REVIEW

Boron acids as protective agents and catalysts in synthesis

Peter J. Duggan * and Edward M. Tyndall

Centre for Green Chemistry and School of Chemistry, PO Box 23, Monash University, Clayton, Melbourne, Victoria, 3800, Australia. E-mail: peter.duggan@sci.monash.edu.au

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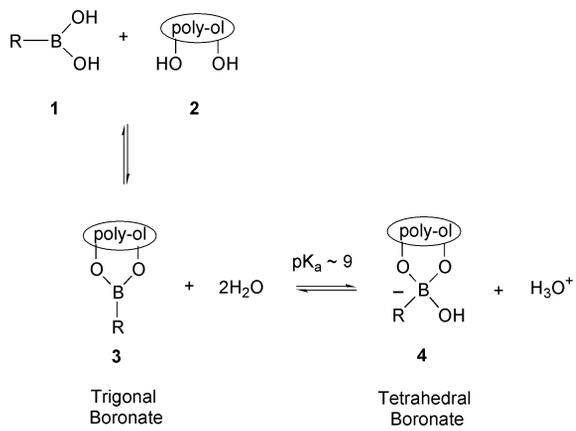
1 Introduction

1.1 Applications of boron acids

Over the last decade there has been a significant expansion in the use of boron acids, with researchers finding a broad range of applications for these versatile compounds. Applications include their use in sugar permeable membranes,[1–3] as carbohydrate sensors[4] and as bioconjugates.[5,6] Boron acids are also being investigated for use in boron neutron capture therapy[7] and as drug delivery agents.[8] Synthetic applications include the use of boronic acids in Suzuki coupling reactions,[9] as part of chiral auxiliaries,[10] in the separation of cyclic *cis*- and *trans*-1,2-diols[11–14] and, occasionally, as precursors to boron enolates.[15] The main focus of this review is the use of boron acids as protective agents and catalysts in organic synthesis. Our attention has been drawn to such applications of boron acids primarily because they present the possibility of more environmentally benign synthetic procedures. This article concentrates on the use of boron acids as reagents which improve reaction selectivities and/or rates, without the boron acids themselves being consumed, such that they could, in principle, be recovered. Most of the work reviewed here employs arylboronic acids, with just a few references to the use of either boric acid or borinic acids.

1.2 A brief summary of relevant boron acid chemistry

Ferrier[16] was a pioneer in the use of boron acids as selective protective agents for carbohydrates and last reviewed the topic in 1978. The reader is referred to that article for a summary of the chemical properties of boron acids and their esters relevant to their use in carbohydrate synthesis. A simplified view will be reiterated here. The core properties making boronic acids (**1**, Scheme 1) attractive protective agents are: a) their ability to form cyclic esters with diols (**2**) much more readily than many other acids, and b) the boronate esters thus formed are stable



Scheme 1

but can be cleaved under relatively mild conditions. Except under basic conditions, the boronate esters adopt a trigonal planar arrangement about the boron (**3**). Ring strain dictates that six-membered trigonal boronate esters form most readily, but five-membered esters can also be prepared from vicinal-diols. The boron in all of these trigonal boronate esters is electron deficient and can co-ordinate with Lewis bases. If the base is strong, such as a hydroxide or alkoxide ion, a fully covalent bond is formed with the boron, which then becomes tetrahedral (as in **4**). The most stable tetrahedral esters are the five-membered esters formed with vicinal-diols. The situation becomes considerably more complicated when, as is often the case, more than two hydroxy groups are present on the substrate.

Most of the synthetic applications of boronic acids described in this article involve trigonal boronate esters. The presence of a third exchangeable group on boric acid, as opposed to only two in the case of boronic acids, means that borate esters formed with diols, and especially poly-ols, consist of a complicated mixture of equilibrating structures, considerably more complex than those formed with boronic acids. This is particularly the case at high pH. These facts, combined with the lack of organic solubility of boric acid, probably explain why borates have been used much less frequently than boronates in organic synthesis.

By 1978,[16] it had been established that boronate esters could be used for the preferential protection of particular pairs of hydroxy groups within poly-hydroxylated compounds and thus provide selective access to organic and inorganic esters, carbamates, ethers and disaccharides. A few examples of nucleophilic displacements and oxidations carried out in the presence of boronate esters were also known at the time. All of these reaction sequences were performed by isolating the crystalline boronate esters prior to the derivatisation step. Little activity was seen in this field in the 1980's, but the area experienced a resurgence in the 1990's. The application of boron acids as catalysts and facilitating reagents in organic transformations has essentially arisen since the time of Ferrier's review.[16]

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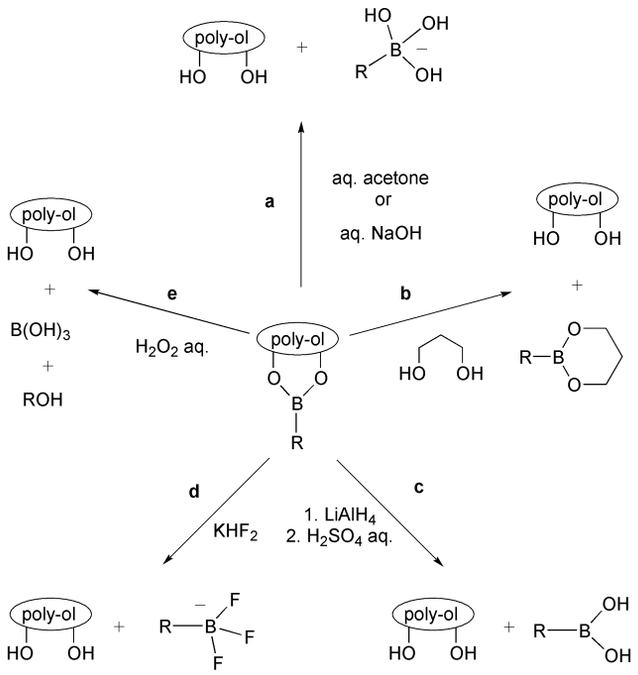
1.3 Formation of boronate esters

A number of methods can be used to prepare boronate esters. The most common procedures involve heating a diol with stoichiometric amounts of a boronic acid, or the corresponding trimeric anhydride (boroxin), in a suitable solvent with azeotropic removal of water. Appropriate solvents include benzene, toluene and dioxane.[16] Inorganic drying agents[17,18] or molecular sieves[19,20] can also be used to remove the water. Acid catalysts have sometimes been used to assist in ester formation.[21] In some cases, treatment of the diol with a boroxin in a solvent such as methanol can lead to precipitation of the crystalline boronate esters,[16] but since many boronate esters are highly susceptible to transesterification, this method is not universally applicable. Further complications may arise if the substrate bears multiple hydroxy groups. For a given poly-ol, a complex solution equilibrium is likely to exist between the various possible boronate esters, and the boronate ester that precipitates may not necessarily be the most stable. For example, a highly crystalline or highly insoluble boronate ester may be the major product of a procedure that relies on precipitation as a method of boronate production. However, once redissolved, a solution phase equilibrium will be re-established, so a subsequent derivatisation reaction may take place with a form other than that which crystallised. It is therefore unwise to assume that the boronate ester that crystallises is the most stable ester in solution, or that it is the actual compound that leads to the major derivatised product.[16]

Duggan and co-workers have recently described a solventless preparation of a diboronate ester that involves grinding together a mixture of an alditol and phenylboronic acid (PBA) and uses heat to remove the water by-product.[22]

1.4 Cleavage of cyclic boronate esters

Boronate esters vary in their susceptibility to cleavage so a range of methods for achieving this have been developed. If the diol component is soluble in organic solvents, some boronate esters are easily cleaved by dissolving them in an organic solvent and washing the resulting solution with aqueous hydroxide. The free diol is then isolated from the organic phase (Scheme 2a).[17,22] Alternatively, treatment with aqueous acetone[23] or exposure to silica,[24] followed by separation of the boronic acid and diol, can be effective. Various ion exchange resins can also be used to effect boronate ester cleavage,[16] including the borate specific resin Amberlite-IRA-743.[25] However, most boronate esters require more elaborate cleavage methods. Transesterification with diols such as ethanediol, propane-1,3-diol, neopentyl glycol† and pinacol is often used, and sometimes relies on the removal of the newly formed boronate ester by distillation to drive the reaction forward and allow the isolation of the deprotected diol in acceptable yields (Scheme 2b).[16] Diols that form exceptionally stable boronate esters are sometimes made more labile by reduction with $LiAlH_4$ to the corresponding tetrahedral borohydride, which can then be hydrolysed to a mixture of the diol and the boronic acid with aqueous acid (Scheme 2c).[26] Very recently, a diethanolamine appended polystyrene has been described which binds PBA quite strongly.[27] This polymer is also likely to have application in the cleavage of boronate esters, particularly because it should allow simple isolation of the diol from the solution phase and efficient recovery of the boronic acid. In fact, all of the above cleavage methods should allow recovery of the boronic acid. With today's increasing focus on Green synthetic practices, the recoverability of boronic acids makes them attractive reagents for use in synthesis.



Scheme 2 Some methods used to cleave boronate esters.

Potassium hydrogenfluoride (KHF_2) can also be used to cleave boronate esters, yielding the free diol and the corresponding potassium trifluoroborate (Scheme 2d).[28,29]

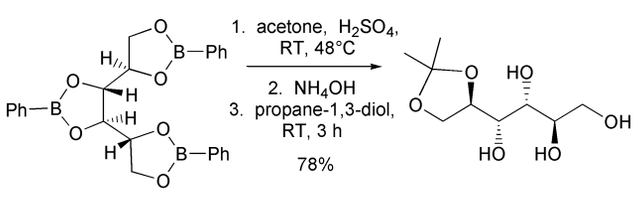
When cleavage cannot be achieved by any of the above methods, oxidation of the boronate to a borate, although less desirable from an environmental stand point, can be very effective. Treatment of phenylboronate esters with molecular bromine gives the deprotected diol, along with boric acid and bromobenzene.[16] Alternately, phenylboronate can be cleaved with H_2O_2, producing the deprotected diol, boric acid and phenol (Scheme 2e).[20,30–33] Alkylboronates can be cleaved by oxidation with *N*-oxides, followed by hydrolysis.[34] Of the three oxidation methods mentioned here, the H_2O_2 protocol is the most widely used as it usually gives very clean reaction mixtures.

2 Boron acids as protective agents

2.1 Protection without activation

The uses of boron acids as protective agents for diols highlighted in this section can be traced back to work published prior to 1978, but it is evident that as the field has matured, more diverse applications have been identified.

In 1976, Stacey and Tierney[16] first described the selective production of acetonylated carbohydrates, assisted by PBA, and in 1980, Griffiths and Weigel[35] published the results of the selective acetonolysis of the 1,2:3,4:5,6-tris-phenylboronates of the alditols, D-sorbitol and D-mannitol in acidified acetone (Scheme 3). Once the acetonolysis of these boronates was

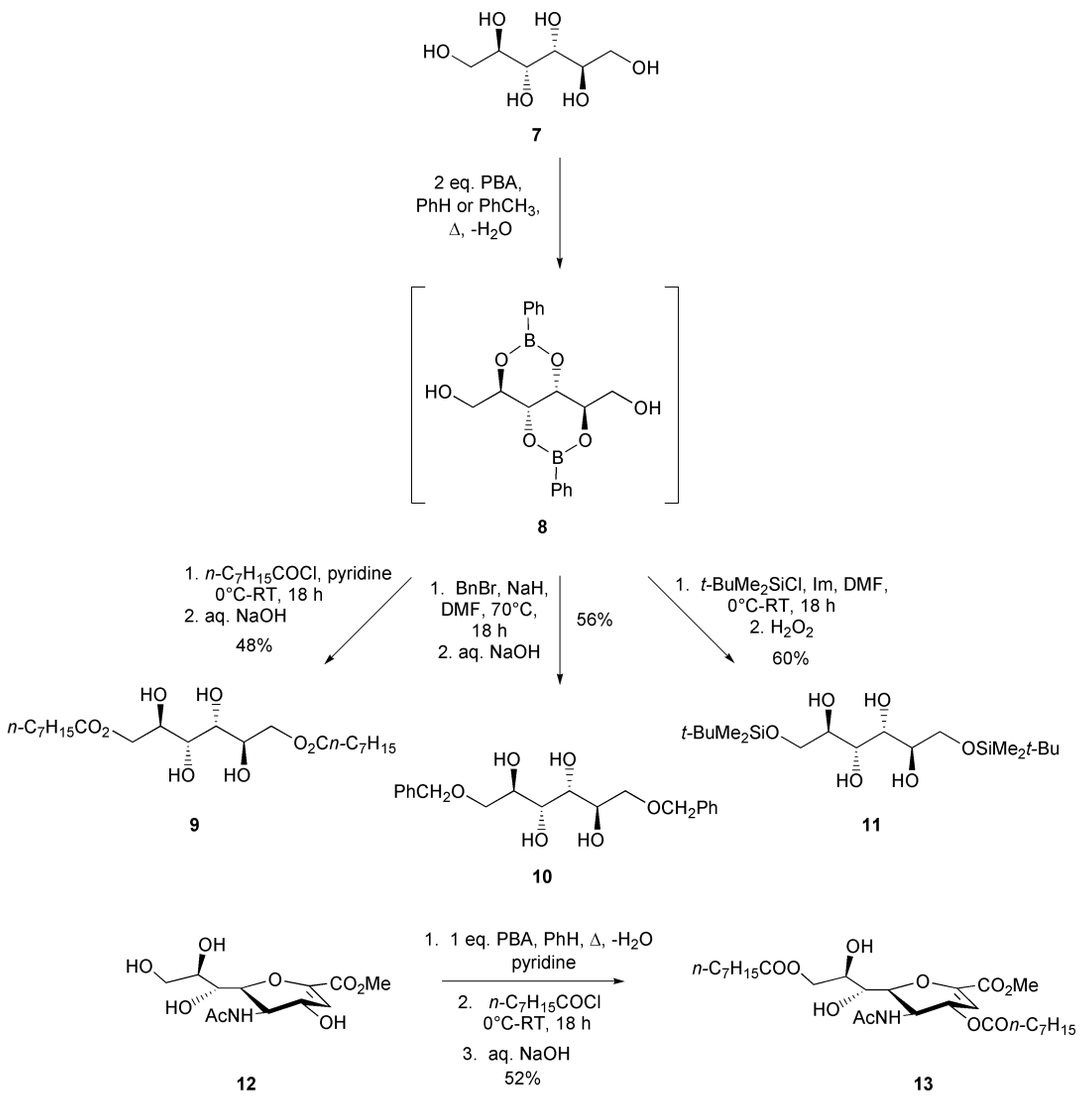


5 **6**

Scheme 3

complete the residual boronate esters were cleaved by transesterification with propane-1,3-diol to produce the tetra-ol and 2-phenyl-1,3,2-dioxaborinane, which could be removed by dis-

† The IUPAC name for neopentyl glycol is 2,2-dimethylpropane-1,3-diol.

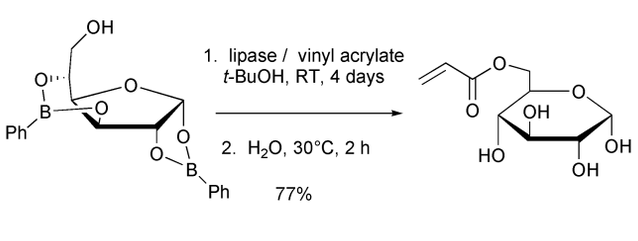


Scheme 4

tillation. The 5,6-acetonide of D-sorbitol and the 1,2-acetonide of D-mannitol (**6**) were thus obtained in 43% and 78% yields, respectively.

The full potential of boronate esters to serve as selective protective agents for alditols is yet to be realised, and has been obscured by the fact that most workers have crystallised the intermediate boronate esters prior to derivatisation. Our group,[22] and others,[16,36] have found that 1,2:3,4:5,6-tris-phenylboronate is the major crystalline product formed from the reaction of D-mannitol with PBA, even when a 2 : 1 ratio of PBA : D-mannitol is used. Sugihara and Bowman showed that esterification of this tris-boronate leads to hexa-acylation,[16] which is of marginal synthetic value. Our interest in the development of synthetic procedures requiring minimal manipulation and purification steps led us to examine the protection of D-mannitol (**7**, Scheme 4) with two equivalents of PBA, followed by derivatisation without the isolation of the intermediate boronate esters. Scheme 4 shows the likely structure (**8**) of the major boronate ester of D-mannitol present in solution before derivitisation, but molecular modelling studies, as well as NMR and electrospray mass spectral evidence suggest that the PBA esters of D-mannitol exist in equilibrium between various mono-, di- and triesters. Acylation and benzylation of this mixture of boronate esters led to the preparation of pure 1,6-acylated or benzylated D-mannitol in yields of up to 56%, without the need for chromatography or recrystallisation.[22] All other reagents and by-products could be removed by simple washing procedures. Similar reactions on unprotected D-mannitol yield multiple products. More recently, we have prepared a 1,6-bis(silyl ether) of D-mannitol (**11**) in 60% yield by a related method.[37] The same general strategy has also been extended to the selective acylation of a sialic acid derivative (**12**), affording the triester (**13**) in 52% yield.[22]

There has been one report of the use of PBA to assist lipase-catalysed esterifications of carbohydrates and alditols (Scheme 5). Thus, Ikeda and Klibanov[38] showed that α-D-glucofuranose



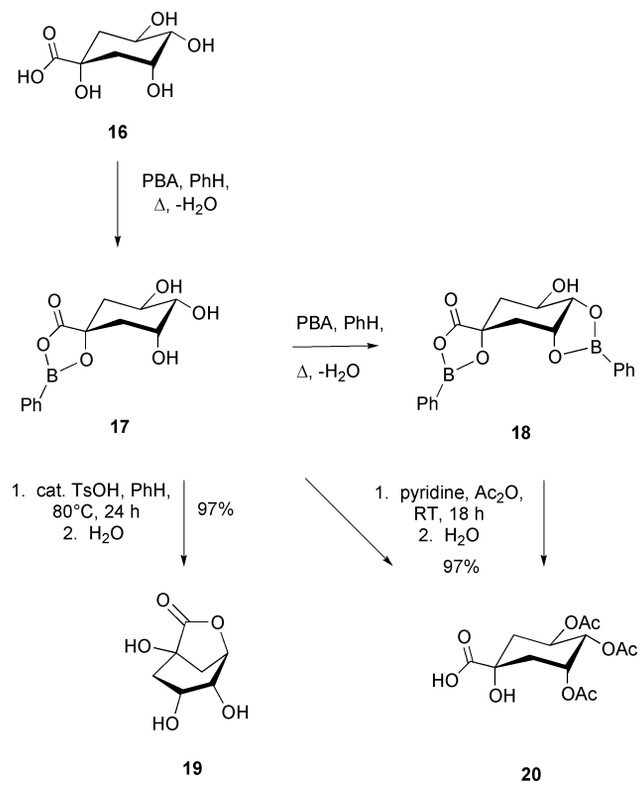
Scheme 5

1,2:3,5-bis-phenylboronate (**14**) could be converted into 6-*O*-acryloylglucose (**15**) in 77% yield by treatment with vinyl acrylate and *Pseudomonas* sp. lipoprotein lipase in *tert*-butyl alcohol, followed by boronate hydrolysis. It is surprising that the enzyme was active in the presence of PBA and its esters, since boronic acids are known to inhibit lipases.[39] This might explain why Ikeda and Klibanov had to employ an enzyme to

boronate ester mass ratio of ~3 : 1. We have performed very similar experiments on D-mannitol and its phenylboronate esters in our laboratory, and found that enzyme assisted acylation only occurred in the absence of PBA, in which case 1,6-acylated D-mannitols were obtained in good yield and purity.[40]

Boronic acids have also found application in another enzymatic reaction: glycosylation catalysed by β-glucosidase. Lee *et al.*[41] treated a mixture of glucose and either phenyl- or *n*-butylboronic acid with β-glucosidase in a hydrocarbon solvent and obtained a range of disaccharides in overall yields of around 25%. These workers suggested that the boronic acid serves to solubilise glucose in the organic solvent, but has no effect on the enzyme structure or the reaction mechanism.

In 1990, Flores-Parra and co-workers[42] described a thorough investigation of the interaction of PBA with quinic acid ‡ (**16**, Scheme 6). They made the interesting observation that the stable



Scheme 6

spiro-1,3,2-dioxaborolan-4-one (**17**) forms when the α-hydroxy acid function of quinic acid is treated with one equivalent of PBA, while the boronate ester (**18**) forms with the remaining *cis*-1,2-diol function of quinic acid if another equivalent of PBA is added. These compounds were used for the efficient preparation of the lactone (**19**) and the triacetate (**20**) in near quantitative yields.

A more subtle form of selectivity was demonstrated by Pis *et al.*[32] when they found that a boronate ester, obtained from an open chain 1,2-diol, was more readily formed than the analogous ester derived from a *cis*-1,2-diol associated with a rigid ring system (Scheme 7). These workers employed this effect in the synthesis of a series of 20-hydroxyecdysone glycosides by first converting the aglycone (**21**) into the 20,22-phenylboronate (**22**) in 93% yield. The unprotected secondary alcohols on **22** could then be glycosylated or acetylated, thus ultimately giving access to the 2-β-D-glucopyranoside of 20-hydroxyecdysone (**23**), as well as the corresponding 3-, 22- and 25-β-D-glucopyranosides.

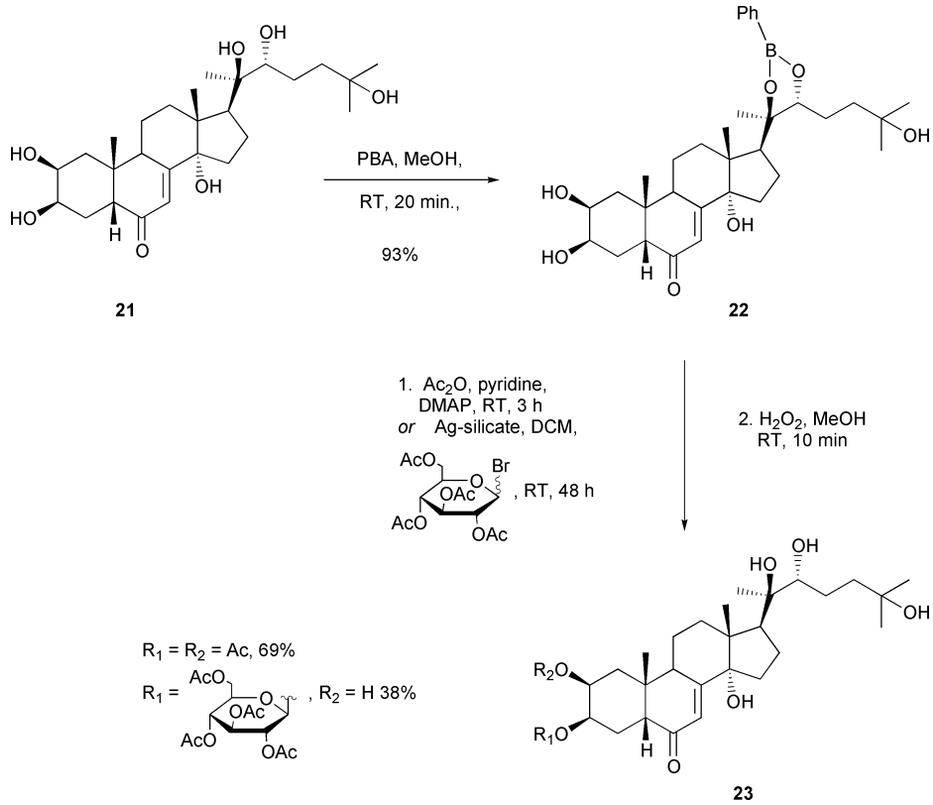
‡ The IUPAC name for quinic acid is 1*R*,3*R*,4*S*,5*R*-tetrahydroxycyclohexanecarboxylic acid.

M^{c}Murry and Erion,[17] in their synthesis of the immunosuppressant K-76, employed PBA to protect a cyclic *cis*-1,2 diol from protonation, so as to allow an acid catalysed cyclisation of a phenol (**26**) onto an olefin contained elsewhere in the molecule (Scheme 8). These workers found that the unprotected vicinal diol present in **24** inhibited the acid-catalysed cyclisation of the phenol because, they reasoned, the basic nature of the diol suppressed the protonation of the B-ring olefin to such an extent that acid-catalysed decomposition was favoured over cyclisation. Support for this conclusion comes from the observation that the compound in which a double bond was present in place of the diol cyclised smoothly to the dihydrobenzofuran. Protection of the cyclic *cis*-1,2-diol in **24** as a phenylboronate (**26**) allowed the production of the desired *O*-methyl K-76 (**25**) in a 45% yield after boronate hydrolysis and chromatographic separation from the isomeric benzopyran.

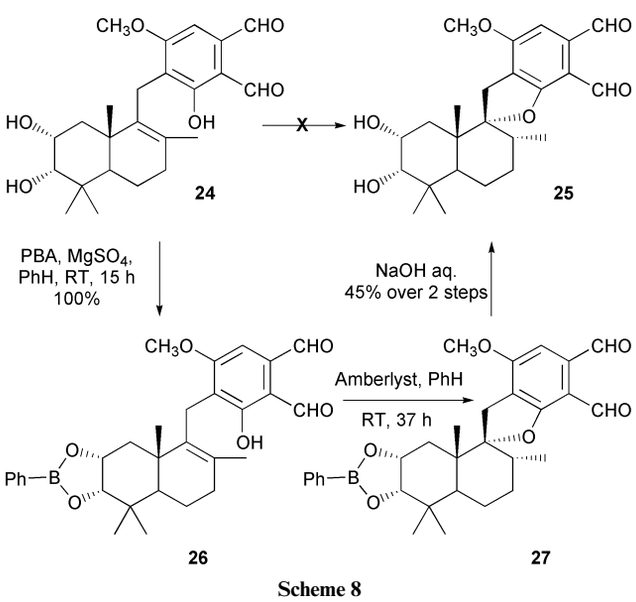
There have been a number of cases where boronate esters have been used to protect alcohols from oxidation. Warrener *et al.* [21] in their study of homoallylic control in Sharpless epoxidation reactions, used PBA to confirm the *cis*-relationship of the 1,3-diol moiety in **28** (Scheme 9). These workers showed that selective formation of the 1,3-boronate (**29**) could be exploited in the oxidation of the unprotected secondary alcohol to the ketone (**30**) using PCC and molecular sieves. Similarly Evans and Polniaszek,[31] in their synthesis of the C_1–C_9 ferensimycin synthon, selectively protected a 1,3-diol (**32**, Scheme 10) with PBA so that a remote secondary alcohol could be oxidised to a β-ketoester (**34**) under Swern conditions. Protection, oxidation and deprotection were completed in 70% overall yield and with no discernible epimerisation at C2. These workers preferred boronate protection over traditional ketal type protection because of the ease of cleavage of boronate esters, feeling that methods used to remove an α-naphthylidene group, for example, would lead to epimerisation of the sensitive β-ketoester (**34**).

In their recent synthesis of prostaglandin $F_{2\alpha}$ analogues, Hacksell and co-workers,[20] employed boronate protection to assist in a broad range of transformations (Scheme 11). Thus, selective protection of the *cis*-cyclopentane-1,3-diol portion of the triol (**36**) with PBA left the exocyclic alcohol free to be oxidised with PCC–Al_2O_3. The resultant aldehyde (**37**) was not isolated, but subjected to a Horner–Wadsworth–Emmons olefination reaction to yield, after boronate cleavage, the α,β-unsaturated ketone (**38**) in 76% yield. Reduction of the ketone gave the triols, **39** and **40**, which were separated by column chromatography. Directed epoxidation of the allylic alcohol residue within these triols was unsuccessful, but appropriate protection with PBA gave, after boronate cleavage, the expected epoxides (*e.g.* **41**) in yields of 60–76% and up to 93% de. The separated diastereomers were then subjected to nucleophilic ring-opening of the epoxide with LiOH or PhSNa, reactions which were again facilitated by preliminary protection of the *cis*-cyclopentane-1,3-diol regions with PBA. These latter reactions were generally stereoselective and gave yields of 33–66% after boronate cleavage. Hacksell did not speculate on how the boronate protection assisted with the epoxidation and ring-opening reactions.

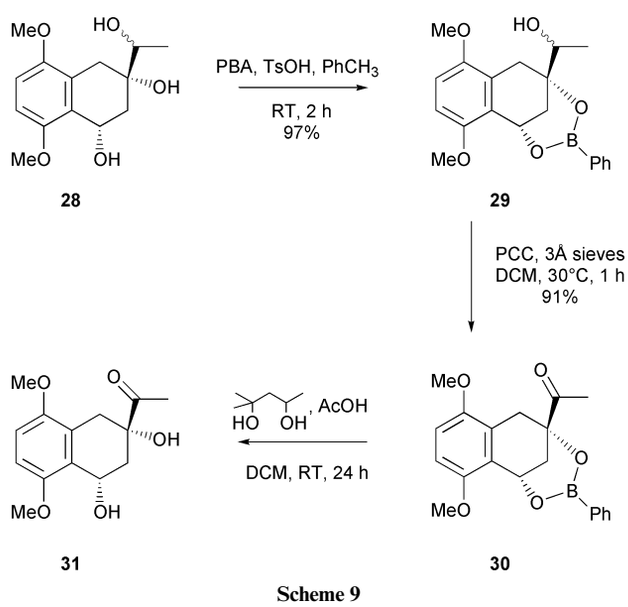
Yamamoto and co-workers,[43,44] in their synthesis of the spermine alkaloids (±)-verbacine, (±)-verbaskine and (±)-verbascenine, have shown that boronic acids can also be used to protect 1,3-diamines (Scheme 12). These workers prepared the macrocycle (**42**) through an antimony(III) ethoxide-promoted macrolactamisation, then performed a selective acylation at *N*-6 following the initial *in situ* formation of the 1,3,2-diazaborinane (**43**) with the electron deficient boronic acid 3,5-$(CF_3)_2C_6H_3B(OH)_2$ giving the monocinnamamide (**44**) in 53% yield. When the boronic acid was omitted only diacylation could be achieved and the use of PBA or tolylboronic acid in the place of 3,5-$(CF_3)_2C_6H_3B(OH)_2$ led to lower yields and poorer regioselectivities.



Scheme 7



Scheme 8

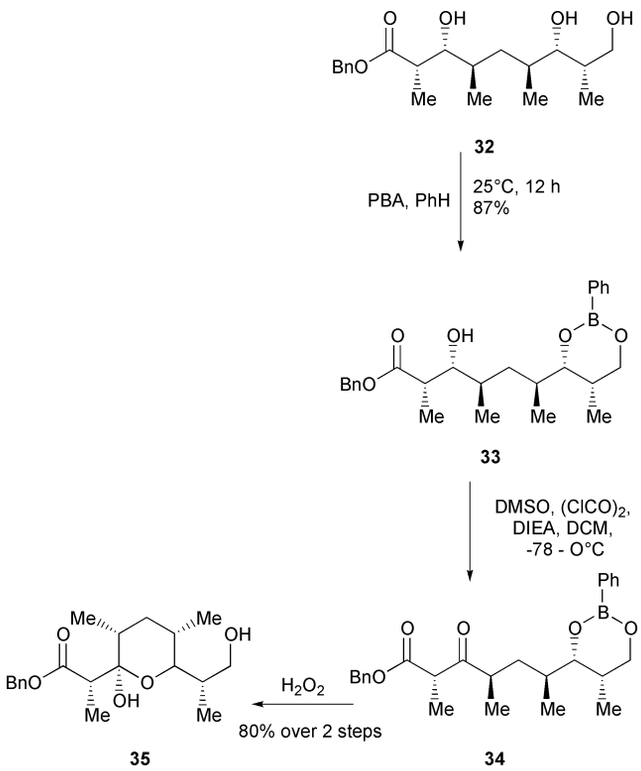


Scheme 9

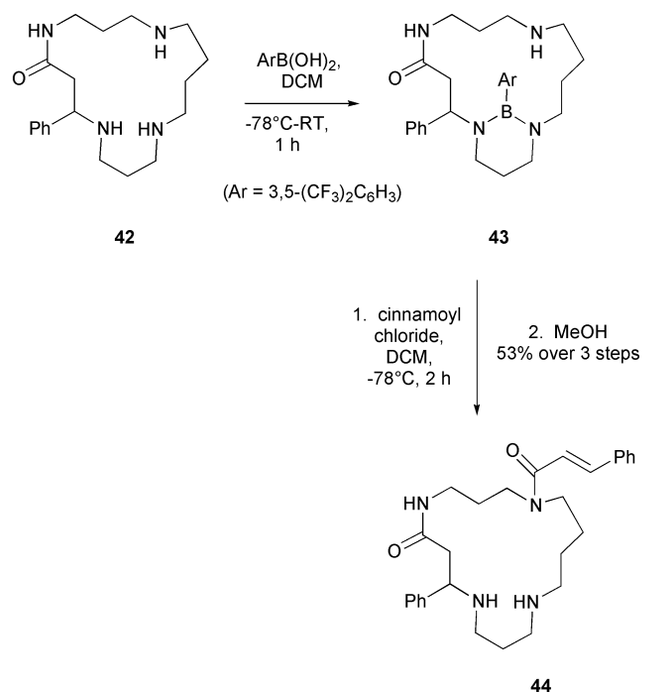
As indicated in Section 1.2, boric acid has found less frequent application as a protective agent in organic synthesis than boronic acids. However, despite the water solubility and the complex equilibria that exist with sugar borate esters, Rendle *et al.*[45] have recently employed boric acid in the efficient synthesis of penta-*O*-acetyl- and penta-*O*-propanoyl-β-D-glucofuranose (Scheme 13). This is an example of a boron acid being used to lock a reactant in one isomeric form rather than being used as a protecting agent. Thus, D-glucose was first solubilised as its 1,2:3,5-bis-borate (**45**) by heating with boric acid in acetic acid, and this was, in turn, partially acetolysed with acetic anhydride, a transformation that was accompanied by anomerisation. Removal of the boric acid, as trimethylborate, followed by further acetylation with acetic anhydride and pyridine gave predominantly (81%) penta-*O*-acetyl-β-D-glucofuranose (**46**). The corresponding pure β-pentapropanoate was obtained in 58% yield by a similar process, thus providing one of the most direct syntheses of a crystalline furanoid derivative of D-glucose. A survey of a range of hexoses and pentoses revealed that the Rendle procedure may also be synthetically useful for the preparation of xylose and idose furanosides, as well as arabinose and galactose pyranosides. In some cases, however, the formation of borate esters under acidic conditions promoted partial anomerisation.

2.2 Protection with activation

Most of the above-mentioned synthetic applications of boron acids have relied upon the protection of diols or amines, so as to prevent them from acting as nucleophiles, *via* cyclic boronate or diazaboracyclohexane formation, followed by reaction at unprotected alcohol or amine centres. In this section examples



Scheme 10

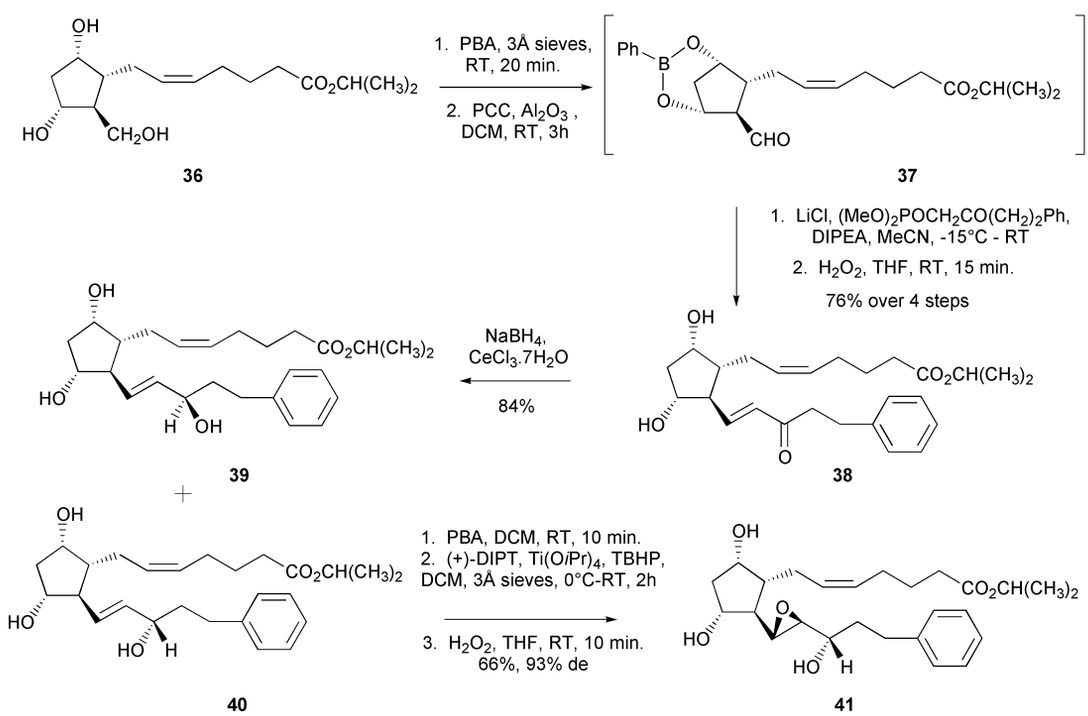


Scheme 12

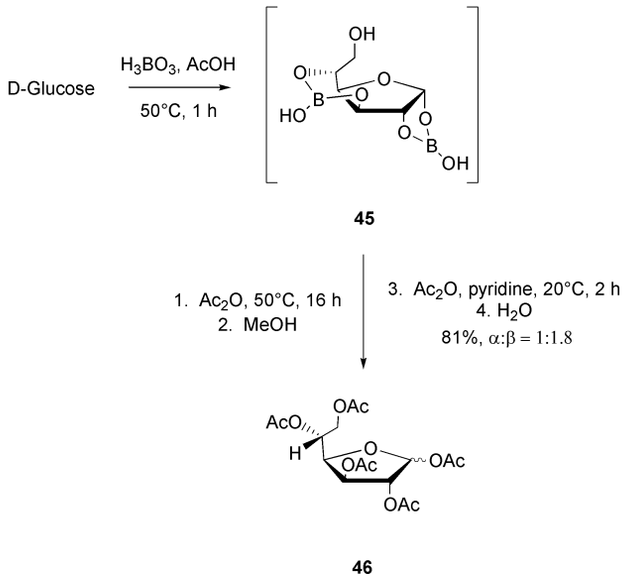
in which boronate ester formation is combined with *activation* of hydroxy groups towards further reaction, are described. Two distinct effects will be discussed; one where the activation is provided by a stannanediyl acetal, and the other where the boronate itself provides the activation.

It is well established that stannanediyl acetals derived from vicinal-diols are activated towards alkylation and acylation, giving higher yields of ethers and esters, as well as reacting more regioselectively than the parent diols.[46] Vasella *et al.*[24] combined this regioselective activation provided by stannanediyl acetals with the protective properties of PBA in the selective benzoylation and sulfonation of methyl α-D-glucopyranoside and methyl β-D-galactopyranoside (Scheme 14). These workers were able to produce the corresponding glucopyranoside 2-sulfate and 2-benzoate (**49**) in yields of 79% and 85%, respectively, and the corresponding galactopyranoside 3-sulfate and 3-benzoate in 85% and 86% yields, respectively. These reactions were significantly more selective and higher yielding than other cases where stannylation was omitted and were comparable, in terms of yield, to those resulting in the corresponding 4,6-ketals, obtained where stannylation was combined with benzylidene or isopropylidene protection instead of boronate formation.

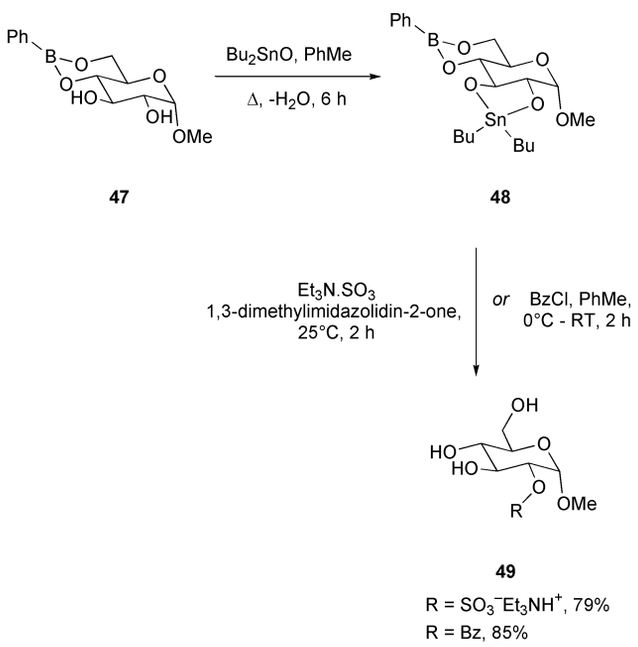
Aoyama *et al.*[18] have taken this approach one step further, by using a combination of reagents that apparently activate oxygen atoms contained within a boronate ester towards alkylation (Schemes 15 and 16). They found that if the 3,4-phenylboronate



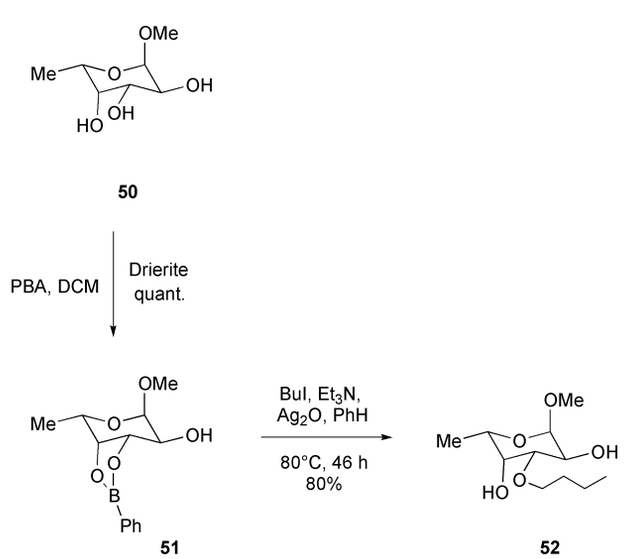
Scheme 11



Scheme 13



Scheme 14



Scheme 15

ester (**51**) of methyl fucopyranoside (**50**) was treated with triethylamine, Ag_2O and iodobutane, the 3-*O*-butyl fucopyranoside (**52**) could be obtained in up to 80% yield as the sole sugar-derived product. The most convincing evidence that an activation process was involved in this reaction was the finding that the parent fucopyranoside (**50**) alone was quite unreactive under the same conditions. Apparently the activation results from amine coordination to the boron atom, leading to a build up of electron density on the boronate oxygen atoms, and the nucleophilic attack of the less hindered *O*-3 on the silver-activated butyl iodide.

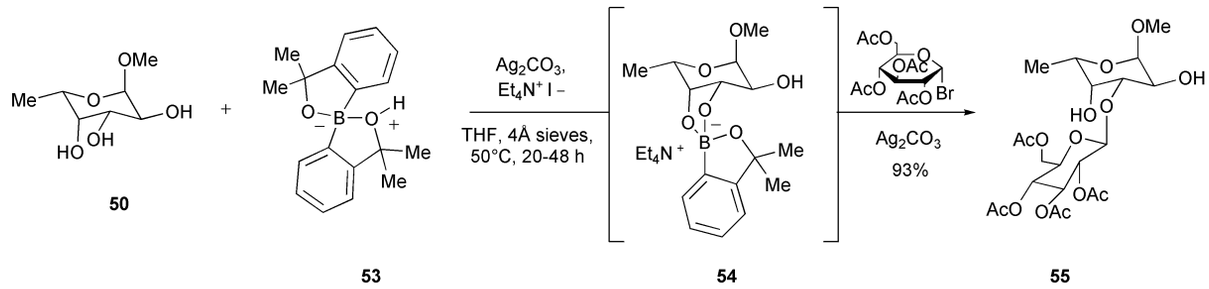
Oshima and Aoyama[19] extended such studies to the synthesis of di- and trisaccharides, this time using intramolecular oxygen coordination to activate the boronate oxygen atom towards glycosylation. In a reaction mixture containing Ag_2CO_3 and molecular sieves, five different pyranosides were treated with a borinate (**53**, Scheme 16), possessing an internally coordinating hydroxy group. This generated the corresponding tetrahedral boronate esters, such as **54**, which were then glycosylated to give disaccharides (*e.g.* **55**) in yields of up to 93%. Following a similar procedure, substrates bearing four hydroxy groups were converted to trisaccharides in up to 84% yield. The observed regioselectivity in the reactions studied can be rationalised if one takes into account the fact that boronic acids form esters with *cis*-1,2-diols and 1,3-diols, in preference to most other diols, and that glycosylation should occur at the least hindered of the three oxygen atoms of the boronate ester thus formed. The authors quite succinctly describe their results as having stemmed from "a remarkable cooperation of selective complexation, intramolecular activation, and steric manipulation" which may "open a hitherto-unexplored route to oligosaccharides without involving (formal) protection/deprotection procedures."

2.3 Boronate esters in solid phase synthesis

Fréchet and Seymour first described the preparation and use of polymeric boronic acids as insoluble alternatives to PBA in 1976,[47] and followed on with a limited series of papers shortly thereafter.[23,48,49] This type of boronic acid was essentially ignored until the late 1990's, but is now emerging as one of the more exciting types of organoboron compound, which is likely to be exploited broadly over the coming years.

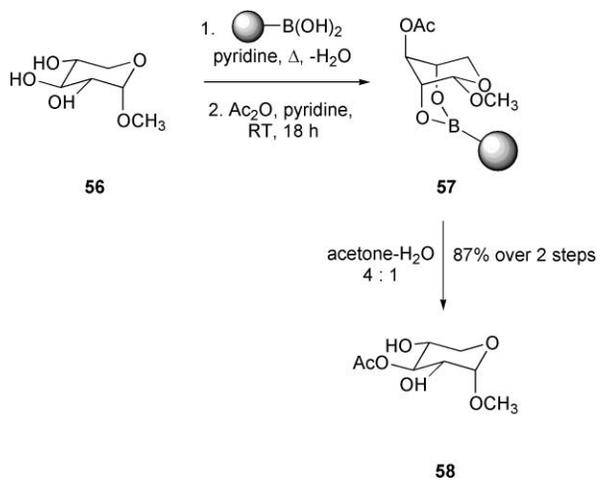
Polystyrylboronic acid resin can be prepared from brominated polystyrene by first treating the resin with *n*-butyllithium then quenching the solid phase organolithium species with a trialkyl borate. The resulting dialkyl boronate can be readily hydrolysed to the free boronic acid by treatment with aqueous acid.[47] Hodge and co-workers[50] have also described preparations of polystyrylboronic acid involving organomercury and organothallium chemistry.

After initially focussing on the use of macroreticular resin,[47] Fréchet and co-workers turned to a cross-linked resin,[48] which is capable of swelling in solvent and which they found gave higher yields. In addition, because the cross-linked resin is less fragile than the macroreticular resin, it could be more readily recycled. They observed that the protecting properties of these polystyrylboronic acids are very much like those of PBA, but the protection and deprotection steps are usually milder than those required for PBA, and higher yields of the desired derivatised product are frequently obtained. This is illustrated by the mono-acetylation at the 3-position of methyl α-D-*xylo*-pyranoside (**56**, Scheme 17). Prior to Fréchet's work, the only effective method for the preparation of the 3-acetate (**58**) required the use of PBA and provided a 42% yield.[16] In contrast, the solid phase method yielded the 3-acetate in 87% yield. This application of arylboronic acids as protective agents is enhanced by the usual benefits of solid phase chemistry, including operational simplicity, easy recovery of unreacted starting material and simple isolation of the product. The resin also



50 53 54 55

Scheme 16

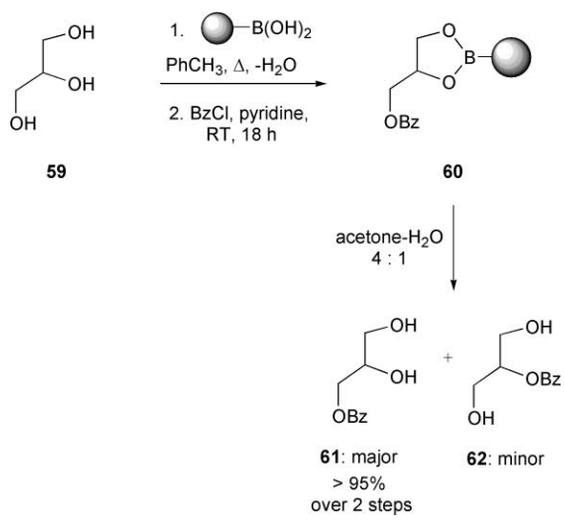


56 57 58

Scheme 17

shows a high capacity for recycling, having been re-used by Fréchet's group many times without loss of activity.

Fréchet and Seymour have also employed polystyrylboronic acid in the protection and monobenzoylation of acyclic triols.[49] An interesting example is the monobenzoylation of glycerol (**59**, Scheme 18). Thus, glycerol was protected with polystyryl-



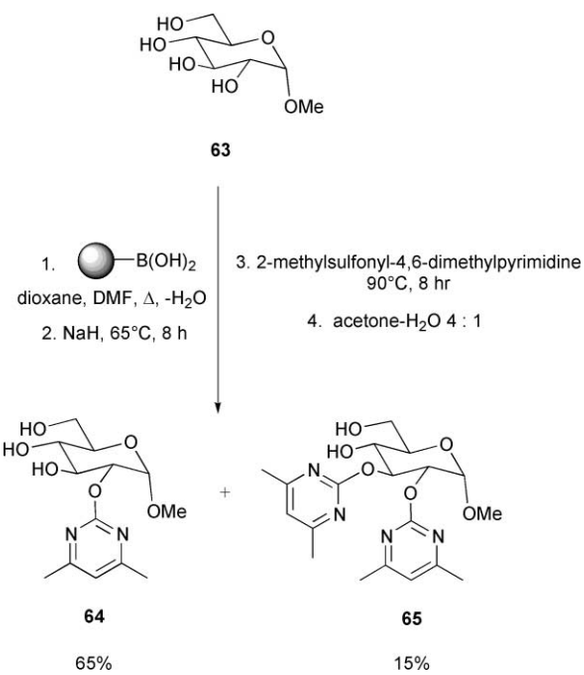
59 60

Scheme 18

boronic acid, and the product (**60**) treated with benzoyl chloride in pyridine, then aqueous acetone, to furnish 1-*O*-benzoyl glycerol (**61**) in >95% yield. As indicated in Section 1.2, six-membered cyclic trigonal boronates usually form more readily than the corresponding five-membered rings, but Fréchet and Seymour's result suggests the intermediacy of the five, rather than the six-membered cyclic boronate. We recently obtained an analogous result with a sialic acid derivative using PBA as the protective agent (Scheme 4). In both examples, however, the terminal mono-acylation products could be derived from a low concentration of the presumably more reactive five-membered cyclic boronates bearing free primary hydroxy groups, which were in equilibrium with the less reactive six-membered counterparts.

Sano and Teno[51] later described the use of polystyrylboronic acid for the protection of the 4- and 6-hydroxy groups of the non-reducing unit of malto-oligosaccharides. This ultimately led to the preparation of materials that could be employed in assays of α-amylase activity.

As an indication of the recent resurgence of interest in polystyrylboronic acid, Liao and Li,[52] have used it to produce, regioselectively, a mono- and di-pyrimidinyl glucopyranoside (**64** and **65**, Scheme 19) in a combined yield of 80%, by treating



63 64 65

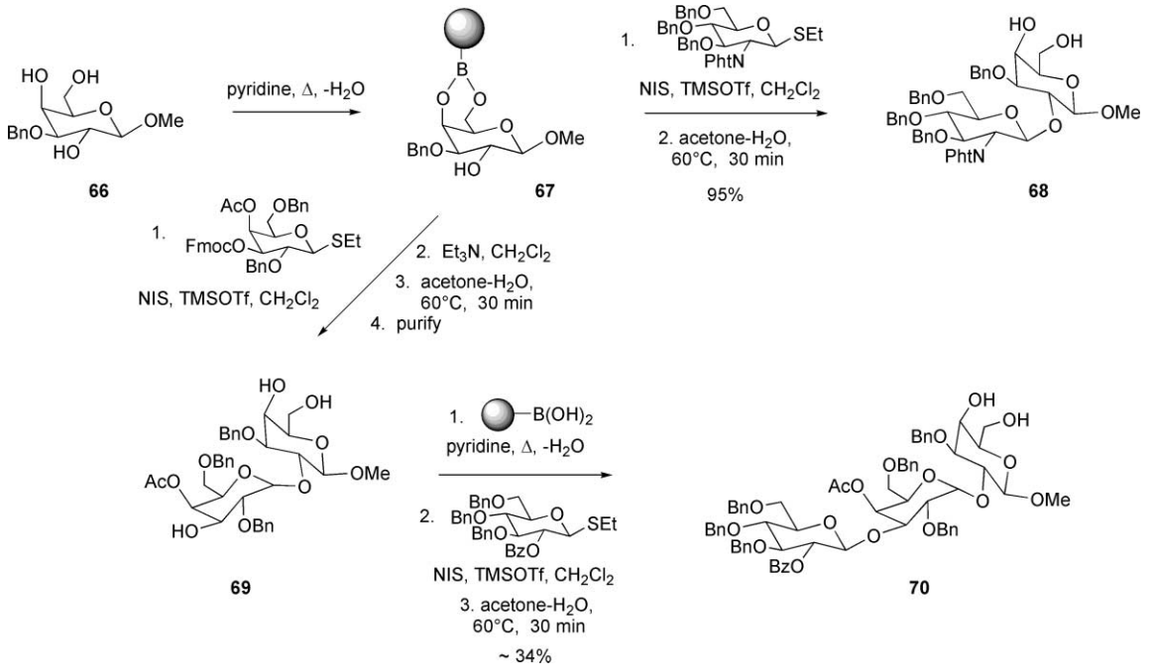
64: 65%

65: 15%

Scheme 19

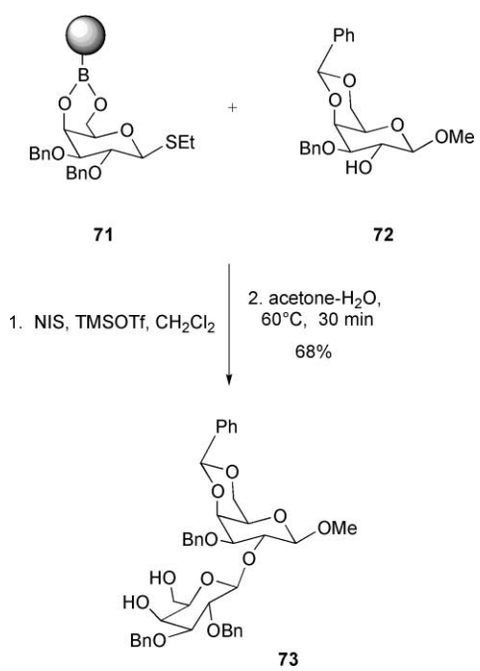
the polystyrylboronate formed from methyl α-D-glucopyranoside (**63**) with 2-methylsulfonyl-4,6-dimethylpyrimidine. A similar reaction performed on the unprotected pyranoside (**63**) produced at least seven products.

In 2000, Boons *et al.* reported the use of polystyrylboronic acid in the synthesis of di- and tri-saccharides (Scheme 20).[53,54] These workers immobilised methyl 3-*O*-benzyl-β-galactoside (**66**) on polystyrylboronic acid and subjected it to a range of glycosylation conditions. One of the more successful reactions led to the production of the β-disaccharide (**68**) in 95% yield. This approach was extended to the synthesis of trisaccharides, incorporating a "loading–release–reloading" strategy. Using this method, the disaccharide (**69**) was prepared on the solid phase in a similar way as before, but in this case the anomeric selectivity was low (α : β = 1.6 : 1.0), so the mixture of disaccharides was cleaved from the solid phase, separated and the α-anomer "reloaded" before the third saccharide was attached. This strategy allowed the synthesis of the tri-saccharide (**70**) in



Scheme 20

anomerically pure form. Attachment of the thioglycosyl donor to the solid phase *via* the boronate tether (**71**) also gave encouraging results (Scheme 21).



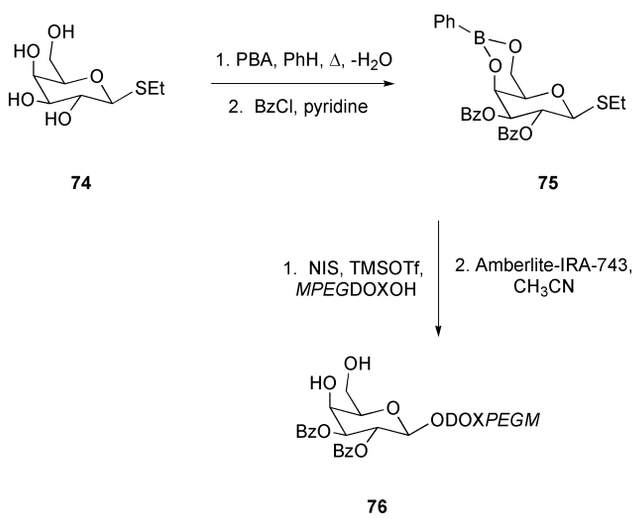
Scheme 21

Related to Boons' work is that of Cross and Whitfield,[25] who, by using PBA to protect the 4- and 6-positions of thioglycosyl donors, were able to prepare disaccharide precursors on the soluble polymer support, polyethylene glycol monomethyl ether (Scheme 22).

The above types of solid phase chemistry of boronates, together with the recent application of boronate esters as cleavable linkers,[55,56] suggests that boronic acids will play an important role in the future development of modern synthetic chemistry.

3 Boron acids as catalysts and facilitating reagents

Boron acids promote a diverse range of reactions, including Mukaiyama aldol reactions, Oppenauer oxidations, amidation



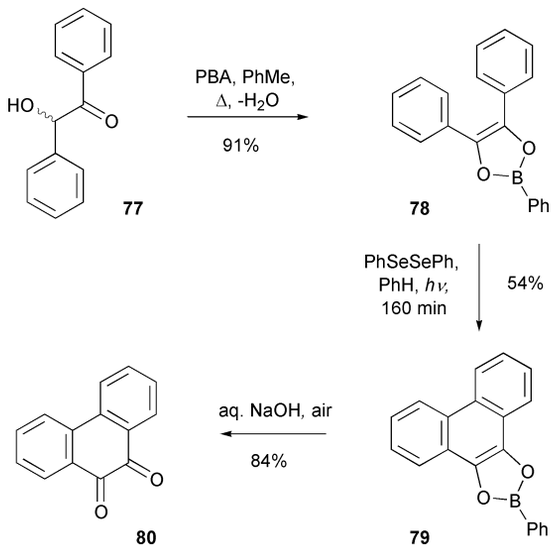
Scheme 22

of carboxylic acids and imine hydrolysis, all of which have recently been reviewed by Ishihara and Yamamoto[57] and will not, therefore, be covered here. In this section, we discuss progress in the use of boron acids as facilitators for cyclisations and for *o*-alkylations of phenols, as well as decarboxylation, epoxide opening and dihydroxylation reactions.

3.1 Cyclisation reactions

The ability of boron acids to form stable esters reversibly, upon reaction with hydroxy groups or enolates, has allowed their exploitation as templates and trapping agents to facilitate cyclisation reactions. Most of the work in this area has been developed since 1978 and deals predominantly with pericyclic reactions, although there has been one report of the use of boric acid as a template for a macrocyclisation reaction.[58]

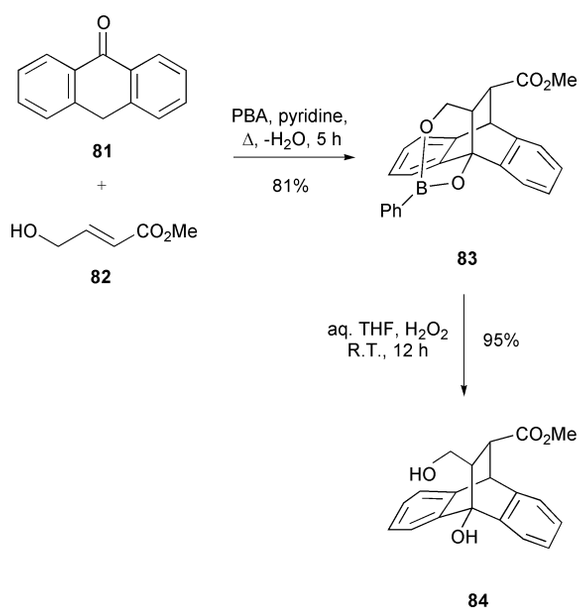
De Vries and Hubbard[59] were the first to describe the use of PBA to facilitate a cyclisation reaction when they reported their study of the reaction of benzoin (**77**, Scheme 23) to give phenanthrene-9,10-quinone (**80**). The formation of the PBA ester (**78**) from benzoin forces the alkene into the *cis* configuration and thus establishes a (*Z*)-stilbene which can undergo photocyclisation. Hence, irradiation of a benzene solution of the boronate ester (**78**) with a mercury lamp in the presence of



Scheme 23

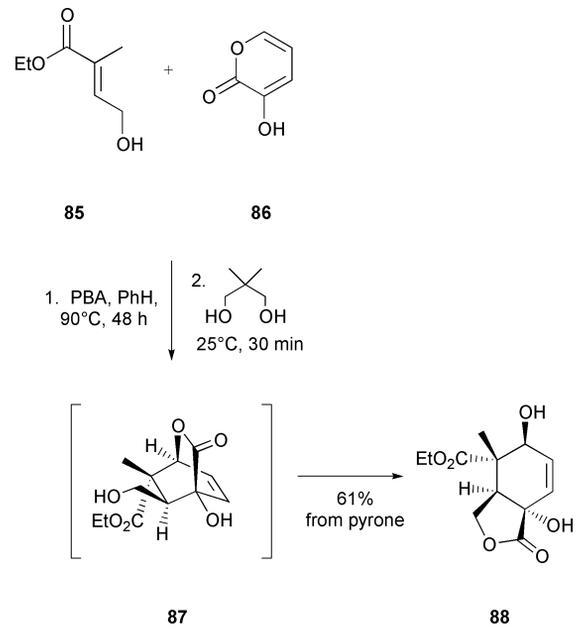
PhSeSePh produced the corresponding dihydroxyphenanthrene boronate (**79**). Hydrolysis of this intermediate with aqueous hydroxide followed by spontaneous aerial oxidation gave the quinone (**80**) in 84% yield.

Narasaka and co-workers[33] later reported two examples in which PBA facilitated intramolecular Diels–Alder reactions to give cycloadducts in high regio- and diastereo-selectivity (Schemes 24 and 25). Anthrone (**81**) was found to react with



Scheme 24

methyl 4-hydroxybut-2-enoate (**82**) in the presence of PBA in refluxing pyridine to give the single Diels–Alder adduct (**83**) in an 81% yield. This adduct (**83**) was apparently produced by a cyclisation reaction of a mixed boronate ester formed from the enol tautomer of anthrone and methyl 4-hydroxybut-2-enoate. The reaction did not occur if either PBA or the hydroxy group on the dienophile were absent. The possibility that PBA traps the Diels–Alder adduct, thus inhibiting the retro-Diels–Alder reaction, can be discounted since no retro-Diels–Alder product was observed upon heating the deprotected product in pyridine for an extended period. Furthermore, the regioselectivity of the PBA-assisted reaction was opposite to that of the corresponding intermolecular Diels–Alder reaction between anthrone (**81**) and methyl acrylate, and consistent with the formation of the proposed boronate. Similar results were obtained with the

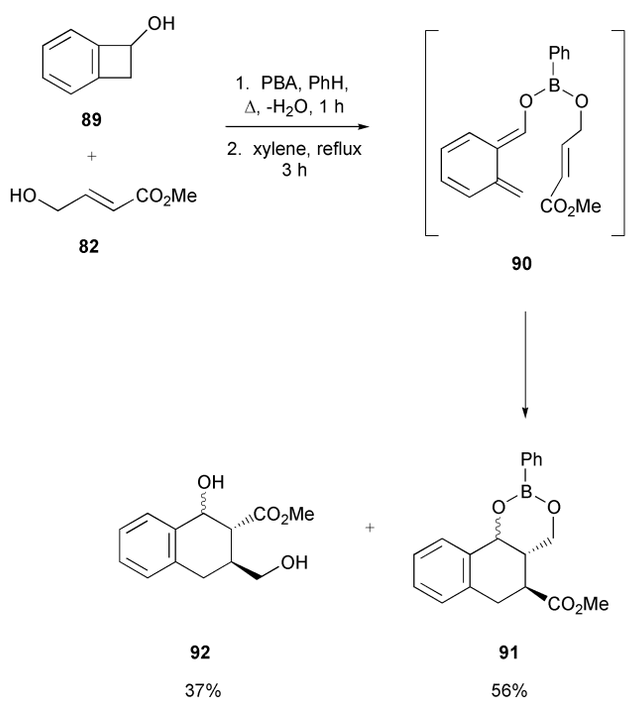


Scheme 25

Diels–Alder reaction between 3-hydroxy-2-pyrone and methyl 4-hydroxybut-2-enoate.

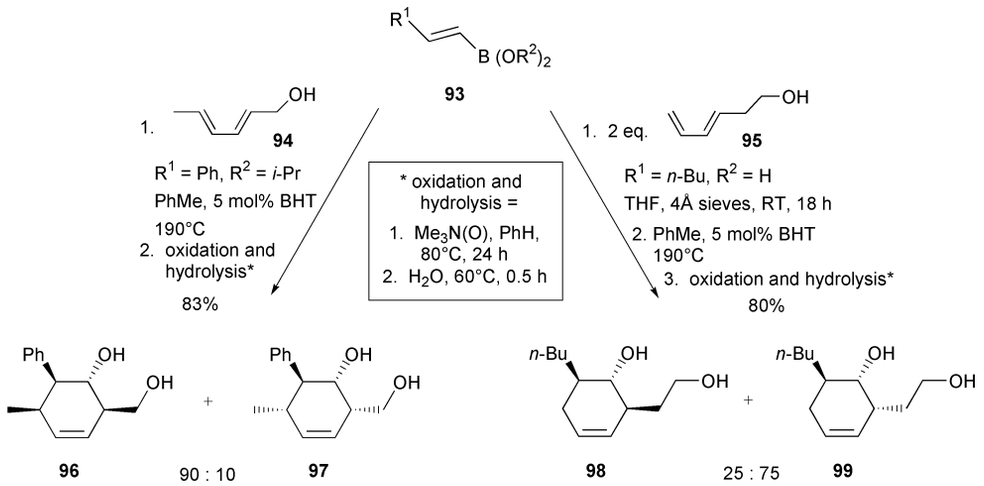
Narasaka's modification of the Diels–Alder reaction has since been utilized in the synthesis of the fully functionalized CD ring system of paclitaxel performed by Nicolaou and co-workers (Scheme 25).[60] The PBA-mediated Diels–Alder reaction of the substituted 4-hydroxybutenoate (**85**) with 3-hydroxy-2-pyrone (**86**) was achieved with complete regiocontrol. Cleavage of the intermediate boronate (**87**) caused the cycloadduct to rearrange spontaneously to the desired γ-lactone (**88**), which was isolated in 61% yield.

Narasaka *et al.*[61] demonstrated the versatility of boron acids by using them simultaneously as templates for intramolecular Diels–Alder reactions and trapping reagents for α-hydroxy-*o*-quinodimethanes (Scheme 26). α-Hydroxy-*o*-quinodimethanes,



Scheme 26

which can be formed by thermolysis of 1,2-dihydrobenzocyclobutene derivatives or by the photochemical isomerisation of *o*-tolylcarbonyl compounds, only undergo Diels–Alder



Scheme 27

reactions with highly reactive dienophiles, and usually isomerise to the *o*-tolylcarbonyl compounds or dimerise, rather than cyclise with an unreactive dienophile. However, Narasaka's group found that α-hydroxy-*o*-quinodimethanes can be stabilised by esterfication with a boronic acid, and that the formation of mixed boronate esters with hydroxylated dieneophiles promotes an intra-molecular Diels–Alder reaction. For example, 1,2-dihydrobenzocyclobuten-1-ol (**89**) dissolved with methyl 4-hydroxybut-2-enoate (**82**) in refluxing benzene containing PBA, gives the intermediate mixed boronate ester (**90**), which, when heated in xylene, undergoes the Diels–Alder reaction to produce (**91**) in 56% yield. The regioisomer (**92**), which can result if the dienophile adds in a reverse sense, most likely through an intermolecular reaction, was obtained in 37% yield. Both products were produced as a 1 : 1 mixture of *endo*- and *exo*-isomers. When 1-hydroxy-2-oxa-1-boraindan, which can only form a boronate with a single alcohol, was used in place of PBA, the Diels–Alder reaction was slower, and the only isolable product was the diol **92** (15%).

Diels–Alder cyclisation reactions in which alkenylboronic acids are used as both the reaction template, and the source of the dienophile, have recently been investigated by Batey *et al.* (Scheme 27).[34] Although this work does not strictly fall within the bounds of this review, as the boron acid in this case is consumed in the reaction, Batey's reactions illustrate a useful extension on the original work of Narasaka. The general approach involved tethering an alkenylboronic acid (**93**) to a diene containing a hydroxy group (**94** or **95**) through a boronate ester, and then heating the compound to induce cyclisation. Oxidative cleavage of the C–B bond in the cyclised product furnished, after hydrolysis, functionalized cyclohexenes (**96**–**99**). The good *endo*-selectivity observed when the tether to the diene consisted of a single methylene (**94**), was reversed to significant *exo*-selectivity when the tether was extended by a second methylene (**95**). The methodology was also found to be effective in the diastereoselective synthesis of bicyclic diols.

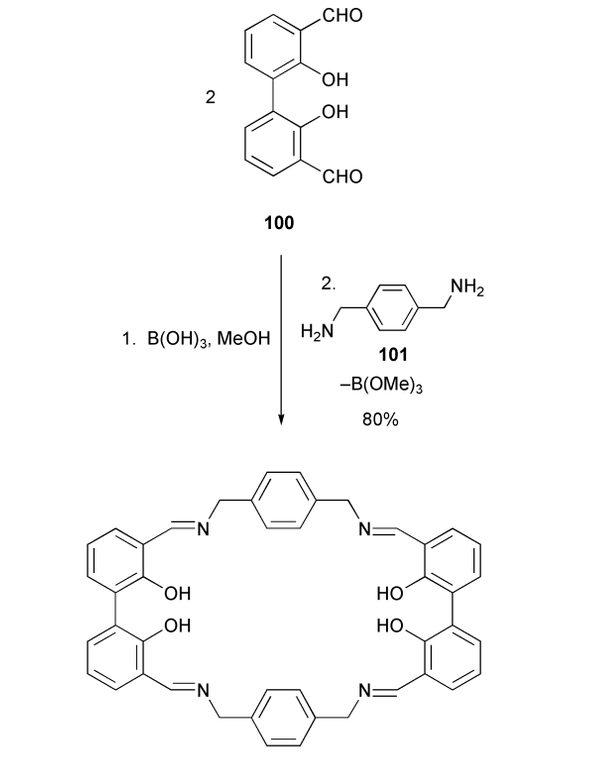
The use of boron acids as templates for cyclisation has not been restricted to pericyclic reactions. In 1982, Corey and co-workers[62] proposed that the borate anion might be used as a template for a macrocyclisation reaction as part of the total synthesis of the boron-containing antibiotic aplasmomycin. Following this suggestion, Pierre *et al.*[58] used boric acid in the first reported boron-templated synthesis of a macrocycle (Scheme 28). These authors found that attempts to cyclise a diphenolic dibenzaldehyde (**100**) *via* imination reactions with various diamines under high dilution conditions, or by use of templates such as barium salts, only led to polymerisation. However, the desired macrocycle (**102**) was synthesised in yields of up to 88% when boric acid was included in the reaction mixture. The cyclisation most likely occurs *via* a dimeric ester formed between two molecules of the diphenolic dibenzaldehyde (**100**) with boric acid, which then reacts with two molecules of diamine (**101**) to produce the cyclic tetra-imine. The boric acid residue is then released from the macrocycle, most likely as trimethyl borate, by reaction with methanol.

3.2 *o*-Alkylation of phenols

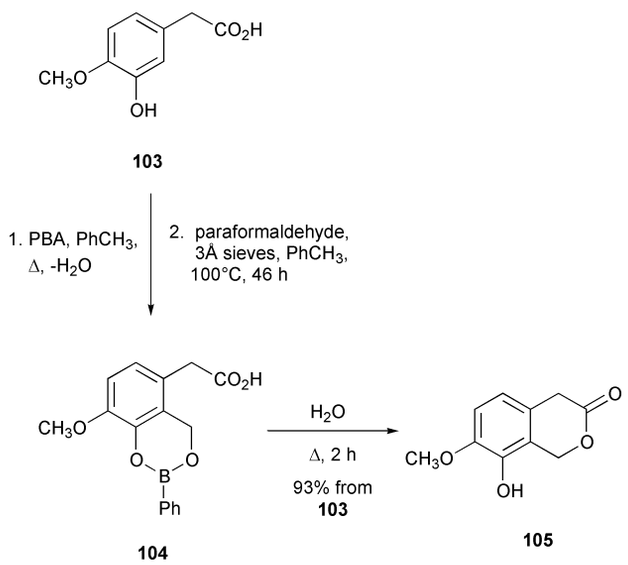
In 1975, Nagata and co-workers[63] described an adaptation of a low yielding reaction, first discovered by Peer,[64] which exploits the Lewis acidity of boron acids in the *o*-hydroxyalkylation of phenols. Peer utilised boric acid, but Nagata's group found that a combination of PBA and a catalytic amount of propionic acid gave synthetically acceptable yields of saligenol [*o*-(hydroxymethyl)phenol] from phenol and paraformaldehyde. Chelation of formaldehyde with the intermediate boronate ester appeared to promote *o*-alkylation strongly, and the generation of the alkylation product as a boronate ester apparently minimised further alkylation. Nagata then used PBA in the hydroxyalkylation of homoisovallinic acid (**103**, Scheme 29), as a key step in a very efficient synthesis of a 9,10-substituted tetrahydroprotoberberine alkaloid. By the incorporation of molecular sieves in the reaction mixture, and the use of a sealed vessel to prevent the loss of paraformaldehyde, Cushman and Dekow[65] were able to improve the yield of the same reaction to 93% (Scheme 29).

Soon after Cushman and Dekow's article appeared, Nagata *et al.*[66] published work that demonstrated the generality of their modification of Peer's procedure, revealing the successful hydroxyalkylation of a range of phenols and aldehydes. Treatment of the phenols with excess aldehyde and a catalytic amount of propionic or trichloroacetic acid in refluxing benzene or toluene, with the azeotropic removal of water, produced the phenylboronate esters of the corresponding *o*-(hydroxymethyl)phenols in high yield. Deprotection then yielded the corresponding saligenol derivative. Electron-rich phenol substrates were found to react more readily than electron-deficient substrates, and electron-donating groups *ortho* to the phenolic hydroxy group were found to retard the reaction significantly. Nagata also found that the reaction was not restricted to the use of formaldehyde. Straight chain aldehydes, branched aldehydes and benzaldehyde all gave the corresponding dioxaborin in yields >40%. The alkylation reaction is thought to occur *via* a [3,3]-sigmatropic rearrangement. A representation of the proposed transition state (**106**) for such a reaction is shown in Fig. 1.

In 1989, Lau and co-workers[67] described the preparation of a new set of dioxaborins, including a benzofuran derivative, using Nagata's method, then demonstrated their utility by converting



Scheme 28



Scheme 29

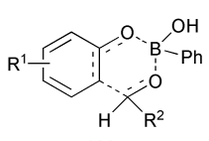


Fig. 1

them into *o*-alkylphenols, *o*-alkylthiomethylphenols and *o*-alkoxymethylphenols.

3.3 Decarboxylations

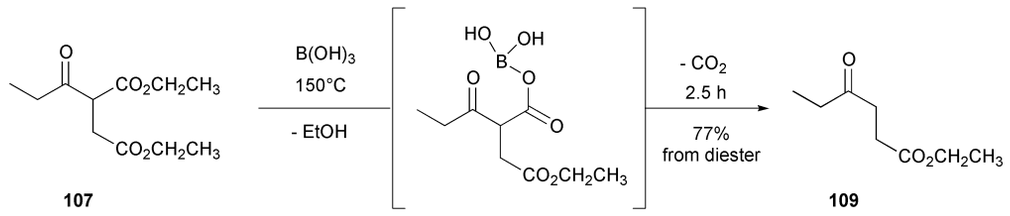
Boron acids are also useful in the promotion of decarboxylation and dehydration reactions. Two groups, in particular, have used boric acid to facilitate decarboxylation reactions. Wehrli and Chu[68,69] reported the production of γ-keto esters from acylated diethyl succinates (Scheme 30). The authors proposed that the γ-keto esters result from a mixed anhydride (**108**) formed by the reaction of boric acid with the β-keto ester (**107**) in the starting succinate derivative. The selectivity of this process was thought to result from complexation of the keto-carbonyl oxygen to the boron atom. Apparently, when this intermediate is heated, a decarboxylation reaction is induced that leads to a boron enolate, and hydrolysis of this boron enolate during workup then produces the free γ-keto ester.

A similar decarboxylation protocol was reported by Lhommet *et al.*[70] for the synthesis of cyclic imines from β-enaminoesters (Scheme 31). For example, when the β-enaminoester (**110**) was heated at 180 °C with two equivalents of boric acid, the corresponding 2-alkyl-cyclic imine (**111**) was obtained in 80% yield. These workers later published a similar method for the regio- and stereo-specific synthesis of cyclic β-enaminones.[71] In particular, heating the β-enaminoketoester (**112**) at 220 °C with excess boric acid, produced the corresponding (*Z*)-β-enaminone (**113**) in 60% yield. In 1991, Lhommet and co-workers[72] summarised the above results and described an additional regioselective boric acid-catalysed decarboxylation reaction, namely that of β-enaminoketodiesters. With these latter substrates, the initial decarboxylation products, enaminone esters, generally underwent a spontaneous cyclisation by intramolecular *C*-acylation to produce the corresponding cyclic β-enaminodiketones in low to moderate yields. For example, the β-enaminoketodiester (**114**) gave the β-enaminodiketone (**115**) in 40% yield. The decarboxylation reaction apparently occurs by concerted loss of CO_2 from an intermediate mixed anhydride similar to that proposed by Wehrli for the decarboxylation of β-ketoesters.

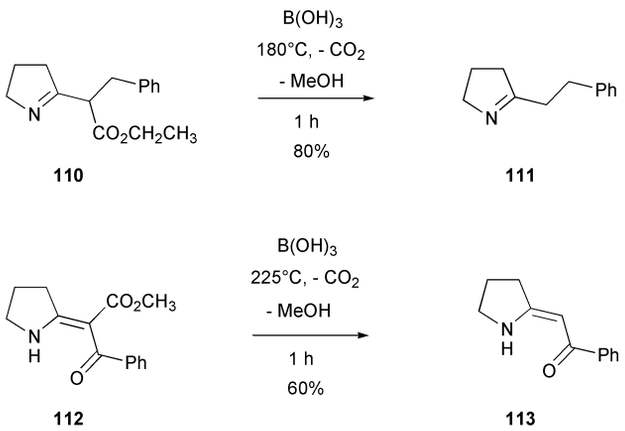
3.4 Opening of epoxides

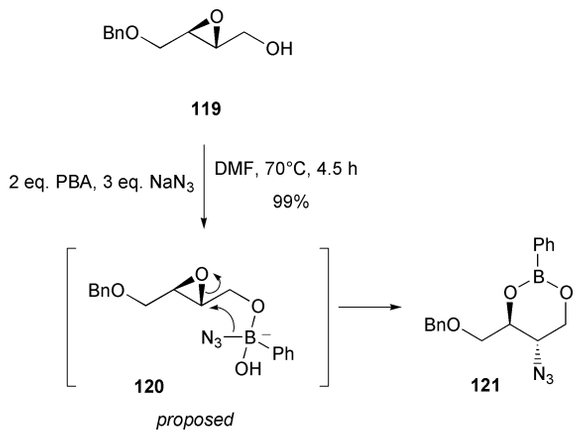
Miyashita and co-workers[73,74] have recently published two papers which describe the application of the weak Lewis acidity of PBA to the stereoselective ring-opening of epoxysulfides and epoxyalcohols (Schemes 32 and 33). In the first reported example of this unusual use of boronic acids, Miyashita *et al.*[73] treated 2,3-epoxysulfides with 1.3 equivalents of PBA in hot benzene and found that the epoxides were converted, quantitatively and stereospecifically, into phenylboronate esters of 2,3-dihydroxysulfides. The reactions of *trans*-2,3-epoxysulfides produced the corresponding 2,3-*syn*-phenylboronates and *cis*-2,3-epoxysulfides produced the corresponding 2,3-*anti*-phenylboronates, all with a diastereoselectivity of >99%. As such, these stereochemical outcomes are unusual, in that they provide access to vicinal-diols from epoxides *via* a double inversion of configuration. The authors proposed that the reaction proceeds *via* an episulfonium intermediate bearing a tetrahedral boronate (**117**), which collapses to the 2,3-diol phenylboronate ester (**118**) *via* attack of a hydroxy group on the boron at the 2-carbon, followed by loss of water. *cis*-Epoxysulfides were observed to react even more rapidly, presumably indicating an improved accessibility of PBA to the epoxide oxygen. The ring opening reaction was also found to proceed more quickly for substrates that contained an ether oxygen on a side chain, possibly reflecting a chelation effect.

The same researchers went on to investigate the use of PBA to facilitate the C2 selective opening of *trans*-2,3-epoxyalcohols by NaN_3 (Scheme 33).[74] The *trans*-4-benzyloxy-2,3-epoxyalcohol (**119**) and the corresponding *trans*-5-benzyloxy-2,3-epoxyalcohol were both treated with three equivalents of NaN_3 and two equivalents of PBA in hot DMF to yield phenylboronates of *trans*-2-azido-1,3-diols as single products in 99% and 94% yields, respectively. Substrates containing a silyloxy group or alkyl group, instead of the benzyloxy group, reacted with lower C2 selectivity, and the only trisubstituted epoxide studied opened in an unselective manner. As with the reactions of the epoxysulfides, epoxyalcohols containing an ether oxygen in their side-chains reacted more quickly, and in this case, with

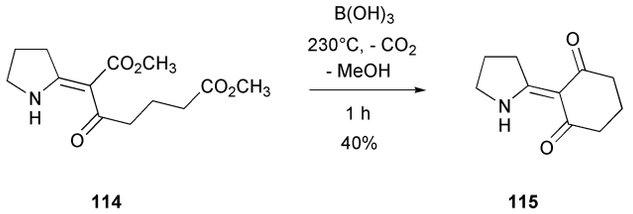


Scheme 30

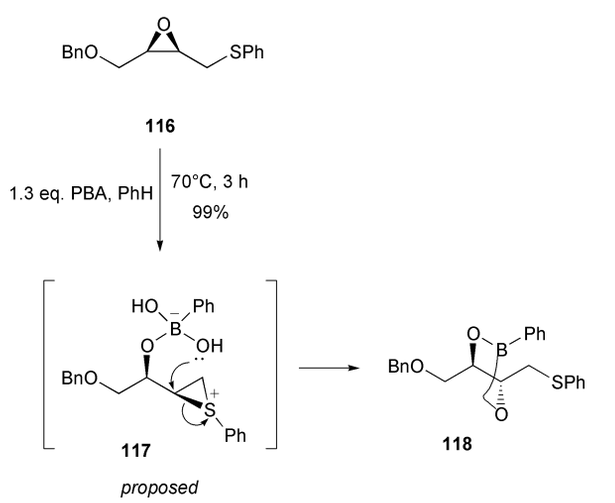




Scheme 33



Scheme 31

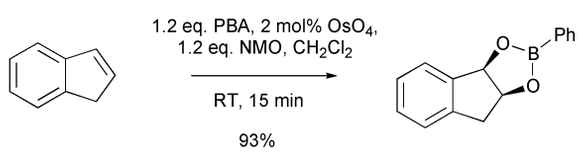


Scheme 32

higher regioselectively, than those with simple alkyl side chains. The preferential reaction at C2 was proposed to result from an intramolecular attack of azide through an intermediate possessing a tetrahedral boron atom (**120**).

3.5 Dihydroxylations

Narasaka *et al.* exploited the ability of boron acids to bind with diols in their development of a convenient method for the *cis*-dihydroxylation of olefins.[75] Traditional procedures for the dihydroxylation of olefins using catalytic amounts of osmium tetraoxide and an amine *N*-oxide co-oxidant, the so-called "Upjohn procedure",[76] often lead to over oxidation of the desired cyclic *cis*-1,2-diols. Aqueous conditions are also usually used to hydrolyse the osmate ester intermediate, which complicates the work-up if the products are water soluble. Narasaka's more recent approach employs diol captors to prevent over-oxidation and to aid in the isolation of the products.[75] Thus, to solutions containing catalytic osmium tetraoxide and *N*-methylmorpholine *N*-oxide (NMO) in dichloromethane at room temperature, various diol captors and indene (**122**, Scheme 34) were successively added at room temperature. Of the diol captors



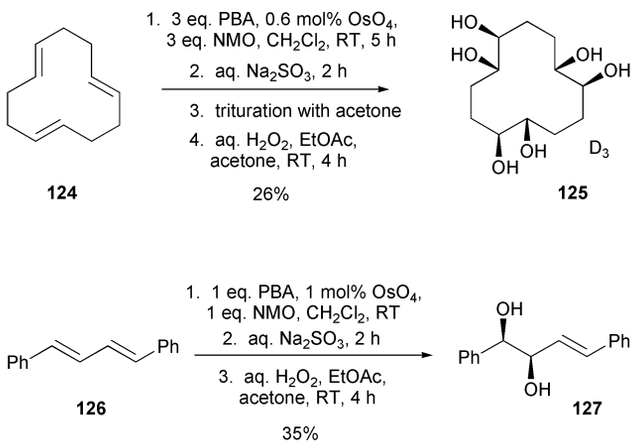
Scheme 34

employed, PBA was the most effective, giving the boronate ester (**123**) in 93% yield after 15 min. The use of $BuB(OH)_2$, boric acid, $Ph_2Si(OH)_2$ and Ph_2SnO instead of PBA gave lower yields and required longer reaction times. In the absence of PBA and using a reaction time of one day, the *cis*-1,2-diol was obtained, together with side products, in 68% yield. This suggests that PBA successfully prevents further oxidation of the *cis*-1,2-diol derivative. The generality of the procedure was demonstrated by the *cis*-dihydroxylation of a range of mono- and di-alkenes, all in high yields. The results of further experiments suggested that as well as acting as a diol captor, PBA might facilitate the reaction by helping to cleave the osmium ester intermediate. For example, the dihydroxylation of indene (**122**) in the presence of PBA was already 80% complete after 10 min. By comparison, dihydroxylations conducted for the same period of time in aqueous solvent systems, and in the absence of PBA, resulted in incomplete reactions, with only 10–35% of the alkene having been consumed. Narasaka *et al.*[77,78] have since utilised this reaction for the synthesis of a diboronate host for the selective complexation of amines.

The only other reported investigation of this procedure has been by Sharpless and coworkers[30] in which they compared Narasaka's method to standard procedures[76] for the dihydroxyl-

ation of polyenes. Their work highlighted the advantages of Narasaka's procedure, particularly the shorter reaction times, the fewer over-oxidised by-products and the high organic solubility of the boronate products. They found that a loading of only 0.2 mol% per alkene of the highly toxic OsO_4 was required, significantly less than the 2 mol% used by Narasaka's group. Sharpless *et al.* commented that the anhydrous conditions used in the Narasaka procedure also allow for a wider range of reaction temperatures than the standard method, but they also require the use of solid, anhydrous NMO, which is much more expensive than the aqueous solution employed in the standard Upjohn protocol.[76]

Sharpless' group also investigated the diastereoselectivity of the Narasaka procedure with a variety of polyene substrates (Scheme 35). Reaction of (*E*,*E*,*E*)-dodecatriene (**124**) under



Scheme 35

standard Upjohn conditions gave a 5 : 95 mixture of the D_3- and C_2-symmetric diastereoisomers, respectively. In contrast, the Narasaka method yielded a 1 : 1 mixture of the corresponding boronates. After trituration with acetone, and cleavage of the boronate esters with peroxide, the desired D_3-isomer (**125**) was obtained in a 26% yield, based on the triene (**124**). The D_3-selectivity was improved to 70 : 30 (D_3 : C_2) when the reaction was performed at −25 °C. These workers also showed that this procedure could be applied to the single dihydroxylation of a conjugated diene, something that cannot be achieved with the standard Upjohn process, because the second dihydroxylation proceeds at a greater rate than the first. Thus, they treated (*E*,*E*)-1,4-diphenylbuta-1,3-diene (**126**) with one equivalent of PBA, one equivalent of NMO and a catalytic amount of osmium tetraoxide at room temperature in dichloromethane and obtained, after oxidative cleavage of the resulting boronate ester, the ene-diol (**127**) in 35% overall yield.

4 Conclusions

Over the last two decades there has been a considerable expansion in the application of boron acids as labile diol protective agents in organic synthesis. Their use in improving the selectivity and yields of standard derivatisation reactions such as esterifications and alkylations has continued, but considerable improvement has been made in their use as protecting agents during alcohol oxidations, Horner–Wadsworth–Emmons olefinations and alkene epoxidations. As a result, boron acids have been used in the total synthesis of a number of complex natural products. Boron acids, which have largely been used in the protection of diols from reagents that cause *O*-derivitisation, have also been shown to be useful in the protection of diamines. Boron acids that *activate* alcohols towards alkylation have also been developed.

One of the most appealing features of boron acids is their ease of attachment to and removal from diols, as well as their potential to be recycled. Particularly relevant to the latter point are investigations into the use of polymer supported boronic acids, a field which is still in its infancy, but is likely to undergo significant growth over the coming decade.

The use of boron acids as facilitating reagents for a number of organic transformations has only been investigated relatively recently. Here we have reviewed cases where boron acids have been used to catalyse or enhance cyclisations, *o*-alkylations of phenols, as well as decarboxylation, epoxide opening and dihydroxylation reactions. Other examples have been reviewed by Ishihara and Yamamoto.[57]

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6 References

1 S. P. Draffin, P. J. Duggan and S. A. M. Duggan, *Org. Lett.*, 2001, **3**, 917.
2 S. J. Gardiner, B. D. Smith, P. J. Duggan, M. J. Karpa and G. J. Griffin, *Tetrahedron*, 1999, **55**, 2857.
3 B. D. Smith and S. J. Gardiner, in *Advances in Supramolecular Chemistry*, ed. G. W. Gokel, JAI Press, Greenwich, 1999, vol. 5, pp. 157–202.
4 T. D. James, K. R. A. S. Sandanayake and S. Shinkai, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1911.
5 D. Larson-Irwin, *Mod. Drug Discovery*, 2000, **3(7)**, 79.
6 M. L. Stolowitz, C. Ahlem, K. A. Hughes, R. J. Kaiser, E. A. Kesicki, G. Li, K. P. Lund, S. M. Torkelson and J. P. Wiley, *Bioconjugate Chem.*, 2001, **12**, 229.
7 R. R. Srivastava, R. R. Singhaus and G. W. Kabalka, *J. Org. Chem.*, 1999, **64**, 8495.
8 J. A. Riggs, K. A. Hossler, B. D. Smith, M. J. Karpa, G. Griffin and P. J. Duggan, *Tetrahedron Lett.*, 1996, **37**, 6303.
9 A. Suzuki, in *Metal Catalysed Cross-Coupling Reactions*, ed. F. Diederich and P. J. Stang, Wiley-VCH, Weinheim, 1998, ch. 2.
10 D. S. Matteson, in *Stereodirected Synthesis with Organoboranes*, ed. K. Hafner, C. W. Rees, B. M. Trost, J.-M. Lehn and P. von Ragué Schleyer, Springer-Verlag, Heidelberg, 1995.
11 E. Bertounesque, J.-C. Florent and C. Monneret, *Synthesis*, 1991, **4**, 270.
12 K. Ravichandran, F. A. J. Kerdesky and M. Cava, *J. Org. Chem.*, 1986, **51**, 2044.
13 Y. S. Rho, S. Y. Kim, I. Cho, H. S. Kang, D. J. Yoo and C. Cheong, *Bull. Korean Chem. Soc.*, 1998, **19**, 1059.
14 M. Machida and K. Oda, *Tetrahedron*, 1985, **41**, 4995.
15 C. J. Cowden and I. Paterson, *Org. React.*, 1997, **51**, 38.
16 R. J. Ferrier, *Adv. Carbohydr. Chem. Biochem.*, 1978, **35**, 31.
17 J. E. McMurry and M. D. Erion, *J. Am. Chem. Soc.*, 1985, **107**, 2712.
18 K. Oshima, E.-I. Kitazono and Y. Aoyama, *Tetrahedron Lett.*, 1997, **38**, 5001.
19 K. Oshima and Y. Aoyama, *J. Am. Chem. Soc.*, 1999, **121**, 2315.
20 C. Liljebris, B. M. Nilsson, B. Resul and U. Hacksell, *J. Org. Chem.*, 1996, **61**, 4028.
21 R. W. Irvine, R. A. Russell and R. N. Warrener, *Tetrahedron Lett.*, 1985, **26**, 6117.
22 V. Bhaskar K., P. J. Duggan, D. G. Humphrey, G. Y. Krippner, V. McCarl and D. A. Offermann, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1098.
23 J. M. J. Fréchet, L. J. Nuyens and E. Seymour, *J. Am. Chem. Soc.*, 1979, **101**, 432.
24 S. Langston, B. Bernet and A. Vasella, *Helv. Chim. Acta*, 1994, **77**, 2341.
25 G. G. Cross and D. M. Whitfield, *Synlett.*, 1998, 487.
26 J. E. A. Luithle and J. Pietruszka, *J. Org. Chem.*, 1999, **64**, 8287.
27 S. Arimori, J. H. Hartley, M. L. Bell, C. S. Oh and T. D. James, *Tetrahedron Lett.*, 2000, **41**, 10291.
28 D. S. Matteson, personal communication.
29 E. Vedejs, R. W. Chapman, S. C. Fields, S. Lin and M. R. Schrimpf, *J. Org. Chem.*, 1995, **60**, 3020.
30 A. Gypser, D. Michel, D. S. Nirschl and K. B. Sharpless, *J. Org. Chem.*, 1998, **63**, 7322.
31 D. A. Evans and P. Polniaszek, *Tetrahedron Lett.*, 1986, **27**, 5683.
32 J. Pis, J. Hykl, M. Budesinsky and J. Harmatha, *Tetrahedron*, 1994, **50**, 9679.

33 K. Narasaka, S. Shimada, K. Osoda and N. Iwasawa, *Synthesis*, 1991, 1171.
34 R. A. Batey, A. N. Thadani and A. J. Lough, *J. Am. Chem. Soc.*, 1999, **121**, 450.
35 C. J. Griffiths and H. Weigel, *Carbohydr. Res.*, 1980, **81**, 17.
36 A. Gupta, A. Kirfel and G. Will, *Acta Crystallogr., Sect. B*, 1977, **33**, 637.
37 V. Bhaskar K., A. D'Elia, P. J. Duggan, D. G. Humphrey, G. Y. Krippner, T. T. Nhan and E. M. Tyndall, *unpublished work.*
38 I. Ikeda and A. M. Klibanov, *Biotechnol. Bioeng.*, 1993, **42**, 788.
39 G. Youssef, S. Ransac and R. Verger, *Biochim. Biophys. Acta*, 1997, **1344**, 6.
40 P. J. Duggan, D. G. Humphrey and V. McCarl, unpublished work.
41 H.-O. Park, D.-S. Lee and S. C. Shim, *Biotechnol. Lett.*, 1992, **14**, 111.
42 A. Flores-Parra, C. Paredes-Tepox, P. Joseph-Nathan and R. Contreras, *Tetrahedron*, 1990, **46**, 4137.
43 K. Ishihara, Y. Kuroki, N. Hanaki, S. Ohara and H. Yamamoto, *J. Am. Chem. Soc.*, 1996, **118**, 1569.
44 Y. Kuroki, K. Ishihara, N. Hanaki, S. Ohara and H. Yamamoto, *Bull. Chem. Soc. Jpn.*, 1998, **71**, 1221.
45 R. H. Furneaux, P. M. Rendle and I. M. Sims, *J. Chem. Soc., Perkin Trans. 1*, 2000, 2011.
46 M. Pereyre, J.-P. Quintard and A. Rahm, in *Tin in Organic Synthesis*, Butterworths, London, 1987, p. 261.
47 J. M. J. Fréchet and E. Seymour, *Tetrahedron Lett.*, 1976, **15**, 1149.
48 J. M. J. Fréchet and E. Seymour, *Tetrahedron Lett.*, 1976, **41**, 3669.
49 J. M. J. Fréchet and E. Seymour, *Isr. J. Chem.*, 1978, **17**, 253.
50 N. P. Bullen, P. Hodge and F. G. Thorpe, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1863.
51 A. Sano and N. Teno, USP 5 300 634/1994 (*Chem. Abstr.*, 1992, **118**, 169525).
52 Y. Liao and Z. Li, *Synth. Commun.*, 1998, **28**, 3539.
53 G. Belogi, T. Zhu and G.-J. Boons, *Tetrahedron Lett.*, 2000, **41**, 6965.
54 G. Belogi, T. Zhu and G.-J. Boons, *Tetrahedron Lett.*, 2000, **41**, 6969.
55 C. Pourbaix, F. Carreaux, B. Carboni and H. Deleuze, *Chem. Commun.*, 2000, 1275.
56 B. Carboni, C. Pourbaix, F. Carreaux, H. Deleuze and B. Maillard, *Tetrahedron Lett.*, 1999, **40**, 7979.
57 K. Ishihara and H. Yamamoto, *Eur. J. Org. Chem.*, 1999, 527.
58 W. Moneta, P. Baret and J.-L. Pierre, *J. Chem. Soc., Chem. Commun*, 1985, 899.
59 J. G. de Vries and S. A. Hubbard, *J. Chem. Soc., Chem. Commun*, 1988, 1172.
60 K. C. Nicolaou, J. J. Liu, C.-K. Hwang, W.-M. Dai and R. K. Guy, *J. Chem. Soc., Chem. Commun.*, 1992, 1198.
61 S. Shimada, K. Osoda and K. Narasaka, *Bull. Chem. Soc. Jpn*, 1993, **66**, 1254.
62 E. J. Corey, B.-C. Pan, D. H. Hua and D. R. Deardorff, *J. Am. Chem. Soc.*, 1982, **104**, 6816.
63 W. Nagata, H. Itazaki, K. Okada, T. Wakabayashi, K. Shibata and N. Tokutake, *Chem. Pharm. Bull.*, 1975, **23**, 2867.
64 H. G. Peer, *Recl. Trav. Chim. Pays-Bas*, 1960, **79**, 825.
65 M. Cushman and F. W. Dekow, *J. Org. Chem.*, 1979, **44**, 407.
66 W. Nagata, K. Okada and T. Aoki, *Synthesis*, 1979, **5**, 365.
67 C. K. Lau, H. W. R. Williams, S. Tardiff, C. Dufresne, J. Scheigetz and P. C. Bèlanger, *Can. J. Chem.*, 1989, **67**, 1384.
68 P. A. Wehrli and V. Chu, *J. Org. Chem.*, 1973, **38**, 3436.
69 P. A. Wehrli and V. Chu, *Organic Syntheses*, ed. W. A. Shepperd, Wiley and Sons, New York, 1978, vol. 58, p. 79.
70 D. Bacos, J.-P. Celerier and G. Lhommet, *Tetrahedron Lett.*, 1987, **28**, 2353.
71 P. Delbecq, D. Bacos, J. P. Celerier and G. Lhommet, *Tetrahedron Lett.*, 1990, **31**, 4873.
72 P. Delbecq, D. Bacos, J. P. Celerier and G. Lhommet, *Can. J. Chem.*, 1991, **69**, 1201.
73 H. Hayakawa, N. Okada and M. Miyashita, *Tetrahedron Lett.*, 1999, **40**, 3191.
74 H. Hayakawa, N. Okada, M. Miyazawa and M. Miyashita, *Tetrahedron Lett.*, 1999, **40**, 4589.
75 N. Iwasawa, T. Kato and K. Narasaka, *Chem. Lett.*, 1988, 1721.
76 V. VanRheenen, D. Y. Cha and W. M. Hartley, *Organic Syntheses*, ed. W. A. Shepperd, Wiley and Sons, New York, 1978, vol. 58, p. 43.
77 K. Narasaka, H. Sakurai, T. Kato and N. Iwasawa, *Chem. Lett.*, 1990, 1271.
78 H. Sakurai, N. Iwasawa and K. Narasaka, *Bull. Chem. Soc. Jpn.*, 1996, **69**, 2585.