

SYNLETT Spotlight 114

Indium Tribromide: A Water-Tolerant Green Lewis Acid

Compiled by Zhan-Hui Zhang



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

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Introduction

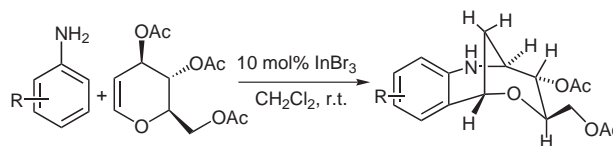
Recently, indium tribromide has received increasing attention as a novel type of water-tolerant green Lewis acid catalyst for organic synthesis with highly chemo-, regio- and stereoselective results.¹ Compared to conventional Lewis acids, it has advantages of water stability, recyclability, operational simplicity, strong tolerance to oxygen- and nitrogen-containing reaction substrates and functional

groups, and it can often be used in just catalytic amounts. This catalyst promotes various transformations including alkylation of aldehydes and *N,O*-acetals,² Michael addition,³ synthesis of 1,3-dioxane derivatives,⁴ conversion of oxiranes to thiiranes,⁵ sulfonation of indoles,⁶ alkynylation of acid chlorides⁷ and synthesis of 2-halo-1,3-dienes.⁸

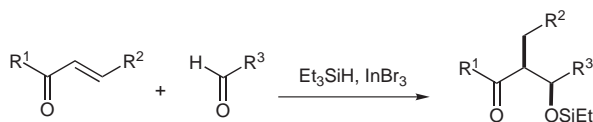
Indium tribromide is conveniently prepared by heating metallic indium in a current of nitrogen and bromine,⁹ and is now also commercially available.

Abstracts

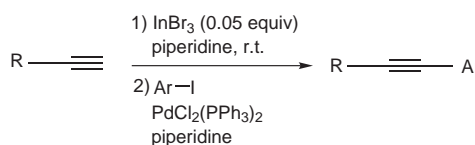
(A) A novel one-pot synthesis of benzo-fused heterobicyclic compounds is achieved in excellent yields and high stereoselectivity using a catalytic amount of InBr_3 in the reaction of glycals with aryl amines under mild reaction conditions.¹⁰ Although the reaction also proceeded with InCl_3 , InBr_3 was found to be superior in terms of yield and reaction rate. This reaction can also be performed with stoichiometric amounts of TMSOTf.



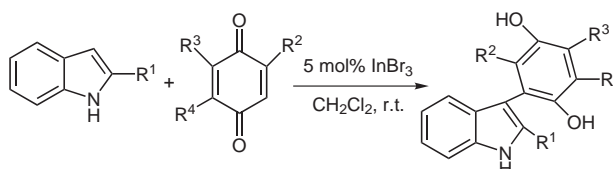
(B) Shibata et al. reported the Et_3SiH -promoted diastereoselective reductive aldol reaction using InBr_3 as catalyst. Indium hydride, generated in situ, promoted a 1,4-reduction of the enone to the indium enolate, which gave the aldolate upon reaction with an aldehyde. This three-component reaction afforded only silyl aldolates as products without any side reactions. The *syn* selectivity is higher than for other known reductive aldol reactions.¹¹



(C) Sakai et al. reported that the $\text{PdCl}_2(\text{PPh}_3)_2$ - InBr_3 reagent system effectively catalyzes the cross-coupling reaction of terminal alkynes with aryl iodides, leading to the corresponding functionalized alkyne derivatives in excellent yields.¹² This method has been applied to a one-pot synthesis of 2-phenylindole through the intramolecular cycloaddition of 2-phenylethynylaniline without the need for a protecting group on the amine.



(D) A practical synthesis of 3-indolylquinones was achieved with this catalyst by the conjugate addition of indoles to *p*-benzoquinones under mild reaction conditions, in high yields and with high selectivity. 1,4-Naphthoquinones also underwent Michael addition with indoles under similar conditions to give 3-indolynaphthoquinones.¹³



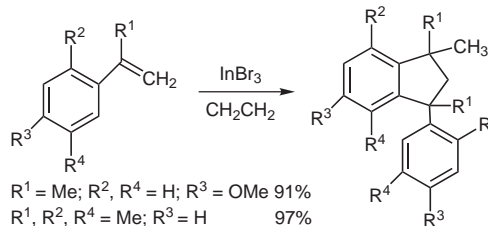
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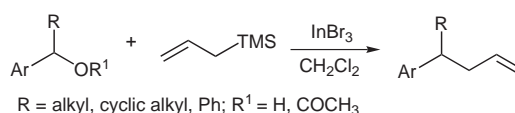
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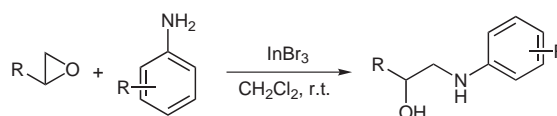
(E) InBr_3 is found to be a mild and efficient catalyst for dimerization of α -substituted vinylarenes. The reaction of vinylarenes containing electron-withdrawing substituents or an *o*-methoxy group leads to acyclic dimers. The acyclic dimers are suitable precursors of polymers. β -Substituted vinylarenes are inert under these conditions.¹⁴ The highlight of this protocol is the rigorous chemoselective control of products, depending on the nature and regiochemistry of the substituents on the aryl portion of the vinylarene.



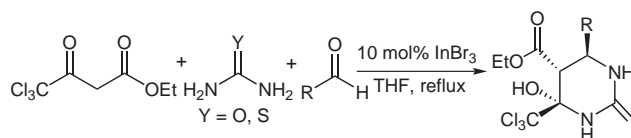
(F) In the presence of a catalytic amount of InBr_3 (5 mol%), benzyl alcohols, allylic and benzylic acetates undergo deoxygenative allylation reaction with allylsilanes to give the corresponding allylation products in high yields.¹⁵



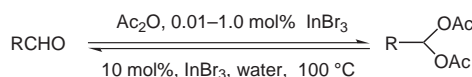
(G) Indium tribromide efficiently catalyzes the aminolysis of epoxides with aromatic amines to afford the corresponding β -amino alcohols, important intermediates for the synthesis of natural products and pharmaceuticals, in high yields with high selectivity.¹⁶ This method is applicable to a variety of epoxides and aromatic amines, especially deactivated and highly hindered amines, as well as other nitrogen heterocycles.



(H) The Biginelli-type three-component cyclocondensation reaction of chlorinated 1,3-dicarbonyl compounds with aldehydes and urea (or thiourea) in the presence of indium tribromide provides trichloromethyl-substituted tetrahydropyrimidinones, instead of the usual Biginelli products (dihydropyrimidinones), in high yields.¹⁷



(I) At a loading as low as 0.01 mol%, InBr_3 can catalyze the chemoselective preparation of acylals under solvent-free conditions. Aliphatic and aromatic aldehydes react with acetic anhydride to afford the corresponding acylals in very good to excellent yields at ambient temperature.^{18a} Indium tribromide is a water-tolerant green Lewis acid, and the cleavage of acylals can be carried out using a catalytic amount of InBr_3 in water at 100 °C.^{18b}



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