J. Org. Chem. **1997,** *62,* 3552−3561

Mechanism of Polyphosphoric Acid and Phosphorus Pentoxide−Methanesulfonic Acid as Synthetic Reagents for Benzoxazole Formation

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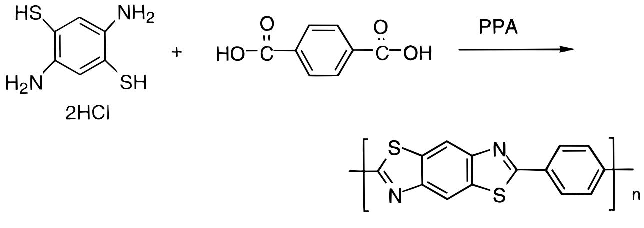
Received March 4, 1996⊗

The mechanism of 2-phenylbenzoxazole formation from benzoic acid and *o*-aminophenol in polyphosphoric acid (PPA) is studied by NMR spectroscopy and chemical analysis. Benzoic acid reacts with PPA to form benzoic−phosphoric anhydride and benzoic−polyphosphoric anhydride. The ratio of mixed anhydride to free carboxylic acid increases dramatically as the P_2O_5 content of PPA increases, but this ratio is independent of reaction temperature and time. When *o*-aminophenol dissolves in PPA, part of the hydroxyl group is converted to phosphate ester, and only protonated amine is detected. Benzoic acid, mixed anhydride, and PPA are in dynamic equilibrium, and so are PPA, *o*-aminophenol, and its phosphate ester. The mixed anhydride and *o*-aminophenol react to form 2-aminophenyl benzoate as the first reaction intermediate which undergoes rapid acyl migration to generate 2-hydroxybenzanilide. Ring closure of 2-hydroxybenzanilide to form 2-phenylbenzoxazole is acid catalyzed. The reactive components in phosphorus pentoxide−methanesulfonic acid (P_2O_5−MSA) which is a convenient alternative to PPA are very similar to those present in PPA. Benzoic acid is also converted into mixed anhydride in P_2O_5−MSA.

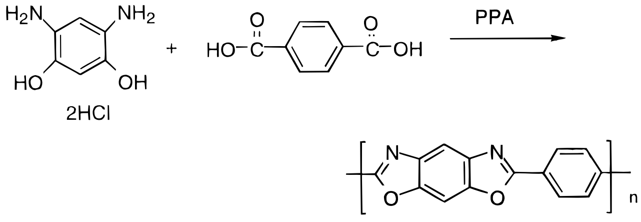
Introduction

Polyphosphoric acid (PPA) is a good solvent for many organic compounds and has been used extensively in organic synthesis. It is one of the most effective reagents for carrying out acylation, alkylation, cyclization, and acid-catalyzed reactions. It is often the reagent of choice for a variety of synthetic transformations such as dehydrations, rearrangements, and synthesis of nitrogen-containing heterocycles.[1−4] PPA has also proved to be very useful in polymer synthesis.[5−7]

2-Phenylbenzoxazole is readily prepared from *o*-aminophenol and benzoic acid in PPA.[8] The reaction is one of the most convenient methods for benzoxazole synthesis and also has very important applications in polymer chemistry. Polybenzimidazoles, poly(benzo[1,2-d:4,5-d′]-bisthiazole-2,6-diyl-1,4-phenylene) (PBT), and poly(benzo-[1,2-d:5,4-d′]bisoxazole-2,6-diyl-1,4-phenylene) (PBO) are synthesized by the reaction of terephthalic acid (TA) with aromatic tetraamines, 1,4-diamino-3,6-dithiohydroxybenzene (DADTB), and 1,3-diamino-4,6-dihydroxybenzene in PPA. PBT and PBO have unique extended rigid-rodlike configurations. These polymers have excellent thermal and oxidative stability and outstanding hydrolytic and solvent resistance. Fibers of these polymers have extremely high tensile strength and tensile modulus. The synthesis, process, and properties of these polymers have been actively pursued.[9−11]



PBT



PBO

In spite of the large number of publications on the synthetic applications of PPA, little is established on how PPA works as a synthetic reagent. The high viscosity and complex composition of PPA make it extremely difficult to investigate the mechanism of reactions occurring in it. Indeed, most of the proposed mechanistic pathways involving PPA are not accompanied with experimental data.

The previously proposed mechanism for PBT and PBO formation involves the generation of a mixed anhydride

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⊗ Abstract published in *Advance ACS Abstracts,* May 1, 1997.

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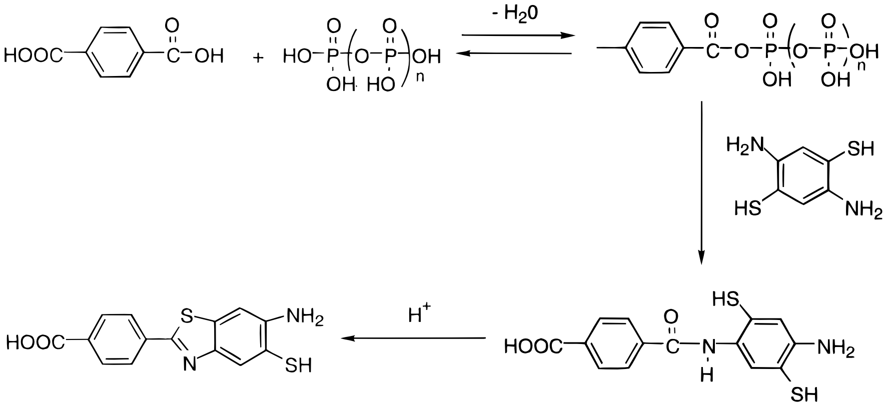
S0022-3263(96)00441-0 CCC: $14.00

Scheme 1



from TA and PPA. The amino group reacts with the activated carbonyl to form an amide which then cyclizes to benzothiazole or benzoxazole.[12,13] The cyclization reaction is acid catalyzed.[14] Scheme 1 shows the proposed reaction mechanism for PBT formation from TA and DADTB in PPA.

In this article, we report the mechanistic study of benzoxazole formation from benzoic acid and *o*-aminophenol in PPA. The fate of benzoic acid and *o*-aminophenol in PPA was studied by NMR spectroscopy. The several roles which PPA plays in this reaction are thoroughly investigated. The results are valuable for understanding other PPA-promoted reactions and providing guidelines to the use of PPA as a synthetic reagent.

A mixture of P_2O_5 and methanesulfonic acid (P_2O_5–MSA) is a convenient alternative to PPA.[15–17] It provides the advantages of a less viscous solution and sometimes better solubility of certain organic compounds. Like PPA, "the important reactant in the P_2O_5–MSA reagent is not certain; most probably it is a very active mixed anhydride."[15] Although MSA anhydride is present in P_2O_5–MSA, a MSA anhydride–MSA solution is a less effective reagent than P_2O_5–MSA for intramolecular acylation and the Beckmann rearrangement, and in other cases such as the synthesis of 2-phenylbenzoxazole, it does not work at all. Pure MSA or a mixture of P_2O_5 and sulfuric acid does not promote the reactions as PPA or P_2O_5–MSA.[18] The components in P_2O_5–MSA are studied by ^{31}P, ^{13}C, and ^{1}H NMR spectroscopy. The reactive species found in P_2O_5–MSA are very similar to those present in PPA.

Results and Discussion

A. Benzoic Acid, Benzoyl Chloride, and Benzoic Anhydride in PPA. PPA is a continuous series of mixtures of condensed phosphoric acid oligomers as represented in Scheme 1. The average chain length depends on the ratio of water to P_2O_5. Small amounts of cyclic and cross-linked molecules are also thought to be present. The ^{31}P NMR spectrum of PPA at 100 °C is shown in Figure 1. Phosphoric acid, chain end phosphorus, and phosphorus in the middle of the chains were distinctively observed. Absorption at −46.2 ppm was attributed to branched phosphorus.[19]

Figure 1 also shows the ^{31}P NMR spectrum of PPA with 17% benzoic acid at 100 °C.[20] Orthophosphoric acid and chain end phosphorus peaks were broadened as compared to those of PPA alone, while peaks for phosphorus in the middle of the chains remained sharp. The absorption peak at −8.0 ppm was attributed to $PhCO_2PO(OH)_2$. The peak for phosphorus bonded to benzoate in $PhCO_2P(O)(OH)[OP(O)(OH)]_nOH$, where $n \geq 1$, had merged with peaks for phosphorus in the middle of free PPA chains at about −30 ppm. At 60 °C, this peak was distinctively observed at −22.0 ppm.

Figure 2 is the ^{13}C NMR spectrum of PPA with 17% benzoic acid in PPA at 100 °C. There were two carbonyl absorptions, assigned as carboxylic acid at 173 ppm and anhydride at 161 ppm. The 161 ppm absorption was broader, and sometimes, at low temperatures, seen as two lines with about 1 ppm separation. One or both of the anhydride peaks must be mixed anhydride with PPA. The presence of benzoic anhydride was investigated by comparing the carbonyl as benzoic–phosphoric and benzoic–polyphosphoric mixed anhydrides from the ^{31}P NMR spectrum with the anhydride carbonyl from the ^{13}C NMR spectrum of the same NMR sample. The number of moles of PPA mixed anhydrides was about equal to that for anhydride carbonyl. The results suggested no significant amount of benzoic anhydride was formed from benzoic acid dissolved in PPA.

Raising the temperature to 120 °C caused the anhydride and acid peaks to broaden and then merge to a single line, in both the ^{13}C and ^{31}P NMR spectra. The benzoic acid–mixed anhydride chemical shift separations (in Hz) are about the same in the ^{13}C NMR spectra (12 ppm × 90 MHz in Figure 2) and the ^{31}P NMR spectra (8 ppm × 145 MHz in Figure 1), and the merger occurred at the same temperature for both nuclei. Peak broadening and merging of peaks at higher temperatures suggested the species are in dynamic equilibrium as shown in Scheme 2.[21]

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[14] (a) Hodd, K. A. *Thermal Analysis*; ICTA: Budapest, 1974; Vol. 2, pp 91–103. (b) Ghaffari, F.; Hodd, K. A. *Thermochim. Acta* **1980**, *41*, 213–224.

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[18] When benzoic acid and *o*-aminophenol were stirred in a mixture of 10 wt % P_2O_5 in sulfuric acid at 50 °C for 4 h, no 2-hydroxybenzanilide nor 2-phenylbenzoxazole was formed.

[19] (a) *Phosphorus-31 NMR, Principles and Applications*; Gorenstein, D. G., Ed.; Academic Press: New York, 1984. (b) *Handbook of Phosphorus-31 Nuclear Magnetic Resonance Data*; Tebby, J. C., Ed.; CRC Press: Boca Raton, FL, 1991.

[20] Percentages are wt % unless specified.

[21] Sandstrom, J. *Dynamic NMR Spectroscopy*; Academic Press: New York, 1982.

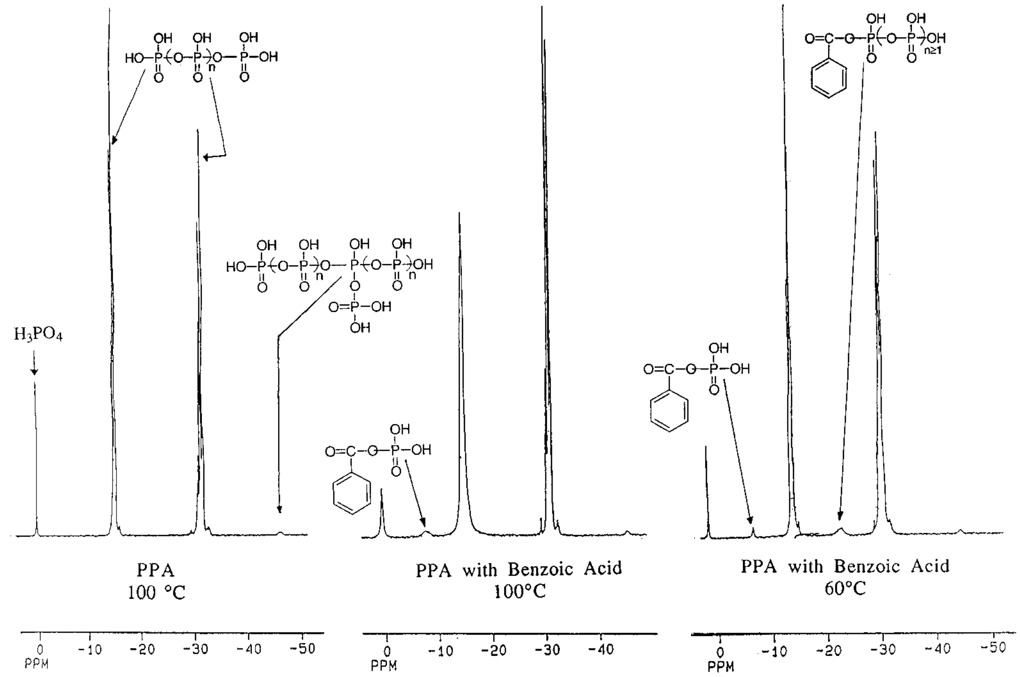
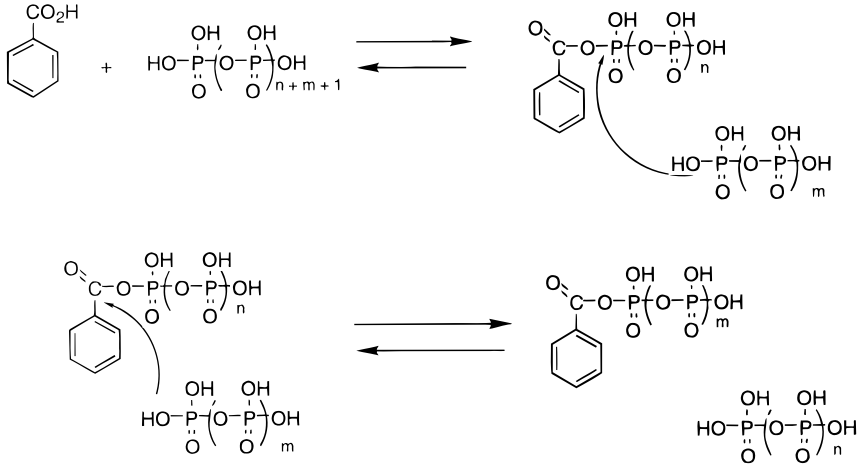


Figure 1. ^{31}P NMR spectra of PPA at 100 °C and PPA with 17% benzoic acid at 100 and 60 °C.

Scheme 2



^{31}P and ^{13}C NMR spectroscopy showed that benzoyl chloride and benzoic anhydride in PPA were converted to benzoic acid and mixed anhydride. A lower percentage of mixed anhydride was observed for samples prepared from benzoic acid in PPA than samples from benzoyl chloride and benzoic anhydride because water was liberated in mixed anhydride formation from benzoic acid. The ratio of acid to mixed anhydride did not seem to change with prolonged heating or with temperature as shown in Table 1.[21] Figure 3 shows phosphorus in the middle of the chains in PPA and PPA with 17% benzoic acid. The percentage of longer chains decreased in the sample of benzoic acid in PPA.

The ratio of benzoic acid to mixed anhydride as a function of P_2O_5 content in PPA was studied, and the results are shown in Table 2. The amount of mixed anhydride increased dramatically when P_2O_5 content changed from 77% to 87%. In PPA with 77% P_2O_5 content, no anhydride was observed, whereas at 87% P_2O_5 content in PPA, the ratio of anhydride to acid was 80:20. In reactions in which a large amount of water is liberated, extra P_2O_5 is required to adjust the P_2O_5 content to keep PPA effective.[7]

Table 1. Ratios of Acid to Anhydrides of Benzoic Acid, Benzoyl Chloride, and Benzoic Anhydride in PPA

initial composition	T (°C)	time (h)[a]	acid:anhydride[b]
17 wt % benzoic acid in PPA	100	1	71:29
	100	12	71:29
	120		2 peaks began to merge
	150		peaks merged
17 wt % benzoyl chloride in PPA	60	1	61:39
	100	2	60:40
8 wt % benzoic anhydride in PPA	60		61:39
	100	1	58:42
	100	2	57:43
	100	3	60:40

[a] Sample in NMR tube was heated for this period of time before data accumulation. [b] Acid:anhydride means the ratio of benzoic acid to total benzoic−phosphoric anhydride and benzoic−polyphosphoric anhydride.

B. Aniline, Phenol, and *o*-Aminophenol in PPA.

Aniline in PPA was studied by NMR spectroscopy. The ^{31}P NMR spectrum of aniline in PPA was the same as

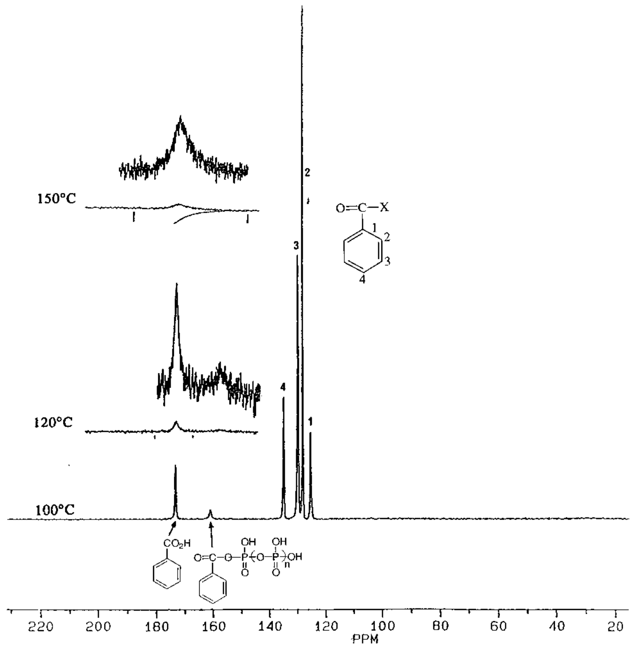


Figure 2. ^{13}C NMR spectra of 17% benzoic acid in PPA at 100 °C.

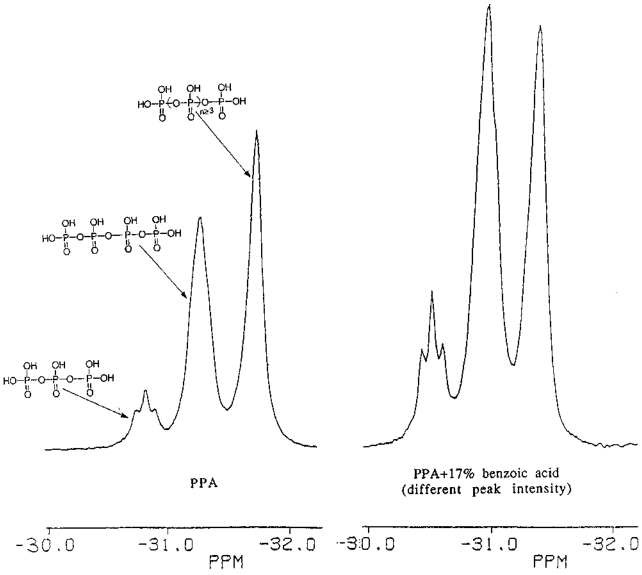


Figure 3. ^{31}P NMR of midchain phosphorus in PPA and PPA with 17% benzoic acid at 100 °C.

that of PPA itself. Both the ^{13}C and ^{1}H NMR spectra were consistent with protonated aniline. Phosphoramide was not formed detectably.

Figure 4 is the ^{31}P NMR spectrum of phenol in PPA which shows peaks attributed to phenol phosphate esters. ^{13}C NMR spectroscopy detected phenol phosphate ester as the only component. Phenol and its phosphate ester were in equilibrium, but phenol in PPA was not detected by this technique.

The ^{31}P NMR spectrum of *o*-aminophenol in PPA is essentially the same as Figure 4. Phenol phosphate esters were observed. Figure 5 displays the ^{13}C NMR spectra of aniline, phenol, and *o*-aminophenol in PPA. The ^{13}C NMR spectrum suggests that the amino group was protonated, and the phenol group existed as free −OH and phosphate ester. Peak intensities suggested the ratio of *o*-aminophenol to *o*-aminophenol phosphate ester to be 1:10.

Table 2. Benzoic Acid to Anhydrides Ratio vs Initial P_2O_5 Content in PPA

initial P_2O_5 content[a,b] (%)	acid:anhydride[c]
77	no anhydride was observed; ^{31}P NMR showed PPA existed mostly as orthophosphoric acid, pyrophosphoric acid, and some linear tripolyphosphoric acid
83.5	71/29
85	52/48
87	20/80

[a] 17 wt % benzoic acid was dissolved in PPA. [b] Temperature was 100 °C. [c] Acid/Anhydride means the ratio of benzoic acid to total benzoic−phosphoric anhydride and benzoic−polyphosphoric anhydride.

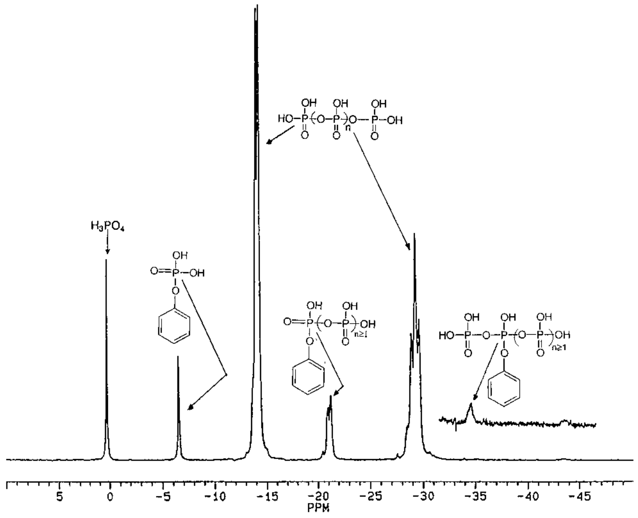
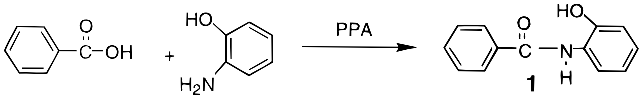
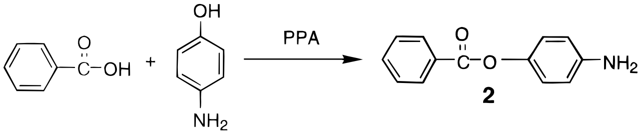


Figure 4. ^{31}P NMR spectra of phenol in PPA at 100 °C.

C. Benzoic Acid and *o*-Aminophenol in PPA.[22] In PPA at 60 °C, benzoic acid and *o*-aminophenol produced 2-hydroxybenzanilide (**1**) as almost the only product with less than 3% of 2-phenylbenzoxazole by GC peak area integration. Conversion of benzoic acid was 80%.



Benzoic acid and *p*-aminophenol, however, reacted in PPA to produce 4-aminophenyl benzoate (**2**) as the only product at 60 or 90 °C.



When *o*-anisidine and *o*-(*N*,*N*-dimethylamino)phenol competed for benzoic acid at 60 or 90 °C in PPA, *o*-(*N*,*N*-dimethylamino)phenyl benzoate was the only reaction product, and unreacted *o*-anisidine was quantitatively recovered.

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(22) A detailed description of this part has been published; see: So, Y. H.; Heeschen, J. P.; Murlick, C. L. *Marcomolecules* **1995**, *28*, 7289−7290.

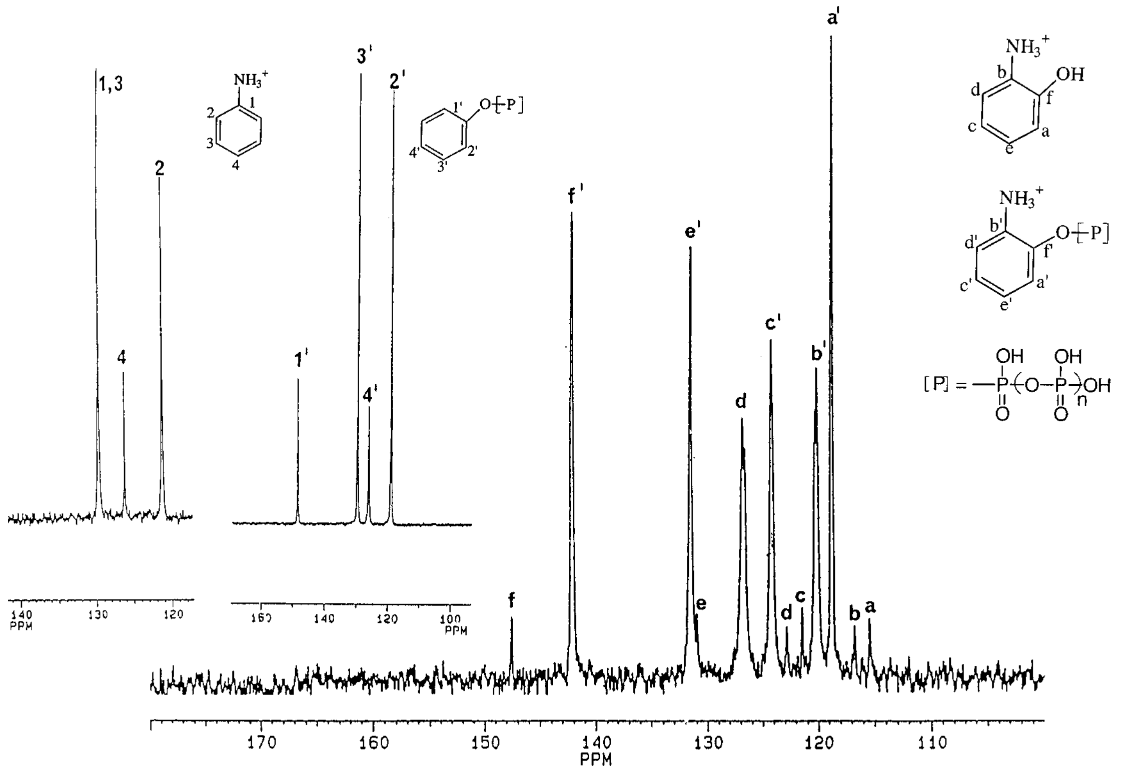
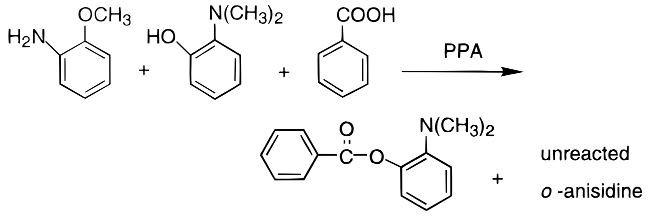


Figure 5. ^{13}C NMR spectra of aniline, phenol, and *o*-aminophenol in PPA at 100 °C.



The above experiments clearly demonstrated that *o*-aminophenol and benzoic acid in PPA first produce the ester,[23] 2-aminophenyl benzoate, which then undergoes rapid acyl migration to form the amide[24] **1**, as shown in Scheme 3.[25] The lack of proximity prevented acyl migration in the case of **2**.

The reaction of *o*-aminophenol and benzoic acid in PPA with different initial P_2O_5 content was monitored. Results in Table 3 shows the reaction was faster with higher initial P_2O_5 content. Higher reaction rates and higher anhydride to benzoic acid ratios (Table 2), when the P_2O_5 content was increased, suggest that the mixed anhydride is the reacting intermediate.

Table 3. Reaction of *o*-Aminophenol with Benzoic Acid in PPA with Different Initial P_2O_5 Content at 70 °C[a]

	initial P_2O_5 content		
time (h)	77%[b]	84%	87%
0.5		44, 56	14, 86, 0.1
2	98, 2	17, 83	
4	97, 3	17, 83	
26	95, 5	10, 90, 0.1	

[a] 4.9% benzoic acid in PPA was used. [b] The first number is percentage of benzoic acid, the second number is the combined percentages of 2-hydroxybenzanilide and 2-phenylbenzoxazole, and the third number is the percentage of a side product, 2-phenyl-5-benzoylbenzoxazole (**3**).[22]

The fate of 2-hydroxybenzanilide in PPA was studied by ^{13}C NMR spectroscopy. A sample of 2-hydroxybenzanilide-*carbonyl*-^{13}*C* was made from benzoic-*carboxyl*-^{13}*C* acid and *o*-aminophenol. A 2% solution of 2-hydroxybenzanilide-*carbonyl*-^{13}*C* in PPA was prepared by stirring the compound in PPA at room temperature. A series of ^{13}C NMR spectra was acquired at 60 °C. The resulting spectra are shown in Figure 6, where the times shown are the mid-points of the scans.

Signals in the range of 160−175 ppm are attributed to benzoxazole and carbonyl carbons. These signals were stronger than others because these carbons had been enriched in carbon-13. The earliest spectrum showed two signals in this region, at 173.5 and 170.1 ppm. The 170.1 ppm line was assigned to the amide C=O of 2-hydroxybenzanilide. It was present at first, then weakened, and became undetectable after 119 min. The line at 173.5 ppm was assigned tentatively to benzoic acid as a hydrolysis product. Figure 6 suggests possibly some 2-hydroxybenzanilide-*carbonyl*-^{13}*C* was converted to benzoic acid and *o*-aminophenol during sample preparation. The oxazole would be seen at 162.3 ppm under these conditions, and no signal was found near that chemical shift. The sample was returned to room temperature after the kinetic run and was unchanged after 6 days. An absorption peak at 159.8 ppm which was assigned as the mixed anhydride was observed when 1000 scans were used for acquisition.

At 60 °C in PPA, the rate of 2-hydroxybenzanilide ring closure to form 2-phenylbenzoxazole is significantly

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(23) Imai and co-workers proposed esters as the intermediates for polybenzoxazole and polybenzothiazole formation based on the observation that high molecular weight polybenzoxazole and polybenzothiazole were prepared much faster than the corresponding polybenzimidazole; see: Imai, J.; Taoka, I.; Uno, K.; Iwakura, J. *Makromol. Chem.* **1965**, *83*, 167−178.

(24) Raiford, L. C.; Couture, J. R. *J. Am. Chem. Soc.* **1924**, *46*, 2305−2318.

(25) In the reaction of benzoyl chloride and *o*-aminophenol in PPA, 2-benzamidophenyl benzoate and 2-hydroxybenzanilide were isolated. The result suggests direct amide formation from *o*-aminophenol and benzoyl chloride is possible.

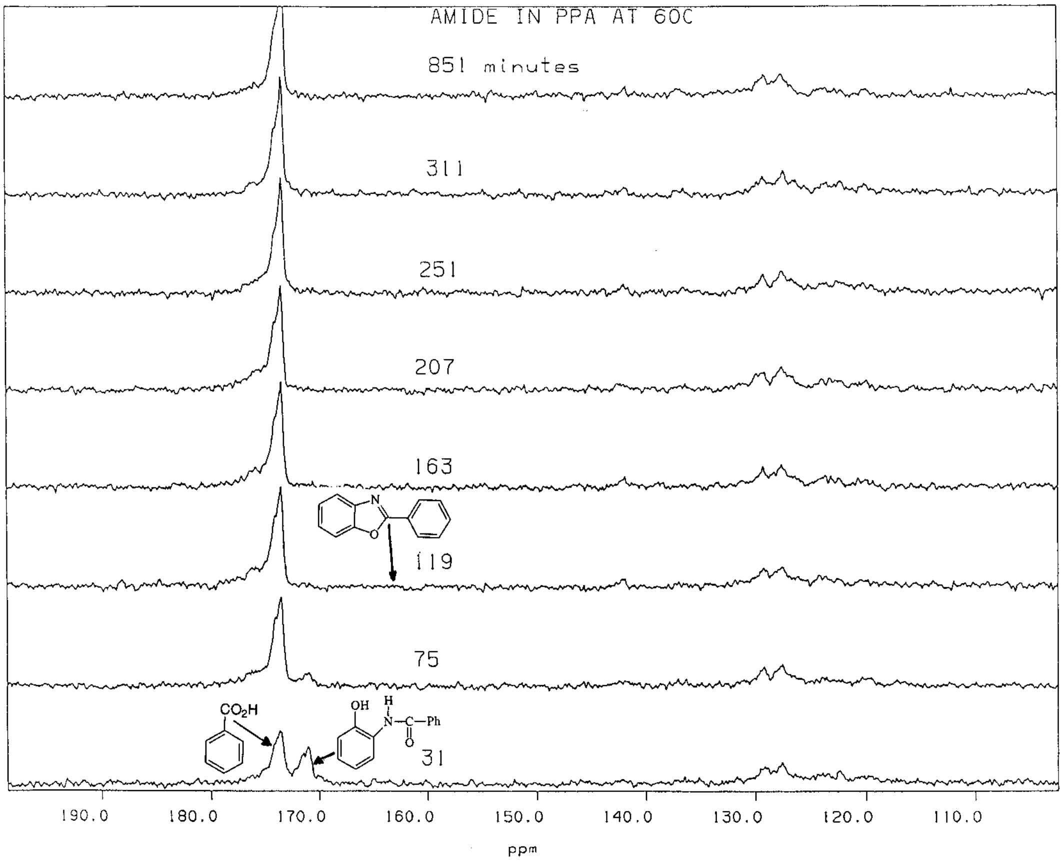
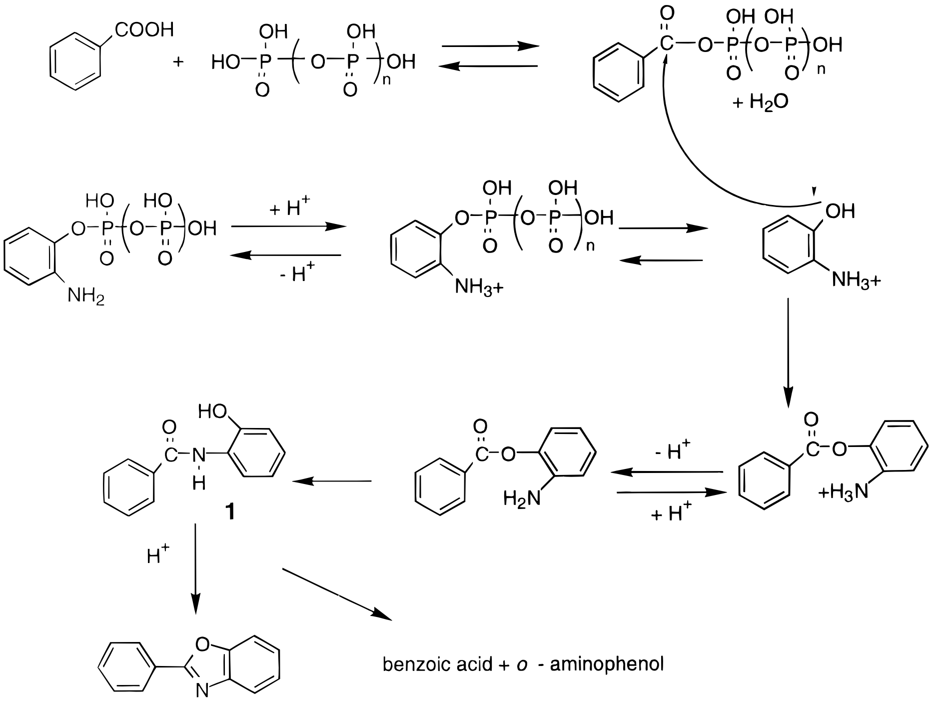


Figure 6. Hydrolysis of 2-hydroxybenzanilide-*carbonyl*-^{13}C in PPA as monitored by ^{13}C NMR spectroscopy.

Scheme 3



slower than the rate of hydrolysis to generate benzoic acid and *o*-aminophenol. Since it was a dilute solution with no agitation, the formation of 2-hydroxybenzanilide from the hydrolyzed products was not detected by this technique.

The reaction mechanism of benzoic acid and *o*-aminophenol in PPA to form 2-phenylbenzoxazole is of high complexity. The proposed pathways which are consistent with our experimental results are shown in Scheme 3. Benzoic acid is activated through the formation of benzoic–phosphoric anhydride. Benzoic acid, mixed anhydride, and PPA are in dynamic equilibrium. The amino group of *o*-aminophenol is protonated, and about 90% of the hydroxyl group exists as phosphate ester. All the *o*-aminophenol derivatives and PPA are also in dynamic equilibrium. 2-Aminophenyl benzoate is proposed as the

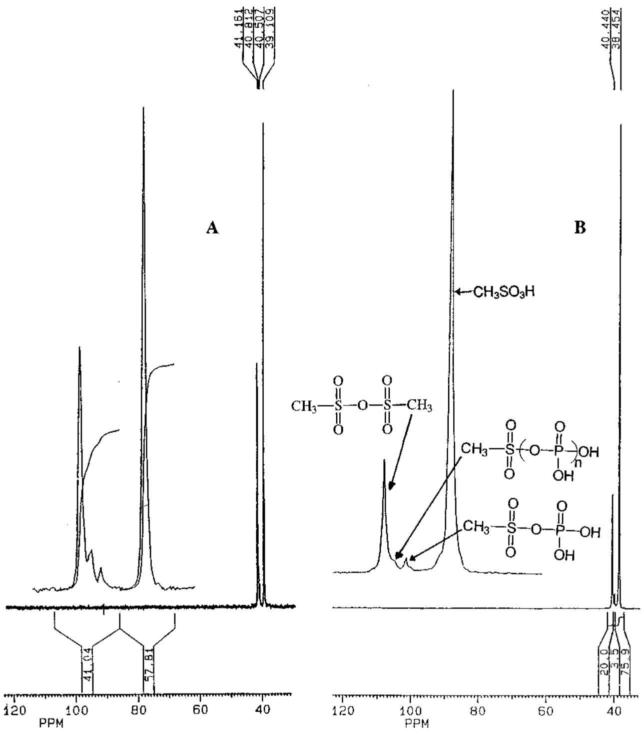
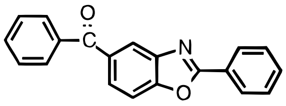


Figure 7. ^{13}C NMR spectra of 25% P_2O_5 in MSA (A) and 10% P_2O_5 in MSA (B) at 60 °C.

first reaction intermediate. Rapid equilibrium is expected between protonated amine, and free amine although only protonated amine is detected by ^{13}C NMR spectroscopy. Rapid acyl migration of the ester generates 2-hydroxybenzanilide which undergoes acid-catalyzed ring closure to generate 2-phenylbenzoxazole.[14,22] This study does not rule out the possibility of 2-aminophenyl benzoate cyclization to form 2-phenylbenzoxazole. Formation of 2-phenyl-5-benzoylbenzoxazole (**3**) suggests that benzoyl cation might be developed in the reaction.



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D. Reactive Species in Phosphorus Pentoxide–Methanesulfonic Acid. The components in P_2O_5–MSA and the fate of benzoic acid in this mixture were studied by ^{31}P, ^{13}C, and ^{1}H NMR spectroscopy. Two samples with 9% and 25% P_2O_5 in MSA were prepared by adding P_2O_5 to MSA with stirring. Figure 7 shows the ^{13}C NMR spectra. Peaks were assigned for CH_3SO_2OH, $CH_3SO_2OP(O)(OH)[OP(O)(OH)]_nOH$ (with $n \geq 0$), and $(CH_3SO_2)_2O$. In the sample with higher P_2O_5 content, a higher percentage of $CH_3SO_2OP(O)(OH)[OP(O)(OH)]_nOH$ was observed. ^{1}H NMR spectroscopy (Figure 8) showed protons in methanesulfonic acid, methanesulfonic anhydride, methanesulfonic–phosphorus anhydride, and methanesulfonic–polyphosphoric anhydride. The percentage of anhydride protons was higher in the sample with 25% P_2O_5.

^{31}P NMR spectra of the two samples showed H_3PO_4 and $CH_3SO_2OP(O)(OH)[OP(O)(OH)]_nOH$, with $n \geq 0$ (Figure 9). ^{13}C, ^{1}H, and ^{31}P NMR spectroscopy demonstrated formation of methanesulfonic anhydride, methanesulfonic–phosphoric anhydride, and methanesulfonic–polyphosphoric anhydride in P_2O_5–MSA. Higher percentage of anhydrides was generated with higher P_2O_5 content. Polyphosphoric chains were formed in P_2O_5–MSA. They are of similar nature to the polyphosphoric acid chains in PPA.

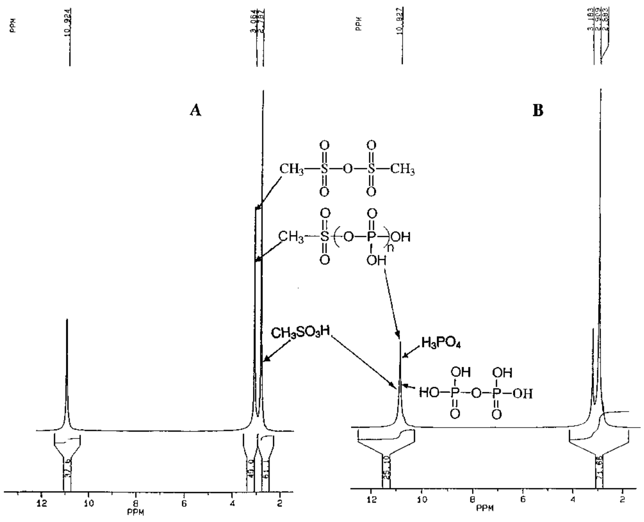

Figure 8. ^{1}H NMR spectra of 25% P_2O_5 in MSA (A) and 10% P_2O_5 in MSA (B) at 60 °C.

Figure 10 is the ^{13}C NMR spectra of benzoic acid in P_2O_5–MSA. They are similar to the ^{13}C NMR spectrum of benzoic acid in PPA. The ^{31}P NMR spectra of benzoic acid in P_2O_5–MSA (Figure 11) are also very similar to that of benzoic acid in PPA. Peaks assigned to phosphorus in benzoic–phosphoric anhydride and benzoic–polyphoshoric anhydrides were observed. Both ^{13}C and ^{31}P NMR spectroscopy demonstrate that part of the benzoic acid was transformed into activated carbonyls, benzoic–phosphoric anhydride, and benzoic–polyphosphoric anhydride.

The components found in P_2O_5–MSA are very similar to those present in PPA. The carboxylic acid group in benzoic acid is transformed to benzoic–phosphoric anhydride and benzoic–polyphosphoric anhydride which are activated for esterification, amidation, acylation, alkylation, and many other reactions. These species are not found in a mixture of P_2O_5 and sulfuric acid. ^{13}C NMR spectrum of a solution of benzoic acid in a mixture of 10% P_2O_5 in sulfuric acid showed only one carbonyl peak at 179.80 ppm which is assigned as carboxylic acid. Neither MSA anhydride-MSA solutions nor pure MSA have the reactive phosphorus species to promote reactions as PPA or P_2O_5–MSA. 2-Phenylbenzoxazole was also made from benzoic acid and *o*-aminophenol in PPA–MSA which is less viscous than PPA and does not require the handling of solid P_2O_5.[26]

Conclusion

The reaction mechanism of benzoic acid and *o*-aminophenol to produce 2-phenylbenzoxazole in PPA is investigated. Benzoic acid reacts with PPA to form mixed anhydride. The ratio of anhydride to free benzoic acid increases dramatically as the P_2O_5 content in PPA increases. In PPA, the amino group of *o*-aminophenol is

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[26] When P_2O_5–MSA or PPA–MSA was used as the reagent for 2-phenylbenzoxazole synthesis from benzoic acid and *o*-aminophenol, both 2-hydroxybenzanilide and 2-methanesulfonamidophenyl benzoate were isolated as reaction intermediates.

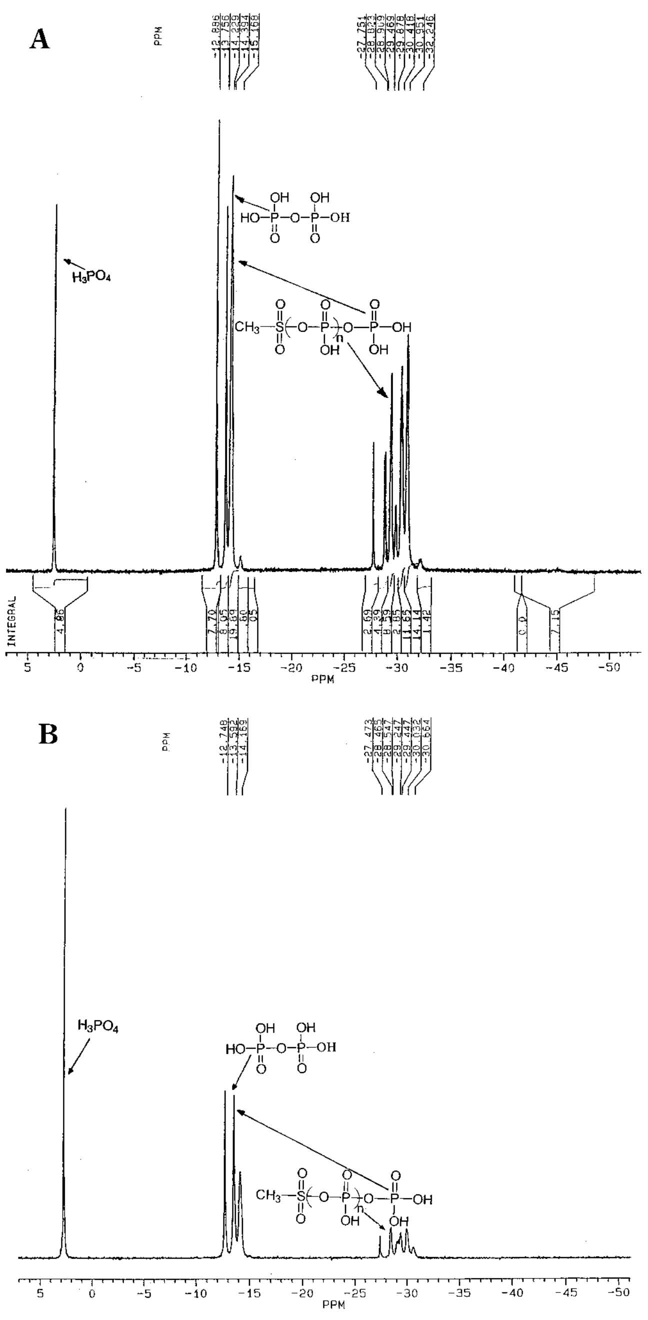

Figure 9. ^{31}P NMR spectra of 25% P_2O_5 in MSA (A) and 10% P_2O_5 in MSA at (B) 60 °C.

protonated, and about 90% of the hydroxyl group exists as hydroxyl phosphate ester. Benzoic acid, mixed anhydride, and PPA are in dynamic equilibrium and so are *o*-aminophenol, *o*-aminophenol phosphate ester, and PPA. NMR spectroscopy is a very valuable tool in studying reaction mechanisms involving PPA.

o-Aminophenol reacts with the activated carbonyl, mixed anhydride, to produce an ester, 2-aminophenyl benzoate, as the first intermediate which undergoes rapid acyl migration to generate 2-hydroxyanilide. Ring closure to form 2-phenylbenzoxazole is acid catalyzed.

PPA plays several roles in this reaction. It activates the carbonyl group, reduces the viscosity of PPA by releasing water in phenol phosphate ester formation at the beginning of the reaction, picks up water of condensation, and catalyzes benzoxazole ring closure. The rate of this reaction is critically influenced by the P_2O_5 content of PPA. Since the water content in this reaction changes continuously, it is extremely difficult to study its kinetics.

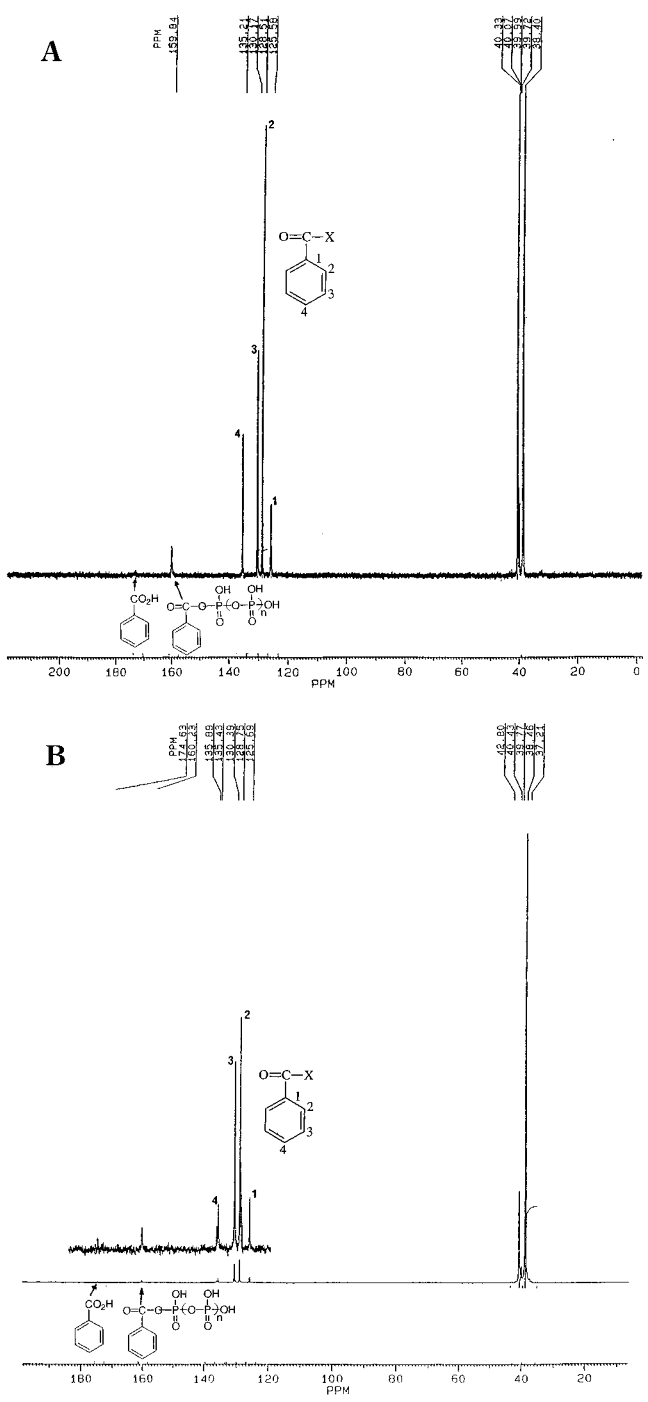

Figure 10. ^{13}C NMR spectra of 7.5% benzoic acid in a mixture of 25% P_2O_5 in MSA (A) and 1.7% benzoic acid in a mixture of 10% P_2O_5 in MSA (B) at 60 °C.

The components in a mixture of P_2O_5 and MSA are very similar to those found in PPA. Benzoic acid in P_2O_5–MSA is also activated through the formation of mixed anhydride. To lower PPA viscosity and also avoid handling of the highly hygroscopic solid P_2O_5, PPA–MSA is a convenient alternative.

Experimental Section

Materials. Benzoic acid, *o*-aminophenol, *o*-anisidine, benzoic-*carboxyl*-^{13}C acid, and PPA were purchased from Aldrich Chemical Co. 2-Phenylbenzoxazole and MSA-d_4 were from

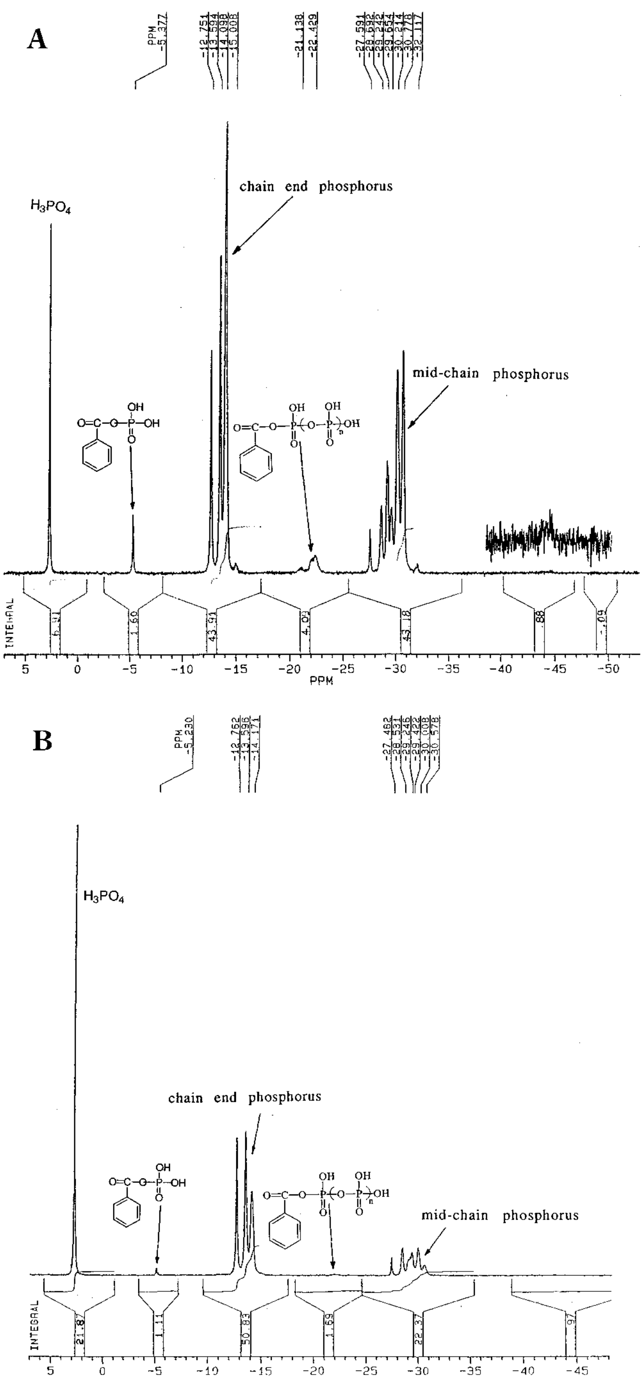

Figure 11. ^{31}P NMR spectra of 7.5% benzoic acid in a mixture of 25% P_2O_5 in MSA (A) and 1.7% benzoic acid in a mixture of 10% P_2O_5 in MSA (B) at 60 °C.

TCI and Cambridge Isotope Laboratories, respectively. The P_2O_5 content in PPA was determined by NaOH titration.[27] Samples with 83.5% P_2O_5 content were used unless specified. The synthesis and characterization of 2-hydroxybenzanilide, 4-aminophenyl benzoate, *o*-(*N*,*N*-dimethylamino)phenol, and *o*-(*N*,*N*-dimethylamino)phenyl benzoate were previously reported.[22] 2-Hydroxybenzanilide-*carbonyl*-^{13}*C* was prepared and isolated with the same procedure as that for the unlabeled compound.

Measurements. GC analysis was performed on a HP5840A chromatograph with a 30 m J&W fused silica gel capillary column. Benzophenone was the internal standard.

NMR spectra were obtained on the following instruments:

instrument	resonance frequency (MHz) ^{1}H	^{31}P	^{13}C
GE Omega-600	600	242	150
Bruker WM-360	360	145	90
IBM AF-300	300		75
GE/Nicolet NT-300	300		75

The conditions used are as follows: field/frequency lock on internal deuterated solvent, proton decoupling for ^{13}C NMR spectra, no proton decoupling for ^{31}P NMR spectra, ambient temperature of 20−25 °C, and pulse-Fourier transform (FT) technique with multiple scans coadded.

^{31}P NMR spectra were obtained using an approximately 45° flip angle and a 5−10 s repeat time. These conditions gave the same signal strength as for spectra run using 2 times the repeat time. ^{13}C NMR spectra were obtained using an approximately 70° flip angle at 6 s repeat time. ^{1}H NMR spectra were obtained using a flip angle of less than 20° and 1−5 s between scans.

Chemical Shift References. The chemical shift is reported as fractional frequency difference, in parts per million, from a reference signal. For ^{1}H and ^{13}C NMR spectra of PPA samples, the reference is TMS in the sample. For ^{31}P NMR, the reference is a separate sample of 85% phosphoric acid set at 0.00 ppm. Measurement was made by sample interchange at a fixed magnetic field value. On the Omega-600 spectrometer, the system gave chemical shift values which were within a few tenths of 1 ppm.

For P_2O_5−MSA samples, the methyl signal of MSA was used as the reference for ^{1}H and ^{13}C chemical shifts because TMS has extremely low solubility in MSA and may be subject to decomposition. The ^{1}H and ^{13}C reference shifts were derived from a MSA solution containing *n*-propanol (10%), tetramethylammonium chloride (2%), and a trace amount of TMS. For ^{31}P shifts in P_2O_5−MSA solutions, the internal H_3PO_4 signal serves as the reference. The ^{31}P chemical shift of H_3PO_4 in P_2O_5−MSA solutions was found to be 2.7 ppm relative to a separate 85% H_3PO_4 sample by sample interchange on the Omega-600 spectrometer. Internal chemical shift reference values for P_2O_5−MSA solutions are listed below, and these shift values are not necessarily the same for a dilute solution in a nonprotonating solvent:

nucleus	Chemical Shift Response in P_2O_5−MSA Solution, ppm H_3PO_4	MSA (CH_3)	Me_4N^+	propanol (CH_3)	TMS
^{1}H		3.16	3.11	0.98	0.00
^{13}C		40.1	56.6	10.27	not detected
^{31}P	+2.7	sample interchange with 85% H_3PO_4			

NMR Samples. NMR sample of benzoic acid in PPA was prepared by stirring 17 g of benzoic acid in 83 g of PPA at 100 °C for 1 h under nitrogen. A portion of the solution was transferred into a 10 mm NMR tube. NMR samples of other compounds in PPA were prepared similarly. A 9% P_2O_5 in MSA mixture was made by adding 9 g of P_2O_5 to 91 g of MSA with stirring. In the preparation of 25% P_2O_5−MSA, solid P_2O_5 was added to MSA at 60 °C. For MSA solutions, a 5−20% addition of MSA-d_4 served as the field/frequency lock; 1 drop of MSA-d_4 was used for the ^{13}C NMR signal lock.

NMR Spectra. In units of ppm, with peak area integration in parentheses.[28]

PPA at 100 °C: ^{31}P NMR 0.351 (H_3PO_4, 4), −14.770, −15.089, −15.157, −16.028 (chain end phosphorus, 45),

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(27) Standard Test Method 01-04-01, Polyphosphoric Acid Assay by Chain Length Determination; Stauffer Chemical Co., Basic Products Group, May 30, 1984.

(28) ^{31}P and ^{13}C NMR spectra signal peaks were assigned with the following references: (a) Reference 19. (b) Kalinowski, H.-A.; Berger, S.; Braun, S. *Carbon-13 NMR Spectroscopy*; Wiley: New York, 1988. (c) Sadtler Spectra, Carbon-13 NMR Collection; BIORAD, Sadtler Division, Philadelphia, PA, 1995. Peak assignments of of ^{13}C NMR spectrum for protonated aniline were based on (c) 6822C which are different from assignments in (b) p 315.

−29.580, −30.801, −31.257, −31.713, −32.729, −33.007 (midchain phosphorus, 50), −46.199 (branched phosphorus, 1).

PPA with 17% benzoic acid at 100 °C: ^{31}P NMR 0.865 (H_3PO_4, 11), −8.00 ($PhCO_2P(O)(OH)_2$, 2), −14.575, −15.434 (chain end phosphorus, 102), −30.055, −30.498, −30.920 (midchain phosphorus, 95), −45.10 (branched phosphorus, 1); ^{13}C NMR 173.24 (71), 160.85 (29), 134.87 (129), 129.66 (297), 128.00 (281), 125.31 (95); mol of carbonyl anhydride in 100 g of sample was 0.29(17/122) = 0.0403.

PPA with 17% benzoic acid at 60 °C: ^{31}P NMR 1.773 (H_3PO_4, 2.47), −7.03 ($PhCO_2P(O)(OH)_2$, 0.83), −13.528, −13.878 (chain end phosphorus, 38.98), −22.01 ($PhCO_2P(O)(OH)[OP(O)(OH)]_nOH$, 3.12), −29.732, −30.160, −30.569 (midchain phosphorus, 53.55), −44.20 (branched phosphorus, 0.78); phosphorus existed as mixed anhydrides = 3.95/99.73 = 3.96%; mol of P_2O_5 in 100 g of sample = (83 × 83.5%)/142 = 0.488; mol of mixed anhydride phosphorus = 0.488 × 2 × 3.96% = 0.0387.

Aniline in PPA at 100 °C: ^{13}C NMR 129.61 (ipso, meta), 126.17 (para), 121.18 (ortho); ^{1}H NMR 11.242, 7.345, 6.658, 6.478; ^{31}P NMR 1.70 (H_3PO_4), −13.860, −14.174, −14.216, −15.142 (chain end phosphorus), −28.938, −29.927, −30.379, −30.827, −31.869, −32.156 (midchain phosphorus), −45.187 (branched phosphorus).

Phenol in PPA at 100 °C: ^{31}P NMR 0.946 (H_3PO_4), −5.127 ($PhOP(O)(OH)_2$), −13.720, −13.996, −14.053 (chain end phosphorus), −20.0 ($PhOP(O)(OH)[OP(O)(OH)]_nOH$), −23.816 (midchain phosphorus); ^{13}C NMR 148.27, 129.28, 125.71, 118.72.

***o*-Aminophenol in PPA at 100 °C:** ^{13}C NMR 147.51 (0.69), 142.06 (14.97), 131.49, 130.95 (15.01), 126.02 (15.78), 124.20 (14.66), 122.01, 121.43 (3.53), 120.14 (13.95), 118.73 (15.61), 116.69, 115.39 (3.30); Figure 5 (a + b + c + d + f)/(a′ + b′ + c′ + d′ + f′) = (3.30 + 3.53 + 0.69)/(15.61 + 13.95 + 14.66 + 15.78 + 14.97) = 1/10; ^{31}P NMR 0.289 (H_3PO_4), −6.526 ($PhOP(O)(OH)_2$), −13.942, −14.183 (chain end phosphorus), −20.438, −20.954, −21.225 ($PhOP(O)(OH)[OP(O)(OH)]_nOH$), −27.559, −28.505, −28.897, −29.284, −29.644, −30.613 (midchain phosphorus).

P_2O_5 (25%)−MSA at 60 °C: ^{13}C NMR 41.161, 40.812, 40.507, 39.109; ^{1}H NMR 10.924 (37.6), 3.064 (anhydrides, 49.0), 2.781 (MSA, 61.1); ^{31}P NMR 2.75 (H_3PO_4, 4.86), −12.886, −13.756, −14.229, −14.394, −15.168 (chain end phosphorus, 36.49), −27.751, −28.823, −28.909, −29.469, −29.878, −30.418, −30.951, −32.246 (midchain phosphorus, 45.73), −45 (branched phosphorus, 7.15).

P_2O_5 (9%)−MSA at 60 °C: ^{13}C NMR 40.440, 38.454; ^{1}H NMR 10.827 (25.10), 3.183, 2.909, 2.883 (CH_3 of anhydrides and MSA, 71.66); ^{31}P NMR 2.75 (H_3PO_4, 22.0), −12.748, −13.592, −14.170 (chain end phosphorus, 53.4), −27.473, −28.544, −29.246, −29.447, −30.031, −30.663 (midchain phosphorus, 23.5).

Benzoic acid (7.5%) in P_2O_5 (25%)−MSA: ^{13}C NMR 172.24 (6.06), 159.84 (9.97), 135.21 (12.91), 130.17 (27.61), 128.51 (27.82), 125.58 (12.62), 40.33, 40.07, 39.99, 39.72, 38.40 (180.26); ^{31}P NMR 2.75 (H_3PO_4, 6.91), −5.377 ($PhCO_2P(O)(OH)_2$, 1.60), −12.751, −13.594, −14.098, −15.008 (chain end phosphorus, 43.91), −21.138, −22.429 ($PhCO_2P(O)(OH)[OP(O)(OH)]_nOH$, 4.09), −27.591, −28.692, −29.242, −29.654, −30.214, −30.778, −32.117 (midchain phosphorus, 43.18).

Benzoic acid (1.7%) in P_2O_5 (9%)−MSA: ^{13}C NMR 174.63 (0.72), 160.23 (0.92), 135.89 (0.54), 135.43 (1.05), 130.39 (3.25), 128.75 (3.20), 125.69 (0.94), 42.80, 40.43, 39.77 (21.70), 38.46, 37.21 (75.79); ^{31}P NMR 2.75 (H_3PO_4, 21.87), −5.230 ($PhCO_2P(O)(OH)_2$, 1.11), −12.762, −13.596, −14.171 (chain end phosphorus, 50.83), −21.5 ($PhCO_2P(O)(OH)[OP(O)(OH)]_nOH$, 1.69), −27.482, −28.531, −29.246, −29.422, −30.008, −30.578 (midchain phosphorus, 22.37).

Study of 2-Hydroxybenzanilide-*carbonyl*-^{13}*C* in PPA by ^{13}C NMR Spectroscopy. A series of ^{13}C NMR spectra was acquired at 60 °C, 256 scans each covering 851 min. Timing started when the sample was dropped into the heated probe. Pulse width was 20 μs, corresponding to a flip angle of 70° or less.

Reaction of *o*-Aminophenol and Benzoic Acid in Different Initial P_2O_5 Content PPA. *o*-Aminophenol (4.36 g, 0.04 mol) and benzoic acid (4.88 g, 0.04 mol) were stirred in 95 g of PPA. Samples were removed from the reactor, quenched with ice water, extracted with ethyl acetate, and analyzed by GC.

Benzoic Acid in P_2O_5−Sulfuric Acid. To 25 g of concentrated sulfuric acid was added 2.5 g of P_2O_5 with stirring. Benzoic acid (2.75 g) was added. The solution was clear. ^{13}C NMR: 179.80, 139.85, 133.28, 131.30, 125.62.

Acknowledgment. We thank Drs. Don McLemore and Nelson Rondan for helpful discussions and Rick DeCaire for assistance.

Supporting Information Available: ^{1}H and ^{13}C NMR and IR spectra of **1**−**3** and *o*-(*N*,*N*-dimethylamino)phenyl benzoate and ^{1}H NMR spectrum of *o*-(*N*,*N*-dimethylamino)phenol (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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