SYNLETT
Spotlight

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

New Uses for Indium(III) Chloride

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Rosana Freitas was born in 1988 in Rio Grande do Sul, Brazil. She received her B.Sc. in Pharmacy (2011) from Estácio de Sá University (UNESA) and her M.Sc. degree in Chemistry (2013) from Federal University of Rio de Janeiro (UFRJ) under the guidance of Professor Carlos A. Manssour Fraga. She is currently a Ph.D. student under the guidance of Professor Carlos A. Manssour Fraga and Professor Edson F. Silva. Her research focuses on the synthesis and pharmacological evaluation of new prototypes of anti-*Trypanosoma cruzi* agents.

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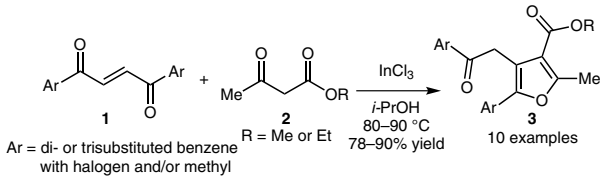
Introduction

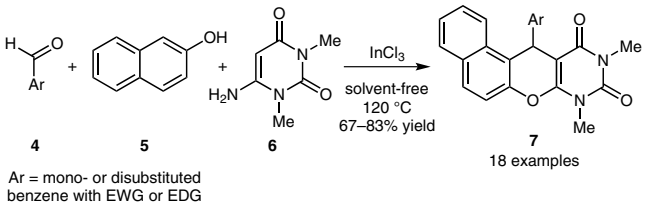
Indium(III) chloride ($InCl_3$) is an inexpensive, commercially available, easy-to-handle, air- and water-stable Lewis acid with moderate toxicity. It shows a high tolerance to most functional groups including oxygen and nitrogen functionalities.[1] Additionally, $InCl_3$ is very attractive for green-chemistry reactions due to its recyclability.[2] Therefore, $InCl_3$ has been described as a catalyst for various reactions, especially multicomponent reactions (MCR),[3] as given below.

Abstracts

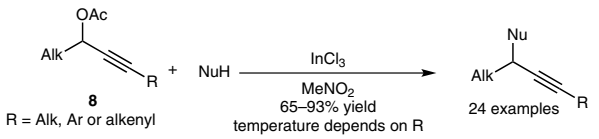
(A) *Synthesis of Furans:*
Dey and co-workers reported a one-pot synthesis of polysubstituted furans (**3**) using but-2-ene-1,4-diones (**1**) and acetoacetates (**2**) under acid catalysis using $InCl_3$. It is an efficient and easy way of obtaining polysubstituted furans in excellent yields.[4] In a similar manner, Suresh and co-workers reported a synthesis of various pyrroles from α-azido chalcones and 1,3-dicarbonyl compounds using acid catalysis with $InCl_3$ in water.[5]



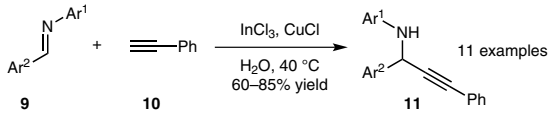
(B) *Multicomponent Reaction:*
A new protocol described a solvent-free, three-component reaction to generate 8,10-dimethyl-12-aryl-12*H*-naphtho[1′,2′:5,6]pyrano-[2,3-*d*]pyrimidine-9,11-diones (**7**) using functionalized aldehydes (**4**), 2-naphthol (**5**), and 6-amino-1,3-dimethyluracil (**6**) with $InCl_3$ as catalyst. The synthesis is conducted in the absence of a co-catalyst and the desired compounds were obtained in good yields and lower reaction times.[6] Several other multicomponent reactions using $InCl_3$ have been described since then.[3]



(C) *Nucleophilic Substitution:*
Lin and co-workers described a versatile and useful methodology for the synthesis of new C(sp^3)–C(sp^2), C(sp^3)–N, C(sp^3)–S and C(sp^3)–O bonds via nucleophilic substitution of secondary alkyl-substituted propargyl acetates (**8**) in $MeNO_2$ using $InCl_3$. Over twenty substrates were tested and the substitution products were obtained in high yields.[7]



(D) *Barbier–Grignard-type Reaction:*
A novel and efficient one-pot synthesis of propargylamines (**11**) via a Barbier–Grignard-type reaction was described for a variety of aldimines (**9**) and phenylacetylenes (**10**) in a bicatalytic system using $InCl_3$ and CuCl in water. The products were obtained in moderate to good yields, without formation of byproducts or hydrolysis of aldimines.[8]



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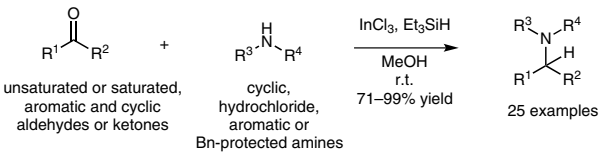
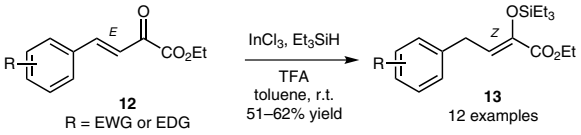
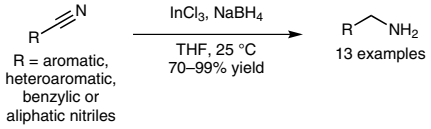
(E) *Reductive Amination:*
$InCl_3$ and Et_3SiH in methanol were able to promote the highly chemoselective reductive amination of various carbonyl compounds. In this methodology, ketones and aldehydes, some of them α,β-unsaturated, and various amines were used, including amines with other functional groups. The proposed mechanism suggests that the reducing agent is formed in situ by a catalytic cycle to generate active indium hydride species $[InHCl_2(MeOH)_{x-1}]$, which then transfers the hydride to an iminium ion intermediate to generate the corresponding amine.[9]



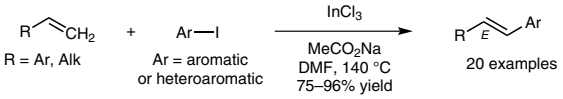
(F) *1,4-Hydrosilylation*:
A new chemo- and stereoselective method for 1,4-hydrosilylation of α,β-enone ester (**12**) to silylenol ether (**13**) was developed by using $InCl_3$, Et_3SiH and TFA in toluene. The products were obtained in moderate yields, and the double bond showed only *Z* configuration indicating the stereoselective course of the reaction.[10]



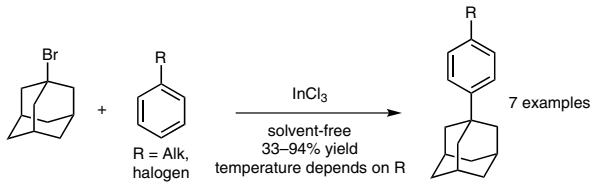
(G) *Reduction of Nitriles:*
Nitriles were reduced to primary amines in excellent yields using $InCl_3$ and $NaBH_4$ in THF. Among the tested substrates were aromatic, heteroaromatic and aliphatic nitriles, indicating the versatility of this new methodology. Species which promote the reduction of nitriles, for example, $HInCl_2$ and BH_3·THF, are generated in situ by reaction with $NaBH_4$ and $InCl_3$.[11]



(H) *Heck Reaction:*
Liu and co-workers reported the discovery of $InCl_3$ as the only catalyst for a Heck reaction between aryl iodides and olefins in the presence of sodium acetate in DMF. The new method was validated by the use of various olefins and functionalized aryl iodides, resulting in the formation of functionalized styrenes or stilbenes in high yields.[12]



(I) *Friedel–Crafts Alkylation:*
$InCl_3$ was effective to catalyze the Friedel–Crafts alkylation of 1-bromo-adamantane and monosubstituted benzenes to generate 1-adamantyl benzenes. Good yields were obtained, and an excellent regioselectivity for the formation of the *para* isomer compared to the *meta* isomer was achieved.[13]



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