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The reaction of pentacyanonitrosylferrate(II) with primary amines as a source of stabilized aliphatic diazonium ions: a new route to secondary amines

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Abstract

Pentacyanonitrosylferrate(II), **1**, reacts with *n*-butylamine to produce di-*n*-butylamine in high yields (81–95%). The absence of rearranged products indicates that the initially produced diazonium ion is stabilized by coordination to the metal. Benzylamine and 1,4-diaminobutane react with **1** to produce dibenzylamine and piperidine, respectively. © 1999 Elsevier Science Ltd. All rights reserved.

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The chemistry of pentacyanonitrosylferrate(II) ($[Fe(CN)_5NO]^{2-}$, **1**) is of great interest for several reasons. Firstly, it is widely used as a vasodilator and its electrophilic nitrosyl ligand might be able to react with amines present in the physiological medium to produce nitrosamines, which are known carcinogens. Moreover, the chemistry of the nitrosyl ligand itself has recently received interest due to its presence in mammals as an important mediator in a number of biological processes such as neural transmission, cytotoxicity and blood pressure regulation.[1] Therapeutical uses of NO coordinated to ruthenium, also a Group 8 element, have been recently reviewed.[2] On the other hand, the reaction of pentacyanonitrosylferrate(II) with aliphatic amines has been postulated to produce diazonium ions as intermediates.[3] These aliphatic diazonium ions could be stabilized by coordination through back donation from the metal to the diazonium salt, as indicated by preliminary calculations performed by our group[4] and by results obtained by Mayer et al.[5] who obtained aromatic diazonium salts stabilized by coordination to ruthenium through the reaction of $[Ru(bpy)_2(NO)Cl]^{2+}$ (bpy is 2,2′-bipyridil) with aniline and other aromatic amines. Similar reactions involving aliphatic amines could provide insight into the chemistry of the extremely reactive aliphatic diazonium salts if coordination to the metal stabilizes them enough to reduce their reaction rates to a measurable timescale, and limited amounts of nucleophiles are present. Reactions of pentacyanonitrosylferrate(II) involving primary[3,6] and secondary

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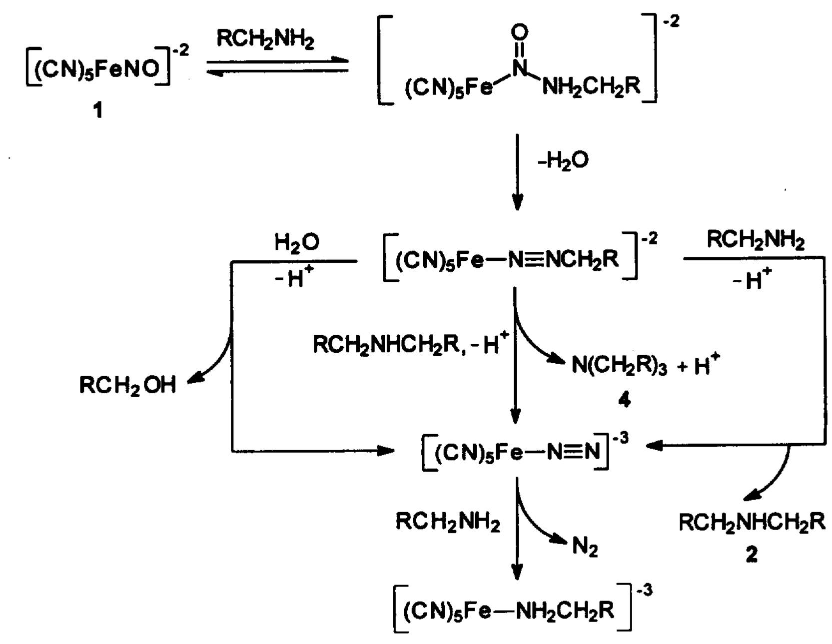
Table 1
Products obtained by the reaction of pentacyanonitrosylferrate(II) with *n*-butylamine[a]

Experiment #	1[b]	2[b]	3[c]	4[c]
Solvent[d]	-	-	CH_3CN	CH_3CN
$[Fe(CN)_5NO]^{2-}$: *n*-butylamine	1:120	1:4	1:120	1:120
Atmosphere	N_2	N_2	Air	N_2
% Dibutylamine (**2**)	81	82	89	95
% N-Butyl-1-butanimine (**3**)	8	<1	3	1
% Tributylamine (**4**)	3	12	2	3
% 2-Butylaminepentanenitrile (**5**)	<1	2	5	5

[a]All reactions were carried out at room temperature. Results are expressed as moles of product per 100 moles of starting complex. [b]Na^+ was present as counterion. [c]NH_4^+ was present as counterion due to the insolubility of the sodium salt in acetonitrile. [d]Dashes indicate that no solvent was added (the starting complex is not soluble in *n*-butylamine).

amines[7] as well as aminoacids[8] have only been studied in aqueous media, where enormous amounts of nucleophile are present in the form of hydroxide or water molecules. In the present work we focus on reactions conducted in non-aqueous solvents, namely acetonitrile and/or amine, in an attempt to get more insight on the chemistry of coordinated diazonium ions and also to elucidate the possible role of pentacyanonitrosylferrate(II) as a nitrosating agent in lipophilic media.

Table 1 shows the amounts of organic products obtained by the reaction of pentacyanonitrosylferrate(II) with *n*-butylamine under different conditions. The main organic product is dibutylamine (**2**). Butylaminepentacyanoferrate(II) is the major iron containing product, (84% isolated yield in experiment #2) although a small amount of prussian blue was obtained as a precipitate in experiments #3 and #4. Nitrogen gas was formed as indicated by previous works[3,6] (89% yield determined volumetrically for experiment #2). Butanol was also observed but could not be quantified because of the similarity of its GC retention time with the huge peak due to *n*-butylamine. Approximately 4 moles of *n*-butylamine react per mole of **1** since two moles of amine are involved in the formation of dibutylamine, one mole is bound to iron in the butylaminepentacyanoferrate(II) complex, and the fourth is acting as counterion. As in previous studies,[3] nucleophilic attack at coordinated NO in **1** by the amine and subsequent loss of water to produce a coordinated diazonium ion followed by reaction with a second equivalent of amine is proposed (Scheme 1, R=propyl). The yields of dibutylamine are very high even in the presence of only stoichiometric amounts of *n*-butylamine (experiment #2). Rearranged products characteristic of carbocations are not observed. These results are largely in contrast with those obtained for the diazotization of butylamine by nitrous acid in water,[9] where only 30% of unrearranged products were obtained, and the rest corresponded to rearrangement and elimination products. Therefore we can conclude that the diazonium ion produced by diazotization of *n*-butylamine with pentacyanonitrosylferrate(II) is stabilized by coordination to the metal until it is attacked by a nucleophile. As depicted in Scheme 1, if this nucleophile is *n*-butylamine, dibutylamine (**2**) is produced. Formation of butanol may be explained in a similar manner by reaction of the coordinated diazonium ion with water, while its reaction with dibutylamine produces tributylamine (**4**). Stabilization of the diazonium ion could be due to back donation from the metal, and/or to steric hindrance effects promoted by the other groups attached to iron.



Scheme 1. Proposed mechanism for the reaction of *n*-butylamine with pentacyanonitrosylferrate(II). (R=propyl)

From experiments #1 and #2 it can be concluded that when the initial ratio **1**:*n*-butylamine decreases, some of the diazonium ion initially formed reacts with dibutylamine to produce tributylamine (**4**, Scheme 1). However, dibutylamine is still the major product, indicating that the more nucleophilic dibutylamine is less reactive than *n*-butylamine, probably due to steric hindrance produced by the coordinated cyanide groups. Experiments carried out independently have shown that under the same conditions as those used for *n*-butylamine, dibutylamine does not react with pentacyanonitrosylferrate(II) either in acetonitrile solution or in the absence of solvent.

The effect of oxygen on the reaction is barely noticeable, as shown by experiments #3 and #4. In the presence of air a small amount of dibutylamine is oxidized to *N*-butyl-1-butanimine (**3**), probably by a mechanism that involves iron(II) oxidation, as it has been suggested before for ruthenium complexes.[10] Alternatively, in the absence of air (experiment #1) **3** might be produced by NO^+ oxidation of the coordinated amine. This is likely considering that reduction of pentacyanonitrosylferrate(II) in acetonitrile occurs at a relatively favorable potential of –0.82 V,[11] and that coordination of amines to transition metals activates the amine toward dehydrogenation, as previously demonstrated for some Ru(II) complexes.[12–14]

By comparing reactions #1 and #4 it can be observed that when the reaction is carried out in acetonitrile 2-butylaminepentanenitrile (**5**) seems to be produced at the expense of *N*-butyl-1-butanimine (**3**). As stated before, prussian blue was detected as a product in small amounts, and it has been found that this compound is formed by decomposition of pentacyanoferrate(II) complexes with the concomitant liberation of cyanide.[15] Since it is known that cyanide adds to iminium ions,[16] it seems reasonable to assume that cyanide could add intermolecularly to **3** (coordinated to iron by exchange with butylamine) therefore producing compound **5**.

The scope of the reaction can be extended, as depicted in Table 2. Benzylamine also produces the corresponding secondary amine (dibenzylamine, **6**), although the yield for this product is not as good as expected due to the formation of *N*-benzylphenylmethanimine (**7**). Since 1,2-diphenylethane and toluene are also obtained, and these products derive from the benzyl radical, it can be assumed that **7** is produced by NO oxidation of benzylamine via a radical pathway. On the other hand, a cyclized amine such as

Table 2
Yields of secondary amines obtained by reaction of **1** with primary amines[a]

Reactant(s)	**Product (yield)** [b]
Benzylamine	Dibenzylamine (**6**) (30%)[c]
1,4-Diaminobutane	Pyrrolidine (**8**) (50%)[d]
Butylamine/Benzylamine (1:3)	Butyl(benzyl)amine (**9**) (58%)[e]

[a] Reaction conditions similar to those applied in exp. #1. [b] Yields in moles of product per 100 moles of starting complex. [c] Other products: N-benzylphenylmethanimine (**7**, 66%), 1,2-diphenylethane (8%), toluene (8%). [d] Other product: N-nitrosopyrrolidine. [e] Other products: N-benzylphenylmethanimine (25%), 1,2-diphenylethane (7%), dibutylamine (24%).

pyrrolidine (**8**) is obtained in good yields from the corresponding diamine, while an unsymmetrical amine (**9**) is produced if two different primary amines are used as reactants.

In conclusion, the absence of rearranged products in the reaction of pentacyanonitrosylferrate(II) with primary amines indicates that the initially produced diazonium ion is stabilized by coordination to iron. Moreover, our results demonstrate that the reaction is a potentially good route for the preparation of symmetrical, unsymmetrical and cyclized secondary amines.

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