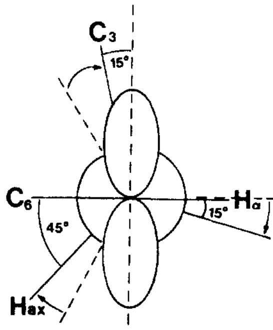
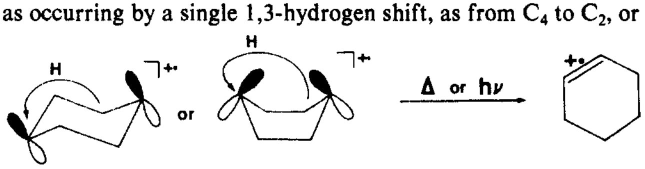


density being taken as 48 and 24 G for the β and α hydrogens, respectively. This model agrees well with the experimental result of a 11.9 G coupling to six equivalent hydrogens. Moreover, this structure is expected to have a strong charge-resonance electronic absorption band,[9] which is consistent with the intense blue color and ease of photobleaching by red light ($\lambda > 620$ nm).

Having characterized the intermediate, its photoinduced or thermal conversion to the cyclohexene radical cation is interpreted as occurring by a single 1,3-hydrogen shift, as from C_4 to C_2, or



2a 2b

conceivably by two consecutive 1,2-hydrogen shifts.[10,11] From a study of the thermal reaction between 77 and 90 K in CF_3CCl_3, the activation energy is estimated to be 4.5 kcal mol^{-1}. Thus, the cyclohexane-2,5-diyl radical cation resides in a shallow potential energy minimum on the reaction path connecting the 1,5-hexadiene and cyclohexene cations, and since it is calculated to be 34 kcal mol^{-1} more stable than the 1,5-hexadiene radical cation,[6] a degenerate radical cation Cope rearrangement is strongly disfavored. Therefore, isomerization to the cyclohexene radical cation may be the only available reaction path in this case.

Finally, we note the striking contrast between the title reaction and the absence of cyclohexene formation in the degenerate Cope rearrangement of neutral 1,5-hexadiene,[12] although the cyclohexane-2,5-diyl radical cation intermediate in the former is isostructural with the transition state[13] or diradicaloid intermediate[14] in the latter, and cyclohexene formation is calculated to be exothermic for both radical cation (36 kcal mol^{-1}) and neutral (21 kcal mol^{-1}) processes. Consequently, if a diradical *intermediate* is formed in the neutral Cope rearrangement, it presumably cannot exist in a very deep potential well since this feature might be expected to allow hydrogen transfer, and therefore cyclohexene formation, to compete with the electrocyclic cleavage reaction.

Acknowledgment. We thank Dr. Clair J. Collins, Dr. Richard M. Pagni, and the referees for their comments on this work. Support of this research was provided by the Division of Chemical Sciences, U.S. Department of Energy (Report No. DOE/ER/02968-174).

Supplementary Material Available: Comparisons of the ESR spectra obtained from γ-irradiated solid solutions of 1,5-hexadiene and cyclohexene: (a) in $CFCl_3$ at 135 K (together with a simulated spectrum of the cyclohexene radical cation) and (b) in $CF_2ClCFCl_2$ at 100 K (2 pages). Ordering information is given on any current masthead page.

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[8] See, e.g.: Gordy, W. *Theory and Applications of Electron Spin Resonance*; Wiley: New York, 1980; Chapter VI, p 198.

[9] The charge resonance band for the "three-electron bond" in the isostructural dithiane radical cation has been described: (a) Shida, T.; Momose, T. *J. Mol. Struct.* **1985**, *126*, 159. (b) Asmus, K.-D. *Acc. Chem. Res.* **1979**, *12*, 436.

[10] The possibility that the hydrogen shift occurs before 1,6-ring closure has also been carefully considered. In this case, the "snakelike" distonic species $CH_2{\cdots}{}^{+}CH{\cdots}CH-(CH_2)_2-CH_2^{\bullet}$ comprised of an allylic cation and an alkyl radical would probably be the intermediate.[11] This species could also give a seven-line hyperfine pattern with an ca. 12-G spacing if the $RCH_2CH_2^{\bullet}$ radical center were to adopt an eclipsed rather than the usual bisected conformation,[8] such that $A(2H_\beta) = 12$ G and $A(2H_\alpha) = 24$ G. However, the line intensity ratios in Figure 1 are inconsistent with this assignment, especially considering that lines 1, 2, 6, and 7 of such a 1:2:3:4:3:2:1 pattern should be selectively broadened at low temperatures by the usual residual α-hydrogen hyperfine anisotropy. Ab initio MO calculations (Bellville, D. J.; Bauld, N. L. *Tetrahedron* **1986**, *42*, 6167) originally suggested that this type of distonic intermediate constitutes a minimum along the path of the "role-reversed" Diels–Alder cycloaddition of *s-cis*-1,3-butadiene radical cation to ethylene, although the barrier to its endocyclization was calculated to be only 2.7 kcal mol^{-1}. With a better basis set, however, this minimum disappears, indicating a concerted reaction (Bauld, N. L.; Bellville, D. J.; Harirchian, B.; Lorenz, K. T.; Pabon, R. A., Jr.; Reynolds, D. W.; Wirth, D. D.; Chiou, H.-S.; Marsh, B. K. *Acc. Chem. Res.* **1987**, *20*, 371, footnote 19).

[11] Additional evidence against an acyclic distonic intermediate produced by a hydrogen shift[10] comes from our very recent studies on 1,1,6,6-tetradeuterio-1,5-hexadiene (Guo, Q.-X.; Williams, F., unpublished results). The ESR spectrum of the intermediate in this case is a sharp 12-G quintet which clearly rules out $CD_2{\cdots}{}^{+}CH{\cdots}CH-(CH_2)_2-CD_2^{\bullet}$ but is nicely consistent with the structure of the cyclized diyl radical cation proposed in the present paper.

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Direct Conversion of Aldehydes to Seleno- and Thioaldehydes

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Received October 13, 1987

The chemistry of molecules having unstable carbon–heteroatom multiple bonds is of great importance and interest. Until quite recently, the chemistry of selenoaldehydes has remained almost undeveloped because of their high reactivity and difficulty of preparation.[1] The isolation of several selenoaldehydes stabilized by electron-donating groups[2] or by coordination to the transition metals such as chromium and tungsten[3a] has been reported. Though monomeric selenoaldehydes have not been isolated as free species without resort to such stabilizations as yet, they have been known to react with 1,3-dienes to give the corresponding Diels–Alder adducts[3b–5] or isomerize to benzoselenane.[6] The utmost important problem in selenoaldehyde chemistry is still to find a practical preparative method. The most efficient method for

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[1] Reviews: *Organic Compounds of Sulphur, Selenium, and Tellurium*; Specialist Periodical Reports; The Chemical Society: London, 1970–1981; Vol. 1–6. Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Baldwin, J. E., Ed.; Pergamon Press: 1986; pp 58–83.

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[3] (a) Fischer, H.; Zeuner, S.; Riede, J. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 726–727. (b) Fischer, H.; Gerbing, U.; Riede, J.; Benn, R. *Ibid.* **1986**, *25*, 78–79.

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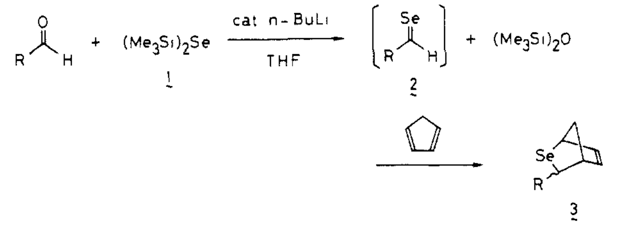
Table I. Generation and Reaction of Selenoaldehydes **2** with Cyclopentadiene

entry	RCHO, R	reaction condn temp (°C)	reaction condn time (h)	isolated yield of **3** (%)	isomer ratio endo:exo[a]
1	C_6H_5	25	7	73	4:1
2	4-Cl-C_6H_4	25	3	72	4:1
3	2-furyl	15	3	85	2:1
4	*n*-C_3H_7	40	6	71	7:1
5	*i*-C_3H_7	40	6	81	10:1
6	*t*-C_4H_9	60	4	45	>20:1

[a] Determined by ^{1}H NMR spectra.

selenoaldehydes known to date would be that of Krafft and Meinke, who reported in 1986 the generation of selenoaldehydes by β-elimination of silicon and cyano moieties from, for example, α-silyl-α-(cyanoselenenyl)toluene [$Me_3SiCH(Ph)SeCN$].[4a] The precursor, however, should be prepared in one or two steps from aldehydes. We now wish to report a very simple method which allows the direct conversion of aldehydes to selenoaldehydes. In the new method, bis(trimethylsilyl)selenide ($Me_3SiSeSiMe_3$, **1**)[7] works not only for the introduction of a selenium atom but also for removal of oxygen. The principle can be extended to thioaldehyde synthesis.

It seemed that for the conversion of relatively stable carbon–oxygen double bond to such an unstable bond as selenium–carbon double bond, a sufficiently large driving force should be supplied by the concomitant change of the reagent used, and any byproducts or reagents should not react with the labile product, selenoaldehyde. The seemingly large energy difference between disilyl selenide ($Me_3SiSeSiMe_3$, **1**) and disiloxane ($Me_3SiOSiMe_3$)[8] was very attractive to us as the driving force of the desired transformation. Thus we studied the reaction of aldehydes with **1** extensively with respect to the catalysts and reaction conditions. Among various candidates including ZnI_2, $TiCl_4$, *n*-BuLi, R_3N, and R_3P examined for the catalyst, only *n*-BuLi has met with success, a typical example being given below. The reaction was carried out in the presence of cyclopentadiene which is known as a good trapping agent for selenoaldehydes[3b,4a,5] (eq 1).

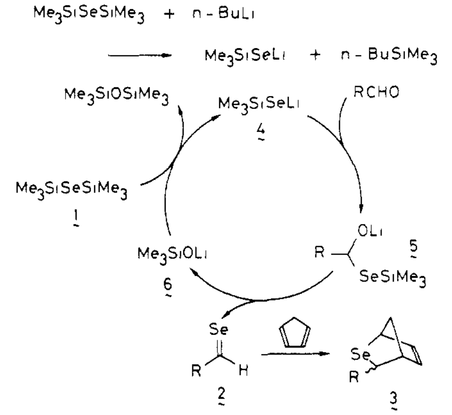


(1)

Butyllithium (1.6 M solution in hexane, 0.063 mL, 0.1 mmol) was added to a solution of bis(trimethylsilyl)selenide (225 mg, 1.0 mmol) in THF (30 mL) at 0 °C under nitrogen. After stirring for 30 min at 0 °C, cyclopentadiene (198 mg, 3.0 mmol) and benzaldehyde (159 mg, 1.5 mmol) were added in that order. The reaction mixture was stirred at 25 °C for 7 h. Evaporation of the solvent followed by a flash chromatography on silica gel (hexane–dichloromethane, 2:1) yielded the selenobenzaldehyde cycloadduct (172 mg, 73% yield) as a 4:1 mixture of endo and exo isomers.

The representative examples are summarized in Table I.[12]

Scheme I



These satisfactory yields of cycloadducts **3** imply that selenoaldehyde generation occurs efficiently under this base-catalyzed condition except for entry 6. Use of 5–10 mol% butyllithium in a highly diluted solution (0.03 M solution of **1** in THF) suppressed the undesired reactions.[13] The Diels–Alder adducts with cyclopentadiene yielded a mixture of endo and exo isomers, with the former predominating in all cases. These results are consistent with those reported by Krafft and Meinke.[4a]

We propose a catalytic cycle illustrated in Scheme I for selenoaldehyde formation. Lithium trimethylsilylselenide ($Me_3SiSeLi$, **4**), generated in situ from the treatment of **1** with butyllithium, attacks the carbonyl carbon of aldehyde to give the corresponding unstable intermediate **5**, which then undergoes elimination of (trimethylsiloxy)lithium (Me_3SiOLi, **6**) probably via the Peterson-type mechanism[14] to give a selenoaldehyde **2** that is immediately trapped by cyclopentadiene to give the observed adduct **3**. The eliminated **6** reacts with **1** to give the siloxane and regenerates the active catalyst **4**.

It appears that the initial addition of the $Me_3SiSeLi$ to the carbonyl is the rate-limiting step, since the 4-chlorobenzaldehyde reacts more than twice as fast as benzaldehyde. This possibility is also substantiated by the higher temperatures required for reactions of the sterically encumbered pivalaldehyde. The cycloaddition step cannot be the slow step since Krafft's procedure requires 2 h at 0 °C for selenobenzaldehyde,[4a] compared with 7 h at 25 °C in this work.[15]

The concept mentioned above can also be applicable to the preparation of thioaldehydes, another interesting class of compounds which are not very easily accessible.[16] Thus, under the similar reaction conditions using $Me_3SiSSiMe_3$,[17] some aldehydes

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(7) It has been reported that bis(trimethylsilyl)selenide smoothly converts sulfoxides, selenoxides, and telluroxides into sulfides, selenides, and tellurides, respectively. See: Detty, M. R.; Seidler, M. D. *J. Org. Chem.* **1982**, *47*, 1354–1356.

(8) From the consideration of hard/soft pairs[9] and also from bond energies estimated for H–O (102 Kcal/mol), H–Se (73 Kcal/mol), Si–O (194 Kcal/mol), and Si–Se (131 Kcal/mol).[10,11]

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(12) All cycloadducts gave satisfactory IR, NMR, mass spectral data, and elemental analyses. See Supplementary Material. We thank Tadashi Koyama, Hajime Saito, and Nakaji Komiyama at Kanazawa University for experimental assistance.

(13) The side reactions are condensation of cyclopentadiene with aldehydes and trimerization of aldehydes or selenoaldehydes.

(14) For a review, see: Ager, D. J. *Synthesis* **1984**, 384–398.

(15) We thank a referee for the discussion.

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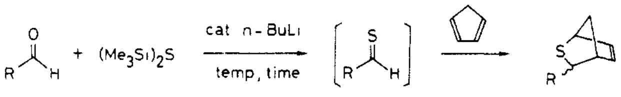
(17) This reagent has once been used for the preparation of thioaldehydes but not directly. In the Steliou's work, the role of $Me_3SiSSiMe_3$ was to convert BCl_3 to the working reagent B_2S_3, see: Steliou, K.; Mrani, M. *J. Am. Chem. Soc.* **1982**, *104*, 3104–3106.

are converted to thioaldehydes in good to excellent yields (eq 2).



				endo:exo
R = C_6H_5	15°C	8h	96%	(4 : 1)
= 2-thienyl	10°C	5h	97%	(5 : 1)
= n-C_3H_7	55°C	7h	80%	(6 : 1)
= t-C_4H_9	55°C	5h	86%	(>20 : 1)

(2)

The described method opens a new route to the generation of seleno- and thioaldehydes and will permit further studies of the reactivity of these exotic molecules. We are currently exploring the various possibilities offered by these preliminary results.

Acknowledgment. This work was supported in part by Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan.

Supplementary Material Available: Full characterization including spectral and elemental analysis for all compounds described (8 pages). Ordering information is given on any current masthead page.

Intrinsic Fluorescence and HPLC Measurement of the Surface Dynamics of Lysozyme Adsorbed on Hydrophobic Silica

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This paper presents results on the direct intrinsic fluorescence and liquid chromatographic measurement of the rate of change of state (weaker to stronger binding) of lysozyme adsorbed at the interface of a hydrophobic surface (*n*-butyl silica gel, C4-RP). To our knowledge, this is the first reported study on the direct kinetic measurement of changes of state while a protein is in contact with an adsorbent surface. There is a great deal of interest within various fields in the study of protein adsorption.[1,2] It is well known that protein conformation and reorientation can take place when the molecule is in contact with a surface.[3] Such changes have been observed by various techniques including intrinsic fluorescence spectroscopy[2,4-7] and chromatography.[8-12] The understanding of these protein surface changes is important in elucidating protein mechanisms of adsorption. In the present case, a first-order rate constant of change of state for lysozyme of 2.7 × 10^{-2} s^{-1} was measured in a 1% methanol buffer at 4 °C. The fluorescence measurements reveal a fast step accompanied by a red shift of the emission wavelength maximum, followed by a slower step associated with a small blue shift and an increase in emission intensity for which the rate constant is determined. In order to demonstrate that this slow step leads to a different state, a C4-RP packed fluorescence cell was incorporated into an HPLC system, and the rate of conversion was separately determined by HPLC.[8-10] The rate constants from the spectroscopic and HPLC methods were found to be in close agreement.

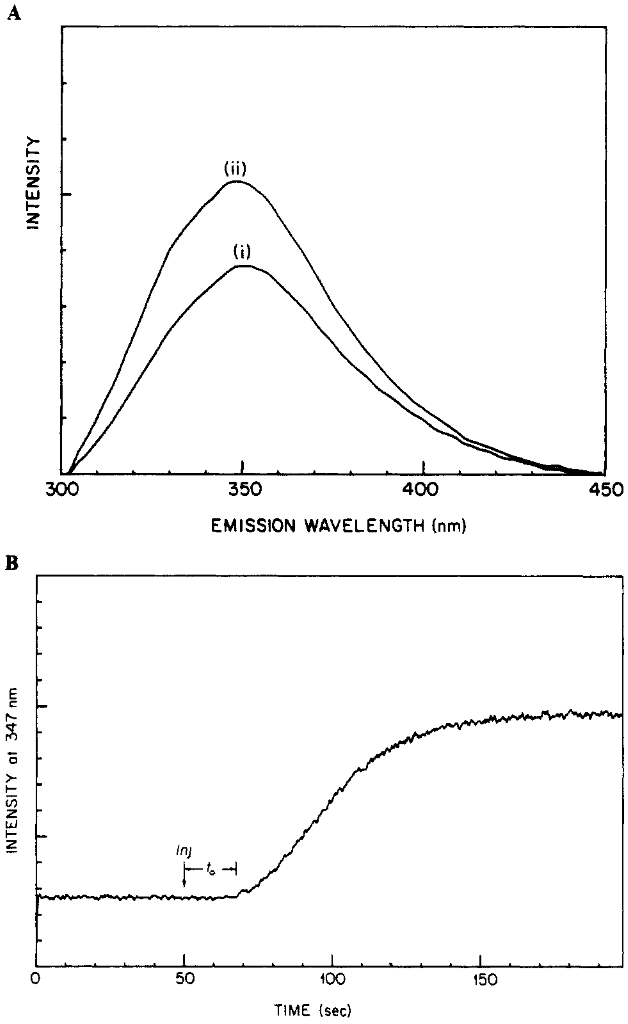

Figure 1. (A) Emission spectra of adsorbed lysozyme collected 15 s after contact (i) and after 90 s incubation (ii): excitation wavelength, 295 nm; slit width, 4 nm; scan rate, 2.5 nm/s; flow rate, 0.3 mL/min. (B) Intensity change as a function of time at an emission wavelength of 347 nm. The arrow indicates the injection time, and t_0 is the time needed for the sample to reach the column. Conditions: 1% methanol in 10 mM phosphoric acid, pH 2.3, 0.3 mL/min, 4 °C, 5 μg of lysozyme injected.

The instrument consisted of a DuPont 8800 liquid chromatograph (DuPont Co., Wilmington, DE) connected to a Suprasil quartz spectroscopic flow cell (35 μL, 11 × 2 mm i.d.) of an SPF-500 spectrofluorometer (SLM-Aminco, Urbana, IL). The flow cell (maintained at 4 °C) was utilized both for fluorescence measurements and as a chromatographic column by slurry packing roughly 25 mg of Vydac silica gel (Separations Group, Hesperia, CA) bonded with *n*-butyltriethoxysilane[13] (particle size 5 μm, pore diameter 300 Å, specific surface area 78 m^2/g). The outlet of the flow cell was connected to an HP 1046A fluorescence HPLC detector (Hewlett Packard, Palo Alto, CA). The sample consisted of 10 μL of 0.5 mg/mL of chicken egg white lysozyme (Sigma Chem. Co., St. Louis, MO) purified by size exclusion chromatography. For the surface fluorescence studies (measured at 90° to the excitation beam), wavelength maxima shifts were determined from a series of spectra taken in the region of 345-360 nm

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