Alkylation of Nitroaromatics with Trialkylborane**

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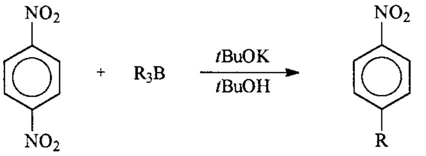
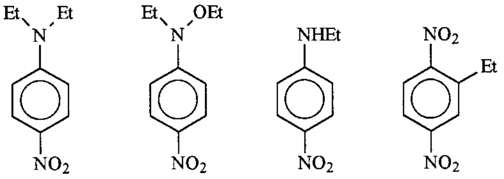
Aromatic substitution is one of the most thoroughly studied reactions.[1] Yet in spite of the wealth of mechanistic knowledge and numerous synthetic applications, this paper reports a facile and hitherto unknown alkylation procedure for nitroaromatics.

When *p*-dinitrobenzene (**1**) is treated with trialkylborane in the presence of potassium *tert*-butoxide in *tert*-butyl alcohol at room temperature for five minutes, it furnishes *p*-alkylnitrobenzene (**2**, Equation 1) in high yield. Equivalent amounts of the three components—**1**, trialkylborane, and base—were found to be essential for the completion of the reaction. When the amount of trialkylborane or base is reduced below this ratio, the substrate is consumed in an amount equivalent to the reagent present in the minimum concentration. Since an excessive amount of base results in the formation of *p*-*tert*-butoxynitrobenzene, a small excess (approximately 10%) of the borane reagent was usually employed. When the reaction was performed with triethylborane, by-products **3**–**6** were isolated in addition to 70% of **2** (R = Et, Scheme 1).



(1)

1 **2**



5% 12% 1.7% trace

3 **4** **5** **6**

Scheme 1. By-products obtained in the reaction of *p*-dinitrobenzene with triethylborane.

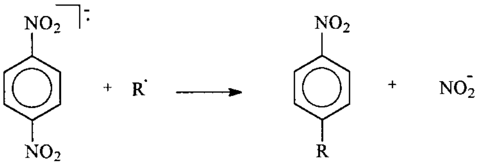
The reaction can also take place in THF. However, the yields are slightly lower with the major difference being the presence of approximately 15% of *p*-*tert*-butoxynitrobenzene amongst the products. Using two equivalents of triethylborane increased the yield to 85% and no *p*-*tert*-butoxynitrobenzene was formed. Temperature sensitivity was also observed. When the reaction was conducted at temperatures below 25°C the rate decreased drastically. At 0°C, for example, the reaction does not progress, to a significant extent, even after 2 hours.

Using tributylborane, the yield of *p*-butylnitrobenzene was also in the range of 70–80% and no isomerization on the butyl chain was observed. However, the reaction failed with triphenylborane. Even after 24 hours no *para* phenylation was observed. When the substrate was changed to *p*-nitrobenzaldehyde and the previous reaction conditions were employed in THF, only 7% of **2** (from departure of CHO) was observed after 12 hours.

Aluminum, the homologue of borane, was found to be much less reactive. Treatment with triethylaluminum, under identical reaction conditions gave only 19% (NMR yield) of *p*-ethylnitrobenzene after 12 h at room temperature although over 40% of **1** was consumed.

The reaction is unlikely to be a radical or a radical–anionic chain mechanism of a type similar to the Srn1 reaction[2] since it also proceeds smoothly in 2-propanol, a solvent which rapidly reacts with free radicals. In addition, no inhibition of the reaction by 5 mol% galvinoxyl is observed and the reaction is not catalyzed by the laboratory light. On the other hand, *p*-dinitrobenzene is known to be a powerful electron acceptor[3] and trialkylboranes are known to yield very rapidly, with a rate constant of $10^8\,\mathrm{M}^{-1}\,\mathrm{s}^{-1}$, alkyl radicals when reacted with oxy-radicals.[4] Based on the nature of the reactants and the aforementioned results a tentative nonchain mechanism can be suggested where all the steps take place in a complex or in a solvent cage. In this mechanism, the alkyl radical formed (Equation 2) reacts with the radical anion of *p*-dinitrobenzene (Equation 3) initially generated by an electron transfer from an anionic species present in the reaction mixture.

$$R_3\dot{B}OtBu \longrightarrow R_2BOtBu + R^{\cdot} \qquad (2)$$



(3)

Experimental Section

Typical procedure: Compound **1** (84 mg, 0.5 mmol) in 1 mL of dry *t*BuOH was injected into a flask which contained a solution of *t*BuOK (56 mg, 0.5 mmol) and trialkylborane (0.55 mmol) in *t*BuOH (5 mL) under argon. After 5 to 10 min at room temperature, the reaction was treated with dilute aqueous HCl (3%), extracted several times with CH_2Cl_2, and dried over anhydrous sodium sulfate. After purification by flash column chromatography, the yield of **2** was 70–80%.

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Metal Ions as Allosteric Inhibitors in Hydrogen-Bonding Receptors**

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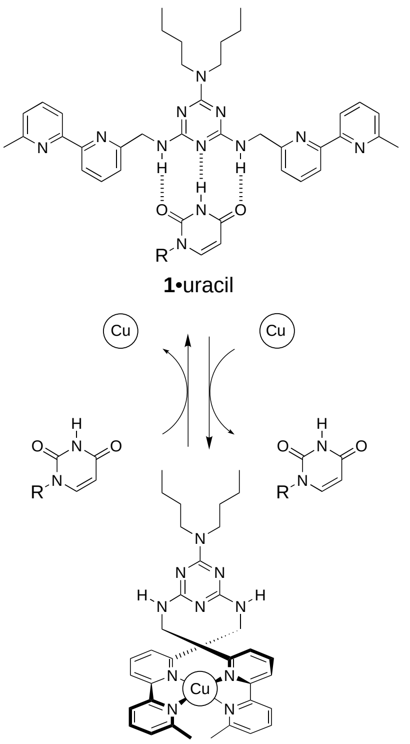
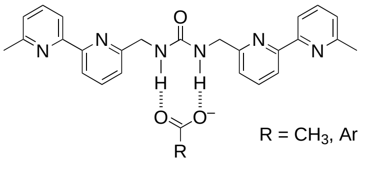
Although there are many examples of artificial systems that display positive allostery,[1] where the induced conformational change increases the receptor's binding efficacy, there are few reports of simple negative allosteric receptors,[2] where the initial interaction with the cofactor results in a decrease in the receptor's binding affinity for its substrate. Of those that have been described, none, as far as we are aware, involve the destruction of well-ordered multipoint hydrogen-bond surfaces that are specific for biologically interesting guest species.

We report here how two novel receptors inhibit substrate binding in the presence of Cu^{I}. Receptor **1** is based on the triaminotriazine scaffold, which presents a donor–acceptor–donor hydrogen-bond surface well suited to act as a host for imide guests such as uracil (Scheme 1) and thymine.[3] When **1** is exposed to the metal ion, the two bipyridine arms swing towards each other and form a metal–ligand coordination compound. It is the Lewis acid that acts as the allosteric inhibitor, as its complexation to the chelating ligands forces two of the triazine's exocyclic C–N bonds to rotate, distorting the hydrogen-bonding surface. When the metal ion is extracted from the coordination pocket, the original hydrogen-bonding surface is reconstructed. This reactivates the receptor.



Scheme 1. Exchange of a substituted uracil and Cu^{I} in receptor **1**. $R = C_4H_9$.

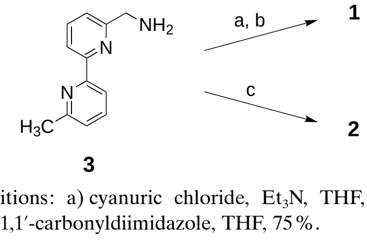
In a similar fashion, urea **2** presents a donor–donor hydrogen-bond recognition site for carboxylate guests.[4] It can exist in its active, natural form in the absence of Lewis acids, or it can be deactivated upon copper complexation.



2•carboxylate

Both receptors can be conveniently prepared from the readily available 6-aminomethyl-6′-methyl-2,2′-bipyridine (**3**)[5] as outlined in Scheme 2. All new species were characterized by multinuclear NMR spectroscopy, IR spectroscopy, and mass spectrometry.

The binding efficacy of receptors **1** and **2** to their substrates was evaluated by analyzing the changes that occurred in the



Scheme 2. Reagents and conditions: a) cyanuric chloride, Et_3N, THF, 72%; b) Bu_2NH, THF, 52%; c) 1,1′-carbonyldiimidazole, THF, 75%.

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