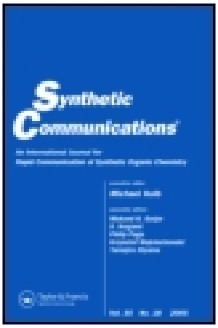

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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To cite this article: Shigekazu Yamazaki (1999): Nickel-Catalyzed Benzylic Oxidation with NaOCl, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 29:13, 2211-2216

To link to this article: http://dx.doi.org/10.1080/00397919908086219

SYNTHETIC COMMUNICATIONS, 29(13), 2211-2216 (1999)

NICKEL-CATALYZED BENZYLIC OXIDATION WITH NaOCl

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ABSTRACT: Ni(bpy)$_2$Cl$_2$ has been found to be an efficient catalyst for the oxidation of various alkylbenzenes with hypochlorite. Substituted toluenes having electron withdrawing group at 4-position were oxidized to the corresponding substituted benzoic acids in excellent yields.

Oxidation is a fundamental transformation in organic synthesis and numerous methods are reported in the literature.[1,2] The laboratory scale liquid-phase benzylic oxidations are generally carried out with a large excess of chromium reagents or manganese reagents.[2] Since the metal residues are environmentally undesirable and often provide problems during work-up, it could be advantageous to develop oxidizing methods requiring only a catalytic amount of metal reagent in combination with appropriate stoichiometric oxidant.[3-7]

In this paper, we present our results on the oxidation of toluenes and alkylbenzenes to the corresponding benzoic acids and carbonyl compounds using NaOCl as the stoichiometric oxidant and a catalytic amount of Ni(bpy)$_2$Cl$_2$. Previously, we have reported that Ni(bpy)$_2$Cl$_2$ is an effective catalyst for epoxidation of olefins with NaOCl.[8] Now we have found that this catalytic system is also effective for benzylic oxidations.

First, the oxidation of toluene was examined in various solvents, and then the influence of the amount of catalyst and oxidant on the oxidation efficiency was examined. The results are summarized in Table 1. A mixture of toluene, nickel catalyst and NaOCl was stirred at room temperature. The oxidation without

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organic solvent proceeded smoothly to give 64% benzoic acid exclusively (Entry 1). The remaining material is toluene only. The use of organic solvent (two-phase system) gave variety of results. The use of acetonitrile as the organic solvent improved the yield of benzoic acid to 76% (Entry 2). The use of benzene or dichloromethane as the solvent afforded a by-product, benzyl chloride (Entries 3, 4).

The initial color of the reaction mixture was black, which indicated the formation of catalytically active nickel species,[8] and the color disappeared when the reaction finished. The oxidant was consumed completely at this time, so the prolonged reaction could not improve the conversion of toluene.

The use of lower amount of catalyst resulted in the formation of a small amount of benzyl chloride (Entries 2, 6), and the use of higher amount of catalyst could improve the yield of benzoic acid only slightly (Entries 2, 7). A large excess of oxidant was required for the higher conversion (Entries 2, 5). This is because a considerable amount of catalytically active species formed by the reaction of nickel complex and NaOCl decomposed non-productively.[8]

The oxidation of toluene with $NiCl_2$ as catalyst was very slow (5% conversion at 6 h). This indicated that bipyridine ligand is essential for this nickel-catalyzed benzylic oxidation.

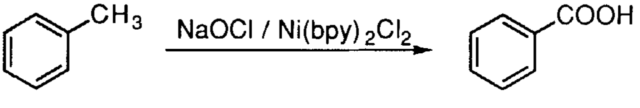

Table 1. Nickel-catalyzed oxidation of toluene with NaOCl [a)]

	NaOCl	$Ni(bpy)_2Cl_2$		Time	Product / %[b)]	
Entry	Mol amt.	Mol amt.	Solvent	min	Benzoic acid	Benzyl chloride
1	10	0.1	-	30	64	0
2	10	0.1	CH_3CN	30	76	0
3	10	0.1	C_6H_6	30	66	15
4	10	0.1	CH_2Cl_2	30	41	8
5	5	0.1	CH_3CN	20	55	trace
6	10	0.05	CH_3CN	45	73	4
7	10	0.2	CH_3CN	15	83	0

a) Reaction at room temperature. b) Isolated yield based on toluene used. The remaining material is toluene.

Oxidation of various substituted toluenes was examined by this catalytic system. The results are summarized in Table 2. The toluenes substituted at 4-position by electron-withdrawing groups such as nitro, chloro, bromo and cyano groups were oxidized smoothly to the corresponding benzoic acids in excellent yields (Entries 1-4). The nitrotoluenes substituted at 2- or 3-position were oxidized to the corresponding benzoic acids in high selectivity, but the conversion is 50% or so under the same reaction conditions as the reaction of 4-nitrotoluene (Entries 5, 6). Oxidation of 4-methoxytoluene, electron-rich toluene, gave a complex mixture which contained ring chlorinated products.

The oxidation of ethylbenzene afforded equal amount of benzoic acid (44%) and acetophenone (45%) (Entry 7). On the other hand, the oxidation of 4-nitroethylbenzene produced 73% of 4-nitrobenzoic acid accompanied with only 2% of

Table 2. Nickel-catalyzed oxidation of substituted toluenes and alkylbenzenes with NaOCl [a)]

Entry	Substrate	Time min	Conv. %	Product (%) [b)]
1	4-Nitrotoluene	60	100	4-Nitrobenzoic acid (98)
2	4-Chlorotoluene	30	100	4-Chlorobenzoic acid (91)
3	4-Bromotoluene	40	100	4-Bromobenzoic acid (85) 4-Bromobenzyl chloride (trace)
4	4-Cyanotoluene	30	100	4-Cyanobenzoic acid (97)
5	2-Nitrotoluene	60	55	2-Nitrobenzoic acid (93) 2-Nitrobenzylchloride (4)
6	3-Nitrotoluene	210	54	3-Nitrobenzoic acid (89) 3-Nitrobenzylchloride (4)
7	Ethylbenzene	70	100	Benzoic acid (44) Acetophenone (45)
8	4-Nitroethylbenzene	180	86	4-Nitrobenzoic acid (73) 4'-Nitroacetophenone (2) 4'-Nitro-1-chloroethylbenzene (3)
9	Diphenylmethane	90	70	Benzophenone (87)

a) Reaction conditions: At room temperature in acetonitrile. Substrate / NaOCl / nickel catalyst = 1 / 10 / 0.1. b) Isolated yield.

4'-nitroacetophenone (Entry 8). Diphenylmethane was oxidized to benzophenone in 87% yield (Entry 9).

The catalytically active species in the nickel complexes catalyzed oxidations are considered to be $LNi^{IV}=O$ or $LNi^{III}OCl$ which were formed by the reaction of oxidant and LNi^{II} complexes.[9-11] The initial step of this benzylic oxidation should involve hydrogen abstraction at benzylic position of the substrates by these nickel species or •OCl formed by dissociation of $LNi^{III}OCl$. The radical mechanism of this nickel-catalyzed benzylic oxidation was supported by the facts of the isolation of chlorinated products at benzylic position in some cases and the formation of benzoic acids from ethylbenzenes (β-scission of alkoxyl radical intermediates and further oxidation).

In general, oxo metal stoichiometric oxidants such as potassium permanganate and chromic acid effectively oxidize toluenes substituted by either electron-withdrawing or -donating groups to the corresponding benzoic acids.[2] Cobalt acetate in combination with bromide ion or manganese acetate is generally used for catalytic liquid-phase oxidation of toluenes with molecular oxygen as primary oxidant in acetic acid as solvent. This oxidation is effective for activated toluenes such as *p*-xylene and cresols, but very difficult for strongly deactivated toluenes such as nitrotoluene.[1] The $RuCl_3$/phase transfer reagent-catalyzed oxidation of toluenes to benzoic acids with NaOCl under pH controlled condition was reported by Sasson and coworkers.[7] The ruthenium-catalyzed oxidation is effective for the ring-deactivated toluenes and gives complex mixture containing chlorinated products for ring-activated toluenes. The method reported in this paper exhibits similar reactivity with Sasson's method.

In summary, oxidation of toluenes and alkylbenzenes with NaOCl catalyzed by $Ni(bpy)_2Cl_2$ provides a convenient method for the transformation of toluenes to carboxylic acid and alkylbenzenes to carbonyl compounds. Especially, substituted toluenes having electron withdrawing group at 4-position were oxidized to the corresponding substituted benzoic acids in excellent yields.

Experimental

The toluenes, alkylbenzenes and amine ligands were commercially available, and used as received. NaOCl was obtained as aqueous solution (1.9-1.5M) and titrated before use. The aqueous $Ni(bpy)_2Cl_2$ catalyst was prepared by dissolving

$NiCl_2 \cdot 6H_2O$ (5.9 g, 25 mmol) and 2 molar amount of the 2,2'-bipyridine (7.8 g, 50 mmol) in distilled water (500 mL) as 0.050 M solution. The catalyst prepared was stood at room temperature for at least 1 day before use.

A typical procedure is as follows: NaOCl (1.84 M, 19.8 mL, 36 mmol) was added to the stirring mixture of 4-nitrotoluene (0.500 g, 3.6 mmol) in acetonitrile (10 mL) and $Ni(bpy)_2Cl_2$ (0.050M aqueous solution, 7.3mL, 0.36 mmol). The mixture was stirred vigorously at room temperature. A fine black precipitate formed in a few minutes upon addition of NaOCl. The reaction mixture got warm at around 15 to 20 min, and the black color of the reaction mixture disappeared within 60 min. After 60 min stirring, the reaction mixture was acidified with conc. HCl (white precipitates), and a small amount of $NaHSO_3$ was added. The mixture was extracted with ethyl acetate (10 mL x 3). The organic layer was washed with brine and dried over anhydrous $Na_2SO_4/MgSO_4$ (1:1 mixture), and then the solvent was distilled out under a reduced pressure. The obtained residue was 4-nitrobenzoic acid (0.596 g, 98%) which was pure by ^1H-NMR analysis.

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(Received in Japan 6 October 1998)