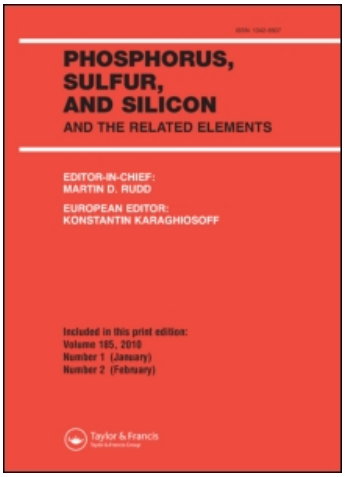

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS OF ALKYL HYDROGEN ALKYLPHOSPHONATES

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To cite this Article Pienaar, André , Erasmus, Cornelis M. , Wentzel, Mauritz and Cowley, Eugene H.(1999) 'SYNTHESIS OF ALKYL HYDROGEN ALKYLPHOSPHONATES', Phosphorus, Sulfur, and Silicon and the Related Elements, 148: 1, 149 — 159
To link to this Article: DOI: 10.1080/10426509908037007
URL: http://dx.doi.org/10.1080/10426509908037007

Phosphorus, Sulfur and Silicon, 1999, Vol. 148, pp. 149-159
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SYNTHESIS OF ALKYL HYDROGEN ALKYLPHOSPHONATES

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(Received 24 November, 1998)

The synthesis of alkyl hydrogen alkylphosphonates **1** was studied. Different synthetic routes were investigated and it was found that alkylphosphonic anhydrides can serve as ideal precursors for the synthesis of those half-acids. It was also shown that isopropyl phosphonic dichloride reacts in a unique fashion to produce alkyl hydrogen isopropylphosphonates in moderate yields.

Keywords: Synthesis; alkylphosphonic anhydride; alkyl hydrogen alkylphosphonates; alkylphosphonic dichloride

INTRODUCTION

A detailed literature search has revealed that alkyl hydrogen alkylphosphonates **1** have not been studied in great detail. Because of their high stability, these compounds are important in the verification of the alleged use of chemical warfare agents, since most G- and V- agents undergo rapid hydrolysis when exposed to the atmosphere for extended periods of time[1,2]. Various methods have been employed for the synthesis of compounds **1**[3]. In a study on the alkaline hydrolysis of phosphonate esters in aqueous dioxane carried out by Christol et al.[4], it was found that both symmetrical and mixed phosponates can be used as substrates for the synthesis of alkyl hydrogen methylphosphonates. Symmetrical phosphonates were hydrolysed with the loss of one ester group to form the correspond-

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ing mono-acid, while with mixed phosphonates the better leaving group was displaced. The starting compounds for these procedures were prepared via known methods, whereby symmetrical phosphonates could be obtained by the reaction of methylphosphonic dichloride and the corresponding sodium alkoxides in anhydrous ether at 0°C. Mixed phosphonates were prepared by first converting methylphosphonic dichloride to the corresponding monoalkyl methylphosphonochloridate through reaction with an alcohol, followed by treatment with the sodium alkoxide of the second alcohol to give the mixed phosphonate in fairly good yield.

The subsequent hydrolysis of the phosphonates was performed by mixing the phosphonate with a more than twofold excess of a 4% solution of sodium hydroxide in a 1: mixture of water and dioxane at 90°C[4]. The reaction time allowed for completion of the hydrolysis before workup, varied between 2 and 100 hours, depending on the nature of the specific phosphonate used as substrate. Similar results were obtained by Rabinowitz[5] and Gryszkiewicz-Trochimowski et al.[6]. These authors have confirmed that phosphonic acid diesters undergo selective alkaline hydrolysis of a single ester group at different reaction rates.

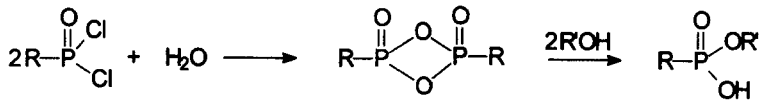
RESULTS AND DISCUSSION

Corbridge[7] states that with boiling aq. NaOH, phosphonic diesters hydrolyse only to the mono-ester salts, and that the rates vary considerably. For example, methyl esters undergo hydrolysis 15 times faster than ethyl and 1800 times faster than neopentyl esters. In addition, the workup of the reaction mixture appears to be tedious. Three different purification procedures[5] have been applied and involve, inter alia, acidification to neutralise the excess alkali, concentration, filtration, extraction and finally distillation.

We have attempted to synthesize ethyl hydrogen methylphosphonate **1a** by heating diethyl methylphosphonate with sodium hydroxide in aqueous dioxane at reflux for 2 hours, followed by acidification with hydrochloric acid at 0°C. The reaction mixture was concentrated by rotary evaporation, acetone was added and the sodium chloride was filtered. The filtrate was concentrated again and in the attempt to purify the residue by distillation, only a small amount of distillate was obtained which contained a number

of unidentifiable compounds. The residue in the distillation flask solidified, so this approach was abandoned. A further disadvantage of this method is the fact that the phosphonic diesters are either not commercially available, or expensive, so that they would have to be synthesized for this purpose.

The more facile procedure introduced by Petrov[3] has been studied in detail by our group and has been shown to provide a general synthetic route for the preparation of a wide range of alkyl hydrogen alkylphosphonates. The Russian authors demonstrated that methylphosphonic anhydride can serve as precursor for that synthesis. The methylphosphonic anhydride was obtained in quantitative yields by the hydrolysis of methylphosphonic dichloride (Scheme 1) and we confirmed their applicability for the synthesis of alkyl hydrogen methylphosphonates. The list of starting alkylphosphonic anhydrides was extended to include both the ethyl and propyl derivatives, as shown in Table I.



SCHEME 1

The phosphonic anhydrides were obtained in quantitative yields by the hydrolysis of the alkylphosphonic dichloride with the calculated amount of water, followed by the subsequent removal of the hydrogen chloride. Each of these anhydrides formed a clear, brittle, glassy mass, which makes stirring as well as uniform heating of the reaction mixture very difficult. For all anhydrides the esterification reaction proceeded smoothly when 50% solutions of the anhydrides in DMF were used, so the reaction was carried out under much milder conditions, and much less side reactions were observed. The solution of an appropriate anhydride in DMF was treated with the desired alcohol at reflux temperature to yield a brown oil. Final purification of the desired hydrogen phosphonates was performed by bulb to bulb distillation. Lower yields were obtained for standard vacuum distillation as a result of decomposition due to the relatively high boiling points and the viscous nature of the products.

TABLE I Alkyl hydrogen alkylphosponates R-P(O)OR'OH

1	*R*	*R'*	*Yield, %*	*Formula*
a	CH_3	CH_3CH_2	25.8*	$C_3H_9PO_3$
b	CH_3	iso-C_3H_7	12.1*	$C_4H_{11}PO_3$
c	CH_3	$CH(CH_3)C(CH_3)_3$	18.2*	$C_7H_{17}PO_3$
d	CH_3	n-C_6H_{13}	33.9*	$C_7H_{17}PO_3$
e	CH_3	C_6H_{11}	46.7	$C_7H_{15}PO_3$
f	CH_3CH_2	CH_3CH_2	41.0	$C_4H_{11}PO_3$
g	CH_3CH_2	iso-C_3H_7	60.0	$C_5H_{13}PO_3$
h	CH_3CH_2	$CH(CH_3)C(CH_3)_3$	67.0	$C_8H_{19}PO_3$
i	CH_3CH_2	C_5H_9	5.0*	$C_7H_{15}PO_3$
j	CH_3CH_2	C_6H_{11}	58.0	$C_8H_{17}PO_3$
k	n-C_3H_7	CH_3	93.7	$C_4H_{11}PO_3$
l	n-C_3H_7	CH_3CH_2	78.1	$C_5H_{13}PO_3$
m	n-C_3H_7	iso-C_3H_7	80.5	$C_6H_{15}PO_3$
n	n-C_3H_7	$CH(CH_3)C(CH_3)_3$	79.0	$C_9H_{21}PO_3$
o	iso-C_3H_7	CH_3	93.3	$C_4H_{11}PO_3$
p	iso-C_3H_7	CH_3CH_2	63.6	$C_5H_{13}PO_3$
q	iso-C_3H_7	iso-C_3H_7	33.0	$C_6H_{15}PO_3$
r	iso-C_3H_7	$CH(CH_3)C(CH_3)_3$	38.7	$C_9H_{21}PO_3$

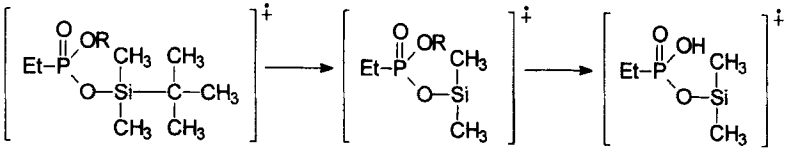
* Reduced yields for vacuum distillation due to decomposition

In the case of the isopropylphosphonic acid analogues, the corresponding anhydride is not commercially available as synthetic precursor. Based on previously tested procedures, it should be possible to synthesize the anhydride by converting isopropylphosphonic dichloride to the corresponding acid, followed by thermal intermolecular dehydration to the anhydride. However, several attempts have failed thus far. We have found that the reaction between isopropylphosphonic dichloride and an alcohol not only produces the dialkyl phosphonate as the expected product, but also a fair amount of the alkyl hydrogen isopropylphosphonate, as well as a small amount of isopropylphosphonic acid. Although the mechanisms for the

formation of the phosphonic acid derivatives are not clear at this stage, we have applied the same procedure to the synthesis of some analogues of alkyl hydrogen isopropylphosphonates (Table I). The isopropylphosphonic dichloride was prepared according to a procedure published by Kinear and Perren[8], whereby isopropyl chloride is treated with phosphorus trichloride in the presence of aluminium trichloride, followed by distillation of the dichloride from the reaction mixture. The dichloride was reacted with the different alcohols at reflux temperature for 3 hours in the absence of any solvent. Bulb to bulb distillation afforded the target compounds in yields ranging from 30 to 90% based on the amount of dichloride used as starting material.

From the NMR spectra of these compounds a number of interesting observations can be made. The far downfield singlet, *ca* 10 ppm of the O-H proton, could be observed for almost every half ester. This value corres- ponds to similar P-O-H chemical shifts reported by Christol and co-workers[4] for a series of alkyl and aryl hydrogen methylphosphonates. Furthermore, the CH function α to phosphorus displays characteristic values of the $^2J_{HP}$=18–20 Hz and $^1J_{CP}$=144–148 Hz couplings.

The mass spectra of the methylphosphonic acid derivatives show very prominent M^++1 peaks owing to the strong tendency of methylphosphonic acid to produce protonated molecular ions[9, 10]. The base peak at m/z 97 indicates the ease of loss of the ester functionality leading to the formation of the acid species. With the ethyl derivatives the base peak at m/z 167 results from the loss of both the ester as well as the trimethyl side of the derivatisation reagent (Scheme 2).



SCHEME 2

It is assumed that the tertiary butyl group is fragmented first since the (M^+- 57) peak is evident in all the compounds studied. Once again an acid moiety is formed that proves to be thermodynamically very stable. In the case of the propylphosphonic acids the loss of the ester functionality

occurs less readily. This gives an indication of the effect the alkyl functionality has on the stability of the P-O-R group. This stabilizing effect is also evident with the isopropylphosphonic derivatives.

The overall frequency range for the phosphoryl stretching vibration (P=O) in compounds which also contain a P-OH group, is 1087–1335 cm^{-1}. More specifically, this frequency range can be narrowed down to 1170–1225 cm^{-1} for alkyl hydrogen alkylphosphonates[11], which closely corresponds to frequencies observed for all the investigated compounds.

Interpretation of the spectra of compounds containg both P-OH and P-OR functionalities is complicated by the fact that they give rise to strong P-O- stretching vibrations which are common to both groups[11]. The same author[11] states that the P-O-C group is always characterized by a strong absorption band in the region of 1000 cm^{-1} for pentavalent organophosphorus compounds such as alkyl hydrogen methylphosphonates. It follows therefore that any assignment of the absorption bands near 1000 cm^{-1} to either the P-OH or the P-OR stretching vibrations cannot be made with any certainty, since it is to be expected that these bands will overlap, resulting in broad and complex absorption patterns in this region of the spectrum. We have indeed observed such patterns in the spectra of our products.

During the synthesis of the pinacolyl derivatives a mixture of two diastereomers was obtained in each case. No attempt was made to separate these diastereomers and the spectra of the mixtures were recorded.

EXPERIMENTAL

Solvents and commercially available reagents were purified by conventional methods before use. FTIR spectra were recorded on a Nicolet 550 Series II Fourier Transfor Infra-red spectrometer, at 15 scans per spectrum for the neat liquid between potassium bromide disks. NMR spectra were recorded on a Varian Gemini 2000 broadband NMR spectrometer, at 300 MHz. Chemical shift values are given in δ (ppm) relative to TMS (^{1}H, ^{13}C) as internal standard, and 85% H_3PO_4 (^{31}P) as external standard. Mass spectra were recorded on a Varian Saturn 3 GC-MS system, utilizing a DB-5 capillary column and operating in EI mode at 70 Ev.

Preparation of alkylphosphonic anhydrides. General procedure

The alkylphosphonic dichloride (1 mole equivalent) was placed in a round bottom flask fitted with a reflux condenser and a dropping funnel. The reaction mixture was cooled in an ice bath and water (1 mole equivalent) was added with stirring at such a rate that the temperature of the reaction mixture did not rise above 20°C. The reaction mixture was heated for 30 minutes at 120°C with the exclusion of atmospheric moisture. After cooling, the hydrogen chloride gas, which was formed during the reaction was removed under reduced pressure to yield a clear, brittle, glassy mass.

Preparation of alkyl hydrogen alkylphosphonates. General procedure

The alkylphosphonic anhydride (1 mole equivalent), preferably as a 50% solution in DMF, was placed in a round bottom flask fitted with a reflux condenser and a dropping funnel. The temperature of the solution was raised to 100°C and the alcohol (2 mole equivalent) was introduced dropwise to the reaction mixture. The mixture was kept at reflux temperature for 30 minutes. After cooling, the brown oil was transferred to a 10 ml round bottom flask and purified by distillation to yield a colourless oil.

Ethyl hydrogen methylphosphonate (**1**) b.p. 110°C/3 mmHg (3.64 g, 25.8%):δ_H: 1.31 (3H, t, J_{HH} 7.2), 1.46 (3H, d, J_{HP} 18.0), 4.06 (2H, dq, J_{HH} 7.2, J_{HF} 8.1), 9.44 (1H, bs); proton decoupled δ_c: 11.53 (d, J_{CP} 147.7), 16.14 (d, J_{CP} 6.6), 61.05 (d, J_{CP} 6.3); δ_P: 34.11. MS, methyl derivative, m/z: 125 (71%), 97 (100%), 79 (98%). FTIR: υ_{PO} 1189, υ_{OH} 2986.

Isopropyl hydrogen methylphosphonate (**2**) b.p. 110–115°C/3 mmHg (2.70 g, 12.1%):δ_H: 1.31 (6H, d, J_{HH} 6.0), 1.45 (3H, d, J_{HP} 17.7), 4.64 (1H, dq, J_{HH} 6.0, J_{HP} 8.4), 7.00 (1H, bs); proton decoupled δ_C: 12.21 (d, J_{CP} 148.3), 23.85 (d, J_{CP} 4.6), 70.66 (d, J_{CP} 6.6); δ_P: 33.35. MS, methyl derivative, m/z: 139 (2%), 125 (72%), 97 (100%), 79 (93%). FTIR: υ_{PO} 1132, υ_{OH} 2981.

Pinacolyl hydrogen methylphosphonate (**3**) b.p. 135°C/3 mmHg (6.92 g, 18.2%):δ_H: 0.89 (9H, s), 1.26 (3H, d, J_{HH} 6.3), 1.45 (3H, d, J_{HP} 18.0), 4.18 (1H, m), 10.17 (1H, bs); proton decoupled δ_C: 12.21 (d, J_{CP} 149.7), 16.74, 25.47, 34.78 (d, J_{CP} 6.3), 80.87 (d, J_{CP} 7.8); δ_P:33.44. MS, methyl derivative, m/z: 181 (4%), 123 (85%), 97 (100%). FTIR: υ_{PO} 1205, υ_{OH} 2964.

(1,3-Dimethyl butyl) hydrogen methylphosphonate (**4**) b.p. 135°C/0.8 mmHg (7.70 g, 33.9%):δ_H: 0.87 (3H,d, J_{HH} 6.9), 0.90 (3H, d, J_{HH} 6.9),

1.27 (1H, m), 1.30 (3H, d, J_{HH} 6.3), 1.44 (3H, d, J_{HP} 18.0), 1.60 (2H, m), 4.58 (1H, m), 9.10 (1H, bs); proton decoupled δ_C: 12.30 (d, J_{CP} 148.9), 22.03, 22.35 (d, J_{CP} 2.3), 22.83, 24.33, 46.89 (d, J_{CP} 6.0), 71.99 (d, J_{CP} 7.2); δ_P: 33.28. MS, methyl derivative, m/z: 194 (9%), 137 (46%), 111 (100%), 93 (44%), 79 (7%). FTIR: υ_{PO} 1163, υ_{OH} 2961.

Cyclohexyl hydrogen methylphosponate (**5**) b.p. 150°C/0.8 mmHg (8.31 g, 46.7%):δ_H: 1.13–1.34 (3H, m), 1.40–1.55 (3H,m), 1.44 (3H,d, J_{HP} 18.0), 1.63–1.86 (2H,m), 1.86–1.94 (2H, m), 4.32 (1H, m), 11.44 (1H, s); proton decoupled δ_C: 12.39 (d, J_{CP} 148.1), 23.59, 25.12, 33.62 (d, J_{CP} 4.2), 75.11 (d, J_{CP} 6.7); δ_P: 33.15. MS, TBDMS derivative, m/z: 211 (11%), 195 (8%), 153 (100%), 75 (14%). FTIR: υ_{PO} 1200, υ_{OH} 2932.

Ethyl hydrogen ethylphosphonate (**6**) b.p. 126°C/0.08 mmHg (5.66 g, 41.0%):δ_H:1.15 (3H, dt, J_{HH} 7.8, J_{HP} 20.1), 1.31 (3H, t, J_{HH} 7.0), 1.72 (2H, dq, J_{HH} 7.8, J_{HP} 18.5), 4.07 (2H, dq, J_{HH} 7.0, J_{HP} 7.0), 9.31 (1H, bs); proton decoupled δ_C: 6.25 (d, J_{CP} 6.7), 16.28 (d, J_{CP} 6.1), 19.01 (d, J_{CP} 145.3), 60.96 (d, J_{CP} 6.6); δ_P: 37.17. MS, TBDMS derivative, m/z: 195 (46%), 167 (100%), 121 (7%), 75 (14%), 73 (6%). FTIR: υ_{PO} 1201, υ_{OH} 2979.

Isopropyl hydrogen ethylphosphonate (**7**) b.p. 160°C/0. 1 mmHg (9.12 g, 60.0%):δ_H: 1.13 (3H, dt, J_{HH} 7.2, J_{HP} 20.4), 1.30 (6H, d, J_{HH} 6.0), 1.70 (2H, dq, J_{HH}7.2, J_{HP} 18.7), 4.65 (1H, dq, J_{HH} 6.0, J_{HP} 6.4), 9.23 (1H, bs); proton decoupled δ_C: 6.20 (d, J_{CP} 6.9), 19.40 (d, J_{CP} 146.0), 23.87 (d, J_{CP} 4.3), 70.03 (d, J_{CP} 7.2); δ_P: 36.17. MS, TBDMS derivative, m/z: 267 (6%), 209 (6%), 167 (100%), 121 (8%), 75 (9%). FTIR: υ_{PO} 1200, υ_{OH} 2932.

Pinacolyl hydrogen ethylphosphonate (**8**) b.p. 160°C/0.1 mmHg (12.99 g, 67.0%):δ_H:0.87 (9H, s), 1.13 (3H, dt, J_{HH} 7.7, J_{HP} 20.2), 1.23 (3H, d, J_{HH} 6.6), 1.70 (2H, dq, J_{HH} 7.7, J_{HP} 20.1), 4.19 (1H, dq, J_{HH} 6.6, J_{HP} 2.1), 9.60 (1H, bs); proton decoupled δ_C: 6.30 (d, J_{CP} 6.9), 16.72 (d, J_{CP} 1.4), 19.53 (d, J_{CP} 148.0), 25.45, 34.78 (d, J_{CP} 6.0), 80.40 (d, J_{CP} 8.4); δ_P: 28.42. MS, TBDMS derivative, m/z: 251 (28%), 225 (47%), 209 (5%), 167 (100%), 121 (13%), 75 (8%). FTIR: υ_{PO} 1188, υ_{OH} 2979.

Cyclopentyl hydrogen ethylphosphonate (**9**) b.p. 155°C/0. 1 mmHg (0.89 g, 5.0%):δ_H: 1.13 (3H, dt, J_{HH} 7.6, J_{HP} 20.1), 1.53–1.83 (10H, m), 4.87 (1H, m); proton decoupled δ_C: 6.25 (d, J_{CP} 6.6), 19.34 (d, J_{CP} 145.9), 22.92, 34.03 (d, J_{CP} 4.6), 78.44 (d, J_{CP} 7.2); δ_P: 28.20. MS,TBDMS derivative, m/z: 167 (100%), 121 (6%), 75 (13%). FTIR: υ_{PO}1242, υ_{OH} 2959.

Cyclohexyl hydrogen ethylphosphonate (**10**) b.p. 155°C/0.1 mmHg (11.1 g, 58.0%):δ_H: 1.14 (3H, dt, J_{HH} 7.7, J_{HP} 20.2), 1.29 (3H, m), 1.50 (2H, m), 1.66 (5H, m), 1.75 (2H, m), 4.37 (1H, m); proton decoupled δ_C: 6.28 (d, J_{CP} 6.6), 19.51 (d, J_{CP} 146.2), 23.49, 25.10, 33.59 (d, J_{CP} 4.0), 74.84 (d, J_{CP} 7.5); δ_P: 36.28. MS, TBDMS derivative, m/z: 307 (3%), 225 (8%), 210 (10%), 167 (100%), 121(5%), 75 (13%). FTIR: υ_{PO} 1279, υ_{OH} 2932.

Methyl hydrogen propylphosphonate (**11**) b.p. 175°C/0.1 mmHg (1.22 g, 93.7%):δ_H: 0.96 (3H, m), 1.60 (2H, m), 2.59 (2H, m), 3.62 (3H, d, J_{HP} 10.8), 9.90 (1H, bs); proton decoupled δ_C: 15.21 (d, J_{CP} 17.7), 16.14 (d, J_{CP} 4.9), 27.49 (d, J_{CP} 140.5), 51.33 (d, J_{CP} 6.3); δ_P:32.63. MS, TBDMS derivative, m/z: 253 (1%), 239 (2%), 195 (100%). FTIR: υ_{PO}1300, υ_{OH} 3700.

Ethyl hydrogen propylphosphonate (**12**) b.p. 180°C/0.1 mmHg (1.12 g, 78.1%):δ_H: 0.96 (3H, m), 1.26 (3H, t, J_{HH} 7.0), 1.61 (2H, m), 2.59 (2H, m), 3.99 (2H, dq, J_{HH} 7.0, J_{HP}10.8), 9.95 (1H, bs); proton decoupled δ_C: 15.16 (d, J_{CP} 17.7), 16.03 (d, J_{CP} 4.9), 16.25 (d, J_{CP} 6.3), 27.97 (d, J_{CP} 141.1), 60.59 (d, J_{CP} 6.3); δ_P: 32.53. MS, TBDMS derivative, m/z:252 (4%), 209 (100%), 181 (93%). FTIR: υ_{PO}1320, υ_{OH} 3800.

Isopropyl hydrogen propylphosphonate (**13**) b.p. 150°C/0.08 mmHg (1.26 g, 80.5%):δ_H: 0.97 (3H, m), 1.28 (6H, dd, J_{HH} 6.3, J_{HP} 0.9), 1.62 (4H, m), 4.63 (1H, m), 11.16 (1H, bs); proton decoupled δ_C: 15.06 (d, J_{CP} 17.7), 15.84 (d, J_{CP} 5.1), 23.87 (d, J_{CP} 4.3), 28.31 (d, J_{CP} 144.0), 69.73 (d, J_{CP} 7.2); δ_P: 34.18. MS, TBDMS derivative, m/z: 281 (5%), 265 (6%), 223 (6%), 181 (100%). FTIR: υ_{PO} 1300, υ_{OH} 3700.

Pinacolyl hydrogen propylphosphonate (**14**) b.p. 180°C/0.08 mmHg (1.55 g, 79.0%):δ_H: 0.88 (9H, s), 0.99 (3H, m), 1.24 (3H, d, J_{HH} 6.3), 1.64 (4H, m), 4.18 (1H, dq, J_{HH} 6.3, J_{HP} 6.3), 11.40 (1H, bs); proton decoupled δ_C: 15.13 (d, J_{CP} 17.8), 15.94 (d, J_{CP} 5.2), 16.72, 25.48, 28.48 (d, J_{CP} 145.4), 34.78 (d, J_{CP} 6.3), 80.36 (d, J_{CP} 8.3); δ_P: 34.19, 34.13. MS, TBDMS derivative, m/z: 265 (35%), 239 (13%), 181 (100%). FTIR: υ_{PO} 1320, υ_{OH} 3700.

Preparation of alkyl hydrogen isopropylphosphonates. General procedure

Isopropylphosphonyl dichloride (1 mole equivalent) was placed in a round bottom flask fitted with a reflux condenser and a dropping funnel. The appropriate alcohol (2.5 mole equivalent) was introduced dropwise to the

reaction mixture. The temperature was raised after all the alcohol was added and the reaction mixture was kept at reflux temperature for 3 hours. After cooling the brown oil was transferred to a 10 ml round bottom flask and purified by bulb to bulb distillation to yield a colourless oil.

Methyl hydrogen isopropylphosphonate (**15**) b.p. 125°C/0.1 mmHg (0.80 g, 93.3%):δ_H1.16(6H, dd, J_{HH} 7.0, J_{HP} 18.7), 1.94 (1H, m), 3.69 (3H, d, J_{HP} 10.5), 8.64 (1H, bs); proton decoupled δ_c: 15.62 (d, J_{CF} 4.6), 25.14 (d, J_{CP} 145.1), 51.35 (d, J_{CP} 7.5); δ_P: 39.22. MS, TBDMS derivative, m/z: 253 (5%), 195 (100%). FTIR: υ_{PO} 1300, υ_{OH} 3700.

Ethyl hydrogen isopropylphosphonate (**16**) b.p. 140°C/0.1 mmHg (1.20 g, 63.6%):δ_H: 1.15 (6H, dd, J_{HH} 7.2, J_{HP}18.5), 1.29 (3H, t, J_{HH} 7.0), 1.94 (1H, m), 4.06 (1H, dq, J_{HH} 7.2, J_{HP} 7.2), 8.98 (1H, bs); proton decoupled δ_C: 15.64 (d, J_{CP} 4.6), 16.20 (d, J_{CP} 6.0), 25.39 (d, J_{CP} 145.1), 60.89 (d, J_{CP} 7.2); δ_P: 38.05. MS, TBDMS derivative, m/z: 267 (5%), 209 (100%), 181 (80%). FTIR: υ_{PO} 1270, υ_{OH} 3700.

Isopropyl hydrogen isopropylphosphonate (**17**) b.p. 175°C/0.1 mmHg (0.34 g, 33.0%):δ_H: 1.14(6H, dd, J_{HH} 7.0, J_{HP} 18.7), 1.29 (6H, d, J_{HH} 6.3), 1.86 (1H, m), 4.66 (1H, m), 10.10 (1H, bs); proton decoupled δ_c: 15.65 (d, J_{CP} 4.9), 23.85 (d, J_{CP} 4.3), 25.64 (d, J_{CP} 146.0), 69.77 (d, J_{CP} 7.5); δ_P: 37.37. MS, TBDMS derivative, m/z: 281 (71%), 267 (50%), 225 (10%), 181 (100%). FTIR: υ_{PO} 1320, υ_{OH} 3700.

Pinacolyl hydrogen isopropylphosphonate (**18**) b.p. 150 °C/0.08 mmHg (0.50 g, 38.7%):δ_H: 0.89 (9H, s), 1.21 (3H, d, J_{HH} 6.9), 1.32 (6H, m), 2.25 (1H, m), 4.37 (1H, m), 4.50 (1H, m); proton decoupled δ_c: 15.77 (d, J_{CP} 4.3), 15.84, 16.06 (d, J_{CP} 5.1), 16.94, 25.44 (d, J_{CP} 5.1), 33.48 (d, J_{CP} 124.2), 34.95 (d, J_{CP} 8.0), 35.04 (d, J_{CP} 6.3), 83.24 (d, J_{CP} 10.0), 83.85 (d, J_{CP} 10.3); δ_P: 49.49, 50.43. MS, TBDMS derivative, m/z: 322 (4%), 265 (31%), 239 (37%), 181 (100%). FTIR: υ_{PO} 1300, υ_{OH} 3700.

Acknowledgements

Financial assistance from the South African Defense Research and Development Board (DRDB) and the input from Prof.T. A. Modro are gratefully acknowledged.

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