

SYNTHESIS OF A NON-AGED NEW ALKOXIDE SOL-GEL HYDROXYAPATITE MONITORED BY SOLUTION STATE ^{31}P NMR

¹G. S. K. Kannangara, ²D. D. Green, ³A. Milev and ⁴B. Ben-Nissan

Department of Chemistry, Materials and Forensic Science,
University of Technology, Sydney, PO Box 123 Broadway, NSW, 2007 Australia
Email: Kamali.Kannangara@uts.edu.au

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INTRODUCTION

It has been established that ageing (24 hours) is necessary to convert starting precursors of calcium diethoxide $[\text{Ca}(\text{OEt})_2]$ and triethyl phosphite $[\text{P}(\text{OEt})_3]$ in an ethanolic sol-gel system to attain stable reaction intermediates. From this study impetus to examine an alternative phosphorous precursor that doesn't require a 24-hour ageing period was initiated. Solution-state ^{31}P NMR spectroscopy was successfully applied to monitor reactions during the ageing period that provided vital characteristics of the alternate phosphorous precursor. Using diethyl phosphite $[\text{H}(\text{O})\text{P}(\text{OEt})_2]$ as an alternate precursor it was possible to produce hydroxyapatite, which did not require ageing of the sol. [1]. However, no attempt was made to postulate mechanism(s) and identification of the intermediate species formed in these sol-gel systems. This current work encompasses both these aspects; mechanism and identification of the reaction intermediates for $\text{P}(\text{OEt})_3$ and $\text{H}(\text{O})\text{P}(\text{OEt})_2$ sol-gel systems. The ^{31}P NMR spectra for both sol systems revealed that phosphorous precursors undergo reaction with alkyl anions to form anions of the monoalkyl ester of hydrogen phosphonate.

MATERIALS AND METHODS

Sol-Gel: Calcium precursor solution was prepared by dispersing 1.5 mmoles of calcium diethoxide $[\text{Ca}(\text{OEt})_2]$, [Kojundo Chemical Lab., Saitama, Japan] in absolute ethanol (EtOH, Riedel-de Haen, Germany) followed by dissolving the calcium diethoxide with ethylene glycol $[\text{Et}(\text{OH})_2]$, Aldrich, USA]. Stoichiometric amount of phosphorous precursor solution was prepared by diluting, either $\text{P}(\text{OEt})_3$ or $\text{H}(\text{O})\text{P}(\text{OEt})_2$ (Aldrich, USA) in absolute EtOH. After complete dissolution of the $\text{Ca}(\text{OEt})_2$, the stoichiometric quantity of phosphorous precursor solution was added dropwise to the calcium precursor solution. Vigorous stirring was maintained throughout the addition and for a further 10 minutes thereafter. Due to the hygroscopic nature of the reactants, the

preparation was carried out in a glove box containing dry nitrogen atmosphere.

NMR: Phosphorus NMR spectra were acquired by employing a Bruker DRX-300 (300MHz for protons and 121MHz for ^{31}P) and a Bruker DRX-500 (500MHz for protons and 202MHz for ^{31}P) spectrometer, using 85% H_3PO_4 as an external reference.

RESULTS AND DISCUSSION:

^{31}P NMR spectral data for $\text{P}(\text{OEt})_3$ sol-gel over 0.5-20-hour time period revealed the presence of five major peaks (Figure 1, Trace: "1"). The single peak at chemical shift (δ) 139.9ppm is attributed to $\text{P}(\text{OEt})_3$ while the two sets of doublets between δ 0-10ppm are attributed to reaction products. The first set of doublet peaks at 9.5 and 4.3 ppm have a first order coupling constant ($^1J_{\text{H-P}}$) of $\sim 629\text{Hz}$.

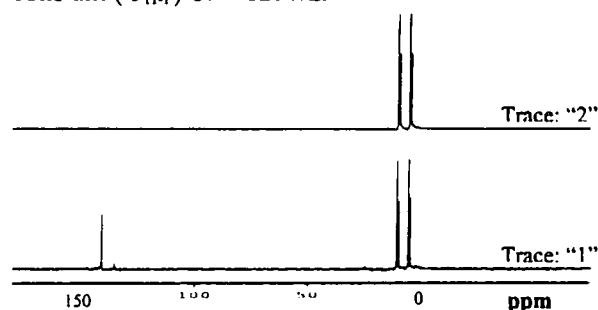


Figure: 1 – ^{31}P NMR (121MHz for ^{31}P) of $\text{P}(\text{OEt})_3$ sol-gel system – Trace: "1" is representative of 15 hours old, Trace: "2" is representative of 24 hours old solution.

Analysis of the sol at the end of the 24 hours using higher resolution NMR (202MHz for ^{31}P) revealed the third order J ($^3J_{\text{P-H}}$) splitting pattern of these two sets of doublets (Figure 2). Trace "A", illustrates two sets of triplets which have a $^3J_{\text{P-H}} \sim 8.5\text{Hz}$. The $^3J_{\text{H-P}}$ triplet line formation is indicative of two protons coupling to the phosphorous nuclei through adjacent (O-C) bond [2].

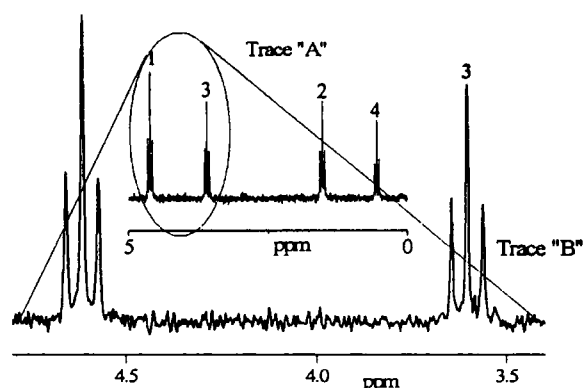


Figure: 2 – ^{31}P NMR (202MHz for ^{31}P) of $(\text{POEt})_3$ sol-gel system, Trace “A” - peaks (1 and 2) and (3 and 4) contributes to the two set of doublets. Expanded region (Trace “B”) shows the $^3J_{\text{H-P}} \sim 8.5\text{Hz}$ triplet line formation.

Knowing that $\text{P}(\text{OEt})_3$ has a septet line configuration, due to six coupling protons (three – CH_2 groups) through the oxygen and no $^1J_{\text{H-P}}$, it is evident that $\text{P}(\text{OEt})_3$ has been converted to a phosphorus species that only contains one ethoxide ligand rather than its original three, accompanied by the new formation of a hydrogen bonded directly to the phosphorus nuclei (P-H).

In contrast to the $\text{P}(\text{OEt})_3$ sol system, $\text{HO}(\text{POEt})_2$ sol-gel system did not undergo a major change during the 24-hour period. The ^{31}P NMR spectrum contains two sets of doublets with $\delta = 5.9, 2.8\text{ppm}$ corresponding to the peaks in the first set of doublet (assigned as nos. 5 and 6) and $4.9, 1.9\text{ppm}$ corresponding to peaks in the second set of doublet (assigned as nos. 7 and 8). Both doublets have a $^1J_{\text{H-P}} \sim 627\text{Hz}$. (Figure 3, Trace “C”). The use of higher resolution NMR (202MHz for ^{31}P) revealed the $^3J_{\text{P-H}}$ splitting of these two sets of doublets is approximately 8.5Hz (Figure 3, trace “D”) [3]. This indicates that there is only one $-\text{O}-\text{CH}_2-$ group rather than the two initial $-\text{O}-\text{CH}_2-$ groups attached to the phosphorous nucleus.

CONCLUSION

The use of high-resolution solution state ^{31}P NMR provided the information required to characterise the reaction species and to propose a reaction mechanism for $\text{HOP}(\text{OEt})_2$ calcium-phosphate sol-gel systems. The fact that there are two sets of doublets in the final ^{31}P NMR spectrum suggests the formation of two different types of hydrogen phosphonates. Because these doublets are $\sim 1\text{ppm}$ apart indicates that both these species have very similar chemical environments in ‘A’ where $\text{R} = -\text{OEt}$ and $-\text{O}(\text{CH}_2)_2\text{OH}$. The differences in

the intensities of the two sets of doublets leads to the conclusion that one alkoxy substituent is favoured over the other. However, it has not yet been determined which ligand exchange relates to these chemical shifts

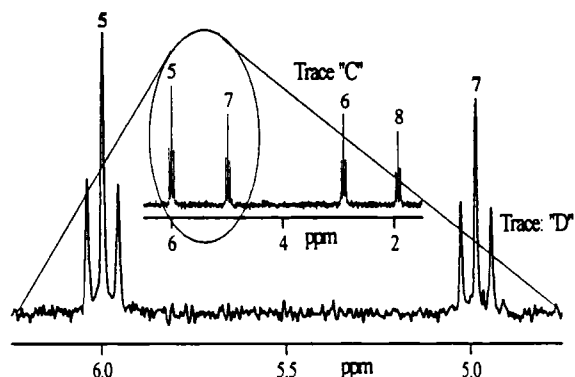


Figure: 3 – ^{31}P NMR (202MHz for ^{31}P) of $\text{HO}(\text{POEt})_2$ sol-gel system, Trace “C” – two set of doublets, peaks nos. 5 and 6 belong to the first set of doublets and peak nos. 7 and 8 belong to the second set of doublets. Expanded region (Trace “D”) shows the $^3J_{\text{H-P}} \sim 8.5\text{Hz}$ (triplet). Both traces are representative of 24 hours old.

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