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Catalytic Dealkylation of Phosphates with Binuclear Boron Compounds

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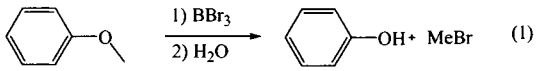
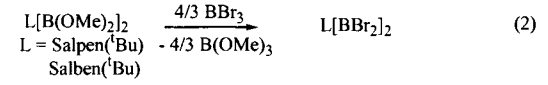
The breaking of a phosphate ester bond is important in many areas such as the destruction of nerve agents (Sarin and VX),[1] pesticides (chloropyrifos),[2] and in biological systems.[3] In recent years, methods for the catalytic cleavage of the P−O bond in phosphate esters have been developed.[4] Most of these are binuclear systems use d-block metals such as cobalt,[5] copper,[6] and zinc.[7] Boron compounds however, have not been examined in this regard, despite the fact that BBr_3 will, through cleavage of the O−C bond, dealkylate alkyl and aryl ethers (eq 1)[8] and silyl ethers.[9] This reagent, however, is ineffective with phosphates since phosphorus is electron-donating (thereby strengthening the alkyl−oxygen bond). For example, BBr_3 does not de-alkylate trimethyl phosphate (less than 2% in 24 h). In an effort to determine whether the presence of a chelate ligand might improve the effectiveness of boron bromides for this reaction, new binuclear boron compounds Salpen(^{t}Bu)[BBr_2]$_2$ (**1**) and Salben(^{t}Bu)[BBr_2]$_2$ (**2**) have been synthesized.[10] These compounds catalytically dealkylate a broad range of phosphate esters through cleavage of an O−C bond.

The binuclear boron bromides (**1** and **2**) are prepared in high yields by combining Salpen(^{t}Bu)[$B(OMe)_2$]$_2$ [11] or Salben(^{t}Bu)-[$B(OMe)_2$]$_2$ [11] with a stoichiometric amount of BBr_3 (eq 2).[12] The ^{11}B NMR shows a broad single peak for **1** and **2** at δ −0.57 and −0.40 ppm, upfield from the related chloride analogue Salpen-(^{t}Bu)[BCl_2]$_2$ [13] (6.21 ppm).





In the structure[14] of **2** (Figure 1), the boron atoms are in a distorted tetrahedral geometry and trans to one another. The angle of the ligand (N−B−O) is 112.8(6)°, which is slightly larger than other Salen-supported binuclear systems such as Salen(^{t}Bu)-[$B(OSiPh_3)_2$]$_2$ [15] (angle = 104.9(3)°). The B−Br bond lengths are 2.023(8) and 2.077(9) Å for **2**, which are slightly longer than those for other four-coordinate boron dibromide compounds such as [(2-Me_2NCH_2)C_6H_4]BBr_2 (with B−Br bond distances of 2.01(1) and 2.02(1) Å).[16]

Salpen(^{t}Bu)[BBr_2]$_2$ cleaves an O−C bond in a multitude of phosphate esters (Table 1).[17] When combined with stoichiometric amounts of various phosphates, **1** produces alkyl bromides and chelated boron phosphates (eq 3). Simple and sterically encumbered (P−O−C) linkages that possess primary and secondary sp^3 α-carbons are cleaved.

The mechanism appears to be one in which a cationic intermediate [(chelate)BBr]$^+$ coordinates the phosphate, allowing a nucleophilic attack by the bromide at the α-carbon. Such cations appear readily accessible by the simple addition of a Lewis base.[18] The cation formation also takes place when excess BBr_3 is added to compound **1**.[19]

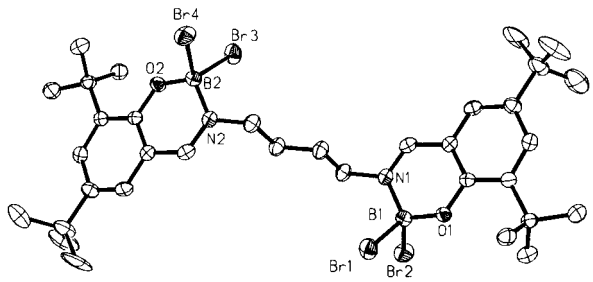
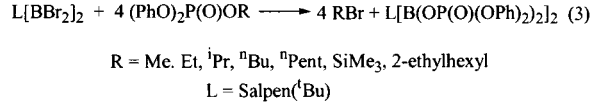


Figure 1. Molecular structure and atom numbering scheme for **2**. Selected bond lengths (Å) and angles (deg): B(1)−O(1), 1.418(9); B(1)−N(1), 1.517(9); B(1)−Br(1), 2.023(8); B(1)−Br(2), 2.077(9), O(1)−B(1)−N(1), 112.8(6); O(1)−B(1)−Br(1), 108.6(5); N(1)−B(1)−Br(1), 112.2(5); Br(1)−B−Br(2), 107.7(3).

Table 1. Percent Dealkylation of Different Phosphates with Salpen(^{t}Bu)[BBr_2]$_2$ (**1**)

phosphate	conversion (%)[a]
$(MeO)_3P(O)$	89
$(EtO)_3P(O)$	63
$(^n BuO)_3P(O)$	99
$(^n PentO)_3P(O)$	98
$(MeO)_2P(O)H$	85
$(MeO)_2P(O)Me$	99
$(^i PrO)_2P(O)H$	63
$(PhO)_2((2\text{-Et})HexO)P(O)$	71
$(Me_3SiO)_3P(O)$	98
$(PhO)_3P(O)$	0

[a] The percent conversion was determined by the amount of phosphate remaining to the amount of alkyl bromide produced in the ^{1}H NMR.



Since Salpen(^{t}Bu)[BBr_2]$_2$ (**1**) can be generated in situ from Salpen(^{t}Bu)[$B(OMe)_2$]$_2$ and BBr_3, the process can be made catalytic. The dealkylation of trimethyl phosphate occurs within 5 min through the addition of catalytic amounts of borate to equimolar trimethyl phosphate and BBr_3 in the trimethyl phosphate to **1** ratio of 20:1.[20] Salpen(^{t}Bu)[$B(OMe)_2$]$_2$ dealkylates $(MeO)_3P(O)$ (75% conversion) with BBr_3 within 30 min at a substrate-to-catalyst ratio of 200:1. Addition of BBr_3 or the borate alone does not effect dealkylation within 24 h. The boron bromide compounds show excellent activity toward the dealkylation of different phosphates. The activity of the boron halide compounds does not decrease with the extension of the alkyl chain on the phosphates. However, the activity of the boron halide compounds shows a slight decrease with the branched phosphates such as $(PhO)_2$((2-Et)HexO)P(O). A

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further positive attribute of this system is that these reactions can be conducted at room temperature. Unlike the synthetic enzyme models, the C−O cleavage appears to occur at only one metal site. For example, preliminary results show that the compound N, -tert-butyl (salicylideneimine) dealkylates trimethyl phosphate. Thus, this might be a general reaction for any type of chelate.

The phosphates dealkylated in this report may be viewed as models for the nerve agent Sarin and the pesticide chloropyrifos since they have similar P−O−C units. Thus, chelated boron bromides appear to be promising candidates for the decontamination of chemical warfare agents such as VX and Sarin gas under organic conditions. More specifically, they may be more efficient than conventional decontamination systems that use hydroxide sources.[21]

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Supporting Information Available: X-ray crystallographic data for **2** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Salpen(^{t}Bu) = (*N*,*N*′-propylenebis(3,5-di-*tert*-butyl(2-hydroxy)benzylideniimine), Salben(^{t}Bu) = (*N*,*N*′-butylenebis(3,5-di-*tert*-butyl(2-hydroxy)-benzylidenimine).
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(12) Experimental details for **1** and **2**: Salpen(^{t}Bu)[BBr_2]$_2$ (**1**). To a stirring solution of Salpen(^{t}Bu)[$B(OMe)_2$]$_2$ (3.0 g, 4.62 mmol) in toluene (50 mL) was added 1M BBr_3 in heptane (6.24 mL, 6.24 mmol). The reaction mixture was stirred for 24 h. The solvent was removed and the solid remaining behind was washed with 10 mL of hexanes. Filtration and vacuum-drying afforded Salpen(^{t}Bu)[BBr_2]$_2$. Yield: 3.28 g (88%); mp 282−285 °C dec. ^{1}H NMR ($CDCl_3$): δ 1.25 [s, 18H, C(CH_3)$_3$], 1.47 [s, 18H, C(CH_3)$_3$], 2.88 [m, 2H, CH_2], 4.12 [m, 4H, NCH_2], 7.30 [d, 2H, C_6H_2], 7.76 [d, 2H, C_6H_2], 8.53 [s, 2H, C*H*N]. ^{11}B NMR ($CDCl_3$): δ −0.57 ($w_{1/2}$ = 78.2 Hz). IR(cm^{-1}): 2963(s), 2870(w), 1626(s), 1575(s), 1472 (m), 1438(m), 1395(m), 1364(s), 1339(m), 1279(m), 1217(w). 1077-(w), 1027(w), 904(w), 846(w), 769(w), 668(m), 641(m). MS: 766(M⊕ − Br, 20), 686(M⊕ − 2Br, 5), 606(M⊕ − 3Br, 100). Anal. Calcd for $B_2C_{33}H_{48}N_2O_2Br_4$: C 47.03(46.96), H 5.74(5.68), N 3.33(3.32). Salben(^{t}Bu)[BBr_2]$_2$ (**2**). To a stirring solution of Salben(^{t}Bu)[$B(OMe)_2$]$_2$ (1.0 g, 1.51 mmol) in toluene (50 mL) was added 1 M BBr_3 in heptane (2.04 mL, 2.04 mmol). The reaction mixture was stirred for 18 h at room temperature. The solution was concentrated to 10 mL, filtered, and dried. Yield: 0.96 g (76%); mp: 279−280 °C dec. ^{1}H NMR ($CDCl_3$): δ 1.27 [s, 18H, C(CH_3)$_3$], 1.42 [s, 18H, C(CH_3)$_3$], 2.21 [m, 4H, CH_2], 4.08 [m, 4H, NCH_2], 7.22 [d, 2H, C_6H_2], 7.78 [d, 2H, C_6H_2], 8.24 [s, 2H, C*H*N]. ^{11}B NMR ($CDCl_3$): δ −0.40 ($w_{1/2}$ = 92.7 Hz). IR (cm^{-1}): 2953(s), 2900-(m), 2870(w), 1627(s), 1573(s), 1469(m), 1440(m), 1395(w), 1362(w), 1253(m), 1220(m), 1136(w), 1083(w), 1024(m), 863(m), 768(w), 641-(w). MS: 780(M⊕ − Br, 100), 700(M⊕ − 2Br, 50), 620(M⊕ − 3Br, 40), 540(M⊕ − 4Br, 10). Anal. Calcd for $B_2C_{34}H_{50}N_2O_2Br_4$: C 47.66 (47.84), H 5.89 (6.22), N 3.27 (3.22).
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(14) X-ray data for **2** were collected on a Nonius CCD unit employing Mo Kα radiation. The structures were refined using the Siemens software package SHELXTL 4.0. All of the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were put into calculated positions. Absorption corrections were not employed. X-ray data for **2**: yellow crystals (0.2 mm × 0.2 mm × 0.16 mm), formula C_{48} H_{66} B_2 Br_4 N_2 O_2 FW 1044.29, monoclinic, $P2_1/c$, a = 14.0520(10) Å, b = 30.708(2) Å, c = 12.2780(10) Å, β = 108.733(10)°, V = 5017.4(6) Å^3, Z = 4, data 8848, parameters 553, R1 = 0.0486 (for $I > 2\alpha I$), wR2 = 0.0755, GOF (on F^2) = 1.078.
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(17) Dealkylation of the phosphate: In a NMR tube, phosphate was added to a equimolar solution of the catalyst (**1** or BBr_3) in $CDCl_3$ and held at room temperature for 30 min. The reaction was monitored by ^{1}H NMR.
(18) In a NMR tube, 5 equiv of THF was added to a solution of **1** in $CDCl_3$ giving a ^{11}B NMR resonance of 4.28 ppm. It is shifted downfield from **1** by 4.85 ppm, indicating the displacement of Br by THF and formation of a cation.
(19) In a NMR tube, 3 equiv of BBr_3 was added to a solution of **1** in $CDCl_3$. ^{11}B NMR: δ 23.10, −0.42, −21.60. Indicating the formation of BBr_4 (−21.60) and Salpen(^{t}Bu)[$BBr_2(BBr)^+$] (−0.42 and 23.40).
(20) Catalytic dealkylation of the phosphate: In a NMR tube, equimolar amounts of $(MeO)_3P(O)$ and BBr_3 were added to a solution of Salpen-(^{t}Bu)[$B(OMe)_2$]$_2$ in $CDCl_3$ in the ratio of 20:1 of phosphate to borate and held at room temperature. The reaction was monitored by ^{1}H NMR. A white precipitate formed during the reaction and is a type of boron phosphate compound with no ligand present.
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