



Counterion effects in indium-catalysed aromatic electrophilic substitution reactions

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Abstract—Indium(III) triflamide ($\text{In}(\text{NTf}_2)_3$) has been prepared in high yield and has been demonstrated to be an efficient, recoverable catalyst for a range of aromatic electrophilic substitution reactions. When compared to other indium(III) complexes, anomalous reactivities suggest a non-innocent role for the counterion in the studied processes. © 2002 Elsevier Science Ltd. All rights reserved.

The efficient preparation of diversely functionalised aromatics has traditionally relied on the use of stoichiometric promoters of electrophilic substitution such as aluminium(III) chloride with the associated purification problems.¹ More recently, efficient catalytic protocols have emerged including the use of Fe(III) exchanged montmorillonite clay,² zeolites,³ bismuth(III) salts,⁴ scandium and lanthanide(III) salts.⁵ In previous work we have demonstrated that commercially available indium(III) triflate functions as an efficient Lewis acid catalyst at low catalyst loadings.⁶ In this communication we wish to report the remarkable consequences of changing the counterion to the less coordinating triflamide anion in a range of aromatic electrophilic substitution processes.

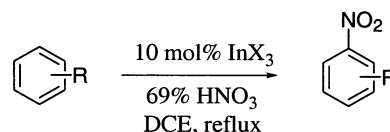
The new indium complex, $\text{In}(\text{NTf}_2)_3$, was easily prepared by the reaction of indium oxide (In_2O_3) with bis(trifluoromethanesulfonyl)imide (Tf_2NH). Thus, heating an aqueous solution of In_2O_3 and Tf_2NH at reflux for 24 h provided $\text{In}(\text{NTf}_2)_3$ in an almost quantitative yield after work-up and drying. The procedure was based on previous reports for the preparation of $\text{Sc}(\text{NTf}_2)_3$.⁷ We decided to test the efficacy of $\text{In}(\text{NTf}_2)_3$ in the clean, catalytic nitration of aromatics where the Lewis acid serves as a replacement for sulfuric acid and the only by-product is water (Scheme 1).

This important area is led by the excellent contributions from Barrett and Braddock who have revealed recyclable catalysts such as lanthanide(III) triflates and the

highly active ytterbium(III) and scandium(III) triflides which promote the nitration of activated and deactivated aromatics.⁸ Although never previously tested, we supposed that indium salts should be effective catalysts given the charge-to-size ratio of 3.75 ($r^{3+}=0.80 \text{ \AA}$) along with their established Lewis acidity in aqueous solvents.

At the outset of the study we examined the nitration of selected aromatics with different indium salts to validate the importance of counterion (Table 1). In a typical experiment we heated a mixture of aromatic (3 mmol), 69% nitric acid (1 equiv.) and indium catalyst (10 mol%) in 1,2-dichloroethane (5 ml) to reflux for 6–18 h. After dilution with water the organic phase was separated, dried and evaporated under pressure to afford the nitration product which could be purified by either recrystallisation or column chromatography. The indium salt could be recovered by evaporation of the aqueous phase and used in subsequent reactions with no significant loss of activity.

In the absence of catalyst a slow background reaction afforded less than 10% of nitration product. It was pleasing to note that indium(III) triflate and indium(III) triflamide were active catalysts for nitration reac-



Scheme 1.

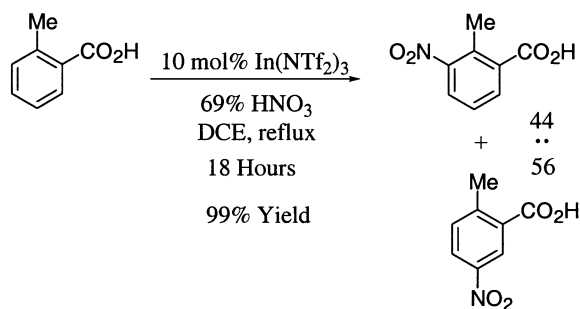
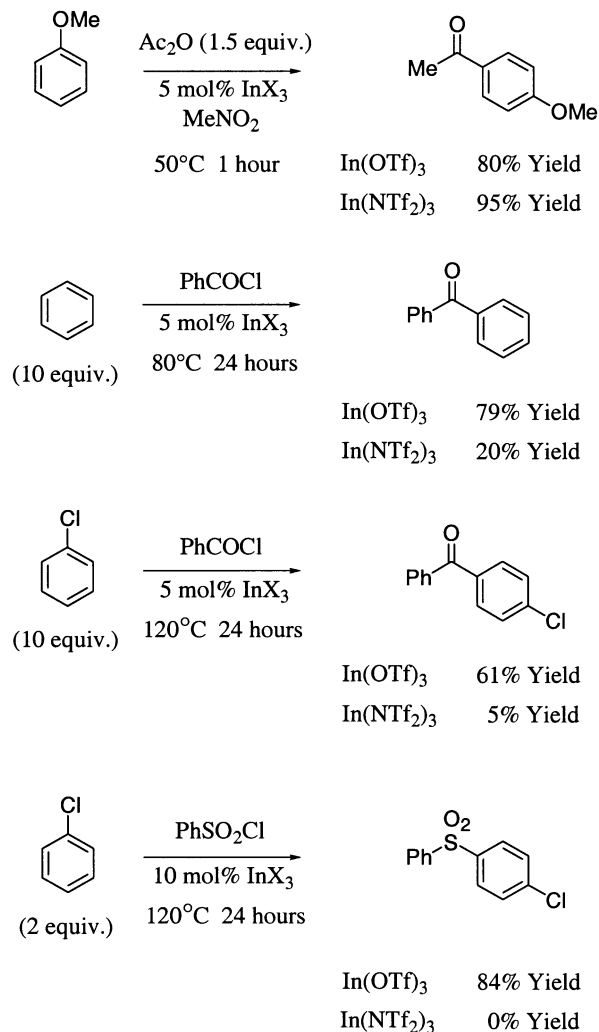
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Table 1. Evaluation of indium catalysts in aromatic nitration

Entry	Catalyst	Aromatic	Time (h)	Yield (%)	Isomer ratio
1	InCl ₃	Toluene	6	<5	–
2	In(OTf) ₃	Toluene	6	99	50:7:43 (<i>o</i> : <i>m</i> : <i>p</i>)
3	In(NTf ₂) ₃	Toluene	6	99	48:7:45 (<i>o</i> : <i>m</i> : <i>p</i>)
4	In(OTf) ₃	<i>m</i> -Xylene	6	95	14:86 (2-NO ₂ :4-NO ₂)
5	In(NTf ₂) ₃	<i>m</i> -Xylene	6	99	14:86 (2-NO ₂ :4-NO ₂)
6	In(OTf) ₃	Bromobenzene	18	89	33:0:67 (<i>o</i> : <i>m</i> : <i>p</i>)
7	In(NTf ₂) ₃	Bromobenzene	18	98	39:0:61 (<i>o</i> : <i>m</i> : <i>p</i>)
8	In(NTf ₂) ₃	Chlorobenzene	18	93	33:0:67 (<i>o</i> : <i>m</i> : <i>p</i>)
9	In(OTf) ₃	2-Nitrotoluene	18	<5	–
10	In(NTf ₂) ₃	2-Nitrotoluene	18	31	35:65 (2,4-NO ₂ :2,6-NO ₂)

tions including the efficient functionalisation of aryl carboxylic acids (Scheme 2). The catalyst loading (In(NTf₂)₃) could be lowered to 1 mol% in the nitration of bromobenzene affording a 47% isolated yield of product. The isolated yields for different aromatic compounds could be correlated to Hammett coefficients and catalyst counterion. Thus, electron-rich aromatics like toluene and *m*-xylene were easily nitrated with both In(OTf)₃ and In(NTf₂)₃, whilst much lower reactivity was observed for 2-nitrotoluene. The difference in activity reveals the crucial and complex role of the counterion. Although proven to be an excellent Lewis acid in aqueous systems, indium(III) chloride does not promote the reaction. A similar lack of activity using lanthanide(III) chlorides is postulated to be as a result of the inability of the chloride ion to transport the nitronium ion into the organic phase where the reaction occurs.⁸ If this is indeed the case the increased solubility of the nitronium triflamide salt as well as acidity considerations contribute to the observed superior activity of In(NTf₂)₃.⁹

As shown in Scheme 3, In(NTf₂)₃ is a superior catalyst for the acetylation of electron-rich aromatics with acetic anhydride.¹⁰ In these examples we presume that the weakly coordinating triflamide anion leads to enhanced

**Scheme 2.****Scheme 3.**

Lewis acidity via a coordination complex. In similar reactions Sc(NTf₂)₃ is more active than Sc(OTf)₃.⁷ However, in more demanding processes such as the benzoylation and sulfonylation of weakly activated or deactivated aromatics we see a pronounced reversal in catalytic performance (with benzoyl and sulfonyl chlorides). The success of In(OTf)₃ may be accounted for by a mechanism involving a ligand exchange (TfO⁻/Cl⁻) at the indium atom affording an acyl triflate (RCO⁺OTf) or mixed sulfonic anhydride (ArSO₂OTf) in situ which are

much more reactive species and thus allow the functionalisation of weakly activated or deactivated aromatics. In the case of acid anhydrides no exchange occurs invoking a method of activation based solely on coordination. This is confirmed in the reaction of benzene with benzoic anhydride where less than 10% of benzophenone product is isolated in the presence of $\text{In}(\text{OTf})_3$. This mechanism was first suggested by Dubac for bis-muth-catalysed Friedel–Crafts reactions and recently elucidated in an excellent review.¹¹ We suggest that the increased acidity of HNtF_2 relative to TfOH precludes any NTf_2/Cl^- exchange and activation can only occur by coordination.¹²

In conclusion, we have presented a new indium catalyst for aromatic electrophilic substitution reactions. In different substitution processes the physical properties of the counterion have been shown to dictate catalytic activity. A better understanding of the function of counterions in other catalytic systems may lead to improved activity and the discovery of new organic transformations.

Acknowledgements

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