

SYNLETT Spotlight 135

1,3-Dibromo-5,5-dimethylhydantoin

Compiled by Ashrafal Alam



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

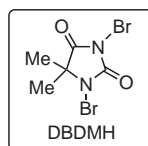
Ashrafal Alam was born in Sherpur, Bangladesh in 1973. After completion of his undergraduate (B.Sc.) and postgraduate degree (M.Sc.) in Organic chemistry at Shahjalal University of Science and Technology, Sylhet, Bangladesh, he joined the research group of Professor Sadao Tsuboi (Okayama University, Japan) to pursue his Ph.D. His prime research interest focuses on the formation of symmetric and asymmetric C–C bonds towards the synthesis of natural products.

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Introduction

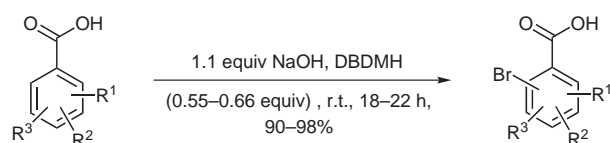
Aromatic bromination with elemental bromine is one of the most widely used and extensively studied reagents.¹ Owing to low reactivity, high toxicity, and handling inconvenience, some alternative brominating agents have been developed. However, a stable, solid reagent is always preferred, particularly for small-scale reactions that require a specific amount of brominating reagent. On the other hand, getting regioselective monobromination is also important, because it is very common to obtain a mixture of monobromides and dibromides.² The commercially available 1,3-dibromo-5,5-dimethylhydantoin (DBDMH) meets most of the requirements mentioned. It is an excellent reagent for the bromination of aromatic rings, particularly for phenols and polyphenols. It gives

excellent yields with a variety of aromatic rings including protected and unprotected phenol and polyphenol derivatives, and those that contain carboxylic acids. The reaction is usually faster and the conditions are mild (at or below room temperature). In addition to the bromination activity, we found it to be an excellent oxidant for the oxidation of thiols to disulfides in extremely high yield.



Abstracts

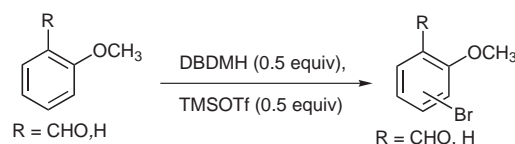
(A) Auerbach et al.³ reported a useful method for bromination of activated benzoic acids using the DBDMH in aqueous NaOH. They reported high yields (90–98%) and purity (99.9%) for bromides of several benzoic acids. It was also shown that DBDMH gave better yield than NBS.



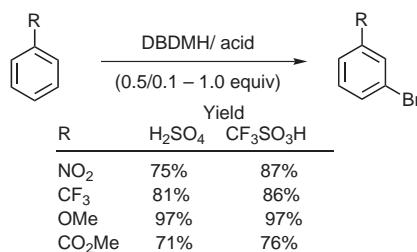
$R^1, R^2, R^3 = 3,4,5\text{-(OMe)}_3$
 $R^1 = R^2 = \text{H}; R^3 = 2\text{-OMe}$
 $R^1 = \text{H}; R^2, R^3 = 2,3\text{-(-OMe)}_2$

$R^1, R^2, R^3 = 3,4,5\text{-(OMe)}_3; 2\text{-Br}; 91\%$
 $R^1 = R^2 = \text{H}; R^3 = 2\text{-OMe}; 5\text{-Br}; 98\%$
 $R^1 = \text{H}; R^2, R^3 = 2,3\text{-(OMe)}_2; 6\text{-Br}; 90\%$

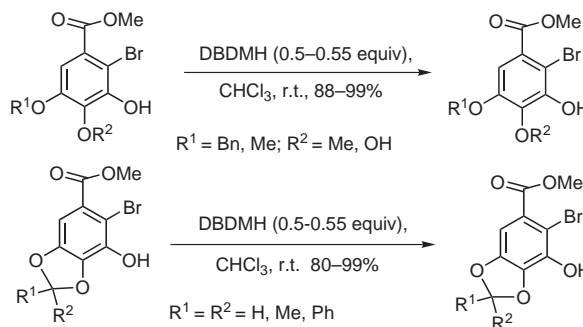
(B) Chassaing et al.⁴ reported the enhanced reactivity of DBDMH in the presence of trimethylsilyl trifluoromethanesulfonate. They obtained very good yield of monobromide in the presence of TMSOTf, whereas without TMSOTf, either a mixture of bromides or starting material was recovered.



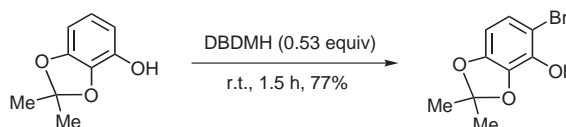
(C) Similarly, Eguchi et al.⁵ used DBDMH in the presence of organic and inorganic acids of pK_a values less than -2 to get the monobromide in excellent yields. It gave very good yields even for aromatics having electron-withdrawing substituents. For some cases, a catalytic amount of acid was sufficient.



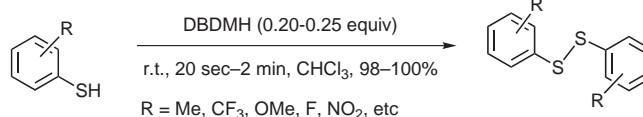
(D) Recently, we investigated the bromination of a wide variety of phenols and polyphenols using DBDMH.⁶ The aim was to prepare pure *ortho*-monobromophenols of different methyl gallates. A simple treatment of various methyl gallates with 0.5–0.55 equivalents of DBDMH resulted in the desired *ortho*-monobromides in very good to excellent yield and purity. Interestingly, we prepared both regioselective bromide units in very high yields for the synthesis of α - and β -DDB.



(E) We also studied⁷ the regioselective bromination of pyrogallol derivatives by DBDMH, which gave regioselective single monobromides in 77% yield in 90 minutes at room temperature.



(F) Very recently,⁸ we found that DBDMH is an excellent oxidizing agent for the oxidation of different thiols to their corresponding disulfides in extremely high yield and in very short reaction time. It was found to be superior to other oxidants, the reaction was very clean, and no other oxidized side-products were found.



References

- (1) (a) Larock, R. C. *Comprehensive Organic Transformations*; Wiley-VCH: New York, **1999**, 2nd Ed., 619. (b) Smith, M. B.; March, J. *March's Advanced Organic Chemistry*; Wiley: New York, **2001**, 5th Ed., 704.
- (2) (a) Zhan, S. L.; Zhang, C. Z. *Chinese Chem. Lett.* **1992**, 3, 29, *Chem. Abstr.* **1992**, 117, 69764. (b) Chang, J.; Chen, R.; Guo, G.; Dong, C.; Zhao, K. *Helv. Chim. Acta* **2003**, 86, 2239. (c) Guo, R.-Y.; He, J.; Chang, J.-B.; Chen, R.-F.; Xie, J.-X.; Ge, Y.-H.; Liu, H.-Q. *Gaodeng Xuexiao Huaxue Xuebao* **2001**, 22, 2018. (d) Matsuoka, Y.; Hosaka, K.; Takeda, S.; Mitsuhashi, H. PTC Japanese Patent 87/00387, *Chem. Abstr.* 1988; 109: 110414, **1987**.
- (3) Auerbach, J.; Weissman, S. A.; Blacklock, T. J.; Angeles, M. R.; Hoogsteen, K. *Tetrahedron Lett.* **1993**, 34, 931.
- (4) Chassaing, C.; Haudrechy, A.; Langlois, Y. *Tetrahedron Lett.* **1997**, 38, 4415.
- (5) Eguchi, H.; Kawaguchi, H.; Yoshinaga, S.; Nishida, A.; Nishiguchi, T.; Fujisaki, S. *Bull. Chem. Soc. Jpn.* **1994**, 67, 1918.
- (6) Alam, A.; Takaguchi, Y.; Ito, H.; Yushida, T.; Tsuboi, S. *Tetrahedron* **2005**, 61, 1909.
- (7) Alam, A.; Takaguchi, Y.; Tsuboi, S. *J. Fac. Environ. Sci. Technol.*; Okayama University, **2005**, 10, 105, *Chem. Abstr.* **2005**, 142, 409887.
- (8) Alam, A.; Takaguchi, Y.; Tsuboi, S. *Synth. Commun.* **2005**, 35, 1329.