ORGANIC LETTERS

2006
Vol. 8, No. 2
207−210

Carbohydrate-Derived Amino-Alcohol Ligands for Asymmetric Alkynylation of Aldehydes

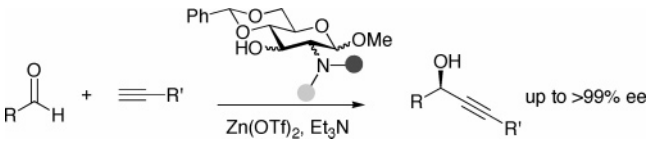
Daniel P. G. Emmerson,[†] William P. Hems,[‡] and Benjamin G. Davis*,[†]

Department of Chemistry, University of Oxford, Chemistry Research Laboratory, Mansfield Road, Oxford OX1 3TA, U.K., and Johnson Matthey Catalysis and Chiral Technologies, 28, Cambridge Science Park, Milton Road, Cambridge CB4 0FP, U.K.

ben.davis@chem.ox.ac.uk

Received October 16, 2005

ABSTRACT



Conformationally restricted amino alcohols based on carbohydrate scaffolds provide flexible and fine-tuneable libraries that greatly expand the range of ligands available in the $Zn(OTf)_2$-mediated addition of alkynes to aldehydes, in some cases with very high stereoselectivities.

Enantioenriched, secondary propargyl alcohols are important synthetic building blocks, but there are few methods for preparing them in consistently high yield and ee. Corey's chiral oxazaborolidine promoted[1] alkynylation and Carreira's zinc triflate catalyzed[2,3] method in which *N*-methylephedrine **A** is the chiral promoter are the two leading examples, giving highly enantiopure, secondary propargyl alcohols (>90% ee). Chan[4,5] and Pu[6,7] have both reported methods involving Ti-BINOL catalysts and alkynylzinc reagents prepared with dialkylzincs and terminal acetylenes, which give high yields and enantioselectivity, especially for aromatic aldehydes. Reduction of prochiral alkynones also provides an alternative means of entry.[8]

The $Zn(OTf)_2$-catalyzed method offers operational advantages over other methods: the alkynylzinc may be prepared by a straightforward procedure that does not require inert atmosphere techniques or high-grade dry solvent. There is still some room for improvement in terms of substrate generality for this reaction,[9] but relatively little investigation into the effect of ligand structure has been undertaken. Indeed, for the zinc triflate catalyzed reaction, to date only one ligand **B**[10,11] has improved upon *N*-methylephedrine. Notably the use of **B** improved yields for reactions of aliphatic aldehydes without α-branching, which had been problematic for the *N*-methylephedrine promoted reaction. No ligand has shown broad reactivity with aromatic aldehydes in this reaction.

Carbohydrates have recently received much attention as sources of chiral ligands for asymmetric catalysis.[12−16] As part of our ongoing studies[17,18] into the application of glucosamine-derived, amino alcohol ligands **4** to promote asymmetric transformations, we report here the first thorough investigation into the influence that ligand structure has on asymmetric, zinc triflate catalyzed alkynylation. In particular, the *trans*-decalin-like framework of such ligands provides a

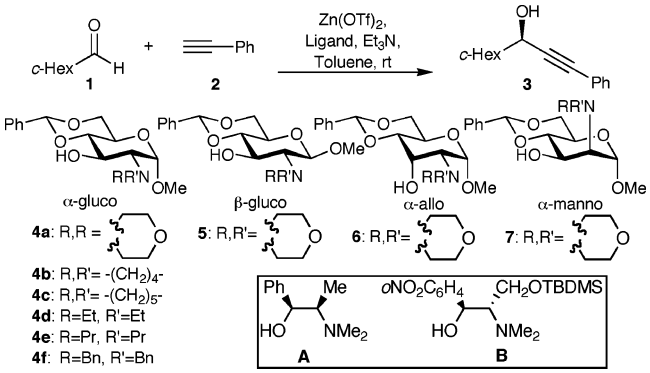
[†] University of Oxford.
[‡] Johnson Matthey Catalysis and Chiral Technologies.

(1) Corey, E. J.; Cimprich, K. A. *J. Am. Chem. Soc.* **1994**, *116*, 3151−3152.
(2) Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 1806−1807.
(3) Frantz, D. E.; Fässler, R.; Tomooka, C. S.; Carreira, E. M. *Acc. Chem. Res.* **2000**, *33*, 373−381.
(4) Lu, G.; Li, X.; Chan, W. L.; Chan, A. S. C. *Chem. Commun.* **2002**, 172−173.
(5) Li, X.; Lu, G.; Kwok, W. H.; Chan, A. S. C. *J. Am. Chem. Soc.* **2002**, *124*, 12636−12637.
(6) Moore, D.; Pu, L. *Org. Lett.* **2002**, *4*, 1855−1857.
(7) Xu, M.-H.; Pu, L. *Org. Lett.* **2002**, *4*, 4555−4557.
(8) Noyori R.; Tomino, I.; Tanimoto; Y. *J. Am. Chem. Soc.* **1979**, *101*, 3129; Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738.
(9) For a recent example of difficulties, see: Marshall, J. A.; Bourbeam, M. P. *Org. Lett.* **2003**, *5*, 3197.
(10) Jiang, B.; Chen, Z.; Xiong, W. *Chem. Commun.* **2002**, 1524.
(11) See also: Yamashita, M.; Yamada, K.; Tomioka, K. *Adv. Synth. Catal.* **2005**, *347*, 1649.

10.1021/ol052503l CCC: $33.50
Published on Web 12/21/2005

rigidity that would allow us to investigate the effects of conformational restriction that contrasts the two ligands **A** and **B** used to date. On the basis of preliminary screening of primary and secondary amines, we selected tertiary amines for this study. We chose to use a ligand family that exhibited both functional and stereochemical diversity and consequently chose α-gluco ligands **4a**−**f** (Scheme 1) with

Scheme 1. Stereochemically and Functionally Diverse Family of Ligands Tested in $Zn(OTf)_2$-Promoted Alkynylation



different C-2 amine substituents, as well as three diastereomers of **4a**, **5**−**7**. In particular, the latter enabled us to precisely investigate the effect of inverting the C-1, C-2, and C-3 stereogenic centers of the ligand in turn (**4a** → **5** or → **7** or → **6**, respectively). The synthesis of these ligands has been described in previous work.[17,18] In brief they may all be derived on a gram scale from *N*-acetyl glucosamine in overall yields of 28−34% for **4a**−**e**, 19% for **4f**, 14% for **5**, 18% for **6**, and 4% for **7**.

We began by using ligand **4a**, phenylacetylene **2**, and cyclohexanecarboxaldehyde **1** following the method of Carreira and co-workers[2] using their optimized conditions[19] (Table 1). The reaction essentially failed at room temperature (entry 1), and only a trace of the desired secondary alcohol was recovered. However, at 40 °C product was isolated in 95% yield and 97% ee (entry 2), a marginally higher ee than for any of the previously reported methods.[2,10] We then applied our other ligands **4b**−**f**, **5**, **6**, and **7** to this model

Table 1. Addition of Phenylacetylene **2** to **1**[a]

	ligand	ligand stereochemistry[b]	R	R′	yield (%)[c]	ee (%)[d] (config)[e]
1	**4a**	α-G[f]	$-(CH_2)_2O(CH_2)_2-$		3	71 (*R*)
2	**4a**	α-G	$-(CH_2)_2O(CH_2)_2-$		95	97 (*R*)
3	**4b**	α-G	$-(CH_2)_4-$		58	99 (*R*)
4	**4c**	α-G	$-(CH_2)_5-$		73	81 (*R*)
5	**4d**	α-G	Et	Et	38	79 (*R*)
6	**4e**	α-G	Pr	Pr	37	54 (*R*)
7	**4f**	α-G	Bn	Bn	96	39 (*R*)
8	**5**	β-G	$-(CH_2)_2O(CH_2)_2-$		94	99 (*R*)
9	**6**	α-M	$-(CH_2)_2O(CH_2)_2-$		92	22 (*R*)
10	**7**	α-A	$-(CH_2)_2O(CH_2)_2-$		8	35 (*R*)

[a] Ratio $Zn(OTf)_2$/ligand/Et_3N/PhC≡CH/*c*-$C_6H_{11}CHO$ = 1.1:1.2:1.2:1.2:1.0. Temperature = 40 °C. [b] Ligand stereochemistry: α/β refers to anomeric stereochemistry, G = glucose, A = allose, M = mannose. [c] Isolated yield, after column chromatography. [d] Determined by chiral GC using a 25 m CDex-β chiral column. [e] Absolute stereochemistry determined by polarimetry on product from entry 2, $[\alpha]^{23}_D = -9.9$ (*c* 1.22, $CHCl_3$) [lit.[1] $[\alpha]^{23}_D$ −10.8 (*c* 1.0, $CHCl_3$)], and thereafter by order of elution. [f] Temperature = 23 °C.

reaction. The results of this screening process improved enantioselectivity yet further: ligands **4b** and **5** both promoted the reaction with almost complete enantioselectivity (entries 3 and 8); **5** also gave an excellent yield. These levels of enantioselectivity represent an improvement in $\Delta\Delta G^{\ddagger}$ for diastereomeric transition states that lead to **3***R* vs **3***S* ($\Delta\Delta\Delta G^{\ddagger}$ (*R*−*S*)), compared to the best prior ligand,[10] of ∼3800 J mol^{-1}.

General trends could also be discerned from the results. First, cyclic amine substituents[20] at C-2 gave enantioselectivities and yields higher than those of noncyclic ones (Table 1, entries 2−4 vs 5−7). Second, β-gluco ligands gave selectivity higher than that of their α−anomers (Table 1, entries 8 vs 2), whereas α-manno ligands gave good yields but low enantioselectivity and α-allo ligands gave only poor yields and low enantioselectivity. The diastereomeric fine-tuning shown, in particular, by β-gluco vs α-gluco ligands highlights the importance of second-sphere/chiral relay effects,[21] which may be readily exploited in carbohydrate ligands as a result of their abundance of stereogenic centers.[17]

Encouraged by these excellent results for ligands **4a** and **5**, we wished to investigate the possibility of developing a catalytic version of this reaction. For this purpose we chose ligand **4a** and varied temperature, solvent, and reagent stoichiometry as shown in Table 2. We tested DCM and THF as alternative solvents for the reaction and found that THF severely hindered the reaction (Table 2, entry 4), whereas DCM caused only a slight deterioration of both yield and ee compared to toluene (Table 2, entry 3). Upon initial use of both sub-stoichiometric $Zn(OTf)_2$ and ligand, yields were reduced (entries 5 and 6). However, experiments using 1 equiv of $Zn(OTf)_2$ and sub-stoichiometric **4a** led to a successful system using 0.55 equiv of ligand (entry 7) in which the yield (86%) and ee (93%) were only slightly reduced compared to the reaction with 1.2 equiv of ligand. A ∼2:1 ratio of Zn(II) to ligand appeared to be the maximum

(12) For reviews, see: Kunz, H.; Rück, K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 336. Hale, K. J. In *2nd Supplements to the 2nd Edition of Rodd's Chemistry of Carbon Compounds*; Sainsbury, M., Ed.; Elsevier: New York, 1993; Vol. 1E−G, pp 217−313. Inch, T. D. *Adv. Carbohydr. Chem. Biochem.* **1972**, *27*, 191. For related organocatalysis, see: Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 488.

(13) Bauer, T.; Tarasiuk, J.; Pasniczek, K. *Tetrahedron: Asymmetry* **2002**, *13*, 77.

(14) Selke, R.; Ohff, M.; Riepe, A. *Tetrahedron* **1996**, *52*, 15079.

(15) Masumoto, S.; Usuda, H.; Suzuki, M.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 5634.

(16) Diéguez, M.; Ruiz, A.; Claver, C. *Dalton Trans.* **2003**, *15*, 2957.

(17) Emmerson, D. P. G.; Villard, R.; Mugnaini, C.; Batsanov, A.; Howard, J. A. K.; Hems, W. P.; Tooze, R. P.; Davis, B. G. *Org. Biomol. Chem.* **2003**, *1*, 3826.

(18) Emmerson, D. P. G.; Hems, W. P.; Davis, B. G. *Tetrahedron: Asymmetry* **2005**, *16*, 213.

(19) Ligand (1.2 equiv) and $Zn(OTf)_2$ (1.1 equiv) were disolved in toluene, followed by addition of Et_3N and then, after 2 h, acetylene followed by aldehyde.

(20) For another example of a chiral morpholino alcohol, see: Nugent, W. A. *Chem. Commun.* **1999**, 1369.

(21) Bull, S. D.; Davies, S. G.; Fox, D. J.; Garner, A. C.; Sellers, T. G. R. *Pure Appl. Chem.* **1998**, *70*, 1501.

Table 2. Catalytic Asymmetric Alkynylation of **2** with **1**

	no. of equiv			temp	time		yield	ee
	$Zn(OTf)_2$	Et_3N	**4a**	(°C)	(h)	solvent	(%)[a]	(%)[b]
1	1.1	1.2	1.2	23	21	PhMe	3	71
2	1.1	1.2	1.2	40	21	PhMe	95	97
3	1.1	1.2	1.2	40	21	DCM	86	89
4	1.1	1.2	1.2	40	48	THF	8	51
5	0.2	0.5	0.22	40	21	PhMe	14	67
6	0.5	0.55	0.55	40	21	PhMe	39	91
7	1.1	1.2	0.55	40	21	PhMe	86	93
8	1.1	1.2	0.22	40	21	PhMe	55	54
9	0.5	1.2	0.22	40	21	PhMe	65	37
10	0.2	0.5	0.22	60	21	PhMe	64	84
11	0.2	1.2	0.22	60	21	PhMe	20	39
12	0.5	1.2	0.22	60	44	PhMe	56	33

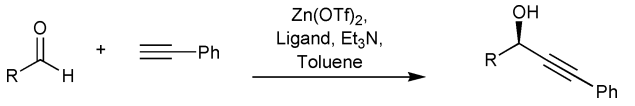
[a] Isolated yield after column chromatography. [b] Determined by chiral GC using 25 m CDex-β column. Absolute configuration (*R*) for all.

that was tolerated (entries 7 vs 8). We then investigated the reaction at 60 °C and found that a good ee (84%) and moderate yield (64%) could be achieved under these conditions with a catalytic (20 mol %) amount of $Zn(OTf)_2$ and base (entry 10).[22] Interestingly, at 60 °C, a larger excess of base with respect to $Zn(OTf)_2$ was detrimental to enantioselectivity (entries 10 and 11).

We then turned our attention to substrate generality using the noncatalytic conditions optimized in Table 1. Using the two most successful ligands **4a** and **5** we first tested addition of phenylacetylene **1** to a range of straight chain and α−branched aliphatic aldehydes and *para*-substituted aromatic aldehydes (Table 3). Cyclopropanecarboxaldehyde, isobutyraldehyde, and pivalaldehyde were chosen as examples of branched chain aldehydes, and in all cases excellent enantioselectivities were obtained in additions of phenylacetylene (entries 1−6, Table 3). Indeed when the ligand **5** was used our results mostly improved upon the best enantioselectivities previously reported for these reactions,[2,10] although in some cases yields using ligand **5** were lower.

The additions of **1** to heptaldehyde and 3-phenylpropionaldehyde were investigated as examples of additions to aliphatic aldehydes without α-branching using ligands **4a**, **4c**, and **5** (entries 7−11). High yielding additions of acetylenes to such aliphatic aldehydes remain a particular challenge using existing ligands.[23] We found that only moderate yields (55%) were possible with heptaldehyde and poor yields (15%) were obtained with 3-phenylpropionaldehyde, although enantioselectivity was high in both cases (92% and 98% ee, entries 7 and 11, Table 3, respectively). Warming to 60 °C for the addition to heptaldehyde improved yield (68%) but drastically reduced ee (26%, entry 9). Aldol self-condensation of straight chain aliphatic aldehydes has been suggested[23] as a reason for reduced yields. We found no such byproducts; rather, in the addition to 3-phenylpropionaldehyde, a product due to aldol reaction followed by crossed-Tishchenko reaction between aldol adduct and unreacted aldehyde was isolated as a 0.8:1 mixture of diastereomers (~50% yield for both ligands **4a** and **5**). An analogous product was observed by NMR and MS from the addition to heptaldehyde. The potential of this tandem aldol-Tishchenko reaction[24−30] is being explored.

Table 3. Alkynylation of Aldehydes with Phenylacetylene



	ligand	R	temp (°C)	time (h)	yield (%)[a]	ee (%)[b]
1	**4a**	*i*-Pr	23	40	80	95
2	**5**	*i*-Pr	23	40	70	97
3	**4a**	*c*-Pr	23	40	64	65
4	**5**	*c*-Pr	23	40	71	94
5	**4a**	*t*-Bu	40	40	51	81
6	**5**	*t*-Bu	40	20	62	97
7	**4a**	n-C_6H_{13}	40	21	55	92
8	**4c**	n-C_6H_{13}	40	21	46	73
9	**4a**	n-C_6H_{13}	60	10	68	26
10	**4a**	$Ph(CH_2)_2$	23	40	4	74
11	**5**	$Ph(CH_2)_2$	23	40	15	98
12	**4a**	Ph	40	24	50	91[c]
13	**5**	p-$CH_3C_6H_4$	23	44	38	97
14	**5**	p-$CH_3C_6H_4$	50	44	19	64
15	**7**	p-$CH_3C_6H_4$	23	44	43	23
16	**4f**	p-$CH_3C_6H_4$	23	44	18	0
17	**5**	p-$CH_3OC_6H_4$	23	44	11	nd
18	**5**	p-$CH_3OC_6H_4$	50	44	12	nd
19	**5**	p-ClC_6H_4	23	44	36	98
20	**5**	p-ClC_6H_4	50	44	62	81
21	**4a**	PhCH=CH	40	72	17	nd
22	**5**	PhCH=CH	40	44	14	nd

[a] As for Table 2. [b] Determined by chiral HPLC (chiracel OD column). [c] Determined by chiral GC (25 m CDex-β column). nd = not determined.

Benzaldehyde, *p*-chlorobenzaldehyde, *p*-tolualdehyde, *p*-anisaldehyde, and the conjugated aldehyde cinnamaldehyde were chosen as representative examples of aromatic aldehydes (entries 12−22). Additions to benzaldehyde using ligand **A** have been reported to give reduced yields due to Canizzaro side-reaction[23] and alkynyl zinc reagents prepared in situ by the reaction of terminal alkynes with dialkyl zincs have usually been employed for aromatic aldehydes.[5,6,31] The only high yield for addition to benzaldehyde using the amino-alcohol/ $Zn(OTf)_2$ system employed ligand **B**[10] and gave 85% yield and 97% ee. We too found reaction with aromatic aldehydes to be problematic, especially for cinnamaldehyde and the aromatic aldehydes with *para* electron-donating groups for which low yields were recorded. In some cases

(22) This compares with selectivities of 86% ee in, e.g., ref 23.

(23) Anand, N. K.; Carreira, E. M. *J. Am. Chem. Soc.* **2001**, *123*, 9687. For another catalytic system developed during the course of this work, see also: Takita, R.; Yakura, K.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 13760.

(24) Bodnar, P. M.; Shaw, J. T.; Woerpel, K. A. *J. Org. Chem.* **1997**, *62*, 5674.

(25) Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447.

(26) Curran, D. P.; Wolin, R. L. *Synlett* **1991**, 317.

(27) Berkhardt, E. R.; Bergman, R. G.; Heathcock, C. H. *Organometallics* **1990**, *9*, 30.

(28) Mahrwald, R.; Costisella, B. *Synthesis* **1996**, 1087. Rohr, K.; Herre, R.; Mahrwald, R. *Org. Lett.* **2005**, *7*, 4499.

(29) Horiuchi, Y.; Taniguchi, M.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1995**, *36*, 5353.

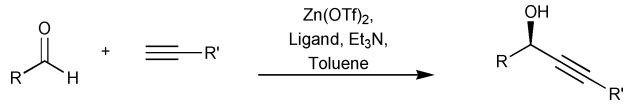
(30) For catalytic variants, see: Mascarenhas, C. M.; Miller, S. P.; White, P. S.; James P. Morken, J. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 601. Gnanadesikan, V.; Horiuchi, Y.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 7783.

(31) Xu, Z.; Wang, R.; Xu, J.; Da, C.-S.; Yan, W.-J.; Chen, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 5747.

Canizzaro products were isolated, but interestingly ketones probably resulting from crossed Canizzaro reaction between aldehyde and product alcohol were also formed. Nonetheless, high enantioselectivity (97% ee) was still achieved in these examples when **5** was used as the ligand despite low yields (entry 13). Increasing the temperature was not greatly successful in improving the yield and often resulted in a reduced ee (entry 14). In the case of benzaldehyde and electron-deficient *p*-chlorobenzaldehyde, better yields (50−62%) were achieved, and once again enantioselectivity was excellent (91−98% ee, entries 12 and 19, Table 3). Increasing the temperature to 50 °C from 23 °C resulted in increased yield but lower (81%) ee (entry 20, Table 3). Encouraged by these results, stereochemical and functional changes in ligand were tested in the addition of **2** to *p*-tolualdehyde. Trends were as for addition to **1**, a slight increase in yield but reduction in ee for α-manno **7** (entry 15, Table 3) and a dramatic loss of activity and enantioselectivity for dibenzylamine **4f** (entry 16).

Finally, we investigated the applicability of our ligands to additions to **1** of a range of terminal acetylenes with different functionalities: silyl ethers, a primary alcohol, and a secondary alcohol under noncatalytic conditions (Table 4).

Table 4. Alkynylation of Aldehydes by Terminal Acetylenes



	ligand	R′	R	temp (°C)	time (h)	yield (%)[a]	ee (%)
1	**5**	$Ph(CH_2)_2$	Cx[d]	23	24	89	95[b]
2	**5**	$Ph(CH_2)_2$	*t*-Bu	23	24	77	>99[b]
3	**4a**	Me_2COH	Cx	23	44	39	94[c]
4	**5**	Me_2COH	Cx	50	44	71	99[c]
5	**5**	Me_2COTMS	Cx	23	44	8	98[c]
6	**5**	Me_2COTMS	Cx	50	20	68	97[c]
7	**5**	$HO(CH_2)_2$	Cx	50	12	90	98[c]
8	**5**	Et_3Si	Cx	23	44	11	>99[c]
9	**5**	Et_3Si	Cx	50	20	42	98[c]

[a−c] As for Table 3. [d] Cx = cyclohexyl.

Ligand **5** was selected since it had given the highest enantioselectivities. 4-Phenylbut-1-yne gave good yields (77−89%, entries 1 and 2) and excellent enantioselectivity, especially for the addition to pivalaldehyde (>99% ee, entry 2). Using 2-methylbut-3-yn-2-ol and its TMS protected analogue, moderate to good yields were achieved at an elevated temperature also in excellent enantioselectivity (entry 4, 99% ee). These results demonstrated the tolerance of the reaction to a secondary alcohol, but silyl ether protection was not severely detrimental to either yield or ee. A high yield (90%) and excellent ee (98%) was also observed for but-3-yn-1-ol (entry 7). Excellent enantioselectivity (>99% ee, entry 8) was observed in the reaction with triethylsilylacetylene but the yield was low (11%); increasing reaction temperature improved yield (42%, entry 9) without severely diminishing ee (98%).

In conclusion, we have found a ligand, **5**, that gives very high enantioselectivities for the addition of terminal acetylenes to aldehydes, generally improving upon results obtained with **A**. For more challenging substrates, such as unbranched aliphatic and aromatic aldehydes, we have recorded excellent enantioselectivities but more disappointing yields. Isolated, characterized byproducts suggest previously unobserved aldol/crossed-Tishchenko or crossed-Cannizaro reactions compete. Moreover, ligand stereochemical diversification revealed that β-gluco **5** gave enhanced enantioselectivity over α-gluco **4a**. Thus, variation of anomeric configuration tunes enantioselectivity ($\Delta\Delta\Delta G^{\ddagger}$ (*R*−*S*) of 2800−5000 J mol^{-1}) and demonstrates that chiral information may be "relayed" to the metal binding site. Variation of stereogenic centers directly adjacent to the *N*,*O*-binding site to create α-allo **6** or α-manno **7** ligands has an even larger effect.

It is interesting that the two most successful ligands bear 2-(4-morpholinyl) moieties; corresponding deoxo, 2-piperidinyl, ligand **4c** showed significantly reduced enantioselectivities. Although, in the absence of investigations into nonlinear effects, we cannot rule out a bimetallic intermediate such as that operating in DIAB-catalyzed addition of dialkylzincs to aldehydes,[32] it seems reasonable to speculate that the morpholinyl oxygen plays an important role in coordinating zinc in a tentative tridentate transition state such as **C** (Figure 1). Basic molecular models, low reactivity in

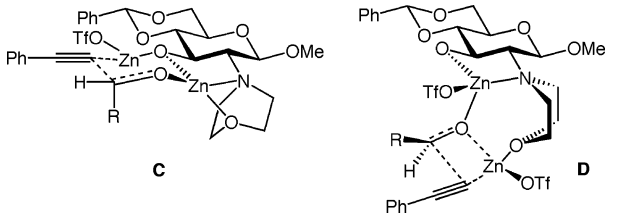


Figure 1. Proposed transition states.

THF (Table 2), and similar suggested coordination in dialkylzinc-aldehyde additions[33] support this possibility. Alternatively, in line with a proposed bifunctional mechanism for dialkynylzinc-aldehyde reaction,[34] this oxygen may act as a Lewis base activating zinc acetylide in a transition state such as **D**.

Acknowledgment. We thank Johnson Matthey Catalysis and Chiral Technologies (D.P.G.E.) for funding.

Supporting Information Available: Experimental procedures and characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

OL052503L

(32) Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028.
(33) Hanyu, N.; Aoki, T.; Mino, T.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2000**, *11*, 4127.
(34) Kang, Y.-F.; Liu, L.; Wang, R.; Yan, W.-J.; Zhou, Y.-F. *Tetrahedron: Asymmetry* **2004**, *15*, 3155.