

Rapid synthesis of (3-bromopropyl)triphenylphosphonium bromide or iodide

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A novel rapid method for the preparation of (3-bromopropyl)triphenylphosphonium bromide was developed. The synthesis was accomplished by microwave irradiation of 1,3-dibromopropane with triphenylphosphine at a ratio of 1:1 for 2 minutes in xylene or toluene or without any solvent. The target compound was isolated in good yield (81–93%) and high purity.

Key words: 1,3-dibromopropane, triphenylphosphine, (3-bromopropyl)triphenylphosphonium bromide, (3-bromopropyl)triphenylphosphonium iodide, solvent effect; microwave irradiation.

INTRODUCTION

(3-Bromopropyl)triphenylphosphonium bromide is a useful compound which can be applied as novel insoluble bactericidal ceramic filler [1]. Its antibacterial activity is used against heterotrophic bacteria in simulated industrial recirculation water. After regenerating, the reused bactericide ceramic could still purify contaminated water [1]. Aqueous solutions of bromoalkyltriphenylphosphonium bromides react with zero-valent metals, causing their dissolution [2]. The reaction initially follows second-order kinetics, with the rate depending on both metal and bromide concentrations. Zero-valent metals similarly react with aqueous methylmercuric acetate and other dissolved organo-metals [2]. Positive ion fast atom bombardment (FAB) mass spectra were reported [3] for a representative series of mono- and bisphosphonium halides derived from triphenylphosphine. The use of laser micro-probe mass spectrometry (LMMS) for structural characterization of thermolabile quaternary phosphonium salts has been evaluated [4]. From 793 screening compounds with evaluable data, 158 were found, including (3-bromopropyl)triphenylphosphonium bromide to have significant inhibitory effects on ovarian cancer stem-like cells (CSC) [5].

In a paper were reported the synthesis and structural characterization of a new family of stable $R_3P^+(CH_2)_nS_2O_3^-$ ($R = Ph$ or Bu , $n = 3, 4, 6, 8$ or 10), which behave as cationic masked thiolate ligands with application to the functionalisation of gold nanoparticles having potential as new diagnostic bio-recognition systems [6]. The hexaflu-

orophosphate salt of the (3-bromopropyl)triphenylphosphonium compound was synthesized by Guarr *et al.* [7].

In this paper we report a rapid (only for 2 min) method for the preparation of (3-bromopropyl)triphenylphosphonium bromide by microwave irradiation. The conversion of bromide salt into iodide salt was performed in water that is the most popular green solvent [8].

EXPERIMENTAL

Materials

Unless otherwise stated, all reagents and solvents used in the synthesis and analysis were obtained from Sigma-Aldrich (St. Louis, MO, USA), Alfa-Aesar (Haverhill, MA, USA) as commercial products of analytical grade and applied without further purification.

Instrumentation

NMR spectra were recorded on a Bruker Avance III 500 MHz instrument (Rheinstetten, Germany) using $CDCl_3$ at 25 °C. (δ) are reported in ppm and referenced directly to the chemical shift of the TMS peak. Chemical shift of ^{31}P signal is not referenced. Melting point temperatures were determined on a Kofler bench apparatus (DDR, Berlin, Germany) and are uncorrected.

Experimental procedure for the preparation of (3-bromopropyl)triphenylphosphonium bromide or iodide

A 100 ml Erlenmeyer flask was charged with triphenylphosphine **2** (13.10 g, 0.05 mol), 1,3-dibromopropane **1** (5.10 ml, 0.05 mol, ratio of 1:1), and 5

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ml xylene or toluene. The flask content was heated in MW oven for up to 2 min at 450 W (stop on every 10 s with intervals of 10 s). A vigorous exothermic reaction was observed. Heating was stopped until the exothermic reaction ceased. After cooling to room temperature the reaction mixture was diluted with 20 ml of acetone and 75 ml of diethyl ether. The precipitate was filtered and air-dried. Yield: 81–93%, m.p. 226–227 °C (lit. m.p. 229–230 °C [2]).

The anion of (3-bromopropyl)triphenylphosphonium bromide could readily be exchanged with iodide. The white precipitate of (3-bromopropyl)triphenylphosphonium bromide (1 g) was dissolved in 5 ml of ethanol and added to 0.012 mol of potassium iodide dissolved in 10 ml of water. The solution was boiled for 10 minutes with stirring and then cooled to room temperature. The resulting white precipitate was filtered and dried in the air. Yield: 80%, m.p. 198–199 °C, no lit. m.p.

¹H-NMR (500 MHz, CDCl₃): 2.19–2.29 (m, 2H, CH₂CH₂), 3.87 (dt, 2H, J = 1.3, 6.2 Hz, CH₂Br), 4.09–4.15 (m, 2H, CH₂P), 7.68–7.76 (m, 6H, PhH), 7.78–7.90 (m, 9H, PhH).

¹³C-NMR (125 MHz, CDCl₃): 21.64 (d, 1C, J = 52.5 Hz, PCH₂), 26.31 (d, 1C, J = 2.7 Hz, CH₂CH₂), 33.54 (d, 1C, J = 20.4 Hz, BrCH₂), 117.98 (d, 3C, J = 86.4 Hz, PhC), 130.59 (d, 6C, J = 12.6 Hz, PhCH), 133.72 (d, 6C, J = 10.0 Hz, PhCH), 135.21 (d, 3C, J = 3.1 Hz, PhCH) [9]

³¹P-NMR (202 MHz, CDCl₃): 24.20 (s, 1P).

ESI+: m/z 384.055 (M+H, calculated 384.064), 386.034 (M+H, calculated 386.062)

RESULTS AND DISCUSSION

Usually (3-bromopropyl)triphenylphosphonium bromide has been prepared in solvents as xylene or toluene from equimolar quantities of 1,3-dibromopropane and triphenylphosphine for 20 h heating in yield up to 90% [10–12]. Another synthetic pathway involves reaction of triphenylphosphine with halogenoalcohols and subsequent replacement of the OH

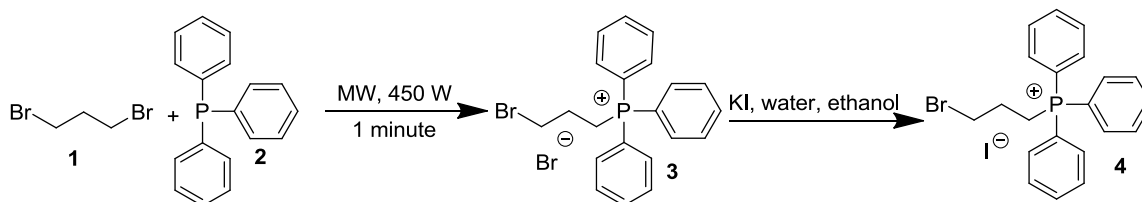
in alcohols by a halogen [6]. An attempt has been made to develop a green synthesis process. In PEG200/400, which recently have been confirmed as eco-friendly solvents [13], a mixture was obtained from mono- and bis-phosphonium salts. Probably this is due to PEG200/400 polarity. The same was obtained in another green solvent – ethyl L-lactate [14]. We found that this compound could be obtained with xylene (toluene) or without any solvent only for up to 2 min heating the reaction mixture in MW oven at 450 W (Scheme 1). The best yield of (3-bromopropyl)triphenylphosphonium was obtained in xylene and toluene corresponding to the similar dH evap [kJ/mol] of both solvents, 33.3 for toluene and 36.2 for xylene, irrespective of their different boiling points. The temperature obtained using microwaves depends on the dielectric constant of the reagent [15]. Microwave irradiation not only affords better yield (81–93%) than conventional heating, but even leads to acquiring a product of higher purity. Our method is much more rapid than most of the available procedures and greatly simplified as well.

The (3-bromopropyl)triphenylphosphonium bromide was proved by melting point, ¹H-NMR (Fig. 1), ¹³C-NMR (Fig. 2), ³¹P-NMR (Fig. 3) and mass spectra.

CONCLUSIONS

The new method for synthesis of (3-bromopropyl)triphenylphosphonium bromide or iodide by microwave irradiation has been described. The present procedure has the advantages of short reaction time (up to 2 minutes), high yields of the products, small reaction volume, a highly reproducible approach, a simple experimental work-up procedure, and easy anion replacement. By preparation of larger amount of (3-bromopropyl)triphenylphosphonium bromide part of the diethyl ether, acetone and xylene (or toluene) could be regenerated.

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Scheme 1. Preparation of 1-(3-bromopropyl)triphenylphosphonium bromide and iodide.

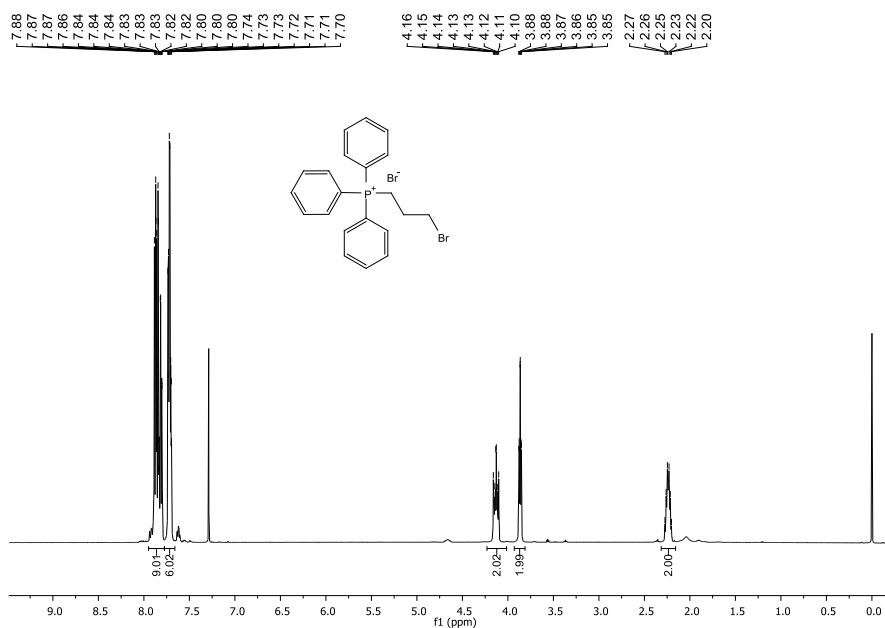


Fig. 1. ¹H-NMR spectra of (3-bromopropyl) triphenylphosphonium bromide.

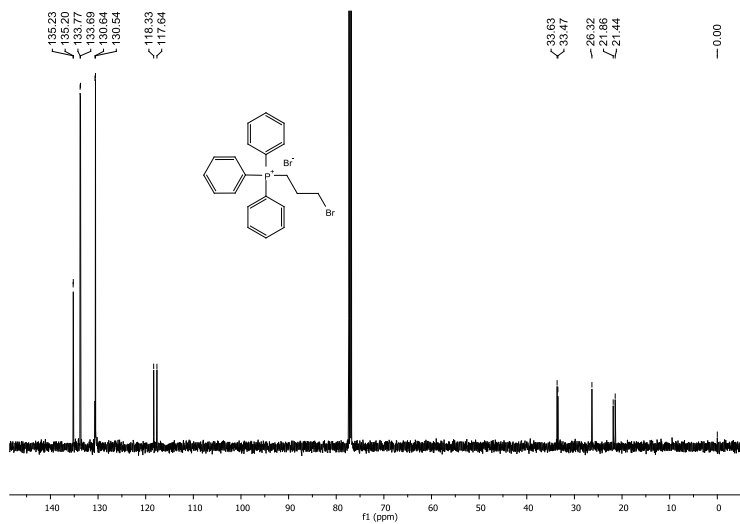


Fig. 2. ¹³C-NMR spectra of (3-bromopropyl) triphenylphosphonium bromide.

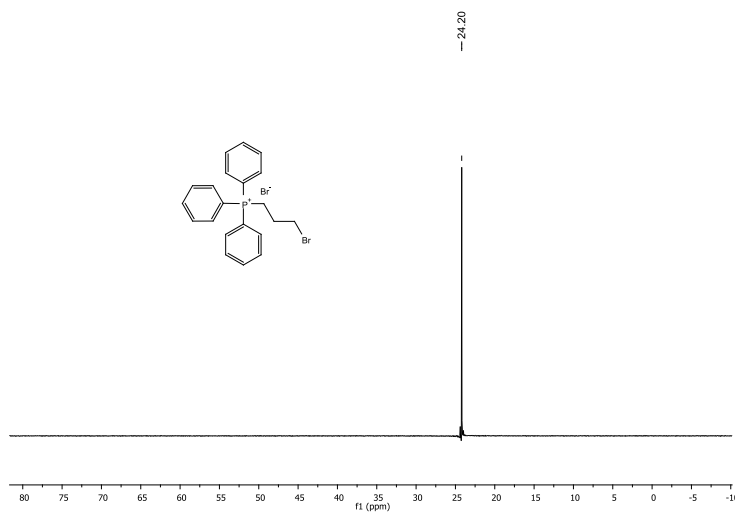


Fig. 3. ³¹P-NMR spectra of (3-bromopropyl) triphenylphosphonium bromide.

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БЪРЗ МЕТОД СИНТЕЗ НА (3-БРОМОПРОПИЛ)ТРИФЕНИЛФОСФОНИЕВ БРОМИД ИЛИ ЙОДИД

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(Резюме)

Разработен е нов бърз метод за получаване на (3-бромпропил)трифенилфосфониев бромид. Синтезът се извършва чрез MW облъчване на 1,3-дибромпропан с трифенилфосфин в съотношение 1:1 за 2 минути в ксилен или толуен или без разтворител. Основното съединение се получава с добър добив (81–93%) и с висока чистота.