

Note

1-Benzyl-4-aza-1-azoniabicyclo[2.2.2]octane tribromide as a regenerable and useful reagent for bromination of phenols under mild conditions

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1-Benzyl-4-aza-1-azoniabicyclo[2.2.2]octane tribromide has been examined over several phenolic compounds under mild conditions. The reaction gives brominated phenols in good to excellent yields. Straightforward work-up of the reaction yields pure products in several cases.

Keywords: Octane tribromide, phenolic compounds, brominated phenols

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The brominated phenolic compounds are very important materials from the point of view of antiseptic hygienic and disinfectant character properties and they are also useful in industry for manufacturing biologically active agrochemicals, antioxidant and flame retardancy¹⁻⁵.

Environmental problems caused by using chemical compounds and solvents⁶ in conventional bromination⁷ are some of the major problems⁵. To solve these problems bromoperoxidase enzyme, such as *Alga* has been used for bromination of organic substance in the presence of bromide and hydrogen peroxide, however these reagents produce a mixture of brominated products⁸.

Other brominating reagents, such as *N*-bromosuccinimide (NBS)⁹, or bromodimethylsulfonium bromide are expensive and generate organic waste¹⁰. Moreover, few groups have investigated the potential advantages of heterogeneous catalysts in halide oxidation¹¹. Stable crystalline quaternary ammonium tribromide (OATB)¹²⁻¹⁴ like Me₄NBr₃, Et₄NBr₃,

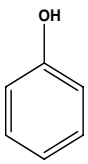
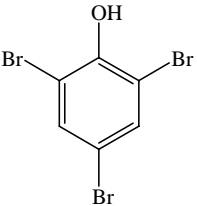
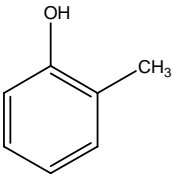
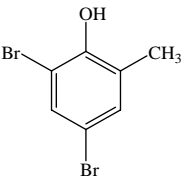
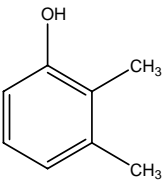
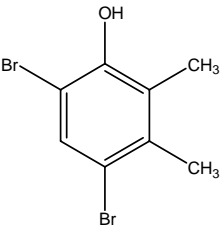
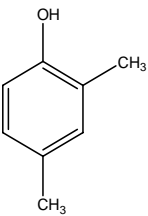
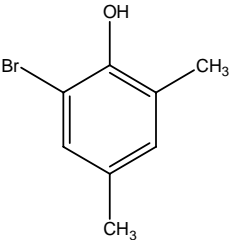
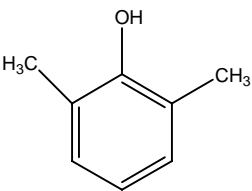
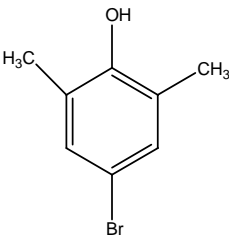
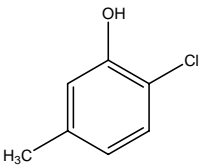
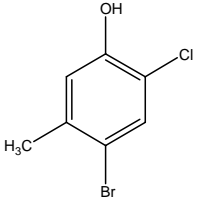
Bu₄NBr₃, pyridinium tribromide, and cetyltrimethylammonium tribromide, have been synthesized from the reaction of the corresponding bromide with V₂O₅ and aqueous H₂O₂. However, this method is expensive. In the course of our studies on developing new reagent in organic synthesis¹⁵ herein we report the synthesis of 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane tribromide **1** as an efficient and new reagent and application of this reagent for bromination of phenol derivatives. Reaction of 1-benzyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide with KBr₃ in water gave **1** as a yellow precipitate in good yield. This reagent showed an intense electronic absorption at 279 nm typical of tribromide (Br₃⁻)¹. Reactions of phenols with **1** in methanol as solvent at room temperature gave polybromophenols in a good to excellent yields. These reactions can be facilitated by addition of calcium carbonate powder to neutralize the generating hydrogen bromide (Table I, Scheme I).

Bromination of 2,6-dimethylphenol with reagent **1** (2 molar equivalent) resulted into a mixture of 4-bromo-2,6-dimethylphenol and 4,4-dibromo-2,6-dimethyl-2,5-cyclohexadienone (2:1) and reaction of phenol with reagent **1** (4 molar equivalent) produced a mixture of 2,4,6-tribromophenol and 2,4,4,6-tetrabromo-2,5-cyclohexadienone (2:1) which indicates the high reactivity of reagent **1**. Interestingly, bromination of deactivated dinitrophenol is very difficult. In our method this compound is directly brominated at room temperature. The presence of methanol markedly facilitates the bromination of phenol by generating methylhypobromite from reaction between reagent **1** and methanol. The reaction of phenols with MeOBr could give polybrominated phenols¹².

Another noteworthy feature of this method is that the reagent **1** can be regenerated quantitatively. After extraction of the bromoaromatic compounds, the aqueous layer was treated with a fresh-bath of the aqueous KBr₃ to regenerate the reagent **1** in quantitative yield.

In conclusion, we report herein an efficient and green method for bromination of phenols which is superior to reported methods from the point of view of straightforward isolation, green chemistry, excellent yields, mildness of conditions and

Table I—Bromination of phenols **2** by reagent **1** — *Contd*

Entry	Starting material 2	Product 3 ^a	Molar ratio 1:2	Time (min)	Yield ^b (%)	m.p. °C or b.p. °C/torr(lit) ¹⁶⁻¹⁹
a			1/1	15	92	90-91 (95-96)
b			2/1	15	95	54-56 (57)
c			2/1	30	70	66-67 (67-68)
d			1/1	15	94	232/760 (231/760)
e			1/1	15	67	78-79 (79.5)
f			1/1	30	94	55-57 (56-57)

— *Contd*

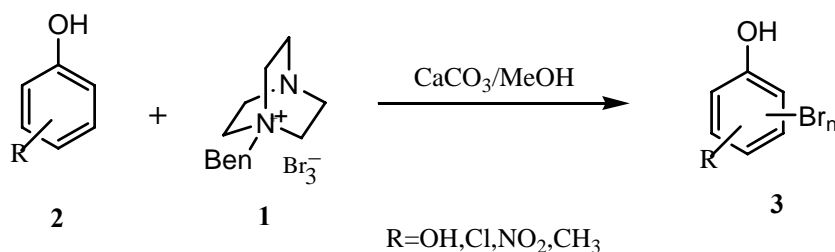
Table I—Bromination of phenols **2** by reagent **1** — *Contd*

Entry	Starting material 2	Product 3 ^a	Molar ratio 1:2	Time (min)	Yield ^b (%)	m.p. °C or b.p. °C/torr(lit) ¹⁶⁻¹⁹
g			1/1	180	85	65-66 (68)
h			1/1	150	90	114 (114)
i			3/1	10	95	95-96 (98-99)
j			3/1	15	80	110-11 (112)
k			1/1	120	90	111-12 (114)
l			2/1	200	85	136-37 (137)

— *Contd*

Table I—Bromination of phenols **2** by reagent **1** — *Contd*

Entry	Starting material 2	Product 3 ^a	Molar ratio 1:2	Time (min)	Yield ^b (%)	m.p. °C or b.p. °C/torr(lit) ¹⁶⁻¹⁹
l			2/1	200	85	136-37 (137)
m			4/1	70	88	278-79 (278-79)
n			4/1	70	90	178-80 (179-81)

^aAll of isolated products are known and their spectra and physical data have been reported in literature.¹⁶⁻¹⁹^bYield of pure product after purification.**Scheme I**

bromination of deactivated phenol derivatives^{1,12,17-18}. On the other hand, the tribromide **1** is a stable crystalline solid which can be easily handled and environmentally benign because of its solid character. Another noteworthy feature of this reagent is that it can be regenerated in quantitative yields.

Experimental Section

General. All yields refer to isolated products. Products were characterized by comparison with authentic samples (IR and ¹H NMR spectra, melting

and boiling points and TLC analysis)¹⁶⁻¹⁹. All ¹H NMR spectra were recorded at 90 and 300 MHz in CDCl₃ or CCl₄ relative to TMS.

Preparation of reagent 1. To a solution of KBr (11.9 g, 0.1 mole) in water (200 mL) was added dropwise bromine (16.0 g, 0.1 mole). The solution was stirred at room temperature for 30 min, the bromine colour disappeared and KBr₃ was formed. To a solution of 1-benzyl-1,4-diazoniabicyclo[2.2.2]octane chloride (24.8 g, 0.1 mole) in water (200 mL) was added the KBr₃ solution dropwise until a yellow

precipitate formed. After 30 min stirring, the mixture was filtered and washed with water (3×30 mL). The filtered cake was dried to give **1** as yellow crystals (40.0 g, 90% yield), which decomposed at 181–83 °C to a dark-brown material. IR (KBr): 3050 (m), 1600 (s), 1460 (s), 1360 (s), 1040(m), 1210 (s), 840 (m), 800 (m) cm⁻¹; ¹H NMR: δ 3.52–3.57 (t, 6H), 3.68–3.72 (t, 6H), 4.73 (s, 2H), 7.57 (s, 5H); ¹³C NMR: δ 131.1, 128.9, 127.5, 124.7, 112.4, 48.8, 42.1; UV (CH₂Cl₂): 279 nm. Anal. Calcd for C₁₃H₁₉N₂Br₃: C, 35.24; H, 4.32; N, 6.32. Found: C, 35.55; H, 4.21; N, 6.53%.

General procedure for bromination of phenols 2a with reagent 1. To a solution of phenol **2a** (0.19 g, 2 mmoles) in methanol (10 mL) was added reagent **1** (2.66 g, 6 mmoles) and CaCO₃ (0.60 g, 6 mmoles). The mixture was stirred for 15 min at room temperature till decolourization of orange solution occurred. When TLC showed complete disappearance of phenol, the solvent was removed *in vacuo* and the solid residue was isolated with ether (4×40 mL) and filtered off. The combined organic layers were washed with water (2×40 mL), dried (magnesium sulfate), and evaporated under vacuum to give 2,4,6-tribromophenol **3a**, which was recrystallized from a mixture of methanol-water (1:3) as a colourless needles in 93% yield (0.62 g).

Regeneration of reagent 1. After the residue was washed with ether and filtered, the filtered cake was washed with water (3×20 mL) and separated from solid residue by filtration. Then to the combined solution was added a bromine solution dropwise (0.96 g, 6 mmoles in 50 mL water) during 30 min to obtain **1** as yellow crystals (2.32 g, 90% yield).

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