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An efficient vanadium-catalyzed bromination reaction

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Abstract—An efficient catalytic oxidative bromination of arenes, alkenes, and alkynes in aqueous media was achieved under relatively mild conditions by using NH_4VO_3 catalyst combined with H_2O_2, HBr, and KBr. Dodecyltrimethylammonium bromide was found to serve as an efficient surfactant to facilitate the NH_4VO_3-catalyzed bromination in aqueous media.

Bromination of organic compounds is one of the important synthetic tools in organic syntheses. Classical bromination involves the use of hazardous elemental bromine. To avoid the use of bromine, the development of environmentally harmonic bromination protocols has been focused on.[1] Vanadium haloperoxidases, which are found in marine algae, catalyze the oxidation of halides to the corresponding hypohalous acids in the presence of hydrogen peroxide, permitting halogenation of organic compounds.[2] Considerable efforts have been devoted to develop efficient bromination systems by using V(V)–H_2O_2.[3] More environmentally harmonic catalytic procedure is to be developed. We herein report an environmentally harmonic vanadium-catalyzed bromination reaction in aqueous media.

The catalytic system consists of NH_4VO_3 (0.02 mmol), H_2O_2 (0.40 mmol), HBr (0.40 mmol), and KBr (0.60 mmol).[4] The oxidative bromination reaction of 1,3,5-trimethoxybenzene (0.20 mmol) was conducted at room temperature with stirring in water (5 mL) for 24 h. For comparison, two-phase ($H_2O/CHCl_3$) reaction[3b] was also examined under the similar conditions. The dibromide was produced quantitatively in both H_2O and $H_2O/CHCl_3$ (Table 1). Anisole similarly underwent the NH_4VO_3-catalyzed bromination in H_2O to give the monobromide and dibromide although only the former derivative was obtained in $H_2O/CHCl_3$. These findings indicate that the oxidative bromination proceeds smoothly in aqueous media. This catalytic system was successfully applied to the oxidative bromination of alkenes and alkynes. A distinct difference of products was observed between aqueous and two-phase media. In the case of *trans*-β-methylstyrene, the corresponding bromohydrin, which is considered to be derived from the intermediary bromonium ion and H_2O, was obtained as a major product in aqueous media. On the contrary, the two-phase reaction resulted in the formation of the dibromide as a major product. It should be noted that the oxidative bromination of α-methylstyrene in H_2O led to the selective and quantitative formation of the bromohydrin. Furthermore, gram-scale oxidative bromination of α-methylstyrene could be performed in H_2O to afford the bromohydrin selectively in 98% yield. Of interest is that the NH_4VO_3-catalyzed bromination of 1-phenyl-1-propyne in H_2O yielded the α,α-dibromoketone[5] as a major product, accompanied by a small amount of the dibromoalkene (Scheme 1).

$$\text{Substrate} \xrightarrow[\text{solvent, Ar, rt, 24 h}]{\substack{NH_4VO_3\ (10\ mol\%) \\ H_2O_2\ (2.0\ eq.) \\ HBr\ (2.0\ eq.) \\ KBr\ (3.0\ eq.)}} \text{Bromination Products}$$

Scheme 1. Oxidative bromination of arenes, alkenes, and alkynes.

In the case of cyclohexene, only 5% yield of the corresponding bromohydrin was obtained in H_2O although oxidative bromination reaction proceeded in $H_2O/CHCl_3$ to give dibromide, α-bromoketone, and bromohydrin derivatives. The NH_4VO_3-catalyzed bromination of cyclohexanone produced the α-bromoketone derivative in both H_2O and $H_2O/CHCl_3$. Contrary to

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Keywords: Catalytic oxidative bromination; NH_4VO_3 Catalyst; H_2O_2; Aqueous media; Surfactant.

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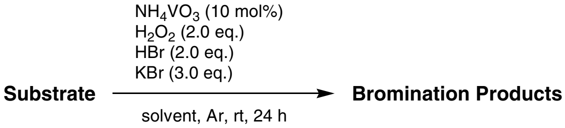
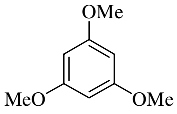
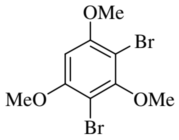
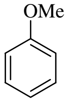
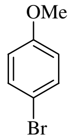
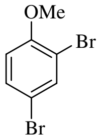
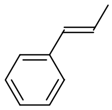
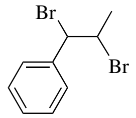
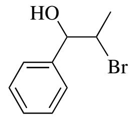
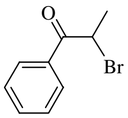
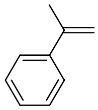
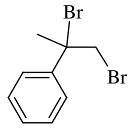
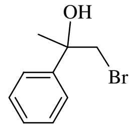
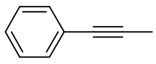
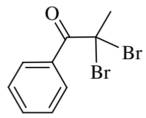
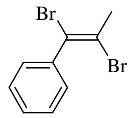
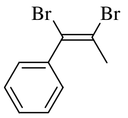
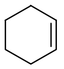
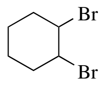
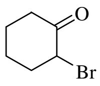
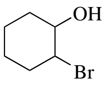
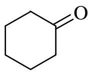
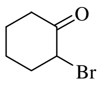
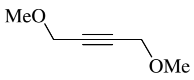
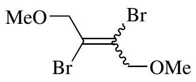
Table 1. Oxidative bromination of arenes, alkenes, and alkyne[a]



Substract	Solvent	Products, NMR yields/%					
	H_2O				100		
	$H_2O/CHCl_3$ (1/1)				98		
	H_2O		48		48		
	$H_2O/CHCl_3$ (1/1)		94		0		
	H_2O		7[b]		75[b]		10[b]
	$H_2O/CHCl_3$ (1/1)		64[b]		0[b]		26[b]
	H_2O		0		100		
	H_2O[c]		0		98		
	$H_2O/CHCl_3$ (1/1)		31		69		
	H_2O		82		12		Trace
	$H_2O/CHCl_3$ (1/1)		Trace		81		13
	H_2O		0		0		5
	$H_2O/CHCl_3$ (1/1)		46		24		20
	H_2O				33		
	$H_2O/CHCl_3$ (1/1)				48		
	H_2O				70		
	$H_2O/CHCl_3$ (1/1)				58		

[a] The reaction was carried out by using a substrate, 10 mol % of NH_4VO_3, 2.0 equiv of H_2O_2, 2.0 equiv of HBr, and 3.0 equiv of KBr in H_2O at room temperature for 24 h.

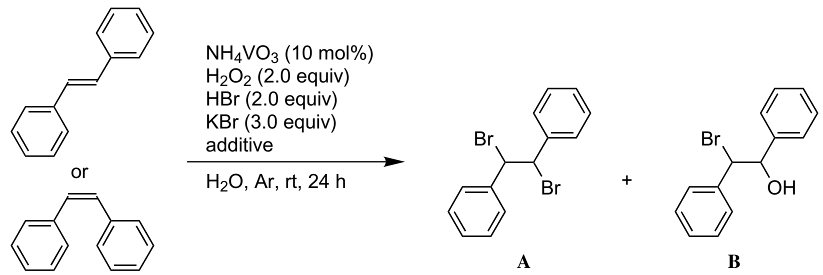
[b] Isolated yield.

[c] The reaction was carried out by using 10 mmol of substrate, 1.0 mmol of NH_4VO_3, 20 mmol of H_2O_2, 20 mmol of HBr, and 30 mmol of KBr in H_2O at room temperature for 24 h.

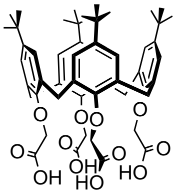
the bromination of 1-phenyl-1-propyne, the dibromide was produced as a major product in the case of 1,4-dimethoxy-2-butyne.

Above-mentioned results indicate synthetic efficiency of the present catalytic oxidative bromination system in aqueous media. To optimize the catalytic system, the effect of an additive in aqueous media was studied, as summarized in Table 2. The presence of a surfactant facilitated the bromination of *trans*-stilbene. Dodecyltrimethylammonium bromide (DTAB) exhibited an advantage over **1** and sodium dodecyl sulfate (SDS) in both yield and selectivity, to afford the dibromide and bromohydrin in 44% (*erythro*/*threo* = 93/7) and 27% yield (*erythro*/*threo* = 100/0), respectively. On the other hand, the poor yields were obtained in the absence of the additive. The similar effect of DTAB was also observed in the bromination of *cis*-stilbene.

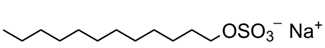
Table 2. Oxidative bromination of stilbenes in water in the presence of an additive[a]



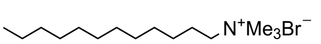
Additive	NMR yields/% (*erythro*/*threo*)			
	From *trans*-stilbene		From *cis*-stilbene	
	A + B	A B	A + B	A B
1	51	{33(88/12)/18(100/0)}	94	{67(13/87)/27(26/74)}
SDS	37	{21(58/42)/16(81/19)}	94	{71(47/53)/23(26/74)}
DTAB	71	{44(93/7)/27(100/0)}	98	{77(17/83)/21(33/67)}
None	10	{7(93/7)/3(100/0)}	86	{62(32/68)/24(25/75)}



1: 10 mol%



SDS: 40 mol%



DTAB: 40 mol%

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[a] The reaction was carried out by using stilbene, 10 mol % of NH_4VO_3, 2.0 equiv of H_2O_2, 2.0 equiv of HBr, 3.0 equiv of KBr, and 10 mol % or 40 mol % of an additive in H_2O at room temperature for 24 h.

In conclusion, the present procedure provides an efficient method for the catalytic oxidative bromination in aqueous media. The more efficient bromination was attained in the presence of the cationic surfactant. Studies on the reaction mechanism and synthetic application are now in progress.

Acknowledgments

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4. *General procedure of the catalytic oxidative bromination*: To a stirred mixture of a substrate (0.20 mmol), NH_4VO_3 (2.34 mg, 0.02 mmol), and KBr (71.4 mg, 0.60 mmol) in H_2O (5 mL) were added 48% HBr (45.5 μL, 0.40 mmol)

and 30% H_2O_2 (40.8 μL, 0.40 mmol). The resulting mixture was stirred under Ar at room temperature for 24 h. The mixture was diluted with chloroform and water, washed with 1 N HCl solution and brine, and dried over Na_2SO_4. The formation of the products was detected by ^1H NMR. Spectral data of the products were identical with those of commercially available and authentic samples.

5. α,α-Dibromoketone might be produced by further bromination of the bromo vinyl alcohol.