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Catalytic Asymmetric Allylation Reactions Using BITIP Catalysis and 2-Substituted Allylstannanes as Surrogates for β-Keto Ester Dianions

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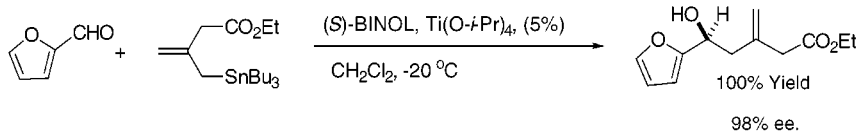
ABSTRACT



Catalytic asymmetric allylation (CAA) reactions using the indicated allylstannane and the BITIP catalysts previously described by us give high yields and enantioselectivities in additions to aldehydes. The products are convertible to β-keto esters by oxidative cleavage of the olefin. These reactions thus provide a useful catalytic enantioselective method for chain extension with introduction of a versatile four-carbon unit.

Previous reports from our laboratories have documented the utility of catalytic asymmetric allylation (CAA) reactions using BITIP catalysis for the enantioselective addition of allyl[1] and methallyl[2] stannanes to aldehydes. These readily prepared BITIP catalysts[3] have also proven useful in other catalytic asymmetric additions to aldehydes, including Mukaiyama aldol reactions to afford thiol esters,[4] reductions using Bu_3SnD for the preparation of labeled primary alcohols,[5] and a formal hetero-Diels−Alder process which adds a functionalized four carbon unit by reaction with Danishefsky's diene.[6] In connection with approaches to synthetic targets under investigation in our laboratories, we have had occasion to examine other 2-substituted allylstannanes in such aldehyde addition reactions. We record herein the results of a very useful new process utilizing an ethylaceto 2-substituted allylstannane in such reactions, which provides, among other possibilities, a very useful asymmetric surrogate for an acetoacetate dianion.[7]

Initial experiments along these lines were conducted with the Chan diene[8] (**1**) in an attempt to carry out a transformation analogous to those previously conducted with the structurally similar Danishefsky's diene. However, despite extensive investigation with a variety of substrates, solvents, reaction conditions, and catalyst preparations, no synthetically useful results were obtained using this approach. In all cases, either the chemical yields or the enantiomeric excess were unacceptably low using reasonable amounts of catalyst. For example, yields and ee's were both typically in the 30% range using 20 mol % of BITIP catalysts (prepared as previously described). Somewhat better results could be obtained using 50 mol % of catalyst (e.g., 60% yield, 72%

(1) (a) Keck, G. E.; Tarbet, K. H.; Geraci, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 8467. (b) Keck, G. E.; Krishnamurthy, D. *Org. Synth.* **1998**, *75*, 12. (c) Keck, G. E.; Geraci, L. S. *Tetrahedron Lett.* **1993**, *34*, 7827.

(2) Keck, G. E.; Krishnamurthy, D.; Grier, M. C. *J. Org. Chem.* **1993**, *58*, 6543.

(3) For the definition of the acronymn, see ref 6.

(4) Keck, G. E.; Krishnamurthy, D. *J. Am. Chem. Soc.* **1995**, *117*, 2363.

(5) Keck, G. E.; Krishnamurthy, D. *J. Org. Chem.* **1996**, *61*, 7638.

(6) Keck, G. E.; Li, X.-Y.; Krishnamurthy, D. *J. Org. Chem.* **1995**, *60*, 5998.

(7) This is a powerful disconnection; for recent examples of syntheses using such reactions, see: (a) Evans, D. A.; Carter, P. H.; Carreira, E. M.; Prunet, J. A.; Charette, A. B.; Lautens, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 2354. (b) Carreira, E. M.; Kruger, J. *Tetrahedron Lett.* **1998**, 7013. (c) Balog, A.; Harris, C.; Savin, K.; Zhang, X.-G.; Chou, T. C.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 2875.

(8) Brownbridge, P.; Chan, T. H.; Brook, M. A.; Kang, G. J. *Can. J. Chem.* **1983**, *61*, 688.

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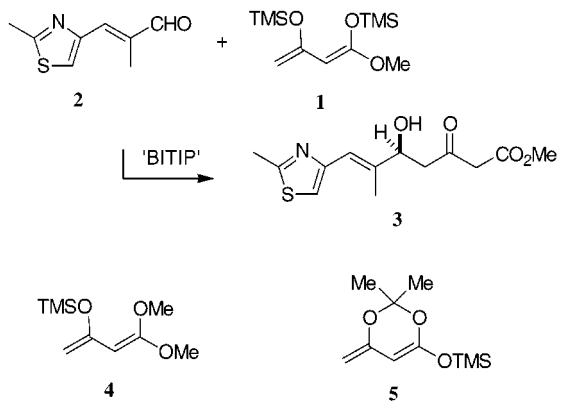
ee) but this is clearly not a preparatively useful process. Likewise, no preparatively useful results could be obtained using the dienes **4** or **5** in these reactions[9,10] (Scheme 1). We were thus led to investigate the use of an allylstannane as a functional equivalent for these highly oxygenated dienes.

Scheme 1



The requisite allylstannane for our purposes (**6**) was prepared in 65−70% isolated yield by heating the known[11] bis-stannane **7** with ethyl chloroformate (Scheme 2). Stannane **6** was found to be quite stable with respect to manipulation and storage. This material was isolated in analytically pure form by chromatography over deactivated (treated with 2% NEt_3 in EtOAc) silica gel, and can be stored in a freezer indefinitely.

Scheme 2

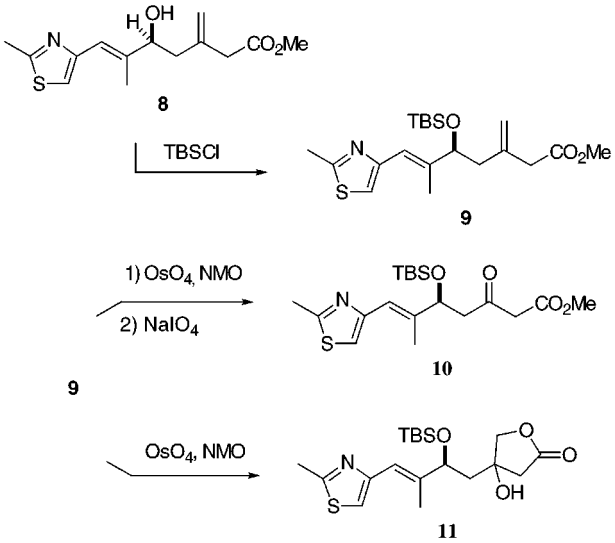
Reactions of this stannane with benzaldehyde and also with thiazole **2** were used to survey conditions (catalyst preparation and solvent) for the catalytic asymmetric addition process. Here it was found that catalyst prepared according to "method B" [12] used in CH_2Cl_2 gave optimal results. Initial experiments used 20 mol % of catalyst, since we were concerned that the electron withdrawing ester substituent might significantly decrease the reactivity of the allylstannane relative to the purely alkyl-substituted cases explored previously. However, use of the catalyst at the 10 mol % level was found to provide virtually identical results. The use of even lower levels of catalyst was examined in one case: addition to furaldehyde gave a quantitative chemical yield of product with 98% ee using 5 mol % of catalyst. Thus it seems likely that even smaller amounts of catalyst could be employed in these reactions, but this has not as yet been investigated since the levels of catalyst employed are quite convenient for most laboratory applications. Results for reactions conducted at the 10 mol % level using the "method B" BITIP catalyst are summarized in Table 1.

Table 1. Isolated Yields and Enantiomeric Excess for BITIP-Catalyzed Reactions of Stannane **6** with Aldehydes RCHO

RCHO	yield (%)	EE (%)
2	60	97
PhCHO	96	98
furaldehyde	100	99
$PhCH_2CH_2CHO$	98	99
PhCH=CHCHO	71	93
$BnOCH_2CHO$	85	97

Use of these materials as precursors to the desired β-keto esters has also been documented, and occurs in good yields. For example, the CAA product (**8**) from addition to **2** was converted to the corresponding TBS ether which was cleaved oxidatively to afford the corresponding β-keto ester (**10**) in 80% isolated yield (Scheme 3). On the other hand, when the reaction mixture from the osmylation of **8** was quenched with sodium bisulfite solution and subjected to normal

Scheme 3



(9) (a) Banville, J.; Brassard, P. *J. Chem. Soc., Perkin Trans. I* **1976**, 1852. (b) Sato, M.; Sunami, S.; Sugita, Y.; Kaneko, C. *Chem. Pharm. Bull.* **1994**, *42*, 839.

(10) For previous examples of asymmetric Mukaiyama aldol reactions using dienes **1** and **5**, see: (a) Sato, M.; Sunami, S.; Sugita, Y.; Kaneko, C. *Heterocycles* **1995**, *41*, 1435. (b) Singer, R.; Carreira, E. M. *J. Am. Chem. Soc.* **1995**, *117*, 12360. (c) Evans, D. A.; Murry, J. A.; Kozlowski, M. C. *J. Am. Chem. Soc.* **1996**, *118*, 5814. (d) Kruger, J.; Carreira, E. M.; *J. Am. Chem. Soc.* **1998**, *120*, 837.

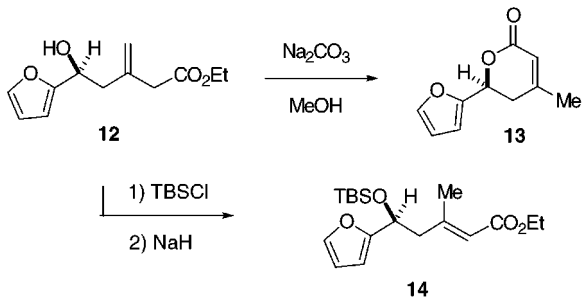
(11) (a) Sano, H.; Orawara, M.; Ueno, Y. *Synthesis* **1984**, *11*, 933. (b) Keck, G. E.; Palani, A. *Tetrahedron Lett.* **1993**, *34*, 3223.

(12) The description of catalyst preparations as methods A−D are used as consistent with our previous reports.[1−6] The sense of asymmetric induction was also the same as previously observed: i.e., benzaldehyde affords *S* product using *S*-BINOL.

extractive workup, the β-hydroxy lactone **11** was obtained exclusively.

In addition to the obvious utility of these materials as precursors of the corresponding β-keto esters, other transformations of these CAA products are possible which make other common structural fragments readily accessible in high enantiomeric excess. For example, treatment of the furaldehyde adduct **12** with Na_2CO_3/MeOH results in cyclization and double-bond isomerization to afford the unsaturated lactone **13**, which is of *Z* stereochemistry with respect to the trisubstituted olefinic unit (Scheme 4). The corresponding

Scheme 4



E unsaturated ester can also be prepared quite simply from the same CAA adduct. Thus, treatment of the corresponding TBS ether with sodium hydride in THF effects double-bond isomerization to afford **14** in good chemical yield (93%) and with surprisingly high (90:1) *E/Z* selectivity.[13,14] Thus, using very simple reactions, such CAA adducts are transformed into materials for which no direct asymmetric C−C bond forming approach is available.

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Supporting Information Available: Full experimental details, spectral and analytical data for new compounds, and copies of ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) This is a curious result, and is clearly a kinetic phenomenon, perhaps associated with a preferred geometry for formation of the enolate anion with sodium as counterion. Use of DBU to effect this transformation affords a 9:1 mixture. After extended reaction times, the sodium hydride promoted process also affords a 9:1 mixture.

(14) **Representative Experimental Procedure: Preparation of Ethyl 3-((2*S*)-2-(2-Furyl)-2-hydroxyethyl)but-3-enoate.** A mixture of (*S*)-(−)-1,1′-binaphthol (115 mg, 0.401 mmol), 1 M Ti(O-i-Pr)$_4$ in CH_2Cl_2 (0.20 mL, 0.20 mmol), 0.1 M CF_3CO_2H in CH_2Cl_2 (60 μL, 6.0×10^{-3} mmol), and oven-dried 4 Å molecular sieves (1.50 g) in 15 mL of CH_2Cl_2 was heated at reflux for 1 h. The resulting red-brown mixture was cooled to room temperature, and 2-furylaldehyde (192 mg, 2.00 mmol) was added. This mixture was stirred at room temperature for 10 min before it was cooled to −78 °C and stannane **6** (1.67 g, 4.00 mmol) was then added. The reaction flask was then placed in a −20 °C freezer for 72 h without stirring. The resulting mixture was quenched by the addition of 10 mL of saturated $NaHCO_3$ solution, stirred for 5 min at room temperature, and then filtered through a plug of Celite. The filtrate was diluted with 200 mL of CH_2Cl_2 and washed with 100 mL of water. The organic layer was dried over anhydrous Na_2SO_4 and then concentrated. The residue was purified by flash chromatography on a silica gel column (2.8 × 25 cm), eluting with acetone/EtOAc/hexane (1.5:1:10) to give 448 mg (100%) of the product as a colorless oil. The enantiomeric excess was determined to be 99% by conversion to the Mosher MTPA ester, and ^{19}F NMR measurement: R_f 0.13 (20% EtOAc/hexane); $[\alpha]_D^{24} = -31.8$ (*c* 2.32, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (dd, $J = 2.0$, 0.7 Hz, 1H), 6.32 (dd, $J = 3.2$, 2.0 Hz, 1H), 6.26 (ddd, $J = 3.2$, 0.7, 0.7 Hz, 1H), 5.11 (dd, $J = 1.0$, 1.0 Hz, 1H), 5.07 (dd, $J = 1.0$, 1.0 Hz, 1H), 4.85 (dd, $J = 7.8$, 5.9 Hz, 1H), 4.15 (q, $J = 7.1$ Hz, 2H), 3.12 (dd, $J = 15.9$, 1.0 Hz, 1 H), 3.05 (dd, $J = 15.6$, 1.0 Hz, 1H), 2.72−2.60 (m, 3H), 1.26 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 156.1, 142.1, 138.4, 118.4, 110.4, 106.2, 65.0, 61.6, 42.8, 41.8, 14.3; IR (neat) 3250 (br), 3081, 1732, 1650, 1501 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.18; H, 7.21.