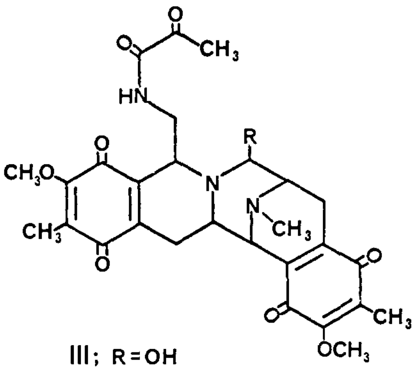

III; R=OH
IV; R=CN

two tyrosine units must condense to generate the basic ring system of this group. Additional studies on naphthyridinomycin are underway to determine the orientation of glycine's incorporation into C-1 and C-2, the role of ornithine in the biosynthesis, and the source of carbons 9 and 9′.

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Registry No. I, 54913-26-7; L-tyrosine, 60-18-4; L-methionine, 63-68-3; glycine, 56-40-6; L-ornithine, 70-26-8.

Composition of Elemental Sulfur in Solution: Equilibrium of S_6, S_7, and S_8 at Ambient Temperatures

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We report that S_8 is partially transformed to S_6 and S_7 at ambient temperatures by its dissolution in polar solvents such as methanol or acetonitrile. In time, an equilibrium is established in which ~1% of the sulfur is present as the smaller rings. In view of the much greater reactivity of S_6[1] and S_7[2] compared to S_8, the discovery of this equilibrium and processes that facilitate its attainment are potentially of value in defining and controlling the chemistry of sulfur. In particular, we may now ask whether reactions of sulfur proceed through S_6, S_7, or intermediates that lead to these compounds.

The chemistry of common sulfur at ambient temperatures is usually regarded as that of S_8. Consequently, we were surprised to find S_6 and S_7 present with S_8 in the mixtures described above, as determined by high-pressure liquid chromatography (HPLC).[3]

Table I. Equilibration of Sulfur in Methanol - Cyclohexane or Acetonitrile

	product distribution,[a] equilibrated mixtures		
reactant	S_6	S_7	S_8
S_6	0.32	0.76	98.9
S_7	0.30	0.77	98.9
S_8	0.30	0.78	98.9

[a] Wt % S_6, S_7, or S_8; quantities by HPLC;[6,7] reaction solvent 80% methanol–20% cyclohexane (similar results were obtained with acetonitrile); sulfur concentration 0.12 mg/mL; period elapsed from solution preparation to analysis, 1 day (S_7 and S_8 equilibrations), 3 days (S_6 equilibration). Rates of equilibration were variable.

We also observed that S_6 and S_7 in methanol at room temperature revert to solutions containing the three rings. To determine whether these mixtures result from an equilibration process, we compared the quantities of S_6, S_7, and S_8 produced from decompositions of the individual compounds. Solvents used for the equilibration reactions were methanol–cyclohexane or acetonitrile. The HPLC analysis (eluant 80% methanol–20% cyclohexane) is based on a scheme for separation of sulfur allotropes reported by Steudel and co-workers.[6,7] The data, presented in Table I, show that the three sulfur compounds yield, within experimental uncertainties, the same final mixture of S_6 (0.30 ± 0.05%), S_7 (0.8 ± 0.1%), and S_8 (98.9%).

A study of the variation of allotropic composition with total concentration provides additional evidence for the existence of the equilibrium and an independent demonstration of the number of sulfur atoms in the molecule associated with a given HPLC peak. Thus for the equilibrium $8S_n \rightleftarrows nS_8$, a plot of $\ln([S_n]/[S_8])$ vs. $\ln[S_8]$ is expected to be linear with a slope of $(n/8) - 1$. We find $n = 6.08 \pm 0.13$ for the "S_6" peak and $n = 7.07 \pm 0.10$ for "S_7". The values summarize data in acetonitrile and methanol–cyclohexane solutions that were originally enriched in S_6 or S_8.

There is a significant variation in the ability of solvents to promote the equilibration of S_6, S_7, and S_8. At room temperature, methanol, acetonitrile, and dimethyl sulfoxide dissolve S_8 to yield solutions in which appreciable quantities (>0.2%) of S_6 and S_7 are detected within minutes to hours. In contrast, solutions of S_8 in cyclohexane at room temperature show little conversion to S_6 or S_7 over weeks, although the smaller rings do appear within hours to days when these solutions are heated above 100 °C.

In Bartlett's study of the conversion of S_6 to S_8 in aromatic solvents, several polar catalysts were reported.[8,9] We find that S_6 and S_7 are much less stable in methanol than in cyclohexane and that partial conversion of these rings toward the equilibrium mixture occurs during HPLC analysis under our conditions[11] with methanol–cyclohexane as eluant. This chromatography routine

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[1] Bartlett, P. D.; Cox, E. F.; Davis, R. E. *J. Am. Chem. Soc.* **1961**, *83*, 103–109. In reactions with triphenylphosphine S_6 is 2 × 10^4 more reactive than S_8 as determined by extrapolation to comparable conditions.

[2] Steudel, R. "Chemistry of the Non-Metals"; W. de Gruyter: New York, 1977; p 208. S_7 is suggested to be more reactive than S_6.

[3] Identification of the S_6 and S_7 peaks follow from their retention volumes being within 1% of those of authentic samples[4] prepared by the method of Schmidt.[5] Mass spectra (MS) of the "S_7" fraction isolated from an equilibrated S_8 source confirmed the identification. The "S_6" peak gave only the MS of S_8, presumably as the result of rapid transformation of S_6 to S_8 on concentration.

[4] Data for the authentic reference samples are given in the following. S_6: found, S, 99.4%; mol wt calcd for S_6 192, found 192 (mass spectrum) and 200 (vapor-pressure osmometry, benzene). S_7: found, S, 99.9%; mol wt calcd for S_7 224, found 224 (mass spectrum) and 225 (vapor-pressure osmometry, benzene). Recrystallization of Fisher (sublimed) sulfur from carbon disulfide or evaporation of a cyclohexane extract of Baker and Adamson (precipitated) sulfur yielded samples of S_8 with less than 0.1% S_6 and S_7.

[5] Schmidt, M.; Block, B.; Block, H. D.; Köpf, H.; Wilhelm, E. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 632–633.

[6] Steudel, R.; Mausle, H. J.; Rosenbauer, D.; Mockel, H.; Freyholdt, T. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 394–395.

[7] We used a Zorbax ODS (octadecylsilane) column, 250 mm × 6.2 mm i.d. The compounds were detected at 254 nm. The reported quantities are corrected for differences in extinction coefficients of S_6, S_7, and S_8 at that wavelength.

[8] Bartlett, P. D.; Lohaus, G.; Weis, C. D. *J. Am. Chem. Soc.* **1958**, *80*, 5064–5069.

[9] $NaAlO_2(SiO_2)_2 \cdot 2H_2O$:[10] surface area 313 m^2/g; pore volume 188 Å^3 was found to facilitate the approach to equilibrium. Bartlett et al.[8] found a non-acid alumina promoted the conversion of S_6 to S_8.

[10] Mahler, W.; Forshey, W. O., Jr. U.S. Patent 4213949.

[11] S_7 was stable in methanol during chromatography under the reported conditions.[6] Catalysts in minute amounts promote the conversion of S_6 to S_8.[12]

[12] Bartlett, P. D.; Colter, A. K.; Davis, R. E.; Roderick, W. R. *J. Am. Chem. Soc.* **1961**, *83*, 109–114.

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was, therefore, useful for quantitative analyses near equilibrium or qualitative assessments when the system was far from equilibrium. To make quantification possible under the latter conditions, we developed an HPLC technique using a column with a polar bonded phase and a mixed fluorocarbon solvent system to separate S_6, S_7, and S_8 without detectable decomposition.[13] This allowed the determination that our preparations[4] of reference samples of S_6 and S_7 yielded products with <1% S_8 as an impurity. The HPLC procedures now available[6,13] yield information on elemental sulfur systems that was not previously accessible.

The allotropic composition of elemental sulfur is perturbed by light. S_8, irradiated with a sunlamp, is converted to a reactive form of sulfur.[14] Irradiation of S_6, S_8, or S_{10} in various solvents is reported to produce S_7.[15] We find that prolonged irradiation of S_8 in methanol at 2537 Å yields mixtures with S_6 and S_7 considerably in excess of the amounts achieved by equilibrations of samples in the dark, sugggesting that a photostationary state can be significantly displaced from the thermal equilibrium. At concentrations of $\sim 10^{-5}$ M, S_6 may be ~40% and S_7 ~20% of total sulfur. The quantities of the less stable S_6 and S_7 in methanol–cyclohexane are also enhanced by heating, as expected. Because of the sensitivity of the system to light and temperature, the data used for establishing the existence of the equilibrium discussed above were obtained with solutions kept in the dark at temperatures near 22 °C.

The presence of S_6 and S_7 in sulfur melts[16] and in gaseous sulfur at high temperatures[17] is well documented. Extrapolations of these measurements to the quite different temperatures and concentrations of the above solutions indicate that in "nonpolar" environments the equilibrium concentrations of $S_6 + S_7$ may be similar to those in polar solvents. In this case, solvent polarity may not drastically shift the position of equilibrium but may increase the rates of interconversion. The possibility that rates in polar solvents are affected by small amounts of impurities[8] is being investigated. An equilibrium position independent of solvent is compatible with S_6 and S_8 having no permanent dipoles while the small moment of S_7 may be further reduced by rapid pseudorotation.[18] Near the completion of this study, a communication by Steudel and Strauss appeared reporting the equilibrium of Se_6, Se_7, and Se_8 in carbon disulfide.[19]

The solvent effects noted above may signal the presence of polar intermediates in the interconversion processes. The intermediates could be structurally related to the ions generated by dissolution of sulfur in polar media[20] or to S_7 ring compounds isolated from oxidations of S_8 in polar solvents,[21] e.g., S_7O.[21c] Extended Hückel calculations indicate that a polar S_7S is only 5–10 kcal above S_8 in energy.[22] The exo sulfur might be transferred to other sulfur rings. Mechanistic studies are underway to elucidate these and related points.

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Note Added in Proof. A wide-ranging article by R. Steudel has appeared in *Topics in Current Chemistry*. Among other subjects it reports the formation of S_6 and S_7 on ultraviolet irradiation of S_8 solutions and the thermal approach to equilibrium of the three rings in CS_2 at 130–150°. We are grateful to Professor Steudel for a preprint of his manuscript.

Registry No. S_6, 13798-23-7; S_7, 21459-04-1; S_8, 10544-50-0.

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(13) Hayman, A. C., to be submitted for publication.

(14) Bartlett, P. D.; Meguerian, G. *J. Am. Chem. Soc.* **1956**, *78*, 3710–3715.

(15) Steudel, R.; Steidel, J.; Pickardt, J.; Schuster, F. *Z. Naturforsch., B* **1980**, *35B*, 1378–1383.

(16) See: (a) Harris, R. E. *J. Phys. Chem.* **1970**, *74*, 3102–3111. (b) Mansle, H. J.; Steudel, R. *Z. Anorg. Allg. Chem.* **1981**, *478*, 177–190. Extrapolation of Harris' data from the melt to room temperature and correction for the difference in concentration between the melt and 10^{-4} M solutions lead to ~1% $S_6 + S_7$ (the main components of his S_π).

(17) (a) Berkowitz, J. In "Elemental Sulfur"; Meyer, B., Ed.; Interscience: New York, 1965; Chapter 7. Extrapolation of the vapor-phase data to 20 °C and 10^{-4} M sulfur leads to S_6 and S_7 concentrations within factors of 3 of those found in methanol solutions. Thus a large dependence of the equilibrium composition on solvent is not predicted: (b) Drowart, J.; Goldfinger, P.; Detry, D.; Rickert, H.; Keller, H. *Adv. Mass Spectrom.* **1968**, *4*, 499–509.

(18) Steudel, R.; Schuster, F. *J. Mol. Struct.* **1978**, *44*, 143–157.

(19) Steudel, R.; Strauss, E. M. *Z. Naturforsch., B* **1981**, *36B*, 1085–1088.

(20) Chivers, T.; Lau, C. *Inorg. Chem.* **1982**, *21*, 453–455.

(21) (a) Burns, R. C.; Gillespie, R. J.; Sawyer, J. F. *Inorg. Chem.* **1980**, *19*, 1423–1432. (b) Passmore, J.; Sutherland, G.; Taylor, P.; Whidden, T. K.; White, P. S. *Ibid.* **1981**, *20*, 3839–3845. (c) Steudel, R.; Shandow, T. *Angew. Chem.* **1978**, *80*, 644–645.

(22) Wasserman, Z. R., unpublished results.

Carbanion-Accelerated Claisen Rearrangements

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The [3,3] sigmatropic rearrangement of allyl vinyl ethers (Claisen rearrangement,[1] Scheme I) has enjoyed widespread application in many facets of organic synthesis over the past 20 years.[1e] It has proved no less attractive to physical and theoretical organic chemists[2] who have contributed greatly to understanding mechanism and energetics of the rearrangement. Modern variants[3] that employ ketene acetal tautomers of carboxylic acid derivatives provide the corresponding amide,[3a–d] ester,[3e,f] acid[3g–i] or thioester[3j,k] upon rearrangement. The increasingly mild conditions required for these variants (Scheme I) amplifies their value as synthetic methods. *We report a new variant of the Claisen rearrangement that is mild and regioselective and produces γ,δ-unsaturated ketones as rearrangement products.*[4]

Our strategy was based on the empirical observation that π-electron donating groups at the 2-position of an allyl vinyl ether accelerate the reaction;[5] cf. Scheme I. We therefore reasoned that the greatest acceleration should be observed with the most powerful π-donor, i.e., a carbanion.[6] Initial experiments involving lithium salts of cyano- and carboethoxy-stabilized anions (Z =

[†] Eastman Kodak Graduate Fellow, 1981–1984.

(1) Reviews: (a) Tarbell, D. S. *Chem. Rev.* **1940**, *27*, 495. (b) Tarbell, D. S. *Org. React.* **1944**, *2*, 1. (c) Rhoads, S. J.; Raulins, R. N. *Ibid.* **1975**, *22*, 1. (d) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227. (e) Bennett, G. B. *Synthesis* **1977**, 589.

(2) (a) Rhoads, S. J. In "Molecular Rearrangements"; deMayo, P., Ed.; Interscience: New York, 1963; Part 1, pp 655–684. (b) Hansen, H. J. In "Mechanism of Molecular Migration"; Thyagarajan, B. S., Ed.; Wiley-Interscience: New York, 1971; Vol. 3, pp 177–236. (c) McMichael, K. C.; Korver, G. L. *J. Am. Chem. Soc.* **1978**, *100*, 2746. (d) Gajewski, J. J.; Conrad, N. D. *Ibid.* **1978**, *100*, 2747. (e) Gajewski, J. J. *Acc. Chem. Res.* **1980**, *13*, 142. (f) Carpenter, B. K.; Burrows, C. J. *J. Am. Chem. Soc.* **1981**, *103*, 6983, 6984.

(3) (a) Wick, A. E.; Felix, D.; Steen, K.; Eschenmoser, A. *Helv. Chim. Acta* **1964**, *47*, 2425. (b) Felix, D.; Gschwend-Steen, D.; Wick, A. E.; Eschenmoser, A. *Ibid.* **1969**, *52*, 1030. (c) Ficini, J.; Barbara, C. *Tetrahedron Lett.* **1966**, 6425. (d) Bartlett, P. A.; Hahne, W. F. *J. Org. Chem.* **1979**, *44*, 882. (e) Johnson, W. S.; Wethermann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T.; Faulkner, D. J.; Peterson, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741. (f) Faulkner, D. J.; Peterson, M. R. *Ibid.* **1973**, *95*, 553. (g) Arnold, R. T.; Searles, S. *Ibid.* **1949**, *71*, 1150. (h) Ireland, R. E.; Mueller, R. H. *Ibid.* **1972**, *94*, 5897. (i) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *Ibid.* **1976**, *98*, 2868. (j) Malherbe, R.; Bellus, D. *Helv. Chim. Acta* **1978**, *61*, 295. (k) Rosini, G.; Spineti, G. G.; Foresti, E.; Pradella, G. *J. Org. Chem.* **1981**, *46*, 2228.

(4) The Carroll modification of the Claisen rearrangement also affords γ,δ-unsaturated ketones. (a) Carroll, M. F. *J. Chem. Soc.* **1940**, 704, 1266; **1941**, 507. (b) Kimel, W.; Cope, A. C. *J. Am. Chem. Soc.* **1943**, *65*, 1992.

(5) This purely intuitive analysis has received qualitative theoretical support recently from Carpenter.[2f] See also: Carpenter, B. K. *Tetrahedron* **1978**, *34*, 1877.

(6) The accelerating effect of a carbanion in the electrocyclic opening of benzocyclobutenes has been documented: Kametani, T.; Tsubuki, M.; Nemoto, H.; Suzuki, K. *J. Am. Chem. Soc.* **1981**, *103*, 1256.

0002-7863/82/1504-4972$01.25/0