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Diphenyl (2,3-Dihydro-2-thioxo-3-benzoxazolyl)phosphonate: A New, Reactive Activating Agent for the Synthesis of Amides and Polyamides

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ABSTRACT: A new activating agent for amide condensations, diphenyl (2,3-dihydro-2-thioxo-3-benzoxazolyl)phosphonate (**1**), was readily prepared at room temperature by the reaction of 2-benzoxazolethiol (**3**) with diphenyl phosphorochloridate (**2**) in the presence of triethylamine (TEA) in benzene. The reaction of carboxylic acids with amines in the presence of **1** was investigated by two procedures, a two-step and a one-step procedure. Both procedures gave corresponding amides in high yields under mild conditions. The direct polycondensation of dicarboxylic acids with diamines by using the activating agent **1** in the presence of TEA proceeded smoothly at room temperature to produce polyamides with inherent viscosities up to 1.2 dL g^{-1}. Furthermore, the activating agent **1** was used successfully 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.

Introduction

Condensation ranks among the most important and fundamental reactions in organic synthesis, and many activating agents for promoting condensations by a two-step or a one-step procedure have been reported. Most such activating agents first react with carboxylic acids to give intermediates, such as acid anhydrides, active esters, or amides, which undergo subsequent nucleophilic attack by amino or hydroxyl groups. Therefore, a primary factor in determining whether or not the activating agents are effective is their ability to activate carboxylic acids.

It is well recognized that increased reactivity of carboxylic acid derivatives toward nucleophiles may be roughly correlated with greater stability of the leaving group anions, that is, the pK_a of the leaving groups. From this point of view, we previously exploited a series of good leaving groups in the synthesis of active esters and amides, demonstrating that the active ester and amide methods are useful in the preparation of high molecular weight polyamides under mild conditions.[1]

Based on the success of those studies, we continued to investigate new activating agents for the synthesis of amides, esters, and polyamides.[2] In the preceding papers, we showed diphenyl 2,3-dihydro-1,3-benzisoxazol-3-yl phosphonate,[3] phenyl bis(2,3-dihydro-2-oxobenzothiazol-3-yl)phosphinate,[4] and diphenyl (2,3-dihydro-2-oxo-3-benzothiazolyl)phosphonate[5] were new activating agents for the synthesis of amides and polyamides.

We now report that amides and polyamides can be easily obtained from carboxylic acids and amines by a two-step and a one-step procedure using the new activating agent diphenyl (2,3-dihydro-2-thioxo-3-benzoxazolyl)phosphonate.

Experimental Section

Materials. Solvents, Amines, and Carboxylic Acids. *N*-Methyl-2-pyrrolidone (NMP) (supplied by Idemitsu Kosan Co., Ltd.) and hexamethylphosphoramide (HMPA) were purified by vacuum distillation and stored over 4-Å molecular sieves. 4,4′-oxydianiline (**12a**) (supplied by Mitsui Toatsu Chemical Industries Ltd.) and 4,4′-methylenedianiline (**12b**) (supplied by Mitsubishi Chemical Industries Ltd.) were purified by recrystallization from tetrahydrofuran and benzene, respectively. Isophthalic acid (**9a**), adipic acid (**9b**), sebacic acid (**9c**), 5-hydroxyisophthalic acid (**14**), 5-aminoisophthalic acid (**16**), and 3,5-diaminobenzoic acid (**18**) were purified by recrystallization. Other reagents and solvents were obtained commercially and used as received.

Diphenyl (2,3-Dihydro-2-thioxo-3-benzoxazolyl)phosphonate (1). To a solution of 2-benzoxazolethiol (**3**) (4.53 g, 0.03 mol) and triethylamine (TEA) (4.2 mL, 0.03 mol) in benzene (35 mL) was added dropwise at room temperature with stirring a solution of diphenyl phosphorochloridate (6.2 mL, 0.03 mol) in benzene (10 mL). The addition was completed in 30 min, and stirring was continued at room temperature for an additional 90

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min. Triethylamine hydrochloride was removed by filtration and the solvent was removed in vacuo. *n*-Hexane was added to the oily residue which then crystallized immediately. Purification by recrystallization from *n*-hexane gave white needles; yield 6.9 g (61%), mp 81–82 °C: IR (KBr) ν 1280 (P=O), 1170, 980 cm^{-1} (P—O—C); UV ($CHCl_3$) λ_{max} 297 nm (ϵ 2.4 × 10^4); ^{13}C NMR ($CDCl_3$) 179.5 ppm (C=S); MS, *m/e* 383 (M^+). Anal. Calcd for $C_{19}H_{14}NO_4PS$: C, 59.53; H, 3.68; N, 3.65. Found: C, 59.6; H, 3.7; N, 3.7.

Model Reaction. Typical examples of the model reactions follow.

Amide (8). General Procedure (Two Step). Activating agent 1 (0.422 g, 1.1 mmol) was added to a solution of the carboxylic acid (1.0 mmol) and TEA (0.14 mL, 1.0 mmol) in NMP (2 mL) at room temperature. After 10 min, the amine (1.0 mmol) was added. Stirring was continued for 10–30 min. The mixture was poured into 1% aqueous sodium hydrogen carbonate. The precipitate was filtered, washed with water, and dried.

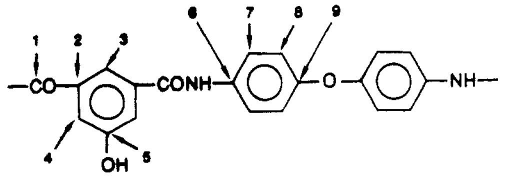
Amide (8). General Procedure (One Step). To a solution of the carboxylic aicd (1.0 mmol), the amine (1.0 mmol), and TEA (1.0 mmol) in NMP (2 mL) was added 1 (1.1 mmol) at room temperature. The solution was stirred for 2 h and poured into 1% aqueous sodium hydrogen carbonate. The precipitate was filtered, washed with water, and dried.

***N,N'*-Isophthaloylbis(benzoxazoline-2-thione) (10a).** To a stirred solution of **9a** (0.166 g, 1.0 mmol) and TEA (0.29 mL, 2.0 mmol) in NMP (2 mL) was added 1 (0.843 g, 2.2 mmol), followed by stirring at room temperature for 30 min. The reaction mixture was poured into water (100 mL). A precipitate formed and it was collected by filtration, washed with water, and dried in vacuo; yield 0.445 g (99%). It was recrystallized from benzene to give yellow needles, mp 200–201 °C (lit.[6] 201–202 °C).

Polycondensation. Typical examples of the polycondensations follow.

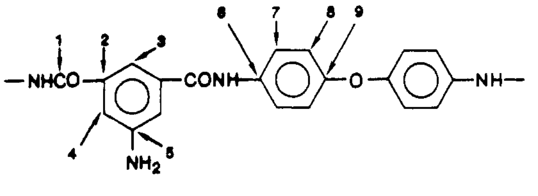
Polyamide 13a from 9a and 12a. Activating agent 1 (0.843 g, 2.2 mmol) was added with stirring to a solution of **9a** (0.166 g, 1.0 mmol) and TEA (0.29 mL, 2.0 mmol) in NMP (1 mL) at room temperature. After 30 min, **12a** (0.200 g, 1.0 mmol) was added to this solution. After 12 h of stirring, the resulting viscous solution was diluted with NMP (9 mL) and poured into methanol (500 mL). The polymer that precipitated was filtered and was refluxed in methanol for 2 h. The fibrous polymer was collected and dried in vacuo at 100 °C. The yield was 0.330 g (99%). The inherent viscosity of the polymer in concentrated sulfuric acid was 0.97 dL g^{-1} at a concentration of 0.5 g dL^{-1} at 30 °C: IR (film) ν 3300 (N—H), 1660 cm^{-1} (C=O).

Polyamide 15 from 14a and 12a. To a solution of **14a** (0.182 g, 1.0 mmol), **12a** (0.200 g, 1.0 mmol), and TEA (0.28 mL, 2.0 mmol) in NMP (2 mL) was added activating agent 1 (0.843 g, 2.2 mmol). The mixture was stirred at room temperature until 1 was dissolved completely in NMP and then at 80 °C for 4 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 0.92 dL g^{-1} at a concentration of 0.5 g dL^{-1} at 30 °C: IR (film) ν 3300 (O—H, N—H), 1660 (C=O); ^{13}C NMR ($(CD_3)_2SO$)



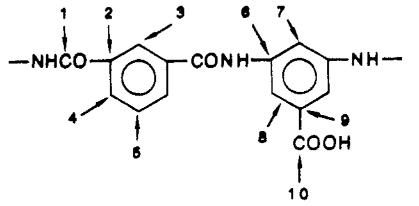
observed value (calculated value) (C-1) 164.6, (C-2) 136.3 (136.4), (C-3) 121.2 (119.6), (C-4) 117.3 (117.7) , (C-5) 157.0 (154.8), (C-6) 134.3 (134.2), (C-7) 121.8 (122.2), (C-8) 118.4 (119.0), (C-9) 152.6 (153.5). Anal. Calcd for $C_{20}H_{14}N_2O_4\cdot 0.8H_2O$: C, 66.58; H, 4.36; N, 7.76. Found: C, 66.59; H, 4.32; N, 7.33.

Polyamide 17 from 16 and 12a. The activating agent 1 (0.843 g, 2.2 mmol) was added at room temperature with stirring to a solution of **16** (0.181 g, 1.0 mmol), **12a** (0.200 g, 1.0 mmol), and TEA (0.28 mL, 2.0 mmol) in NMP 4 mL. The mixture was stirred at this temperature for 24 h. The polymer was isolated as described above. A 99% yield of the polymer having an inherent viscosity of 0.72 dL g^{-1} in NMP (c = 0.5 g dL^{-1} at 30 °C) was obtained: IR (film) ν 3300 (N—H), 1660 cm^{-1} (C=O); ^{13}C NMR ($(CD_3)_2SO$)



(C-1) 165.4, (C-2) 135.8 (135.9), (C-3) 122.0 (117.1), (C-4) 119.8 (117.1); 5: 144.1 (145.9); 6: 134.6 (134.2), (C-7) 121.8 (122.2) (C-8) 118.4 (119.0), (C-9) 152.6 (153.5). Anal. Calcd for $C_{20}H_{15}N_3O_3\cdot H_2O$: C, 66.10; H, 4.71; N, 11.55. Found: C, 66.69; H, 4.67; N, 10.60.

Polyamide 19 from 9a and 18. This polymer was prepared as described above, using **9a** and **18** as monomers for 2.5 h. The inherent viscosity was 0.53 dL g^{-1} in NMP (c = 0.5 g dL^{-1} at 30 °C): IR ν 3300 (N—H, O—H), 1710, 1660 cm^{-1} (C=O); ^{13}C NMR ($(CD_3)_2SO$)



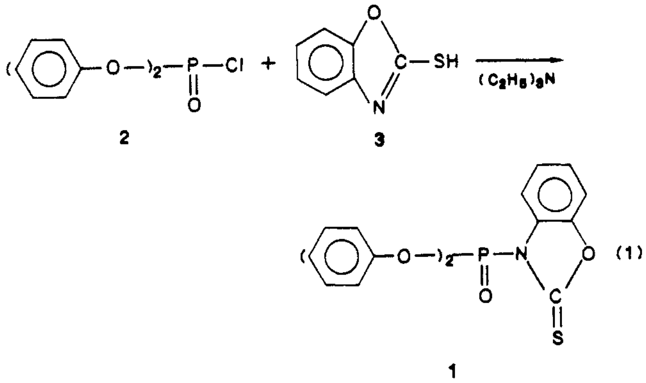
(C-1) 164.9, (C-2) 134.7 (135), (C-3) 126.9 (126.9), (C-4) 130.7 (130.4), (C-5) 128.4 (127.9); (C-6) 139.3 (139.2); (C-7) 116.3 (117.8), (C-8) 116.7 (117.9), (C-9) 131.2 (130.4), (C-10) 166.7. Anal. Calcd for $C_{15}H_{10}N_2O_4\cdot 0.5H_2O$: C, 61.86; H, 3.81; N, 9.61. Found: C, 61.9; H, 4.2; N, 9.7.

Results and Discussion

Preparation of Activating Agent, Diphenyl (2,3-Dihydro-2-thioxo-3-benzoxazolyl)phosphonate (1).

We already reported that active dithiol esters and diamides derived from 2-benzoxazolethiol (3) reacted with diamines at room temperature and produced high molecular weight polyamides.[6] This finding prompted us to develop a new activating agent, diphenyl (2,3-dihydro-2-thioxo-3-benzoxazolyl)phosphonate (1), for the syntheis of amides and polyamides by the direct procedure.

The new activating agent 1 was conveniently prepared from 3 and diphenyl phosphorochloridate (2) in the presence of TEA in dry benzene at room temperature. Phosphorylation of 3 might be expected to yield the *S*- or *N*-phosphoryl product, because of the tautomerism of 3. The above reaction conditions gave preferentially the more thermodynamically stable *N*-phosphoryl product (eq 1).



The structure of 1 was assigned on the basis of elemental analysis, IR, UV, ^{13}C NMR, and mass spectroscopy. The IR spectrum showed the P=O absorption at 1280 cm^{-1} and P—O—C absorptions at 1170 and 980 cm^{-1}. The UV absorption maxima of 1 was observed at 297 nm that is very close to that characteristic of 3-benzoylоxazoline-2-thione

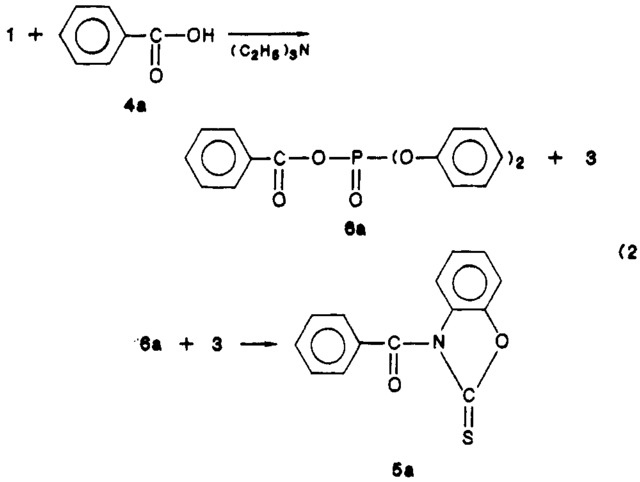
Table I
Preparation of Amides 8 Using Activating Agent 1[a] (Two-Step Procedure)

R—COOH	R′—NH$_2$	time,[b] min	product	yield, %
C_6H_5— (**4a**)	C_6H_5— (**7a**)	10	*N*-phenylbenzamide (**8a**)	98
C_6H_5— (**4a**)	$C_6H_5CH_2$— (**7b**)	30	*N*-benzylbenzamide (**8b**)	87
C_6H_5— (**4a**)	c-C_6H_{11}— (**7c**)	30	*N*-cyclohexylbenzamide (**8c**)	97
n-C_5H_{11}— (**4b**)	C_6H_5— (**7a**)	10	*N*-phenylhexanamide (**8d**)	77
n-C_5H_{11}— (**4b**)	$C_6H_5CH_2$— (**7b**)	10	*N*-benzylhexanamide (**8e**)	65
$C_6H_5CH{=}CH$— (**4c**)	C_6H_5— (**7a**)	10	*N*-phenylcinnamamide (**8f**)	98
$C_6H_5CH{=}CH$— (**4c**)	$C_6H_5CH_2$— (**7b**)	10	*N*-benzylcinnamamide (**8g**)	97
$C_6H_5CH{=}CH$— (**4c**)	c-C_6H_{11}— (**7c**)	10	*N*-cyclohexylcinnamamide (**8h**)	96
o-$CH_3C_6H_5$— (**4d**)	C_6H_5— (**7a**)	30	*N*-phenyl-*o*-tolylamide (**8i**)	91
$C_6H_5CO(CH_2)_2$— (**4e**)	C_6H_5— (**7a**)	10	*N*-phenyl-3-benzoylpropionamide (**8j**)	73
C_6H_5— (**4a**)	*p*-HOC_6H_5— (**7d**)	10	*N*-(4′-hydroxyphenyl)benzamide (**8k**)	87

[a] Reaction was carried out with 1.0 mmol of the reactants in the presence of TEA (1.0 mmol) in NMP (2 mL) at room temperature. [b] Reaction time, step 1, 10 min; reaction time, step 2, 30 min.

(λ_{max} 289 nm).[7] Furthermore, the ^{13}C NMR resonance of C=S in 1 was observed at 179.5 ppm.

Two-Step Procedure. The two-step procedure involves two separate steps: (1) activation of the carboxylic acid component, i.e., generation of the active intermediate from 1 and the carboxylic acid, and (2) condensation of this intermediate with the amine. In order to clarify the reaction pathway in the two-step procedure, the reaction of 1 with benzoic acid (**4a**) was carried out in NMP at room temperature for 10 min in the presence of TEA as a tertiary base. The reagent 1 reacted rapidly with **4a** to give 3-benzoylbenzoxazoline-2-thione (**5a**) in 90% yield. The compound **5** has been characterized by high reactivity toward aminolysis. The above observations point to the following pathway. The activating agent 1 reacts first with **4a** to form the mixed carboxylic-phosphoric anhydride (**6a**), a highly activated acylating agent, which reacts rapidly with available nucleophile **3** to give the active amide (**5a**) (eq 2).



(2)

The conversion of carboxylic acids into amides by using the activating agent 1 was carried out by the two-step procedure of eq 3. The mixture of 1 and the carboxylic

$$1 + 4 \xrightarrow[\text{step 1}]{\text{base}} 5 \xrightarrow[\text{step 2}]{R'NH_2\ 7} \underset{8}{RC(=O)NHR'} \qquad (3)$$

acid **4** was stirred at room temperature for 10–30 min, and then the amine **7** was added. The reaction proceeded smoothly to give the corresponding amides **8** in good yields. The amines, as expected from their generally greater reactivity in nucleophilic reactions, react more rapidly than alcohols with the active amides **5**. This difference in reactivity permitted the selective N-acylation of *p*-aminophenol (**7d**). These results are summarized in Table I.

Then, the reaction of dicarboxylic acids with the activating agent 1 was performed to determine if the method gave the desired active amides **10** in high enough yield to give promise as a polymer-forming reaction. The desired active diamides were obtained in excellent yields (Table II) (eq 4).

Table II
Preparation of Active Amides 10 Using Activating Agent 1[a] (Two-Step Procedure)

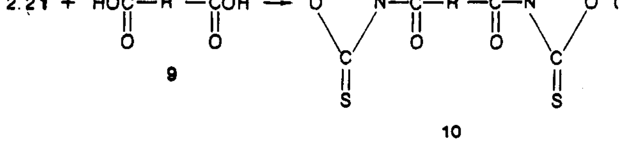
HOOC—R—COOH	time, min	product	yield, %
m-C_6H_4— (**9a**)	10	*N,N*′-isophthaloylbis(benzoxazoline-2-thione) (**10a**)	87
m-C_6H_4— (**9a**)	30	*N,N*′-isophthaloylbis(benzoxazoline-2-thione) (**10a**)	99
—$(CH_2)_4$— (**9b**)	30	*N,N*′-adipolybis(benzoxazoline-2-thione) (**10b**)	87
—$(CH_2)_8$— (**9c**)	30	*N,N*′-sebacoylbis(benzoxazoline-2-thione) (**10c**)	92

[a] Reaction was carried out with 1.0 mmol of the reactants in the presence of TEA in NMP (1 mL) at room temperature.

Table III
Preparation of Diamides 11 Using Activating Agent 1[a] (Two-Step Procedure)

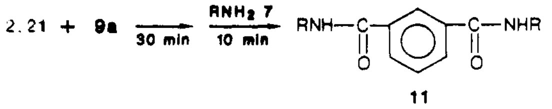
R—NH$_2$	product	yield, %
C_6H_5—	isophthalanilide (**11a**)	99
$C_6H_5CH_2$—	*N,N*′-dibenzylisophthalamide (**11b**)	94
c-C_6H_{11}—	*N,N*′-dicyclohexylisophthalamide (**11c**)	94
p-HOC_6H_4—	*N,N*′-bis(4′-hydroxyphenyl)isophthalamide (**11d**)	97

[a] Reaction was carried out with isophthalic acid **9a** (1.0 mmol) and amine (1.0 mmol) in the presence of TEA in NMP (2 mL) at room temperature. Reaction time: step 1, 30 min; step 2, 10 min.



(4)

Furthermore, diamides (**11**) were prepared from isophthalic acid (**9a**) and amines **7** by using the activating agent 1 (eq 5). Condensation proceeded rapidly at room



(5)

Table IV
Polycondensation of Dicarboxylic Acids 9 with Diamines 12 Using an Activating Agent[a] (Two-Step Procedure)

HOOC—R—COOH	$H_2NC_6H_5$—R′—$C_6H_5NH_2$	solvent (mL)	reaction time step 1, min	 step 2, h	polymer	η_{inh},[a] dL g^{-1}
m-C_6H_4—	—O— (**12a**)	NMP (1)	30	12	**13a**	0.97
m-C_6H_4—	—CH_2— (**12b**)	NMP (1) HMPA (1)	120	2	**13b**	0.63
m-C_6H_4—	—CH_2— (**12b**)	HMPA (1)	180	24	**13b**	0.48
—$(CH_2)_8$—	—O— (**12a**)	HMPA (1)	20	24	**13c**	0.34

[a] Polycondensation was carried out with 1 mmol of the monomers using activating agent 1 (2.2 mmol) in the solvent at room temperature. [b] Measured at a concentration of 0.5 g dL^{-1} in concentrated sulfuric acid 30 °C.

Table V
Polycondensation of Isophthalic Acid (9a) with Hexamethylenediamine Using an Activating Agent[a] (Two-Step Procedure)

activating agent, mmol	LiCl, mmol	solvent (mL)	reaction time step 1, h	 step 2, h	polymer yield, %	 η_{inh},[b] dL g^{-1}
2.0		HMPA (1.0)	2	24	92	0.31
2.1		HMPA (1.0)	2	24	97	0.51
2.2		HMPA (1.0)	2	24	97	0.41
2.1		NMP (0.5)	1	24	98	0.56
2.1		HMPA (0.5) NMP (0.5)	1	24	97	0.57
2.1		NMP (0.5) HMPA (0.5)	1	5[c]	99	0.61
2.1	2.0	NMP (0.5)	1	7	96	0.57
2.1	2.0	HMPA (1.0)	2	6	92	0.34

[a] Polycondensation was carried out with 1 mmol of the monomers in the presence of TEA at room temperature. [b] Measured at a concentration of 0.5 g dL^{-1} in concentrated sulfuric acid at 30 °C. [c] Reaction temperature: step 2, 60 °C.

temperature and gave the desired diamides in excellent yields (Table III).

Polycondensation (Two-Step Procedure). On the basis of these studies, the two-step polycondensation of dicarboxylic acids **9** with aromatic diamines **12** was carried out by using the activating agent **1** in polar aprotic solvents at room temperature (eq 6).

$$2.21 + \underset{\mathbf{9}}{\mathrm{HOC({=}O)RC({=}O)OH}} \xrightarrow[\text{step 1}]{} \xrightarrow[\text{step 2}]{\mathrm{H_2NR'NH_2}\ (12)} \underset{\mathbf{13}}{-(\mathrm{C({=}O)RC({=}O)NHR'NH})_n-} \tag{6}$$

A 10 mol % excess of the reagent **1** based on each monomer was appropriate, and 1 mL of NMP was found to be enough for the reaction on a 1.0-mmol scale. Table IV indicates that polyamides **13** were easily produced in quatitative yields with inherent viscosities of 1.0 dL g^{-1}.

Although the direct polycondensation has been applied successfully for the synthesis of polyamides from dicarboxylic acids and aromatic diamines, only one method afforded relatively high molecular weights of aliphatic polyamides with limited success.[8] As described by Ogata,[8] the difficulty of synthesizing aliphatic polyamides may be ascribed to the high basicity of aliphatic diamines which presumably causes significant side reactions such as the formation of stable P–N linkages.

As mentioned above, dicarboxylic acids were converted to the corresponding active amides **10** in quantitative yields in the presence of the activating agent **1**. Therefore, we decided to undertake the synthesis of polyamides from aliphatic diamines by the two-step procedure. Polycondensation of **9a** with hexamethylenediamine was carried out by using the activating agent **1**, and the results are summarized in Table V. The polyamides with inherent viscosities up to 0.6 dL g^{-1} gave values which are comparable to that obtained by the polycondensation of the active diamides **10a** with hexamethylenediamine.[6]

Table VI
Preparation of Amides 8 Using Activating Agent 1[a] (One-Step Procedure)

R—COOH	R—NH_2	product	yield, %
C_6H_5—	C_6H_5—	benzanilide	99
$C_6H_5CH{=}CH$—	C_6H_5—	*N*-phenylcinnamamide	99
n-C_5H_{11}	C_6H_5—	*N*-phenylhexanamide	99
C_6H_5—	*p*-HOC_1H_5—	4′-hydroxybenzanilide	98

[a] Reaction was carried out with 1 mmol of the reactants using activating agent 1 (1.1 mmol) in the presence of TEA in NMP (2 mL) for 2 h at room temperature.

Table VII
Polycondensation of Isophthalic Acid 9a with Aromatic Diamine 12 Using Activating Agent 1[a] (One-Step Procedure)

diamine	NMP, mL	time, h	η_{inh},[b] dL g^{-1}
12a	1	2	0.97
12a	2	10	1.2
12b	2	7	1.2

[a] Polycondensation was carried out with 1 mmol of the monomers using activating agent 1 (2.2 mmol) in the presence of TEA in NMP at room temperature. [b] Measured at a concentration of 0.5 g dL^{-1} in concentrated sulfuric acid at 30 °C.

One-Step Procedure. We next studied the synthesis of amides by the one-step procedure. This procedure consists of adding the activating agent **1** to a solution of the carboxylic acid and the amine in the presence of TEA. Once the mixed anhydride **6** was formed, it reacted in situ with the amine to give the amide. The advantage of this method over the two-step procedure is that more reactive **6** in place of **5** is used in the aminolysis (eq 7).

$$1 + \underset{\mathbf{4}}{\mathrm{RC({=}O)OH}} + \underset{\mathbf{7}}{\mathrm{RNH_2}} \xrightarrow[(\mathrm{C_2H_5})_3\mathrm{N}]{} \underset{\mathbf{8}}{\mathrm{RC({=}O)NHR'}} \tag{7}$$

The results of several representative amide syntheses by the one-step procedure are summarized in Table VI. Condensations proceeded smoothly and gave the corresponding amides in higher yields than did the two-step procedure. Furthermore, selective N-acylation of *p*-aminophenol (**7d**) was performed in quantitative yield. However, when the aliphatic amines were used, the formation of phosphoramides together with the desired amides was observed. Thus, this procedure is not adequate for the synthesis of amides from aliphatic amines.

On the basis of these results, the direct polycondensation of isophthalic acid (**9a**) with aromatic diamines **12** was carried out with the activating agent **1** in the presence of TEA in polar aprotic solvents. Table VII indicates that polyamides were easily produced in quantitative yields with inherent viscosities up to 1.2 dL g^{-1}.

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

Table VIII
Polycondensation of 5-Hydroxyisophthalic Acid 14 with 12a Using Activating Agent 1[a] (One-Step Procedure)

solvent, mL	temp, °C	time, h	η_{inh},[b] dL g^{-1}
1	20	4	0.42
2	60	4	0.48
2	20	24	0.55
2	80	4	0.92

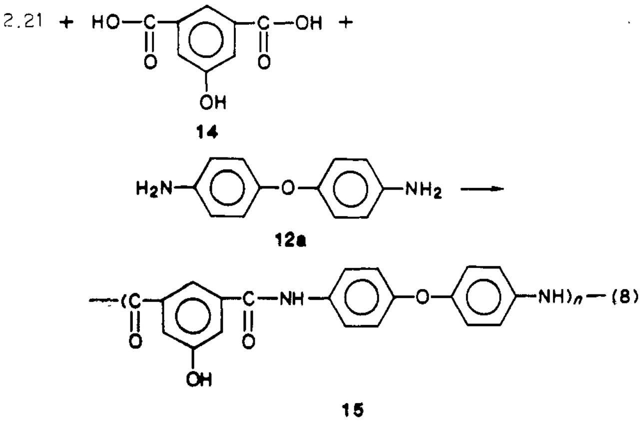
[a] Polycondensation was carried out with 1 mmol of the monomers using activating agent 1 (2.2 mmol) in the presence of TEA in NMP at room temperature. [b] Measured at a concentration of 0.5 g dL^{-1} in concentrated sulfuric acid at 30 °C.

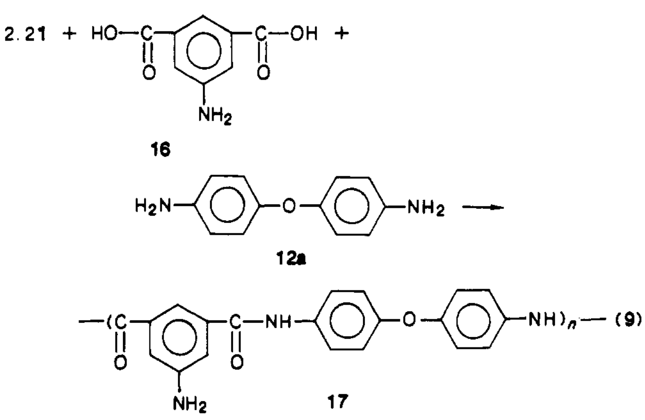
Table IX
Polycondensation of Isophthalic Acid 9a with 3,5-Diaminobenzoic Acid 18 Using Activating Agent 1[a] (One-Step Procedure)

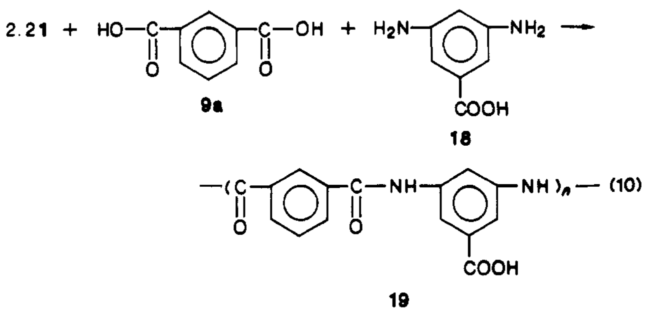
activating agent, mmol	solvent, mL	time, h	η_{inh},[a] dL g^{-1}
2.05	4	24	0.21
2.1	4	2.5	0.53
2.1[c]	2	12	0.46

[a] Polycondensation was carried out with 1 mmol of the monomers using activating agent 1 in the presence of TEA in NMP at room temperature. [b] Measured at a concentration of 0.5 g dL^{-1} in NMP at 30 °C. [c] Two-step procedure.

In order to further demonstrate the preparative utility of our method, it was applied to the chemoselective polyamidation. It has been a generally accepted principle that the lower the selectivity the greater the reactivity. In our method, the reactive intermediate is the mixed-anhydride 6 or the active amide 5, the reactivity of which toward nucleophiles is lower than that of acid chlorides. Thus, the chemoselective polyamidation would be expected. As described above, the selective N-acylation of 7 was performed in the presence of 1. First, the synthesis of polyamide from 5-hydroxyisophthalic acid (14) and 12a was tried with our method (eq 8). The direct polycondensation of 14 and 12a was carried out with the activating agent 1 in NMP. A relatively high molecular weight polyamide 15 was obtained at room temperature. The reaction temperature on the polycondensation showed a favorable effect on the molecular weight of polymer, where polyamide 15 with inherent viscosity up to 0.92 dL g^{-1} was obtained (Table VIII). Second, the direct polycondensation of 5-aminoisophthalic acid (16) with 12a was performed (eq 9). Although a gel formed at the high monomer concentration (16%), a high molecular weight polyamide 17 with the inherent viscosity of 0.7 dL g^{-1} was obtained at the monomer concentration of 9%. Finally, polyamide synthesis from 9a and 3,5-diaminobenzoic acid (18) was performed by using the activating agent 1 (eq 10). Polycondensation proceeded smoothly and gave a polyamide with inherent viscosity of 0.52 dL g^{-1}. For the comparison of polymer structure, the same polyamide was prepared by the two-step procedure (Table IX).







Transparent films cast from the solution of polyamides 15, 17, and 19 in aprotic solvents showed a high degree of toughness and flexibility. IR and ^{13}C NMR spectroscopy and elemental analyses of these polymers indicated materials corresponding to the expected polyamides.

Through these polymerizations, we observed the following. The active intermediate, mixed-anhydride 6 or active amides 5, does not react with an OH group less nucleophilic than a NH$_2$ group. Intermediate 6 or 5 can differentiate the more nucleophilic amino group in 12a from the amino group in 16. Reagent 1 can also differentiate the carboxyl group between 9a and 18.

In summary, our studies indicate that the new activating agent 1 is very useful for the preparation of amides and high molecular weight polyamides under mild conditions. We also achieved highly chemoselective polyamidation of multifunctional dicarboxylic acids and diamines without special protection of the acylation-sensitive groups. This method will be utilized for the synthesis of polymers which requires such chemoselectivity.

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Registry No. **1**, 111160-56-6; **2**, 2524-64-3; **3**, 2382-96-9; **4a**, 65-85-0; **4b**, 142-62-1; **4c**, 621-82-9; **4d**, 118-90-1; **4e**, 2051-95-8; **7a**, 62-53-3; **7b**, 100-46-9; **7c**, 108-91-8; **7d**, 123-30-8; **8a**, 93-98-1; **8b**, 1485-70-7; **8c**, 1759-68-8; **8d**, 621-15-8; **8e**, 6283-98-3; **8f**, 3056-73-3; **8g**, 57152-94-0; **8h**, 6750-98-7; **8i**, 7055-03-0; **8j**, 17649-94-4; **8k**, 15457-50-8; **9a**, 121-91-5; **9b**, 124-04-9; **9c**, 111-20-6; **10a**, 80292-82-6; **10b**, 80292-83-7; **10c**, 111160-57-7; **11a**, 13111-32-5; **11b**, 41882-29-5; **11c**, 82292-41-9; **11d**, 1245-91-6; **13a** (SRU), 26026-92-6; **13b** (SRU), 25667-73-6; **13b** (copolymer), 25668-18-2; **13a** (copolymer), 27616-35-9; **13c** (SRU), 31549-47-0; **13c** (copolymer), 52825-24-8; (**14**)(**12a**) (copolymer), 111160-58-8; (**14**)(**12a**) (SRU), 111160-59-9; (**18**)(**9a**) (copolymer), 51202-70-1; (**18**)(**9a**) (SRU), 31808-02-3; (**9a**)(H$_2$N(CH$_2$)$_6$NH$_2$) (copolymer), 25722-07-0; (**9a**)(H$_2$N(CH$_2$)$_6$NH$_2$) (SRU), 25668-34-2.

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Syndiotactic Polymerization of Styrene: Mode of Addition to the Double Bond

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ABSTRACT: By ^{1}H NMR analysis of a syndiotactic copolymer of perdeuteriostyrene with *cis*-styrene-*β*-*d*, it is observed that the mode of addition of the growing chain end to the double bond of the monomer is cis.

Introduction

Syndiotactic polymerization of styrene in the presence of catalytic systems consisting of hydrocarbon-soluble compounds of titanium or zirconium, such as tetrabenzyltitanium and tetrabenzylzirconium, and methylaluminoxane has been reported in previous papers.[1-3] In these papers it has been also reported that the statistical model of the stereospecific propagation is Bernoullian[1] and that the insertion of the monomer into the reactive metal–carbon (or even metal–hydrogen, in the initiation step) bonds is secondary,[2,3] e.g.,

$$\text{Mt–P} + C_8H_8 \rightarrow \text{MtCH}(C_6H_5)\text{CH}_2\text{–P}$$

where Mt = metal of the catalytic complexes and P = growing polymer chain.

In order to complement the basic information concerning the stereochemical reaction mechanism we report in this paper the mode of addition of the growing chain end to the double bond of the monomer.

Results and Discussion

A syndiotactic polymer can be described as a sequence of mirror-related syndiotactic dyads. According to the literature,[7] the allowed conformations of a syndiotactic dyad, in solution, are those shown in Figure 1. The population of the TT conformer P_{TT}[8] is larger than that of the GG conformer P_{GG} ($P_{TT} + P_{GG} = 1$). By considering the Karplus function describing the magnitude of the vicinal proton–proton coupling constant J as a function of the dihedral angle in the H–C–C–H bond system[9] and the averaging of the J's arising from fast equilibration with each other of the conformers of Figure 1,[10] one could anticipate that the coupling constants between the methylene and the methine protons of syndiotactic polystyrene would be

$$\bar{J}_{12} = \bar{J}_{34} = P_{TT}J_t + P_{GG}J_g$$

$$\bar{J}_{13} = \bar{J}_{24} = P_{TT}J_g + P_{GG}J_t$$

where $\bar{J}_{ij}$ is the coupling constant between vicinal protons i, j averaged for the interconversion of the two conformers, P_{TT} and P_{GG} are the populations of the two conformers, and J_g and J_t are the coupling constants of the H–C–C–H bond system for H–C–C–H dihedral angles of 60° and 180°, respectively.

As discussed in a previous paper concerning syndiotactic polypropylene[11] $P_{TT}J_t + P_{GG}J_g$ and $P_{TT}J_g + P_{GG}J_t$ cannot be determined simply from the ^{1}H NMR spectrum of syndiotactic polymers because the resonance of the chemically equivalent methylene protons (Figure 2A), coupled to each other, is a deceptive triplet. These coupling constants[11] can be determined from the ^{1}H NMR spectrum of syndiotactic polystyrene-*β*-*d* reported in Figure 2B. In this case the resonance of the methylene protons is a doublet of doublets and the larger spacing ($9._0$ Hz) corresponds to $P_{TT}J_t + P_{GG}J_g$ while the smaller spacing ($5._4$ Hz) corresponds to $P_{TT}J_g + P_{GG}J_t$. The resonance of the methine protons is less resolved because of the coupling with two vicinal deuteriums, which broadens the components of the resonance. The assignments

$$P_{TT}J_t + P_{GG}J_g = \bar{J}_{12} = \bar{J}_{34} = 9._0 \text{ Hz}$$

$$P_{TT}J_g + P_{GG}J_t = \bar{J}_{13} = \bar{J}_{24} = 5._4 \text{ Hz}$$

are a consequence of the fact, previously mentioned, that $P_{TT} > P_{gg}$ and that, according to the Karplus equation, $J_t > J_g$. When a small amount of, e.g., styrene-*β*-*d* is copolymerized with a large amount of perdeuteriostyrene, most of the *β*-*d* units will be flanked by perdeuterio units. As a consequence, most of the methylene protons will be coupled with only one methine proton (e.g., H^1) and the spectrum of the aliphatic protons will consist of two doublets. The spacing between the components of the doublet will be either $P_{TT}J_t + P_{GG}J_g = \bar{J}_{12} = 9._0$ Hz or $P_{TT}J_g + P_{GG}J_t = \bar{J}_{13} = 5._4$ Hz, depending on the structure (cis or trans) of the styrene-*β*-*d* and the mode of addition (cis or trans) of the growing chain end to the double bond of the monomer.

One can easily visualize by ball-and-stick models that cis addition to the double bond of the trans monomer and trans addition to the double bond of the cis monomer will lead to the syndiotactic dyad shown in a TT conformation in Figure 3a, while trans addition to the trans monomer and cis addition to the cis monomer will lead to the syndiotactic dyad shown in Figure 3b.

The ^{1}H NMR spectrum of the syndiotactic copolymer of cis styrene-*β*-*d* (15% mole fraction) with perdeuteriostyrene (85% mole fraction) is reported in Figure 2C. The resonance of the aliphatic protons consists of two doublets at 1.23 (methylene) and 1.75 ppm (methine). The spacing between the components of the doublets is $9._0$ Hz. The spacing corresponds to $\bar{J}_{12}$ thus showing that the methylene and the methine protons are arranged as in Figure 3b. As just discussed, this shows that the actual mode of addition

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