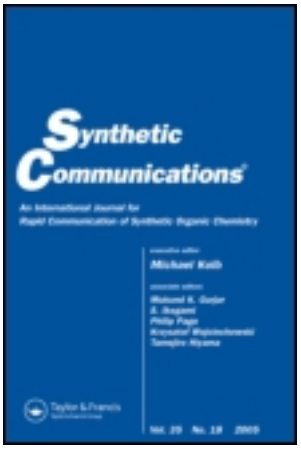

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Synthesis and Reactivity Studies of a New Reagent, Ethyltriphenylphosphonium Tribromide

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SYNTHESIS AND REACTIVITY STUDIES OF A NEW REAGENT, ETHYLTRIPHENYLPHOSPHONIUM TRIBROMIDE

Latonglila Jamir, B. Alimenla, Anil Kumar, Dipak Sinha, and Upasana B. Sinha

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A new reagent, ethyltriphenyl phosphonium tribromide (ETPPTB), has been synthesized and studied. Results show that the reagent is quite efficient for various reactions such as organic bominations, acylations, and isothiocyanate preparation.

Keywords: Acylation; bromination; desulfurization; dithiacarbamate; ethyltriphenyl phosphonium tribromide; isothiocyanates

INTRODUCTION

Organic phosphonium tribromides are the structural analogs of organic ammonium tribromides, with expectedly similar properties.[1] However, while organic ammonium tribromides have become very popular in recent years and a number of reports are available discussing the importance of these reagents in various types of organic transformations,[2] unfortunately the phosphonium tribromides do not seem to have received a similar kind of attention as yet. Nevertheless, these reagents merit an amount of investigation, especially because they are reported to have milder reactivity than organic ammonium tribromides.[3] Accordingly, an attempt was made to synthesize one such phosphonium tribromide and then study its reactivity profile. Thus, through this article we report the first synthesis of ethyltriphenyl phosphonium tribromide (ETPPTB), its crystal structure,[4] and its efficacy in various reactions such as bromination reactions, acylation reactions, and the synthesis of isothiocyanates.

RESULTS AND DISCUSSION

Ethyl triphenylphosphine tribromide (ETPPTB), molecular formula $C_{20}H_{20}PBr_3$, is a deep orange, solid crystalline compound that melts at 135 °C. It is soluble in polar aprotic solvents such as acetonitrile and dimethylformamide (DMF) as well as nonpolar aprotic solvents such as chloroform and dichloromethane (DCM) and is sparingly soluble in polar protic solvents such as ethanol and methanol. It is

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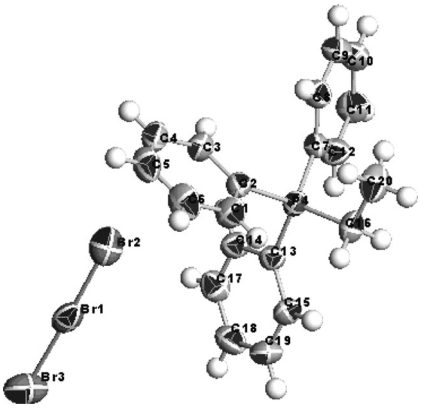
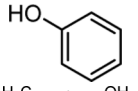
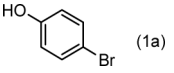
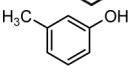
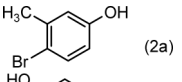
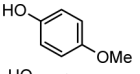
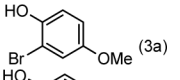
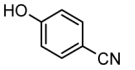
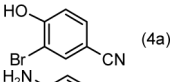
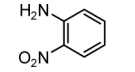
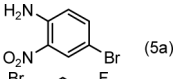
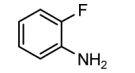
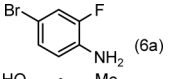
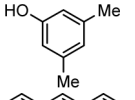
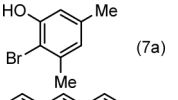
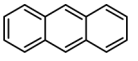
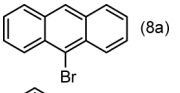
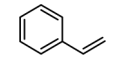
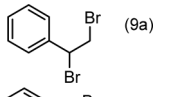
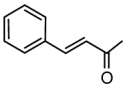
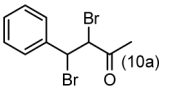


Figure 1. ORTEP view of ETPPTB with atom numbering scheme.

Table 1. Bromination reactions with ethyl triphenyl phosphonium tribromide[a]

Entry	Substrate	Time (min)	Product[b]	Yield (%)[c]
1		20	 (1a)	78
2		15	 (2a)	81
3		15	 (3a)	84
4		15	 (4a)	61
5		35	 (5a)	73
6		25	 (6a)	76
7		35	 (7a)	58
8		15	 (8a)	68
9		20	 (9a)	76
10		45	 (10a)	65

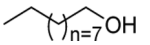
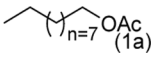
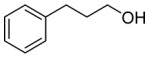
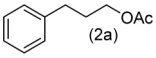
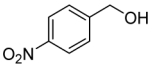
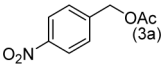
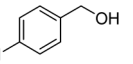
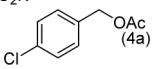
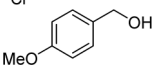
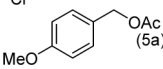
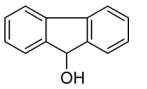
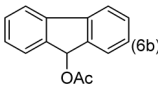
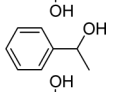
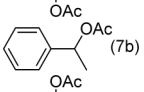
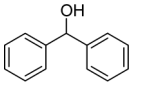
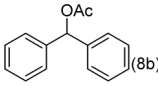
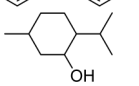
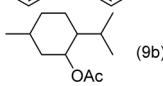
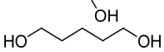
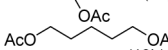
[a]Reactions were monitored by TLC.
[b]Products were characterized by IR, ^{1}H NMR, and ^{13}C NMR.
[c]Isolated yield.

nonhygroscopic, air stable, and has a prolonged shelf life at room temperature without loss of activity. The crystal structure of the compound reveals a monoclinic structure with space group P2(1)/n and an independent, nearly symmetric, and linear tribromide ion and an independent ethyltriphenylphosphonium ion. The tribromide ion has bond lengths of 2.525 Å (Br_1–Br_2) and 2.563 Å (Br_1–Br_3) and a bond angle of 178.43 Å (Fig. 1).

To study the versatility of ETPPTB as brominating agent, representative examples of different types of organic substrates were taken (Table 1). It was observed that bromination reactions were quite facile, and the products were obtained in moderate to excellent yields. The results have been summarized in Table 1. The products were identified by comparison of their melting points, infrared (IR) absorption, and NMR spectra with the authentic samples.[5]

Acylations of protic nucleophiles such as alcohols, amines, and thiols are important in synthetic organic chemistry because the resulting esters, amides, and thioesters serve as important functional components and/or intermediates in synthetic chemistry.[6] Thus, some acylation reactions were attempted (Table 2). The results were encouraging, revealing that ETPPTB can act well as an acylating reagent.

Table 2. Acylation of alcohols with ethyl triphenyl phosphonium tribromide[a]

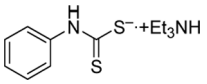
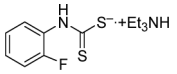
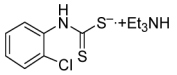
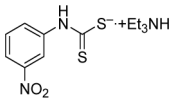
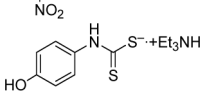
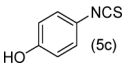
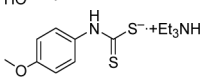
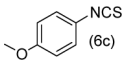
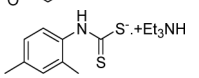
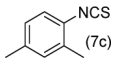
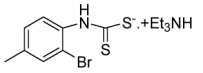
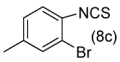
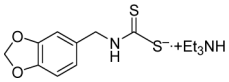
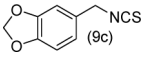
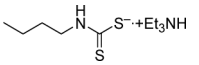
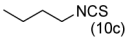
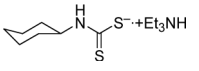
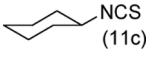
Entry	Substrate	Time (min)	Product[b]	Yield (%)[c]
1		15		82
2		15		78
3		25		75
4		15		79
5		15		80
6		45		73
7		45		70
8		55		67
9		50		74
10		10		69

[a]Reactions were monitored by TLC.
[b]Products were characterized by IR, ^{1}H NMR, and ^{13}C NMR.
[c]Isolated yield.

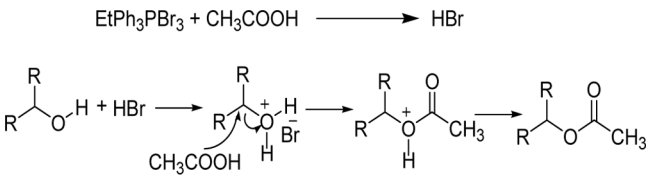
Isothiocyanates are some of the most important synthetic intermediates for the preparation of both sulfur- and nitrogen-containing organic compounds, especially for heterocycles.[7] The functionality is frequently encountered in natural products including marine sesquiterpenes. Additionally, synthetic isothiocyanates have been proved to have some biological activity and act as antiproliferatives[8] and enzyme inhibitors for the HIV virus.[9] Numerous methods for the preparation of isothiocyanates have been reported, and the most widely used procedure seems to be the decomposition of dithiocarbamates using heavy metals,[10] thiophosgene iodine,[11] ethyl chlorocarbonate,[12] and claycop.[13] However, most of the methods suffer from poor yields and the use of environmentally unattractive reagents.

Through this work, we observed that ETPPTB works well as a desulfurizing agent for synthesis of isothiocyanate from the corresponding dithiocarbamate precursor (Table 3). The dithiocarbamic acid salts were prepared following a modified

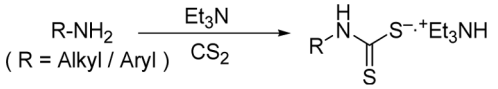
Table 3. Preparation of isothiocyanates with ethyl triphenyl phosphonium tribromide[a]

Entry	Substrate	Product[b]	Yield (%)[c]
1			83
2			69
3			71
4			70
5			68
6			74
7			87
8			70
9			67
10			65
11			68

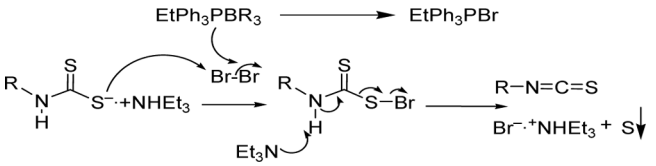
[a]Reactions were monitored by TLC.
[b]Products were characterized by IR, ^{1}H NMR, and ^{13}C NMR.
[c]Isolated yield.



Scheme 1. Mechanism for acylation of alcohols.



Scheme 2. Preparation of dithiocarbamate salt.



Scheme 3. Proposed mechanism for formation of isothiocyanate.

procedure of the reported methodology,[14] which can be represented as shown in Scheme 2.

The proposed mechanism for the transformation is given in Scheme 3. The precipitation of elemental sulfur supports the proposed mechanism.[15]

CONCLUSION

ETPPTB has been synthesized and its reactivity studied. Its ease of preparation, mildness, and efficacy in organic reactions such as bromination, acylation and isothiocyanate preparation shows that the reagent could be a useful addition to the existing lot of reagents.

EXPERIMENTAL

Preparation of the Reagent

An amount of V_2O_5(10 mg, 0.1 mmol) was added to 30% H_2O_2(9 mL, 79.74 mmol) and stirred in a precooled beaker at 0–4 °C until V_2O_5 completely dissolved and the solution attained a clear reddish brown color. To this content, 110 mL of water were added. Then, a solution of ETPPB (5 g, 13 mmol) and potassium bromide (KBr) (3.57 g, 30 mmol) in 100 mL of water was added. Later, 40 mL of 1 M H_2SO_4 was added in small portions, and the mixture was stirred for another 3h. ETPPTB precipitated out as fine yellow microcrystals, which were filtered under suction using Whatman 40 filter paper and dried in a vacuum desiccator using

self-indicating coarse silica gel. It was further recrystallized in ethyl acetate/hexane (99:1%). The yield was 92%.

Typical Procedure for Bromination Reaction

In a typical reaction, the phenol (**1**, Table 1) (282 mg, 3 mmol) was taken in acetonitrile (3 mL) and ETPPTB (1.59 g, 3 mmol), and dissolved acetonitrile (5 mL) was added dropwise with constant stirring at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was worked up to remove the spent reagent. The crude product thus obtained was concentrated and then subjected to column chromatography over a pad of silica gel to get 78% of the product.

Typical Procedure for Acylation Reaction

ETPPTB (159 mg, 0.3 mmol) was added to a solution of octadecyl alcohol (**1**, Table 2) (810 mg, 3 mmol) in acetic acid (3 mL). The reaction mixture was refluxed, and the progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was poured into a saturated solution of $NaHCO_3$ (15 mL) and then extracted with ethyl acetate (2×15 mL). The organic layer was separated and dried over anhydrous Na_2SO_3, and the crude product was isolated. Further purification was achieved by passing the compound through a short column of silica gel. The product yield was 82%.

Typical Procedure for Preparation of Isothiocyanate from Dithiocarbamate Salt

Carbondisulfide (1.5 mL, 25 mmol) was added dropwise to an ice-cooled mixture of the aniline (930 mg, 10 mmol) and triethylamine (4.15 mL, 30 mmol) with constant stirring. The reaction mixture was stirred further at room temperature for 2h. The resultant salt was filtered, washed with hexane/ethylacetate (9/1%), and dried in air.

Triethylamine (622 μL, 4.5 mmol) was added to a stirred, ice-cooled suspension of freshly prepared phenyl dithiocarbamate salt (**1**, Table 3) (810 mg, 3 mmol) in acetonitrile (5 mL). ETPPTB (1.59 g, 3 mmol) dissolved in acetonitrile (5 mL) was added dropwise over a period of 15 min. During the addition of the reagent, sulfur precipitated out as a light-yellow compound along with the spent reagent. After the completion of the reaction, the precipitated sulfur and spent reagent were filtered off. The organic layer was evaporated and admixed/extracted with hexane (15 mL), which was further washed with 1 N HCl (2×5 mL) and water (1×5 mL). The organic layer was dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified over a short column of silica gel (100% hexane) to give 83% yield of the product (**1a**).

Crystallographic Description

Crystal data were collected with a Bruker Smart Apex-II CCD diffractometer using graphite monochromated MoKα radiation ($\lambda = 0.71073$ Å) at 298 K. Cell

parameters were retrieved using SMART software and refined with SAINT on all observed reflections. Data reduction was performed with the SAINT software and corrected for Lorentz and polarization effects. Absorption corrections were applied with the program SADABS. The structure was solved by direct methods implemented in SHELX-97 program and refined by full-matrix least-squares methods on F2. All nonhydrogen atomic positions were located in difference Fourier maps and refined anisotropically. The hydrogen atoms were placed in their geometrically generated positions. The orange crystal was isolated in rectangular shapes from acetonitrile/hexane (9:1) at room temperature.

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4. (a) CCDC-627535 contain the supplementary crystallographic data for this article. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request.cif. Crystallographic description of ETPPTB (Fig 1): Crystal dimension (mm), $0.50 \times 0.28 \times 0.18$, $C_{20}H_{20}Br_3P$, $M_r = 531.06$; monoclinic, space group P2(1)/n; a = 10.1571(3) Å, b = 12.2399(3) Å, c = 16.9416(5) Å, $\alpha = \gamma = 90°$, $\beta = 90.678(2)°$, V = 2106.06(10) $Å^3$, Z = 4, ρcal = 1.675 Mg/m^3; reflections collected = 18784; 18784; refinement method = full-matrix least-squares on F^2; final R indices [I > 2sigma(I)] $R_1 = 0.0409$, $wR_2 = 0.0924$; R indices (all data) $R_1 = 0.0856$, $wR_2 = 0.1089$; goodness of fit = 1.005.
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