Metal Complex and Phase Transfer Catalysed Nitric Oxide Reactions

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Benzyl bromides are converted into oxime ethers by bubbling nitric oxide through a solution of the bromide in t-pentyl alcohol–3 M aqueous sodium hydroxide containing a palladium or ruthenium complex as catalyst and a quaternary ammonium salt as phase transfer agent; this provides the first example of a catalytic reaction of halides which involves free or co-ordinated nitric oxide and is also the first report of a phase transfer reaction utilizing nitric oxide as a reactant.

Phase transfer catalysis[1] is a useful method for effecting a variety of metal catalysed processes.[2] One of the most important classes of such reactions are carbonylations, the key step usually being the insertion of carbon monoxide *via* a ligand migration pathway.[3,4]

Splendid work by Bergman and co-workers[5] has shown that co-ordinated nitric oxide can undergo migratory insertion into a metal–alkyl bond. The first examples of the insertion of nitrosonium ion into a metal–carbon bond of a mononuclear[6] and a cluster[7] complex have recently been disclosed. These are, of course, stoicheiometric reactions. There are no examples, to our knowledge, of the reaction of organic substrates with nitric oxide under phase transfer catalysis conditions, in either the absence or the presence of a transition metal complex. This communication describes the conversion of benzylic bromides into oxime ethers using nitric oxide, a palladium, ruthenium, or rhodium complex as the metal catalyst, and a quaternary ammonium salt as the phase transfer agent.

When nitric oxide was bubbled through a solution of t-pentyl alcohol containing benzyl bromide (**1**, Ar = Ph) and tetrakis(triphenylphosphine)palladium(0), 3 M aqueous sodium hydroxide, and benzyltriethylammonium chloride as

$$\underset{(\mathbf{1})}{\mathrm{ArCH_2Br}} + \mathrm{NO} \rightarrow \underset{(\mathbf{2})}{\mathrm{ArCH{=}NOCH_2Ar}}$$

Reagents: $Pd(PPh_3)_4$, PPh_3, $Bu_4N^+HSO_4^-$, 3 M NaOH, t-pentyl alcohol, room temp., 1 atm.

Table 1. Metal complex and phase transfer catalysed reaction of benzylic bromides with nitric oxide.[a]

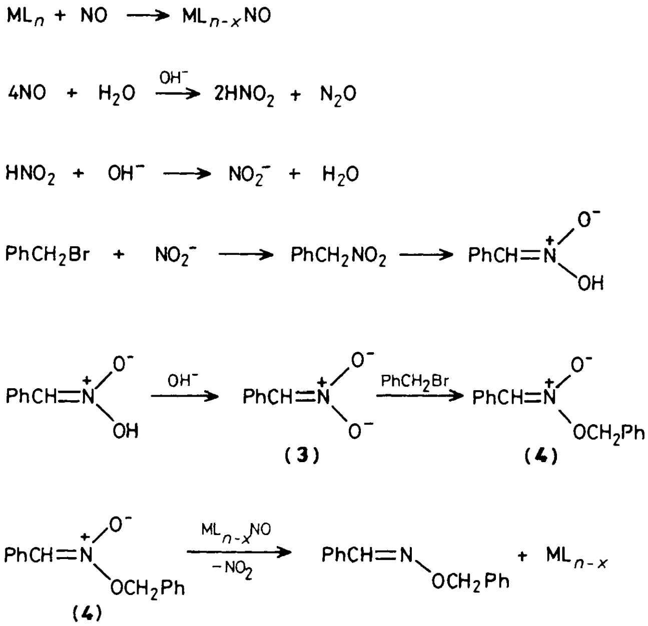
Ar in (**1**)	ML_n	PPh_3	$R_4N^+X^-$[b]	(**2**), %	$(ArCH_2)_2O$, %	Other products, %
Ph	$Pd(PPh_3)_4$	No	A	20[c]	1	
	$Pd(PPh_3)_4$	No	B	23	25	$PhCH_2OH$, 26
	$Pd(PPh_3)_4$	Yes	B	38	4	$PhCH_2OH$, 30
	$Pd(PPh_3)_4$	(PBu_3)	B	36	3	
	$Pd(PPh_3)_4$	Yes	—	—	Trace	
	—	No	B	8	13	$PhCH_2OH$, 35
	$Pd(dba)_2$	No	B	30[d]	6	
	$RuCl_2(PPh_3)_3$	No	B	31	5	
	$RuCl_2(PPh_3)_3$	Yes	B	29	16	
	$Ru(NO)_2(PPh_3)_2$	Yes	B	32	5	
	$[Rh(hd)Cl]_2$	No	B	26[d]	12	
Ph[e]	$Pd(PPh_3)_4$	Yes	B	4[d]	n.d.[f]	
p-MeC_6H_4	$Pd(PPh_3)_4$	Yes	B	33	6	
m-MeC_6H_4	$Pd(PPh_3)_4$	Yes	B	40	19	
o-MeC_6H_4	$Pd(PPh_3)_4$	Yes	B	25	9	
p-FC_6H_4	$Pd(PPh_3)_4$	Yes	B	34	7	
2-$C_{10}H_7$	$Pd(PPh_3)_4$	Yes	B	40	n.d.[f]	

[a] Using 3 M NaOH, t-pentyl alcohol, room temp. for 17 h. Yields are of *pure* materials. [b] A = $PhCH_2NEt_3^+Cl^-$; B = $Bu_4N^+HSO_4^-$. [c] 45 h reaction. [d] 42 h reaction. [e] $PhCH_2Cl$. [f] Yield was not determined.

the phase transfer agent, for 45 h at room temperature, the *O*-benzyl oxime ether (**2**, Ar = Ph) was isolated in 20% yield (+ 1% of dibenzyl ether).† The ratio of substrate : $Pd(PPh_3)_4$: $PhCH_2NEt_3^+Cl^-$ was 25 : 1 : 2. Use of tetrabutylammonium hydrogen sulphate as the phase transfer catalyst, and a 17 h reaction time, afforded the oxime ether in slightly higher yield (23%); however, substantial quantities of dibenzyl ether and benzyl alcohol were also formed (see Table 1 for results). If triphenylphosphine is added to the latter reaction, equimolar with respect to the palladium catalyst, then the yield of oxime ether increases to 38%, and much less dibenzyl ether is formed. Tri-n-butylphosphine is almost as useful as triphenylphosphine. Note that (**2**) is not formed in the absence of the quaternary ammonium salt and base, using benzene or t-pentyl alcohol as the organic phase. The oxime ether is obtained, albeit in 8% yield, in the absence of the palladium catalyst and triphenylphosphine.

Other metal catalysts which can promote the conversion of benzylic bromides into oxime ethers include bis(dibenzylideneacetone)palladium(0) [$Pd(dba)_2$], dichlorotris(triphenylphosphine)ruthenium, dinitrosylbis(triphenylphosphine)ruthenium, and the dimer of chloro(hexa-1,5-diene) rhodium(I) $[Rh(hd)Cl]_2$. Note that added triphenylphosphine does not have a beneficial effect on the ruthenium complex catalysed reactions.

Oxime ethers were isolated in 25—40% yields (*pure* products) from a variety of benzylic bromides using tetrakis(triphenylphosphine)palladium and triphenylphosphine as the metal catalyst system, and tetrabutylammonium hydrogen sulphate as the phase transfer agent. Product yields were significantly lower using benzene or methylene chloride as the organic phase. The reaction is not useful in the case of benzyl chloride, and 1-bromonaphthalene and bromocyclohexane are inert.



Scheme 1

It is conceivable that these reactions proceed *via* the oxime (formed by base catalysed tautomerism of the nitrosoarylmethane)[8] which, under the basic phase transfer conditions, is deprotonated and reacts with additional benzyl halide to give the oxime ether (**2**). The nitrosoarylmethane may arise from a metal (Pd, Ru, or Rh) complex containing nitrosyl and benzylic ligands which then undergoes migratory insertion. The fact that not even traces of an oxime were detected in any of the reactions studied indicates that the reaction may not be

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† The following general procedure was used. A mixture of the quaternary ammonium salt (0.4 mmol) in 3 M NaOH (12.5 ml), and the metal complex (0.20 mmol, also 0.20 mmol of PPh_3 if added) in t-pentyl alcohol (10 ml) was stirred under a nitric oxide atmosphere at room temperature. The benzylic bromide (5.0 mmol) in t-pentyl alcohol (2.5 ml) was then added, drop-by-drop, to the stirred solution and nitric oxide was slowly bubbled through the reaction mixture overnight at room temperature. The layers were separated, and the organic layer was washed with aqueous NaCl, dried, and concentrated. Pure oxime ether was obtained by silica gel thin-layer or column chromatography.

proceeding by such a pathway. An alternative mechanism, not involving a free oxime intermediate, is outlined in Scheme 1 (illustrated for benzyl bromide). Some of the nitric oxide may react with base to form nitrite ion.[9] Indeed, when NO was bubbled overnight through a solution of 3 M NaOH at room temperature (*i.e.* no phase transfer or metal catalyst), and then bis(triphenylphosphine)iminium chloride (PPN^+Cl^-) was added, $PPN^+NO_2^-$ was isolated and identified by elemental analysis, m.p. (223—226 °C; lit.[10] 225—226 °C), and fast atom bombardment mass spectrometry. Reaction of benzyl bromide with nitrite ion under phase transfer conditions would give phenylnitromethane and then the nitronate anion (**3**). Compound (**4**) would then arise by *O*-alkylation.[11] Deoxygenation of (**4**) by a metal nitrosyl would afford the oxime ether and NO_2. Therefore one role of the metal complex may be in the last step in the reaction sequence.

The question arises as to whether nitrite ion alone (*i.e.* without NO) can effect the same transformation as nitric oxide. Sodium nitrite can do so, but in reduced product yield. Repetition of the reaction described in entry 3, Table 1, using $NaNO_2$ instead of NO, affords the oxime in 29% yield (compared with 38%). Therefore, in addition to some of it being converted into NO_2^-, nitric oxide does contribute to the conversion of halide into oxime ether. Also, note that the oxime ether is obtained by reaction of benzyl bromide with sodium nitrite in the absence of a metal catalyst but the yield is significantly lower (16%).

There has been considerable interest in the application of transition metal nitrosyls in organic synthesis.[12] Indeed, the *stoicheiometric* reaction of benzyl halides with $Bu_4N^+[Co(CO)_2(NO)X]^-$ (ref. 13) and with $Ru(NO)_2(PPh_3)_2$ (carbon monoxide atmosphere)[14] to give benzaldehyde oximes and other products has previously been described. Although the product yields are not high, the present reaction is nevertheless the first example of a *catalytic* reaction of halides involving free or co-ordinated nitric oxide (and nitrite). Furthermore, as noted above, it is the first case of any phase transfer process utilizing nitric oxide.

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