geometry and the intensity ratio a measure of the C-S-S bond angles, ^{2,8} the observed spectral changes mean that the geometry of the disulfide linkages is more uniform in solution than in the solid state and that the C-S-S bond angles are smaller in solution.^{2,8} The line at 724 cm⁻¹ was assigned to the C-S stretching of trans-methionines by Lord and Yu.² When a comparison is made between the powder and solution spectra, a slight sharpening of the 724-cm⁻¹ line is noticeable.

In the amide III region (1220-1300 cm⁻¹), two resolved lines were observed at 1239 and 1260 cm^{-1} in the powder spectra. According to a recent study on the Raman spectra of glucagon in various conformational states, Yu and Liu¹¹ concluded that the α helical, random coil, and β structure of a protein should have the amide III vibrational frequencies at 1266, 1248, and 1232 cm⁻¹, respectively. On the other hand, the Xray diffraction studies of RNase A¹² and RNase S^{6,13} have revealed that the main chain of the molecule may roughly be divided into two parts with three sections of α helix (2–12, 26–33, and 50–58, totaling approximately 15% of the molecule) in the first half, and the bulk of the β structure (somewhat irregular) in the second half. With this information at hand, we assigned the line at 1239 cm⁻¹ to the β structure and the one at 1260 cm⁻¹ to the α helices. Upon dissolution, the 1260-cm⁻¹ line shifted to 1265 cm^{-1} and both lines sharpened.

Other manifestations of the conformational changes occur near 810 and between 870 and 980 cm^{-1} .

It is interesting to note that although the molecule consists of two distinct structural components in the main chain, the amide I region does not show this. Since the α helix and β structure are expected to have the amide I frequencies near 1660 and 1672 cm⁻¹, respectively,¹¹ the observed single line at 1669 cm⁻¹ in the powder spectra (or 1667 cm⁻¹ in the solution spectra) is probably the superposition of these two lines.

At the present time we are investigating the Raman spectra of RNase A crystals to determine whether the structure of the enzyme in crystals is the same as in solution or resembles that in the lyophilized powder. We are also investigating the S-peptide-S-protein binding interaction of RNase S both in crystals and in solution. Results on this aspect of the work will be presented in a future publication.

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Selective Formation of Symmetrical Bissulfides

Sir:

We report a remarkable selectivity in the dialkylation of ethanedithiol with alkyl halides of general formulas 1 and 2. The model halides 1 were easily prepared in high yields by treatment of acyl isocyanates² with N,Ndimethyl-p-phenylenediamine in acetonitrile at room temperature or with *p*-nitrophenylacetamide in boiling dioxane.



In a typical experiment, a solution of ethanedithiol (10 mol) and triethylamine (22 mmol) in 50 ml of acetonitrile was added to a suspension of $1_1(10 \text{ mmol})$, mp 195-196°, and 2₂ (10 mmol), mp 164.5-165.0°, in 200 ml of acetonitrile with stirring at room temperature over a period of 2 hr. Stirring was continued for an additional 12 hr at room temperature. The reaction mixture was evaporated, treated with water, and dried in vacuo. The resulting brown solid gave 3_1 (38%), mp 236.0-236.5° dec (DMF-acetonitrile) [Anal. Calcd for $C_{24}H_{32}N_6O_4S_2$: C, 54.13; H, 6.06; N, 15.78; S, 12.02. Found: C, 54.11; H, 5.89; N, 15.95; S, 12.16], and 4_2 (31%), mp 194–195° dec (acetonitrile) [Anal. Calcd for $C_{26}H_{28}N_6O_{10}S_2$: C, 48.15; H, 4.35; N, 12.96; S, 9.87. Found: C, 48.07; H, 4.24; N, 12.83; S, 10.16], on successive treatments with boiling DMF-acetonitrile, acetonitrile at room temperature, and boiling acetonitrile. No unsymmetrical bissulfide $(5_{1,2})$ could be isolated from the residual solid. All the results are summarized in Table I. The structural assignment of the bissulfides is based on their elemental analyses and the infrared and nmr spectra. The infrared spectra of 3_1 , 4_1 (mp 172–175° dec), and $5_{1,1}$ ³ [Anal. Calcd for $C_{24}H_{28}N_6O_7S_2$: C, 50.00; H, 4.90; N, 14.58; S, 11.11. Found: C, 49.81; H, 4.73; N, 14.85; S, 11.02] were readily distinguishable. The structures of bissulfides were further confirmed by

(1) All new compounds in this paper gave satisfactory elemental analytical values.

(2) A. J. Speziale and L. R. Smith, J. Org. Chem., 27, 3742 (1962).

⁽³⁾ The DTA curve of 51,1, which was recrystallized from dichloroethane, under a nitrogen atmosphere, showed two endothermic peaks at 126 and 175°, suggesting that 51,1 might be a liquid crystal. In addition, this compound is vellow in a solvent and turned pale orange in This change in color is reversible. air.



Figure 1. Plots of the yields of the corresponding symmetrical bissulfides vs. reaction time for 2_2 (\blacktriangle) and 9 (\odot) in acetonitrile at 26.0°. The yields are based on the weight of the bissulfides practically isolated.

Table I. Reaction^{*a*} of Ethanedithiol with 1_m and 2_n

Chlorides (1 and 2)		Time,	Temp,	Reac-	Yield, ^e % (isolated)		
m	п	hr	°C	tion ^b	3_m	4 _n	$5_{m,n}$
1	1	12	26	Α	35	27	4
1	2	12	26	Α	38	31	0
2	2	12	26	Α	36	30	4
1	2	4	70	В	34	18	0
2	2	6	45	В	36	29	5

^a Solvent, CH₃CN; concentration, 0.04 *M*. ^b A, heterogeneous; B, homogeneous. ^c Yields are calculated in such a way that complete conversion of 1_m and 2_n to 3_m and 4_n or to $5_{m,n}$ is 50 and 50 or 100%, respectively. It was shown by the that 4 involves a very small amount of 3.

ammonolysis. For example, treatment of 4_2 with ammonia in methanol gave the corresponding acylurea derivative 6 (75%), mp 243.5–244.0° dec, and *p*-nitrophenylacetamide (75%).

$$4_2 \xrightarrow{\text{NH}_3} (\text{CH}_2\text{SCH}_2\text{CH}_2\text{C}-\text{N}-\text{C}\text{NH}_2)_2 + 2\text{H}_2\text{NCCH}_2 \longrightarrow \text{NO}_2$$

The showed that $5_{1,1}$ was neither destroyed nor converted into a mixture of 3_1 and 4_1 under the conditions shown in a typical experiment.⁴ The data in Table I clearly indicate that the two symmetrical bissulfides (3 and 4) are formed selectively under both heterogeneous and homogeneous conditions. This result demonstrates conclusively that the selectivity is neither ascribed to the reaction being heterogeneous nor due to solubility differences between 1 and 2.

It is suggested that hydrogen bonding plays an important role⁵ in this selectivity. Reaction⁶ with a pair

(4) It should be noted that 96% of 3_1 , 94% of $5_{1,1}$, and 88% of 4_1 were indeed recovered from the mixture of these three bissulfides by the procedure described in a typical experiment.

(5) Because of low solubility in chloroform, the infrared spectra of 1 and 2 could not be measured by employing the dilution technique. However, it has been demonstrated that some acylurea derivatives form strong N-H \cdots O intermolecular hydrogen bonds in chloroform: T. Mukaiyama, T. Endo, and S. Noguchi, *Tetrahedron Lett.*, 2291 (1971). (6) This reaction proceeded much more slowly than that with 1 and 2. The residual solid proved to consist of at least five unknown products other than the three bissulfides by tlc. Low yields of the three bissulfides are presumably due to the formation of these unknown by products.

of chlorides 7 (mp 140.0-140.5°) and 8 (mp 110-112°),



model compounds probably incapable of forming intermolecular hydrogen bonding, under the same conditions as in a typical experiment gave two symmetrical bissulfides [8% (mp 222.0-222.5° dec) and 10% (mp 163.5-164.5°)] and the unsymmetrical one (20%), mp 140-144° dec. This product ratio (8:20:10) is nearly identical with that (1:2:1) statistically expected.

In addition, when the reaction of 1_1 and 2_1 (mp 170.5-171.5°) was carried out in 2:1 DMSO-acetonitrile solution in the presence of 5 equiv of urea at room temperature, only 3_1 could be isolated in 28% yield. This finding suggests that intermolecular hydrogen bonding in 1 is kept under these unfavorable conditions and that 2 forms weaker hydrogen bonding than 1.

The substituents, *p-N,N*-dimethylaminophenyl and *p*-nitrophenyl groups, were originally introduced into this system on the assumption that charge-transfer interaction would assist in controlling the orientation of a pair of model compounds 1 and 2. The next experiment, however, demonstrated that this interaction is not so significant in bringing about the selectivity. Treatment of ethanedithiol with 1_1 and 1-(3-chloropropionyl)-3-(phenylacetyl)urea (an analog of 2_2 having no nitro group), mp 88–89°, gave 3_1 (27%), the other symmetrical bissulfide (30%, mp 166–167°), and the unsymmetrical one (3%, mp 123–127°).

The above-mentioned findings indicate that selective formation of two symmetrical bissulfides is due to selective intermolecular association mainly through *homotropic* intermolecular hydrogen bonding which plays a significant role in keeping two respective reaction sites of 1 and 2 in close proximity to each other as shown below.



Next, concerning rate acceleration by approximation,⁷ many interesting papers dealing with inclusion compounds⁸ or micelles have recently been reported. The new type of approximation through intermolecular hydrogen bonding shown in this experiment has been found to lead to rate acceleration. The yields of symmetrical bissulfides obtained by treatment of ethanedithiol with 2_2 , a model compound⁹ capable of forming

⁽⁷⁾ T. C. Bruice in "The Enzymes," P. D. Boyer, Ed., Vol. II, 3rd ed, Academic Press, New York, N. Y., 1970, Chapter 4.

⁽⁸⁾ R. Breslow and L. E. Overman, J. Amer. Chem. Soc., 92, 1075 (1970).

⁽⁹⁾ In the case of 9, the reaction was carried out under homogeneous conditions, but the faster reaction with 2_2 was heterogeneous.

intermolecular hydrogen bonding, or with N-phenethylchloroacetamide (9) (mp 67.0-67.5°), a model compound probably incapable of forming such intermolecular hydrogen bonds, were plotted against time. Figure 1 clearly indicates that reaction with 2_2 is completed within 1 hr and that 2_2 reacts *ca*. nine times as fast as 9 with ethanedithiol at this stage.

From the above results, it seems reasonable to conclude that selective intermolecular association leads to specific synthesis and rate acceleration.

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An Even-Electron, Paramagnetic Silicon Species, Cl₂Si(bipyridyl)₂^{1,2}

Sir:

In 1968 Herzog and Krebs³ reported the synthesis of the intense dark green solid $Cl_2Si(bipy)_2$ (bipy = 2,2'bipyridyl), slightly soluble in benzene and tetrahydrofuran, by the reaction of SiCl₄ · bipy with Li₂bipy in tetrahydrofuran.

 $SiCl_4 \cdot bipy + Li_2bipy \longrightarrow Cl_2Si(bipy)_2 + 2LiCl_3$

The intense green color of the compound is most unusual since all other silicon adducts with nitrogen bases are colorless or nearly so. Recently Kummer, et al.,⁴ have found that the same compound is formed in a few minutes at room temperature by the reaction of Si₂Cl₆ with bipyridyl in tetrahydrofuran.

$$Si_2Cl_6 + 3bipy \longrightarrow Cl_2Si(bipy)_2 + SiCl_4 \cdot bipy$$

The former authors suggested that this compound contained silicon in an oxidation state of +2 and would thus be formulated as a bipyridyl complex of dichlorosilylene, Cl₂Si:, the silicon analog of dichlorocarbene.



In the present study we have found that the solid material exhibits paramagnetic behavior as shown by magnetic susceptibility and epr measurements. The solid as well as the dilute dark green solutions in benzene, toluene, and tetrahydrofuran gave strong, sharp epr signals. The epr signal could be grown controllably in a sealed epr tube by combining Si₂Cl₆, bipyridyl, and tetrahydrofuran at liquid nitrogen temperature, sealing the tube, mixing at -64° , and then

(1) This report is based in part on portions of a thesis to be submitted by P. M. Broudy to the Graduate School of the University of Pennsylvania in partial fulfillment of the requirements for the degree of Doctor of Philosophy. Partial financial support of P. M. B. by the Frankford Arsenal, Philadelphia, Pa., is gratefully acknowledged.

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Figure 1. Epr spectrum of a frozen solution of Cl₂Si(bipy)₂ in toluene at -160° ($\nu = 9.137$ GHz) recorded at different amplications to show: A, half-field signal; B, center signal; C, triplet signals ($\Delta M = 1$).

measuring the signal at -160° . Only a very weak signal was first observed. On warming to room temperature for approximately 3 min on consecutive occasions, the characteristic green color of Cl₂Si(bipy)₂ appeared and the signal (at -160°) grew enormously in intensity. Maximum color and intensity of the signal was reached after about 9 min at room temperature. Identical epr spectra were obtained for samples of Cl₂- $Si(bipy)_2$ synthesized either from Si_2Cl_6 and bipyridyl or from SiCl₄ · bipy and Li₂bipy.

The epr spectrum of Cl₂Si(bipy)₂ in the form of a solid powder at -160° consisted of a sharp signal at g = 2.002 and a weak half-field ($\Delta M_s = 2$) of two different paramagnetic species. The intense sharp signal (width of band envelope, 5 G) at g = 2.002 is believed to be associated with a weakly coupled triplet radical pair. The resonances on either side of the center peak (Figure 1) are clearly due to a triplet species $(g_{x,y})$ $= 2.003; g_z = 2.001; D = 172$ G). A half-field signal characteristic of a triplet species was also observed (Figure 1). The epr spectra do not show any resolvable nuclear hyperfine splitting. Hyperfine structure is rarely observed in triplets and is not found in the spectra of the related compounds, Be(bipy)₂ and Mg(bipy)₂, studied by Weissman, et al.5

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