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Chromium Salen

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CONTRIBUTION FOR:
ELECTRONIC ENCYCLOPEDIA OF REAGENTS FOR ORGANIC SYNTHESIS

(1R,2R)-(-)-[1,2-Cyclohexanediamino-N,N'-bis(3,5-di-t-butylsalicylidene)]chromium(III) chloride. Cl(Cr(Salen)

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(1R,2R)-(-)-[1,2-Cyclohexanediamino-N,N'-bis(3,5-di-t-butylsalicylidene)]chromium(III) chloride

[164931-83-3] $C_{36}H_{52}ClCrN_2O_2$ MW 632.28

Reagent used as a catalyst or reagent for a wide range of asymmetric transformations

Physical Data: Brown powder, mp 375.5 - 398 °C (dec).°C

Solubility: Low solubility in CH_3CN, Et_2O, THF, *t*BuOMe

Form: Solid

Purification: Recrystallisation from CH_3CN

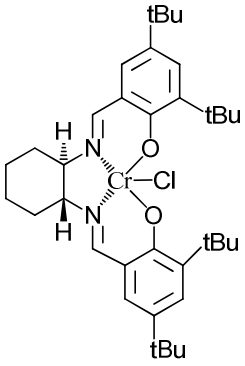
Handling, Storage and Precautions: H302, H312, H332. P280. Stable under recommended storage conditions, avoid strong oxidising agents. Hazardous decomposition products formed under fire conditions.

Introduction.

The use of salen as a versatile and effective ligand has been reported for over 100 years[1] and were first studied systematically in the 1930s by Pfeiffer and co-workers,[2] who also introduced the first non-racemic salen ligand. Salen metal complexes are considered privileged catalysts, demonstrated by their successful application in many challenging asymmetric reactions. The straightforward preparation of the chiral ligand and their modular structure allows a wide structural modification owing to the development of many asymmetric transformations.

Cr(Salen) as a Lewis Acid.

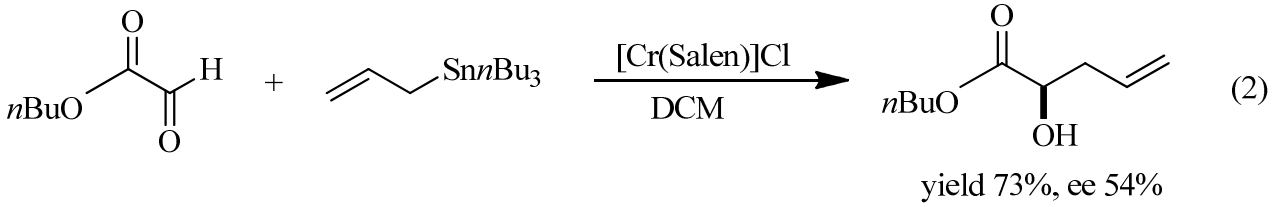
Cationic [Cr(Salen)] complexes (eq 1) have demonstrated their utility in Lewis acid mediated processes.



(1)

For instance, chiral cationic tetradentate [Cr(Salen)BF_4] complexes catalyse the asymmetric hetero Diels–Alder (HDA) reaction between 1-methoxy-3-[(trimethylsilyl)oxy]buta-1,3-diene ('Danishefsky's diene') and carbonyl compounds in a highly stereocontrolled manner.[3] The addition of 4Å molecular sieves is necessary for the reactions to proceed to completion, probably due to the presence of coordinated water molecules to [Cr(Salen)]. Jacobsen and coworkers have investigated the reaction mechanism that seems to point toward a concerted [4+2] process.[4] The efficiency of this process was improved by Jacobsen by the synthesis of a new class of chiral tridentate chromium(III) catalysts.[5] The influence of conformation of the [Cr(Salen)] catalyst is evident in the diastereomeric (*R,R*)-[Cr(Salen)] and (*R,S*) complexes described by Katzuki that show opposite senses of enantioselectivity.[6]

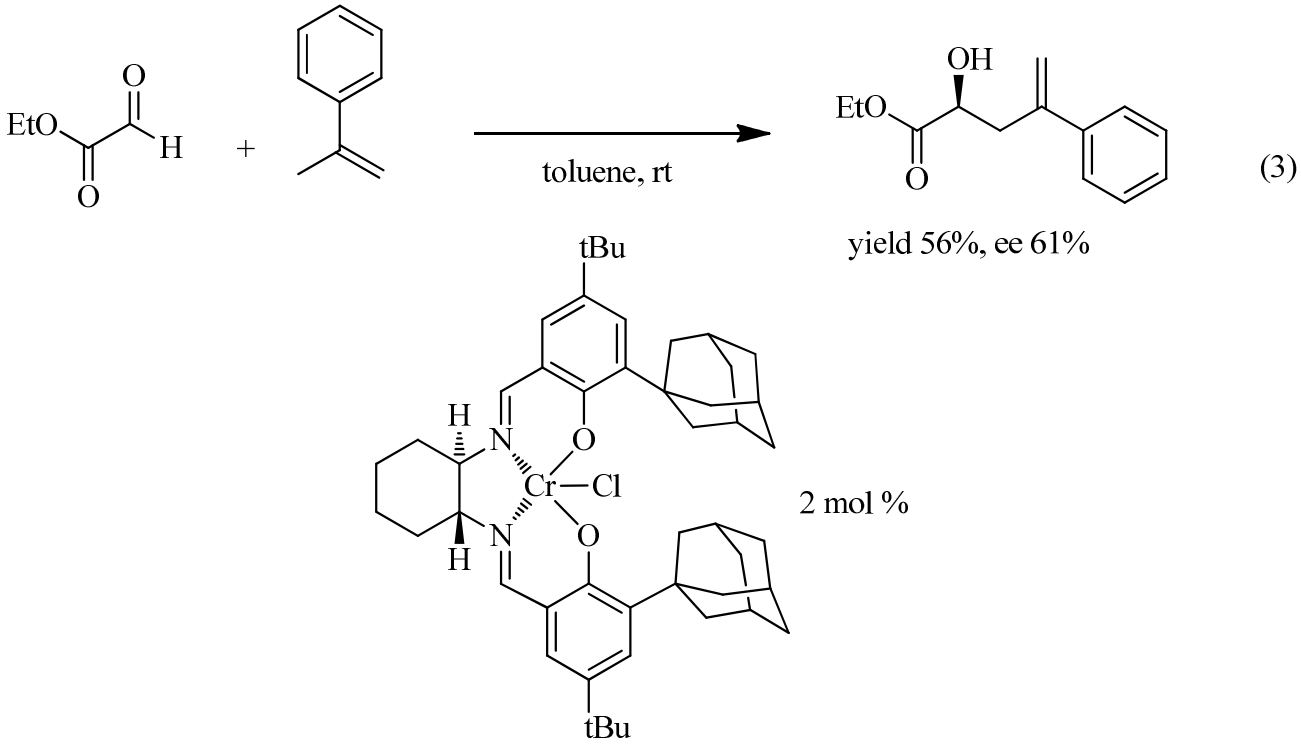
Chromium(III)Salen has also been utilized in the enantioselective [4+2] cycloaddition of buta-1,3-dienes to alkyl glyoxylates, thermal and high-pressure [4+2] cycloadditions of buta-1,3-diene, cyclohexa-1,3-diene, and 2,3-dimethylbuta-1,3-diene to alkyl glyoxylates of type 2 (R= n-Bu, i-Pr, t-Bu). In the enantioselective allylation of alkyl glyoxylates, the Cr(salen) complex has afforded high yields and moderate enantioselectivities (eq 2).[7]



Ene and Mukaiyama Reactions.

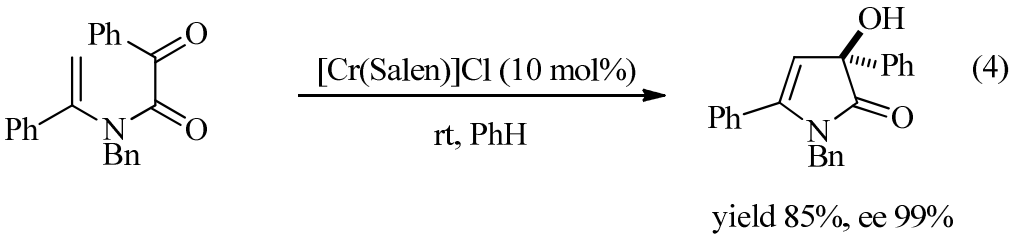
Mukayiama-type reactions were described by Katsuki with Cr(Salen). Cationic (*R*,*R*)-[Cr(Salen)] complex was found to catalyse the enantioselective addition of 2-(trimethylsilyloxy)furan to aldehydes to give 5-substituted butenolides, though diastereoselectivity was only modest. The presence of a small amount of water is essential for achieving high enantioselectivity.[9]

An enantioselective carbonyl-ene reaction of alkyl glyoxylates with various 1,1-disubstituted olefins, catalysed by chiral [Cr(III)(Salen)BF_4] complexes, has been studied. It was found that a chromium complex bearing adamantyl substituents at the 3,3′-positions of the salicylidene moiety catalysed the reaction with much greater selectively than the classic Jacobsen-type catalyst. The reaction proceeded effectively under undemanding conditions in the presence of 2 mol % of the catalyst in an acceptable yield and with 59–92% ee (eq 3).[10]



Recently, the formation of quaternary stereogenic centers was induced by the use of Cr(Salen). The catalytic asymmetric intramolecular nucleophilic addition of tertiary enamides to a carbonyl group

to give highly functionalized 1*H*-pyrrol-2(3*H*)-one derivatives in excellent yield and enantiomeric excess (eq 4).[11]

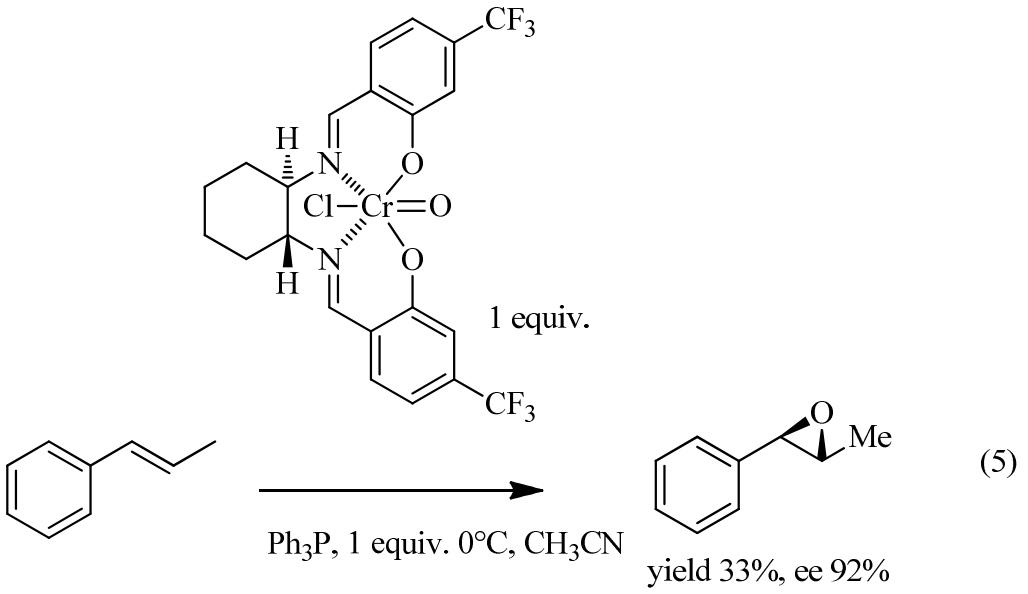


(4)

yield 85%, ee 99%

Cr(Salen) in oxidation reactions.

The important breakthrough in asymmetric epoxidation (AE) by salen metal complexes was reported independently by Katsuki[12] and Jacobsen[13]. Studies led to the synthetic design of the salen ligands suitable for application in the epoxidation reaction. In addition the catalytic cycle and the mode of reaction of the active species involved have been identified. The reaction is also influenced by other factors such as additive and co-oxidants. Cr(Salen)-mediated epoxidations were developed by Gilheany with enantioselectivities of up to 92% reported (eq 5).[14]

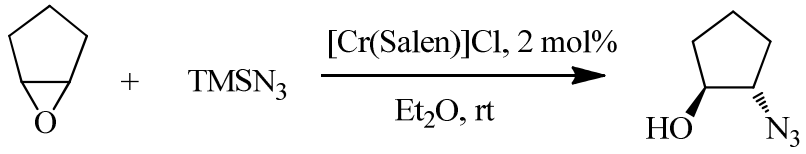


(5)

yield 33%, ee 92%

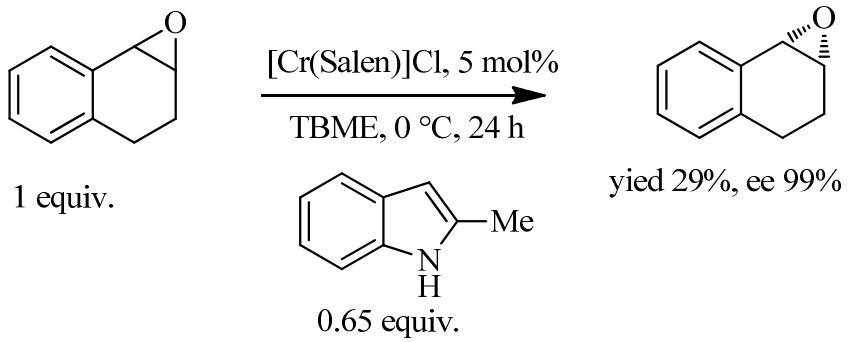
Cr(Salen) in the asymmetric opening of epoxides.

Jacobsen has reported the application of [Cr(Salen)Cl] in the asymmetric ring-opening of *meso*-epoxides by nucleophiles. In his pioneering study, Jacobsen opened expoxides with Me_3SiN_3 (eq 6).[15]



(6)

If the epoxide is opened under strictly anhydrous conditions the Cr(Salen) is an inactive system. Traces of water are essential in the production of HN_3 by hydrolysis of Me_3SiN_3. The key point in the chemistry was to understand that a second-order dependence of the reaction rate on the catalyst, indicating that two molecules of catalyst are involved in the rate determining step. As in many other reactions, the chiral chromium complex is capable of activing both the reaction partners in a bimetallic transition state.[16] Further studies have expanded the scope of the nucleophile, and several nucleophiles have been shown to open epoxides with appreciable stereoselectivity.[17] The nucleophilic attack can be also used for kinetic resolution of epoxides[18] and in particular to acces epoxides that are difficult to prepare with other reactions (eq 7).[19]

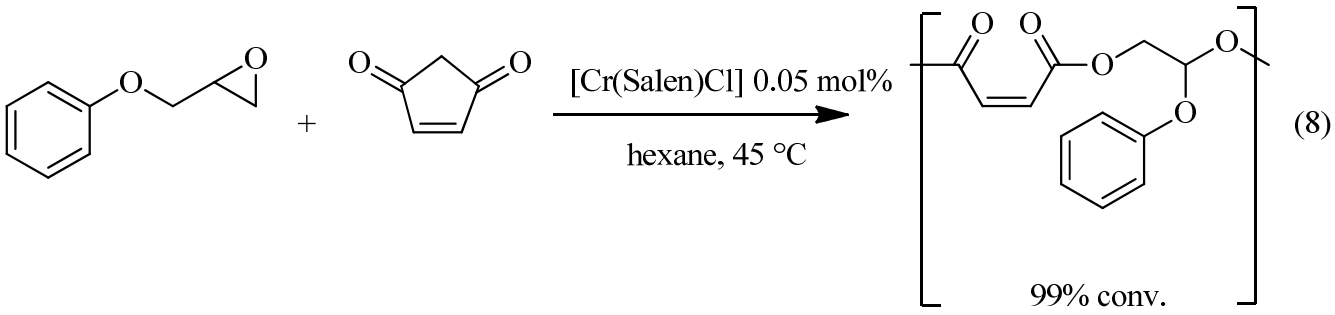


(7)

A regio-, diastereo-, and enantioselective aminolysis of racemic *trans*-1,2-disubstituted aromatic epoxides with anilines catalysed by [Cr(Salen)Cl] complex was described.[20]

Cr(salen) in polymerization and co-polymerization of epoxides.

(Salen)chromium(III) in the presence of addivites was found to be an active catalyst system for the coupling of CO_2 with epoxides and aziridines.[21] Coates has reported the ring-opening copolymerization of maleic anhydride with a variety of epoxides catalysed by chromium(III) salen. The method provides access to a range of new unsaturated polyesters with versatile functionality, as well as the first synthesis of high molecular weight poly(propylene fumarate) (eq 8).[22]



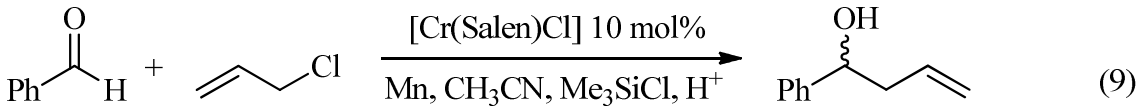
(8)

[Cr(Salen)] and redox catalysis.

An important characteristic associated with metallo–Salen systems is their ability to support redox processes on the metal center. [M(Salen)] complexes can act as 'molecular batteries' storing and releasing electrons.[23] The Salen backbone is also able to stabilize metals in different oxidation states.[24]

If a M(Salen) metal complexes is employed in low oxidation state, the corresponding oxidative addition can occur. Cr(Salen) can support a catalytic redox process employing a metal being the stoichiometric reductant. The reductant (usually a metal) is capable of restoring the catalytic active Cr(Salen) (II) complex. When the C-C bond formation is occuring between the Cr(III)Salen organometallic species and an electrophile (aldehyde or ketone) a strong Cr-O bond is formed, and by the use of a 'scavenger'the organic fragment is liberated from the Cr(Salen) reagent.

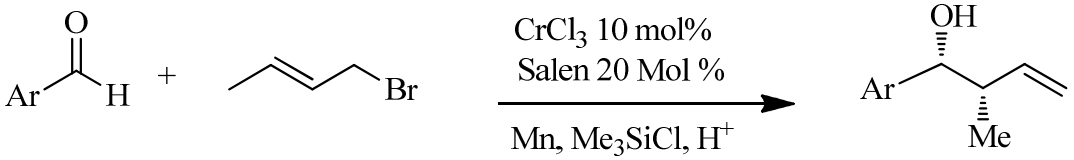
One of the most powerful methodologies for the construction of new C–C connections is the Nozaki– Hiyama–Kishi (NHK) reaction.[25] Such a procedure results in the chemo- and regio-selective addition of organo-chromium complexes to carbonyls compounds. In the first asymmetric example, Cozzi and co-workers utilized Cr(Salen) as the ligand and reported enantioselectivities of up to 84% for the allylation of benzaldehyde (eq 9).[26]



(9)

yield 67%, ee 84% (*R*)

The Cr(Salen) mediated addition of halides to aldehydes has shown a broad scope and different halides have been employed, including crotyl bromide. A remarkable feature of this reaction is the *syn* selectivity (eq 10). Normally, the Cr mediated allylation is stereoconvergent and favours the *anti* product, however in the case of Cr(Salen) the diastereoselectivity can be significantly altered by changing the amount of ligand.[27]



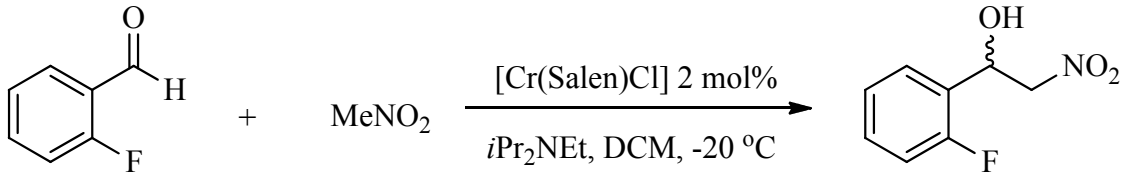
(10)

Ar = Ph, pBrPh, pFPh, pMePh, pPhPh

yield 43-56%, dr 2.4:1-4.8:1, ee syn 82-90

Cr(Salen) catalysed addition of nucleophiles.

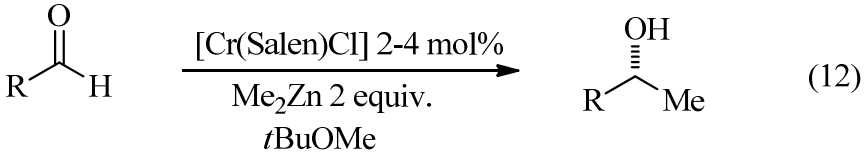
Cr(Salen) mediated Henry reactions have been reported by a number of research groups. Skarzewski has utilised chiral chromium(salen) complexes to catalyse the enantioselective Henry reaction of a range of aldehydes with nitromethane, with moderate yields and enantioselectivities (eq 11).[28]



(11)

yield 80%, ee 62% (*S*)

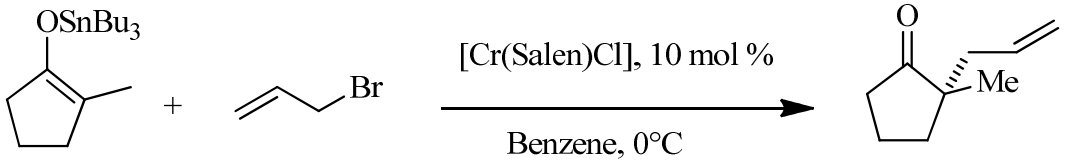
Cozzi and co-workers that Zn(Salen) metal complexes are able to promote the addition of Et_2Zn to aldehydes with moderate enantioselectivities.[29] Cr(Salen) has also been used to promote the addition of Me_2Zn to aldehydes (eq 12).[30] Kozlowski and co-workers have exploited this concept through the tailored design of new Salen Schiff bases, able to coordinate electrophiles and nucleophiles which are in close proximity.[31]



(12)

yields 40-95%, ee 71-99%

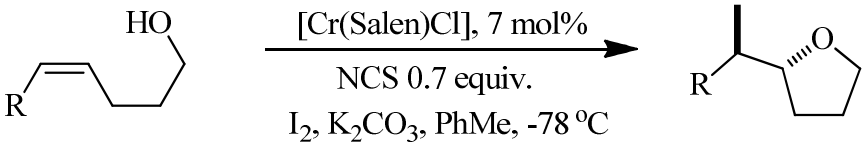
Salen metal complexes are useful transfer catalysts for alkylation of enolates and Jacobsen has used these properties associated with Cr(Salen) in the alkylation of tin enolated of ketones (eq 13).[32] In the proposed mechanism, Cr(Salen) was acting either to activate the tin enolate, or form an activated species with the electrophile.



(13)

yield 84 %, ee 94%

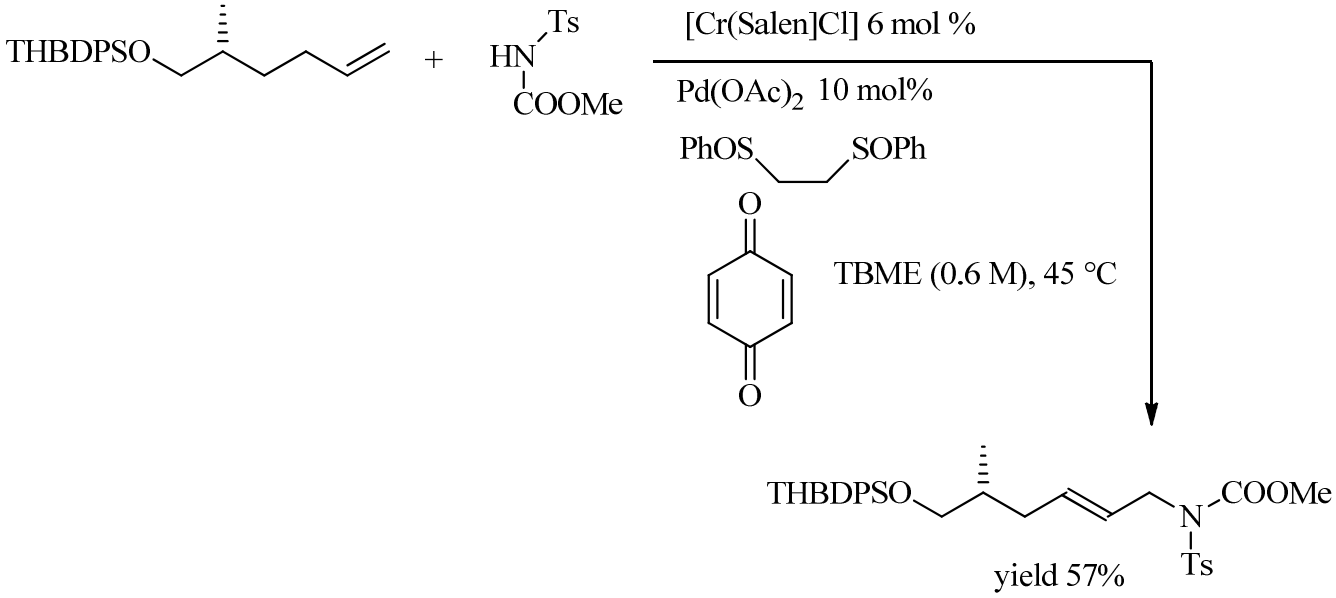
Refinement of the conditions established a novel catalytic enantioselective iodocyclization protocol using iodine in the presence of 7 mol% of [(*R,R*)-Cr(Salen)Cl] complex activated by 0.7 equivalent of NCS in toluene to induce 74 to 93% ee (eq 14).[33]



(14)

ee 74-93%

An interesting use of Cr(Salen) was reported by White in the catalytic intermolecular linear allylic C-H Amination *via* heterobimetallic catalysis. [Cr(III)(Salen)] complexes increase the rate of π-allylPd functionalization with acetate, suggesting that this catalyst may promote π-allyl functionalization. It was found that the addition of 6 mol % commercial (salen)Cr(III)Cl complex with 10 mol % with commercial bis-sulfoxide/$Pd(OAc)_2$ complex gave linear (*E*)-allylic amine in with remarkable regio- and stereoselectivities (eq 15).[34]



(15)

Recycling of Catalysts.

The recovery and re-use of catalysts is important for both economic and environmental reasons. Efforts have been made to utilise ionic liquids or anchor the catalysts on solid supports. Kureshy has reported the use of a chiral recyclable dimeric and polymeric [Cr(III)Salen] complex as a catalyst for the enantioselective production of trans 1,2 aminoalcohols through aminolytic kinetic resolution of *trans*-stilbene oxide and *trans*-β methyl styrene oxide with anilines using a microwave.[35]

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