Synthesis of Polyamides by Direct Polycondensation with 5-Methyl-2-chloro-3-phenyl-2,3-dihydro-1,3,4,2-oxadiazaphosphole as a New Condensing Agent

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ABSTRACT: A new condensing agent, 5-methyl-2-chloro-3-phenyl-2,3-dihydro-1,3,4,2-oxa-diazaphosphole (2) prepared from β-N-acetyl-phenylhydrazine (1) and phosphorus trichloride was used for the synthesis of amides and polyamides. The condensing agent was useful for the preparation of amides from carboxylic acids and amines. The direct polycondensation of dicarboxylic acids with aromatic diamines using the condensing agent in the presence of pyridine proceeded at room temperature to produce polyamides with inherent viscosities up to $1.9 \, dl \, g^{-1}$.
    KEY WORDS   Condensing Agent / 5-Methyl-2-chloro-3-phenyl-2,3-dihydro-1,3,4,2-oxadiazaphosphole / Direct Polycondensation / Polyamides /

The direct polycondensation using condensing agents had been initiated to realize for the *in situ* activation of dicarboxylic acids, followed by condensation under mild conditions. Now this method has been developed into an useful procedure for the synthesis of polyamides, polyesters, and other condensation polymers.[1]

A number of condensing agents are available, but most of them have disadvantage of requiring either multi-step syntheses or not easily available starting materials. Therefore, alternative new convenient condensing agents are always of interest. In the course of the study on the synthesis of new condensing agent, we found that halo dihydroxadiazaphospholes were very suitable condensing agent for amide syntheses. These condensing agents have the following advantages: simple preparation, long shelf-stability at room temperature, and very good solubility in all solvents. These characteristics prompted us to employ them for the preparation of polyamides as condensing agents.

In this paper, we report that amides and polyamides can be easily obtained from car-boxylic acids and amines by a direct procedure using the new condensing agent 5-methyl-2-chloro-3-phenyl-2,3-dihydro-1,3,4,2-oxadiazaphosphole.

EXPERIMENTAL

Materials

The condensing agent 5-methyl-2-chloro-3-phenyl-2,3-dihydro-1,3,4,2-oxadiazaphosphole (2) was prepared from β-N-acetylphenylhydrazine (1) and phosphorus trichloride in benzene by modifying the method reported by Italinskaya.[2]

To a suspension of β-N-acetylphenylhydrazine (1) (20.0 g, 0.133 mol) and triethylamine (TEA) (26.9 g, 0.267 mol) in dry benzene (200 ml) was added dropwise a solution of phosphorus trichloride (18.3 g, 0.133 mol) in dry benzene (50 ml) with stirring. During the addition period the temperature was maintained at 8—10°C by appropriate cooling with an ice bath. After addition was completed, the mixture was stirred at this temperature for 1 h, and then heated at 60°C for 1 h. The mixture

was cooled to room temperature. TEA·hydrochloride was removed by filtration and solvent was removed *in vacuo*. The residual oil was distilled *in vacuo* to give a colorless liquid. The yield was 25.7 g (90%), bp 110°C [1.5 mmHg (0.2 kPa)] (lit. 97°C [0.2 mmHg (27 Pa)][2]). IR (NaCl) v 2910 (C–H), and 1625 cm^{-1} (C=N), ^{1}H NMR (CDCl$_3$) δ 2.34 (3H, s, CH$_3$) and 7.2 ppm (5H, m, phenyl), MS m/z 214.5 (M$^+$).

Dicarboxylic Acids. Succinic acid (**6a**), glutaric acid (**6b**), adipic acid (**6c**), sebacic acid (**6d**), isophthalic acid (**6e**), and terephthalic acid (**6f**) were purified by recrystallizaition.

Diamines. 4,4'-Oxydianiline (**7a**), 4,4'-methylenedianiline (**7b**), and *p*-phenylenediamine (**7c**) were purified by recrystallization.

Solvents and Reagents. Pyridine (Py), *N*-methyl-2-pyrrolidone (NMP), *N,N*-dimethylformamide (DMF), tetrahydrofuran (THF), and dimethylsulfoxide (DMSO) were purified by vacuum distillation and stored over 4 Å molecular sieves. The other reagents and solvents were obtained commercially and used as received.

Model Reaction

Typical example of the model reaction is as follows.

Benzanilide (**5a**). Condensing agent **2** was added to a stirred solution of benzoic acid (0.20 g, 1.6 mmol) in Py (3.3 ml) at 0°C. After 5 min, aniline (0.15 g, 1.6 mmol) was added. Stirring was continued for 3 h at room temperature. The mixture was poured into 1% hydrochloric acid. The precipitate was filtered and washed with water and dried. The yield was 0.31 (97%), mp 164—165°C (lit. 163°C[3]).
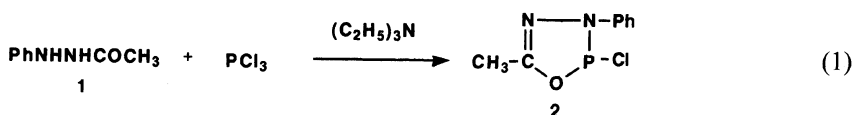
Polycondensation

Typical examples of the polycondensation are as follows.

Polyamide (**8ca**) *from Adipic Acid* (**6c**) and 4,4'-*Oxydianiline* (**7a**). To a solution of **6c** (0.292 g, 2.0 mmol) and Py (2.5 ml) in NMP (2.5 ml) was added condensing agent **2** (0.858 g, 4.0 mmol) at 0°C. The mixture was stirred for 5 min, then **7a** (0.400 g, 2.0 mmol) was added at room temperature. Stirring was continued for 24 h. The resulting viscous solution was diluted 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 0.620 g (99%). The inherent viscosity of the polymer in concentrated sulfuric acid was 1.49 dl g^{-1}, measured at a concentration of 0.5 g dl^{-1} at 30°C. IR (film) v 3300 (N–H), 1650 (C=O) cm^{-1}.

Polyamide (**8ea**) *from Isophthalic Acid* (**6e**) and **7a**. The condensing agent **2** was added to a solution of **6e** (0.249 g, 1.5 mmol), **7a** (0.300 g, 1.5 mmol) and Py (4.0 ml) in NMP (1.0 ml) at 0°C. The mixture was stirred at this temperature for 5 min, then at 60°C for 24 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 1.2 dl^{-1} ($c = $ 0.5 g dl^{-1} at 30°C). IR (film) v 3300 (N–H), 1650 (C=O) cm^{-1}.

RESULTS AND DISCUSSION

5-Methyl-2-chloro-3-phenyl-2,3-dihydro-1,3,4,2-oxadiazaphosphole (**2**) was readily prepared by the reaction of β-*N*-acetylphenylhydrazine (**1**) with phosphorus trichloride in benzene at 60°C (eq 1).

$$\text{PhNHNHCOCH}_3 \ + \ \text{PCl}_3 \ \xrightarrow{\ (C_2H_5)_3N\ } \ \begin{array}{c} \text{CH}_3-\text{C} \end{array} \hspace{2em} (1)$$

1   **2**

Model Reaction

In order to clarify the reactivity of condensing agent **2**, we first studied the synthesis of amides (**5**) by the one-pot procedure. This procedure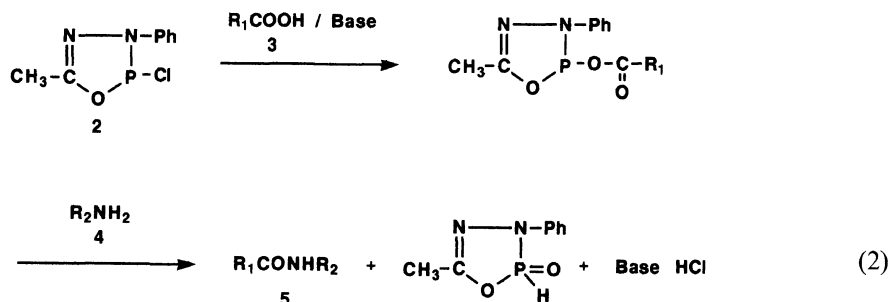 involves two separate steps: (1) activation of the carboxylic acid **3**, *i.e.*, generation of the active intermediate from the carboxylic acid and **2**, and (2) condensation of this intermediate with the amine **4** (eq 2).

Table I. The preparation of benzanilide in various tertiary amines using **2**[a]

| Tertiary amine	pK_a	Benzanilide Yield/%[b]
Pyridine	5.25	97
β-Picoline	5.52	90
α-Picoline	5.97	63
γ-Picoline	6.03	65
2,6-Lutidine	6.99	20
N-Ethylmorpholine	7.67	5
Triethylamine	10.75	trace

[a] Reaction was carried out with 2.5 mmol of benzoic acid and aniline at room temperature for 4 h.
[b] Based on benzoic acid used.

Table II. Synthesis of various amides using **2**[a]

Carboxylic acid R_1	Amine R_2	Yield[b] %
CH_3	C_6H_5	90
C_6H_5	C_6H_5	97
C_6H_5	$C_6H_5CH_2$	86
$CH_3{>}CH$ CH_3	C_6H_5	90
$CH_3{>}CH$ CH_3	$C_6H_5CH_2$	90
$CH_3{>}CH$ CH_3	c-C_6H_{11}	84
CH_3	c-C_6H_{11}	98
$CH_3(CH_2)_7$	C_6H_5	99
$CH_3(CH_2)_7$	$C_6H_5CH_2$	82
	C_6H_5	99

[a] Reaction was carried out with 2.5 mmol of each reactants in pyridine (5 ml) at room temperature for 4 h.
[b] Yield of crude carboxamides. All these crude crystals melted within one degree of melting points reported in the literature.

Tertiary bases play important role on the activation of carboxylic acids using organophosphorus reagents.[4] Therefore, in order to determine the influence of base strength in the condensation reaction using **2**, tertiary amines with a wide range of pK_a values were tested. The results are shown in Table I. When triethylamine was used as a base-solvent, the reaction mixture changed in color to a reddish brown which indicated some side reactions, and benzanilide was little obtained. The reaction in the presence of N-ethylmorpholine was also colored in orange and only a small amount of benzanilide was obtained. On the other hand, among the tertiary amines examined, pyridine (Py) and β-picoline with pK_a value in the range of 5.2—5.6 were specially effective for the condensation reaction. Thus, the reaction was performed by stirring **3** and **2** in Py at 0°C for 5 min, and then **4** was added. The results are summarized in Table II. The

reactions proceeded smoothly to give the corresponding amides **5** in excellent yields.

It is interesting that amides from the aliphatic amines such as cyclohexylamine and benzylamine were obtained in good yields although they could not generally get in stisfactory yields by use of phosphite esters as condensing agents.[5] This may be due to the presence of chlorine in phosphite ester **2** used as condensing agent, since certain halogen containing organophosphorus compounds[6] were efficient for the synthesis of amides from aliphatic amines.

Then, the reaction of isophthalic acid **6e** with aniline in the presence of **2** was carried out to determine if the method gave the desired diamides in high enough yield to give promise as a polymer-forming reaction. The desired diamides, isophthalanilide was obtained in quantitative yield.

The most probable reaction pathway in the condensation reaction using **2** is as follows (eq 3).

$$
\begin{array}{c}
\text{(structure 2)} \xrightarrow[\text{Py}]{\underset{\text{3}}{R_1COOH}} \text{(intermediate)} \xrightarrow[\text{4}]{R_2NH_2} \\[2em]
R_1CONHR_2 \;+\; \text{(structure)} \;+\; PyH^+Cl^-
\end{array}
\qquad (3)
$$

As described above, Py was most effective for this condensation reaction. It seems that Py paticipates in the reaction in addition to its roles as a solvent and acid acceptor. Yamazaki et al.[7,8] have reported that the high reactivity of diphenyl phosphite–pyridine system for the preparation of the peptides and the polyamides could be explained by formation of acyloxy N-phosphonium salt of Py as an active intermediate by releasing phenolate anion from the diphenylphosphite (eq 4).

$$
(PhO)_2\text{-P-OH} \xrightarrow[\text{Py}]{RCOOH} \;\; \overset{Py^+ \; O^-Ph}{\underset{HO \;\; OPh}{H-P-O-CO-R}}
\qquad (4)
$$

Therefore, we assume that condensing agent **2** may also react with carboxylic acids in Py to form the acyloxy N-phosphonium salt of Py by releasing chloride anion from **2** as shown in eq 3. This activated intermediate is less stable and its enhanced reactivity causes it to react rapidly with amines to give amides in excellent yield. Further, it seems that nitrogen and oxygen atom of condensing agent **2** favour the condensation reaction by contributing as intramolecular general base catalysis (anchimericassistance).[9]

Polycondensation

On the basis of these studies, a direct polycondensation of dicarboxylic acids with diamines was carried out using **2** in Py/polar aprotic solvents (eq 5).

$$
\underset{\text{6}}{HOOC\text{-}R_3\text{-}COOH} \;+\; \underset{\text{7}}{H_2N\text{-}R_4\text{-}NH_2} \xrightarrow[\text{Py / NMP}]{\text{2}} \underset{\text{8}}{\left(\!OC\text{-}R_3\text{-}CONH\text{-}R_4\text{-}NH\!\right)_n}
\qquad (5)
$$

R₃ : —(CH₂)₂— , —(CH₂)₃— , —(CH₂)₄— , —(CH₂)₈— , [structure 6e] , [structure 6f]

6a   6b   6c   6d   6e   6f

R₄ : [structure 7a] , [structure 7b] , [structure 7c]

7a   7b   7c

To determine the optimum conditions for the polycondensation, the polycondensation of adipic acid (**6c**) with 4,4'-oxydianiline (**7a**) was studied. The polycondensation was performed with 2 mmol of each monomer at room temperature for 24 h. Table III shows the solvent effect on the polycondensation. Polymer precipitations occurred at early stage of polycondensation in DMF and THF. On the other hand , the polycondensation proceeded in homogeneous solution in NMP and gave a quantitative yield of polyamide (**8ca**) having an inherent viscosity of $1.49 \, dl \, g^{-1}$.

Table IV shows the effect of concentration of the reactants on the degree of polymerzation. The preferred concentration range for this type of solution polycondensation was 0.3—0.7 $mol \, dm^{-3}$ of solvent. Higher concentrations made the solution difficult to stir and yielded polyamides with lower molecular weights.

The effect of amount of Py on the polycondensation in a mixed solvent of NMP and Py is shown Figure 1. The inherent viscosity of the polymer reached its highest value in a mixed solvent of NMP and Py of 50% content in volume (corresponding to 2.5 ml of Py).Further addition of Py caused inferior results because of the precipitation of the resulting polymer.

Figure 2 shows the course of the polymerization in terms of inherent viscosity of the resulting polymer. Polymerization was essentially completed in 5 h, and then proceeded very slowly until 24 h.

On the basis of these studies, the direct polycondensation of aliphatic dicarboxylic acids with aromatic diamines was carried out

Table III. Effect of various solvent systems on polycondensation of **6c** and **7a** using **2**

Solvent system	(ml/ml)	Polymer	
		Yield/%	$\eta_{inh}/dl \, g^{-1 \, b}$
NMP/Py	2.50/2.50	99	1.49
NMP/Py	4.03/0.97	99	0.75
NMP/β-Picoline	4.03/0.87	99	0.94
DMF/Py	2.50/2.50	97	0.58
THF/Py	2.50/2.50	98	0.23
DMSO/Py	2.50/2.50	57	0.04

[a] The polycondensation was carried out with 2 mmol of each monomer using 4 mmol of **2** at room temperature for 24 h.
[b] Measured at a concentration of $0.5 \, g \, dl^{-1}$ in concentrated sulfuric acid at 30°C.

Table IV. Effect of monomer concentration on the polycondensation of **6c** and **7a** using **2**[a]

Concentration of **6c** $(mol \, dm)^{-3}$	Polymer	
	Yield/%	$\eta_{inh}/dl \, g^{-1 \, b}$
0.2	98	0.43
0.3	99	1.22
0.4	99	1.49
0.6	99	1.39
0.7	99	1.25
0.8	92	0.55
1.0	80	0.35

[a] The polycondensation was carried out with the amount of **2** equivalent to **6c** in 2.5 ml of NMP and 2.5 ml of Py at room temperature for 24 h.
[b] Measured at a concentration of $0.5 \, g \, dl^{-1}$ in concentrated sulfuric acid at 30°C.

using condensing agent **2** in Py/NMP. Table V indicates that polyamides were easily produced in quantitative yields with inherent viscosities
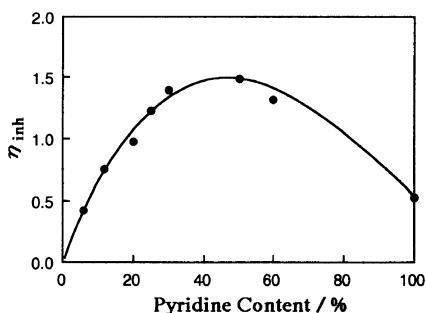
Figure 1. Effect of the amount of pyridine on the poly-condensation of **6c** and **7a** using **2**. Reactant concn, $[6c] = [7a] = 0.4 \, mol \, dm^{-3}$, $[2] = 0.8 \, mol \, dm^{-3}$; solvent, $(NMP + Py) = 5 \, ml$; temp, room temp; time, 24 h.
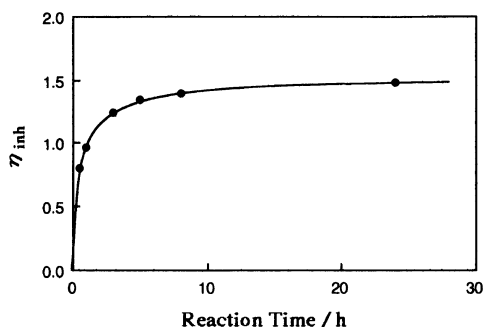

Figure 2. Rate of the polycondensation of **6c** and **7a** using **2**. Reactant concn, $[6c] = [7a] = 0.4 \, mol \, dm^{-3}$, $[2] = 0.8 \, mol \, dm^{-3}$; solvent, $Py/NMP = 2.5/2.5$ (ml/ml); temp, room temp.

Table V. Synthesis of polyamides (**8**) by the direct polycondensation of aliphatic dicarboxylic acids (**6**) with aromatic diamines (**7**) using **2**[a]

Dicarboxylic acid	Diamine	Polymer	
		Yield/%	$\eta_{inh}/dl \, g^{-1}$ [b]
6a	**7a**	98	0.53
6b	**7a**	99	1.90
6b	**7b**	99	1.78
6c	**7a**	99	1.49
6c	**7b**	99	0.97
6c	**7c**	97	0.96
6d	**7a**	99	1.06
6d	**7b**	98	0.92

[a] The polycondensation was carried out with 2 mmol of each monomer using 4 mmol of **2** in 2.5 ml of NMP and 2.5 ml of Py at room temperature for 24 h.
[b] Measured at a concentration of $0.5 \, g \, dl^{-1}$ in concentrated sulfuric acid at 30°C.

up to $1.90 \, dl \, g^{-1}$.

Next, the synthesis of polyamides from aromatic dicarboxylic acids was performed under conditions similar to those described for the preparation of polyamide **8ca**. The direct polycondensation of **6e** with **7a** proceeded smoothly, but the inherent viscosity of polyamide (**8ea**) obtained remained $0.37 \, dl \, g^{-1}$. In the typical direct polycondensation method, Yamazaki–Higashi method[10] based upon a pyridine–triphenylphosphite system, the amount in the mixed solvent and the reaction temperature are the most important factors to obtain high molecular-weight polyamides.[8,11]

Therefore, the effect of amount of Py on the polycondensation of **6e** with **7a** was then performed again to improve the molecular

weight of polyamides. The mixed solvent system of Py (4 ml) and NMP (1 ml) was found to be effective for the polycondensation on a 2.0 mmol scale. In this system, polyamide **8ea** with the inherent viscosity of $0.73 \, dl \, g^{-1}$ was obtained at room temperature. Furthermore, the reaction temperature on the inherent viscosity of the resulting polymer was examined. The reaction temperature was also effective, and polymer **8ea** with an inherent viscosity as high as $1.20 \, dl \, g^{-1}$ was obtained at 60°C.

On the basis of these results, the direct polycondensation of dicarboxylic acids with aromatic diamines was carried out with condensing agent **2** in the mixed Py/NMP solvent. Table VI indicates that polyamides from **6e** were easily produced in quantitative yields with inherent viscosities up to $1.2 \, dl \, g^{-1}$.

The direct polycondensation method falls into two main groups, one-pot method and one-step method.[1b] The latter method consists of adding the condensing agent to a mixed solution of dicarboxylic acid and diamine in the presence of a base (eq 6).

Therefore, the one-step method was tested to determine whether this method was suitable

Table VI. Synthesis of polyamides (**8**) by the direct polycondensation of aromatic
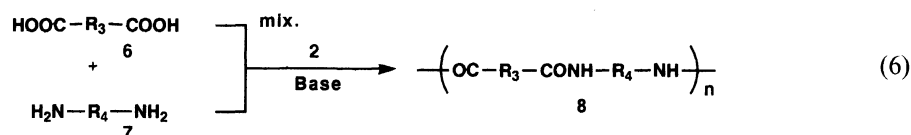dicarboxylic acids (**6**) with aromatic diamines (**7**) using **2**[a]

Dicarboxylic acid	Diamine	NMP/Py	Temperature	Polymer	
		ml/ml	°C	Yield/%	$\eta_{inh}/dl\,g^{-1}$[b]
6e	7a	2.5/2.5	rt[c]	95	0.37
6e	7a	1.0/4.0	rt	99	0.73
6e	7a	1.0/4.0	60	99	1.20
6e	7b	1.0/4.0	60	99	1.01
6e	7c	1.0/4.0	60	99	0.96
6f	7a	1.0/4.0	60	98	0.56[d]
6f	7b	1.0/4.0	60	97	0.42[d]

[a] The polycondensation was carried out with 2 mmol of each monomer using 4 mmol of **2** for 24 h.
[b] Measured at a concentration of $0.5\,g\,dl^{-1}$ in concentrated sulfuric acid at 30°C.
[c] Room temperature.
[d] 2 wt% LiCl was added.

$$HOOC-R_3-COOH \quad \underset{6}{} \quad + \quad \underset{7}{H_2N-R_4-NH_2} \quad \xrightarrow[\text{Base}]{\text{mix.} \atop 2} \quad \underset{8}{\left(\!OC-R_3-CONH-R_4-NH\!\right)_n} \tag{6}$$

or not for the direct polycondensation using condensing agent **2**. The direct polycondensation of **6c** with **7a** was carried out in the presence of **2** in the mixed Py/NMP solvent system at room temperature for 24 h. Polyamide **8ca** were also produced in quantitative yield with an inherent viscosity of $1.4\,dl\,g^{-1}$.

The polymers obtained were identified as polyamides (**8**) by comparing their IR spectra with those of authentic polyamides.

In summary, our studies indicate that the new condensing agent **2** is useful for the preparation of amides and high molecular-weight polyamides under mild condition.

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