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Tetrahedron Letters 47 (2006) 3107–3109

Tetrahedron Letters

An efficient method for the esterification of phosphonic and phosphoric acids using silica chloride

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Received 19 December 2005; revised 16 February 2006; accepted 27 February 2006
Available online 20 March 2006

Abstract—Silica chloride is used as an effective heterogeneous catalyst for the rapid esterification of alkyl/aryl phosphonic/phosphoric acids to their corresponding alkyl/aryl phosphonates/phosphates under mild conditions with quantitative yields.

Organophosphorus compounds are important both in living systems as well as in commercial applications such as pesticides, fungicides, fire retardants and lubricants. Alkyl/aryl phosphonates/phosphates are also important for the synthesis of various bioactive compounds[1] serving as natural products, phosphates, phosphonopeptides, amino acid analogues, prodrugs, pharmacological agents and as important synthetic precursors.[1–7] Furthermore, phosphonates have also been recognized as 'markers' of chemical warfare agents, for verification purposes of the chemical weapons convention (CWC)[8,9] and are covered in the CWC text under schedule 2 B4 category.[9] Due to their wide utility and our interest in their properties, we intended to reinvestigate their synthesis. A plethora of effective chemical approaches have been devised from the corresponding phosphites (dialkyl phosphites/trialkyl phosphites)[10,11] in the presence of alkyl halides. Among these methods, only a few can be carried out as convenient laboratory methods for the syntheses of the title compounds. Most of the reported methods are time consuming,[12] require a strong base,[13] the use of solvent, high temperature,[14] tedious work-up and chromatographic techniques are often used to afford the compounds of desired purity.

In recent years, the use of reagents and catalysts on solid supports has received significant attention.[15] Silica gel is one of the extensively used surface material supports for different chemical transformations in organic chemistry.[16] One such modified silica is silica chloride (SiO_2–Cl), which has been reported to be an efficient reagent for the synthesis of many organic compounds.[17] The efficiency of silica chloride, under operationally simple conditions, has prompted us to explore the possibility of this catalyst for the esterification of phosphonic/phosphoric acids. Our aim in undertaking this work was to overcome the limitations and drawbacks of the reported methods. Herein, we report a rapid, efficient, economic, environmentally benign and easy to scale-up method for the effective conversion of alkyl/aryl phosphonic/phosphoric acids to their corresponding alkyl/aryl phosphonates/phosphates at room temperature using silica chloride as a heterogeneous catalyst. This particular catalyst can be prepared very easily and has found infrequent application in synthetic organic chemistry. The method developed has allowed us to obtain quantitative yields of the required products in reduced reaction times. The room temperature (20–25 °C) reaction of phosphonic acids with various alcohols in the presence of silica chloride afforded the corresponding alkyl/aryl phosphonates in 20–40 min with excellent yields (Table 1).

The reactions were carried out using 1:1:4 molar ratios of alkyl phosphonic acid, silica chloride and alcohol; dry alcohol was added to the mixture dropwise at 0 °C and the desired phosphonates were obtained in excellent yield with acceptably high purities.[18] Esterification with alicyclic and primary alcohols was complete in 20–25 min, while secondary alcohols, phenols and aromatic alcohols took comparatively longer times (40 min) for complete esterification, whilst tertiary alcohols did not react at all. Probably, the reaction is slow essentially

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Keywords: Phosphonate; Phosphate; Silica chloride; Heterogeneous catalyst; Dialkyl phosphite; Trialkyl phosphite; CWC; CWA.

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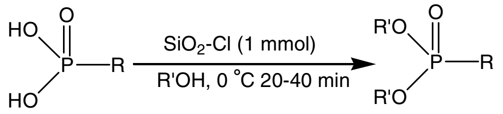
doi:10.1016/j.tetlet.2006.02.159

Table 1. Synthesis of phosphonates using silica chloride



Entry	R	R′	Yield (%)[a]	^{31}P NMR (ppm)[b]
1	CH_3	CH_3	89	32.3
2	CH_3	C_2H_5	88	30.1
3	CH_3	n-C_3H_7	80	29.8
4	CH_3	i-C_3H_7	92	27.8
5	CH_3	n-C_4H_9	90	28.9
6	CH_3	C_6H_{11}	90	29.2
7	C_2H_5	CH_3	94	33.3
8	C_2H_5	C_2H_5	90	33.9
9	C_2H_5	n-C_3H_7	92	32.8
10	C_2H_5	i-C_3H_7	89	32.1
11	C_2H_5	n-C_4H_9	91	32.6
12	n-C_3H_7	CH_3	89	32.6
13	n-C_3H_7	C_2H_5	88	32.2
14	n-C_3H_7	n-C_3H_7	90	29.2
15	i-C_3H_7	CH_3	92	32.6
16	i-C_3H_7	C_6H_5	90	30.2

All compounds were characterized by IR, NMR and MS.

[a] Isolated yield.

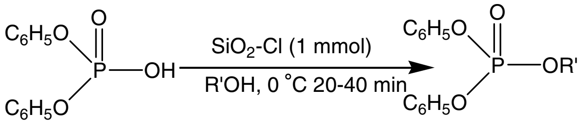
[b] ^{31}P NMR spectra were recorded in $CDCl_3$ at 400 MHz.

because of the bulkiness of the corresponding alcohol. The applicability of this method was further extended to the synthesis of phosphates from diaryl phosphoric acids (Table 2).

It is likely that silica chloride acts as a source of acid, which protonates the phosphonic/phosphoric acid followed by attack of an alkoxide ion on the phosphorus atom, which results in esterification of the corresponding acids. The structures of the products were confirmed on the basis of their spectral data (^{1}H NMR, ^{31}P NMR and MS).[19] The advantage of using silica chloride is that it can be prepared from readily available material[20] and can also be removed easily from the reaction mixture.

In conclusion, an efficient and simple method for the synthesis of alkyl/aryl phosphonates and phosphates has been described using silica chloride as a heterogeneous catalyst. The main advantage of this method is that it requires mild reaction conditions, short reaction times, takes place at ambient temperature with operational simplicity and with excellent yields.

Table 2. Synthesis of phosphates using silica chloride



Entry	R′	Yield (%)[a]	^{31}P NMR (ppm)[b]
1	CH_3	89	−15.1
2	C_2H_5	88	−15.4
3	n-C_3H_7	90	−14.8
4	i-C_3H_7	92	−14.5
5	n-C_4H_9	90	−12.4
6	C_6H_{11}	95	−12.2

All compounds were characterized by IR, NMR and MS.

[a] Isolated yield.

[b] ^{31}P NMR spectra were recorded in $CDCl_3$ at 400 MHz.

Acknowledgements

We thank Shri K. Sekhar, Director DRDE, Gwalior for his keen interest and encouragement.

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18. Typical experimental procedure for the synthesis of alkyl/aryl phosphonates/phosphates: To a mixture of alkyl phosphonic/phosphoric acid (1 mmol) and silica chloride (1 mmol), dry alcohol (4 mmol) was added dropwise at 0 °C. The reaction mixture was stirred for 10–20 min. The progress of reaction was monitored by ^{31}P NMR. After disappearance of the phosphonic/phosphoric acid signal in ^{31}P NMR, the reaction mixture was filtered and the solvent was evaporated under reduced pressure. The residue was distilled under vacuum to afford the pure compound. The mass spectrometric and ^{31}P NMR data of the synthesized compounds were matched with the spectral library available in the latest official database of the Organization for the Prohibition of Chemical Weapons (e-OCAD).
19. Organization for the Prohibition of Chemical Weapons (OPCW) Central Analytical database (e-OCAD) v, 5 April 2004.
20. Typical procedure for the preparation of silica chloride: To well-stirred silica gel (20 g) in CH_2Cl_2 (50 mL) was added dropwise $SOCl_2$ (20 g) at room temperature. Evolution of copious amounts of HCl and SO_2 occurred instantaneously. After stirring for 1 h, the solvent was removed to dryness under reduced pressure (1 Torr). The SiO_2–Cl could be stored in sealed vessels for 6 months without any critical decline in activity.