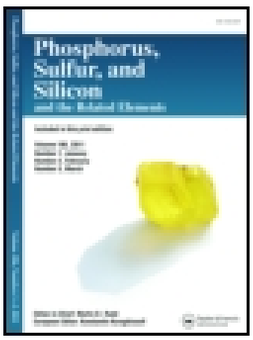

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Synthesis of α-hydroxyphosphonate cyclotriphosphazene under solvent-free conditions with a basic catalyst

Lisheng Zhou, Guangcheng Zhang*, Jianwei Li, Yunjie Feng

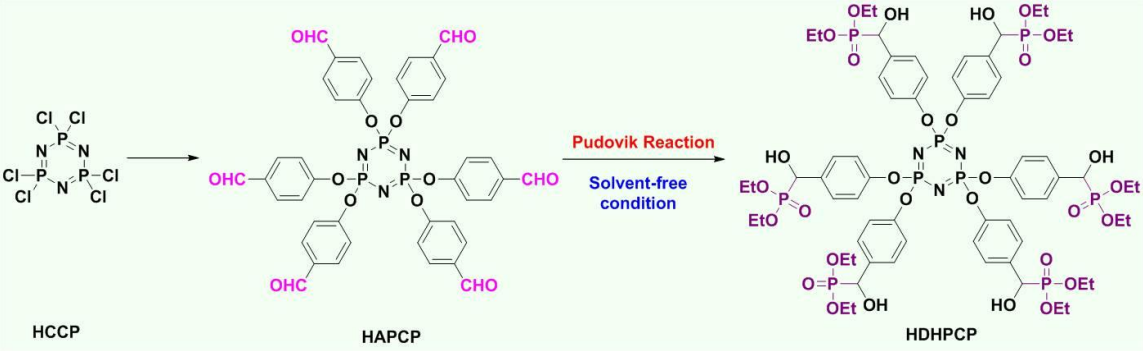
MOE Key Lab of Applied Physics and Chemistry in Space, Department of Applied Chemistry, College of Science, Northwestern Polytechnical University, Xi'an, 710072, China

*Corresponding Author E-mail: zhangguc@nwpu.edu.cn

Abstract

An α-hydroxyphosphonate cyclotriphosphazene compound, hexa-(4- diethylphosphate-hydroxymethyl- phenoxy)-cyclotriphosphazene) (HDHPCP), was synthesized in two steps. Firstly, the intermediate hexa-(4-aldehyde-phenoxy)-cyclotriphosphazene (HAPCP) was synthesized by the elimination reaction of hexachlorocyctriphosphazene (HCCP) with 4-hydroxybenzaldehyde. Then, HDHPCP was obtained by Pudovik reaction under solvent free condition. In this step, the effects of the type and amount of catalyst on reaction time and yield were investigated, and it was found that triethylamine (TEA) has better activity than KF and K_2CO_3. When the molar ratio of HAPCP to TEA was 1:5, the reaction gave an excellent yield of 95.4% in 70 min. Under these conditions, the reaction was easy to work-up, time-saving, environmentally benign and with high yield. FTIR, NMR and elemental analysis results confirmed

that HDHPCP was synthesized successfully, and the TGA measurement indicated that it presents good thermal stability and high char residual.



Keywords

cyclotriphosphazene, α-hydroxyphosphonate, Pudovik reaction, solvent-free condition

Introduction

Organophosphorus compounds have drawn much attention in recent years, because these compounds have a wide range of applications in the areas of medicinal, agricultural and industrial chemistry according to their biological and physical properties[1-6]. Hexachlorocyclotriphosphazene (HCCP), with a six-membered ring backbone of alternating phosphorus and nitrogen atoms, is the most important intermediate in the field of polyphosphazenes. In HCCP, the P-Cl bonds with high activity are easy to react with nucleophilic reagents, such as sodium alkoxides or aryloxides, primary or secondary amines, or organometallic compounds. Therefore, cyclophosphazene derivatives with diverse physical and chemical properties have been prepared by reaction with different nucleophiles[7]. The special structures of cyclophosphazenes provide these materials with good fire resistant behaviors due to their high phosphorus content [8-12]. Besides, the functional materials based on cyclophosphazenes, which with properties of optical[13-15], photoresponsive liquid-crystalline[16], or biological activities[17, 18], have also been reported.

Meanwhile, among known organophosphorus compounds, phosphonates have received considerable attention due to their biological activities[19, 20], flame retardant properties[21-24], metal chelating properties[25, 26] and biodegradabilities[27]. α-Hydroxyphosphonates are compounds of significant biological activities, such as renin inhibitors[28, 29], HIV proteases[30], antibacterial agents[31, 32], and enzyme inhibitors[33]. α-Hydroxyphosphonates are most frequently synthesized

using the so-called Pudovik reaction, which is the addition of dialkyl or diaryl H-phosphonates to carbonyl compounds[34, 35]. This atom-economic and straightforward protocol can be successfully performed under environmentally friendly conditions. Fully esterified phosphites such as the addition of triethyl or trimethyl phosphite to carbonyl compounds are synthesized by the so-called Abramov reaction (seen in Scheme 1)[1]. In the structure, R^1 represents organic group, R^2 and R^3 represent organic groups or H atoms, respectively. In recent years, solvent-free reactions in the field of organic synthesis have drawn much attention. Solvent free conditions have advantages compared with tradition organic reactions in a solvent medium, such as being environmentally benign, economically beneficial, usually time saving, and with high yields[36, 37].

By considering all of the above aspects, we synthesized an α-hydroxyphosphonate cyclotriphosphazene, hexa-(4- diethylphosphate- hydroxymethyl- phenoxy)-cyclotriphosphazene) (HDHPCP), in two steps. In the first step, the intermediate HAPCP was synthesized according to the literature[10, 38]. In the second step, the target molecule HDHPCP was obtained by Pudovik reaction under solvent-free condition with base catalyst. As reported by Kamalakar[39] that in the Pudovik reaction, acid catalysts had less activities than base catalysts, so we chose three bases, KF, K_2CO_3 and TEA, as catalysts. The chemical structure of HDHPCP was characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, elemental analysis, and its thermal stability was evaluated by TGA.

Results and discussion

Synthesis of HDHPCP

HDHPCP was prepared in two steps from HCCP (Scheme 2). In the first step, HAPCP was obtained by the elimination reaction of HCCP with 4-hydroxybenzaldehyde. In the second step, HDHPCP was synthesized by a Pudovik reaction between HAPCP and diethyl phosphate in the presence of a base as catalyst under solvent free condition. In this step, three different bases (KF, K_2CO_3 and TEA) were chose as catalysts to optimize of the experimental conditions.

Table 1 shows the results of HAPCP reacting with diethyl phosphate at different type and amount of catalysts. When KF and K_2CO_3 are selected as catalysts, the investigated molar ratios of HAPCP to catalyst are 1:6, 1:12, 1:18 and 1:24, respectively. With an increasing amount of catalyst, the reaction time decreased, but the yields show different situations. Because the reaction proceeds under solvent free condition, the reaction mixture usually became solidified when it is completed, this can also act as a criterion for the end of the reaction. As the reaction progressed, the viscosity of the mixture increased gradually until it can't be stirred, which proved to be the ending of the reaction. The preferable molar ratios for HAPCP to KF and K_2CO_3 were found to be 1:24 and 1:12. When TEA is selected as the catalyst of this reaction, there are some differences of experimental conditions and reaction phenomena from those observed when KF and K_2CO_3 acting as catalyst.

The molar ratios of HAPCP to TEA are investigated at the range from 1:1 to 1:6. When the molar ratio is 1:1, no desirable product is detected after the reaction was stirred at room temperature for 24 h. It can also be found that when the molar ratio is 1:5 an excellent yield 95.4% was obtained in 70 min. Not only acting as a catalyst, we speculate that TEA still acts as solvent in some extent. Because unlike being solidified when KF and K_2CO_3 act as catalyst, the reaction mixture can be stirred continually, which is also benefit for the reaction to continue and produce a high yield. By contrasting these three catalysts, TEA shows better catalytic effect in yields and reaction times.

Characterization of HDHPCP

The chemical structures of HAPCP and HDHPCP were characterized by ^{1}H, ^{13}C, ^{31}P NMR and FTIR spectroscopy. The NMR and FTIR data obtained for HAPCP are in agreement with previous studies[8, 10, 38]. The ^{1}H NMR spectrum of HDHPCP is shown in Figure S 1 (available online in Supplemental Materials). The signal peaks at 7.27 ppm and 6.96-6.72 ppm are contributed to benzene ring protons, the peak at 5.00 ppm is assigned to hydroxyl protons. The ethyl protons are detected at 3.99 ppm and 1.39-1.03 ppm. In the ^{13}C NMR spectrum of HDHPCP (Figure S 2), C-6 is found with different chemical shifts (63.1 and 63.5 ppm), this may attribute to the P atom being attached to a chiral carbon (C-5), and thus the substituents on the P atom are nonequivalent. Furthermore, being affected by the adjacent P atom, the C-5 is detected as split peaks at 68.9 and 70.5 ppm. Other chemical shifts (ppm) are assigned to the aromatic carbon

resonances: 149.9 (C1), 134.1 (C3), 128.5 (C4), 120.5 (C2). In the corresponding ^{31}P NMR spectrum (Figure S 3), two peaks at chemical shifts at 21.8 and 9.3 ppm are assigned to the phosphorus atoms in phosphonate and cyclotriphosphazene structure of HDHPCP, respectively. The FTIR spectrum of HDHPCP (Figure S4) exhibits absorption peaks at 1210 cm^{-1} and 1180 cm^{-1} corresponding to the P = N stretching vibration of cyclophosphazene ring. The strong absorption peaks at 1160 cm^{-1} and 955 cm^{-1} reveal the presence of a phosphazene structure (P-O-Ph). The spectrum of HAPCP shows the absorption peaks at 2825, 2733 and 1707 cm^{-1} illustrating the presence of the aldehyde group (-CHO), whereas in the spectrum of HDHPCP, these peaks disappear, and strong absorption peak at 3278 cm^{-1} takes place corresponding to the hydroxyl stretching (-OH). Furthermore, the absorption peaks at 2980 and 2906 cm^{-1} are attributed to the stretching vibration -CH_2CH_3.

The characterization results of FTIR, NMR and elemental analysis confirm the chemical structure of HDHPCP, indicating that HDHPCP was successfully synthesized. Although the compound has been reported, the synthesis method presented in this paper is different compared with the reported method[40, 41]. And the results indicate that the solvent free condition is convenient to operate, time saving and high yield compared with tradition method.

Thermal analysis of HDHPCP

The thermal stability of HDHPCP was investigated using themogravimetric analysis (TGA) and derivative thermogravimetry (DTG) in the temperature range from room temperature to 850°C in air, and the corresponding TGA/DTG curve is shown in Figure 1. The slight weight loss occur below 150°C may attributed to the evaporation of the residual solvent and loss of adsorbed water. The initial decomposition temperature (T_5) of HDHPCP is 196°C. According to the DGT curve, the thermal degradation occurs mainly in four steps. The first weight loss interval at 169-255°C (weight loss = 18.4 wt%), with the maximum degradation rate at 220°C, is probably due to the cleavage of P-OEt bonds. The second weight loss interval is in range of 255-330°C and the maximum degradation rate peak appears at 282°C. During this stage, 6.8 wt% weight loss of original sample occurs, which may be attributed to the intramolecular or intermolecular dehydration of the hydroxyl groups. The third decomposition stage in the temperature range of 355-435°C may be related to the release of phosphoric acid or metaphosphoric acid, with a minor weight loss (2.8 wt%). The last stage loss occurs at higher temperature range from 570 to 810°C probably due to the cleavage of aryloxy groups. Above 700°C, the TGA curve becomes more flat. The char yields of HDHPCP at temperature of 600°C and 800°C are 53.7% and 18.0%, respectively, meaning that this compound has good thermal stability.

Experimental Section

Materials

Hexachlorocyclotriphosphazene (HCCP) was purchased from Shandong Lanyin Chemical Co. Ltd., China. Diethyl phosphate and *p*-hydroxybenzaldehyde were purchased from Sinopharm Chemical Reagent Co. Ltd. Anhydrous KF was obtained from Aladdin Industrial Inc. K_2CO_3 and triethylamine were purchased from Tianjin Kemiou Chemical Reagent Co. Ltd., China. All solvents were purchased from commercial sources and purified by standard methods.

Characterization

^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker Advance 400-MHz spectrometer operated at 400, 101 and 162 MHz, respectively. The spectra were recorded with TMS as internal standard or with 85% phosphoric acid aqueous as external reference. Fourier transform infrared (FTIR) spectra were characterized on potassium bromide discs and Perkin Elmer 400 spectrometer (USA). TGA measurements were carried out on a TA thermogravimetric analyzer Q50. Specimens of about 20 mg were heated from room temperature to 850°C at a rate of 20°C/min in air. Elemental analyse was determined on a Perkin Elmer 2400 CHNS/O Analyzer.

Synthesis of HAPCP and HDHPCP

Synthesis of hexa-(4-aldehyde-phenoxy)-cyclotriphosphazene (HAPCP)

In a three-neck round-bottom flask equipped with a reflux condenser and a constant drip funnel, HCCP (5.0 g, 14.4 mmol) and K_2CO_3 (25.8 g, 187.0 mmol) were stirred in THF (100 mL) in an ice bath under nitrogen atmosphere. Simultaneously, *p*-hydroxybenzaldehyde (12.3 g, 10.1

mmol) in THF (50 mL) was added into the above mixture dropwise. Then, the reaction mixture was heated to reflux and then allowed to stir vigorously for 24 h. After that, the mixture was filtered and the filtration was concentrated on a rotary evaporator. The obtained crude product was recrystallized from chloroform/petroleum ether and then washed by ethanol and dried in vacuum. Finally, HAPCP was obtained as white solid powder.

Yield: 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 7.74 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.5 (-CHO), 154.5, 133.8, 131.5, 121.3(-C_6H_4). ^{31}P NMR (162 MHz, $CDCl_3$) δ 7.3.

Synthesis of hexa-(4- diethylphosphate- hydroxymethyl- phenoxy)-cyclotriphosphazene) (HDHPCP)

HAPCP (1 eq.) and diethyl phosphate (7 eq.) were placed in a round-bottom flask, and stirred at room temperature for 30 min. A certain amount of catalyst (KF, K_2CO_3 or TEA) was added to the above mixture and stirred until it completed. The crude product was dissolved in DCM, extracted and the obtained solvent was concentrated to yield HDHPCP as a white solid (hygroscopic). Further purification of HDHPCP was by recrystallization from DCM/ petroleum ether.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 16.3 Hz, 12H), 6.96-6.72 (m, 12H), 5.00 (dd, *J* = 25.0, 13.2 Hz, 6H), 3.99 (dd, *J* = 35.7, 7.0 Hz, 24H), 1.39 -1.03 (m, 36H). ^{13}C NMR (101 MHz, $CDCl_3$)

δ 149.9, 134.1, 128.5, 120.5 (-C_6H_4), 69.3 (-C-OH), 63.4 (-CH_2CH_3), 16.4 (-CH_2CH_3). ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.8, 9.3. Anal. Calcd for $C_{66}H_{96}N_3O_{30}P_9$: C, 46.90; H, 5.73; N, 2.49. Found: C, 46.84; H, 5.76; N, 2.47.

Conclusion

α-Hydroxyphosphonate cyclotriphosphazene, HDHPCP, was successfully synthesized in two steps from hexachlorocyclotriphosphazene. In the synthesis of HDHPCP from HAPCP, solvent free condition was used and three base catalysts were selected and explored the effects of different catalyst and amount to the reaction times and yields. The results indicated that TEA had better catalytic effect compared to KF and K_2CO_3. When the molar ratio of HAPCP to TEA is 1:5 gives an excellent yield of 95.4% in 70 min, which is much faster and higher yield than tradition method in organic solvent. It is speculated that this may because TEA not only act as catalyst during the reaction, but also play the role of solvent to be convenient for the molecular motion, thus promoting the reaction. The chemical structure of HDHPCP was characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, elemental analysis, and the thermal stability was measured by TGA. According to the obtained results, HDHPCP may has potential flame retardant property, and the performance of related research will be done in our later works. In conclusion, we have develpoed a highly efficient, environmentally friendly synthesis of α-hydroxyphosphonate cyclotriphosphazene under solvent free condition with base catalyst. This method provides method

for the preparation of α-hydroxyphosphonates and will be increasingly necessary for phosphazene commercialization.

Acknowledgements

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References

[1] Olszewski, T. K. *Synthesis* **2014**, 46, 403-429.

[2] Quittmann, U.; Lecamp, L.; El Khatib, W.; Youssef, B.; Bunel, C. *Macromol Chem Phys.* **2001**, 202, 628-635.

[3] Wolschke, H.; Sühring, R.; Xie, Z.; Ebinghaus, R. *Environ Pollut.* **2015**, 206, 488-493.

[4] Quin, L. D. *A Guide to Organophosphorus Chemistry*. John Wiley & Sons, Inc.; **2000**.

[5] Hartley, F. R. *The Chemistry of Organophosphorus Compounds*. John Wiley & Sons; **1996**.

[6] Levchik, S. *Phosphorus-Based FRs. Non-Halogenated Flame Retardant Handbook*. John Wiley & Sons, Inc.; **2014**, 17-74.

[7] Bilge, S.; Demiriz, Ş.; Okumuş, A.; Kılıç, Z.; Tercan, B.; Hökelek, T.; Büyükgüngör, O. *Inorg. Chem*. **2006**, 45, 8755-8767.

[8] Xu, G. R.; Xu, M. J.; Li, B. *Polym. Degrad. Stabil.* **2014**, 109, 240-248.

[9] Stewart, F. F. *Organophosphorus Chem*. **2014**, 43, 366-412.

[10] Qian, L. J.; Ye, L. J.; Xu, G. Z.; Liu, J.; Guo, J. Q. *Polym. Degrad. Stabil*. **2011**, 96, 1118-1124.

[11] Lu, S. Y.; Hamerton, I.; *Prog. Polym. Sci*. **2002**, 27, 1661-1712.

[12] You, G.; Cheng, Z.; Peng, H.; He, H. *Chinese J. Appl. Chem*. **2014**, 31, 993-1009.

[13] Kagit, R.; Yildirim, M.; Ozay, O.; Yesilot, S.; Ozay, H. *Inorg. Chem*. **2014**, 53, 2144-2151.

[14] Hu, X. M.; Chen, Q.; Zhou, D.; Cao, J.; He, Y. J.; Han, B. H. *Polym. Chem*. **2011**, 2, 1124-1128.

[15] Çoşut, B.; Yeşilot, S.; Durmuş, M.; Kılıç, A. *Dyes Pigments* **2013**, 98, 442-449.

[16] Jiménez, J.; Pintre, I.; Gascón, E.; Sánchez-Somolinos, C.; Alcalá, R.; Cavero, E.; Serrano, J. L.; Oriol, L. *Macromol. Chem. Phys*. **2014**, 215, 1551-1562.

[17] Işıklan, M.; Asmafiliz, N.; Özalp, E. E.; İlter, E. E.; Kılıç, Z.; Çoşut, B.; Yeşilot, S.; Kılıç, A.; Öztürk, A.; Hökelek, T.; Koç Bilir, L. Y.; Açık, L.; Akyüz, E. *Inorg. Chem*. **2010**, 49, 7057-7071.

[18] Asmafiliz, N.; Kılıç, Z.; Hayvalı, Z.; Açık, L.; Hökelek, T.; Dal, H.; Öner, Y. *Spectrochim. Acta A*. **2012**, 86, 214-223.

[19] Zhou, L. S.; Yang, K. W.; Feng, L.; Xiao, J. M.; Liu, C. C.; Zhang, Y. L.; Crowder, M. W. *Bioorg. Med. Chem. Lett*. **2013**, 23, 949-954.

[20] Santhisudha, S.; Sreelakshmi, P.; Jayaprakash, S. H.; Vijaya, K. B.; Suresh, R. C. *Phosphorus, Sulfur Silicon Relat. Elem.* **2015**, 190, 1479-1488.

[21] Zhao, W.; Li, B.; Xu, M.; Zhang, L.; Liu, F.; Guan, L. *Polym. Eng. Sci.* **2012**, 52, 2327-2335.

[22] Spontón, M.; Ronda, J. C.; Galià, M.; Cádiz, V. *Polym. Sci. Pol. Chem*. **2007**, 45, 2142-2151.

[23] Li, Y.; Zheng, H.; Xu, M.; Li, B.; Lai, T. *J. Appl. Polym.Sci*. **2015**,132, n/a-n/a.

[24] Chang, S.; Condon, B.; Graves, E.; Uchimiya, M.; Fortier, C.; Easson, M.; Wakelyn, P. *Fibers Polym*. **2011**, 12, 334-339.

[25] Zhang, Y.; Li, X.; Cao, Z.; Fang, Z.; Hull, T. R.; Stec, A. A. *Ind. Eng. Chem. Res.* **2015**;54(13):3247-3256.

[26] Gomes, R. D.; Dacheux, N.; Pellet-Rostaing, S.; Faur, C.; Bouyer, D.; Monge, S. *Polym. Chem.* **2015**, 6, 5264-5272.

[27] Huang, J.; Su, Z.; Xu, Y. *J. Mol. Evol*. **2005**, 61, 682-690.

[28] Patel, D. V.; Rielly-Gauvin, K.; Ryono, D. E. *Tetrahedron Lett*. **1990**, 31, 5587-5590.

[29] Patel, D. V.; Rielly-Gauvin, K.; Ryono, D. E.; Free, C. A.; Rogers, W. L.; Smith, S. A.; DeForrest, J. M.; Oehl, R. S.; Petrillo, E. W. *J. Med. Chem*. **1995**, 38, 4557-4569.

[30] Stowasser, B.; Budt, K. H.; Jian, Q. L.; Peyman, A.; Ruppert, D. *Tetrahedron Lett*. **1992**, 33, 6625-6628.

[31] Kafarski, P.; Lejczak, B. *J. Mol. Catal. B-Enzym*. **2004**, 29, 99-104.

[32] Kategaonkar, A. H.; Pokalwar, R. U.; Sonar, S. S.; Gawali, V. U.; Shingate, B. B.; Shingare, M. S. *Eur. J. Med. Chem.* **2010**, 45, 1128-1132.

[33] Sikorski, J. A.; Miller, M. J.; Braccolino, D. S.; Cleary, D. G.; Corey, S. D.; Font, J. L.; Gruys, Kenneth, J.; Han, C. Y.; Lin, K. C.; Pansegrau, P. D.; Ream, J. E.; Schnur, D.; Shah, A.; Walker, M. C. *Phosphorus, Sulfur Silicon Relat. Elem.* **1993**, 76, 115-118.

[34] Cherkasov, R.; Galkin, V.; Kurdi, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **1990**, 49, 61-64.

[35] Semenzin, D.; Etemad-Moghadam, G.; Albouy, D.; Diallo, O.; Koenig, M. *J. Org. Chem.* **1997**, 62, 2414-2422.

[36] Nagendrappa, G. *Reson* **2002**, 7, 59-68.

[37] Zheng, J.; Feng, X.; Yu, Y.; Zhen, X.; Zhao, Y. *Phosphorus, Sulfur Silicon Relat. Elem.* **2012**, 188, 1080-1087.

[38] Huang, X.; Xiao, Y.; Lang, M. *Macromol. Res*. **2011**, 19, 113-1121.

[39] Kamalakar, P. N.; Jitendra, P. N.; Vijay, S. P.; Bhosale, S, V. *Chem. Biol. Interface* **2012**, 2, 314-321.

[40] Li, J.; Hu, W.; Zhang, X. CN 104877173 A. **2015**.

[41] Yang, R.; Hu, W.; Xu, L.; Song, Y.; Li, J. *Polym. Degrad. Stabil*. **2015**, 122, 102-109.

Table 1. Synthesis of HDHPCP with different amounts of catalysts[a]

Entry	Catalyst	Molar ratio[b]	Time	Yield[c] %
1	KF	1:6	4.5 h	66.3
2	KF	1:12	2 h	82.7
3	KF	1:18	1.5 h	76.5
4	KF	1:24	40 min	83.2
5	K_2CO_3	1:6	10 h	89.8
6	K_2CO_3	1:12	6 h	90.3
7	K_2CO_3	1:18	5 h	80.1
8	K_2CO_3	1:24	2 h	77.0
9	TEA	1:1	24 h	No Reaction
10	TEA	1:2	6 h	77.6
11	TEA	1:3	4 h	79.6
12	TEA	1:4	1.5 h	92.9
13	TEA	1:5	70 min	95.4
14	TEA	1:6	40 min	93.9

[a]Reaction condition: 1 mmol HAPCP, 7 mmol diethyl phosphate, catalyst, r.t.

[b]Molar ratio of HAPCP with catalyst

[c]Isolated purified product.

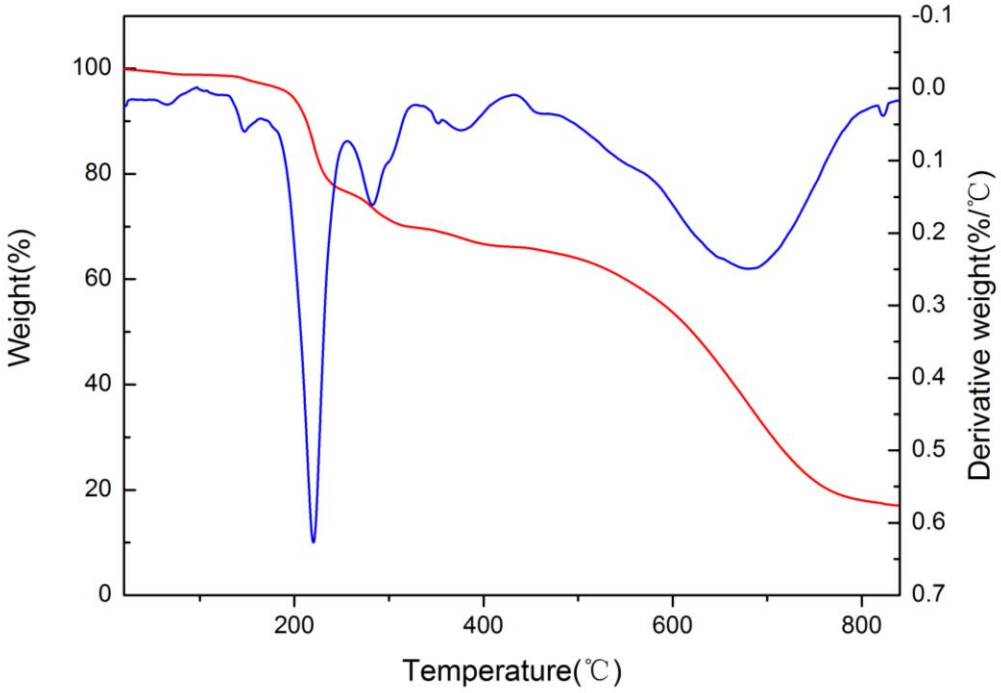
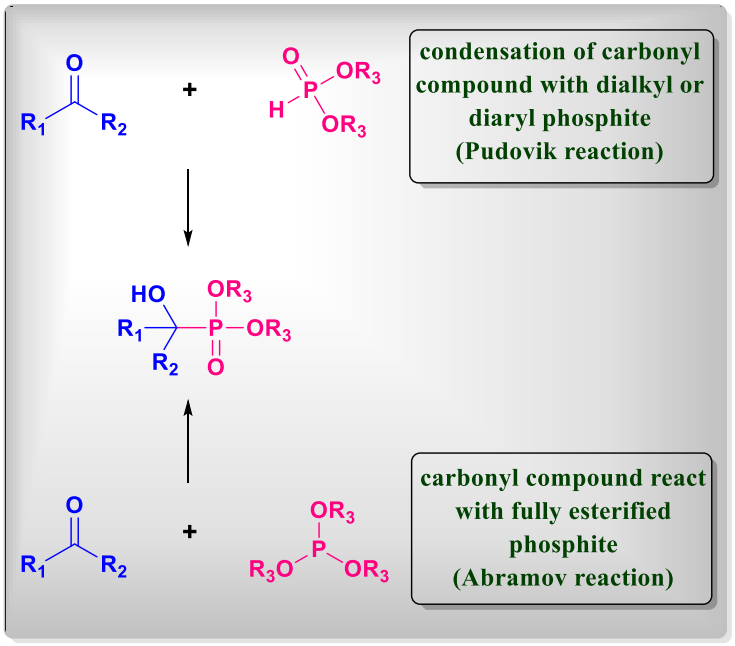
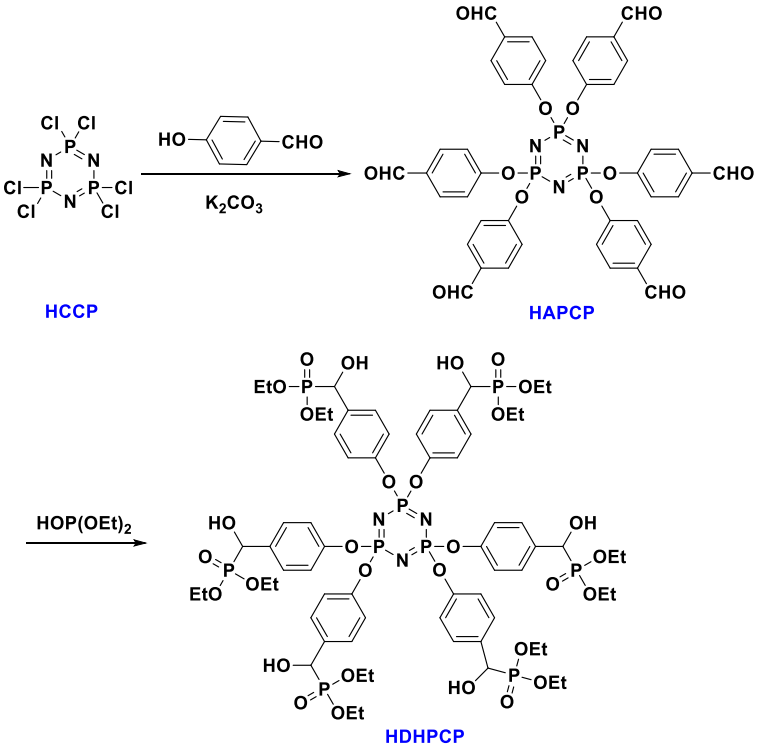


Figure 1. TGA/DTG curve of HDHPCP



Scheme 1. Synthesis protocols of α-hydroxyphosphonates



Scheme 2. Synthetic route for HDHPCP