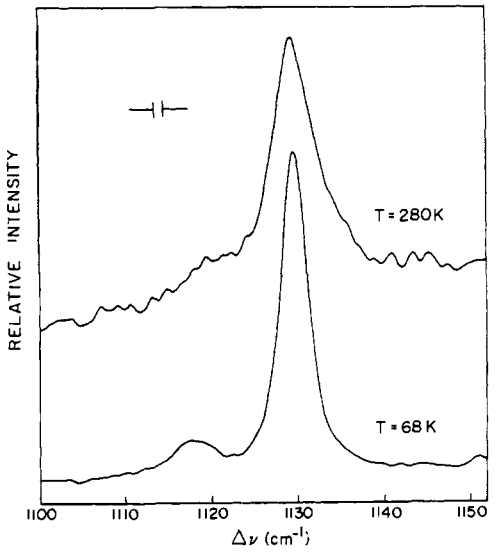

Figure 3. High resolution (1 cm^{-1}) unpolarized Raman spectra of the 1130-cm^{-1} line of ferrocytochrome *c*.

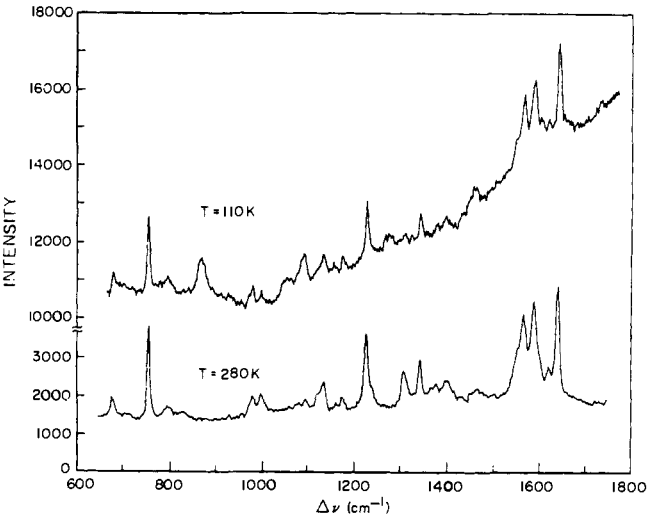

Figure 4. Raman spectra (unpolarized) of oxyhemoglobin using 5817-Å laser excitation at 15-mW incident power. The excitation frequency is quite close to the α band, which shows no sign of splitting but does shift from 5775 to 5720 Å as the temperature is lowered to 110 K. The extra features in the low temperature run are due primarily to the glassy solvent, ethylene glycol. Intensity differences are due to the shift of the Q_{00} band.

the signal to noise is decreased in this low temperature measurement due to increased fluorescent emission, the Raman peak positions can still be determined accurately and compared with the spectrum of oxyhemoglobin in the liquid state. The data show that, as with ferrocytochrome *c*, there is no apparent shift of line positions as the sample is frozen. This is strong evidence that the heme group is perturbed very little, if at all, in going from liquid to solid solutions.[8] This result should be quite encouraging to those who routinely perform spectroscopic measurements at cryogenic temperatures with little knowledge of the effects on the heme site produced by the liquid-to-solid transition.

One of the most interesting aspects of resonance Raman scattering in heme proteins is the strong variation in intensities and polarization properties as the laser frequency is scanned through the absorption bands. A rise in the scattering cross section occurs when either the incident or scattered photon is in resonance with the Q_{00} transition. As the transition sharpens up at low temperature, this dispersion in the scattering efficiency becomes more pronounced and more abrupt. This is the principal explanation for the changes in Figure 2. The depolarization ratio, $\rho_l = I_\perp/I$, also varies with laser frequency for several Raman bands. This dispersion has been noted by several workers and is not well understood. For at least some of the bands, it appears to reflect interferences between Q_{00} and Q_{01} resonances, and between nondegenerate Q_{00x} and Q_{00y} resonances. The low temperature spectra for cytochrome *c* show both these effects. In particular, there is a very pronounced dip in ρ_l near the α band for the 1585-cm^{-1} mode. This dip is in quantitative agreement with our earlier predictions.[9] It becomes more pronounced as the widths of the α band components decrease relative to their splitting (cf. Figure 1).

A more complete account of the low temperature Raman spectra of several cytochromes will be published elsewhere. In this report, we merely wish to point out that excellent Raman spectra can be obtained at low temperature, that the dispersion effects near resonance are more pronounced at low temperature, and that the heme group vibrational frequencies are not detectably modified upon freezing.

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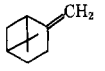
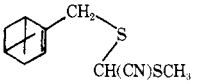
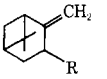
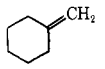
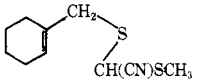
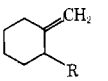
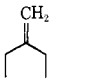
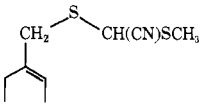
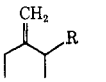
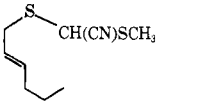
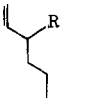
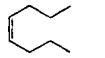
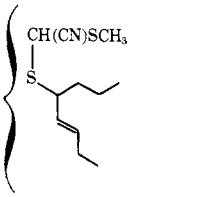
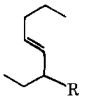
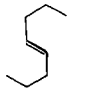
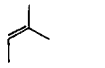
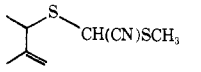
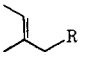
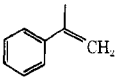
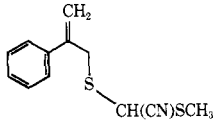
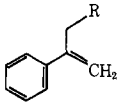
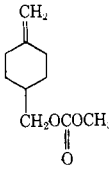
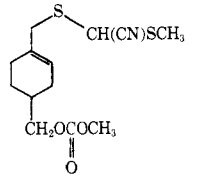
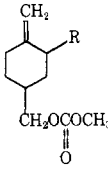
Allylic Cyanobis(methylthio)methylation. Insertion of a Functionalized Carbon in an Allylic Carbon–Hydrogen Bond

Sir:

A procedure that would allow the unambiguous insertion of a functionalized carbon atom into an allylic carbon–hydrogen bond would be of great synthetic value. At present procedures exist which lack regiospecificity since an allylic carbanion, carbonium ion or radical is an intermediate.[1] A method that proceeds by an ene reaction[2] followed by a [2,3] sigmatropic rearrangement as does the selenium dioxide oxidation of olefins[3,4] would allow an unambiguous functionalization of an alkene without double bond migration. Since allylic sulfides are known to undergo [2,3]-sigmatropic rearrangements readily on deprotonation,[5] our goal was to convert an alkene to an allylic sulfide by an ene reaction. Hexafluorothioacetone reacts readily with a variety of alkenes at −78 °C to give ene adducts which are allylic sulfides.[6] Unfortunately, these are of limited synthetic value. Methyl cyanodithioformate (**1**) is readily available[7] and is known to function as a dienophile in Diels–Alder reactions.[8] Furthermore, the expected ene adduct **2** should possess a relatively acidic hydrogen which could be easily abstracted to give an anion which

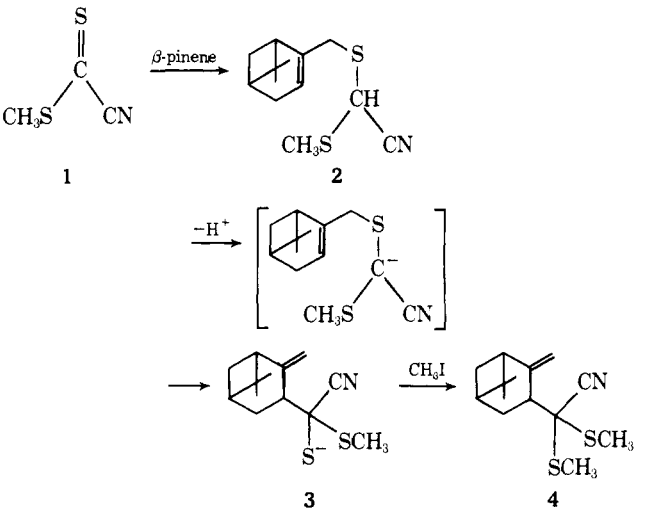
Table I. Allylic Cyanobis(methylthio)methylation

	Alkene	Reactn time (h)	Ene adduct	% yield	Rearrangement product R = $C(SCH_3)_2CN$	% yield
1		5		83[a]		72
2		5		76		70
3		16		72[b]		86
4		48		43[c]		56
5		72		28[c,d]		70[c]
6		72		74[c,e]		73[c]
7		46		45[f]		70[g]
8		6		70		91
9		8		22		77[h]

[a] Analysis of the NMR signals of the thioacetal methine indicated a 78:22 mixture of diastereomers is present. [b] The NMR spectra showed broad signals at δ 3.48 and 3.35 in the ratio of 21:79 which are assigned to the *Z* and *E* olefin isomers, respectively.[11] [c] Analysis of NMR coupling constants indicated that the double bond was mainly trans. [d] Analysis of the NMR signals due to the thioacetal methine indicated a 45:55 mixture of diastereomers was present. [e] Analysis of the NMR signals due to the thioacetal methine indicated a 71:29 mixture of the same diastereomers described in *d* was present.[10] [f] Analysis of the NMR signals due to the thioacetal methine indicated a ca. 1:1 mixture of diastereomers was present. [g] This is formed predominantly as the *E* isomer. [h] This is formed as a ca. 85:15 mixture of trans and cis isomers, respectively.

should rearrange to the thiolate **3**, giving the desired allylic insertion of an appropriately functionalized carbon atom. The realization of these expectations is described below.

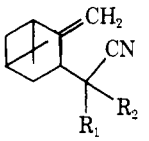
The ene reactions of **1** with alkenes are carried out by heating a 1 M solution of **1** in toluene with an excess of alkene in a sealed tube at 100–110 °C until the purple color of **1** disappears (see Table I). Cases 1, 5, 6, and 7 are capable of giving two diastereomers depending on whether endo or exo addition occurs. These can be clearly observed in the NMR of the dithioacetal methine although at present they can only be assigned on the assumption that the nitrile prefers to add endo.[9-11] Furthermore, the double bond formed in cases 4, 5 and 6 appears to be formed primarily trans by analysis of NMR coupling constants. Case 3 gives a 79:21 mixture of *E* and *Z* double bond isomers, respectively,[12] as one would expect from an analysis of the transition state of the ene reaction.[2] Experiments with highly substituted or endocyclic olefins give little ene adduct.[13]

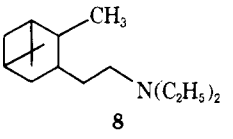


1 2 3 4

Preparation of the anion of the ene adduct is straightforward using either butyllithium or lithium diisopropylamide in tetrahydrofuran. However, [2,3]-sigmatropic rearrangement does not occur under these conditions. Addition of methyl iodide or deuterium oxide gives the ene adduct with the hydrogen replaced by methyl or deuterium.[14] Extended reaction times give only decomposition. Addition of 25% HMPA to the solvent allows the rearrangement to proceed readily (less than 1 h at −20 °C). The function of the HMPA is presumably to convert a tight ion pair into a solvent separated ion pair.[15] The thiolate resulting from rearrangement is trapped with methyl iodide giving the products shown in Table I. As one would expect, the trans olefins are the predominant products (>90%) and in case 7 the isomer shown predominates. In a typical experiment lithium diisopropylamide was formed in situ from 0.46 ml of diisopropylamine (3.14 mmol) and butyllithium (2.93 mmol) in 20 ml of 3:1 tetrahydrofuran:HMPA at 0 °C. The solution was cooled to −20 °C. The ene adduct of **1** with β-pinene (**2**) (0.506 g, 2 mmol) in THF was added slowly. After 1 h at −20 °C the solution was quenched with 0.5 ml of methyl iodide and allowed to warm to room temperature. After 2 h the reaction was worked up giving 0.386 g (72%) of **4** which was >95% pure by NMR analysis.

We are presently engaged in investigating the chemistry of the cyanobis(methylthio)methyl group. Preliminary results indicate that treatment of **4** with deactivated W-4 Raney nickel[16] for 24 h in refluxing ethanol cleanly affords **5** in 83% yield. Treatment of **4** under the same conditions with W-4





8

5, $R_1, R_2 = H$
6, $R_1 = SCH_3$; $R_2 = H$
7, $R_1, R_2 = O$

Raney nickel affords **8** in 90% yield. Stirring **4** in ethanol with aluminum amalgam[17] converts **4** to the monothioether **6** in 72% yield. This compound can be obtained as the corresponding anion by treatment of **4** with methyllithium or butyllithium in tetrahydrofuran (2 h, −78 to 0 °C) in 75 and 68% yield, respectively. The alkyllithium procedures are of special interest since they give an acyl anion equivalent directly.[18] Attempted hydrolysis of **4** to the acyl nitrile **7** has been unsuccessful due to the sensitivity of **4** to oxidizing agents and acidic conditions.

We are presently engaged in investigating the uses of the above compounds in synthesis as well as other routes to the allylic insertion of a functionalized carbon atom.

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(13) Cyclohexene, 1-methylcyclohexene, 2,3-dimethylbutene, *l*-carvone, and α-pinene gave <10% ene adduct. In all cases the other products are unreacted olefin and 2,3-bis(methylmercapto)maleonitrile, a dimer of the enophile.[6]
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Book Reviews

Scanning Electron Microscopy. By OLIVER C. WELLS (IBM Thomas J. Watson Research Center). McGraw-Hill Book Co., New York, N.Y. 1974. xviii + 421 pp. $22.95.

This book comes at an appropriate moment because there have been a considerable number of important advances in scanning electron microscopy during the past several years. Those advances have led to this form of microscopy being applied to an increasing number of different areas of science. Already these applications have led to much new and valuable information about structures.

The book has been written not only by Dr. Wells, but considerable portions have been contributed by Alan Boyde, Eric Lifshin and Alex Rezanowich. The aim of the volume is to give a detailed account of the problems of the design and use of scanning electron microscopes. The authors naturally also give useful accounts of the applications to the physical sciences, and also in biology and medicine. The level of writing is appropriate for those using scanning electron microscopy in their research work, and the authors are to be congratulated on striking an interesting balance between descriptive material and also at the same time giving a satisfactory mathematical treatment of the problems of signal-to-noise ratio in electron microscopy, electron penetration, bulk scattering, secondary electron emission, and the problem of the optical design of small current probe forming systems.

In addition to excellent chapters covering the above topics, it was pleasing to note that there is a valuable introductory chapter which gives an interesting account of not only the different types of scanning electron microscopes but also a useful survey of the history of the development of this important instrument.