A Novel and Efficient Ceric Ammonium Nitrate Catalyzed Oxidative Nuclear Chlorination of Activated Aromatic Compounds by Acetyl Chloride

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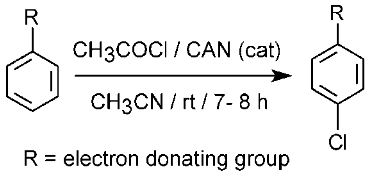
Abstract: A mild and efficient oxidative chlorination of activated aromatic compounds have been achieved in excellent yields using acetyl chloride in the presence of a catalytic amount of ceric ammonium nitrate at room temperature. However, chlorination failed to occur with deactivated aromatic rings.

Key words: ceric ammonium nitrate, nuclear chlorination, acetyl chloride

Halogenation of aromatic systems is one of the most vastly investigated organic reactions and it has been discussed in a wealth of chemical literature.[1] Aromatic chlorides have a wide diversity of uses. They can serve as precursors for numerous functionalities, such as phenols, aromatic ethers and thioethers, aryl amines, aryl hydrazines, benzonitriles, benzaldehydes, fluoroaromatics, silylated aromatics, and aromatic hydrocarbons.[2] There are two fundamental routes to prepare chloro aromatic compounds. The first is through electrophilic aromatic substitution by chlorine[3] and the other is through organometallic intermediates (ArLi or ArMgCl).[4]

Some of the representative chlorinating agents, which replace the traditional use of molecular chlorine in presence of a catalyst including sulfuryl chloride,[5] iodine trichloride,[6] titanium(IV)chloride,[7] copper(II)chloride,[8] antimony(V)chloride,[9] tellurium(IV)chloride,[10] trichloroisocyanuric acid,[11] and poly(*N*-chloromaleimide).[12] Many of these reagents are used either in the presence of an acid or an oxidizing agent. However, some of the regents are unstable and have to be prepared freshly just before their use. Recently, a new chlorinating agent, benzyltrimethylammonium tetrachloroiodate (BTMA ICl_4) has been disclosed[13] with its versatile applications for aromatic compounds. But this methodology is not suitable for substrates containing acid sensitive functionalities as it uses acetic acid as solvent. Depending on the reaction conditions many of the existing aromatic chlorination protocols suffer from nuclear coupling, side chain attack in alkyl benzenes, disproportionation and polymerization.

As a part of our exploration of ceric ammonium nitrate (CAN) as a single electron oxidant,[14] we have found that acetyl chloride acted as an efficient chlorinating agent for activated aromatic compounds in the presence of a catalytic amount of CAN. Acetyl chloride by itself is commonly used for acetylation reactions and has never been reported to chlorinate aromatic compounds. We report here, for the first time, the use of a stoichiometric amount of acetyl chloride as a reagent for monochlorination[15] of activated aromatic nucleus in the presence of a catalytic amount of CAN in acetonitrile (Scheme 1). Thus, a number of activated aromatic compounds were subjected to chlorination reaction and the results are summarized in Table 1.



Scheme 1

The aromatic compounds shown in the Table 1 were converted to their corresponding monochloro derivatives without any detectable dichloro compounds. Aniline and phenol, as expected, furnished solely acetanilide and phenyl acetate respectively with one equivalent of acetyl chloride. It is noteworthy that the use of an excess (2.2 equiv) of acetyl chloride for aniline with an expectation of yielding acetylated monochloro products, furnished uncharacterizable material. Nevertheless, pure acetanilide (entry 8, Table 1) when subjected to the chlorination conditions, furnished solely the corresponding monochlorinated product in good yield. However, *N*,*N*-dimethyl and *N*,*N*-diethyl anilines, two tertiary aromatic amines, were found to afford the corresponding monochloro-products in good yields.

The reaction did not proceed at all with deactivated aromatic compounds such as nitrobenzene, benzaldehyde, ethyl benzoate and benzoic acid. However, while all the other aromatic compounds shown in the Table 1 afforded solely the monochloro compounds, 1,2-methylenedioxybenzene afforded the symmetrical 1,2-dichloro-4,5-methylenedioxybenzene when two equivalents of acetyl chloride and 10 mol% of CAN were used. It is noteworthy that some of the aromatic compounds furnished the nitro aromatics in 5–6% yields along with the monochloro compounds. When stoichiometric amounts or excess of CAN was used, nuclear nitration[16] occurred solely without a trace of chlorinated products.

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Table 1 CAN Catalyzed Chlorination of Activated Aromatic Compounds by Acetyl Chloride

Entry	Substrate	Product	Yield (%)
1	Toluene	4-Chlorotoluene-2-Chlorotoluene (70:30)[a]	70
2	Anisole	4-Chloroanisole-2-Chloroanisole (75:25)[a]	85
3	*p*-Xylene	1-Chloro-2,5-dimethylbenzene	86
4	1,3-Dimethoxy benzene	1-Chloro-2,4-dimethoxybenzene	82
5	1,2-Methylenedioxy benzene	1-Chloro-3,4-methylenedioxy benzene	80
6	*N*,*N*-Dimethylaniline	4-Chloro-*N*,*N*- dimethyl aniline	66
7	*N*,*N*-Diethylaniline	4-Chloro-*N*,*N*- diethyl aniline	62
8	Acetanilide	4-Chloroacetanilide	86
9	Naphthalene	1-Chloronaphthalene	84
10	1-Methoxynaphthalene	4-Chloro-1-methoxy naphthalene	78
11	2-Methoxynaphthalene	1-Chloro-2-methoxy naphthalene	74

[a] Ratio of the two regioisomers

In summary, we have successfully achieved a mild, efficient and novel method of monochlorination of electron rich aromatic moieties by using the cheap and commercially available acetyl chloride in the presence of a catalytic amount of ceric ammonium nitrate.

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(15) General Procedure. To a stirred mixture of the aromatic substrate (1.5 mmol) and freshly distilled acetylchloride (1.52 mmol) in acetonitrile (10 mL), was added ceric ammonium nitrate (0.15 mmol) in one portion under N_2 at room temperature. The reaction mixture was allowed to stir for 7–8 h. After completion of the reaction (the progress of the reaction was monitored by TLC), the reaction mixture was diluted with diethyl ether (25 mL) and washed thoroughly with saturated aqueous $NaHCO_3$ solution (3 × 10 mL), brine (3 × 10 mL) and dried (Na_2SO_4). Volatiles were removed under reduced pressure and the residue obtained was purified by column chromatography over silica gel (2% ethyl acetate in light petroleum) to yield the pure chlorinated product.

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