InCl$_3$: A Versatile Catalyst for Synthesizing a Broad Spectrum of Heterocycles
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ABSTRACT: This review deals with the recent applications of the indium trichloride (InCl$_3$) catalyst in the synthesis of a broad spectrum of heterocyclic compounds. Over the years, a number of reviews on the applications of InCl$_3$-catalyzed organic synthesis have appeared in the literature. It is evident that InCl$_3$ has emerged as a valuable catalyst for a wide range of organic transformations due to its stability when exposed to moisture and also in an aqueous medium. The most attractive feature of this review is the application of the InCl$_3$ catalyst for synthesizing bioactive heterocyclic compounds. The study of InCl$_3$-catalyzed organic reactions has high potential and better intriguing aspects, which are anticipated to originate from this field of research.

1. INTRODUCTION
Lewis acid catalysis has brought a radical change in the approach toward the synthesis of a large number of important organic intermediates and heterocyclic compounds having significant biological activity.$^{1a}$ The common Lewis acids which are generally used for various organic transformations include AlCl$_3$, BF$_3$, Et$_2$O, ZnCl$_2$, TiCl$_4$, and SnCl$_2$. Although indium (In) belongs to the same group in the periodic table as boron (B) and aluminum (Al), the study of indium and its salts was unexplored until recently.$^{1b}$ Indium and its salts have found applications in the preparation of alloys to be used as medical diagnostic agents for the health sector and equipment for the electronic industry.$^{2a-d}$ The ability of indium(III) salts to react with organic compounds to form in situ organoindium species has largely eliminated the use of sensitive, toxic, and explosive organometallics.$^{3a,b}$ The effectiveness of InCl$_3$ as a Lewis acid catalyst has sustained immense interest due to its moisture compatibility, which enhances its use in a wide range of solvents including water. Moreover, nontoxicity, abundance, recyclability, and excellent catalytic activity$^{3b}$ of InCl$_3$ afforded high chemo- and regioselectivity in various organic transformations.$^{2a-d}$ These advantages of InCl$_3$ inspired us to write a review highlighting its catalytic applications in the synthesis of a broad range of heterocycles.

2. SYNTHESIS OF N-HETEROCYCLES
N-Heterocycles constitute the core scaffolds of many natural products and pharmaceutical agents. The syntheses of these N-heterocycles are very challenging, and the development of methodologies for their synthesis provided us with unique metal catalysts, but many of them are hazardous and expensive. Among them, InCl$_3$ was found to be inexpensive, moisture friendly, and reactive even in mild conditions.$^{2a-d,3a,b}$ Nandi et al.$^{3c}$ accomplished a one-pot synthesis of highly substituted pyrrole 3 directly by reacting propargyl alcohol 1 with β-ketoimide 2 in the presence of InCl$_3$ catalyst (Scheme 1) in good yields.

Scheme 1. InCl$_3$-Catalyzed Synthesis of Tetrasubstituted Pyrroles from Propargyl Alcohol and Ketoimide

In 2011, Meng et al.$^{3d}$ reported the synthesis of various C-pyrrolyl glycoside 6 in moderate to good yields through a tandem (hemiacetal intermediate) condensation of aminosugar
Cook et al. disclosed the catalytic activity of InCl₃ to favor an intramolecular Friedel–Crafts reaction of simple arenes incorporated with allylic bromides to give the corresponding arene-fused heterocycle (Scheme 3).

Perumal et al. reported the synthesis of quinoline derivatives. The reaction proceeds via an imino Diels–Alder reaction of N-arylaldimine or with cyclopentadiene in the presence of the InCl₃ catalyst (Schemes 4 and 5). They also demonstrated that 3,4-dihydro-2H-pyran and indene underwent a Diels–Alder reaction under the same condition.

Menéndez et al. reported the synthesis of C-4-substituted 1,2,3,4-tetrahydroquinoline by reacting aromatic amine with N-allylindole-2-carbaldehyde in the presence of 20 mol % of InCl₃ catalyst (Scheme 7).

The same group also reported an excellent catalytic activity of InCl₃ in acetonitrile or impregnated in silica gel toward the synthesis of diastereomeric pyrano/thiopyranodquinoline derivatives.
Scheme 6. InCl₃-Catalyzed Synthesis of C-4-Substituted 1,2,3-Trihydroquinolines

Scheme 7. InCl₃-Catalyzed Synthesis of Fused Hydroquinolines

Scheme 8. InCl₃-Catalyzed Synthesis of Pyrimidine-Annulated Fused Hydroquinolines

Scheme 9. InCl₃-Catalyzed Synthesis of Thiopyranoquinolines via Intramolecular Imino-Diels–Alder Reaction

29 and 30 through an intermolecular imino-Diels–Alder reaction (Scheme 9).

An efficient three-component one-pot synthesis of diastereomeric ellipticine derivatives was reported by Nagarajan et al. through an imino-Diels–Alder reaction of 3-aminocarbazole 31 and substituted benzaldehyde 32 with an electron-rich alkene 33, such as 3,4-dihydro-2H-pyran, 2,3-dihydrofuran, or ethyl vinyl ether in the presence of 10 mol % of InCl₃ catalyst in an...
ionic liquid at 100 °C (Scheme 10). In the case of substituted benzaldehydes, reductive amination was also observed. Ranu et al.\textsuperscript{3e} demonstrated the InCl\textsubscript{3}-catalyzed three-component one-pot synthesis of dihydropyrimidin-2(1\textsubscript{H})-one \textsuperscript{39} in good to excellent yields by reacting 1,3-dicarbonyl \textsuperscript{36}, aldehyde \textsuperscript{37}, and urea/thiourea \textsuperscript{38} (Scheme 11).

Li et al.\textsuperscript{4g} synthesized diastereoselective tetrahydroquinolines by reacting aromatic amine \textsuperscript{40} and cyclic enol ether \textsuperscript{41} or 2-hydroxy cyclic ether \textsuperscript{42} in the presence of a catalytic amount of InCl\textsubscript{3} in water. The reaction followed an aza-Diels−Alder path to yield \textit{cis}-selective tetrahydroquinolines as major products (Scheme 12).

Juaristi et al.\textsuperscript{5a} have reported the asymmetric synthesis of \textit{R}-selective 4-phenyldihydropyrimidinone derivative \textsuperscript{50} in a one-pot Biginelli condensation by reacting acetoacetate ester \textsuperscript{45} with benzaldehyde \textsuperscript{46} and urea \textsuperscript{47} in THF in the presence of a catalytic amount of InCl\textsubscript{3} and chiral ligands (Scheme 13).
The enantiomeric ratio (er) of the product was found to be 62:38 (for \( R, R \)-48) with an excellent yield of up to 93%.

Prajapati et al.\(^5_b\) have developed an InCl\(_3\)-catalyzed neat synthesis of tetra-substituted pyridine derivative \(^5_3\) via Michael addition of 1,3-dicarbonyl \(^5_1\) with \( \alpha, \beta \)-unsaturated oxime \(^5_2\) followed by a ring-closing reaction (Scheme 14).

Dobbs et al.\(^5_c\) reported the cyclization reaction of silylated homoallyl alcohol \(^5_4\) and aldehyde \(^5_5\) (even epoxides) in the presence of a catalytic amount of InCl\(_3\) to yield diastereoselective unsaturated heterocycle \(^5_6\) (Scheme 15).

Yadav et al.\(^5_d\) have reported an InCl\(_3\)-catalyzed condensation of \( o \)-phenylenediamine \(^5_7\) with 4,6-di-O-alkyl-2,3-dideoxyaldehyde-\( D - erythro \)-trans-hex-2-enose \(^5_8\) followed by cyclization under mild conditions to afford 1,5-benzodiazepine \(^5_9\) in good yield (Scheme 16).

Am mild, efficient InCl\(_3\)-catalyzed multicomponent one-pot synthesis of highly substituted pyrroles was developed by Liu et al.\(^5_e\)
Interestingly, they found that the reaction involved propargylation, amination, followed by cycloisomerization in a single step to afford pyrrole from propargyl alcohol, 1,3-dicarbonyl, and primary amine in very good yields (Scheme 17).

Adimurthy et al.5f developed a highly efficient and regioselective method for the synthesis of 1,8-naphthyridine directly from substituted 2-aminopyridine and ethyl acetoacetate in the presence of a catalytic amount of InCl₃ in ethanol at 100 °C for 33−48 h (Scheme 18).

Mahadevan and co-workers6a reported an advanced efficient method for the synthesis of various cis-2-methyl-4-amido-1,2,3,4-tetrahydroquinoline derivative by reacting aromatic amine and N-vinyl caprolactam or N-vinyl pyrrolidone in the presence of a catalytic amount of InCl₃ in an aqueous medium in good to excellent yields. These 2,4-disubstituted tetrahydroquinolines showed cis diastereoselectivity (Scheme 19).

Khurana et al.5g reported an appealing synthetic protocol which utilized water as the solvent and InCl₃ as the promoter for the three-component combinatorial synthesis of a variety of bioactive pyrimidine and pyrazole derivatives. The latter derivatives were synthesized from aldehyde, electron-rich amino heterocycles such as 6-amino-1,3-dimethyl uracil and 3-methyl-1-phenyl-1H-pyrazol-5-amine, and 1,3-dicarbonyl compound under refluxing conditions. Following the same reaction conditions, the synthesis of a new class of pyrimidine derivative was also reported. The reactions were environmentally benign; the reaction product could be isolated easily, and the catalyst could be recycled (Scheme 20).

A facile and regioselective synthesis of polysubstituted pyrroles have been reported by Muthusubramanian and co-worker from azido chalcones and 1,3-dicarbonyl compounds via an InCl₃ catalyst in water under microwave irradiation (Scheme 21).

Lavilla et al.4h achieved a successful InCl₃-catalyzed three-component reaction of dihydropyridine, aldehyde, and p-methylaniline to afford a diastereomeric mixture of highly substituted tetrahydroquinolines which contained cis-isomer as the major product (Scheme 22).
Li et al. reported an intermolecular 1,3-dipolar cycloaddition of methyl α-diazoacetate with alkyne in water in the presence of \( \text{InCl}_3 \) catalyst to afford substituted pyrazole compounds and quinoxalines in good yields (Scheme 23).

Ranu et al. developed a one-pot synthesis of quinoline by reacting aniline with alkyl vinyl ketone on the solid surface of silica gel impregnated with \( \text{InCl}_3 \) under microwave irradiation (Scheme 24). The products were obtained in excellent yields.

An efficient and eco-friendly synthesis of structurally diversified 2-quinolinones from coumarin-3-carboxylic acid and primary amine in the presence of a catalytic amount of \( \text{InCl}_3 \) in aqueous medium at ambient temperature was reported by Mahadevan et al. (Scheme 25).

Gogoi et al. reported an \( \text{InCl}_3 \)-catalyzed condensation of \( \text{O} \)-phenylenediamine with ketone and 1,2-dicarbonyl to afford various 1,5-benzodiazepine and quinoxaline, respectively, with excellent yields (Scheme 26).

Very recently, Jeong et al. reported a synthesis of novel 3-amino-2-benzoyl-1-aryl-1H-pyrazolo[1,2-b]phthalazine-5,10-dione derivative via a one-pot three-component reaction of phthalhydrazide, aldehyde, and arylacetonitrile in the presence of \( \text{InCl}_3 \) (20 mol %) catalyst under solvent-free environmentally friendly conditions. Similarly, they reported the synthesis of 3-amino-2-benzoyl-1-aryl-1H-pyrazolo[1,2-a]pyridazine-5,8-dione derivatives but used maleic hydrazide instead of \( \text{92a} \) (Scheme 27).

3. SYNTHESIS OF O-HETEROCYCLES

Indium and its salts have been extensively used for alkylation, allylation, and alenylation reactions in water. Therefore, \( \text{InCl}_3 \)-catalyzed synthesis of bioactive compounds in water is the decent choice for researchers for the development of pharmaceutical agents with less or no toxicity. Among various O-heterocycles, chromanes were found in many important natural products and reported to have significant biological importance.

Kang et al. reported an intramolecular allylation of carbonyl/imine in the presence of \( \text{InCl}_3 \) and \( \text{Pd(PPh}_3)_4 \) in water with high yield (Scheme 28).

The main advantage of using indium along with \( \text{InCl}_3 \) was to generate active \( \text{InCl} \), which was responsible for the generation of an organoindium complex via transmetalation from an organopalladium complex followed by allylation.
Li et al.11a demonstrated InCl₃-mediated highly diastereoselective tandem carbonyl allylation−Prins cyclization of aldehyde 68 with 3-trimethylsilylallyltributylstannane 97 to afford 2,6-dialkyl-5,6-dihydropyran 98 with a cis diastereoselectivity (Scheme 29).

Loh et al.11b accomplished a one-pot Prins cyclization of aldehyde 68 with allylchlorosilane 99 to afford corresponding 2,4,6-trisubstituted tetrahydropyran 100 in the presence of InCl₃ catalyst (Scheme 30). They also observed that α,β-unsaturated aldehydes also respond to the reaction equally.

Yadav et al.12a found that, in the presence of 10 mol % of InCl₃, 1,4-benzoquinone 102 could react with electron-rich alkene 101 to afford the corresponding 2,3-dihydrobenzofuran 103 in excellent yield. It was noted that the reaction underwent a [3 + 2] cycloaddition pathway to produce a trans-selective product (Scheme 31).

Balasubramanian et al.11c reported the synthesis of 2-(D-glycero-1,2-dihydroxyethyl)furan 105, an optically active furandiol from glucal 104 in the presence of a catalytic amount of InCl₃·3H₂O in acetonitrile at room temperature (Scheme 32).

Ishii et al.11d have developed a catalytic Baeyer−Villiger oxidation of KA-oil (a mixture of cyclohexanone 106 and cyclohexanol 107) with molecular oxygen. The reaction has been done in the presence of a catalytic amount of InCl₃ and N-hydroxyphthalimide to afford ε-caprolactone 108 (Scheme 33).

An efficient InCl₃-catalyzed synthesis of substituted pyran 110 was demonstrated by Lee et al.11e by reacting 1,3-dicarbonyl 70 with α,β-unsaturated aldehyde 109 in acetonitrile under refluxing conditions with moderate yield (Scheme 34).

Perumal et al.11f developed InCl₃-catalyzed cyclization of o-hydroxylidine 111 with vinyl enol ether 41, resulting in the formation of diastereoselective benzopyran derivatives (syn-112 and anti-113) at ambient temperature with excellent yield and high diastereoselectivity (Scheme 35).

Scheme 31. InCl₃-Catalyzed Synthesis of 2,3-Dihydrobenzofuran Derivatives

Scheme 32. InCl₃-Catalyzed Rearrangement of Dihydropyran to Puran

Scheme 33. InCl₃-Catalyzed Baeyer−Villiger Oxidation of KA-Oil to ε-Caprolactone

Scheme 34. InCl₃-Catalyzed Synthesis of Substituted Pyrans

Scheme 35. Diastereoselective Synthesis of Purano/Pyranobenzopyran Derivatives

Scheme 36. InCl₃-Catalyzed C-Alkylation of Indoles with Cyclic Enol Ether

Scheme 37. InCl₃-Catalyzed Synthesis of Substituted Coumarins
Yadav and co-workers also developed the methodology for the synthesis of 2-methyl-3-perhydrofuro[2,3-b]oxepin-4-yl-1H-indole derivative \( 116 \) by reacting substituted 2-methylindole \( 114 \) with 2,3-dihydrofuran \( 115 \) in the presence of a catalytic amount of \( \text{InCl}_3 \) under mild reaction conditions. The yield and diastereoselectivities of the products were found to be excellent.

On the other hand, 5,5-di(1H-3-indolyl)-1-pentanol derivative \( 118 \) was formed in high yields when indole \( 117 \) and 3,4-dihydro-2H-pyran \( 33 \) were reacted under similar reaction conditions (Scheme 36).

Kalyanam et al. synthesized coumarin \( 121 \) in a single step with a condensation reaction of substituted phenol \( 119 \) and acetylenic ester \( 120 \) in the presence of a catalytic amount of \( \text{InCl}_3 \) under solvent-free conditions (Scheme 37).

Ranu et al. developed an easy and efficient methodology that demonstrated \( \text{InCl}_3 \)-catalyzed masking of carbonyl \( 122 \) to 1,3-dioxolane \( 123 \) and dialkyl acetal \( 124 \) with good to excellent yields (Scheme 38).

Tocco et al. reported that 2,2′-dihydroxybiphenyl \( 125 \) and bis(2-hydroxyphenyl)methane \( 127 \) reacted with carbonyl \( 122 \) to afford dibenzo(d,g)-(1,3)dioxepine \( 126 \) and 12H-dibenzo-(d,g)-(1,3)dioxocin \( 128 \), respectively, in the presence of a catalytic amount of \( \text{InCl}_3 \) (Scheme 39).

van Lier et al. have shown a facile oxidation of 2′-hydroxychalcone \( 129 \) and hydroflavanone \( 130 \) to afford the corresponding flavone \( 131 \) in the presence of silica gel impregnated with 15–20 mol % of \( \text{InBr}_3 \) or \( \text{InCl}_3 \) under solvent-free conditions (Scheme 40).

Chen and co-workers reported an \( \text{InCl}_3 \)-catalyzed three-component reaction of aryglyoxal monohydrate \( 132 \), phenol \( 133 \), and \( p \)-toluenesulfonamide \( 134 \) to afford 2-aryl-3-amino-benzofuran \( 135 \) in good to excellent yields (Scheme 41).

Raghunathan et al. reported the \( \text{InCl}_3 \)-catalyzed synthesis of 1,3,5-trioxane \( 136 \) by the cyclotrimerization of aldehyde \( 68 \) in excellent yields under solvent-free conditions (Scheme 42).

Prajapati and Gohain have synthesized a cis-trans mixture of pyrano[2,3-d]pyrimidines \( 140 \) and \( 141 \) from a multicomponent domino Knoevenagel/hetero-Diels–Alder reaction of 1,3-dimethyl barbituric acid \( 137 \) and an aromatic aldehyde \( 138 \) followed by vinyl ether \( 139 \) addition, in the presence of 1 mol % of \( \text{InCl}_3 \) (Scheme 43).

Yadav et al. also reported that hexose sugar \( 142 \) underwent a coupling reaction with 1,3-dicarbonyl \( 143 \) in the presence of...
10 mol % of InCl₃ in water at 80 °C to afford C-furyl glycosides in high yields (Scheme 44). The pentose sugars with 1,3-dicarbonyls gave the corresponding furan derivatives, and reaction of cyclic ketones with hexose sugars gave the corresponding tetrahydrobenzofuranyl glycoside derivatives.

Perumal et al.² developed an InCl₃-catalyzed three-component one-pot synthesis of spirooxindoles under both conventional and solvent-free microwave irradiation conditions. Isatin 145 first

Scheme 45. Synthesis of Spirooxindoles from Isatin and Malonitriles

Scheme 46. InCl₃-Catalyzed Synthesis of Amino Chromenes

Scheme 47. InCl₃-Catalyzed Synthesis of Naphthapyranopyrimidines

Scheme 48. InCl₃-Catalyzed Synthesis of Dihydropyranochromenediones
condenses with malononitrile 146a or ethyl cyanoacetate 146b to form α,β-unsaturated nitrile or acetate derivatives which undergo a C-alkylation reaction with 1-naphthol 147c or 2-naphthol 147d followed by nucleophilic addition of the phenolic OH group onto the cyano moiety, forming spirooxindoles 148 and 149, respectively (Scheme 45).

The same group further reported a convenient three-component one-pot synthesis of 2-aminochromene 153 from salicylaldehyde 150, malononitrile 151, and Hantzsch dihydropyridine ester 152 in aqueous ethanol using InCl₃ catalyst (Scheme 46).¹³e

Singh et al.¹⁴ have reported an InCl₃-catalyzed three-component one-pot coupling of β-naphthol 154, aldehydes 155, and 6-amino-1,3-dimethyluracil 156 under solvent-free conditions to give 8,10-dimethyl-12aryl-12H-naphtho[1′,2′:5,6]pyrano[2,3-d]pyrimidine-9,11-dione 157 in high yields (Scheme 47).

Reddy et al.¹⁵ reported a novel three-component one-pot synthesis of dihydroxypyran [3,2-β]-chromenedione derivative 160 from kojic acid 158, aldehyde 159, and dimedone 70 in the presence of 10 mol % of InCl₃ under solvent-free conditions at 120 °C. The product 2-(hydroxymethyl)-7,7-dimethyl-10-phenyl-7,8-dihydroxypyran [3,2-β]-chromene-4,9(6H,10H)-dione (160) was obtained in 90% yield (Scheme 48).

Balalaie et al.¹⁶ reported an efficient approach for the synthesis of pyranoquinoline 162 through InCl₃-catalyzed activation of alkyne 161. Intramolecular hydroamidation of alkynes can proceed through alkyne activation by indium(III) chloride and then 6-exo-dig cyclization, leading to a fused pyran ring with high selectivity, high atom economy, and good yields (Scheme 49).

4. SYNTHESIS OF S-CONTAINING HETEROCYCLES AND OTHERS

Muthusamy et al.¹⁸ reported an InCl₃-catalyzed synthesis of 1,3-dithiolane 164 by reacting carbonyl 122 with 1,2-ethanedithiol 163 in methanol at room temperature in excellent yields (Scheme 50).

Ranu et al.¹⁷ also developed a method for trans-thioacetalization of O,O-acetal 165 by thiol 166 in 1,2-dichloroethane (DCE) to afford 167 in the presence of a catalytic amount of InCl₃ in good yields (Scheme 51).

Muthusamy et al.¹⁸ reported an InCl₃-catalyzed atom-economical diastereoselective synthesis of indenodithiepines and indenodithiocines via a domino reaction of propargylic
alcohol 168 and dithioacetal 169 (Scheme 52). The reaction works efficiently with remarkable accessibility of a wide variety of indene-fused sulfur heterocycles (e.g., functionalized dithiepines and dithiocines) with good to excellent yields (up to 96%).

Sakai et al. reported the direct conversion of lactone 171 into thiolactone 172 with elemental sulfur (S8) catalyzed by InCl3/PhSiH3 in a one-pot reaction (Scheme 53). This catalytic system was successfully applied to the novel preparation of selenolactones from lactones and selenium.

Gharpure and co-workers reported an inter- as well as intramolecular thia-Pictet−Spengler cyclization of N-tethered thiol and carbonyl compound to yield nitrogen-fused thiazinoindole derivative 175 in excellent yields (Scheme 54).

The strategy was extended to a one-pot, sequential Friedel−Crafts alkylation/Pictet−Spengler cyclization and the synthesis of thiazinoxepinoindole.

Scheme 54. InCl3-Catalyzed Synthesis of Nitrogen-Fused Thiazinoindole Derivatives

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\begin{align*}
\text{Scheme 55. InCl3 catalyzed synthesis of tetrahydrochomanoquinolines} \\
\begin{array}{c}
\text{Scheme 56. InCl3 catalyzed synthesis of oxazoloquinolines} \\
\text{Scheme 57. InCl3-Catalyzed Synthesis of Oxa-Aza Bicyclononene Derivatives}
\end{array}
\end{align*}
\]

Perumal et al. have discovered the intramolecular imino Diels−Alder reaction of aldmines derived from aromatic amines 40 and O-allyl salicylaldehydes 176 to give a diastereomeric...
mixture of tetrahydrochromano[4,3-b]quinolines in the presence of InCl$_3$ catalyst in excellent yields under mild reaction conditions (Scheme 55). The products were obtained as a mixture of cis 177 and trans 178 isomers in 1:1 ratio.

Pak et al.\textsuperscript{21} reported an InCl$_3$ catalyzed Beckmann rearrangement of 3-acyl-4-quinolinone ketoximes 179 to obtain predominantly an oxazoloquinoline 180 as the major product; an iso-oxazoloquinoline 181 was isolated as a minor product without rearrangement (Scheme 56).

Yadav et al.\textsuperscript{12d} developed a synthetic methodology for the synthesis of oxa-aza bicyclononene scaffolds which have presumed importance in the field of drug discovery. They have demonstrated a three-component coupling (3CC) of glycal 182, 1,3-dicarbonyl compound 51, and arylamine 40 in the presence of 10 mol % of InCl$_3$ in DCE under refluxing conditions. This reaction afforded oxa-aza bicyclononene 183 in 93% isolated yield and high stereoselectivity (Scheme 57).

For more than a decade, our group also worked on the InCl$_3$-catalyzed synthesis of heterocycles.\textsuperscript{22} We explored the use of the InCl$_3$ catalyst in the synthesis of four different types of heterocyclic compounds, which included substituted furans, pyrroles, bipyrroles, and pyrones. We reacted 1,2-diarylethylene 184 with various $\beta$-dicarbonyls 51 in the presence of a catalytic amount of InCl$_3$, which resulted in the formation of tetra-substituted furan 186. In the presence of ammonium acetate (NH$_4$OAc), the reaction between 51 and 184 yielded substituted pyrrole 187. The treatment of diarylacetylene 185 with 51 and NH$_4$OAc yielded ($\pm$)-3,3$'$-bipyrrole 188. In the absence of NH$_4$OAc, 51 reacted with 185 to afford substituted 2-pyrene 189 in very good yield and not the expected($\pm$)-3,3$'$-bifuran 190 (Scheme 58).

Reddy et al.\textsuperscript{23} developed a novel one-pot synthesis of oxa-aza bicycle 194 from the $\delta$-hydroxy-$\alpha$-$\beta$-unsaturated sugar aldehyde (Perlin aldehyde) 191, arylamine 192, and 1,3-dicarbonyl compound 193 in the presence of 10 mol % of InCl$_3$ in acetonitrile at 80 °C. Initially, the aryl amine reacted with the
1,3-dicarboxyl to form β-enamino ketones, which subsequently coupled with the Perlin aldehyde to produce oxo-aza bicycles in good yields with high selectivity (Scheme 59).

Yadav et al.\textsuperscript{12f} found that in the presence of a catalytic amount of InCl\textsubscript{3}, a tandem Michael addition and intramolecular Friedel–Crafts-type cyclization occurred under mild conditions between δ-hydroxy-α,β-unsaturated aldehyde 195 and arylamine 196 to afford fused heterocycle 197 in good yield and excellent stereoselectivity (Scheme 60).

A systematic and comprehensive study on the synthesis of 3H-(pyrrol-1-yl)indolin-2-one 200 was reported by Ji et al.\textsuperscript{24} Various isatin derivatives 198 and 4-hydroxyproline 199 were reacted in the presence of 10 mol % of InCl\textsubscript{3} under ambient reaction conditions to afford the products in excellent yields up to 99% (Scheme 61).

Yadav et al.\textsuperscript{12f} described a cycloaddition reaction of aryl amine 40 with 3,4-dihydro-2H-pyran 33 in the presence of the InCl\textsubscript{3} catalyst under mild reaction conditions to afford the corresponding pyran[3,2-c]quinoline 201 with high diastereoselectivity (Scheme 62).

Raghunathan et al.\textsuperscript{25} demonstrated the synthesis of tetrahydro-pyrazole[4,3′:5,6][1]thiopyran[4,3-b]quinolines catalyzed by InCl\textsubscript{3} under mild conditions (Scheme 63). The products were obtained as a diastereomeric mixture of cis-isomer 204 as the major product and the trans-isomer 205 as the minor product.

5. CONCLUSIONS

This review encompasses catalytic applications of InCl\textsubscript{3} for synthesizing a wide range of heterocycles. It is evident from the above discussion that InCl\textsubscript{3} is a valuable Lewis acid catalyst for the synthesis of many heterocyclic scaffolds. The most attractive feature of this review is the application of InCl\textsubscript{3} to catalyze reactions in both organic and/or aqueous media with almost equal feasibility. It exhibits unique activity in this area owing to its high coordination number and fast coordination–dissociation equilibrium maintenance. In contrast, the application of InCl\textsubscript{3} along with a chiral auxiliary in asymmetric synthesis is still largely unexplored. Thus, the future of this area lies in the development of an enantioselective InCl\textsubscript{3} catalyst which may be air- and water-insensitive. Hence, InCl\textsubscript{3}-catalyzed reactions have a huge potential for application in organic synthesis and green chemistry.

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Notes
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REFERENCES

(1) Santelli, M.; Pons, J.-M. Lewis Acids and Selectivity in Organic Synthesis; CRC Press: Boca Raton, FL, 1995. (b) Schinzer, D., Ed. Selectivities in Lewis Acid Promoted Reactions; Kluwer Academic Publishers: Amsterdam, The Netherlands, 1989; pp 1–314.

(2) For recent reviews, see: (a) Babu, G.; Perumal, P. T. Synthetic Applications of Indium Trichloride Catalysed Reactions. Aldrichimica Acta 2000, 33, 16–22. (b) Singh, M. S.; Raghuvanshi, K. Recent advances in InCl₃-catalyzed one-pot organic synthesis. Tetrahedron 2012, 68, 8683–8697. (c) Cornil, J.; Connard, L.; Bensoussan, C.; Serra-Muns, A.; Gnamm, C.; Commandeur, C.; Commandeur, M.; Reymond, S.; Guérinot, A.; Cossy, J. Iron- and Indium-Catalysed Reactions toward Nitrogen- and Oxygen-Containing Saturated Heterocycles. Acc. Chem. Res. 2015, 48 (3), 761–773. (d) Pathipati, S.; van der Werf, A.; Selier, N. Indium (III)-Catalyzed Transformations of Alkenes: Recent Advances in Carbo- and Heterocyclization Reactions. Synthesis 2017, 49, 4931–4941 and references cited therein.

(3) (a) Li, J.; Li, C. J. Synthesis of tetrahydropyran derivatives via a novel indium trichloride mediated cross-cyclization between epoxides and homoallyl alcohols. Tetrahedron Lett. 2001, 42, 793–796. (b) Li, X.-R.; Loh, T.-P. Indium trichloride-promoted tin-mediated carbonyl allenylation in water: High simple diastereo- and diastereofacial selectivity. Tetrahedron: Asymmetry 1996, 7, 1535–1538. (c) Nandi, G. C.; K. S. Catalyst-Controlled Straightforward Synthesis of Highly Substituted Pyrroles/Furans via Propargylation/Cycloisomerization of α-Oxoketene-S-N-acetals. J. Org. Chem. 2016, 81, 11909–11915. (d) Li, B.; Wang, G.; Li, Z.; Meng, X. InCl₃-catalyzed synthesis of C-pyrrolyl glycosides via tandem condensation of aminosugars and 1,3-dicarbonyl compounds in water. Tetrahedron Lett. 2011, 52, 3891–3894. (e) Ranu, B. C.; Hajra, A.; Jana, U. Indium(III) Chloride Catalyzed One-Pot Synthesis of Dihydropyrimidinones by a Three-Component Coupling of 1,3-Dicarbonyl Compounds, Aldehydes, and Urea: An Improved Procedure for the Biginelli Reaction. J. Org. Chem. 2000, 65, 6270–6272. (f) (7) (a) Hazarika, P.; Gogoi, P.; Konwar, D. Efficient and Green Method for the Synthesis of 1,5-Benzodiazepine and Quinoxaline Derivatives in Water. Synth. Commun. 2007, 37, 3447–3454. (b) Jadhav, A. M.; Balwe, S. G.; Kim, J. S.; Lim, K. T.; Li, J.; V. T. Indium(III) chloride catalyzed synthesis of novel 1,3-benzodiazepine [2,1-b]pyrazine-5,10-diones and 1H-pyrazolo[1,2-a]pyridazine-5,8-dioxo derivatives under solvent-free conditions. Tetrahedron Lett. 2019, 60, 560–565. (c) (a) Bhuuyan, G.; Hashimoto, A.; Yamamoto, A. Indium nitride (InN): A review on growth, characterization, and properties. J. Appl. Phys. 2003, 94, 2779–2808. (b) Anderson, C. J.; Welch, M. J. Radiometal-Labeled Agents (Non-Technetium) for Diagnostic Imaging. Chem. Rev. 1999, 99, 2219–2234. (d) Chao, L.-C.; Rieke, R. D. Activated metals. IX. New reformatsky reagent involving activated indium for the preparation of beta-hydroxyphthalide derivatives. J. Org. Chem. 1975, 40, 2253–2255.

(10) Nguyen, V. C.; Kim, Y.-T.; Yu, Y.-K.; Kang, H.-Y. Synthesis of Chromane Derivatives by Palladium-Catalyzed Intramolecular Allylation of Aldehydes with Allylic Acetates or Chlorides Using Indium and Indium (III) Chloride. Bull. Korean Chem. Soc. 2005, 26, 711–712.

(11) (a) Viswanathan, G. S.; Yang, J.; Li, C.-J. A Novel Stereoselective Cyclization to Functionalized Dihydropyran. Org. Lett. 1999, 1, 993–995. (b) Chan, K.-P.; Loh, T.-P. Lewis acid-catalyzed one-pot crossed Prins cyclizations using allylchloroalane as allaylating agent. Tetrahedron Lett. 2004, 45, 8387–8390. (c) Sobhana Babu, B.; Balasubramaniam, K. K. A Facile Synthesis of a Chiral Furan Diol from Glycals Catalyzed by Indium Trichloride. J. Org. Chem. 2000, 65, 4198–4199. (d) Fukuda, O.; Sakaguchi, S.; Ishii, Y. A new strategy for catalytic Baeyer–Villiger oxidation of KA-ol with molecular oxygen using N-hydroxypthalimide. Tetrahedron Lett. 2001, 42, 3479–3481. (e) Lee, Y. R.; Kim, D. H.; Shim, J.-J.; Kim, S. K.; Park, J. H.; Cha, J. S.; Lee, C.-S. One-Pot Synthesis of 2H-Pyran by Indium (III) Chloride-Catalyzed Reactions.
Efficient Synthesis of Pyrano[3,4-c]chromenones, Pyrano[3,4-b]chromones, and Pyrano[3,4-c]quinolinones. Bull. Korean Chem. Soc. 2002, 23, 998–1002. (1) Annyappan, M.; Muralidharan, D.; Perumal, P. T. Diastereoselective synthesis of cis-fused pyrano and furanobenzopyranos catalyzed by indium trichloride or triphenylphosphonium perchlorate. Tetrahedron 2002, 58, 10301–10307. (g) Kalyanam, N.; Nagarajan, A.; Majeed, M. A Single-Step Assembly of Coumarin Ring Skeleton from Oxogenated Phenols and Acetylenic Esters by Catatytic Indium Chloride Catalysis in the Absence of Solvent. Smtih. Commun. 2004, 34, 1909–1914. (h) Ahmed, N.; Ali, H.; van Lier, J. E. Silica gel supported InBr3 and InCl3: new catalysts for the facile and rapid oxidation of 20-hydroxychalcones and flavanones to their corresponding flavones under solvent free conditions. Tetrahedron Lett. 2005, 46, 253–256. (i) Chen, C.-X.; Liu, L.; Yang, D.-P.; Wang, D.; Chen, Y.-J. Indium Trichloride Catalyzed Synthesis of 2-Aryl-3-amino benzofuran Derivatives by a Three-Component Reaction of Phenols, Aryl glyoxals and para-Toluenesulfonamide. Synlett 2005, 13, 2047–2051. (12) (a) Yadav, J. S.; Reddy, B. V. S.; Kundaji, G. InCl3-Catalyzed [3 + 2] Cycloaddition Reactions: A Facile Synthesis of trans-Dihydrobenzofurans and Substituted Cyclobutane Derivatives. Synthesis 2003, 2003, 1100–1104. (b) Yadav, J. S.; Reddy, B. V. S.; Satheesh, G.; Prakash, A.; Kunwar, A. C. Unprecedented InCl3-catalyzed formation of cis-fused perhydrofuro[2,3-b] oxepines. Tetrahedron Lett. 2003, 44, 2221–2224. (c) Yadav, J. S.; Reddy, B. V. S.; Sreenivas, M.; Satheesh, G. Indium (III) Chloride/Water: A Versatile Catalytic System for the Synthesis of C-Furyl Glycosides and Trihydroxyalkyl Furan Derivatives. Synthesis 2007, 2007, 1712–1716. (d) Yadav, J. S.; Reddy, B. V. S.; Srinivas, M.; Divyavani, C.; Kunwar, A. C.; Madavi, C. The first examples of cyclizations of a glycal with enamines leading to oxo-aza bicyclononene scaffolds. Tetrahedron Lett. 2007, 48, 8301–8305. (e) Yadav, J. S.; Reddy, B. V. S.; Padmavani, B. InCl3-Catalyzed Tandem Michael/Friedel–Crafts Cyclization: A Novel Protocol for Chiral 2,4-Disubstituted Tetrahydroquinolines. Synthesis 2004, 3, 405–408. (f) Yadav, J. S.; Reddy, B. V. S.; Rao, R. S.; Kumar, S. K.; Kunwar, A. C. InCl3-Catalyzed hetero-Diels–Alder reaction: an expeditious synthesis of pyranoquinolines. Tetrahedron 2002, 58, 7891–7896. (13) (a) Ranu, B. C.; Jana, R.; Samanta, S. A Simple, Efficient and General Procedure for Acetalization of Carbonyl Compounds and Deprotection of Acetals under the Catalysis of Indium (III) Chloride. Adv. Synth. Catal. 2004, 346, 446–450. (b) Tocco, G.; Begala, M.; Delogu, G.; Picciau, C.; Podda, G. Indium(III) chloride catalyzed one step synthesis of some new dibenzo[d, f][1,3]dioxepines and 12H-dibenzo[d, g] (1,3) dioxin derivatives. Tetrahedron Lett. 2004, 45, 6909–6913. (c) Elamparuthi, E.; Ramesh, E.; Raghu Nathan, R. InCl3 as an Efficient Catalyst for CyclotrimORIZATION of Aldehydes: Synthesis of 1, 3, 5-Trioxane under Solvent-Free Conditions. Synth. Commun. 2005, 35, 2801–2804. (c) Prapatj, D.; Gohain, M. An efficient synthesis of novel pyrano[2,3-d] and furanopyrano[2,3-d] pyrimidines via indium-catalyzed multi-component domino reaction. Beilstein J. Org. Chem. 2006, 2, 1–5. (e) Shanthi, G.; Perumal, P. T. An eco-friendly synthesis of 2-aminochromones and indolyl chromones catalyzed by InCl3 in aqueous media. Tetrahedron Lett. 2007, 48, 6785–6789. (14) Nandi, G. C.; Samai, S.; Singh, M. S. First InCl3-Catalyzed, Three-Component Coupling of Aldehydes, β-Naphthol, and 6-Amino-1, 3-dimethyluracil to Functionalized Naphthopyranopyrimidines. Synlett 2010, 2010, 1133–1137. (15) Reddy, B. V. S.; Reddy, M. R.; Narasimhulu, G.; Yadav, J. S. InCl3-catalyzed three-component reaction: a novel synthesis of dihydopyrano[3,2-b]chromenediones under solvent-free conditions. Tetrahedron Lett. 2010, 51, 5677–5679. (16) Balalaie, S.; Mirzaie, S.; Nikbakht, A.; Hamdan, F.; Rominger, F.; Navari, R.; Bijanazadeh, H. R. Indium-Catalyzed Intramolecular Hydroamidation of Alkynes: An Exo-Dig Cyclization for the Synthesis of Pyranoquinolines through Post-Transformational Reaction. Org. Lett. 2017, 19, 6124–6127. (17) Ranu, B. C.; Das, A.; Samanta, S. Highly Efficient Trans-thioacetalization of O-O-Acetals Catalyzed by Indium(III) Chloride. Synlett 2002, 2002, 0727–0730. (18) Muthusamy, S.; Sivaguru, M.; Suresh, E. Indium (III) chloride catalyzed highly diastereoselective domino synthesis of indenothiophenes and indenodithiocines. Chem. Commun. 2015, 51, 707–710. (19) Sakai, N.; Horikawa, S.; Ogawa, Y. Indium-Catalyzed Direct Conversion of Lactones into Thiolactones and Selenolactones in the Presence of Elemental Sulfur and Selenium. Synthesis 2018, 50, 565–574. (20) Gharpure, S. J.; Nanda, S. K. Stereoselective synthesis of thiadiazino[4,3-a]indoles using the thia-Pictet–Spengler reaction of indoles bearing N-tethered thiols and vinyllogous thiocarbonates. Org. Biomol. Chem. 2016, 14, 5586–5590. (21) Yoo, K. H.; Choi, E. B.; Lee, H. K.; Yoon, G. H.; Yang, H. C.; Pak, C. S. Beckmann Rearrangement Using Indium(III) Chloride: Synthesis of Substituted Oxazoloquinolines from the Corresponding Ketoximes of 3-Acyl-1H-quinolin-4-ones. Synthesis 2006, 2006, 1599–1612. (22) (a) Dey, S.; Nandi, D.; Pradhan, P. K.; Giri, V. S.; Jaisankar, P. Indium trichloride catalyzed efficient one-pot synthesis of highly substituted furans. Tetrahedron Lett. 2007, 48, 2573–2575. (b) Dey, S.; Pal, C.; Nandi, D.; Giri, V. S.; Zaidlewicz, M.; Krzeminski, P.; Smentek, L.; Hess, B. A.; Gawronsji, J.; Kowit, M.; Babu, N. J.; Nangia, A.; Jaisankar, P. Lewis Acid-Catalyzed One-Pot, Three-Component Route to Chiral 3,3′-Bipyroles. Org. Lett. 2008, 10, 1373–1376. (c) Mahato, S. K.; Vinayagam, J.; Dey, S.; Timiri, A. K.; Chatterjee, S.; Jaisankar, P. InCl3 Catalysed One-Pot Synthesis of Substituted Pyrroles and 2-Pyriones. Aust. J. Chem. 2013, 66, 241–251. (23) Reddy, B. V. S.; Divyavani, C.; Begum, Z.; Yadav, J. S. Three-Component Reaction of a δ-Hydroxy-α,β-Unsaturated Aldehyde with Aroylamines and 1,3-Diketones: A Novel Synthesis of Oxa-Aza Bicycles. Synthesis 2010, 2010, 1719–1723. (24) Shen, S. S.; Ji, S. J.; Wang, S. Y. A Highly Efficient Synthesis of 3H-(Pyrrol-1-yl)indolin-2-ones Catalyzed by InCl3. Chin. J. Chem. 2008, 26, 15–18. (25) Manian, R. D. R. S.; Jayashankaran, J.; Ramesh, R.; Raghu Nathan, R. Rapid synthesis of tetrahydroquinolines by indium trichloride catalyzed mono- and bis-intramolecular imino Diels–Alder reactions. Tetrahedron Lett. 2006, 47, 7571–7574.