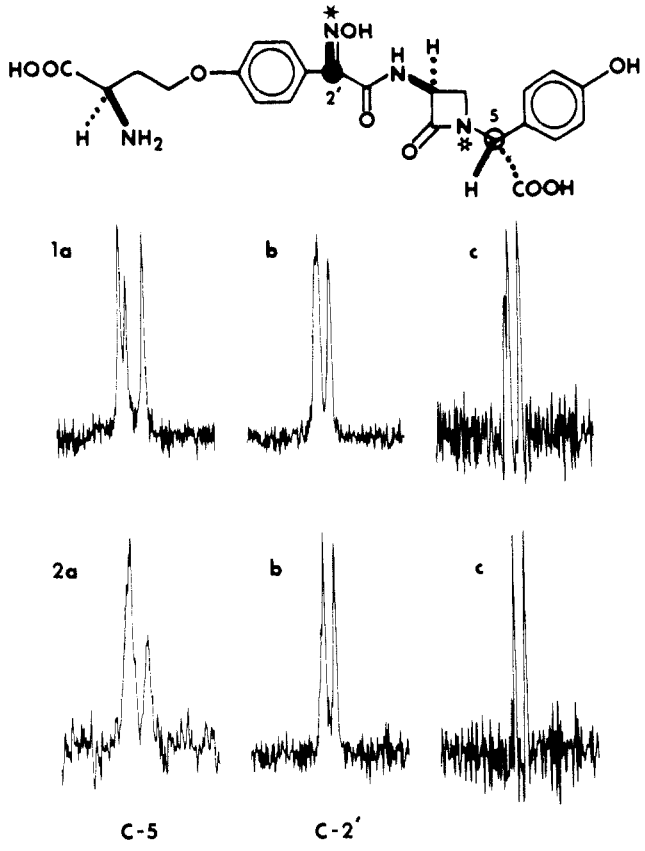

Figure 1. Partial $^{13}C\{^1H\}$ NMR spectra (expansions 50 Hz wide) obtained at 100.54 MHz on a Varian XL-400 spectrometer. Spectra 1(a-c) are of nocardicin A (20.4 mg/3.0 mL D_2O) derived from incorporation of [2'-^{13}C,^{15}N]epinocardicin G (**6**): (a) 500 transients, C-5 singlet 61.6 ppm, doublet 1.75 Hz upfield, $^1J_{CN}$ = 7.5 Hz, (b) 4000 transients, C-2' singlet 153.8 ppm, doublet 2.6 Hz upfield, $^1J_{CN}$ = 3.4 Hz, (c) 4000 transients, C-2' resolution enhanced RE = 0.225, AP = 0.675. Spectra 2(a-c) are of nocardicin A (7.1 mg/3.0 mL D_2O) derived from incorporation of [2'-^{13}C,^{15}N]nocardicin G (**5**): (a) as above, 50 000 trasients, (b) as above, 40 000 transients, (c) as above, 40 000 trasients.

as shown in Figure 1. Spectral expansions from the incorporation of the LLD-diastereomer **6** are represented in 1(a-c) and those from the DLD-diastereomer **5** are shown in spectra 2(a-c). The data are arrayed in each instance as (a) C-5 (61.6 ppm), (b) C-2' (153.8 ppm), and (c) C-2' after resolution enhancement. For [2'-^{13}C,^{15}N]epinocardicin G (**6**) carbon label was found to randomize totally into C-5 and C-2' of nocardicin A, 22% and 20%, respectively, accompanied by 25-30% loss of ^{15}N (*). It is quite apparent that this substrate was efficiently degraded to doubly-labeled PHPG prior to utilization. However, in sharp contrast [2'-^{13}C,^{15}N]nocardicin G (**5**) gave a 21% incorporation of label selectively at C-2' [spectrum 2(b), a remarkably high value for a whole-cell experiment] with negligible attendant ^{15}N-exchange (<5%). Amplification of the C-5 region [spectrum 2(a)] revealed an approximately 2.5% incorporation of carbon label at this locus accompanied by significant loss of ^{15}N, presumably owing to limited degradation of the precursor or possibly of a diastereomeric impurity.[10]

In conclusion, we have prepared a doubly-labeled sample of nocardicin G (**5**), the structurally simplest member of the nocardicin family, and have demonstrated its intact incorporation into nocardicin A (**1**). This finding establishes the central intermediate of the pathway and suggests the existence of an at present unknown precursor composed of most probably two D-PHPG units and L-serine. As evidenced by the rapid degradation of epinocardicin G (**6**), the presence of D-PHPG residues may confer proteolytic stability to both this hypothetical precursor and to nocardicin G to allow elaboration of the latter by amine oxidation and reaction with methionine to the other members of this antibiotic group.

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Registry No. 1, 39391-39-4; **5**, 65309-11-7; **6**, 99297-19-5.

Preparation of Polysilanes in the Presence of Ultrasound

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Sonochemical synthesis of organometallic compounds has recently received considerable amount of attention.[1] Not only have higher yields been reported but also new compounds have also been prepared. Sonochemistry is based on the implosive collapse of cavities with very high pressures and temperatures existing locally for a short time. Sonochemical reductive coupling of chlorosilanes with lithium leads to the formation of disilenes and cyclotrisilanes.[2] We have used a similar method for the preparation of high molecular weight polysilanes.[3] The latter materials have exciting photochemical and photophysical properties which confirmed earlier theoretical predictions concerning conjugation of the catenated Si-Si bonds in linear polymers.[4] The properties of polysilanes depend on the degree of polymerization[5] and structure-properties relationships should be established for well-defined species with controlled molecular weight and low polydispersities.

Polysilanes are typically prepared by reductive coupling with molten sodium in boiling toluene or xylene.[5] Polymers formed in this process have polymodal molecular weight distributions and, in addition to cyclics (Si_5 or Si_6), a low molecular weight polymer ($\bar{M}_n \approx 10^3$) and a high molecular weight polymer ($\bar{M}_n > 10^5$) are found. The polymer is separated from cycles by precipitation in, e.g., isopropyl alcohol, but polymer fractionation is usually difficult. Formation of a bimodal polysilane has been explained by diffusion phenomena;[4e] however, the alternative explanation could be based on multiple mechanisms of polymerization which operate simultaneously. For example, reactive intermediates involved in

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Table I. Results of the Sonochemical Synthesis of Different Polysilanes[a]

monomer	$PhMeSiCl_2$	$PhMeSiCl_2$	$PhMeSiCl_2$	$(n\text{-Hex})2SiCl_2$	$(n\text{-Hex})_2SiCl_2$	$PhMeSiCl_2$ + $(nHex)_2SiCl_2$ (1:1)	$PhMeSiCl_2$ + Ph_2SnCl_2 (1:1)
solvent	$PhCH_3$	$PhCH_3$	$PhCH_3$	$PhCH_3$	$PhCH_3$ (+25% diglyme)	$PhCH_3$	$PhCH_3$
°C	110	60	40	60	60	60	60
ultrasound		imm	cl bath	imm	imm	imm	imm
% polymer	55	12	11.1	0	24	12	75
HP/LP	1/3(1/9)	1/0	1/0		1/0	1/0*	3/1 #
M_n[d]·10^{-5} (HP)	1.07	1.04	1.3		0.45	1.75	
M_n·10^{-3} (LP)	3.3						1.0
M_w/M_n	1.81 (1.7)	1.5	1.20		1.73	1.66	(3.7)

[a] $[M]_0$ = 0.32 mol/L, toluene, $[Na]_0/[Si\text{-}U]_0$ = 1.2. [b] Reaction time: 60 min (thermal and immersion), 180 min (cleaning bath). imm (immersion type); cl bath (cleaning bath). [b] Ratio of $[PhMeSi]/[(n\text{-Hex})_2Si]$ in a copolymer was 1.5/1.0. [c] Ratio of $[PhMeSi]/[Ph_2Sn]$ in a low molecular weight copolymer; high polymer was insoluble in common organic solvents. [d] Molecular weights are based on polystyrene standards; vpo and light scattering measurements indicate that "true" molecular weights of polysilanes are approximately two times larger.

the reductive coupling could be radicals, anions, silylenes, strained cyclosilanes, or disilenes. High and low molecular weight chains could be formed by two different mechanisms. Various chemical reactions have different activation energies, and, by changing temperatures, different contributions of these reactions to the chain growth are expected. However, a decrease of temperatures below 100 °C leads to the formation of solid sodium which cannot react with dichlorosilanes.

We have used sonochemical synthesis of polysilanes at ambient temperatures, and we have found the formation of monomodal high molecular weight polymers. The polydispersities of these polymers could be below $\bar{M}_w/\bar{M}_n < 1.2$. Polysilanes are prepared with an immersion type probe or with usual ultrasonic cleaning baths.[6]

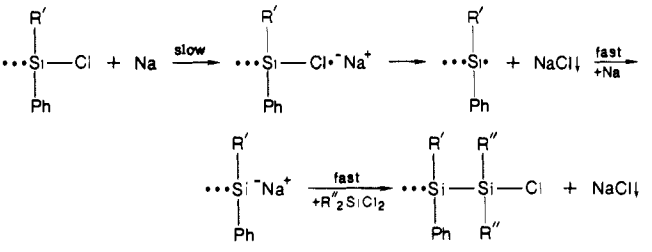
Three phenomena may be related to the formation of monomodal polymers. The first one is the preferential contribution of one type of intermediates in the sonochemical reductive coupling. The second one accounts for the formation of high quality sodium dispersion[7] which is continuously regenerated during the coupling process. The third phenomenon is related to the selective degradation of polysilanes with higher molecular weights.

Sonochemical homopolymerization of dichlorosilanes is successful at ambient temperatures in nonpolar aromatic solvents (toluene, xylenes) only for monomers with α-aryl substituents. Dialkyldichlorosilanes do not react with sodium dispersion under these conditions, but they can be copolymerized with phenylmethyldichlorosilane. Copolymers that contain 30–45% dialkylsilanes are formed from equimolar mixtures. Copolymerization might indicate anionic intermediates. A chloro-terminated chain end can participate in a two-electron-transfer process with sodium.[8] The polymeric silyl anion can react with both dichlorosilanes although only phenylmethyldichlorosilane can react with sodium. Therefore, dialkyl monomers can copolymerize, but they cannot homopolymerize under sonochemical conditions. The growth via radical intermediates should lead to a homopolymer of phenylmethylsilane and unreacted dialkyldichlorosilane unless an extensive transfer process would operate. Large yields of cycles (<80%) which are products of end-biting reaction of anions with Cl-terminated chains also support anionic intermediates. Anions can react with both monomeric dichlorides in an S_N2 type reaction providing a copolymer.

Table II. Effect of Sonication Time on Molecular Weights and Polydispersities of Poly(phenylmethylsilylene)[a]

	during addition			after addition			
time (min)	5	10	15	30	60	80	120
M_n·10^{-5}	3.8	2.24	2.30	1.82	1.48	1.06	0.40
M_w·10^{-5}	17.3	6.68	6.35	3.73	2.57	1.57	0.47
M_w/M_n	4.5	2.98	2.71	2.05	1.73	1.48	1.17

[a] $[PhMeSiCl_2]_0$ = 0.32 mol/L, toluene, $[Na]_0/[Si\text{-}Cl]_0$ = 1.2, T = 60 °C, immersion type probe. Polysilane separated from the reaction mixture and sonicated in the presence of 0.2 equiv of Na degraded in the similar way.



The reductive coupling must start at the slow reaction between sodium and monomer and is followed by the much fast reactions involving polymeric species. Otherwise, no high polymer could be formed with an excess of sodium. The macromolecular silyl chloride should react with sodium in a two-electron-transfer reaction to form silyl anion. This anion reacts faster with a dichlorosilane than with a macromolecular silyl chloride. Thus, polymerization would resemble a chain growth process with a slow initiation and a rapid propagation.

Dialkyldichlorosilanes could be homopolymerized sonochemically at ambient temperatures only in the presence of etheral solvents.[9] For example, we prepared poly(di-*n*-hexylsilylene) with molecular weight $\bar{M}_n$ = 75000 in mixtures toluene/diglyme (1:1). Sonochemical synthesis has also been successfully applied to the preparation of copolysilanes and copolystannanes from mixtures of phenylmethyldichlorosilane and diphenyldichlorotin (cf. Table I).

The active surface of sodium dispersion may increase under ultrasonication.[7] This has the origin in the cavitational erosion of sodium malleable at this temperature. Ultrasound also assures local excess of sodium by the continuous regeneration of the metal surface. Similar effects were reported in the sonochemical hydrogenation with Ni catalysts.[10]

(6) Phenylmethyldichlorosilane (Petrarch) was distilled prior to use and dried over CaH_2. Toluene was distilled from CaH_2 and dried over CaH_2. Known amounts of sodium were placed in a flask filled with toluene and purged with dry argon. This flask was placed in the ultrasonic bath (75-1970 Ultramet II Sonic Cleaner, Buehler Ltd.) until stable dispersion of sodium was formed. In some experiments an immersion-type ultrasonic probe which allows better temperature control was used (W-140, Heat Systems-Ultrasonics, Inc.). A toluene solution of dichlorosilane was added to the reaction flask in a controlled manner under inert gas. The reaction was quenched after the required time by using equimolar mixtures of water and ethanol. The organic phase was later added to a large excess of isopropyl alcohol leading to the precipitation of the polymer. The polymer was dried, and the yield was determined gravimetrically. Molecular weights and polydispersities were determined by GPC by using polystyrene standards. The compositions of the polymers were measured by NMR. The filtrate remaining after the evaporation of the isopropyl alcohol was analyzed by GC/MS, GPC, and HPLC.

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We have found that high molecular weight polysilanes are rapidly degraded in the presence of ultrasound (cf. Table II). A similar effect has previously been observed for polystyrene, poly(methylmethacrylate), dextran, and other polymers.[11] Selective degradation is of a mechanical nature caused by friction forces between macromolecules and solvent molecules during the cavitation process. Larger molecules are more resistant to flow, have larger shear forces, and rupture more frequently than shorter macromolecules. Beyond certain molecular weight, shear forces are smaller than bond strengths, and polymers cannot degrade. This selective degradation not only reduces molecular weights to a certain value but also descreases polydispersity.

Thus, although low polydispersities can be explained by the selective degradation of polysilanes, the absence of low molecular weight polymers has the origin in the suppression of side reactions and probably in the promoting of the polymerization with anionic intermediates.

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Registry No. $PhMeSiCl_2$(homopolymer), 31324-77-3; $PhMeSiCl_2$-(SRU), 76188-55-1; $(n\text{-Hex})_2SiCl_2$(homopolymer), 97036-67-4; $(n\text{-Hex})_2SiCl_2$ (SRU), 94904-85-5; $(PhMeSiCl_2)((n\text{-Hex})_2SiCl_2)$(copolymer), 113925-33-0; $(PhMeSiCl_2)(Ph_2SnCl_2)$(copolymer), 113925-34-1.

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Mechanism of Adenylate Kinase. 3. Use of Deuterium NMR To Show Lack of Correlation between Local Substrate Dynamics and Local Binding Energy[1]

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The fact that enzymes utilize binding energy to bring about entropically unfavorable events and thus facilitate catalysis[2] suggests that enzymes are fundamentally involved in the control of substrate motion. We have examined the local motions of AMPPCP bound to adenylate kinase (AK) in order to examine the relationships between local rigidity of a bound substrate, binding energy, and catalysis by AK.

Chicken muscle AK was titrated with AMPPCP[3] deuteriated upon the phosphonate chain and upon the adenine ring[4] and followed by measuring the deuterium NMR line width ($\Delta\nu_{1/2}$) of the single peak which results from the average of the bound and free AMPPCP. Plots of $\Delta\nu_{1/2}$ versus $[AMPPCP]_{bound}/[AMPPCP]_{total}$ were linear, as shown in Figure 1. The line shapes of the observed peaks were usually Lorentzian, and limited T_1 inversion recovery data taken were always monoexponential. Upon

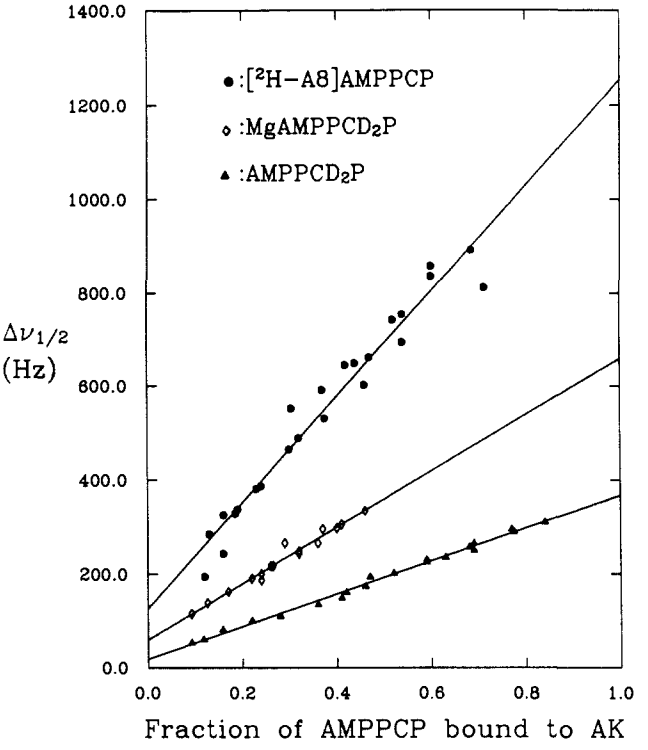

Figure 1. ^2H NMR (46.1 MHz) line widths ($\Delta\nu_{1/2}$ in Hz) of ^2H-labeled AMPPCP and MgAMPPCP ($[Mg^{2+}]/[AMPPCP] = 4$) as a function of fractions bound to AK, obtained by titrating 1-2 mM AK with the nucleotides. Sample conditions: pH 7.0 in ^2H-depleted H_2O with 45 mM Hepes-K^+ or imidazole-HCl, 117 mM KCl, 1-8 mM dithiothreitol, and 0.1 mM EDTA in a 10-mm NMR tube (starting volume of 1.75 ml) at 10 °C. Spectral conditions: digital resolution 1 Hz/point (narrow signals) to 15 Hz/point (very broad signals), 90 °C pulse width 12 μs. The reported $\Delta\nu_{1/2}$ have been corrected for line broadening (1-10 Hz). The fraction of AMPPCP bound to AK was calculated by using K_d values of 210 μM for AMPPCP and 190 μM for MgAMPPCP determined in our lab and elsewhere.[19,25]

increasing temperature from 5 °C to 35 °C, the line widths decreased with a magnitude approximately proportional to the decreasing solution viscosity. Thus, our data meet "fast-exchange" criteria, and the line widths of the fully bound species can be determined from linear extrapolations to fraction bound = 1.[5] Indeed very little extrapolation is required for two of the curves. The line widths obtained are listed in Table I. The effective rotational correlation times (τ_c) for isotropic motions were then calculated from the well-known relationship between line width ($1/\pi T_2$) and τ_c.[6-8] The contributions of two-bond ^2H-^{14}N and ^2H-^{31}P scalar and dipolar couplings to the observed $\Delta\nu_{1/2}$ were insignificant. The validity of the τ_c data determined from such analysis was further supported by the fact that the same τ_c values (within experimental errors) were obtained from T_1 experiments

(1) Abbreviations: AMPPCP, adenylyl (β,γ-methylene)diphosphonate; AK, adenylate kinase; ATP, adenosine 5'-triphosphate; AMP, adenosine 5'-monophosphate; EDTA, ethylenediamine tetraacetate; Hepes, *N*-(2-hydroxy ethyl)piperazine-*N*-2-ethanesulfonic acid; PPPi, triphosphate; T_1, spin-lattice relaxation time; T_2, spin-spin relaxation time.

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(3) It is assumed that AMPPCP interacts with AK in a motionally and energetically similar manner as ATP, since the observed binding energies (based on K_d) for ATP and AMPPCP are similar (-5.2 and -5.1 kcal/mol, respectively).

(4) [8-^2H]AMPPCP was prepared by heating AMPPCP in D_2O at pH_{obsd} = 10 for 3-6 h at 95 °C. $AMPPCD_2P$ was synthesized by modified literature procedures.[20,21]

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(7) We assume effectively isotropic motion (on an NMR time scale) since $\tau_c \ll$ [quadrupolar coupling constant]$^{-1}$. We also assume purely quadrupolar relaxation because of the relatively high quadrupolar coupling constants exhibited by deuteriated hydrocarbons due to aspherical electronic symmetry and because there are no reasons to expect a competing mechanism. For our calculations we utilized an asymmetry parameter of zero which is quite reasonable due to the axial symmetry of the electric field gradient of the deuterium nuclei in our compounds. Finally, we assume quadrupolar coupling constants of 178 MHz for [8-^2H]AMPPCP and 168 MHz for both $AMPPCD_2P$ and $MgAMPPCD_2P$. These values were chosen through chemical analogy with [8-^2H]AMP[22] and deuteriated malonic acid.[23] This is reasonable since ^2H quadrupolar coupling constants are quite invariant with even major covalent electronic perturbations.[23]

(8) Viscosity measurements were also performed (at room temperature) which suggest that the total viscosity change which occurred during the titrations is only ~5%.

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