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α -Aminophosphonate derivatives of triethoxysilane for the synthesis of surface-modified silica

Maksim A. Kolosov^a (D), Yulia I. Chuyko^a, Olesia G. Kulyk^a (D), Alexander V. Mazepa^b, Vladimir V. Zavarzin^c, and Yuriy V. Kholin^a

^aSchool of Chemistry, V.N. Karazin Kharkiv National University, Kharkiv, Ukraine; ^bA.V. Bogatsky Physico-Chemical Institute of the NAS of Ukraine, Odessa, Ukraine; ^cSchool of Physics, V.N. Karazin Kharkiv National University, Kharkiv, Ukraine

ABSTRACT

A convenient synthetic route for the preparation of α -aminophosphonate derivatives of triethoxysilane, attractive precursors for silica surface functionalization, was developed. The condensation of commercially available APTES with carbonyl compounds followed by Pudovik reaction of imines with diethyl phosphite yielded desired N-phosphonomethyl functionalized (3-aminopropyl)triethoxysilanes in high yields without further purification. The chemical structures of obtained products were undoubtedly proved by $^1\text{H},\ ^{13}\text{C}$ and ^{31}P NMR spectroscopy, elemental analysis and mass spectrometry.





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KEYWORDS

3-Aminopropyltriethoxysilane; α-aminophosphonates; Kabachnik-Fields reaction; modified silica: Pudovik reaction

Introduction

3-Aminopropyltriethoxysilane (APTES) is a widely used coupling agent for introducing amine groups onto the surface of SiO₂ to prepare the aminopropyl-modified materials.^[1] Grafting and co-hydrolysis (sol-gel route) are two general methods to functionalize the surface of SiO₂. The grafting process includes the interaction of APTES with the surface silanol and/or silanolate groups via the electrostatic interactions, hydrogen and/or siloxane bonds,^[2] while the sol-gel procedure assumes the simultaneous co-condensation of APTES with tetraethoxysilane (TEOS) in the presence of water.^[3] Obtaining the proper structure and density of NH₂-terminated outermost layer is very crucial with regard to further surface functionalization.^[2a,4] Indeed, the subsequent attachment of functional moieties allows one to tune the structural and physicochemical properties of SiO₂-based materials. However, a precise control of the number of

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CONTACT Maksim A. Kolosov 🖾 kolosov@univer.kharkov.ua 🝙 School of Chemistry, V.N. Karazin Kharkiv National University, Svobody sq., 4, Kharkiv 61022, Ukraine.



Scheme 1. Two general approaches to the synthesis of α -aminophosphonates: three-component Kabachnik–Fields and two-component Pudovik reactions.^[7,8]

fragments linked to the outer NH_2 -groups cannot be achieved in a reproducible manner due to the varying ratio of functionalized and non-reacted NH_2 -groups.^[5] Hence, the incomplete modification of SiO₂ surface is one of the main issues in this field, and the best way to afford the uniform surface of *N*-functionalized aminopropylsilica is to use the preformed *N*-substituted APTES precursors. Among a variety of the latter, α -aminophosphonate derivatives of trialkoxysilane are of particular interest due to the presence of both proton donating (amine) and proton accepting (phosphoryl) groups. This provides a prospective opportunity to study the chelating properties with metals as well as the selective binding, recognition and transfer of various substrates into the siloxane architectures.^[6] The most widely used synthetic routes toward α -aminophosphonates are the three-component Kabachnik–Fields condensation of primary or secondary amines, carbonyl compounds and dialkyl phosphites,^[7] and the two-component Pudovik (also known as aza-Pudovik) reaction of imines and dialkyl phosphites (Scheme 1).^[8]

Although a lot of various α -aminophosphonates have been successfully prepared so far, only one report on the synthesis of *N*-phosphonomethyl functionalized trialkoxysilanes is known to date. Specifically, Stoikov and coworkers described the synthesis of α -aminophosphonates bearing the triethoxysilane moiety *via* the one-pot Kabachnik–Fields condensation of ketones, dialkyl phosphite and APTES in the presence of *p*-toluenesulfonic acid in good yields.^[6a] With the desire to further explore the synthetic potential of *N*-phosphonomethyl APTES derivatives, herein we propose the alternative approach to their preparation involving a base-promoted Pudovik condensation of dialkyl phosphite and preformed imines.

Results and discussion

As a starting point we synthesized imines 1a and 1b by stirring commercially available APTES with the appropriate carbonyl compound in the presence of molecular sieves to absorb water (Scheme 2).^[9]

Noteworthy, imine **1b** was also synthesized in 78% yield by refluxing starting reagents in toluene using Dean–Stark apparatus to remove water. However, taking into consideration the low boiling point of acetone, the protocol with dehydration by activated molecular sieves seems to be more general.

The chemical formulas of imines **1a** and **1b** were unambiguously established by mass spectrometry, ¹H and ¹³C NMR spectroscopy. Interestingly, ¹H NMR spectrum of **1a**



Scheme 2. Synthesis of imines 1a,b.



Scheme 3. Synthesis of target N-phosphonomethyl APTES derivatives 2a,b.

depicts two singlets at 1.91 and 1.74 ppm relating to the non-equal Z- and E-CH₃-groups (for details see Supplementary information).

It should be noted that as-prepared imines are air and moisture sensitive and should be stored under inert atmosphere. Upon the improper or long-term storage of 1a and 1b, the doubling of signals in their ¹H NMR spectra was revealed, suggesting the occurrence of polymerization or other undesirable processes. It should be also emphasized that imines 1a and 1b are appealing building blocks for the reactions with various H–P donors.

For preparing target *N*-phosphonomethyl APTES derivatives **2a** and **2b**, imines **1a,b** were thermally condensed with diethyl phosphite (DEP) in the presence of 4dimethylaminopyridine (DMAP) under solvent-free conditions (Scheme 3). The completion of the reaction was monitored by ¹H and ³¹P NMR spectroscopy. Desired products **2a** and **2b** were isolated in >90% yields as viscous orange liquids.

Compounds **2a** and **2b** were thoroughly characterized by ¹H and ¹³C NMR spectroscopy, elemental analysis and mass spectrometry.

Additionally, we have attempted to obtain **2b** *via* one-pot Kabachnik–Fields reaction (Scheme 4) using conditions developed by Stoikov and coworkers for the synthesis of α -aminophosphonate derivatives of trialkoxysilane.^[6a] In contrast to two-component Pudovik reaction (Scheme 3), three-component condensation of APTES, DEP and benzaldehyde in THF in the presence of *p*-toluenesulfonic acid afforded desired **2b** with poor purity and modest yield (Scheme 4a). Unfortunately, the purification using routine chromatography techniques was complicated due to the reaction of **2b** with the stationery phase (e.g., SiO₂, Al₂O₃). Meanwhile, the vacuum distillation of **2b** was also difficult to perform because of its high boiling point – about 250 °C at 1 mbar (calc.).

Furthermore, conditions developed for two-component synthesis of **2b** (Scheme 3) were extended toward three-component approach (Scheme 4b). However, the heating of APTES, DEP and benzaldehyde in toluene at 100 °C in the presence of DMAP gave **2b**



Scheme 4. Synthesis of **2b** *via* three-component Kabachnik–Fields reaction using conditions developed: (a) by Stoikov and coworkers^[6a] and (b) by our group for two-component Pudovik reaction.

with lower yield (58%) compared with that of 2b (92%) obtained by two-component route. Hence, Pudovik condensation is better optimized for the synthesis of 2b in high yields without further purification.

Conclusion

In summary, we have developed a two-step protocol to obtain α -aminophosphonate derivatives of triethoxysilane starting from commercially available APTES, benzaldehyde, acetone and DEP. Accordingly, the condensation of APTES with carbonyl compounds followed by two-component Pudovik reaction of as-obtained imines with DEP in the presence of DMAP afforded target **2a** and **2b** in high yields. These results open up the route to investigate the grafting process of **2a,b** onto the surface of SiO₂ with the formation of uniform *N*-functionalized outermost layer. The remarkable propensity of *N*-phosphonomethyl groups to chelate metals is intriguing in view of the design of novel SiO₂-based materials to be used in selective water purification from heavy metals.

Experimental part

¹H NMR spectra were registered in CDCl₃ ($\delta_{\rm H}$ =7.26 ppm) at 400 MHz using Varian MR-400 spectrometer (Varian, CA, USA) with $Si(CH_3)_4$ as an internal standard, chemical shifts are given in ppm and coupling constants are given in Hz. Resonance multiplicity was described as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad signal). ¹³C NMR spectra were registered in CDCl₃ ($\delta_{\rm C}$ =77.16 ppm) at 100 MHz using Bruker Avance 400 spectrometer (Bruker, MA, USA) and at 125 MHz using Bruker Avance 500 spectrometer (Bruker, MA, USA) with Si(CH₃)₄ as an internal standard. ³¹P NMR spectra were registered in CDCl₃ at 202 MHz using Bruker Avance 500 spectrometer (Bruker, MA, USA). Mass spectra (EI, 70 eV) were obtained on an MKh-1321 instrument (Nauchpribor, USSR). Elemental analyses were performed using EuroVector EA-3000 instrument (EuroVector, Italy). Toluene was distilled before use and stored under molecular sieves (4Å). Dichloromethane (DCM) was stored under K₂CO₃. K₂CO₃ was activated by heating at 400 °C for 3 h. Molecular sieves (CaA or NaA from "Reakhim" (Reakhim, USSR)) were activated by heating at 400 °C for 3 h. SiO₂ (400-230 mesh from "Swambe Chemicals" (Swambe Chemicals, India)) was used as it is. The inert atmosphere was maintained using Ar-filled balloons equipped with a syringe and needle that was used to penetrate the silicon stoppers. Starting 3aminopropyltriethoxysilane (APTES), acetone, benzaldehyde and diethylphosphite (DEP) were distilled before use. All reagents, materials and solvents were commercially available.

Typical procedure for the preparation of diethyl {[3-(triethoxysilyl)propyl]amino}methylphosphonates (2a,b)

A mixture of imine **1a** or **1b** (1 eq.), DEP (1.6 eq.) and 4-dimethylaminopyridine (DMAP, 0.1 eq.) was heated at 100°C under argon for 20 h. After cooling to r.t., the mixture was filtered through small layer (1.5 cm) of SiO₂ and the filter washed with dry DCM. The filtrate was evaporated under reduced pressure to give **2a** (98%) or **2b** (92%) as orange viscous liquids.

Full experimental detail, ¹H and ¹³C NMR data of all compounds can be found via the "Supplementary material section" of this article's webpage.

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ORCID

Maksim A. Kolosov (b) http://orcid.org/0000-0002-6714-0513 Olesia G. Kulyk (b) http://orcid.org/0000-0003-0303-6941 Yuriy V. Kholin (b) http://orcid.org/0000-0003-1369-741X

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