Selective Oxidation of Methylarenes with Pyridinium Chlorochromate

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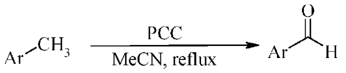
Abstract: A simple and selective method for oxidation of methylarenes, using pyridinium chlorochromate (PCC) is described. This reagent can efficiently oxidize methylarenes to the corresponding aldehydes under mild aprotic conditions.

Key words: methylarenes, PCC, benzylic oxidations, aldehydes

Oxidation of methyl groups on aromatic rings is a frequently used procedure in organic synthesis.[1–6] Most commonly used are transition metal oxidants. In these cases, the initial oxidation products are often more susceptible to oxidation than the starting material. Once a methyl group is attacked, it is likely to be oxidized to the carboxylic acid.[7] While such reactions readily give benzoic acids in high yields, they are rather difficult to stop at the aldehyde stage. Several special procedures have been developed to suppress further oxidation of the aldehyde to the corresponding acid. Basically, there are two approaches: first, the use of special oxidants that oxidize the aromatic methyl group to the aldehyde, but not further,[1] and second, the application of specific reagents that trap the aldehyde formed.[8] The reagents reported for oxidation of benzylic hydrocarbons include benzeneseleninic anhydride,[1] 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ),[2] Co/Mn/Br^-,[3] $Ag(Py)_4S_2O_8$,[4] $Ce(NH_4)_2(NO_3)_6$,[5] O_2/NBS,[6] Ce(IV)/methanesulfonic acid,[9] $RhCl(PPh_3)$,[10] $KMnO_4/Al_2O_3$,[11] O_2/Laccase/ABTS–$(NH_4)_2$[12] and CrO_3/Me_3SiCl.[13] However, all of these procedures exhibit some disadvantages, such as the need for drastic reaction conditions, rather poor yields and long reaction times.

Pyridinium chlorochromate (PCC), a readily available and stable reagent, can oxidize a wide variety of organic substrates such as primary and secondary alcohols with high efficiency.[14] It has also been used for the oxidation of active methylenes (benzylic and allylic) to their corresponding ketones.[15] In our best knowledge there is no report concerning oxidation of methylarenes to their corresponding aldehydes using PCC. We now wish to report here another use of PCC in organic synthesis: the selective oxidation of methylarenes to the corresponding aldehydes under very mild conditions (Scheme 1).



Scheme 1 Oxidation of methylarenes using PCC

To gain some preliminary information on this synthetically useful reaction, *p*-xylene was chosen as a model substrate. We have studied the influence of temperature, mole ratio of oxidant to substrate and solvent to obtain the optimum conditions. Our observations revealed that, amongst the various solvents used, acetonitrile was the most effective and gave high yields with a molar ratio of 1:1 substrate:reagent under reflux condition. Under the optimum conditions, different methyl-substituted aromatic compounds were oxidized to the corresponding aldehydes. The results are presented in the Table 1.

As indicated in Table 1, *o*-, *m*-, *p*-xylenes are oxidized to their corresponding aldehydes in relatively high yields when treated with PCC in refluxing acetonitrile. Under these reactions only one methyl group is oxidized and further oxidation to the corresponding carboxylic acid and also the oxidation of other methyl group did not occur, even using higher molar ratios of PCC and longer reaction times. This indicates the selective oxidation nature of PCC in these reactions. To confirm further, we have examined 1,3,5-trimethylbenzene and durene and observed that, similar to xylenes, only one methyl group was transformed to the aldehyde group. Similarly, toluene and *p*-methoxytoluene under these reaction conditions gave high yields of benzaldehyde and *p*-methoxybenzaldehyde, respectively. Introduction of electron-withdrawing groups, such as bromine and nitro groups, on the aromatic ring retards the oxidation reaction.

In order to investigate the applicability of this procedure in industry, we have carried out the oxidation of *p*-xylene under our optimum reaction conditions on large scale (15–20 mmol) and obtained almost the same yields as in the small-scale reaction. It is also noteworthy that, unlike other oxidative methods, the major drawback of overoxidation of the aldehyde to the carboxylic acid was not observed.

In conclusion we have introduced another efficient use of PCC as a readily available reagent in organic oxidation reactions.

General Procedure for Oxidation of Methylarenes with PCC

To a solution of 1 mmol of PCC in 10 mL of dried MeCN, 1 mmol of the aromatic compound was added, and then the mixture was refluxed for the specified time. After completion of the reaction, the reagent (PCC) was removed by filtration and washed with CH_2Cl_2.

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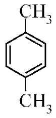
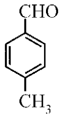
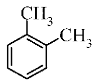
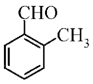
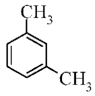
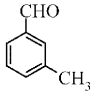
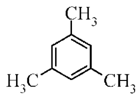
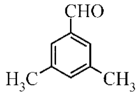
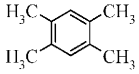
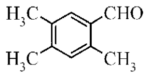
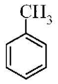
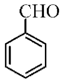
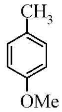
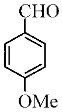
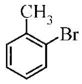
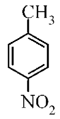
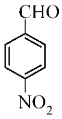
Table 1 Oxidation of Methylarenes Using PCC

Entry	Substrate	Product[a]	Time (h)	Yield (%)[b]
1			2	78
2			3.5	67
3			3	79
4			3	79
5			4	76
6			3	89
7			2.5	82
8			8	10
9			18	–

[a] Products were confirmed by comparison with authentic samples (mp, ^{1}H NMR, GC).

[b] Yield of isolated pure aldehydes.

The CH_2Cl_2 phase was washed with H_2O. The combined extracts were dried with $MgSO_4$. Evaporation of the solvent gave the corresponding aldehyde derivatives. Further purification of products was carried out by column chromatography and then the products were characterized by ^{1}H NMR, GC and comparison with authentic samples.

Acknowledgment

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