European Journal of Chemistry 2 (2) (2011) 269-271

European Journal of Chemistry
Journal homepage: www.eurjchem.com

Novelties of solid-liquid phase transfer catalyzed synthesis of benzyl diethyl phosphate from the sodium salt of diethyl phosphate

Na Ge[a], Yumin Zhang[a], Dongmin Shi[a], Qiang Gu[a,*], Xuefeng Zhu[b] and Zhiyong Ding[b]

[a] *College of Chemistry, Jilin University, Changchun, 130012, China*
[b] *Daqing New Century Fine Chemicals Co. Ltd., Daqing, Heilongjiang Province, 163511, China*

**Corresponding author at: College of Chemistry, Jilin University, Changchun, 130012, China. Tel.: +86.431.85168470(3); fax: +86.431.85168420.*
E-mail address: guqiang@jlu.edu.cn (Q. Gu).

COMMUNICATION INFORMATION

Received: 24 August 2010
Received in revised form: 29 November 2010
Accepted: 08 December 2010
Online: 30 June 2011

KEYWORDS

Benzyl diethyl phosphate
Sodium salt of diethyl phosphate
Solid-liquid phase transfer catalysis
Nucleophilic substitution
Organic phosphate
Mechanism

ABSTRACT

Solid-liquid phase transfer catalysis coupled with mixed solvents, which could be recycled, as a green chemistry procedure, was applied to the synthesis of phosphate from the sodium salt of diethyl phosphate. The benzyl diethyl phosphate was synthesized in good yield via one-pot method from the reaction of the industrial by-product sodium salt of diethyl phosphate with benzyl chloride in solid-liquid phase transfer catalysis and toluene-water mixed solvents. The effects of catalyst structure, the amounts of catalyst, the raw material molar ratio, water loading, and reaction temperature on the conversion of the reaction were investigated. The structure of the benzyl diethyl phosphate generated was confirmed by Elemental Analysis, IR, ^{1}H NMR and GC/MS.

1. Introduction

Organic phosphates play an important role in a variety of chemical processes, such as catalysts for condensation reaction [1] and epoxidation reaction [2], pro-drugs [3] to increase the water solubility and bio-availability of the agents in biological chemistry [4], solvent extraction processes and insecticides in agriculture applications [5], and so on. The preparation of most phosphates is based on the phosphorylation of alcohols or phenols with some sort of "activated phosphoric acid" in the literature [6-9]. Recently, the cross-coupling reaction of substituted benzyl diethyl phosphates with arylboronic acids and arylmagnesium reagents has been explored by McLaughlin [10] and Kofink *et al.* [11], respectively. The generally reported method for the preparation of a series of substituted benzyl diethyl phosphates was the corresponding substituted benzyl alcohols by phosphorylation with diethyl chloro-phosphate in the presence of triethylamine or pyridine, and the yields were low [12-14]. Clearly, there is a need for improving synthesis of substituted benzyl diethyl phosphates. It is known that sodium salt of diethyl phosphate was very poor nucleophilic agent and its nucleophilic substitution with organic halides was rarely studied to be of any preparative importance [15].

The sodium salt of diethyl phosphate is an inconveniently disposed and contaminates environment side-product of industrial products, which derive from fluorescent brightener 2,2'-(2,2'-(1,4-phenylene) *bis*(ethene-2,1-diyl)) dibenzonitrile (ER) by employing triethyl phosphite as catalyst, and increases year after year. Therefore, it is more important to utilize sodium salt of diethyl phosphate, which not only reduce environmental pollution but also bring out considerable economic value.

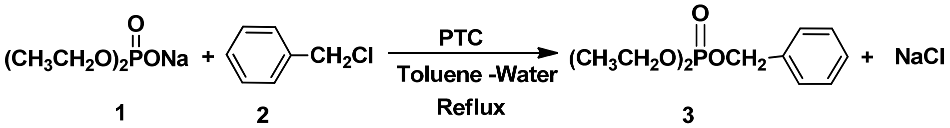
To the best of our knowledge, the research on sodium salt of diethyl phosphate reused and prepared available organic phosphate has hardly been reported. It is now demonstrated that phosphorylation of benzyl chloride (**2**) by means of sodium salt of diethyl phosphate (**1**) in toluene-water at reflux temperature in solid-liquid system with tetrabutyl ammonium bromide (TBAB), affording the good yield of benzyl diethyl phosphate (**3**) (Scheme 1). This one-pot procedure is a facile and efficient method for the synthesis of benzyl diethyl phosphate, with the advantages of mild reaction conditions, simple operations, clean technology and high yields. Besides, the catalyst is inexpensive, basically nontoxic, highly stable and easily available. Moreover, this method is suitable for the synthesis of phosphate ester by using all the sodium salts of dialkyl phosphate as initial material, including sodium salt of diethyl phosphate, the by-product by employing triethyl phosphite as catalyst in the basic condition. So it is significant to this research further.

2. Experimental

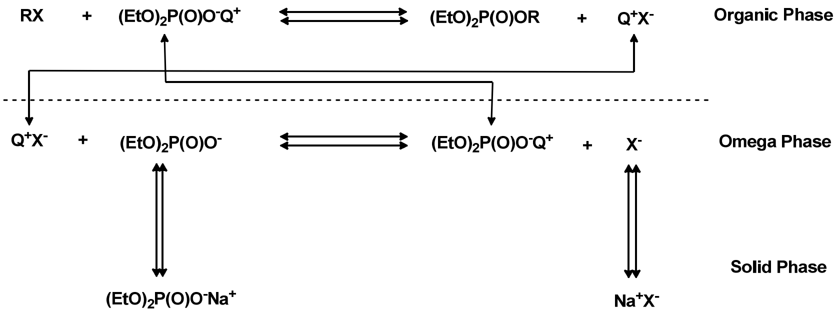
2.1. Instrumentation

IR spectrum was prepared on an Alpha Centauri FT-IR spectrometer. ^{1}H NMR spectrum was measured using a Varian Mercury-300 NMR spectrometer with TMS as an internal standard. Mass spectra was collected with an Agilent 5975/6890N GC/MS spectrometer. Thin layer chromatography was carried out on silica gel GF-254 plates with petroleum ether:ethyl acetate (8:1) as developing agent. Refractive Index (uncorrected) was measured using a Shanghai Abbe Refractometer-2WAJ, and compared with the literature value.

ISSN 2153-2249 (Print) / ISSN 2153-2257 (Online) © 2011 EURJCHEM
DOI:10.5155/eurjchem.2.2.269-271.261



Scheme 1



Scheme 2

2.2. Materials

All the reagents aside from sodium salt of diethyl phosphate were analytical pure reagent and were used without further purification. Sodium salt of diethyl phosphate derived from the by-product of fluorescent brightener ER in the factory was used with further purification.

2.3. Synthesis

The optimal synthesis condition is as follows: Sodium salt diethyl phosphate (0.05 mol), TBAB (0.003 mol), 20 mL toluene and 2 mL water were mixed in the three-neck round-bottomed flask. Then benzyl chloride (0.05 mol) was added and stirred at the reflux temperature until TLC analysis (petroleum ether:ethyl acetate, 8:1, v:v) monitored completion of the reaction. Then the mixture was cooled and poured into toluene (20 mL), filtered and the residue was taken up in toluene. The toluene layer was washed with saturated sodium bicarbonate (2x15 mL), water (2x15 mL), saturated sodium chloride (1x20 mL), and dried over anhydrous magnesium sulfate. After the removal of the low boiling solvent, benzyl diethyl phosphate was collected. The benzyl diethyl phosphate was obtained as light yellow oil. Yield (10.94 g, 89.67%). n_D^{22} 1.4895 (Lit. [16] n_D^{20} 1.4846). Anal. Calcd. for $C_{11}H_{17}PO_4$: C, 54.10; H, 7.02 %. Found: C, 54.40; H, 7.20 %. IR (ν_{max} , film, cm^{-1}): 2983, 2865, 1498 (CH_3); 2933, 2908, 2855, 1456 (CH_2); 1275 (P=O); 1034, 976 (P-O-C). ^{1}H NMR (300 MHz; $CDCl_3$, δ_H): 1.28-1.32 (t, J=7.5 Hz, 6H), 4.06-4.13 (m, J=7.5 Hz, 4H), 5.05-5.08 (d, J=8.5 Hz, 2H), 7.33-7.39 (m, 5H). MS (m/z, I_r/%): 246 (2.2), 245 (15.6), 244 (29.2), 215 (15.5), 188 (15.7), 187 (24.7), 153 (10.3), 125 (25.9), 107 (78.6), 91 (100).

3. Results and discussion

A possible mechanism for the reaction can be described as shown in Scheme 2, which involves the dissolution of solid $(EtO)_2P(O)O^-$ into ω-phase, followed by the anion-exchange reaction with the quaternary ammonium salt Q^+X^- to form the active ion pair $(EtO)_2P(O)O^-Q^+$ in the ω-phase, a layer around the solid phase and organic phase, then $(EtO)_2P(O)O^-Q^+$ is transferred to the organic phase, where the diethyl phosphate anion substitution on benzyl chloride takes place. Addition of small quantities of water also facilitates the distribution of the quaternary salt between the organic phase and solid phase (Scheme 2).

To obtain the high yield, we attempted to optimize the reaction conditions on the different phase transfer catalysts. The results were as shown in Table 1, triethyl benzyl ammonium chloride (TEBA), cetyl trimethyl ammonium bromide (CTAB), and polyethylene glycol-400 (PEG-400) to be less effective than TBAB in our laboratory (entries 1-4). This is because the catalyst TBAB cation Q^+ possess the better distribution in the organic phase, $(EtO)_2P(O)O^-$ could efficiently be transferred to the organic phase by Q^+, further enhanced the nucleophilic property of $(EtO)_2P(O)O^-$. The results were in agreement with the published literature [17-20]. To adequately utilize the side-product of industrial products sodium salt of diethyl phosphate, the effect of molar ratios of sodium salt of diethyl phosphate to benzyl chloride were studied for 1:1, 1:1.2, 1:1.5, and 1:2 under otherwise similar conditions (entries 4, 10-12). The yield of the product was not obviously enhanced with the use of higher concentration of the TBAB catalyst (up to 8 mol%, based on the sodium salt of diethyl phosphate, entries 4-9) and a 1.2~2.0 times excess benzyl chloride (entries 10-12), due to the fact that the concentration of $(EtO)_2P(O)O^-Q^+$ extracted into the ω-phase retains almost constant with the ion-exchange reaction proceeding. This phenomenon is also observed in most other solid-liquid phase transfer catalyzed reactions [21,22]. Furthermore, considering the cost of consumed materials, 6 mol% of TBAB and the molar ratio 1:1 of sodium salt of diethyl phosphate to benzyl chloride was taken for all the reactions. However, surprisingly, the yield of the product was notably enhanced when a little water was introduced. In the present study, the effect of the amount of water on yields was also investigated (entries 4, 13-16). Previous literature generally indicated that adding a little water to form the ω-phase, which would enhance the rate of the reaction [23]. For clarity, it was observed that small quantities of water (1 mL or 2 mL) substantially increase the yield and purity of product compared to those under adding more water above 5mL.

Table 1. Preparation of benzyl diethyl phosphate from sodium salt of diethyl phosphate and benzyl chloride under various conditions[a].

Entries	Raw material ratio [b]	PTC (%mol) [c]	Solvent toluene/water (mL/mL)	Temperature (°C)	Yield [d,e] (%)
1	1:1	6% CTAB	20/3	reflux	38.44
2	1:1	6% TEBA	20/3	reflux	23.60
3	1:1	6% PEG-400	20/3	reflux	11.15
4	1:1	6% TBAB	20/3	reflux	64.30
5	1:1	3% TBAB	20/3	reflux	42.70
6	1:1	4% TBAB	20/3	reflux	50.90
7	1:1	5% TBAB	20/3	reflux	59.84
8	1:1	7% TBAB	20/3	reflux	67.54
9	1:1	8% TBAB	20/3	reflux	69.15
10	1:1.2	6% TBAB	20/3	reflux	65.24
11	1:1.5	6% TBAB	20/3	reflux	64.51
12	1:2	6% TBAB	20/3	reflux	68.61
13	1:1	6% TBAB	20/0	reflux	00.00
14	1:1	6% TBAB	20/1	reflux	88.11
15	1:1	6% TBAB	20/2	reflux	89.67
16	1:1	6% TBAB	20/5	reflux	29.48
17	1:1	6% TBAB	20/2	70	60.74
18	1:1	6% TBAB	20/2	80	70.16
19	1:1	6% TBAB	20/2	100	86.13

[a] Reaction time (11.5 h).

[b] Raw material ratio (sodium salt of diethyl phosphate:benzyl chloride).

[c] The amount of PTC is based on sodium salt of diethyl phosphate.

[d] Refractive index 1.4860 (Lit. [16] n_D^{20} 1.4846).

[e] Isolated yields.

The yield and purity consumedly shrank when the water addition was more than 5 mL. Further addition of water rendered the conversion of the system from S(reagent)-L(ω)-L(org) to L(ω)-L(org) PTC, leading to a dramatic decrease in the effective concentration of $(EtO)_2P(O)O^-Q^+$ in the organic phase, in return the overall reaction rate fell. Thus, the 2 mL water loading helps to the reaction. At the same time, it was found when the temperature was low, the reaction did not occur.

The effect of temperature on the yield of the product was studied in the range of 70-100 °C (entries 4, 17-19). The yield was observed to increase with an increase in the reaction temperature up to reflux for 11.5 h. However, the yield declined a little when reaction temperature was further increased to 100 °C, which may be resulted in an evaporation of the ω-phase water at this temperature. As a result, the reflux temperature was chosen to be the optimized temperature.

In conclusion, at the optimized reaction conditions, the catalytic efficiency was TBAB > CTAB > TEBA > PEG-400. The amounts of catalyst was 6 mol% TBAB. The raw material ratio of sodium salt of diethyl phosphate to benzyl chloride was 1:1. The quantity of water added was 2 mL per 0.05 mol sodium salt of diethyl phosphate. The reaction temperature is the reflux temperature of the mixed solvents.

Acknowledgements

The authors wish to acknowledge their gratitude to Daqing New Century Fine Chemicals Co., Ltd. for the by-product of fluorescent brightener support.

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