PART - II

Ferric Chloride Mediated Michael Addition of Dicarboxylic Acid Esters to $\alpha$-$\beta$-Unsaturated Ketones

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PART II

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II.1. Introduction

The Michael addition reaction, one of the most studied and widely applied C-C bond forming reactions was introduced into synthetic organic chemistry more than a century ago by Michael himself in the 1880s, and first report appeared in the year 1887. When introduced, the reaction was defined by Arthur Michael as the addition of an enolate of a ketone or an aldehyde to the $\beta$-carbon of an $\alpha,\beta$-unsaturated carbonyl compound. Since then, in the past more than a hundred years old history, the scope of the Michael addition reaction has been widened to cover a large number of substrates and reagents. The Michael addition is now defined as the addition of a nucleophile, including non-carbon nucleophiles, to the $\beta$-position of a carbon-carbon double bond of an $\alpha,\beta$-unsaturated ketone, aldehyde, nitrile, or carboxylic acid derivatives. It belongs to the larger class of conjugate additions. A general representation of Michael addition reaction is shown in Scheme II.1.1.

R = H, alkyl, aryl
EWG = Electron withdrawing group such as ester, keto, aldehyde, cyano, nitro, etc.

Scheme II.1.1
Most of the reported nucleophiles are carbon-nucleophiles, which are carbanions, and often derived from compounds containing active methylene groups or organometallics. Some favourite pro-nucleophiles are malonates,\textsuperscript{6,7} $\beta$-keto esters,\textsuperscript{8} cyano esters,\textsuperscript{9} nitroalkanes,\textsuperscript{10,11} thiols,\textsuperscript{8,12} etc. Silyl enolates\textsuperscript{13-15} have also been reported as nucleophiles. Other versions of Michael addition reaction such as aza-Michael addition, oxy-Michael addition involve N-nucleophile and O-nucleophile respectively in place of usual C-nucleophiles. These versions of Michael additions are also considered as powerful tools for the carbon-heteroatom bond forming reactions.\textsuperscript{16}

The Michael addition reactions are catalyzed by both Lewis acids and Lewis bases, and several procedures involving such catalysts are already reported in innumerable articles.\textsuperscript{17-19} An elaborate account on the use of such catalysts is a part of a Ph.D. thesis submitted to Gauhati University.\textsuperscript{20} Following is a brief account on reported Michael addition reactions selectively picked up from among the hundreds of articles and communications published in the recent past.

**II.1.1 Lithium-mediated Michael additions**

Lithium-mediated Michael addition reactions are wide-spread. Followings are two interesting examples selected from many such others.

(i) Stereoselective asymmetric intramolecular Michael addition reaction using $\alpha$-lithiated vinylic sulfoxides as Michael donors was reported by N Maezaki and coworkers (Scheme II.1.2).\textsuperscript{21} This was claimed to be the first ever example of the use of vinylic sulfoxide as the Michael donor.
(ii) Another interesting LDA-mediated Michael addition reaction involving addition of $\alpha$-hydroxy acid derivatives to $\alpha,\beta$-unsaturated esters is described by Jang and coworkers (Scheme II.1.3).^{22}

(iii) Using LHMDS as the base similar Michael addition of the camphor-derived tetrahydropyran-desymmetrized glycineamide to nitroolefins, $\alpha,\beta$-unsaturated ketones, esters and lactones was carried out to afford enantiomerically enriched, functionally dense building block (Scheme II.1.4).^{50}
II.1.2 Aluminium-mediated Michael addition reaction

(i) In recent years chiral metal complexes have been used as efficient catalysts for the Michael reaction\textsuperscript{18-23} the development of multi functional lanthanide BINOL

\[ \text{Sodium-aluminium-SALEN complex (catalyst)} \]

\[ \text{Scheme II.1.5} \]

\[ R^1 = \text{H, Me} \]
\[ R = \text{Me, Et, } \text{i-Pr, } \text{t-Bu, Bn} \]
Part II.1

... being the most significant development in this area.\textsuperscript{29} It has been established by researchers that alkali metal-aluminium alkoxides act as efficient catalysts for Michael addition reactions.\textsuperscript{28-30} It is also reported that the presence of sodium as the counter cation is superior than lithium in this reaction (Scheme II.1.5).\textsuperscript{31}

(ii) Polymer supported aluminium-complex catalyst (ALB) has been developed and used in asymmetric Michael reaction by Jayaprakash and Sasai (Scheme II.1.6).\textsuperscript{32}

\begin{center}
\begin{tikzpicture}
\node at (-2,0) {\text{\textbf{Scheme II.1.6}}};
\node at (-2,2) {\text{The catalyst ALB carries Li as the counter cation.}};
\node at (-2,4) {A similar heterobimetallic complex prepared from a chiral SALEM ligand and Red-Al is reported\textsuperscript{33} as an efficient catalyst in the Michael reaction between various dialkyl malonates and cycloalkenones to afford products in high yields with ee's upto 58\%.}
\end{tikzpicture}
\end{center}
II.1.3 Nickel-complex in Michael addition reactions

Itoh et al have reported the use of an interesting aqua organonickel complex along with an amine in the Michael addition of malononitrile to alkenamides.\textsuperscript{34} They reported results that suggested that the nickel-complex / amine combination worked to doubly activate the substrate to afford the Michael adducts in high chemical yields with satisfactory enatioselectivity up to 87% (Scheme II.1.7).

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{CN} \\
\text{R} & \quad \text{CN}
\end{align*}
\]

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{CN} \\
\text{R} & \quad \text{CN}
\end{align*}
\]

\[
\begin{align*}
\text{R} & = \text{Me, n-Pr, i-Pr, t-Bu}
\end{align*}
\]

Aqua organonickel complex (catalyst)

Scheme II.1.7

Amines used are proton sponge, \textit{i-Pr}_2\text{EtN}, DBU, N,N-dibenzylamine, N,N-dicyclohexylamine, TMP.
II.1.4 Copper-complex in Michael addition reaction

(i) Chiral Cu(II) bisoxazoline (box) Lewis acid has been developed as catalysts for the Michael addition of enolsilanes to unsaturated ester derivatives. It is observed that (E)-enolsilanes give anti products and (Z) enolsilanes afford syn adducts (Scheme II.1.8).48

(ii) Use of another chiral Cu-complex is reported in an asymmetric so called aza-Michael addition reaction involving the addition of a nitrogen-based nucleophile to α,β-unsaturated malonates (Scheme II.1.9)35 by G Cardillo and others with good enantioselectivity.
II.1.5 Aza-Michael addition reactions

(i) TBAF-mediated stereoselective aza-Michael addition involving BnNH₂ as the nucleophile has been exploited by Sharma et al.\textsuperscript{36} as a mild and efficient route for the synthesis of glycosyl β-amino acid esters (Scheme II.1.10).

(ii) Iodine-alumina catalyzed aza-Michael addition under solvent free conditions has been reported by M. Saikia and coworkers.\textsuperscript{49} Several amines – both primary and secondary, cyclic as well as acyclic – have been examined (Scheme II.1.11).
II.1.6 Pd-complex catalyzed Michael addition

An interesting aza-Michael addition reaction involving allyl carbamates as the source of N-nucleophile is reported\(^\text{37}\) in the presence of Pd(PPh\(_3\))\(_4\) as the catalyst in THF at room temperature (Scheme II.1.12). With high diastereoselectivity the reaction is an excellent method for creating \(\alpha\)-allyl \(\beta\)-amino ketones having two contiguous stereocentres.

\[
\text{R} + \text{R'}\text{NH}_2 \xrightarrow{\text{I}_2\text{-Alumina}} \text{R'HN} + \text{R}
\]

\(
\text{R} = \text{CN, CO}_2\text{Me}
\)

\(
\text{R'} = \text{HOCH}_2\text{CH}_2, \text{Bn, PhCH}_2\text{CH}_2, \text{H}_2\text{NCH}_2\text{CH}_2
\)

Scheme II.1.11

II.1.7 Titanium-mediated Michael addition

Enantio-enriched allenyltitaniums, prepared \textit{in situ}, undergo Michael addition to alkylidene malonates to afford the Michael addition products with high optical purity (Scheme II.1.13).\(^\text{38}\) The procedure is a noval asymmetric method for construction of an acyclic carbon skeleton bearing two adjacent alkyl substituents.
II.1.8 Base-catalyzed crown ether-mediated oxy-Michael addition

Base-catalyzed crown ether-mediated highly diastereoselective oxy-Michael addition (Scheme II.1.14) is reported by Buchanan and coworkers. The procedure has been successfully used to afford the enantio-enriched aldol products in quantitative yields.

Scheme II.1.14
II.1.9 Amide and selenomide as nucleophiles in Michael addition

Unlike ester, keto or cyano-activated methylene nucleophiles, amide nucleophiles, although scarcely reported, nonetheless provide useful procedures for synthetic organic chemists. One such procedure provides an access to enantiomerically enriched trans-3,4-disubstituted δ-lactones via asymmetric Michael reaction of pseudoephedrine amides (Scheme II.1.15).\(^{40}\)

\[
\begin{align*}
\text{Ar} & \text{N} & \text{Me} & \text{Ph} \\
\text{Me} & \text{OH} & \text{LHMDS, TMEDA, } 0^\circ\text{C} & \text{MeO}_2\text{C} & \text{O} & \text{Me} & \text{Ph}
\end{align*}
\]

\[
\begin{align*}
\text{R} & \overset{\text{CO}_2\text{R}}{\searrow} \\
\text{Ar} & \text{N} & \text{Me} & \text{OH} & \text{R}\text{''} & \overset{\text{O}}{\longrightarrow} & \text{O}
\end{align*}
\]

Scheme II.1.15

T Murai has reported Michael addition of selenoamides to α,β-unsaturated carbonyl compounds. Mediated by LDA, the reaction is facilitated by formation of lithium eneselenolates from selenomides (Scheme II.1.16).\(^{41}\)

\[
\begin{align*}
\text{R} & \overset{\text{Se}}{\searrow} & \overset{\text{NR}_2}{\uparrow} & \overset{\text{i) LDA}}{\longrightarrow} & \text{R} & \overset{\text{R}}{\searrow} & \overset{\text{Se}}{\uparrow} & \overset{\text{NR}_1}{\uparrow} \\
\text{R} & \overset{\text{NR}_1}{\uparrow} & \overset{\text{R}}{\searrow} & \overset{\text{R}}{\searrow} & \overset{\text{O}}{\longrightarrow} & \text{R} & \overset{\text{R}}{\searrow} & \overset{\text{R}}{\searrow} & \overset{\text{Se}}{\uparrow} & \overset{\text{NR}_2}{\uparrow}
\end{align*}
\]

Scheme II.1.16
II.1.10  Rubidium salt catalyzed Michael addition

Rubidium salt of L-proline catalyzes the asymmetric Michael addition of malonate anions to prochiral enones and enals. The method has been successfully applied to a wide range of substrates to give adducts with a predictable absolute configuration (Scheme II.1.17).42

![Scheme II.1.17](image)

II.1.11  Electrochemically-induced Michael addition

An unusual electrochemically-induced Michael addition is reported by Palombi and coworkers.43 The procedure has been used to attend stereoselective conjugate addition of several chiral β-dicarbonyl derivatives to methyl vinyl ketone. With respect to the metal-catalyzed methods, the electrochemical, metal-free conditions resulted in enhanced reactivity of the electrogenerated enolates, so that the Michael addition was found to occur under mild conditions and short reaction times, affording products with significant diastereoisomeric excesses (Scheme II.1.18).

![Scheme II.1.18](image)
Other reports on electrochemically induced Michael addition of both C-nucleophiles\textsuperscript{44} and N-nucleophiles\textsuperscript{45} are also available.

### II.1.12 Organocatalysts in Michael addition

Apart from metal-based catalysts, a large number of organic molecules showing remarkable catalytic activity on Michael addition reactions are reported. Only a handful of them are cited here.

(i) Michael additions of aldehydes to enones catalyzed by imidazolidinone are reported by Peelen and coworkers\textsuperscript{46}. Use of a phenol as the co-catalyst in the procedure is noteworthy (Scheme II.1.19).

(ii) Antibody-catalyzed asymmetric intramolecular Michael addition to yield the disfavoured \textit{cis}-product is not only intriguing but also significant from biochemical point of view. The Scheme II.1.20 projects an intramolecular Michael addition of aldehydes and ketones catalyzed by antibody Ab38C2.\textsuperscript{47}
(iii) Michael addition reactions of 2-nitropropane with substituted chalcones catalyzed by chiral azacrown ethers is reported (Scheme II.1.21).\textsuperscript{50}

![Scheme II.1.20](image)

Both the type of substituents on the chalcone and the size of the catalyst show significant influence on the enantioselectivity of the reaction.

(iv) N Mase and coworkers have reported Michael reaction of ketones and aldehydes with β-nitrostyrene in brine using bifunctional organic molecules as the
catalyst (Scheme II.1.22). Some of the bifunctional catalysts examined are I, II, III and IV. I and IV are found to be the best performer in terms of yields.

\[
\text{O} + \text{PhNO}_2 \xrightarrow{\text{Catalyst (0.1 eq)}} \text{PhNO}_2
\]

Brine, 25 °C, 24 h

(v) The organocatalyzed asymmetric aza-Michael addition of hydrazones to cyclic enones has been achieved in good yield and stereoselection using cheap and commercially available cinchona alkaloids as catalysts (Scheme II.1.23).
II.1.13 Enamines and imines in Michael addition reactions

Use of enamines and imines as donors are extensively reported in Michael addition reactions. A selected few from the publications in the recent past are recorded here.

(i) Enamines from vinyl bromides, generated in situ, have been reacted with alkylidene malonates to provide Michael adducts (Scheme II.1.24). The procedure, in fact, is the virtual use of vinyl bromides as Michael donors.

(ii) Michael addition reaction of enamino esters with methyl vinyl ketone with high ee's of 93-96% is reported as a tool for synthesis of Hagemann type esters (Scheme II.1.25). Hagemann esters are useful building blocks in the synthesis of a variety of complex natural and bioactive molecules such as terpenes, alkaloids, taxane core, steroids and flavones.
(iii) R A Schenato et al has reported Michael addition of enamine to methyl vinyl ketone en route to synthesis of chiral naphthalenone – a building block in the synthesis of (-)-dehydrofukinone, a naturally occurring sesquiterpene (Scheme II.1.26).^[33]

(iv) The enantio-selective Michael addition of a chiral imine with phenyl crotonate has been used to synthesize a building block required for the synthesis of (+)-valencenol, a bioactive molecule (Scheme II.1.27).^[34]
(v) In another report, Revial and coworkers have used the stereoselective Michael addition reaction of a chiral imine of 4-isopropylidene-2-methylcyclohexanone to phenyl crotonate to obtain a building block required for the synthesis of (+)-α-vetivone, an odoriferous constituent of vetiver oil (Scheme II.1.28).
II.1.14 Quaternary ammonium salts in Michael addition

(i) Chiral ammonium bifluoride catalyzed highly enantioselective Michael addition of silyl nitronates to α,β-unsaturated aldehydes is reported by Ooi and coworkers (Scheme II.1.29).91

(ii) A similar N-spiro C₂-symmetric chiral quaternary ammonium bromide has been used as a catalyst under mild phase-transfer conditions to afford highly enantioselective Michael addition of diethyl malonate to chalcone derivatives (Scheme...
The procedure was found to be quite effective for various chalcone derivatives, including those with heteroaromatic substituents.

\[
\begin{align*}
\text{An}^1 \text{O} \text{Ar}^1 & \text{C} \text{OH} + \text{CO}_2 \text{Et} \\
\text{PhMe, } -20 \degree \text{C} & \rightarrow \\
\text{An}^2 \text{O} \text{Ar}^2 & \text{C} \text{OH} \text{Et} \\
\text{Catalyst (3 mol\%)} & \\
\text{K}_2 \text{CO}_3 (10 \text{ mol\%}) & \\
\text{Yield 94 to 99\% (85 - 94\% ee)} & \\
\text{Scheme II.1.30}
\end{align*}
\]

(iii) Use of another chiral quaternary ammonium salt in biphasic medium has been reported by Zhang and Corey in enantio- and diastereoselective Michael reaction of silylenol ethers and chalcones (Scheme II.1.31).
II.1.15 Phosphorus-based catalysts in Michael addition

Hexamethylphosphorus triamide (HMPT) and other phosphoramidites and phosphates have been found to be efficient catalysts for the Michael reaction of alkenones and alkynones with malonates, α-cyano esters, β-keto esters, and nitro compounds. Some of the catalysts used are (MeN)₃P, (MeO)₃P, PhP(OMe)₂ (Scheme II.1.32).⁵⁷

\[
\begin{align*}
\text{Catalyst} & \quad \text{anti / syn} \quad 20 : 1 \ (92\% \ ee)
\end{align*}
\]
Among the suggested catalysts, HMPT is found to be the most effective organocatalysts. A catalytic cycle has also been proposed.

**II.1.16 Iridium-complex in Michael addition**

In a recent publication,\(^5^8\) M Janka and coworkers have reported the use of a Ir(III)-complex in a tandem Nazarov cyclization-Michael addition sequence to afford high diastereoselectivity in a reaction that created three new stereocentres (Scheme II.1.33).

![Scheme II.1.33](image)

**II.1.17 Intramolecular Michael cyclization of nitro-diene**

An interesting stereoselective intramolecular Michael addition of an \(\omega\)-nitro-\(\alpha,\beta,\gamma,\omega\)-unsaturated ester has been reported. The cyclization is initiated by a chemoselective conjugate addition (Scheme II.1.34).\(^5^9\)
II.1.18 Virtual asymmetric Michael addition of hydrogen sulfide

Using a complex chiral odorless thiol K Nishide and coworkers had reported a virtual asymmetric Michael addition of hydrogen sulfide to α-substituted α,β-unsaturated carbonyl compounds (Scheme II.1.35).61
II.1.19 Michael addition of thiols and thiophenols

Michael addition of thiols and thiophenols to α-enones in ionic liquids is reported. Seventeen organocatalysts were tested for their activity to catalyze the addition of thiophenols to chalcones in ionic liquid [bmim]PF₆. High yields were observed but no stereoselectivity (Scheme II.1.36).⁶⁷

![Scheme II.1.36](image)

II.1.20 Nitrosoalkenes as Michael acceptor

Michael addition of nucleophilic reagents such as ammonia, amines, and optically active amino esters to nitrosoalkenes to afford α-amino phosphine oxides and phosphonates in a highly regioselective fashion is described (Scheme II.1.37).⁶⁸

![Scheme II.1.37](image)
II.1.21 Triflic acid catalyzed Michael addition

Triflic acid-catalyzed Michael addition reactions of indole and pyrrole compounds with α,β-unsaturated ketones in water is reported (Scheme II.1.38).⁶⁹

\[
\begin{align*}
\text{R}^2 \begin{array}{c}
\text{N} \\
\text{R}
\end{array} + \text{R}^1 \begin{array}{c}
\text{C} \text{= O}
\end{array} \rightarrow \text{HOTf (1 mol\%)} & \rightarrow \text{R}^2 \begin{array}{c}
\text{N} \\
\text{R}
\end{array} \begin{array}{c}
\text{C} \text{= O}
\end{array}
\end{align*}
\]

Scheme II.1.38

II.1.22 Oxazoles and oxazolines as Michael acceptors

Stereoselective Michael addition of alcohols, amines, thiols, and halides to C(2)-alkynyl oxazoles and oxazolines as a versatile route to afford heterocyclic building blocks is reported by Wipf and Graham (Scheme II.1.39).⁷⁰

\[
\begin{align*}
\text{MeO}_2\text{C} \begin{array}{c}
\text{N}
\end{array} \begin{array}{c}
\text{C} \text{= C}
\end{array} & \rightarrow \text{R-XH} \rightarrow \text{MeO}_2\text{C} \begin{array}{c}
\text{N}
\end{array} \begin{array}{c}
\text{C} \text{= C}
\end{array}
\end{align*}
\]

\[X = S \text{ or } N\]
\[R = \text{Et, Ph, Bn, etc.}\]
\[\text{Additive } = K_2\text{CO}_3 \text{ or } n\text{-Bu}_3\text{P}\]

Scheme II.1.39
II.1.23  Molecular iodine-catalyzed Michael addition

Molecular iodine-catalyzed Michael addition of indole and pyrrole to nitroolefins is reported.\(^7\) Short reaction time and high yield of products are noteworthy features. Molecular iodine promoted Michael addition is operationally simple and efficient method compared to many other known Lewis acids or rare earth metal catalysts (Scheme II.1.40).

\[
\text{Ar} = \text{Me, Ph} \\
n = 0 \text{ or } 1 \\
R_1 = \text{Me, Et, n-Pr, n-Bu}
\]

Scheme II.1.40

II.1.24  Lithium hydroxide-catalyzed Michael addition

Lithium hydroxide mediated Michael addition of malonate- and succinate-carbanion to several \(\alpha,\beta\)-unsaturated ketones have been successfully carried out by Deka and Sukanya in methanol or under microwave irradiation without solvent (Scheme II.1.41).\(^{19,20}\)

\[
X = \text{H, OMe, Cl} \\
R = \text{Me, Ph} \\
n = 0 \text{ or } 1 \\
R' = \text{Me, Et, n-Pr, n-Bu}
\]

Scheme II.1.41
II.1.25 Double Michael addition

Double Michael addition leading to simultaneous formation of two C-C or carbon-heteroatom bonds has been reported on several occasions. Three of them are reproduced here.

(i) A double Michael addition reaction leading to formation of a heterocycle is reported. Reactions in which two C-C bonds of a heterocycle are formed simultaneously by a double Michael reaction are scarcely observed (Scheme II.1.42).

(ii) Double Michael addition of diphenylphosphine to 4,4-dimethyl-2,5-cyclohexadienone and phenylphosphine to cyclo-2,7-octadienone have been reported (Scheme II.1.43).
(iii) Stereocontrolled total synthesis of recemic culmorin via the intramolecular double Michael addition is reported (Scheme II.1.44).65

![Stereocontrolled total synthesis of recemic culmorin via the intramolecular double Michael addition](image)

**Scheme II.1.44**

II.1.26 Ferric chloride mediated Michael addition

Ferric chloride as a Lewis acid has diverse applications in organic reactions. It is inexpensive and environmentally benign. Ferric chloride catalyzed Sonogashira reactions,72 addition of 1,3-dicarbonyl compounds to aromatic olefins,73 1,2-addition reactions of aryl aldehydes with aryloboronic acid to yield biaryl methanols,74 direct alkylation of active methylene compounds with benzylic and allylic alcohols,75 alkenylation of arenes,76 nucleophilic substitution of propargylic alcohols,78 hydroarylation of styrenes,77 deprotection of acetals,79 deprotection of oximes and hydrazones,84 etc are only a few examples to cite. However, ferric chloride catalyzed Michael addition reaction is scarcely reported. Ferric chloride catalyzed Michael addition of Grignard reagents and a number of cyclic and acyclic dicarbonyls to various acceptors are reported, and a few of them resketch here.
(i) Ferric chloride hexahydrate (FeCl₃·6H₂O) catalyzed Michael addition of a number of cyclic and acyclic dicarboxyls was considered by Christoffers (Scheme II.1.45).80,81

\[
\begin{array}{c}
\text{O} & \text{O} \\
\text{X} & \text{Me}
\end{array}
\xrightarrow{\text{FeCl₃·6H₂O (1.5 mol%)}}
\begin{array}{c}
\text{O} & \text{O} \\
\text{X} & \text{Me}
\end{array}
\]

Scheme II.1.45

(ii) Ferric ion-exchanged fluorotetrasilieic mica is reported by Shimizu and coworkers82 as acting as a highly effective and reusable catalyst for the solvent free Michael addition reaction of α-ketoesters with vinyl ketones under mild conditions (Scheme II.1.46).

\[
\begin{array}{c}
\text{O} & \text{O} \\
\text{Et} & \text{Me}
\end{array}
\xrightarrow{\text{Fe³⁺ (1 mol%)}}
\begin{array}{c}
\text{O} & \text{Et} \\
\text{CO₂Et} & \text{Me}
\end{array}
\]

Scheme II.1.46

The immobilized catalyst shows higher activity than homogeneous Fe³⁺ catalysts, FeCl₃·6H₂O and Fe(NO₃)₃·9H₂O.

(iii) Anhydrous ferric chloride-mediated Michael addition of mercaptans to α,β-unsaturated ketones and esters under solvent free conditions is reported.83 Addition of
various thiols to $\alpha,\beta$-unsaturated ketones was completed rapidly in the presence of a catalytic amount (2-3 mol%) of anhydrous ferric chloride under solvent free conditions and under air atmosphere. Anhydrous ferric chloride is more active than other ferric salts (Scheme II.1.47).

(iv) Feric chloride hexahydrate was shown to be an efficient catalyst for the conjugate addition of 2,3-allenoates with alkyl-, aryl-, or vinyl-Grignard reagents to synthesize polysubstituted $\beta,\gamma$-unsaturated alkenoates with high regio- and stereoselectivity (Scheme II.1.48).
II.1.27 Relevance of ferric chloride in Michael addition reactions

Volumes of reports and published works on Michael addition reaction in the recent past speaks loud enough that the Michael addition reaction is one of the most favourite reaction among the synthetic organic chemists. It is, however, noteworthy that in spite of definite advantages fullest potentiality of ferric chloride catalyzed Michael addition of malonates and succinates could not be traced.

Ferric chloride is a non-hazardous chemical having wide spread applications in research laboratories as well as in large scale industries. Anhydrous ferric chloride has a relatively low melting point and boils at around 315 °C. It is deliquescent, forming hydrated hydrogen chloride mists in moist air. It is soluble in water, alcohol and ether. The vapour consists of the dimmer Fe$_2$Cl$_6$ which increasingly dissociates into monomeric FeCl$_3$ at higher temperatures. The colour of ferric chloride crystals depends on the viewing angle – by reflected light the crystals appear dark green, but by transmitted light they appear purle-red.$^86$

The ordinary yellow ferric chloride of commerce is the hexahydrate, FeCl$_3$.6H$_2$O. It is exceedingly soluble in water. The solubility curve shows a number of breaks corresponding to the various hydrates that exist.$^{87,88}$

When dissolved in water, ferric chloride undergoes hydrolysis to give an acidic solution and give off heat in an exothermic reaction. The resulting brown, acidic, and corrosive solution is used as a coagulant in sewage treatment and drinking water production, and as an etchant for copper-based metals in printing circuit boards. Though corrosive, ferric chloride solution is not absorbed through skin.
Anhydrous ferric chloride is a fairly strong Lewis acid, and it is used as a catalyst in organic synthesis. In industry ferric chloride is used as a catalyst for the reaction of ethylene with chlorine, forming ethylene dichloride, an important industrial chemical, which is mainly used for the production of vinyl chloride, the monomer of making PVC.

In the laboratory ferric chloride is commonly employed as a Lewis acid for catalyzing reactions such as chlorination of aromatic compounds and Friedel-Crafts reaction of aromatics. It is less powerful than aluminium chloride, but in some cases this mildness leads to higher yields.\(^8^9\)
References to Part II.1

   33, 1016.
   690, 2989.


86. From internet – *Wikipedia the Free Encyclopedia.*


