Catalytic, enatioselective Michael addition reactions

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Dedicated to Professor S.V.Kessar on the occasion of his 70th birthday

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Abstract

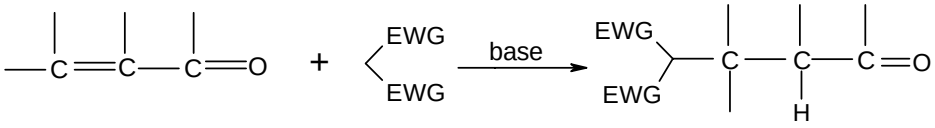
This review summarizes the tremendous achievements in the field of catalytic enantioselective Michael addition reaction involving the attack of soft nucleophiles on α,β- unsaturated systems. The reaction has evolved during past two decades, from stoichiometric to catalytic. A large number of efficient catalytic systems have been used to generate chiral Michael adducts in high optical purity. Several chiral alkaloids were used for the enantioselective addition of thiols and dialkylmalonates to cyclic and linear enones to give product in moderate to high enantioselectivity. Chiral crown ethers in conjugation with metal alkoxides were found to be the catalyst of choice for the addition of substituted α-phenylesters to linear enones. Proline derived catalysts gave product in moderate in moderate to high enantioselectivity where NO_2 group was present as an activator in either Michael donor or acceptor. BINAP based catalysts were found to be superior in Michael addition of α-nitrile substituted esters to linear enones. A new class of heterobimetallic catalysts based on BINOL ligand was found to be highly versatile for an array of Michael donors and acceptors to provide products in very high optical purity. Metal complexes based on chiral N,N-dioxides were found to be superior for the addition of arylthiols to both linear and cyclic enones to have product in high enantiomeric excess.

Keywords: Michael addition, nucleophiles, catalysis, chiral ligands, enantioselectivity, heterobimetallic

Contents

1. Introduction

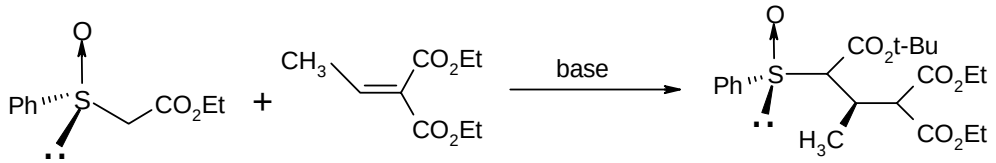
Michael addition reaction refers to the addition of carbanion to unsaturated systems in conjugation with an activating group. As enormous amount of work has been documented in this area, we will survey only the work involving catalytic enantioselective addition of stabilized soft nucleophiles (eqn. 1).



(1)

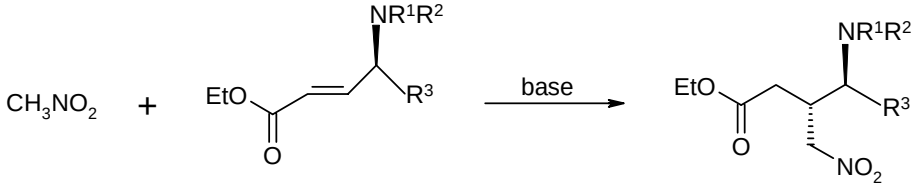
EWG = CO_2R, CO_2NR_2, CN, NO_2 etc.

Essentially there are three ways to generate chiral adducts using Michael reaction namely,
(a) Addition of chiral Michael donor to achiral Michael acceptor – here the source of chirality is present in the Michael donor which controls the new stereogenic center formed in the product. (eqn. 2).



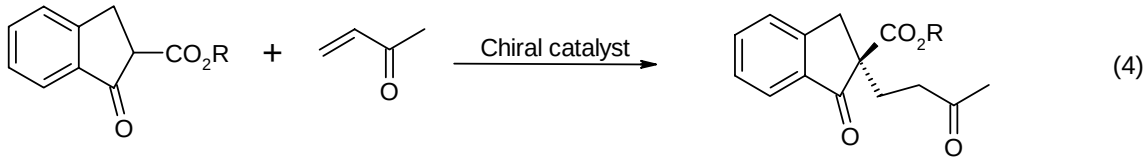
(2)

(b). Addition of achiral Michael donor to chiral Michael acceptor – here the source of chirality is present in the Michael acceptor which controls the new stereogenic center formed in the product (eqn. 3).



(3)

(c). Both the reactants *i.e.* Michael donor and Michael acceptor are achiral however the catalyst used for the reaction is chiral (eqn. 4)



(4)

It is the last type of reaction which has received much attention in recent times mainly because of the easy availability of the starting reactants (as they are achiral or racemic) and also because of the fact that reaction could be promoted by the use of chiral additive in catalytic amount. The asymmetric Michael reaction could be categorized in two groups:
(i). Enantioselective addition of prochiral enolates *i.e.* Michael donor to acceptor.
(ii). Enantioselective addition of enolates to prochiral Michael acceptor (Figure 1).

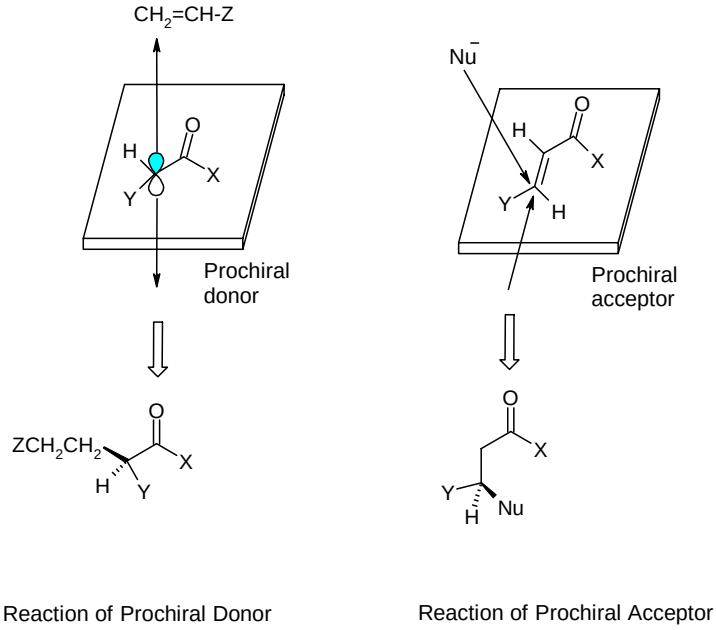


Figure 1

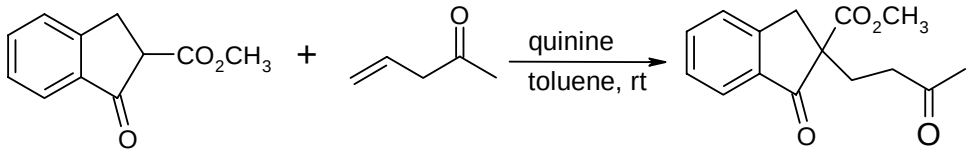
In the former reaction, there is discrimination of the enantioface of the prochiral Michael donor, and the asymmetric centers are formed on the donor. In the latter reaction, there is discrimination of the enantioface of the prochiral Michael acceptor and the resulting asymmetric centers are formed on the Micahel acceptor. Since the first reported[1] example of catalytic enantioselective Michael addition reaction by Wynberg in 1975, there has been plethora of publications in this area and the reaction has become one of the important methods for the enantioselective C-C bond formation. Several chiral additives have been used for promoting the reaction including chiral alkaloids, chiral diamines, chiral alkoxides, chiral amino acids, chiral lanthanoide complexes etc. Due to the wide variations in the nature of catalyst used for the

reaction, it becomes important to classify Michael reaction according to the kind of catalyst used. Broadly they can be categorized in two groups *viz.* organo catalysts and organometallic catalysts.

2. Organo Catalysts

2.1. Optically active alkaloids

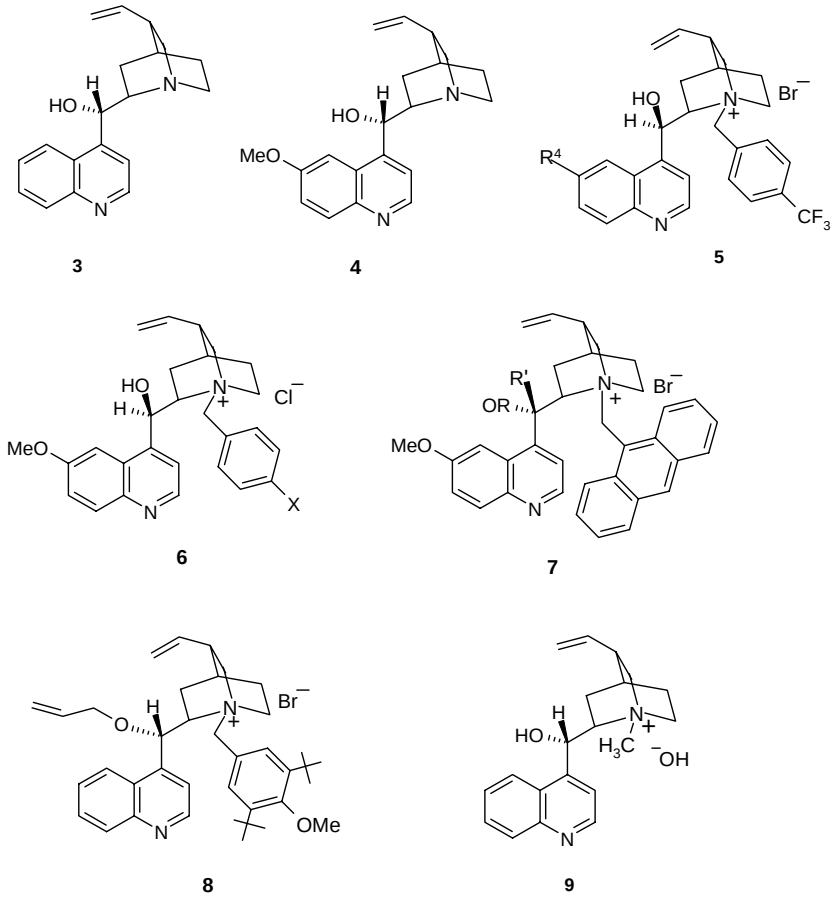
Various alkaloids based on cinchona and ephedra have been used for the enantioselective Michael addition. Indeed the catalytic enantioselective Michael reaction first reported[1] by Wynberg utilized optically active quinine as catalyst for the addition of 1-oxo-2-indane-carboxylate (**1**) to methyl vinyl ketone giving Michael adduct (**2**) in 68 % *ee* (eqn- 5).



(5)

1 2 (68% *ee*)

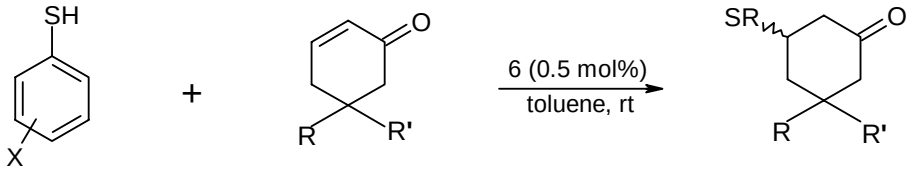
Various chiral cinchona alkaloids which have been used for Michael addition reaction are shown in Figure 2.



3 4 5 6 7 8 9

Figure 2

Addition of aromatic thiols to conjugated cycloalkenones was also reported. Quinine or *N*-(p-nitrobenzyl) quininium chloride (**6**) showed comparable catalytic activity (eqn. 6).[2, 3]



(6)

Catalysts containing the β-hydroxy amine moiety (cinchona and ephedra) gave higher reaction rates and higher *ee* than the catalyst without a hydroxyl functionality. Polar solvents and concentrated reaction solutions were counterproductive for the enantioselectivity. It was proposed[4] that *erythro* cinchona and ephedra alkaloids catalyze the reaction *via* tight transition state complex comprising all the three species viz. thiol, enone and the catalyst (Figure 3).

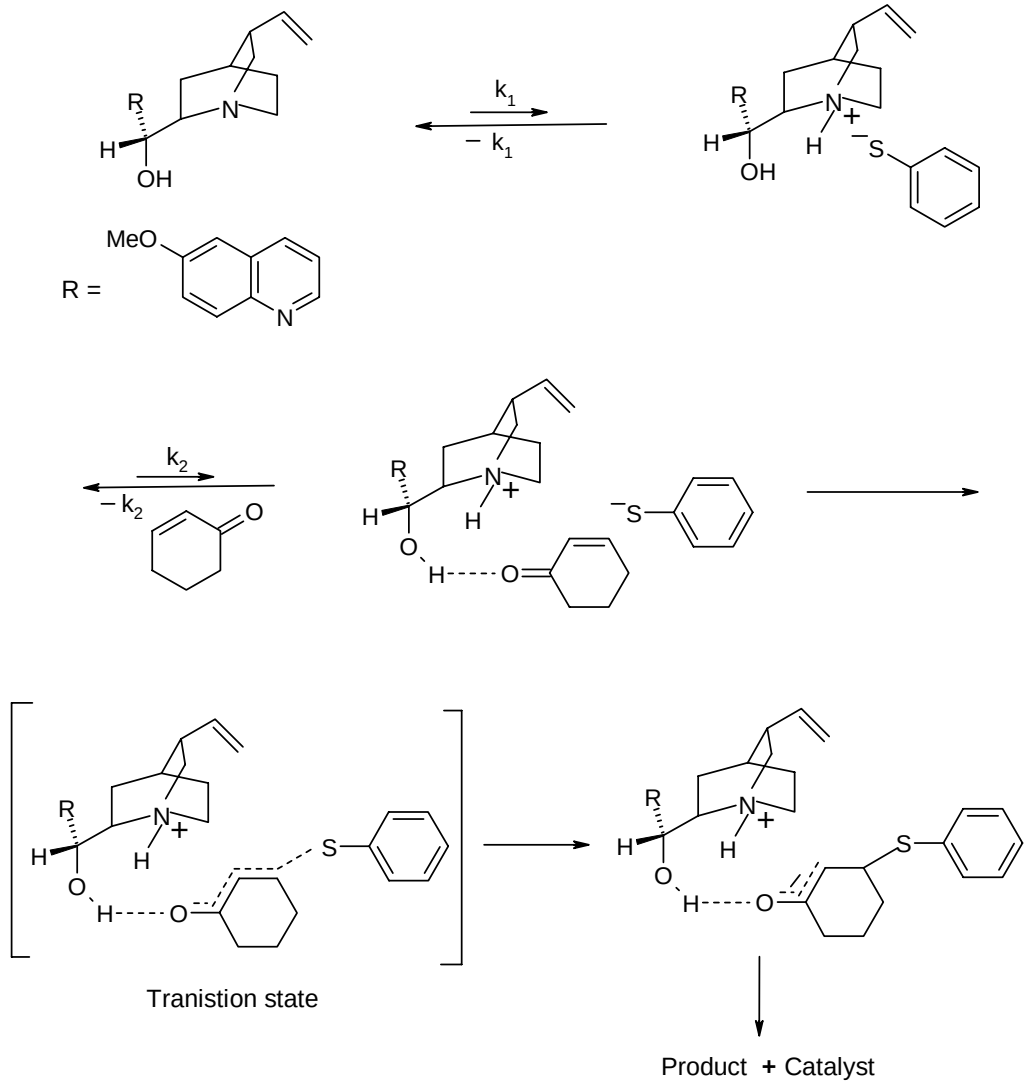
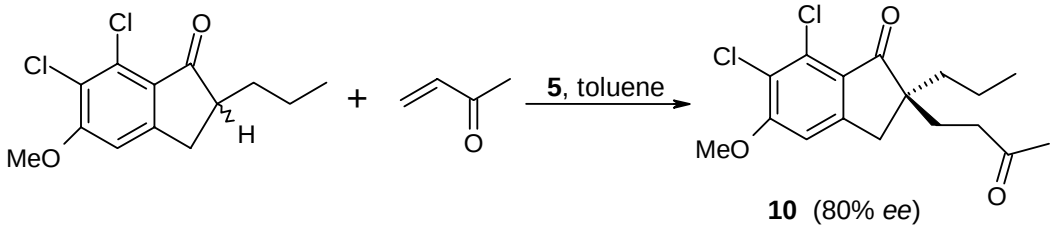


Figure 3

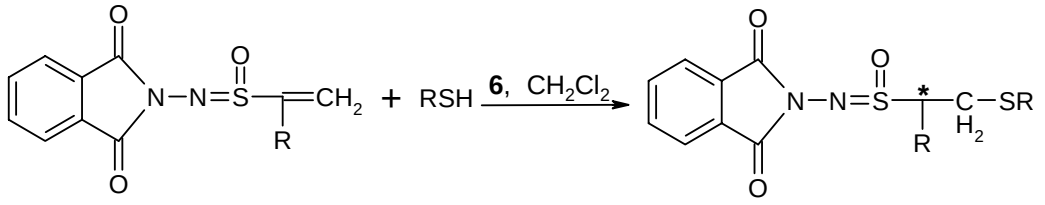
An electrostatic interaction between the thiol anion and the ammonium cation and a hydrogen bond between the catalyst hydroxyl group and the enone carbonyl group stabilizes the geometry of these complexes whereas steric factors imposes a free energy difference between the two possible orientations of the enone which results in the formation of unequal amounts of *R* and *S* products. Threo cinchona alkaloids and the catalyst without a hydroxyl group lack at least one of the stabilizing interactions leading to less stabilized transition states and consequently lower enantioselectivity.

Conn et. al. reported[5] enantioselective addition of 2-alkylindanones to methyl vinyl ketone. Using [p-(trifluoromethyl)benzyl] cinchoninium bromide (**5**) the Michael adduct (**10**) was obtained in upto 80% *ee* and in 95% overall yield (eqn.7).



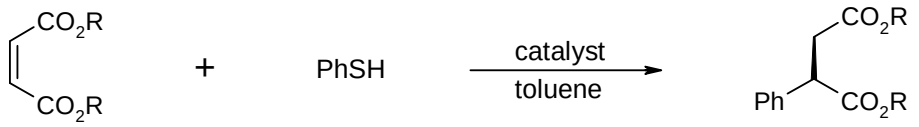
10 (80% *ee*) (7)

Colonna et. al. reported[6] the addition of thiols to α,β-unsaturated sulphoximides to obtain the product, albeit in low enantiomeric excess. Several catalysts like quinine, N-benzyl quininium chloride (**6**), *N*-dodecyl-*N*-methyl ephedrinium bromide were examined (eqn. 8).



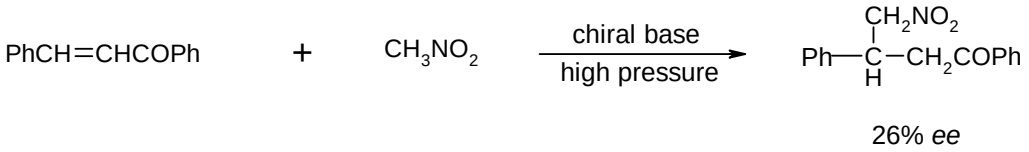
13% *ee* (8)

Mukaiyama et. al. reported[7] asymmetric addition of thiophenol to dialkyl maleate using catalysts like cinchonine, cinchonidine, quinine, quinidine. Although product with *ee* as high as 86% was obtained the overall yield was only 7% that to after several days of stirring at 0 ^{0}C. However reaction at 20 ^{0}C gave product (**11**) in 92% yield and in 55% *ee* (eqn.9).



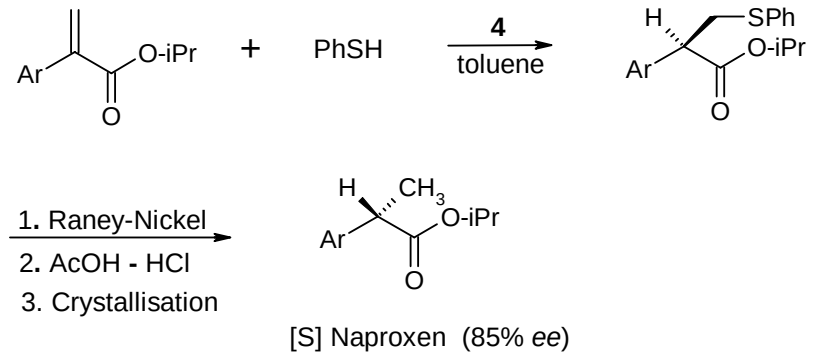
11 (9)

Matsumoto et. al. carried out addition of nitromethane to chalcone under high pressure. Various cinchona based alkaloids were used for the reaction , quinidine giving the best result[8] with up to 26% enantioselectivity (eqn. 10).



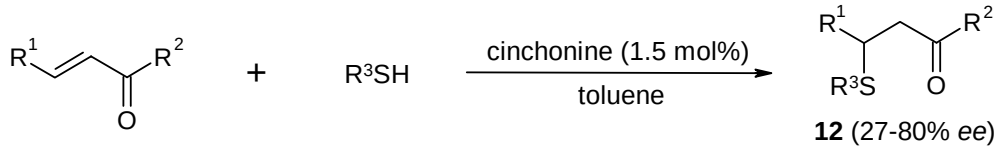
(10)

A novel synthesis of optically active 2-phenylpropionic acid or esters which can be used for the synthesis of [*S*]-naproxen, a non steroidal anti-inflammatory agent, was reported by Dike et. al.[9] The key step in the reaction was the enantioselective protonation of the prochiral carbanion generated in the addition of benzene thiol to α-aryl acrylates catalyzed by cinchona alkaloids. Amongst various alkaloids used, quinidine gave the best result. An interesting feature of this addition was the formation of a new chiral center one atom away from the incoming sulphur atom. The benzene thiol group can be removed easily by standard Raney-nickel desulphurization to give the corresponding α-aryl propionates (Scheme-1).



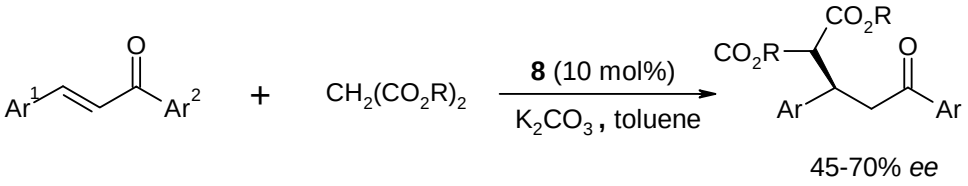
Scheme 1

Recently Skarzewski et. al. reported[10] enantioselective addition of thiophenols to chalcones in the presence of cinchonine to give Michael adduct (**12**) in up to 80% *ee* (eqn. 11).



(11)

Kim et. al. reported[11] the addition of malonates and nitromethane to chalcone using chiral quaternary ammonium salts derived from cinchona. Cinchona derived alkaloids (e.g. **8**) were used giving product in up to 70% *ee* (eqn. 12 & 13).



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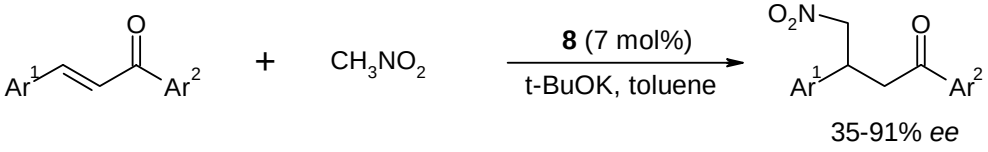
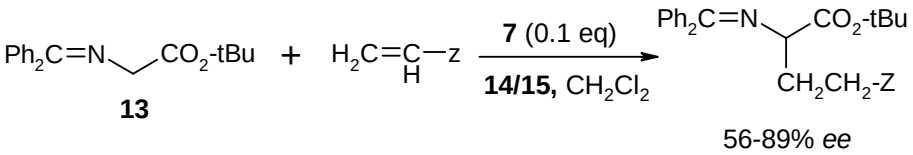


(13)

O'Donell et. al. reported[12] the preparation of optically active unsaturated α-amino derivatives by the conjugate addition of schiff base ester derivatives (**13**) to Michael acceptor using cinchona derivatized (**7**) along with non ionic phosphazene bases (Schwesinger bases) BEMP(**14**) or BTPP (**15**).



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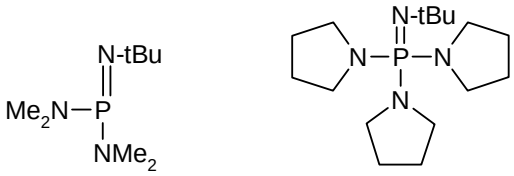


BEMP (**14**) BTPP (**15**)

In addition to cinchona based alkaloids, ephedra based alkaloids have also been used (Figure 4).

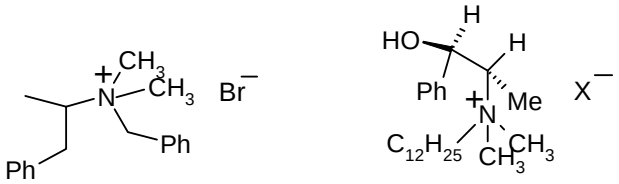
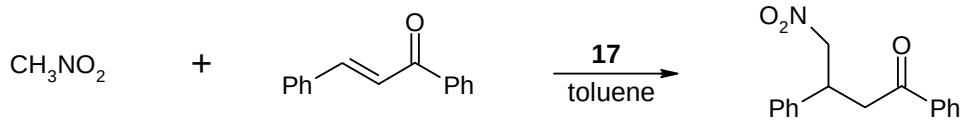


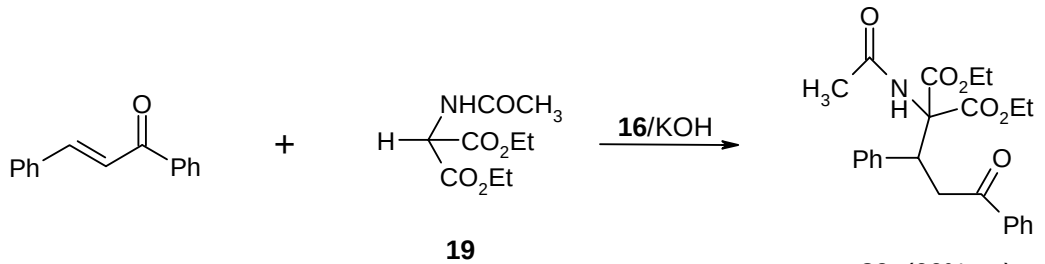
Figure 4

Wynberg et. al. reported[13] the addition of nitromethane to chalcone using *N*-dodecyl fluoride of *N*-methyl ephedrine (**17**) to obtain product (**18**) in 23% *ee* (eqn. 15).



18 (23% *ee*) (15)

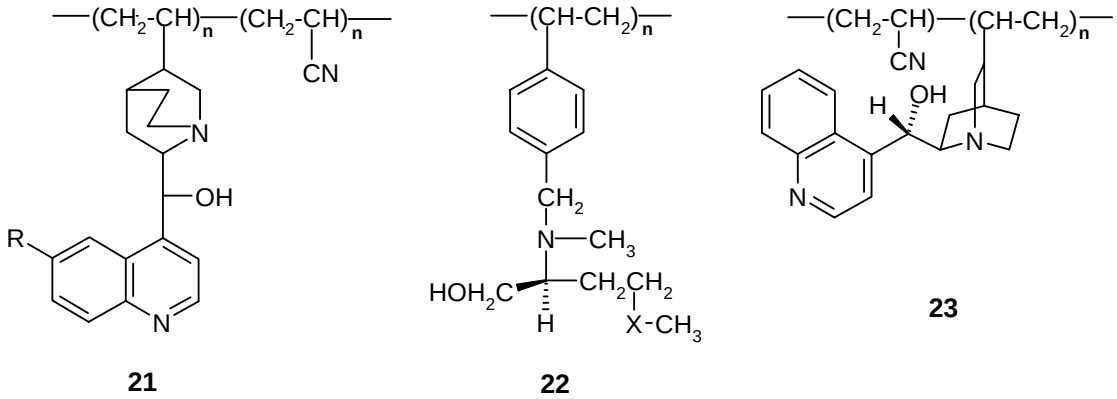
Loupy et. al. reported[14] the addition of diethylacetylamine malonate (**19**) to chalcone using *N*-methyl-*N*-benzyl ephedrinium bromide (**16**) to give product (**20**) in 66% *ee* (eqn. 16).



19 **20** (66% ee) (16)

2.2. Polymer supported catalysts

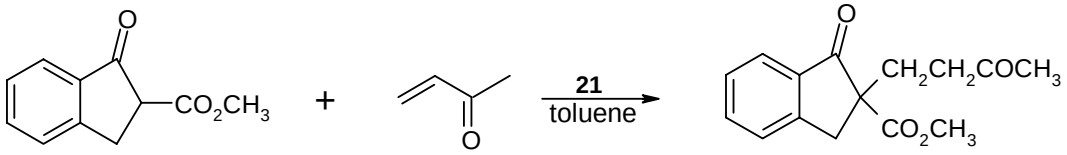
The principal drawback in the use of alkaloid catalysts is the relative difficulty of separating the product from the catalyst. One way to overcome this drawback would be to fix the alkaloid on a solid support in a way that retains the stereochemistry of the alkaloid. To serve this purpose, various polmer supported alkaloids were prepared (Figure 5).



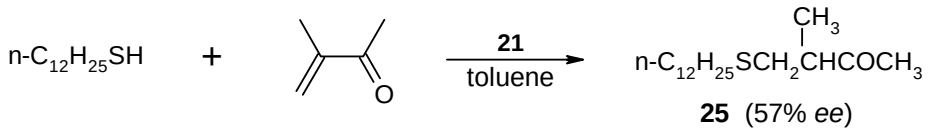
21 **22** **23**

Figure 5

Burri et. al. carried out[15] addition of 1-oxo-2-indane carboxylate to methyl vinyl ketone using **21** to obtain **24** in 42% *ee*. The same group reported the addition of dodecanethiol to iso-propenyl methyl ketone to obtain **25** in 57% *ee* (eqn. 17 & 18).

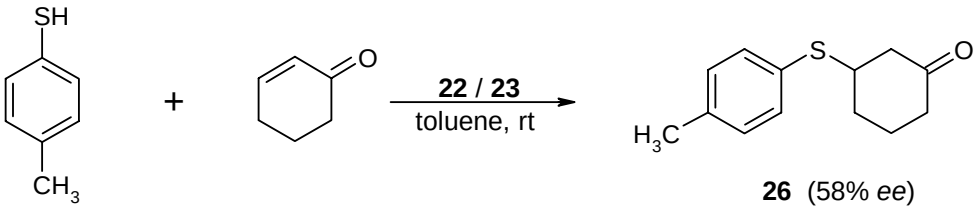


24 (42% *ee*) (17)



25 (57% *ee*) (18)

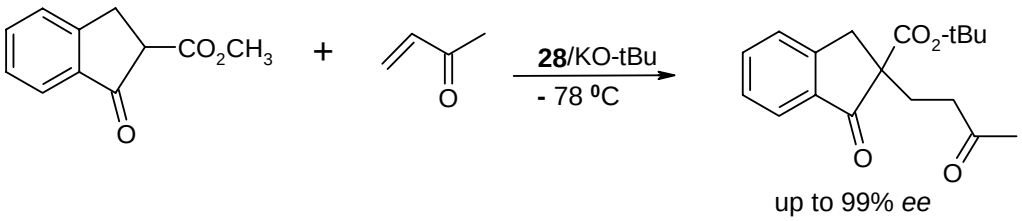
Hodge et. al. carried[3] out the addition of p-methyl thiophenol to cyclohexenone using **22** and **23** to obtain product (**26**) in almost quantitative yield (eqn. 19).



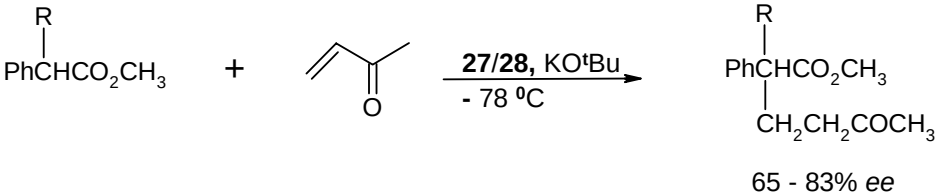
26 (58% *ee*) (19)

2.3. Crown ethers

Crown ethers of wide structural variations have been used for the asymmetric Michael addition reactions. Since the first report[16] by Cram et. al. using chiral crown complexes based on optically active *R/S* – BINOL, much progress has been made in this area. Some of the chiral crown ethers which have been used for this purpose are shown in Figure 6.

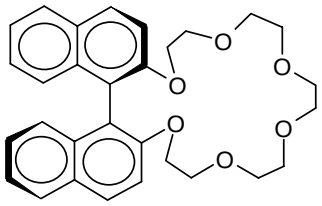


up to 99% *ee* (20)



65 - 83% *ee* (21)

Cram et. al. carried out the addition of methyl-1-oxo-2-indane carboxylate to methyl vinyl ketone using 20 mol% of crown ether **27**/**28** (eqn. 20). They also reported[16] the addition of substituted methylphenyl acetate to methyl vinyl ketone (eqn. 21).



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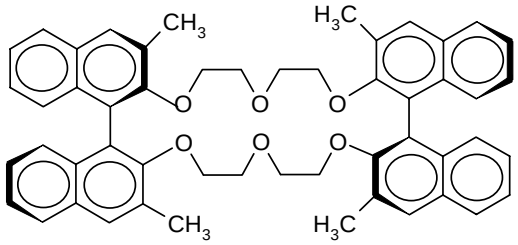

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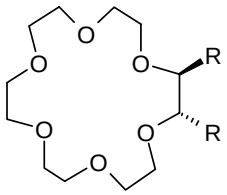

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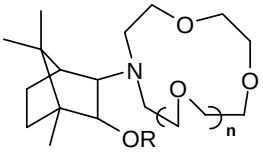

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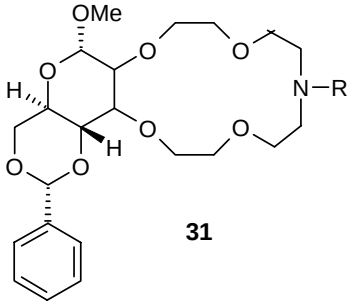

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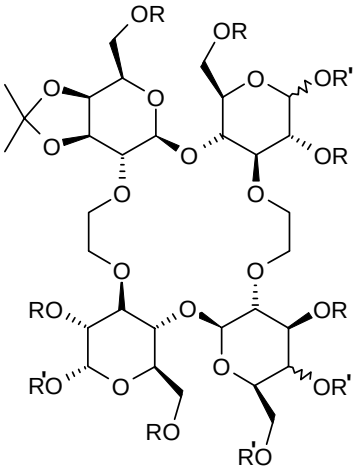

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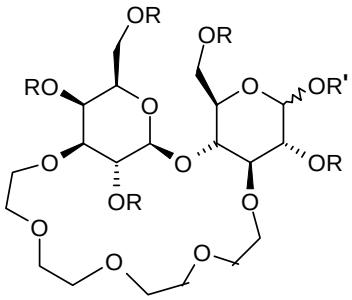

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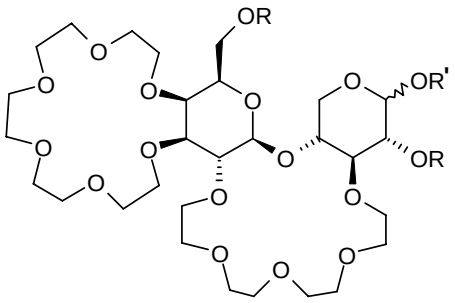

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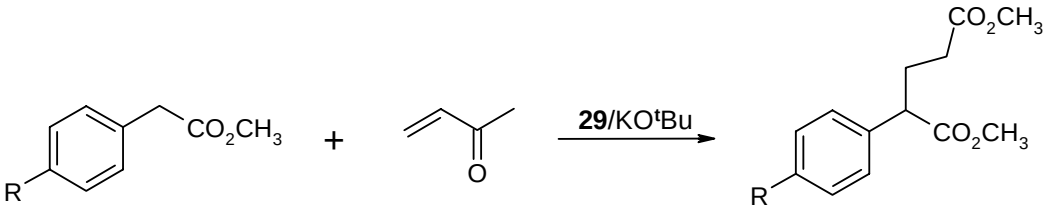
Figure 6

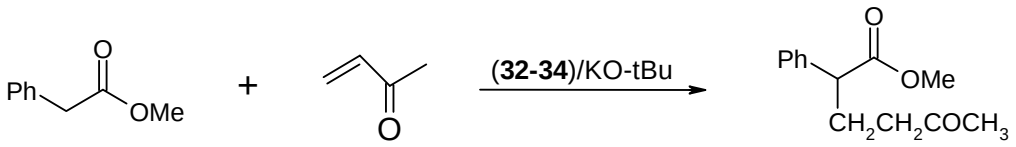
Koga et al. reported[17] the addition of methylphenyl acetate to acrylates using the crown ether **29** (eqn. 22).



(22)

up to 88% *ee*

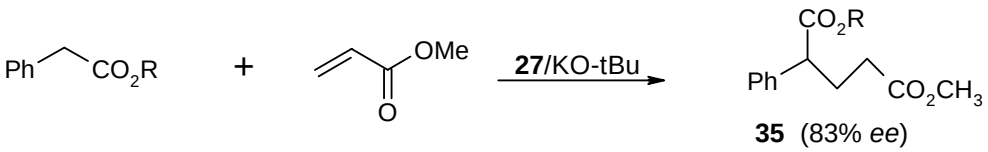
Penandes et. al. prepared[18] several *bis* lacto-18-crown-6 ethers (**32-34**) and examined their efficiency for the enantioselective addition of methyl phenyl acetate to methyl vinyl ketone (eqn. 23).



(23)

7-44% *ee*

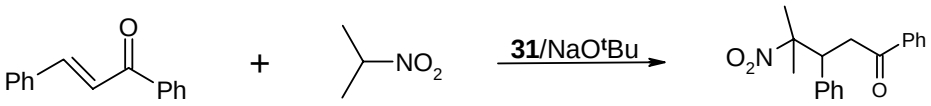
Camphor derived crown ether **30** was used by Brunet et. al.[19] for the addition of alkyl phenyl acetate to methyl acrylate to obtain the product **35** up to 85% yield (eqn. 24).



(24)

35 (83% *ee*)

Toke et. al. reported[20] the addition of nitroalkanes to chalcone using crown **31** (eqn. 25).



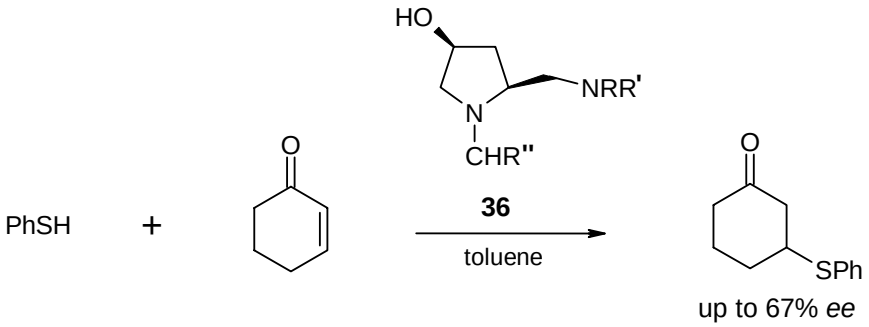
(25)

60% *ee*

2.4. Chiral diamines

Mukaiyama et. al. reported[21] the enantioselective addition of thiols to cyclohexenone using chiral diamines. The best results were obtained using (*2S,4S*)-2-anilinomethyl-1-ethyl-4-hydroxy pyrrolidine (**36**) as the catalyst to realize the product in up to 67% optical purity and in 24-90% yield (eqn. 26).

It was proposed that the product formation takes place *via* formation of an ammonium thiolate complex where the ammonium counterpart has a 5,5-fused ring structure (Figure 7).



(26)

Such rigid structure was supposed to be a crucial factor in the enantioselection because the enantioselectivity decreased when the substituent of the amine was replaced by bulkier groups and therefore this structure no longer remained a preferred one. Also in a solvent like toluene, the thiolate anion is stabilized by the π-π interaction and the freedom of its location is further limited by the interaction with the aromatic ring of the catalyst. Approach of cyclohexenone to complex-A takes place with a hydrogen-bond interaction between the carbonyl group and the hydroxyl group of the catalyst. In a protic solvent like ethanol this interaction is reduced resulting in no enantioselection. It was also postulated that the attack of thiolate anion to the enone occurs where two pathways B and C are possible (Figure 7). In case of the pathway C, the steric congestion of the aniline group and the cyclohexenone ring prevents the complex-A and the enone from reaching a favorable transition state leading to a preferential attack on the *Re* face of the cyclohexenone through pathway B resulting in the predominant formation of the [*R*]-enantiomer.

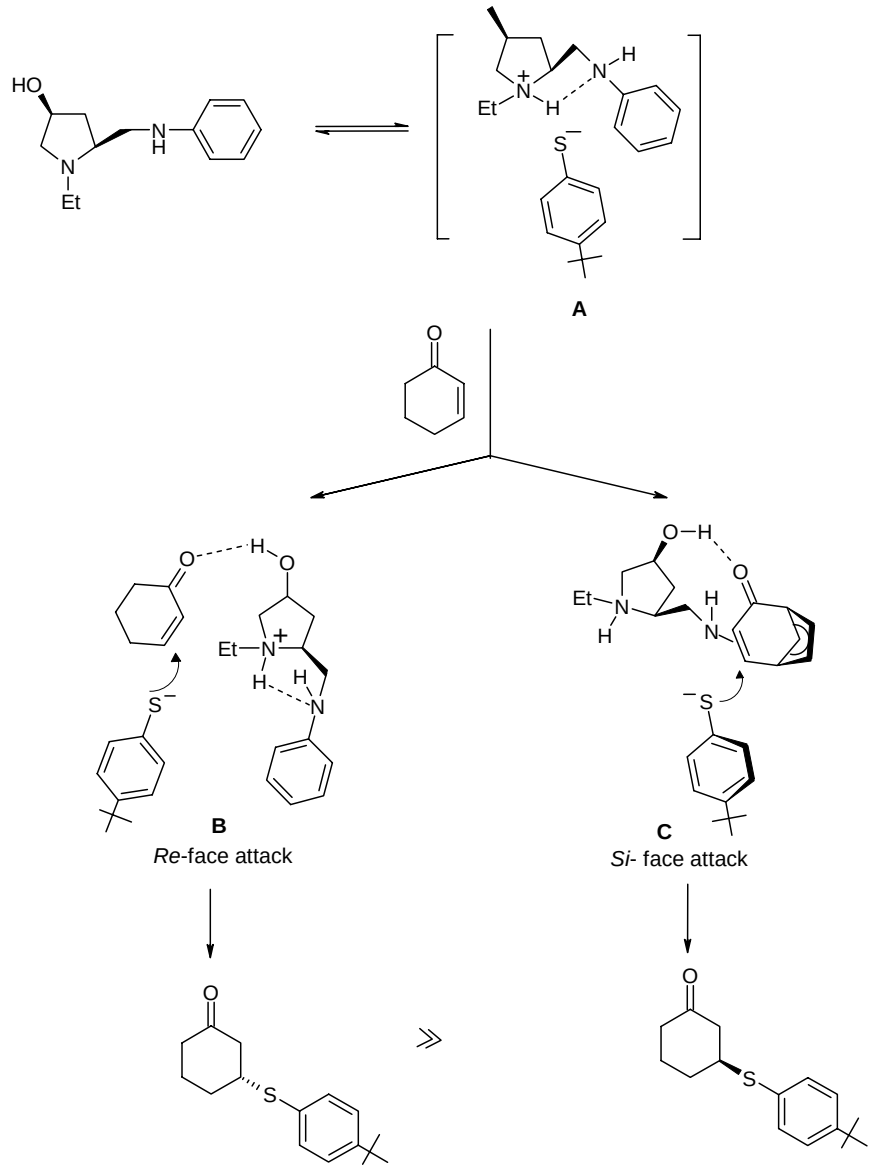
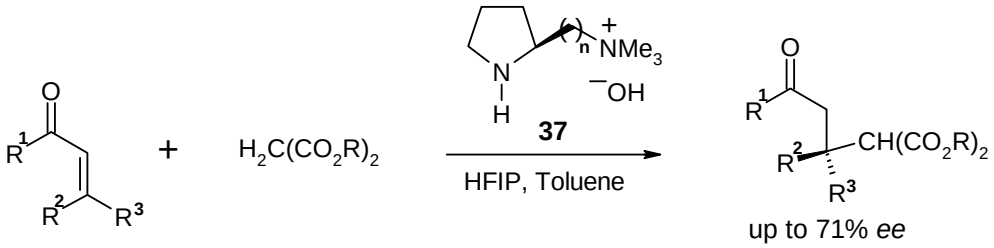


Figure 7

2.5. Amino acid and their derivatives

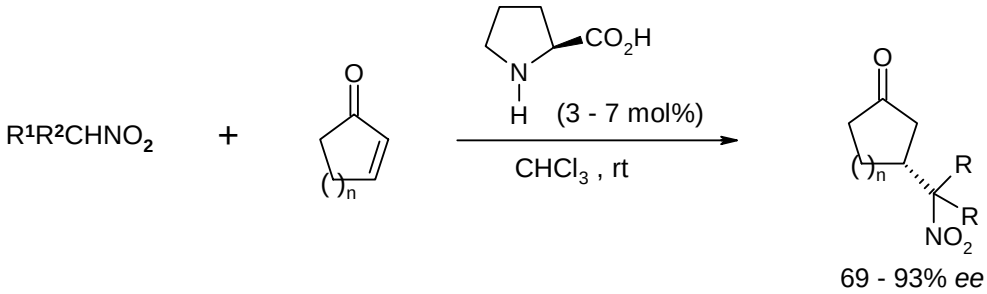
Taguchi et. al.[22] used [*S*]-*N*-(2-pyrrolidylmethyl)-*N*,*N*,*N*-trimethylammonium hydroxide (**37**) for the addition of soft nucleophiles to enones giving product with moderate to high optical purity (eqn. 27).



(27)

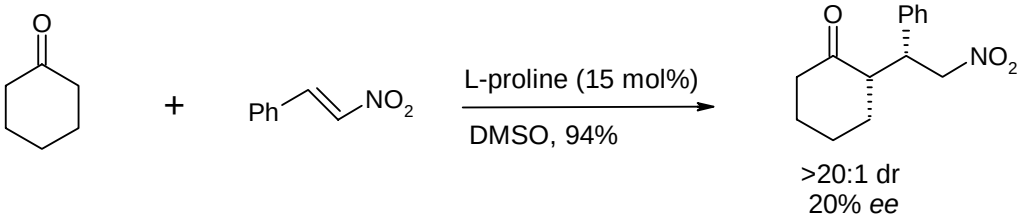
A test reaction done between dibenzyl malonate and cyclohexenone using the catalyst **37** gave the product in 88% yield with 3.5% *ee*. Taguchi *et. al.* concluded that due to strong basicity of the catalyst direct attack of malonate to the enone causes lowering of the enantioselectivity. HFIP (1,1,1,3,3,3-hexafluoro-2-propanol) was therefore added to reduce basicity and to control the imminium intermediate formation which resulted in product with up to 70% *ee*. These results suggested that the face selective attack on enone was controlled through the reversible imminium intermediate.

Hanessian et. al. reported[23] the conjugate addition of nitroalkanes to cycloalkenones using L-proline as the catalyst (eqn. 28).



(28)

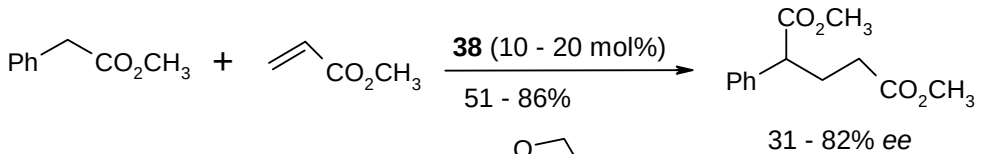
List et. al. reported[24] the addition of cyclohexanone to 2-phenyl-1-nitroethane also using L-proline (eqn. 29).



(29)

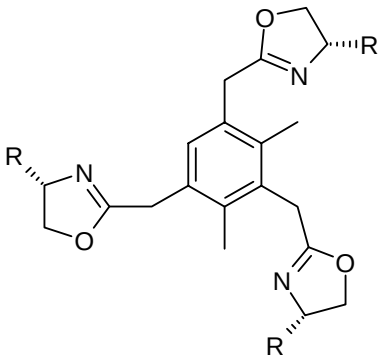
2.6. Chiral oxazoline

Ahn et. al. reported[25] the Michael addition catalyzed by chiral tripodal oxazoline (38) in conjuction with KO^{t}Bu (eqn. 30).



31 - 82% *ee*

(30)

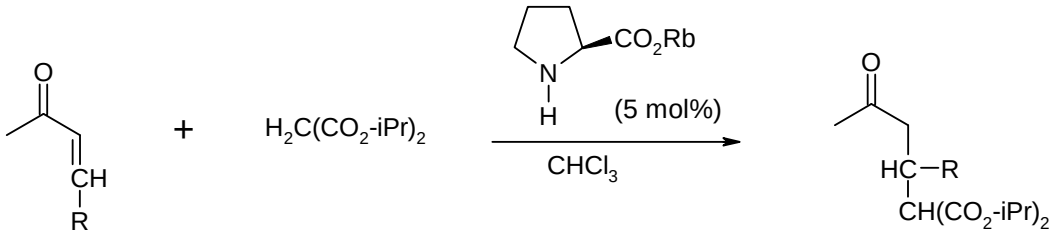


38 - (S,S,S)- BTO

3. Organometallic Catalysts

3.1. Metal salts of amino acids

Yamaguchi et. al. reported[26] the first catalytic asymmetric Michael addition of a simple maolnate to prochiral enones and enals employing readily available rubidium salt of L-proline (eqn. 31).



35 - 76% *ee*

(31)

The catalyst was found to be associated with water of hydration and the reaction rate was considerably lowered in the presence of molecular sieves 4A. In fact, small amount of water was found to promote the reaction. Rubidium salts of *N*-methyl-proline, pyrrolidine or trimethyl amine were found to be ineffective for the reaction showing that the secondary amine and the metal carboxylate moieties of the catalyst are essential for high catalytic activity. It was proposed that the asymmetric induction takes place through enantioface differentiation of the Michael acceptor (Figure 8).

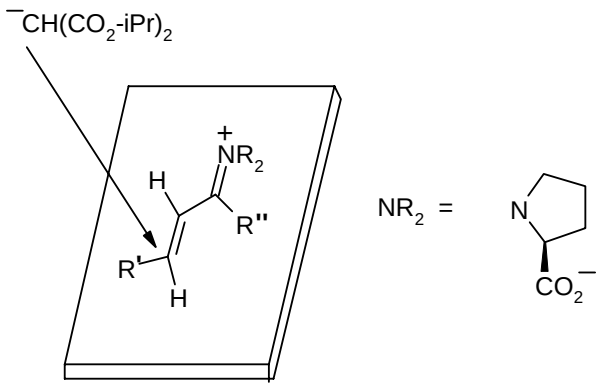
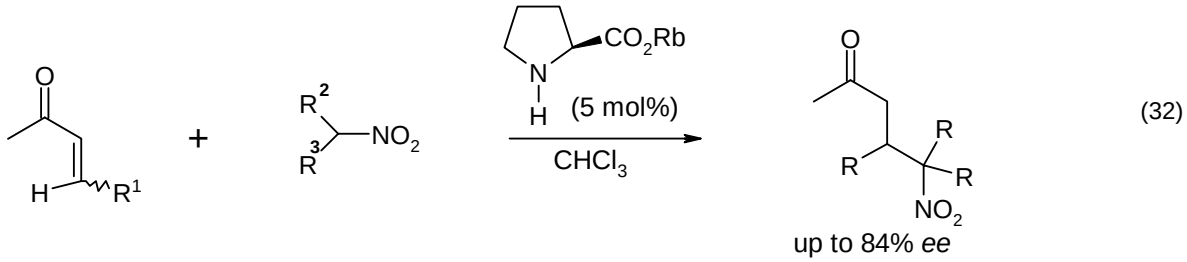


Figure 8

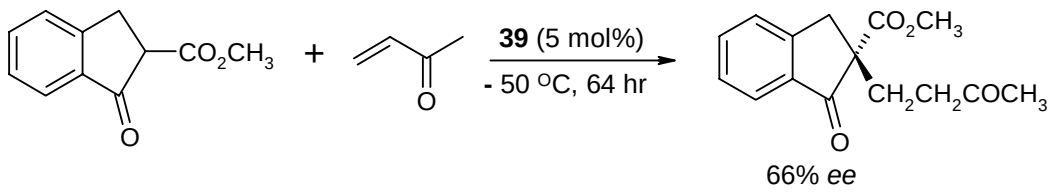
The same group later reported[27] the addition of nitroalkanes to enones and enals by using rubidium salt of L-proline to obtain the product in up to 84% *ee* (eqn. 32). [*R*]-adducts were obtained from cyclic [*Z*]-enones and [*S*]-adducts from acyclic [*E*]-enones.



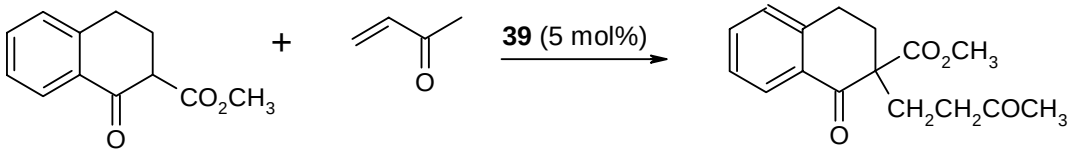
(32)

3.2. Metal-diamine complexes

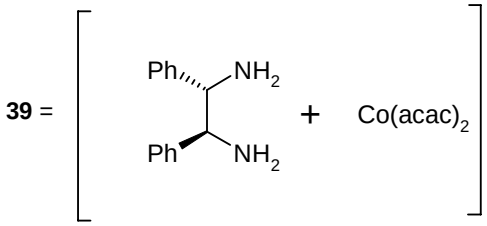
Michael reaction catalyzed by inorganic salts is widely reported.[28-35] Along with these reports, the use of metal-diamine complexes[36] is also known. Brunner et. al. reported[37] the first transition metal catalyzed Michael addition using cobalt(II)-diamine complex. It was postulated that an octahedral complex involving Co(II), diamine and 2-indane carboxylates first formed, which then undergoes stereoselective Michael addition to methyl vinyl ketone (eqn. 33 & 34).



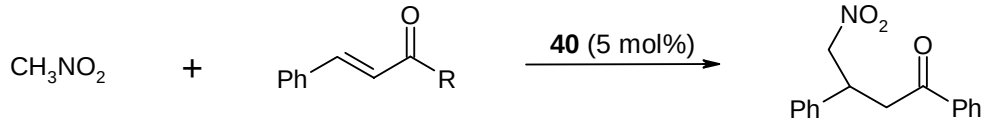
66% *ee* (33)



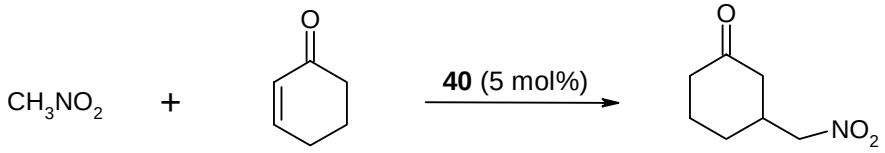
39% *ee* (34)



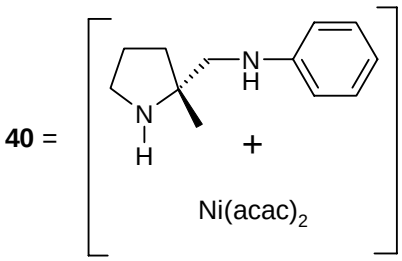
Botteghi et. al. prepared[38] Ni(II) complexes with chiral chelating nitrogen ligands such as 2,2'-bipyridines, 1,10-phenanthroline and 1,2-diamines for the addition of nitromethane to benzalacetone, chalcone and 2-cyclohexenone. Catalyst derived from $Ni(acac)_2$ and (+)-(*S*)-2-(anilinomethyl)-pyrrolidine (**40**) showed good catalytic activity providing up to 24% *ee* (eqn. 35 & 36).



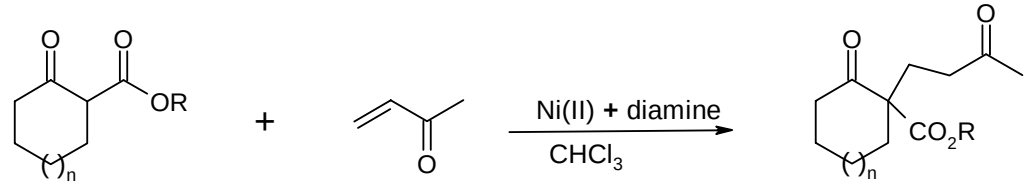
up to 24% *ee* (35)



up to 24% *ee* (36)



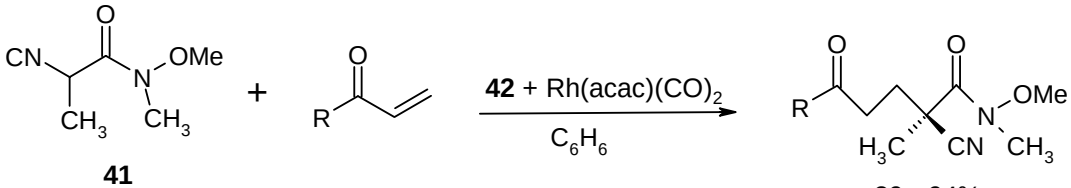
Recently Christoffers et. al.[39] created quaternary chiral centers using catalyst derived from $Ni(OAc)_2.2H_2O$ and (*R*,*R*)-1,2-cyclohexane diamine (eqn. 37).



(37)

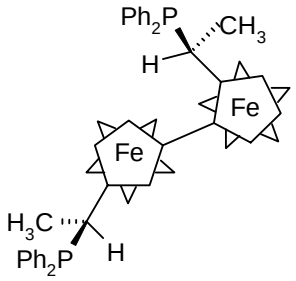
3.3. Transition metal complexes

Ito et. al. reported[40] the addition of *N*-methoxy-*N*-methyl-2-cyanopropionamide (**41**) to vinyl ketones or acrolein using 0.1-1 mol% of rhodium catalyst prepared in situ from $Rh(acac)(CO)_2$ and dipsosphine ligand (*S*,*S*)-(*R*,*R*)-PhTRAP (**42**) (eqn. 38).



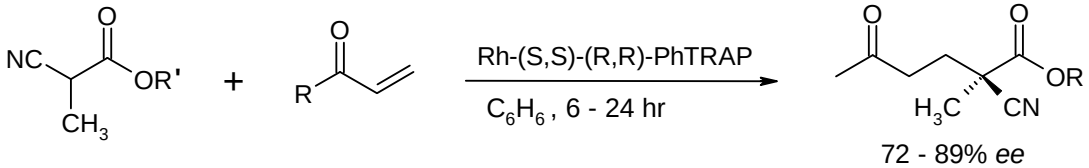
41

(38)



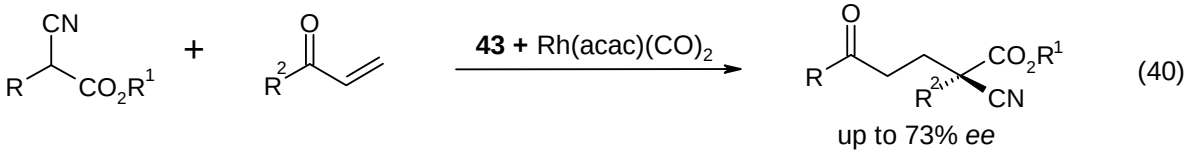
42 (*S*,*S*)-(*R*,*R*)-PhTRAP

They also reported[41] the addition of alkyl-2-cyano carboxylate to vinyl ketones using Rh-(*S*,*S*)-(*R*,*R*)-PhTRAP complex giving the product in more than 90% yield and up to 89% *ee* (eqn. 39).

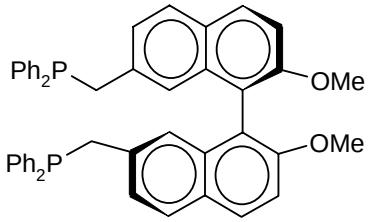


(39)

Nozaki et. al. used[42] chiral bisphosphine ligand (**43**) and prepared a chiral Rh(I) complex which was used for the addition of α-cyano esters to vinyl ketones (eqn. 40).

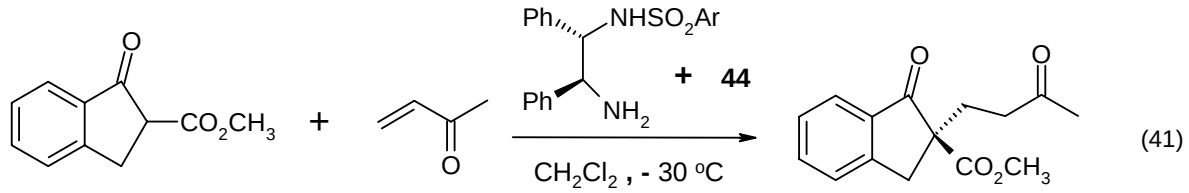


(40)

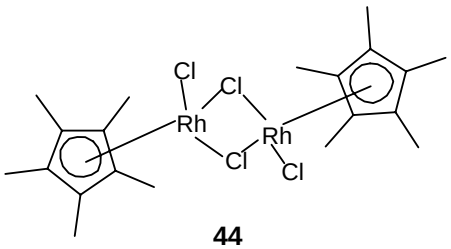


43

Suzuki et. al. prepared rhodium complex[43] for the addition of methyl-1-oxo-2-indane carboxylate to methyl vinyl ketone (eqn. 41).

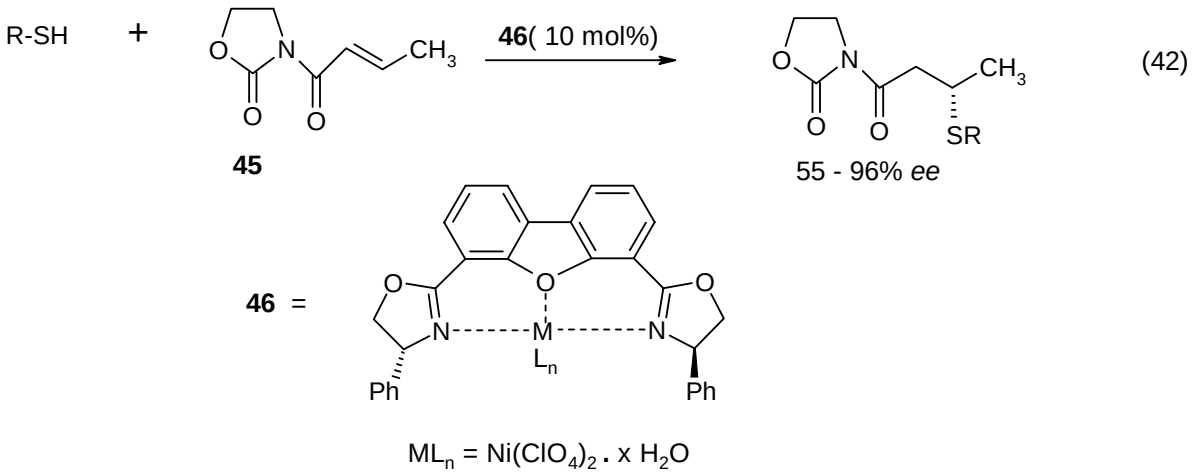


(41)



44

Kanemasa et. al. reported[44] the asymmetric conjugate addition of thiols to 3-(2-alkenoyl)-2-oxazolidinone (**45**) catalyzed by chiral cationic Ni(II) complex (**46**) (eqn. 42).



3.4. Heterobimetallic complexes

Heterobimetallic complex in which each metal plays a different role in the enantiodifferentiation represents another class of potent catalyst for enantioselective Michael reaction. The development of the multifunctional alkalimetal lanthanide-BINOL catalyst by Shibasaki *et al.*[45, 46] marked the milestone in this area enabling efficient catalytic conjugate additions of malonates to acyclic as well as cyclic substrates with high enantioselectivities. These complexes are depicted in Figure 9.

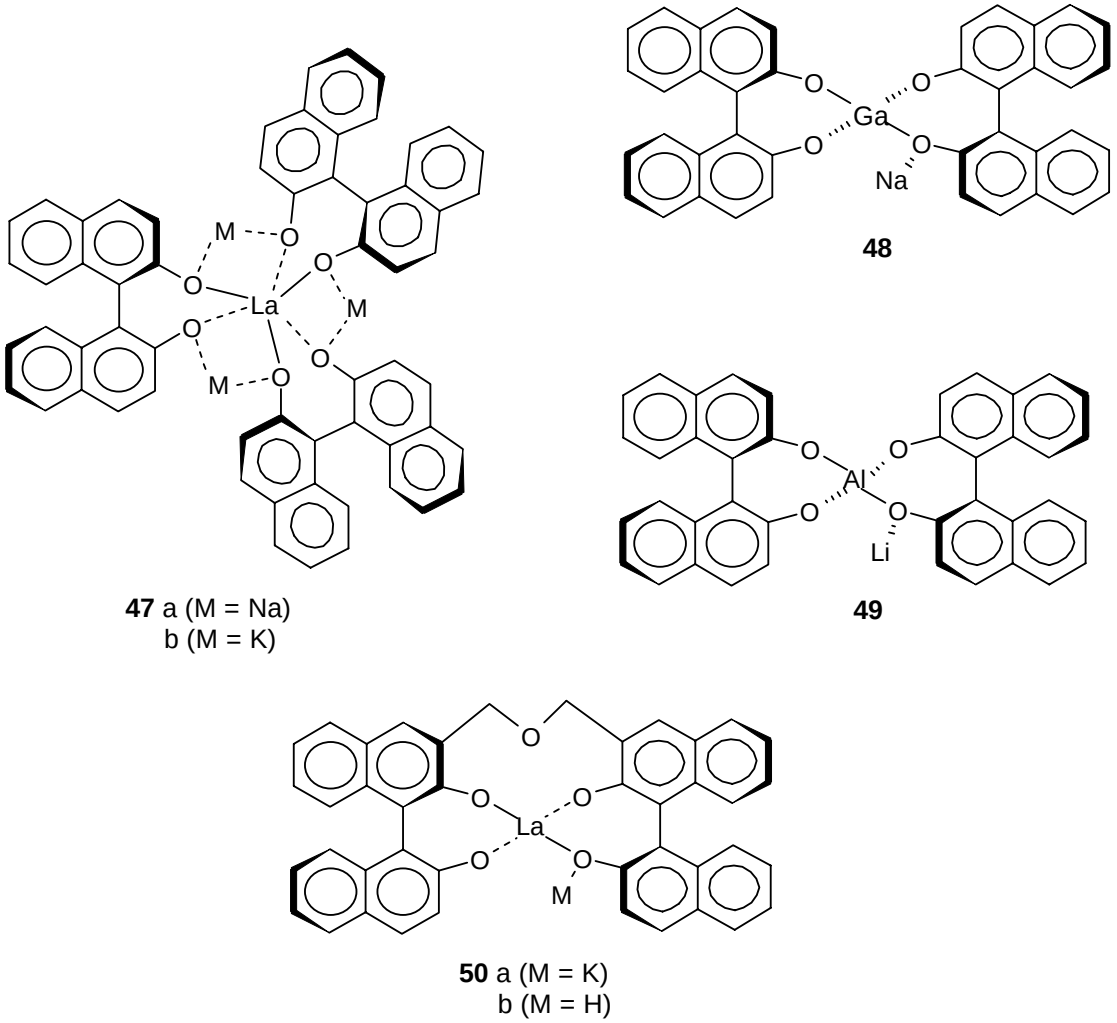
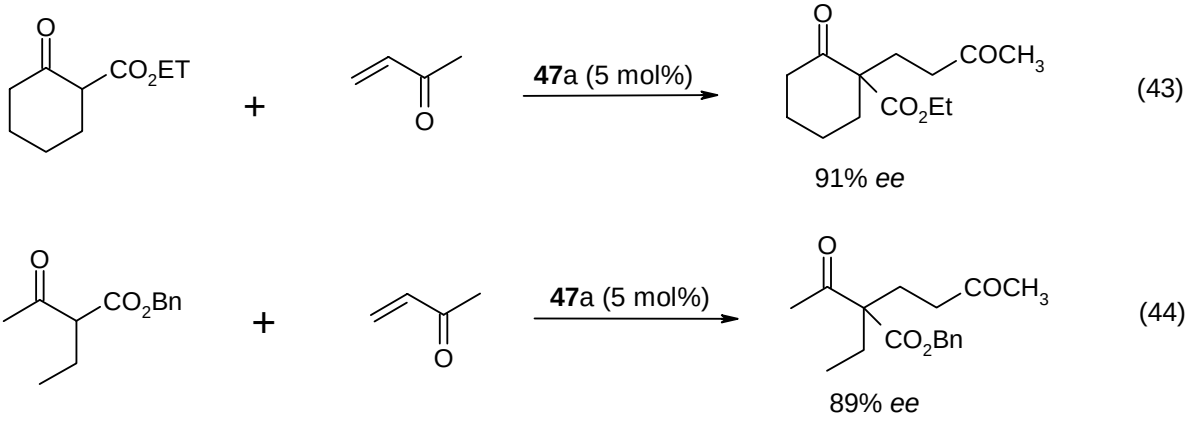
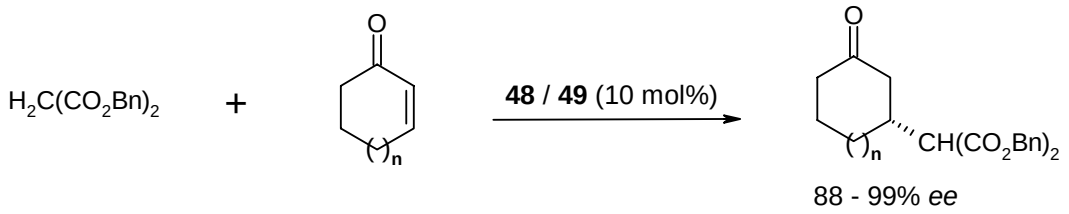


Figure 9

Extensive studies showed[47-49] that the lanthanum-sodium-BINOL complex (LSB) (**47**a) is very selective in the addition of prochiral β-keto esters to methyl vinyl ketone (eqn. 43 & 44).

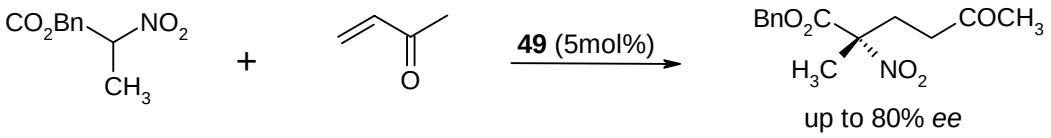


However for cyclic enones of different ring-size, the gallium-sodium complex (GSB) (**48**) and the aluminium lithium complex (**49**) proved[50] to be the catalyst of choice (eqn. 45).



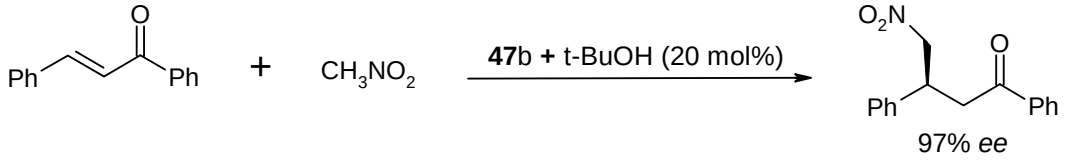
(45)

Feringa et. al. demonstrated[51] that the conjugate addition reactions catalyzed by (**49**) can be extended to α-nitro esters as nucleophiles to get the product in up to 80% *ee* (eqn. 46).



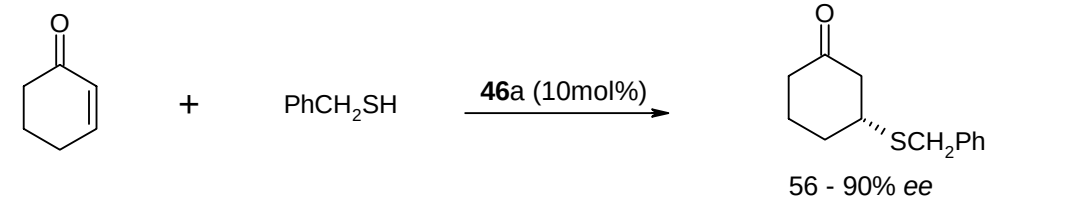
(46)

By the use of 20 mol% of **47**b as catalyst, Shibasaki et al.[52] were able to obtain the addition product of nitromethane to chalcone in 97% *ee* (eqn. 47).



(47)

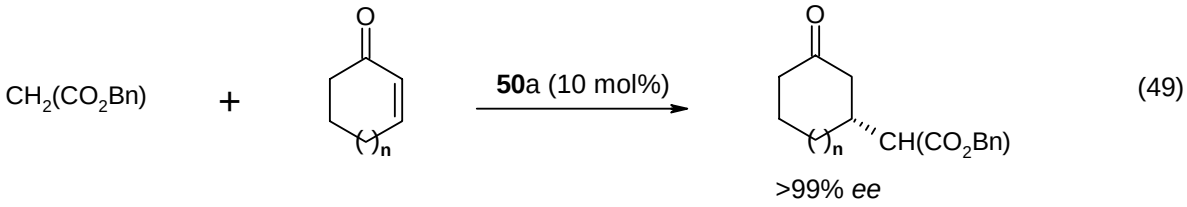
Besides carbon nucleophiles, thiols were also subjected to 1,4-addition to cyclic enones furnishing the corresponding Michael adducts with good yields and high enantioselectivities. Amongst various heterobimetallic complexes, the lanthanum catalyst **47**a showed the highest level of stereoselectivity. Thus the reaction of benzylmercaptan and cyclohexenone in the presence of 10 mol% of **47**a afforded the Michael adduct[53] in 90% *ee* (eqn. 48).

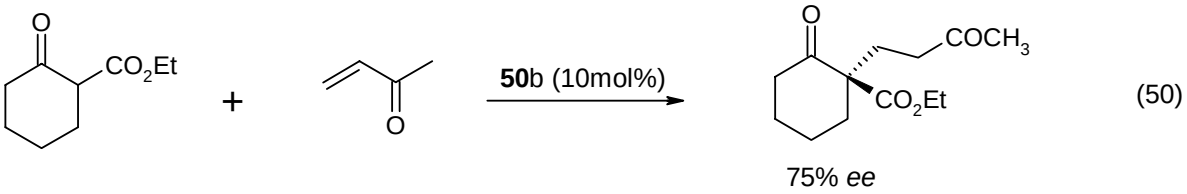


(48)

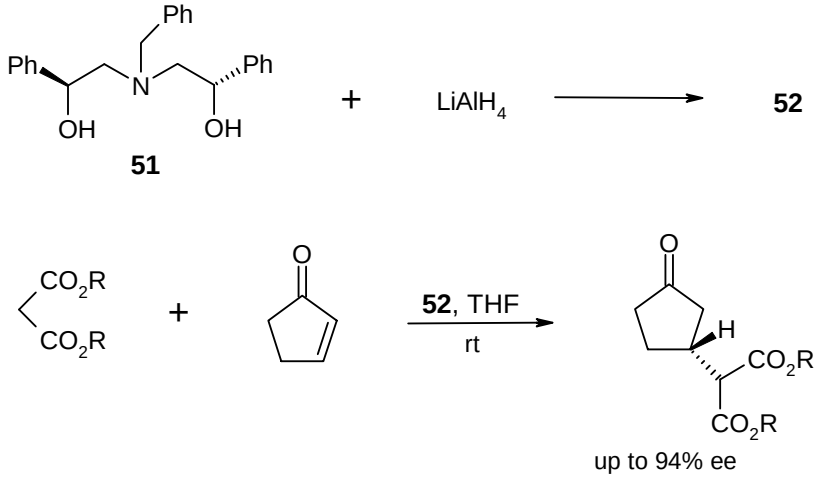
The same group later reported[54,55] the structurally modified catalyst **50** in which two BINOL-moieties were linked by an ether group. This heterobimetallic complex (**50**a) gave only moderate selectivities in the conjugate addition of dibenzyl malonate to cyclic enones whereas alkali metal

free lanthanum catalyst (**50**b) displayed perfect enantioselection in the addition of malonates to cyclic enones (eqn. 49 & 50).



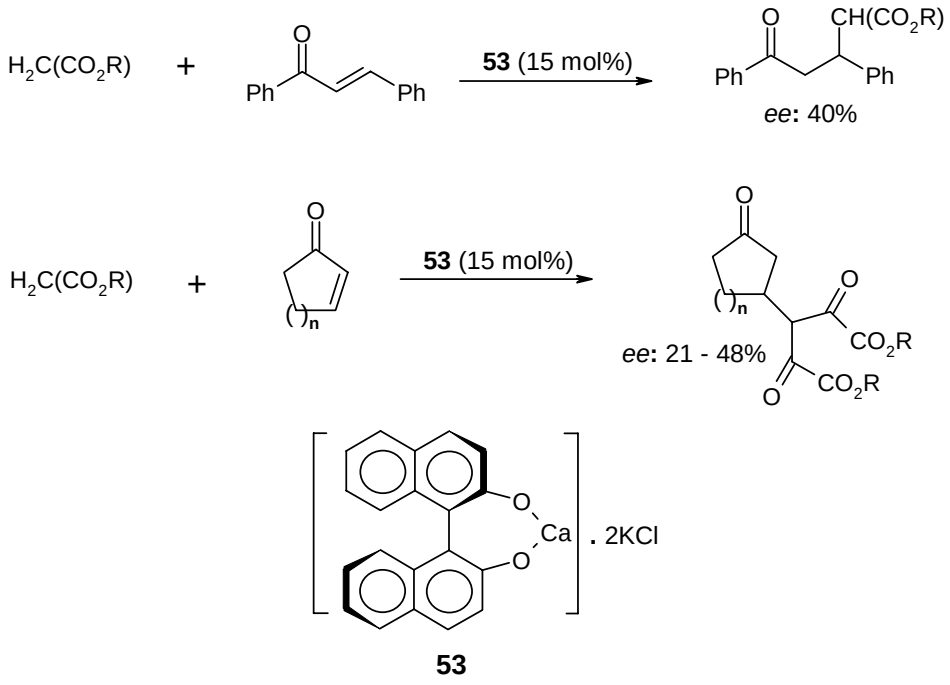


Sundarajan et. al. used[56] chiral amino diol (**51**) for preparing the heterobimetallic complex with lithium aluminium hydride (Scheme-2).



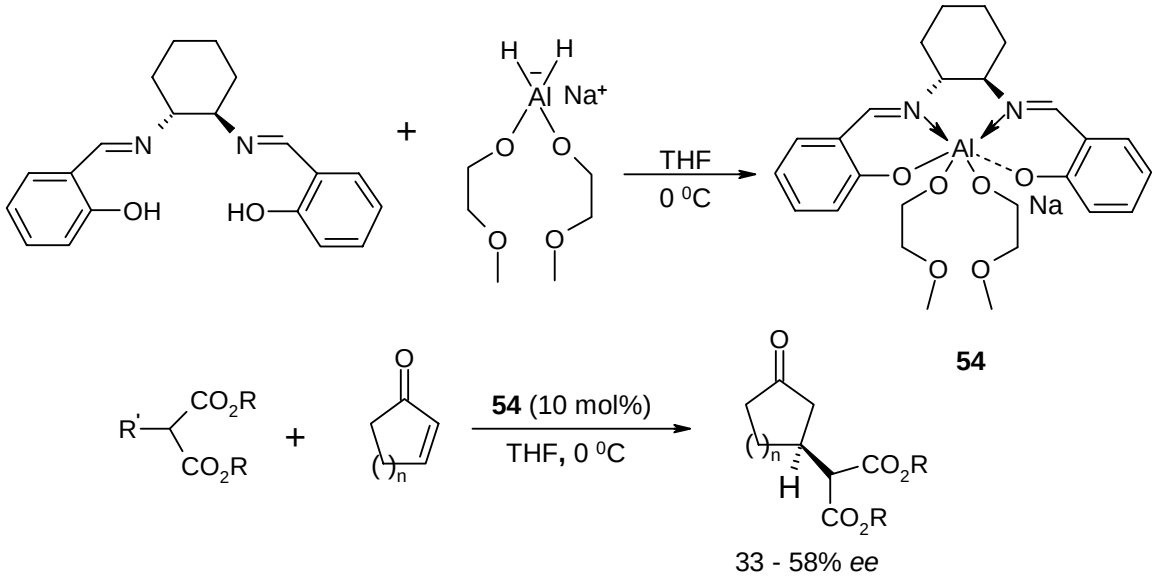
Scheme 2

Kumaraswamy et. al. reported[57] a new calcium-BINOL (**53**) catalyst for asymmetric addition of malonates to chalcone and cycloalkenones (Scheme-3).



Scheme 3

We have recently reported[58] a new aluminium-salen complex for the enantioselective addition of various alkylmalonates to cycloalkenones (Scheme-4).

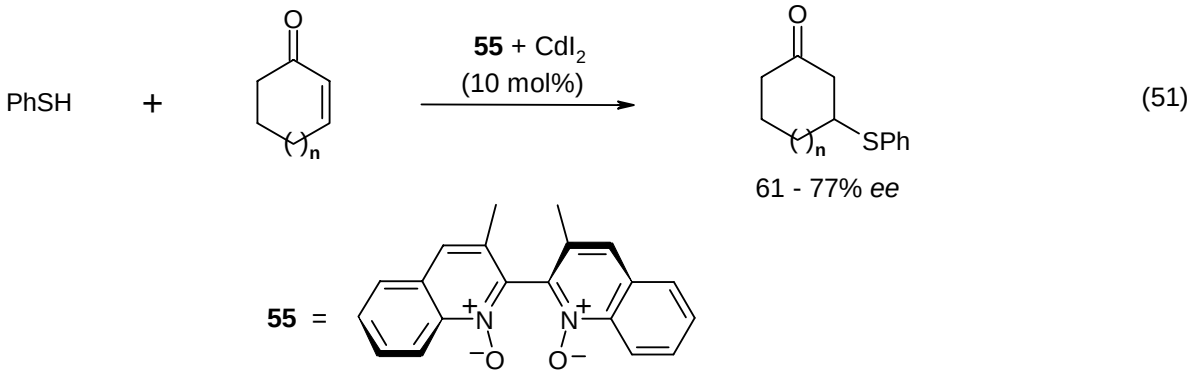


Scheme 4

We postulate that sodium phenoxide moiety acts as a Bronsted base abstracting the proton from the Michael donor while central aluminium metal complexes with the carbonyl functionality of the Michael acceptor due to its Lewis acidic nature.

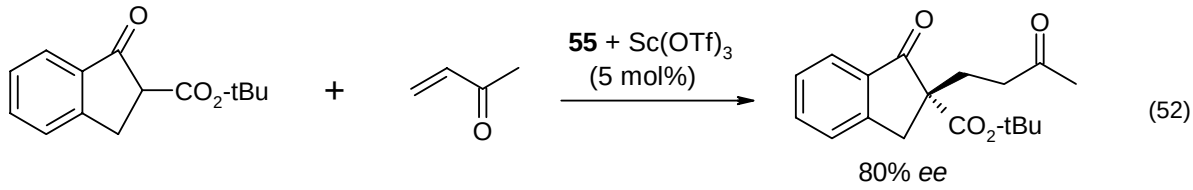
3.5. Chiral N,N-dioxides

The *N*-oxide functional group is known to form complexes with a variety of metals[59] due to its strong electron donating ability. However only a limited number of attempts to employ *N*-oxides as chiral catalysts have been reported.[60-67] Nakajima et. al. developed[68] a cadmium catalyst containing (*S*)-3,3'-dimethyl-2,2'-bisquinoline-*N*,*N*'-dioxide (**55**) as a chiral ligand. With this system, the conjugate addition of thiophenol to enones was carried out to obtain the desired products in 61-81% *ee* (eqn. 51).



(51)

The same group also reported[69] the enantioselective Michael addition of β-ketoesters to methyl vinyl ketone employing **55** along with scandium triflate. The Michael adduct was obtained in 90% yield with up to 80% *ee* (eqn. 52).



(52)

The predominant formation of [*R*] adduct was explained by the transition state model (Figure 9). The bulky tert-butyl ester moiety should be located on the *si*-face of the keto ester plane in order to avoid steric repulsion with the quinoline moiety which leads the attack of MVK at the *re*-face preferentially.

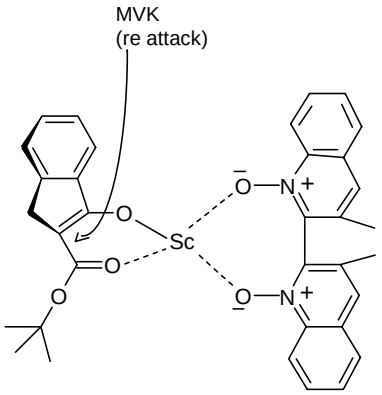
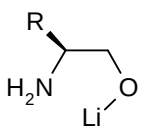


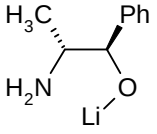
Figure 10

3.6. Miscellaneous catalysts

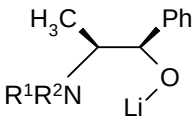
Koga et. al. examined[70] various chiral lithium-2-amino alkoxides(**56-58**) for catalyzing enantioselective Michael addition of methyl phenyl acetate and methyl acrylates. Product with as high as 84% ee was obtained. However the chiral alkoxides were effective only in stoichiometric amount (eqn. 53).



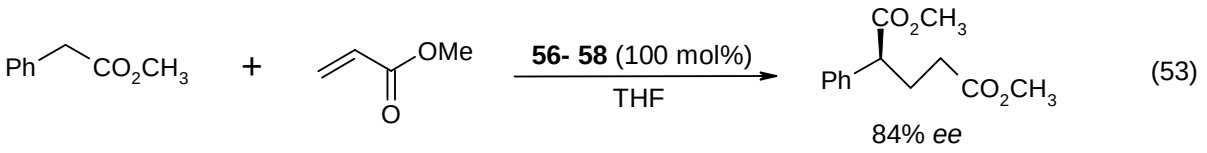
56



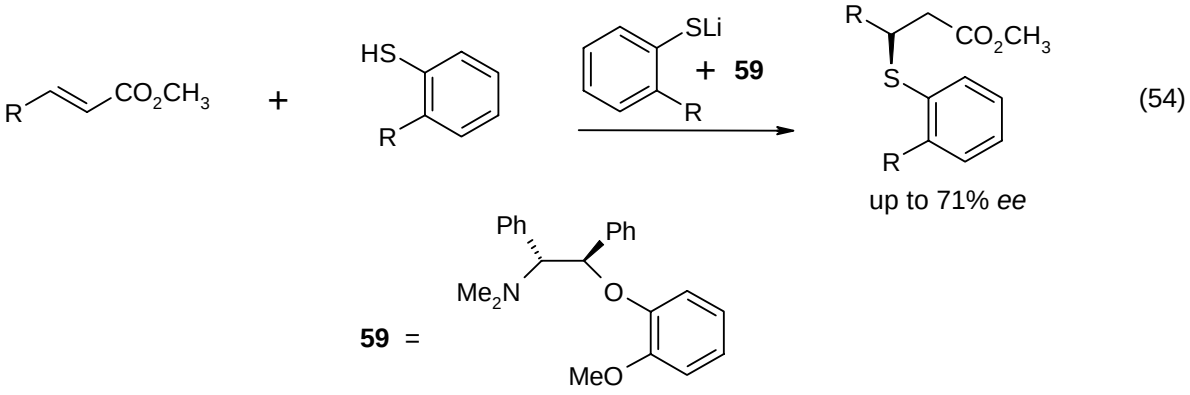
57



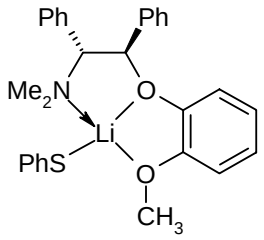
58



Tomioka et. al. reported[71] the addition of thiols to acrylate derivatives in the presence of chiral ligand (**59)** and lithium phenolate (eqn. 54).



The existence of bicyclo[3.3.0] complex (**60**) as active species in the reaction was postulated.



60

4. Conclusions

Catalysts with wide structural variations have been used for asymmetric Michael addition reactions. Organocatalyst include chiral diamines, chiral crown ethers, chiral alkaloids, chiral aminoacids and chiral oxazolines. Organometallic catalysts include salts of amino acids, metal-diamine complexes, schiff base-metal complexes, transition metal complexes, heterobimetallic complexes and metal-N,N-dioxide complexes. There is no single catalyst discovered so far, that is good for the entire range of Michael reaction. However some recent developments have made it possible to select an efficient catalyst for a particular series of transformation

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