one mole eq.); the aldehyde-acetal equilibrium is reached instantaneously. The addition of trimethyl orthoformate shifts the equilibrium towards the dimethyl acetal. Trimethyl orthoformate also acts as a water scavenger allowing the use of the commercially available hydrated lanthanide salts.

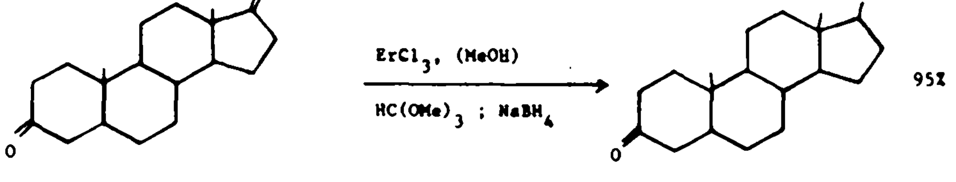
$$\mathrm{RCHO + MeOH \xrightarrow[HC(OMe)_3]{LnCl_3} RCH(OMe)_2}$$

The reaction is very fast at room temperature (10 min.) and yields are often nearly quantitative. Interestingly, the yields depend on the nature of the lanthanide ion. La, Ce and Nd are the most effective for acetal formation from aliphatic aldehydes. Er and Yb seem to be best for aromatic and heterocyclic aldehydes. The precise role of the catalyst has not been studied.

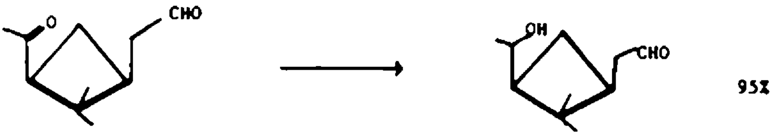
Aromatic ketones and $\alpha$-enones remain unaffected by the reaction conditions leading to acetals. Aliphatic and alicyclic ketones gave unexpected results with various lanthanide ions, suggesting the formation of hemiketals. This fact was used to advantage in performing the selective reduction by $NaBH_4$ of keto groups in the presence of an aldehyde.[91] Indeed, a convenient one-pot process was set up; one example is indicated below:

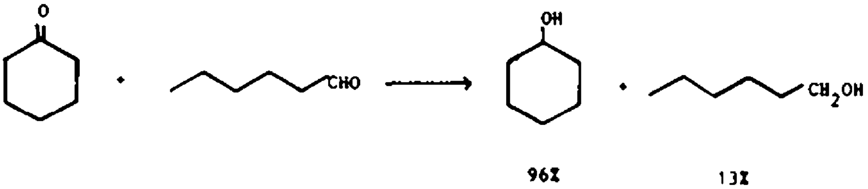


A related procedure allows the isolation of the acetal intermediates in some cases. It is also possible to take advantage of differences in reactivity between two keto groups in a molecule for the *in situ* protection of the more reactive one. Thus, androstane-3,17-dione was transformed into 17 $\beta$-hydroxy-androstan-3-one with high yield:



A simpler method for the selective reduction of ketones in the presence of aldehydes was devised by Luche and Gemal[92] which avoids the formation of a ketal intermediate and its subsequent hydrolysis. It was found that selective reduction occurs with an equimolar mixture of an aldehyde and a ketone in aqueous ethanol (EtOH–$H_2O$, 1 : 1.5) in the presence of $CeCl_3$, 6 $H_2O$ and 1 molar equiv. of $NaBH_4$. Under these conditions the aldehyde is protected against reduction, while the secondary alcohol is usually produced in high yields (after 10 min.). Some representative results are indicated below:



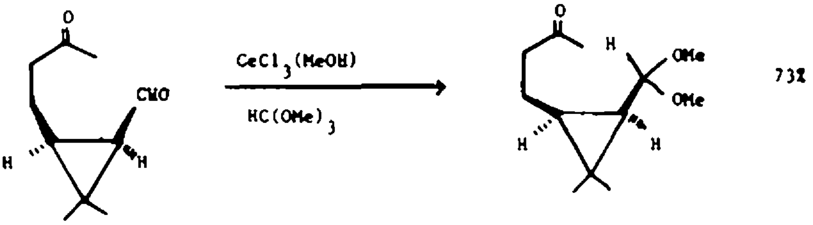


The authors assumed that the high selectivity for ketone reduction was the result of the rapid formation of the geminal diol or hemiacetal from the aldehyde group under condition which leave the keto group unchanged.

In some cases $CrCl_3$ gave comparable results to $CeCl_3$ or $ErCl_3$.[93]

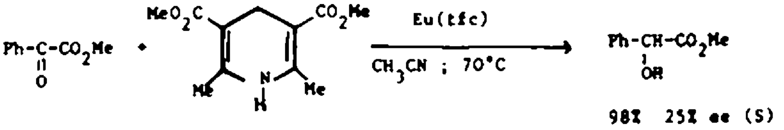
Selective reductions by $NaBH_4$ in aqueous ethanol solution was extended to the couple conjugated aldehydes/non-conjugated aldehydes.[94] It is known that conjugated aldehydes usually give hydrates more easily than non-conjugated ones. Indeed, by using the combination EtOH–$H_2O$–$ErCl_3$–$NaBH_4$ a number of selective reductions were obtained.

Ketalization in presence of $CeCl_3$ and $HC(OMe)_3$ was utilized by Smith during the formation of the key ketal group in the synthesis of milbemycin-$\beta_3$.[94] Preferential acetal formation from a ketoaldehyde was also achieved by this procedure:[95]



Hydrogen peroxide (30% aqueous solution) is able to oxidize aldehydes to acids in the presence of $(NH_4)_6Mo_7O_{24}$, 4 $H_2O$ and potassium carbonate. The reaction is greatly accelerated by cerium trichloride, presumably through the enhanced *in situ* formation of a hydrate of aldehyde the actual species which is oxidized.[96]

4.3.2. *Asymmetric reduction catalyzed by chiral shift reagents*. NAD analogs with a dihydropyridine moiety are able to reduce conjugated ketones in the presence of $Mg(ClO_4)_4$ as a catalyst. It was found[97] that catalytic amounts of chiral europium $\beta$-diketones (0.1 mol eq.) are able to promote the slow transformation of methyl phenylglyoxylate to methyl mandelate:



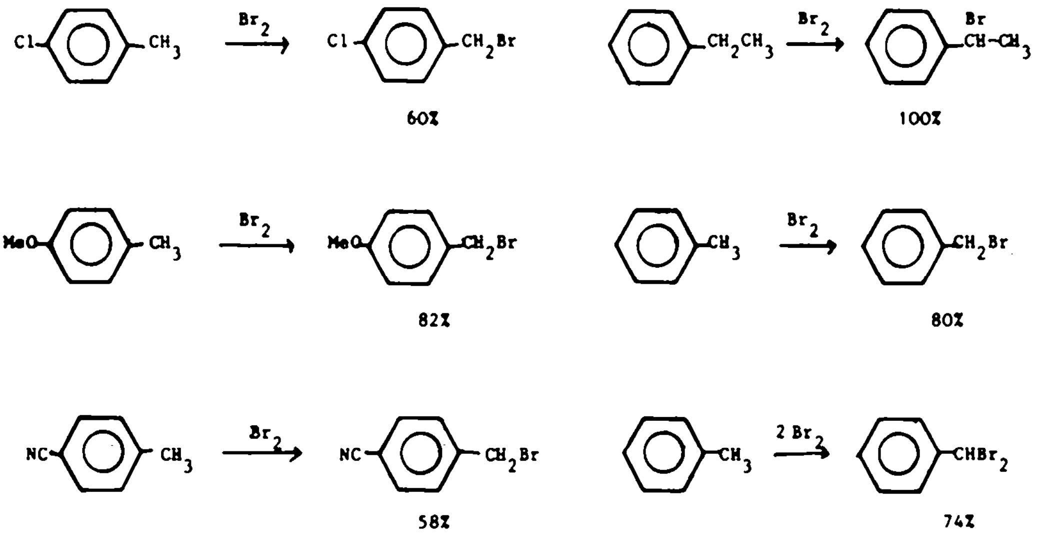
The reaction is slower in methylene chloride at room temperature (28% yield) but the ee is increased to 55%.

4.3.3. *Friedel–Crafts reactions*. The old patent literature gave reports of the use of $CeCl_3$ as a catalyst in the Friedel–Crafts acylation of aromatic compounds by acyl chlorides. In these cases the cerium powder used as the catalyst precursor was transformed *in situ* into cerium trichloride.[98] $CeCl_3$ was also described as a good catalyst (in the presence of $HgCl_2$) for the addition of HCl to acetylenes and olefins. Friedel–Crafts reactions catalyzed by lanthanide salts were recently reinvestigated by Fujiwara *et al.*[99]

A wide variety of anhydrous rare earth halides were checked as catalysts (catalyst/substrate = 1 : 3) in the alkylation of benzene with benzyl bromide. Diphenylmethane was formed in yields up to 74% (with $DyCl_3$). Interestingly, the catalysts can be recovered easily and re-used.[99]

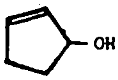
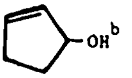
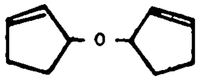
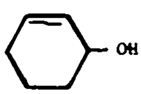
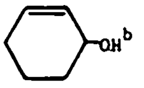
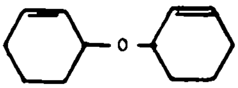
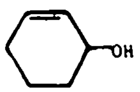
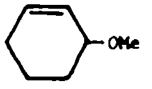
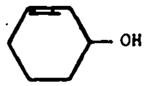
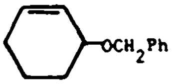
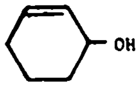
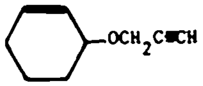
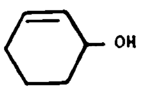
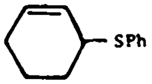
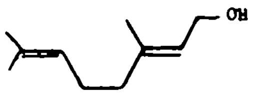
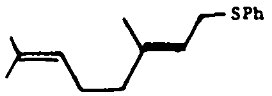
4.3.4. *Benzylic brominations*. The benzylic bromination with NBS-bromine is seldom used because of competitive nuclear bromination; it requires special experimental conditions such as UV irradiation and high temperatures. It was found that various alkyl aromatics can be selectively brominated in the benzylic position by bromine in presence of catalytic amounts of lanthanum triacetate.[100] The substrate is dissolved in $CCl_4$ with 0.1 mol eq. of $La(OAc)_3$ (which remains in suspension). One equivalent of bromine (in $CCl_4$) is slowly added to the solution maintained at 60° at the visible light or under a standard laboratory light. After a few hours the reaction is complete, the product is isolated in excellent yield. Some dibromides were also prepared when two equivalents of bromine are added. The reaction failed with aromatic rings which are too electron-rich and prone to electrophilic attack. For example, cresols or methylnaphthalenes give mixture of products. The mechanism of the reaction was studied[101] $Ln(OAc)_3$ is completely insoluble in $CCl_4$ and rapidly adsorbs bromine (or 0.3 mol eq.). Ambiant light is necessary to initiate the process, presumably by dissociation of adsorbed bromine. A free radical bromination then takes place close to the surface of the solid. Benzylic bromination was also observed with other lanthanide derivatives [$SmCl_3$, $La(CF_3CO_2)_3$, $Sm_2O_3$], these compounds being more efficient than various other metallic salts [$BaCl_2$, NaOAc or $Cu(OAc)_2$]. Representative examples of benzylic brominations are indicated below:

Benzylic bromination catalyzed by $La(OAc)_3$[100]



4.3.5. *Ether formation from allylic alcohols*. The behaviour of various allylic alcohols in the presence of catalytic amounts of $SmCl_3$ has been studied.[102] In many cases dialkyl ethers were obtained in good yields (Table 9). The procedure is very simple since it involves refluxing an allylic alcohol with 0.1 mol eq. of $SmCl_3$ in 1,2-dichloroethane for a few hours. Saturated alcohols, benzylic alcohol and propargyl alcohol do not give ether formation under these experimental conditions. This property allowed the preparation of mixed ethers containing only one allyl group by heating an allylic alcohol in the presence of a few equivalents of another alcohol and catalytic amounts of

Table 9. Synthesis of ethers and thioethers from allylic alcohols catalyzed by SmCl$_3$[102]

| Allylic alcohol[a] | Nucleophile (mol eq) | Products (isolated yield %)[c] | |
|---|---|---|---|
|  |  |  | (69) |
|  |  |  | (80) |
|  | MeOH<br>(5) |  | (48) |
|  | PhCH$_2$OH<br>(2) |  | (74) |
|  | HC≡C—CH$_2$OH<br>(2) |  | (73) |
|  | PhSH<br>(2) |  | (95) |
|  | PhSH<br>(3) |  | (56) |

[a] In ClCH$_2$CH$_2$Cl (5 mmol allylic alcohol in 20 ml), 12 h at reflux; 0.1 mol eq of SmCl$_3$.

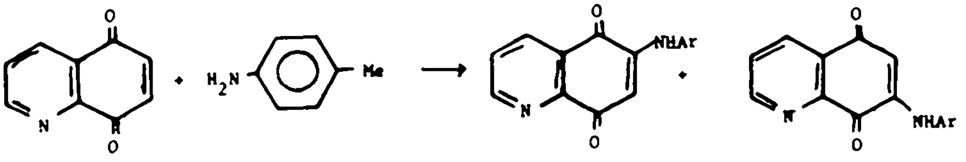
[b] The total amount of allylic alcohol is given in note *a*.

[c] Isolation by column chromatography. The starting allylic alcohol accounts for the material balance.

SmCl$_3$ (Table 9). In some cases, thiophenol can replace the alcohols giving rise to allylic thioethers (Table 9).

The mechanism which was proposed[102] is based on the formation of an electrophilic moiety derived from the allylic alcohol. The allylic cation is then attacked by the protic nucleophile (alcohol or thiophenol).

4.3.6. *Regioselective reactions of quinones with aromatic amines.* One of the earliest of the application of lanthanide compounds to problems of organic synthesis seems to be the report of Pratt[103] who showed that CeCl$_3$ (as the heptahydrate) is a superior catalyst for the regioselective addition of aromatic amines to various unsymmetrical 1,4-naphthoquinones or 5,8-quinolinequinones (followed by reoxidation). Thus 5,8-quinolinequinone and *p*-toluidine lead to the following results:

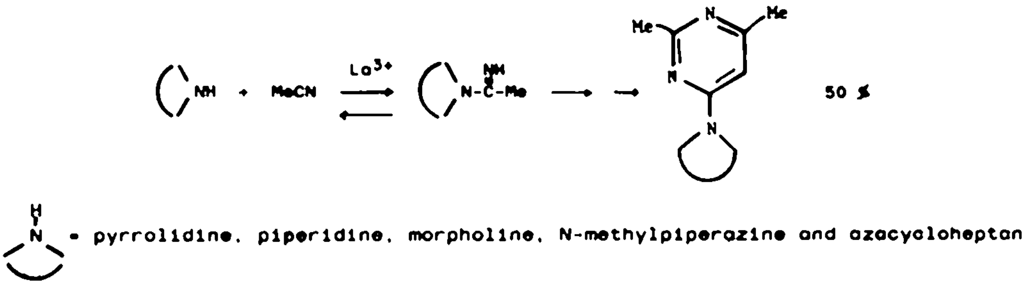


| | | |
|---|---|---|
| without CeCl$_3$ | 30% | 24% |
| 0.1 mol.eq CeCl$_3$ | 69% | 0 |

The powerful catalytic effect of cerous chloride was interpretated as an activation through coordination involving nitrogen and the proximate carbonyl, which orients the reaction to the position α to the second carbonyl.

4.3.7. *Formation of 4-substituted-2,6-dimethylpyrimidines.* Anhydrous La(ClO$_4$)$_3$ [or Pr(ClO$_4$)$_3$]

in small amount catalyzes the reaction between various secondary amines in acetonitrile as solvent.[104] The lanthanide ion seems to catalyze amidine formation from acetonitrile and the amine and may also be involved in subsequent steps of the reaction.



4.3.8. *Diels–Alder reactions*. It is well-known that Diels–Alder reactions are often appreciably accelerated by catalytic amounts of a Lewis acid such as $AlCl_3$. It was recently observed that milder Lewis acids such as lanthanide tris-$\beta$-diketonates (used as nmr shift reagents) catalyze various Diels–Alder and hetero Diels–Alder reactions. The main results are summarized in Table 10. Danishefsky *et al.*[106–110] made a detailed study of the hetero Diels–Alder reactions catalyzed by $Yb(fod)_3$ or $Eu(fod)_3$. The activated dienes and various aldehydes gave many types of oxygen heterocycles which were used as intermediates in natural product synthesis. The cyclocondensation were often stereoselective. It was even possible to realize an asymmetric synthesis (entry 9, Table 10) by taking the chiral complex $Eu(hfc)_3$ as catalyst.

A new catalytic system ($Ce(OAc)_3$–$BF_3$, $OEt_2$) was developed[110] to obtain a good stereochemical control into a specific diastereomer (entry 5, Table 10).

Homo Diels–Alder reactions between conjugated aldehydes (but not $\alpha,\beta$-unsaturated ketones) and several dienes were also observed,[100] some results are reported in Table 10. The lanthanide catalysis is becoming a useful method for Diels–Alder reactions involving highly substituted reactants.

4.3.9. *Meerwein–Ponndorf–Verley–Oppenauer reactions*. Meerwein–Ponndorf–Verley reductions and Oppenauer oxidations are useful reactions. However, a drastic limitation to their use for a wide range of organic substrates is the requirement of large amounts of metal alkoxides. There are a few reports of systems using catalytic amounts of metal alkoxide. It was found[114] that secondary lanthanides alkoxides $ROLnI_2$ are good catalysts for the MPV/O reactions. When Ln = Sm or Yb the alkoxide is easily obtained as follows:

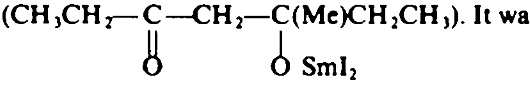
$$t\text{-BuOO}t\text{-Bu} + LnI_2 \xrightarrow[rt]{THF} 2\,t\text{-BuOLnI}_2$$

For Ln = Ce the diiodoisopropoxide was prepared by reaction of cerium metal with iodine and 2-propanol:

$$Ce + I_2 + i\text{-PrOH} \xrightarrow[rt]{THF} i\text{-PrOCeI}_2 + 1/2\,H_2$$

Most of the MPV/O reactions were achieved with 0.1 mol eq. of $t$-BuOSmI$_2$ as catalyst in THF at 65° for 24 hours. Some of the results are indicated in Table 11 (entries 1–10).

Recently a more active system based on the use of $SmI_2$ (0.1 mol eq.) in THF was devised.[115] For example, the oxidation of 2-octanol by 2-butanone in presence of $t$-BuOSmI$_2$ gives a 90% yield after 24 hours at 65°C (entry 1, Table 11). Replacement of $t$-BuOSmI$_2$ by $SmI_2$ led to the same yield, but the reaction was complete after 24 hours at room temperature (entry 11, Table 11). Other results are indicated in Table 11 (entries 11–14). A preliminary investigation showed that $SmI_2$ rapidly disappeared with concurrent appearance of the aldolisation product of butanone $(CH_3CH_2\text{—}\underset{\underset{O}{\|}}{C}\text{—}CH_2\text{—}\underset{\underset{O\,SmI_2}{|}}{C}(Me)CH_2CH_3)$. It was established that this compound is the true catalyst.



The lanthanide catalysis of MPV/O reactions seems of wide application but suffers from the following drawbacks: the reaction has to be anhydrous (water deactivates the catalyst) and $\alpha$- or $\beta$-ketols are not oxidized, presumably because of strong chelation which blocks coordination sites

Table 10. Diels–Alder reactions catalyzed by lanthanide tris-β-diketonates

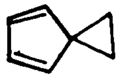
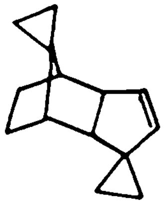
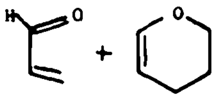
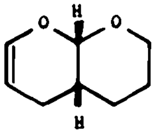
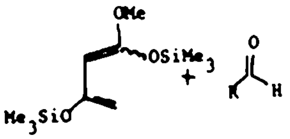
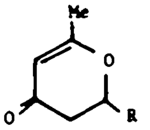
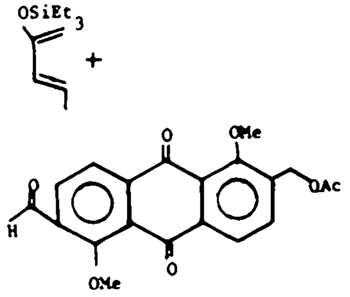
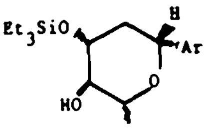
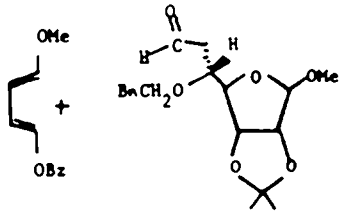
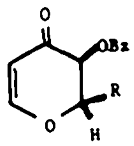
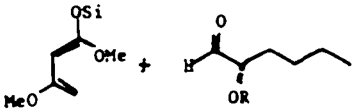
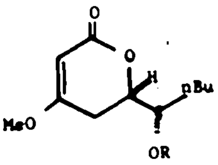
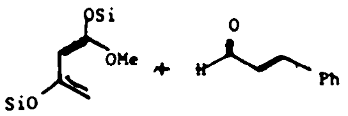
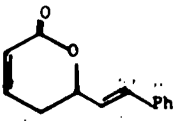
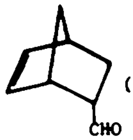
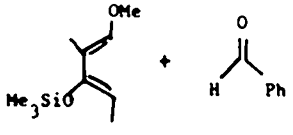
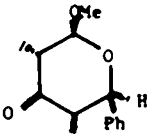
| Reactants | Catalyst | Product(s) (yield %) | Ref |
|---|---|---|---|
|  | $Eu(tfn)_3$ |  | 105 |
|  | $Yb(fod)_3$ |  | 107 |
|  | $Eu(fod)_3$ |  R=Ph (85)<br>R=n-$C_6H_{13}$ (73) | 108 |
|  | $Eu(fod)_3$ |  (70) | 109 |
|  | $Ce(OAc)_3$<br>$BF_3 \cdot Et_2O$ |  (45) | 110 |
|  | $Eu(hfc)_3$ |  (98) | 111 |
|  | $Eu(fod)_3$ |  (84) | 112 |

Table 10. (*cont.*)

| Reactants | Catalyst | Product(s) (yield %) | Ref |
|---|---|---|---|
|  | Eu(fod)$_3$<br>25° |  (endo/exo=15:1) (86) | 113 |
|  | Eu(hfc)$_3$<br>−10° |  58% ee (71) | 106 |

around samarium. Unexpectedly, alcohols with an unhindered terminal double bonds (i.e. $CH_3$—$CH(OH)(CH_2)_4CH$=$CH_2$) do not give the Oppenauer oxidation with either *t*-BuOSmI$_2$ or SmI$_2$ as catalysts.[115] This seems to indicate an interaction between the double bond and the lanthanide, which would be quite unusual in 4f-element chemistry.

4.3.10. *Selective catalyzed-rearrangement of terminal epoxides to methyl ketones*. The rearrangement of epoxides is a well-documented reaction. The main product is a carbonyl compound (ketone or aldehyde) when the reaction is catalyzed by an acid. A terminal olefin is usually mainly transformed into an aldehyde in presence of a Lewis acid. It was found that some lanthanide catalysts give a conversion into methyl ketones I with the complete absence of aldehydes II.[116]

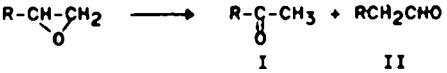


Table 11. Oppenauer oxidations and Meerwein–Ponndorf–Verley reductions catalyzed by lanthanide derivatives[114,115]

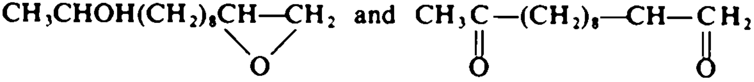
| | Substrate | Reactant (equiv)[a] | Reaction time (h) | Product | Yield (%) |
|---|---|---|---|---|---|
| 1 | 2-octanol | 2-butanone (8) | 24 | 2-octanone | 90 |
| 2 | α-methylbenzyl alcohol | 2-butanone (8) | 24 | acetophenone | 98 |
| 3 | 1-octanol | 2-furaldehyde (8) | 5 | octanol | 69 |
| 4 | 4-*tert*-butylbenzyl alcohol | 2-furaldehyde (1) | 24 | 4-*tert*-butylbenzaldehyde | 82 |
| 5 | *cis*-carveol | acetone (4) | 24 | carvone | 62 |
| 6 | geraniol | 2-furaldehyde (3) | 24 | citral (E+Z) | 62 |
| 7 | cholesterol | cyclohexanone (4) | 48 | 4-cholesten-3-one | 78 |
| 8 | 2-octanone | 2-propanol (4) | 7 | 2-octanol | 86 |
| 9 | octanal | 2-propanol (4) | 7 | 1-octanol | 66 |
| 10 | ethyl pyruvate | 2-propanol (4) | 7 | ethyl lactate | 80 |
| 11 | 2-octanol | 2-butanone (8) | 24 | 2-octanone | 90 |
| 12 | 2-cyclohexen-1-ol | 2-butanone (8) | 2 | 2-cyclohexen-1-one | 70 |
| 13 | dicyclopropyl methanol | 2-butanone (8) | 24 | dicyclopropylketone | 80 |
| 14 | 6-methyl-5-hepten-2-ol | 2-butanone (8) | 24 | 6-methyl-5-hepten-2-one | 80 |

[a] Temperature: 65° (entries 1–10) or 20° (entries 11–14).

[b] Catalyst: *t*BuOSmI$_2$ (0.1 mol eq) in entries 1–10 or SmI$_2$ (0.1 mol eq) in entries 11–14. Solvent: THF.

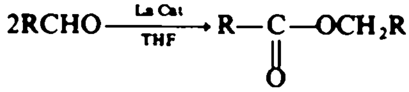
The catalysts were iodoalcoholates such as *t*-BuOSmI$_2$, Ce(O-*i*Pr)I$_2$. THF solutions of SmI$_2$ oxidized either by air or by an epoxide are also able to catalyze the rearrangement of epoxides.

Reactions were performed in THF at room temperature for 20 h with 0.1 mol eq. of catalyst. For example *t*-BuOSmI$_2$ catalyzes the formation of I (R = n-$C_8H_{17}$) in 90% yield, and of I (R = $C_6H_5CH_2$) in 82% yield. More vigorous conditions are necessary for rearrangement of internal epoxides into ketones (60°, 4 h). Thus epoxycyclooctane gave cyclooctanone (83%) and trans n-$C_4H_9CH$—$CH$—$C_4H_9$) gave 5-decanone (78%). A limitation of the lanthanide catalysts appears to be their deactivation by functional groups present in the molecule. Thus $CH_3CHOH(CH_2)_8\underset{\diagdown O \diagup}{CH—CH_2}$ and $CH_3\underset{\|\atop O}{C}—(CH_2)_8—CH—\underset{\|\atop O}{C}H_2$ were not rearranged in the presence of *t*-BuOSmI$_2$.



The mechanism of the catalytic rearrangement was discussed.[116] It was assumed that the selectivity of the reaction arose from the mild Lewis activity of the lanthanide center combined with nucleophilic ring-opening by iodide. The mechanism was compared to that of the $Co_2(CO)_8$/MeOH system, which is also able to perform epoxide rearrangements very similar to those observed with lanthanide catalysts.

4.3.11. *Tischenko reaction*. The Tischenko reaction has recently been catalyzed by several types of lanthanide derivatives:[14,115,117]

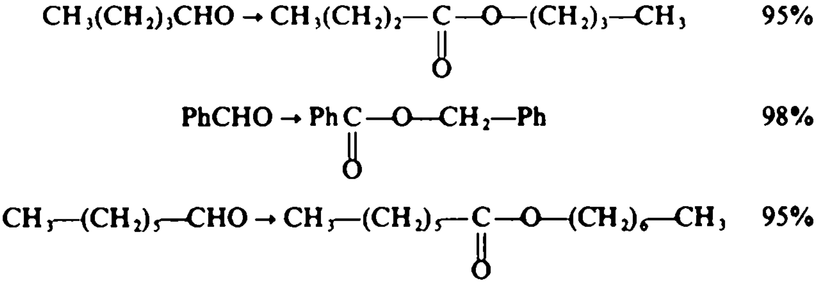


$$2RCHO \xrightarrow[THF]{Ln\ Cat} R—\underset{\|\atop O}{C}—OCH_2R$$

An organolanthanide was prepared in THF from Nd, Sm or Pr metal and $IC_2H_5$.[117]

Fujiwara *et al.* assumed that *β*-elimination yields ethylene and HLnI$_2$. This latter seems to be the catalyst precursor for the Tischenko reaction. The reactivity is not very high: the reaction was performed with 0.5 to 1 mol eq. of the lanthanide species. A more active catalyst prepared by the reaction of iodobenzene with cerium turnings at 50° was mentioned by Imamoto.[13] Several aromatic aldehydes were converted into the corresponding esters in 49–98% yields on treatment with this catalyst (*ca.* 10 mol%).

The most efficient lanthanide catalyst reported to date is one derived from SmI$_2$. It was recently observed[115] that 1% mol eq. of SmI$_2$ in THF catalyzes the transformation at room temperature over 6 hours of many aldehydes to the Tischenko esters, for example:



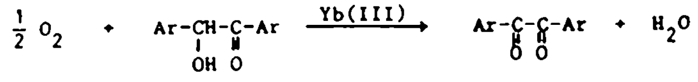
$$CH_3(CH_2)_3CHO \rightarrow CH_3(CH_2)_2—\underset{\|\atop O}{C}—O—(CH_2)_3—CH_3 \qquad 95\%$$

$$PhCHO \rightarrow Ph\underset{\|\atop O}{C}—O—CH_2—Ph \qquad 98\%$$

$$CH_3—(CH_2)_5—CHO \rightarrow CH_3—(CH_2)_5—\underset{\|\atop O}{C}—O—(CH_2)_6—CH_3 \qquad 95\%$$

4.3.12. *Oxidation of allylic alcohols by tert-butyl hydroperoxide catalyzed by lanthanide alkoxides.* Ln(O*i*Pr)$_3$ is a catalyst for oxidation of allylic alcohols in the case of Ln = La, Ce, Sm, Dy, Ho and Lu.[118] Geraniol gave 2,3-epoxy geranial and geranial in relative amounts depending on Ln. Ln(O*i*Pr)$_3$ appears to be a less selective catalyst when compared to early transition metal catalysts (i.e. Ti, V, Mo).

4.3.13. *Oxidation of benzoins to benzils catalyzed by ytterbium trinitrate.* Excellent yields (close to 90%) of benzils were obtained by heating benzoins in aqueous glyme in presence of aqueous HCl and 0.2 mol eq. of Yb(NO$_3$)$_3$:

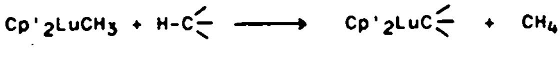


$$\frac{1}{2}O_2 + Ar—\underset{\mid\atop OH}{CH}—\underset{\|\atop O}{C}—Ar \xrightarrow{Yb(III)} Ar—\underset{\|\atop O}{C}—\underset{\|\atop O}{C}—Ar + H_2O$$

The $NO_3^-$ ion is the actual oxidizing agent. In the presence of the $Yb^{3+}$ ion as the catalyst, the nitrite ion formed is then reoxidized to nitrate by molecular oxygen.[119]

4.3.14. *Catalysis by organolanthanides with cyclopentadienyl-type ligands.* The interest in this field originated from the finding that some lanthanide derivatives are active as olefin polymerization catalysts. The main references to the original publications can be found in several reviews.[120,121]

Watson *et al.*[122] devised a method to prepare $Cp'_2LnCH_3$ where Cp′ = pentamethylcyclopentadienyl and Ln = Yb or Lu. The bulky ligands provide an interesting new chemistry for these highly electron deficient complexes (which exhibit a rapid monomer-dimer equilibrium in solution). $Cp'_2LnCH_3$ was found to be an excellent soluble model for Ziegler–Natta catalysis.[122,123] Insertion of propene into Ln—$CH_3$ provided $Cp'_2LnCH_2CH(CH_3)_2$.[123,124] The reverse reaction (β-alkyl elimination) was also observed. Competitive β-hydrogen elimination reaction from $Cp'_2LnCH_2CH(CH_3)_2$ gave $Cp'_2LnH$ and isobutene (the reverse reaction, insertion of isobutene into a Ln—H bond, was also operating). The β-H elimination was studied by Evans in the family $Cp_2LnC(CH_3)_3$ and was found to be quite difficult.[125] One interesting consequence of the research on the lanthanide model for Ziegler–Natta catalysis was the finding that $Cp'_2LnCH_3$ is able to react with various kinds of C—H bonds (vinylic, aromatic or aliphatic):[126]



The most striking result[127] was the activation of methane according to the following exchange reaction (at 70°).

$$Cp'_2Lu{}^{12}CH_3 + {}^{13}CH_4 \rightarrow Cp'_2Lu{}^{13}CH_3 + {}^{12}CH_4$$

The above reactions concerning C—H activation could become of importance for catalytic reactions of C—H bonds. Recently, Marks, Schumann *et al.*[128,129] described a systematic investigation of the preparation and properties of $Cp'_2LnR$ complexes (R = $CH(SiMe_3)_2$ or H, Ln = La, Nd, Sm, Lu). The two-step synthesis is as follows:

$$LnCl_3 + 2\,LiCp' \xrightarrow[2)\ \text{ether}\ (Et_2O)]{1)\ \text{THF}} Cp'_2LnCl_2^- Li(\text{ether})_2^+ + LiCl$$

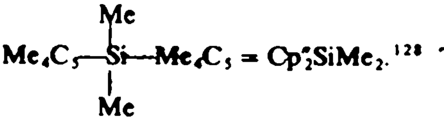
$$Cp'_2LnCl_2^- Li(\text{ether})_2^+ + LiCH(Si(Me)_3)_2 \rightarrow Cp'_2LnCH(SiMe_3)_2 + 2\,LiCl + 2\,\text{ether}$$

These complexes were easily isolated and characterized. They gave access to the corresponding hydrides by a fast, quantitative hydrogenolysis:

$$Cp'_2LnCH(SiMe_3)_2 + H_2 \xrightarrow[\text{pentane}]{0^\circ} \frac{1}{2}(Cp'_2LnH)_2 + CH_2(SiMe_3)_2$$

$Cp'_2LnH$ complexes display extraordinarily high catalytic activities in the homogeneous polymerization of ethylene[128] and in some olefin hydrogenations.[130] The highest turnover frequency was observed for Ln = Lu (exceeding 1800 $s^{-1}$ at 25° under 1 atm of ethylene pressure). In the case of the hydrogenation of 1-hexene to *n*-hexane, the catalytic activities decrease in the order Lu > Sm > Nd > La, the highest turnover number being 120,000 $h^{-1}$ (25°, 1 atm of $H_2$). It is interesting to compare this value to the activities of other homogeneous transition metal catalysts under similar conditions:

$RhCl(PPH_3)_3$ = 3000 $h^{-1}$, $Ir(COD)P(\text{cyclohexyl})_3^+ PF_6^-$ = 6400 $h^{-1}$. The scope of these $Cp'_2LnH$ catalysts is not yet known. Exploratory experiments indicate that internal olefins (*cis* or *trans*-2-hexene), as well as *trans*-stilbene and the exocyclic double bond of limonene are easily hydrogenated.[129] The two Cp′ ligands could be replaced in these complexes by the chelating ligand



$Me_4C_5{-}Si(Me)_2{-}Me_4C_5$ = $Cp''_2SiMe_2$.[128] The corresponding complexes $(Cp''_2SiMe_2)LnH$ are also excellent catalysts for hydrogenation. One can expect in the near future exciting developments in catalysis using the well-defined organolanthanides which are now available[122–130] and which are susceptible to many structural modifications.

## LANTHANIDES(IV)

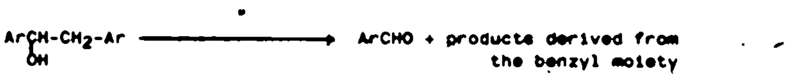
### 5.1. *Introduction*

The tetravalent oxidation state of the lanthanides is also an uncommon one. Tetravalent species of Ce, Pr, Nd, Tb and Dy have been prepared, but only those of cerium are readily accessible. Furthermore, the only tetravalent aquo ion of the lanthanides is that of cerium. The standard electrode potential, $E°(Ce^{4+}/Ce^{3+})$ is unknown. The formal potential for equal concentrations of cerium(IV) and cerium(III) varies considerably with the nature and concentration of the acidic medium. In 1M $H_2SO_4$ it is 1.44 V: in 8M $HClO_4$ it is 1.87 V. This unusually large variation is attributed mainly to hydrolysis of $Ce^{4+}$ (aq) which is reduced at high acidity and to strong complexation of $Ce^{4+}$ (aq) by anions such as $SO_4^{2-}$ and $NO_3^-$ which are normally regarded as weak complexing agents.[131]

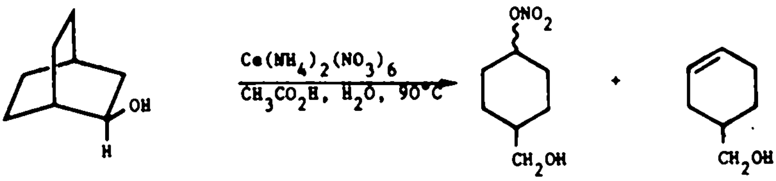
The synthetic utility of the strong oxidizing power of the ceric ion, to organic chemists started to be explored about thirty years ago. In 1973, Ho reviewed synthetic aspects of ceric ion oxidations.[2] In this paper, the oxidation of various functional groups on treatment with ceric ammonium nitrate (*CAN*) or ceric ammonium sulfate are reported. The main results are the following.

a. Depending on its structural features an alcohol may undergo either direct oxidation to a carbonyl compound, fragmentation or both processes:

$$ArCH_2OH \xrightarrow[CH_3CO_2H,\ H_2O,\ 90\ C]{Ce(NH_4)_2(NO_3)_6} ArCHO$$

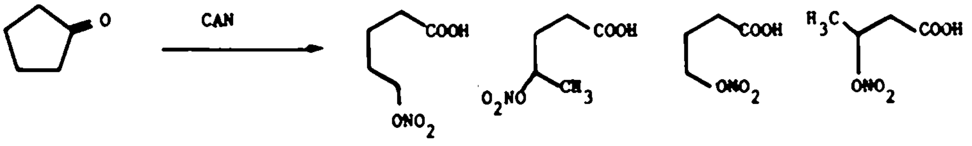


$$ArCH(OH)\text{-}CH_2\text{-}Ar \xrightarrow{\bullet} ArCHO + \text{products derived from the benzyl moiety}$$

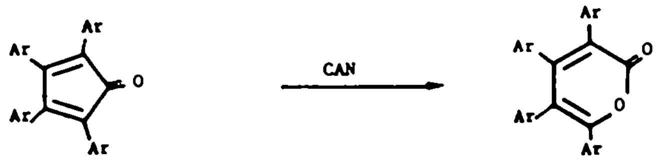


b. Vicinals glycols and polyhydric alcohols are quantitatively cleaved by ceric ion.

c. Aldehydes and ketones are susceptible to ceric ion oxidation. The main products isolated from the reaction of certain cyclic ketones are nitrato-carboxylic acids.

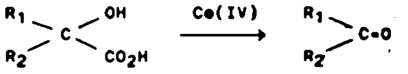


d. Some ketones undergo an extremely rapid Bayer–Villiger oxidation.



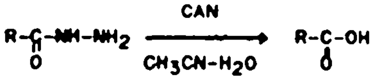
e. Oximes and semi-carbazones are rapidly cleaved by CAN to give the parent carbonyl compounds.

f. Carboxylic acids are resistant to ceric oxidation. However, oxalic acid and malonic acid are readily oxidized by ceric ion to $CO_2$ and $H_2O$ and α-hydroxycarboxylic acids are degraded by ceric sulfate or CAN to carbonyl compounds having one fewer carbon atom.



$$R_1R_2C(OH)CO_2H \xrightarrow{Ce(IV)} R_1R_2C{=}O$$

g. Carboxylic acids can be isolated in good yields after contact of a solution of carboxylic acid hydrazides with CAN.



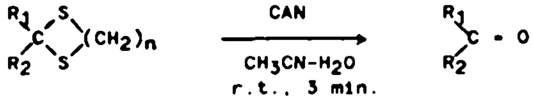
$$R{-}\underset{O}{\overset{\|}{C}}{-}NH{-}NH_2 \xrightarrow[CH_3CN-H_2O]{CAN} R{-}\underset{O}{\overset{\|}{C}}{-}OH$$

h. Dihydroquinones are quickly converted to quinones with CAN.

i. Polynuclear aromatic hydrocarbons are oxidized by CAN, but the reaction is extremely complex. The major products are quinones.

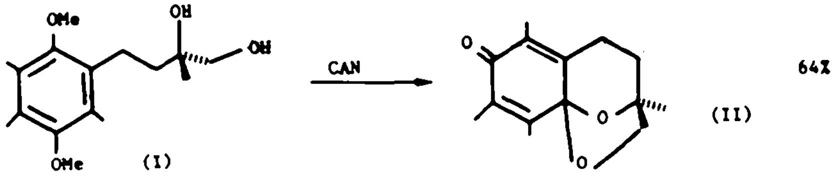
j. Benzylic methyl and methylene groups can be converted to carbonyl functions by treatment with CAN in an acidic medium. The reaction normally stops at the mono-carbonyl stage.

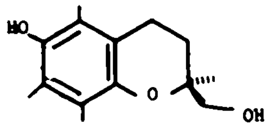
k. CAN promotes selective oxygenation of diarylsulfides to sulfoxides at room temperature in excellent yields. Sulfones are not formed. This method is not suitable for aliphatic sulfides. Dithianes and 1,3-dithiolanes are readily degraded to the parent carbonyl compounds.



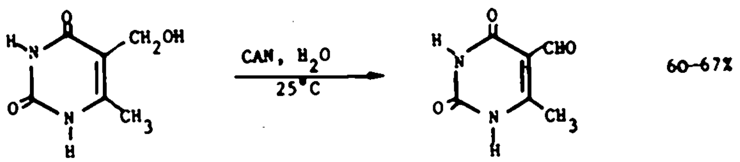
Within the past ten years, ceric oxidations have been often used in the course of various syntheses of polyfunctional compounds.

*For example*, oxidation of the diol(I) to ketal(II) with CAN is a key step in the synthesis of the vitamin E precursor:[132]

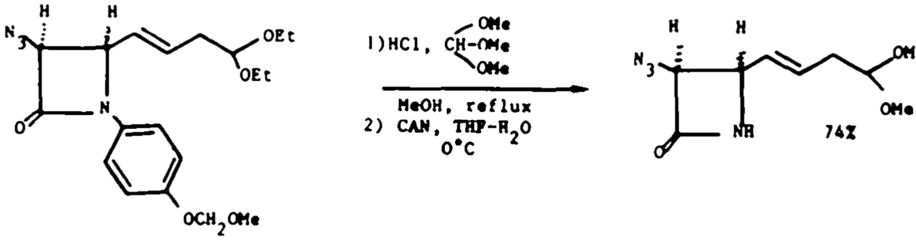




In the total synthesis of (+)-sparsomycin, CAN is used as an oxidant to produce an aldehyde:[133]



Fukuyama *et al.* used CAN for the oxidative removal of an N protecting group in the total synthesis of the racemic antibiotic 593A:[134]



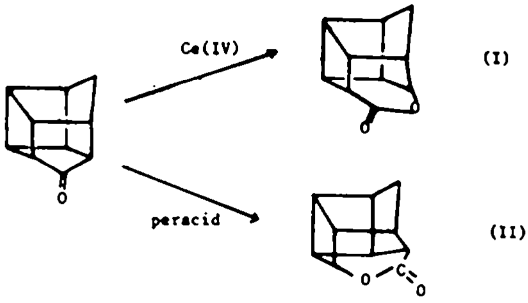
We present here new reagents, new reactions and new methodology or improvements in ceric oxidations of organic compounds. Kinetic and mechanistic studies are beyond the scope of this review.

### 5.2. *New reactions or improvements in reactions using CAN as a reagent*

CAN is a commercially available, stable, soluble salt of cerium(IV); for these reasons its properties are still being widely investigated.

It has been shown that ceric oxidation of adamantone furnishes the corresponding Baeyer–Villiger lactone in good yield.[135] A study on three pentacyclic ketones demonstrated that these also undergo efficient Baeyer–Villiger oxidations.[136]

It is interesting to note that pentacyclo[5,3,0,0$^{2,5}$,0$^{3,9}$,0$^{4,8}$]decan-6-one give the lactone (I) in 78% yield whereas peracid oxidation furnishes the other isomer (II).



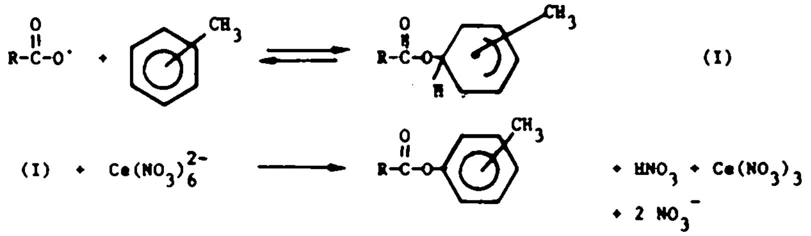
Kurtz *et al.* studied the decomposition of dialkyl peroxydicarbonates in the presence of two molar equivalents of CAN in toluene. Tolyl alkyl carbonates are obtained in yields of 75–90% based on two carbonate moieties from each peroxide molecule.[137]

$$(\mathrm{iPrOCO_2})_2 + 2\,\mathrm{CAN} + 2\,\mathrm{C_6H_5CH_3} \xrightarrow[60^\circ-24\,\mathrm{h}]{\mathrm{CH_3CN}} 2\,\mathrm{iPrOCO_2C_6H_4CH_3}$$

(the ortho isomer is the major product)

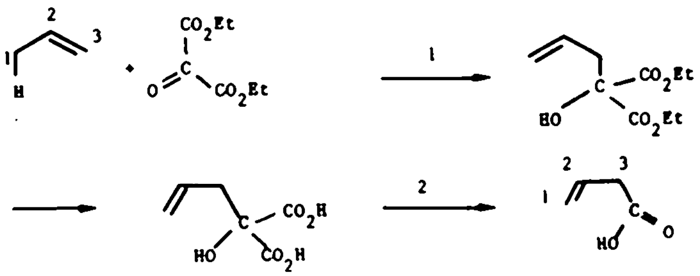
$$+\mathrm{Ce(NO_3)_3} + \mathrm{NH_4NO_3} + 2\,\mathrm{HNO_3}$$

The proposed mechanism is the following:



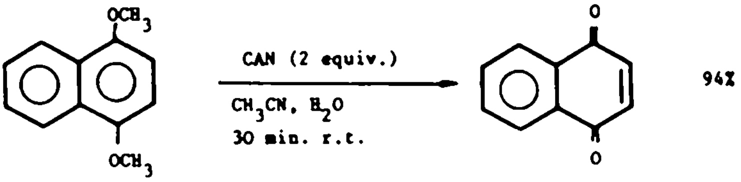
R = iPrO, sec BuO, $C_6H_5$

Allyl carboxylic acids can be prepared according to the scheme below, which is synthetically equivalent to an ene reaction of carbon dioxide.[138]

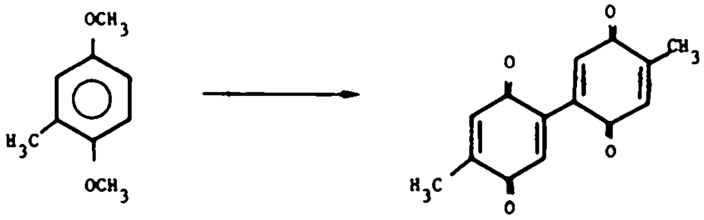


The second step, an oxidative bis decarboxylation of α-hydroxymalonic acid can be achieved with good yields using CAN in acetonitrile instead of sodium periodate.

A reaction which should find broad application is the oxidative demethylation of hydroquinone dimethyl ether with CAN, which lead to quinones generally in good yields.[139]

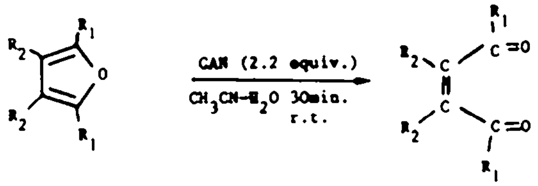


The reaction can be carried out in the absence of strong acid and is generally quite fast at room temperature. Various functional groups are tolerated. With some hydroquinone dimethyl ethers, however, the major is a dimer:

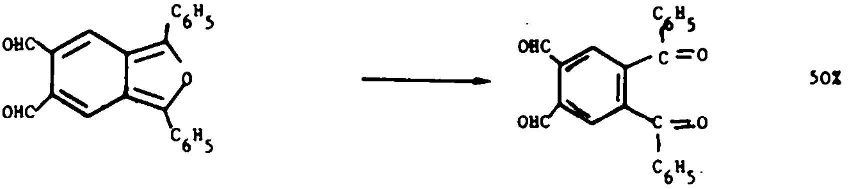


The method can be improved (no condensation side reactions) by using pyridine-2,6-dicarboxylic acid N-oxide as a ligand of CAN.[140]

Aldehydic and ketonic 1,4-dicarbonyl compounds can be prepared in good yields by oxidative cleavage of furans, isobenzofurans and furo[3,4d]pyridazines with CAN.[141]

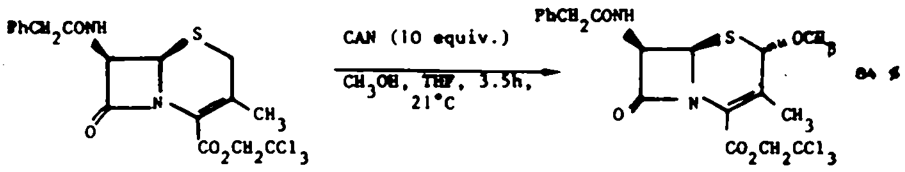


Interestingly, certain sensitive groups present in the molecule are not affected:



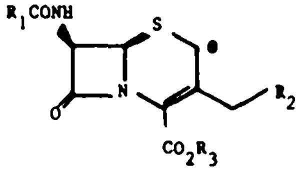
It is worthy of note that CAN does not cleave the methoxy groups in 4,7-dimethoxy-1,3-diphenylisobenzofuran:

A new, operationally simple method for stereospecific 2-alkoxylation of cephalosporins using CAN in an alcoholic medium was reported recently.[142,143]

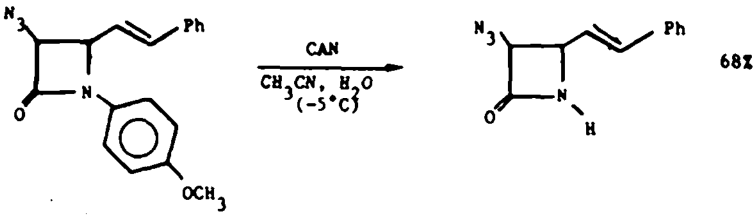


(Ethanol, isopropanol and benzyl alcohol can also be used in these reactions.)

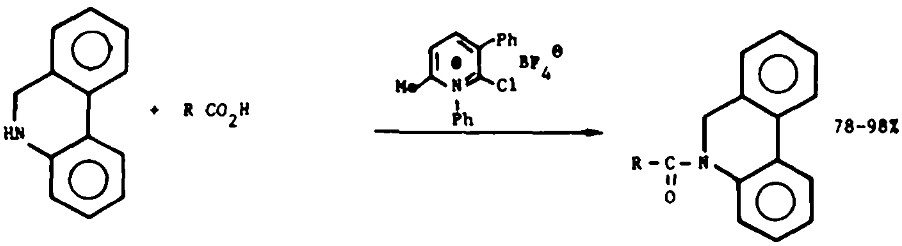
The mechanism of the reaction proceeds via one electron oxidation of the sulfur atom by the Ce(IV) reagent and subsequent formation of the sulfur-stabilized carbocation which is trapped by the nucleophilic solvent.



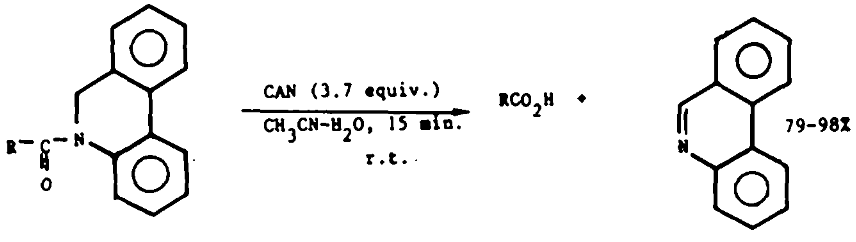
CAN has been used for the oxidative removal of protecting groups. Related to the oxidative demethylation of hydroquinone dimethylether (see above) is the oxidative N-dearylation of azetidinones with CAN.[144,145]



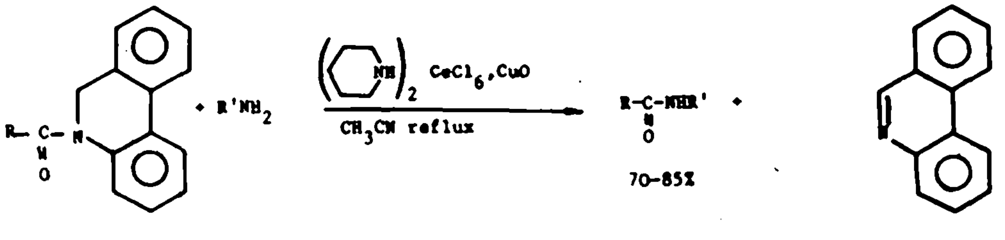
Mukaiyama *et al.* found that the carboxyl group can easily be protected as the amide derived from 5,6-dihydrophenanthridines under appropriate conditions.[146]



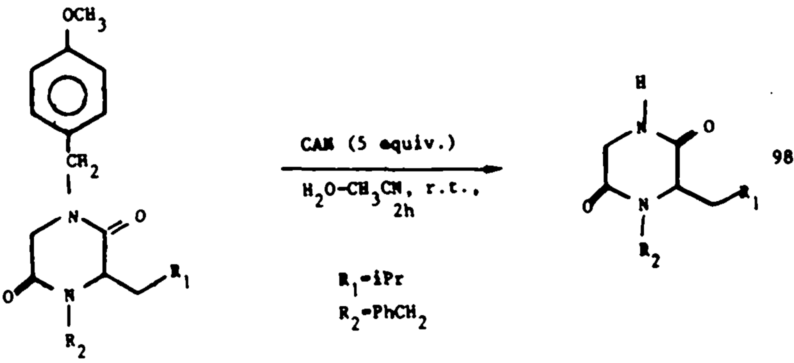
The resulting amides are stable under basic or acidic hydrolytic conditions. They can be easily oxidatively cleaved with CAN under relatively mild conditions to regenerate the carboxylic acid :



If the protected carboxylic acid is treated in the presence of a primary amine with the combination ceric pyridinium chloride and cupric oxide, the carboxylic acid is not regenerated ; it is transformed to the corresponding amide.[147]

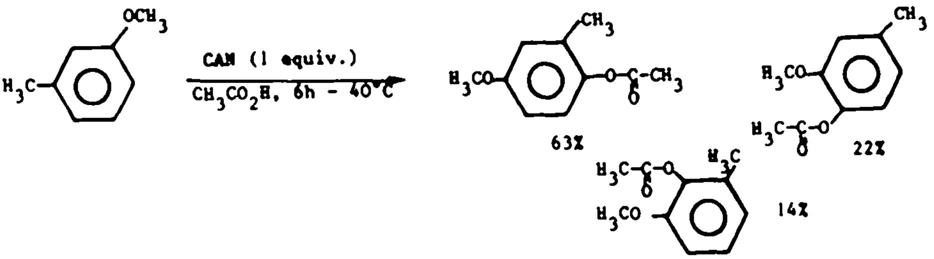


Very recently, it was shown that the 4-methoxybenzyl group can be easily introduced onto the 2,5-piperazine dione skeleton as a suitable N-protecting group which is smoothly removed by CAN oxidation under mild conditions.[148]

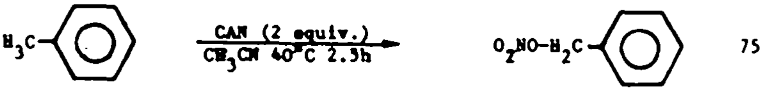


The oxidation of alkyl derivatives of aromatic hydrocarbons by Ce(IV) is an extensively studied reaction. The mechanisms has been widely investigated. The products distribution is strongly dependent on the experimental conditions. This aspect of cerium chemistry was reviewed in 1981 by Beletskaya and Makhon'kov.[149] Very recently some interesting results concerning this topic have been published.

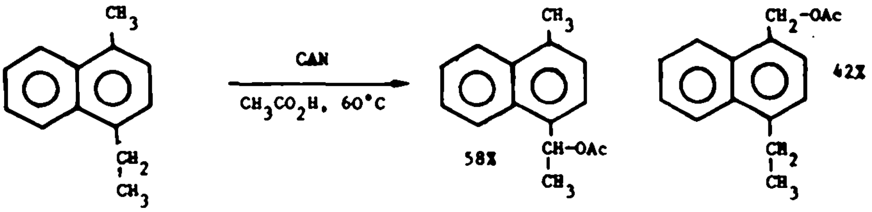
The distribution between nuclear and side chain substitution products in the oxidation of some alkylaromatic compound by CAN in acetic acid has been studied by Baciocchi *et al.*[150] It was shown that under the experimental conditions used (except in the case of p-methoxytoluene), nuclear acetoxylation is the predominant or almost exclusive reaction.



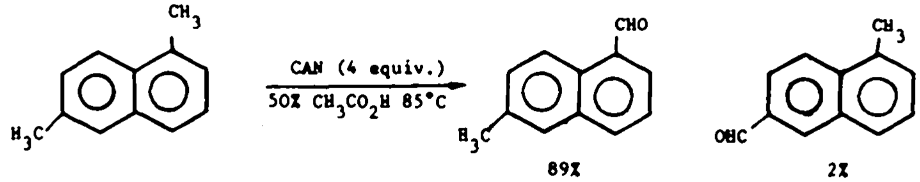
The same authors studied the reaction of CAN with methylbenzenes under irradiation in acetonitrile. A clean side-chain oxidation takes place under very mild conditions leading to high yields of benzyl nitrates.[151]



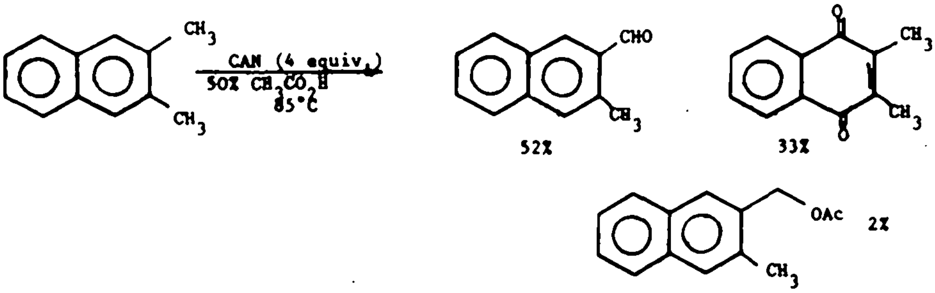
Reaction of an alkylnaphthalene *with CAN in acetic acid at 60°* has been investigated, it was observed that side chain acetoxylation takes place exclusively with 1-ethyl and 1-methyl-4-ethylnaphthalene.[152]



On the contrary the oxidation of isomeric dimethyl naphthalenes *with CAN in 50% acetic acid at 85°* leads to the corresponding monoaldehydes in yields better than 80%.[153] In each case the methyl group attached to C-1 is oxidized with a selectively better than 11 : 1.



Under the same experimental conditions methylnaphthalenes with no group in a peri position give aldehydes in fair yields, accompanied by significant amounts of 1,4-naphthoquinone.[154]



The side-chain oxidation of *p*-methoxytoluene with CAN in methanol proceeds smoothly yielding anisaldehyde (90%). Electrooxidation of the recovered cerium (III) salts can be performed in methanol to give a solution of CAN which can be used for a subsequent oxidation. Thus, an indirect electrooxidation is realized.[155] Indirect electrooxidation procedures involving the recycling of electron carriers such as cerium ions have been reviewed recently by Torii.[156]

### 5.3. *New Ce(IV) reagents and their use in organic chemistry*

CAN is a widely used reagent, nevertheless the oxidations with CAN suffer from:

(1) Highly acidic conditions which are not suitable for the oxidations of acid sensitive compounds.

(2) Reactions usually proceed in a mixture of water and a polar organic solvent which complicates work-up of the reaction.

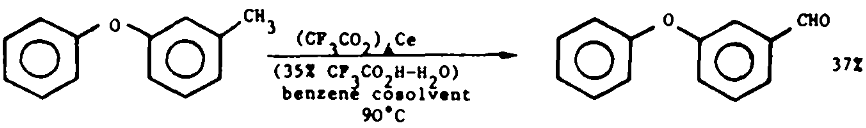
(3) In many cases CAN leads to a complex mixture of products.

To obviate these difficulties other Ce(IV) reagents have been prepared:

The reaction of Ce(IV) hydroxide with trifluoracetic acid gives the basic salt $Ce(OH)_2(O_2CCF_3)_2$ which on further treatment with the same acid and its anhydride yields Ce(IV) trifluoroacetate.[157] This compound is soluble in coordinating solvents (e.g. acetone, 1,2-dimethoxyethane, dimethylsulfoxide and acetonitrile).

The reactions of this salt with benzenoid hydrocarbons were studied. With electron rich compounds, oxidation is rapid at room temperature. The products are biaryls, diarylmethanes and trifluoroacetates esters, the proportions of which depends on the structure of the aromatic compounds.

This reagent has been also found to be especially effective for the oxidation of activated toluenes to the corresponding aldehydes.[158] Ceric ion is consumed in stoichiometric amounts but can be electrochemically regenerated at high current efficiencies (95%).



Recently Firouzabadi *et al.* have developed several Ce(IV) reagents in order to perform oxidations in aprotic organic solvents under neutral conditions. They are prepared according to the following schemes

•$Ce(OH)_4 + 3(C_2H_5)_3N \xrightarrow[NO_3H,\ 0°]{concentrated} [Ce(Et_3NH)_2](NO_3)_6$

ceric triethylammonium nitrate (CTAN)[159]

•$K_2Cr_2O_7 + 2\,Ce(NH_4)_2(NO_3)_6 \xrightarrow{H_2O} [Ce(NO_3)_3]_2CrO_4 + 2\,NO_3K + 4\,NH_4NO_3 + CrO_3$

bis[(trinitratocerium(IV))]chromate (BTNCC)[160,161]

•$CeCl_3,\ 7\,H_2O \xrightarrow[2)\,H_2O_2]{1)\,NH_4OH} Ce(OH)_3O_2H$ Ceric trihydroxyhydroperoxide (CTH)[162]

•$K_2Cr_2O_7 + Ce(NH_4)_2(NO_3)_6 \xrightarrow{H_2O} [Ce(NO_3)_2]CrO_4,\ 2\,H_2O + CrO_3 + 2\,NO_3K + 2\,NH_4NO_3$

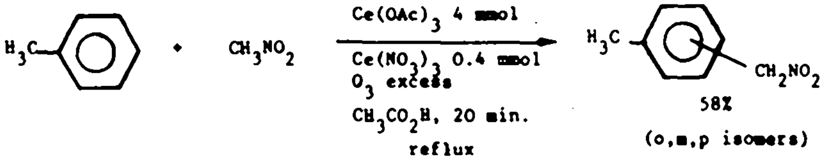
dinitratocerium (IV) chromate dihydrate (DCCD)[163]

•$K_3H_2IO_6 + 3\,Ce(NH_4)_2(NO_3)_6 \rightarrow [(NO_3)_3Ce]_3H_2I_6 + 6\,NO_3NH_4 + 3\,NO_3K$

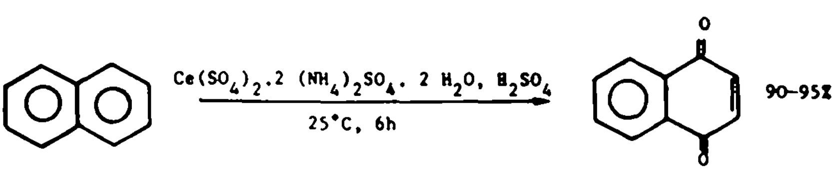
tris[trinitratocerium(IV)] paraperiodate (TTNCPP)[164]

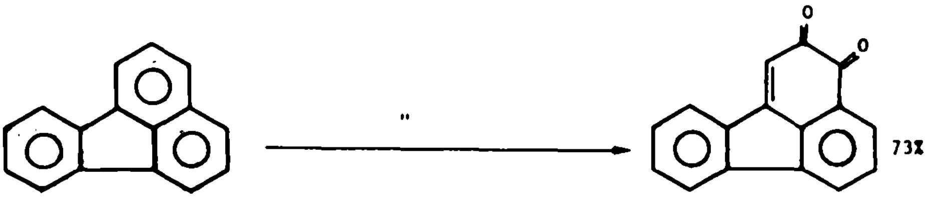
These new reagents perform interesting oxidations, some of which are tabulated below (Table 12). CTAN and BTNC oxidize α-hydroxyketones to the corresponding diketones with high yields, BTNCC oxidizes alkyl, aryl, and benzyl phenyl carbinols to the corresponding carbonyl compounds without cleavage of C—C bonds. This reagent also allows conversion of thiols to their disulfides very smoothly in good yields. This reaction was also performed with CTH; the reagent can be regenerated by the addition of a solution of $H_2O_2$ to the remaining Ce(III) compound. TTNCPP is a very effective oxidant for the cleavage of 1,2-diols and for the oxidation of cinnamyl alcohol to cinnamaldehyde.

CAN is capable of effecting aromatic nitromethylation of the aromatic ring with nitromethane. Unfortunately, other products are formed in high yields. It was found that cerium (IV) acetate generated in solution by ozonolysis of either cerium (III) nitrate or a mixture of cerium (III) acetate and cerium (III) nitrate in acetic acid promotes high yields of nitromethylation products. Furthermore, this reaction is free of side-products.[165]



The oxidation of polycyclic aromatic hydrocarbons to quinones has been improved by using ceric ammonium sulfate instead of CAN.[166]





Recently, it has been found that cerium (IV) alkoxides can be readily prepared in a one step synthesis using CAN as the starting material.[167]

$$(NO_3)_6Ce(NH_4)_2 + 4\,ROH + 4\,NH_3 \rightarrow Ce(OR)_4 + 6\,NH_4NO_3$$

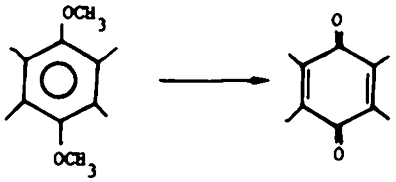
$$(NO_3)_6Ce(NH_4)_2 + 4\,ROH + 6\,NaOCH_3 \rightarrow Ce(OR)_4 + 6\,NaNO_3 + 2\,NH_3 + 6\,CH_3OH$$

These alkoxides have not yet been tested for the oxidation of organic compounds.

### 5.4. *New methodology*

The strong oxidizing power of tetravalent cerium salts sometimes is of limited synthetic value because it often leads to undesired and over-oxidized products. In order to overcome these difficulties various new procedures have been developed.

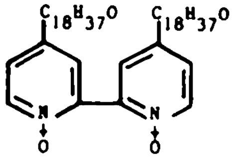
5.4.1. *Two-phase oxidations.* Oxidations (1) and (2) have been carried out in the two-phase system ($H_2O$, cyclohexane) by CAN and an appropriate catalyst.



(1)

$$ArCH_3 \rightarrow ArCHO + ArCH_2ONO_2 \qquad (2)$$

Both

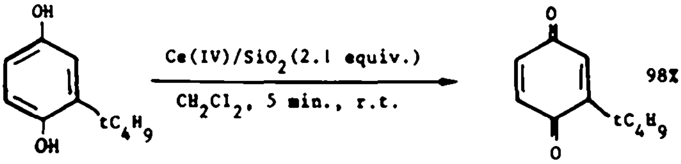


a 4,4'-dialkoxy-2,2' bipyridine-1,1'-dioxide

and the anionic surfactan, sodium dodecyl sulfate (SDS) have been tested. In the latter case, it was concluded that the catalytic action is due to the binding of aromatic compounds and Ce(IV) ions to the surface of the SDS micelles.[168,169] It seems that the micellar oxidant has a high oxidation potential which should allow oxidation of the comparatively nonreactive substrates.

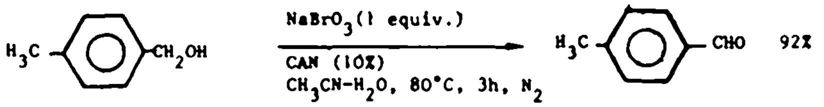
5.4.2. *Oxidations by silica supported cerium (IV) salts.* Owing to their mildness, ease of operation, and enhanced reactivity, heterogeneous organic reactions effected by reagents supported on porous solids have become important for laboratory-scale synthesis. Chawla and Mittal have developed a procedure which uses silica gel supported ammonium nitrate for the controlled oxidative nitration of some naphthalene derivatives.[170]

Treatment of polynuclear arenes and hydroxynaphthalenes with CAN absorbed on silicagel in the absence of solvent affords mononitro derivatives, whereas the reaction of the same substrates with CAN in solution leads to a considerable percentage of dinitroderivatives or the corresponding quinones. Fisher and Henderson used a reagent prepared by coating silica with CAN, which was obtained as a free-flowing yellow powder. Oxidations of hydroquinones or catechols were performed. Pure quinones were obtained in high yield.[171]



5.4.3. *Catalytic systems.* The practicality of cerium (IV) oxidations in preparative chemistry has been limited by the requirement for large quantities of reagent. This is due to the combined factors that cerium (IV) ion can accept only one electron and that such oxidants have relatively high molecular weights.

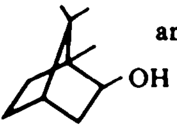
Ho *et al.* have found that the dual oxidant system $Ce^{4+}/BrO_3^-$ allows the use of cerium (IV) as a catalyst. Several organic oxidations have been investigated. The cerium (IV) ion is the true reagent; it is continuously replenished by the action of the bromate anion. With this system hydroquinones are oxidized to quinones, sulfides are oxidized to sulfoxides and arylmethanols are transformed into the corresponding carbonyl compounds in good yields.[172,173]



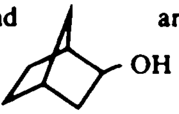
Secondary alcohols are also oxidized to ketones in excellent yields with the system CAN/$BrO_3^-$.[174]

$$\text{cyclodecanol} \xrightarrow[\text{CAN (10\%), } CH_3CN-H_2O;\ \text{reflux; 30 min}]{NaBrO_3\ \text{(1 equiv.)}} \text{cyclodecanone 98\%}$$

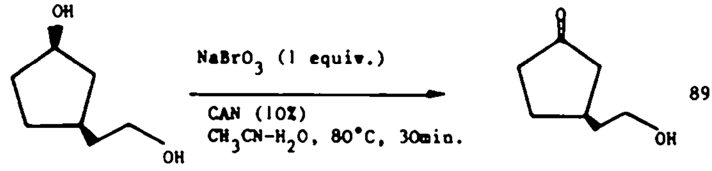
Cerium (IV) sulfate can be used instead of CAN. Primary alcohols are not oxidized, but PhCH(OH)—CO—Ph,



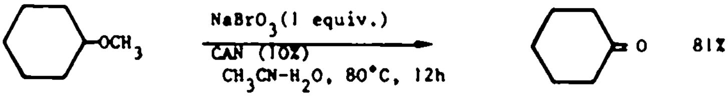
and



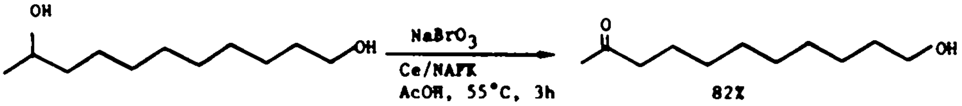
are cleanly transformed to the corresponding ketones in contrast to their treatment with stoichiometric amounts of CAN. The treatment of primary secondary diols with this technique affords hydroxyketones arising from selective oxidation of the secondary alcohols.



A new oxidative cleavage of ethers has been performed with the same catalytic system. Alkyl and silyl ethers are readily cleaved to afford the corresponding carbonyl compounds.[175]



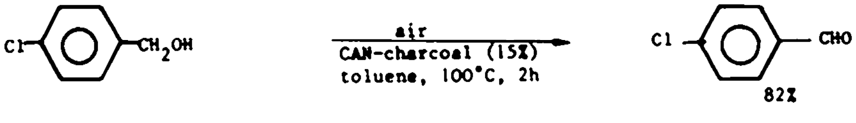
A polymer supported catalyst (Ce/NAFK) prepared by treatment of Nafion (R) 511 with CAN was also found to be an effective catalyst for the selective oxidation of diols by $NaBrO_3$.



Furthermore Ce/NAFK catalyzes the oxidation of secondary alcohols with *t*-BuOOH.[176]

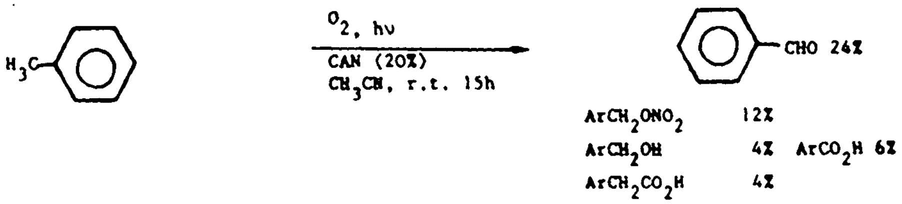
$$\text{4-t-butylcyclohexanol} \xrightarrow[\text{Ce/NAFK (27\%) benzene; 6 h; 80°}]{\text{tBuOOH (4 equiv.)}} \text{4-t-butylcyclohexanone } 98\%$$

CAN adsorbed on activated charcoal catalyzes the air oxidation of benzyl and related alcohols to the corresponding carbonyl compounds in good to high yield.[177] Recently, Beleskaya *et al.* have shown that $PhCH_2OH$ can be quantitatively converted into PhCHO under aerobic conditions in trifluoroacetic acid in presence of catalytic amounts of CAN (3%).[178] The catalytic oxygen oxidation of anthracene into anthraquinone has been reported[179] using CAN as the catalyst. The catalyst can be restored on addition of $HNO_3$. The experimental conditions have been optimized.

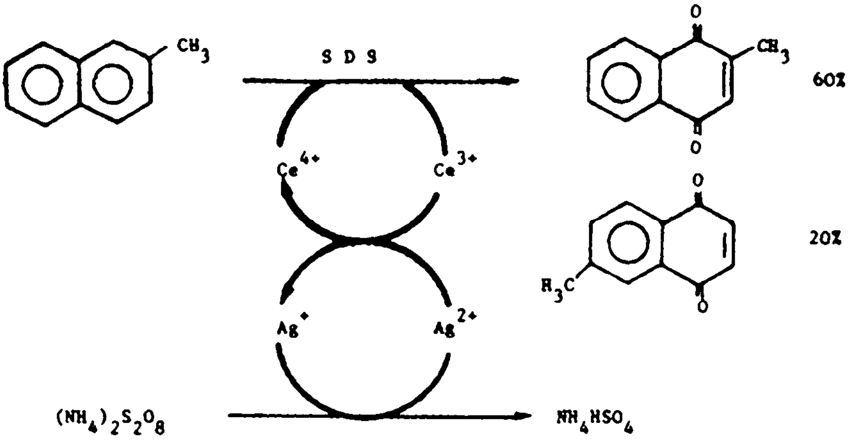


Very recently it was found that CAN is able to catalyze the photochemical autooxidation of alkyl benzenes under mild conditions. This process is enhanced by the presence of added acids ($HClO_4$, $HNO_3$).[180] The reaction is probably promoted by $NO_3$ radicals generated by the photochemical decomposition of CAN.

Another catalytic system using Ce(IV) ammonium sulfate (CAS) has been studied for the oxidation of polycyclic hydrocarbons to quinones. It takes advantage of the fact that Ce(III) is readily converted into Ce(IV) by persulfate with Ag(I) ion as a catalyst. The reaction was performed

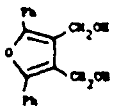
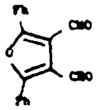
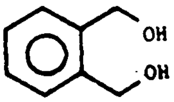
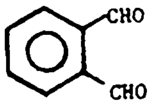


under biphasic conditions (cyclohexane-water) with sodium dodecylsulfate (SDS) as an anionic surfactant.[181]



Substrate = 4.16 mmol; CAS: 2.5 mmol; $AgNO_3$: 0.75 mmol; SDS: 0.023 mmol; $(NH_4)_2S_2O_8$: 16.6 mmol; $H_2SO_4$: 13.75 ml; solvent: $H_2O$-cyclohexane (25 ml + 15 ml); 50°; 6 h.

Table 12

| Reagent | Substrate | Product | Oxidant Reactant | Reaction time (h) | Isolated yield (%) |
|---|---|---|---|---|---|
| CTAN | p-methoxybenzylic alcohol | p-methoxybenzylic alcohol | 1.2 | 1 | 97 |
| CTAN | benzoin | benzil | 2 | 2.4 | 85 |
| CTAN |  |  | 0.5 | 0.5 | 85 |
| BTNCC | piperonol | piperonal | 2 | 0.6 | 85 |
| BTNCC | phenylbenzylcarbinol | phenylbenzylketone | 2 | 0.7 | 85–90 |
| BTNCC | thiophenol | phenyl disulfide | 2 | 4 | 80–90 |
| BTNCC | benzylmercaptan | benzyl disulfide | 2 | 8 | 70–80 |
| BTNCC | cyclohexyl mercaptan | cyclohexyl disulfide | 2 | 6 | 75–80 |
| BTNCC | benzoin | benzil | 2 | 2 | 85–90 |
| CTH | p-anisyl alc. | p-anisyl ald. | 2 | 0.5 | 95 |
| CTH | furoin | furil | 2 | 5 min | 95 |
| CTH | p-toluidine | 4,4-dimethyl azobenzene | 2 | 1 | 55–65 |
| CTH | 2-mercapto benzothiazole | 2-benzothiazol disulfide | 2 | 0.25 | 95 |
| CTH | mandelic acid | benzaldehyde | 2 | 1 | 95 |
| DCCD | phenyl benzyl carbinol | phenyl benzyl ketone | 2 | 1.5 | 95 |
| DCCD |  |  | 4 | 2 | 85 |
| DCCD | benzyl amine | benzaldehyde | 2 | 1.25 | 100 |
| DCCD | 2-mercapto benzothiazole | 2-benzothiazol disulfide | 2 | 4.5 | 75 |
| TNCPP | 1,2-diphenyl ethylene glycol | benzaldehyde | 2 | 0.5 | 90–95 |
| TNCPP | 1-phenylethylene glycol | benzaldehyde | 2 | 1.5 | 95–100 |
| TNCPP | benzyl mercaptan | benzyl disulfide | 2 | 1 | 90–100 |
| TNCPP | furoin | furil | 2 | 1 | 100 |

## 6. CONCLUSION

The field of rare earths was stagnant for many years as far as organic chemistry (except ceric oxidations) was concerned. The use of shift reagents in the 1970s familiarized organic chemists with this unusual family of elements. After an induction period where new reagents were found to be useful in synthesis, it seems that we are now reaching the stage of exponential growth. Organometallics as well as various salts were found to catalyze or to promote many different types of reaction. Lanthanide derivatives are beginning to be used for selective transformations of quite complex molecules, thus it can be anticipated the near future will bring many new developments in this area.

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