Table III. Synthesis and Properties of 5,6,7,8-Tetrahydrotetrazolo[1,5-*b*][1,2,4]triazines

compound	mp, °C	yield, %
11a: $R_1 = R_2 = H$	147	95
11b: $R_1 = CH_3$; $R_2 = H$	141	
11c: $R_1 = H$; $R_2 = CH_3$	125	92
11d: $R_1 = R_2 = CH_3$ (cis)	131	
11e: $R_1 = R_2 = CH_3$ (trans)	164 dec	98

reduced to **10c** and **10d**. The yields and melting points are summarized in Table II. ^{1}H NMR: **10a** (DMSO-d_6) δ 4.20 (d, J = 2.0 Hz, 2 H), 7.4 (t, 1 H, J = 2.0 Hz), 7.85 (br s, 1 H). **10c** ($(CD_3)_2CO$) δ 1.50 (d, J = 6.0 Hz, 3 H), 3.0 (br s, 1 H), 4.68 (dxq, J = 2.0, J = 6.0 Hz, 1 H), 7.4 (d, J = 2.0 Hz, 1 H). **10d** ($(CD_3)_2CO$) δ 1.50 (d, J = 6.0 Hz, 3 H), 2.20 (s, 3 H), 4.50 (q, J = 6.0 Hz, 1 H), 7.3 (br s, 1 H).

5,6,7,8-Tetrahydrotetrazolo[1,5-*b*][1,2,4]triazines (11a-e). In a 250-mL Erlenmeyer flask equipped with a thermometer and stirring bar was placed 1.22 g (10 mmol) of tetrazolo[1,5-*b*]-[1,2,4]triazine, **6a**, and 50 mL of methanol. This solution (slurry) was stirred, and the temperature was adjusted to 10 °C (ice bath); then sodium borohydride 0.5 g (13 mmol) was added in one portion. After the mixture was stirred for 30 min, the methanol was removed at reduced pressure, 50 mL of water was added, and this was removed at reduced pressure. The resulting solid was recrystallized from a mixture of water to give the pure product. In a similar fashion a mixture of **6b** and **6c**, pure **6c** and **6d** were reduced to give respectively a mixture of **11b** and **11c**, pure **11c**, and a mixture of **11d** and **11e**. The yields and melting points of the products are summarized in Table III. ^{1}H NMR: **11a** (DMSO-d_6) δ 3.30 (m, 4 H), 7.00 (t, J = 6.0 Hz), 7.70 (br s, 1 H). **11b** ($(CD_3)_2CO$) δ 1.25 (d, J = 6.0 Hz, 3 H), 2.90-3.80 (m, 3 H), 6.2 (d, J = 10.0 Hz, 1 H, exchanges), 6.80 (br s, 1 H). **11c** ($(CD_3)_2CO$) δ 1.30 (d, J = 6.0 Hz, 3 H), 2.90-3.80 (m, 3 H), 6.70 (dxd, J = 3.0 Hz, J = 9.0 Hz, 1 H), 7.30 (br s, 1 H). **11d** ($(CD_3)_2CO$) δ 0.95 (d, J = 6.0 Hz, 3 H), 1.05 (d, J = 6.0 Hz, 3 H), 2.9-3.7 (m, 2 H), 7.15 (d, J = 5.0 Hz, 1 H), 7.75 (br s, 1 H). **11e** ($(CD_3)_2CO$) δ 1.05 (d, J = 6.0 Hz, 3 H), 1.15 (d, J = 6.0 Hz, 3 H), 2.3-3.2 (m, 2 H), 6.75 (d, J = 10.0 Hz, 1 H), 7.25 (br s, 1 H).

5,8-Dinitro-5,6,7,8-tetrahydrotetrazolo[1,5-*b*][1,2,4]triazine (12). In a 25-mL round-bottom flask equipped with a magnetic stirring bar was placed 8.0 mL of 100% nitric acid. This was cooled to 0 °C, and 4 mL of acetic anhydride was added dropwise over 2 min. This mixture was stirred for 10 min. The temperature was then lowered to -20 °C, and 1.26 g (10.0 mmol) of **11a** was added in small portions over 10 min. The mixture was stirred at 0 °C for 10 min and then quenched on ice. After the ice melted, the crude product was isolated by filtration and dried in a vacuum to give 2.1 g (9.5 mmol, 95%) of crude product. The product can be recrystallized by dissolving it in acetone at room temperature and precipitating it out by adding water. The purified product has a mp of 102-104 °C dec. ^{1}H NMR ($(CD_3)_2CO$) δ 4.60 (t, 2 H, J = 5.5 Hz), 5.00 (t, 2 H, J = 5.5 Hz).

8-Nitro-7,8-dihydrotetrazolo[1,5-*b*][1,2,4]triazine (13). Nitration of 0.62 g (5 mmol) of **10a** with acetic anhydride (4 g) and nitric acid (8.0 g) by the procedure described for **12** gave 0.82 g (4.7 mmol, 95%) of **13**. The compound decomposes when recrystallized. The melting point of the crude product is 124-126 °C dec. ^{1}H NMR ($(CD_3)_2CO$) δ 5.50 (d, J = 2.0 Hz, 2 H), 8.2 (t, J = 2.0 Hz, 1 H).

7-Nitro-5,6-dihydro-7*H*-imidazolo[1,2-*d*]tetrazole (14). In a 25-mL ratio round-bottom flask equipped with a magnetic stirring bar was placed 10 g of acetic anhydride. This was cooled to 0 °C (salt-ice bath), and 10 g 100% nitric acid was added dropwise over 10 min. This nitrating solution was stirred for 20 min; then 5.55 g (50 mmol) of 5,6-dihydro-7*H*-imidazolo[1,2-*d*]-tetrazole[11] was added in small portions over 10 min. The solution was stirred for 20 min and then quenched on 50 g of crushed ice. The crude product was collected, washed with water, and dried. The yield was 5.9 g of colorless crystals (37 mmol; 75% yield). Recrystallization from acetone-water gave the pure product, mp 160 °C dec. ^{1}H NMR (CD_3SOCD_3) δ 4.75 (m, 2 H, H_5), 5.05 (m, 2 H, H_6).

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Supplementary Material Available: Tables of atomic coordinates and isotropic thermal parameters for **11b** and **12** and diagrams with atom numbering (2 pages). Ordering information is given on any current masthead page.

An Unusual Ring Reorganization of a *N*-Styrylisothiazolethione to a 2-Styrylthiazole

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Although the excited-state rearrangement of isothiazoles to thiazoles and the reverse reaction have been well documented,[2] the ground-state version of this type of rearrangement has never been reported so far. We now report the first example of this skeletal reorganization reaction.

In the course of our synthetic efforts on 1,4-thiazepine systems,[3] we have found that attempted Pummerer reaction of 2,3-dihydro-2,7-diphenyl-5-methoxy-1,4-thiazepine 1-oxide (**1**) gave 3-oxo-5-phenyl-(*Z*)-*N*-styrylisothiazole, which, on heating, was quantitatively isomerized to the corresponding *E* isomer (**2**).[4] Treatment of **2** with phosphorus pentasulfide gave a fairly labile product in 78% yield, which could not be purified fully. Nevertheless, the structure of this product can safely be assigned to the expected 3-thioxo-5-phenyl-(*E*)-*N*-styrylisothiazole (**3**) as inferred from the available spectral data. Thus, the ^{1}H NMR spectrum of **3** definitely shows the presence of a β-substituted (*E*)-styryl grouping as exemplified by an AB quartet at δ 6.08 and 7.92 with J_{AB} = 14.3 Hz. Furthermore, the IR spectrum of **3** reveals a thiocarbonyl absorption at 1178 cm^{-1} instead of the corresponding carbonyl absorption at around 1660 cm^{-1}.[4] These spectral findings strongly suggest that no skeletal rearrangement occurred during the reaction of **2** with phosphorus pentasulfide (Scheme I).

To convert the thione **3** into the isothiazolium ion salt **4**, compound **3** was treated with trimethyloxonium tetrafluoroborate in dichloromethane at room temperature for 2 h. Instead of the anticipated product (i.e., 3-(methyl-

(1) Current address: Department of Chemistry, Nara University of Education, Takabatake-cho, Nara 630, Japan.

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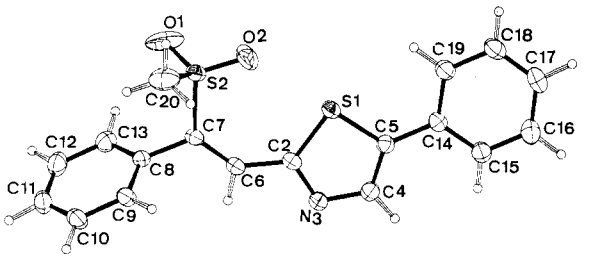
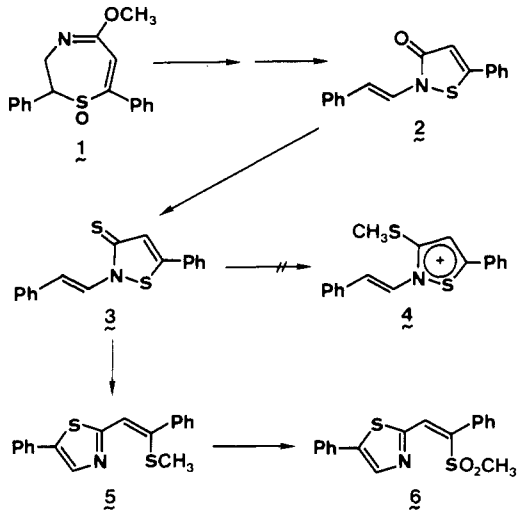
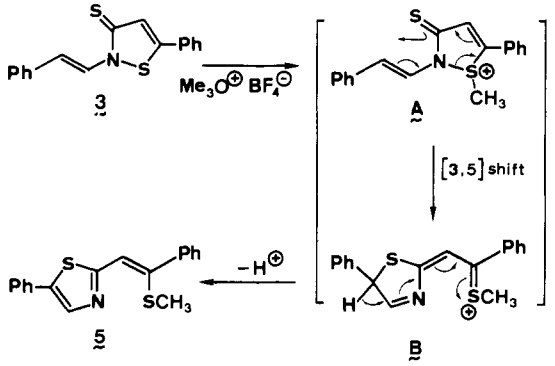


Figure 1. An ORTEP view of the sulfone **6**, showing the atom numbering scheme. Selected distances are as follows: S(1)–C(2) 1.730 (3), S(1)–C(5) 1.714 (3), C(2)–N(3) 1.316 (4), C(2)–C(6) 1.459 (4), N(3)–C(4) 1.358 (4), C(4)–C(5) 1.362 (4), and C(6)–C(7) 1.337 (4) Å.

Scheme I



Scheme II



thio)-5-phenyl-*N*-styrylisothiazolium ion (**4**)), a new compound **5** was obtained in 61% yield whose ^{1}H NMR and mass spectra indicated the presence of methylthio and two phenyl groups. Although the compound **5** possesses two sulfur atoms, one was not susceptible to oxidation. Thus, *m*-chloroperbenzoic acid oxidation (2 equiv) of **5** gave the monosulfone **6**. This suggests that one of the sulfur atoms might be incorporated in a π-excess heteroaromatic ring.[5] Neither the reactivity nor the analysis of routine NMR, IR, UV, and mass spectra provided sufficient information to unequivocally assign the structure of **5**. Therefore, we turned to single-crystal X-ray structural analysis of the sulfone **6** to establish the structure of **5**. The structure of **6** is shown in Figure 1. Hence, the compound **5** can be assigned with confidence as (*Z*)-2-[2-(methylthio)-2-phenylethenyl]-5-phenylthiazole.

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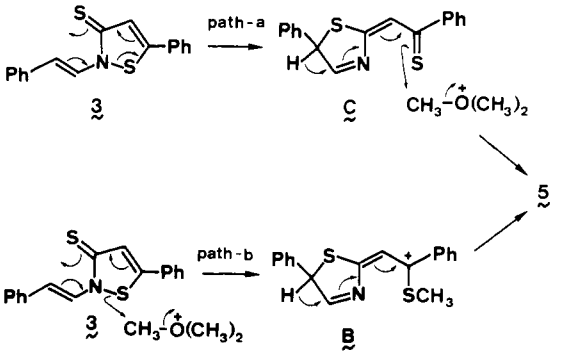
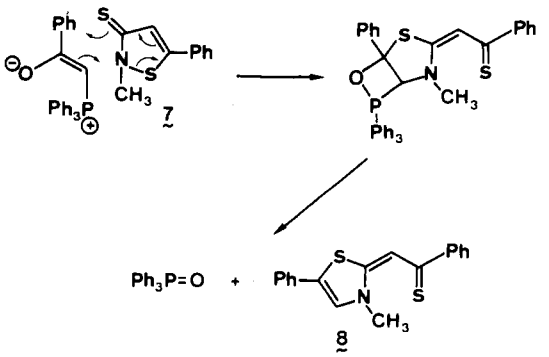
Scheme III



Scheme IV



At first we propose a mechanism (Scheme II) to account for the unusual transformation **3** → **5**. Although **3** possesses three potential nucleophilic centers that could be methylated by Meerwein reagent, only a sulfonium ion (A) produced by the reaction at ring sulfur atom would have led to the second intermediate (B) by way of eight-electron pericyclic process (apparent [3,5]sigmatropic shift of the N–S$^+$ bond) followed by deprotonation (Scheme III). This mechanism provides the simplest explanation for the observed product; however, methylation of the ring sulfur atom rather than the thione seems unusual.[6] A possible explanation is that the hard acid, trimethyloxonium tetrafluoroborate, may prefer to alkylate on the ring sulfur (possibly harder than usual because of adjacent nitrogen). Therefore, it would be interesting to see if the use of methyl iodide, a weaker acid, would give alkylation in the thioxo group.[7] In this context, we have examined the reaction of **3** with methyl iodide. Although, on treatment with methyl iodide, the simple *N*-alkyl-5-arylisothiazoline-3-thiones are known to give the corresponding isothiazolium iodides,[8] the same reaction of **3** afforded only tarry material. Presumably, this failure is due to the presence of a *N*-styryl group in our compound **3**. Thus, a most plausible mechanism to account for the rearrangement would be that either the rearrangement happens first to give the intermediate (C), which can be trapped by the Meerwein reagent (Scheme III, path a), or the methylation occurs concertedly with the rearrangement to afford the intermediate (B) followed by deprotonation (path b).[9]

As to these pericyclic processes, a precedent for the transformation of *N*-methyl-5-phenylisothiazole-3-thione

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(9) We thank referees for pointing out this mechanism.

(7) into the thiazole skeleton 8 on treatment with phenacylidene-triphenylphosphorane (Scheme IV) was found in the literature.[10] The novel ring reorganization reported in this paper may be viewed as an intramolecular version of the above intermolecular reaction.

Experimental Section

Melting points were uncorrected. IR spectra were recorded on a JASCO A-100 spectrophotometer. ^1H NMR spectra were recorded in $CDCl_3$ on a Varian XL-100 spectrometer. ^{13}C NMR spectra were taken on JEOL FX-90Q spectrometer. All chemical shifts are reported in δ units downfield from Me_4Si, and the J values are given in hertz. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet. Mass spectra were obtained with a JEOL JMS-01SG-2 spectrometer at 75 eV. UV spectra were measured on a Hitachi 340 recording spectrophotometer. All reactions were carried out under a nitrogen atmosphere.

3-Thioxo-5-phenyl-(*E*)-*N*-styrylisothiazole (3). To a solution of 3-oxo-5-phenyl-(*E*)-*N*-styrylisothiazole (2) (84.5 mg, 0.303 mmol) in pyridine (1.3 mL) was added phosphorus pentasulfide (76.6 mg, 0.345 mmol) by portions. The mixture was stirred for 3 h at room temperature. After addition of water the mixture was extracted with CH_2Cl_2, and the extracts were washed with 2 N HCl and saturated aqueous $NaHCO_3$ and then dried over Na_2SO_4. Removal of the solvent gave 70 mg (78% yield) of crude 3 as orange crystals, which, without purification, was subjected to the following reaction: ^1H NMR δ 6.08 (s, 1 H), 6.08 (d, 1 H J = 14.3 Hz), 7.0-7.7 (m, 10 H), 7.92 (d, 1 H, J = 14.3 Hz); IR ($CHCl_3$) 1178 cm^{-1}; MS, m/z (relative intensity) 295 (M^+, 16%).

(*Z*)-2-[2-(Methylthio)-2-phenylethenyl]-5-phenylthiazole (5). To a solution of 3 (56.5 mg, 0.19 mmol) in 2 mL of dichloromethane was added 28.3 mg (0.19 mmol) of freshly prepared trimethyloxonium tetrafluoroborate. The resulting mixture was stirred at room temperature for 2 h. To the stirred solution was added aqueous K_2CO_3 solution. The mixture was extracted with dichloromethane, and the combined extracts were dried over Na_2SO_4. The solvent was removed, and the residue was chromatographed on silica gel (containing 5% water), eluting with chloroform to give 5 (36.3 mg, 61% yield) as orange crystals. Recrystallization from ether gave a sample: mp 59-60 °C; ^1H NMR δ 2.15 (s, 3 H), 7.20 (s, 1 H), 7.34-7.65 (m, 10 H), 8.02 (s, 1 H); IR (KBr) 1585, 1485, 1475, 1442, 1150, 780, 755 cm^{-1}; UV (cyclohexane) λ_{max} (log ϵ) 242 (4.05), 279 (3.91), 360 (4.43) nm; MS, m/z (relative intensity) 309 (M^+, 100), 294 (49), 276 (42), 262 (39), 134 (42). Anal. Calcd for $C_{18}H_{15}NS_2$: C, 69.78; H, 4.89; N, 4.53; S, 20.72. Found: C, 69.77; H, 4.91; N, 4.54; S, 20.55.

(*Z*)-2-[2-(Methylsulfonyl)-2-phenylethenyl]-5-phenylthiazole (6). A solution of MCPBA (80%, 109 mg, 0.51 mmol) in CH_2Cl_2 (2.6 mL) was added dropwise with stirring at 0 °C to a solution of 5 (78 mg, 0.25 mmol) in CH_2Cl_2 (3.4 mL). After further stirring at room temperature for 2.5 h, the solution was washed with 5% aqueous $NaHSO_3$ and saturated aqueous $NaHCO_3$ and then dried over Na_2SO_4. Removal of the solvent gave 6 quantitatively as pale yellow crystals: mp 164-165 °C (recrystallized from ethyl acetate); ^1H NMR δ 3.03 (s, 3 H), 7.27-7.62 (m, 10 H), 7.29 (s, 1 H), 8.05 (s, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 42.96, 127.1, 128.8, 129.1, 129.3, 129.4, 129.6, 130.8, 133.6, 135.5, 139.6, 142.0, 145.2, 157.8; IR (KBr) 1605, 1295, 1130, 800 cm^{-1}; UV (cyclohexane) λ_{max} (log ϵ) 260 (3.69), 346 (4.37); MS (75 eV), m/z 341 (M^+, 18), 340 (39), 262 (100), 134 (40). Anal. Calcd for $C_{18}H_{15}NO_2S_2$: C, 63.32; H, 4.43; N, 4.10; S, 18.78. Found: C, 63.15; H, 4.32; N, 4.15; S, 18.52.

Single-Crystal X-ray Diffraction Analysis of (*Z*)-2-[2-(Methylsulfonyl)-2-phenylethenyl]-5-phenylthiazole (6). The crystal data for 6 (single crystal obtained via recrystallization from ethyl acetate) are as follows: $C_{18}H_{15}NO_2S_2$, M = 341.43, monoclinic, space group $P2_1/a$, a = 9.290 (2) Å, b = 22.938 (3) Å, c = 8.521 (1) Å, β = 117.39 (1)°, V = 1612.1 (4) Å^3, Z = 4, D_c = 1.41 g cm^{-3}. Intensity data were collected by a Syntex R3 diffractometer in the range of $2 < 2\theta < 55°$ by using the monochromated Mo Kα radiation (λ = 0.71069 Å). The intensities of the three standard reflections were monitored every 100 reflections, and no significant variation was observed throughout the date collection. The data were corrected for Lorentz and polarization effects. Of 3783 collected reflections, 2826 were considered observed at the level of ($|F_o| \geq 3\sigma|F_o|$). The structure was solved by the direct method (MULTAN78) and refined anisotropically by the full-matrix least-squares process. All the hydrogen atoms, located on a difference Fourier map, were included in the final part of the refinement with the isotropic temperature factors to give the final agreement indices R = 0.050 and R_w = 0.046. The weights were of the form $w = 1/\sigma^2(F_o)$. The final difference electron density map was featureless with the largest residual peak of 0.26 e/Å^3.[11] All the calculations were carried out on a HITAC M-200H computer at Hiroshima University with the structure analysis program system UNICS3.[12]

Registry No. 2, 110567-91-4; 3, 116503-11-8; 5, 116503-12-9; 6, 116503-13-0.

Supplementary Material Available: Tables of atomic coordinates, anisotropic thermal parameters, interatomic distances, and interatomic angles for 6 (3 pages). Ordering information is given on any current masthead page.

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(11) Tables of atomic coordinates, anisotropic thermal parameters, bond lengths, and bond angles for 6 have been deposited as supplementary material.

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NMR Spectroscopic Investigation of Previtamin D_3: Total Assignment of Chemical Shifts and Conformational Studies

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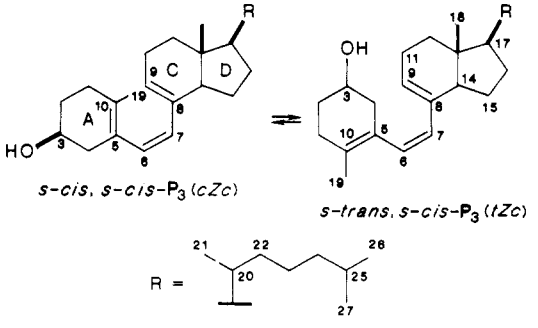
The two different classes of conformations of previtamin D_3 (P_3) are thought to lead upon irradiation to different products (ground-state conformational control,[2a] NEER principle[2b]). The two types of conformations proposed are shown in the following scheme. The thermal formation of vitamin D_3 occurs predominantly from one specific *cZc* conformation:[3]



(1) Recipient of a Feodor Lynen-Fellowship of the Alexander von Humboldt-Stiftung 1986-1988.

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