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Bisorthoesters as Polymer Intermediates. III.* Oligomers Containing Purine Rings

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ABSTRACT

Hexa-n-propyl orthoisophthalate, hexa-n-propyl orthoterephthalate, and in one case hexaethyl orthooxalate were condensed with aminomalondiamine dihydrochloride or aminomalonamideamidine dihydrochloride in DMSO or DMF between 100° C and the boiling point of DMF to oligomers containing adenine and hypoxanthine rings. For example, hexa-n-propyl orthoisophthalate and aminomalonamidamidine dihydrochloride in dimethyl sulfoxide at 100° C gave an oligomer of poly (2,8-hypoxanthinediyl-1,3-phenylene). The condensation was limited to oligomers of relatively low molecular weight, partly because of the low solubility of the oligomers under reaction conditions and partly also because the four reactive amino groups of the aminomalonamideamidine and the aminomalondiamidine did not react simply as difunctional tetramines to form linear aromatic polymers; this unequal reactivity of the amine functions caused side reactions to occur. Such side reactions have not been observed in the reactions of bisorthoesters with tetrafunctional aromatic orthodiamines, such as 3,3',4,4'-tetraaminobiphenyl.

*For the preceding papers in this series, see C. D. Dudgeon and O Vogl, J. Polym. Sci. Polym. Chem. Ed., in press [1, 2].

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INTRODUCTION

Purine, pteridine and pyrimidine ring systems are of considerable biological interest because they are produced in nature by various plants or animals. Two purine derivatives, adenine and guanine, are building blocks of RNA and DNA. Other purine derivatives are the active components of plants.

Almost 20 years ago it was found that orthoesters (but no other carboxylic acid derivatives) when reacted with aminomalonamidamidine dihydrochloride or aminomalondiamidine dihydrochloride gave hypoxanthine or adenine derivatives [3] in good yield. Hypoxanthine and adenine themselves were prepared when triethyl orthoformate was used as the cyclization reagent. Triethyl orthoacetate and triethyl orthopropionate were used to prepare 2,8-dimethyl, 2-8-diethyl-, and 2,8-diphenylhypoxanthine and adenine. This cyclization provided the best method for the preparation of hypoxanthine and adenine as well as their 2,8-dialkyl or diaryl substituted derivatives. The reaction was simple, and purines were produced in high yield [3].

Purines may be formed from properly substituted pyrimidines, imidazoles or open chain compounds by cyclization with carboxylic acid derivatives including orthoesters. The cyclization of 4,5-diaminopyrimidines with orthoesters has been investigated extensively [4-25] and has usually been carried out by heating a 4,5-diaminopyrimidine derivative with an excess of an orthoester such as triethyl orthoformate. Acetic anhydride was often added as co-reactant because of its reaction with orthoesters to form 1,1-dialkoxyalkyl acetates. Cyclizations of diaminopyrimidines with orthoesters are believed to proceed through an iminoester.

Although not covered as extensively, the conversion of substituted imidazoles to purine derivatives has also been studied. With triethyl orthoformate, 4-amino-5-carboxamidoimidazole gave in good yield hypoxanthine [26] and 4-aminoimidazole-5-hydroxamic acid gave hypoxanthine-1-N-oxide [27]. As is usual with orthoester cyclizations, only a short time (20 min) was required to complete the reaction [28].

Few examples for the preparation of purine derivatives from open chain compounds have been reported [3]. Adenine and hypoxanthine have been prepared from aminomalondiamidine dihydrochloride and aminomalonamidamidine dihydrochloride respectively by heating with an excess of triethyl orthoformate in dimethylformamide (DMF) [29], and with other trialkyl orthocarboxylates, 2,8-disubstituted hypoxanthines and adenines were obtained. Triethyl orthoacetate or triethyl orthopropionate readily gave 2,8-dimethyl- and 2,8-diethyladenine. Much longer reaction times were required for the preparation of 2,8-disubstituted hypoxanthines. Aminomalonamidamidine

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dihydrochloride and triethyl orthoacetate gave after 15 min 2-methyl-4-(1-methoxyethylideneamino)imidazole-5-carboxamide, which could be converted to 2,8-dimethylhypoxanthine methyl ether by continued heating in DMF for 20 hr or by vacuum sublimation of the isolated product at 250° C.

It was noted [3] that a side reaction occurred during this reaction in the presence of excess hydrogen chloride. The intermediate product, 2-methyl-4-(1-methoxyethylideneamino)imidazole-5-carboxamide, was converted to 2-methyl-4-acetylaminoimidazole-5-carboxamide and this compound could not be converted to 2,8-dimethylhypoxanthine. This observation suggested that carboxylic acid derivatives other than orthoesters could not be used for this cyclization.

Bisorthoesters have only recently been investigated as polymer intermediates [1, 30].

It was expected that aromatic bisorthoesters or hexaalkyl orthooxalate could react with aminomalonamidamidine or aminomalondiamidine to form polymers containing purine rings as it was found that they reacted with aromatic tetraamines and gave polybenzimidazoles. Because of the good thermal stability of these heterocyclic systems, the purine as well as the benzimidazole polymers were considered attractive candidates for high temperature polymers and complexing agents.

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EXPERIMENTAL

Materials

Bisorthoesters were synthesized and purified according to earlier procedures [29, 30].

N,N-Dimethylacetamide (Aldrich Chemical Co.), was fractionally distilled at reduced pressure (bp 55-58° C/11 Torr) and stored over activated 4 Å molecular sieves. No water was observed by gas chromatography.

N,N-Dimethylformamide (Eastman Kodak Co.), was dried over $MgSO_4$, filtered, fractionally distilled at reduced pressure (bp 78-80° C/40 Torr) and stored over activated 4 Å molecular sieves.

Dimethyl sulfoxide (Aldrich Chemical Co.), was fractionally distilled at reduced pressure from CaH_2 (bp 70.5-71° C/10 Torr) and collected over activated 3 Å molecular sieves. The resulting DMSO had only a very faint odor. The water level was found by gas chromatography to be 40 ppm.

Malononitrile (Aldrich Chemical Co.), mixed with P_2O_5 was fractionally distilled at reduced pressure (bp 81-83° C/4.7 Torr).

Ethyl cyanoacetate (Eastman Kodak Co.), was washed with 10%

aqueous Na_2CO_3, water, dried over anhydrous Na_2SO_4 and fractionally distilled at reduced pressure (bp 70° C/1.5 Torr).

Phenylazomalonamidamidine hydrochloride (PAMA·HCl) and phenylazomalondiamidine dihydrochloride (PMDA·2HCl) were synthesized from ethyl cyanoacetate and malononitrile according to a modified [30] procedure developed earlier by Shaw [31, 32].

Special Drying Procedures

Because of the ease of hydrolysis of orthoesters to normal esters, special precautions were taken to remove any possible sources of moisture. It was found to be most convenient to dry all glassware for at least 2 hr at 150° C, assemble hot, allow to cool in vacuo, and fill with prepurified nitrogen. Solvents used for polymerizations were transferred from their storage containers under nitrogen via syringe. For the drying of solutions containing orthoesters neutral or basic drying agents, such as anhydrous potassium carbonate, were employed.

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Preparation of Monomers and Polymers

Aminomalonamidamidine Dihydrochloride (AMAA · 2HCl)

To a 500-ml Parr shaker bottle was added PAMA·HCl (50 g, 0.21 mole), 10% palladium on carbon (2.5 g), and 50% aqueous ethanol (250 ml). PAMA was reduced under an initial hydrogen pressure of 40 psi, requiring 4 hr for the uptake of 33 psi (0.42 mole). The catalyst was removed by filtration and the filtrate concentrated on a rotary evaporator at 20 Torr until a second oily layer formed. The solution was extracted with ethyl ether (3 × 50 ml), and hydrochloric acid (30 ml) was added to the aqueous solution. The solution was concentrated on a rotary evaporator at 20 Torr to 50 ml and transferred to a 50-ml Erlenmeyer flask; absolute ethanol (100 ml) and ethyl ether (250 ml) were added, and AMAA · 2HCl separated as an oil which soon crystallized. The flask was tightly stoppered with a rubber stopper and stored in a refrigerator overnight to complete the crystallization. AMAA · 2HCl was isolated by filtration, washed with a small amount of absolute ethanol, and dried in a desiccator over KOH at 20 Torr to give 32 g (82%). The crude product was dissolved in water (2ml/g), decolorizing carbon was added, and the solution was stirred for 1 hr. The suspension was filtered and absolute ethanol (5 ml/ml water) was added followed by a large amount of ethyl ether. AMAA · 2HCl separated as a colorless oil which soon crystallized and the mixture was stored in a refrigerator overnight to complete crystallization. Pure AMAA · 2 HCl was

isolated by filtration, washed with absolute ethanol, dried in a desiccator over KOH at 0.01 Torr, and gave 20 g (51%) of a white powder, mp 210-215° C (lit. [31] 209-210° C).

Analysis. Calculated for $C_3H_{10}N_4Cl_2O$: C, 19.05%; H, 5.29%; N, 29.63%. Found: C, 18.98%; H, 5.37%; N, 29.66%.

Aminomalondiamidine Dihydrochloride (AMDA · 2 HCl)

To a 500-ml Parr shaker bottle was added PMDA · 2 HCl (50 g, 0.18 mole), 50% aqueous ethanol (200 ml), and 10% palladium-on-carbon (2 g). PMDA was reduced under an initial hydrogen pressure of 40 psi requiring 3 hr for the uptake of 28 psi (0.36 mole) of hydrogen. The suspension was filtered and the filtrate concentrated on a rotary evaporator at 20 Torr until a second oily layer formed. The solution was then extracted with ether (3 × 50 ml), concentrated on a rotary evaporator at 20 Torr to 50 ml, and decolorized with activated carbon. Absolute ethanol (250 ml) and ethyl ether (500 ml) were then added to precipitated AMDA · 2HCl as a fluffy white solid. The suspension was filtered, and the solid was washed with absolute ethanol (50 ml) and dried in a desiccator over KOH at 20 Torr to give 21 g (63%) of AMDA · 2 HCl. AMDA · 2 HCl could be further purified by dissolving in a minimum amount of distilled water and decolorizing with activated charcoal; then absolute ethanol (5 ml/ml water) and a large amount of ethyl ether were added to precipitate pure AMDA · 2 HCl. After filtration it was washed with a small amount of absolute ethanol and dried in a desiccator over KOH at 0.01 Torr; mp 300° C.

Analysis. Calculated for $C_3H_{11}N_5Cl_2$: C, 19.15%; H, 5.85%; N, 37.34%; Cl, 37.77%. Found: C, 19.43%; H, 5.83%; N, 37.08%; Cl, 37.82%.

Adenine-Containing Oligomers

Poly(2,8-adeninediyl-1,4-phenylene) from AMDA · 2HCl and HPOT in DMSO. To a dry, 50-ml three-necked flask was added AMDA · 2HCl (0.460 g, 2.45 mmole), HPOT (1.11 g, 2.45 mmole), dry DMSO (30 ml), and dry pyridine (3 ml). The flask was fitted with a mechanical stirrer, nitrogen capillary inlet tube and nitrogen exit connected to a paraffin oil bubbler. The solution was stirred under a slow stream of nitrogen for 15 min, placed in an oil bath at 100° C, and heated with stirring under nitrogen for 12 hr. The solution was cooled to room temperature and concentrated on a rotary evaporator at 0.1 Torr to approximately 5 ml. Poly(2,8-adeninediyl-1,4-phenylene) was precipitated as a brown product by adding the solution dropwise with stirring to 50 ml of water. The suspension was stirred overnight, filtered, the polymer dried over NaOH at 100° C/0.01 Torr and gave 0.250 g (49%) of gold-brown powder, η_{inh} = 0.10 dl/g (0.5% in DMSO at 30° C).

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Analysis. Calculated for $(C_{11}H_7N_5)_n$: C, 63.16%, H, 3.35%; N, 33.49%. Found: C, 58.97%; H, 4.84%; N, 24.22%.

PMR (DMSO-d_6) showed two overlapping singlets at 8.05δ (2H) and 8.18δ (4H) (aromatic and $-NH_2$) as well as absorptions attributed to propyl ester groups ($-O-CH_2-$ at 4.25δ, $-CH_2-$ at 1.70δ, $-CH_3$ at 0.98δ). The IR spectrum (thin film on NaCl plate) showed absorptions at 3300, 3200 (–N–H stretch), 1710 (ester C=O stretch), 1660 (–C=N– stretch), and 1585 cm^{-1} (aromatic C=C ring stretch). The UV spectrum showed one band at 285 nm ($E^{1\%}_{1cm}$ 1470). Thermal analysis under nitrogen showed weight losses of 2.5%, 30%, and 45% at 200, 400, and 600° C.

Poly(2,8-adeninediyl-1,3-phenylene) from AMDA · 2HCl and HPOI in DMSO. To a dry 50-ml three-necked flask was added AMDA · 2HCl (0.460 g, 2.45 mmole), HPOI (1.11 g, 2.45 mmole), dry DMSO (30 ml), and dry pyridine (3 ml). The flask was fitted with a mechanical stirrer, nitrogen capillary inlet tube and nitrogen exit connected to a paraffin oil bubbler. The solution was stirred under a slow stream of nitrogen for 15 min, placed in an oil bath at 100° C, and heated with stirring under nitrogen for 12 hr. The solution was cooled to room temperature and concentrated on a rotary evaporator at 0.1 Torr to approximately 5 ml. Poly(2,8-adeninediyl-1,3-phenylene) precipitated as a light brown product when the solution was added dropwise with stirring to 50 ml of water. The suspension was stirred overnight and filtered; the polymer was dried over NaOH at 100° C and 0.1 Torr and gave 0.125 g (25%) of light brown powder, η_{inh} = 0.12 dl/g (0.2% in DMSO at 30° C).

Analysis. Calculated for $(C_{11}H_7N_5)_n$: C, 63.16%; H, 3.35%; N, 33.49%. Found: C, 58.16%; H, 5.25%; N, 22.64%.

PMR (DMSO-d_6) showed a broad singlet at 8.06 δ (2H, $-NH_2$) on top of a number of overlapping broad peaks from 6.55δ to 8.75δ (4H, aromatic). Absorptions attributed to propyl esters were also observed ($-O-CH_2-$ at 4.25δ, $-CH_2-$ at 1.65δ, and $-CH_3$ at 0.90δ). The IR spectrum (thin film on NaCl plate) showed absorptions at 3300, 3200 cm (–N–H stretch), 1720 cm (ester C=O stretch), 1660 cm (–C=N– stretch), and 1580 cm^{-1} (aromatic C=C ring stretch). The UV spectrum showed one band at 248 nm ($E^{1\%}_{1cm}$ 1552). Thermal analysis under nitrogen showed weight losses of 3.6, 29, and 44% at 200, 400, and 600° C.

Hypoxanthine-Containing Polymers

Poly(2,8-hypoxanthinediyl-1,4-phenylene) from AMAA · 2HCl and HPOT IN DMSO. To a dry, 50-ml three-necked flask was added AMAA · 2HCl (0.46 g, 2.4 mmole), HPOT

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(1.1 g, 2.4 mmole), dry DMSO (30 ml), and dry pyridine (3 ml). The flask was fitted with a mechanical stirrer, nitrogen capillary inlet tube and nitrogen exit connected to a paraffin oil bubbler. The solution was stirred under a slow stream of nitrogen for 15 min, placed in an oil bath at 100° C, and heated with stirring under nitrogen for 12 hr. The solution was cooled to room temperature and concentrated on a rotary evaporator at 0.1 Torr to approximately 5 ml. Poly(2,8-hypoxanthinediyl-1,4-phenylene) was precipitated as a dark powder by adding the solution dropwise to 50 ml of methanol. The polymer was Soxhlet-extracted for 12 hr with methanol, dried over NaOH at 100° C and 0.1 Torr and gave 0.46 g (91%), n_{inh} = 0.10 dl/g (0.5% in DMSO at 30° C).

Analysis. Calculated for $(C_{11}H_6N_4O)_n$: C, 62.86%; H, 2.86%; N, 26.67%. Found: C, 59.63%; H, 4.14%; N, 21.29%.

PMR (DMSO-d_6) showed a singlet at 8.15δ (4H, aromatic). Absorptions attributed to propyl ester groups were also observed (–OC<u>H</u>$_2$– at 4.25δ, –C<u>H</u>$_2$– at 170δ and –C<u>H</u>$_3$ at 0.98δ). The IR spectrum (thin film on NaCl plate) showed absorptions at 3400-3200 (N–H stretch), 1710 (ester C=O stretch), 1680-1650 (lactam C=O stretch and –C=N– stretch), and 1600 cm^{-1} (aromatic C=C ring stretch). The UV spectrum showed one band at 319 nm ($E^{1\%}_{1cm}$ 496). Thermal analysis under nitrogen showed weight losses of 0.5%, 21%, and 41% at 200, 400, and 600° C.

<u>Poly[(5-carboxamido-4,2-imidazolediyl)-1,4-phenylene(methoxymethylene) nitrilo] from AMAA · 2HCl and HMOT in DMF.</u> To a dry 50-ml three-necked flask fitted with nitrogen capillary inlet tube and reflux condenser protected by a $CaCl_2$ drying tube was added AMAA · 2HCl (1.00 g, 5.3 mmole), HMOT (1.51 g, 5.3 mmole), and dry DMF (30 ml). The flask was placed in an oil bath at 165° C and heated under a slow stream of nitrogen for 12 hr. During this time a dark solid precipitated from the solution. The flask was cooled to room temperature and the suspension filtered. The resulting dark green solid was washed with ethanol and dried over KOH at 100° C and 20 Torr, giving 0.70 g (55%).

PMR (DMSO-d_6) showed two overlapping broad singlets at 8.08-8.25δ (6H, aromatic, O=C–<u>N</u>H$_2$) and a singlet at 3.9δ (3H, –O–<u>C</u>H$_3$) The IR spectrum (KBr) showed absorptions at 3350, 3180 (N-H stretch), 2900-2700 (aliphatic C–H stretch), 1680 (amide C=O stretch), and 1600 cm^{-1} (aromatic –C=C– ring stretch).

<u>Poly[(5-carboxamido-4,2-imidazolediyl)-1,4-phenylene(methoxymethylidene) nitrilo] from AMAA · 2HCl and HMOT in DMAc.</u> To a dry 50-ml three-necked flask fitted with nitrogen capillary inlet tube and reflux condenser protected

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by a $CaCl_2$ drying tube was added AMAA · 2HCl (1.00 g, 5.3 mmole), HMOT (1.51 g, 5.3 mmole), and dry DMAc (30 ml). The flask was placed in an oil bath at 165° C and heated under a slow stream of nitrogen at 165° C for 12 hr. During this time a dark solid precipitated from the solution. The flask was cooled to room temperature and the suspension filtered. The resulting dark green solid was washed with ethanol, dried over KOH at 100° C and 20 Torr, and gave 0.80 g (62%), η_{inh} = 0.10 dl/g (0.2% in DMSO at 30° C).

The IR spectrum (KBr) showed absorption at 3350, 3180 (N–H stretch), 2900-2700, (aliphatic C–H stretch), and 1680 cm^{-1} (amide C=O stretch).

Poly(2,8-hypoxanthinediyl-1,4-phenylene) from poly[(5-carboxamido-4,2-imidazolediyl)-1,4-phenylene(methoxymethylidene) nitrilo]. To a clean 8-ml vial was added poly[(5-carboxamido-4,2-imidazolediyl)-1,4-phenylene(methoxymethylidene) nitrilo] (0.300 g, 1.25 mmole). The vial was placed in an 8-in. 33-mm ID glass tube which was evacuated to 0.01 Torr and heated in an electric tube heater to 260° C. The tube was held at 260° C.for 5 hr, then cooled to room temperature; 0.216 g (83%) of poly(2,8-hypoxanthinediyl-1,4-phenylene) was obtained as a dark brown-black powder, η_{inh} = 0.10 dl/g (0.2% in DMSO at 30° C).

PMR (DMSO-d_6) showed a broad singlet at 8.4δ (4H, aromatic) and a broad absorption peak at 4.2-4.4δ (O=C(H)–O–CH_3). The IR spectrum (thin film on NaCl plate) showed absorptions at 3400-3200 (N–H stretch), 1690 (lactam C=O stretch), 1650 (–C=N– stretch), and 1600 cm^{-1} (aromatic –C=C– ring stretch). Except for a weaker lactam stretching band, the spectrum was superimposable on that obtained for the one-step synthesis of poly(2,8-hypoxanthinediyl-1,4-phenylene).

Poly(2,8-hypoxanthinediyl-1,3-phenylene) from AMAA · 2HCl and HPOI in DMSO. To a dry 50-ml three-necked flask was added AMAA · 2HCl (0.46 g, 2.4 mmole), HPOI (1.1 g, 2.4 mmole), dry DMSO (30 ml), and dry pyridine (3 ml). The flask was fitted with a mechanical stirrer, nitrogen capillary inlet tube, and nitrogen exit connected to a paraffin oil bubbler. The solution was stirred under a slow stream of nitrogen for 15 min, placed in an oil bath at 100° C, and heated with stirring under nitrogen for 12 hr. The solution was cooled to room temperature and concentrated on a rotary evaporator at 0.1 Torr to approximately 5 ml. A dark product precipitated when the solution was added dropwise with stirring to 50 ml methanol. The polymer was Soxhlet-extracted for 12 hr with methanol and dried over NaOH at 100° C/0.01 Torr, yielding 0.235 g (47%) of brown powder, η_{inh} = 0.08 dl/g (0.5% in DMSO at 30° C).

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Analysis. Calculated for $(C_{11}H_6N_4O)_n$: C, 62.86%; H, 2.86%; N, 26.67%. Found: C, 59.31%; H, 4.13%; N, 21.21%.

PMR (DMSO-d_6) showed three broad overlapping peaks from 8.75-7.65δ (4H, aromatic) and absorptions attributed to propyl groups (–O–C<u>H</u>$_2$– at 4.25δ, –C<u>H</u>$_2$– at 1.70δ and –C<u>H</u>$_3$ at 0.93δ). The IR spectrum (thin film on NaCl plate) showed absorptions at 3400-3200 (N–H stretch), 1710 (ester C=O stretch), 1690-1640 (lactam C=O stretch and –C=N– stretch), and 1600 cm^{-1} (aromatic C=C ring stretch). The UV spectrum showed two bands at 300 and 230 nm ($E^{1\%}_{1cm}$ 1504, 928). Thermal analysis under nitrogen showed weight losses of 0.63, 21, and 42% at 200, 400, and 600° C.

<u>Poly[(5-carboxamido-4,2-imidazolediyl)-1,3-phenylene(methoxymethylidene) nitrilo] from AMAA · 2HCl and HMOI in DMF.</u> To a dry 50-ml three-necked flask fitted with nitrogen capillary inlet tube and reflux condenser protected by a $CaCl_2$ drying tube was added AMAA · 2HCl (1.00 g, 5.3 mmole), HMOI (1.51 g, 5.3 mmole) and dry DMF (30 ml). The flask was placed in an oil bath at 165° C and heated under a slow stream of nitrogen at 165° C for 2 hr. The solution was cooled to room temperature and the DMF removed on a rotary evaporator at 0.1 Torr. Water was added to separate poly[(5-carboxamido-4,2-imidazolediyl)-1,3-phenylene(methoxymethylidene) nitrilo] as a brown-green solid which was isolated by filtration, dried over P_2O_5 at 78° C/20 Torr for 24 hr, yielding 0.82 g (64%).

PMR (DMSO-d_6) showed a broad multiplet at 7.2-8.8δ (6H, aromatic and O=C–<u>N</u>H$_2$) and a singlet at 3.92δ (3H, –O–C<u>H</u>$_3$). The IR spectrum (thin film on NaCl plate) showed absorptions at 3350, 3180 (N–H stretch), 1680-1650 (amide C=O stretch and –C=N– stretch), and 1600 cm^{-1} (aromatic –C=C ring stretch).

<u>Poly[(5-carboxamido-4,2-imidazolediyl)-1,3-phenylene(n-propoxymethylidene) nitrilo] from AMAA · 2HCl and HPOI in DMAc.</u> To a dry 50-ml three-necked flask fitted with a mechanical stirrer, nitrogen capillary inlet tube, and reflux condenser protected by a $CaCl_2$ drying tube was added AMAA · 2HCl (0.660 g, 3.50 mmole), HPOI (1.59 g, 3.50 mmole) and dry DMAc (20 ml). The soltuion was stirred under a slow stream of nitrogen for 30 min, then placed in an oil bath at 165° C and heated with stirring under nitrogen for 2 hr. The solution was cooled to room temperature, concentrated to approximately 5 ml on a rotary evaporator at 0.1 Torr, and poly[(5-carboxamido-4,2-imidazolediyl)-1,3-phenylene(n-propoxymethylidene) nitrilo] was precipitated by adding the solution dropwise with stirring to acetone (50 ml). The product was filtered, Soxhlet-extracted for 12 hr, and dried over KOH at 100° C/20 Torr, giving 0.540 g (57%) of light tan powder, η_{inh} = 0.10 dl/g (0.2% in DMSO at 30° C).

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PMR (DMSO-d_6) showed three broad peaks at 8.80δ, 8.35δ and 7.65δ (6H, aromatic and O=C(–NH$_2$)), a triplet at 4.35δ (–O–CH$_2$–), a multiplet at 1.90δ (–CH$_2$–), and a triplet at 1.0δ (–CH$_3$). The IR spectrum (thin film on NaCl plate) showed absorptions at 3320, 3180 (N–H stretch), 2980 (aliphatic C–H stretch), 1680-1650 cm^{-1} (amide C=O stretch and –C=N– stretch), and 1600 cm^{-1} (aromatic C=C stretch).

Poly(2,8-hypoxanthinediyl-1,3-phenylene) from poly[(5-carboxamido-4,2-imidazolediyl)-1,3-phenylene(methoxymethylidene) nitrilo]. To a clean 8-ml vial was added poly[(5-carboxamido-4,2-imidazolediyl)-1,3-phenylene(methoxymethylidene) nitrilo] (0.217 g, 0.87 mmole). The vial was placed in a 200 mm × 33 mm ID test tube which was evacuated to 0.01 Torr and heated in an electric tube heater to 260° C. The tube was held at 260° C for 5 hr, then cooled to room temperature to give 0.16 g (88%) of poly(2,8-hypoxanthinediyl-1,3-phenylene) as a dark brown-black powder.

PMR (DMSO-d_6) showed three broad overlapping peaks at 8.65δ (1H), 8.15δ (2H) and 7.60δ (1H) (aromatic) and a broad resonance peak at 3.5δ attributed to methyl ester groups. The IR spectrum (thin film on NaCl plate) was superimposable with that obtained for the one-step synthesis in DMSO.

Poly(2,8-hypoxanthinediyl-1,4-phenylene) from poly[(5-carboxamido-4,2-imidazolediyl)-1,4-phenylene(n-propoxymethylidene) nitrilo]. To a clean 8-ml vial was added poly[(5-carboxamido-4,2-imidazolediyl)-1,4-phenylene(n-propoxymethylidene) nitrilo] (0.085 g, 0.315 mmole). The vial was placed in a 200 mm × 33 mm ID test tube which was evacuated to 0.01 Torr and heated in an electric tube heater to 250° C. The tube was held at 250° C for 30 hr, then cooled to room temperature to give 0.066 g (100%) of light brown powder.

PMR (DMSO-d_6) showed three broad overlapping peaks from 9.1-8.0δ (4H, aromatic) and absorptions attributed to propyl ester groups (–O–CH$_2$– at 4.6δ, –CH$_2$– at 2.05δ, and –CH$_3$ at 1.28δ). By infrared spectroscopy the polymer was identical to that prepared in DMSO.

Poly(2,8-hypoxanthinediyl) from AMAA · 2HCl and HEOO in DMSO. To a dry 50-ml three-necked flask was added HEOO (0.50 g, 1.7 mmole), AMMA · 2HCl (0.32 g, 1.7 mmole), dry DMSO (30 ml), and dry pyridine (3 ml). The flask was fitted with a mechanical stirrer, nitrogen capillary inlet tube, and nitrogen exit connected to a paraffin oil bubbler. The solution was stirred under a slow stream of nitrogen for 15 min, placed in an oil bath at 100° C, and heated with stirring under nitrogen for 12 hr. The solution was cooled to room temperature and concentrated on a rotary evaporator at 0.1 Torr to approximately 5 ml. Poly(2,8-hypoxanthinediyl) precipitated as a dark product by adding the solution dropwise with

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stirring to 50 ml of methanol. The polymer was Soxhlet-extracted for 12 hr with methanol, and dried over NaOH at 100° C/0.01 Torr, giving 0.2 g (88%) of brown powder, η_{inh} = 0.06 dl/g (0.2% in DMSO at 30° C).

Analysis. Calculated for $(C_5H_2N_4O)_n$: C, 44.78%; H, 1.49%; N, 41.79%. Found: C, 46.96%; H, 3.92%; N, 27.46%. The IR spectrum (KBr) showed absorptions at 3400-3200 (N–H stretch) and 1690-1640 cm (lactam C=O stretch and –C=N– stretch). The UV spectrum showed two bands at 310 and 261 nm ($E^{1\%}_{1cm}$ 300, 279). Thermal analysis under nitrogen showed weight losses of 0.33, 23, and 43 at 200, 400, and 600° C.

Model Compounds

2,8-Diphenyladenine

AMDA · 2HCl (1.5 g, 8 mmole), dry DMSO (30 ml), and TMOB (2.8 ml, 2.97 g, 16 mmole), after heating at 100° C for 1 hr, gave crude 2,8-diphenyladenine (1.25 g, 55%), which after vacuum sublimation at 230° C/0.01 Torr and recrystallization from ethanol gave pure 2,8-diphenyladenine, mp 299.0-299.5° C.

Analysis. Calculated for $C_{17}H_{13}N_5$: C, 71.08δ; H, 4.53%; N, 24.39%. Found: C, 71.21%; H, 4.93%; N, 24.49%.

PMR (DMSO-d_6) showed a multiplet at 7.9δ (6H, m, p aromatic) and a multiplet at 7.4δ (6H, aromatic and $-NH_2$). The IR spectrum (KBr) showed absorptions at 3250 (N–H stretch), 3150 (aromatic C–H stretch), 1630 (–C=N– stretch), and 1580 cm^{-1}, 1570, and 1440 cm^{-1} (aromatic and heterocyclic ring stretch).

2,8-Diphenylhypoxanthine

Prepared in DMF. AMAA · 2HCl (3.6 g, 19 mmole), TMOB (17.4 g, 96 mmole), and dry DMF (15 ml) after 20 min at 160° C gave yellow 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide which separated as an oil, but crystallized after standing at room temperature [28]. After recrystallization from ethanol, it gave 4.4 g (72%) of off-white powder, mp 194-195° C. (lit [29] 155-160° C). PMR (DMSO-d_6) showed a singlet at 4.03δ (3H, $CH_3O-\overset{|}{C}=N-$), a singlet at 7.4δ (10H, aromatic) and a multiplet at 7.85 (2H, $H_2N-\overset{|}{C}=O$).

2-Phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide (1.0 g, 3 mmole) was sublimed at 230° C/0.015 Torr. 2,8-Diphenylhypoxanthine was obtained as a light yellow solid, which was recrystallized and dried to give 0.47 g (52%) of 2,8-diphenylhypoxanthine as

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a white solid, mp 388-390°C (lit. [29] 380°C). PMR (DMSO-d_6) showed a multiplet at 7.40-7.65δ (6H) and a multiplet at 7.95-8.15δ (4H). The IR spectrum (KBr) showed absorptions at 3000 (C–H stretch), 1640 (–C=N– stretch), 1540, 1440, and 1360 cm^{-1} (heterocyclic ring stretch). The UV spectrum showed two absorption bands at 257 nm ($E^{1\%}_{1\ cm}$ 862) and 308 nm ($E^{1\%}_{1cm}$ 527).

Prepared in DMSO. AMAA · 2HCl (3.78 g, 0.02 mmole), TMOB (6.9 ml, 7.3 g, 0.04 mmole), dry DMSO (50 ml), and dry pyridine (7 ml) after 15 min at 100°C gave crude 2,8-diphenylhypoxanthine (4.4 g, 76%). PMR (DMSO-d_6) showed the product to be almost pure 2,8-diphenylhypoxanthine with only a small amount of 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide remaining as shown by the very small –OCH_3 peak at 4.0δ. The product was recrystallized and vacuum sublimed at 230°C/0.015 Torr to give pure 2,8-diphenylhypoxanthine.

Measurements

Infrared spectra were recorded on a Perkin-Elmer Model 727 or a Perkin-Elmer Model 521 spectrophotometer. Infrared spectra were measured either on KBr pellets or on a thin film cast on a sodium chloride plate from a hexafluoroisopropanol solution. Peak assignments were made to the nearest 10 cm^{-1}.

PMR spectra were measured on either a 60 MHz Hitachi Perkin-Elmer R-24, a 60 MHz Perkin-Elmer R-12, or a 90 MHz Perkin-Elmer R-32 spectrophotometer. All samples were measured as solutions in deuterated dimethyl sulfoxide using TMS as an internal standard.

Gas chromatographic analyses were carried out on a Varian model 1400 gas chromatograph with a thermal conductivity detector. For the determination of water content, a 3 ft × 1/8 in. Porapak Q column was used, while the analysis of orthoesters required a 5 ft × 1/8 in. Carbowax 20M (5% on 100/120 Chromosorb W, AW, DMCS) column. The determination of water at the ppm level required a 10 μl sample The size of the water peak was compared to a calibration curve prepared from ethanol-water solutions. The calibration curve was previously found to be accurate ± 10 ppm by Karl Fischer titration. Orthoesters were analyzed by gas chromatography as a 2 μl sample of a 50% solution in dry hexane.

Ultraviolet spectra of polymers and model compounds were recorded on a Beckman DK-2A spectrophotometer using concentrated sulfuric acid as the solvent.

The thermal properties of the polymers were determined on a Perkin-Elmer DSC-1B differential scanning calorimeter and on a Perkin-Elmer TGS-1 thermobalance at a scan rate of 10°C/min.

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Melting points were determined on a Mel-Temp capillary melting point apparatus and are uncorrected.

Microanalyses were done by the Microanalytical Laboratory, Office of Research Services, University of Massachusetts, Amherst, Mass.

RESULTS AND DISCUSSION

Oligomers of low molecular weight were prepared by the condensation of aminomalondiamidine dihydrochloride (AMDA · 2HCl) and aminomalonamidamidine dihydrochloride (AMAA · 2HCl) with hexapropyl orthoterephthalate (HPOT), hexapropyl orthoisophthalate (HPOI), or hexaethyl orthooxalate (HEOO). Bisorthoesters were of polymerization grade quality, as they gave high molecular weight polymers with 3,3',4,4'-tetraaminobiphenyl and other aromatic tetramines. AMDA · 2HCl and AMMA · 2 HCl were prepared and purified to a quality which was believed to be sufficient for the preparation of high polymers. Side reactions, which also seemed to occur in the preparation of model compounds, are believed to be responsible for the poorer results in our polycondensation reaction. Upon evaluation of our polymerization results and comparing them with the results of preparation of model compounds, it was clear that substituted orthoesters had a lower reactivity than that of orthoformates, which condensed with AMDA · 2HCl or AMMA· [HCl and gave adenine and hypoxanthine in more than 70% yield; the yield of the 2,8-diphenyl derivatives from orthobenzoates were lower and longer reaction times were required. Furthermore, the complete ring closure of the pyrimidine ring required, especially in the case of the hypoxanthine synthesis, temperatures above 200°C. For comparison, trimethyl orthobenzoate, when condensed with o-phenylenediamine, produced in quantitative yield relatively high purity 2-phenylbenzimidazole, the model compound of the benzimidazole polymers, even at 100°C.

Synthesis of Monomers and Model Compounds

The syntheses of AMDA · 2HCl and AMAA · 2HCl were basically the synthetic routes initially described by Shaw [31]; they were, however, modified when needed.

AMDA · 2HCl, for which a good synthesis has never been reported, was prepared by a four-step procedure from malononitrile [Eq. (1b)]; this method is analogous to the synthesis of AMAA · 2HCl [Eq. (1a)]. Dry hydrogen chloride was passed through a solution of malononitrile

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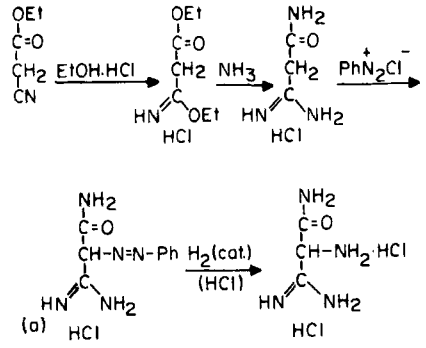
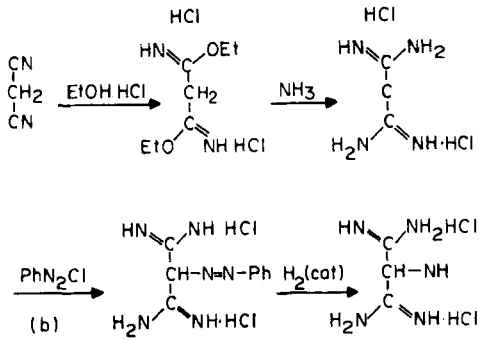


(1a)



(1b)

and ethanol in 1,4-dioxane at 0°C, which gave the diiminoether dihydrochloride in 94% yield. The use of diethyl ether as the solvent resulted in the rapid precipitation of the monoimino ether hydrochloride, and further reaction did not occur. The progress and the optimization of the reaction was followed by analyzing the individual products by Volhard titration.

The resultant 1,3-diethoxy-1,3-diiminopropane dihydrochloride was converted to malondiamidine dihydrochloride by treatment with half-saturated cold NH_3 in ethanol in 88% yield. An essentially quantitative reaction was obtained by addition of benzenediazonium chloride to malondiamidine dihydrochloride. In order to obtain maximum yield, most of the acid was neutralized with sodium bicarbonate and then the pH was adjusted with saturated sodium acetate solution to pH 4.

Phenylazomalondiamidine dihydrochloride was hydrogenated in a Parr shaker with palladium on carbon under an initial pressure of 40 psi and gave in 63% yield AMDA · 2HCl. After evaporation of the solvent, aniline was extracted with ether and AMDA · 2HCl recrystallized from aqueous ethanol and washed with ether; if necessary, the

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solution was decolorized with charcoal. At higher temperatures AMDA · 2HCl degraded, but did not melt up to 350°C.

AMAA · 2HCl was synthesized in a five-step synthesis from ethyl cyanoacetate with an overall 27% yield [Eq. (1a)]. The first three steps were very similar to the synthesis reported earlier [31], but some improvements were made; (attempts were also made to prepare the methyl amino ether, but it was too unstable).

Azo coupling with malonamidamidine hydrochloride has been reported to give an excellent yield (90%) of phenylazomalonamidamidine hydrochloride [31]. When repeated as described, only a low yield (30%) of very impure azo compound was obtained. Shaw's procedure used only 1.8 mole of hydrochloric acid for each mole of aniline, not enough to convert all of the aniline to benzenediazonium chloride. We increased the amount of 6 N hydrochloric acid from 35 ml to 45 ml (2.5 mole HCl/mole of aniline) and increased the yield of phenylazomalonamidamidine hydrochloride from 30% to 95%. After addition of malonamidamidine hydrochloride to the benzenediazonium chloride, pH control was found to be essential for optimum yield. The pH was adjusted to 4 by the addition of sodium acetate, and maintained at 4 for from 4-6 hr.

AMAA · 2HCl was prepared by the catalytic hydrogenation of phenylazomalonamidamidine hydrochloride over palladium on carbon [33] which was carried out in a Parr shaker using 50% aqueous ethanol as the solvent. After removal of the catalyst and evaporation of the ethanol, aniline was removed by extracting with ether. Aniline had to be removed at this point to prevent its subsequent conversion to aniline hydrochloride which would separate out with AMAA · 2HCl. The product was isolated at this point and gave the monohydrochloride as an oil which did not readily crystallize. However, the addition of concentrated hydrochloric acid followed by ethanol and ether resulted in the formation of the dihydrochloride of AMAA which separated as an oil but which rapidly crystallized from the mixture and was recrystallized from 95% ethanol.

Catalytic hydrogenation of phenylazomalonamidamidine hydrochloride has been reported by several different methods [33-35]. The hydrogenation of phenylazomalonamidamidine hydrochloride with palladium on carbon at atmospheric pressure has been reported to yield directly AMAA · 2HCl [33]. When attempted, several days were required for the theoretical volume of hydrogen to be absorbed.

AMDA · 2HCl with triethyl orthoformate in DMF at 155°C gave a 72% yield of adenine [29]. In our hands, a 43% yield of adenine was obtained which was identified by comparison of the infrared spectrum and PMR spectrum. The position of the 6-amino group in the PMR spectrum (7.43 δ) was shifted downfield from the value reported for adenosine triacetate (6.37 δ) [36]. The N–H protons of purine derivatives are known to be shifted downfield when DMSO is used as the PMR solvent [37] because of hydrogen bonding.

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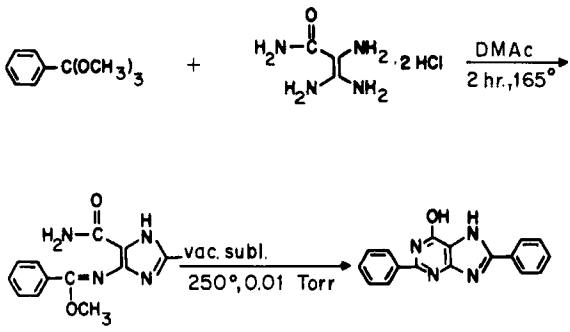

(2)

AMDA · 2HCl condensed with TMOB 1 hr in DMSO at 100°C to yield light yellow crystals of 2,8-diphenyladenine. Both the imidazole and pyrimidine rings were closed in one step, and no evidence for the presence of 2-phenyl-4-(α-methoxybenzylideneamino) imidazole-5-carboxamidine was observed. Vacuum sublimation at 230°C/0.01 Torr gave pure 2,8-diphenyladenine which was identified by microanalysis and by PMR; there was no evidence of C_2 and C_8 protons, but the presence of the two monosubstituted aromatic rings as well as a chemical shift of 7.4δ for the 6-amino group were observed for 2,8-diphenyladenine.

Hypoxanthine was prepared from AMAA · 2HCl with triethyl orthoformate in DMF in a 65% yield and was identified by its PMR and infrared spectrum; it was soluble in DMF but was not soluble in TEOF or in the reaction mixture and precipitated when formed. Using the stoichiometric amount of TEOF without excess resulted in a lower yield of hypoxanthine.

AMAA · 2HCl has been reported to condense with TMOB to give in 58% yield 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide, which upon subsequent vacuum sublimation at 250°C was converted to 2,8-diphenylhypoxanthine [29]; our yield was only 41% [Eq. (2)]. Because this condensation is the model reaction of the polymer forming reaction, it was studied extensively. The condensation of AMAA · 2HCl with TMOB in DMF gave in excellent yield 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide as yellow crystals. The crude product was recrystallized from ethanol and gave a 75% yield of an off-white powder. The yield depended upon the purity of the TMOB, AMAA · 2HCl and the solvent. The use of unpurified DMF resulted in a dark brown product instead of light yellow crystals. Increasing the reaction time did not increase further the product yield.

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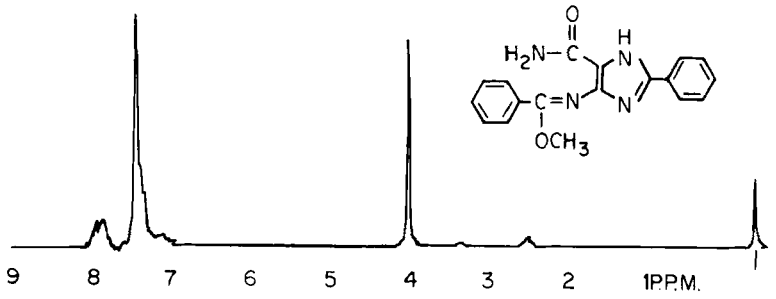

FIG. 1. PMR Spectrum of 2-phenyl-4-(α-methoxybenzylideneamino) imidazole-5-carboxamide.

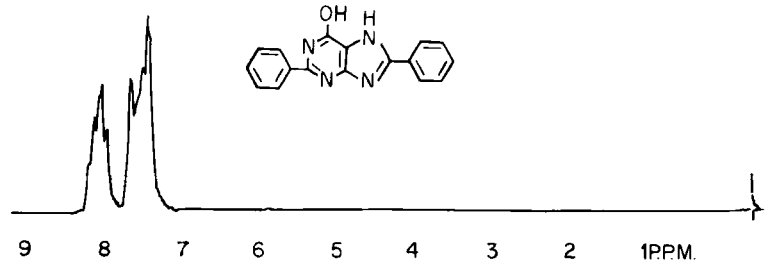

FIG. 2. PMR Spectrum of 2,8-diphenylhypoxanthine.

The melting point observed for the compound was much higher than that previously reported (191°C vs 155-160°C); however, 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide as previously reported was the hydrate which probably explains the lower melting point. The reported 155-160°C melting point was reported as being followed by immediate resolidification which suggested conversion to 2,8-diphenylhypoxanthine. The higher melting point observed in this study was also followed by immediate resolidification.

Pure 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide (Fig. 1) was identified by PMR and by its conversion to 2,8-diphenylhypoxanthine by vacuum sublimation (Fig. 2). The distinguishing feature of the PMR spectrum of 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide was the singlet at 4.4δ of the aliphatic methoxy group. In the aromatic region were absorptions of the aromatic protons of the two phenyl groups and the two amide protons. The N–H proton of the imidazole ring was not

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observed in the 0-10δ region. This is a common feature of the PMR spectrum of substituted imidazoles with the N–H proton generally appearing at 13δ [38].

Vacuum sublimation of 2-phenyl-4-(α-methoxybenzylideneamino)-imidazole-5-carboxamide at 230°C/0.015 Torr gave, after recrystallization, a good yield (52%) of pure 2,8-diphenylhypoxanthine, which was identified by melting point and by PMR and showed the absence of the methoxy protons at 4.4δ; only the 10 aromatic protons of the two phenyl groups were observed. This, together with the absence of an –OH stretching band in the 3500-3300 cm^{-1} region and the presence of a carbonyl stretching band at 1650 cm^{-1} indicates that the actual structure of 2,8-diphenylhypoxanthine is that of the 1H-purine-6-one rather than that of the 6-hydroxypurine.

As noted before, the melting of 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide at 191°C was followed by immediate resolidification which was assumed to be due to conversion to the higher melting 2,8-diphenylhypoxanthine. To see if heating above the melting point would be sufficient to give the desired 2,8-diphenylhypoxanthine without vacuum sublimation, a sample of 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide (Fig. 1), was melted and allowed to resolidify, and the resolidified product air dried. The product was identified by PMR as 2,8-diphenylhypoxanthine but the melting point (230°C) was well below the 380°C observed for pure 2,8-diphenylhypoxanthine (Fig. 2). Vacuum sublimation was found to be the only method which could be used to purify the crude compound.

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Various solvents were studied for use in this condensation reaction of AMAA · 2HCl and TMOB. In DMF or DMAc condensation proceeded at the same rate but temperatures of 155-165°C were required for good results. PMR studies showed, however, that condensation in DMSO occurred efficiently at 100°C; the amount of TMOB was also found to affect the composition of the product which was obtained. In the previously reported synthesis of 2,8-diphenylhypoxanthine [28], a large excess of TMOB was used and the orthoester was in effect a co-solvent for the reaction. When the condensation of AMAA · 2HCl with TMOB was carried out in DMSO at 100°C with a large excess of orthoester the product was found by PMR to be the 50:50 mixture of 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide and 2,8-diphenylhypoxanthine. When only the desired amount of TMOB was used, the product obtained was almost pure 2,8-diphenylhypoxanthine with only a trace of 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide.

DMSO did have the disadvantage, however, of turning dark when heated to 100°C for extended periods of time. The use of a nitrogen blanket did not decrease the amount of discoloration but addition of a small amount of pyridine to the reaction mixture eliminated this problem.

The condensation of AMAA · 2HCl with TMOB in DMSO at 100°C gave a crude yield of 76% of 2,8-diphenylhypoxanthine as a light tan powder from which white crystals of the pure compound could be obtained by vacuum sublimation.

Preparation of Oligomers

Adenine-Containing Oligomers

AMDA · 2HCl was condensed with HPOT in DMSO in the presence of some pyridine at 100°C for 12 hr and gave in 50% yield a condensation product which was soluble in DMSO and also in trifluoroacetic acid. From model compound studies it was known that both the imidazole and the pyrimidine ring of the purine would probably be closed in 1 hr reaction time but the extended period was allowed to insure completeness of reaction. The reaction product had an inherent viscosity of 0.1 dl/g, and its PMR spectrum showed end group absorptions at 4.25δ, 1.70δ and 0.98δ, similar to those [39] observed for n-propyl benzoate (4.25δ, 1.76δ, and 1.07δ). On the basis of this investigation the molecular weight of our product was estimated to be 600-800. Similar results were obtained in another experiment carried out on a larger scale. Thermal analysis gave a 30% weight loss at 400°C (Fig. 3).

Attempts to carry out a successful condensation of HPOT with AMDA · 2HCl to poly(2,8-adeninediyl-1,4-phenylene) in DMAC at 165°C were unsuccessful. AMDA · 2HCl is not soluble at room temperature and decomposes at 165°C; no cyclization occurred, as judged by PMR at 100°C.

AMDA · 2 HCl condensed with HPOI in DMSO at 100°C and gave a reaction product in 25% yield which had an inherent viscosity of 0.12 dl/g. Attempts to produce condensation products of higher molecular weight by further purification of solvents and reactants and by carrying out the condensation on a larger scale were without improved results.

PMR measurements of the compound showed PMR signals in the aromatic region which was dominated by a multiplet from 6.55 to 8.75δ, typical for a meta-disubstituted benzene ring. Overlapping this multiplet was a broad singlet at 8.06δ which was assigned to the C_6 amino group. The location of this amino peak was identical to that observed for the amine peak in poly(2,8-adeninediyl-1,4-phenylene) samples. Again the propyl ester groups were observed at 4.25δ, 1.65δ, and 0.90δ. The infrared spectrum, consistent with a nitrogen heterocyclic compound, showed absorption bands for aromatic rings, –C=N– and –N–H functions. Thermal degradation started at 260°C and showed a 30% weight loss by 400°C (Fig. 3).

An attempt was also made to liberate the free base in situ from

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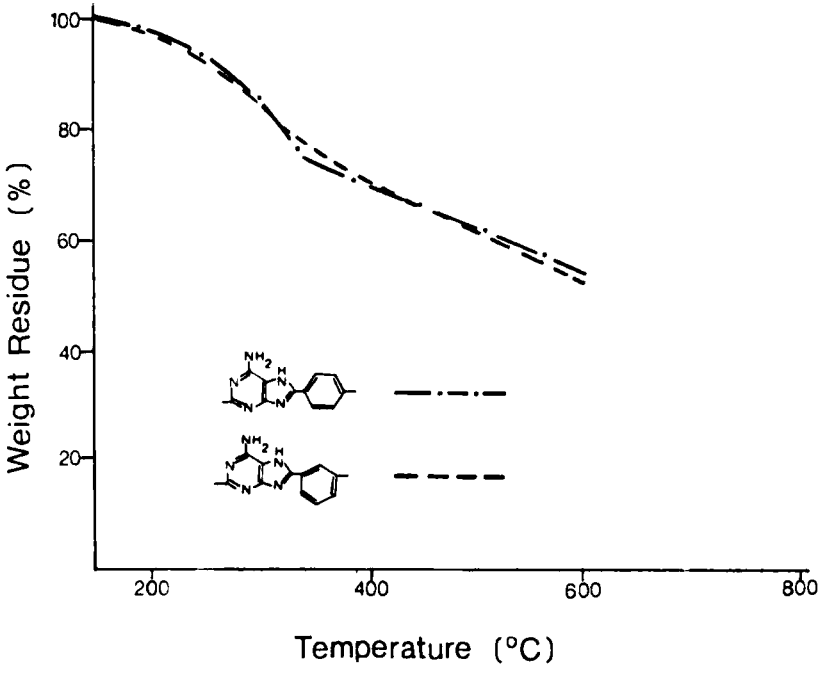

FIG. 3. TGA of adenine oligomers.

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AMDA · 2HCl in DMAc and Ag_2O and then allow it to condense with HMOI. After 1 hr condensation time a brown solid separated which was insoluble in all solvents including concentrated sulfuric acid (Table 1). Unsuccessful were also the attempts to condense HEOO with AMDA · HCl to obtain poly(2,8-adeninediyl).

Condensation of bisorthoesters was expected to occur according to the general scheme of the model compounds as depicted in Eq. (2), which in the case of the hypoxanthine derivative would go in two distinct steps. Adenines would react directly as has been previously demonstrated in this paper [Eq. (3)].

The polymer reaction for the preparation of adenine derivatives is shown in Eq. (4), and expecially the hypoxanthine derivatives were expected to go via the open chain products. Such intermediates, which have some similarities to the polyamic acids, the intermediates of the polyimide synthesis, were expected to provide a polymeric precursor of purine containing polymers or intermediates which could be fabricated and the ring then closed in a second step [Eq. (5)].

AMDA and AMAA are penta- and tetrafunctional derivatives which, however, for cyclization reactions can act as difunctional monomers,

TABLE 1. Adenine-Containing Oligomers: AMDA · 2HCl + Bisorthoester

Bisorthoester	Solvent type	Temp, (°C)	Yield, (%)	Color	η (DMSO)
HPOT	DMSO (Py 10)	100	49	gold	0.01
HMOT	DMAc	170	67	gray	insoluble
HPOI	DMSO (Py 10)	100	25	light brown	0.12
HMOI	DMAc	170	61	gray	insoluble
HEOO	DMSO (Py 10)	100	gum		

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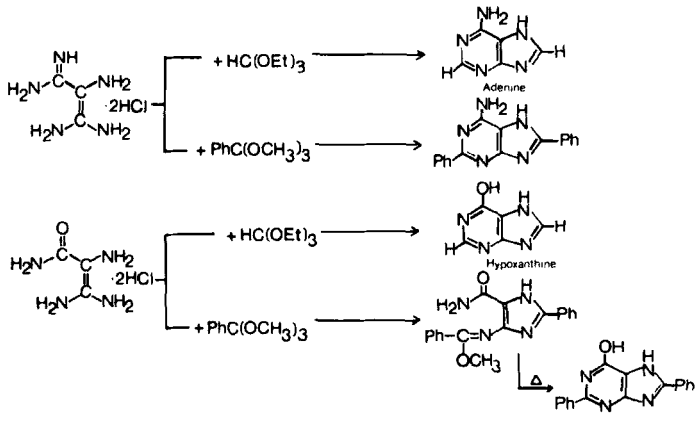
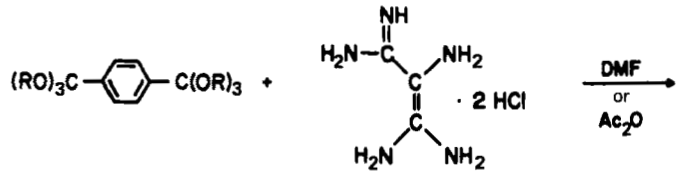
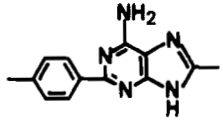


(3)

conceptionally similar to the aromatic tetramines which are used for the preparation of polybenzimidazoles. What is different in such condensations of AMDA and AMAA is that they must react in the enamine form. Furthermore, all amino groups are basically aliphatic amines, which are more reactive than aromatic amines but are not stable as the free bases and must be kept as the 2HCl salts. This may be the reason why even model reactions do not give 100% yields of condensation products as in the case of the formation of benzimidazoles or polybenzimidazoles.

One other point should be mentioned: purines are basically unsymmetric molecules and can be arranged in a polymer structure as





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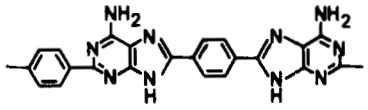

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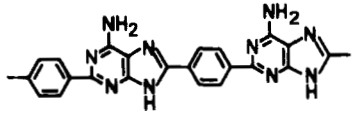

or

OH instead of NH_2 (5)

head-to-tail or head-to-head structures or a random mixture of both [Eq. (6)] [40]. We believe that the head-to-head structure should be favored because the imidazole ring is more easily closed than the pyrimidine ring. If this likely suggestion is correct it might also explain why our condensation reaction of bisorthoesters and AMAA did not give high polymers.

Hypoxanthine-Containing Oligomers

AMAA · 2HCl with HPOT in DMSO at 100°C gave after 12 hr reaction time and precipitation a dark brown powder in 91% yield with an inherent viscosity of 0.10 dl/g. Infrared and PMR spectra are consistent with a heterocyclic ring system but with strong propyl ester end groups in the PMR and with a 1H-purine-6-one structure. Thermal analysis showed a weight loss beginning at 250°C and a 20% loss at 400°C.

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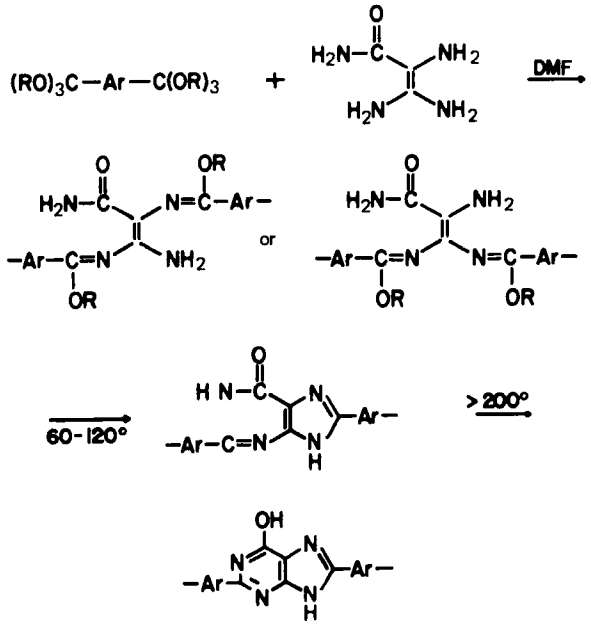

(6)

Poly(2,8-hypoxanthinediyl-1,4-phenylene) was also prepared in two steps. The condensation of AMAA · 2HCl with hexamethyl orthoterephthalate (HMOT) in either DMF or DMAc at 165° C for 2 hr afforded a low yield (55-62%) of a material in which the imidazole ring but not the pyrimidine ring was closed. The two identical products were identified by inspection of their PMR and infrared spectra. The PMR spectrum showed two overlapping broad singlets at 7.40-8.10δ. The absorption at 8.10δ was assigned to the four equivalent p-phenylene protons while the one at 7.40δ was assigned to the carboxamide protons. The methyl imino ether protons were observed as a singlet at 3.9δ. The PMR spectrum was very similar to that observed for the model compound 2-phenyl-4-(α-methoxybenzylideneamino)imidazole-5-carboxamide. The inherent viscosity of this imidazole polymer was also 0.10 dl/g.

Conversion to poly(2,8-hypoxanthinediyl-1,4-phenylene) was accomplished thermally. The conditions for this ring closure were determined by DSC. A sample of poly[(5-carboxamido-4,2-imidazolediyl)-1,4-phenylene(methoxymethylene) nitrilo] when heated in a DSC-1B apparatus showed an exothermic transition at 250-300° C.(Fig. 4). At

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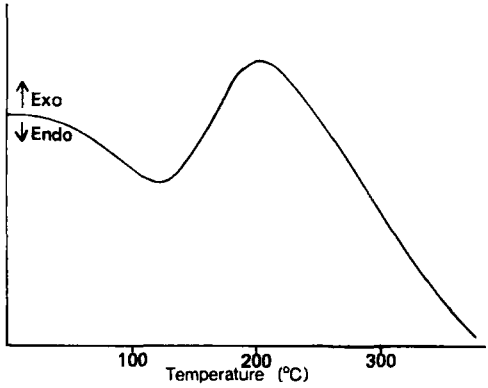

FIG. 4. DSC scan of poly[5-carboxamido-4,2-imidazolediyl)-1,4-phenylene(methoxymethylene) nitrilo].

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the same time the effulent analyzer showed that a volatile material was being released. This volatile material was trapped in a 10 cm gas cell and identified by infrared as methanol. On the basis of this information, poly[(5-carboxamido-4,2-imidazolediyl)-1,4-phenylene-(methoxymethylene) nitrilo] was heated in vacuo to 260° C for 5 hr to give a good yield (83%) of dark brown poly(2,8-hypoxanthinediyl-1,4-phenylene). The polymer had an inherent viscosity of 0.10 dl/g. Poly(2,8-hypoxanthinediyl-1,4-phenylene) was identified by inspection of the PMR spectrum. The PMR spectrum showed only a single broad peak at 8.4δ for the four equivalent p-phenylene protons. As for all of the imidazole containing materials produced, the imidazole N–H proton was not observed in the 0-10δ range. The presence of methyl end groups as a singlet at approximately 4.0δ suggested that the product was also of low molecular weight. The absence of an exothermic DSC transition at 250-300° C eliminated the possibility that this methyl signal was due to incomplete closure of the pyrimidine ring.

AMAA · 2HCl condensed with HPOI in DMSO at 100° C to give a 47% yield of oligomer of an inherent viscosity of 0.08 dl/g. It showed three broad peaks in the PMR spectrum from 8.75δ to 7.65δ and the propyl ester end group. Thermal degradation of the material started at 280° C, and 20% weight was lost at 400° C (Fig. 5). The same material was also prepared in a two-step synthesis in DMAc (Table 2).

Poly(2,8-hypoxanthinediyl-1,3-phenylene) was also prepared by a two-step procedure in which the intermediate was a poly[(5-carboxamido-4,2-imidazolediyl)-1,3-phenylene(alkoxymethylidene) nitrilo] which could be converted to poly(2,8-hypoxanthinediyl-1,3-phenylene)

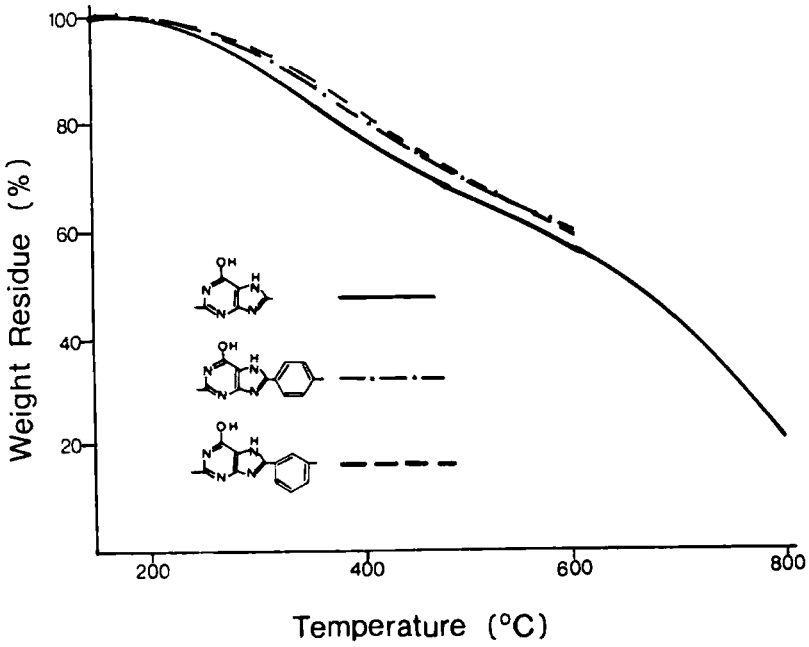

FIG. 5. TGA of hypoxanthine oligomers.

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by thermally closing the pyrimidine ring. This condensation was carried out with two different orthoesters and in three different solvents. AMAA · 2 HCl condensed with HMOI at 165°C and gave poly[(5-carboxamido-4,2-imidazolediyl)-1,3-phenylene(methoxymethylidene) nitrilo]. The PMR spectrum showed a broad multiplet at 7.2δ to 8.8δ for the four aromatic and two amide protons while the methoxy protons gave a singlet at 3.9δ. Under the same conditions, the condensation of AMAA · 2HCl and HMOI with HMPA as the solvent, no product could be isolated.

The condensation of AMAA · 2HCl with HPOI in DMAc gave poly[(5-carboxamido-4,2-imidazolediyl)-1,3-phenylene(n-propoxymethylidene) nitrilo] in a 5% yield with an inherent viscosity of 0.10 dl/g. The PMR spectrum was similar to that observed by condensing AMAA · 2HCl with HMOI in DMAc. Propyl groups were observed as absorption peaks at 4.35δ, 1.90δ, and 1.00δ. Both intermediates were ring closed by heating at 250°C for 30 hr in vacuo; the ring-closed compound was obtained in nearly quantitative yield. The two-step procedures had, however, no advantages over the one-step synthesis in DMSO.

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TABLE 2. Hypoxanthine-Containing Oligomers, AMAA · 2HCl + Bisorthoester

Bisorthoester	Solvent type	Temp (12 hr) (°C)	Yield (%)	Color	η (DMSO)
HPOT	DMSO (Py 10)	100	91	dark	0.10
HMOT	DMF	165	55	dark green	not ring closed
HMOT	DMAc	165	62	dark green	not ring closed
	ring closure:	260 (5 hr)	83	brown black	0.10
HPOT	DMSO (AgO, K_2CO_3)	100	30	brown	-
HPOI	DMSO (Py 10)	100	47	brown	0.08
HMOI	DMF	165	64	dark green	not ring closed
HMOI	DMAc	165	60	dark brown	-
HMOI	HMPA	170 (20 min)		black gum	-
HPOI	DMAc	165	57	light tan	0.10
	ring closure:	260 (5 hr)	88	brown black	not ring closed
		250 (30 min)	100	light brown	-
HEOO	DMSO (Py 10)	100	88	brown	0.06

TABLE 3. UV Data for Purine Oligomers and Model Compounds

	λ_{max} (nm)[a]	$E^{1\%}_{1cm}$
Adenine	257	1000
	261	1000
2,8-Diphenyladenine	250	735
	339	2283
Hypoxanthine	242	1080
	249	820
2,8-Diphenylhypoxanthine	257	862
	308	527
Poly(2,8-adeninediyl-1,4-phenylene)	285	1470
Poly(2,8-adeninediyl-1,3-phenylene)	248	1552
Poly(2,8-hypoxanthinediyl-1,4-phenylene)	319	496
Poly(2,8-hypoxanthinediyl-1,3-phenylene)	300	1504
	230	928
Poly(2,8-hypoxanthinediyl)	310	300
	261	279

[a]The ultraviolet absorption spectra were measured on concentrated sulfuric acid solutions of the polymers.

AMAA · 2HCl condensed with HEOO in DMSO and gave the reaction product in 88% yield and an inherent viscosity of 0.06 dl/g. PMR was not useful because of the absence of protons in the repeat unit which fall in the 0-10 ppm range.

Analysis of the resulting products was not easy because of the inherent problems associated with analyzing purine derivatives by C, H and N analysis. End-group analysis by PMR had indicated that the materials were of low molecular weight.

We have now tried to fit the data from the PMR end-group analysis, information from the UV (Table 3) and infrared spectra, and particularly the careful examination of the results from the C, H, and N elemental analysis, and we believe that our condensation products have the structures I-III.

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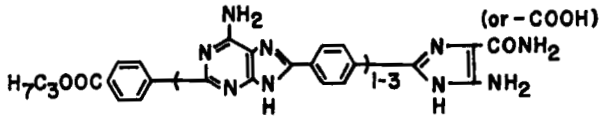

I

Amide Structure, n = 1: C, 60.35%; H, 4.66%; N, 25.34%.
Calculated, n = 2: C, 61.18%; H, 4.28%; N, 27.75%.

Acid Structure, n = 1: C, 60.23%; H, 4.45%; N, 22.48%.
Calculated; n = 2: C, 61.09%; H, 4.13%; N, 25.73%.

Found for para-compound: C, 58.97%; H, 4.84%; N, 24.22%.
meta-compound: C, 58.16%; H, 5.25%; N, 22.64%.

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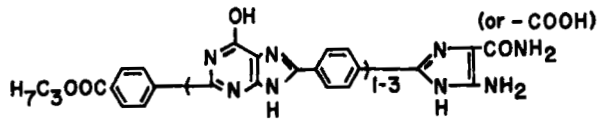
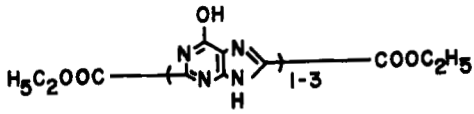


II

Amide Structure, n = 1: C, 60.23%; H, 4.45%; N, 22.48%.
Calculated, n = 2: C, 61.01%; H, 3.98%; N, 23.72%.

Acid Structure, n = 1: C, 60.11%; H, 4.27%; N, 19.63%.
Calculated, n = 2: C, 58.30%; H, 3.67%; N, 20.78%.

Found for para compound: C, 59.31%; H, 4.13%; N, 21.21%.
meta compound: C, 59.63%; H, 4.14%; N, 21.29%.



III

Calculated for $C_{16}H_{14}N_8O_6$, n = 2: C, 46.38%; H, 3.41%; N, 27.05.
Found: C, 46.96%; H, 3.92%; N, 27.46%.

CONCLUSIONS

We have prepared oligomers from HPOT, HPOI, HEOO and AMDA · 2HCl and AMAA · 2HCl which, after isolation have one to three purine rings in the chain and ester as one end group and probably an acid or amide group as the other end group. This results indicates that the ring closure of the pyrimidine ring does not function properly under the conditions that we employed for this reaction to be used as a polymer-forming reaction. We cannot decide exactly whether this is caused by some impurity in the amidines or whether this is inherent in the reaction, but we suspect the latter to be the case.

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