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Indium trichloride: a useful catalyst for ionic Diels–Alder reactions[†]

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Abstract

Indium trichloride (20 mol%) in nitromethane permits ionic Diels–Alder reaction of a variety of 2,3-olefinic acetals to form the corresponding cycloadducts in good yields with good *endo* selectivities.

Keywords: ionic Diels–Alder reaction; indium trichloride; asymmetric catalysis.

The ionic Diels–Alder (IDA) reaction,[2] using a 2,3-olefinic acetal instead of an α,β-unsaturated carbonyl compound as a dienophile, is a useful variation of the conventional Diels–Alder reaction in cases where Lewis acids cause polymerization of dienophiles or thermal means do not readily lead to the expected adducts. Gassman and co-workers[3] systematically studied this reaction and several new aspects were reported by them in a series of excellent papers. Additionally, Grieco et al.[4] have reported that $LiClO_4 \cdot Et_2O$ (4 M or 5 M solution) along with 1% camphorsulfonic acid permits the ionic Diels–Alder reaction. In this study an important observation that addition of 1% camphorsulfonic acid is necessary, otherwise $LiClO_4 \cdot Et_2O$ does not give any desired adduct, deserves special mention. We have also reported[5] that $LiClO_4$ in nitromethane (4 M solution), without the addition of camphorsulfonic acid, leads to the desired ionic Diels–Alder adducts from a variety of olefinic acetals. This change in the dipole moment of 1.33 D of diethyl ether to 3.4 D of nitromethane was attributed as the possible cause of the success of the reaction using $LiClO_4$–CH_3NO_2 since ionic Diels–Alder reactions involve charged intermediate species. In addition to this, we also reported that Nafion-H[5] acts as an excellent solid catalyst for the ionic Diels–Alder reaction and in some cases with improved selectivity.

Apart from this there have been efforts[6,7] to study the asymmetric variance of IDA reactions in the literature. Our endeavors[5] in this direction involved utilization of chiral acetals containing

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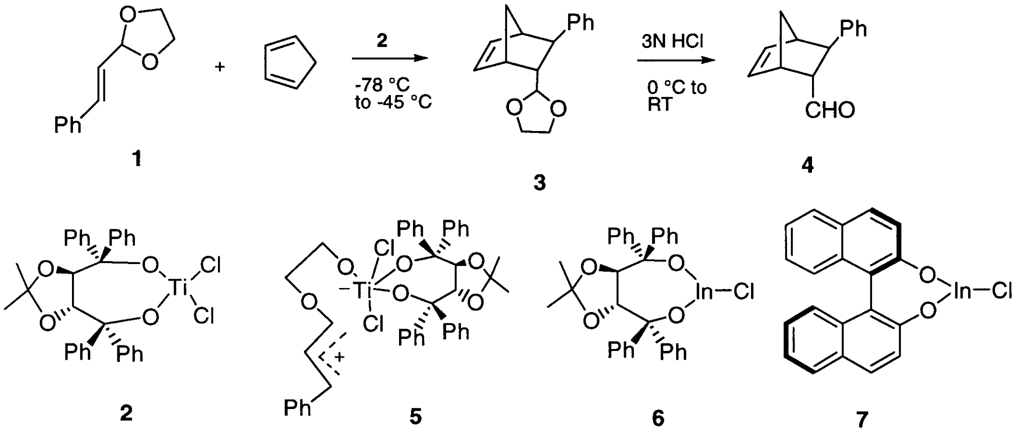
dienophiles with a side chain appendage using $TiCl_4$, $BF_3 \cdot Et_2O$ and $TiCl_2(iPrO)_2$ as catalysts. On the other hand, our efforts to study[8] these reactions with achiral olefinic acetals in the presence of chiral catalysts have met with little success. Thus, reaction of olefinic acetal **1** (Scheme 1) with cyclopentadiene in the presence of chiral catalyst **2**,[9] derived from TADDOL, gave the expected IDA adduct **3** in 71% yield. This was then hydrolyzed to the known aldehyde **4** which, however, had rather low enantioselectivity (10.4% ee)[10] possibly because of the flexible transition state **5** as a result of very high reactivity of the catalyst **2**, even at low temperatures (−78 to −45°C).

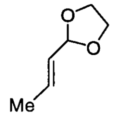
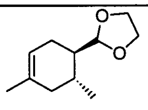
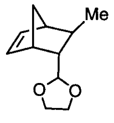
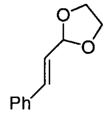
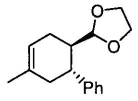
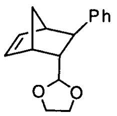
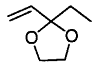
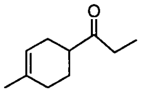
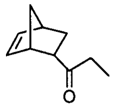
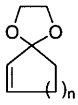
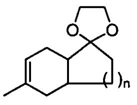
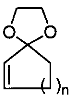
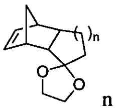
In order to perform asymmetric IDA reactions, it would thus be desirable to use a catalyst which is moderately reactive so that it permits transition states of type **5** to remain rather close to cause diastereomeric differentiation. Clearly, such catalysts should also be capable of interacting with chiral ligands and yet bear sufficient reactivity towards IDA reactions. Towards this effect, we considered $InCl_3$,[11–16] $Yb(OTf)_3$[17] and $Sc(OTf)_3$[17] as catalysts which have, in recent years, gained importance owing to their Lewis acidic character and which could also be maintained in aqueous medium. As a result of this property, several reactions such as Diels–Alder,[12,17] hetero Diels–Alder,[13] aldol,[14] Friedel–Crafts[15] and Ferrier reactions,[16] with some advantages over the traditional Lewis acids have appeared in the literature. Additionally, use of chiral ligands such as TADDOL and (*R*)- or (*S*)-BINOL to modify $Yb(OTf)_3$ and $Sc(OTf)_3$ to effect asymmetric induction has enjoyed some success.[17] To the best of our knowledge, no report is known where $InCl_3$, $Yb(OTf)_3$ or $Sc(OTf)_3$ have been employed in IDA reactions. This aspect, coupled with the fact that an appropriate bidentate ligand could modify[17] each of these into a chiral catalyst, led us to examine their behavior in IDA reactions.



Scheme 1.

Indeed $InCl_3$ was found to be an excellent catalyst in IDA reactions but surprisingly, however, with neither $Yb(OTf)_3$ nor $Sc(OTf)_3$ were IDA reactions clean and no cycloadduct was formed indicating thereby that $InCl_3$ is indeed a unique catalyst for these reactions. A variety of acyclic and cyclic olefinic acetals undergo reactions with isoprene and cyclopentadiene in the presence of 20 mol% of $InCl_3$ to form the corresponding cycloadducts in good yields (Table 1). Among the various solvents nitromethane was found to be the best in terms of reaction time and yield, indicating once again that the transition state does impart some ionic character. In the case of cyclopentadiene based reactions, the *endo*/*exo* ratio was fairly good and comparable to the $LiClO_4$[4,5] and Nafion-H[5] based reactions. All the cycloadducts were hydrolyzed to the corresponding carbonyl compounds and their spectral data compared with the literature[5] values.

Table 1
Ionic Diels–Alder reaction using $InCl_3$

Entry	Dienophile	Diene	Cycloadduct	% Yield/ Time (h)/ (*Endo:Exo Ratio*)
1		Isoprene		63 /4
2		Cyclopentadiene		73/1/(80:20)
3		Isoprene		64 /13
4		Cyclopentadiene		75/2/(89:11)
5		Isoprene		64/1[a]
6		Cyclopentadiene		72/1/(88:12)[a]
7	 n = 1	Isoprene	 n = 1	64/1
8	n = 2		n = 2	66/1
9	n = 3		n = 3	70/1
10	 n = 1	Cyclopentadiene	 n = 1	74/1/(94:6)
11	n = 2		n = 2	75/1/(94:6)
12	n = 3		n = 3	75/1/(92:8)

[a] The corresponding cyclic acetals were not isolable from the reaction mixture. [b] All the cycloadducts are known[5] compounds and they gave satisfactory spectral and analytical data.

For the asymmetric variation, $InCl_3$ was then treated with TADDOL and (*R*)-BINOL separately in the presence of NaH (or Et_3N) in THF to form catalysts **6** and **7** (Scheme 1), respectively, and further reacted in situ with **1** and cyclopentadiene in nitromethane. Unfortunately, however, no IDA reaction was found to occur, perhaps indicating that the modified indium catalysts are not sufficiently electrophilic to permit opening of the olefinic acetals for ionic Diels–Alder reactions.

Nevertheless, the success of indium chloride as a catalyst for achiral IDA reactions is important and this suggests that other more reactive derivatives of indium such as indium triflate based chiral catalysts may be useful for asymmetric IDA reactions. Work towards this end is in progress.

General experimental procedure: To a stirred solution of a dienophile (2 mmol) and freshly distilled diene (6 mmol) (isoprene or cyclopentadiene) in nitromethane (4 mL) was added anhydrous $InCl_3$ (20 mol%) (10 mg hydroquinone was also added while using isoprene) at 15–20°C. The progress of the reaction was monitored by TLC and after completion the reaction mixture was extracted with CH_2Cl_2 (3×20 mL), washed with water, brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent and purification by column chromatography gave the desired cycloadducts.

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References

1. Kumareswaran, R.; Pachamuthu, K.; Vankar, Y. D. *Synlett* **2000**, 1652.
2. (a) Gassman, P. G.; Singleton, D. A.; Wilwerding, J. J.; Chavan, S. P. *J. Am. Chem. Soc.* **1987**, *109*, 2182. (b) Pascal-Teresa, B. D.; Houk, K. N. *Tetrahedron Lett.* **1996**, *37*, 1759. (c) For a short review, see: Sanghi, R.; Vankar, P. S.; Vankar, Y. D. *J. Ind. Chem. Soc.* **1998**, *75*, 709.
3. Gassman, P. G.; Chavan, S. P. *Tetrahedron Lett.* **1990**, *31*, 6489.
4. Grieco, P. A.; Colins, J. L.; Handy, S. T. *Synlett* **1995**, 1155.
5. Kumareswaran, R.; Vankar, P. S.; Reddy, M. V. R.; Pitre, S. V.; Roy, R.; Vankar, Y. D. *Tetrahedron* **1999**, *55*, 1099.
6. Alexakis, A.; Mangeney, P. *Tetrahedron*: *Asymmetry* **1990**, *1*, 477.
7. Sammakia, T.; Berliner, M. A. *J. Org. Chem.* **1994**, *59*, 6890.
8. Kumareswaran, R. PhD dissertation, IIT Kanpur, 1998.
9. Seebach, D.; Dahinden, R.; Marti, R. E.; Beck, A. E.; Plattner, D. A.; Kuhnle, N. M. *J. Org. Chem.* **1995**, *60*, 1788.
10. The rotation value of $[\alpha]_D^{25}=+14$ (*c* 1, CH_2Cl_2) was observed for the aldehyde **4** and the ee was calculated by comparing the rotation value with the literature value, cf. Ishihara, K.; Kurihara, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 3049.
11. Babu, G.; Perumal, P. T. *Aldrichim. Acta* **2000**, *33*, 16.
12. Loh, T.-P.; Pei, J.; Lin, M. *Chem. Commun.* **1996**, 2315.
13. Babu, G.; Perumal, P. T. *Tetrahedron* **1999**, *55*, 4793.
14. Loh, T.-P.; Pei, J.; Cao, G.-Q. *Chem. Commun.* **1996**, 1819.
15. Miyai, T.; Onsihi, Y.; Baba, A. *Tetrahedron* **1999**, *55*, 1017.
16. Babu, B. S.; Balasubramanian, K. K. *Tetrahedron Lett.* **2000**, *41*, 1271.
17. (a) Kobayashi, S.; Hachiya, I.; Takahori, T.; Araki, M.; Ishitani, H. *Tetrahedron Lett.* **1992**, *33*, 6815. (b) Arseniyadis, S.; Rodriguez, R.; Yashunsky, D. V.; Camara, J.; Ourisson, G. *Tetrahedron Lett.* **1994**, *35*, 4843. (c) Kobayashi, S. *Synlett* **1994**, 689. (d) Kobayashi, S.; Ishitani, H.; Araki, M.; Hachiya, I. *Tetrahedron Lett.* **1994**, *35*, 6325.