



Factors affecting reactions of trialkylcyanoborates with imidoyl chlorides/trifluoroacetic anhydride



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ARTICLE INFO

Article history:

Received 9 April 2015

Received in revised form 2 June 2015

Accepted 9 June 2015

Available online 15 June 2015

Keywords:

Cyanoborate
Rearrangement
Hydroboration
Imidoyl chloride

ABSTRACT

Methods for generating *tert*-alkyl organoboron species are in high demand as they are invaluable intermediates for the synthesis of quaternary carbon centres. Herein we report investigations into generation of *tert*-alkyl organoboron species using imidoyl chlorides as reagents in the organoboron cyanidation reaction. Although alkenyl side-products predominate in particularly hindered cases, *tert*-alkyl organoboron species can be successfully generated for less hindered examples.

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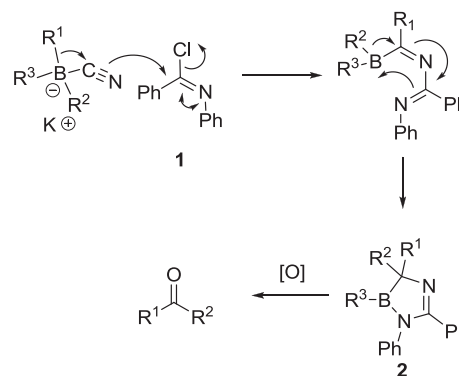
1. Introduction

The formation of C–C bonds using boron-to-carbon alkyl group migrations is an invaluable transformation in organic chemistry.¹ Such reactions can involve one, two or three migrations, depending on the number of available leaving groups. There has been considerable interest of late in such migration reactions that give rise to *tert*-alkyl organoboron species, as there are protocols available to use these in the generation of otherwise difficult to synthesise quaternary carbon centres.^{2–8}

Several organoboron reactions have been developed that utilize all three alkyl groups of a trialkylborane, giving a *tert*-alcohol as the final product following oxidation of the *tert*-alkyl organoboron intermediate.^{9–12} Of these reactions, the cyanidation reaction is particularly useful as it proceeds under mild conditions, is tolerant of sensitive functional groups and the doubly-migrated ketone product is also accessible using the appropriate reaction conditions.^{11,13–15}

Although trifluoroacetic anhydride (TFAA) or benzoyl chloride is usually the acylating reagent used in the cyanidation reaction, it has been shown that *N*-phenylbenzimidoyl chloride (**1**) successfully induces two boron–carbon migrations to give the intermediate **2**, which on oxidation gives the ketone product (Scheme 1).¹⁵ Since it

is possible to envisage introducing chirality into the imidoyl chloride, it was of interest to us to investigate whether a third migration could be induced in the cyanidation reaction when using an imidoyl chloride as the acylating reagent.



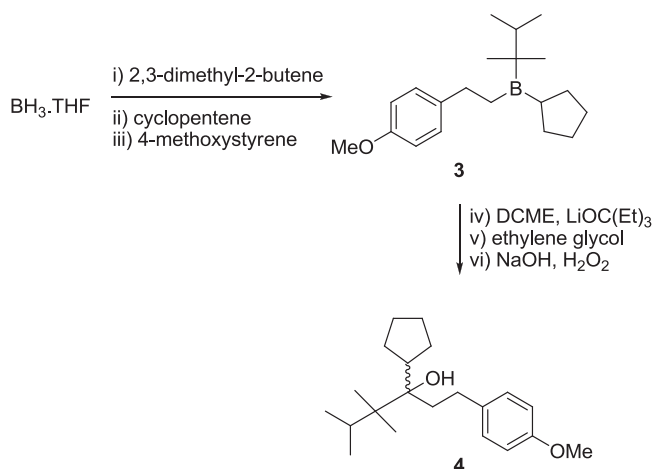
Scheme 1. Imidoyl chloride-induced cyanidation reaction.

It was reasoned that by adding excess trifluoroacetic anhydride (TFAA) to the intermediate of type **2** (Scheme 1), acylation would occur on nitrogen, thereby promoting the migration of the third and final alkyl group, as occurs in the direct reaction of trialkylcyanoborates with excess TFAA.¹³ Our results indicate that such a process is indeed possible in cases when the trialkylborane is not extremely hindered.

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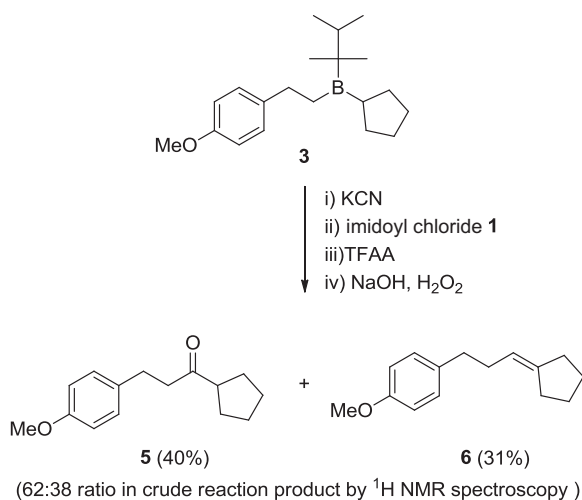
2. Results/discussion

The mixed trialkylborane **3** was chosen as the first substrate to be studied, as a chiral *tert*-alcohol product would allow evaluation of any future cyanidation reactions utilizing chiral imidoyl chlorides. An authentic sample of racemic *tert*-alcohol **4** was prepared by the sequential hydroboration of 2,3-dimethyl-2-butene, cyclopentene and 4-methoxystyrene to give **3**, which was subsequently taken through the dichloromethyl methyl ether (DCME) protocol to give **4** (Scheme 2).¹²



Scheme 2. Formation of a chiral tertiary alcohol by the DCME reaction.

Mixed organoborane **3** was converted into its cyanoborate by stirring under nitrogen with powdered potassium cyanide for 1 h. This was then stirred overnight at room temperature with *N*-phenylbenzimidoyl chloride (**1**), before excess TFAA was added and the reaction mixture heated to 40 °C for 14 h. ¹H NMR analysis following oxidation and work-up showed the presence of ketone **5** and novel alkene **6** (Scheme 3) in a 62:38 ratio, respectively, with no presence of *tert*-alcohol **4**. After chromatographic separation, compound **5** was isolated in 40% yield and compound **6** in 31% yield.



Scheme 3. Reaction of imidoyl chloride **1** with mixed trialkylborane **3**.

Ketone **5** is almost certainly the product from the oxidation of the intermediate of type **2** following two migrations, whilst alkene **6** may be the product of protodeboronation of intermediate **2**, along with elimination of amine, facilitated by small amounts of acid

present in the TFAA. Such alkenyl species have been reported as minor side products in the traditional cyanidation reaction when using particularly hindered trialkylboranes,¹¹ and also in the DCME reactions of certain borinic esters¹⁶, which, upon heating, give the alkenyl products almost quantitatively.¹⁷

Many factors (both steric and electronic in nature) affect boron-to-carbon migrations,¹ and so imidoyl chlorides **7–9** were chosen to probe whether the electronic and/or steric characteristics of the imidoyl chloride could influence the reaction in such a way as to promote the third alkyl group migration to give, after oxidation, tertiary alcohol **4**. Imidoyl chlorides **7** and **8** (Fig. 1) were chosen to test whether an electron-withdrawing substituent could promote the third migration, while imidoyl chloride **9** was chosen to probe whether the third migration could be promoted by the alleviation of steric hindrance around boron.¹

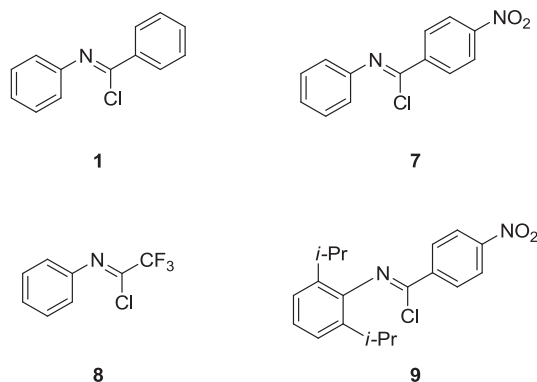


Fig. 1. Imidoyl chlorides chosen for study.

Imidoyl chlorides **7–9** were added to the potassium cyanoborate salt of **3** and, following stirring at room temperature overnight, an aliquot was taken, oxidised and worked-up. Ketone **5** was clearly visible as the major product by ¹H NMR analysis of the products when using imidoyl chlorides **7** and **9**, indicating that the first two migrations had been successful. When using imidoyl chloride **8**, however, only the alcohols arising from the oxidation of **3** could be seen in the ¹H NMR spectrum of the product. An aliquot taken after heating the reaction mixture of **8** overnight at 80 °C contained only trace amounts of **5**, while further heating resulted in darkening of the solution and formation of a black polymeric material. Imidoyl chlorides possessing electron-withdrawing substituents are known to be less prone to attack by nucleophiles,¹⁸ which could explain the apparent lack of reactivity of imidoyl chloride **8** with the potassium cyanoborate salt of **3**.

Excess TFAA was added to the reaction mixtures involving **7** and **9**, and the reaction mixtures were heated to 40 °C overnight (Table 1). ¹H NMR analysis following work-up for both reactions showed an identical ratio of **5** and **6**, with no sign of *tert*-alcohol **4** (Table 1). The presence of the bulky isopropyl groups of **9** seemed to have had minimal effect on the course of the reaction, whilst the addition of a nitro group into the 4-position of the aryl ring of **7** increased the production of alkene **6**.

Given that alkene side-products of type **6** are seen in traditional cyanidation reactions (using TFAA alone as the acylating reagent) only when particularly bulky trialkylboranes are used,¹¹ it was reasoned that boranes lacking the bulky *tert*-butyl (2,3-dimethyl-2-butyl) group of intermediate **10** might allow the third migration to give a *tert*-alcohol product. Attempts were therefore made to displace the *tert*-butyl group from **10**.

Using **7**, intermediate **10** was heated to 100 °C with excess 1-octene in an attempt to replace the *tert*-butyl group with an *n*-octyl group via a displacement reaction (Entry 5, Table 1).¹⁹ ¹H NMR analysis following subsequent reaction with TFAA and oxidation showed the presence of **5** (ca. 61% yield) and 1-octene (ca. 79%

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