

A Convenient and Selective Method for the *para*-Bromination of Aromatic Compounds with Potassium Bromide in the Presence of Poly(4-vinylpyridine)-Supported Peroxodisulfate in Nonaqueous Solution*

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Abstract—A convenient and selective procedure for the *para*-bromination of aromatic compounds has been developed using potassium bromide in the presence of poly(4-vinylpyridine)-supported peroxodisulfate in nonaqueous solution.

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Bromoarenes are useful precursors of organometallic reagents which have been used in the synthesis of biologically active and pharmaceutically important compounds [1–3]. Preparation of brominated aromatic compounds with molecular bromine is a well-known reaction in organic chemistry, but it generally requires transition metal-based catalysts and generates toxic and corrosive hydrogen bromide. Furthermore, direct treatment of activated aromatic compounds with elemental bromine usually resulted in complex mixtures of mono-, di-, and polysubstituted products [4–6].

Besides Br₂ itself (with or without a catalyst), many reagent systems including pyridinium tribromide [7], KBr/sodium peroxyborate [8], tetrabutylammonium tribromide [9], cetyltrimethylammonium tribromide [10], HBr/DMSO [11], LiBr/CAN (ceric ammonium nitrate) [12], KBr/H₂O₂ [13], and tetrabutylammonium peroxodisulfate [14] have also been reported. In most of these methods, the electrophilic species is Br⁺ which is generated *in situ* by reaction of bromide ion with an oxidant [12].

In our studies on the halogenation of aromatic compounds [15–17] we have used poly(4-vinylpyridine)-supported peroxodisulfate and KBr for direct bromination of some activated aromatic rings. In the present communication we report on the use of poly(4-vinylpyridine)-supported peroxodisulfate as mild oxidant

and potassium bromide as source of bromine for the bromination of some activated aromatic compounds under heterogeneous conditions. The results are given in table.

All reactions were performed first at room temperature and then the mixture was heated under reflux for an appropriate time. According to the obtained results, methoxyarenes were converted into the corresponding monobrominated products in excellent yields (see table, run nos. 1–7). *N*-Methylaniline, *N,N*-dimethylaniline, and naphthalen-1-amine were also converted into the *para*-substituted products in high to excellent yields (run nos. 8–10). Diphenylamine yields finally the disubstituted product when the KBr–oxidant–substrate molar ratio is 2:2:1 (Table 1, run no. 11). *o*-Nitroaniline gave rise to 4-bromo-2-nitroaniline in good yield (run no. 12). The bromination of phenol and *o*-chlorophenol also produced the corresponding *para*-substituted products (run nos. 13, 14). Weakly activated arenes such as acetanilide and 6-methoxy-1,2,3,4-tetrahydronaphthalen-1-one were also subjected to the bromination under analogous conditions. However, from the former we obtained only 20% of the brominated product, while the latter was recovered unreacted even after heating for 10 h in boiling acetonitrile (run nos. 15, 16). When the *para* position is blocked, no reaction occurs, and the initial compound is recovered from the reaction mixture (run no. 17). Thus the described procedure ensures selective *para*-bromination

* The text was submitted by the authors in English.

Bromination of aromatic compounds with KBr^a in the presence of poly(4-vinylpyridine)-supported peroxodisulfate

| Run no. | Substrate | Product ^b | Reaction time, h | Yield, ^c % |
|---------|--|--------------------------------------|------------------|-----------------------|
| 1 | Anisole | 4-Bromoanisole | 3 | 98 ^d |
| 2 | 2-Methylanisole | 4-Bromo-1-methoxy-2-methylbenzene | 2 | 97 |
| 3 | 1,3-Dimethoxybenzene | 4-Bromo-1,3-dimethoxybenzene | 4 | 95 |
| 4 | 1,2,4-Trimethoxybenzene | 5-Bromo-1,2,4-trimethoxybenzene | 3 | 95 |
| 5 | 1,2,3-Trimethoxybenzene | 4-Bromo-1,2,3-trimethoxybenzene | 2 | 97 ^e |
| 6 | 1-Methoxynaphthalene | 1-Bromo-4-methoxynaphthalene | 3 | 92 ^f |
| 7 | 2-Methoxynaphthalene | 1-Bromo-2-methoxynaphthalene | 3 | 96 ^g |
| 8 | <i>N,N</i> -Dimethylaniline | 4-Bromo- <i>N,N</i> -dimethylaniline | 2 | 95 ^h |
| 9 | Naphthalen-1-amine | 4-Bromonaphthalen-1-amine | 1.5 | 80 |
| 10 | <i>N</i> -Methylaniline | 4-Bromo- <i>N</i> -methylaniline | 2 | 75 |
| 11 | Diphenylamine | 4,4'-Dibromodiphenylamine | 4 | 80 |
| 12 | 2-Nitroaniline | 4-Bromo-2-nitroaniline | 3 | 90 |
| 13 | Phenol | 4-Bromophenol | 3 | 83 ⁱ |
| 14 | 2-Chlorophenol | 4-Bromo-2-chlorophenol | 4 | 84 ^j |
| 15 | <i>N</i> -Phenylacetamide | <i>N</i> -(4-Bromophenyl)acetamide | 10 | <20 |
| 16 | 8-Methoxy-1,2,3,4-tetrahydronaphthalen-1-one | No reaction | 15 | – |
| 17 | 4-Bromoanisole | No reaction | 15 | – |

^a KBr-to-substrate molar ratio 1.2:1, except for run no. 11 (2:1).^b Products were characterized by their physical constants, comparison with authentic samples, and IR and NMR spectra.^c Yield of isolated product.^d Published data: TBHP/HBr, yield 76% [18]; DBDMH, 18 h, yield 85% [19].^e Published data: CAN/LiBr, 1 h, yield 95% [12]; TBAPD/LiBr, 36 h, yield 83% [14].^f Published data: H₂O₂/KBr, 5 h, yield 72% [20]; Oxone/NaBr, 24 h, yield 85% [21].^g Published data: H₂O₂/KBr, 5 h, yield 72% [20]; TBAPD/LiBr, 24 h, yield 85% [14].^h Published data: CAN/LiBr, 5 h, yield 70% [12]; NBS/HZSM-5, 5 h, yield 80% [22].ⁱ Published data: TBAP/V₂O₅/H₂O₂, 2 h, yield 20% [23]; 4,4-dibromopyrazolone, 20 h, yield 85% [24].^j Published data [25]: NBS/HBF₄·Et₂O, 1.5 to 24 h, yield 78%.

of activated aromatic compounds. Some of the obtained results were compared with those reported in the literature for other methods (see table). It can be seen that our procedure is superior in terms of yield and reaction time.

To conclude, the proposed procedure is advantageous due to accessibility and low cost of the reagents, simple and clean work-up, high product yields, short reaction time, mild and heterogeneous conditions, and excellent selectivity, which make it a useful supplement to the known methods for the bromination of activated aromatic compounds.

EXPERIMENTAL

All products were identified by comparison of their spectral and physical data with those of authentic samples. The purity of the products was checked by

TLC on Polygram SIL G UV 254 silica gel plates. Potassium bromide and other chemicals were purchased from Merck. Cross-linked poly(4-vinylpyridine) was purchased from Fluka.

Preparation of poly(4-vinylpyridine)-supported peroxodisulfate. Concentrated hydrochloric acid, 10 ml, was added to a solution of 8.0 g of potassium peroxodisulfate in 150 ml of distilled water. Poly(4-vinylpyridine), 5 g, was then added, and the mixture was stirred for 2 h and filtered. The precipitate was washed with distilled water (4×20 ml) and dried for 12 h at 40°C. We thus obtained 8.6 g of polymer-supported reagent, 0.6 g of which is equivalent to 1.0 mmol of peroxodisulfate.

General procedure for the bromination of aromatic compounds with potassium bromide in the presence of poly(4-vinylpyridine)-supported peroxodisulfate. An aromatic compound, 1 mmol, was

added to a mixture of 0.143 g (1.2 mmol) of KBr and 0.72 g of poly(4-vinylpyridine)-supported peroxodisulfate (equivalent to 1.2 mmol of peroxodisulfate) in 5 ml of acetonitrile, and the mixture was stirred on heating under reflux for a time indicated in table. The progress of the reaction was monitored by TLC (carbon tetrachloride–diethyl ether, 4:2, or carbon tetrachloride–*n*-hexane, 8:2). When the reaction was complete, the mixture was cooled to room temperature and filtered. Excess bromine was removed from the filtrate by dropwise adding a 1 M sodium sulfite solution. Methylene chloride, 5 ml, was added, and the organic layer was separated in a separatory funnel. After drying over magnesium sulfate and evaporation of the solvent, the crude product was purified by recrystallization or column chromatography on silica gel. The yields are given in table.

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