Polymer Journal, Vol. 20, No. 6, pp 477—483 (1988)

Synthesis of Polyamides by Direct Polycondensation with Propylphosphonic Anhydride as an Activating Agent

Mitsuru UEDA and Tsukasa HONMA

Department of Polymer Chemistry, Faculty of Engineering, Yamagata University, Yonezawa 992, Japan

(Received January 20, 1988)

ABSTRACT: A 50 wt% solution of the propylphosphonic anhydride in NMP as an activating agent was used for the synthesis of amides and polyamides. The activating agent was useful for the preparation of amides from carboxylic acids and amines. The direct polycondensation of dicarboxylic acids with aromatic diamines using the activating agent in the presence of pyridine proceeded at 100°C to produce polyamides with inherent viscosities up to 1.6 dl g^{-1}. Furthermore, the activating agent was used for the chemoselective polyamidation; that is, polyamides from dicarboxylic acids and diamines containing various functional groups were prepared without special protection of the acylation-sensitive groups.

KEY WORDS Polyamides / Direct Polycondensation / Propylphosphonic Anhydride / Activating Agent / Dicarboxylic Acid / Diamine /

A direct polycondensation using activating agents has been developed as a useful method for the synthesis of polyamides under mild conditions, where organophosphorus reagents have been found useful for activation of carboxylic acid groups.

In the preceding papers, we showed phosphorus-based activating agents, such as, diphenyl 2,3-dihydro-1,3-benzisoxazol-3-yl phosphonate,[1] phenyl bis(2,3-dihydro-2-oxobenzothiazol-3-yl)phosphonate,[2] and diphenyl(2,3-dihydro-2-oxo-3-benzothiazolyl)-phosphonate[3] to be useful for the synthesis of amides and polyamides.

Recently, alkylphosphonic anhydrides were found suitable activating agents for peptide syntheses.[4] These reagents have the following advantages: simple preparation, long shelf-stability at room temperature, very good solubility in all solvents, and little tendency to racemization. These characteristics prompted us to employ them for the preparation of polyamides as activating agents.

In this paper, we report the synthesis of polyamides by the direct polycondensation of dicarboxylic acids with diamines using propylphosphonic anhydride as an activating agent.

EXPERIMENTAL

Materials

The reagent propylphosphonic anhydride was prepared according to the reported procedure[4] and a 50 wt% solution of propylphosphonic anhydride in NMP (**1**) was used as the activating agent.

Diamines. 4,4′-Oxydianiline (ODA), 4,4′-methylenedianiline (MDA), 4,4′-diaminodiphenyl sulfone (DDS), and 3,5-diaminobenzoic acid (DAB) were purified by recrystallization.

Dicarboxylic Acids. Isophthalic acid (**4a**), sebacic acid (**4b**), 5-hydroxyisophthalic acid (**4c**), and 5-aminoisophthalic acid (**4d**) were purified by recrystallization.

Solvents and Reagents. *N*-Methyl-2-pyrrolidone (NMP) (supplied by Mitsubishi Chemical Industries Ltd.), and hexamethylphosphoramide (HMPA) were purified by vacuum distillation and stored over 4 Å molecular sieves. The other reagent and solvents were obtained commercially and used as received.

Model Reaction

Typical example of the model reaction is as follows.

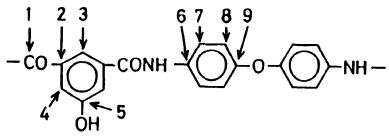
Benzanilide (**2a**). A 50 wt% solution of propylphosphonic anhydride in NMP **1** (0.63 ml, 1.0 mmol) was added to a stirred solution of benzoic acid (0.122 g, 1.0 mmol), aniline (0.09 ml, 1.0 mmol), and pyridine (0.16 ml, 1.0 mmol) in NMP (1 ml) at room temperature. The solution was stirred at 80°C for 2 h, and poured into water (100 ml). The precipitate was collected and dried. The yield was 0.185 g (94%). mp 162°C (lit.[5] 162°C)

Polycondensation

Typical examples of the polycondensation are as follows.

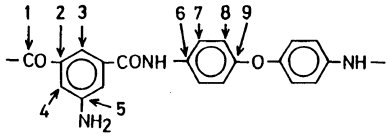
Polyamide (**5a**) *from Isophthalic Acid* (**4a**) *and ODA.* To a mixture of isophthalic acid **4a** (0.166 g, 1.0 mmol), ODA (0.200 g, 1.0 mmol), and pyridine (0.32 ml, 2.0 mmol) was added the activating agent solution (1.26 ml, 2.0 mmol). The solution was stirred at 100°C for 2 h. The resulting viscous solution was diluted with NMP (10 ml) and poured into methanol (500 ml). The polymer that precipitated was filtered and refluxed in methanol for 2 h. The fibrous polymer was collected and dried *in vacuo* at 100°C. It weighed 0.320 g (97%). The inherent viscosity of the polymer in concentrated sulfuric acid was 1.1 dl g^{-1}, measured at a concentration of 0.5 g dl^{-1} at 30°C. IR (film) ν 1660 (C=O), 3240 cm^{-1} (N–H).

Polyamide (**6**) *from 5-Hydroxyisophthalic Acid* (**4c**) *and ODA.* A mixture of the activating agent solution (1.26 ml, 2.0 mmol), **5**-hydroxyisophthalic acid **4c** (0.182 g, 1.0 mmol), ODA (0.200 g, 1.0 mmol) and pyridine (0.32 ml, 2.0 mmol) was stirred at 80°C for 2 h. The polymer solution was worked up as described above. The yield was essentially quantitative. The inherent viscosity of the polymer in concentrated sulfuric acid was 0.82 dl g^{-1}, measured at a concentration of 0.5 g dl^{-1} at 30°C. IR (film) ν 1660 (C=O), 3300 cm^{-1} (N–H, O–H).



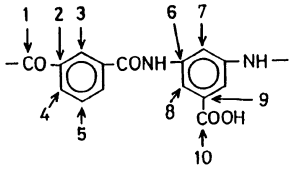
^{13}C NMR ((CD$_3$)$_2$SO): observed value (calculated value) (C-1) 164.6, (C-2) 136.3 (136.4), (C-3) 121.5 (119.6), (C-4) 117.9 (117.7), (C-5) 152.7 (154.8), (C-6) 134.3 (134.2), (C-7) 121.8 (122.2), (C-8) 118.4 (119.0), (C-9) 152.6 (153.5).

Polyamide (**7**) *from 5-Aminoisophthalic Acid* (**4d**) *and ODA.* This polymer was prepared as described above, using **4d** and ODA for 24 h. The inherent viscosity was 0.59 dl g^{-1} in NMP (c=0.5 g dl^{-1} at 30°C). IR (KBr) ν 3300 (N–H), 1660 cm^{-1} (C=O); ^{13}C NMR ((CD$_3$)$_2$SO):



(C-1) 165.4, (C-2) 135.8 (135.9), (C-3) 116.6 (117.1), (C-4) 120.1 (117.1), (C-5) 148.6 (145.9), (C-6) 134.5 (134.2), (C-7) 121.7 (122.2), (C-8) 118.3 (119.0), (C-9) 152.5 (153.5).

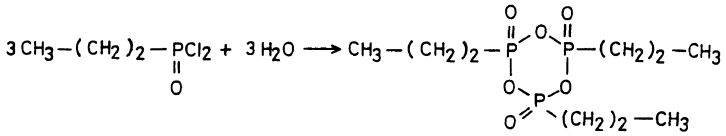
Polyamide (**8**) *from Isophthalic Acid* **4a** *and 3,5-Diaminobenzoic Acid* (*DAB*). This polymer was prepared as descrbed above, using **4a** and DAB at 80°C for 12 h. The inherent viscosity was 0.36 dl g^{-1} in NMP (c= 0.5 g dl^{-1} at 30°C). IR (KBr) ν 3300 (N–H, O–H), 1710, 1660 cm^{-1} (C=O); ^{13}C NMR ((CD$_3$)$_2$SO)



(C-1) 165.2, (C-2) 134.8 (135), (C-3) 128.4 (126.9), (C-4) 131.4 (130.4), (C-5) 128.8 (127.9) (C-6) 139.3 (139.2), (C-7) 116.6 (117.8), (C-8) 116.7 (117.9), (C-9) 131.4 (130.4), (C-10) 166.9.

RESULTS AND DISCUSSION

Propylphosphonic anhydride was readily prepared by the reaction of propylphosphonic dichloride with water in a more ratio of 1 : 1, and a 50 wt% solution of the anhydride in NMP (**1**) was used as the activating agent (eq 1).



(1)

1

Model Reaction

Various peptides have been prepared from *N*-protected amino acids and amino acid ester hydrochlorides by treatment with activating agent **1** at room temperature for 24 h. However, the synthesis of amides by the reaction of carboxylic acids with aromatic amines has not yet been investigated. Therefore, we first studied the synthesis of benzanilide (**2a**) from benzoic acid and aniline in the presence of activating agent **1** by a direct procedure. This procedure consisted of adding **1** to a solution of carboxylic acids and amines in NMP that containes a tertiary organic base to form carboxylate anion.

The following factors influencing the preparation of **2a** were studied: temperature and time of reaction, and the base strength of tertiary amines. The results shown in Table I, reveal that the reaction proceeded slowly at room temperature, but was complete in 2 h at 80°C. A 2 molar equivalent of pyridine based on benzoic acid was required to accept a 2 molar equivalent of phosphonic acid residue formed in the reaction, as shown in the reaction pathway later. It was thought that the condensation in the presence of activating agent **1** proceeds rapidly at room temperature, as would be expected from the anhydride bond of **1**. However, the reaction was slow at room temperature and required 24 h for completion. The rate of condensation was much slower than that of the reaction in the presence of various phosphonates.[1-3] One of the reason for this low rate may be the steric effect of propyl group. Many more phosphonic anhydrides in this series should be accumulated to elucidate this phenomenon.

Table I. Preparation of benzanilide **2a** using activating agent **1**[a]

Base	Temp	Time	Yield
mmol	°C	h	%
None	r.t.	1	25
TEA[b] 1	r.t.	1	54
TEA 2	r.t.	1	64
TEA 2	r.t.	2	68
TEA 2	r.t.	24	73
TEA 2	80	2	80
Py[c] 2	r.t.	2	75
Py 2	r.t.	24	90
Py 2	80	2	94

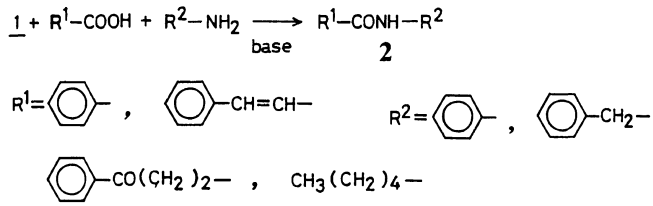
[a] The reaction was carried out with 1 mmol of each reactant using 1 mmol of **1** in 1 ml of NMP.
[b] TEA, triethylamine.
[c] Py, pyridine.

Table II. Preparation of amides **2** using activating agent **1**[a]

Carboxylic acid	Amine	Base	Product	Yield/%
Benzoic acid	Aniline	Py	Benzanilide (**2a**)	94
Benzoic acid	Benzylamine	TEA	*N*-Benzylbenzamide (**2c**)	85
Cinnamic acid	Aniline	Py	*N*-Phenylcinnamamide (**2d**)	92
Cinnamic acid	Benzylamine	TEA	*N*-Benzylcinnamamide (**2e**)	93
Benzoylpropionic acid	Aniline	Py	*N*-Phenylbenzoylpropionamide (**2f**)	93
Benzoylpropionic acid	Benzylamine	TEA	*N*-Benzylbenzoylpropionamide (**2g**)	93
Capronic acid	Aniline	Py	*N*-Phenylcapronamide (**2h**)	94
Capronic acid	Benzylamine	TEA	*N*-Benzylcapronamide (**2i**)	70

[a] The reaction was carried out with 1 mmol of each reactant using 1 mmol of **1** in the presence of 2 mmol of base in 1 ml of NMP at 80°C for 2 h.

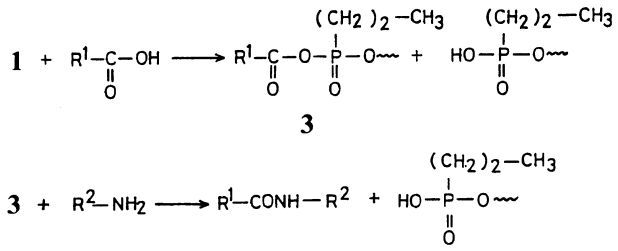
On the basis of these results, various amides (**2**) were prepared (eq 2).



(2)

The results of several representative amide syntheses are summarized in Table II. Triethylamine (TEA) as the base was used for the preparation of amides from benzylamine. The condensation proceeded smoothly and gave the corresponding amides in good yields.

The most probable reaction pathway is as follows (eq 3):



(3)

Activating agent **1** first reacts with carboxylic acids to form mixed carboxylic–phosphonic anhydrides **3**, which react *in situ* with amines to give amides. This reaction pathway is similar to that using a phosphorus-based activating agent.[1-3]

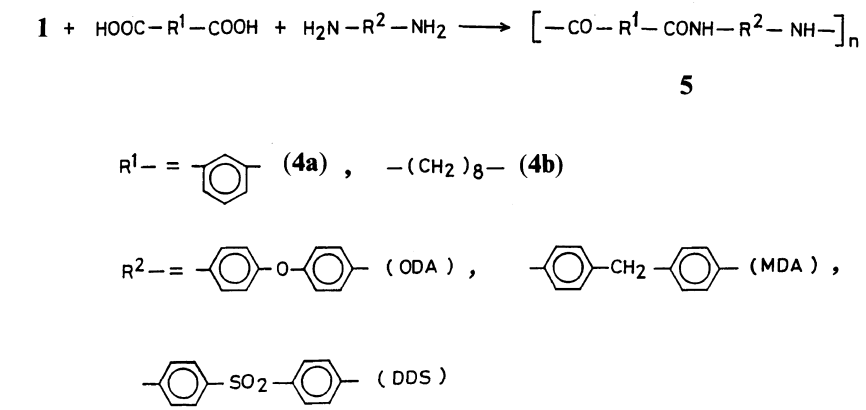
Polycondensation

On the basis of these results, the direct polycondensation of dicarboxylic acids with aromatic diamines was carried out with activating agent **1** in the presence of pyridine (eq 4).

Table III. Polycondensation of dicarboxylic acids with diamines using activating agent **1**[a]

Dicarboxylic acid **4**	Diamine	Temp / °C	Time / h	Polymer: Type	Polymer: Yield / %	Polymer: η_{inh}[b] / dl g^{-1}
4a	ODA	80	4	**5a**	94	0.95
4a	ODA	100	2	**5a**	99	1.1
4a	MDA	80	6	**5b**	99	0.88
4a	DDS	80	24	**5c**	99	0.45
4a	DDS	100	10	**5c**	99	0.42
4a	DDS	100	24	**5c**	99	0.47
4b	ODA	80	1	**5d**	99	0.45
4b[c]	ODA	80	10	**5d**	99	0.41
4b	ODA	100	1	**5d**	99	0.63
4b[d]	ODA	100	1	**5d**	99	1.6

[a] Polycondensation was carried out with 1 mmol of each monomer using 2 mmol of **1** in the presence of 4 mmol of Py.
[b] Measured at a concentration of 0.5 g dl^{-1} in concentrated sulfuric acid at 30°C.
[c] HMPA (1 ml) was added.
[d] NMP (4.5 ml) and Py (12 mmol) were added.

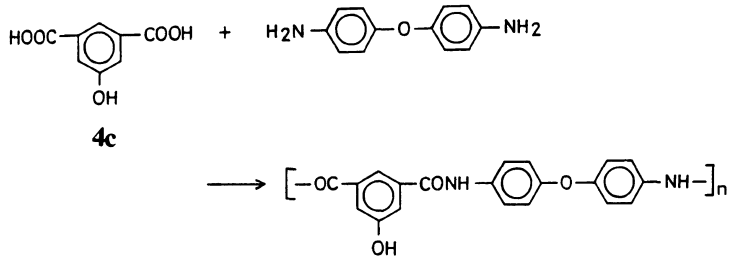


In the case of the polycondensation of sebacic acid (**4b**) with 4,4′-oxy-dianiline (ODA), the precipitation of the polymer occurred in 5 min. To improve the solubility of the polymer, the polycondensation was conducted in a more dilute system. The polymer again separated out within 20 min. However, a polymer with an inherent viscosity up to 1.6 dl g^{-1} was obtained.

On the other hand, the polycondensation of isophthalic acid (**4a**) with ODA or 4,4′-methylenedianiline (MDA) proceeded in homogeneous solution in NMP and resulted in a polymer having an inherent viscosity up to 1.1 dl g^{-1}. A moderate molecular weight polymer (**5d**) with an inherent viscosity of 0.5 dl g^{-1} was obtained from 4,4′-diaminodiphenyl sulfone (DDS) with low basicity.

In order to further demonstrate the preparative utility of our method, it was applied to chemoselective polyamidation. It is generally accepted that the lower the selectivity, the greater is the reactivity. In our method, the reactive intermediate was mixed anhydride **3**, the reactivity of which toward nucleophiles was lower than that of acid chlorides. Thus,

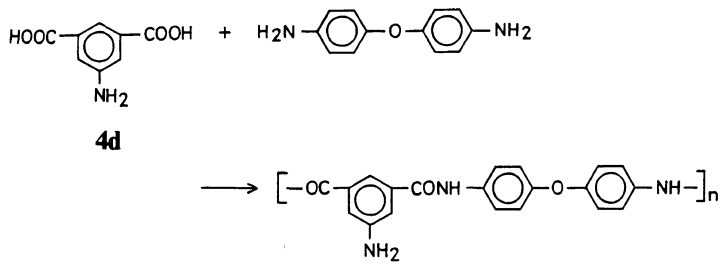
chemoselective polyamidation was expected. First, the synthesis of polyamide **6** from 5-hydroxyisophthalic acid (**4c**) and ODA was tried. The direct polycondensation of **4c** with ODA was carried out with activating agent **1** at 80°C for 2 h (eq 5):



4c **6** (5)

Polyamide **6** was easily produced in a quantitative yield with an inherent viscosity of $0.82\,dl\,g^{-1}$.

Secondly, the direct polycondensation of 5-aminoisophthalic acid (**4d**) with ODA was conducted (eq 6).



4d **7** (6)

Table IV. Polycondensation of 5-aminoisophthalic acid **4d** with ODA using activating agent **1**[a]

NMP	Temp	Time	Polymer	
			Yield	η_{inh}[b]
ml	°C	h	%	$dl\,g^{-1}$
0.5	r.t.	24	87	0.59
1	r.t.	24	63	0.19
1	60	5	80	0.38
3	80	2	Gel	

[a] Polycondensation was carried out with 1 mmol of each monomer using 2 mmol of **1** in the presence of 4 mmol of pyridine.
[b] Measured at a concentration of $0.5\,g\,dl^{-1}$ in NMP at 30°C.

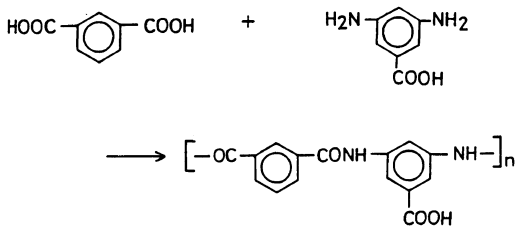
Table V. Polycondensation of isophthalic acid **4a** with 3,5-diaminobenzoic acid (DBA) using activating agent **1**[a]

NMP	Temp	Time	Polymer	
			Yield	η_{inh}[b]
ml	°C	h	%	$dl\,g^{-1}$
0.5	r.t.	24	Gel	
1	r.t.	24	81	0.21
2	80	12	Gel	
4	80	12	80	0.36

[a] Polycondensation was carried out with 1 mmol of each monomer using 2 mmol of **1** in the presence of 4 mmol of pyridine.
[b] Measured at a concentration of $0.5\,g\,dl^{-1}$ in NMP at 30°C.

A gelation was observed at 80°C because of the small difference of the basicity in amino groups between **4d** and ODA. A moderate molecular weight polyamide (**7**) with an inherent viscosity of 0.59 dl g^{-1} was obtained at room temperature (Table IV).

Finally, polyamide synthesis from 3,5-diaminobenzoic acid (DAB) and isophthalic acid **4c** was performed using activating agent **1** (eq 8).



8

In this case, a gel also formed at a high reaction temperature or in a high monomer concentration. Under optimum conditions, polyamide **8** with an inherent viscosity of 0.36 dl g^{-1} was obtained (Table V).

The polymers obtained were identified as polyamides by comparing their IR and ^{13}C NMR spectra with those of authentic polyamides.

In summary, it was found that activating agent **1** was very useful for the preparation of amides and high molecular weight polyamides under mild conditions. Furthermore, chemoselective polyamidation was achieved from multifunctional dicarboxylic acid and diamines without special protection of the acylation-sensitive groups.

REFERENCES

1. M. Ueda and H. Oikawa, *J. Polym. Sci., Polym. Chem. Ed.*, **23**, 1607 (1985).
2. M. Ueda and A. Mochizuki, *Macromolecules*, **18**, 2353 (1985).
3. M. Ueda, A. Kameyama, and C. Ikeda, *Polym. J.*, **19**, 673 (1987).
4. H. Wissmann and H. J. Kleiner, *Angew. Chem. Int. Ed., Engl.*, **19** (1980).
5. H. Franzen, *Ber. Dtsch. Chem. Ges.*, **42**, 2466 (1909).