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Reaction of boranephosphonate diesters with pyridines or tertiary amines in the presence of iodine. Synthetic and mechanistic studies.

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Keywords: boranephosphonates; pyridiniumboranephosphonates; oxidation with iodine; mechanism; nucleotide analogues

Abstract:

Boranephosphonate diesters react with heteroaromatic and certain tertiary amines in the presence of an oxidant (I_2) to afford the boron-modified phosphodiester analogues containing a P-B-N structural motif. Our multinuclear ^{31}P and ^{11}B NMR spectroscopy studies lend support for a two steps mechanism involving generation of a λ^3-boranephosphonate intermediate that immediately coordinates an amine in the solvent cage, leading to *B*-pyridinium or *B*-ammonium boranephosphonate betaine derivatives. We found that type of the solvent used (*e.g.*, dichloromethane *vs* acetonitrile) significantly affected course of the reaction resulting either in the formation of boron-modified derivatives or lost of the boron group with a subsequent oxidation of the phosphorus atom. In aprotic, electron-donating, polar solvents. *e.g.*, acetonitrile (ACN), tetrahydrofuran (THF), a λ^3-boranephosphonate intermediate can also coordinate solvent molecules forming P-B-ACN or P-B-THF complexes that may influence the type of the products formed.

INTRODUCTION

During the last decades boranephosphonate analogues emerged as important bioisosters of nucleic acids and their components.[1] New properties imparted by the presence of the BH_3 group, located in a nonbridging position of the phosphate function, *e.g.*, chirality at the phosphorus center, resistance to nucleases, high lipophilicity, low toxicity, *etc*.[2] constituted basis for potential applications of these analogues as antisense/antigene agents, siRNA gene modulators,[1a,2a,3] alternative substrates for polymerase chain reaction (PCR),[4] or new structural motifs for nucleic acids-based diagnostics.[5]

Apart from these biology-related applications, there has been an increasing interest in exploring boranephosphonates/boranephosphinates as new, potentially important synthetic equivalents for P(III) phosphorus synthons with the hidden P-H functionality (*e.g*. H-phosphonate or H-phosphinate esters). Temporary conversion of the P-H function into the P-BH_3 one, freezes these compounds in a $\lambda^5\sigma^4$ phosphonate form that, in contrast to that of the parent P-H compounds, cannot isomerize to a nucleophilic $\lambda^3\sigma^3$ tervalent form with a lone electron pair on the phosphorus. Thus, boranephosphonates are generally more resistant to various chemical transformations than H-phosphonate derivatives, but the P-H function and its reactivity can be retrieved at the end of synthesis and subject, if so desired, to additional synthetic tasks. The feasibility and usefulness of such an approach has been successfully demonstrated in the synthesis of biologically important phosphorus compounds.[6]

Recently, Caruthers *et al*.[7] exploring further chemistry of boranephosphonates proposed the P-B bond as a new chemical marker for a postsynthetic modification of oligonucleotides, and showed that the BH_3

group under mild, oxidative conditions (*e.g.*, in the presence of iodine) can be stereospecifically replaced by various nucleophiles, *e.g.*, amines, alcohols, thiols, *etc*, forming the corresponding P(V) derivatives. When such oxidative transformation is carried out in the presence of pyridine (or other heteroaromatic, or certain 3° amines), boranephosphonate diester derivatives bearing a pyridine or a 3° amine moiety attached to the borane group, are formed.[8] The authors showed that a pyridiniumboranephosphonate modification, when present in oligonucleotides, facilitated cellular uptake of such molecules,[8] and modulated reducing properties of borane-modified nucleic acids during formation of DNA-templated metal nanostructures.[8-9]

With a focus on chemistry of boranephosphonates as important nucleotide analogs and potentially valuable synthetic intermediates, we recently investigated mechanistic aspects of a formal replacement of the BH_3 group by amines, promoted by iodine.[10] In contradistinction to the literature report[7] we found that this transformation occurred with total inversion of the configuration at the phosphorus center and involved the intermediacy of the corresponding H-phosphonate diesters.[10] These findings are of importance in the context of a possible use of boranephosphonate analogues in postsynthetic modifications of nucleic acids.

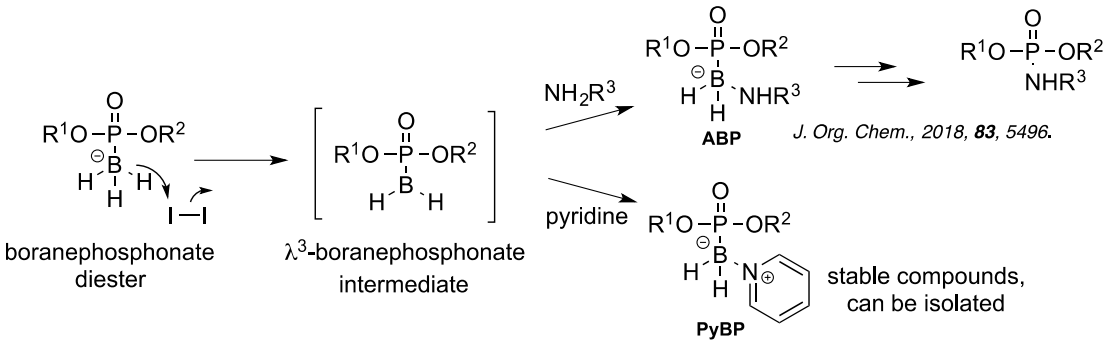
In this paper we investigated the reaction of boranephosphonate diesters with heteroaromatic and 3° amines, promoted by iodine.[8] This reaction, in contrast to that involving 1° or 2° amines,[7] preserves the P-B bond in boranephosphonates, and leads to the formation of a new structural motif, P-B-N, where N is part of a heteroaromatic or 3° amine.[8] Taking into account the potential importance of *B*-modified boranephosphonate nucleotide analogues in nucleic acid chemistry, medicinal chemistry, or metal nanotechnology, we undertook these studies to gain better understanding of the underlying chemistry, evaluate substrate scope of this reaction in term of

the kind of the amine used, and to clarify some mechanistic aspects that can be of synthetic relevance. We used in our studies multinuclear NMR spectroscopy to detect putative intermediates and define a mechanistic framework of the whole transformation. As a model system for our studies we chose a reaction of diethyl boranephosphonate diester **1** with pyridine (or its derivatives), or certain 3° amines promoted by iodine under various experimental conditions.

RESULTS AND DISCUSSION

For the reaction of boranephosphonate diesters with 1° and 2° amines in the presence of iodine, and that with heteroaromatic and certain 3° amines, two distinct mechanisms have been advocated. For that involving 1° and 2° amines, a nucleophilic substitution of the activated borane group by iodide to form the corresponding iodophosphate with inversion of the configuration at phosphorus, was proposed as a key reaction step.[7] For the second reaction, that makes use of heteroaromatic or 3° amines as substrates and preserves the borane group in the molecule, a different mechanism, involving a four center addition of an *N*-iodoammonium species to the borane moiety with a simultaneous oxidation of the boron-bound hydride, was suggested.[8]

Studies from our laboratory showed that the mechanism suggested for the reaction of boranephosphonates with 1° and 2° amines was incorrect.[10] We proposed that the most likely reaction pathway for this process involved the intermediacy of an electron deficient λ^3-boranephosphonate species that coordinated the amine present in the reaction mixture to form aminoborane intermediate, followed by its dissociation to the corresponding H-phosphonate, and finally after oxidation, a phosphoramidate diester (Scheme 1).



R^1, R^2 = alkyl, aryl, or a nucleoside moiety; R^3 = alkyl or aryl;
ABP = aminoboranephosphonate; **PyBP** = pyridiniumboranephosphonate

Scheme 1. Reaction of boranephosphonate diesters with amines, promoted by iodine.

As for the reaction of boranephosphonate diesters with heteroaromatic and 3° amines promoted by iodine, our working hypothesis was that the initial, key mechanistic steps were the same as those proposed for 1° and 2° amines, *i.e.*, involved formation of an electron deficient λ^3-boranephosphonate species, followed by coordination of the amine used (Scheme 1). The fate of the reaction is probably determined by stability of the formed intermediates, *i.e.*, complexes of λ^3-boranephosphonate with amines (**ABP** *vs* **PyBP**, Scheme 1). In case of instability of an aminoboranephosphonate complex (*e.g* **ABP**), the reaction proceeds further to the corresponding P(V) derivative, but if the complex is stable enough (*e.g.*, pyridiniumborane complex **PyBP**), it may remain the final product of the reaction. This hypothesis was based on the expected reactivity of boranephosphonate diesters towards oxidants, the known affinity of electron-deficient boron species towards amines, and some preliminary ^{31}P NMR spectroscopy experiments on this reaction.

Although the conversion of boranephosphonate diesters into the corresponding pyridiniumborane- or ammoniumboranephosphonate derivatives formally looks like a simple two steps reaction, a careful scrutiny

of the reaction conditions revealed that it might be a complex process with various competing reaction pathways and multiple equilibria systems involved. In agreement with these, Caruthers *et al*.[8] reported on the formation on variable amounts of phosphates in this reaction (the lost of the borane group and oxidation at the phosphorus centre), and a complex dependency on the amount of pyridine and the oxidant used. For our part, we observed also irreproducibility of certain experiments that can point to sensitivity of the reaction to factors that have not been fully appreciated.

To get a deeper insight into the mechanistic features of the investigated reaction and to pinpoint synthetically important factors, we carried out series of experiments to identify the intermediates involved, clarify the role of the solvents used, and to elucidate a possible involvement of amine-oxidant complexes in the oxidation step.

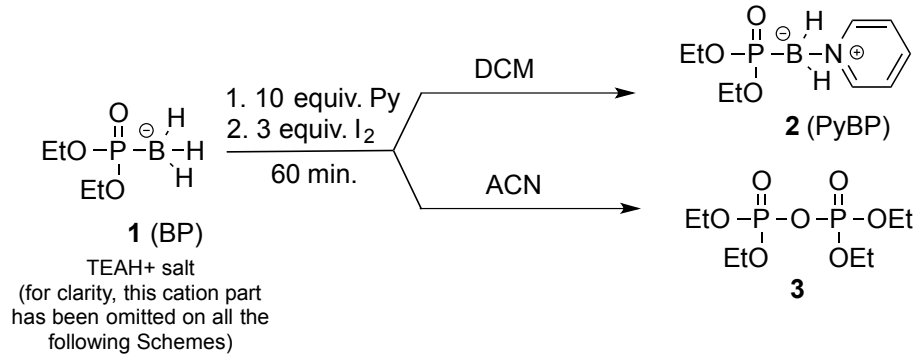
Reaction of boranephosphonate 1 with pyridine promoted by iodine in different solvents.

Preliminary experiments showed that simple diethyl boranephosphonate **1** reacted with pyridine in the presence of iodine analogously to the derivatives containing more complex esters residues (*e.g.*, nucleoside moieties), and for this reason we selected it as a model boranephosphonate diester for our studies. We expected that type of the solvent used for this reaction can be important on at least two counts. Firstly, iodine is known to form brown- or violet-colored solutions depending upon the solvent. Brown solutions, which contain iodine coordinated to the solvent molecules appear to be more reactive than those with presumably free iodine molecules, the violet ones.[11] Secondly, assuming an electron-deficient borane intermediate to be involved in the investigated reaction (Scheme 1), the coordination ability or electron-donating properties of the solvent may be of particular importance for stabilization of such species. Thus, taking into

account solubility requirements for the substrates and the theoretical premises mentioned above, we chose dichloromethane (DCM) and acetonitrile (ACN) as two differing solvents for the studied reaction.

*Reaction of diethyl boranephosphonate **1** with pyridine and iodine in dichloromethane vs acetonitrile.*

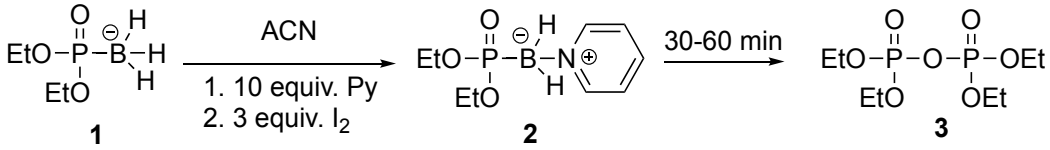
A standard protocol for the investigated reaction consisted of adding iodine (3 equiv.) to a ca. 0.1 M solution of boranephosphonate **1** ($TEAH^+$ salt) in a selected solvent containing a heterocyclic or 3° amine (10 equiv.). First, we run the reaction in DCM with pyridine as a heterocyclic amine. Inspection of the ^{31}P NMR spectrum after 1 h since the addition of iodine showed a complete disappearance of the starting material **1** (δ_P = 94.2 ppm) and the presence of two signals at δ_P = 59.8 ppm (m, ca. 80%) and δ_P = 45.0 ppm (m, ca. 20%). The compound resonating at ca. 60 ppm was isolated from the reaction mixture and identified (^1H, ^{13}C, ^{11}B NMR, and HRMS) as the expected product, diethyl pyridiniumboranephosphonate **2** (Scheme 2, PyBP). For identification of the side product at δ_P = 45.0 ppm, see later in the text.[12]



Scheme 2. Different courses of the reaction **1** + pyridine + iodine in dichloromethane (DCM) *vs* acetonitrile (ACN). For the relevant ^{31}P and ^{11}B NMR spectra, see Fig. S1 and Fig. S2 in the supporting information.

The analogous reaction of BP **1** with pyridine and iodine in ACN took completely different course and afforded tetraethyl pyrophosphate **3** (δ_P = -

13.0 ppm) as the sole phosphorus containing product (Scheme 2). This indicated deboronation occurring during the course of the reaction but its mechanistic pathway was far from clear. To get some insight into a possible mechanism, we followed progress of the reaction in acetonitrile by ^{31}P NMR spectroscopy. In the first ^{31}P NMR spectrum recorded (after ca. 5 min.), a compound resonating at ca. δ_P = 60 ppm (m, ca. 80%) appeared in the reaction mixture and during 30-60 min it gradually faded away to be converted into the final product of this reaction, pyrophosphate **3**. The shape of the signal and its chemical shift values (δ_P = 59.8 ppm and δ_B = -13.4 ppm) strongly suggested formation of PyBP **2** but, in contradistinction to the reaction in DCM, this species was unstable under the reaction conditions and ultimately (within 60 min) produced pyrophosphate **3** (Scheme 3).



Scheme 3. A transient formation of PyBP **2** in the reaction of **1** with pyridine and iodine in acetonitrile. For the relevant ^{31}P and ^{11}B NMR spectra, see Fig. S1 in the supporting information.

Since the isolated PyBP **2** was found to be completely stable in an acetonitrile solution, to prove its intermediacy in the investigated reaction, we reacted BP **1** with pyridine (10 equiv.) and iodine (3 equiv.) in ACN in the presence of the added putative intermediate, PyBP **2** (1 equiv.). Somewhat surprisingly, in this experiment BP **1** was converted into PyBP **2** that did not undergo further transformation (few hours) to the expected under these conditions final product **3**. However, when we doubled the amount of iodine and pyridine in the above reaction, both substrates (BP **1** and PyBP **2**) were converted into tetraethyl pyrophosphate **3** (Fig. 1). Thus, in this context, two questions should be addressed: (i) why sometimes the produced PyBP **2** was

stable even when the investigated reaction was run in acetonitrile, and related to it, (ii) what is a possible mechanism of transformation of PyBP **2** into pyrophosphate **3** during the course of the reaction in acetonitrile?

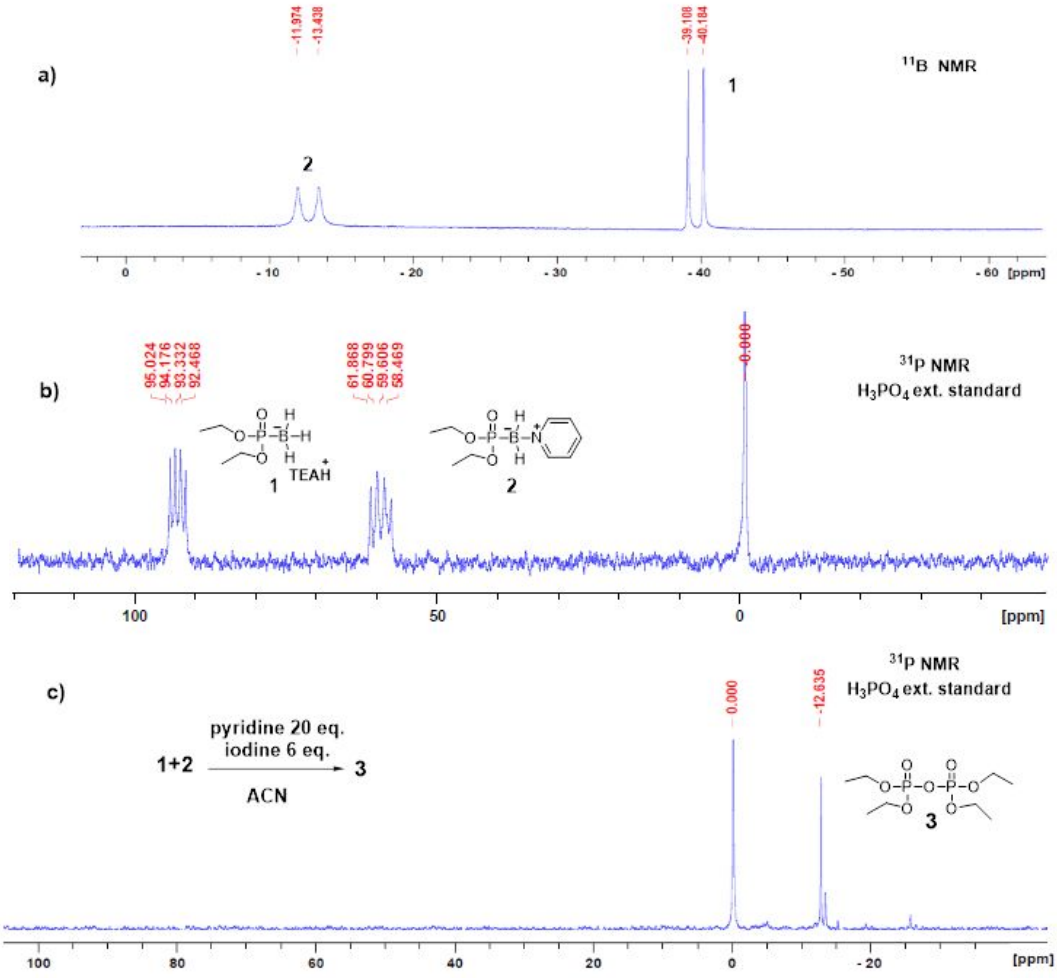
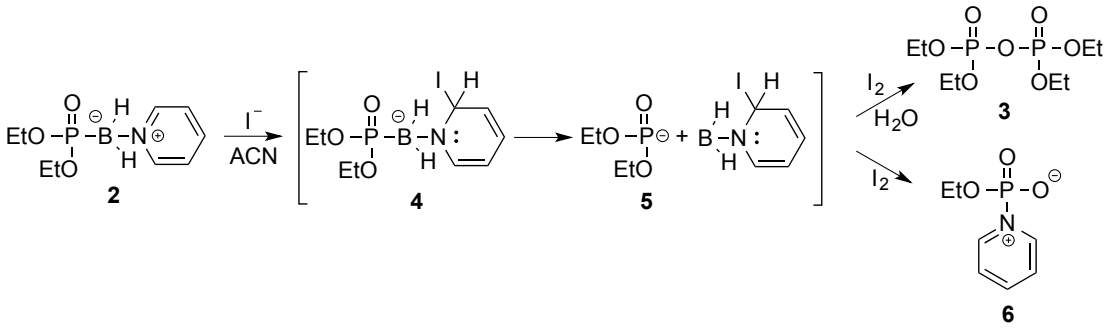


Fig. 1. The reaction of boranephosphonate **1** with pyridine (20 equiv.) in acetonitrile mediated by iodine (6 equiv.), in the presence of the added postulated intermediate, pyridiniumboranephosphonate **2** (1 equiv.). (a) ^{11}B NMR spectrum of **1**+**2** before the addition of iodine; (b) ^{31}P NMR spectrum of the same reaction mixture as in (a); (c) ^{31}P NMR spectrum of the reaction mixture as in (b) but after a few minutes after adding iodine.

The transformation of PyBP **2** into pyrophosphate **3** during the course of the reaction in ACN (Scheme 3) occurred without any detectable by the ^{31}P NMR spectroscopy intermediates, and thus no mechanistic clue existed to this

process. However, on a chemical ground one can assume as plausible an initial nucleophilic attack of iodide (present in the reaction mixture) on carbon C2 of the pyridinium cation moiety[13] in **2** to form aminoboranephosphonate intermediate **4** (Scheme 4). Such a species, or its protonated form, was expected to be unstable and should dissociate to generate first phosphonate anion **5** (or the corresponding H-phosphonate),[10] and after its oxidation by iodine in the presence of spurious water, pyrophosphate **3**. This reaction pathway was partly supported by the findings that under strictly anhydrous conditions, also pyridinium adduct of metaphosphate **6** was formed.[14]

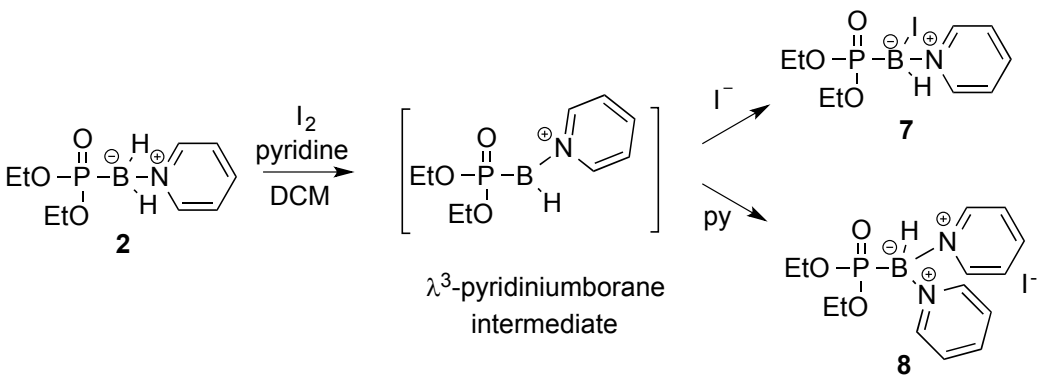


Scheme 4. A putative mechanism for the conversion of PyBP **2** during the reaction of BP **1** with pyridine and iodine in acetonitrile.

As for the variable persistence of PyBP **2** during the reaction in acetonitrile, we carried out a series of experiments in which we reacted BP **1** with pyridine (10 equiv.) by varying the amount of iodine (0.5, 1, 1.5, 2, and 3 equiv.). We observed that with less iodine (0.5 - 1.5 equiv.), the produced PyBP **2** was stable under the reaction conditions (24 h), while larger excess of iodine (2-3 equiv.) favoured decomposition of **2** into tetrasubstituted pyrophosphate **3** (ca. 1h). These can be rationalized in light of the mechanism in Scheme 4, by assuming a possible formation of polyiodides[15] with excess of iodine that could be more effective nucleophiles than iodides.

Another important aspect of the reaction in acetonitrile, in contrast to that run in DCM, was absence of the side-product resonating at ca. $\delta_P = 45$

ppm. This could be of synthetic importance and possibly might provide an additional mechanistic insight into the investigated reaction. Since the most likely scenario for the formation of side-products in this reaction was a subsequent oxidation of the initially formed PyBP **2** by iodine, first we doubled the amount of iodine and pyridine (6 and 20 equiv., respectively) in the reaction in DCM. Unfortunately, this did not result in an increase in side-product formation. However, repeated addition of new portions of iodine and pyridine to the reaction mixture (three times 3 and 10 equivalents, respectively) each time generated more by-product resonating at ca. $\delta_P = 45$ ppm (increase of ca. 20% upon each addition).[16] A similar phenomenon was also observed when isolated PyBP **2** was subjected to the incremental addition of iodine and pyridine in DCM. We speculated that a plausible explanation why the reaction demanded a repeated addition of several portions of fresh iodine and pyridine could be that oxidation of PyBP **2** apparently required more reactive oxidizing species than that involved in oxidation of BP **1**. Such species could be a short lived and transiently generated upon mixing of iodine with pyridine (more on iodine-pyridine complexes, see later in the text). At this point we opted for two possible structures for this side-product, namely, iodopyridiniumboranephosphonate **7** (compound with a betaine structure) and dipyridiniumboranephosphonate **8** (a cationic species), shown in Scheme 5.



Scheme 5. A possible outcome of oxidation of PyBP **2** with iodine-pyridine reagent system.

Propitiously enough, we succeeded in isolation from the reaction mixture of the side-product resonating at δ_P = 45.0 ppm and found that it contained two pyridine moieties (^{1}H NMR). This, and other spectral analysis data (^{13}C, ^{31}P, ^{11}B NMR, and HRMS) allowed us to determine the structure of this side-product as derivative of dipyridiniumboranephosphonate **8**.

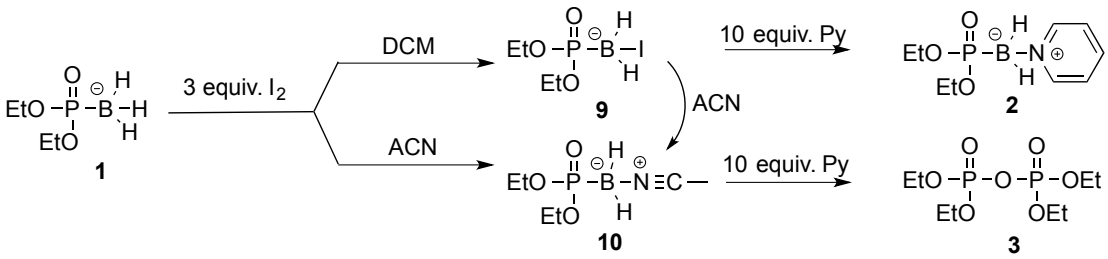
Since formation of the side-product **8** was not observed when the investigated reaction was run in acetonitrile, it seemed that further oxidation of PyBP **2** by iodine did not occurred in this solvent. This paralleled our previous observation that also oxidation of BP **1** in acetonitrile was slower than that in dichloromethane and usually required more iodine.[10]

*Preactivation of boranephosphonate **1** with iodine in dichloromethane vs acetonitrile.*

The widely differing reactivity of BP **1** in dichloromethane compared to acetonitrile (Scheme 2) prompted us to investigate what were the initial products of activation of boranephosphonate diesters with iodine in these solvents. To this end we reacted BP **1** with 3 equiv. of iodine separately in DCM and in ACN, and followed progress of these reactions by the ^{31}P and ^{11}B NMR spectroscopy. We found that in DCM, the major reaction product (>70%) resonated at ca. δ_P = 69 ppm and δ_B = -39 ppm, and in ACN at δ_P = 75 ppm and δ_B = -25 ppm (also the major product, >70%). Upon mixing these two reaction mixtures, only one signal in the ^{31}P NMR (at ca. 75 ppm) and one in the ^{11}B NMR (at ca. -25 ppm) spectra, were observed. This might have indicated that the same product was formed in both reactions, and the observed differences in chemical shifts values were due to differences in the solvents' polarity. However, additional experiments testified to something to the contrary. When to the reaction mixture in ACN, dichloromethane was

added (1:1, v/v), this did not affect the chemical shift values of the signals in ^{31}P (ca. 75 ppm) and ^{11}B NMR (-25 ppm) spectra. However, addition of acetonitrile to the reaction mixture in DCM (1:1, v/v), resulted in an immediate change in the positions of the NMR signals from δ_P = 69 and δ_B = -39 ppm to those observed in the reaction mixture in ACN (δ_P = 75 and δ_B = -25 ppm). By adding only limited amounts of acetonitrile to the reaction mixture in DCM, two resonances in the ^{31}P NMR (at ca. 67 ppm and 75 ppm) and in ^{11}B NMR spectra (at ca. -39 and -25 ppm) could be observed. These experiments strongly suggested that (i) in the preactivation reaction of BP **1** with iodine in DCM and in the reaction in ACN, different products were formed, and (ii) the product formed in DCM was apparently converted to that formed in acetonitrile, upon addition of the later solvent.

Although none of these preactivation products could be isolated, the MS spectra of the crude reaction mixtures and the observed reactivity of the intermediates formed, pointed to iodoboranephosphonate **9** (the preactivation in DCM, δ_P = 69 and δ_B = -39 ppm) and to a new type of complex of acetonitrile-λ^3-boranephosphonate **10**, (the preactivation in ACN, δ_P = 75 ppm and δ_B = -25 ppm), as the most likely structures (Scheme 6). Mechanistic aspects of how these intermediates could be formed will be discussed later in this work.

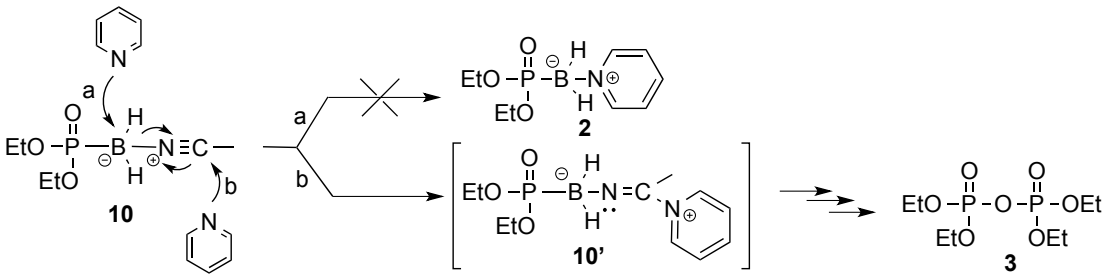


Scheme 6. Products of the preactivation of BP **1** with iodine in DCM and in ACN, and their subsequent reactions with the added pyridine.

As a next step we studied reactivity of the generated intermediates **9** and **10** towards pyridine. We found that addition of pyridine (10 equiv.) to the reaction mixture containing the putative iodoborane intermediate **9** in DCM afforded immediately the expected product, pyridiniumboranephosphonate **2**, presumably *via* a nucleophilic substitution at the boron center (Scheme 6). This might have supported the view that **9** could be an intermediate involved in the reaction of boranephosphonate diesters with pyridine promoted by iodine. However, the analogous reactions with the added 2,6-lutidine or triethylamine did not produce the anticipated products,[17] *i.e.*, the corresponding 2,6-lutidiniumborane- or triethylammoniumboranephosphonate, although these were formed in the reactions without the preactivation step (compounds **12b** and **12l**, *vide infra*). On this basis, and assuming that the same mechanism operated for all the investigated amines, we could dismiss iodoboranephosphonate **9** as a common reaction intermediate, and considered instead a path *via* a four-center transition state addition, or a mechanism involving the intermediacy of an electron-deficient λ^3-boranephosphonate species (*vide infra* and Scheme 1) for the formation of products **2** and **12a-l**.

The reactivity of intermediate **10** generated in acetonitrile turned out to be somewhat unexpected since the addition of pyridine (10 equiv.) resulted in an immediate formation of pyrophosphate **3** (Scheme 6). This reaction, in contradistinction to that in Scheme 3, was fast, proceeded without pyridiniumboranephosphonate **2** as an intermediate, and thus could be an alternative reaction pathway leading to pyrophosphate **3**. A possible explanation for the observed reactivity of **10** could be that a betaine-type of structure of this complex should make the B-N bond stronger and effectively prevent a nucleophilic substitution of the acetonitrile moiety by pyridine at the boron center (path *a* in Scheme 7). On the other hand, the presence of a

positive charge on the nitrile nitrogen in **10**, might invite a nucleophilic attack of pyridine on the nitrile carbon (path b in Scheme 7) possibly generating an aminoborane intermediate **10'**. This step, which can be considered analogous to that in the Pinner[18] or the Ritter[19] reaction, should lead to labilization of the P-B bond and dissociation of the aminoborane intermediate **10'** into phosphonate anion **5** and the borane part, and then in the presence of iodine, to subsequent P-oxidation reactions, as it was discussed above for the transformation shown in Scheme 4.



Scheme 7. A possible mechanism for the reaction of acetonitrile-λ^3-boranephosphonate complex **10** with pyridine in the presence of iodine.

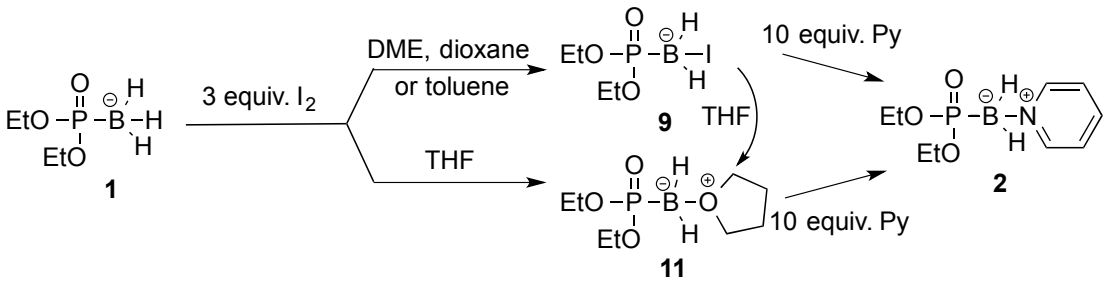
In line with the mechanism suggested in Scheme 7, the added 2,6-lutidine (10 equiv.) or triethylamine (10 equiv.) reacted similarly as pyridine with acetonitrile-borane complex **10**,[20] to afford pyrophosphate **3** (see also later in the text).

*Reactivity of boranephosphonate **1** in other solvents.*

High sensitivity of boranephosphonate diesters to the nature of the solvent used for the reaction, prompted us to investigate the activation process of BP **1** and its reaction with amines mediated by iodine in different organic solvents, namely, monoglyme (1,2-dimethoxyetane, DME), dioxane, tetrahydrofuran (THF), *N,N*-dimethylformamide (DMF), and toluene. The reactions of **1** with iodine alone (3 equiv.; the preactivation process) in

monoglyme, dioxane, and toluene occurred similarly, but less efficiently than that in DCM, producing iodoboranephosphonate **9** (Scheme 6 and 8) as a minor product (*e.g.*, in DME, 50% of unreacted **1**, 25% of **9**, and 25% of diethyl phosphoroiodidate). In DMF the reaction of BP **1** with iodine afforded immediately only deboronated products without any detectable by the ^{31}P NMR spectroscopy intermediates.

We observed that the produced iodoboranephosphonate **9** was much less stable in monoglyme or dioxane than in DCM (>24 h) and decomposed (deboronation and oxidation) to phosphate derivatives within 1 h.



Scheme 8. Preactivation of BP **1** with iodine in monoglyme (DME), dioxane, toluene, and THF.

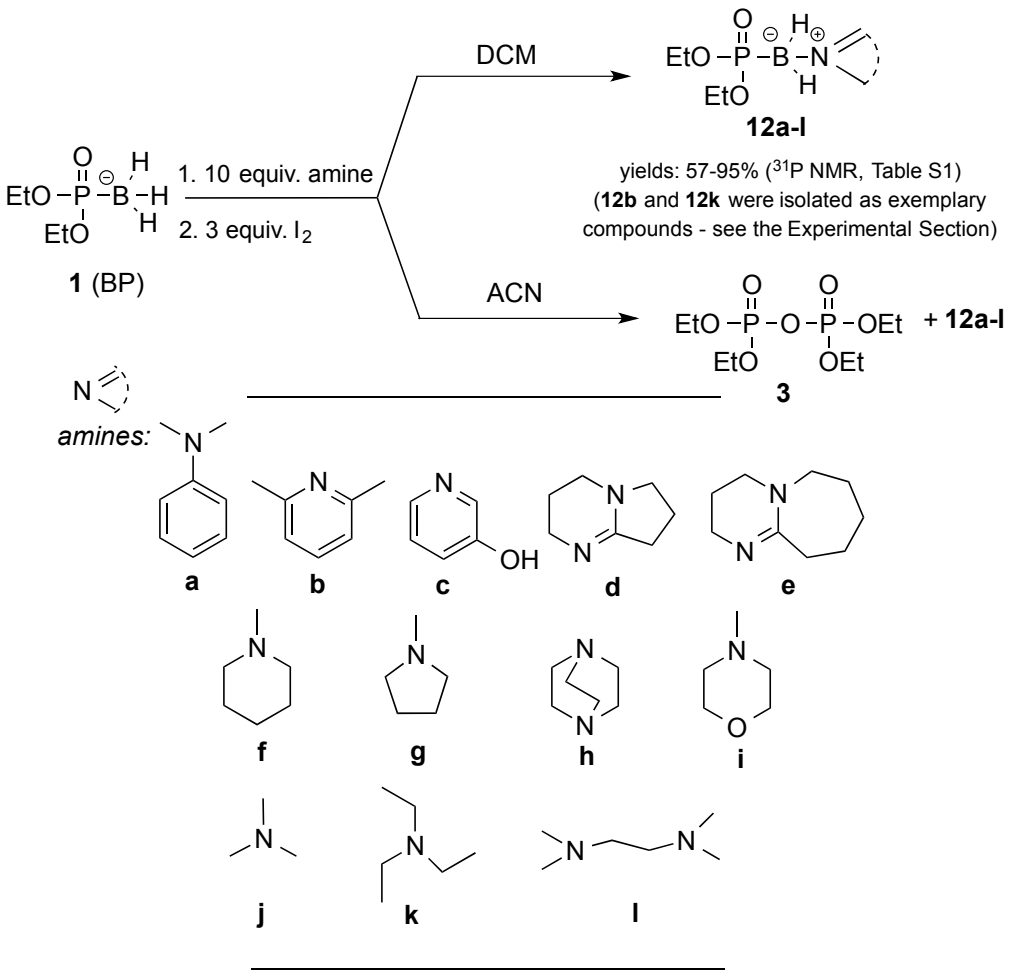
The preactivation of BP **1** with iodine in THF did not afford iodoboranephosphonate **9**, but a new compound resonating in the ^{31}P NMR spectrum at 78.2 ppm, and in the ^{11}B NMR, at -7.3 ppm. This later chemical shift value indicated presence of a boron-oxygen bond, and thus we tentatively identified this compound as a THF-λ^3-boranephosphonate complex **11** (Scheme 8), analogously to that containing the acetonitrile instead of the THF moiety (compound **10** in Scheme 6). This assignment was substantiated by the experiment in which iodoboranephosphonate **9**, generated in DCM (δ_P = 69.4 ppm and δ_B = -38.7 ppm), was converted into the putative THF-λ^3-boranephosphonate complex **11** (δ_P = 78.2 and δ_B = -7.3 ppm) upon the addition of THF (20 equiv.). In light of these it seems that THF, in

contradistinction to monoglyme or dioxane, is a strongly participating solvent, resembling in this respect ACN. One should note, however, that the bonding pattern in THF-λ^3-boranephosphonate **11** is quite different from that in the acetonitrile complex **10**. This probably made complex **11** susceptible to a nucleophilic substitution by pyridine at the boron center[21] to form pyridiniumboranephosphonate **2** (Scheme 8), in contradistinction to the acetonitrile complex **10**, where this reaction pathway was disfavored (Scheme 6).

In all the investigated solvents the reaction of BP **1** with pyridine (10 equiv.), and iodine (3 equiv.) without the preactivation proceeded similarly as in DCM and afforded the expected product Py-BP **2** together with small amounts of dipyridiniumboranephosphonate **8** (10-20%) as a side-product.

The substrate scope of the investigated reaction

To explore the substrate scope of the investigated reaction we appended the series of *N*-nucleophiles used by Caruthers *et al*.[8] by additional heteroaromatic and 3° amines **a**-**l** with diverse structural features (aromatic amines, pyridine derivatives, bicyclic amidines, aliphatic acyclic, cyclic and bicyclic amines, *etc*; Scheme 9).



Scheme 9. Substrate scope of the reaction of diethyl boranephosphonate **1** with tertiary amines.

To have comparison with the reactivity of pyridine, we reacted amines **a**-**l** both with BP **1** in DCM, ACN, and THF in the presence of iodine, and also separately with the products of activation of BP **1** with iodine, *i.e.*, iodoboranephosphonate **9** (reactions in DCM), acetonitrile-λ^3-boranephosphonate **10** (reactions in ACN) and tetrahydrofuran-λ^3-boranephosphonate **11 (**reactions in THF**)**. The analysis of data from Table S1 (see the supplementary information) revealed some general trends regarding the reactivity of the tested amines. In dichloromethane, amines **a**-**l** reacted promptly with BP **1**, but less cleanly than pyridine, to afford the corresponding *B*-modified boranephosphonate derivatives **12** (^{31}P NMR experiments, δ_P = 58 - 65 ppm, broad signals) and some deboronated products

(ca. 5-20%). In all instances, presence of additional boron-containing products (up to 20%), resonating at ca. 40 ppm in the ^{31}P NMR spectra, could be detected.[22] A similar reactivity was observed for the reactions in ACN and THF (participating solvents), and the yields of the P-B-N products of type **12** were usually noticeable higher in THF than those in ACN or DCM. For certain amines, however, *e.g.*, **b**, **d** in ACN, and **a**, **b** in THF, only the deboronated products were formed. For the reaction of amines **a**-**l** (10 equiv.) with the generated iodoboranephosphonate intermediate **9** (reactions in DCM), formation of **12** with variable proportions of tetraethyl pyrophosphate **3** (20-60%) was observed. Certain sterically hindered amines (*e.g.*, **b**, **e**, **i**, **j**, **k**), apparently could not substitute the iodide at the boron center in **9**, and produced only the deboronated products (phosphate derivatives). This may have a mechanistic bearing concerning a possible intermediate involved in the investigated reaction.

In the instance of acetonitrile-λ^3-boranephosphonate complex **10**, no formation of the P-B-N derivatives of type **12** was observed for all the tested amines, analogously to the reaction with pyridine (Scheme 7). In sharp contrast to the reactivity of **10**, tetrahydrofuran-λ^3- boranephosphonate complex **11** reacted smoothly with amines **c**-**l** giving the P-B-N derivatives **12** usually in higher yields than in the reaction of BP **1** in DCM. This was most apparent for amidine bases **d** and **e**. Sterically hindered amines of low basicity, *e.g.*, *N*,*N*-dimethylaniline (**a**) and 2,6-lutidine (**b**), were not able to substitute the THF moiety in complex **11**, but instead they probably facilitated further oxidation of the borane group eventually producing deboronated products (phosphate derivatives).

The broad substrate scope of this reaction is consistent with studies by Caruthers *et al*.[8] but with a notable exception of 2,6-lutidine and triethylamine, for which no formation of complexes of type **12** was reported,

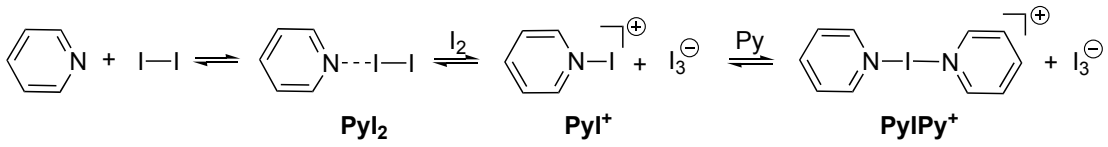
due to the claimed extensive steric hindrance. Contrary to these we found that in DCM compounds **12b** (2,6-lutidine derivative) and **12k** (triethylamine derivative) could be formed and their structures were confirmed by spectroscopic methods (^{1}H, ^{13}C, ^{31}P, ^{11}B NMR, and HRMS) after silica gel chromatographic isolation. This highlighted the importance of the solvent used and might pointed to the intermediacy of an electron-deficient borane species in this reaction (see Scheme 1). In agreement with these, in the reaction of boranephosphonate diesters with sterically hindered amines, participating solvents (*e.g.*, dioxane in the Caruthers' studies[8], and acetonitrile or THF in the present work) may efficiently prevent capturing of the borane intermediate by the amines, in contrast to non-participating solvents (*e.g.*, dichloromethane), where the transient λ^3-borane intermediate can be intercepted even by sterically hindered amines to form *B*-modified boranephosphonate dieters of type **12**.

Mechanistic aspects of the reaction of boranephosphonate diesters with amines promoted by iodine.

The issue of the oxidizing species - iodine-amine complexes.

Although iodine is implicated as an oxidant in the investigated reaction, a chemical nature of the oxidizing entity involved is far from clear. The problem can be particularly difficult to resolve for oxidative transformations involving amines[7-8] since these are known to form with iodine various type of complexes, connected *via* complex equilibria systems,[23] that ultimately undergo time- and concentration-dependent decomposition processes.[23d,24] The interaction of amines with halogens has been the subject of numerous investigations since almost a century[11b,23c,25] and in recent years these studies have received new stimuli due to the revival of the concept of a N-X-N halogen bonding[26] as a new molecular motif in rational drug design

and in material sciences.[27] For a pyridine/iodine mixture, a typical equilibria system that is established in organic solvents is shown in Scheme 10.[23c,28]



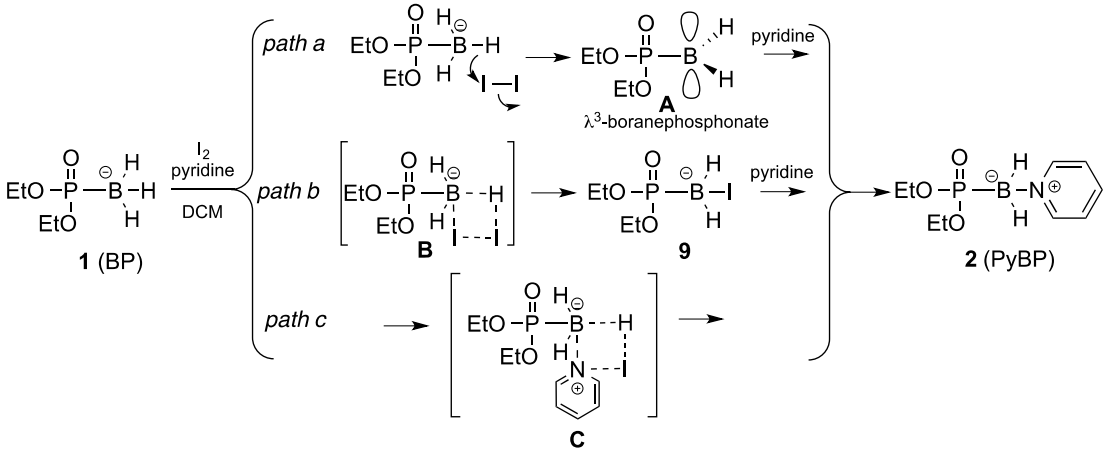
Scheme 10. A putative (simplified) equilibria system for iodine and pyridine in organic solvents.

An increase in iodine concentration is shifting the equilibrium in Scheme 10 towards *N*-iodopyridinium cationic species PyI^+, while an increase in base concentration (pyridine) favours formation of a charge transfer complex PyI_2 (K_a ca. 100-200 M^{-1}) and another cationic species, *N*-iododipyridinium $PyIPy^+$.[28a,29] In nonpolar solvents, the charge transfer complexes of type PyI_2 are relatively stable but in polar systems, they tend to dissociate to form ionic species PyI^+ and $PyIPy^+$ that undergo slow decomposition.[28a] According to the Schuster's and Roberts' ^1H- and ^{13}C NMR studies,[30] in nonpolar solvents iodine and pyridine are in fast equilibrium with PyI_2, while the equilibrium between PyI_2 and $PyIPy^+$ is slow on the NMR time scale. In line with these, our ^1H NMR experiments on 2:1 mixture of pyridine and iodine in DCM revealed only one set of signals from the pyridine moiety, indicating a rapid equilibrium of iodine and pyridine with the charge transfer complex PyI_2. For the ACN solutions, an additional set of signals, attributed to the formation of cationic species $PyIPy^+$ (ca. 15%), was observed in the ^1H NMR spectra (data not shown). We could also confirm that solutions of iodine with pyridine were not completely stable (even in DCM) as judging from the inferior results of the formation of pyridiniumboranephosphonates **2**, when pyridine with and iodine were mixed 15-60 min prior to the reaction with BP **1**.[31] Due to complexity of the system and its sensitivity to various factors (*e.g.*, kind of the solvent used, concentration and the ratio of the reactants, instability in time), no attempt

was made to identify, which of the species, elemental iodine, charge transfer complex PyI_2, PyI^+, or $PyIPy^+$ was the reactive entity accepting a hydride ion from the borane group during synthesis of **2**. However, selected experiments shed some light on this problem. Since that there was no discernible difference in the rate of oxidation of boranephosphonate **1** in DCM with iodine alone (the preactivation process), and with iodine in the presence of pyridine (the reaction to produce **2**, *vide supra*), we assumed for the purpose of our studies that reactivity of elemental iodine was probably similar to that of the other complexes formed by iodine with pyridine (Scheme 10). For this reason in our mechanistic discussion we found it justified to invoke the participation of elemental iodine or its complexes with pyridine as possible oxidants.

*Reaction pathways for oxidative transformation of boranephosphonate **1** into pyridiniumboranephosphonate derivative **2**.*

All the experiments discussed above cumulatively pointed to three possible reaction pathways for the conversion of BP **1** into pyridiniumboranephosphonates of type **2** that are summarized in an abbreviated form in Scheme 11.



Scheme 11. Some possible reaction pathways for the formation of pyridiniumboranephosphonate **2**.

At the present stage of this study *path a* in Scheme 11 seems most likely because all the synthetic results discussed above can be simply accounted for by assuming the intermediacy of λ^3-boranephosphonate **A** with a vacant *p*-orbital on the boron atom. In line with this, in non-participating solvents such as DCM, the formation compounds of type **12** with the P-B-N functionality bearing even highly sterically hindered amines, was observed. While the generated in the preactivation process in DCM iodoboranephosphonate **9** also reacted smoothly with pyridine and other 3° amines (Table 1S), it failed to provide the corresponding P-B-N derivatives in the reaction with certain sterically hindered amines, *e.g.*, 2,6-lutidine (**b**), DBU (**e**), *N*-methylmorpholine (**i**), trimetylamine (**j**), and triethylamine (**k**) (Table 1S). By this token, *path b*, that assumed iodoboranephosphonate **9** as an alternative common intermediate in this reaction, must be rejected. Thus, in the light of our previous studies[10] *path a* may constitute a uniform mechanism for the iodine-mediated reactions of boranephosphonate diesters with amines, regardless of the type of final products formed, *i.e.*, the corresponding phosphoramidates (for 1° and 2° amines)[10] or *B*-modified boranephosphonate derivatives (for 3° and heteroaromatic amines, this study).

Another possible way for the formation of pyridiniumboranephosphonate **2** can be *path c* that involves a 4-center transition state **C** (Scheme 11) in which oxidation of the borane hydride and coordination of the pyridine moiety occurs simultaneously. Such a mechanism was previously proposed by Caruthers *et al*[8] to explain a different course of the mediated by iodine reaction of boranephosphonate diesters with pyridine *vs* 1° or 2° amines. This seems reasonable in light of the oxidizing species present in the reaction mixture, but on the geometrical ground, a

transition state of type **C** would call for a square pyramidal arrangement of the substituents around the boron center, and require a frontside attack of the amine moiety. While probably possible for pyridine, this scenario can be somewhat problematic for sterically hindered bases. Thus, we suggest that if PyI^+ would be involved as a reactive oxidizing species, the B-H bond breaking (oxidation of the borane hydride) might run significantly ahead of the B-N bond formation, and the transition state could adopt all the characteristic of λ^3-boranephosphonate **A** intermediate with the pyridine molecule nearby the boron center, available for coordination. We refer to such a mechanism as occurring *via* λ^3-boranephosphonate **A** intermediate in a solvent cage. A similar scenario can be envisaged for iodine or its charge-transfer complex with pyridine (PyI_2) acting as an oxidizing species (*path a*), where the incipient λ^3-boranephosphonate **A** intermediate could be intercepted by pyridine present in the solvent cage. Assuming the above mechanism, it can be expected that in participating solvents (ACN and THF, see Table 1S) competitive capture of intermediate **A** by the solvent molecules may occur. This would lead to the formation of acetonitrile-λ^3-boranephosphonate complex **10** (reactions in ACN) or tetrahydrofuran-λ^3-boranephosphonate complex **11** (reactions in THF). Since compound **10** cannot be converted into P-B-N products (see Scheme 6 and Table 1S), lower yields of the desired products **12** would be expected for the reaction in acetonitrile. This is indeed apparent from the data in Table 1S. In addition, for certain amines, *e.g.*, 2,6-lutidine (**b**) and DBN (**d**), only deboronated products were formed in ACN, probably due to complete capture of **A** by the solvent molecules. This interpretation is congruous with the data for the reactions in THF (Table 1S). In this instance the interception of the putative intermediate **A** by the solvent molecules to form tetrahydrofuran-λ^3-boranephosphonate complex **11**, should not have a detrimental effect on the efficiency of the P-B-N compounds formations, because unlike the complex with acetonitrile **10**, complex **11**

would return the desired products **12** upon the reaction with amines. Indeed, for the most part, the yields of products **12** in the reactions in THF were higher than in acetonitrile and comparable with those in DCM. The exception here were *N,N*-dimethylaniline (**a**) and 2,6-lutidine (**b**) that, as it was mentioned before, could not substitute the tetrahydrofuran moiety in **11**, but instead, promoted its degradation to deboronated products. Considering this reactivity and the assumption that during the course of the reaction of BP **1** with amines, intermediate **A** can be captured by the solvent molecules to form **11**, the formation of P-B-N products for amines **a** and **b** was not observed in THF.

Finally, a possible mechanism for the formation of the preactivation products from BP **1** with iodine in DCM (compound **9**), ACN (compound **10**), and THF (compound **11**), deserved some comments. Iodoboranephosphonate **9** can be formed, in principle, *via* (i) the initial generation of intermediate **A,** followed by coordination of iodide present in the reaction mixture, (ii) in a one step reaction *via* a 4-center transition state **B**, analogous to **C**, or (iii) coordination of the iodide anion by the insipient λ^3-boranephosphonate **A** in a solvent cage, as it was suggested above for the reactions with amines. Since reactivity of iodine alone, and iodine in the presence of amines, towards boranephosphonate diesters seems to be comparable, at this stage of our investigations we tend to favour the last option. As to the formation of acetonitrile-λ^3-boranephosphonate **10** and tetrahydrofuran-λ^3-boranephosphonate **11**, direct coordination of the solvent molecules (acetonitrile and tetrahydrofuran, respectively) by λ^3-boranephosphonate **A** most likely prevailed due significantly higher concentration of the solvent molecules compared to iodide, but some participation of **9** cannot be completely excluded.

To closing this part, it should be remembered that reactions of boranephosphonate diesters with amines mediated by iodine are also very sensitive to the ratio of the reagents used, as it was shown above for the model amine, pyridine. This can have a quantitative and qualitative impact on the outcome of these reactions.

CONCLUSIONS

We found that the reaction of diethyl boranephosphonate **1** with pyridine promoted by iodine in dichloromethane afforded the corresponding pyridiniumboranephosphonate **2** and ca. 20% of dipyridiniumboranephosphonate derivative **8**. In an analogous reaction in acetonitrile, a complete deboronation occurred, with tetraethyl pyrophosphate **3** as a final product. It seems that the formation of different products in dichloromethane *vs* acetonitrile was most likely due to instability of the formed pyridiumboranephosphonate derivative under the reaction conditions or an alternative reaction pathway (formation of acetonitrile adduct **10**) in the later solvent. A similar course of the reaction was observed for other pyridine derivatives and 3° amines investigated. Preactivation of BP **1** with iodine in dichloromethane *vs* acetonitrile without amine also produced distinct intermediates, namely, the corresponding iodoboranephosphonate **9** (in DCM) and the hitherto unknown complex of λ^3-boranephosphonate with acetonitrile **10** (in ACN). These, upon addition of pyridine afforded the desired diethyl pyridiniumboranephosphonate **2**, and tetraethyl pyrophosphate **3**, respectively. We also found that THF in this reaction acted as a strongly participating solvent forming BP-THF complex **11** that, in contradistinction to the analogous complex with acetonitrile **10**, reacted with the added pyridine yielding PyBP **2**.

On the basis of ^{31}P and ^{11}B NMR spectroscopy we formulated a general mechanism for the reaction of boranephosphonate diesters with 1°, 2°, 3°, and heteroaromatic amines mediated by iodine. It features, as key mechanistic steps, generation of an electron-deficient intermediate λ^3-boranephosphonate **A** (Scheme 11), followed by its coordination by the amine present to form compounds with a P-B-N structural motif. Given the overall complexity of this reaction, two distinct mechanisms can also be envisaged, one *via* 4-center transition state of type **C**, for less sterically hindered amines (*e.g.,* 1° and 2° amines, pyridine), and the other, *via* a λ^3-boranephosphonate intermediate **A**, for sterically hindered amines (*e.g.,* 2,6-lutidine).

EXPERIMENTAL SECTION

All reagents were of analytical grade, obtained from commercial suppliers and used without further purification. Diethyl boranephosphonate **1** was prepared as previously described.[10] Anhydrous solvents used for the reactions were stored over molecular sieves 4 Å. TLC analyses were carried out on Merck silica gel 60 F 254 precoated plates using CH_2Cl_2–MeOH 9:1 (v/v) solvent system. All evaporations were carried out on rotatory evaporators under reduced pressure at 40 °C.

The NMR spectra were recorded using Bruker Avance II 400 MHz instrument. The chemical shifts are reported in ppm, relative to solvent peaks (^1H, ^{13}C NMR), 2% H_3PO_4 solution in D_2O (^{31}P NMR), and BF_3 diethyl etherate (^{11}B NMR). Assignment of the NMR signals was accomplished on the basis of the expected chemical shift values, splitting pattern of the signals, and 2D correlation experiments. High-resolution mass spectra (HRMS) were recorded on Thermo Fisher Scientific Q-Exactive Orbitrap mass spectrometer. Identification of intermediates observed in the ^{31}P and ^{11}B NMR spectra of the reaction mixtures was done on the basis of the expected chemical shifts, coupling constants, shapes of the multiples, and spiking of the reaction samples with compounds of known structures.

Purity of the isolated compounds was >97% (^1H NMR spectroscopy) unless it was stated otherwise.

General protocol for ^{31}P and ^{11}B NMR experiments

To a solution of diethyl boranephosphonate **1** (0.5 mmol) and pyridine (5 mmol, 10 equiv.) in CH_2Cl_2 (3 mL), iodine (1.5 mmol, 3 equiv.) was added, and the reaction mixture was kept at room temperature with a continuous stirring. Progress of the reaction was checked by ^{31}P and ^{11}B NMR spectroscopy by taking samples in time

intervals and recording the spectra. Analogous reactions were run also in other solvents *(e.g*. acetonitrile, THF) and with other heteroaromatic and 3° amines (for details, see in the text). To detect possible intermediates involved, **1** in a suitable solvent was reacted with variable amounts of iodine in the absence of an amine (see, the preactivation experiments). Reactivity of the intermediates formed was studied by adding to the reaction mixture suitable reactants as indicated in the text.

To prove chemical identity of the formed compounds, selected reactions were run on a preparative scale, and the products were isolated by silica gel chromatography. The isolated compounds were characterized by spectroscopic methods and, is so desired, subjected to additional reactions as specified in the text.

*Preactivation of diethyl boranephosphonate **1** with iodine in dichloromethane.*

Diethyl boranephosphonate **1** (TEAH+ salt, 127 mg, 0.5 mmol) was dissolved in CH_2Cl_2 (10 mL) and evaporated repeatedly (3 x) the added solvent (3 x 10 mL CH_2Cl_2). The residue was dissolve in CH_2Cl_2 (3 mL) and iodine (380 mg, 1.5 mmol, 3 equiv.) was added. Progress of the reaction was checked by ^{31}P and ^{11}B NMR spectroscopy by taking samples in time intervals and recording the spectra. After ca 10 min upon mixing the reagents, the major signal (>70%) at ca 69 ppm in the ^{31}P NMR or at ca -39 ppm in ^{11}B NMR spectrum, appeared. This was tentatively identified as iodoboranephosphonate **9** on the basis of its reactivity towards pyridine and acetonitrile, and by MS spectra of the crude reaction mixture. For more details, see also Scheme 6 and the discussion in the text.

*Preactivation of diethyl boranephosphonate **1** with iodine in acetonitrile.*

Diethyl boranephosphonate **1** (TEAH+ salt, 127 mg, 0.5 mmol) was dissolved in acetonitrile(10 mL) and evaporated repeatedly (3 x) the added solvent (3 x 10 mL acetonitrile). The residue was dissolve in acetonitrile (3 mL) and iodine (380 mg, 1.5 mmol, 3 equiv.) was added. Progress of the reaction was checked by ^{31}P and ^{11}B NMR spectroscopy by taking samples in time intervals and recording the spectra. After ca 15 min upon mixing the reagents, the major signal (>75%) at ca 75 ppm in the ^{31}P NMR or at ca -25 ppm in ^{11}B NMR spectrum appeared. This was tentatively identified as iodoboranephosphonate **9** on the basis of its reactivity towards pyridine and by MS spectra of the crude reaction mixture. For more details, see also Scheme 6 and the discussion in the text.

*Synthesis of diethyl pyridiniumboranephosphonate **2***

Diethyl boranephosphonate **1** ($TEAH^+$ salt, 254 mg, 1mmol) was placed in a 100 mL pear-shaped flask and evaporated twice the added anhydrous dichloromethane (2 × 20 mL). The residue was dissolved in the same solvent (5 mL), and then pyridine (10 mmol) and elemental iodine (3 mmol) were added. The mixture was stirred and progress of the reaction was monitored by ^{31}P NMR spectroscopy. After 10 min excess of iodine was decomposed by the addition of an aqueous ethanethiol (25%, 0.2 mL), the solvents evaporated under reduced pressure, and the product was purified by

a silica gel column chromatography using a gradient of water in acetonitrile (0−5%, v/v). Fractions containing the desired product were collected and evaporated to yield pyridiniumboranephosphonate as a colorless oil (167 mg). Yield 73%. HRMS m/z: $[M+H^+]^+$ calcd for $C_9H_{18}BNO_3P$, 230.1117; found, 230.1103. ^1H NMR ($CDCl_3$, 400 MHz, δ): 1.15 (t, 6H, $^3J_{HH}$ = 7.1 Hz), 3.90 (q, 4H, $^3J_{HH}$ = 7.0 Hz), 7.60 (t, 2H, $^3J_{HH}$ = 13.8 Hz), 8.03 (t, 1H), 8.61 (d, 2H, $^3J_{HH}$ = 6.1 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ): 16.6 ($^3J_{PC}$ = 5.6 Hz), 58.6 ($^2J_{PC}$ = 6.6 Hz), 126.0 ($^2J_{PC}$ = 1.9 Hz), 140.8 ($^4J_{PC}$ = 3.2 Hz), 148.0 ($^3J_{PC}$ = 6.8 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz, δ): 60.16 (br m). ^{11}B NMR ($CDCl_3$, 128.4 Hz, δ): -13.27 ($^1J_{PB}$ = 175.7 Hz, $^1J_{BH}$ = 105.6 Hz, dt).

*Synthesis of diethyl dipyridiniumboranephosphonate **8***

Diethyl dipyridiniumboranephosphonate **8** was isolated as a side product during the synthesis of pyridiniumboranephosphonate **2** (see above). To this end a reaction mixture from a separate run was quenched by aqueous ethanethiol (25%, 0.2 mL), evaporated to dryness, and dissolved in dichloromethane (100 mL). The organic layer was extracted with water (3 x 75 mL), the aqueous phase containing the product was evaporated to dryness, and the residue was purified by reverse silica gel column chromatography using as an eluent acetone/water (a linear gradient 0−15%, v/v of water). Fractions containing the desired product were collected and evaporated to yield dipyridiniumboranephosphonate **8** as a colorless oil (34 mg). Yield 12%. HRMS m/z, $[M^+]$ calcd for $C_{14}H_{21}BN_2O_3P^+$, 307.1377; found, 307.1366.^1H NMR ($CDCl_3$, 400 MHz): δ 1.27 (t, 6H, $^3J_{HH}$ = 7.0 Hz), 4.14 (m, 4H), 8.07 (t, 4H, $^3J_{HH}$ = 6.9 Hz), 8.57 (t, 4H, $^3J_{HH}$ = 7.8 Hz), 8.97 (d, 2H, $^3J_{HH}$ = 5.8 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 15.7 ($^3J_{PC}$ = 5.0 Hz), 62.1 ($^3J_{PC}$ = 7.5 Hz), 128.1, 145.9, 147.5 ($^3J_{PC}$ = 7.8 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 44.28 (br m). ^{11}B NMR ($CDCl_3$, 128.4 MHz, δ): -1.29 ($^1J_{PB}$ = 212.2 Hz, d).

*Synthesis of diethyl 2,6-dimethylpyridiniumboranephosphonate **12b***

Diethyl 2,6-dimethylpyridiniumboranephosphonate **12b** was obtained analogously to diethyl pyridiniumboranephosphonate **2** but using 2,6-dimethylpyridine (10 mmol) as a nucleophile instead of pyridine. The desired product was isolated as a yellowish oil (164 mg). Yield 64%. HRMS m/z: $[M+H^+]^+$ calcd for $C_{11}H_{22}BNO_3P$, 258.1430; found, 258.1416. ^1H NMR ($CDCl_3$, 400 MHz, δ): 1.28 (t, 6H, $^3J_{HH}$ = 7.0 Hz), 2.97 (s, 6H), 4.02 (m, 4H), 7.36 (d, 2H, $^3J_{HH}$ = 7.8 Hz), 7.77 (m, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ): 16.66 ($^3J_{PC}$ = 5.5 Hz), 25.4, 58.6 ($^2J_{PC}$ = 6.9 Hz), 125.6, 139.8, 159.6. ^{31}P NMR ($CDCl_3$, 162 MHz, δ): 62.93 (br m). ^{11}B NMR ($CDCl_3$, 128.4 MHz, δ): -18.50 ($^1J_{PB}$ = 187.5 Hz, $^1J_{BH}$ = 175.7101.3 Hz, dt).

*Synthesis of diethyl triethylammoniumboranephosphonate **12k***

Diethyl triethylammoniumboranephosphonate **12k** was obtained analogously to diethyl pyridiniumboranephosphonate but using as a nucleophile triethylamine (10 mmol) instead of pyridine. The desired product was isolated as a yellowish oil (155 mg). Yield 62%. HRMS m/z: $[M+H^+]^+$ calcd for $C_{10}H_{28}BNO_3P$, 252.1899; found, 252.1885. ^1H NMR ($CDCl_3$, 400 MHz, δ): 1.16 (m, 15H), 2.99 (q, 6H, $^3J_{HH}$ = 7.3 Hz), 3.84 (4H).$^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ): 8.2, 16.6 ($^2J_{PC}$ = 5.7 Hz), 51.7 ($^2J_{PC}$ = 8.2 Hz), 58.2 ($^2J_{PC}$ = 6.7 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz, δ): 60.39 (br m). ^{11}B NMR ($CDCl_3$, 128.4 MHz, δ): -16.36 ($^1J_{PB}$ = 185.7 Hz, $^1J_{BH}$ = 95.9 Hz, dt).

Supporting information

^{1}H, ^{13}C, ^{31}P, and ^{11}B NMR spectra (pdf) of the synthesized compounds and selected reaction mixtures.

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(16) The addition of more iodine or pyridine alone to the reaction mixture did not increase the formation of the by-product.

(17) The reaction of the generated iodoboranephosphonate **9** with 2,6-lutidine (10 equiv.) afforded diethyl phosphoroiodidate as a sole phosphorus-contaning product (δp ca. -40 ppm). Apparently, due to steric hindrance, 2,6-lutidine acted as a base facilitating further oxidation of **9** into di- or triodo derivatives, and ultimately, into the iodophosphate. The reaction of **9** with triethylamine gave a complex mixture of the deboronated products together with unreacted starting material. In this instance the incomplete reaction was probably due to competeting decomposition of iodine by rather strongly basic triethylamine.

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(22) The side-products resonating at ca. 40 ppm in the ^{31}P NMR spectrum could not be isolated and their structures remain cryptic. It seems, however, that in contradistinction to the the analogous product from the reaction with pyridine (compound **8**, Scheme 5), they most likely did not contain an additional amine residue, but instead an iodine atom (structures analogous to that of **7** in Scheme 5). This was suggested by the chemical shifts values in the ^{11}B NMR spectra of these side-products (signals at ca. -39 ppm *vs* - 1 ppm for **8**).

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(31) For triethylamine or other 3° amines, solutions with iodine in DCM or ACN were loosing their oxidation capacity much faster (within few to several minutes; decoloration or development of deep dark coloration togther with precipitate formation).

Graphical Abstract