# Preparation of Chiral Allenylmetal Reagents from Enantioenriched Allenyl Iodides and Propargylic Mesylates. A Comparison of Indium, Bismuth, and Tin Derivatives

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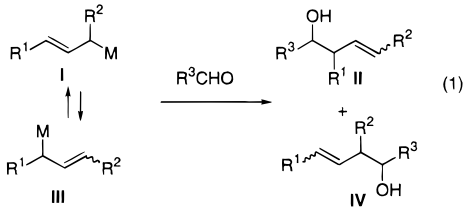
Chiral allenylmetal halides were prepared starting from enantioenriched (∼95% ee) 1-octyn-3-ol mesylate (**1**) and 3-butyn-2-ol mesylate (**7**). Addition of these transient metallo species to aldehydes in situ afforded mainly anti homopropargylic alcohol adducts of varying ee. Three approaches were explored. In the first, the mesylates were converted to allenylstannanes with $Bu_3SnLi$·CuBr and the allenylmetal halide was prepared from the resulting enantioenriched allenylstannane by transmetalation with $InBr_3$, $BiBr_3$, and $SnCl_4$ in the presence of cyclohexanecarboxaldehyde. The configurational stability of the transient allenylmetal halide was estimated from the ee of the derived adduct. The second approach involved metalation of the allenyl iodides prepared from mesylates **7** and **1** through $S_N2'$ displacement with $LiCuI_2$. From these experiments, it was determined that allenylindium bromides and allenyltin bromides are configurationally stable under the reaction conditions. The adduct obtained from the allenylbismuth bromide was nearly racemic. A superior procedure was developed in which the propargylic mesylates **7** and **1** were converted to allenylindium iodide intermediates through treatment with InI and 5 mol % of a Pd(0) dppf catalyst in THF−HMPA, THF−DMSO, or THF−DMPU. Under these conditions, α-branched aldehydes were converted to anti adducts (∼95:5 anti/syn) of >90% ee. Additions to unbranched aldehydes were less diastereoselective, but afforded adducts of high ee. Additions of enantiomeric allenylindium iodide reagents to (*R*)-*β*-ODPS-α-methylpropanal (**13**) afforded diastereomeric adducts (anti,anti and anti,syn) **14**, **15** and **18**, **19** with excellent diastereoselectivity indicative of a high degree of reagent control. A convenient procedure for the preparation of InI from In and $I_2$ is also described.

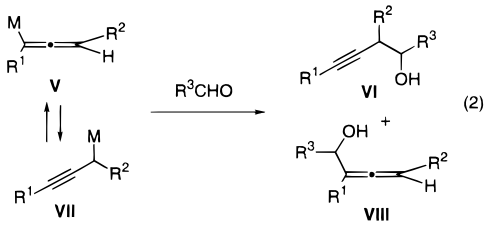
Allylmetal compounds, particularly boranes/boronates, stannanes, and to a lesser extent, allylic zinc, chromium, and silane reagents, have been well utilized for the stereoselective synthesis of acyclic intermediates with two or more contiguous stereocenters (eq 1).[1] The major-




(1)

ity of these applications have employed the crotyl species **I** ($R^1$ = Me, $R^2$= H), in which the metal is attached to a primary carbon thereby favoring formation of the branched product **II** by an $S_E2'$ pathway. The situation becomes more complex with secondary allylmetal reagents (**I**; $R^1$, $R^2$ = alkyl or aryl) because of possible allylic interconversion of **I** and **III** and subsequent formation of isomeric adducts **II** and **IV**.

An analogous scenario is applicable to allenylmetal reagents.[2] Here the interconversion of allenic and propargylic isomers **V** and **VII** can lead to propargylic and allenic adducts **VI** and **VIII** (eq 2). These adducts have the potential for further elaborations of the alkynyl and allenyl functions.




(2)

We have been interested in the generation of enantioenriched allenylmetal reagents and their subsequent addition to aldehydes to afford enantioenriched propargylic adducts.[3] Such applications are feasible only if the allenylmetal intermediate (1) is more reactive than the propargyl isomer or (2) does not interconvert with the propargyl isomer and (3) reacts with the aldehyde faster than it racemizes. These requirements are met by a number of allenyltin derivatives. Configurationally stable allenyltin reagents **X** of high ee can be prepared through $S_N2'$ displacement of enantioenriched propargylic mesylates **IX**.[4] They undergo syn-selective additions to aldehydes in the presence of Lewis acids such as $BF_3$·$OEt_2$. Anti-selective additions can also be effected, but only after conversion to a more electron-deficient allenylmetal compound **XIII** through tin−metal exchange with $SnCl_4$ or $InCl_3$. These metathesis reactions occur with inversion

(1) Review: Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.

(2) Reviews: Yamamoto H. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, Chapter 1.3, pp 81−98. Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31.

(3) (a) Marshall, J. A.; Perkins, J. F.; Wolf, M. A. *J. Org. Chem.* **1995**, *60*, 5556. (b) Marshall, J. A.; Palovich, M. R. *J. Org. Chem.* **1997**, *62*, 6001.

(4) (a) Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1990**, *55*, 6246. (b) Marshall, J. A.; Wang, X−j. *J. Org. Chem.* **1991**, *56*, 3211. (c) Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1992**, *57*, 1242.

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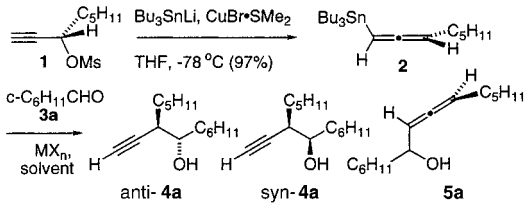
**Table 1. Addition of Allenylmetal Reagents Prepared from Allenylstannane 2 to Aldehyde 3a**

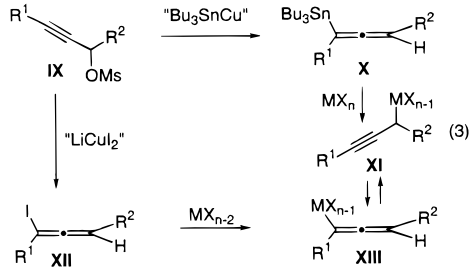



| $MX_n$ | solvent | yield, % | anti/syn | **4:5** | $[\alpha]_D$[a] | ee,[a] % |
|---|---|---|---|---|---|---|
| $InBr_3$ | THF | 98 | 96:4 | 95:5 | −12.9 | 90[b] |
| $BiBr_3$ | THF[c] | 64 | 88:12 | 93:7 | +1.2[d] | 8[e] |
| $SnCl_4$ | $CH_2Cl_2$ | 59 | 97:3 | 95:5 | +11.6[d] | 81 |
| $BF_3$·$OEt_2$ | $CH_2Cl_2$ | 72 | 22:78 | 99:1 | +14.9 | *f* |

[a] Major product. [b] From $^1$H NMR analysis of *O*-methyl mandelates. [c] −40 °C to rt. [d] Enantiomer of *anti*-**4a**. [e] From optical rotation comparison with first entry. [f] Not determined.

of configuration in the former case and mainly retention in the latter case.[3,4]

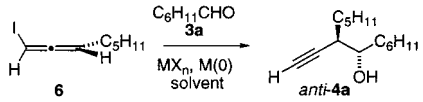
Although the foregoing allenylmetal additions proceed in high yield with excellent diastereo- and enantioselectivity and the reagents are easily prepared from readily available enantioenriched propargylic alcohols, they suffer from several drawbacks. These include the need to handle toxic tin byproducts and the difficulty in separating these byproducts from the reagents and final products. Accordingly, we decided to explore an alternative route to chiral allenylmetal compounds **XIII** by way of allenic iodides **XII**. These are available by $S_N2'$ displacement of propargylic mesylates with $LiCuI_2$.[5]




Our initial studies were designed to compare the configurational stability of allenic tin, indium, and bismuth halides. Organoindium and bismuth reagents fulfill the aforementioned criteria of accessibility and low toxicity.[6] They have the additional advantage of being relatively moisture insensitive. Allenyindium halides react with aldehydes to afford anti homopropargylic alcohol adducts[3b] via a cyclic transition state. A priori, allenylbismuth halides might be expected to react by an analogous pathway.

Using the chiral allenylstannane **2**, prepared by $S_N2'$ displacement of the mesylate of (*S*)-1-octyn-3-ol[7] (**1**, >95% ee), as the allenylmetal precursor (Table 1) we examined transmetalations with $InBr_3$, $BiBr_3$, and $SnCl_4$ in the presence of cyclohexanecarboxaldehyde (**3a**) to establish the regio-, diastereo-, and enantioselectivity of the transient halometal reagents. THF proved superior to other solvents (EtOAc, $CH_2Cl_2$, DMF, MeCN) for the $InBr_3$ and $BiBr_3$ transmetalations with regard to speed of reaction and yields of adducts whereas the $SnCl_4$ reactions were best conducted in $CH_2Cl_2$. For product comparison we also carried out additions of **2** promoted by $BF_3$·$OEt_2$, in $CH_2Cl_2$ , along previously reported lines.[3,4] The $InBr_3$ and $BiBr_3$ reactions showed excellent regio- and diastereoselectivity. When the aldehyde was initially present, the $SnCl_4$ reaction afforded a 1:1 mixture of propargyl and allenyl adducts indicative of a rapid $S_E2'$ transmetalation and a slower 1,3-isomerization of the resulting propargylic $SnCl_3$ intermediate.[3] However, if the addition of aldehyde was delayed by 30 min to allow for equilibration of the stannane reagent, the propargyl adduct was formed in large predominance. As expected from our previous studies, the propargyl adducts, *anti*-**4a**, from the $InBr_3$ and $SnCl_4$ experiments were enantiomeric and of high ee.[3b] In contrast, the $BiBr_3$-derived adduct was nearly racemic. Evidently, the allenylbismuth intermediate and/or its presumed propargyl precursor are not configurationally stable under these conditions. The $BF_3$-promoted addition gave the syn adduct, *syn*-**4a**, as the major product, in line with previous findings.[3]

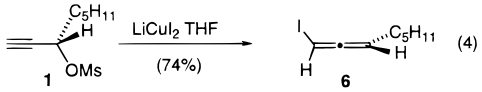
**Table 2. Additions of Allenylmetal Reagents Prepared from Allenyl Iodide 6 to Aldehyde 3a**




| $MX_n$ | M(0) | solvent | yield, % | anti/syn[a] | $[\alpha]_D$ | ee,[b] % |
|---|---|---|---|---|---|---|
| | In | THF−$H_2O$[c] | 96 | 95:5 | −8.7 | 65 |
| | In | DMF−$H_2O$[c] | 95 | 95:5 | −6.8 | 50 |
| | In | DMA−$H_2O$[c] | 98 | 95:5 | −9.4 | 70 |
| $InBr_3$ | Zn | THF | 92 | >95:5 | −6.4 | 48 |
| $InBr_3$ | Zn | THF[d] | 99 | >95:5[e] | −8.7 | 65 |
| $SnBr_2$ | Zn | THF | 77 | 85:15[e] | −8.1 | 60 |
| $BiBr_3$ | Zn | THF | 89 | 95:5[f] | −1.0 | 7 |

[a] The ratios were determined by $^1$H NMR analysis. [b] Anti isomer. [c] 5−10% v/v water/solvent. [d] −78 °C to rt. [e] A trace of allenyl product **5** was formed. [f] −40 °C to rt.

A second set of experiments was conducted in which the allenylmetal reagents were generated *in situ* from allenyl iodide **6**. Iodide **6** was prepared by $S_N2'$ displacement on the aforementioned (*S*)-1-octyn-3-ol mesylate (**1**) with CuI and LiI in THF (eq 4).[5]




The reaction of **6** with indium metal powder did not take place in anhydrous THF but occurred readily when 5−10% of water was added.[8] Comparable results were obtained in 95:5 DMF−$H_2O$ or DMA−$H_2O$ as solvents. A reactive form of indium metal could also be generated *in situ* from $InBr_3$ and zinc powder. In each case, the anti propargylic adduct **4a** was isolated in excellent yield, but with some loss of ee (Table 2). Addition of $SnBr_2$ in the presence of Zn powder afforded enantioenriched adduct

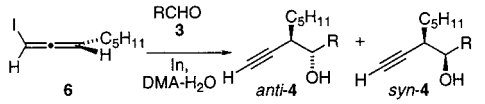
(5) (a) Elsevier: C. J.; Vermeer, P.; Gedanken, A.; Runge, W. *J. Org. Chem.* **1985**, *50*, 364. (b) D'Aniello, F.; Mann, A.; Taddei, M.; Wermuth, C.-G. *Tetrahedron Lett.* **1994**, *35*, 7775. (c) Montury, M.; Gore, J. *Synth. Commun.* **1980**, *10*, 873.

(6) Reviews: (a) Indium reagents: Marshall, J. A. *Chemtracts−Org. Chem.* **1997**, *10*, 481. (b) Bismuth reagents: Marshall, J. A. *Chemtracts−Org. Chem.* **1997**, *10*, 1064.

(7) Aldrich Chemical Co., Milwaukee, WI.

(8) A recent report suggests that allyl bromide reacts with indium metal in water to form allylindium(I) bromide, which adds in situ to ketones to afford homoallylic alcohols. Chan, T. H.; Yang, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3228. Although this pathway could also be involved in the present additions, the high anti/syn product ratios are more consistent with allenyl $InX_2$ species.

**Table 3. Additions of Allenylindium Reagent Prepared from Allenyl Iodide 6 to Aldehydes 3a−d**




| R | yield, % | anti/syn[a] | ee, % |
|---|---|---|---|
| c-$C_6H_{11}$, **3a** | 98 | 95:5 | 65[b] |
| $C_6H_{13}$, **3b** | 91 | 87:13 | 42[b] |
| (*E*)-BuCH=CH, **3c** | 88 | 71:29 | *c* |
| 2-furyl, **3d** | 96 | 52:48 | *c* |

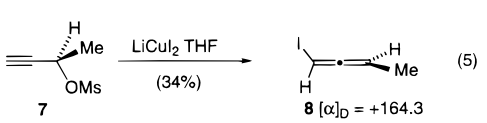
[a] The ratios were determined by GC analysis. [b] Based on optical rotation. [c] Not determined.

*anti*-**4a** of comparable ee to the organoindium reactions.[9] The % ee of this adduct was estimated from analysis of the $^1$H NMR spectrum of the *(R)*- and *(S)*-*O*-methyl mandelates.[10] A control experiment yielded less than 10% of adducts from allenyl iodide **6** and Zn metal in the absence of the metal halide salt. This reaction also gave rise to numerous byproducts.

The reaction involving $InBr_3$ and Zn in THF at room temperature afforded adduct *anti*-**4a** of lower ee than the experiment in which indium metal powder was employed to generate the allenylindium intermediate in THF−$H_2O$. However, when the former reaction was conducted at −78 °C, an adduct of ee comparable to that of the indium powder experiment was formed. Samples of unreacted allenyl iodide taken from a Zn/$InBr_3$ reaction in progress showed no loss of optical rotation. Evidently racemization of the allenylindium reagent is promoted by $ZnBr_2$.

The In powder methodology was examined with enantioenriched allenyl iodide **6** and several representative aldehydes in order to probe the scope of the reaction (Table 3). Addition to heptanal (**3b**) proceeded with anti diastereoselectivity somewhat lower compared to cyclohexanecarboxaldehyde (**3a**). Additions to (*E*)-2-heptenal and 2-furfuraldehyde (**3d**) were distinctly less selective. The absolute configuration and % ee of adducts *anti*-**4a** and -**4b** were estimated from the optical rotation values.

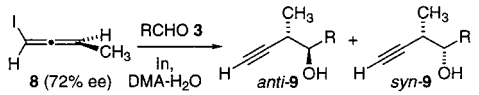
The foregoing experiments show that enantioenriched allenylindium and tin reagents can be prepared from allenyl iodide **6**, albeit with some loss of ee. As we were unable to establish the ee of iodide **6**, we could not determine the enantioselectivity of the metalation reactions. To probe that question we prepared iodide **8** of established configuration and ee.[5a] Thus, treatment of the mesylate derivative **7**, prepared from *(R)*-3-butyn-2-ol of 95% ee,[7] with $LiCuI_2$ afforded the allenyl iodide **8** of 72% ee, based on comparison of the optical rotation with the reported value (eq 5).[5a] The low yield of this iodide is attributable to its volatility.




(5)

Additions of the derived allenylindium reagent, generated from In powder, to aldehydes **3a**−**d** in DMA−$H_2O$ gave results comparable to those observed for the pentyl

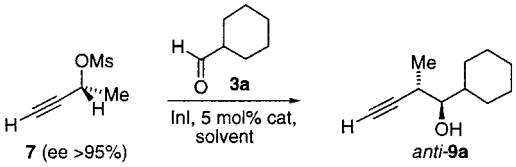
**Table 4. Additions of Allenylmetal Reagents Prepared from Allenyl Iodide 6 to Aldehyde 3a**




| R | yield, % | anti/syn | ee,[a] % |
|---|---|---|---|
| c-$C_6H_{11}$, **3a** | 84 | 95:5 | 40 |
| $C_6H_{13}$, **3b** | 56 | 86:14 | 40 |
| (*E*)-BuCH=CH, **3c** | 89 | 69:31 | 38 |
| 2-furyl, **3d** | 86 | 53:47 | 40 |

[a] For the anti isomer by GC analysis on an α-DEX column.

**Table 5. Variations of Solvent in Additions of Allenylindium Reagents Derived from Mesylate 7 to Cyclohexanecarboxaldehyde**




| catalyst | solvent[a] | yield, % | anti/syn[b] | ee,[c] % |
|---|---|---|---|---|
| none | 3:1 THF−HMPA | 66 | 96:4 | 0 |
| Pd(dppf)$Cl_2$[d] | 3:1 THF−HMPA | 76 | 95:5 | 95 |
| Pd(dppf)$Cl_2$[e] | 3:1 THF−HMPA | 95 | 95:5 | 90 |
| Pd(dppf)$Cl_2$ | 20:1 THF−HMPA | 66 | 93:7 | 91 |
| Pd(dppf)$Cl_2$ | 3:1 THF−DMPU | 63 | 87:13 | 87 |
| Pd(dppf)$Cl_2$ | 1:1 THF−DMPU | 80 | 91:9 | 90 |
| Pd(dppf)$Cl_2$ | 1:1 DMSO−THF | 78 | 94:6 | 92 |
| Pd(dppf)$Cl_2$ | 3:1 DMSO−THF | 84 | 95:5 | 95 |

[a] DMPU = *N*,*N*-dimethylpropylene urea. [b] Analysis by gas chromatography on an α-cyclodextrin column. [c] Major isomer. [d] dppf = diphenylphosphinoferrocene. [e] Freshly prepared InI was employed.

analogue **6**, but with somewhat lower yield and diastereoselectivity (Table 4). These adducts, unlike those derived from **6**, could be analyzed by gas chromatography to determine the ee of both anti and syn adducts. In all cases there was considerable loss of ee, indicating a significant degree of racemization in the metalation reaction. Control experiments revealed negligible racemization of the allenyl iodide occurred under the reaction conditions. The absolute configuration of the first three entries of Table 4 were determined by comparison of the optical rotation values with those of known samples of these adducts.[11]

At this point, it was clear that the use of allenyl iodides as precursors to enantioenriched allenylmetal reagents was plagued by two problems: (1) partial racemization in the formation of the iodides and (2) partial racemization in the metalation of the iodides. We therefore conducted a number of metalation experiments on the propargylic mesylate (*R*)-**1** under Barbier conditions with cyclohexanecarboxaldehyde (**5a**) as the electrophile.

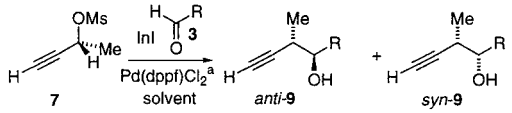
Treatment of mesylate (*R*)-**1** with In powder in the presence of **5a** in THF, THF−$H_2O$, or THF−HMPA afforded no adduct. The aldehyde was recovered. However, when InI was employed, metalation took place in 3:1 THF−HMPA and the adduct **4a** was isolated as a 96:4 anti/syn mixture in 66% yield (Table 5). Unfortunately, this adduct was racemic. We next explored the possibility of effecting a nucleophilic metalation of an allenylpalla-

(9) Wada, M.; Ohki, H.; Akiba, K. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1738.

(10) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. D. *J. Org. Chem.* **1986**, *51*, 2370.

(11) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1999**, *64*, 5201.

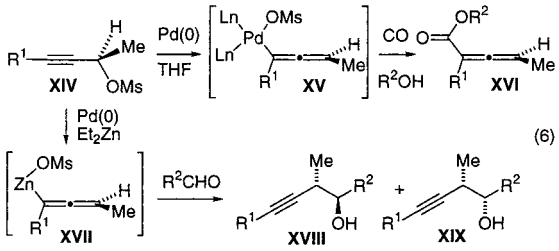
**Table 6. Additions of Transient Chiral Allenylindium Reagents from Mesylate 7 to Representative Achiral Aldehydes**




| R | solvent | yield, % | anti/syn[b] | ee,[b,c] % |
|---|---|---|---|---|
| c-$C_6H_{11}$, **3a** | 3:1 THF−HMPA | 76 | 95:5 | 95 |
| c-$C_6H_{11}$, **3a** | 3:1 THF−HMPA | 79[d] | 93:7 | 94 |
| c-$C_6H_{11}$, **3a** | 1:1 DMSO−THF | 78 | 94:6 | 92 |
| $C_6H_{13}$, **3b** | 3:1 THF−HMPA | 73 | 82:18 | 96 |
| $C_6H_{13}$, **3b** | 1:1 DMSO−HF | 70 | 84:16 | 95 |
| 1-heptynyl, **3e** | 3:1 THF−HMPA | 62 | 72:28 | 95 |
| 1-heptynyl, **3e** | 1:1 DMSO−THF | 57 | 52:48 | 93 |

[a] dppf = diphenylphosphinoferrocene. [b] Analysis by gas chromatography on an α-cyclodextrin column. [c] Major isomer. [d] The InI was prepared from In and $I_2$.

dium intermediate derived from mesylate (*R*)-**1**. We have previously shown that analogous allenylpalladium species undergo alkoxycarbonylation with CO and various alcohols to afford allenic esters **XVI** of high enantiomeric excess.[12] Formation of the allenylpalladium intermediate proceeds with inversion and the ensuing carbonylation with retention of configuration (eq 6). We have also found that the transient nonracemic allenylpalladium species can be converted to an allenylzinc reagent by $Et_2Zn$.[11] This transmetalation process proceeds with retention of configuration in the presence of aldehydes to afford anti adducts **XVIII** as major products.

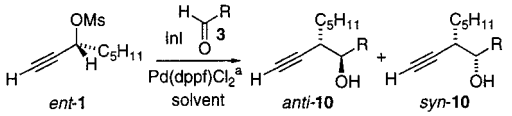



In fact, when mesylate **7** of 95% ee was treated with 5 mol % of $Pd(dppf)Cl_2$ in the presence of cyclohexanecarboxaldehyde (**3a**) and InI in 3:1 THF−HMPA, a 95:5 mixture of the anti and syn adducts **9a** was formed in 76% yield. The ee of the anti adduct was 95%, indicating that the reaction is highly enantioselective (Table 5).[13] Comparable results were obtained when THF−DMPU or THF−DMSO were employed as solvents. The reaction could also be effected with $Pd(OAc)_2 \cdot PPh_3$ as the catalyst precursor in 3:1 THF−HMPA.[11] The use of $Pd(PPh_3)_4$ resulted in lower yields and product ee.

A brief survey of results with mesylate **7** and several achiral aldehydes in 3:1 THF−HMPA and 1:1 DMSO−THF is summarized in Table 6. Two trends can be seen. (1) The two solvent pairs give comparable results with the aldehydes examined. (2) Additions to the branched aldehyde **3a** are more diastereoselective than additions to the unbranched aldehydes **3b** and **3e**. In all cases, the anti adducts are formed with high ee.

Comparable results were obtained with the 1-octynyl mesylate *ent*-**1** (Table 7). Interestingly, the size of the

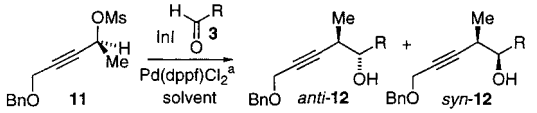
**Table 7. Additions of Transient Chiral Allenylindium Reagents from Mesylate *ent*-1 to Representative Achiral Aldehydes**




| R | solvent | yield, % | anti/syn[b] | ee,[c,d] % |
|---|---|---|---|---|
| c-$C_6H_{11}$, **3a** | 3:1 THF−HMPA | 74 | 97:3 | 86 |
| c-$C_6H_{11}$, **3a** | 3:1 THF−HMPA | 79[e] | 95:5 | 89 |
| c-$C_6H_{11}$, **3a** | 1:1 DMSO−THF | 73 | 95:5 | 89 |
| $C_6H_{13}$, **3b** | 3:1 THF−HMPA | 77 | 84:16 | 95 |
| $C_6H_{13}$, **3b** | 1:1 DMSO−THF | 83 | 86:14 | 96 |
| *i*-Pr, **3f** | 3:1 THF−HMPA | 74 | 94:6 | 93 |
| *i*-Pr, **3f** | 1:1 DMSO−THF | 64 | 96:4 | 95 |

[a] dppf = diphenylphosphinoferrocene. [b] Analysis by gas chromatography on an α-cyclodextrin column. [c] Major isomer. [d] The ee was determined by $^1H$ NMR analysis of the *O*-methyl mandelates. [e] The InI was prepared from In and $I_2$.

**Table 8. Additions of Transient Chiral Allenylindium Reagents from Mesylate 11 to Representative Achiral Aldehydes**




| R | solvent | yield, % | anti/syn[b] | ee,[b,c] % |
|---|---|---|---|---|
| c-$C_6H_{11}$, **3a** | 3:1 THF−HMPA | 81 | 96:4 | 94 |
| c-$C_6H_{11}$, **3a** | 3:1 THF−HMPA | 72[d] | 96:4 | 94 |
| c-$C_6H_{11}$, **3a** | 1:1 DMSO−THF | 86 | 94:6 | 95 |
| $C_6H_{13}$, **3b** | 3:1 THF−HMPA | 72 | 82:18 | 94 |
| $C_6H_{13}$, **3b** | 1:1 DMSO−THF | 73 | 85:15 | 95 |
| (*E*)-BuCH=CH, **3c** | 3:1 THF−HMPA | 72 | 74:26 | *e* |

[a] dppf = diphenylphosphinoferrocene. [b] Analysis by gas chromatography on an α-cyclodextrin column. [c] Major isomer. [d] The InI was prepared from In and $I_2$. [e] Not determined.

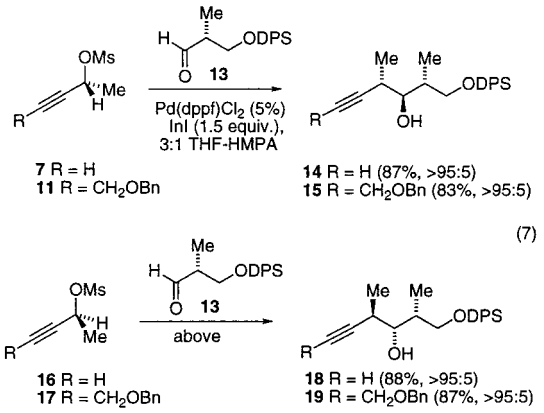
carbinyl substituents ($C_5H_{11}$ vs $CH_3$) does not significantly affect the anti/syn diastereoselectivity.

The benzyloxymethyl-substituted mesylate **11**[3] could also be employed in these additions (Table 8). As expected, the outcome was similar to that observed with the unsubstituted analogue **7**. In none of these reactions were allenylcarbinol products detected. This finding implies that the intermediate allenylindium mesylates are regioisomerically stable under the reaction conditions. When the allenylindium reagent was preformed prior to addition of the aldehyde adducts of lower ee were produced. Thus, racemization of the allenylindium reagent does take place, but at a slower rate than addition to the aldehyde substrates.

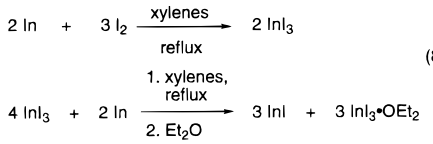
As a probe of double diastereoselectivity, we examined additions of the allenylindium reagents derived from mesylates **7**, **11** and their enantiomers **16**, **17** to the (*S*)-α-methyl-*β*-ODPS aldehyde **13** (eq 7).[14] These reactions proceeded in high yield. In each case, the anti diastereomer was virtually the sole adduct, indicative of a strongly reagent controlled process. The high diastereoselectivity observed in additions leading to the anti,syn adducts **18** and **19** are especially noteworthy. The corresponding additions of an allenylindium chloride, generated through transmetalations of allenylstannanes, af-

(12) Marshall, J. A.; Wolf, M. A.; *J. Org. Chem.* **1996**, *61*, 3238.
(13) A portion of this study was reported in preliminary form. Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 696.
(14) Roush, W. R.; Palkowitz, A. D.; Palmer, M. A. *J. Org. Chem.* **1987**, *52*, 316.

ford nearly 1:1 mixtures of anti,syn and anti,anti diastereomers.[3b]

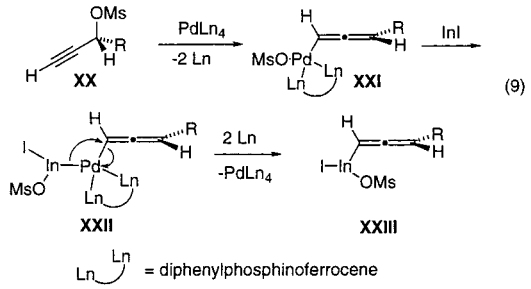



Two sources of InI were employed in these studies. The commercial material comes in the form of small spheres that were crushed prior to use to increase surface area and reactivity.[7] Alternatively, InI can be prepared by reaction of indium metal with $I_2$ (eq 8).[15] Material




prepared in this way is isolated as a highly reactive powder that can be used directly. Our preparation differs somewhat from the published version in stoichiometry and ease of execution. The $InI_3$ formed in the second step of the reaction sequence can be recycled with no loss of yield. A one-step conversion of In to InI is not possible because the actual product from step two of eq 8 is a stable complex, $In(InI_4)$, which is broken up by addition of ether to form a mixture of insoluble InI and a soluble $InI_3$ complex. Most of the addition reactions with InI were performed with the commercial material because we did not examine the noncommercial material until relatively late in our studies. However, we have repeated the preparation of adduct **14** numerous times on various scales with consistent results, which suggests that both sources of InI will give comparable results for all systems studied. We have included an *Organic Synthesis*-type procedure for InI and adduct **14** in the Experimental Section. It is possible to regenerate In metal by electrolysis of the water soluble salts recoverd after isolation of the aldehyde allenyl indium adduct by extraction.[16] This option might be desireable for large-scale applications. However, we did not explore that methodology in the present work.

A possible catalytic cycle for the Pd/In metathesis reaction is depicted in eq 9. The overall process may be viewed as an oxidative transmetalation. The reported in situ generation of allylic zinc,[17] allylic tin,[18] and allylic samarium[19] intermediates may proceed through an analogous pathway. The present process is particularly noteworthy by virtue of the high degree of enantioselectivity attending the transmetalation and the high degree of reagent control exhibited in the additions to α-chiral aldehydes.[13]




## Experimental Section

**Indium(III) Iodide.** To a 1 L, oven-dried, round-bottomed flask flushed with argon and equipped with a magnetic stirrer was added xylenes (500 mL). The solvent was degassed and the flask equipped with a reflux condenser. Indium powder (5.00 g, 43.55 mg-atoms) was added followed by iodine (16.57 g, 65.32 mmol). The mixture was vigorously stirred and refluxed (bath temperature ~160−170 °C) under argon for 1−1.5 h or until the indium metal was consumed. If the metal was not fully consumed, a crystal of iodine was added, and stirring at reflux was resumed. The reaction was considered complete when the added iodine was not consumed after 15 min at reflux. The solution was hot filtered with suction and allowed to cool to room temperature. The resulting bright yellow crystals were filtered and washed with two 10-mL portions of cold benzene to remove traces of $I_2$. The filtrate was concentrated to 1/4−1/3 volume and cooled to 0 °C. The yellow crystals of $InI_3$ were filtered and washed with cold benzene (10 mL). The product was dried in vacuo to yield 18.30 g (85%) of indium(III) iodide as a fine yellow powder. **Note:** indium(III) iodide is very hygroscopic.

**Indium(I) Iodide.** To a 1 L, oven-dried, round-bottomed flask flushed with argon and equipped with a magnetic stirrer was added xylenes (400 mL). The solvent was degassed, and the flask was equipped with a reflux condenser. Indium(III) iodide (18.30 g, 36.93 mmol) was added to the flask followed by indium powder (2.12 g, 18.46 mmol). The mixture was vigorously stirred at reflux under argon for 18 h. The resulting yellow suspension was allowed to cool to room temperature, diluted with ether (400−500 mL), and stirred for 1 h. The resulting burgundy precipitate was filtered and washed with ether (100 mL). The product was dried in vacuo to yield 6.14 g (92%) of indium(I) iodide. The filtrate was concentrated to dryness to yield 14.43 g (105%) of recovered indium(III) iodide as a fine yellow powder.

***(R)*-3-Butyn-2-ol Methanesulfonate (7).** To a 1 L, oven-dried, round-bottomed flask flushed with argon and equipped with a magnetic stirrer were added $CH_2Cl_2$ (713 mL) and (*R*)-(+)-3-butyn-2-ol (10.00 g, 0.143 mol). The mixture was cooled to −78 °C, and $Et_3N$ (39.66 mL, 0.285 mol) and methanesulfonyl chloride (16.56 mL, 0.214 mol) were added. The resulting mixture was stirred at −78 °C for 1 h, quenched with saturated $NaHCO_3$ solution, and allowed to warm to room temperature. The layers were separated, and the organic layer was washed with brine and concentrated under aspirator pressure. The residue was diluted with 500 mL of ether and washed with water followed by brine. The aqueous layer was extracted with ether. The combined extracts were dried over anhydrous $Na_2SO_4$ and concentrated under aspirator pressure to yield 20.13 g (95%) of methanesulfonate **7**. The material

(15) Freeland, B. H.; Tuck, D. G. *Inorg. Chem.* **1976**, *15*, 475.
(16) Tokuda, M.; Satoh, S.; Katoh, Y.; Suginome, H. *Electrochemical Synthesis*; Little, R. D., Weinberg, N. L., Eds.; Dekker: New York, 1991; p 83. Cited in: Paquette, L. A.; Lobben, P. C. *J. Org. Chem.* **1998**, *63*, 5604.
(17) Masuyama, Y.; Kinugawa, N.; Kurusu, Y. *J. Org. Chem.* **1987**, *52*, 3702. Qui, W.; Wang, Z. *J. Chem. Soc., Chem. Commun.* **1989**, 356.
(18) Takahara, J. P.; Masuyama, Y.; Kurusu, Y. *J. Am. Chem. Soc.* **1992**, *114*, 2577.
(19) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 215. Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 1195.

was used without further purification. A sample was purified by chromatography on silica gel: $[\alpha]^{20}_D$ +108.4 (*c* 2.39, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 5.29 (qd, $J$ = 6.8, 2.0 Hz, 1H), 3.12 (s, 3H), 2.70 (d, $J$ = 2.0 Hz, 1H), 1.66 (d, $J$ = 6.8 Hz, 3H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 80.1, 76.6, 67.4, 39.0, 22.3. Anal. Calcd for $C_{13}H_8O_2S$: C, 40.53; H, 5.44. Found: C, 40.54; H, 5.52.

**(2*R*,3*S*,4*S*)-1-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethyl-5-hexyn-3-ol (14).** An oven-dried, 100 mL, one-necked flask equipped with a magnetic stirring bar was purged with argon. The flask was charged with aldehyde **13**[14] (3.00 g, 9.17 mmol) and mesylate **7** (1.50 g, 10.09 mmol). THF (29.4 mL) and HMPA (7.4 mL) were added by means of a syringe, and the solution was cooled in an ice bath for a few minutes. The bath was removed, and $PdCl_2$(dppf) (335 mg, 0.46 mmol) and indium(I) iodide (2.66 g, 11.00 mmol) were added sequentially. The resultant dark suspension was stirred vigorously for 1 h, at which time the reaction was judged complete by TLC.[20] The reaction mixture was quenched by the addition of $H_2O$ (30 mL), and ether (20 mL) was added. After the mixture was stirred for 2 min, the layers were separated and the ether layer was washed with brine. The aqueous layer was extracted with ether, and the combined extracts were dried over anhydrous $Na_2SO_4$. Filtration and concentration in vacuo followed by flash chromatography on silica gel provided 2.64 g (76%) of the anti,anti adduct **14**[12,13] as a clear oil and 201 mg (8%) of the anti,syn diastereomer.[12,13]

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**Supporting Information Available:** Experimental procedures for all new compounds and $^1H$ NMR spectra of key intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) On occasion, the reaction will stop before completion. When this happens, a white spot at $R_f$ = 0.5−0.6 appears on the TLC plate. This spot is the dppf ligand resulting from decomposition of the catalyst. In such cases, the procedure is best terminated. If the reaction stops without appearance of the ligand, it can be restarted with additional InI. The premature termination appears to be related to the quality of the InI powder. When this problem is encountered with a particular batch of InI, the use of 9:1 THF−HMPA as solvent and 10 mol % catalyst is recommended in subsequent applications of the procedure.