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STEREOSPECIFIC FUNCTIONALIZATION OF (R)-(-)-1,1'-BI-2-NAPHTHOL TRIFLATE[1]

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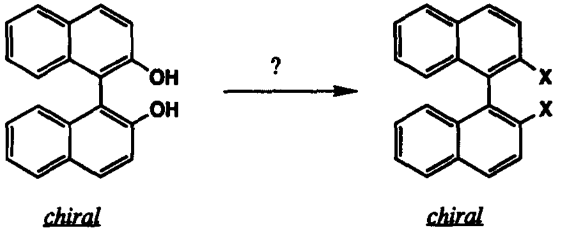
Summary: Several examples of transition metal mediated functionalization of chiral 1,1'-bi-2-naphthol triflate are described which proceed with complete retention of substrate chirality. The transformations described demonstrate the potential of Pd(0) mediated reactions for the stereoselective transformation of the C-O bonds in this substrate.

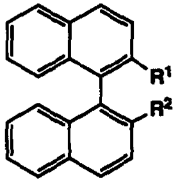
In recent years, chiral 2-substituted-1,1'-binaphthyls have been shown to be useful agents for asymmetric induction in a variety of organic reactions.[2] These substances can serve well as stoichiometric auxiliaries or as ligands in catalytic transition metal mediated processes. As part of a program to generate additional binaphthyls for study in this area, we have examined the potential of functionalizing the readily available[3] (R)-(-)-1,1'-bi-2-naphthol triflate (1). Although functionalization at the O-H bond of chiral 1,1'-bi-2-naphthol is well known,[4] transformations which convert the C-O bonds into other relevant functionality for asymmetric induction (equation 1) are not well documented. Many examples of transition metal mediated functionalization of aryl triflates are known[5] but at the time that this work was undertaken[6] we were unable to find reports of such reactions with the subject triflate. Preservation of the substrate's chiral integrity throughout the transformation is an obvious criterion for success of this approach. Murdoch[7] has shown that a diazotization/lithiation sequence performed on (R)-(+)-2,2'-diamino-1,1'-binaphthyl can be useful under certain conditions. The diazotization approach has been applied to the synthesis of binaphthyl selenides.[2m] As a preface for embarking on the synthesis of novel binaphthyls from 1-1'-bi-2-naphthol we studied two representative reactions of the derived triflate: Pd(0) mediated phosphorylation and Ni(0) mediated cyanation. The results described below bode well for the use of such reactions in the stereospecific functionalization of chiral 1,1'-bi-2-naphthol via its triflate.



(1)

X = PR_2, NR_2, SR, CR_3, etc.

The phosphorylation of the triflate 1 had the most obvious relevance given the key achievements made possible with BINAP type ligands.[2a-h, k] The availability of chiral binaphthyl phosphonates could in principle allow rapid construction of a variety of chiral binaphthyl phosphines variously substituted at phosphorus. Using a method published for such a conversion[8], the substrate reacted sluggishly; under vigorous conditions (140° C, 44 hr, Et_3N, 2.9 equiv. $HPO(OEt)_2$, 0.1 equiv. $Pd(PPh_3)_4$), incomplete conversion of 1 gave a 32 % yield of the monosubstitution product 3.[9] Only triflate cleavage was observed using Ph_2POH under these conditions. Starting material could be recovered unracemized from these reactions.[10]



(-)-1 $R^1, R^2 = OTf$
(+)-2 $R^1 = OTf, R^2 = POPh_2$
(-)-3 $R^1 = OTf, R^2 = PO(OEt)_2$
(-)-4 $R^1 = OH\ R^2 = POPh_2$
(-)-5 $R^1 = OH, R^2 = PO(OEt)_2$
(+)-6 $R^1 = H\ R^2 = POPh_2$
(-)-7 $R^1 = H, R^2 = PO(OEt)_2$
(-)-8 $R^1 = H, R^2 = OTf$
(-)-9 $R^1 = OTf, R^2 = CN$
(-)-10 $R^1, R^2 = CN$

More efficient conversion of 1 could be carried out by using the expedient described by Dolle, *et. al.*[11] In DMSO at 80 - 90° C containing 3 - 4 equiv. of the phosphorylating agent and 6 equiv. of $EtN(i\text{-}Pr)_2$, 1 was completely consumed after 18 hr when the catalyst system $Pd(OAc)_2$/dppp/NaOCHO (0.1 equiv./0.1 equiv./0.22 equiv.) was used. Monosubstitution products 2[9] and 3[9] were isolated in yields of 65 - 77 % along with their respective hydrogenolysis products 6[9] (20 %) or 7[9] (11 %). In reactions taken to completion, the remainder of the material (up to 10 %) often could be accounted for by the triflate hydrolysis[12a] products 4[9] and 5.[9] Bis-phosphorylation products were not apparent as significant products in the crude reaction mixture. All of the products were formed with enantiomeric purity equal to that of the starting binaphthol (> 99 %) thus demonstrating the stereospecific nature of the reactions.[10]

Several observations suggest that the hydrogenolysis products 6 and 7 form by initial monohydrogenolysis of the ditriflate 1 followed by phosphorylation rather than by hydrogenolysis of the monosubstitution products. Under conditions which resulted in complete conversion of 1 to 1,1'-binaphthalene ($Pd(OAc)_2$ (0.1 equiv.), dppp (0.1equiv.), NaOCHO (0.22 equiv.), $EtN(i\text{-}Pr)_2$ (6 equiv.), DMSO, 80 - 90° C, 14 hr)[12], 2 and 3 are not converted to 6 and 7. Monotriflate 8,[9] prepared from (R)-1,1'-binaphthalene-2-ol[13] stereospecifically couples with Ph_2POH to form 6.

The conditions of Widdowson[14] described for triflate cyanation were also applied to 1. Although short catalyst lifetime appeared to limit the efficiency of the reaction with this hindered substrate, both mono and disubstitution products 9[9] and 10[9] were obtained stereospecifically[10] under the described conditions ($NiBr_2$ (0.1 equiv.), Ph_3P (0.4 equiv.), Zn powder (0.3 equiv.), KCN (1.1 equiv), MeCN ; yield at 66 % completion = 40 % 9 , 10 % 10). Attempts to force the reaction to complete disubstitution by using >2 equivalents of KCN were unsuccessful.

While these studies address only two of the many possible transition metal mediated reactions of aryl triflates, we feel that they serve to illustrate the point that substitution reactions of this type can be used to stereospecifically functionalize the axially chiral binaphthalene nucleus. The design and preparation of novel chiral ligands or auxiliaries based on this observation should help expand the important role of axially chiral reagents in asymmetric synthesis.

Typical experimental procedure (2 and 4): A mixture of 5.00 g 1, 40 mL DMSO, 3.67 g Ph_2POH, 0.204 g $Pd(OAc)_2$, 0.375 g 1,3-bis(diphenylphosphino)propane and 9.5 mL $EtN(i\text{-}Pr)_2$ is purged for 20 minutes with a N_2 stream. The mixture is heated in an oil bath at 90° C for 16 hr., cooled to ambient temperature and partitioned with 500 mL Et_2O and 300 mL water. The organics are separated and washed four times with water (250 mL), twice with 5% aqueous HCl (250 mL), twice with water (250 mL), once with saturated aqueous $NaHCO_3$ (250 mL) and once with brine (250 mL). During the acid wash, solids may develop. These are filtered and washed with Et_2O (200 mL) to remove occluded product. The Et_2O is combined with the main organic workup stream and, after drying ($MgSO_4$), concentrated to yield 5.07 g of a yellow foam. This material may be purified at this point using silica gel chromatography ($PhCH_3$:MeCN 19:1->9:1) to yield 2 as a white, friable foam (4.24 g, 77%) . Alternatively, the crude foam is dissolved in 75 mL THF and a solution of 3.5 g $LiOH\cdot H_2O$ in 25 mL H_2O is added. The mixture is stirred for 15 hr. at ambient temperature and partitioned with Et_2O (300 mL) and 5% HCl (100 mL). The organics are washed twice with water (200 mL), once with brine (200 mL), dried ($MgSO_4$) and concentrated to 3.94 g of a yellow solid. This material is purified by silica gel chromatography (CH_2Cl_2:THF 15:1) to yield 4 as a white solid (3.21 g, 75% from 1, m.p.: 148-150 °C (decomp.)). The byproduct 6 may also be revocered as a white foam (0.61 g).

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References and Notes:

†- Analytical and Environmental Research

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2. (a) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Amer. Chem. Soc.*, **1980**, *102*, 7932. (b) Miyashita, A.; Takaya, H.; Souchi, T.; Noyori, R. *Tetrahedron*, **1984**, *40*, 1245. (c) Takaya, H.; Mashima, K.; Koyano, K.;

Yagi, M.; Kumobayashi, H.; Taketoi, T.; Akutagawa, S.; Notori, R. *J. Org. Chem.*, **1986**, *51*, 629. (d)Tani, K.; Yamagata, S.; Akutagawa, S.; Kumobayashi, H.; Taketomi, T.; Takaya, H.; Miyashita, A.; Noyori, R.; Otsuka, S. *J. Amer. Chem. Soc.* **1984**, *106*, 5208 . (e) Noyori, R.; Ohta, M.; Hsiao, Y.; Kitamuar, M.; Ohta, T.; Takaya, T. *J. Amer. Chem. Soc.*, **1986**, *108*, 7117. (f) Takaya, H.; Ohta, T.;Sayao, N.; Kumobayashi, H.; Akutagawa, S.; Inoue, S.; Kasahara, I.; Noyori, R. *J. Amer. Chem. Soc.*, **1987**, *109*, 1596. (g) Ohta, T.; Takaya, H.; Kitamura, M.; Nagai, K.; Noyori, R. *J. Org. Chem.*, **1987**, *52*, 3174. (h) Noyori, R.; Ohkuma, T.; Kitamura, M.; Takaya, H.; Sayo, N.; Kumobayashi, S.; Akutagawa, S. *J. Amer. Chem. Soc.*, **1987**, *109*, 5856. (i) Hayashi, T.; Matsumoto, Y.; Ito, Y.; *J. Amer. Chem. Soc.* **1989**, *111*, 3426. (j) Mikami, K.; Terada, M.; Nakai, T. *J. Amer. Chem. Soc.*, **1989**, *111*, 1940. (k) Kitamura, M.; Ohkuma,; Inoue, S.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Ohta, T.; Takaya, H.; Noyori, R. *J. Amer. Chem. Soc.*, **1988**, *110*, 629. (l) Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *J. Amer. Chem. Soc.*, **1988**, *110*, 310. (m) Tomoda, S.; Iwaoka, M.; *J. Chem. Soc., Chem. Comm.*, **1988**, 1283. (n) Sakamoto, A.; Yamamoto, Y.; Oda, J. *J. Amer. Chem. Soc.*, **1987**, *109*, 7188. (o) Fuji, K; Node ,M.; Tanaka, F.; Hosoi, S. *Tetrahedron Lett.*, **1989**, *21*, 2825.

3. Vondenhof, M.; Mattay, J. *Tetrahedron Lett.*, **1990**, *31*, 985.

4. For an example of functionalization leading to interesting host molecules see: Cram, D.J.; Helgeson, R.C.; Koga, K.; Kyba, E.P.; Madan, K.; Sousa, L.R.; Siegel, M.G.; Moreau, P.; Gokel, G.W.; Timko, J.M.; Sogah, G.D.Y. *J. Org. Chem.*, **1978**, *43*, 2758 and Cram, D.J.; Sogan, G.D. *Tetrahedron Lett.*, **1981**, 22, 625. For an example of a ligand prepared by this approach see: Grubbs, R.H.; DeVries, R.A. *Tetrahedron Lett.*, **1977**, *18*, 1879.

5. See: (a) Huth, A.; Beetz, I.; Schumann, I. *Tetrahedron*, **1989**, *45*, 6679 . (b) Hirota, K.; Isobe, Y.; Maki, Y. *J. Chem. Soc., Perkin Trans.1*, **1989**, 2513. (c) Chen, Q-Y; He, Y.B. *Synthesis*, **1988**, 896. (d) Peterson, G.A.; Kunng, F.-A.; Mc Callum, J.S.; Wulff, W.D. *Tetrahedron Lett.*, **1987**, *28*, 1381. (e) Chen, Q.-Y.; Yang, Z.-Y. *Tetrahedron Lett.*, **1986**, *27*, 1171. (f) Cacchi, S.; Ciattini, P.C.; Morera, E.; Ortar, G. *Tetrahedron Lett.*, **1986**, *45*, 5541. (g) Moraj, S.; McMurry, J.E. *Tetrahedron Lett.*, **1983**, *27*, 2723. (h) Echavarren, A.M.; Stille, J.K.*J. Amer. Chem. Soc.*,**1987**, *109*, 5478 and references 7, 11 and 12 for some examples.

6. While this work was in progress a report appeared describing the carbonylation of 1: Hotta, H.; Suzuki, T.; Miyano, S.; Inoue, Y. *J. Mol. Cat.*, **1989**, *54*, L5.

7. (a) Brown, K.J.; Berry, M.S.; Waterman, K.C.; Lingenfelter, D.; Murdoch, J.R. *J.Amer. Chem. Soc.*, **1984**, *106*, 4717. (b) Brown, K.J.; Murdoch, J.R. *J.Amer. Chem. Soc.*, **1984**, *106*, 7843. (c) Brown, K.J.; Berry, M.S.; Murdoch, J.R. *J. Org. Chem.*, **1985**, *50*, 4345.

8. Lu, X.; Zhu, J. *Synthesis*, **1987**, 726. See also: Petrakis, K.S.; Nagabhushan, T.L. *J. Amer. Chem. Soc.* **1987**, *109*, 2831.

9. Analytical data in full agreement with the assigned structure was obtained for this compound. Characterization was carried out on representative samples and included ^1H, ^{13}C, and ^{31}P (if appropriate) NMR, IR, MS and HRMS for verification of molecular formula. For representative samples optical rotations were: 1, $[\alpha]_D$ = -149.6° (c = 1.00, CH_2Cl_2); 2 ,$[\alpha]_D$ = 6.29° (c = 1.00, CH_2Cl_2); 3, $[\alpha]_D$ = -15.00° (c = 0.63, CH_2Cl_2); 4, $[\alpha]_D$ = -108.3° (c = 1.00, CH_2Cl_2); 5 ,$[\alpha]_D$ = -137.7° (c = 1.22, CH_2Cl_2); 6, $[\alpha]_D$ = 18.14° (c = 1.02, CH_2Cl_2); 7 $[\alpha]_D$ = -34.89° (c = 1.00, CH_2Cl_2); 8 $[\alpha]_D$ = -8.97° (c = 0.50, CH_2Cl_2); 9 $[\alpha]_D$ = -33.33° (c = 1.00, CH_2Cl_2); 10 $[\alpha]_D$ = -53.95° (c = 1.01, CH_2Cl_2).

10. Enantiomeric purity for these compounds was determined by chiral HPLC on Daicell-OT® columns (Daicell Chemical Industries) verified with samples prepared from the opposite enantiomer of 1,1'-binaphthol. Detection limits for minor enantiomers were determined to be <1 % for these cases.

11. Dolle, R.E.; Schmidt, S.J.; Kruse, L.I. *J. Chem. Soc., Chem. Comm.*, **1987**, 904.

12. (a) Cabri, W; De Bernardinis, S.; Francalanci, F.; Penco, S.; Santi, R. *J. Org. Chem.*, **1990**, *55*, 350. (b) Saa', J.M.; Dopico, M.; Martorell, G.; Garcie-Raso, A. *J. Org. Chem.*, **1990**, *55*, 991.

13. See Tamai, Y; Nakano, T.; Sinji, K.; Kawahara, K.; Miyano, S. *Chem. Lett.*, **1989**, 1135.

14. Chambers, M.R.I.; Widdowson, D.A. *J. Chem. Soc., Perkin Trans. 1*, **1989**, 1365. See also Takagi, K.; Sakakibara, Y. *Chem. Lett.*, **1989**, 1957.

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