1 / VOL. 3, NO. 2
THE CHEMICAL EDUCATOR
© 1998 SPRINGER-VERLAG NEW YORK, INC.
ISSN 1430-4171
http://journals.springer-ny.com/chedr
10.1007/s00897980191a

Laboratories and Demonstrations

Bromination of Aromatics With Pyridinium Hydrobromide Perbromide: An Organic Laboratory Experiment

W. PRESTON REEVES*, RUFUS M. KING, II, LYNETTE L. JONAS, OYVIND HATLEVIK, CUONG V. LU, AND BRIAN SCHULMEIER
Department of Chemistry
Texas Lutheran University
Seguin, Texas 78155
reeves_p@txlutheran.edu

These experiments may be conducted on either the microscale or the macroscale level.

Bromination of aniline and anisole derivatives with pyridinium hydrobromide perbromide (PHP) has been selectively achieved. By selecting appropriate reaction conditions, monobrominated, dibrominated, and, in some instances, tribrominated products may be obtained. PHP provides a safe and environmentally friendly way to conduct aromatic brominations. Pedagogic opportunities for this experiment are wide-ranging. GC-MS may be used for the separation of product mixtures. Steric and solvent effects may also be discussed as the scope and limitations of this technique are investigated in the organic laboratory.

Bromination, as an example of electrophilic aromatic substitution, has long been a fixture in the organic laboratory [1].

ISSN 1430-4171
http://journals.springer-ny.com/chedr
S 1430-4171 (98) 02191-5

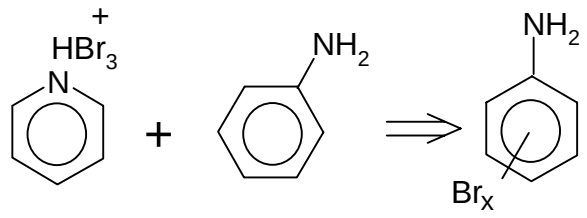

FIGURE 1. BROMINATION OF ANILINE BY PHP.

In recent years, microscale experimentation and safety factors have made the use of molecular bromine less attractive for these reactions. As part of an ongoing undergraduate research project, we have found that pyridinium hydrobromide perbromide (PHP) is an effective reagent for brominating activated aromatics (Figure 1), particularly aniline [2] and anisole [3] derivatives.

By careful selection of PHP reaction conditions, one may selectively obtain monobrominated, dibrominated, and, in some instances, tribrominated products from aromatic amines. If mixtures are obtained, they may be analyzed by GC-MS, which provides an additional pedagogic opportunity for this experiment. Analysis by GC-MS provides an excellent tool for isotope-ratio discussions about the incorporation of various numbers of bromine atoms into the products. The products are generally easily separated by GC, and their mass spectral data are quite distinctive.

Relative reactivities of substrates may be compared by allowing mixtures to compete for a limited amount of PHP. Once again, GC-MS is used for product identification. Generally, monosubstitution products consist of mixtures of ortho and para isomers. The ratio of these products is controlled by steric and electronic factors. *N*,*N*-Dimethylaniline, for example, gives monobromo-*N*,*N*-dimethylaniline in 95% yield, with an ortho/para (*o/p*) ratio of 1:94.

These reactions have been successfully conducted with numerous examples of both aromatic amines and aromatic ethers. Table 1 and Table 2 give results for suggested reactions that may be suitable for an instructional organic laboratory.

All of the above reactions are suitable for use in the undergraduate organic laboratory. However, time constraints may limit the use of some of the less reactive substrates in some cases.

ISSN 1430-4171
http://journals.springer-ny.com/chedr
S 1430-4171 (98) 02191-5

TABLE 1. Bromination of Amines.

Starting Material	% monosubstitution	ortho/para	% disubstitution
Aniline	87	(19/68)	5
Aniline*	-	-	98
N,N -Dimethylaniline	95	(1/94)	1
o -Anisidine	82	(17/65)	7
p -Anisideine	77	-	16
m -Anisidine	68	-	19
o -Toluidine	79	(15/64)	13
p -Toluidine	81	-	11
m -Toluidine	76	(1/2)	11
N -Methylaniline	86	(8/78)	2
N -Ethylanililne	91	(6/85)	-
o -Ethylaniline	91	(12/79)	-
p -Nitroaniline*	76	-	-
Ethyl-*p* -aminobenzoate	75	-	-
2-Methoxy-5-methylaniline	91	-	-
2-Aminopyridine	92	-	-

In these reactions, the amine/THF solution was treated with 5 m 1 of 10% HCIL of 10% prior to HCI before adding the PHP

As would be expected, the reactions are facilitated by electron-releasing substituents on the aromatic system. This allows for the possibility of considerable variation in the organic laboratory. These experiments may be conducted on either the microscale or the macroscale level. With the wide variations possible with inexpensive substrates, and the ease of experimental technique, these preparations are ideal for interfacing the organic laboratory with instrumental techniques.

ISSN 1430-4171
http://journals.springer-ny.com/chedr
S 1430-4171 (98) 02191-5

TABLE 2. Bromination of Ethers.

Starting Material	Product	Time/hours	Yield
Anisole	*p* -Bromoanisole	4	95% isolated
p -Methylanisole	2-Bromo-4-methylanisole	5	60% GC
Anisole	2,4-Dibromoanisole	25	74% isolated
1,4-Dimethoxybenzene	Bromodimethoxybenzene	9	60% GC
1,4-Dimethoxybenzene	Dibromodimethoxybenzene	19	80% isolated
1-Methoxynaphthalene	Bromomethoxynaphthalene	1	100%

Experimental Safety Precautions

The aromatic amines and aromatic ethers used are flammable and are considered irritants. They should be handled with gloves, and under a hood or in a well-ventilated area. Pyridinium hydrobromide perbromide is corrosive and classified as a lachrymator. This compound should be transferred under a hood and handled with gloves. Pyridinium hydrobromide perbromide may be purchased from Aldrich or prepared as described by Fieser [4].

Preparation of Monobrominated Aromatic Amines

Pyridinium hydrobromide perbromide (0.001 mol) dissolved in tetrahydrofuran (25 mL) was added dropwise over a 45-minute period to a stirred solution of aromatic amine (0.001 mol) in THF (25 mL). In some cases, decane was added as an internal gas-chromatographic standard. The solution was then stirred for an additional 15 minutes. The mixture was filtered, if any salt had separated, treated with 10% aqueous sodium bisulfite (2×25 mL) to remove any excess bromine, dried ($MgSO_4$), and analyzed by GC-MS. In several instances the product was isolated by distillation. Yields of 75–95% may be anticipated.

Preparation of Dibrominated Aromatic Amines

The reactions were carried out as described above, except that 0.002 mol PHP was added to 0.001 mol of amine. In the dibromination reactions, the solvent was either

ISSN 1430-4171
http://journals.springer-ny.com/chedr
S 1430-4171 (98) 02191-5

25 mL of glacial acetic acid or 20 mL THF containing 5 mL of water. Yields of 70–95% were obtained.

Preparation of Tribrominated Aromatic Amines

For tribromination, a solution of 0.003 mol PHP was added dropwise over 1 hour to 0.001 mol amine in 20 mL acetic acid containing 5 mL of water. From aniline, monobromoaniline was obtained in 87% yield (*o/p* ratio 19/68), dibromoaniline in 95% yield, and tribromoaniline in 95% yield.

Preparation of Monobromoanisole

Anisole (0.109 mL, 0.001 mol) was dissolved in glacial acetic acid (10 mL). This solution was placed in an ultrasonic cleaning bath (Branson, Model 5200) and a warm solution of pyridinium hydrobromide perbromide (0.640 g, 0.002 mol) in 10 mL acetic acid was added. The mixture was sonicated for one hour.

The solution was treated with solid sodium bisulfite to remove any remaining bromine, suction filtered, and the filtrate was rinsed with ether. The solution was extracted with ether (2 × 20 mL) and washed with 10% sodium bicarbonate (3 × 20 mL). The combined ether layers were dried ($MgSO_4$), the ether was evaporated, and the product analyzed by GC-MS. In some cases, the product was then isolated by distillation. The yield of monobromoanisole was 94%.

Preparation of Dibromoanisole

The preparation was conducted as described for the monobromination, except that 0.003 mol PHP in 15 mL of glacial acetic acid was added to the anisole (0.001 mol) contained in 8 mL of acetic acid and 2 mL of 48% hydrobromic acid. The isolated yield of 2,4-dibromoanisole was 74%.

Competitive Reaction Studies

In a typical study, two substrates (0.002 mol each) were dissolved in 50 mL of a solvent mixture of 10% water, 40% acetic acid, and 50% diethyl ether. This magnetically stirred mixture was treated with 0.0005 mol of PHP. The reaction was

ISSN 1430-4171
http://journals.springer-ny.com/chedr
S 1430-4171 (98) 02191-5

generally complete after 1 minute as indicated by a discharge of color. The products were then analyzed by GC-MS.

ACKNOWLEDGEMENT

We wish to thank the Robert A. Welch Foundation for financial support during the development of these experiments.

REFERENCES

1. Adams, R.; Johnson, J. J. *Laboratory Experiments in Organic Chemistry***,** 4th ed.; Macmillan: New York, 1949; p 333.

2. Reeves, W. P.; King, R. M., II. *Synthetic Communications*, **1993,** *23*, 855.

3. Reeves, W. P.; Lu, C. V.; Schulmeier, B.; Jonas, L. L.; Hatlevik, O. *Synthetic Communications*, **1998,** *28*, 499.

4. Fieser, L. F. Experiments in Organic Chemistry, 3rd ed.; Heath: Boston, 1957; p 65.