The Nature of meso- and pyro-Borate Precatalysts to the VANOL and VAPOL BOROX Catalysts

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Abstract  
The structures of the meso- and pyro-borate esters generated by treatment of the VANOL and VAPOL ligands with triphenylborate have been revisited. These species were previously identified as precatalysts that could be in situ converted into VANOL and VAPOL BOROX catalysts by an imine substrate. The complete assignment of all protons for both the meso- and pyro-borate esters of both ligands was aided by the $^1H$ NMR spectrum of each generated from pentadeuterophenol. There were significant differences between the chemical shifts for certain protons in the meso- and pyro-borate species in both the VANOL and VAPOL derivatives. Optimized structures for the meso-borates and two different isomers of the pyro-borates were determined by DFT calculations for each ligand. For each ligand the cyclic pyro-borate was found to be lower in energy than the corresponding linear pyro-borate at the B3LYP/6-311+G(d,p) level of theory. The structures of the cyclic pyro-borate esters were more consistent with the observed $^1H$ NMR chemical shifts than the linear pyro-borates for each ligand and thus the structures of the pyro-borates esters of VANOL and VAPOL have been re-assigned as the cyclic isomers.

Keywords  
meso- and pyro-borate esters, VANOL and VAPOL ligands, VANOL and VAPOL BOROX Catalysts, imine substrate

We have found that chiral BOROX catalysts derived from the VAPOL (and VANOL) ligand are effective catalysts for a number of asymmetric reactions including cis-aziridinations,1 trans-aziridinations,2 heteroatom Diels–Alder reactions,3 aza-Cope rearrangements,4 three-component Ugi reactions,5 and quinoline reductions.6 The BOROX catalysts were originally prepared from a precatalyst which was generated by heating the VAPOL ligand with three equivalents of B(OPh)$_3$ for one hour followed by removing all volatiles at the same temperature at 0.133 mbar (Scheme 1).1,7 The precatalyst was previously determined to be a mixture of two compounds that were identified as the meso-borate 2 and the pyro-borate 3.8 The BOROX catalyst was then generated by treating the precatalyst mixture with an imine 4 at room temperature.9 The overall yield of the BOROX catalyst 5 can be quite high since B(OPh)$_3$ is not removed under the conditions for the generation of the precatalyst. Later it was found that generation of the precatalyst is not necessary as the treatment of the VAPOL ligand with imine 4 and B(OPh)$_3$ leads to the formation of the BOROX catalyst 5 in less than ten minutes at room temperature.7

The ratio of the meso-borate 2 to the pyro-borate 3 varies depending on conditions and can range from 10:1 in favor of the meso-borate 2 to 1:20 in favor of the pyro-borate 3.8 Under the conditions indicated in Scheme 1 the ratio is typically ca. 1:4 in favor of 3.8 Neither species could be obtained in completely pure form by crystallization or by silica gel chromatography since they are hydrolytically sensitive and thus were characterized as mixtures.8 One of the distinctive NMR handles that can be used to characterize these compounds is the bay proton on carbon 5 (Scheme 2) of each of the phenanthrene rings which for VAPOL appears as a doublet at $\delta = 9.79$ ppm (CDCl$_3$) which is well outside the range of the normal aromatic protons due to the diamagnetic anisotropy present in phenanthrenes. Since the precatalyst consists of a mixture of meso- and pyro-borates and since all of the protons in each molecule are aromatic, analysis of the $^1H$ NMR spectrum was quite challenging. The assignment of the bay protons to the meso- and pyro-borates was made by an analysis of the precatalyst mixture prepared from $tris-p$-tolyl borate (Scheme 2).8 Under the conditions shown in Scheme 2, a 1:1:3 mixture of borates was formed, and the VAPOL ligand was completely consumed. A different ratio of borates 6 and 7 was obtained by heating VAPOL with four equivalents of B(O-p-Tol)$_3$, and one equivalent of H$_2$O in toluene at 80 °C for one hour and then removal of all volatiles at 80 °C for 0.5 hours which gave a 1:8:4 ratio of 6/7. This allowed for a correlation of the two different methyl protons of the tolyl group with a particular
bay proton. The integration of the bay proton at $\delta = 9.63$ ppm against the tolyl methyl group at $\delta = 2.50$ ppm was found to be 1:1.8 for 6 (1:1.5 expected), and the integration of bay proton at $\delta = 9.35$ ppm against the tolyl methyl group at $\delta = 2.24$ ppm was found to be 1:3.5 for 7 (1:3.0 expected).

High resolution mass spectroscopic analysis of the 1:1.3

Scheme 1

Scheme 2
mixture of 6/7 revealed two parent ions with an intensity ratio of 1:1.3, and the calculated mass for each ion matched that expected for the two borates. There was not any evidence to definitively distinguish between the isomeric pyro-borates 7 and 9 (or 3 and 8). A tentative assignment of the pyro-borate as the linear structure 3 rather than the cyclic structure 8 was made on the basis of the $^{11}$B NMR spectrum. Three coordinate borate esters present a broad absorption at $\delta = 16–18$ ppm and for a 1:8 mixture of 6/7 this broad absorption appeared as two equal peaks that were slightly separated. The linear pyro-borate 3 would be expected to have two different borons, and the symmetric cyclic pyro-borate 8 would be expected to have a single boron. However, since the presence of other borate esters including B(OPh)$_3$ could not be rigorously excluded, assignment of the pyro-borate ester as the linear isomer 3 on this basis can only be classified as tentative.

In our original publication all of the protons for the meso-borate 2 and the pyro-borate 3 were not assigned from the mixture of the two.$^8$ A subsequent effort to do so began with a consideration of the $^1$H NMR spectrum of 1:4.3 mixture of 2/3 (Figure 1). There is at most a trace of the free VAPOL ligand remaining, and thus essentially all of the VAPOL is incorporated into two $C_2$-symmetrical species since both bay protons in each species appears as one doublet rather than two. The other two protons that stand out from the rest of the aromatic protons are the two doublets at $\delta = 6.49$ and 6.64 ppm (Figure 1). Based on the chemical shifts, one possibility for these protons is that they are the ortho hydrogens in the phenoxy groups in the borate esters 2 and 3. However, while the integration of the absorptions at $\delta = 6.49$ to that at $\delta = 9.33$ ppm is 4:2 and consistent with the structure 3, the integration of the absorptions at $\delta = 6.64$ to that at $\delta = 9.60$ ppm is also 4:2 and thus not consistent with structure 2.

![Figure 1](https://example.com/image1.png)

**Figure 1** $^1$H NMR spectrum (CDCl$_3$) of a 1:4.3 mixture of meso-borate 2 to pyro-borate 3

![Scheme 3](https://example.com/scheme3.png)

**Scheme 3**
If these are in fact the ortho hydrogens of the phenoxy groups, then one would have to conclude that the spectral data would likely be most consistent with a mixture of the linear and cyclic pyroborates 3 and 8. This prompted a series of new NMR experiments that would lead to a complete assignment of all of the protons in the two borate species and to the reassignment of the linear pyroborate species 3 as the cyclic pyroborate 8.

We have found that cleaner formation of the meso-borate 2 can be achieved by heating VAPOL with one equivalent of BH₃·SMe₂ complex and one equivalent of phenol in toluene at 100 °C and then removal of all volatiles at the same temperature under vacuum (Scheme 3). This gives a 17:1 mixture of meso-/pyro-borate esters. This greatly simplifies the aromatic region of the ¹H NMR spectrum as shown in Figure 2 (a). To even further simplify the aromatic region...
region, the meso-borate 2 was prepared in the same way but with pentadeuterophenol to remove the three protons of the phenoxy group from the mix (Figure 2, b). The most interesting fact emerging from the two spectra in Figure 2 is that the doublet at δ = 6.64 ppm is not from the ortho proton in the phenoxy group of meso-borate 2. Since it is a doublet integrating to four protons, it can only be assigned to the ortho protons of the two phenyl groups in the 2- and 2′-positions of the VAPOL ligand. By subtraction of the two spectra, the protons of the phenoxy group in meso-borate 2 can thus be assigned as a doublet at δ = 7.16 ppm, a triplet at δ = 7.30 ppm, and a triplet at δ = 7.39 ppm.

The pyro-borate complex of VAPOL could be prepared as an 8:1 mixture with the meso-borate 2 from BH$_3$SMe$_2$ and phenol as indicated in Scheme 4. In this case, three equivalents of B(OAr)$_3$ is freshly prepared by heating three equivalents of BH$_3$SMe$_2$ and 12 equivalents of phenol at 80 °C for one hour, and then the volatiles and excess phenol are removed at 80 °C under vacuum for 0.5 hours. Then the VAPOL ligand and one equivalent of water are added and the mixture heated at 80 °C for one hour, and then the volatiles were removed at 80 °C under vacuum. This procedure gives an 8:1 mixture of pyro-/meso-borates and the spectra for this mixture prepared from C$_6$H$_5$OH and C$_6$D$_5$OH are shown in Figures 3 (a) and (b), respectively. Water is added since the formation of a B-O-B linkage requires one equivalent of water. Note that when commercial B(OPh)$_3$ is used to prepare the pyroborate, the addition of water is usually not necessary since commercial B(OPh)$_3$ is usually partially hydrolyzed to the point that the formation of both pyro-borates and BOROX catalysts (Scheme 1) are facile. Since the original assignment of the pyro-borate was only tentatively made as the linear isomer 3, both the linear and cyclic structures 3 and 8 need to be considered going forward.

In contrast to the situation for the meso-borate 2, the most upfield doublet at δ = 6.49 ppm in the pyro-borate is lost when the pyro-borate is prepared from C$_6$D$_5$OH (Figures 3, a vs. 3, b). From the difference of Figures 3 (a) and (b), the protons from the phenoxy group in the pyro-borate can be identified as a doublet at δ = 6.49, triplet at δ = 6.99, and a triplet at δ = 7.05 ppm. A doublet integrating to four protons for the ortho hydrogens of the phenyl group in the pyro-borate can only reside in the multiplet at δ = 7.09–7.18 (Figure 3, b). Thus it is interesting to note that the ortho hydrogens of the phenyl and phenoxyl groups switch places in the meso- and pyro-borates. The ortho hydrogens of the phenyl group move from δ = 6.64 ppm in the meso-borate to δ = 7.09–7.18 ppm in the pyro-borate.

In contrast, the ortho hydrogens of the phenoxyl group move from δ = 7.16 ppm in the meso-borate to δ = 6.49 in the pyro-borate.

In order to gain some insight into the chemical shifts observed for the meso- and pyro-borates, energy-minimized structures of VAPOL and its borates were determined at the B3LYP/6-31G(d) level of theory for VAPOL, the meso-borate 2, both isomers of the pyro-borates 3 and 8, and the minimized structures are shown in Figure 4. The lowest-energy structure in the gas phase for the VAPOL ligand was found to have a dihedral angle of 81.1° between the two phenanthrene rings. The crystal structure of five different forms of VAPOL have been determined, and all have dihedral angles in the range of 73.0–88.5°. The first issue of note is that of the two isomeric pyro-borates, the cyclic pyro-borate 8 is significantly more stable (5.63 kcal/mol) than the linear pyro-borate 3. A unique feature among the
structures is that the cyclic pyro-borate 8 has an ortho hydrogen of each phenoxy group pointing directly at the central ring of each of the phenanthrene ring systems. The distance of $d = 4.555 \, \text{Å}$ is in the range of that expected for a CH–π interaction as defined by the standard practice of measuring the distance from the carbon bearing the hydrogen to the centroid of the arene ring with which it interacts.13–15 This would explain the upfield shift of the ortho hydrogens of the phenoxy hydrogens of the pyro-borate species ($\delta = 6.49 \, \text{ppm}$) relative to those of the meso-borate 2 ($\delta = 7.16 \, \text{ppm}$) if the pyro-borate existed as the cyclic structure 8. Neither the linear pyro-borate species 3 nor the meso-borate 2 have any potential CH–π interactions with distances less than 5.5 Å.

Thus the computational and $^1$H NMR studies both indicate that the better assignment for the pyro-borate species is the cyclic structure 8 rather than the linear structure 3. The $^{11}$B NMR spectrum of the 8:1 mixture of pyro-/meso-borates shown in Figure 3 (a) reveals a broad peak at $\delta = 16.33 \, \text{ppm}$ with a smaller shoulder peak at $\delta = 18.26 \, \text{ppm}$ (see Supporting Information). This is not necessarily taken as evidence that the pyro-borate contains two different borons since the shoulder peak could be due to the presence of other unidentified three-coordinate borates. Instead, the assignment is made as the cyclic pyro-borate 8 on the basis of all of the other evidence gathered in the present study. The assignment of all of the protons for the meso-borate 2 and the pyro-borate 8 are presented in Table 1 along with those for phenol and triphenylborate for comparison. The ortho hydrogens ($H_k$) of the phenoxy groups in B(OPh)$_3$ are...
at $\delta = 7.15$ ppm and thus the ortho-phenoxy protons in the meso-borate 2 at $\delta = 7.16$ ppm are in a ‘normal’ position for an aryl borate ester. It is the ortho hydrogens of the phenoxy groups of the pyro-borate 8 that are anomalous with a chemical shift of $\delta = 6.49$ ppm and as illustrated in the structures in Figure 4, and this can be accounted for by the CH–$\pi$ interaction with the central ring of the phenanthrene unit.

With regard to the chemical shift of the ortho hydrogens of the phenyl group ($H_h$), the chemical shift of $H_h$ in the meso-borate 2 ($\delta = 6.64$ ppm) is very close to those of the free VAPOL ligand 1 ($\delta = 6.72$ ppm). In contrast, the chemical shift of $H_h$ in the pyro-borate 8 is shifted downfield to 7.09–7.18 ppm. The two phenyl groups in VAPOL 1 and in the meso-borate 2 are close to parallel and are within the $\pi$–$\pi$ stacking distance (3.4–3.6 Å). The phenyl rings are offset such that the ortho hydrogens of these phenyl groups

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### Table 1

$^1$H NMR Data for VAPOL, VAPOL Borates 2 and 8, Phenol, and Triphenylborate

<table>
<thead>
<tr>
<th></th>
<th>VAPOL 1</th>
<th>VAPOL meso-borate 2</th>
<th>VAPOL pyro-borate 8</th>
<th>Phenol</th>
<th>B(OPh)$_3$</th>
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<tbody>
<tr>
<td>$H_a$</td>
<td>9.79</td>
<td>9.60</td>
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<td>7.37</td>
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<td>–</td>
</tr>
<tr>
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<td>7.61</td>
<td>7.68–7.74</td>
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<td>–</td>
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<tr>
<td>$H_d$</td>
<td>7.98</td>
<td>7.95</td>
<td>8.01</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>$H_{(e)}$</td>
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<td>7.72</td>
<td>7.82</td>
<td>–</td>
<td>–</td>
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<tr>
<td>$H_{(f)}$</td>
<td>7.86</td>
<td>7.83</td>
<td>7.88</td>
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<tr>
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<td>7.55</td>
<td>7.80</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>$H_h$</td>
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<td>6.64</td>
<td>7.09–7.18</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
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<td>–</td>
<td>–</td>
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<td>$H_l$</td>
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<tr>
<td>$H_m$</td>
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<td>7.30</td>
<td>6.99</td>
<td>6.95</td>
<td>7.11</td>
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</table>

*a CDCl$_3$ as solvent.

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**Scheme 5**

(S)-VANOL (10)

1) B(OAr)$_3$ (3 equiv)

H$_2$O (1 equiv)

toluene, 80 °C, 1 h

2) 80 °C, Hg (0.5 mm), 0.5 h

pyro/meso = 2.3–2.5:1
should be shielded which is consistent with their upfield shifts. The phenyl groups H₈ in the pyro-borate complex 8 are also nearly parallel at a distance of 3.77 Å and are also offset. However, these protons are deshielded and appear at δ = 7.09–7.18 ppm.

An investigation of the structures in Figure 4 leads to a possible explanation of this deshielding of the H₈ protons in complex 8. The protons H₈ are within H-bonding distance of O1 of the pyro-borate bridge with an O–H distance of 2.457 Å. This distance is uniquely short for complex 8 as this distance is ca. 0.5–1.0 Å larger for all other structures. Such an H-bonding interaction would be expected to lead to deshielding, and an observed shift of ca. 0.5 ppm relative to the meso-borate 2 would be consistent with this expectation.

A similar type of NMR and computational analysis was carried out on the meso- and pyro-borates of VANOL, and the results essentially mirrored those obtained with the meso- and pyro-borates of VAPOL. In this way the pyro-borate of VANOL was reassigned as the cyclic pyro-borate 13 (Scheme 5) rather than its linear isomer. The details of this analysis can be found in the Supporting Information.

We have determined the complete assignments of the ¹H NMR signals for the meso-borates and pyro-borates of the vaulted biaryl ligands VANOL and VAPOL. This spectroscopic analysis coupled with computational studies has led to the reassignment of the pyro-borates of both ligands as the cyclic isomers as opposed the linear isomers. This new information concerning the structures of the pyro-borates esters of VANOL and VAPOL shed some light on understanding how the mixtures of meso- and pyro-borates are transformed by the presence of an amine or imine base into boroxinate (BOROX) catalysts due to the similarity between the structures of the cyclic pyro-borates and the catalysts suggesting that the cyclic pyro-borates on the pathway to the boroxinates and this possibility should serve to stimulate experiments to test this possibility.

Acknowledgment
This work was supported by a grant from the National Institute of General Medical Sciences (GM094478).

Supporting Information
Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1378707. Included are experimental procedures, ¹H NMR and ¹¹B NMR spectra of compounds 2, 8, 11, and 13 and pdb files for DFT energy-minimized structures for 1–3, 8, 10–13.

Primary Data
Primary data for this article are available online at http://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00000083 and can be cited using the following DOI: 10.4125/pd0067th.

References and Notes

     (c) Zhang, Y.; Lu, Z.; Wulff, W. D. Synlett 2009, 2715.


Preparation of VAPOL meso-borate 2 (Procedure A)

To a flame-dried 25 mL Schlenk flask equipped with a stir bar and flushed with nitrogen was added phenol (113 mg, 1.20 mmol, 12.00 equiv), dry toluene (2 mL), and BH3·SMe2 (2 M in toluene, 0.10 mmol, 1.0 equiv). The flask was sealed, and the resulting mixture was stirred at 100 °C for 1 h. The volatiles were then carefully removed via high vacuum and left under high vacuum at 100 °C for 0.5 h. The residue was then dissolved in ca. 0.7 mL CDCl3 and the resultant meso-borate 2 was subjected to 1H NMR and 11B NMR analysis. To locate the five aromatic protons in the phenol moiety in meso-borate 2, procedure A described above was repeated with phenol-2,3,4,5,6-pyro-borates with phenol was 13:1.

Spectral Data for 2 (from Phenol, Figure 2, a)

1H NMR (500 MHz, CDCl3): δ = 6.64 (dd, 4 H, J = 8.3, 1.0 Hz), 7.00 (t, 4 H, J = 7.8 Hz), 7.13–7.18 (m, 4 H), 7.35–7.40 (m, 4 H), 7.55 (s, 2 H), 7.68–7.74 (m, 4 H), 7.80 (s, 2 H), 7.83 (d, 2 H, J = 8.5 Hz), 7.95 (dd, 2 H, J = 7.8, 1.2 Hz), 9.60 (d, 2 H, J = 8.5 Hz).

Preparation of pyro-Borate 8 (Procedure B)

To a flame-dried 25 mL Schlenk flask equipped with a stir bar and flushed with nitrogen was added phenol (113 mg, 1.20 mmol, 12.00 equiv), dry toluene (2 mL), and BH3·SMe2 (2 M in toluene, 150 μL, 0.300 mmol, 3.00 equiv). The flask was sealed, and the resulting mixture was stirred at 80 °C for 1 h. The volatiles were then carefully removed via high vacuum and left under high vacuum at r.t. for 0.5 h yielding a white solid. To this solid was added VAPOL (54 mg, 0.10 mmol, 1.0 equiv), dry toluene (2 mL), and H2O (1.8 μL, 0.10 mmol, 1.0 equiv). The mixture was stirred at 80 °C for 1 h. The volatiles were carefully removed via high vacuum and left under high vacuum at 80 °C for 0.5 h. The residue was then dissolved in ca. 0.7 mL CDCl3 and transferred to a quartz NMR tube, and the pyro-borate 8 was subjected to 1H NMR and 11B NMR analysis. To locate the five aromatic protons in the phenol moiety in 8, the procedure B described above was repeated with phenol-2,3,4,5,6-pyro-borates with phenol was 8:1 and with the pentadeuterophenol was 8:1.

Spectral Data for 8 (from Phenol, Figure 3, a)

1H NMR (500 MHz, CDCl3): δ = 6.49 (d, 4 H, J = 7.8 Hz), 6.99 (t, 2 H, J = 7.2, 1.3 Hz), 7.05 (t, 4 H, J = 7.8 Hz), 7.09–7.18 (m, 10 H), 7.68–7.74 (m, 4 H), 7.80 (s, 2 H), 7.83 (d, 2 H, J = 8.5 Hz), 7.88 (d, 2 H, J = 9.0 Hz), 8.01 (dd, 2 H, J = 7.3, 2.0 Hz), 9.29–9.34 (m, 2 H).

Spectral Data for 8 (from Pentadeuterophenol, Figure 3, b)

1H NMR (500 MHz, CDCl3): δ = 7.09–7.18 (m, 10 H), 7.68–7.74 (m, 4 H), 7.80 (s, 2 H), 7.81 (d, 2 H, J = 9.0 Hz), 7.88 (d, 2 H, J = 9.0 Hz), 8.01 (dd, 2 H, J = 7.3, 2.0 Hz), 9.29–9.34 (m, 2 H).

(10) Preparation of VAPOL-meso-borate 2 (Procedure A)
(11) Preparation of pyro-Borate 8 (Procedure B)

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