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Studies on Polyphosphazenes-bound Wittig Reactions

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포스파젠 고분자를 이용한 Wittig반응에 관한 연구

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Abstract: Polyphosphazene-bound Wittig reagents such as $[NP(OC_6H_5)_{1.7}(OC_6H_4P(Ph)_2{=}CHCH_2CH_2CH_3)_{0.3}]_n$ were synthesized by treating $[NP(OC_6H_5)_{1.7}(OC_6H_4Br)_{0.3}]_n$ with n-butyllithium, diphenylchlorophosphine, and n-butyl iodide. Polymeric reactions were carried out according to the reaction conditions with cyclic trimers such as $[N_3P_3(OC_6H_5)_5(OC_6H_4P(Ph)_2)]$. The desired alkene and polymer-bound phosphine oxide were prepared successfully by the reaction of polyphosphazene-bound Wittig reagents with benzophenone.

요 약: $[NP(OC_6H_5)_{1.7}(OC_6H_4P(Ph)_2{=}CHCH_2CH_2CH_3)_{0.3}]_n$과 같은 포스파젠 고분자에 부착된 Wittig 시약을 $[NP(OC_6H_5)_{1.7}(OC_6H_4Br)_{0.3}]_n$에 n-butyllithium, diphenylchlorophosphine, 그리고 n-butyl iodide 등으로 처리하여 만들었다. 고분자의 반응들은 $[NP(OC_6H_5)_5(OC_6H_4P(Ph)_2)]$와 같은 고리형 삼중체를 이용한 모델반응 조건들을 고려해 이루어졌다. 포스파젠 고분자에 부착된 Wittig 시약과 benzophenone을 반응시켜 원하는 알켄과 고분자에 부착된 phosphine oxide를 성공적으로 만들었다.

1. Introduction

In recent years there has been a considerable interest in the use of polymer-supported reagents in organic synthesis[1-3]. One of the major advantages of polymer-supported reagents is that the separation of the insoluble polymeric byproduct from the reaction mixture is possible by simple filtration [4].

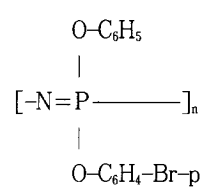
Wittig reaction, which is one of the most famous reactions in organic synthesis[5], is known to have some separation problems[6]. For example, the triphenyl phosphine oxide byproduct from Wittig reactions in solution is often hard to separate from the product olefins[7]. Howerever, polymer-supported Wittig reagents allow the separation of phosphine oxide by simple filtration[8-9].

Earlier papers on polymer-supported Wittig reagents reported synthesis of olefin in widely variable yields, depending on the particular reaction conditions and the polymer used[10-12]. Heitz and Michels used polystyrene as a support material for Wittig reaction[13].

Polyphosphazenes are a diverse new class of synthetic polymers that have been investigated as support materials[14-16]. Because of the substitu-

tive mode of synthesis used for poly(organophosphazenes)[17], several properties such as solubilities, molecular flexibility, surface character, chemical resistance, and coordination behavior can be easily modified by different synthetic pathways[18-21]. So we investigated several possible polyphosphazenes to find the most efficient polymer supports. In the present work we have explored the use of a poly[bis(aryloxy)phosphazene] as a support material because these phosphazene polymers possessed good solubility and stability[22].

Allcock and Fuller found that poly[bis(bromophenoxy)phosphazene] can easily reacted with n-butyllithium and diphenylchlorophosphine to form triphenyl phosphine functional group[23]. After several approaches, polymer(1) was found to be the best starting material for polymer-supported Wittig reactions.



(1)

(n=15,000)

Before our polymer attempts, it has been our practice to perform exploratory reactions with small molecule models[24]. Hence, cyclic trimeric phosphazenes such as trimer(2) have been used as preliminary models for the reactions of high polymer (1).

$[N_3P_3(OC_6H_5)_5(OC_6H_4P^+(Ph)_2RX^-)]$ (2)

(Ph=phenyl)

This paper describes the sequential pathways to cyclic model systems and polyphosphazene-bound Wittig reagents with phenoxy p-bromo-phenoxy cosubstituted polyphosphazenes.

2. Experimental Section

2. 1. Equipment

^{31}P NMR spectra were obtained in the Fourier transform mode at 40.5 MHz with a JEOL PS-100 FT spectrometer and processed with a Nicolet 1080 computer. Polymer separations were carried out with a Waters Associates Prep LC/system 500, using two silica columns. Approximate polymer molecular weights were determined with a Waters Associates AlC/GPC 501 instrument fitted with a 120 cm × 1cm 10^6 Styragel column.

2. 2. Materials

All experimental manipulations were performed under an atomsphere of dry nitrogen(Matheson). Tetrahydrofuran(THF)(EM) and dioxane(EM) were freshly distilled under nitrogen from sodium benzophenone ketyl. Hexachlorocyclotriphosphazene(m. p. 110~112℃) was obtained from a trimer-tetramer mixture(Ethyl Corp.) after two fraction vacuum sublimations at 60℃/0.5 Torr, two recrystallization from heptane and two further vacuum sublimations. Poly(dichloro phosphazene)$[NPCl_2]_n$ was prepared by the melt polymerization of $[NPCl_2]_3$. n-Butyllithium was used as received(Aldrich). Phenol, p-bromophenol(Aldrich), diphenylchlorophosphine(Organomet), sodium hydride(Aldrich) were used as received.

2. 3. General Procedure for the Synthesis of Trimers with the Formulars$[N_3P_3(OC_6H_5)_5Cl]$(4)

150g of $[NPCl_2]_3$(0.43mol) was dissolved in THF (1 ℓ, dry). To this solution was added 90g of NaH (60% active, 2.24mol) and this solution was cooled to 0℃ and 210g(2.24mol) of phenol dissolved in THF (200ml) was added dropwise over a 4h period. Solution was slowly warmed to room temperature and stirred for 26h. ^{31}P NMR yielded multiplet and a singlet due to $[N_3P_3(OC_6H_5)_5Cl]$ and $[NP(OC_6H_5)_2]_3$ mixture. Centrifugation(1000 RPM) and a filtering funnel(1 inch silica gel) were used to remove $NaOC_6H_5$. Solvent was removed under reduced pressure to yield the product as white crystals in 50% yield.

2. 4. General Synthetic Routes to $[N_3P_3(OC_6H_5)_5(OC_6H_4Br)]$(5)

80g(0.126mol) of trimer(4) was dissolved in THF

(400ml). To this solution was added NaH 6g(60% active, 1.2mol), followed by the dropwise addition of p-bromophenol 261g(1.2mol) dissolved in THF (150ml). The reaction mixture was allowed to stir at reflux for 48h. Centrifugation(1000 RPM) and filtering funnel(1 inch silica gel) were used to remove excess $NaOC_6H_4Br$. Oil obtained was allowed to crystallize in refrigerator.

2.5. General Synthetic Routes to $[N_3P_3(OC_6H_5)_5(OC_6H_4P(Ph)_2)]$(7)

20g(0.026mol) of trimer(5) was dissolved in THF(1 ℓ). This solution was then cooled to -80℃ and n-butyllithium(34ml, 0.517mol) was added. The reaction mixture was stirred for 2 minutes at -80 ℃, and diphenylchlorophosphine(9.3ml, 0.052mol) was added. The reaction mixture was stirred at -80 ℃ for 3h, allowed to warm to 25℃, and stirred for 24h. The solution was added to 2 ℓ ethanol and the solvent was slowly removed on the rotaryevaporator to yield a white oil.

2.6. General Synthetic Routes to $[N_3P_3(OC_6H_5)_5(OC_6H_4P(Ph)_2{=}CH_2)]$(9), and Wittig Reaction

3g(0.0034mol) of trimer(7) was dissolved in THF(100ml). To this solution was added 0.425ml (0.0069mol) of methyl iodide. The mixture was allowed to stir at 25℃ for 2h. To the solution of $[N_3P_3(OC_6H_5)_5(OC_6H_4P^+(Ph)_2CH_3I^-)]$(8) was added 2.2ml(0.023mol) of n-butyllithium. The solution was allowed to warm to 25℃, and stirred for 24h. ^{31}P NMR revealed that -23ppm peak had disappeared. To this solution was added 0.62mg of benzophenone(0.0034mol). This mixture was allowed to stir for 24h. The ^1H NMR spectrum of 1,1-diphenylethylene possessed a multiplet at 7.2~7.5ppm from aromatic hydrogens and a sharp singlet at 5.4ppm from ethylene unit.

2.7. General Procedure for the Synthesis of Polymers with the Formulars $[NP(OC_6H_5)_{1.7}(OC_6H_4Br\text{-}P)_{0.3}]_n$ (13)

Sodium p-bromophenoxide was prepared by adding a solution of p-bromophenol in dioxane(100ml) to a stirred suspension of a molar excess of sodium hydride and dioxane(100ml). After 4h, the reaction mixture was heated to reflux and filtered. The filtrate was added to a stirred solution of poly (dichlorophosphazene) in dioxane(150ml). The reaction mixture was stirred for 4-8h at 25℃ and then added to a solution of sodium phenoxide, prepared in a similar manner to the preparation of sodium p-bromophenoxide, in boiling dioxane(250ml). The reaction mixture was refluxed for 168h and concentrated by rotaryevaporation, and the concentrate was added to water. The precipitated was collected, washed with ethanol, redissolved in tetrahydrofuran, and the polymer was isolated by precipitation into water. The polymer was purified by further reprecipitations from THF into water(twice) and into hexane(twice).

2.8. General Synthetic Routes to $[NP(OC_6H_5)_{1.7}(OC_6H_4P(Ph)_2)_{0.3}]_n$(15)

The polymers(13) (15% p-bromophenoxy group) were dissloved in THF(200ml). The polymer solution was cooled to -40℃ to -60℃ by means of a dryice-acetone bath. n-Butyllithium(15~20ml) was then added to the polymer solution via syringe. Reaction times with n-butyllithium were in the range of 0.5~1min. To this solution was added diphenylchlorophosphine(15~20ml) via syringe. The low reaction temperature was maintained for 3h, and the reaction mixture was then allowed to warm to 25℃. Ethanol(100ml) was added to the reaction mixture which was then concentrated by rotaryevaporation until the polymer precipitated from solution. The polymeric precipitate was collected by filtration, washed with ethanol, dissolved in THF, and precipitated into heptane.

2.9. General Synthetic Routes to $[NP(OC_6H_5)_{1.7}(OC_6H_4P^+(Ph)_2CH_2CH_2CH_2CH_3I^-)_{0.3}]_n$(16)

A sample of polymer(15) (0.5g, 0.0014mol) was dissolved in THF(200ml) and an excess of n-butyl iodide(2g, 0.01mol) was added. The reaction mix-

ture was stirred for 6h at reflux temperature. To this reaction mixture was added ethanol(300ml). The polymeric product was purified by reprecipitations from acetonitrile into water and from acetonitrile into ethanol. The polymer exhibited only two ^{31}P NMR resonance at +24ppm (phosphonium salt phosphorous) and -20ppm (phosphazene phosphorous).

2. 10. General Synthetic Routes to $[NP(OC_6H_5)_{1.7}(OC_6H_4P(Ph)_2{=}CHCH_2CH_2CH_3)_{0.3}]_n$(17), $[NP(OC_6H_5)_{1.7}(OC_6H_4P(Ph)_2{=}O)_{0.3}]_n$(18), and Wittig Reaction

The polymer(16) (0.87g, 0.00266mol) was dissolved in dry THF(100ml). To this solution was added n-butyllithium(2.72ml, 0.0042mol). The solution color was changed into deep orange. The reaction mixture was stirred for 6h. The polymer product(17) was precipitated into heptane, and dried in vacuum line. This polymer(17) (0.5g, 0.0015mol) was dissolved in THF(100ml). To this solution was added benzeophenone (0.28g, 0.0015mol). The reaction mixture was stirred for 12h, and the polymeric product was precipitated into heptane. The ^{31}P NMR spectra of polymer(18) possessed two resonances at +26ppm and -19ppm. The ^1H NMR spectrum of 1,1-diphenyl-pentane(19) possessed a multiplet at 7.2~7.5ppm from aromatic hydrogens, and several complicated multiplets at alkane hydorgen shift aresa.

3. Results and Discussion

3. 1. Synthesis of Cyclic Trimeric Model Systems

The specific reaction sequences used for the phosphazene cyclic trimers are outlined in Scheme 1. Mixed-substituent trimers of type(5), containing both p-bromophenoxy and phenoxy groups, were synthesized by the initial interaction of (3) with five equivalents of sodium phenoxide, followed by treatment with an excess of sodium p-bromophenoxide. ^{31}P NMR spectra revealed that this solution had a small amount of hexaphenoxy cyclic trimer $[N_3P_3(OC_6H_5)_6]$.

Trimer(5) was separated from reaction mixture by HPLC, using a mixture of methylene chloride and hexane(60:40) as a solvent. The phosphination reactions for trimer(7) was performed by n-butyllithium and diphenylchlorophosphine. The phosphinated trimer had a chemical shift at 5.58ppm for the phosphine phosphorous in the ^{31}P NMR spectrum.

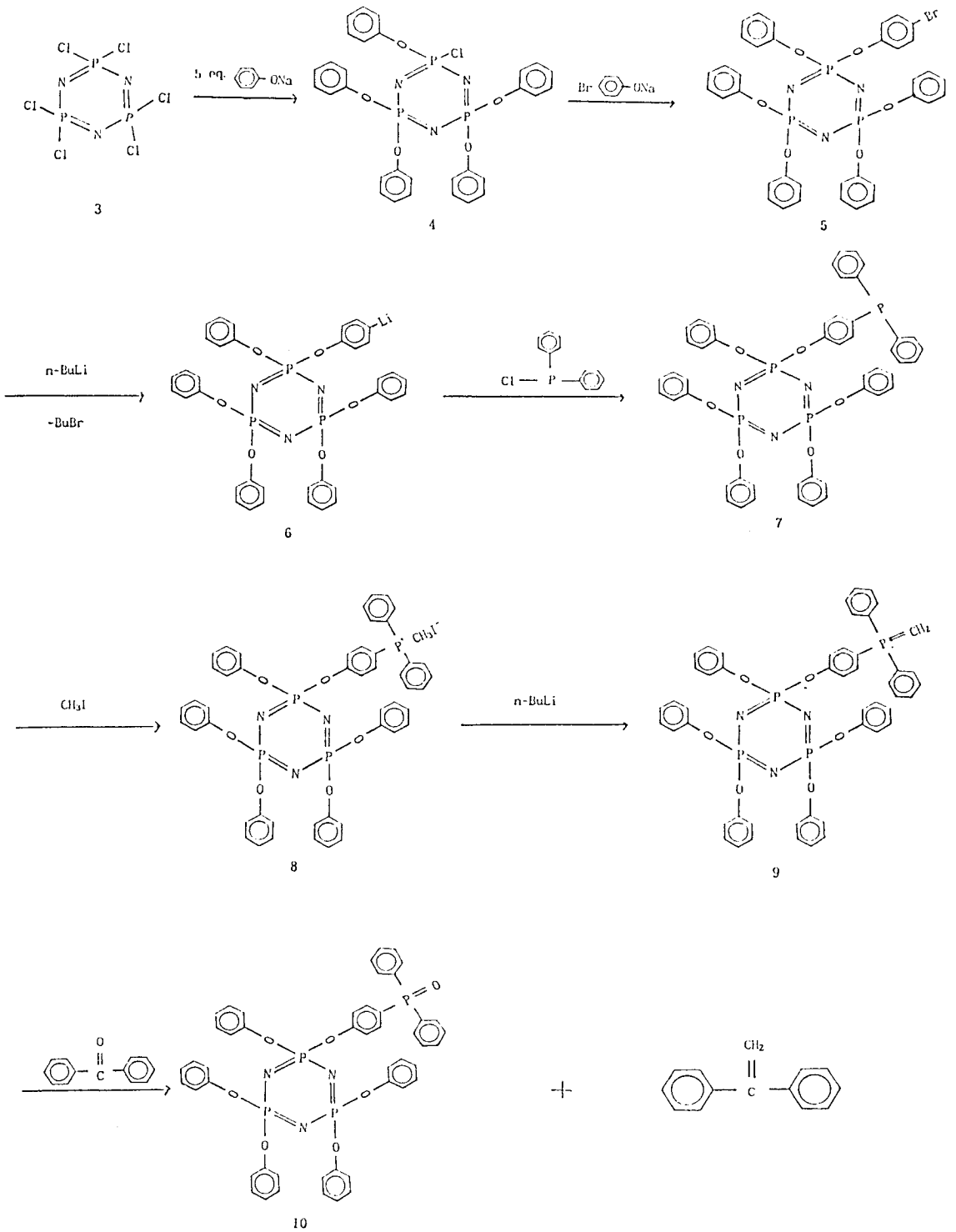
The quaternization reaction of trimer(7) was carried out at room temperature in THF using methyl iodide to yield trimer(8). ^{31}P NMR spectra of trimer (8) possessed a resonance at +23ppm which was compatible with the presence of phosphonium salt.

The trimer(9) was synthesized by the reaction of n-butyllithium with trimer(8) at 0℃. The ^{31}P NMR spectrum revealed that -23ppm peak from phosphonium salt had disappeared. To this trimer solution (9) was added a stochiometric amount of benzophenone. The ^{31}P NMR spectra of the final trimer(10) possessed a resonance at +26.96ppm which was compatible with the presence of a phosphine oxide. The ^1H NMR spectrum of 1,1-diphenylethylene possessed a multiplet at 7.2-7.5ppm from aromatic hydrogens and a sharp singlet at 5.4ppm from ethylene unit. The trimer-supported Wittig reaction occurred with high efficiency as expected.

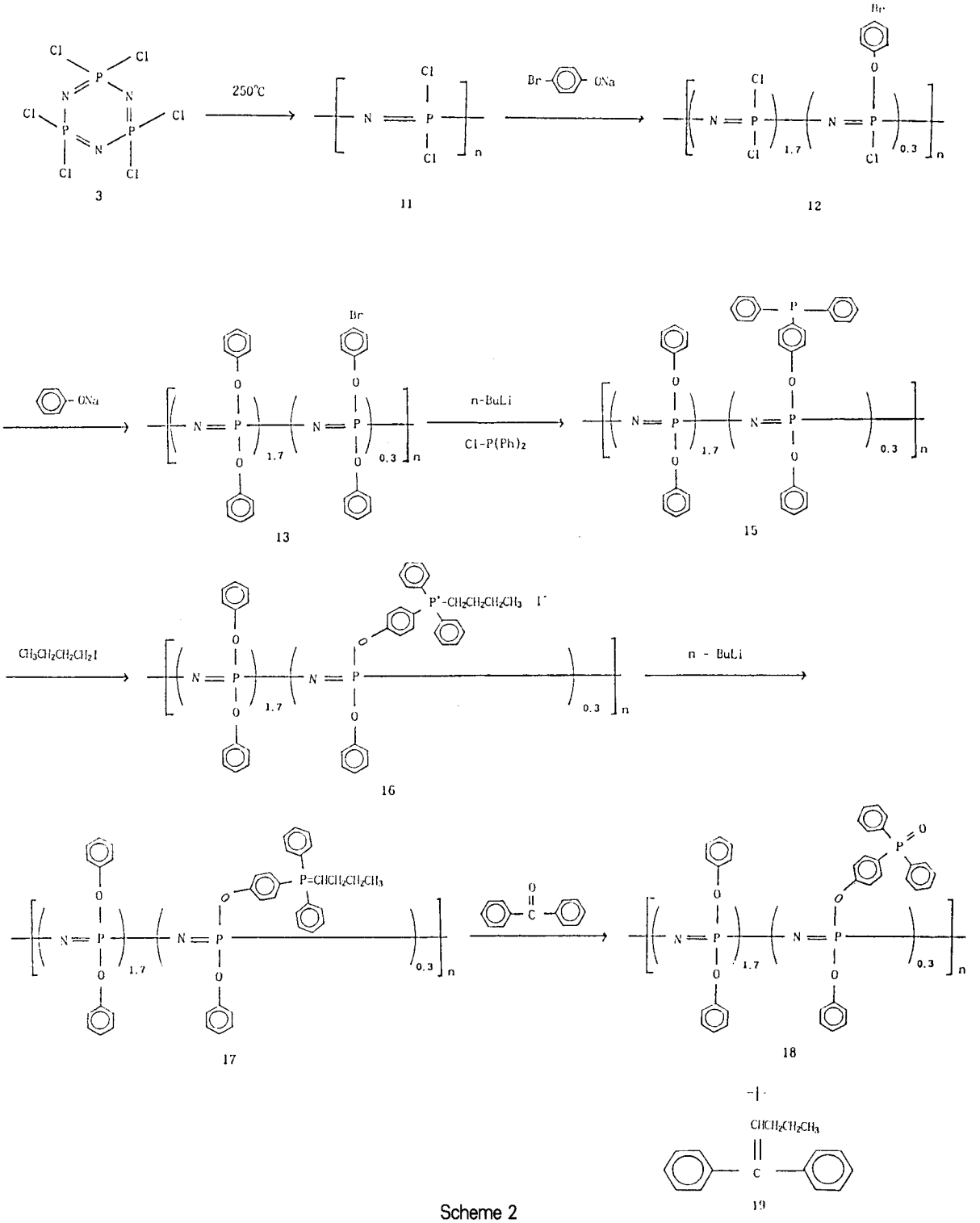
3. 2. Synthesis of the High Polymeric Derivatives

The reaction sequences shown in Scheme 2. involve six discrete steps, 1) the preparation of poly (dichlorophosphazene)(11) with high molecular weight, 2) the synthesis of 15% bromophenoxy 85 % phenoxy polyphosphazene(13), 3) the replacement of the bromine atoms in polymer(13) by lithium with the use of a metal-halogen exchange reaction with n-butyllithium, 4) the reaction of lithiophenoxy polyphosphazene of type(14) with diphenylchlorophosphine, 5) the reaction of phosphinated polymer(15) with n-butyl iodide, 6) the reaction between benzophenone and polyphosphazene-bound Wittig reagents.

Ploymer(13) was prepared by the initial interaction of polymer(11) with a deficient of sodium p-bromo phenoxide, followed by treatment with an ex-



Scheme 1



Scheme 2

cess of sodium phenoxide. The ^{31}P NMR spectrum of polymer(13) possessed a single resonance at -19ppm. The phosphination reaction for polymer (15) was performed by n-butyllithium and diphenylchlorophosphine. The ^{31}P NMR spectrum of polymer(15) possessed two resonances at -19ppm and + 5.64ppm which was compatible with the presence of a phosphine unit. The quaternization reaction was carried out with n-butyl iodide to yield polymer (16). The ^{31}P NMR spectrum of polymer(16) possessed two single resonances at -19ppm and +24ppm which was compatible with the presence of a phosphonium unit.

The polyphosphazene-bound Wittig reaction was carried out by the initial interaction with polymer (16) with n-butyllithium, followed by the reaction between polymer(17) and benzophenone. The ^{31}P NMR spectrum of the final polymer product(18) possessed two single peaks at -19ppm from phenoxy phosphazene phosphorous and at +27ppm from a phosphine oxide unit. The ^{1}H NMR spectrum of 1, 1-diphenyl 1-pentene(19) possessed a multiplet at 7.2-7.5ppm from aromatic hydrogens, triplet from ethylenic hydrogen, and several complicated multiplets at alkane hydrogen shift areas.

4. Conclusions

The conclusions of this study on polyphosphazene -bound Wittig reactions can be summarized as follows :

1. Cyclic trimer systems were studied first to find the appropriate conditions for high polymer reactions.

2. All the trimer reaction steps were successfully identified by instrumental analysis of each product.

3. 15% Bromophenoxy 85% phenoxy polyphosphazene was used as the starting material to form polymer-bound Wittig reagents.

4. The reaction between benzophenone and polyphosphazene-bound Wittig reagent was carried out at room temperature and produced polymer-bound phosphine oxide and alkene.

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References

1. P. Hodge and D. C. Sherrington, Eds., "Polymer -Supported Reactions in Organic Synthesis", Wiley, London(1980).
2. A. Akelah and D. C. Sherrington, *Chem. Rev.*, **81**, 557(1982).
3. E. Roman and G. Valenzuela, *J. Polym. Sci.*, **21**, 2057(1983).
4. J. Frechet and C. Schnerch, *J. Am. Chem. Soc.*, **93**, 492(1971).
5. J. Frechet, *Tetrahedron*, **37**, 663(1981).
6. F. Camps, J. Castells, and J. Fout, *Tetrahedron lett.*, 1971, 1715(1971).
7. M. Bernard and W. T. Ford, *J. Org. Chem.*, **48**, 326(1983).
8. J. Castells and J. Font, *J. Chem. Soc., Perkin Trans.*, **1**, 1(1979).
9. A. Akelah, *Eur. Polym. J.*, **18**, 559(1982).
10. S. Clarke, C. R. Harrison, and P. Hodge, *Tetrahedron lett.*, **21**, 1375(1980).
11. P. Hodge and J. Waterhouse, *Polymer*, **22**, 1153 (1981).
12. W. Heitz and R. Michels, *Justus Liebigs, Ann. Chem.*, 1973, 227(1973)
13. W. Heitz and R. Michels, *Angew. Chem., Int. Ed. Engl.*, **11**, 298(1972).
14. H. R. Allcock, *Chem. Rev.*, **72**, 315(1972).
15. H. R. Allcock and T. J. Fuller, *Macromolecules*, **13**, 1338(1980).
16. H. R. Allcock and S. Kwon, *Macromolecules*, **19**, 1502(1986).
17. H. R. Allcock, *Chem. Eng. News*, **63**, 22(1985).
18. H. R. Allcock and S. Kwon, *Macromolecules*, **22**, 75(1989).
19. H. R. Allcock, S. Kwon, and R. J. Riding,

Biomaterials, **9**, 509(1988).
20. H. R. Allcock, M. Gebura, and S. Kwon, *Biomaterials*, **9**, 500(1988).
21. H. R. Allcock and S. Kwon, *Macromolecules*, **21**, 1980(1988).
22. H. R. Allcock, "Phosphorous-Nitrogen Compounds", Academic Press, New York,(1972).
23. H. R. Allcock, J. F. Fuller, and T. L. Evans, *Macromolecules*, **13**, 6, 1326(1980).
24. P. E. Austin, G. H. Riding, and H. R. Allcock, *Macromolecules*, **16**, 719(1983).