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Organic Syntheses Using Indium-Mediated and Catalyzed Reactions in Aqueous Media

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I. Introduction

While the development of boron and aluminum reagents for synthetic purposes has been one of the major achievements in organic chemistry in this century, the study of indium reagents has remained largely unexplored until very recently.[1] The earliest study of using indium for synthetic purposes was carried out briefly earlier this century.[2] In the 1970s, Rieke developed various active metals (including indium), now commonly referred to as

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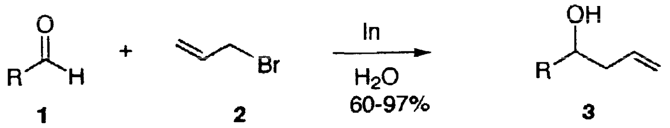
the Rieke metals, for synthetic purposes.[3] In the late 1980s, Araki and co-workers contributed to the more extensive exploration of indium reagents for organic synthesis in anhydrous solvents.[4] In the 1990s, the use of indium for synthetic purposes has seen a stellar development. Most recent interests in indium-mediated reactions have been focused on its unique ability of mediating and catalyzing organic reactions in aqueous media, which were initiated by the two authors of this report about a decade ago.[5]

Because of economical and environmental concerns, the use of water as solvent for organic reactions has been of interest recently. In addition, there is the practical convenience of not having to handle flammable and anhydrous organic solvents. The tedious protection-deprotection processes for certain acidic-hydrogen containing functional groups can be simplified, which contributes to the overall synthetic efficiency. Water-soluble compounds, such as carbohydrates, can be used directly without the need of derivatization. Among the many reactions carried out in water, the use of indium and indium compounds appears special. This report summarizes recent developments in the use of indium metal and indium compounds for organic synthetic purposes in aqueous media with a focus on representativeness rather than comprehensiveness. We hope that the report will provide non-specialists with some insight into this field and serve as a helpful tool in designing synthetic strategies in their research.

II. Indium-Mediated Barbier-Type Reactions

2.1. The Reaction

The use of indium for mediating Barbier-Grignard type reactions in water was first reported in 1991 (Eq. 1).[5] The work was an outgrowth of developing an aqueous chemical strategy toward the synthesis of sialic acids, *e.g.* (+)-3-deoxy-D-*glycero*-D-*galacto*-nonulosonic acid (KDN), 3-deoxy-D-manno-octulosoic acid (KDO) and N-acetyl-neuraminic acid. It was envisioned that such natural products can be synthesized through the coupling of a sugar with ethyl (2-bromomethyl)acrylate. While the reactions of carbonyl compounds with (2-bomomethyl)acrylate mediated by zinc[6] and tin[7] were known at the time, they are not suitable for the sialic acid synthesis owing to the harsh conditions associated with these reactions. Hence, an effort was made to seek more reactive metals.



(Eq. 1)

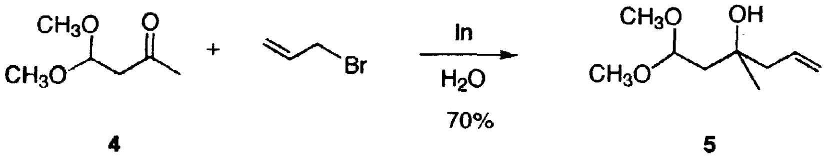
The transferring of electrons from metals to organic substrates plays important roles in many metal mediated reactions. The ionization potential of an element is directly related to its ability of giving off electrons. Thus, by examining the first ionization potentials of different elements,[8] it was found that indium has the lowest first ionization potential relative to the other metal elements near it in the periodic table. In fact, the ionization potential of indium is on the same level with the most active alkali metals and is much lower than that of zinc or tin, or even magnesium (Table 1). On the other hand, unlike those more reactive alkali metals, indium metal is not sensitive to boiling water or alkali and does not form oxides readily in air. Such special properties of indium indicate that it is perhaps a promising metal for aqueous Barbier-Grignard type reactions. Indeed, it appears that indium is by far the most effective metal for such reactions. With the initial success, Chan and Li also reported the first synthetic application (KDN synthesis) of the indium-mediated reaction in water.[9]

Table 1. First Ionization Potential of Some Metals

Metal	Indium	Magnesium	Zinc	Tin	Lithium	Sodium
First Ionization Potential (ev)	5.79	7.65	9.39	7.43	5.39	5.12

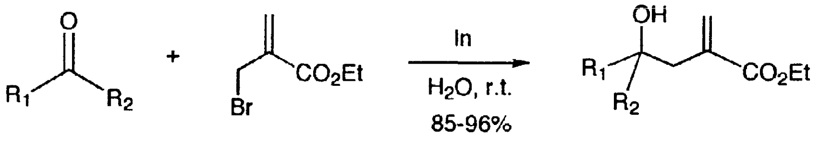
Cited from *CRC Handbook of Chemistry and Physics*. 75th ed., CRC Press, 1994.

When the allylation was mediated by indium in water, the reaction went smoothly at room temperature without any promoter, whereas the use of zinc and tin usually requires acid catalysis, heat, or sonication. An organic co-solvent is not necessary either. The mildness of the reaction conditions makes it possible to use the indium method to allylate a methyl ketone **4** in the presence of an acid sensitive acetal functional group to generate **5** (Eq. 2). Attempts to achieve such transformations with zinc and tin have not been successful under the usual acidic conditions related to these reactions. Furthermore, the coupling of ethyl 2-(bromomethyl)acrylate (**6**) with carbonyl compounds proceeds equally well under the same reaction conditions, which later makes the synthesis of sialic acids possible (Eq. 3).



4 **5**

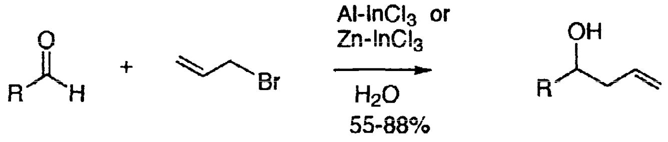
(Eq. 2)



6 **7**

(Eq. 3)

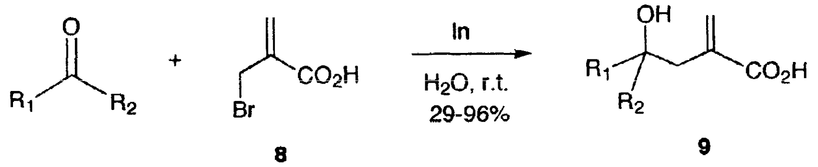
Araki *et al.* found that the allylation of aldehydes and ketones in aqueous medium can be carried out by using catalytic amounts of indium(III) chloride in combination with aluminum or zinc metal (Eq. 4).[10] This reaction was typically performed in a THF-water (5:2) mixture at room temperature. However, with this method, the conversion is much slower, relative to the same reaction mediated by use of a stoichiometric amount of indium; it requires days to complete. When the reaction was carried out in anhydrous THF, the yield dropped considerably, while side-reaction (such as reduction of the aldehyde to alcohol) increased. The combinations of Al-$InCl_3$ or Zn-$InCl_3$ gave comparable results.



(Eq. 4)

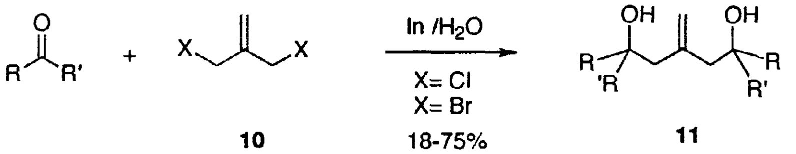
On the other hand, Whitesides and co-workers examined in a greater detail the effect of substituents and co-solvents on the allylic moiety on the indium mediated reactions in water.[11] They also found that the use of indium at room temperature gave results comparable to those of tin-mediated reactions carried out at reflux. Replacement of the aqueous phase with 0.1 N HCl further increased the rate of the reaction by shortening the initiation time. The indium-mediated reactions also provide cleaner products than the tin mediated ones. Various carbohydrates were allylated in good yields with high diastereoselectivity. Propargyl bromide also reacted to give a mixture of allylation and propargylation products.

More recently, Chan *et al.* reported that the carboxylic acid functionality on allyl halides is compatible with the indium-mediated reactions (Eq. 5).[12,13] Thus, when 2-(bromomethyl)acrylic acid (**8**), instead of its ester, was treated directly with carbonyl compounds and indium in water, the corresponding γ-hydroxyl-α-methylenecarboxylic acids **9** were generated in good yields. On the other hand, the same reaction in a mixture of THF/water generated the corresponding α-methylene-γ-lactone.[14]

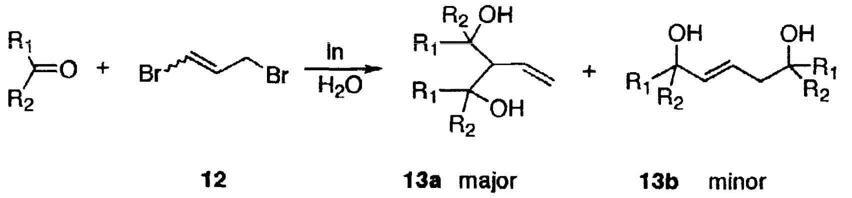


(Eq. 5)

Li reported that combination of 2-halomethyl-3-halo-1-propene **10** with carbonyl compounds mediated by indium in water generates bis-allylation products **11** (Eq. 6).[15] Such a system effectively constitutes a trimethylenemethane dianion equivalent in water. The bis-allylation of 1,3-dibromo-propene **12** with carbonyl compounds mediated by indium in water was reported by Li *et al.* (Eq. 7).[16] The reaction gave predominately 1,1-bis-allylation product **13a**.

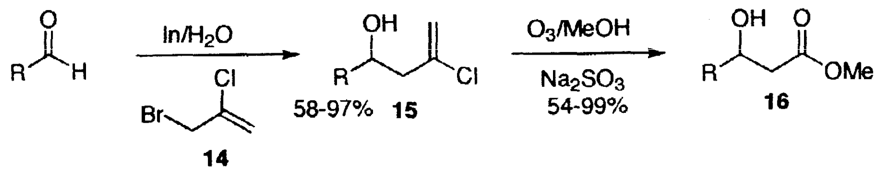


(Eq. 6)



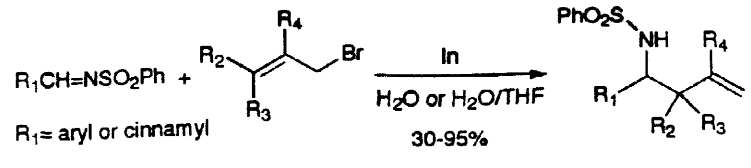
(Eq. 7)

In an effort to synthesize biologically important polyhydroxylated carboxylic acid derivatives, a general and effective methodology for the preparation of β-hydroxyl carboxylic esters is desired. While no apparent reaction was observed between indium and these substrates, it was found that various aldehydes can be alkylated with 3-bromo-2-chloro-1-propene (**14**) very efficiently mediated by indium in water at room temperature. Subsequent treatment of the compound **15** with ozone in methanol followed by work-up with sodium sulfite provided the desired hydroxyl esters **16** in high yield (Eq. 8).[17a] Very recently, Paquette and co-workers reported an indium-mediated reaction of methyl (E)-4-bromo-3-methoxycrotonate to aldehydes in water to give β-hydroxyesters. After hydrolysis of these esters, Knoevenagel-like adducts were generated.[17b]



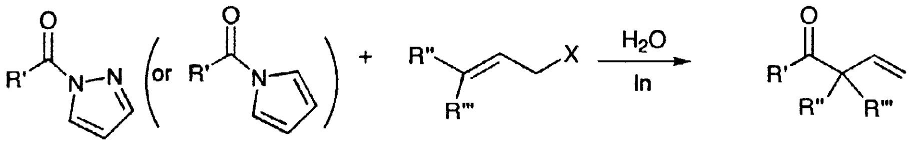
(Eq. 8)

In addition to the allylation of aldehydes and ketones, allylation of sulfonimines **17** (Eq. 9) to give homoallyl sulfonamides **18** was reported by Chan.[18] His group also reported the allylation of acyloyl-imidazoles **19** and pyrazoles **20** to give β,γ-unsaturated ketones **21** (Eq. 10).[19]



(Eq. 9)

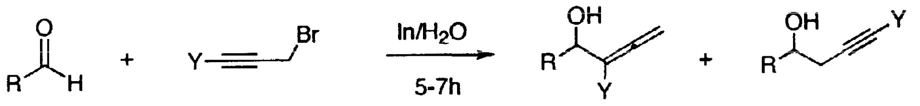
17 **18**



(Eq. 10)

19 **20** **21**

Chan *et al.* reported the behavior of aldehydes with propargyl bromides in aqueous medium mediated by indium (Eq. 11).[20] They found that simple prop-2-yn-1-yl bromide reacted with both aliphatic and aromatic aldehydes in water, to give mainly the homopropargyl alcohols. In contrast, when propargyl bromide is γ-substituted the coupling products were predominantly or exclusively the allenylic alcohols.



(Eq. 11)

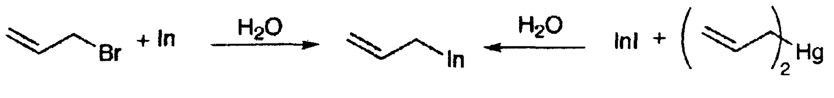
22 23 24

Y= H	Minor	Major
Y= alkyl, aryl, or silyl	Major or exclusive	Minor

2. 2. *Mechanism of Indium-Mediated Barbier-Type Reactions*

While it is not the intention of this review to discuss in full detail the mechanism of the indium-mediated Barbier-type reactions in water, it is nevertheless useful to give a brief description of our current understanding of the mechanism, since this will prove important for further development of the scope of such reactions and their applications in organic synthesis.

When the reaction was first discovered, it was proposed that the aqueous indium-mediated allylation reaction proceeds on the metal surface with a single electron transfer (SET) from the metal to the allyl bromide to generate a reactive radical anion species. Subsequently, it is accepted that an allylindium intermediate may actually be involved based on the experimental observation of Whitesides and his coworkers.[11] They found that an allylindium intermediate, whatever its structure, generated from the reaction of allylmagnesium bromide and indium trichloride in ether, can react with carbohydrates in ethanol/water (10/1) to give the corresponding homoallylic alcohols. More recently, Chan and Yang established that the transient but discrete diallylindium intermediate, generated in the reaction of allyl bromide with indium in water, has the allylindium (I) (**25**) structure.[21] Other experimental confirmation of the formation of allylindium (**25**) has alson been obtained from the reaction of diallylmercury (**26**) with indium (I) iodide in water.



25 **26**

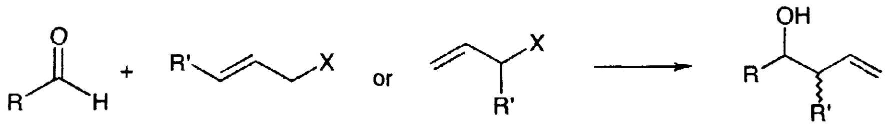
(Eq. 12)

The formation of indium(I) instead of indium(III) compounds from the reactions of allyl halides with indium metal is consistent with the previous observation that indium has a relatively low first ionization potential but relatively high second or third ionization potentials. In terms of the implication for organic synthesis, the reactions of other organoindium(I) compounds with electrophiles in water should be examined.

2.3. The Regio- and Stereochemistry of Indium-Mediated Reactions

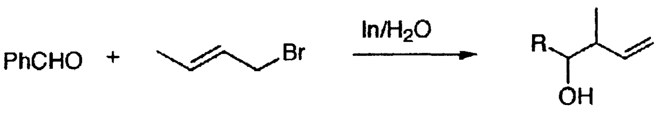
Regioselectivity

In terms of the regioselectivity of indium-mediated allylation in water, both electronic and steric effects operate. As in the case of allylations mediated by other metals in water, the carbon-carbon bond usually forms at the more substituted carbon of the allyl halide, irrespective of the position of halogen in the starting material (Eq. 13). However, the carbon-carbon bond forms at the less substituted carbon when the γ-substituents of allyl halides are large enough (e.g., trimethylsilyl or tert-butyl) as shown by Chan *et al.*[22] They have studied the regioselectivity in detail and several conclusions can be drawn.



(Eq. 13)

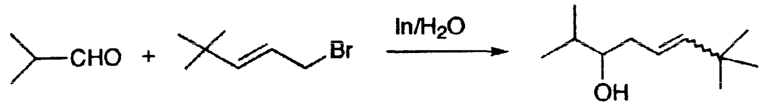
In general, the reaction gives the regioisomer where the substituent is alpha to the carbon-carbon bond to be formed. For example, in the coupling of crotyl bromide with benzaldehyde by indium in water, the product is exclusively the γ-coupled isomer **27** (Eq. 14).



(Eq. 14)

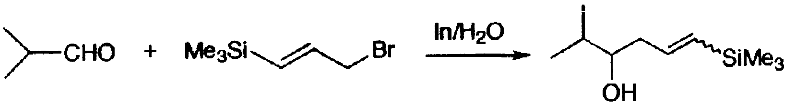
27

The regioselectivity is governed by the steric size of the substituent but not by the degree of substitution. This can be illustrated by the coupling of isobutyraldehyde with either the allyl bromide **28** or **30** to give **29** and **31** respectively. On the other hand, γ,γ-dimethylallyl bromide or the pinenyl bromide **33** reacted with benzaldehyde to give the adducts **32** and **34** respectively inspite of the high degree of substitution at the double bond (Eq. 15-18).



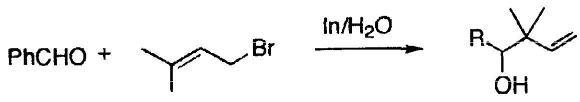
(Eq. 15)

28 29



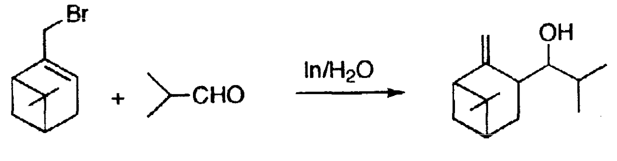
(Eq. 16)

30 31



(Eq. 17)

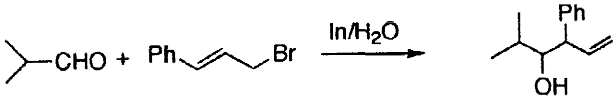
32



(Eq. 18)

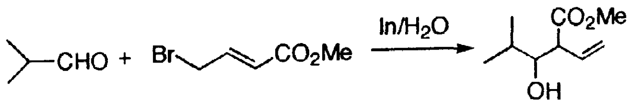
33 34

The presence of conjugation to the double bond does not affect the regiochemistry. This is shown in the coupling of E-cinnamyl bromide or methyl 4-bromo-E-crotonate with isobutyraldehyde (Eq. 19, 20). In both cases, the products **35** and **36** (both deconjugated) were obtained as the reaction product.



(Eq. 19)

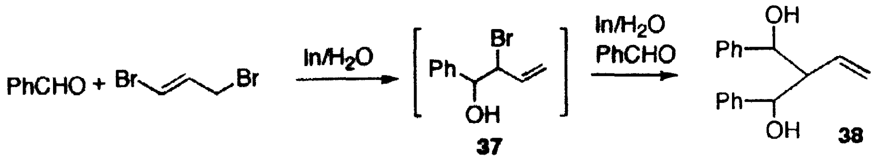
35



(Eq. 20)

36

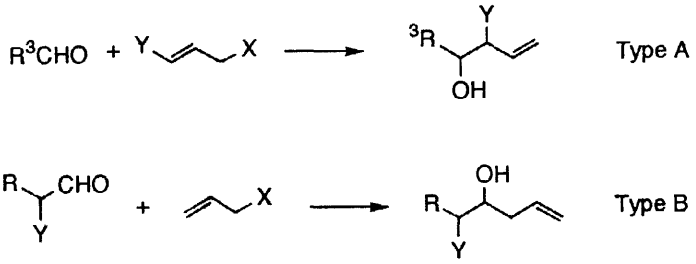
In addition, the regioselectivity is independant of the geometry of the double bond or the initial location of the substituent on the double bond. For example, either E- or Z-cinnamyl bromide coupled with isobutyraldehyde to give the same regioisomer **35**. In the reaction of 1,3-dibromopropene with benzaldehyde, the intermediate allylic bromide **37** must have the bromine α- to the substituent, and the second coupling must have occurred regioselectively to give the adduct **38** (Eq. 21).



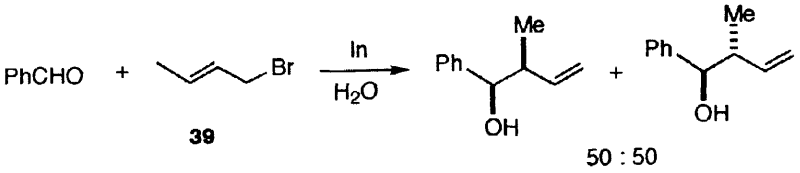
(Eq. 21)

Diastereoselectivity

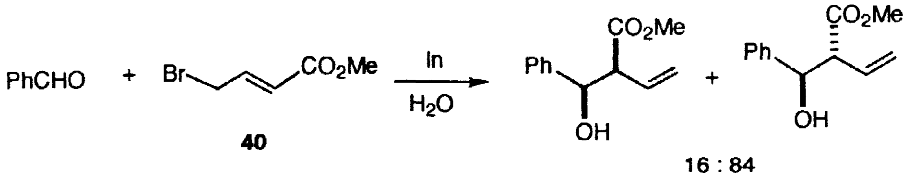
In terms of diastereoselectivity of the indium-mediated allylation reaction in water, two types of situation prevail (Type A and Type B).



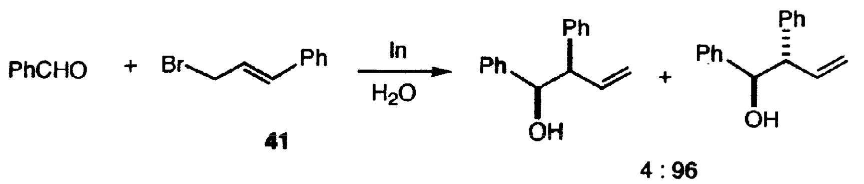
Within the type A situation, the diastereoselectivity depends on the substituents on both the aldehyde and the allylic halide, but not on the geometry of the double bond of the allylic halide as shown in Eqs. 22-24. For example, with **41**, the use of either the E- or the Z-cinnamyl bromide gave nearly the same diastereoselectivity. On the other hand, the reaction of **41** with different aldehydes resulted in diastereoselectivity which is dependant on the steric size of the substituent on the aldehyde. As the size increases from **42** to **43** to **44**, the anti-diastereoselectivity increases as well for the allylation (Eq. 25-27). Chan *et al.* explained the selectivity by involving a Zimmerman type transition state with the allylindium species and the carbonyl compounds as illustrated in Figure 1. However, when an adjacent heteroatom is present on the aldehyde moiety (e.g., glyoxylic acid and 2-pyridinecarboxaldehyde), syn selectivity was obtained.



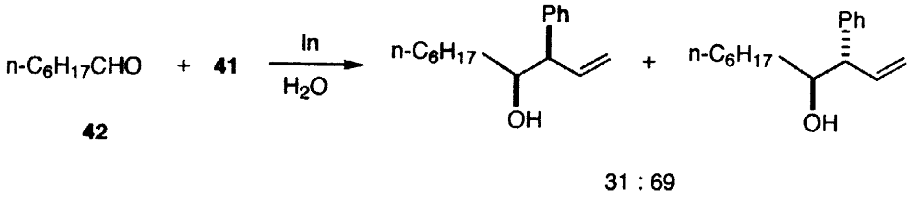
(Eq. 22)



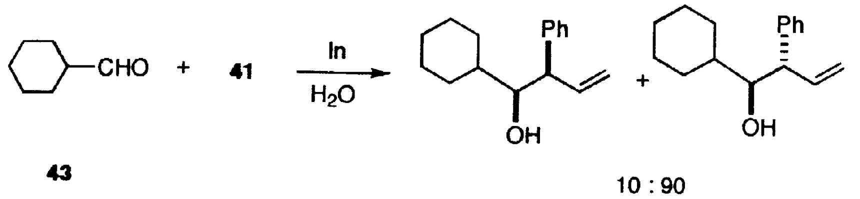
(Eq. 23)



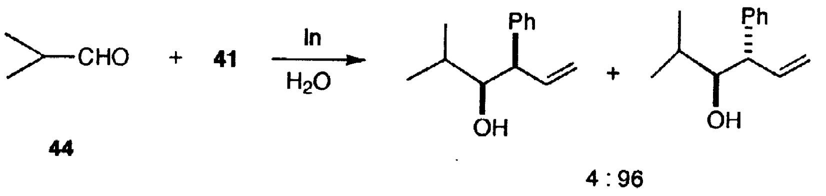
(Eq. 24)



(Eq. 25)



(Eq. 26)



(Eq. 27)

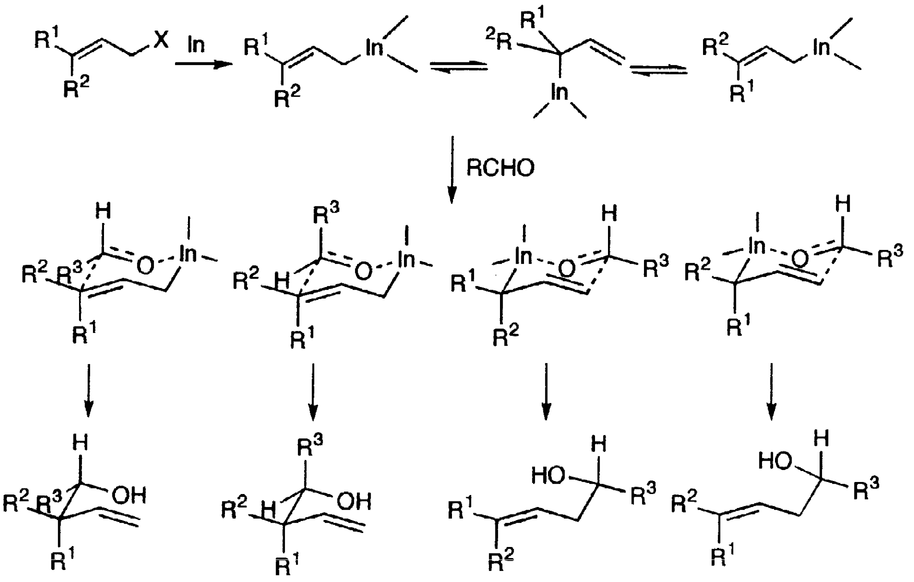
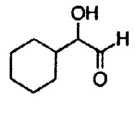
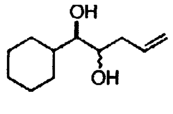
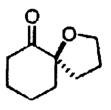
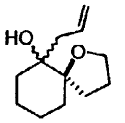
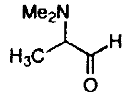
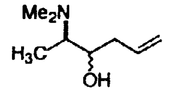
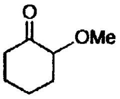
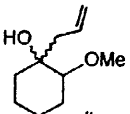
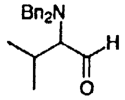
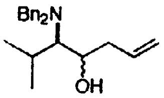
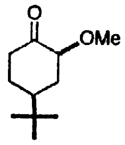
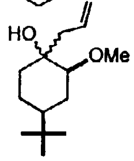
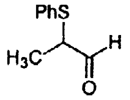
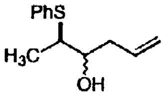
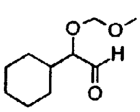
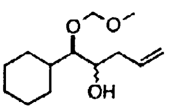
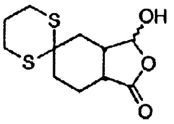
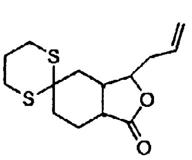
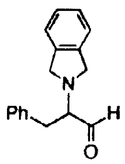
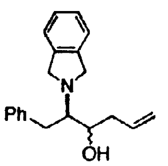
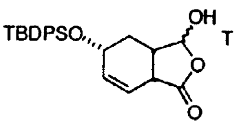
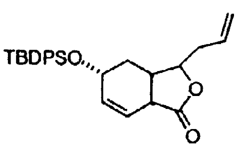


Figure 1.

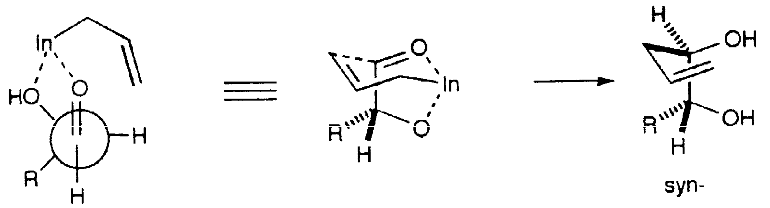
For the Type B situation, either syn or anti- diastereoselectivity can be favored depending on the properties of the α-substituents. The presence of a strong α-chelating group, such as a hydroxyl, generally leads to syn product, whereas a non α-chelating group, such as a methyl, produces anti-product. In the early studies by Chan and Li,[9] as well as Whitesides and co-workers,[11] significant diastereoselectivity was observed during allylation of carbohydrates with indium in water. However the presence of an α-alkoxyl group (a weak chelating group) often generates the non-chelating product in the aqueous organometallic reactions.[23] Thus, the anti-preference was obtained in the reactions of α-alkoxyaldehydes with allyl bromide/indium in water.[24]

The diastereofacial control of indium mediated allylations in aqueous media has been studied comprehensively by Paquette and co-workers by using many elegantly designed substrates involving various chelating groups and heteroatoms (including oxygen, sulfur and nitrogen, some examples are listed in Table 2).[25] It is argued that in this case, the allylindium intermediate coordinates with both the hydroxy and the carbonyl function as in **45**, leading to the syn adduct. In addition, Paquette and co-workers found that the presence of salts has a dramatic effect on the diastereofacial selectivity of the allylation reaction.

Table 2. Selected Examples of Chelation/Non-chelation Allylation of Aldehydes with Allyl Bromide and Indium in Water

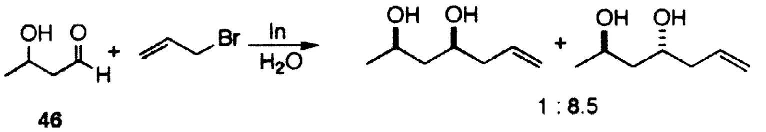
substrates	allylation products (chelate: non-chelate)		substrates	allylation products (chelate: non-chelate)	
		9.8 :1			2.7:1
		99:1			12.5:1
		1 :4			>97:3
		1 :4			
		2.1 :1			(β/α=) 6.5:1
		8.2:1			(β/α=) 9.6:1

For more detailed information, please see Ref. 25 by Paquette and co-workers.



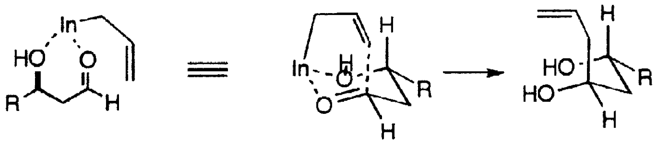
45

The same coordination is used to account for the observed anti- preference in the allylation of 3-hydroxybutanal (**46**) with allyl bromide/indium in water (Eq. 28). The intermediate **47** leads to the anti- product **48**. In support of the intramolecular chelation model, it is found that if the hydroxy group is converted to the corresponding benzyl or t-butyldimethylsilyl ether, the reaction is not stereoselective at all and gives nearly equal amounts of syn- and anti- products. Long range diastereofacial control with chelating groups on allylindium moiety has also been examined by both Mulzer's and Paquette's groups (Eq. 29).[26]

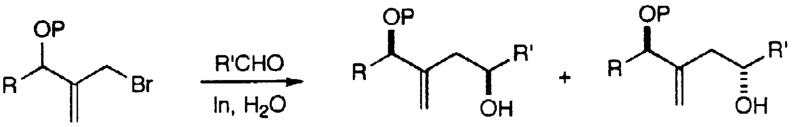


46

(Eq. 28)



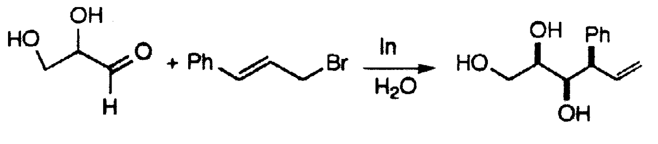
47 **48** anti-



(Eq. 29)

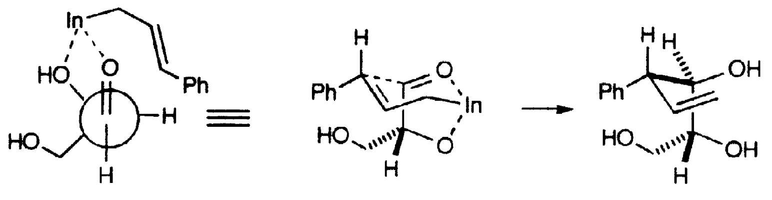
R=$(CH_3)_2CH$, P=TBS, R'=$(CH_3)_2CH$ 99:1

When both the type A and the type B situations are combined in the coupling of a chiral aldehyde with a substituted allylic halide, multi-stereogenic centers are formed. For example, in the coupling of unprotected aldoses (e. g., glyceraldehyde) with cinnamyl bromide (Eq. 30) two new stereogenic centers are created. The syn-, syn- isomer **49** is formed preferentially in this case. To account for the syn- syn- stereochemistry, chelation of the allylindium species with the hydroxy aldehyde function with intramolecular attack through the cyclic transition state **50** is postulated.[25]



(Eq. 30)

49 syn-, syn-



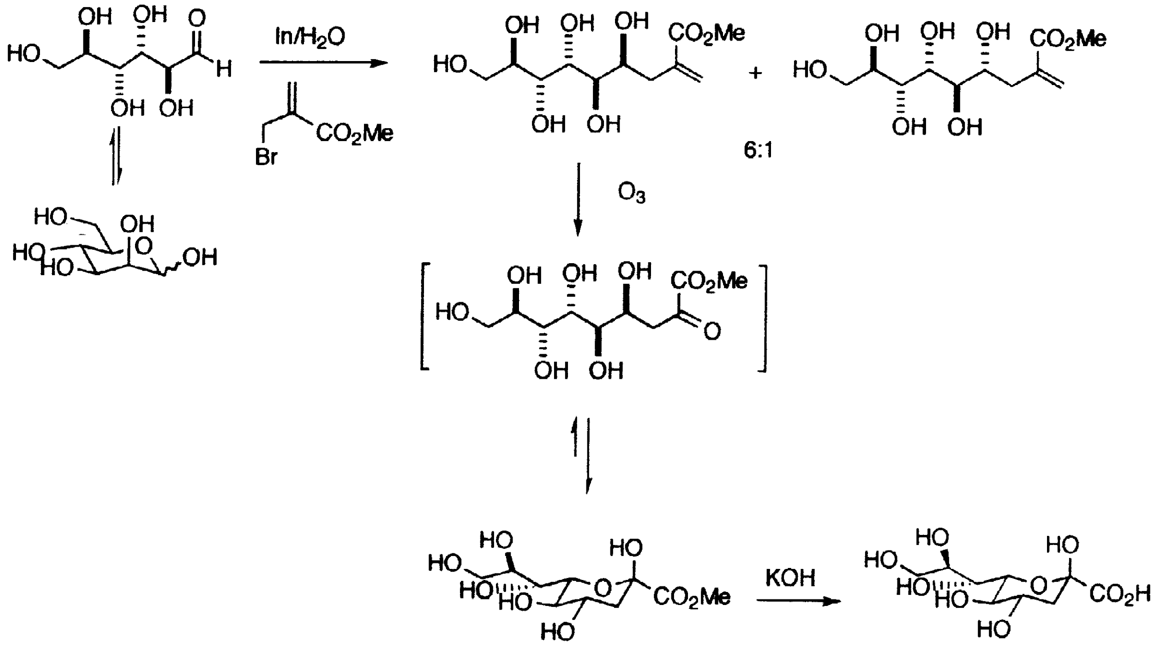
50

49 syn-, syn-

2.4. Synthetic Applications of Indium-Mediated Reactions

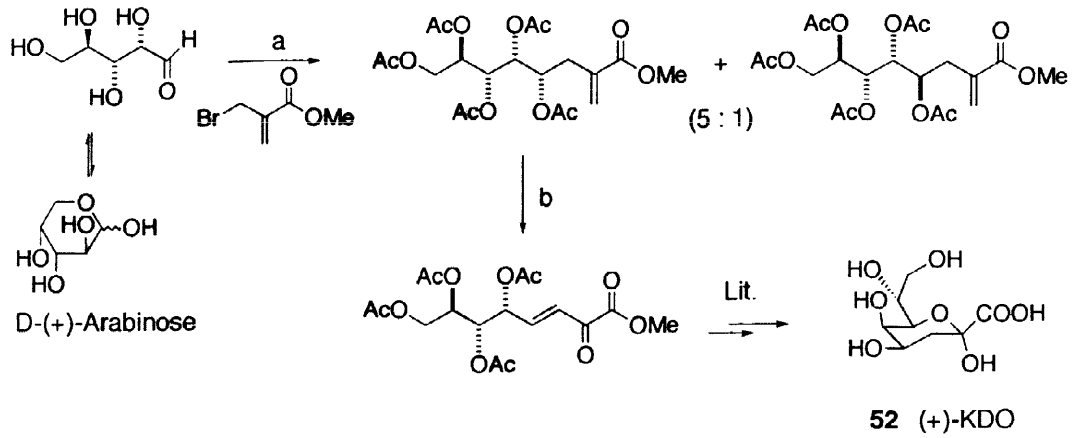
2.4.1. Synthesis of Sialic Acids and Carbohydrate Homologations

Following their success in accomplishing the indium-mediated allylation reaction in water, Chan and Li reported[9] an efficient synthesis of (+)-3-deoxy-D-*glycero*-D-*galacto*-nonulosonic acid (KDN, **51**)(Scheme 1). A similar attempt toward 3-deoxy-D-manno-octulonate (KDO, **52**) led primarily to the undesired diastereomer.[27]



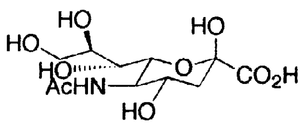
51 (+) KDN

Scheme 1.



Scheme 2. a). In/ H_2O, vigorous stirring, then Ac_2O/pyridine/DMAP, 79%; b). O_3/methylene chloride -78°C to r.t., then column chromatography, 67%

Whitesides and co-workers reported the synthesis of N-acetyl-neuraminic acid (**53**),[28] as well as other sialic acid derivatives (**54** and **55**), based on the indium strategy. The use of indium is essential for the carbon-carbon bond forming step in these sialic acid syntheses. KDO was synthesized *via* indium-mediated allylation of 2,3:4,5-di-O-isopropylidene-D-arabinose (Scheme 3).[29] In this case, the desired diastereomer predominated due to the protection of α-hydroxyl group.



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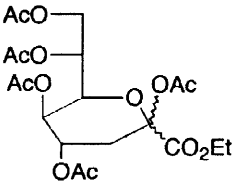

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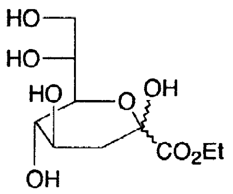

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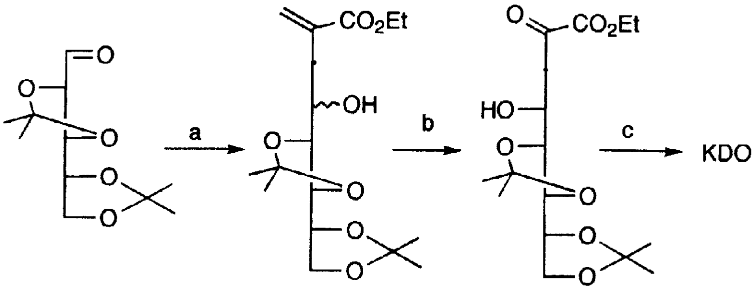
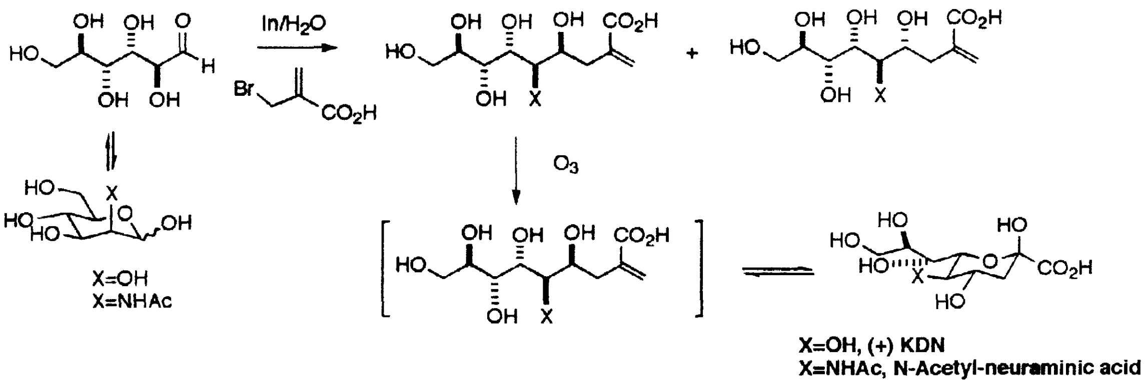


erythro: threo = 2: 1

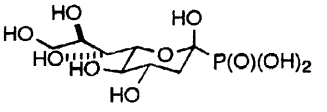
Scheme 3. a). In/ethyl a-(bromomethyl)acrylate, 10% formic acid, aqueous MeCN, 61%; b). O_3, MeOH, -78°C to r.t. 92%, c). TFA, NH_4OH, 55%.

Recently, Chan *et al.* made more progress in sialic acid synthesis and have further shortened the already short route to two steps through the indium mediated reaction of α-(bromomethyl)acrylic acid with sugars (Scheme 4). Both KDN and N-acetyl-neuraminic acid were synthesized in this way.[30]

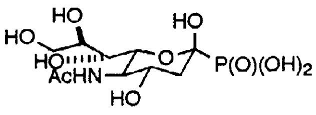


Scheme 4.

Phosphonic acid analogues **56** and **57** of both KDN and N-acetylneuraminic acid have been synthesized using the indium-mediated coupling of the lower carbohydrates with dimethyl 3-bromopropenyl-2-phosphonate (**58**) in water.[31]



56



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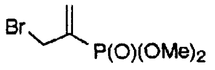
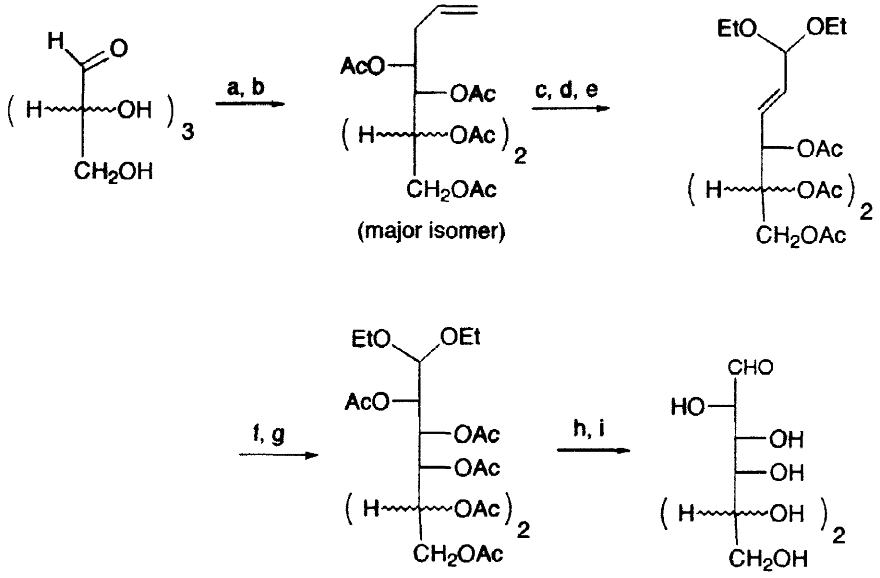
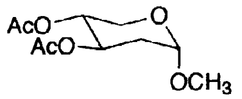


58

Following their early studies on tin-mediated carbohydrate homologation,[32] Whitesides and co-workers examined the homologation of various carbohydrates by using indium-mediated allylation reactions.[11] The indium-mediated reaction was found to provide cleaner product and better diastereoselectivity than the corresponding tin-mediated reactions. The indium-mediated allylation reaction has been applied by Schmid *et al.* to the elongation of the carbon chain of carbohydrates in forming higher analogs (Scheme 5)[33] and to deoxy sugars (**59-62**).[34] Many carbohydrate compounds were converted to their higher analogs by this method. The reaction has also been applied to erythrose.[35]



Scheme 5. a. In/allyl bromide, ultrasound; b. Ac_2O/pyridine/DMAP; c. OsO_4, KIO_4; d. TBAF; e. $H^+/HC(OEt)_3$; f. OsO_4, NMNO; g. Ac_2O/pyridine/DMAP; h. NaOMe/MeOH; i. H^+.



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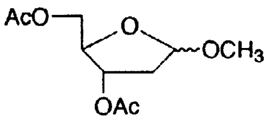

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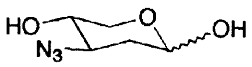

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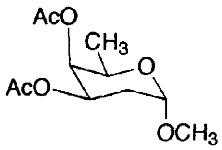
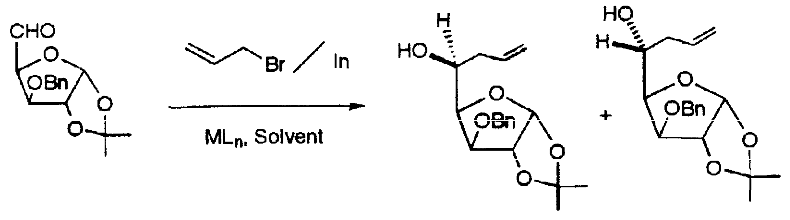


62

Loh *et al.* reported the reaction of the glucose-derived aldehyde with ally bromide mediated by indium (Eq. 31).[36] The reaction again gives a non-chelation product as the major diastereomer. The use of an organic co-solvent increases the diastereoselectivity. The addition of ytterbium trifluoromethanesulfonate [Yb(OTf)$_3$] enhances both the reactivity and the diastereoselectivity. Other Lewis acids also catalyze the reaction.[37]

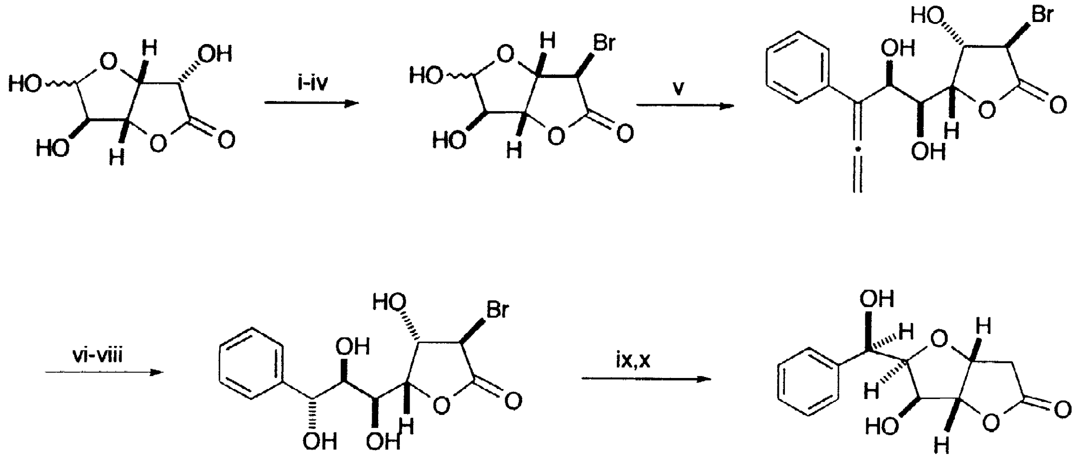


(Eq. 31)

H_2O (10h)	41/59
H_2O-THF(4/1) (10h)	24/76
H_2O-DMF(4/6) (2h)	17/83
H_2O-DMF(4/6)-Yb(OTf)$_3$ (1h)	6/94

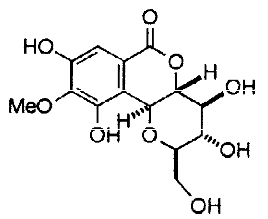
2.4.2. *Styryl Carbohydrates*

There are a number of styryl carbohydrates found in nature that possess important biological activities. By using the indium-mediated allenylation reaction, Li and co-workers developed the synthesis of the aniti-viral, anti-tumor compound (+)-goniofufurone (**63**),[38] a key component isolated from the Asian trees of the genus *Goniothalamus* (Scheme 6).[39] (+)-Bergenin (**64**) is another styryl carbohydrate derivative that exhibit various biological activities **65**.[40] During their studies of total synthesis of (+)-bergenin, Li *et al.* reported the formation of aryl δ-lactones, a key step toward the synthesis of bergenin and its derivatives, by using the indium methods.[41] The solvent was found to have an effect on the product formation. For example, indium-mediated coupling between the bromde and benzaldehyde under indentical conditions resulted, instead of the δ-lactone, in a 1,3-butadiene derivative **66** as the major isolated product in which the two aromatic moieties located on the same side of the carbon-carbon double bond existed in a cis relationship (Eq. 32).[42]

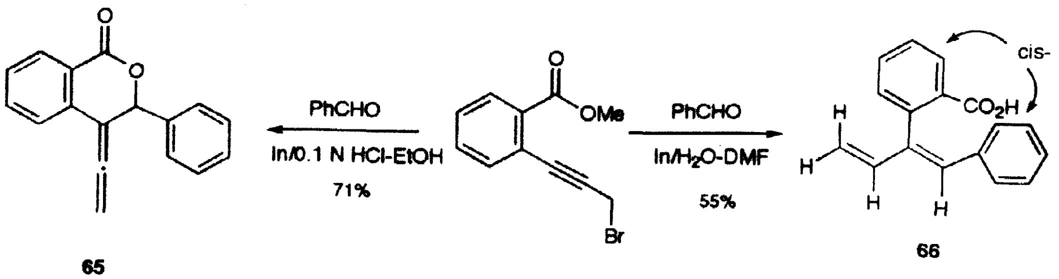


63 (+)-Goniofufurone

Scheme 6: i). acetone, H_2SO_4, r.t., 5h, 86%; ii). Tf_2O, Py, CH_2Cl_2, -40°C, 94%; iii). LiBr, acetone, r.t., 1h, 97%; iv). TFA-H_2O (3:1), r.t., 4.5 h, 98%; v). Phenylpropargyl bromide, In, 0.1 N HCl-EtOH (1:9), r.t., 14 h; vi). O_3, MeOH, -78°C, then Me_2S; vii). $NaBH_4$, MeOH, -10°C, 30 min, then AcOH quench; viii). H_2SO_4, Ac_2O, r.t., 75% for three steps; ix). Na_2SO_3, MeOH-H_2O, r.t., 3 h, quant.; x). HCl(g), MeOH, r.t., 2d, 44% for two steps.



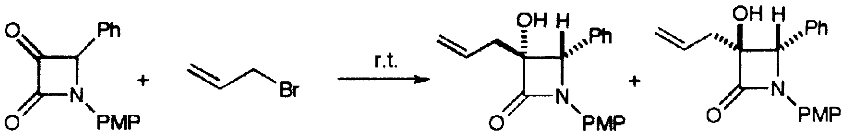
64 (+)-Bergenin



(Eq. 32)

2.4.3. *β-Lactams*

Both Bose[43] as well as Paquette[44] have applied the indium-mediated allylation in water to the synthesis of β-lactams. Bose reported that the allylation of azetidin-2,3-diones with allyl bromide and indium in water/THF mixture provided consistently high yield in a case in which zinc gave a very poor results (Eq. 33). In addition, a single diastereomer was obtained with the indium method, whereas the use of zinc often provides a 1:1 mixture of diastereomers. When crotyl bromide was used, diastereo-control was able to be achieved with indium in water/THF over three stereogenic centers in one step. A more comprehensive investigation of related reactions was carried out by Paquette and co-workers.[44]

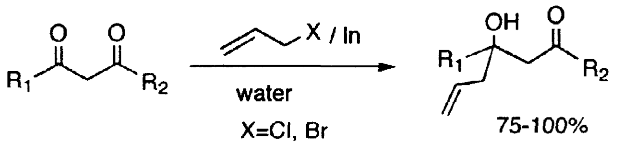


(Eq. 33)

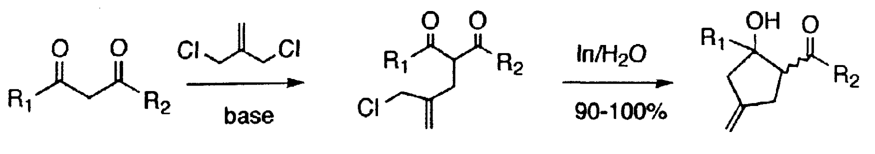
Zn/NH$_4$Cl, THF	1:1
In/H$_2$O, THF	*anti* only

2.4.4. *Carbocycles*

Li *et al.* reported that enolizable 1,3-dicarbonyl compounds undergo efficient carbonyl allylation reactions in aqueous medium (Eq. 34).[45] The reaction is general and a variety of 1,3-dicarbonyl compounds have been alkylated successfully using allyl bromide or allyl chloride in conjunction with either tin or indium. The corresponding 1,3-carbonyl cyano compound can be allylated similarly.[46] The reaction can be used readily for the synthesis of cyclopentane derivatives (Eq. 35).[47]

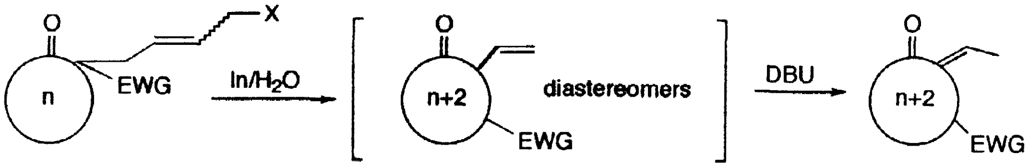


(Eq. 34)



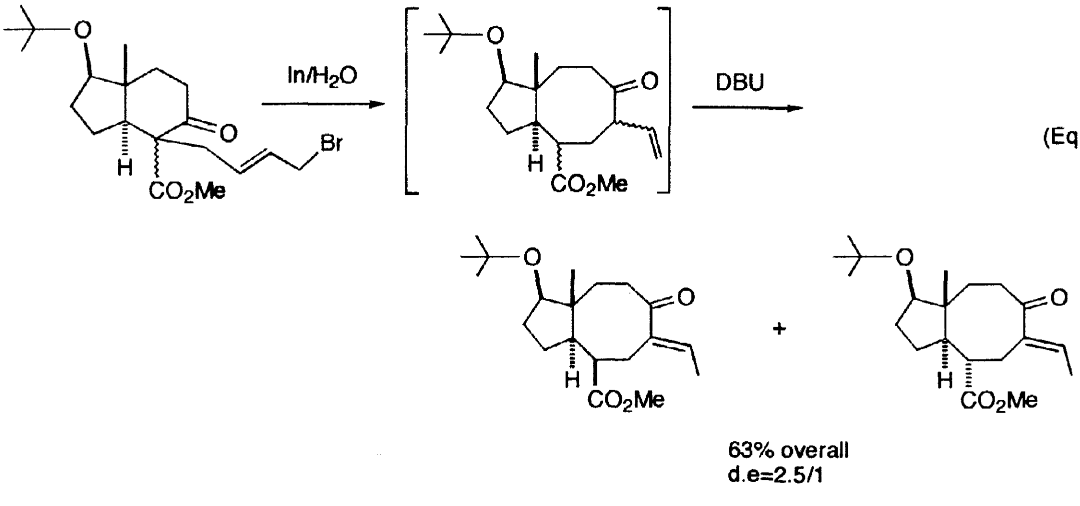
(Eq. 35)

A related application of aqueous Barbier-type reaction in organic syntheses is a carbocycle ring enlargment methodology developed by Li *et al.*[48] By using the indium-mediated Barbier-type reaction in water, five-, six-, seven-, eight-, and twelve-membered rings are enlarged by two carbon atoms into seven-, eight-, nine-, ten-, and fourteen-membered ring derivatives respectively (Eq. 36). The use of water as a solvent was found to be critical for the success of the reaction. Similar ring expansion in organic solvents was not successful. The ring expansion has also been applied to the synthesis of a heterocyclic medium ring.[49] One carbon-ring expansions were reported similarly.[50]

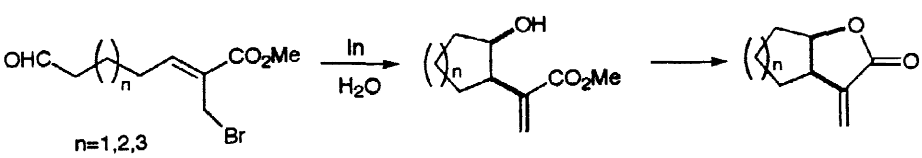


(Eq. 36)

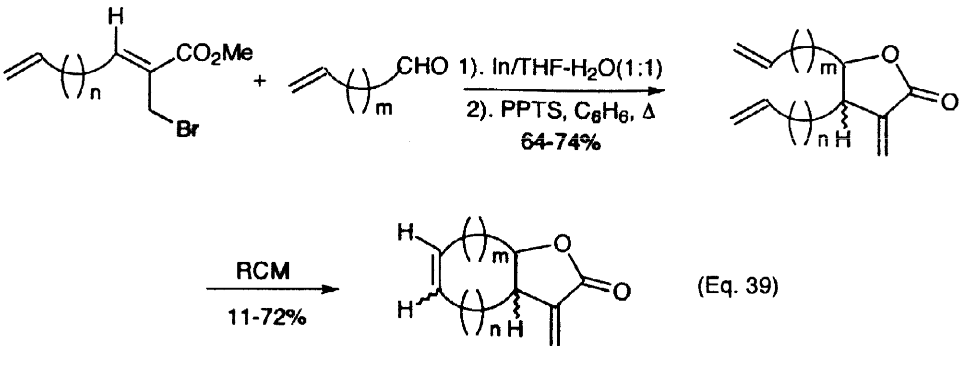
A five-six fused ring system was also efficiently transformed into a five-eight fused ring compound (Eq. 37).[51] Indium-mediated intramolecular carbocyclization in aqueous media generated fused α-methylene-γ-butyrolactones (Eq. 38).[52] An indium-mediated α-methylene-γ-butyrolactone formation and a ruthenium catalyzed ring-closing metathesis (RCM) was eligantly combined by Paquette and co-workers recently to form α-methylene-γ-butyrolactone fused to medium and large rings (Eq. 39).[53]



(Eq. 37)



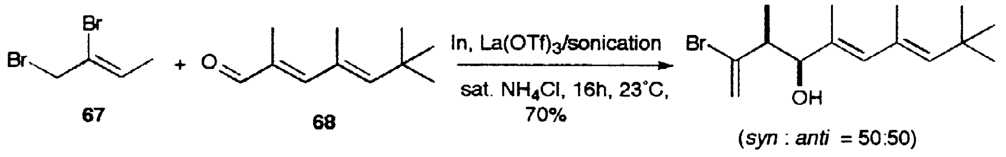
(Eq. 38)



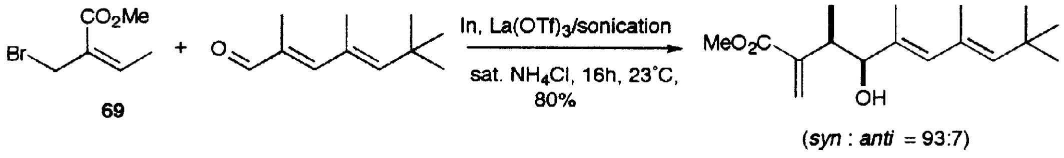
(Eq. 39)

2.4.5. Other Examples

Indium-mediated allylation of aldehyde[54] was used to synthesize an advanced intermediate in the synthesis of antillatoxin,[55] a marine cyanobacteria (*Lyngbya majuscula*) which is an ichthyotoxic compound isolated from a marine plant. In the presence of a lanthanide triflate, the indium-mediated allylation of Z-2-bromocrotyl chloride **67** and aldehyde **68** in saturated NH_4Cl under sonication yielded the desired advanced intermediate in a 1:1 mixture of diasteromers in 70% yield (Eq. 40). Loh *et al.*[56] then changed the halide compound to methyl (Z)-2-(bromomethyl)-2-butenoate (**69**) and coupled it with aldehyde **68** under the same conditions to yield the desired homoallylic alcohol in 80% yield with a 93:7 *syn:anti* selectivity (Eq.41).

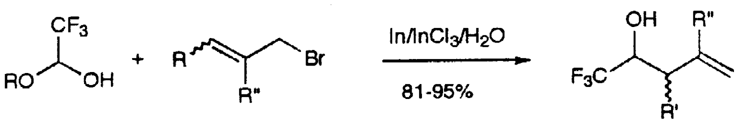


(Eq. 40)



(Eq. 41)

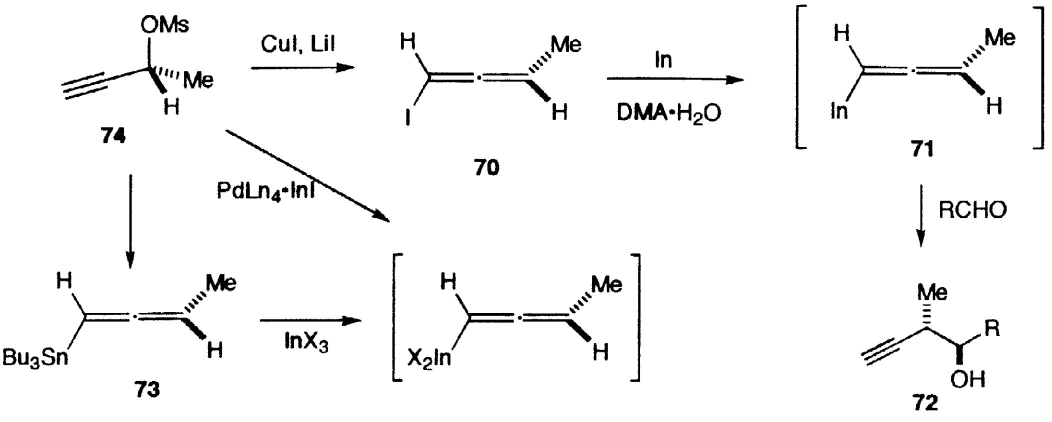
The indium-mediated allylation of trifluoroacetaldehyde hydrate (R=H) or trifluoroacetaldehyde ethyl hemiacetal (R=Et) with an allylic bromide in water yielded α-trifluoromethylated alcohols (Eq. 42).[57] Lanthanoid triflate-promoted indium-mediated allylation of aminoaldehyde in aqueous media generated β-aminoalcohols stereoselectively.[58]



(Eq. 42)

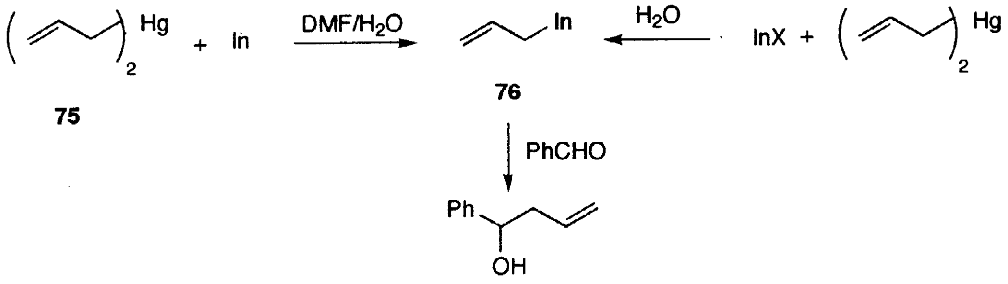
III. Transmetalation Reactions with Indium Metal or Indium Salts

Less explored but potentially useful is the formation of the transient, or even stable, organoindium reagents through transmetallation reactions. The earliest example was the reaction of allylmagnesium bromides with indium trichloride. An allylindium intermediate was presumably formed, and the transient reagent reacted with carbohydrates in ethanol/water (10/1) to give the corresponding homoallyl alcohols.[11] Marshall *et al.* reported[59] that the allenyliodide **70** reacted with indium in DMA/H_2O to give the presumed allenylindium intermediate **71** which coupled with aldehydes to give the corresponding homopropargyl alcohols **72**. The same presumed allenylindium intermediate can be generated from allenylstannane **73** and indium(III) halides or from the palladium (Pd(dppf)Cl_2] catalyzed reaction of propargyl mesylate **74** with indium(I) iodide in organic solvents (Scheme 7).



Scheme 7.

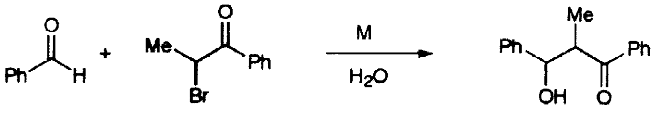
Chan *et al* reported that diallylmercury **75** which is stable in water can undergo transmetalation reaction with either indium or indium(I) iodide in aqueous media to give the corresponding allylindium(I) (**76**) (Scheme 8).[21] The reagent coupled with aldehydes and ketones to give the corresponding homoallyl alcohols. One synthetic advantage of generating the allylindium reagent in this manner is that functional groups which are reduced by the metal may still be tolerated under these conditions.



Scheme 8.

IV. Other Indium-Mediated Reactions

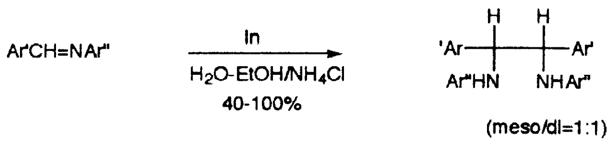
Indium was also found to effect cross-aldol and Reformatsky-type reactions of aromatic aldehydes with α-halogenated carbonyl compounds.[12] Compared with the reactions mediated by tin or zinc, the cross-aldol reaction between an aldehyde and a secondary α-bromo-ketone mediated by indium in water resulted in a slight improvement in yield but a sharp increase in diastereoselectivity (Eq. 43). Similar cross-coupling between aromatic aldehydes and α-halogenated caroxylic acids or their esters resulted in a modest yield of the products (0-52%).



(Eq. 43)

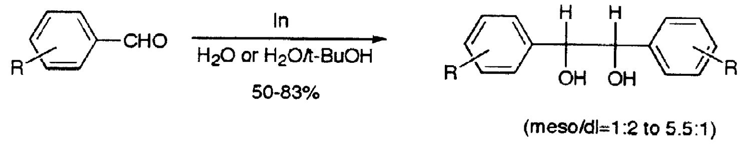
method	yield (%)	*erythro:threo*
Zn, 45°C	82	2.5:1
Sn, 80°C	67	1:1.1
In, r.t.	85	12:1

Reductive coupling of aldimines obtained frorm aromatic aldehydes and aromatic amines to generate vicinal diamines mediated by indium was carried out in aqueous ethanol (Eq. 44).[60] Small indium rods were used in this study. No side product due to unimolecular reduction was observed. The presence of NH_4Cl was found to accelerate the reaction. The reaction fails completely in CH_3CN, DMF, or wet DMF. The use of non-aromatic substrates also resulted in the failure of the reaction.



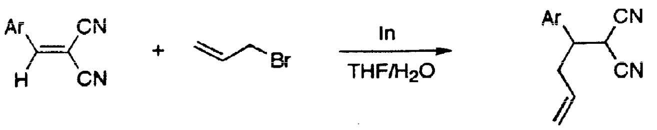
(Eq. 44)

Under sonication, Kim and co-workers[61] found that aromatic aldehydes homo-coupled to generate pinacol-type products (Eq. 45). The reaction occurred in neutral aqueous media over 8 to 22 hrs. In the absence of sonication, the reaction was much slower and the yield of the product was decreased by a factor of 2 to 3. Interestingly, the reaction did not proceed under nitrogen protection! Water alone or a 1:1 mixture of water and t-BuOH were used in these reactions. Aliphatic aldehydes and ketones are inert under the reaction conditions. Solid aldehydes resulted in poor yield of the product or no product.



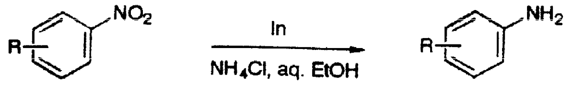
(Eq. 45)

It was reported that indium-mediated Michael addition of allyl bromide to 1,1-dicyano-2-arylethenes proceeded well in aqueous medium (Eq. 46).[62] By reacting indium and α-bromoketones with sodium alkyl thiosulfates, phenacyl sulfides was generated in water (Eq. 47).[63] On the other hand, a similar reaction with diselenides generated α-selenoketones.[64] Coupling of sulfonyl chlorides with alkyl bromides in water mediated by indium was reported to generate sulfones.[65] A novel synthesis of allyl and propargyl selenides in aqueous media promoted by indium was reported by Zhang and co-workers.[66] Recently, indium in aqueous medium has been used by Moody and Pitts in the reduction of nitro aromatics to anilines and the reduction of heterocyclic rings in quinolines, isoquinolines and quinoxalines (Eq. 48, 49).[67]

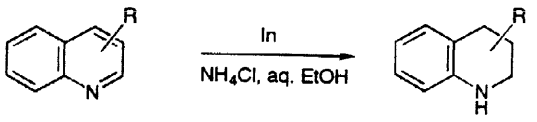


(Eq. 46)

(Eq. 47)



(Eq. 48)



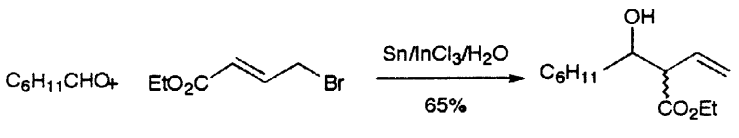
(Eq. 49)

V. *Indium Salts as Water-Tolerant Lewis Catalysts*

Earlier, under anhydrous conditios, Mukaiyama *et al.*[68] have used the $InCl_3$-TMSCl catalyst system for the reaction of O-trimethylsilyl monothioacetals with triethylsilane and other silylated carbon nucleophiles and the $InCl_3$-TBSCl catalyst system[69] for the reaction of aldehydes with t-butyldimethylsilyl enol ethers to yield the corresponding aldol adducts. The effectiveness of indium triflate on the Pd-catalyzed trimethylenemethane (TMM) reaction yielding a five membered ring through a conjugate addition followed by cyclization was reported by Trost.[70] The addition of 10 mol% of indium redirects the reaction from 1,4 addition to 1,2 addition with enones. Indium trichloride has also been used in the allyltin reaction of carbonyl compounds.[71] More recently, the use of indium salts as water-tolerant Lewis acids has been investigated in several reactions.

5.1. *Barbier-Type Reactions*

The use of a catalytic amount of indium trichloride in combination with stoichiometric amounts of zinc or aluminum for carbonyl allylation in water was initially investigated by Araki.[10] The reaction was much less effective than the use of indium metal. Allylindium was proposed as the reaction intermediate. Marshall[70] observed that indium trichloride allylation of cyclohexanecarboxaldehyde with allyltin proceeded well in aqueous ethanol. On the other hand, Loh *et al.* reported that in the presence of indium trichloride, tin-mediated additions of allyl bromides to aldehydes and aldoses leads to the adduct (Eq. 50).[72]

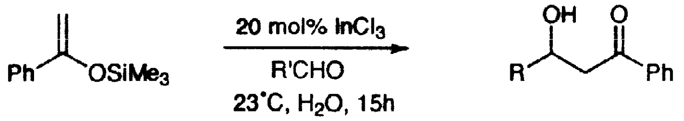


ant:syn = 99:1

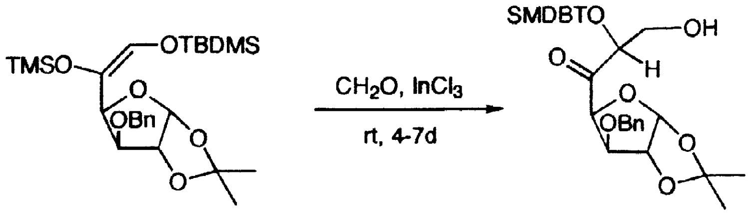
(Eq. 50)

5.2. *Mukaiyama-Aldol Reactions*

Indium trichloride is an efficient catalyst in Mukaiyama type reactions of silyl enol ethers and aldehydes in water at room temperature to yield the corresponding aldol products in good yields (Eq. 51).[73] However, it was found that the use of a micellar system by adding a small amount of surfactant in water is more effective as the media for such reactions.[74] The reaction has been applied to the carbon-chain elongation of a glucose derivative (Eq. 52).[75]

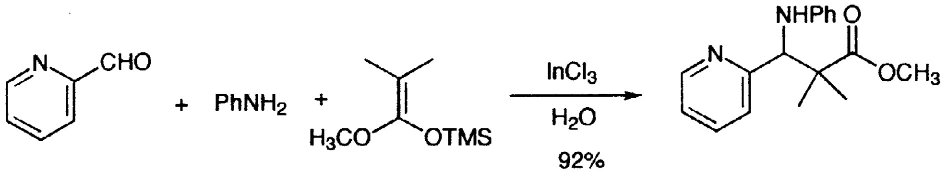


(Eq. 51)



(Eq. 52)

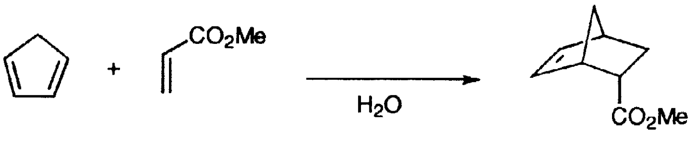
A closely related reaction is the addition of silyl enol ethers to imines. In the presence of 20 mol% indium trichloride, an aldehyde, an amine, and an ester derived silyl enol ether were reacted in water in a one-pot Mannich-type reaction to yield ß-amino ketones and esters (Eq. 53).[76] In the absence of indium trichloride, only starting material was recovered.



(Eq. 53)

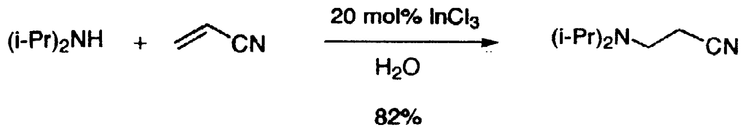
5.3. *Other Reactions*

For Diels-Alder reactions in water, indium trichloride has been used as a catalyst. Several dienes were reacted with different dienophiles at room temperature, in the presence of 20 mol % of indium trichloride (Eq. 54). The reaction works well with either cyclic or acylic dienes. The reaction of acrolein with cyclopentadiene with 20 mol% indium trichloride was complete in two hours with 100% yield and 90:10 *endo/exo* selectivity while the same reaction without indium trichloride had a 60% yield and a 74:26 *endo/exo* selectivity.[77] Indium trichloride also catalyzed conjugate addition of amines to α,β-ethylenic compounds in water (Eq. 55).[78] On the other hand, indium triflouride was found to be effective in catalyzing the addition of TMSCN to aldehyde in water.[79]



(Eq. 54)

20 mol% $InCl_3$ 100% endo:exo=90:10
without $InCl_3$ 100% endo:exo=74:26



(Eq. 55)

VI. Conclusions

The synthetic advantages of using indium-mediated reactions in aqueous has been demonstrated in this review. However, the full synthetic potential of such reactions is still waiting to be explored. It can be expected that the use of indium-mediated and -catalyzed reactions in aqueous solvents for synthetic purposes will gain further attention.

VII. Acknowledgments

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Note Added in Proof.

Indium-mediated Barbier-type allylation and propargylation reactions of 6-oxopenicillanate and 7-oxocephalosporanate was reported by Cho *et al.* see: Cho, Y.S.; Lee, J.E.; Koh, H.Y. *Tetrahedron Lett.* **1999**, *40*, 1725; Indium-promoted formation of α-methylene-γ-butyrolactams from 2-(bromomethyl)acrylic acid and aldimines was reported by Yus *et al.* see: Choudhury, P. K.; Foubelo, F.; Yus, M. *J. Org. Chem.* **1999**, *64*, 3376; A novel, simple, chemoselective and practical protocol for the reduction of azides using In/NH_4Cl was reported by Reddy *et al.* see: Reddy, G.V.; Rao, G.V.; Iyengar, D.S. *Tetrahedron Lett.* **1999**, *40*, 3937.

XII. References

1. For earlier reviews related to indium reactions, see: Cintas, P. *Synlett* **1995**, 1087; Chan, T.H. *Pure Appl. Chem.* **1996**, *68*, 919; Hashmi, A. S. K. *J. Prakt. Chem. Chem. Zeit.* **1998**, *340*, 84; Paquette, L. A. in *Green Chemistry, frontiers in benign Chemical Syntheses and Processes*, Eds. Anastas, P. and Williamson, T. C. Oxford University Press, New York 1998; Li, C. J.; Chan, T. H. *Organic Reactions in Aqueous Media*, John Wiley & Sons, New York 1997. See also: Li, C. J.*Chem. Rev.* **1993**, *93*, 2023; Chan, T. H.; Li, C. J.; Lee, M. C.; Wei, Z. Y. *Can. J. Chem.* **1994**, *72*, 1181; Li, C. J.*Tetrahedron* **1996**, *52*, 5643; Lubineau, A.; Auge, J.; Queneau, Y. in *Organic Synthesis in Water*, Ed. Grieco, P. A. Blackie Academic & Professional, Glasgow, 1998.
2. Gilman, H.; Jones, R. G. *J. Am. Chem. Soc.* **1940**, *62*, 2353.
3. Chao, L. C.; Rieke, R. D. *J. Org. Chem.* **1975**, *40*, 2253; Rieke, R. D.; Hanson, M. V. *Tetrahedron* **1997**, *53*, 1925-1956.
4. For examples, see: Araki, S.; Shimizu, T.; Johar, P. S. *J. Org. Chem.* **1991**, *56*, 2538 and refs. cited therein.
5. Li, C. J.; Chan, T. H. *Tetrahedron Lett.* **1991**, *32*, 7017.
6. Nokami, J.; Tamaoka, T.; Ogawa, H.; Wakabayash, S. *Chem. Lett.*. **1986**, 541; Uneyama, K.; Ueda, K.; Torii, S. *Chem. Lett.* **1986**, 1201; Talaga, P.; Schaeffer, M.; Benezra, C.; Stampf, J. L. *Synthesis* **1990**, 530; Zhou, J. Y.; Lu, G. D.; Wu, S. H. *Synth. Commun.* **1992**, *22*, 481.
7. Mattes, H.; Benezra, C. *Tetrahedron Lett.* **1985**, *26*, 5697.
8. Li, C. J. *Ph. D. Thesis*, McGill University, 1992.
9. Chan, T. H.; Li, C. J., *J. Chem. Soc., Chem. Commun.* **1992**, 747.

10. Araki, S.; Jin, S. J.; Idou, Y.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1736.
11. Kim, E.; Gordon, D. M.; Schmid, W.; Whitesides, G. M. *J. Org. Chem.* **1993**, *58*, 5500.
12. Chan, T. H.; Li, C. J.; Lee, M. C.; Wei, Z. Y. *Can. J. Chem.* **1994**, *72*, 1181.
13. Chan, T. H.; Lee, M. C. *J. Org. Chem.* **1995**, *60*, 4228.
14. Choudhury, P. K.; Foubelo, F.; Yus, M. *Tetrahedron Lett.* **1998**, *39*, 3581.
15. Li, C. J. *Tetrahedron Lett.* **1995**, *36*, 517.
16. Chen, D. L.; Li, C. J. *Tetrahedron Lett.* **1996**, *37*, 295.
17. a). Yi, X.H.; Meng, Y.; Li, C. J. *Tetrahedron Lett.* **1997**, *38*, 4731; b). Paquette, L. A.; Kern, B. E.; Mendez-Andino, J. *Tetrahedron Lett.* **1999**, *40*, 4129.
18. Chan, T. H.; Lu, W. *Tetrahedron Lett.* **1998**, *39*, 8605.
19. Bryan, V. J.; Chan, T. H. *Tetrahedron Lett.* **1997**, *38*, 6493.
20. Issac, M. B.; Chan, T. H. *J. Chem. Soc., Chem. Commun.* **1995**, 1003.
21. Chan, T. H.; Yang, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3229.
22. Isaac, M. B.; Chan, T. H. *Tetrahedron Lett.* **1995**, *36*, 8957.
23. Chan, T. H.; Li, C. J. *Can. J. Chem.* **1992**, *70*, 2726.
24. Paquette, L.; Mitzel, T. M. *J. Am. Chem. Soc.* ***1996***, **118**, 1931.
25. For a review, see: Paquette, L. A. in *Green Chemistry, frontiers in benign Chemical Syntheses and Processes*, Eds. Anastas, P. and Williamson, T. C. Oxford University Press, New York 1998. For more detailed information, see: Paquette, L. A.; Rothhaar, R. R.; Isaac, M.; Rogers, L. M.; Rogers, R. D. *J.Org. Chem.* **1998**.*63*, 5463; Lobben, P. C.; Paquette, L. A. *J.Org. Chem.* **1998**.*63*, 6990; Paquette, L. A.; Mendez-Andino, J. L. *J.Org. Chem.* **1998**.*63*, 9061; Paquette, L. A.; Mitzel, T. M.; Isaac, M. B.; Crasto, C. F.; Schomer, W. W. *J. Org. Chem.* **1997**, *62*, 4293; Paquette, L. A., Bennett, G. D., Chhatriwalla, A., Isaac, M. B. *J. Org. Chem.* **1997**, *62*, 3370; Isaac, M. B., Paquette, L. A. *J. Org. Chem.* **1997**, *62*, 5333; Bernardelli, P., Paquette, L. A. *J. Org. Chem.* **1997**, *62*, 8285; Paquette, L. A.; Lobben, P. C. *J. Am. Chem. Soc.* **1996**, *118*, 1917; Paquette , L. A.; Mitzel, T. M. *J. Org. Chem.* **1996**, *61*, 8799; Paquette, L. A.; Stepanian, M.; Mallavadhani, U. V.; Cutarelli, T. D.; Lowinger, T. B.; Klemeyer, H. J. *J. Org. Chem.* **1996**, *61*, 7492.
26. Paquette, L. A., Bennett, G. D., Chhatriwalla, A., Isaac, M. B. *J.Org. Chem.* **1997**, *62*, 3320. Maguire, R. J.; Mulzer, J.; Bats, J. W. *J. Org. Chem.* **1996**, *61*, 6936.
27. Chan, T. H.; Li, C. J. 203rd National Meeting of the American Chemical Society, San Francisco, CA; April 1992, Abstract ORGN435.
28. Gordon, D. M.; Whitesides, G. M. *J. Org. Chem.* **1993**, *58*, 7937.
29. Gao, J.; Harter, R.; Gordon, D. M.; Whitesides, G. M. *J. Org. Chem.* **1994**, *59*, 3714.
30. Chan, T. H.; Lee, M. C. *J. Org. Chem.* **1995**, *60*, 4228.
31. Chan, T. H.; Xin, Y. C. *Chem. Commun.* **1996**, 905; Chan, T. H.; Xin, Y. C.; Von Itzstein, M. *J. Org. Chem.* **1997**, *62*, 3500; Chio, S. K.; Lee, S.; Whitesides, G. M. *J. Org. Chem.* **1996**, *61*, 8739.
32. Schmid, W.; Whitesides, G. M. *J. Am. Chem. Soc.* **1991**, *113*, 6674.
33. Prenner, R. H.; Binder, W. H.; Schmid, W. *Libigs Ann. Chem.*, **1994**, 73.
34. Binder, W. H.; Prenner, R. H.; Schmid, W. *Tetrahedron* **1994**, *50*, 749.
35. Carda, M.; Castillo, E.; Marco, J.A. *Tetrahedron: Asym.* **1998**, *9*, 1117.
36. Wang, R.; Lim, C. M.; Tan, C. H.; Lim, B. K.; Sim, K. Y.; Loh, T. P. *Tetrahedron: Asym.* **1995**, *6*, 1825.
37. Loh, T. P.; Diana, S. C. H.; Sim, K. Y. *Synlett* **1996**, 263.
38. Yi, X. H.; Meng, Y.; Li, C. J. *Chem. Commun.* **1998**, 449; Yi, X. H.; Meng, Y.; Hua, X. G.; Li, C. J. *J. Org. Chem.* **1998**, *63*, 7472.
39. Fang, X. P.; Anderson, J. E.; Chang, C. J.; Fanwick, P. E.; McLaughlin, J. L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1655.
40. Tschitschibabin, A. E.; Kirssanov, A. W.; Korolev, A. J.; Woroschzow, N. N. Justus, *Liebigs Ann. Chem.* **1929**, *469*, 93; Yoshida, T.; Seno, Y.; Takama, Y.; Okuda, T. *Phytochemistry* **1982**, *21*, 1180; Chen, X. M.; Yoshida, T.; Hatano, T.; Fukushima, M.; Okuda, T. *Phytochemistry* **1987**, *26*, 515;

Hattori, M.; Shue, Y. Z.; Tomimori, T.; Kobashi, K.; Namba, T. *Phytochemistry* **1989**, *28*, 1289; and Ramaiah, P. A.; Row, L. R.; Reddy, D. S.; Anjaneyulu, A. S. R.; Ward, R. S.; Pelter, A. *J. Chem. Soc. Perkin Trans. 1* **1979**, 2313; refs. cited therein.

41. Hua, X. G.; Mague, J. T.; Li, C. J. *Tetrahedron Lett.* **1998**, *39*, 6837.
42. Mague, J. T.; Hua, X. G.; Li, C. J. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1998**, *C54*, 1934.
43. Jayaraman, M.; Manhas, M. S.; Bose, A. K. *Tetrahedron Lett.* **1997**, *38*, 709.
44. Paquette, L. A.; Rothhaar, R. R.; Isaac, M.; Rogers, L. M.; Rogers, R. D. *J. Org. Chem.* **1998**, *63*, 5463.
45. Li, C. J.; Lu, Y. Q. *Tetrahedron Lett.* **1995**, *36*, 2721.
46. Sarrazin, L.; Mauze, B. *Synth. Commun.* **1996**, *26*, 3179.
47. Li, C. J.; Lu, Y. Q. *Tetrahedron Lett.* **1996**, *37*, 471.
48. Li, C. J.; Chen, D. L.; Lu, Y. Q.; Haberman, J. X.; Mague, J. T. *J. Am. Chem. Soc.* **1996**, *118*, 4216. Li, C. J.; Chen, D. L.; Lu, Y. Q.; Haberman, J. X.; Mague, J. T. *Tetrahedron*, **1998**, *54*, 2347.
49. Li, C. J.; Chen, D. L. *Synlett* **1999**, 0000.
50. Haberman, J.X.; Li, C. J.*Tetrahedron Lett.* **1997**, *38*, 4735.
51. Mague, J. T.; Li, C. J.; Chen, D. L.; Lu, Y. Q.; Haberman, J. X. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1996**,*C52*, 2597.
52. Bryan, V. J.; Chan, T. H. *Tetrahedron Lett.* **1996**, *37*, 5341.
53. Paquette, L. A.; Mendez-Andino, J.*Tetrahedron Lett.* **1999**, *40*, 4301.
54. Loh, T. P.; Cao, G.Q.; Pei, J.*Tetrahedron Lett.* **1998**, *39*, 1457.
55. Orjala, J.; Nagle, G. D.; Hsu, L. V.; Gerwick, W. H. *J. Am. Chem. Soc.* **1995**, *117*, 8281.
56. Loh, T. P.; Cao, G.Q.; Pei, J. *Tetrahedron Lett.* **1998**, *39*, 1457.
57. Loh, T. P.; Li, X. R. *J. Chem. Soc., Chem. Commun.* **1996**, 1929.
58. Loh, T. P.; Wang, R. B.; Sim, K. Y. *Main Group Met. Chem.* **1997**, *20*, 237.
59. Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 696.
60. Kalyanam, N.; Venkateswara Rao, G. *Tetrahedron Lett.* **1993**, *34*, 1647.
61. Lim, H. J.; Keum, G.; Kim, Y. *Tetrahedron Lett.* **1998**, *39*, 4367.
62. Wang, L.; Sun, X.; Zhang, Y. *Synth. Commun.* **1998**, *28*, 3263.
63. Zhan, Z.; Zhang, Y.; Ma, Z. *J. Chem. Res.* **1998**, 130.
64. Bao, W.; Zhang, Y. *Synlett.* **1996**, 1187.
65. Wang, L.; Zhang, Y. *J. Chem. Res.* **1998**, 588.
66. Bao, W.; Zheng, Y.; Zhou, J. *Tetrahedron Lett.* **1996**, *37*, 9333.
67. Moody, C. J.; Pitts, M. P. *Synlett* **1998**, 1028; Moody, Pitts, M. P. *Synlett* **1998**, 1029.
68. Mukaiyama, T.; Ohno, T.; Nishimura, T.; Han, J. S.; Kobayashi, S. *Chem. Lett.* **1990**, 2239.
69. Mukaiyama, T.; Ohno, T.; Han, J. S.; Kobayashi, S. *Chem. Lett.* **1991**, 949.
70. Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1; Trost, B. M.; Miller, M. L. *J. Am. Chem. Soc.* **1988**, *110*, 3687; Trost, B. M.; Chan, D. M. *J. Am. Chem. Soc.* **1983**, *105*, 2326.
71. For examples, see: Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1995**, *60*, 1920; Yasuda, M.; Miyai, T.; Matsuda, H. *Tetrahedron Lett.* **1995**, *36*; 9497.
72. Li, X. R.; Loh, T. P. *Tetrahedron Asym.* **1996**, *7*, 1535.
73. Loh, T. P.; Pei, J.; Cao, G. Q. *J. Chem. Soc., Chem. Commun.* **1996**, 1819; Loh, T. P.; Pei, J.; Koh, K.S.V.; Cao, G. Q.; Li, X. R. *Tetrahedron Lett.* **1997**, *38*, 3465; *Corrigendum* 3993.
74. Kobayashi, S.; Busujima, T.; Nagayama, S. *Tetrahedron Lett.* **1998**, *39*, 1579; see also Kobayashi, S.; Nagayama, S.; Busujima, T. *J. Am. Chem. Soc.*, **1998**, *120*, 8287.
75. Loh, T. P.; Chua, G. L.; Vittal, J. J.; Wong, M. W. *Chem. Commun.* **1998**, 861.
76. Loh, T.P.; Wei, L.L. *Tetrahedron Lett.* **1998**, *39*, 323.
77. Loh, T. P.; Pei, J.; Lin, M. *J. Chem. Soc., Chem. Commun.* **1996**, 2315.
78. Loh, T. P. ; Wei, L. L. *Synlett* **1998**, 975.
79. Loh, T. P.; Xu, K. C.; Ho, D. S. C.; Sim, K. Y. *Synlett* **1998**, 369.

Biographical sketch

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