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Mendeleev Commun., 1994, **4(6)**, 223–224
Mendeleev Communications

Bromination of Aniline with Pyridinium Hydrobromide Perbromide: some Mechanistic Considerations

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In aqueous polar solvents it is suggested that both pyridinium hydrobromide perbromide and molecular bromine are involved in the bromination of aniline.

In the presence of molecular bromine aromatic systems are capable of undergoing electrophilic substitution.[1] In response to a very diverse range of reactivity a number of techniques have appeared for selectively brominating aromatic systems.[2]

Pyridinium hydrobromide perbromide (PHP)[3] has been used for bromination of ketones,[4] for the addition of bromine to alkenes[5] and has received limited attention as a reagent for aromatic bromination.[6,7] Our laboratory has recently reported PHP as a good reagent for monobromination of aromatic amines.[8]

Our present interest is in the mechanism of the bromination process. We would like to determine which species (PHP or Br_2) is acting as the brominating agent in these reactions. Analysis of the products formed in a series of reactions involving the bromination of aniline with PHP or Br_2 in tetrahydrofuran (THF), aqueous THF, ethanol and aqueous ethanol suggest that both the PHP and Br_2 are involved in the bromination process.†

Since the PHP reagent is relatively large compared to molecular bromine, we chose to focus on the amount of *ortho* bromination (*o*/*p* ratio) as a mechanistic probe. The percentage of *ortho* substitution (Table 1) suggests which brominating species is involved in the reaction. Since PHP is very large and the *ortho* position is somewhat hindered, this results in a lower *o*/*p* ratio for the trial using PHP as compared to bromination with molecular bromine in THF.

Additional support for the importance of steric requirements at the *ortho* position comes from competitive bromination experiments starting with *ortho*- and *para*-bromoanilines.‡ The production of the 2,4-dibromoaniline is more facile when starting with *ortho*-bromoaniline. This suggests that the *para* position is more available for formation of an intermediate leading to the dibromoaniline than is the *ortho* position.

In reactions 1 and 2, the *o*/*p* ratio is higher with molecular bromine than with the bulky PHP. This suggests that steric hindrance is a factor between the bulky PHP complex and the amine group of the aniline. As reaction 1 demonstrated, there is a slow release of molecular bromine from the PHP into the solution to give some *ortho* substitution. Reactions 5 and 6 suggest that there must be some molecular bromine being released into the system as the percent of *ortho* substitution is nearly equivalent using PHP and Br_2.

Because PHP is a salt, its ability to release Br_2 into the solution can be enhanced by increasing the polarity of the reaction mixture. This is accomplished by addition of water. This enhancement is demonstrated in reactions 3 and 4 where 10% water (5 ml) was added to the solution producing nearly equivalent *o*/*p* ratio with both PHP and molecular bromine. The decrease in *o*/*p* ratio in both reactions 3 and 4, as compared to reactions 1 and 2, may be accounted for by the formation of HBr and HOBr as shown in part A of Scheme 1.

In reactions 5 and 6, the *o*/*p* ratio is still smaller than in reaction 1 and 2, but it is larger than in reactions 3 and 4. This variation may be accounted for by the formation of an EtOBr species, as shown in part B of Scheme 1. (Gervat and coworkers have reported a similar reaction in which MeOBr is used to brominate anilines.[8])

† A solution of solvent (25 ml) containing 0.001 mol of brominating reagent was added dropwise over a period of 1 h to a magnetically stirred solution of 0.001 mol of aniline contained in 25 ml of solvent. After addition was complete, the mixture was stirred for an additional 15 min. The reaction was then quenched with sodium hydrogensulfite, filtered, dried and analysed by GC-MS (Hewlett-Packard instrument) with a selective ion monitoring (SIM) program for HPG 1034B software for a MS ChemStation (DOS series).

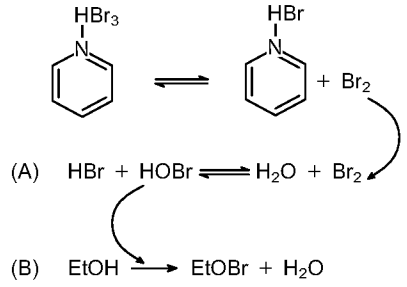
The ratio percent of product ion fragments is obtained by autointegration of the chromatogram where ion peak with the largest area is designated as 100%. Relative ratios of products are obtained by comparison of the ratio percent of product ion fragments to the ratio percent of ion fragments from a standard solution containing 0.001 mol aniline, 0.001 mol *o*-bromoaniline, *p*-bromoaniline and 0.001 mol dibromoaniline.

‡ All reactions were conducted by stirring the reactants at room temperature. Aliquots were removed periodically and the reaction rapidly quenched by treatment with aqueous sodium hydrogensulfite. The products were analysed using a Hewlett-Packard GC-MS instrument with selective ion monitoring software. All experiments were conducted at least in triplicate and all GC-MS data are averages of at least three analyses.

Table 1 Percentage of products formed and percentage of *o*-bromoaniline formed in THF, THF/10% H_2O, ethanol, ethanol/10% H_2O solutions.[a]

Reaction	Solvent	Br(+) source	Aniline (%)	*o*-Bromoaniline (%)	*p*-Bromoaniline (%)	*o*/*p* Ratio	Dibromoaniline (%)
1	THF	PHP	30	16	53	0.30	1
2	THF	Br_2	29	36	23	1.57	12
3	THF/H_2O	PHP	36	7.5	56	0.13	0.5
4	THF/H_2O	Br_2	34.5	6.5	52.5	0.12	6.5
5	EtOH	PHP	42.5	7	36.5	0.19	14
6	EtOH	Br_2	47	4.5	35.5	0.13	13
7	EtOH/H_2O	PHP	56	4.5	18	0.25	21.5
8	EtOH/H_2O	Br_2	58.5	4.5	22.5	0.20	14.5

[a] Yields reported are the averages of several trials.



Scheme 1

This species (EtOBr) is more compatible than the HOBr with the alcoholic solution. Also, the ethyl group by virtue of its electron releasing ability should enhance the stability of the EtOBr. These factors may have provided the slight increase in the *o*/*p* ratio in reactions 5 and 6 compared to reactions 3 and 4. In reactions 7 and 8, the amount of *ortho* substitution was as expected. The reaction in EtOH/H_2O was more polar than reactions 5 and 6. Therefore, it is to be expected that there was an increase in Br_2 being released and subsequently an increase in the amount of *ortho* substitution. Reactions 7 and 8 also produced a larger *o*/*p* ratio compared to reactions 3 and 4. This increase in *o*/*p* ratio may be due to HOBr reacting with the solvent EtOH to produce EtOBr, which acts as the brominating species. As we previously stated, the EtOBr is superior to the HOBr in the alcoholic solution and gives a different substitution ratio. The formation of dibromoaniline from bromination of aniline seems more likely to occur with increased solvent polarity and is enhanced by the formation of EtOBr.

It is apparent that both steric factors and the release of molecular bromine are important in determining the substitution orientation. From these experiments we wish to suggest that both PHP and Br_2 are involved in the bromination reaction. This conclusion is also supported by the work of Sharma *et al.*[10] involving the bromination of phenols and anisoles.

We have demonstrated that the addition of water to reaction mixtures containing PHP can give brominated aniline products in yields nearly equivalent to those obtained by identical reactions with molecular bromine. We feel that the ability to control the release of bromine from PHP by the addition of water to the reaction mixture may be a potentially useful and efficient way to do bromination chemistry while avoiding the hazards of working directly with molecular bromine.

We gratefully acknowledge the Robert A. Welch Foundation for generous financial support of this research project.

References

1 R. O. C. Norman and R. Taylor, *Electrophilic Substitution in Benzenoid Compounds*, Elsevier, New York, 1965, p. 119; C. A. Buebler and D. E. Pearson, *Survey of Organic Synthesis*, Wiley-Interscience, New York, 1970, p. 392.
2 D. E. Pearson, R. D. Wysong and C. V. Breder, *J. Org. Chem.*, 1967, **32**, 2358; W. D. Watson, *J. Org. Chem.*, 1985, **50**, 2145; K. Smith and M. Butters, *Synthesis*, 1985, 1157; G. A. Olah, L. Ohannesian and M. Arvanaghi, *Synthesis*, 1986, 868.
3 PHP prepared according to L. F. Fieser, *Experiments in Organic Chemistry*, D. C. Heath and Company, Boston, 1957, p. 65.
4 C. Djerassi and C. R. Scholz, *J. Am. Chem. Soc.*, 1948, **70**, 417.
5 L. F. Fieser, *J. Chem. Educ.*, 1954, **31**, 291; C. L. Arcus and H. E. Strauss, *J. Chem. Soc.*, 1952, 2669.
6 R. E. Banks, R. N. Haszeldine, J. V. Latham and I. M. Young, *J. Chem. Soc.*, 1965, 594.
7 K. Piers, C. Meimaroglou, R. V. Jardine and R. K. Brown, *Can. J. Chem.*, 1963, **41**, 2399.
8 W. P. Reeves and R. M. King II, *Synth. Commun.*, 1993, **23**, 855.
9 S. Gervat, E. Leonel, J. Barraud and V. Ratovelomanana, *Tetrahedron Lett.*, 1993, 2115.
10 S. Sharma, J. Rajaram and J. C. Kuriacose, *Indian J. Chem.*, 1977, **15B**, 294, 372.

Received: Cambridge, 22nd July 1994
Moscow, 4th August 1994; Com. 4/04513K