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SELECTIVE BROMINATION OF AROMATIC ETHERS WITH PYRIDINIUM HYDROBROMIDE PERBROMIDE

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ABSTRACT: In aqueous polar solvents, various aromatic ethers were selectively brominated using pyridinium hydrobromide perbromide.

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 aromatics.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}

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As previously reported, we have found PHP to be a good reagent for selective monobromination of aromatic amines.⁸

We now wish to report the extension of this method to include aromatic ethers. By judicious choice of reaction conditions (see experimental part), we have selectively mono- and dibrominated anisole, p-methylanisole and p-dimethoxybenzene. Monobromination products also have been obtained from o-methoxybenzaldehyde and from 1-methoxynaphthalene. Attempted bromination of propiophenone was not successful. Starting material was recovered.

These findings suggested that electronic effects are very important in this process. Consideration of the electronic effects leads one to predict an increase in the relative rate of reaction for mono and dibromination as the number of electron releasing groups increases. However, comparative studies indicated that anisole reacted more rapidly than either of the para substituted analogues. This indicates that steric factors are also important.

Additional comparative rate studies were conducted allowing two reactants to compete for a limited amount of brominating agent (PHP). Both o-methylanisole and 1,3-dimethoxybenzene proved to be more reactive than anisole. 1,3-dimethoxybenzene is in turn more reactive than the mmethylanisole. The "empty" para site is both electronically activated and sterically open and thus seems to be the preferred position for substitution when available.

The decrease in the rate of monobromination with *para* substitution suggests that the bromination species is probably a large complex involving the

pyridinium moiety. This could account for the decrease in reaction rate even though substitution is on a system with more electron releasing groups. The ensuing conversion to the dibromo compounds occurs only with difficulty.

Solvent effects are also important in these reactions. Increased solvent polarity, as a general trend, gives a more facile bromination. This trend was also noted in our previous work with the amine series.^{8,9}

With varying reaction conditions, we have been able to selectively mono and dibrominate anisole, p-methylanisole, and p-dimethoxybenzene with the use of PHP. Comparative reactivity suggests that steric as well as electronic and solvent effects are important in the facility of this reaction. With the selectivity offered by PHP as well as the ease of handling and safety of this reagent, it would be worthy of serious consideration for bromination of activated aromatic systems.

EXPERIMENTAL

GC-MS analyses were conducted on a Hewlett-Packard 5890 instrument using the HPG 1034B software for MS ChemStation (DOS series). NMR spectra were obtained on a Varian Unity Plus 300 MHz instrument.

Monobromination of Anisole: Anisole (0.001 mol) was added to PHP (0.002 mol) dissolved in 50 ml of a solvent mixture of 10% water, 40% acetic acid, and 50% ethyl ether. The solution was stirred magnetically for 4 hours. The reaction was then quenched by treatment with sodium hydrogen sulfite, filtered, dried (MgSO₄) and analyzed by GC-MS.

For isolations, the quenched reaction was saturated with sodium chloride and extracted with ethyl ether. The ether solution was washed with 5% aqueous hydrochloric acid (3 x 50 ml), then with 5% sodium bicarbonate, then water and finally dried (anhydrous MgSO₄). Distillation yielded p-bromoanisole in 94.9% yield, bp 223° (lit¹⁰ bp 223°). ¹H NMR δ :s(3H) 3.79, d(2H) 6.79, d(2H) 7.38.

Dibromination of Anisole: The reaction was conducted as above except a PHP:anisole ratio of 4:1 was used in a solvent of 40% water and 60% acetic acid was used and the solution stirred for 25 hours. Isolated yield 74%, mp $60^{\circ}-62^{\circ}$, (lit¹¹ mp = 61.3°). ¹H NMR δ :s(3H) 3.41, d(2H) 6.30, dd(2H) 6.91, d(1H) 7.20. ¹³C NMR δ :56.6, 112.7, 113.0, 113.3, 131.4, 135.6, 155.6.

Monobromination of 4-Methylanisole: A PHP:4-methylanisole ratio of 3:1 was stirred for 5 hours in a solvent of 10% water, 40% acetic acid and 50% ether. GCMS and GC indicated monobromination of starting material in about 60% yield. This product was not isolated.

Dibromination of 4-Methylanisole: A PHP:4-methylanisole ratio of 5:1 was stirred for 7 hours in a solvent of 70% water and 30% acetic acid. GC and GCMS indicated a mixture of dibromomethylanisoles in 90% yield. No attempt was made to separate these products. Monobromination of p-dimethoxybenzene: A PHP:p-dimethoxybenzene ratio of 2:1 was stirred for 70 hours in a solvent mixture of 10% water, 40% acetic acid and 50% ethyl ether. Periodic monitoring of this reaction revealed a 60% conversion to monobromo product after 9 hours. GC-MS analysis indicated formation of 2-bromo-1, 4-dimethoxybenzene. After 70 hours, the product distribution was 93% monobromodimethoxybenzene and 7% dibromodimethoxybenzene. These products were not isolated.

Dibromination of p-dimethoxybenzene: A PHP:p-dimethoxybenzene ratio of 4:1 in a solvent of 40% water and 60% acetic acid was stirred for 19 hours. A quantitative conversion to 2,5-dibromo-1,4-dimethoxybenzene was obtained. Isolated yield 80.6% of a solid mp 142°, (lit¹² mp = 142°). ¹H NMR δ :s(3H) 3.85, s(1H) 7.11. ¹³C NMR δ :57.0, 110.5, 117.2, 150.6.

Monobromination of 1-methoxynaphthalene: PHP:1-methoxynaphthalene in a ratio of 2:1 was stirred for one hour in a solvent of 10% water, 40% acetic acid and 50% ether. A similar flask was sonicated in a laboratory ultrasonic cleaner for one hour. In both cases GC-MS indicated a quantitative conversion to a monobromomethoxynaphthalene. Attempts to dibrominate were not successful.

Monobromination of o-methoxybenzaldehyde formed a brominated product in low yield (8%).

Comparative Reaction Studies:¹³ Two reactive substrates (0.002 mol of each) were dissolved in 50 ml of a solvent mixture of 10% water, 40% acetic acid and 50% diethyl ether. This was then treated with 0.0005 mol of PHP. The reaction, monitered by GCMS, was complete after 1 minute. Both 2-methylanisole and 3-methoxyanisole were more reactive than anisole, however, anisole was more reactive than 1,4-dimethoxybenzene. 1,3-dimethoxybenzene was more reactive than the 3-methylanisole.

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REFERENCES

- Norman, R.O.C. and Taylor, R. "Electrophilic Substitution in Benzenoid Compounds," Elsevier, New York, 1965, p. 119; Buehler, C.A. and Pearson, D.E. "Survey of Organic Synthesis," Wiley-Interscience, New York, 1970, p. 392.
- Pearson, D.E., Wysong, R.D. and Breder, C.V. J. Org. Chem. 1967, 32, 2358; Watson, W.D., J. Org. Chem. 1985, 50, 2145; Smith, K. and Butters, M., Synthesis, 1985, 1157; Olah, G.A., Ohannesian, L. and Arvanaghi, M. Synthesis, 1986, 368.
- 3. PHP prepared according to L.F. Fieser. "Experiments in Organic

PYRIDINIUM HYDROBROMIDE PERBROMIDE

Chemistry," D.C. Heath and Company, Boston, 1957, p. 65.

- 4. Djerassi, C. and Scholz, C.R. Am. Chem. Soc. 1948, 70, 417.
- Fieser, L.F. J. Chem. Educ. 1954, 31, 291; Arcus, C.L. and Strauss, H.E. J. Chem. Soc. 1952, 2669.
- 6. Banks, R.E., Hasszeldine, R.N., Latham, J.V. and Young, I.M. J. Chem. Soc., 1965, 594.
- 7. Piers, K., Meimaroglou, C., Jardine, R.V. and Brown, R.K. Can. J. Chem. 1963, 41, 2399.
- 8. Reeves, W.P. and King II, R.M. Synth. Commun. 1993, 23, 855.
- 9. Reeves, W.P. Lu, C.V. and Russel, J.S. Mendeleev Commun. 1994, 223.
- Shriner, R.L., Fuson, R.C. and Curtin, D.Y., "The Systematic Identification of Organic Compounds," 4th Edition, John Wiley and Sons, Inc., New York, 1956, P. 307.
- Heilborn, I., "Dictionary of Organic Compounds, Vol. II," Oxford Univ. Press, New York, 1953, p. 104.
- Beilstein, "Handbuch Der Organischen Chemie," Band VI, Edwards Brothers, Inc., Ann Arbor, Michigan, 1943, p. 854.
- 13. We wish to thank a referee for suggesting these experiments.

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