



Chiral Selection in the Formation of Borates from Racemic Binaphthols and Related Diols

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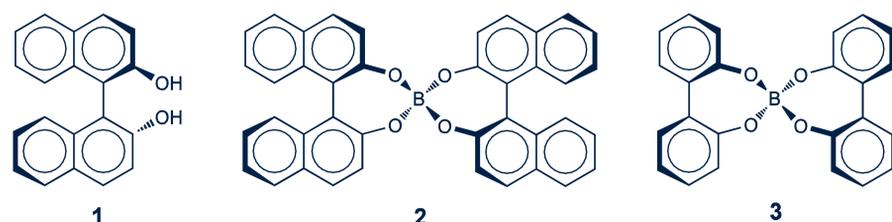
Jevgenij A. Raskatov,^{†‡} John M. Brown[†] and Amber L. Thompson^{†§}

[†] Department of Chemistry, Oxford, UK; [‡] California Institute of Technology, Pasadena, CA, USA; [§] Chemical Crystallography, Oxford, UK.

Contact – amber.thompson@chem.ox.ac.uk or raskatov@caltech.edu

Chiral Counterions and BINOL

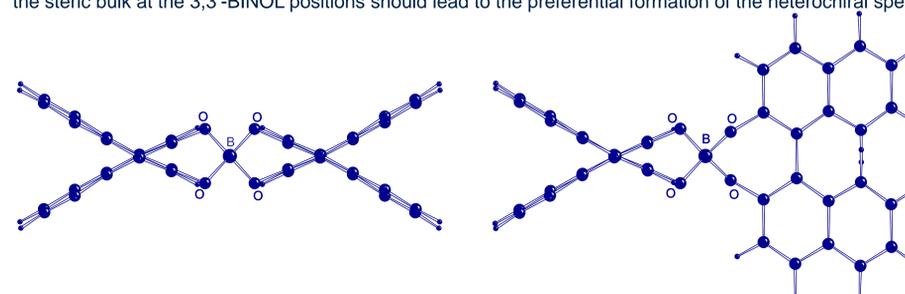
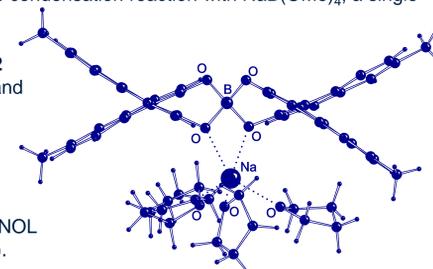
- Chiral counterions have received increasing attention from the asymmetric catalysis community in recent years.¹
- BINOL (**1**) is axially chiral; the chiral backbone of BINOL is stereochemically stable (*atropos*) and the enantiomers can be readily resolved.²
- As one of the most extensively used motifs in the creation of chiral anions, some high-profile applications of BINOL-based chiral phosphates in asymmetric catalysis have been demonstrated.^{3,4}
- The *bis*-BINOL borate (**2**), initially introduced by Periasamy for the purpose of resolving amino alcohol derivatives,⁴ has been studied less extensively in the asymmetric catalysis context.⁵
- The synthesis of *bis*-BINOL borates from racemic BINOL can yield the homochiral (*R,R*)_{ax} and (*S,S*)_{ax} or the heterochiral (*R,S*)_{ax} diastereomers.
- Recent studies of *bis*-BINOL or *bis*-biphenol borates by Wuest and co-workers (**2** & **3** respectively) have demonstrated that both form homochiral anions upon crystallisation from a racemic solution in the presence of various amines as well as other counterions.⁶



- As part of a project designed to study chiral ion pairs of relevance to asymmetric catalysis,⁷ homochiral racemates of various substituted *bis*-BINOL borates with sodium as counterion were required.
- A series of racemic or stereochemically labile chiral borate anions based on the 2,2'-biphenol motif was investigated.⁸

Atropos Borates

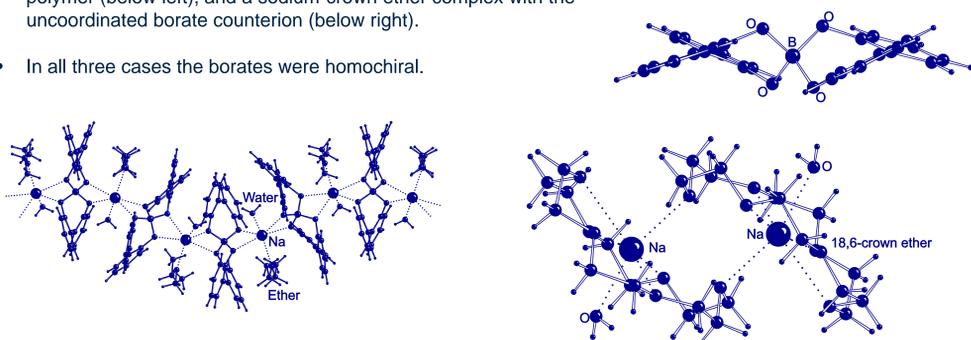
- When two equivalents of *rac*-BINOL were subjected to the condensation reaction with NaB(OMe)₄, a single compound was obtained.
- NMR indicated it was the racemate of the sodium salt of **2** with each anion being homochiral i.e. containing (*R,R*)_{ax} and (*S,S*)_{ax} rather than the heterochiral, (*R,S*)_{ax} and (*S,R*)_{ax}.
- The yield was greater than 90%, demonstrating diastereoselection in favour of the homochiral species.
- An analogous result was obtained for the 6,6'-dimethyl BINOL and the crystal structure of the salt was determined (right).
- DFT calculations were carried out on the homochiral and the heterochiral *bis*-BINOL-borate anions, but at the isolated anion level, thermodynamic differentiation was essentially negligible (0.4 kcal/mol in favour of the heterochiral diastereomer).
- The shape of the homo- and heterochiral species were very different (below). This suggested that increasing the steric bulk at the 3,3'-BINOL positions should lead to the preferential formation of the heterochiral species.



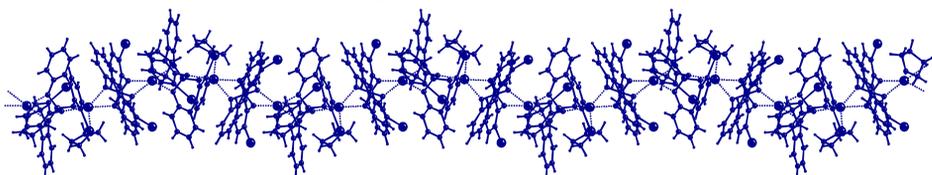
- DFT calculations identified 3,3'-diiodo-2,2'-binaphthol and 9,9'-biphenanthrol as suitable precursors with a substantial thermodynamic preference for the heterochiral anion (4.9 and 3.2 kcal/mol, respectively).
- Single crystal structures of the sodium salts gave the homochiral species and solution NMR of the single crystals confirmed these were representative of the bulk.

Tropos Borates

- All three *atropos* borate structures consisted of the sodium cation coordinated by two of the borate oxygen atoms on one face and THF/water on the other. If this structure reflected the solution behaviour the sodium could be key to the formation of the homochiral species.
- The *tropos* analogue of *bis*-BINOL, *bis*-biphenol (**3**) was used to prepare the sodium salt of the borate and crystals were grown from THF and diethylether.
- An excess of 18,6-crown ether was also used to "capture" the sodium cation and disrupt the structure.
- Three structures were observed: sodium coordinated by the borate and THF (as before); a sodium-borate polymer (below left), and a sodium-crown ether complex with the uncoordinated borate counterion (below right).
- In all three cases the borates were homochiral.

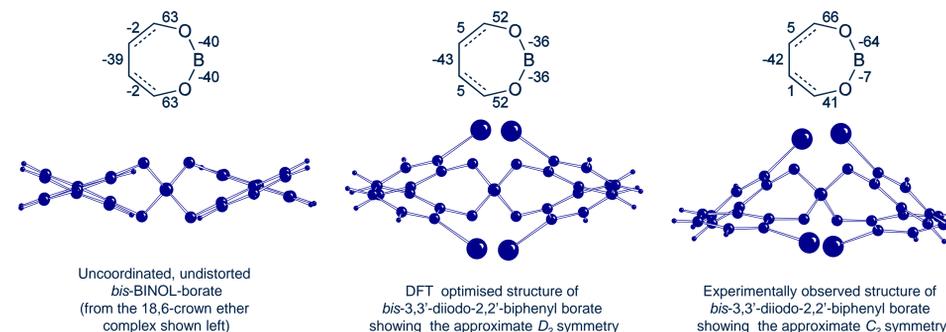
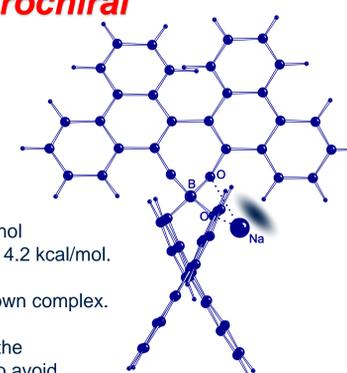


- A similar sodium-borate polymer was observed with the *bis*-3-iodo-2,2'-biphenol borate, in this case forming helices (below) which crystallised as a conglomerate, the only borate to do so in this study.



Homochiral vs. Heterochiral

- In the homochiral borate structures the sodium was coordinated by the borate oxygen atoms and THF/water.
- Since a similar binding mode in the heterochiral species would be more sterically hindered (right), it was thought this could be key to the chiral selection.
- DFT analysis of the borate anion formed from 3,3'-diiodo-2,2'-biphenol predicted a thermodynamic preference for the heterochiral anion by 4.2 kcal/mol.
- This was not seen in the crystal structure of the the sodium 18,6-crown complex.
- The DFT structure predicts an approximately *D*₂-symmetric form of the homochiral anion, but this leads to close I...I interactions. In order to avoid these, the borate distorts to yield a *C*₂-symmetric form in the solid state (torsion angles shown below). The adjacent charged counterion, a dimeric sodium-crown ether pair, may well contribute to stabilising the alternative form, thus the DFT derived predictions can only be used as a guide.



- Although we did not observe a heterochiral borate, the recent report⁹ of a heterochiral aluminate suggests that a heterochiral borate may be accessible with sufficient steric bulk at the 3,3'-position, however it is unclear what influence the increased radius of the aluminium may have had in the preparation of this material.

1. Lacour J. & Frantz R. (2005). *Org. Biomol. Chem.*, 3, 15; Terada M. (2008). *Chem. Commun.*, 4097.
2. Oki, M. (1983). *Top. Stereochem.*, 14, 4193.
3. Akiyama, T., Itoh, J., Yokota K. & Fuchibe, K. (2004). *Angew. Chem., Int. Ed.*, 43, 1566; Hamilton, G. L., Kang, E. J., Mba M. & Toste, F. D. (2007). *Science*, 317, 496; Terada, M., Soga K. & Momiyama, N. (2008). *Angew. Chem., Int. Ed.*, 47, 4122.
4. Periasamy, M., Ramanathan C. R. & Kumar, N. S. (1999). *Tet.: Asym.*, 10, 2307; Periasamy, M., Kumar, N. S., Sivakumar, S., Rao, V. D., Ramanathan C. R. & Venkatraman, L. (2001). *J. Org. Chem.*, 66, 3828.

5. Llewellyn, D. B., Adamson D. & Arndtsen, B. A. (2000). *Org. Lett.*, 2, 4165; Carter, C., Fletcher S. & Nelson, A. (2003). *Tet.: Asym.*, 14, 1995; Chen, D., Sundararaju, B., Krause, R., Klankermayer, J., Dixneuf P. & Leitner, W. (2010). *ChemCatChem*, 2, 55.
6. Tu, T., Maris, T. & Wuest, J. D. (2008). *J. Org. Chem.*, 73, 5255; Voisin, E., Maris, T. & Wuest, J. D. (2008). *Cryst. Growth Des.*, 8, 308.
7. Raskatov, J. A., Thompson, A. L., Claridge, T. D. W. & Brown, J. M., *in preparation*; Raskatov, J. A. (2009). D.Phil thesis, Oxford.
8. Raskatov, J. A., Brown J.M. & Thompson, A. L. (2011). *CrystEngComm*, 13, 2923.
9. Straub, B. F., Wrede, M. Schmid K. & Rominger, F. (2010). *Eur. J. Inorg. Chem.*, 1907.