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Reactions of phosphite triesters with alkyl boranes

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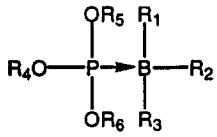
Abstract: *The reactions of BF_3, BCl_3 and several alkyl boranes with the trimethyl and the triethyl phosphite are reported. The reactions with the dialkyl and monoalkyl boranes led to the formation of several alkyl boron phosphite complexes in yield up to 100%. Their ^{31}P NMR spectra are reported.*

Recently[1] it has been shown that phosphoboranate oligonucleotides bind reasonably well to their complementary RNA strand and that these hybrids are substrates for RNAse H. The preparation of the borano phosphate oligonucleotides proceeds through the introduction of the borane group at the trialkyl phosphite moiety when using phosphoramidite chemistry[2] or at the dialkyl silyl phosphite group for the H-phosphonate approach.[3] Because of our interest in this subject,[4] we decided to investigate the stability of complexes for substituted boranes with trialkyl phosphite. In a series of model reactions, we first attempted to prepare complexes with triethyl and trimethyl phosphite because very few examples[5] of these complexes are reported in literature.

SCHEME 1



R_1, R_2 and R_3 = alkyl
R_4, R_5 and R_6 = H or alkyl

We first investigated the reaction of the trihaloboranes BF_3 and BCl_3 with $P(OEt)_3$, since it seemed interesting to study the effects of electron-withdrawing groups on boron in order to improve its electrophilicity and thus make the complex between phosphorus and boron more stable. For both the reactions, the ^{31}P NMR showed sharp singlets (for BCl_3 at 167 ppm and for BF_3 at 130 ppm which corresponded to the reported chemical shift of their halo esters[6]) without any evidence of the quartet pattern due to the phosphorus-boron coupling. The products of these reactions are most likely the monohalo derivatives[7] of the starting materials.

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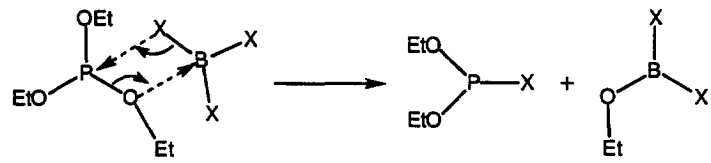
PII: S0040-4039(99)00208-7

SCHEME 2



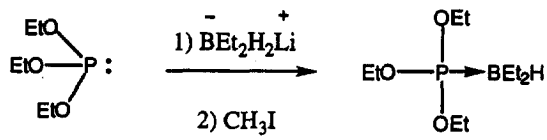
X = Cl, F

We then studied the reactions of the trialkyl borane derived from α-methyl styrene[6] and the less bulky triethylborane. Neither of them formed a complex with the triethyl phosphite, even after standing for one week.

Since the trialkyl boranes did not show the desired reactivity, we investigated dialkyl boranes, hoping that less bulky reagents would give the desired complexes. The first borane we used was the readily available 9-BBN. The reaction of the latter with the triethyl phosphite at r.t in an equimolar amount worked in the desired way, giving a P-B complex, showing a broad quartet around 98 ppm in ^{31}P NMR and also the presence of unreacted starting material. When the reaction was carried out with a 4-fold excess of 9-BBN the conversion of the phosphite to the complex was around 88%. The second dialkylborane investigated was prepared[8] from the cyclohexene and BH_3•SMe_2 at 0° C. This borane was allowed to react in a two fold excess with the triethyl phosphite at r.t. to give the desired complex in 25% yield plus unreacted starting material. The ^{31}P NMR showed a broad quartet around 105 ppm. When we did the reaction using a large excess of the borane we recorded a larger conversion of the starting material as showed in the table. The third dialkyl borane we used was the (+)-$B(Ipc)_2H$, synthesized from BH3•SMe_2 and (+)-α-pinene.[9] This borane reacted with triethyl phosphite at r.t. to give the P-B complex that showed a broad quartet around 105 ppm in ^{31}P NMR. Using a 5-fold excess of borane the yield of the complex was 50%. Since the large dialkyl boranes did not form the complex quantitatively, we next prepared the sterically less demanding diethyl borane, first synthesized by Brown in a two step procedure.[10]

We adapted this procedure to our purposes by reacting triethyl borane with $LiAlH_4$ to give $LiBEt_2H_2$, easily stored at r.t. under nitrogen for a long time without decomposition. Mixing it with the trimethyl phosphite at r.t. followed by addition of an equimolar amount of methyl iodide rapidly gave the desired complex[11] as shown from ^{31}P NMR (a quartet around 105 ppm) in 75% yield when the ratio was 2 to 1 in favor of the borane.

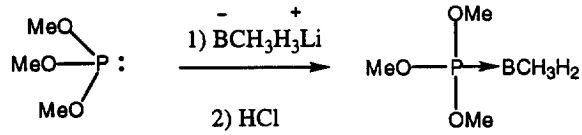
SCHEME 3



It did not react with a dinucleotide phosphite triester, so that no further work was done to optimize the complex formation.

We then looked at the monoalkyl borane as possible reagents for the synthesis of the P-B complexes. In fact, being less bulky, this class of boranes should be favored in approaching the phosphite group. Very few monoalkyl boranes have been synthesized up to now because of their high reactivity toward olefins and one of these is the thexylborane; this borane reacted[12] with the triethyl phosphite at 0° C quantitatively as shown from ^{31}P NMR (a sharp quartet around 106 ppm). As we wanted to study the reactivity of monoalkyl boranes carrying a small alkyl group we also used the methyl borane.[13] We adapted the original Brown procedure for our purposes by firstly reacting[14] methylboronic acid with $LiAlH_4$ to give $LiBCH_3H_3$, easily stored at r.t. under nitrogen for a long time without decomposition and then mixing it with the trimethyl phosphite at r.t. followed by addition of a dry 1M ethereal HCl solution.

SCHEME 4



The monomethyl borane reacted in this way with the trimethyl phosphite at r.t. to afford the phosphorus-boron complex in 80% yield, besides unreacted starting material, as shown from ^{31}P NMR (a sharp quartet at 115 ppm). The results are summarized in the table below .

Borane	Phosphite	^{31}P NMR	ΔJ_{P-B} (Hz)	Yield(%)	RatioB/P
9-BBN	$P(OEt)_3$	98.3 ppm	95.1	28 (88)	1 (4)
$B(Ipc)_2H$	$P(OEt)_3$	104.5 ppm	96.4	50	5
$B(Chex)_2H$	$P(OEt)_3$	99.1 ppm	broad	25 (91)	2 (6)
BEt_2H	$P(OMe)_3$	105.4 ppm	98.2	75	2
$B(CH_3)H_2$	$P(OMe)_3$	115.9 ppm	82.0	80	1.5
$ThexylBH_2$	$P(OEt)_3$	106.3 ppm	78.5	100	1.5

In conclusion trialkyl phosphite does form complexes with dialkyl and monoalkylborane, as shown from the ^{31}P NMR data. On the other hand, we found trialkylboranes not useful for the formation of these complexes. Finally the haloboranes are not suitable for our purpose because they lead to the formation of phospho-haloderivatives.

ACKNOWLEDGMENTS

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REFERENCES AND NOTES

(1) Higson, A.P.; Sierzchala, A.; Brummel H.; Zhao, Z.; Caruthers, H. *Tetrahedron Lett.* **1998**, *39*, 3899-3902.

(2) Sood, A.; Shaw, B.R.; Spielvogel, B.F. *J. Am. Chem. Soc.* **1990**, *112*, 9000-9001.

(3) Zhang, J.; Terhorst, T.; Matteucci, M.D. *Tetrahedron Lett.* **1997**, *38*, 4957-4960.

(4) (a) Yi, J.; Just, G. *Tetrahedron Lett.* **1998**, *39*, 6429-6432; (b) Yi, J. and Just, G. *ibid.* **1998**, *39*, 6433-6436.

(5) Sood, U.; Sood, C.K.; Hall, T. H.; Spielvogel, B. F. *Tetrahedron*, **1991**, *47*, 6915-6930 and references cited therein; Paul, V.; Roberts, B.P. *J. Chem. Soc. Perkin Trans II* **1989**, 1183; Verdake, J.G.; King, R.W. ; Heitsch, C.W. *Inorg. Chem.* **1964**, *6*, 884.

(6) Joan Mason in Multinuclear NMR, *Plenum Press*, New York, **1987**.

(7) Gerard, W.; Lindsay, M. *Chem. and Ind.* **1960**, 152.

(8) Brown, H.C. in Organic syntheses via Boranes, *John Wiley and Sons*, New York, **1975**.

(9) Brown, H.C.; Singaram, B. *J. Org. Chem.* **1984**, *49*, 945-947.

(10) Brown, H.C.; Rangaishenvi, M.V.; Racherla U.S. *J. Org. Chem.* **1987**, *52*, 728-730.

(11) The ^{11}B NMR of this complex showed a broad quartet at -18.1 ppm.

(12) 1mmol of $(EtO)_3P$ was added via syringe to a stirred solution of thexylborane (1.5 mmol in 2 mL of dry THF) under nitrogen at 0° C. An aliquot was taken to perform the ^{31}P and ^{11}B after 10 minutes. The ^{11}B NMR of this complex showed a sharp quartet at - 29.5 ppm. The mixture was stirred for a further 0.5 hour before the solvent and the excess thexylborane was removed under reduced pressure. ^1H NMR (300 MHz, $CDCl_3$) δ 0.76 (6H, s, C-Me_2), 0.78 (6H, m, CH-$\underline{Me}_2$), 0.83 (1H, m, $\underline{CH}$-Me_2), 1.23 (3H, t, J = 7.1 Hz, $\underline{CH}_3$-CH_2-O), 4.02 (2H, q, J = 7.1 Hz, CH_2-O).

(13) Brown, H.C.; Cole, T.E.; Srebnik, M.; Kim K.W. *J. Org. Chem.* **1986**, *51*, 4925-4930.

(14) 1 mmol of $(MeO)_3P$ was added to a solution of $LiBCH_3H_3$ (1.5 mmol in 10 mL of Et_2O) via syringe, under N_2 atmosphere. The solution was stirred for 5 minutes and then a dry 1M ethereal HCl solution (1.5 ml) was carefully added. An aliquot was taken to perform the ^{31}P and ^{11}B after 2 hours. The ^{11}B NMR of this complex showed a sharp quartet at -35.9 ppm.