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Synthesis, Characterization and Structure of DBU-hydrobromide-perbromide: A Novel Oxidizing Agent for Selective Oxidation of Alcohols to Carbonyl Compounds

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A new and efficient reagent for the conversion of primary and secondary alcohols into their corresponding aldehydes and ketones is introduced. The reagent was easily prepared from the reaction of DBU with molecular bromine in $CHCl_3$. The structure of the reagent as $DBUH^+Br_3^-$ was determined by single crystal X-ray diffraction analysis.

Key Words: DBU hydrobromide-perbromide, Oxidation, Alcohols

Introduction

The conversions of functional groups to each other have been the center of attention in organic synthetic methodology. For instance, the selective oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones is of great importance in chemistry and industry.[1] Organic tribromide salts as mild reagents are good candidates for this selective conversion, because they are not only stable, crystalline solids, and relatively soluble in most organic solvents but also can be handled more conveniently than liquid bromine and can be used successfully for this purpose. Although they are used as brominating agents of aromatic rings,[2] α-bromination of ketones,[3-6] and ketals,[3,7] electrophilic addition,[3,4,8-14] and substitution,[4,13,15-19] they are also used as catalyst for the oxidation of aromatic aldehydes to carboxylic acids[20] or ω-bromoesters,[21] and dialkyl and alkyl aryl sulfides to sulfoxides,[22] protection of carbonyl,[23] and hydroxyl groups,[24] cleavage of ethers and dithioacetals[25] and conversion of thioamides into amides.[26] They can also be applied in the synthesis of heterocyclic ring systems such as aziridines[27] and benzothiazoles.[28]

Experimental

Preparation of the $DBUH^+Br_3^-$ complex. A solution of bromine (28 mmol, 10.0 g) in dry chloroform (50 mL) was added dropwise with stirring to a solution of DBU (14 mmol, 4.5 g) in dry chloroform (50 mL) at 0 ~ 5 °C. As the bromine is added, an orange solid is appeared. The mixture was stirred for an additional 2 h, and then the residue was collected by filtration and washed with chloroform (20 mL). (Yield = 12 g (87%), mp = 123 ~ 124 °C, *lit.*[15] mp = 120 ~ 122 °C).

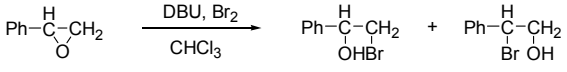
General procedure for the oxidation of primary and secondary alcohols. To a mixture of $DBUH^+Br_3^-$ (1 mmol, 0.47 g) in dichloromethane (5 mL) and water (2 mL), an appropriate amount of alcohol (1 mmol) in dichloromethane (2 mL) was added. The reaction mixture was stirred at room temperature until the orange color of the complex disappeared although the progress of the reaction was monitored by TLC using petroleum ether/ethyl acetate (7:3) as eluent. While the completion of the reaction, the organic layer was separated and the aqueous layer washed with dichloromethane. The combined organic layer was washed with 1% HCl (10 mL), 5% $NaHCO_3$ (10 mL) and water (10 mL), respectively. After the organic layer was dried over anhydrous Na_2SO_4, the solvent was removed under reduced pressure to afford the pure corresponding carbonyl compounds. The physical and spectral data of the purified products were in accordance with the authentic samples.

Results and Discussion

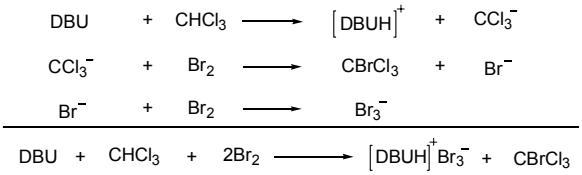
It has been reported that polyhalide ions such as X_3^- or X_5^- are involved in the regioselective ring opening of unsymmetrical epoxides when elemental halogens are applied in the presence of a suitable catalyst.[29-32] According to the proposed mechanism the polyhalide ion as a bulky nucleophile can be obtained through interaction of the catalysts lone-pair electrons with elemental halogen. In this respect we became interested to examine the catalytic efficiency of 1,8-diazabicyclo[5.4.0] undec-7-ene (DBU) for regioselective ring opening of epoxides by bromine. The ring opening of styrene epoxide as a model experiment was examined by adding dropwise of a bromine solution in chloroform to a stirred solution of styrene epoxide and DBU in chloroform. (Scheme 1) After usual work up, a mixture of regioisomers was obtained.

Initially formed *in situ* catalyst was filtered off from the reaction mixture for further characterization, and also was prepared by the same procedure in the absence of epoxide.

Our other efforts to regioselective ring opening of styrene oxide by newly prepared reagent failed and a mixture of regioisomers was obtained. This unusual behavior of DBU in comparison with other nitrogen possessing catalysts promoted us to explore the structure of the initially formed catalyst in this



Scheme 1



Scheme 2

reaction. Herein we wish to report on the synthesis and structural characterization of the bromine complex and its application in selective oxidation of alcohols to the corresponding aldehydes and ketones. The reagent was easily prepared from the reaction of DBU with molecular bromine in dry chloroform at 0 ~ 5 °C. As the dropwise addition of bromine was progressed, an orange solid was formed. The solid was filtered off and washed with chloroform. DBU-hydrobromide perbromide ($DBUH^+Br_3^-$) was formed *in situ*, instead of DBU-bromonium tribromide ($DBUBr^+Br_3^-$). It can be argued that $DBUH^+Br_3^-$ is responsible for the lack of regioselectivity in the ring opening of epoxide, where electrophilic ring opening competes seriously with nucleophilic ring opening reaction. The reagent obtained was pure enough to conduct the next experiment. A literature survey disclosed that there is only one reference cited in the literature dealing with DBU, HBr and Br_2 in AcOH as a brominating agent with the proposed structure as DBU-hydrobromide-perbromide on the basis of its ^{1}H NMR and UV spectral data.[15] We have now exploited a new synthesis of this reagent together with its 3D-structure by X-ray crystallography and examined its oxidation potential for functional group transformations. The suggested mechanism for the preparation of the reagent can be depicted as in Scheme 2. Initially, the deprotonation of $CHCl_3$ by DBU was performed before attacking the bromine molecule.[33]

The resulting $DBUH^+Br_3^-$ reagent has the advantages of being a non-hygroscopic and homogeneous solid which is not affected by exposure to light and moisture. It also showed a remarkable stability at room temperature for a long time.

In order to determine the structure, the red-orange crystal of the compound $DBUH^+Br_3^-$ complex having approximate dimensions 0.15 mm × 0.10 mm × 0.10 mm was sealed in a glass capillary and the crystallographic data and structure refinement parameters for the compound were studied and the results were given in Table 1.

The solid-state structural description of the compound with atom numbering scheme is given in Fig. 1 and its selected bond lengths and bond angles are summarized in Table 2.

The $DBUH^+Br_3^-$ complex crystallized in the monoclinic space group $P2_1/m$ with four molecules in the unit cell. The C10A-N1 bond distance, 1.336(4) Å, is longer than carbon and nitrogen double bond in the DBU which is confirming the DBU conversion to $DBUH^+$ cation. The Br_3^- anion has two different distance, Br4-Br5 2.7397(7) Å and Br5-Br6 2.4225(8) Å. The discrepancy is due to Br4 attendance in intermolecular hydrogen bond with N1 which result in electron density decrement and length increment in Br4-Br5 bond (Fig. 2).

Table 1. Crystal data and structure refinement for $DBUH^+Br_3^-$

compound	
Empirical formula	$C_9H_{17}Br_3N_2$
Formula weight	392.98
Temperature	100(2)
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/m$
Unit cell dimensions	a = 9.0076(5) Å b = 12.8644(8) Å; β = 107.5470(10)° c = 11.8897(7) Å
Volume	1313.64(13) Å^3
Z	4
Density (calculated)	1.987 g/cm^3
Absorption coefficient	9.182 mm^{-1}
F(000)	760
Crystal size	0.15 × 0.10 × 0.10 mm^3
Theta range for data collection	1.80 to 30.00°.
Index ranges	$-12 \le h \le 12$, $-18 \le k \le 18$, $-15 \le l \le 16$
Reflections collected	15671
Independent reflections	3947 [$R_{(int.)}$ = 0.0379]
Completeness to theta = 30.00°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.400 and 0.279
Refinement method	Full-matrix least-squares on F^2
Data /restraints /parameters	3947 /0 /136
Goodness-of-fit on F^2	1.007
Final R indices [for 2849 reflections with I > 2σ(I)]	R_1 = 0.0320, wR_2 = 0.0662
R indices (all data)	R_1 = 0.0561, wR_2 = 0.0745
Largest diff. peak and hole	0.673 and −0.733 e. Å^{-3}

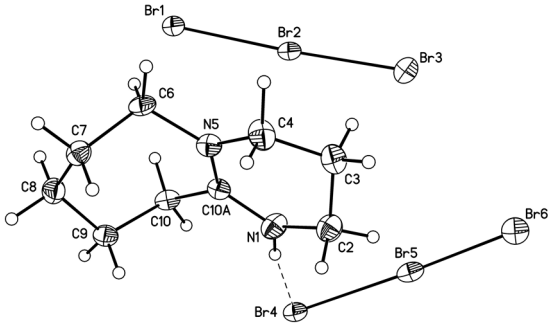


Figure 1. Molecular structure and atomic labeling scheme (50% probability level).

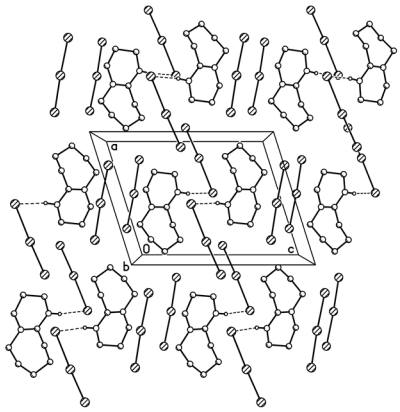


Figure 2. Fragment of crystal packing (along *c* crystal axes). Hydrogen atoms that do not take part in hydrogen bonding are not depicted for clarity.

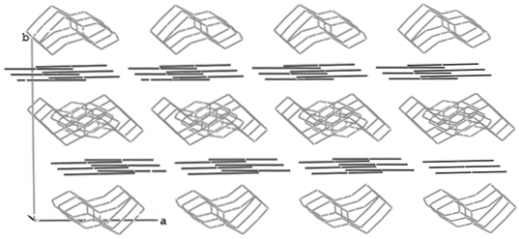


Figure 3. Cationic and anionic layers in $DBUH^+Br_3^-$ along the *b* axis.

Moreover, along the *b* axis, $DBUH^+$ and Br_3^- molecules are arranged in successive cationic and anionic layers (Fig. 3). Crystallographic data for the structure reported here have been deposited with the Cambridge Crystallographic Data Centre (Deposition No. CCDC696011).[34]

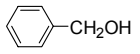
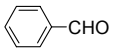
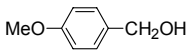
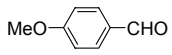
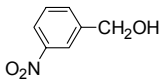
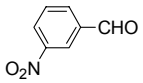
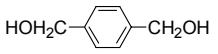
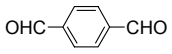
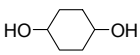
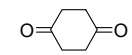
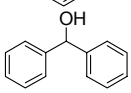
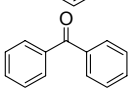
On the other hand, the generality of this reagent was examined in the selective oxidation of benzylic, allylic, primary and secondary alcohols into their corresponding carbonyl compounds on stirring in a mixture of dichloromethane and water at room temperature (Scheme 3). The reaction is generalized through entries 1-9 as shown in Table 1.

The resulting data in Table 1 shows the yields and times of the oxidation for each alcohol are appropriate and no over oxidation to carboxylic acid products were observed. Importantly, the amount of active species can be tuned by regulating the

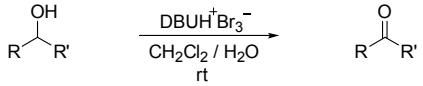
Table 2. Selected bond lengths (Å) and bond angles (°) for $DBUH^+Br_3^-$

Br(1)-Br(2)	2.5957(6)	Br(3)-Br(2)-Br(1)	177.24(2)
Br(2)-Br(3)	2.5139(7)	Br(6)-Br(5)-Br(4)	177.75(3)
Br(4)-Br(5)	2.7397(7)	C(10A)-N(1)-C(2)	121.6(3)
Br(5)-Br(6)	2.4225(8)	C(10A)-N(1)-H(1N)	117.4
N(1)-C(10A)	1.336(4)	C(2)-N(1)-H(1N)	120.4
N(1)-C(2)	1.475(4)	N(1)-C(2)-C(3)	110.1(3)
N(1)-H(1N)	0.9119	C(4)-C(3)-C(2)	111.6(3)
C(2)-C(3)	1.489(5)	N(5)-C(4)-C(3)	113.1(3)
C(3)-C(4)	1.486(5)	C(10A)-N(5)-C(4)	121.6(3)
C(4)-N(5)	1.454(4)	C(10A)-N(5)-C(6)	121.9(3)
N(5)-C(10A)	1.312(4)	C(4)-N(5)-C(6)	116.2(3)
N(5)-C(6)	1.485(4)	N(5)-C(6)-C(7)	112.0(2)
C(6)-C(7)	1.527(4)	C(8)-C(7)-C(6)	113.8(3)
C(7)-C(8)	1.520(5)	C(9)-C(8)-C(7)	114.5(3)
C(8)-C(9)	1.515(4)	C(8)-C(9)-C(10)	114.6(3)
C(9)-C(10)	1.534(4)	C(10A)-C(10)-C(9)	111.8(2)
C(10)-C(10A)	1.497(4)	N(5)-C(10A)-N(1)	122.2(3)
		N(5)-C(10A)-C(10)	120.8(3)
		N(1)-C(10A)-C(10)	116.9(3)

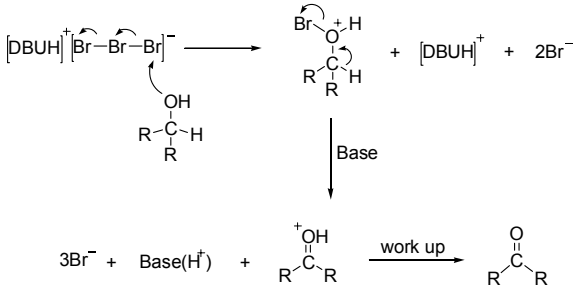
Table 3. Oxidation of alcohols to carbonyl compounds with $DBUH^+Br_3^-$ [a]

entry	substrate	time (h)	product	yield (%)[b]
1		1.45		89
2		2		92
3		1.15		95
4		4		80
5		0.45		85[c]
6		3		90
7		1		83
8		2		88
9		1.5		78

[a]All the reactions was carried out with substrate (1 mmol) and $DBUH^+Br_3^-$ (1 mmol) in CH_2Cl_2:H_2O (7:2) at room temperature except entries 4 and 7 which $DBUH^+Br_3^-$ (2 mmol) was used. [b]Isolated yields. [c]GC yield.



Scheme 3



Scheme 4

amount of the reagent, an operation that is rather difficult in the direct use of liquid bromine or a bromine solution. The reaction of 2-propen-1-ol (entry 5) gave the desired acrolein without damaging the double bond. This product could not be isolated from the reaction mixture, but it was confirmed by GC. It is notable that no brominations take place either at the double bond or α-positions of carbonyl compounds, for instance entries 5 and 8. Likewise, the phenyl group is also unaffected under the experimental conditions. When the reaction of benzyl alcohol (entry 1) as a model experiment was carried out in the presence of excess $DBUH^+Br_3^-$, only the corresponding aldehyde was obtained without any overoxidation product and any other by-products. The oxidation reaction was also examined in an equimolar concentration of benzyl alcohol, 1-phenylethanol and $DBUH^+Br_3^-$. It showed the reaction is chemoselective and only the primary alcohol was oxidized.

The suggested mechanism for the conversion of alcohols into the corresponding aldehydes or ketones for a typical alcohol is depicted in Scheme 4.

In summary, we have presented here a new synthesis for DBU-hydrobromide-perbromide as an efficient oxidizing agent for oxidation of alcohols to carbonyl compounds together with characterization of its 3D-structure by X-ray crystallography. This promising, non-metallic, water and atmospheric stable reagent have the potential to find new scope and application in organic synthesis.

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