Ring-Opening Bulk Polymerization of Five- and Six-Membered Cyclic Phosphonates Using Maghnite, a Nontoxic Proton Exchanged Montmorillonite Clay

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ABSTRACT: A new method of preparation of poly(alkylene H-phosphonate)s by ring-opening bulk polymerization of the five- and six-membered cyclic phosphonates monomers using the nontoxic Maghnite-H^+ as the initiator is described. Cyclic phosphonate monomers have been first synthesized. In particular, a new one-step synthesis of 2-hydro-2-oxo-1,3,2-dioxaphospholane is reported with a yield of 70%. The efficiency of the montmorillonite sheet silicate clay which exchanged with protons, called Maghnite-H^+, as cationic initiator has been proved and the resulting biomimetic poly(alkylene H-phosphonate)s have been characterized. The Maghnite-H^+ regenerated after one turn-over has showed to be still efficient as initiator for the ring-opening polymerization. © 2011 Wiley Periodicals, Inc. J Appl Polym Sci 122: 891–897, 2011

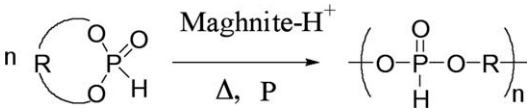
Key words: cationic polymerization; ring-opening polymerization; cyclic phosphonate; clay; poly(alkylene H-phosphonate)

INTRODUCTION

In recent years, synthetic biodegradable polymers have raised increasing interest for various biomedical applications.[1–5] Polymers with phosphoester repeating units in the backbone are of particular interest for drug delivery research.[6–14] Their degradation by simple hydrolysis of the ester backbone in aqueous environments, such as body fluids, leads to harmless low molecular weight products ultimately metabolized to carbon dioxide and water.[15] In particular, poly(alkylene H-phosphonate)s have been extensively investigated because of their biocompatibility,[9,16–21] low cytotoxicity,[22,23] and the possibility to convert secondary phosphonates in the backbone into a number of interesting functional groups, leading for example to mimicking backbone of natural biomacromolecules like nucleic acids.[7,13,24–29] Poly (alkylene H-phosphonate)s can be prepared according to three complementary methods: (i) polycondensation of dialkyl phosphonate with diols,[30,31] (ii) transesterification of phosphonate oligomers,[7,32,33] and (iii) ring-opening polymerization of cyclic phosphonate monomers.[34,35] For this last method, anionic and coordination-insertion initiators, such as C_2H_5ONa, *tert*-C_4H_9OK, *n*-C_4H_9Li, or (i-$C_4H_9)_3Al$, were used.[34,35] Cationic ring-opening polymerization can be induced by $(C_2H_5)_3O^+SbS_6^-$ and $Ph_3C^+SbF_6^-$, whose separation from the polymer may not be possible.[36] The presence of toxic initiator prohibited use of these polymers in medical procedures.

Montmorillonites have both Brönsted and Lewis acid sites and when exchanged with cations having a high charges density, as protons, produce highly-active catalysts for acid-catalyzed reactions.[37] These exchanged montmorillonites have been successfully used as initiators for polymerization reactions.[38]

Herein we report the synthesis of poly(alkylene H-phosphonate)s (Scheme 1) by cationic ring-



Scheme 1 Ring-opening bulk polymerization of five- and six-membered cyclic phosphonate monomers initiated by Maghnite-H^+.

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opening polymerization in bulk of cyclic phosphonates using an algerian proton exchanged montmorillonite clay called Maghnite-H^+ (Mag-H^+), a new nontoxic cationic initiator[39] which has proven its efficiency as a catalyst for the cationic polymerization of a number of vinylic and heterocyclic monomers.[40–43] Mag-H^+ can be easily separated from the polymer product and regenerated by heating to a temperature above 100°C.[44]

The resulting poly(alkylene H-phosphonate)s obtained from the five- and six-membered cyclic phosphonate monomers previously synthesized according to a transesterification procedure[45,46] have been characterized. The influence of the chemical structure of the cyclic monomers, i.e., the number of atoms of the cycle and the presence of substituents, as well as the polymerization conditions are discussed, together with the mechanism of polymerization. Finally, the efficiency of Maghnite-H^+ as regenerated initiator has been investigated.

EXPERIMENTAL

Materials

All chemicals products were purchased from Acros unless otherwise noted. Ethylene glycol (99%, bp_{27Pa} = 70°C), (±)-propane-1,2-diol (99%, $bp_{11\ Pa}$ = 55°C), propane-1,3-diol (98%, $bp_{27\ Pa}$ = 85°C), and diethyl phosphite (99%, $bp_{27\ Pa}$ = 50°C) were distilled *in vacuo* and were stored at −15°C after purification. Solvents were purified according to conventional methods. The 2,2-dimethylpropane-1,3-diol (99%) and $CDCl_3$ (Euriso-Top; 99.9%) were used as received. Maghnite-H^+ was prepared according to the procedure reported by Belbachir and coworkers[39,44] from raw-Maghnite purchased from Bental.

General characterization

NMR spectra were recorded on a Bruker Avance 200 spectrometer using chloroform or $CDCl_3$/TFA (3/1) as the solvent and tetramethylsilane, 2,2-dimethyl-2-silapentane-5-sulfonate (DSS), and H_3PO_4, respectively, as a reference for ^1H, ^{13}C, and ^{31}P nuclei. Coupling constants and chemical shifts are reported in hertz and in parts per million (ppm), respectively. FTIR spectra were recorded using a Nicolet avatar 370 DTGS spectrometer in transmittance mode. High resolution mass spectra (HR-MS) were recorded on a Waters-Micromass® GCT Premier™ (GC, CI+, methane) using a HP 6890 GC apparatus equipped with a chromatographic column of 25 m, diameter 250 μm, thickness 0.25 μm. The sample was warmed at a temperature of 40°C for 5 min and then further heated at a heating rate of 10°C min^{-1} up to 220°C.

General monomer synthesis procedure

A mixture of diol (0.1 mol) and diethyl phosphite (0.105 mol, 5% excess) was placed in a 50-mL round-bottom flask equipped with a Claisen head, a condenser, and a receiving flask. The mixture was heated to 160°C under atmospheric pressure (except for the 2-hydro-4-methyl-2-oxo-1,3,2-dioxaphospholane: $T_{1333\ Pa}$ = 100°C), and ethanol started to distill slowly. When the ethanol evolution ceased, the reaction mixture was allowed to cool to room temperature. The cyclic monomers were purified by distillation under reduced pressure.

2-hydro-2-oxo-1,3,2-dioxaphosphorinane (C6)

$Bp_{27\ Pa}$ = 130°C. Yield: 74%. ^1H NMR ($CDCl_3$, 200 MHz), δ (ppm): 6.92 (d, 1H, P*H*, $^1J_{PH}$ = 670 Hz), 4.35–4.61 (m, 4H, O—CH_2), 1.76–2.43 (m, 2H, —CH_2—). ^{13}C NMR ($CDCl_3$, 50 MHz), δ (ppm): 67.23 (d, O—CH_2, $^2J_{PC}$ = 6 Hz), 25.88 (d, CH_2, $^3J_{PC}$ = 8.5 Hz). ^{31}P NMR ($CDCl_3$, 81 MHz), δ (ppm): 3.25. IR: 2970 (ν_{C-H}); 2904 (ν_{C-H}); 2430 (ν_{P-H}); 1480 (ν_{P-O-C}); 1262 ($\nu_{P=O}$). HR-MS (CI). Calcd for $C_3H_7PO_3 + H^+$: 123.0211. Found: 123.0218.

2-hydro-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinane (C6S)

$Bp_{13\ Pa}$ = 115°C. Yield: 83%. ^1H NMR ($CDCl_3$, 200 MHz), δ (ppm): 6.93 (d, 1H, P*H*, $^1J_{PH}$ = 680 Hz), 3.91–4.13 (m, 4H, —CH_2—), 1.28 (s, 3H, —CH_3), 0.98 (s, 3H, —CH_3).^{13}C NMR ($CDCl_3$, 50 MHz), δ (ppm):, 76 (d, O—CH_2, $^2J_{PC}$ = 5.5 Hz), 32.17 (d, —$C(CH_3)_2$, $^3J_{PC}$ = 6.5 Hz), 21.51 (s, CH_3), 20.70 (s, —CH_3). ^{31}P NMR ($CDCl_3$, 81 MHz), δ (ppm): 3.81. IR: 2969 (ν_{C-H}); 2879 (ν_{C-H}); 2408 (ν_{P-H}); 1474 (ν_{P-O-C}); 1268($\nu_{P=O}$). HR-MS (CI). Calcd for $C_5H_{11}PO_3 + H^+$: 151.0524. Found: 151.0519.

2-hydro-2-oxo-1,3,2-dioxaphospholane (C5)

$Bp_{5\ Pa}$ = 103°C. Yield: 70%. ^1H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.38 (d, 1H, P*H*, $^1J_{PH}$ = 700 Hz), 4.29–4.39 (m, 4H, O—CH_2). ^{13}C NMR ($CDCl_3$, 50 MHz), δ (ppm): 68.19 (d, O—CH_2, $^2J_{PC}$ = 6.5 Hz). ^{31}P NMR ($CDCl_3$, 81 MHz), δ (ppm): 23.13. IR: 2953 (ν_{C-H}); 2449 (ν_{P-H}); 1243 ($\nu_{P=O}$); 970 (ν_{P-O-C}). HR-MS (CI). Calcd for $C_2H_5PO_3 + H^+$: 109.0055. Found: 109.0054.

2-hydro-4-methyl-2-oxo-1,3,2-dioxaphospholane (C5S)

$Bp_{5\ Pa}$ = 115°C. Yield: 55%. ^1H NMR ($CDCl_3$, 200 MHz), δ (ppm): 7.35 (d, 1H, P*H trans*, $^1J_{PH}$ = 718 Hz), 7.32 (d, 1H, P*H cis*, $^1J_{PH}$ = 716 Hz), 3.50–4.94 (m, 3H, C*H*—CH_2), 1.53 (d, 3H, CH_3 *cis*, J_{H-H}

= 6Hz), 1.45 (d, 3H, CH_3 *trans*, J_{H-H} = 6 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz), δ (ppm): 74.94 (d, O—CH_2, $^2J_{PC}$ = 6 Hz), 71.22 (d, O—CH, $^2J_{PC}$ = 9.05 Hz), 19.31 (t, —CH_3 *cis*, $^3J_{PC}$ = 6.5 Hz), 19.00 (t, —CH_3 *trans*, $^3J_{PC}$ = 5.5 Hz). ^{31}P NMR ($CDCl_3$, 81 MHz), δ (ppm): 22.49 (*trans*), 21.70 (*cis*). [35] IR: 2980 (ν_{C-H}); 2444 (ν_{P-H}); 1244 ($\nu_{P=O}$); 970 (ν_{P-O-C}). HR-MS (CI). Calcd for $C_3H_7PO_3 + H^+$: 123.0211. Found: 123.0209.

General polymerization procedure

The polymerizations were carried out in a heterogeneous system. 8×10^{-3} mol of monomer and 0.05 g of Maghnite-H^+ were introduced in a Schlenk tube. The mixture was stirred with a magnetic stirrer, back-filled with nitrogen, and was heated to 155°C (for C6, C6S, and C5) or 95°C (C5S). After a definite period of time, the mixture was cooled to room temperature. Solvent (CH_2Cl_2 for poly(C6) and poly(C6S), CH_2Cl_2/trifluoroacetic acid (TFA) (3/1) for poly(C5)) and poly(C5S) was added and the suspension was filtered off to remove Maghnite-H^+. The polymers were then precipitated into a large excess of diethyl ether for poly(C5) and poly(C5S), toluene for poly(C6S), and cyclohexane for poly(C6) and dried under vacuum until constant weight. Molecular weights of these polymers cannot be determined due to their insolubility in THF used as an eluent for SEC analysis.[29,35]

Poly(2-hydro-2-oxo-1,3,2-dioxaphosphorinane) poly(C6)

Yield: 82%. ^{1}H NMR ($CDCl_3$, 200 MHz), δ (ppm): 6.80 (d, 1H, P*H*, $^1J_{PH}$ = 700 Hz), 3.95–4.65 (m, 4H, OCH_2), 1.75–2.45 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 50 MHz), δ (ppm): 57.88 (d, PH(O)CH_2, $^2J_{PC}$ = 7.5 Hz), 30.46 (t, CH_2, $^3J_{PC}$ = 8Hz). ^{31}P NMR ($CDCl_3$, 81 MHz), δ (ppm): 7.78. IR: 2966 (ν_{C-H}); 2912 (ν_{C-H}); 2430 (ν_{P-H}); 1474 (ν_{P-O-C}); 1270 ($\nu_{P=O}$).

Poly(2-hydro-5,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinane) poly(C6S)

Yield: 21%. ^{1}H NMR ($CDCl_3$, 200 MHz), δ (ppm): 6.80 (d, 1H, P*H*, $^1J_{PH}$ = 720 Hz), 3.5–4.1 (m, 2H, OCH_2), 1.25 (s, CH_3), 1.05 (s, CH_3). ^{13}C NMR ($CDCl_3$, 50 MHz), δ (ppm): 71.74 (d, OCH_2, $^2J_{PC}$ = 4.5 Hz), 30.2 (d, —$CH_2C(CH_3)CH_2$—, $^3J_{PC}$ = 6.5 Hz), 21.00 (s, CH_3), 21.33 (s, CH_3). ^{31}P NMR ($CDCl_3$, 81 MHz), δ (ppm): 8.00. IR: 2967 (ν_{C-H}); 2886 (ν_{C-H}); 2432 (ν_{P-H}); 1458 (ν_{P-O-C}); 1200 ($\nu_{P=O}$).

Poly(2-hydro-2-oxo-1,3,2-dioxaphospholane) poly(C5)

Yield: 45%. ^{1}H NMR ($CDCl_3$/TFA, 400 MHz), δ (ppm): 6.90 (d, 1H, P*H*, $^1J_{PH}$ = 692 Hz), 3.45–4.25 (m, CH_2). ^{13}C NMR ($CDCl_3$/TFA, 100 MHz), δ (ppm): 68.3 (d, OCH_2, $^2J_{PC}$ = 9.5 Hz). ^{31}P NMR ($CDCl_3$/TFA, 81 MHz), δ (ppm): 7.6. IR: 2880 (ν_{C-H}); 2420 (ν_{P-H}); 1455 (ν_{P-O-C}); 1200 ($\nu_{P=O}$).

Poly(2-hydro-4-methyl-2-oxo-1,3,2-dioxaphospholane) poly(C5S)

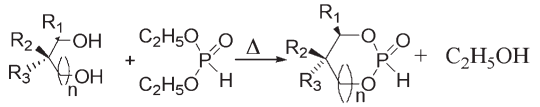
Yield: 26%. ^{1}H NMR ($CDCl_3$/TFA, 200 MHz), δ (ppm): 6.96 (d, 1H, P*H*, $^1J_{PH}$ = 727 Hz), 3.5–5.5 (m, C*H*—CH_2), 1.29 (d, 3H, CH_3, $^2J_{PC}$ = 6 Hz), 1.3 (d, 3H, CH_3, $^2J_{PC}$ = 6 Hz). ^{13}C NMR ($CDCl_3$/TFA, 50 MHz), δ (ppm): 73.3 (d, $OCH(CH_3)CH_2$, $^2J_{PC}$ = 6 Hz), 70.62 (t, CH_2, $^3J_{PC}$ = 5 Hz), 17.88 (t, CH_3, $^3J_{PC}$ = 6 Hz), 15.51 (t, CH_3, $^3J_{PC}$ = 6 Hz). ^{31}P NMR ($CDCl_3$/TFA, 81 MHz), δ (ppm): 7.15. IR: 2887 (ν_{C-H}); 2424 (ν_{P-H}); 1456 (ν_{P-O-C}); 1260 ($\nu_{P=O}$).

RESULTS AND DISCUSSION

Cyclic phosphonate monomers synthesis

Cyclic phosphonates are mainly synthesized by reaction of phosphorus trichloride with diols followed by hydrolysis,[47] directly from phosphonic acid and the corresponding cyclic ether[48] or diol,[49] or by transesterification reaction of dialkyl phosphonates with appropriate diols.[45] This latter synthetic procedure (Scheme 2) has been chosen as it leads to cyclic phosphonates with high yields.[46] Four different monomers have been synthesized leading to substituted and unsubstituted five- and six-membered cyclic phosphonates. Table I summarizes the reaction conditions and yields of each synthesized cyclic phosphonate monomer.

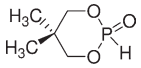
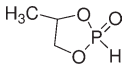
First, the cyclic phosphonates were synthesized via the conditions described by Ostwald,[45] i.e., a pressure of 27 Pa and a temperature of 60°C (Table I, Entries 1, 5, 7 and 11). The conversions have been calculated from ^{1}H (^{31}P) NMR according to the integrals of the signal assigned to the hydrogen atom of the P—H group in the monomers at 6.92, 6.93, 7.38, and 7.32 (*cis*)/7.35 (*trans*) ppm for C6, C6S, C5, and C5S, respectively, and the integrals of the signal assigned to the hydrogen atom of the P—H group of diethyl phosphite at 6.77 ppm. The results showed a low conversion. The initial conditions have then been modified. The use of a reduced pressure and a



n = 0 R_1, R_2, R_3 = H (**C5**) n = 1 R_1, R_2, R_3 = H (**C6**)
n = 0 R_1 = CH_3, R_2, R_3 = H (**C5S**) n = 1 R_1 = H, R_2, R_3 = CH_3 (**C6S**)

Scheme 2 Synthesis of the five- and six-membered cyclic phosphonate monomers.

TABLE I
Conversion and Yields for the Cyclic Phosphonates Prepared by Transesterification

Monomer	Entry	Pressure (Pa)	Temperature (°C)	Time (h)	Conv.[a] (%)	Yield[b] (%)
 **C6**	1	27	60	3	20	–[c]
	2	1333	100	15	59	22
	3	2666	100	9	39	22
	4	101,325	160	4	87	74
 **C6S**	5	27	60	4	5	–[c]
	6	101,325	160	6	75	83
 **C5**	7	27	60	4	27	–[c]
	8	1333	100	14	41	23
	9	2666	100	8	7	–[c]
	10	101,325	160	6	86	70
 **C5S**	11	27	60	3	36	–[c]
	12	1333	100	8	62	55
	13	2666	100	8	15	–[c]
	14	101,325	160	6	0	–

[a] Monomer conversion determined by ^{1}H NMR.
[b] Yield after distillation.
[c] Not distilled.

temperature of 100°C (Table I, Entries 2, 3, 8, 9, 12, and 13) allowed to increase the conversion up to 62% for C6, C5, and C6S but only C5S was obtained with an acceptable yield of 55% after distillation. Finally, the best conditions to reach high conversions and yields are an atmospheric pressure and a temperature of 160°C. C6 and C6S have been obtained with a yield of 74 and 83%, respectively, (Table I, Entries 4 and 6). The structures of monomers C6, C6S, and C5S were confirmed by NMR spectroscopy and high resolution mass spectroscopy (HR-MS). C5S is obtained as a diastereoisomeric mixture as evidenced by ^{31}P NMR spectroscopy: $\delta_{P,\ cis} = 21.7$ ppm and $\delta_{P,\ trans} = 22.49$ ppm, and the coupling constants in ^{1}H NMR: $J_{PH,\ cis} = 716$ Hz and $J_{PH,\ trans} = 718$ Hz are in accordance with those reported in the literature.[35]

For the monomer C5, which the one-step synthesis is only reported in the literature as a by-product of a ribozymomimetic phosphonylation[50] obtained in a 4% yield and not isolated, the use of the same conditions, i.e., an atmospheric pressure and a temperature of 160°C, allowed to obtain the pure monomer with a yield of 70% (Table I, Entry 10). Although this compound was found to be very air- and water-sensitive, the structure of C5 has been confirmed by HR-MS and by ^{1}H NMR (see experimental part) which shows a doublet centered at 7.38 ppm attributed to the P—H bond and a coupling constant of $J_{P-H} = 720$ Hz attributed to the P—H group of the pentavalent phosphorus.

Poly(alkylene H-phosphonate)s synthesis

Cationic ring-opening polymerization was first investigated with each monomer in the presence of Maghnite-H^+ powder in bulk at 155°C for 7 h, which are the conditions used by Lapienis and Penczek[36] for the cationic ring-opening polymerization of cyclic phosphonates with $(C_2H_5)_3O^+SbF_6^-$ and CH_3O-SO_2CF_3 as initiators (Scheme 1 and Table II). Molecular weights of the resulting polymers could not be determined due to the insolubility of poly(alkylkene H-phosphonate)s in THF used as the eluent for SEC analysis.[29,35] The conversions have thus been calculated from ^{1}H (^{31}P) NMR according to the integrals of the signal assigned to the hydrogen atom of the P—H group in the polymers at 6.80, 6.80, 6.90, and 6.96 (7.78, 8, 7.6, and 7.15 ppm) for poly(C6), poly(C6S), poly(C5), and poly(C5S), respectively, and the integrals of the signal assigned to the hydrogen (phosphorus) atom of the P—H group in the monomer at 6.92, 6.93, 7, and 7.32 (*cis*)/7.35 (*trans*) ppm (3.23, 3.81, 23.13, and 21.70 (*cis*)/22.49 (*trans*) ppm) for C6, C6S, C5, and C5S, respectively. As shown in Table II, conversions from ^{1}H NMR and ^{31}P NMR are in very good agreement. C5 and C6 have been converted in 80 and 90% yield, respectively, (Table II, Entries 1 and 11). Increase of the reaction time to 24 h for C5 allowed to reach a 95% conversion (Table II, Entry 12). These conditions applied for C5S led to the degradation of the monomer (Table II, Entry 7). The use of a lower temperature, i.e., 95°C,

TABLE II
Experimental Results for the Ring-Opening Bulk Polymerization of Cyclic Phosphonates Catalyzed by Maghnite-H^+

Monomer	Entry	*n* (mmol)	Maghnite % w/w	Temp. (°C)	Time (h)	Conv.[a]; RMN^{1}H (%)	Conv.[a]; RMN^{31}P (%)	Yield (%)	Polymer solubility	$\overline{M_{n,NMR}}$[b]
C6	1	8	5	155	7	80	81	80	CH_2Cl_2	510
	2	8	0	155	7	0	0	0	–	–
C6S	3	6.6	5	155	7	29	–[c]	12	CH_2Cl_2	
	4	6.6	5	155	24	35	27	21	CH_2Cl_2	470
	5	6.6	5	95	24	0	0	0	–	–
	6	6.6	0	155	7	0	0	0	–	–
C5S	7	8	5	155	24	–[d]	–[d]	–[d]	–	–
	8	8	5	95	7	94	90	23	TFA/CH_2Cl_2 (1/3)	–
	9	8	5	95	24	98	91	26	TFA/CH_2Cl_2 (1/3)	3310
	10	8	0	95	7	0	0	0	–	–
C5	11	9	5	155	7	>95	90	45	TFA/CH_2Cl_2 (1/3)	–
	12	9	5	155	24	>95	95	17	TFA/CH_2Cl_2 (1/3)	560
	13	9	0	155	7	0	0	0	–	–

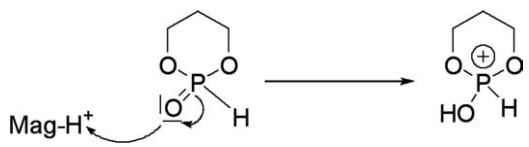
[a] Monomer conversion determined by ^{1}H NMR.
[b] Determined by the ratio of the integral intensities of P-H protons in the repeating units toward that of the end groups.[23]
[c] Superposition of the signals of the polymer and residual diethyl phosphite.
[d] Degradation of the monomer.

allowed to polymerize C5S with a conversion up to 90% (Table II, Entries 8 and 9).

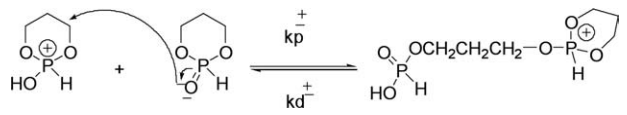
Concerning C6S, the conversion is limited to 30% (Table II, Entries 3 and 4), probably due to a polymer–monomer equilibrium that was not investigated in this work. It is well known that six-membered cyclic phosphorus esters are much less strained and that substitution of the cycle leads to a decrease in polymerizability.[51] The overall effect of temperature on polymerization is complex due to the presence of this propagation-depropagation equilibrium. Polymerization of monomer C6S was attempted at a lower temperature (95°C, see Table II, Entry 5) but these conditions did not shift the equilibrium.

At the end of the reaction, the mixture has been diluted in dichloromethane and filtered to separate Maghnite-H^+ from the polymer. The resulting solution has been precipitated in diethyl ether. Except for poly(C6), which is obtained with a 82% yield (Table II, Entry 1), the yields obtained for the other polymers are rather low, because of the solubility of the oligomers in the precipitating solvent, as demonstrated by NMR characterization. Poly(C6) and poly(C6S) are soluble in CH_2Cl_2 and insoluble in THF, C_6H_6, and C_6H_{12}; poly(C5) and poly(C5S) are insoluble in common solvents and soluble in hexafluoroisopropanol or in trifluoroacetic acid/CH_2Cl_2 in 1/3:v/v ratio. Isolated polymers are rubbery, transparent solid materials.

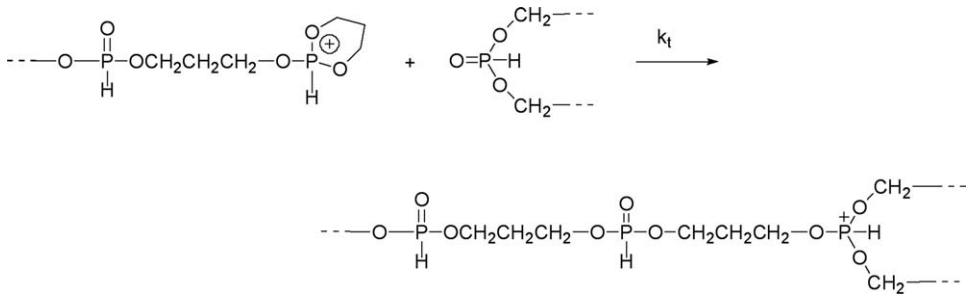
The efficiency of Maghnite-H^+ in the cationic ring-opening polymerization in bulk has been checked by conducting ring-opening polymerization of the monomers without Maghnite-H^+. No conversion was observed whatever the monomer used (Table II, Entries 2, 6, 10, and 13). The Maghnite-H^+, a proton exchanged montmorillonite clay, is thus effective as an initiator of the cationic ring-opening polymerization of cyclic phosphonates. The structures of the polymers were confirmed by NMR. The different coupling constants for the ^{13}C NMR spectrum of the polymer when compared to the monomer, evidences the formation of a polymer that incorporates phosphorous into the polymer backbone. Additional evidence is given by the presence of a broad signal at 7.15 ppm on the ^{31}P NMR spectrum of poly(C5S), in contrast to the two narrow peaks observed at 21.70 and 22.49 ppm for the corresponding monomer. A single signal was observed in the proton-decoupled ^{31}P NMR spectrum for each polymer, indicating the existence of only one type of phosphorous atom, which evidenced obtaining of linear polymer chains. The chemical shifts are in agreement with the literature data.[35] The structure of poly(C5), obtained from 2-hydro-2-oxo-1,3,2-dioxaphospholane, was also



Scheme 3 Initiation step of the polymerization of 2-hydro-2-oxo-1,3,2-dioxaphosphorinane.



Scheme 4 Propagation step during polymerization of 2-hydro-2-oxo-1,3,2-dioxaphosphorinane.



Scheme 5 Termination step during polymerization of 2-hydro-2-oxo-1,3,2-dioxaphosphorinane.

evidenced by ^{1}H NMR: a broadening of the peaks corresponding to the proton attached to phosphorus is observed in the polymer compared to the signals of the monomer.

Mechanism of polymerization

The polymerization of cyclic phosphonates is considered to be initiated by proton addition from Maghnite-H^+ to monomer and the Maghnite takes place as a counter-ion. The protonation leads to an ion with a tetrahedral structure and the observed equivalency of H atoms in polymer (in contrast to monomer) suggests a conformationally mobile substance.[24] Indeed, the replacement of the P═O bond by a H—O—P bond is a source of the absence of any preferred conformation (Scheme 3).

Propagation (Scheme 4) and termination (Scheme 5) can take place by a conventional cationic mechanism.[24] The termination of heterocyclic monomers proceeds through the reaction of the growing species with a polymer segment as evidenced by Penczek.[24]

Initiator reuse

Maghnite-H^+, removed from the mixture by filtration, was regenerated by washing with CH_2Cl_2 and drying in a vacuum oven operating at 105°C for 3 h. The dried material was then reused as an initiator for the polymerization of 2-hydro-4-methyl-2-oxo-1,3,2-dioxaphospholane (C5S). Polymerization using the reused catalyst was carried out at 95°C for 24 h and reached 60% conversion (calculated by ^{1}H NMR) thus confirming the efficiency of regenerated Maghnite-H^+.

CONCLUSIONS

Maghnite-H^+, a proton exchanged montmorillonite clay, is an effective initiator for the cationic ring-opening bulk polymerization of the five- and six-membered cyclic phosphonate monomers. The one-step synthesis of the 2-hydro-2-oxo-1,3,2-dioxaphospholane (C5) has been performed and the resulting structure has been confirmed by mass spectroscopy high resolution (HRMS). Maghnite-H^+ can be easily separated from the polymer product, which is free of toxic impurities thus allowing its use for medical applications. Maghnite-H^+ has been regenerated by heating at a temperature above 100°C and reused successfully as polymerization initiator. Chemical modification of the reactive P—H groups in repeating units of the synthesized poly(alkylene H-phosphonate)s by biocompatible polymer chains using Atherton-Todd reaction[26–28] in combination with "click" chemistry is currently investigated and will be reported in due course.

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