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Synthesis of acetylenes via dehydrobromination using solid anhydrous potassium phosphate as the base under phase-transfer conditions

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ABSTRACT

Phase-transfer catalyzed preparation of acetylenes from the corresponding vicinal dibromo compounds via double dehydrobromination using the mild solid base, anhydrous potassium phosphate, under very mild conditions is reported.

One of the most significant achievements of phase-transfer catalysis (PTC) in synthetic chemistry is the beneficial replacement of hazardous and sensitive bases such as sodamide, sodium hydride or potassium *tert*-butoxide in various processes with the benign and robust aqueous sodium hydroxide. Weakly acidic substrates with a pK_a of up to 24 could be readily deprotonated using 50% aqueous NaOH in the presence of a PTC. Notwithstanding the success of PTC/OH systems,[1] some fundamental limitations still exist that restrict the widespread utility of this system. These are mainly related to the presence of water in hydroxide solutions. Water cannot be avoided in PTC/OH systems primarily due to the highly hygroscopic nature of caustic bases. Consequently, reactions under PTC/OH conditions are susceptible to side reactions such as hydrolysis. This prompts us to offer a general solution for this limitation by utilizing the solid mild base, potassium phosphate. This base, in comparison with hydroxide ions, is milder, less basic, far less hygroscopic and, most importantly, does not produce water upon neutralization with acidic compounds which otherwise results in side reactions.

Potassium phosphate has been recognized previously as a solid base which possesses unique highly basic sites, particularly when dehydrated upon calcination at 400 °C. Tada[2] determined the basic strength of potassium phosphate as $H_0 = 17.2$ using acidic indicators and tested its catalytic activity for the decomposition of diacetone alcohol (4-hydroxy-4-methylpentan-2-one) in the liquid phase at 30–55 °C. Higuchi et al.[3] examined the activity of potassium phosphate and other solid bases in the cyanosilylation of carbonyl compounds at 0 °C and measured the maximum base strength as $18.4 > H_0 > 15.0$ after calcination of the phosphate at 180 °C.

Potassium phosphate has been utilized as an auxiliary mild base in homogeneous metal-catalyzed processes, particularly in the presence of base-sensitive functional groups. Buchwald disclosed K_3PO_4 as an auxiliary base for the arylation of amides and ketones using copper or palladium catalysts.[4] Potassium phosphate was also the base of choice in the Suzuki cross-coupling reactions of aryl triflates or halides and aryl boronic acids with Pd or Ni catalysts.[5]

We realized that potassium phosphate, despite its relatively low basicity in aqueous medium (pK_a of K_3PO_4 is approximately[6] 12), is a very potent solid base in anhydrous systems, and is substantially more active than potassium carbonate and potassium fluoride in the formation and subsequent reactions of carbanion, azanions, and oxanions.[7] K_3PO_4 has also been utilized for various other reactions such as nitroaldol[8] and the Knoevenagel condensation.[9] Hydrated K_3PO_4 has frequently been used in transition metal catalyzed cross-coupling reactions.[10]

In our laboratory we have studied alkylations of different carbon acids and oxidative couplings of thiols to the corresponding disulfides using solid K_3PO_4 as the base under phase-transfer conditions.[7,11] In the present study potassium phosphate was applied for the synthesis of acetylenes from olefins through double dehydrobromination under PTC conditions. Acetylenes are essential and versatile intermediates in organic synthesis.[12] They are also utilized extensively for the preparation of conjugated polyacetylenes with potential applications in the emerging areas of molecular electronics and nanotechnology,[13] as well as for the preparation of nonlinear optical devices and linear chemical probes.[14]

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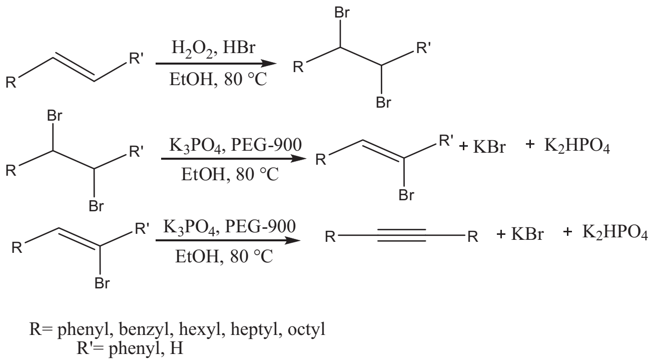


Scheme 1. General process for the conversion of olefins to acetylenes.

As described in the original procedure, the synthesis of phenyl acetylene is achieved by heating β-bromostyrene with KOH in ethylene glycol at 200 °C to give the product in 67% yield.[15] Application of a PTC for the synthesis of acetylenes via base-induced β-elimination was reported by Dehmlow who demonstrated that dehydrohalogenation of 1,2-dihalides into acetylenes proceeded satisfactorily in a liquid–solid system using KOH and highly lipophilic tetraoctylammonium bromide as the phase-transfer catalyst.[16] It was also shown that the use of less lipophilic tetra-*n*-butylammonium salts as the PT catalysts in these reactions was not successful.[17] A breakthrough in this field was made by Kimura and Regen[18] who applied pentaethylene glycol as the catalyst in the dehydrobromination of alkyl bromides or dibromides in the presence of 60% aqueous KOH to generate olefins and acetylenes. Typically, a 96% yield of phenyl acetylene was obtained in the reaction of dibromostyrene at 70 °C after 16 h. Reasonable catalytic activity in the latter system was also realized when pentaethylene glycol was grafted onto a polystyrene polymer. As expected, the presence of the highly concentrated caustic base resulted in side reactions such as hydrolysis and polymerization of the products. Rathore et al. used polyethylene glycol with KOH for diarylacetylene synthesis and obtained good yields but a very high temperature (~190 °C) was required.[19]

We report herein the application of the mild solid base, potassium phosphate, in the solid–liquid phase-transfer catalyzed double dehydrobromination reaction of vicinal dibromides to yield acetylenes in excellent yields. The selected catalyst for the process was PEG-900. When combined with a preceding oxybromination step this methodology offers a general practical strategy for the conversion of olefins into acetylenes (Scheme 1). Initially an alkene was reacted with aqueous hydrogen peroxide and concentrated hydrobromic acid in ethanol at 80 °C to yield the corresponding vicinal dibromide.[20] The latter was then reacted with solid potassium phosphate in ethanol in the presence of 25 mol % of PEG-900 at 80 °C for 1.5–5 h to yield the corresponding acetylene. The elimination reaction occurs as a stepwise process in which the first mole of HBr is eliminated almost instantly while the elimination of the second mole of HBr required several hours under our conditions.

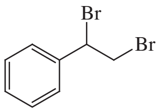
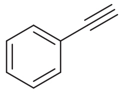
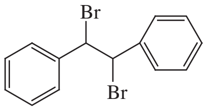
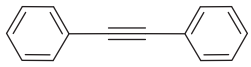
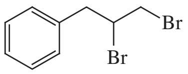
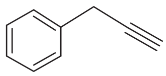
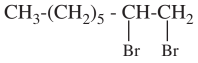
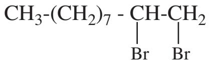
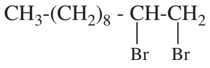
The best results were achieved when solid potassium phosphate was added in two equivalent portions. The second portion was preferably introduced after the first mole of HBr had been eliminated to yield the intermediate bromo olefin. Kinetic measurements revealed that at 80 °C the first step was complete within only 10 min.

This synthetic protocol (Scheme 1) was applied with several olefins and the results are summarized in Table 1. Complete conversion was confirmed in all the experiments using TLC and GC analysis. The only side product detected was the corresponding intermediate bromo olefin. We confirmed that the reaction could be driven to completion upon addition of an excess amount of K_3PO_4 and applying a prolonged reaction time. The product acetylene could be distilled from the mixture after removal of the solvent.

The reaction did not proceed at all in aprotic solvents such as toluene or *N*,*N*-dimethylformamide. The reaction rate in *n*-butanol was 50% lower than in ethanol. Potassium phosphate was completely insoluble in ethanol at temperatures below 100 °C. The presence of polyethylene glycol did not affect this solubility. Conversely, when K_3PO_4 was mixed with ethanol in the presence of PEG, and following the removal of solid potassium phosphate by filtration, the filtrate was found to be substantially basic, however it did not contain phosphate, as was confirmed by ^{31}P NMR spectroscopy. The transfer of basicity to the organic phase could not therefore be attributed to extraction of phosphate. Upon addition of an electrophile such as benzyl chloride to the ethanol/K_3PO_4/PEG mixture, benzyl ethyl ether was formed instantly under ambient conditions. We concluded that the anion transferred to the

Table 1

Double dehydrobromination of vicinal dibromo compounds to the corresponding acetylenes under phase-transfer conditions via Scheme 1

Entry	Reactant	Time (h)	Product	Isolated yield (%)
1		1.5		93
2		5.0		85
3		5.0		76
4	 $CH_3\text{-}(CH_2)_5\text{-}CH(Br)\text{-}CH_2Br$	5.0	$CH_3\text{-}(CH_2)_5\text{-}C\equiv CH$	61
5	 $CH_3\text{-}(CH_2)_7\text{-}CH(Br)\text{-}CH_2Br$	5.0	$CH_3\text{-}(CH_2)_7\text{-}C\equiv CH$	54
6	 $CH_3\text{-}(CH_2)_8\text{-}CH(Br)\text{-}CH_2Br$	5.0	$CH_3\text{-}(CH_2)_8\text{-}C\equiv CH$	52

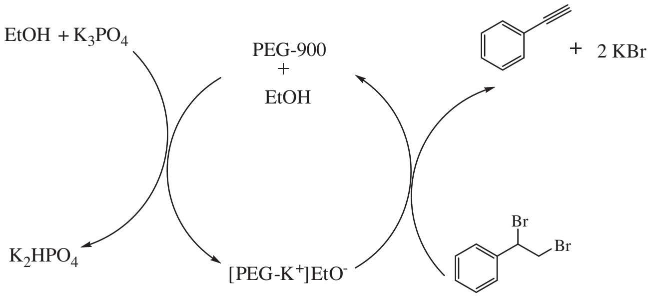


Figure 1. Proposed mechanism for the polyethylene glycol catalyzed dehydrobromination in the presence of solid K_3PO_4.

organic phase was ethoxide which is formed according to the following heterogeneous equilibrium:

$$EtOH + K_3PO_4 \rightleftharpoons EtO^-K^+ + K_2HPO_4$$

Figure 1 illustrates the proposed mechanism for the PEG catalyzed dehydrobromination reaction in the presence of K_3PO_4. Ethanol is deprotonated on the surface of potassium phosphate, and potassium ethoxide is extracted into the bulk ethanol with the aid of PEG along with the formation of K_2HPO_4. This forms the basis of the rationale for the outstanding activity of alcohols in reactions catalyzed by phosphates, such as Knoevenagel and Michael reactions.[7] Potassium ethoxide in the bulk ethanol may form the complex[18] [PEG-K^+]EtO^- which contributes to the enhanced reactivity of the EtO^- anion. In the second step, dehydrobromination of the substrate occurs due to the action of [PEG-K^+]EtO^- to produce a vinylic bromide with both one mole of KBr and K_2HPO_4. The final step is a second dehydrobromination to produce the corresponding acetylene.

We could not identify any poisoning effect of KBr and K_2HPO_4 on the reaction (Scheme 1), and so conclude that the latter is not deposited on the surface of the phosphate base, where it would block access to the active sites.

To conclude, we have demonstrated the application of anhydrous K_3PO_4 as a mild solid base that is more potent than common solid bases such as carbonates, oxides, or fluorides and is also more selective than KOH or NaOH in the facile dehydrobromination of vicinal dibromo compounds. The corresponding acetylenes were obtained in high yields and purities under simple and mild reaction conditions. We believe that the methodology described here can be developed for numerous synthetic applications on laboratory and industrial scale.

General procedures: synthesis of vicinal dibromides from olefins

To a mixture of olefin (16.8 mmol) and EtOH (60 mL) at 80 °C was added concentrated (48%) HBr (7.2 mL) dropwise over a period of 30 min followed by dropwise addition of 30% H_2O_2 (4.8 mL). During H_2O_2 addition the color of the solution changed to brown (the characteristic color of bromine). Stirring was continued until the color disappeared. The mixture was allowed to cool to room temperature, and further neutralized by addition of aqueous $NaHCO_3$ solution until pH 6.

In the case of solids (Table 1, entries 1–3), the products were separated by filtration, washed thoroughly with water and dried in air. In the case of liquids (Table 1, entries 4–6), the products were separated by extraction with CH_2Cl_2. The organic phase was dried over Na_2SO_4 and evaporated under vacuum, to afford pure dibromo compounds which were used as the reactants for the synthesis of acetylenes (as detailed below).

Synthesis of acetylenes from vicinal dibromides

A mixture of vicinal dibromide (5 mmol), anhydrous K_3PO_4 (5 mmol), PEG-900 (1.25 mmol), and EtOH (10 mL) was stirred at 80 °C. The progress of the reaction was monitored by analysis of the samples using TLC and gas chromatography. When the vicinal dibromide had been completely converted into the monobromo product, a second portion of K_3PO_4 (5 mmol) was added.

Following completion of the reaction the mixture was filtered and the filtrate was diluted with CH_2Cl and washed several times with H_2O. The organic phase was dried over $MgSO_4$ and evaporated under vacuum to afford a mixture of product and the monobromo derivative. The acetylene was separated by vacuum distillation. The identity and purity of the products were confirmed by GC–MS and ^1H NMR spectroscopy.

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