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Novel Protocol for the Synthesis of Organic Ammonium Tribromides and Investigation of 1,1′-(Ethane-1,2-diyl)dipiperidinium Bis(tribromide) in the Silylation of Alcohols and Thiols

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A novel and efficient protocol for the synthesis of organic ammonium tribromides (OATBs) is developed by using inexpensive and eco-friendly periodic acid as an oxidant for the conversion of Br^- to Br_3^-. The method does not use any mineral acid and metal oxidants. The protocol is utilized to synthesize a new bis(tribromide) viz., 1,1′-(ethane-1,2-diyl)dipiperidinium bis(tribromide) (EDPBT). EDPBT is investigated as a catalyst in the silylation of alcohols and thiols by HMDS (hexamethyldisilazane) under solvent-free conditions.

Tribromide reagents, particularly organic ammonium tribromides (OATBs), have received considerable interest in the recent past due to their wide applicability as reagents and catalysts in a variety of organic reactions.[1] Tribromides, often known as solid bromine, have already been established to be superior to liquid bromine, NBS, Br_2/HBr, and many other traditional brominating reagents because of their easy-handling, nonhazardous nature, mildness, efficiency, and selectivity.[2] Among the various tribromides, quaternary ammonium tribromides (QATBs), viz., tetrabutylammonium tribromide (TBATB),[3] benzyltrimethylammonium tribromide (BTMATB),[4] pyridinium hydrotribromide (PyHTB),[5] and cetyltrimethylammonium tribromide (CTMATB)[3] are often used as useful reagents and catalysts for a variety of organic functional group transformations. Moreover, *N*-heterocyclic tribromides such as quinoline hydrotribromide (QHTB),[6] *N*-methylpyrroline-2-one hydrotribromide (MPHT),[7] DABCO tribromide,[8] and [BBIm]Br_3[9] have been well documented in the literature as useful reagents and catalysts in important organic transformations. A few *N*,*N*′-heterocyclic bis(tribromide)s, which are relatively less common, but most interesting are also found in literature.[10] Recently, Patel et al. have prepared 1,1′-(ethane-1,2-diyl)dipyridinium bis(tribromide) as stable bis(tribromide) by using oxone.[11] The compound is found to have vast utility in organic reactions like bromination of organic substrates (alkene, alcohols, and amines) and synthesis of heterocyclic compounds.[12]

Conventionally, OATBs are prepared using liquid Br_2 and/or HBr, which are perilous and not favorable from an environmental point of view.[13] Over the last two decades or so, many improved methods for the syntheses of tribromides, which are considered to be environmental benign, have been reported in the literature. A few of them worth mentioning are V_2O_5/H_2O_2,[14] MoO_4^{2-}/H_2O_2,[15] MnO_4^-/H^+,[16] $(NH_4)_2S_2O_8/H^+$,[17] $NaOCl/H^+$,[18] oxone,[11] etc. In spite of several advantages, many of such methods usually involve metals and mineral acids, which still cause environmental concerns. Therefore, development of newer strategies that do not require the use of metals and mineral acids is still a challenge for synthetic chemists. Periodic acid (H_5IO_6) is known to be used extensively in the oxidation of alcohols to aldehydes and acids in the presence of a catalyst like KBr and CrO_3.[19] Its role as an oxidant in the conversion of Br^- to Br^+ in a catalytic cycle for transformation of alcohols to aldehydes is known in the literature.[19a] However, an extensive literature survey reveals that H_5IO_6 has never been used as an oxidant in the conversion of Br^- to Br_3^- leading to the synthesis of a wide variety of organic tribromide reagents. Moreover, it is cheap, nontoxic, efficient, and easy to handle.

In the context of application of tribromides as a catalyst, attention may be drawn to the importance of silylation of alcohols and thiols by HMDS (hexamethyldisilazane). Protection of functional groups are indispensable in multistep reactions for the synthesis of polyfunctional compounds.[20] Formation of silyl ether from a hydroxy or thiol group is most popular and a widely used method specially in analytical chemistry.[21] The silylating reagents that are commonly used in the traditional and conventional processes are SiCl,[22] MeSiN=C(Me)OSiMe,[23] Me_3SiCl or MeSiOTf in presence of a base,[24] etc. However, many of these methods have demerits such as the lack of reactivity, time consuming, difficulty in removing by-products, and the use of cobases during silylation reactions.[25] HMDS is commercially available, cheap, noncorrosive, and easy to handle for the formation of trimethylsilyl ether, which generates only ammonia gas as by-product.[26] A variety of catalysts, $CuSO_4 \cdot 5H_2O$, $Al(OTf)_3$, trichloroisocyanuric acid and I_2, etc., have been reported previously for the efficient synthesis of silylated products.[25,27] To our knowledge, *N*,*N*′-heterocyclic bis(tribromide)s have never been used as a catalyst in silylation reactions. As a part of our continuous endeavor[16–18] to develop new protocols for the synthesis of OATBs, we report herein a new synthetic procedure for the synthesis of OATBs including a new *N*,*N*′-heterocyclic bis(tribromide) compound viz., 1,1′-(ethane-1,2-diyl)dipiperidinium bis(tribromide) (EDPBT). The application of EDPBT as a catalyst in silylation of some selectively chosen alcohols and thiols is also presented in this paper.

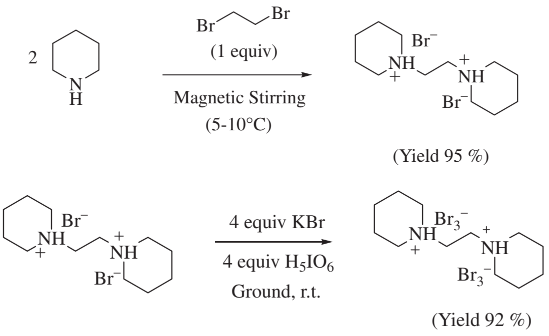
A variety of QABs (quaternary ammonium bromides) were converted to the corresponding tribromides by H_5IO_6 under solvent-free conditions without the help of a mineral acid. In a typical reaction, 10 mmol of tetrabutylammonium bromide was mixed with 20 mmol of KBr and 20 mmol of H_5IO_6. The mixture was agitated in a mortar for ca. 5 min where upon a bright red orange color compound was observed, indicating the formation of a Br_3^- anion. The product thus formed was extracted with a minimum volume of ethyl acetate and dried over anhydrous Na_2SO_4. The solvent was removed in vacuum to obtain the corresponding tribromide compound in nearly quantitative yield (Scheme 1).

$$R_4NBr \xrightarrow[\text{2 equiv } H_5IO_6\text{, ground, r.t.}]{\text{2 equiv KBr}} R_4NBr_3$$

(82-93 %)

Where
R_4N= Me_4N
Et_4N
n-Bu_4N
cetyl-Me_3N
benzyl-Me_3N

Scheme 1. Scheme depicting the synthesis of QATBs.



Scheme 2. Formation of EDPBT from corresponding dibromide.

$$HIO_4{\cdot}2H_2O + Br^- \longrightarrow HOBr + IO_3^- + 2H_2O$$

$$H^+ (H_5IO_6) + HOBr + 2Br^- \longrightarrow Br_3^- + H_2O$$

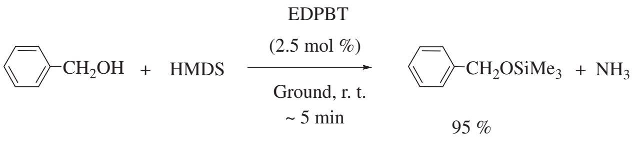
$$H^+ + H_5IO_6 + 3Br^- \longrightarrow Br_3^- + IO_3^- + 3H_2O$$

Scheme 3. A plausible mechanism showing the function of H_5IO_6 in the tribromide synthesis.

The synthesis of bis(tribromide) was carried out in two steps. The first step involves the exothermic reaction of piperidine (10 mmol) with 1,2-dibromoethane (5 mmol) under cold conditions (5–10 °C) to generate 1,1′-(ethane-1,2-diyl)dipiperidinium dibromide. In the second step, the dibromide thus synthesized was converted to the corresponding bis(tribromide) with the help of 4 equiv of KBr and 4 equiv of H_5IO_6 (Scheme 2).

The plausible mechanism of tribromide formation has been depicted in Scheme 3. H_5IO_6 converts Br^- to HOBr, which in the presence of an acid (inherent acidic property exerted by periodic acid itself) transforms three equiv of Br^- to Br_3^-. The tribromide thus formed was extracted with a minimum volume of ethyl acetate.

All the synthesized tribromides are characterized by UV–visible and FT-IR spectroscopic analysis. The anion, Br_3^- exhibits a strong absorption band in the range 260–280 nm and a vibrational stretching frequency at 170 cm^{-1}, characteristic of the tribromide anion.[15,28] Additionally, they were also analyzed by elemental analysis. The results obtained are consistent with theoretical values. The new tribromide, EDPBT is characterized by elemental analysis, UV–vis, FT-IR, and NMR (^1H and ^{13}C) spectroscopy. In the ^1H NMR spectrum of EDPBT, a peak at δ 3.20 is certainly for the ethylene protons attached to the N-atoms. However, no such peak was observed in the ^1H NMR spectrum of piperidine. A similar result can be observed in the ^{13}C NMR spectrum of EDPBT where the peak at δ 44.6 is for the ethylene carbon. The spectral data of the synthesized tribromide compound is as follows. EDPBT: Orange compound; Yield: 92% (0.603 g); UV–visible: 269 nm; FT-IR (KBr, cm^{-1}): 3276, 2933, 1467, 1443, 745, 187; ^1H NMR δ: 9.0 (s, 2H), 3.20 (t, $J = 5.6$ Hz, 4H), 1.99–1.94 (m, 8H), 1.74–1.69 (m, 12H); ^{13}C NMR δ: 22.2, 22.4, 44.6, 77.01; Anal. Calcd for $C_{12}H_{26}N_2Br_6$ (MW: 677.75): Calcd. C, 21.26; H, 3.87; N, 4.13; Br, 70.74%. Found: C, 21.21; H, 3.81; N, 4.03; Br, 70.67%.



Scheme 4. Silylation of benzyl alcohol catalyzed by EDPBT.

After the successful synthesis of EDPBT in nearly quantitative yield, the next step is the investigation of its efficacy as a catalyst in the silylation reaction. For this purpose, benzyl alcohol (**5a**) was chosen as a model substrate (Scheme 4). The reaction was carried out in the absence of solvent at room temperature taking HMDS as the silylating agent. Initially, 20 mmol of **5a** was mixed with catalytic amounts of EDPBT and a small amount of silica gel, and the whole reaction mixture was ground well followed by the addition of HMDS (dropwise) at room temperature. TLC was run to monitor the reaction (10% EtOAc/hexane). It took ca. 5 min to complete the reaction with 95% yield. The catalyst amount used for this trial reaction is 2.5 mol %. We have varied the catalyst amount from 1 to 10 mol % and observed that from 2.5 to 10 mol % of the catalyst, the yields and reaction times are almost the same for different silylation products. However, when the catalyst amount was less than 2.5 mol %, the reaction times were too long for obtaining a significant yield of the products. The potential of HMDS as a reagent was examined for the silylation of **5a** both in the presence and absence of solvents (ethyl acetate, MeCN, and DMSO) using a catalyst. It was observed that a solvent-free reaction leads to better yield of the product in lesser time. Moreover, solvent-free reactions are preferable from the viewpoint of the environment.

After achieving success with **5a**, we tried silylation by choosing a host of substrates, which include aromatic, aliphatic, and acyclic alcohols and thiols. All of these substrates were silylated by pursuing similar reaction conditions mentioned for **5a** affording products in very high yield, 80–95% and in a short reaction time, 5–17 min (Table 1).

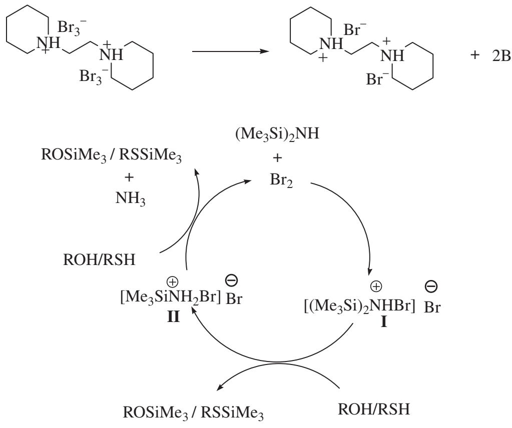
A plausible mechanism[16b] of alcohol and thiol silylation catalyzed by tribromide may be depicted via Scheme 5. From the mechanism, it is observed that the Br_2 molecule generated from EDPBT, in fact acts as the catalyst. Intermediate **I** and **II** are produced in the catalytic loop. In the final step, silyl ether and/or silyl thioether are formed along with NH_3 as a by-product and regeneration of Br_2.

In conclusion, the present work demonstrates an efficient and environmentally acceptable procedure for the development of OATBs and a new bis(tribromide) compound. Bis(tribromide) namely, 1,1′-(ethane-1,2-diyl)dipiperidinium bis(tribromide) is studied for its efficacy as a catalyst in the silylation of thiols and

Table 1. Silylation of alcohols and thiols by HMDS taking EDPBT as catalyst

Entry	Reactant[a]	Products[b]	Yield[c] /%	Time /min
1	n-BuOH (**1a**)	n-BuOSiMe$_3$ (**1b**)	93	7
2	i-PrOH (**2a**)	i-PrOSiMe$_3$ (**2b**)	87	9
3	t-BuOH (**3a**)	t-BuOSiMe$_3$ (**3b**)	88	6
4	PhC_2H_4OH (**4a**)	$PhC_2H_4OSiMe_3$ (**4b**)	90	10
5	$PhCH_2OH$ (**5a**)	$PhCH_2OSiMe_3$ (**5b**)	95	5
6	4-MeOPhCH$_2$OH (**6a**)	4-MeOPhCH$_2$OSiMe$_3$ (**6b**)	80	7
7	$C_6H_{11}OH$ (**7a**)	$C_6H_{11}OSiMe_3$ (**7b**)	83	13
8	$C_{10}H_7OH$ (**8a**)	$C_{10}H_7OSiMe_3$ (**8b**)	82	17
9	n-BuSH (**9a**)	n-BuSSiMe$_3$ (**9b**)	87	6
10	$C_6H_{11}SH$ (**10a**)	$C_6H_{11}SSiMe_3$ (**10b**)	90	10
11	$PhCH_2SH$ (**11a**)	$PhCH_2SSiMe_3$ (**11b**)	85	11
12	PhSH (**12a**)	$PhSSiMe_3$ (**12b**)	91	8
13	4-MePhSH (**13a**)	4-MePhSSiMe$_3$ (**13b**)	88	9
14	$C_{10}H_7SH$ (**14a**)	$C_{10}H_7SSiMe_3$ (**14b**)	82	14

[a]Reactions were conducted at room temperature using catalyst to substrate to HMDS molar ratio of 1:40:20 under solvent-free condition. [b]All the products were first checked in TLC and then identified by spectroscopic techniques (see Supporting Information). [c]Isolated yield.



Scheme 5. Plausible mechanism of EDPBT-catalyzed silylation.

alcohols by HMDS. The encouraging results obtained on silylation suggest that the procedure may serve as an efficient alternative route for the protection of alcohols and thiols.

Supporting Information is available electronically on J-STAGE.

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