Pergamon

Tetrahedron Letters, Vol. 38, No. 5, pp. 753-756, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(96)02453-7

A Potentially General Intramolecular Biaryl Coupling Approach to Optically Pure 2,2'-BINOL Analogs

Bruce H. Lipshutz,* Brian James, Shelly Vance, and Isaac Carrico

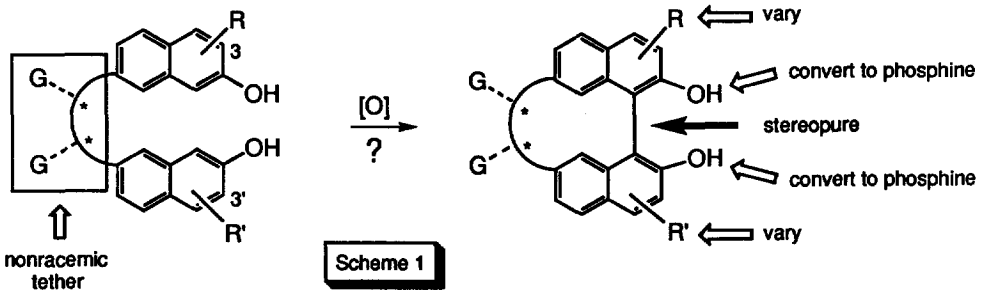
Department of Chemistry

University of California, Santa Barbara, CA 93106

[Fax: 805-893-8265; E-Mail: lipshutz@sbmm1.ucsb.edu]

Abstract. Tethering of two equivalents of mono-protected 2,7-dihydroxynaphthalene gives an intermediate which allows for eventual copper-catalyzed intramolecular biaryl coupling to afford a new nonracemic BINOL documenting a new strategy to modified binaphthyl ligands.

That the 2,2'-binaphthyl system is of tremendous importance in asymmetric synthesis is hardly a matter of debate.[1] Within this family of reagents lies the parent, BINOL,[2] uses of which continue to provide impressive advances in chiral, nonracemic molecule constructions. But what if a modified BINOL catalyst is desired? Classical[3] or enzymatic[4] resolution procedures may not be applicable. How are 3,3'-disubstituted derivatives, known to modify activity, prepared?[5] Typically, expensive BINOL is the starting material. And how would an unsymmetrically (*e.g.*, 3-) mono-substituted derivative of nonracemic BINOL be realized?[6] Other noteworthy features not easily addressed with BINOL include: (1) How can its solubility characteristics be altered?; (2) How can BINOL be attached to a Merrifield (heterogeneous)[7] or PEG (soluble)[8] polymer support? Lastly, what are the prospects for incorporating these features into the corresponding BINAP system? It is toward these goals that we now describe our preliminary results; that is, the successful demonstration of an intramolecular biaryl coupling strategy initially leading to a new nonracemic BINOL equivalent, a strategy which has the potential for applications to more highly substituted analogs of both the BINOL and BINAP arrays (Scheme 1).



Scheme 1

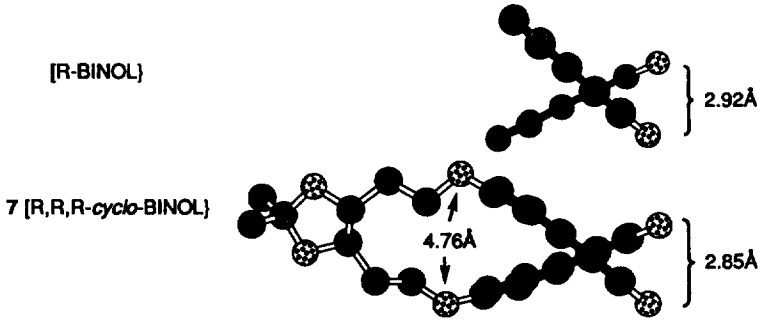
Several desirable features were initially outlined at the planning stage of ligand design. Chief among these was the source of chirality in the tether, which was anticipated to arise from a Sharpless asymmetric dihydroxylation (AD),[9] rather than, *e.g.*, a carbohydrate precursor, which might require extensive manipulation. Moreover, since the tether remains as part of any new BINOL system, competition for metal complexation by oxygen atoms therein must be minimized. Lastly, the sequence should rely on readily available, inexpensive chemicals and provide optically pure material.

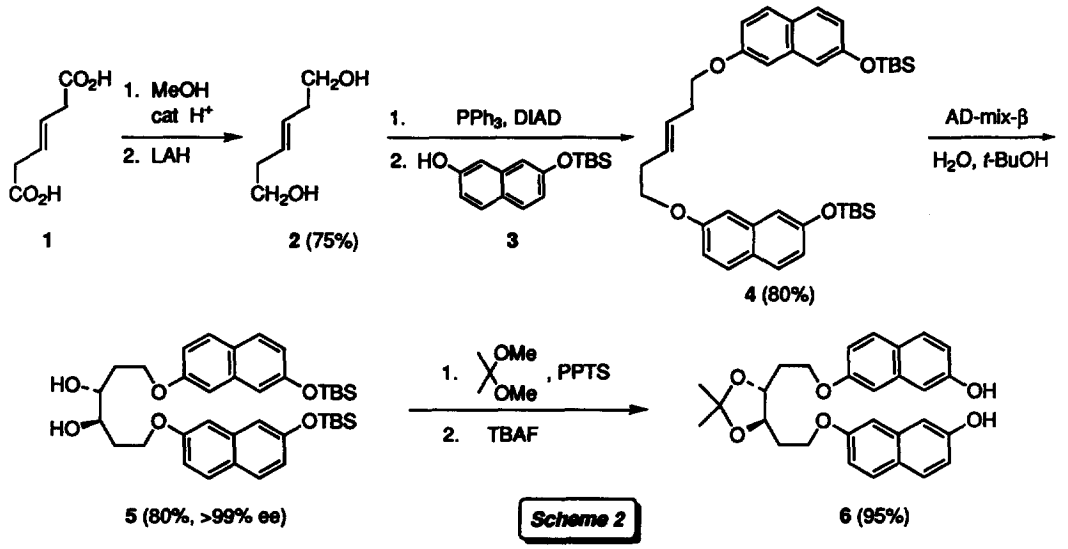
Starting with commercially available *E*-β-hydromucconic acid **1**, esterification and LAH reduction gave diol **2** (Scheme 2). A double Mitsunobu reaction[10] using monosilylated naphthalene-diol[11] **3** afforded **4** and set the stage for the Sharpless AD. Using AD-mix-β,[9] diol **5** was obtained, which by ^{19}F NMR analyses of the *bis* Mosher's ester,[12] appears to be a single enantiomer. Acetonide formation and fluoride-based desilylation resulted in the biaryl precursor **6**.

Exposure of **6** in CH_2Cl_2 (0.001 M) to 8 mol % CuCl(OH)•TMEDA complex[13] in the presence of $^3O_2$ gives rise to the desired 8-*cyclo*-BINOL[14] **7** in 90-95% isolated yield as a 12:1 mix of separable diastereomers (Equation 1). Use of concentrations greater than 0.001 M led to increasing amounts of polymeric, baseline materials. Addition of precursor **6** *via* syringe pump, however, allowed for realization of **7** at final concentrations of 0.01 M. Other metal salts (*e.g.* Mn(II),[15h] Fe(III)[15f,g] salts, etc.) commonly used for these purposes, required in stoichiometric amounts, gave inferior yields of biaryl.

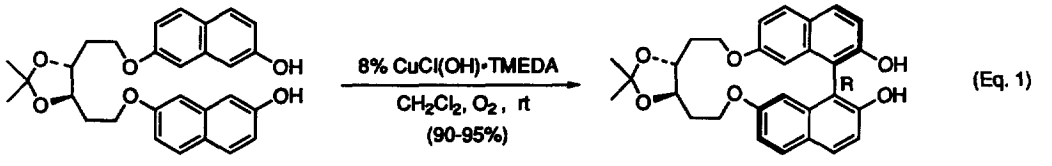
To test the effectiveness of **7**, Keck allylations[16a,b] were performed in side-by side experiments along with optically pure BINOL. As illustrated in Scheme 3, *identical* results, both in terms of yields and ee's, were realized employing either benzaldehyde or cyclohexanecarboxaldehyde as educt.[17] In line with these observations, a Chem3D[18] view of tethered biaryl **7** appears to be superimposable with that of BINOL (Figure 1). When the 12 : 1 mix of (RRR) : (RRS) isomers **7** (*i.e.*, 85% de, Eq. 1) was applied to benzaldehyde, the product[16c] obtained (86%) was of comparable ee (92%), suggesting a nonlinear effect (NLE)[19] as seen previously in these allylations with the parent BINOL.[20]

Figure 1

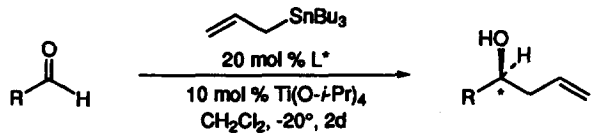




Scheme 2



Scheme 3



Ligand (L*)	Yield (%)	ee (%)		RCHO
R-BINOL	98	95	(literature)[15]	CHO
	84	95	(this work)	
(R,R,R)-*cyclo*-BINOL 7	84	95	(this work)	
R-BINOL	59	83	(literature)[15]	CHO
	56	88	(this work)	
(R,R,R)-*cyclo*-BINOL 7	58	85	(this work)	

In summary, the synthesis of the first member of the *cyclo*-BINOL series,[14] **7**, described herein represents a "proof of principle" example of our approach toward a wealth of novel, finely tuned, nonracemic BINOLs.[21] Compound **7** is a white, stable solid (mp 118-120 °C) which can be prepared in six steps in 41% overall yield. Its synthesis relies on readily available and inexpensive materials. Further developments of this and related routes to substituted *cyclo*-BINOL and derived *cyclo*-BINAP[22] analogs will be reported in due course.

Acknowledgements. We warmly thank the NIH and NSF for financial support of our programs. Suggestions and comments provided by Prof. Keck (Utah) are greatly appreciated.

References and Notes

1. Rosinio, C.; Franzini, L.; Raffaelli, A. Salvadori, P. *Synthesis*, **1992**, 503.
2. (a) Cram, D. J.; Cram, J. M. *Acc. Chem. Res.* **1978**, *11*, 8. (b) Jacques, J.; Fouquay, C. *Tetrahedron Lett.* **1971**, 4617. (c) Noyori, R.; Tomino, I.; Tanimoto, Y. *J. Am. Chem Soc.* **1979**, *101*, 3129.
3. (a) Jacques, J.; Fouquay, C. *Org. Synth.* **1988**, *67*, 1. (b) Truesdale, L. *Org. Synth.* **1988**, *67*, 13. (c) Mazalerat, J. -P.; Wakselman, M. *J. Org. Chem.* **1996**, *61*, 2695.
4. (a) Fujimoto, Y.; Iwadate, H.; Ikekawa, N. *J. Chem. Soc., Chem. Commun.* **1985**, 1333. (b) Kazlaukas, R. J. *J. Am. Chem. Soc.* **1989**, *111*, 4953.
5. For examples, see Ishihara, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 1561; Bao, J.; Wulff, W.D. *ibid.*, **1993**, *115*, 3814.
6. See, *e.g.*, Maruoka, K.; Saito, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1995**, *117*, 1165.
7. Barany, G.; Merrifield, R.B. in *The Peptides*, Gross, E., Meienhofer, J., Eds., Academic Press, N.Y., 1979, Vol 2, p 1.
8. Han, H.; Janda, K.D. *J. Am. Chem. Soc.* **1996**, *118*, 7632.
9. Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.
10. (a) Hughes, D. L. *Org. React.* **1992**, *42*, 335; (b) Mitsunobu, O. *Synthesis* **1981**, 1.
11. As no procedure exists for the monosilylation of aromatic diols, a statistical ratio of products was obtained upon treatment of 2,7-dihydroxynaphthalene with TBDMS-Cl in the presence of Et_3N and DMAP.
12. (a) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. (b) Dale, J. A.; Mosher, H. S. *J. Am.. Chem.. Soc.* **1973**, *95*, 512.
13. Noji, M.; Nakajima, M.; Koga, K. *Tetrahedron Lett.* **1994**, *35*, 7983.
14. We suggest that *cyclo*-BINOLs be named according to tether length. Compound **7** is an 8-*cyclo*-BINOL, which is modified by the oxygens at the 1" and 8" positions; hence 1",8"-di-O-8-*cyclo*-BINOL.
15. Cu(II): (a) Feringa, B.; Wynberg, H. *Tetrahedron Lett.* **1977**, 4447. (b) Sakamoto, T.; Yonehara, H; Pac, C. *J. Org. Chem.* **1994**, *59*, 6859. (c) Brusee, J.; Groenedijk, J. L. G.; te Koppele, J. M.; Jansen, A. C. A. *Tetrahedron* **1985**, *41*, 3313. (d) Kushioka, K *J. Org. Chem.* **1983**, *48*, 4948. (e) Noji, M.; Nakajima, M.; Koga, K. *Tetrahedron Lett.* **1994**, *35*, 7983. Fe(III): (f) Pummerer, R.; Rieche, A. *Chem. Ber.* **1926**, 59. (g) Toda, F.; Tanaka, K.; Iwata, S. *J. Org. Chem.* **1989**, *54*, 3007. Mn(III): (h) Dewar, M. J. S.; Nakaya, T. *J. Am. Chem. Soc.* **1968**, *90*, 7134.
16. (a) Keck, G. E.; Tarbet, K. H.; Geraci, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 8467; see also Costa, A.L.; Piazza, M.G.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *ibid.*, **1993**, *115*, 7001. (b) Keck. G. E.; Geraci, L. S. *Tetrahedron Lett.* **1993**, *34*, 7827. (c) Brown, H.C.; Jadhav, P.K. *J. Am. Chem. Soc.* **1983**, *105*, 2092; (d) Faller, J.W.; Sams, D.W.I.; Liu, X. *ibid.*, **1996**, *118*, 1217; (e) Weigand, S.; Bruckner, R. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1077; (f) Yu, C-M.; Choi, H-S.; Jung, W-H.; Lee, S-S. *Tetrahedron Lett.* **1996**, *37*, 7095.
17. The catalyst could be routinely recovered from each reaction mixture in 70-75% yields.
18. Molecular Mechanics calculations were performed using the MM3 force field as applied by the Chem3D modeling program version 3.1. Copyright 1986-1995, CambridgeSoft Corporation.
19. Guillaneux, D.; Zhao, S.-H.; Samuel, O.; Rainford, D.; Kagan, H.B. *J. Am. Chem. Soc.* **1994**, *116*, 9430.
20. Keck, G.E.; Krishnamurthy, D.; Grier, M.C. *J. Org. Chem.* **1993**, *58*, 6543.
21. For related work with biphenyls, see Harada, T.; Ueda, S.; Yoshida, T.; Inoue, A.; Takeuchi, M.; Ogawa, N.; Oku, A.; Shiro, M. *J. Org. Chem.* **1994**, *59*, 7575.
22. Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 7180.

(*Received in USA* 4 *November* 1996; *accepted* 9 *December* 1996)