Oxidative Esterification of Aromatic Aldehydes Using Polymer-Supported Green Bromine

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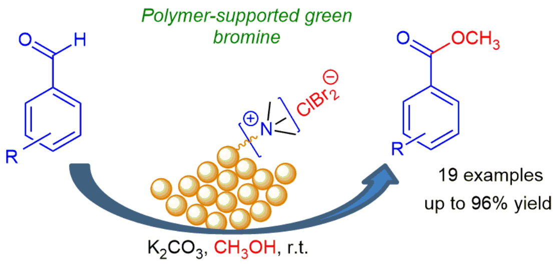

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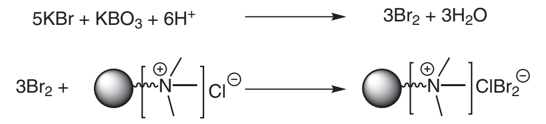
Abstract A facile one-pot green chemical conversion of aromatic aldehydes to alkyl esters is described using polymer-supported bromine chloride resin in the presence of potassium carbonate at room temperature. This eco-friendly methodology with simple workup procedure and recovery and recyclability of the resin makes the transformation simple and efficient.

Key words bromine chloride resin, esterification, oxidation, aldehyde, hypobromite ion

The oxidative one-pot transformation of an aldehyde to an ester is an extremely useful functional-group interconversion in organic synthesis. Several protocols have been reported for this transformation using different transition-metal oxidants such as V_2O_5,[1] $Fe(ClO_4)_3$,[2] $ZnBr_2$,[3] palladium,[4] gold,[5] halogen-derived oxidants such as *N*-halosuccinimide,[6] hypohalites,[7] pyridinium hydrobromide perbromide,[8] molecular bromine,[9] molecular iodine,[10] hypervalent(III)iodine,[11] *N*,*N*-dibromo-*p*-toluenesulfonamide,[12] and $NaIO_4$/LiBr.[13] Despite intensive efforts into the oxidative esterification of aldehydes, the development of a more effective, mild, and eco-friendly method still remains a challenge since many reported methods require heavy-metal oxidants, anhydrous conditions, and extended reaction time or give poor yields of the products.

Application of polymer-supported reagents in organic synthesis has grown over the years due to the convenience in handling, easy workup procedures, and recyclability of the reagents. Polymer-supported iodate,[14] periodate,[15] bromate,[16] hypochlorite, and dichloroiodo resins,[17] used as oxidizing agents, have reported in the literature. However, there is no report on polymer-supported bromine chloride resin in oxidation reactions. In this paper, we describe the preparation of a polymer-supported bromine chloride resin and oxidation reactions of aromatic aldehydes carried out with this reagent.

Gopalakrishnan et al.[18] have reported the preparation of polymer-supported bromine chloride resin by treating commercially available Amberlite IRA-400 chloride resin with bromine in carbon tetrachloride. Since this method involves the use of elemental bromine and carbon tetrachloride, we simplified the preparation of the same bromine chloride resin by treating commercially available, oven-dried IRA-400 resin with a mixture of potassium bromate and potassium bromide in the presence of dilute hydrochloric acid. Bromine liberated from a bromate–bromide mixture in acid medium converts IRA-400 chloride resin into the bromine chloride resin (Scheme 1).



Scheme 1 Preparation of bromine chloride resin using a bromide–bromate mixture

The bromine chloride resin prepared by both methods possesses the same amount of bromine, as indicated by the same increase in the weight of the IRA-400 resin and also by volumetric estimation with $Na_2S_2O_3$ (Table 1). There was no appreciable change in the bromine content after exposure to microwave irradiation for five minutes or storage for five days (Table 2 and Table 3).

Bromine can behave as a mild oxidizing agent under basic conditions due to the formation of hypobromite. This was confirmed through UV-Vis absorption spectral studies. UV absorption spectra were recorded for Winkler's solution, containing potassium carbonate and an aqueous sus-

Table 1 Determination of Bromine Content in the Bromine Chloride Resin

Weight of the resin (g)	Increase in the weight (g)	Volume of $Na_2S_2O_3$(0.05 N) (mL)	Bromine content (mmol/g)	
			Prepared by Br_2/CCl_4	Prepared by Br^-/BrO_3^-
0.5	0.129	10.4	0.8125	0.8062
1	0.258	20.9	1.6187	1.6125
1.5	0.386	31.2	2.4250	2.4125

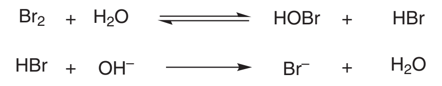
Table 2 Stability of Bromine Chloride Resin under Microwave Irradiation

Entry	Microwave time (min)	Bromine content (mmol/g)
1	0	1.6125
2	0.5	1.6063
3	1	1.5938
4	2	1.5688
5	3	1.5438
6	5	1.5125

Table 3 Stability of Resin during Storage

Entry	Days	Bromine content (mmol/g)
1	0	1.6125
2	1	1.5750
3	2	1.5250
4	3	1.4875
5	4	1.4652
6	5	1.4375

pension of bromine chloride resin, and also for a mixture containing bromine chloride resin and potassium carbonate (Figure 1). The UV spectrum showed absorption bands at λ = 389, 265 nm for Winkler's solution and the aqueous suspension of bromine chloride resin, corresponding to molecular bromine and hypobromite ion, respectively,[19] due to the equilibrium established between molecular bromine and hypobromite ion. Basic potassium carbonate can, however, shift the equilibrium towards hypobromite ion (Scheme 2).



$$Br_2 + H_2O \rightleftharpoons HOBr + HBr$$

$$HBr + OH^- \longrightarrow Br^- + H_2O$$

Scheme 2 Equilibrium of bromine in water

The UV spectrum of Winkler's solution and bromine chloride resin containing potassium carbonate showed an intense absorption band at λ = 265nm corresponding to the hypobromite ion. These observations lead to the conclusion that both Winkler's solution and the bromine chloride resin derived from commercially available Amberlite IRA 400 chloride produces the hypobromite ion in basic medium. In addition, titration with $Na_2S_2O_3$ using starch as an indicator, when one equivalent of potassium carbonate was added to resin containing one equivalent of bromine, also indicated the conversion of bromine into hypobromite. This observation prompted for the use of K_2CO_3 and the resin in equimolar amounts with regard to bromine content for oxidation reactions.

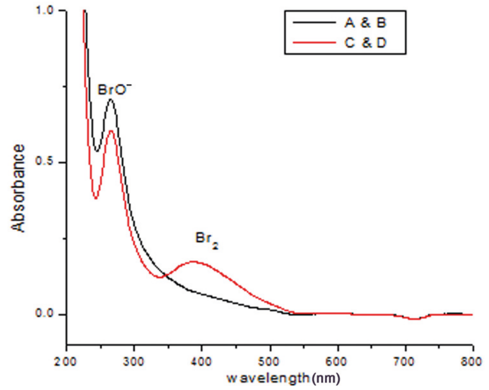
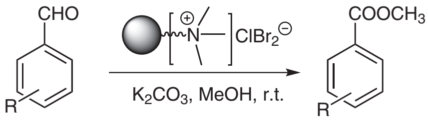


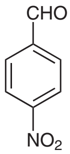
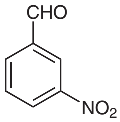
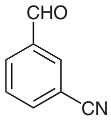
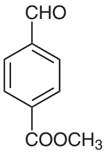
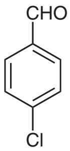
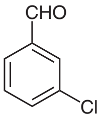
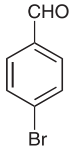
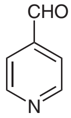
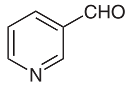
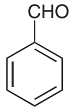
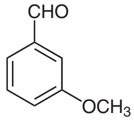
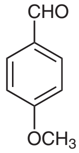
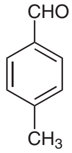
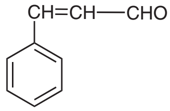
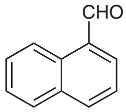
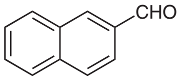
Figure 1 A & B: winkler's solution and aqueous solution of bromine chloride resin. C & D: base + winkler's solution and aqueous solution of bromine chloride resin

For optimizing reaction conditions, oxidation of benzaldehyde was carried out using methanol as solvent in the presence of potassium carbonate. The highest yield of methyl benzoate was obtained in the presence of K_2CO_3 at room temperature. A series of aromatic aldehydes was subjected to similar oxidative esterification using methanol as solvent at room temperature, and the corresponding methyl esters were obtained in good yields (Table 4). Aromatic aldehydes with electron-withdrawing substituents required shorter reaction times than aromatic aldehydes with electron-donating substituents. In all the reactions, isolation of the product was very simple. However, aldehydes with *ortho* substituents gave lower yields, presumably due to steric interactions. Lower yields were obtained when reactions were carried out with ethanol and isopropanol (Table 5), and this may also be attributed to the increased steric crowding in the hemiacetal intermediate. These observations support the probable mechanism of formation of hemiacetal intermediate followed by oxidation of the hemiacetal to the ester (Figure 2).

Table 4 Oxidation of Aldehyde to Methyl Ester Using Bromine Chloride Resin



R = H, CN, NO$_2$, CH$_3$, OCH$_3$, Cl etc

Entry	Substrate	Product **2**	Time (h)	Substrate/ reagent/base	Yield (%)[a]
1		**2a**	0.75	1:2:2	94
2		**2b**	0.5	1:2:2	96
3		**2c**	1	1:3:3	92
4		**2d**	1	1:3:3	91
5		**2e**	4	1:3:3	82
6		**2f**	4	1:3:3	80
7		**2g**	4	1:3:3	86
8		**2h**	2	1:3:3	89
9		**2i**	2	1:3:3	92
10		**2j**	4	1 :3:3	71
11		**2k**	2	1:3:3	82
12		**2l**	2	1:3:3	85
13		**2m**	4	1:3:3	72
14		**2n**	2	1:3:3	50:50[b]
15		**2o**	5	1:3:3	54
16		**2p**	5	1:3:3	62

[a] Isolated yield.
[b] Based on ^{1}H NMR yield.

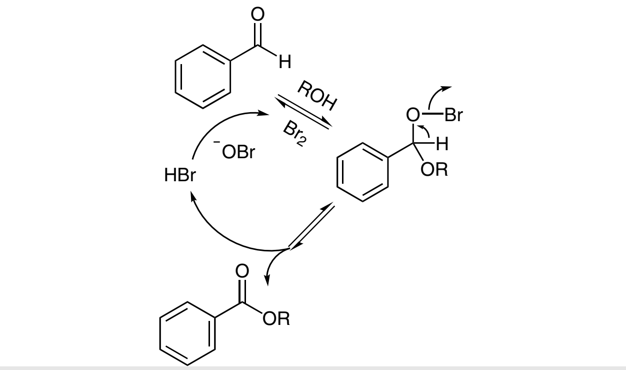


Figure 2 Plausible mechanism for the oxidative esterification of the aldehyde

To study the recyclability of the resin, after the completion of reaction, the resin was collected by filtration, subjected to bromination, and reused in the oxidation of *m*-nitrobenzaldehyde in the presence of methanol and K_2CO_3. This process was repeated six times, and results indicate that the reagent can be reloaded and reused at least five times without significant decrease in the yield as indicated in Table 6.

In conclusion, we have achieved a green chemical method for a facile one-pot conversion of aromatic aldehydes to their respective methyl esters in good yield at room temperature using polymer-supported bromine chloride in the presence of respective methanol and K_2CO_3.[20,21] The bromine chloride resin is prepared by treating commercially available IRA-400 chloride resin with a mixture of potassium bromate and potassium bromide solutions in the presence of dilute hydrochloric acid. The recovery and reusability of the reagent makes the methodology economical.

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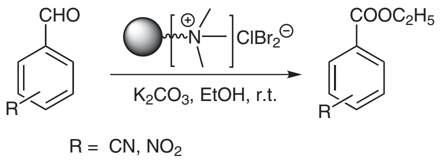
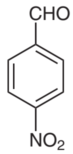
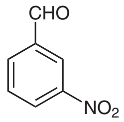
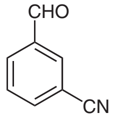
Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1561347.

Table 5 Oxidation of Aldehyde to Ethyl Ester Using Bromine Chloride Resin



Entry	Substrate	Product **3**	Time (h)	Substrate/reagent/base	Yield (%)[a]
1		**3a**	5	1:5:5	68
2		**3b**	5	1:5:5	72
3		**3c**	5	1:5:5	65

[a] Isolated yield.

Table 6 Recyclability of the Resin

Number of recycles	Recovered resin (g)	Product yield (%)[a]
1	0.98	94
2	0.96	92
3	0.95	91
4	0.95	91
5	0.93	90
6	0.87	89

[a] Isolated yield.

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(20) **General Procedure for the Oxidation**
A mixture of bromine chloride resin and K_2CO_3 in MeOH–H_2O (8:2) 3 mL was placed in a round-bottom flask fitted with a magnetic stirrer. To this, the aldehyde (1 mmol, 1 equiv) was added dropwise, and the reaction mixture stirred at r.t. The progress of the reaction was monitored by TLC. After completion of the reaction the mixture was filtered, and the filtrate was extracted with Et_2O. The ether layer was washed with H_2O, brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography, if required, over silica gel (60–120 mesh) using a mixture of PE and EtOAc (9:1) as eluent.

(21) **Procedure for the Preparation of Bromine Chloride Resin**
A solution of 0.1 M KBr–$KBrO_3$ (20 mL) was added to a flask. Oven-dried Amberlite IRA-400 chloride resin (10 g) was added to the flask followed by 5 mL of HCl–H_2O (1:1). The solution was stirred for 5 min. The resin was filtered and washed with H_2O and dried.