Macromolecules 1988, *21*, 1995–2001

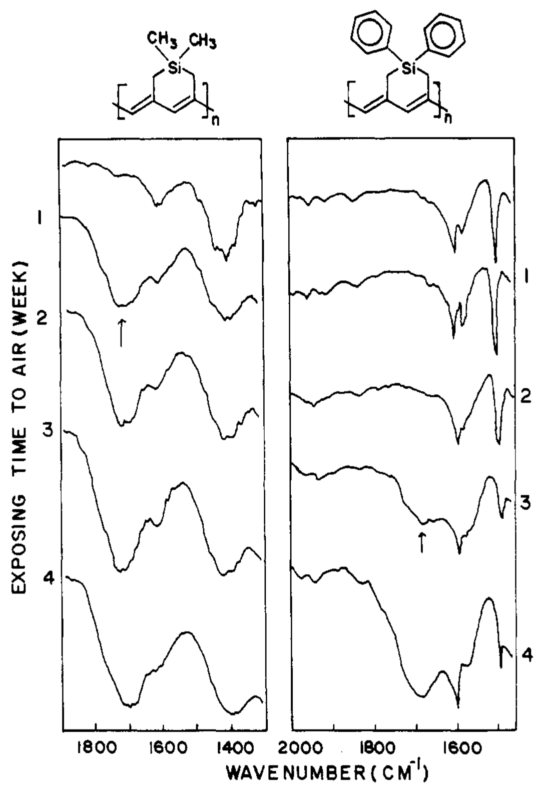

Figure 7. Comparison of oxidation stability to air at room temperature of poly(dimethyldipropargylsilane) and poly(diphenyldipropargylsilane).

were also more stable to oxidation than those having a smaller substituent.

In conclusion, (1) the catalytic activity of $MoCl_5$ was generally greater than that of WCl_6 in this cyclopolymerization; (2) $MoCl_5$ alone was the most effective catalyst for the cyclopolymerization; (3) cyclopolymers having bulkier substituents have better properties such as solubility, air stability, and thermal stability than those having smaller substituents.

In the present study, we found that these polymers had good solubilities in common organic solvents. We are now attempting to increase electric conductivity by homogeneous film casting.

Registry No. PDMPS, 114199-11-0; PMPPS, 114199-13-2; PDPPS, 114199-14-3; $MoCl_5$, 10241-05-1; Bu_4Sn, 1461-25-2; $EtAlCl_2$, 563-43-9; WCl_6, 13283-01-7; $TiCl_4$, 7550-45-0; $PdCl_2$, 7647-10-1; I_2, 7553-56-2.

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Site-Selective Derivatization of Oligoethylenimines Using Five-Membered-Ring Protection Method

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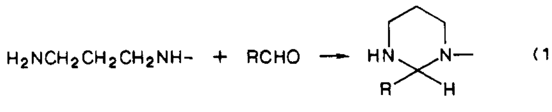
ABSTRACT: Application of modified Ganem's method was found to be effective for derivatization of oligoethylenimines (diethylenetriamine, triethylenetetramine, and pentaethylenehexamine) to site-selectively substituted products. The method involves protection of amino groups with aldehydes by formation of five-membered rings, resulting in only necessary NH groups remaining at which substituents should be introduced. The protective five-membered ring was readily deprotected to recover the amino groups after the necessary substitution reactions were carried out. This protecting method was applied to site-selective thiourea derivatizations and synthesis of completely linear heptaethyleneoctamine. The results suggest the protecting method to be highly promising in designing oligoethylenimine derivatives for a variety of applications including monomers in condensation polymerization.

Introduction

Selective reactions of $—NH_2$ and $=NH$ groups in oligoethylenimines have been a challenging problem in organic and polymer chemistry. It has been highly difficult to derivatize oligoethylenimines at the desired amino groups. The reason is that the basicities of primary (NH_2) and secondary (NH) amino groups differ only slightly, i.e., by 2 pK_a units at most.[1,2] Recently, Ganem[3,4] opened a new route to site-specific derivatization of naturally occurring oligoamines, i.e., spermine, spermidine, and other related amines, by reacting aldehydes to form six-membered protecting rings (eq 1). His basic concept is based on the stability of the six-membered ring that is the highest compared with those of the rings containing other numbers of member.



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Since oligoethylenimines are commercially available, their potential importance on an industrial scale as well

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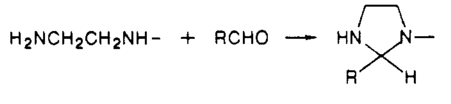
as on a laboratory scale has been well established. However, the usefulness of oligoethylenimines has been largely limited, especially with respect to sophisticated molecular designs based on the oligoamine chains. For instance, it has been difficult to prepare terminally mono- or disubstituted oligoamines of high purities, completely linear heptaethylenoctamine, and so on.

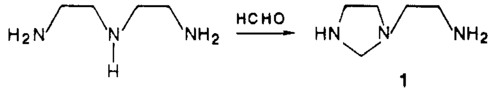
It is well-knwon that the stability of five-membered rings is somewhat lower than that of six-membered rings, but the stabilities of these rings are much higher than those of three-, four-, seven-, eight-, and higher membered rings. Hence, we tried to apply Ganem's protecting method to oligoethylenimines, in believing that five-membered rings should be formed in a high predominance in these cases (eq 2). As a result, we found that this five-membered-ring


(2)

protecting method is quite useful for site-selective derivatizations of diethylenetriamine, triethylenetetramine, and pentaethylenehexamine. At the same time, a new effective deprotection method (eq 17) was also developed.

Results and Discussion

Reaction of Diethylenetriamine with Formaldehyde. Simple mixing of equimolar amounts of diethylenetriamine and HCHO in aqueous solution under ice-cooling afforded 2-imidazolidyl-1-aminoethane (1) quantitatively (eq 3). Compound 1 showed a characteristic singlet signal due to the NCH_2N methylene proton at 3.42 ppm in ^1H NMR.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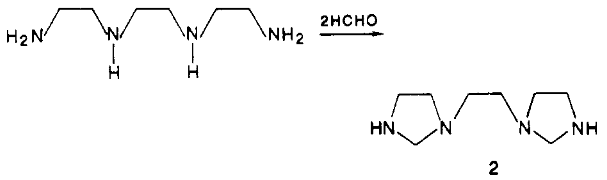
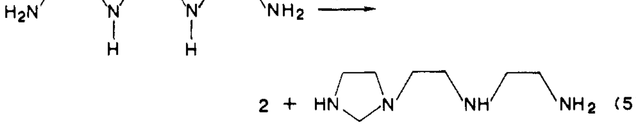
Reaction of Triethylenetetramine with Formaldehyde. Mixing of triethylenetetramine with HCHO in a molar ratio of 1:2 in water or in EtOH under ice-cooling gave generally quantitative yields of 1,2-bis(*N*-imidazolidyl)ethane (2, eq 4). However, in some cases the


(4)

2

reaction in water gave paraformaldehyde or gellike materials during the reaction. Hence, we recommend the use of ethanol as the solvent rather than water, though 35–37% aqueous formalin solution is employed in the reaction.

When the amount of HCHO was adjusted to a slight excess relative to a 1:1 molar ratio, a mixture of 2 and monocyclic product, 2-(*N*-imidazolidyl)-2′-aminodiethylamine (3) as the predominant one, was obtained (eq 5).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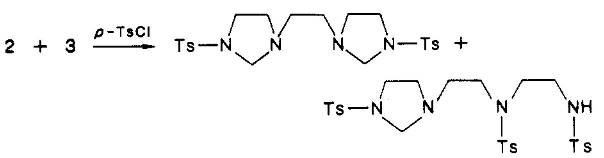
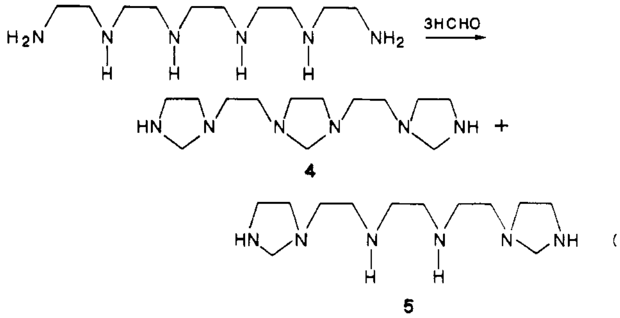
Tosylation of the mixture gave the ditosylate of 2 and the tritosylate of 3 (eq 6), respectively. The latter tosylate was isolated in a pure form from the mixture by extraction with boiling ethyl acetate.


(6)

Reaction of Pentaethylenehexamine with Formaldehyde. We observed that mixing of this oligoamine with excess HCHO in EtOH under ice-cooling gave the desired tricyclic product (4). But in this case it was rather difficult to avoid the formation of bicyclic byproduct 5 (eq 7).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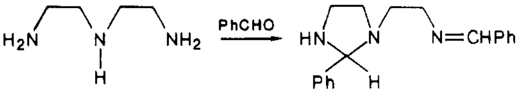
5

The desired tricyclic compound 4 was found to be effectively synthesized by reacting with dry HCHO generated from paraformaldehyde upon heating in the anhydrous EtOH solution of pentaethylenehexamine. When an excess amount of HCHO was reacted, the NMR spectrum of the product became somewhat complicated, suggesting the formation of certain higher molecular weight compounds. This difficulty was overcome by controlling the termination of the protection reaction by NMR spectroscopically monitoring the relative intensities of NCH_2N and NH proton signals of the reacting mixture to agree with the theoretical values.

Reaction of Diethylenetriamine with Benzaldehyde. The reactions of diethylenetriamine with PhCHO were somewhat different from those with HCHO, i.e., a Schiff base moiety (6) was produced in addition to the formation of a five-membered ring at the same time (eq 8), in accordance with the Ganem's observation.[4] This protecting method is useful for derivatization of this amine at the only terminal NH group.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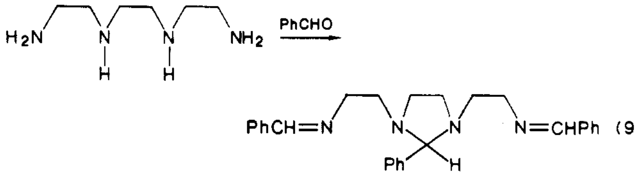
Reaction of Triethylenetetramine with Benzaldehyde. Contrary to the expectation for obtaining the bicyclic compound of the diphenyl derivative of 2, this reaction gave 1,3-bis(2-(benzalamino)ethyl)-2-phenylimidazolidine (7, eq 9), when a large excess amount of HCHO was reacted. Namely, only one five-membered ring was formed at the central portion of the tetramine, and two Schiff bases were attached to both ends of the molecule. The structure was identified by estimating its molecular weight from the gel permeation chromatography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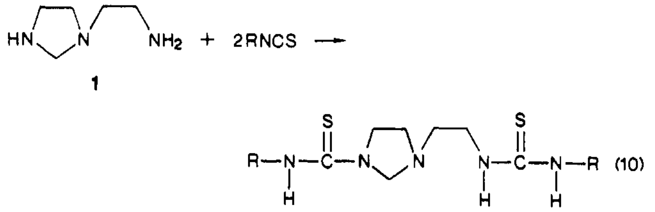
7

(GPC) diagram and by comparing its IR and ^{1}H NMR spectra with those of the corresponding Schiff base of $EtNH_2$. Absence of NH groups in 7 was confirmed by the fact that no ^{1}H NMR spectral change was observed by addition of a small amount of D_2O. Interestingly however, compound 7 was found to be usable for terminal bisderivatization as long as PhNCS was reacted (vide infra). For preparation of a protected compound with two five-membered rings alone it seems necessary to adjust carefully the reaction conditions including the molar ratio of the tetramine to benzaldehyde. This is not realized at present.

Derivatizations of Protected Oligoethylenimines. (A) Reaction with Isothiocyanates. For test experiments of site-selective derivatization of the protected oligoethylenimine, phenyl isothiocyanate (PhNCS) or dehydroabietyl isothiocyanate (DANCS) was reacted. The former isothiocyanate was chosen as a typical example of derivatization with simple substituents, and the latter with sterically very bulky hydrophobic substituents. As expected, reaction of DANCS (RNCS in eq 10) with compound 1 proceeded to give a terminally bisthioureanized product (8).



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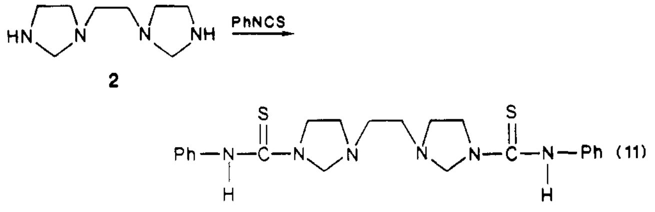
8 (10)

The reaction of 2 with PhNCS gave a terminally bisthioureanized product 9, also as expected (eq 11).



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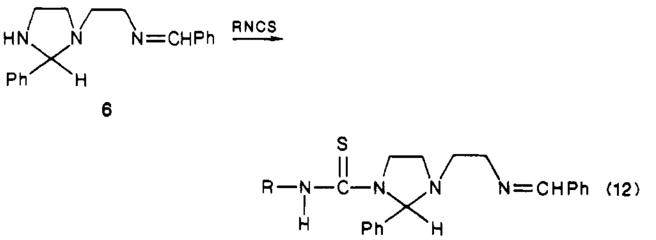
9 (11)

The reaction of benzaldehyde-protected triamine 6 with DANCS formed a terminally monosubstituted compound (eq 12). However, the corresponding tetramine 7 was



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10′ (12)

found to react in an unexpected way, i.e., the protecting groups (two terminal Schiff bases and a central five-membered ring) rearranged to two protecting five-membered rings at the expense of one molecule of benzaldehyde, and the bisderivatization with PhNCS occurred at the terminals of the tetramine 11 (eq 13). This behavior of 7 suggests that the Schiff base type protection is unstable relative to the five-membered-ring-type protection, and the interconversion from the former to the latter occurs with considerable readiness. This is probably because the Schiff base is the precursor of the imidazolidine ring closure.

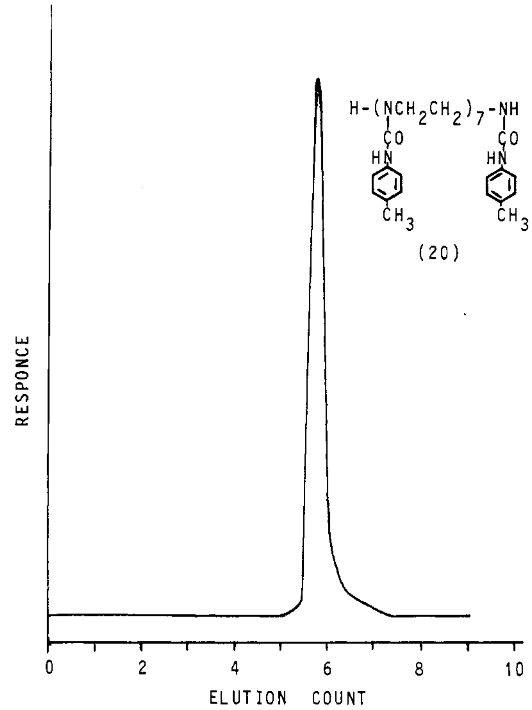
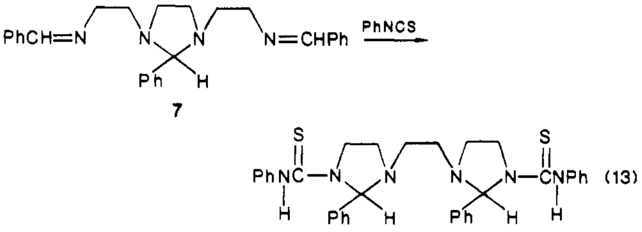


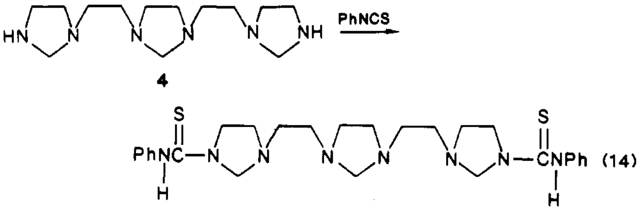
Figure 1. GPC diagram of octakis(*N*-*p*-tolylcarbamoyl)heptaethylenoctamine (**20**).



7

11 (13)

The reaction of PhNCS with the tris-ring-protected hexamine 4 gave a bis-terminally thioureanized product (12, eq 14) in a considerably high yield, judged from the GPC diagram and spectral data. Purification of this product with an effective procedure is under investigation.



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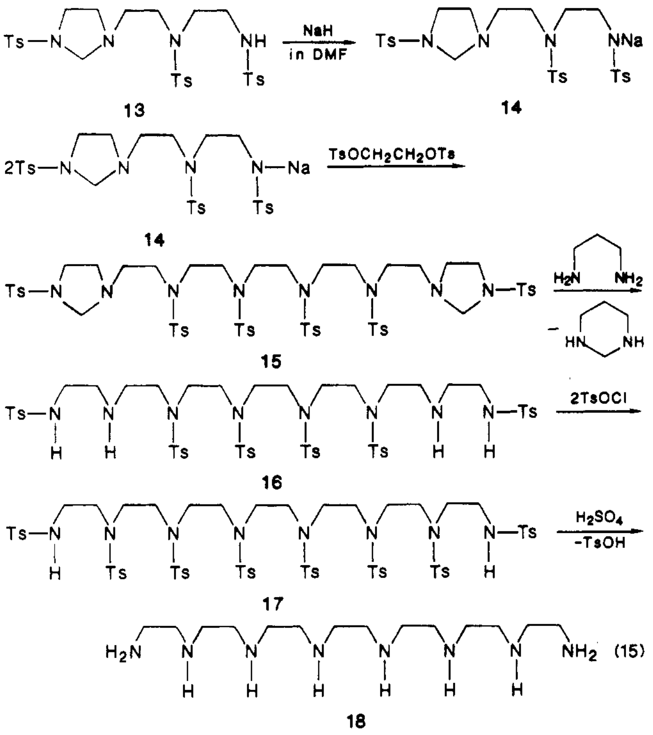
12 (14)

(B) Chain Elongation from Tetramine to Linear Octamine. The most stringent objective of our finding an effective site-specific derivatization of oligoamines is to synthesize the completely linear heptaethyleneoctamine in a preparative scale. It is because this linear octamine is the key backbone-chain compound of our highly interesting "pendantly ureanized octameric oligomers",[5-15] which were prepared by ring-opening polymerization of the corresponding ureanized aziridines.[16,17] For identification of the "true active species" in the polymerized oligomer mixtures having molecular weight distributions, the pure candidate compound has had to be synthesized.

The linear heptaethyleneoctamine has been commercially unavailable. In addition, attempted chain elongation from the unprotected triethylenetetramine with ethylene dibromide or with some related disubstituted ethylene compounds always gave a branched octamine, although the branched octamine is also an important backbone molecule for a series of our study of "urea oligomers".[9]

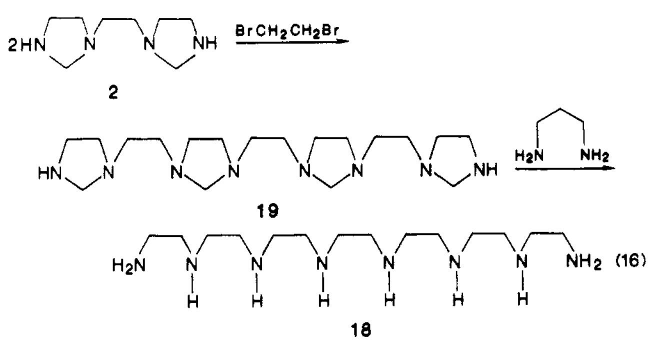
The approach of linear dimerization of triethylenetetramine was challenged in two ways: The first (procedure 1) involves metallation of the tritosylate formed in eq 6 (13) with NaH followed by the dimerization with ethylene ditosylate to 15 and subsequently deprotection with triethylenediamine to give the hexatosylate of heptaethyleneoctamine (16), tosylation to octatosylate (17), purification of 17, and finally detosylation of 17 to obtain linear heptaethyleneoctamine (18, eq 15).

procedure 1



The second (procedure 2) involves direct dimerization of compound 2 with ethylene dibromide (eq 16) to 19,

procedure 2



followed by deprotection with triethylenediamine to give free heptaethyleneoctamine (18); 18 was then purified carefully by distillation in vacuo, removing triethylenetetramine and polymerized higher oligoamines.

Although procedure 1 is found successful in obtaining the desired linear octamine, this route is usable only for synthesis of very small amounts of the product. This is due to the difficulty in the process of detosylation after dimerization. On the other hand, procedure 2 is found to be more convenient, although it requires careful distillation of 18 or 19.

The heptaethyleneoctamine 18 obtained showed no NCH_2N methylene proton signal in ^1H NMR. The octamine 18 was further reacted with *p*-tolyl isocyanate to obtain octakis(*N*-*p*-tolylcarbamoyl)heptaethyleneoctamine (20), which showed an extremely sharp single peak in GPC (Figure 1) at the expected elution count, i.e., almost correctly on the linear line of log MW versus elution count observed for two series of the pure samples of tosylate and ureanized compounds (Figure 2). In addition, the analytical values observed for 20 agreed almost satisfactorily with the theoretical values.

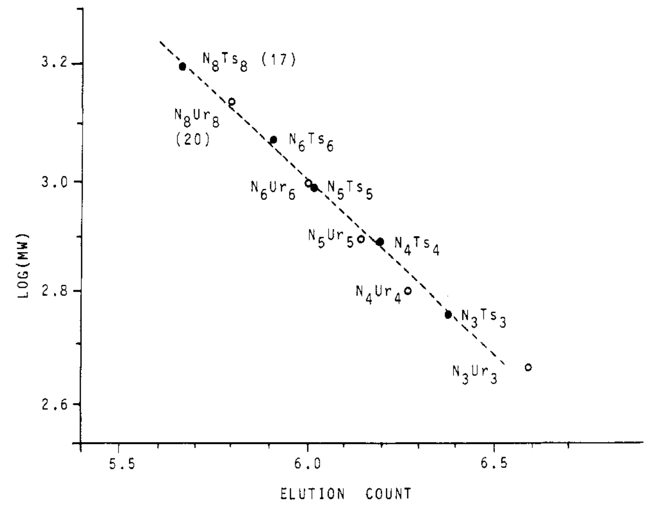
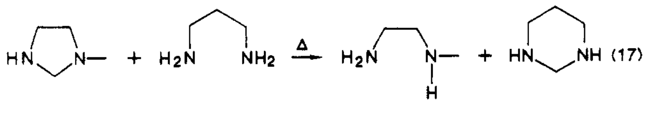


Figure 2. Linear relation between log MW versus GPC elution count for tosylated and ureanized oligoamines: (●) per(*N*-tosyl)oligoethylenimines from diethylenetriamine tritosylate (N_3Ts_3) to heptaethylenoctamine octatosylate (N_8Ts_8); (○) per(*N*-arylcarbamoyl)oligoethylenimines from tris(*N*-arylcarbamoyl)diethylenetriamine (N_3Ur_3) to octakis(*N*-arylcarbamoyl)heptaethylenoctamine (N_8Ur_8).

Deprotection of the Five-Membered-Ring Compounds. The most advantageous point of the five-membered-ring protection compared with the Ganem's six-membered-ring protection is that it is possible to use a "ring-exchange method" for deprotection. For the six-membered deprotection, treatment with acid is a standard method. However, since the five-membered ring is somewhat unstable relative to the six-membered ring, treatment of the five-membered imidazolidyl compounds with trimethylenediamine resulted in a volatile six-membered hexahydropyrimidine and the deprotected oligoamines. The key reaction is shown in eq 17, and in practice



the procedure was readily performed by simply heating the five-membered protected oligoamines with the diamine in dioxane (whose boiling point is nearly identical with hexahydropyrimidine), followed by distillation of the solvent.

Importantly, this process can be carried out in a "basic condition", and no salt is formed with the oligoamines after deprotection. This is highly favorable for simplifying the overall synthetic procedures and also for preventing loss of the purity and yields of the final oligoamines.

The deprotection method is typically exemplified in the synthesis of heptaethyleneoctamine (involved in eq 15 and 16), which was applied to the synthesis after examinations with a variety of site-selectively derivatized oligoamines described in the former sections. In all cases of formaldehyde protection, the reaction of eq 17 proceeded quite smoothly. In the case of benzaldehyde protection, however, the resulting phenylhexahydropyrimidine is more difficult to remove from the reaction system because of its high boiling point. In this case the normal acid treatment followed by distillation or extraction of benzaldehyde and then alkaline treatment were more convenient.

Note that the deprotection by trimethylenediamine is not suitable for the compounds having thiourea residues, because the C=S group in the thiourea groups transfers into hexahydropyrimidinethienone, resulting in decomposed primary amines.

Further Potential Applications of the Site-Selective Derivatization of Oligoethylenimines. Although we have tested the site-selective derivatization methods for a few types of reactions, far-reaching applications of the method will be expected. One of them is the application to the polymerization in which free or protected oligoamine units are incorporated, and hence a variety of basic and polycationic hydrophilic polymers can be designed. Some basic features of application of this method to the polymer synthesis are being investigated progressively[18] and will be published elsewhere.

Other potential application is modification of various type of compounds by introducing the oligoamine tails having affinities for biological tissues, especially polyanions. Our observations reported here by using dehydroabietyl groups suggest that considerably bulky lipophilic compounds can be modified by our methods. Further, this method may be also significant for the synthesis of macrocyclic amines and their derivatives.

Thus, the modifications of Ganem's approaches made in the naturally occurring oligoamines[3,4] will also contribute extensively to the synthetic oligoethyleneimines, which have more industrial and scientic possibilities in a wide range of chemistry. Ganem's work will be of much greater value than he described.

Experimental Section

Materials. Diethylenetriamine, triethylenetetramine, and tetraethylenepentamine were commercially supplied and used without further purification. Commercial pentaethylenehexamine was carefully distilled in vacuo to remove contaminated tetraethylenepentamine. Formalin (35 to 37%) solution was used for formaldehyde protection. In the case of formaldehyde protection for pentaethylenehexamine, commercial paraformaldehyde was used as the formaldehyde source. Other reagents were commercially obtained and used without further purification.

Apparatus. A Shimadzu-Du Pont Model-830 apparatus (HSG-15 gel, 50 cm) was used for probing molecular weight and/or its distribution, since a difference of one phenyl group caused a detectable difference in the elution time. In this case estimation of molecular weight was made by using precalibrated values. A Nihon Denshi Model JNM-MH-100, a Hitachi Model 260-50, a Nihon Bunko Model UVIDEC-510, and a Nihon Bunko Model DIP-140 apparatuses were used for measurements of ^{1}H NMR, IR, UV-vis spectra, and optical rotation, respectively.

Synthesis of Dehydroabietyl Isothiocyanate (DANCS). According to the general method for conversion of amines to isothiocyanate,[19] 100 mL of benzene solution of dehydroabietylamine (0.1 mol) was added dropwise to 50 mL of ice-cooled aqueous solution containing 0.1 mol of CS_2 and 0.1 mol of NaOH at 10–15 °C with stirring. Then the reaction temperature was gradually elevated and kept at 75–85 °C for 2 h. The resulting red solution was cooled to 35–40 °C, and 0.1 mol of $ClCO_2Et$ was slowly added. The benzene layer was separated, evaporated, and dried in vacuo. The crude product was adsorbed on the SiO_2 gel packed in a 20 × 200 mm glass column. The fraction eluted with benzene was collected, and the eluent was adsorbed on a new SiO_2 gel column. Fractionation was then carried out by eluting with *n*-hexane, and pure fractions were collected by monitoring with GPC. The product was a pale yellow viscous oil: GPC (THF) 7.09 count, single peak; $[\alpha]_D$ −33.4° (*c* 2.3, C_6H_6); IR (KBr) 2100 and 2200 cm^{-1} ($\nu_{N=C=S}$); NMR, characteristic AB quartet due to $CH_2N=$ centered at δ 3.4 appeared.

General Method of Formaldehyde Protection of Oligoamines. Method a.[20] To an ice-cooled aqueous solution of oligoamine, 37 or 35% formalin was added dropwise for 20 min with stirring. After being stirred for a further 1 h, the reaction mixture was concentrated in vacuo. Then, tablets of KOH were carefully added to the condensate under ice-cooling until a two-phase solution was obtained. The oily upper phase was extracted with $CHCl_3$, followed by extraction of the aqueous phase with $CHCl_3$. After the extracts were combined, the $CHCl_3$ solution was dried with Na_2SO_4 and filtered, and then the $CHCl_3$ was removed in vacuo.

Method b. To a dried ethanol solution of oligoamine, dry paraformaldehyde was suspended, and the mixture was heated to boiling for ca. 15 min. The reflux was stopped before unexpectedly complicated signals were observed in the ^{1}H NMR spectrum upon monitoring the aliquots of the reaction mixture.

Synthesis of 2-Imidazolidyl-1-aminoethane (1) from Diethylenetriamine. The use of method a together with 0.1 mol of diethylenetriamine (50 mL of H_2O) and an equimolar amount of HCHO (8.5 g of formalin) gave a quantitative yield of colorless viscous liquid of the desired product: NMR ($CDCl_3$) 10 H (δ 2.42–3.20, m, NCH_2CH_2N and NH_2), 2 H (3.42, s, NCH_2N), and 1 H (8.14, m, =NH).

Synthesis of 1,2-Bis(*N*-imidazolidyl)ethylenediamine (2) from Triethylenetetramine. The use of method a together with 0.1 mol of triethylenetetramine (70 mL of H_2O) and 0.22 mol of HCHO (18.9 g of formalin) gave a quantitative yield of pale yellow viscous liquid of the desired product: NMR ($CDCl_3$) 2 H (2.28, s, =NH), 12 H (2.40–3.24, m, NCH_2CH_2N), and 4 H (3.57, s, NCH_2N).

Synthesis of 2-(*N*-Imidazolidyl)-*N*-(2-ethylamino)ethylamine (3) from Triethylenetetramine. The use of method a together with 0.07 mol of triethylenetetramine (50 mL of H_2O) and 0.07 mol of HCHO (5.5 g of formalin) gave the viscous oily compound **3** as main product containing a small amount of compound **2** in a high yield: NMR ($CDCl_3$) ca. 3 H (2.28, s, =NH), 12 H (2.40–3.24, m, NCH_2CH_2N), and ca. 2 H (3.57, s, NCH_2N).

Synthesis of 1,3-Bis(*N*-imidazolidyl)imidazolidine (4) from Pentaethylenehexamine. The use of method b together with 1.38 g of pentaethylenehexamine (100 mL of EtOH) and 0.62 g (3.2 molar excess) of paraformaldehyde gave a quantitative yield of pale yellow viscous liquid of the desired product: NMR ($CDCl_3$) 22 H (2.7–3.1, m, NCH_2CH_2N plus =NH), 6 H (3.48, br s, NCH_2N); IR (KBr) closely resembles that of the compound **2**.

General Method of Benzaldehyde Protection of Oligoamines. Method c. To an ethanol solution of oligoamine more than 2 mol equiv of benzaldehyde was added dropwise at room temperature with stirring. After being stirred for further 8–40 h, the solvent was removed in vacuo. If necessary, the residue was recrystallized from a suitable solvent such as ethanol.

Synthesis of 2-(2-Phenylimidazolidyl)-1-(benzalamino)ethane (6) from Diethylenetriamine. The use of method c together with 0.01 mol of diethylenetriamine (20 mL of $EtOH/Et_3N$ (1:1 v/v)) and 0.02 mol of PhCHO gave 98% yield of a pale yellow viscous liquid of the desired product: NMR ($CDCl_3$) 8 H (2.2–3.1 and 3.3–3.7, two m's, NCH_2CH_2N), 1 H (3.75, s, CH), 10 H (7.3, 7.7, two m's, Ph), and 1 H (8.15, s, CH=N); IR (KBr) 1640 cm^{-1} ($\nu_{C=N}$).

Synthesis of 1,3-Bis(2-(benzalamino)ethyl)-2-phenylimidazolidine (7) from Triethylenetetramine. The use of method c together with 0.068 mol of triethylenetetramine (100 mL of EtOH) and 0.206 mol of PhCHO gave viscous material after evaporation of the solvent. The product was recrystallized from ethanol: yield 35%; mp 87.2–87.9 °C; NMR ($CDCl_3$) 12 H (2.2–3.1 and 3.3–3.7, two m's, NCH_2CH_2N), 1 H (3.75, s, CH), 15 H (7.3, 7.7, two m's, Ph), and 2 H (8.15, s, CH=N); IR (KBr) 1640 cm^{-1} ($\nu_{C=N}$).

The structure of **7** was confirmed by comparing the spectroscopic behaviors of the corresponding EtN=CHPh, i.e., NMR ($CDCl_3$) 3 H (3.4–3.8, m, NCH_2 and CH), 5 H (7.3, 7.7, two m's, Ph), and 2 H (8.18, s, CH=N); IR (KBr) 1640 cm^{-1} ($\nu_{C=N}$).

General Methods of Deprotection. Method 1. To the formaldehyde-protected oligoamine a considerably large amount of dioxane solution containing an excess amount of trimethylenediamine was added and heated to reflux. After a given reflux period, dioxane was distilled out under a moderately reduced pressure. Pure dioxane was then added to the residue, and it was distilled out again. This procedure was repeated until no hexahydropyrimidine was observed in the dioxane distillate.

Method 2. To a solution of the formaldehyde-protected oligoamine a given amount of aqueous HCl was added, and the mixture was heated for a given period until the formaldehyde formed was evaporated. Then, the mixture was neutralized, and the desired deprotected product was extracted with a suitable solvent.

Method 3. To a solution of the benzaldehyde-protected oligoamine an excess amount of trimethylenediamine was added and heated to ca. 100 °C under effective agitation. The solvent was then removed under reduced pressure. Since the residue contains 2-phenylhexahydropyrimidine, it is necessary to remove this compound by extraction with a suitable solvent such as ether.

Method 4. To a solution (e.g., ethanol) of the benzaldehyde-protected oligoamine a given amount of aqueous HCl was added, and the mixture was heated for a given period until the smell of benzaldehyde became very strong. The mixture was then neutralized, and the solvent was removed by moderate blowing of N_2 to the remaining aqueous phase. Ether extraction gave the desired deprotected product without benzaldehyde. The product was transferred into a suitable organic layer (e.g., benzene/*n*-PrOH (2:1 v/v)) under a concentrated alkaline condition.

General Method of Thioureanization of Protected Oligoamines.[20] To an aqueous solution of oligoamine a given amount of isothiocyanate was added dropwise as suitable solution (e.g., THF for PhNCS and benzene for DANCS) at room temperature. After 1 h of agitation, the reaction mixture was refluxed for 24 h and cooled, and the solvent removed in vacuo. In the case of reaction with PhNCS, the crude product was washed with Et_2O or *n*-hexane to give white powdery product. In the case of reaction with DANCS, the crude product was purified by washing with Et_2O followed by *n*-hexane.

The examples of products and their deprotections were as follows:

2-(3-Dehydroabiethylthiocarbamoylimidazolidyl)-*N*-(dehydroabiethylthiocarbamoyl)ethanamine (8) was prepared from **1** and DANCS to give a yellow tacky solid: GPC (THF) single peak at 6.08 count (corresponds to MW ca. 800 (calcd 769 as bisthioureanized). The GPC peak of DANCS at 7.2 count was completely eliminated. Characteristic NMR signals of the DA moiety was observed in addition to the NCH_2N singlet signal at δ 4.45. Deprotection by using method 2 gave ^1N,^3N-bis(*N*-dehydroabietylthiocarbamoyl)diethylenetriamine in 57% yield. The δ 4.45 signal due to the NCH_2N signal disappeared almost completely. Instead, a prominent NH proton signal was newly formed at δ 2.15. GPC (THF) 6.08 count.

1,2-Bis(*N*-(*N'*-phenylthiocarbamoyl))-1,2-diaminoethane (9) was prepared from **2** and PhNCS to give a white powder (32%): mp 162.8–163.9 °C; GPC (THF) main peak at 6.45 count (corresponds to MW ca. 410 (calcd 440 as bisthioureanized) with slight impurities of higher MW; IR (KBr) 1525 cm^{-1} (ν_{CSNH}); NMR (DMSO-d_6) 10 H (2.2–3.4 and 3.4–4.4, two m's, NCH_2CH_2N), 4 H (ca. 4.3, two s's, NCH_2N), 10 H (7.1–7.4, br m, Ph), 1 H (9.0, s, NH), and 1 H (9.7, s, NH).

Synthesis of ^{1}*N*-(Dehydroabietylthiocarbamoyl)diethylenetriamine (10) via 2-[3-(Dehydroabietylthiocarbamoyl)-2-phenylimidazolidyl]-1-(benzalamino)ethane (10′): Reaction of DANCS (0.01 mol) with the protected triamine Schiff base **6** (0.01 mol in benzene) followed by recrystallization from benzene/*n*-hexane gave the compound **10′** as an almost single species in GPC. The thioureanized protected Schiff base **10′** was deprotected with acid (method 4) to give a single species (GPC 6.8 count) in 61% yield. NMR showed reasonable proton ratios for NCH_2 to aromatic protons and methyl protons in the dehydroabietyl moiety; in addition, a prominent NH proton signal was newly formed at δ 1.2.

Synthesis of Bis[(3-phenylthiocarbamoyl)-2-(phenylimidazolidyl)]ethane (11) from 1,3-Bis(2-(benzalamino)ethyl)-2-phenylimidazolidine (7). Reaction of **7** with 10 molar excess of PhNCS in THF (72 h at room temperature) gave the oily product. It was washed with *n*-hexane followed by drying, resulting in an 84% yield of white powder: GPC (THF) single peak at 6.46 count (corresponding to tetraphenyl substitution); mp 114.1–115.7 °C; NMR ($CDCl_3$) 12 H (2.7–4.2, m, NCH_2CH_2N), 2 H (4.15, s, CH), 15 H (7.0–7.6, m, Ph), 1 H (8.25, s, NH), and 1 H (9.65, s, NH); IR (KBr) 1625 ($\nu_{C=N}$, m) and 1520 cm^{-1} (ν_{CSNH}, s).

Synthesis of Linear Heptaethylenoctamine (18) from the Protected Triethylenetetramine 2. Procedure 2. An EtOH solution (100 mL) containing 6 g of **2** was refluxed for 0.5 h with 0.5 molar equiv of 1,2-ethylene dibromide in EtOH solution (100 mL) in the presence of solid KOH with vigorous stirring. After filtration the solvent was evaporated in vacuo, resulting in a viscous oily material (**19**): NMR ($CDCl_3$) ca. 30 H (2.4–3.3, m, NCH_2CH_2N) and ca. 8 H (3.59, s with slight satellite signals, NCH_2N). The product **19** (3 g) was deprotected by the use of method 1 with 50 mL of dioxane and 10 mL of trimethylenediamine. The residue (3 g) was distilled in vacuo with a molecular distillation device, and a fraction of heptaethylenoctamine (**18**) was collected, whose boiling range was 150–200 °C: yield 33%, NMR ($CDCl_3$) 10 H (1.61, s, =NH) and 28 H (2.3–3.0, two m's centered at 2.50 and 2.82 NCH_2CH_2N). In the NMR spectrum the signal due to the NCH_2N proton completely disappeared. IR showed only a simple pattern of common alkylamines. The eight amino groups of **18** were completely ureanized with 10 molar excess of *p*-tolylisocyanate in THF (20 mL) at 55 °C to give a pale yellow powdery product after purification by using SiO_2 gel column chromatography eluting with THF/benzene (1:9 v/v): yield 20%; mp 145–148 °C; GPC (THF) single peak at 5.8 count accurately corresponds to the octaphenyl derivative, i.e., the count was correctly on the calibration line made by a series of pendant urea oligomers from di- to hexapendant pure compounds. Anal. Calcd for $C_{78}H_{94}H_{16}O_8$ (1382): C, 67.34; H, 7.20, N, 16.11. Obsd: C, 67.18; H, 7.04; N, 15.48.

Procedure 1.[20] An aqueous alkaline solution (250 mg of NaOH) of the mixture of the monoprotected tetramine (**3**) containing a small amount of bis-protected tetramine **2** (total 1 g) was tosylated in a usual manner with tosyl chloride (2.79 g) and NaOH (400 mg) in H_2O (total 19 mL) and ether (5 mL) to give a mixture of tris- (**13**) and bis-tosylated (**2**-Ts_2) compounds. Extraction of the mixture with boiling ethyl acetate, followed by deposition upon cooling to room temperature gave pure tris-tosylated product (**13**): GPC (THF) single peak at 6.41 count; NMR ($CDCl_3$) 9 H (2.39 and 2.43, two s's, aromatic CH_3), 4 H (2.62 and 3.38, two m's, ring NCH_2CH_2N), 8 H (3.15, m, acyclic NCH_2CH_2N), 2 H (4.14 s, NCH_2N), 1 H (6.90, br, =NH), and 12 H (7.28, br d, and 7.70, q, aromatic H). Compound **13** (2.34 g) in DMF was monometallated with NaH (DMF-soluble portion was used) by carefully controlling the temperature between 100 and 120 °C and by monitoring the gas evolution. After the monometallation was completed, 0.76 g of ethylene glycol ditosylate was added dropwise at 100 °C and the mixture was stirred for 3 h. DMF was evaporated at 60 °C in vacuo, then the residue was extracted with $CHCl_3$, and the extract (**15**) was washed with ether several times: GPC (THF) single peak at 5.8 count as expected from the calibration line made with a series of pure oligoamine tosylates from tri- to hexamine; NMR ($CDCl_3$) 18 H (2.40, s, aromatic CH_3), 18 H (2.80, and 3.30, two m's, NCH_2CH_2N), 4 H (4.14, s, NCH_2N), and 24 H (7.36 and 7.74, m and d, aromatic H). The hexatosylated and bis-protected heptaethylenoctamine **15** thus obtained was first deprotected by the use of method 1 with trimethylenediamine. The product was directly tosylated with *p*-tosyl chloride and NaOH as described above to result in compound **17**: GPC (THF) single peak at 5.6 count as correctly on the same calibration line as above; NMR ($CDCl_3$) 24 H (2.40, s, aromatic CH_3), 28 H (2.7–3.6, br m, NCH_2CH_2N), and 32 H (7.42 and 7.70, two br s's, aromatic H). The two =NH protons were found to overlap the 7.70 aromatic H signal. The compound **17** was hydrolyzed with concentrated H_2SO_4 (95%); the resulting *p*-toluenesulfonic acid and H_2SO_4 were then removed by repeating the elution through Amberlite columns. The resulting aqueous solution was concentrated in vacuo and alkalized with NaOH, and the residue was carefully extracted with $CHCl_3$, dried with Na_2SO_4, and extracted again with $CHCl_3$. The resulting highly viscous tacky solid (**18**) after evaporation of $CHCl_3$ showed no phenyl signals in NMR, and the IR spectrum was almost identical with those of common alkylamines. The reaction product of **18** and excess of PhNCO was found to contain octakis(*N*-phenylcarbamoyl)heptaethylenoctamine (**20′**) as shown by GPC peak observed at 5.85 count, which agreed with the expected value from the calibration line. But it was rather difficult to separate the product (**20′**) from a large amount of the byproduct diphenylurea.

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Nitrobenzyl Ester Chemistry for Polymer Processes Involving Chemical Amplification

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ABSTRACT: Three esters, 2-nitrobenzyl, 2,4-dinitrobenzyl, and 2,6-dinitrobenzyl tosylate, were synthesized and evaluated as photoprotected toluenesulfonic acids. These materials are of interest because they are nonionic, highly soluble agents for the deep UV photogeneration of acid and may be particularly useful in certain microelectronic applications where the demand for a low dielectric constant material dictates the use of nonionic materials in processing. The effectiveness of these tosylate esters as photogenerators of acid was evaluated by determining their quantum efficiency and thermal and hydrolytic stability and by comparing the lithographic sensitivities of resist systems consisting of the esters and poly[*p*-[(*tert*-butoxycarbonyl)oxy]-α-methylstyrene]. The quantum efficiencies ranged from 0.02 to 0.18 depending upon nitro substitution patterns and did not change significantly with excimer laser exposure.

Introduction

Photochemically labile protective groups are known to have numerous synthetic applications[1] and have also been shown to exhibit utility in microlithography.[2,3] Materials that generate acidic species are of particular interest for this latter application. Onium salts that photochemically generate strong acids may be employed in chemical amplification resist processes,[4–6] while 2-nitrobenzyl photochemistry has been used in the development of solution-inhibition, deep-UV resists.[3,7–9] Recently, the nitrobenzyl protecting group was utilized in chemical amplification resist systems.[10] An ester-based system exhibits a number of advantages over alternative acid precursors[11] for electronic applications. Specifically, the nitrobenzyl derivatives are easily synthesized, are soluble in a variety of organic solvents, are nonionic in character, and contain no refractory elements such as arsenic or antimony. In addition, their absorption characteristics are well suited for deep-UV exposure. In this study, we examine 2-nitrobenzyl ester photochemistry and its utility in chemical amplification processes. The thermal and solvolytic stability of selected esters is investigated, and the effect of substitution on the quantum yield for acid generation is examined. The results are discussed in relation to the lithographic performance of these materials.

Experimental Section

1. **Materials.** The syntheses of *p*-[(*tert*-butoxycarbonyl)oxy]-α-methylstyrene and its corresponding polymer were adapted from the literature.[4,12] Organic starting materials were obtained from the Aldrich Chemical Co. with the exception of 2,4-di-

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