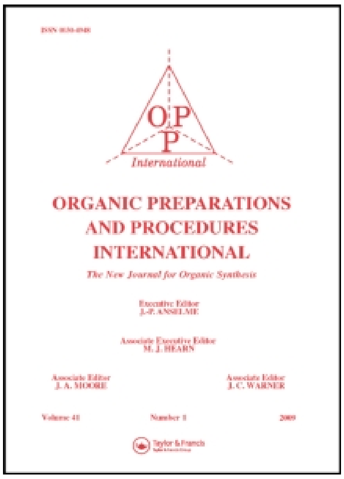

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LANTHANIDES IN ORGANIC SYNTHESIS

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I. INTRODUCTION

The bulk of the world's supply of the rare earth or lanthanide elements are extracted from an intrusive igneous carbonatite orebody in Mountain Pass, California which contains twelve percent of a nonradioactive rare earth fluocarbonate mineral, bastnasite.[1] Lanthanides have familiar uses which include europium phosphors in television screens, samarium-alloys in magnets,[2] and several applications in catalysis.[3]

The utility of the lanthanide elements as reagents in synthesis has only recently been appreciated by organic chemists. In the past few years, there has been an explosion in the number of reports on the use of lanthanides to mediate organic reactions. In large part this is due to the pioneering efforts of Kagan and Luche. The usefulness of the methods developed by these and other groups is evidenced by the number of citations which have rapidly appeared.

The lanthanides are familiar to every organic chemist as NMR shift reagents.[4] Another commonly used lanthanide based methodology is found in cerium(IV) oxidations.[5] These aspects of lanthanide chemistry have been reviewed elsewhere and will not be discussed here. This review will focus on the rather exciting chemistry involving the lanthanide (II) and (III) oxidation states, as well as organolanthanide chemistry of particular interest to the synthetic organic chemist.

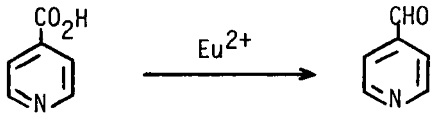
This review, which covers the literature to early 1983, intends to convey the heightened interest of synthetic chemists upon the discovery and exploration of a new area of organic methodology.

II. LANTHANIDE(II) REAGENTS

In the lanthanide (II) oxidation state, the usual driving force for reactions is electron transfer to give the lanthanide (III) species, hence the use of lanthanide (II) reagents involve reductions and reductive couplings. Samarium is perhaps the best candidate for reactions of this type because of its reduction potential, among the highest known for species soluble in organic media: E_0 aq $Sm^{2+}/Sm^{3+} = - 1.55$ V.[31]

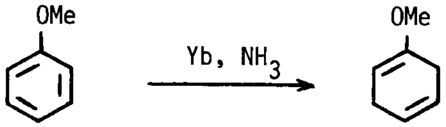
1. Electron Transfer Reductions

An early example of the use of the lanthanide (II) was the report of the reduction of isonicotinic acid to isonicotinal (Eq. 1), and the preliminary report that the corresponding pyridinium salt was reduced to its "dihydro" derivative, which was not completely characterized.[6]



(1)

White and Larson subsequently reported an example of a lanthanide (II) Birch reduction system with ytterbium in liquid ammonia, which presumably proceeds *via* the ytterbium (II).[7] The ytterbium-ammonia system represents a useful reducing agent whose potency resembles that of the alkali metal solutions. Thus, anisole is reduced to 1-methoxy-1,4-cyclohexadiene (Eq. 2), benzoic acid to 1,4-dihydrobenzoic acid (Eq. 3) and 4-octyne to *trans*-4-octene (Eq. 4).



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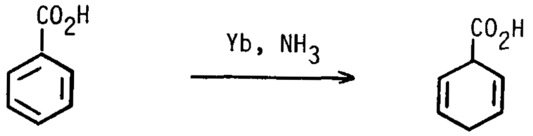

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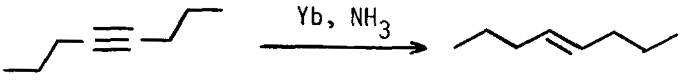

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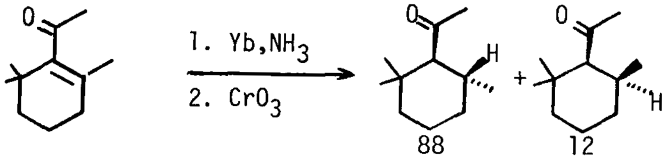

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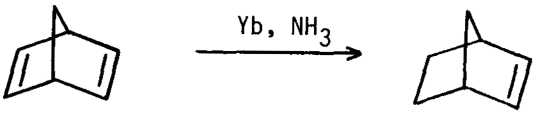
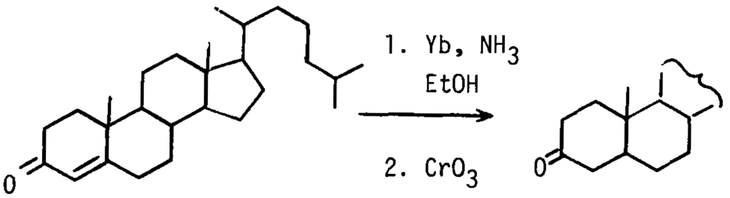


(6)

1,4-Enones undergo conjugate reduction (Eq. 5), which invariably contained mixtures of ketones and the corresponding alcohols. In these cases, the crude reaction mixtures were treated with Jones reagent to facilitate the isolation of the resultant ketone from the reaction mixture. In addition, two noteworthy examples were the hydrogenation of certain reactive alkenes (Eq. 6) and the dimerization of cholest-4-en-3-one in the absence of ethanol (Eq. 8); the latter compound underwent conjugate reduction in the presence of ethanol, after oxidative work-up (Eq. 7).



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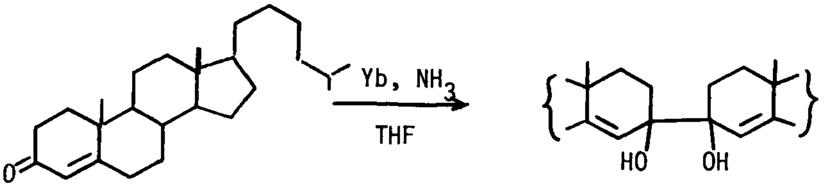

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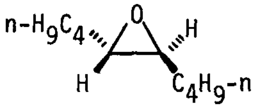
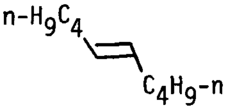
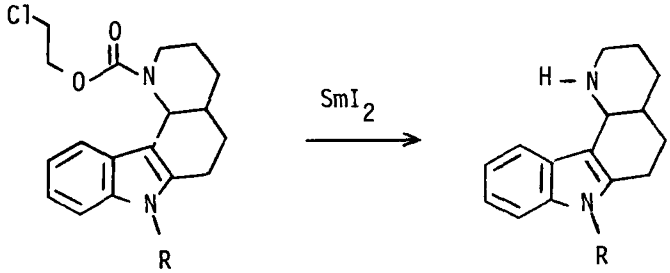
The utility of lanthanide(II) reagents was greatly expanded by Kagan who developed a convenient and high yield preparation of samarium(II) or ytterbium(II) in THF solutions.[8] These workers amplified their initial report by several interesting and useful functional group transformations carried out on a preparative scale (Scheme I). Thus epoxides are deoxygenated to alkenes (Eq. 9) and sulfoxides deoxygenated to sulfides (Eq. 10). Alkyl halides and sulfonate esters are reduced to hydrocarbons (Eq. 11) and benzyl halides dimerize (Eq. 12). Aldehydes are reduced rapidly (Eq. 13), and α,β-unsaturated esters undergo conjugate reduction (Eq. 14) to the corresponding saturated esters.[9a]

In a very recent report, Kagan has observed that aromatic imines and nitro groups are reduced to amines (Eq. 84 and 86).[9b] Oximes (Eq. 85) give complex mixtures, the mechanism is not yet elucidated.[9b]

Other investigators have applied this reagent as a useful one-electron transfer reagent. Thus Magnus and coworkers utilized samarium diiodide to selectively deprotect N-chlorocarbonates and xanthates.[10] The 2-chloroethylcarbamate (Eq. 15) was resistant to Zn-AcOH, $CrCl_2$-HCl, tri-n-butyltin hydride-AIBN and Zn-H_2O-THF-aquo-vitamin B_{12} but was cleanly reduced to the amine with samarium diiodide in 70% yield. The generation of radicals for fragmentation of steroidal 11α-xanthates to seco-steroids was also studied by Magnus. While tri-n-butyltin hydride

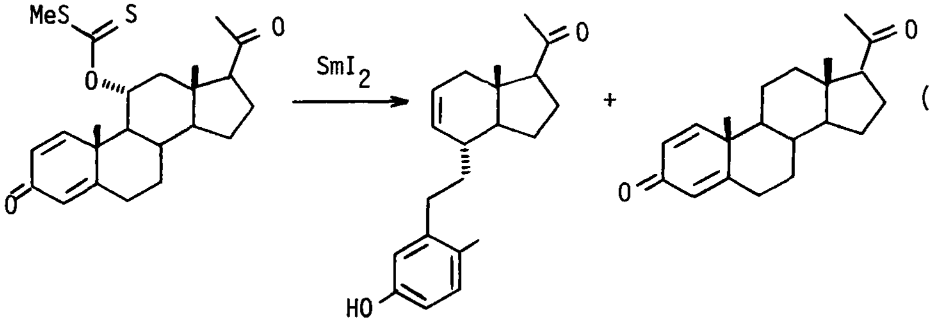
Scheme I. Electron Transfer Reduction with Samarium Diiodide.

Equation	Starting Material	Product	Reference
9			9a
10	$Ph_2S{=}O$	Ph_2S	9a
11	$CH_3(CH_2)_{10}CH_2OTs$	$CH_3(CH_2)_{10}CH_3$	9a
12	$PhCH_2Br$	$PhCH_2CH_2Ph$	9a
13	$CH_3(CH_2)_6CHO$	$CH_3(CH_2)_6CH_2OH$	9a
14	$PhCH{=}CHCO_2Et$	$PhCH_2CH_2CO_2Et$	9a
84	$PhCH{=}NPh$	$PhCH_2NHPh$	9b
85	$PhCH{=}NOH$	$PhCH(NH_2)CH_2Ph$ (75) $PhCH_2NH_2CH_2Ph$ (25)	9b
86	m-$NCC_6H_4NO_2$	m-$NCC_6H_4NH_2$	9b



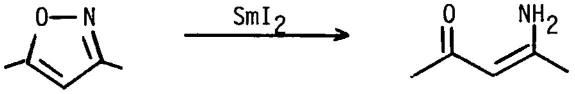
(15)

R = p-$CH_3OC_6H_4SO_2$-



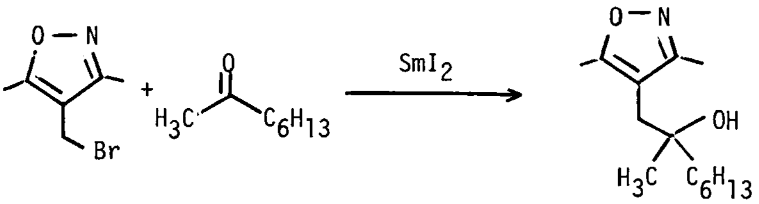
(16)

gave a 1:1 mixture of desired seco-steroid and reduction by-product (Eq. 16), samarium diiodide gave seco-steroid in 88% yield with no detectable reduction by-product. A recent report on the reductive ring opening of isoxazoles to enamino ketones further illustrates the usefulness of this reagent (Eq. 17).[11]



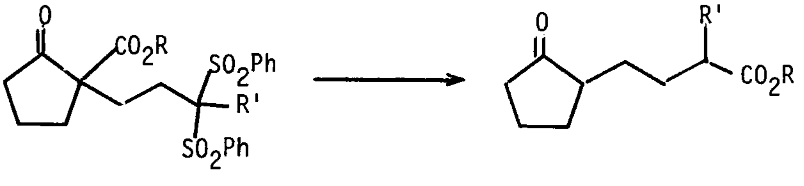
(17)

In one example, the bromoisoxazole shown in Eq. 18 underwent predominant "halogen-lanthanide" exchange. In further studies, trapping with electrophiles leads to a mixture of dimer and of the desired product (Eq. 18). This method for carbon-carbon bond formation requires very carefully controlled experimental conditions to minimize reductive ring opening and dimer formation.[11b]



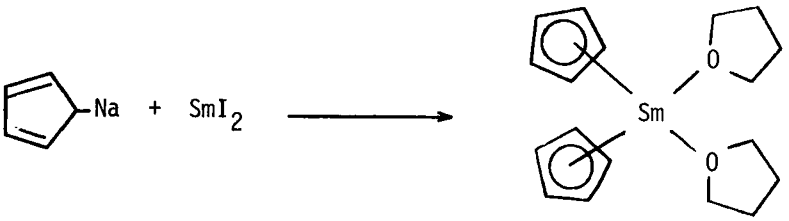
(18)

Reduction of sulfone keto-esters with samarium diiodide was attempted by Trost to study the carbanionic behavior of the incipient nucleophile; however, no fruitful results were obtained. The reaction depicted (Eq. 19) did proceed with lithium phenanthrenide in aprotic media.[17] Two groups have reported the preparation of organic-soluble



(19)

divalent samarium derivatives which hold much promise of future development as synthetic reagents. Kagan reports simple ligand metathesis with samarium diiodide and sodium cyclopentadienide (cp) to give bis(cp)Sm (Eq. 20),[8b] as its bis-THF-adduct.



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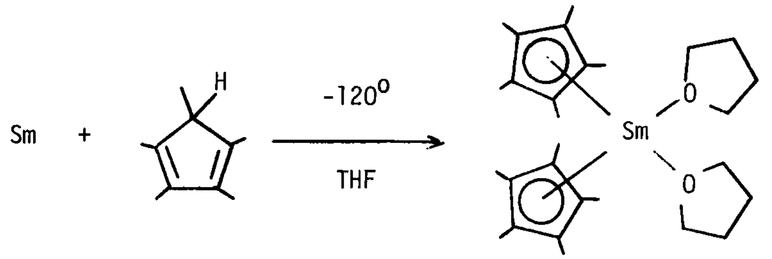
Evans utilized metal vapor techniques to prepare bis(pentamethylcyclopentadienyl) samarium (Eq. 21), which could be crystallized and was found by X-ray studies to be a bis-THF adduct. It reacted rapidly with



(21)

CO, NO, 3-hexyne, HgR_2 and $Co(PR_3)_4$ to form trivalent products. The same adduct also initiated the polymerization of ethylene and functioned as a catalyst precursor for catalytic hydrogenation of 3-hexyne to >99% cis-3-hexene under mild conditions.[47]

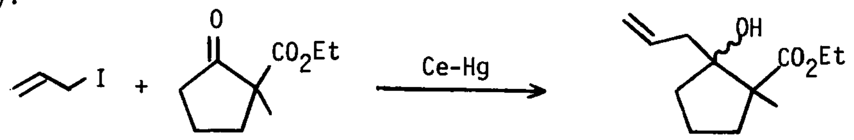
2. Carbon-Carbon Bond Formation via Reductive Coupling

Divalent Grignard type reagents with lanthanide elements was first reported by Evans (Eq. 22).[12a] Perfluorocarbon organic lanthanide

$$\text{Ph-I} + \text{Yb} \longrightarrow \text{Ph-Yb-I} + \text{PhCOPh} \longrightarrow \text{Ph}_3\text{COH} \qquad (22)$$

reagents were prepared by Deacon by transmetalation from $(R_F)_2Hg$ and ytterbium metal.[12b]

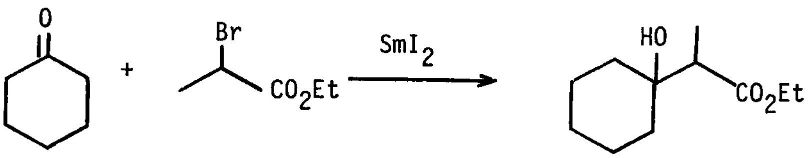
Reductive couplings have also been accomplished with cerium reagent systems (Eq. 23)[12c] and with diorgano ytterbium reagents (Eq. 24).[12d]



(23)

$$(Ph(CH_2)_2)_2Yb \quad + \quad PhCHO \quad \longrightarrow \quad PhCH_2CH_2CH(OH)Ph \qquad (24)$$

Kagan has explored in some detail the lanthanide-Barbier reaction.[9] Because of the sluggish reduction of ketones, addition of ketone and halide to a solution of samarium diiodide gives the coupling product in excellent yields on a preparative scale (Eq. 25). Aliphatic aldehydes can be coupled with allylic or benzylic halides (Eq. 26).[13] The reaction proceeds very rapidly, usually in minutes. Complications



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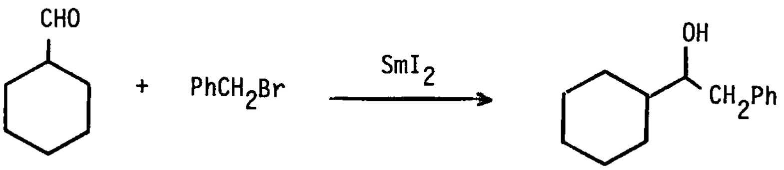
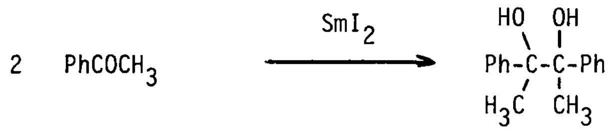


(26)

such as the Meerwein-Ponndorf-Verley reduction, arise with less reactive halides and aromatic aldehydes give pinacols. In fact, in the absence of halide, aromatic aldehydes and ketones give pinacols in excellent yields (Eq. 27);[15a] this reaction can also be accomplished with cerium and iodine.[15b]



$$2\ \mathrm{PhCOCH_3} \xrightarrow{\mathrm{SmI_2}} \mathrm{Ph{-}C(OH)(CH_3){-}C(OH)(CH_3){-}Ph}$$

(27)

Acid chlorides couple readily to yield α-diketones in the presence of samarium diiodide (Eq. 28).[14a] Trapping studies indicate that this reaction proceeds <u>via</u> acyl anion intermediates.[14b]

$$2\ \mathrm{PhCOCl} \xrightarrow{\mathrm{SmI_2}} \mathrm{PhCOCOPh} \qquad (28)$$

3. Mechanistic Studies

Kagan's exploration of the mechanism of samarium diiodide reactions has primarily focused on the isolation of products consistent with free-radical and radical-anion intermediates.[16]

Thus halide reduction is likely to proceed by the Scheme below

$$\mathrm{RX} + \mathrm{Sm}^{2+} \longrightarrow \mathrm{RX}^{\bullet-} + \mathrm{Sm}^{3+}$$

$$\mathrm{RX}^{\bullet-} \longrightarrow \mathrm{R}^{\bullet} + \mathrm{X}^{-}$$

$$\mathrm{R}^{\bullet} + \mathrm{Sm}^{2+} \longrightarrow \mathrm{R}^{-} + \mathrm{Sm}^{3+}$$

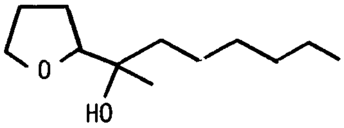
$$\mathrm{R}^{\bullet} + \mathrm{SH} \longrightarrow \mathrm{RH} + \mathrm{S}^{\bullet}$$

$$\mathrm{R}^{-} + \mathrm{SH} \longrightarrow \mathrm{RH} + \mathrm{S}^{-}$$

SH = solvents

The dimerization of benzylic halides can be explained by postulating the formation of stable radicals which can diffuse outside the coordination sphere of samarium. Another hypothesis involves the generation of carbanions that are sufficiently stable and abundant for further reaction with unreacted halides.

In the reduction of 2-octanone, small amounts of the pinacol as well as an adduct with the solvent adduct with THF (Eq. 29) are detected, again, supporting the presence of ketyl radical anions.



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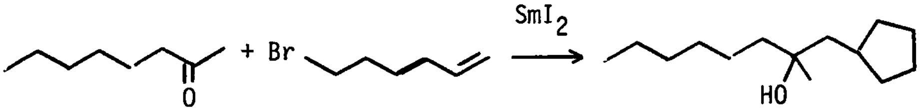
When coupling reactions are carried out in the presence of the radical trap, 1-bromo-5-hexene, the cyclization product (Eq. 30) is



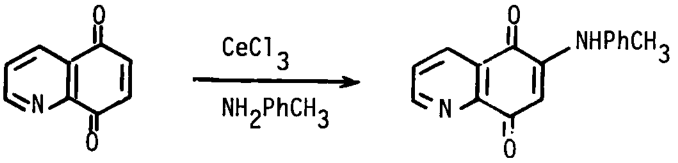
(30)

observed, thus suggesting that a radical species was involved during the course of the reaction. Optically active 2-bromooctane reacts with cyclohexanone at room temperature to give racemic tertiary alcohol. This result is expected, at this temperature, if radicals and/or carbanions are involved. A laser fluorescence mechanistic study of lanthanide catalyzed deoxygenation of carbonyl compounds suggested that the assumed products arise from diradicals, although no details on the organic products were provided.[29] From the point of view of synthetic utility, this result appears worthy of reinvestigation.

Although an overall picture of the mechanisms is gradually emerging, more mechanistic studies will be necessary to fully explain the reactivity of samarium diiodide. Especially intriguing is the role that coordination of Sm(II) and Sm(III) derivatives play in promoting selective transformations.

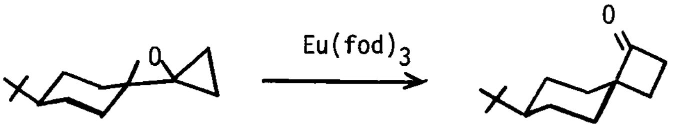
III. LANTHANIDE(III) REAGENTS

One of the earliest observations of the synthetic utility of lanthanide(III) additions was the report of Pratt on the regioselective addition of p-toluidine to the 6-position of 5,8-quinolinequinone (eq. 87). This reaction in the absence of lanthanide additive gives about a 1:1 mixture of regioisomers.[18a]



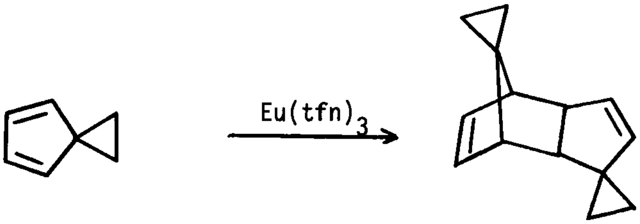
(87)

Another synthetic application of lanthanides was the report of Trost on the rearrangement of epoxides to spiroketones catalyzed by shift reagents (Eq. 31).[18b] Since that report, numerous other applications



(31)

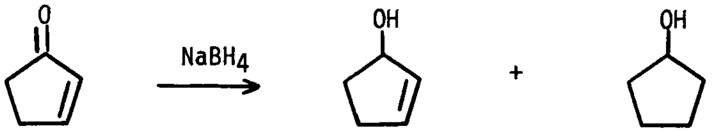
which take advantage of the Lewis acidity of lanthanide(III) compounds, have been discovered. Morrill has reported that shift reagents catalyze the Diels-Alder reaction shown (Eq. 32).[18c]



(32)

1. 1,2-Reduction of Enones

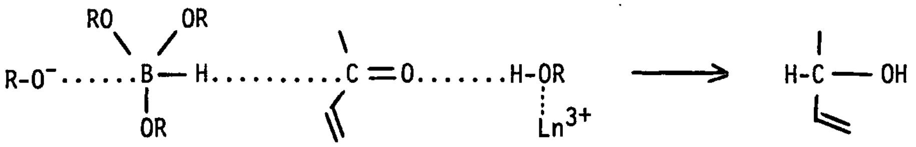
The reduction of cyclopentenone with sodium borohydride is usually complicated by over-reduction to cyclopentanol. Luche and co-workers have found that lanthanide(III) additives change the course of this reaction in a significant manner; for example the reaction in methanol proceeds rapidly to give 1,2-reduction in high yield.[19] The efficiency of this reagent system has allowed widespread application as an allylic alcohol preparation (Eq. 33).



(33)

Additive	%	%
none	---	100
$CeCl_3$	97	3
$SmCl_3$	94	6
$YbCl_3$	93	7

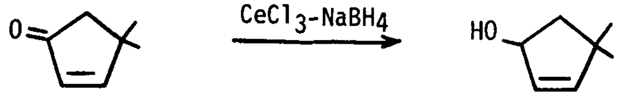
Luche and Gemal proposed the mechanistic interpretation shown in Eq. 34,



(34)

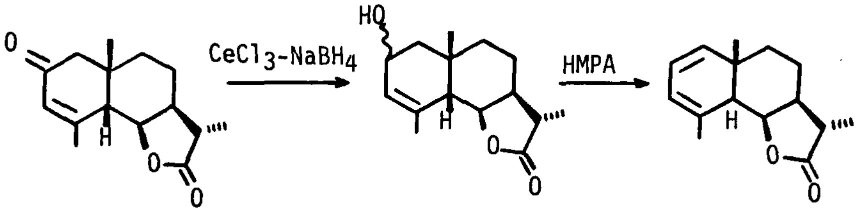
which takes into account both the active reducing species of trimethoxyborohydride and the effect of the lanthanide cation.[20,24] The rationale is also in accordance with the Hard and Soft Acid and Base theory (HSAB). It appears that investigations into the known lanthanide borohydrides could also be fruitful.[46]

Jefford and coworkers report the 1,2-reduction of 3,3-dimethylcyclopentenone (Eq. 35).[32] The high yield (90-93%) and high purity of the product obtained were cited as advantages by the authors.



(35)

In a total synthesis of (-) dictyolene, Greene has reported the selective reduction of the enone lactone below (Eq. 36) occurred regioselectively to give the allylic alcohol lactone. The stereochemistry here was not an important issue as the next step was elimination to the diene lactone.[33] Greene has also used this method for a synthesis of prostaglandin $PGF_{2\alpha}$. Reduction of the carbonyl provided a 1:1 mixture of C-15 epimers (Eq. 37).[34]



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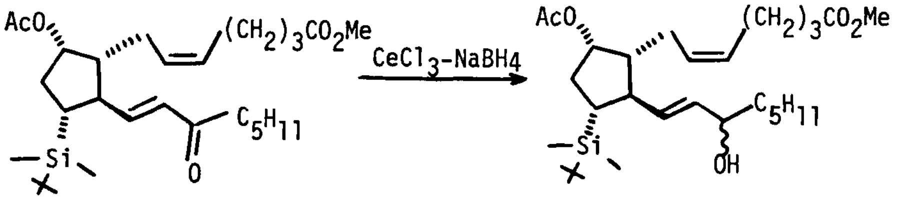
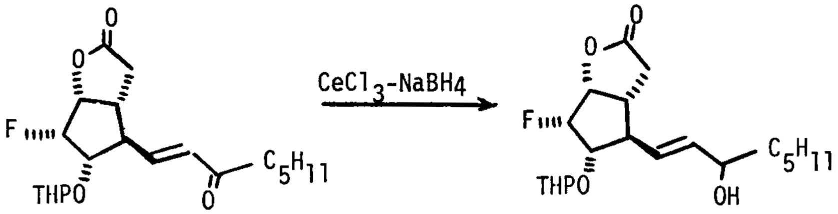


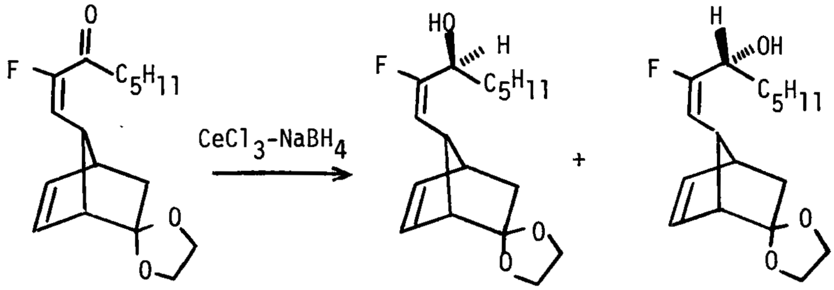
(37)

In his syntheses of fluorinated analogs of prostaglandins (Eq. 38), Grieco has utilized this efficient 1,2-reduction and obtained a 1:1 mixture of epimers, as determined by ultimate transformation to (±)-10α-fluoroprostaglandin $F_{2\alpha}$ methyl ester and its C-15 epimer.[35]



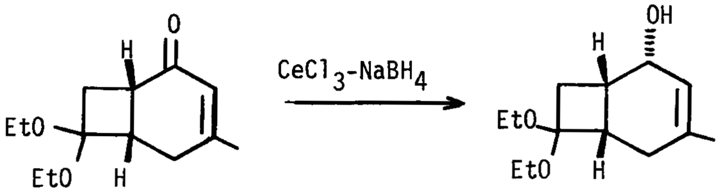
(38)

In an analogous preparation of 14-fluoro prostaglandin $F_{2\alpha}$ methyl esters, reduction of the intermediate fluoroenone gave a 1:1 mixture of allylic alcohol in 95% yield which were readily separable by chromatography (Eq. 39). The allylic alcohols were eventually converted to 14-fluoroprostaglandin $PGF_{2\alpha}$ methyl ester and its C-15 epimer.[36]



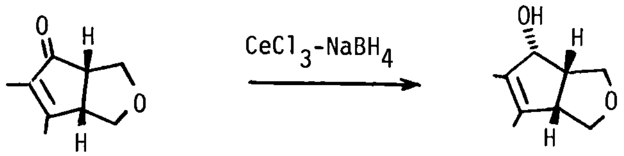
(39)

Smith has also explored the stereochemistry of the $NaBH_4/CeCl_3$ reduction of the enone which afforded a single allylic alcohol (Eq. 40).



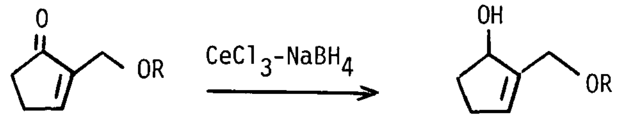
(40)

Reduction of the enone gave rise to a single allylic alcohol. Although the same stereochemical outcome was obtained with DIBAL/toluene, the lanthanide-mediated borohydride procedure was stated to be considerably more convenient.[37] Further support of the predicted stereochemical outcome has been reported by Smith and the identity of the product alcohol was proven by eventual transformation to methylenomycin-A (Eq. 41).[37]



(41)

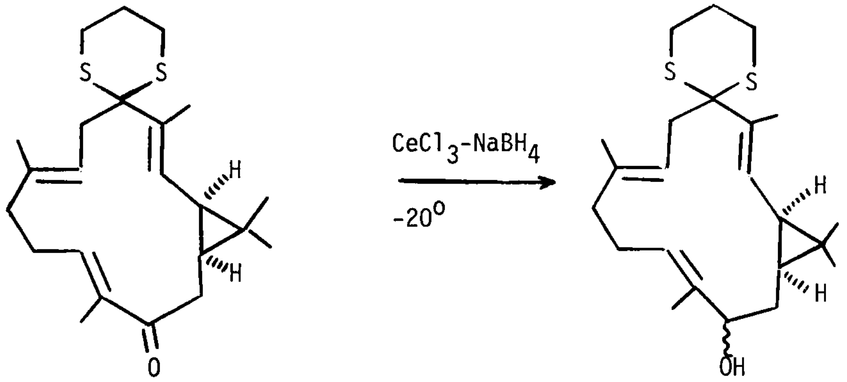
The Luche procedure was used to prepare epi-pentenomycins I, II and III from a common intermediate (Eq. 42) (R=H below).[27,38]



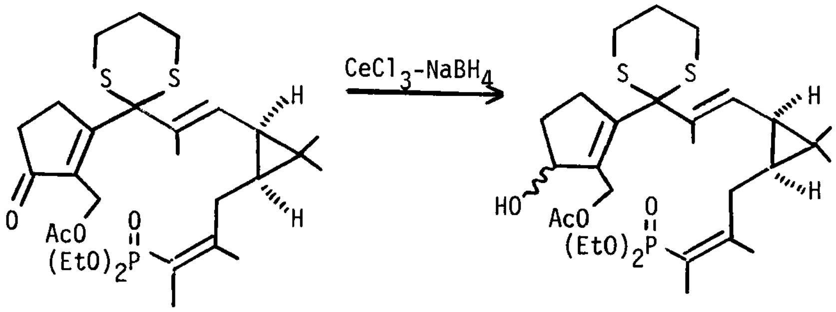
(42)

R = t-$BuMe_2Si$- or Ac-

Smith has recently accomplished two very selective examples of the Luche reduction. In the total synthesis of casbene (eq. 88) and a synthetic approach to bertyadinol (eq. 89). Both illustrate useful functional group selectivity. Dithiane and phosphonate groups are stable under the reaction conditions.[40]

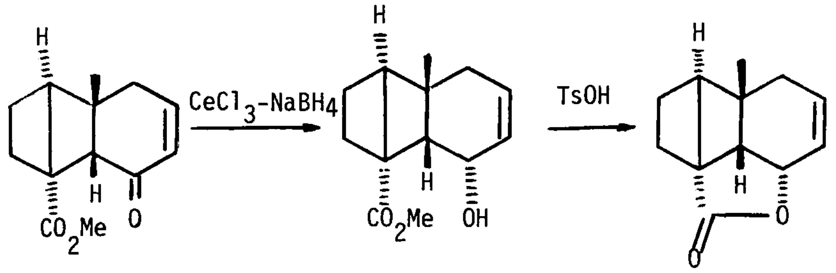


(88)



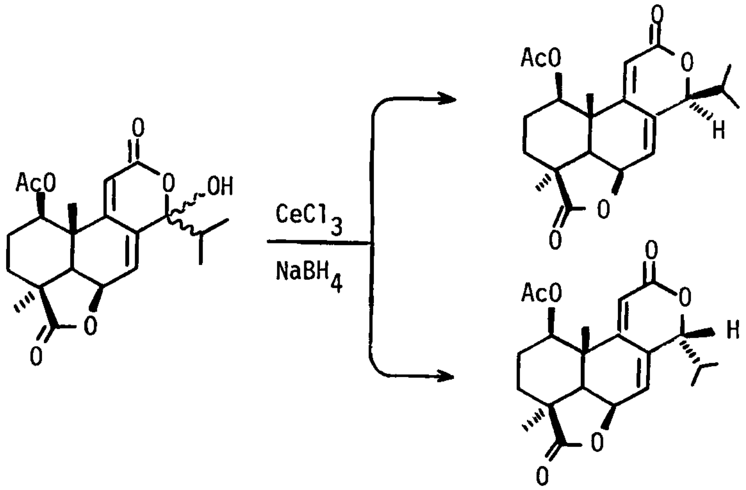
(89)

Wender utilized the $NaBH_4/CeCl_3$ procedure with success in a total synthesis of (±)-isabelin (Eq. 43). The stereochemistry of the reduction was important as intramolecular lactone formation was the next step in the sequence. Borohydride alone in this reaction gave largely a lactone arising from 1,4-followed by 1,2-hydride addition.[62]



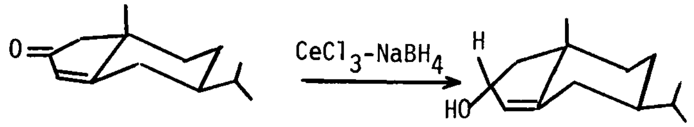
(43)

In a study of norditerpenoid dialactones, Hayashi and Matsumoto[63] observed the selective 1,2-reduction of an α,β-unsaturated hemi-ketal in the presence of both saturated and unsaturated lactones. The epimers were obtained in a 1:1 ratio (Eq. 44).



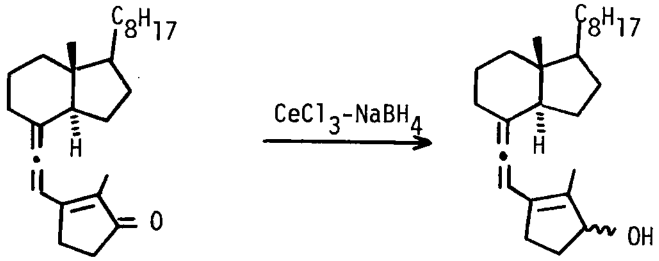
(44)

Reduction of the enone shown in Eq. 45 succeeded with the Luche procedure, while it failed with DIBAL, 9-BBN and L-selectride. The product consisted of at least a 4:1 ratio of epimers, with the major product shown below.[64]



(45)

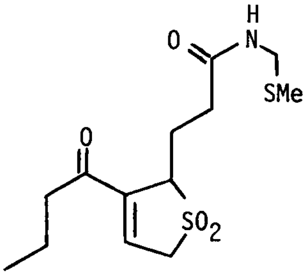
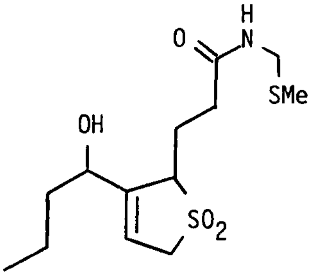
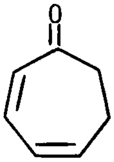
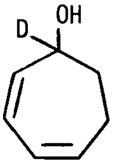
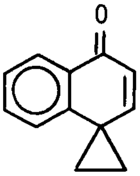
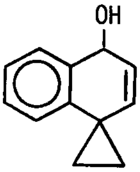
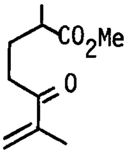
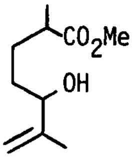
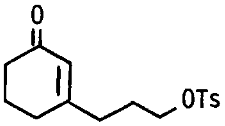
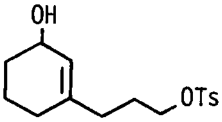
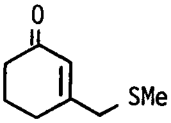
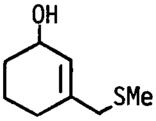
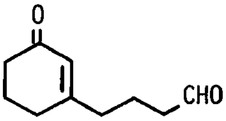
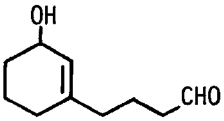
The synthesis of A-norvinylallenes related to vitamin-D required 1,2-reduction as a key step (Eq. 46). Okamura observed that while this could be successfully accomplished by the Luche method, reduction in the absence of $CeCl_3$ resulted in apparent carbon-carbon double bond reduction.[41]



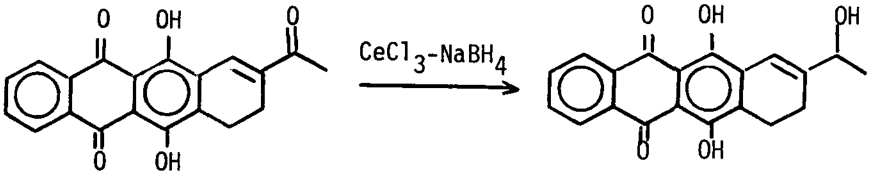
(46)

Weinreb has made use of the Luche procedure to reduce an enone in the presence of amide, sulfide and vinyl sulfone moieties (Eq. 47).[42] Paquette has used Luche's procedure for specific deuterium introduction in a mechanistic study of antarafacial cyclizations (Eq. 48).[43] Olah found that the spiro-allyl alcohol could be obtained by the Luche reaction (Eq. 49).[44] Torii used the Luche reduction to prepare intermediates in his study of electrooxidative cleavage of carbon-carbon linkages (Eq. 50).[45] Godleski has utilized cerium mediated reactions to synthesize starting materials for his study on palladium catalyzed spirocyclization. The examples reported illustrate useful functional group selectivity obtainable with these reagent systems. The 1,2-reduction of enones could be accomplished in the presence of primary tosylates (Eq. 51) and allyl sulfides (Eq. 52). The enone reduction could also be

Reductions with Sodium Borohydride in the presence of Cerium Trichloride

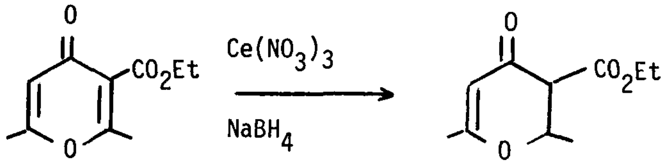
Equation	Starting Material	Product	Comment	Reference
47				42
48			$NaBD_4$	43
49				44
50				45
51				28
52				28
53			-15° aq. EtOH	28

performed in the presence of an aldehyde (Eq. 53) (see section III.3).[28] Cava has recently used the Luche protocol in a key reduction in the course of the synthesis of (+)-4-demethoxy-daunomycinone (eq. 90).[65]



(90)

The reduction of the pyranone shown in Eq. 54 a gives 65% yield of 2,3-dihydro-4H-pyranone (Eq. 54).[67] This method represents a regioselective transformation which is normally difficult to achieve.



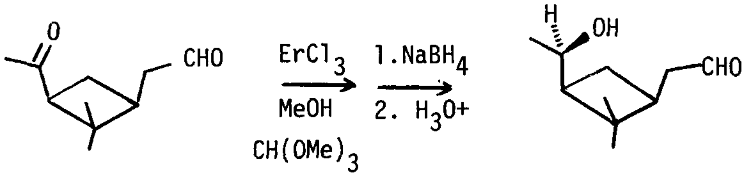
(54)

2. Acetal Formation

Luche and Gemal have found that lanthanide chlorides are effective catalysts for the formation of acetals. The reaction proceeds at room temperature and maximum yield is obtained within a few minutes. An added advantage is the ease of operation. The best results were obtained with erbium and ytterbium chlorides.[21]

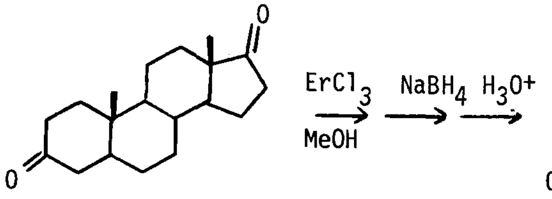
$$\text{Ph-CH=CHCHO} \xrightarrow[\text{CH(OMe)}_3]{\text{ErCl}_3\text{,MeOH}} \text{Ph-CH=CHCH(OMe)}_2 \qquad (55)$$

The protection of ketones proceeds more sluggishly, and selective acetal formation can be accomplished, thus allowing the selective reduction of a ketone in the presence of an aldehyde. Protection of the aldehyde, reduction of the ketone, and subsequent deprotection can be accomplished as illustrated below.[22]



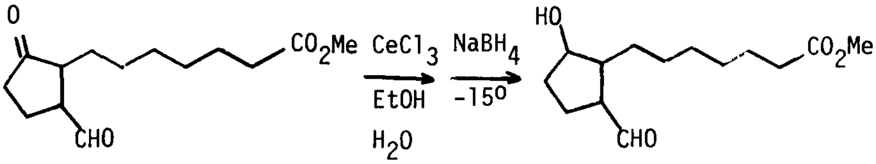
(56)

This process could also be used to reverse the reduction selectivity of ketones (Eq. 57). Thus the more reactive C-3 ketone of androstane-3,17-dione is protected in situ, and reduction followed by deprotection gives 17,β-hydroxy-androstan-3-one in 95% yield.[22]



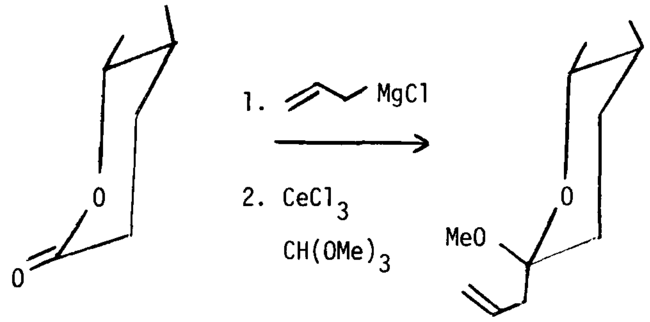
(57)

Another approach to this problem of selective reduction of a ketone in the presence of an aldehyde often can be used when the above method fails (Eq. 58). The aldehyde and ketone mixture is first treated with an aqueous ethanolic solution of cerium trichloride. The flask is cooled to -15° and sodium borohydride added. The aldehyde is recovered almost quantitatively and the secondary alcohol is generated in high yield.



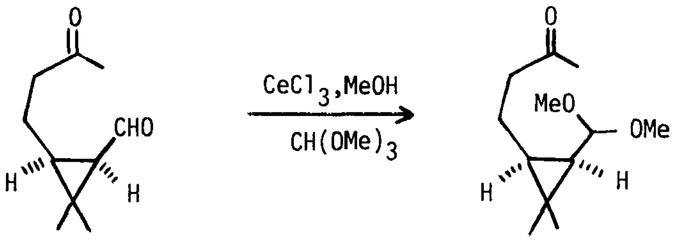
(58)

This procedure represents the first direct solution to the problem of reverse selectivity. The authors propose that the aldehyde is protected in situ by the formation of a geminate diol.[23] Smith has utilized this ketalization for the preparation of a key intermediate in his synthesis of milbemycin-β_3 (Eq. 59).[39]



(59)

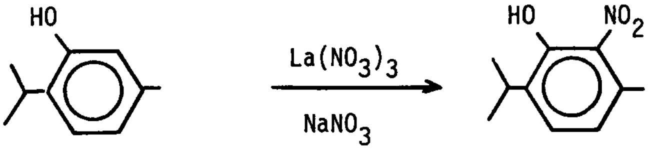
In a synthesis of a bicyclo[5.1.0]enone to serve as a versatile intermediate, Smith utilized a selective acetalization (Eq. **84**).[30]



(84)

3. Nitration and Oxidation with Lanthanide(III) Nitrates

The mononitration of phenols can be accomplished at room temperature (Eq. 60). A two-phase system was used (water-ether) and sodium nitrate in the presence of HCl and a catalytic amount of $La(NO_3)_3$.[26] In



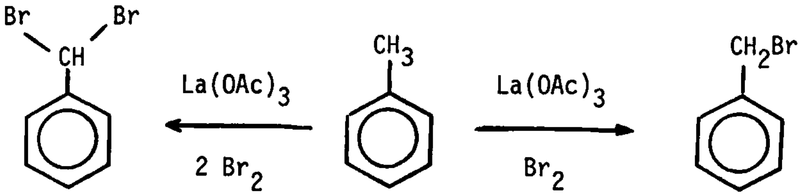
(60)

contrast ytterbium nitrate oxidizes benzoins to benzils (Eq. 61).[25]

$$\mathrm{PhCOCH(OH)Ph} \xrightarrow[\mathrm{HCl}]{\mathrm{Yb(NO_3)_3}} \mathrm{PhCOCOPh} \qquad (61)$$

4. Bromination of Benzylic Hydrocarbons

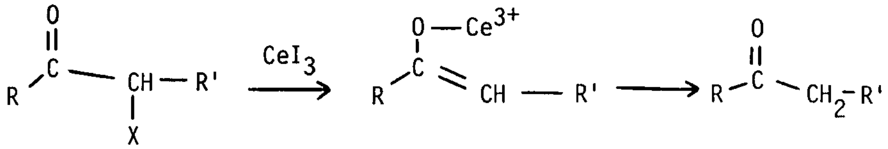
Many benzylic bromides have been prepared using 1% lanthanum acetate as a catalyst (Eq. 62).[48] Several lanthanide salts showed this enhancement of reactivity. Selective benzylic bromination did not proceed in the dark, or in the absence of $La(OAc)_3$ although this salt is completely insoluble in the reaction medium. gem-Dibromomethyl arenes were obtained with two equivalents of bromine.



(62)

5. Dehalogenation of α-Halocarbonyl Compounds

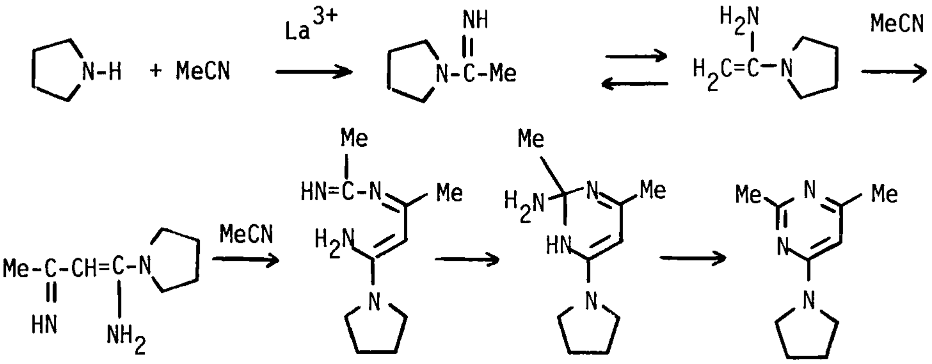
Ho has reported on the dehalogenation of α-halocarbonyl compounds using lanthanide(III) reagents (Eq. 63).[49]



(63)

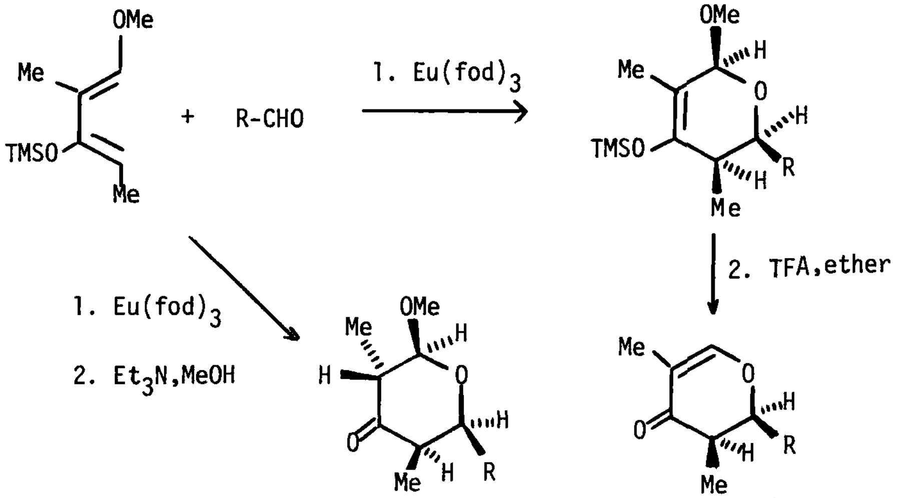
6. Heterocyclic Synthesis

Lanthanide(III) ions catalyze an interesting formation of 4-substituted-2,6-dimethylpyrimidines from monodentate cyclic secondary amines and acetonitrile.[50] The mechanism proposed by the authors is shown below (Eq. 64).



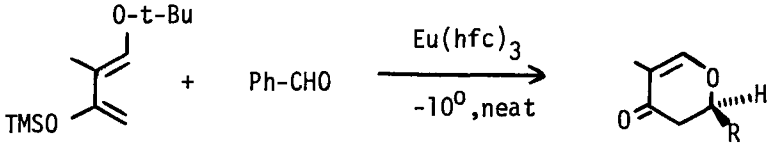
(64)

Danishefsky has recently reported an exciting new finding utilizing europium shift reagents for mediating hetero Diels-Alder reactions. A trace amount of the shift reagent, tris-(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium ($Eu(fod)_3$) was sufficient as a catalyst in the stereospecific synthesis of carbon branched pyranosides shown in Eq. 65. Endoselectivity is maintained, and three chiral centers are established through this suprafacial endo-cycloaddition process. A fourth center at C_2 is controlled through apparent axial protonation of silyl enol ethers.[51] Further study by Danishefsky has revealed that



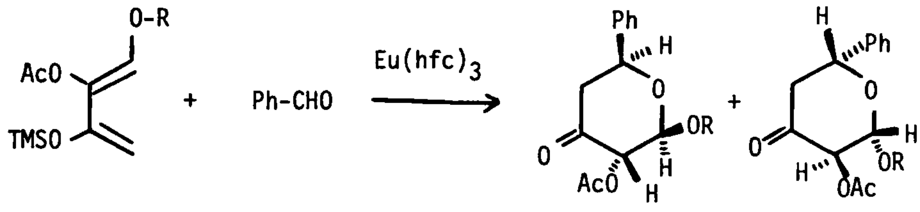
(65)

tris(6,6,7,8,8,8-heptafluoro,-2,2-dimethyl-3,5-octanedionato) europium ($Eu(hfc)_3$) can be used in the cyclocondensation of aldehydes with siloxydienes to obtain modest asymmetric induction (Eq. 66). While the causes of the induction are not presently understood, there is no change in % e.e. by increasing the amount of $Eu(hfc)_3$ to 10 mole %. Typically, 1 mole % of the catalyst is necessary.[52]



58%e.e. (66)

The chiral shift reagent has a pronounced interaction with chiral auxiliaries in the hetero Diels-Alder reaction, and Danishefsky has exploited this methodology to pioneer a new route to L-glycolipids (Eq. 67). Comparison of $Eu(hfc)_3$ and $Eu(fod)_3$ (value in parenthesis) as catalysts in the hetero Diels-Alder reaction with d-menthyloxydienes

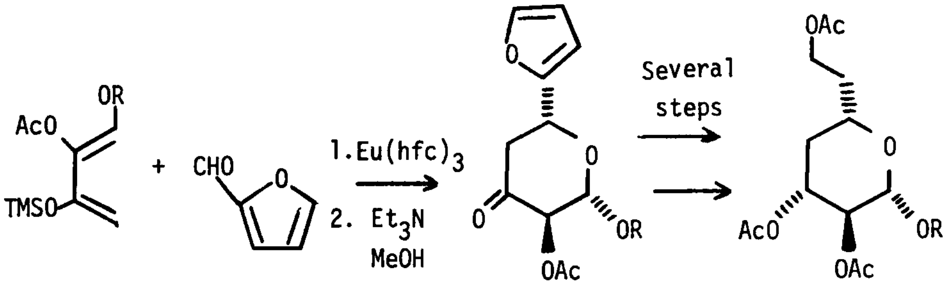


(67)

R = d-menthyl	41 (45)	59 (55)
R = l-menthyl	7 (55)	93 (45)

(values in parenthesis are ratios obtained with Eu(fod)$_3$ as catalyst)

revealed little interaction among the chiral elements. The case of Eu(hfc)$_3$ catalyzed reactions with l-menthyloxydienes however showed a striking interaction of the two chiral elements. A strong "L-pyranose" preference is expressed by interaction with the chiral catalyst. The utility of this procedure is illustrated by the synthesis of an optically pure β-4-deoxy-L-glucoside of l-menthol (Eq. 68).[52]



(68)

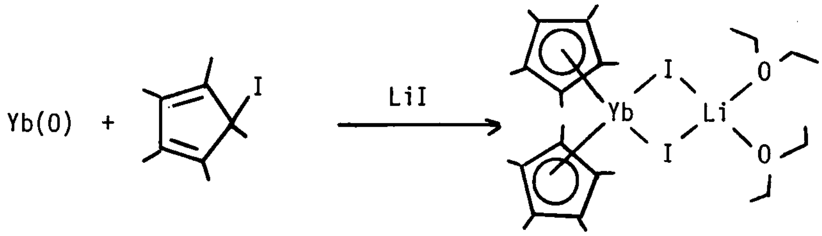
IV. MISCELLANEOUS USES OF ORGANOLANTHANIDES

1. Organolanthanide Chemistry

The π-complex chemistry of the lanthanides has been relatively undeveloped compared to that of the d-block elements, and has been recently reviewed by Marks.[53] The purpose of this section is to highlight those transformations of special interest to the synthetic organic chemist. Future development of synthetic organic methodology with the lanthanide elements will depend on a more complete understanding of the coordination chemistry of the central lanthanide metal atom, and the role this coordination plays in determining the chemical and especially stereochemical transformations in the vicinity of the lanthanide metal. Exciting studies are presently underway which may provide the keys to unlock these mysteries of the lanthanides.

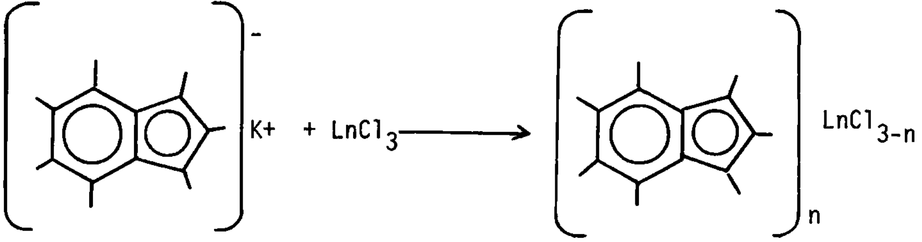
To the bench chemist, stable forms of reagents are a valuable asset. Developments leading to stable organometallic complexes of the lanthanides have taken two approaches (i) optimization of electrostatic interactions and (ii) saturation of the coordination sphere of the metal with bulky ligands in order to sterically block decomposition pathways.[54] The pentamethyl cyclopentadienyl anion ligand has found extensive application because of the above-mentioned stability-lending steric bulk. It also adds considerable solubility and crystallinity to the resulting complexes.

One approach to such complexes is direct metal oxidation, followed by ligand-for-halide metathesis reactions. This method has been utilized by Watson for the formation of several ytterbium and lutetium complexes (Eq. 69).[55] For the larger, early members of the lanthanide series, even simple classes of complexes are unstable with respect to disproportionation. Recently dicyclopentadienyl lanthanide halides have been prepared for La, Ce, Pr, Nd, and Sm.[56] Another approach to new complexes involves metal vapor techniques.[47,57] The heptamethyl indenyl ligand allows the isolation of some previously unavailable types of organo lanthanide



(69)

complexes. The potassium salt can be isolated as a crystalline solid and the complexes n = 1,2,3 were prepared by simply using the proper stoichiometry (Eq. 70).[58]



(70)

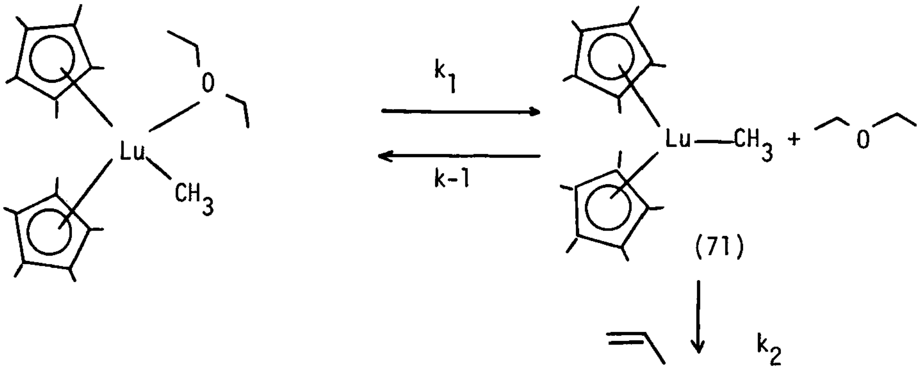
Ln = La, Er, Nd

As greater numbers of crystalline and isolable organolanthanide complexes become available, the stage is set for major advances in organic synthetic methodology.

2. Ziegler-Natta Polymerization

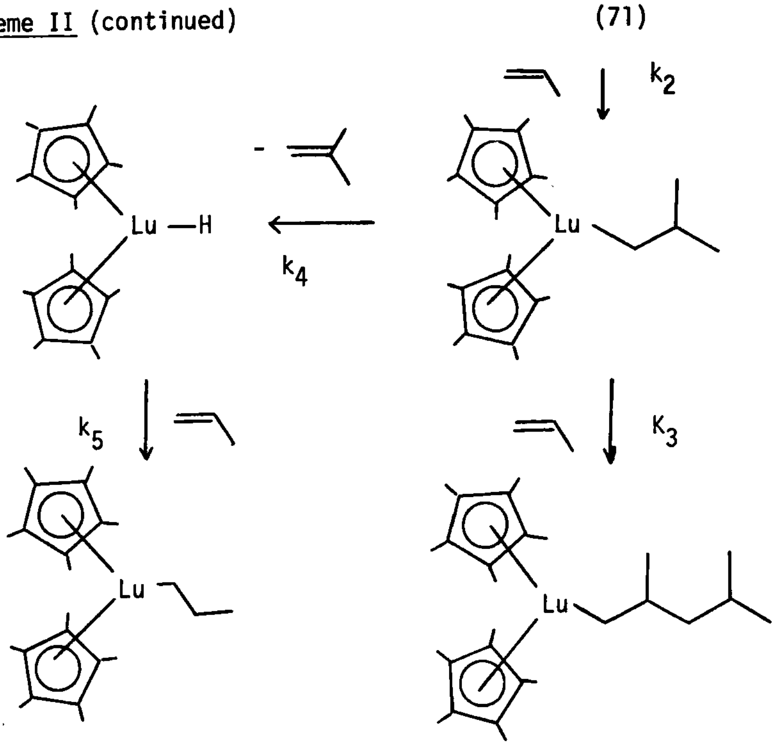
In the course of investigations into the reactivity of lanthanide carbon bonds, Watson has observed insertion of a variety of olefins and acetylenes into the ytterbium and lutetium methyl bonds of $M(\eta^5\text{-}C_5Me_5)_2CH_3$ ether (M = Yb, Lu) (Eq. 71). This system provides a clear experimental model for coordination catalysis of olefin polymerization (Scheme II).[59] Both β-hydrogen elimination from lanthanides-alkyls (step k_4) and olefin insertion into lanthanide-alkyl (step k_2) and lanthanide-hydride (step k_5) bonds are important observable reactions in this model.

Scheme II



(71)

Scheme II (continued)



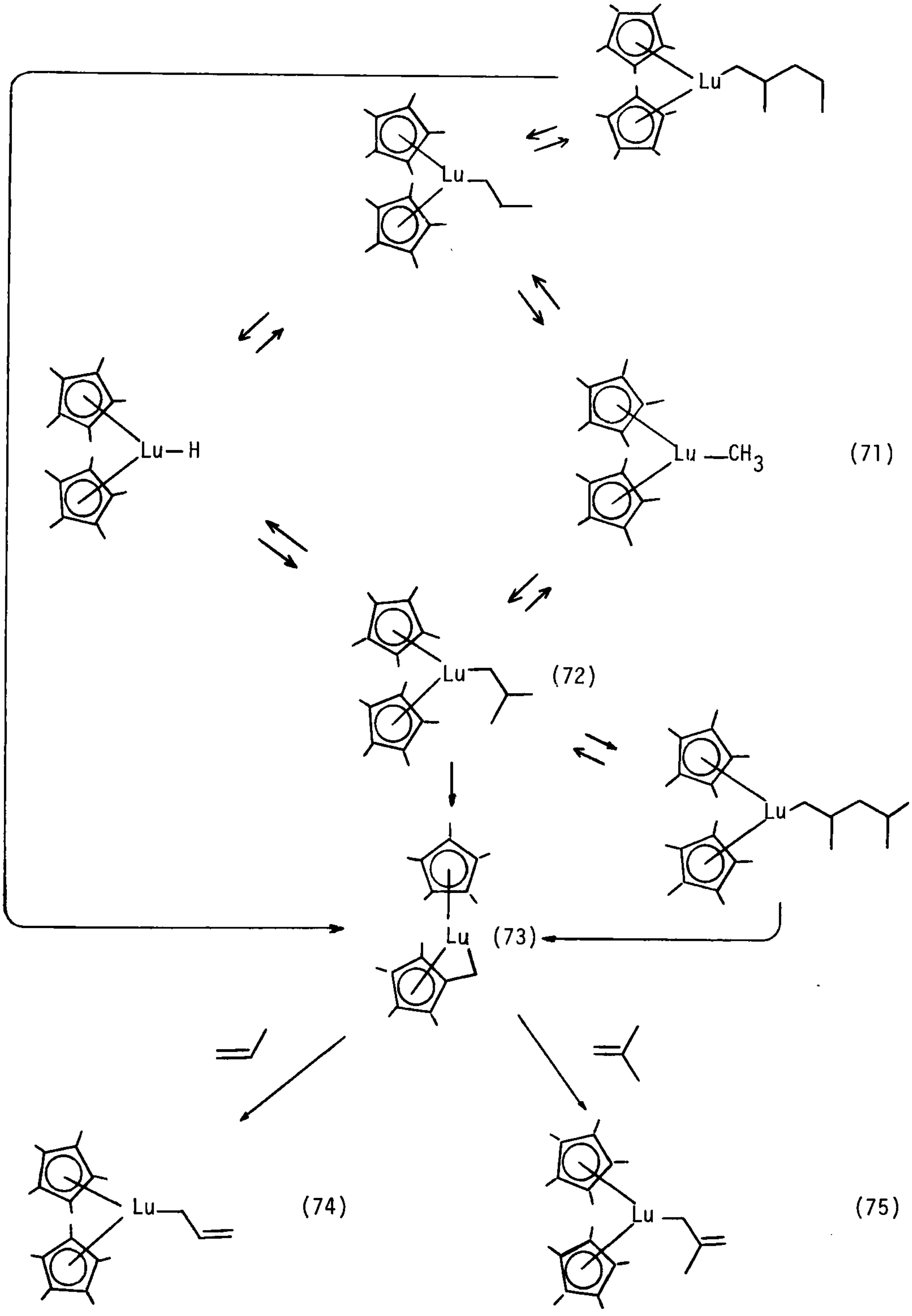
3. β-Alkyl Transfer

During propene oligomerization, β-hydrogen elimination and β-alkyl-elimination lead to chain termination. Watson was able to observe β-alkyl elimination by studying the thermal decomposition of an isobutyl lutetium complex (Eq. 72) in Scheme III. The decomposition is not mechanistically simple but results from the summation of several processes. Especially intriguing is the intermediate complex (Eq. 73) postulated for the production of allyl lutetium products (Eq. 74 and 75).

4. C-H Bond Activation

The activation of C-H bonds has been accomplished by Watson using lutetium and ytterbium organolanthanide complexes (Scheme IV).[61] Pyridine coordinates with the lutetium alkyl and this is followed by metalation in the 2-position (Eq. 76). Phosphorus ylids also undergo intramolecular

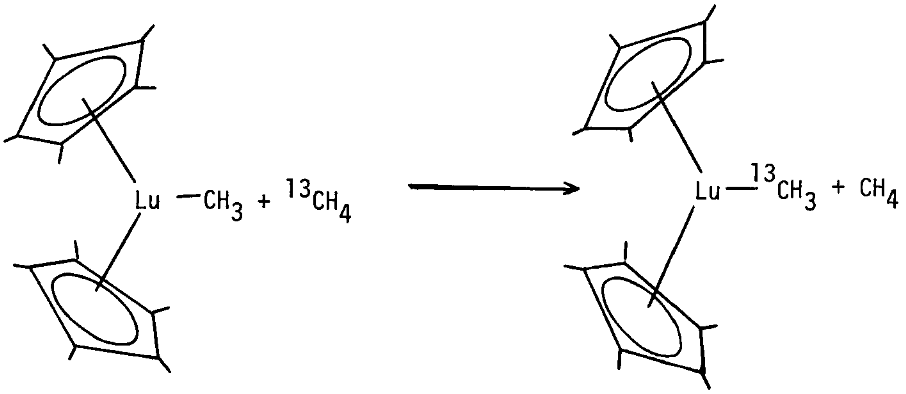
Scheme III



aryl C-H bond activation, presumably after initial coordination by the ylid to yield the lutetium metallacycle (Eq. 77). Tetramethylsilane cleanly eliminates methane, and forms the corresponding methylidene trimethyl silane lutetium complex (Eq. 78).

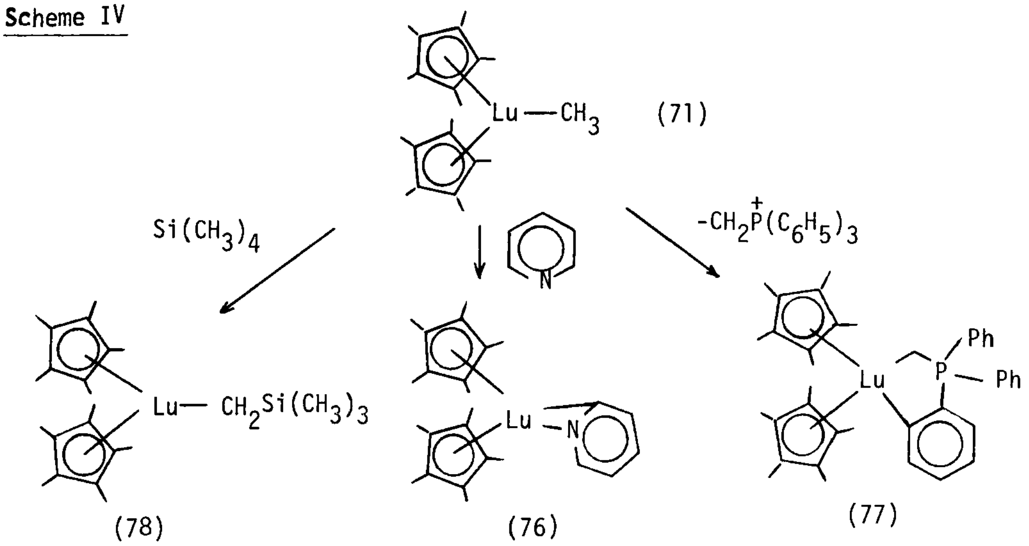
Lutetium hydrides also show C-H bond activation (Scheme V). Watson reported that diethyl ether undergoes loss of ethylene to form a lutetium alkoxide (Eq. 79). Reaction of benzene with the lutetium hydride complex gives an aryllutetium product (Eq. 80) which will undergo further reaction with an additional equivalent of lutetium hydride to give an interesting bridged μ-aryllutetium product (Eq. 81) shown in the Scheme. Perdeuterated benzene reacts with the lutetium hydride to give the lutetium deuteride complex (Eq. 82) and pentadeuterobenzene.

Of all carbon-hydrogen bonds, the most difficult to activate are those of methane, where the bond energy is 104 kilocalories per mole. The first unequivocal instance of activation of a methane C-H bond was reported recently by Watson. ^{13}C-Labeled methane reacts with a lutetium complex, shown below (Eq. 83) to give labeled complex and unlabeled methane, indicating that the complex has cleaved a C-H bond of the substrate.

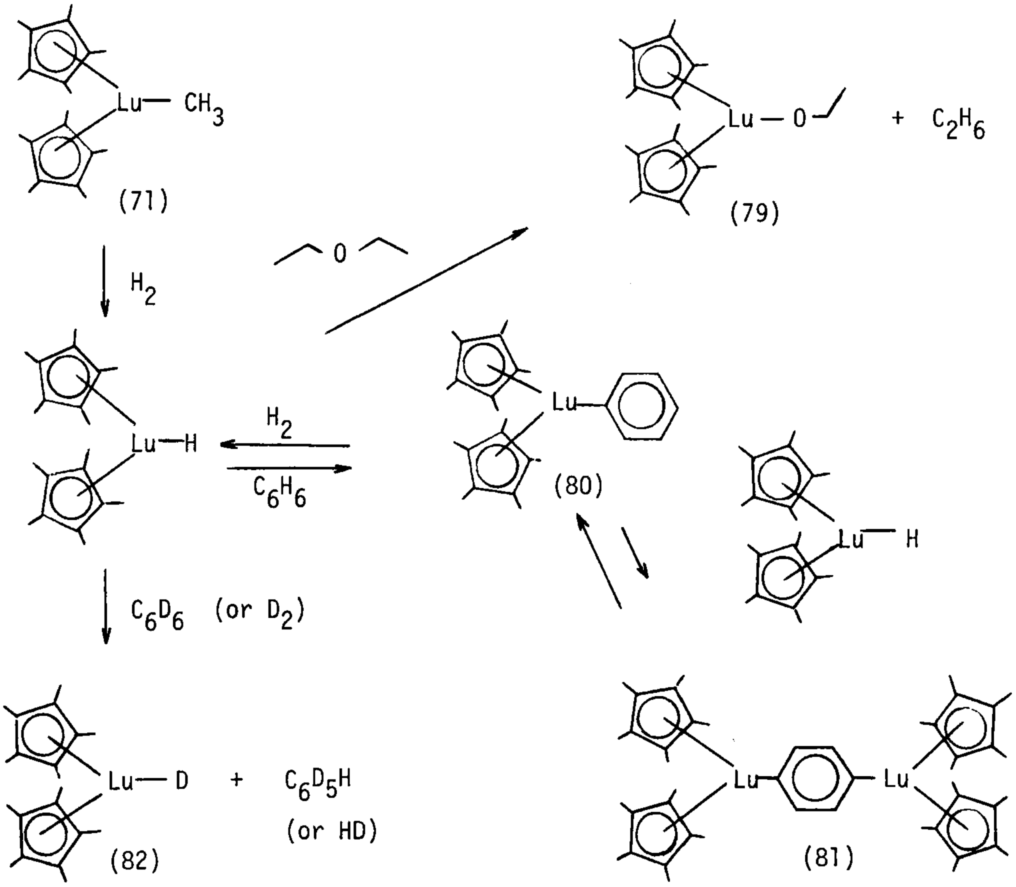


(83)

Scheme IV



Scheme V



In general, the C-H activation reactions of lanthanides proceed in high yield and under mild conditions. These investigations are opening new avenues to the catalytic and synthetic chemist for obtaining transformations and selectivity not available by the more traditional methods.

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