ine at 20° and μ = 0.1. In general, the basicity of the SeH group is considerably lower than that of the SH group. On the other hand, there is a fair correlation between the mercury-proton coupling constants and the electronegativity (Se, 2.4; S, 2.5; N, 3.0) or covalent radius (Se, 1.16; S, 1.02, N, 0.75 Å) of the coordination atoms. These results suggest high covalency of the CH_3Hg-Se bond which involves d_π-d_π back-bonding. In view of the fact that selenium compounds afford excellent protection against mercury intoxication,[10] our finding herein that the selenohydryl group has a high affinity for the mercury compound is of particular interest.

Acknowledgment. Gratitude is due to M. Ohara for assistance with the manuscript.

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(6) In the infrared spectrum of the isolated complex, the presence of $\nu(NH_3^+)$ near 3000 cm^{-1} and the disappearance of ν(SeH) at 2575 cm^{-1} in the free ligand revealed that selenocysteamine coordinates to methylmercury through the selenium atom only, consistent with a methylmercury coordination number of one.

(7) The sample was prepared by mixing the D_2O solution of the ligand (0.2 M) and the dioxane-d_8 solution of methylmercuric chloride (0.2 M) just before the ^1H NMR measurements, as the sample solution showed signs of precipitation after a few minutes.

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(9) The pH independence of the chemical shifts and coupling constant in an equimolar solution of methylmercury and selenocysteamine (or cysteamine) indicates the complex formation of methylmercury by the ligand over the pH range 1–12.

(10) The action of selenocysteamine on mercury toxicity was investigated in male Wister rats (ca. 150 g) in a dose of 10 μmol/kg sc. The percentage of living animals was 20% in those treated with the mercury compound only (20 μmol/kg ip). A concurrent treatment of selenocysteamine resulted in an increase to 90%.

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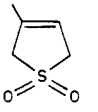
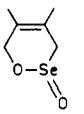
(2 + 4) (π + $\pi\pi$) and (2 + 4) (n + $\pi\pi$) Modes of Addition in the Reaction between SO_2 and a Diene. Kinetic vs. Thermodynamic Control

Sir:

Since de Bruin suggested a cyclic sulfone structure **1** for the crystalline monoadduct obtained from the reaction of liquid sulfur dioxide and isoprene at room temperature,[1] subsequent investigations, conducted in part by Backer and Strating in our laboratories,[2] proved this assumption to be correct and many examples of this 1,4-cycloaddition to dienes have been reported. The industrial value of this type of reaction can be judged from the fact that the sulfur dioxide addition to butadiene is the key step in the synthesis of sulfolane. Although selenium dioxide was at first expected to react with 1,3-dienes in an analogous way, it was show by ^1H NMR spectroscopy that cyclic seleninic esters[3] (e.g., **2**) are formed, thus indicating that (2 + 4) (π + $\pi\pi$) instead of (2 + 4) (n + $\pi\pi$) reactions[4] had taken place between the dienes and selenium dioxide. This difference in chemical behavior combined with the fact that rearrangements of sulfinic esters to sulfones[5] were likely to occur under the conditions employed for almost all sulfur dioxide additions,[6] prompted us to investigate the addition of both dioxides to 1,2,5,6-tetramethyl-3,4-dimethylenetricyclo[3.1.0.0^{2,6}]hexane **3**,[7] which had been shown before to be highly reactive in Diels–Alder processes.[8]



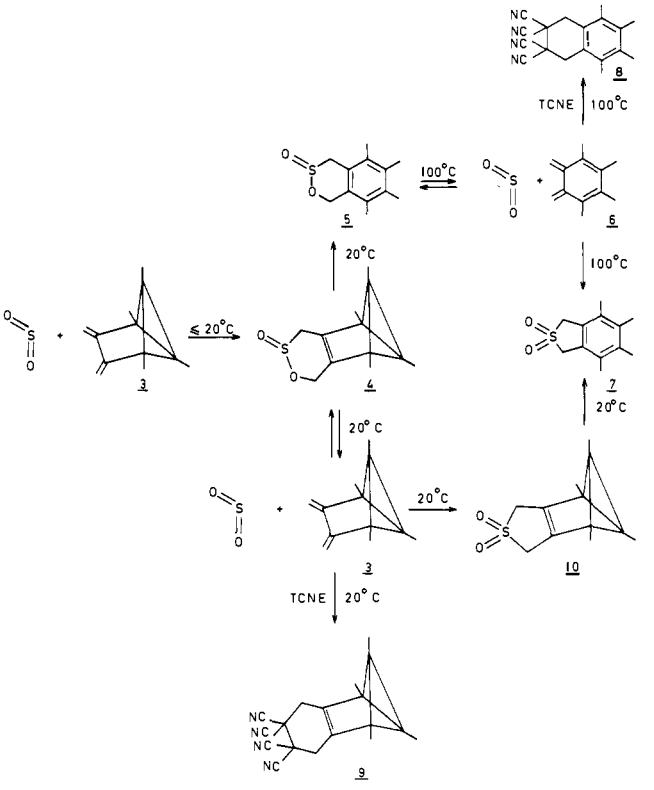
1



2

When sulfur dioxide (dried over phosphorus pentoxide) was introduced at or below room temperature into a stirred chloroform[9] solution of tricyclic diene **3**, an instantaneous reaction took place leading to the kinetically-controlled formation of the sulfinic ester **4**[10] by a (2 + 4) (π + $\pi\pi$) cycloaddition. The ester is not stable at room temperature and rearranges thermally via two possible pathways, namely, preferentially (isolated 90%) to the aromatic ester **5**[11] by an isomerization of the bicyclobutane moiety, and to sulfone **10**[12] (Scheme I).[13]

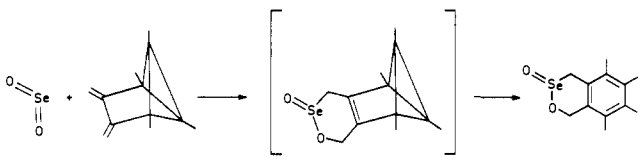
Scheme I



Heating the aromatic ester **5** in *o*-dichlorobenzene at 80–100 °C caused dissociation into sulfur dioxide and the *o*-xylene derivative **6**, followed by recombination[14] yielding in a thermodynamically controlled (2 + 4) (n + $\pi\pi$) cycloaddition the aromatic sulfone **7**[15] (98% isolated). This sulfone was also obtained by isomerization of the bicyclobutane moiety in sulfone **10** at room temperature.

The thermal rearrangement of cyclic β,γ-unsaturated sulfinic esters to sulfones has been shown to proceed via a retro-Diels–Alder reaction.[14] Confirmation of this cycloreversion has now been obtained in the case of both the polycy-

clic and aromatic sulfinic esters **4** and **5** by isolation from their solutions at 20° in the former and at 100° in the latter case of the corresponding tetracyanoethylene (TCNE) adducts **9**[7,16] (7%) and **8**[8] (isolated 90%), respectively (instead of the corresponding sulfones **10** and **7**), on addition of TCNE.



3 11 12

The addition of sulfur dioxide thus bears a close resemblance to the reported selenium dioxide addition to 1,3-dienes. Also with diene **3** at room temperature in chloroform a seleninic ester **12**[17] was formed probably via the intermediacy of **11**, and was isolated in 70% yield. Heating of compound **12** to 180° in *o*-dichlorobenzene did not lead to any rearrangement to the corresponding selenone.

The established reaction sequence as stated in Scheme I suggests that at least in the case of highly reactive dienes more examples of kinetically controlled (2 + 4) (π + $\pi\pi$) vs. thermodynamically controlled (2 + 4) (n + $\pi\pi$) cycloadditions of sulfur dioxide are to be expected.

Acknowledgment. We are grateful to Professor J. Strating for a discussion of the subject and for reading the manuscript.

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(9) If benzene is chosen as the solvent the same applies.
(10) ^{1}H NMR ($CDCl_3$, 30°) δ 1.24 (s, 3 H), 1.34 (s, 3 H), 1.52 (s, 3 H), 1.60 (s, 3 H), 5.07 and 5.25 (SCH_2, 2 H), 5.59 and 5.76 (OCH_2, 2 H); ^{13}C NMR ($CDCl_3$, 30°; δ relative to internal Me_4Si; noise decoupled) δ 3.4, 4.2, 8.5, and 11.9 (CH_3-carbons), 44.0, 57.0, 71.5, and 87.3 (quaternary carbons), 105.5 and 106.9 (CH_2-carbons), 146.7 and 147.6 (sp^2-carbons). Too unstable (i.e., isomerization to **5**) to be isolated.
(11) ^{1}H NMR ($CDCl_3$, 30°) δ 2.23 (s, 6 H), 2.25 (s, 6 H), 3.50 and 4.41 (AB-quartet, J_{AB} = 16 Hz, 2 H), 5.18 (s, 2 H). If dissolved in *o*-dichlorobenzene an asymmetric solvent-induced shift (ASIS) occurs, revealing a second AB-system; ^{1}H NMR (*o*-dichlorobenzene, 30°) δ 1.58 (s, 6 H), 1.66 (s, 6 H), 2.96 and 3.73 (AB-quartet, J_{AB} = 16 Hz, 2 H), 4.57 and 4.74 (AB-quartet, J_{AB} = 14 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 30°, δ relative to internal Me_4Si; noise decoupled) δ 14.5, 15.4, 16.2, and 16.6 (CH_3-carbons), 53.1 and 60.4 (CH_2-carbons), 121.2, 128.8, 129.5, 132.3, 134.5 and 135.1 (sp^2-carbons); ir (Nujol mull) 1105 cm^{-1} (S=O); MS M$^+$ peak at *m/e* 224. Anal. Calcd for $C_{12}H_{16}SO_2$: C, 64.25; H, 7.19; S, 14.29. Found: C, 64.24; H, 7.22; S, 14.31. Compound **5** rearranges prior to melting.
(12) ^{1}H NMR ($CDCl_3$, 30°) δ 1.69 (s, 6 H), 1.71 (s, 6 H), and 3.44 (s, 4 H). Too unstable (i.e., isomerization to **7**) to be isolated.
(13) If the diene **3** is added to liquid sulfur dioxide, condensed at −50° in an open tube, only the aromatic sulfinic ester **5**, due to a sulfur dioxide catalyzed rearrangement, can be isolated; the same isomerization can be induced by treating the polycyclic ester **4** with $AgClO_4/Na_2CO_3$ or with CCl_3COOH. Compare ref 8.
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(15) ^{1}H NMR ($CDCl_3$, 30°) δ 2.13 (s, 6 H), 2.18 (s, 6 H), and 4.27 (s, 4 H); ^{13}C NMR ($CDCl_3$, 37°, δ relative to internal Me_4Si; noise decoupled) δ 16.1 and 17.2 (CH_3-carbons), 57.1 (CH_2-carbons), 127.2, 130.3, and 135.6 (sp^2-carbons); ir (Nujol mull) 1300 and 1130 cm^{-1} (O=S=O); MS M$^+$ peak at *m/e* 224. Anal. Calcd for $C_{12}H_{16}SO_2$: C, 64.25; H, 7.19; S, 14.29. Found: C, 64.29; H, 7.17; S, 14.26; mp 212.0–212.5 °C.
(16) Since no recombination to sulfone **10** is observed in this experiment it is concluded that in the absence of TCNE the rearrangement via **10** to **7** proceeds in 7% yield. The isomerization of **4** to **5** occurs thus in 93% yield. The data are obtained by comparing the relative areas of the absorptions due to the methylene protons in **9** and **5**, respectively, these compounds being the only products formed under these conditions.
(17) ^{1}H NMR ($CDCl_3$, 30°) δ 2.28 (s, 6 H), 2.33 (s, 6 H), 3.43 (d, J = 14 Hz, 1 H), 4.93 (d, J = 14 Hz, 1 H), 4.99 and 5.40 (AB-quartet, J_{AB} = 13 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 37°, δ relative to internal Me_4Si; noise decoupled) δ 15.3; 15.9, 16.8, and 17.0 (CH_3-carbons), 55.4 and 62.4 (CH_2-carbons), 123.3, 130.8, 132.5, 134.3, 135.3, and 135.8 (sp^2-carbons); ir (Nujol mull) 838 cm^{-1} (Se=O); MS M$^+$ peaks at *m/e* 268, 269, 270, 272, and 274 ($_{34}Se^{76}$ = 9.02, $_{34}Se^{77}$ = 7.58, $_{34}Se^{78}$ = 23.52, $_{34}Se^{80}$ = 49.82, $_{34}Se^{82}$ = 9.19% natural abundance). Anal. Calcd for $C_{12}H_{18}SeO_2$: C, 53.15; H, 5.95; Se, 29.11. Found: C, 52.83; H, 5.81; Se, 28.71. Compound **12** decomposes prior to melting (T > 170°).

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Synthesis of 2-Methyl-3-cephem Derivatives[1]

Sir:

In the past decade there has been considerable interest in the chemical modification of penicillins and cephalosporins. We also have developed a useful procedure for the preparation of modified β-lactam derivatives from penicillins via disulfide **1** and penam bromide **2**.[2] In the preceding paper we reported on the synthesis of a new tricyclic β-lactam **3** from **2**;[3] we now report the conversion of **3** via intramolecular cyclopropane ring opening into 2-methyl-3-cephem derivative **4**. The key step, opening the cyclopropane ring while preserving the labile β-lactam ring, was achieved with Lewis acids[4] and yielded all of the possible stereoisomers **4, 5, 6,** and **7** of the 2-methylcephem systems.

Treatment of tricyclic sulfide **3** in CH_2Cl_2 with $AlBr_3$ for 1 h at 0 °C gave a mixture of 3-cephems **4** and **5**, and 2-cephem **6**. Chromatographic separation afforded in 80% yield 2α-methyl-3-cephem **4**, mp 175–178 °C (ir 1790 cm^{-1} (β-lactam C=O); NMR δ (in $CDCl_3$) 1.46 (d, J = 7.5 Hz, 2-CH_3), 3.62 (m, 2-H), 6.66 (d, J = 6 Hz, 3-H), 4.92 (d, J = 4.5 Hz, 6-H), 5.94 (dd, J = 4.5 and 9 Hz, 7-H)), and in 2–3% yields, respectively, 2β-methyl-3-cephem **5**, mp 120–122 °C (ir 1775 cm^{-1} (β-lactam C=O); NMR δ (in $CDCl_3$) 1.50 (d, J = 8 Hz, 2-CH_3), 3.88 (m, 2-H), 6.41 (d, J = 2 Hz, 3-H), 5.11 (d, J = 5 Hz, 6-H), 5.85 (dd, J = 5 and 9 Hz, 7-H)), and 2-methyl-2-cephem **6**, mp 136–137 °C (ir 1780 cm^{-1} (β-lactam C=O); NMR δ (in $CDCl_3$) 1.94 (t, J = 1.5 Hz, 2-CH_3),[5] 5.00 (m, 4-H), 5.59 (m, 3-H), 5.18 (d, J = 4.5 Hz, 6-H), 5.70 (dd, J = 4.5 and 9 Hz, 7-H)).

The configuration of **4** was based on the NMR analysis of its β-sulfoxide **8**,[6] mp 173–175 °C, prepared by oxidation with *m*-chloroperbenzoic acid ($CHCl_3$, 0°, 1.5 h); similarly, **5** was oxidized (*m*-chloroperbenzoic acid, $CHCl_3$, 0°, 1 h) to β-oxide **9**,[6] mp 160–161 °C.

The 2-methyl configuration was assigned α for **4** and β for **5** on the following evidence: (i) the 2-CH_3 signal of **8** (1.25 ppm) is more shielded than that of **9** (1.63 ppm);[7] (ii) in **8**, a 1.0 Hz long-range coupling is present between 2-H and 7-H,[8] and furthermore, a 7% NOE is observed between 6-H and 2-CH_3; (iii) in **9**, on the other hand, 1.5 Hz long-range coupling is present between 2-H and 6-H;[9,10] and (iv) the $J_{2,3}$ values of 6 Hz for **8** and 2 Hz for **9** are in agreement with dihedral angles estimated from molecular models.

In contrast, treatment of **3** in CH_2Cl_2 with $TiCl_4$ for 2.5 h at room temperature gave selectively 2-cephem **7**, mp 108.5–110.5 °C (ir 1770 cm^{-1} (β-lactam C=O); NMR δ (in $CDCl_3$) 1.99 (t, J = 1 Hz, 2-CH_3),[5] 4.68 (m, 4-H), 5.68 (m, 3-H), 5.06 (d, J = 4 Hz, 6-H), 5.56 (m, 7-H)), 70%