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Stereoisomerism Based on High-energy Inversion Barrier of Pentathiepane Ring: Preparation and Isolation of Conformers

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Abstract: Sulfuration of acenaphtho[1,2-*a*]acenaphthylene (**1**) with elemental sulfur gave a pentathiepane derivative (**2**). Dynamic NMR analyses revealed that the two naphthalene rings of **2** are chemically nonequivalent up to 100 °C due to freezing of the inversion of the pentathiepane ring. Thus, sulfuration of 5-phenylacenaphtho[1,2-*a*]acenaphthylene gave a pair of conformers which were isolable and whose steterochemistry was determined by X-ray diffraction analysis. These conformers isomerized slowly to each other in solution at room temperature.

Recent isolation of biologically active benzopentathiepin derivatives, varacin and lissoclinotoxins,[1] from marine organisms has much inspired synthetic, structural, and physiological interest in cyclic oligosulfides.[2] The above naturally occurring benzopentathiepins were claimed to be chiral because of slow inversion of the pentathiepin ring on the NMR time scale.[2d,e] Ring inversion parameters of 1,2,3,4,5-pentathiepins, where two sulfur atoms are bonded to sp^2 carbon atoms, were estimated by molecular orbital[3] and molecular mechanics[2e] calculations, and very recently conformers based on slow inversion of the benzopentathiepin ring were isolated.[4] Although 1,2,3,4,5-pentathiepanes, where two sulfur atoms are bonded to sp^3 carbons, are produced together with 1,2,3-trithiolanes by sulfuration of cyclic alkenes, such as norbornene[5] and dibenzobarrelene,[6] with elemental sulfur, conformational analysis of them has not been examined in detail. We report here a new stereoisomerism due to slow inversion of a pentathiepane ring which enabled us to isolate a pair of conformers in pure form.

Sulfuration of acenaphtho[1,2-*a*]acenaphthylene (**1**)[7] with elemental sulfur (1 molar amount as S_8) in DMF at 130 °C gave the pentathiepane **2**, with a [5.3.3]propellane structure, as the sole product in 88% yield. The trithiolane **3**, which has a more strained [3.3.3]propellane structure, was not formed, in contrast to the sulfuration of norbornene[5] and dibenzobarrelene.[6] The pentathiepane **2** was obtained as colorless crystals, decomposing at 248 °C to form **1** and sulfur. The ^1H NMR spectrum of **2** showed a pair of doublets of doublets and a pair of four doublets in the aromatic region, and the ^{13}C NMR spectrum showed twelve peaks in the range δ 120-144 due to the aromatic carbons and one peak at δ 97 due to the bridgehead carbons,[8] revealing the nonequivalency of the two naphthalene rings. Dynamic ^1H NMR in toluene-d_8, monitored up to 100 °C, did not show the coalescence of signals. Reduction of **2** with $LiEt_3BH$, followed by treatment with MeI, gave a 66% yield of the bis-sulfide **4** whose two naphthalene rings are equivalent in ^1H and ^{13}C NMR.[9] These observations are in harmony with the given chair structure **2** with a C_S symmetry where two naphthalene rings are placed in a different environment. The boat conformation **2'**, although it can also explain the NMR data,

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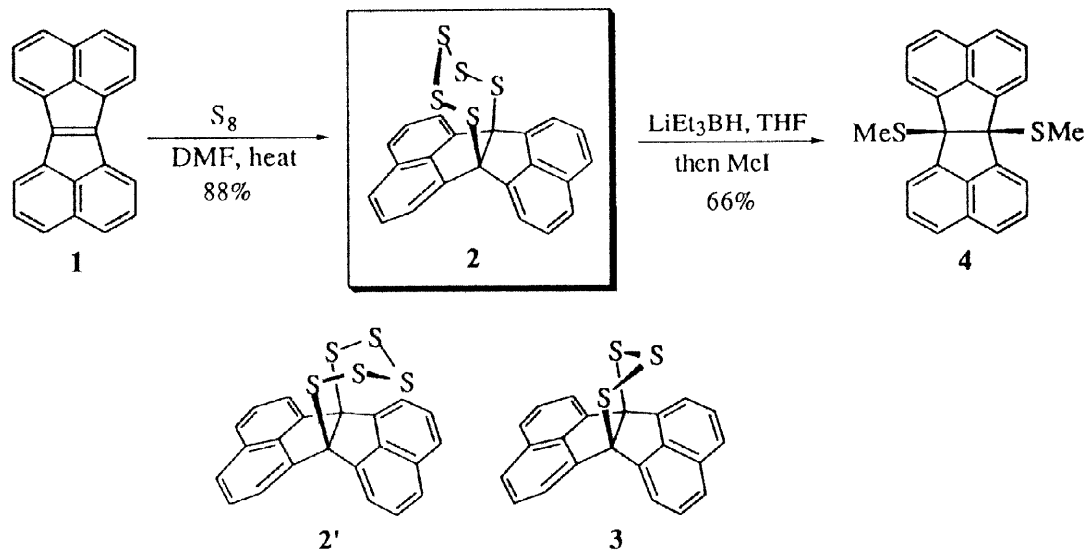
would be unfavorable because of repulsive interactions between the sulfur ring and the naphthalene ring.[10] Nonequivalency of the naphthalene rings of the present system is ascribed to the high-energy barrier of inversion of the pentathiepane ring.



The crystalline structure of **2** was determined by X-ray single crystallographic analysis. An ORTEP drawing of **2** is given in Figure 1 with selected bond lengths and angles data.[11] In agreement with the prediction by NMR, the pentathiepane ring adopts a typical chair conformation in which it is fixed over one of the naphthalene rings.

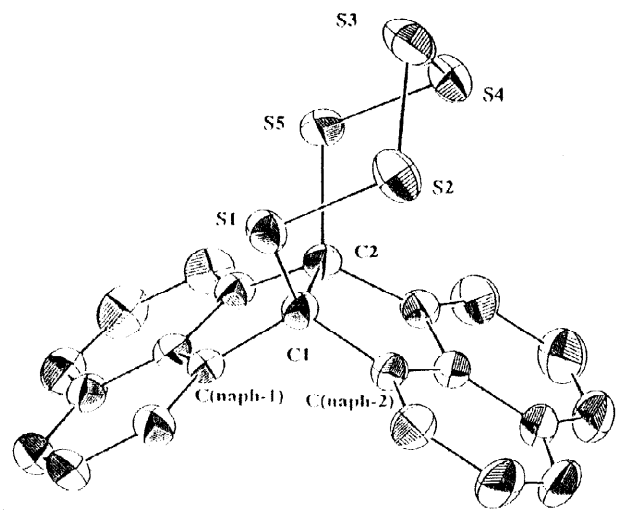
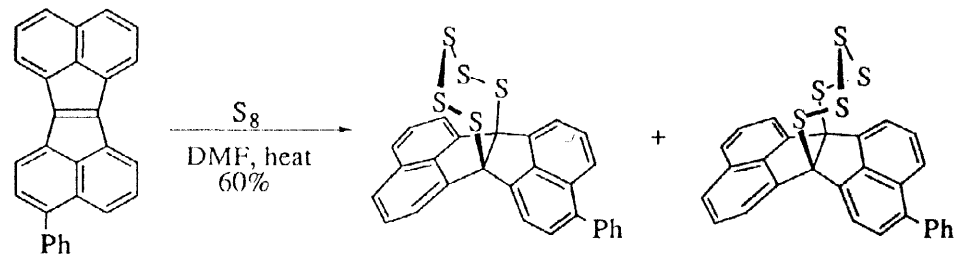


Figure 1. An ORTEP drawing of **2**. Selected bond lengths (Å) and angles (°) on the average: C(1)-C(2), 1.633(3); C(1)-S(1), 1.840(3); S(1)-S(2), 2.038(1); S(2)-S(3), 2.055(2); C(1)-C(2)-S(5), 119.5(1); C(1)-S(1)-S(2), 105.8(1); S(1)-C(1)-C(naph-1), 102.6(2); S(1)-C(1)-C(naph-2), 113.0(2); S(1)-S(2)-S(3), 104.1(1); S(2)-S(3)-S(4), 104.1(1).

The C(1)-C(2) bond length, 1.633(3) Å, is much longer than bond lengths of common $C(sp^3)$-$C(sp^3)$ bonds,[12,13] probably because the pentathiepane ring constitutes a part of the rigid [5.3.3]propellane structure.

The C(1)-S(1), S(1)-S(2), and S(2)-S(3) bond lengths are 1.840(3), 2.038(1), and 2.055(2) Å, respectively. These values are comparable to the corresponding bond lengths of benzopentathiepins.[3] The S(1)-C(1)-C(naph-2) bond angle, 113.0(2)°, is much larger than S(1)-C(1)-C(naph-1), 102.6(2)°, due to electronic and steric repulsions between the pentathiepane ring and the naphthalene ring containing C(naph-2) atom. These results reveal that the pentathiepane ring of 2 is more strained than those of the previously reported pentathiepins which adopt chair conformations.

These observations mean that, if we introduce a proper substituent into one of the napthalene rings of **2**, a pair of separable conformers would be formed. Unfortunately, nitration and Friedel-Crafts acylation of **2** did not give the expected pentathiepanes under conventional conditions. We therefore synthesized 3-ethyl- and 3-phenylacenaphtho[1,2-*a*]acenaphthylenes (**5** and **6**) by coupling of 5-ethyl- and 5-phenylacenaphthylenes with 1,8-diiodonaphthalene.[7] Although sulfuration of **5** with elemental sulfur gave a complex mixture from which no expected pentathiepane could be isolated, that of **6** did give the expected pentathiepane in 60% yield as a mixture of two conformers **7** and **8**,[14] in the equilibrium ratio of 55:45, together with **6** in 23%. The isomers **7** and **8** were separated by HPLC as colorless crystals, which decomposed at 150 °C and 144 °C, respectively, to form **6** and sulfur. Assignment of the stereochemistry of **7** and **8** was impossible by spectroscopic methods. Therefore, the stereochemistry of **8** in which the pentathiepane and phenyl group are placed in syn-orientation was determined by X-ray diffraction analysis at –120 °C (Figure 2).[15]



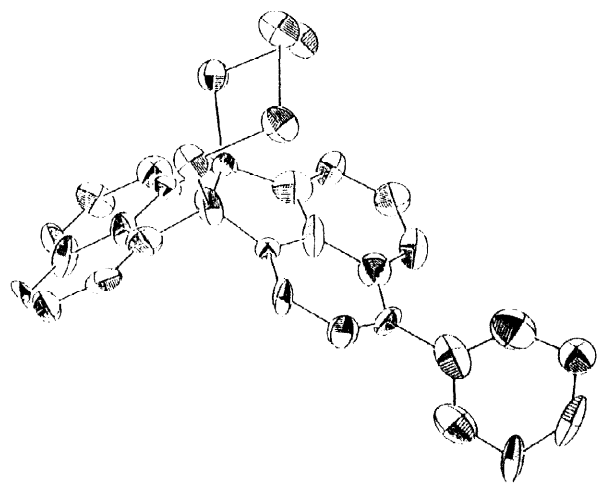


Figure 2. An ORTEP drawing of **8**. CS_2 was omitted for clarity.

The both isomers **7** and **8** isomerized slowly to each other in solution at room temperature. In 2.0 mM $CHCl_3$ solution, the rate constants of the isomerization from **7** to **8** were 0.73, 1.54, 2.99, and 4.03 x 10^{-5} s^{-1}

and those from **8** to **7** were 0.90, 1.76, 3.65, and 4.86 x 10^{-5} s^{-1} at 293, 298, 303, and 308 K, respectively. The final equilibrium ratio of **7** to **8** was about 55:45 at these temperatures. These results gave the activation parameters, Ea = 103.9 kJ•mol^{-1}, $\Delta H^{\neq}$ = 101.4 kJ•mol^{-1}, and $\Delta S^{\neq}$ = 2.9 J•K^{-1}•mol^{-1} (for isomerization from **7** to **8**), and Ea = 103.8 kJ•mol^{-1}, $\Delta H^{\neq}$ = 101.3 kJ•mol^{-1}, $\Delta S^{\neq}$ = 4.2 J•K^{-1}•mol^{-1} (from **8** to **7**).[15]

In conclusion we have found a new stereoisomerism based on high-energy inversion barrier of a pentathiepane ring, which has enabled us to prepare isolable conformers.

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8. **2**: colorless crystals (CS_2-$CHCl_3$), mp 248 °C (dec); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 7.0 Hz, 2H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 7.0 Hz, 2H), 7.66 (dd, *J* = 7.0, 8.1 Hz, 2H), 7.61 (dd, *J* = 7.0, 8.1 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3/CS_2$): δ 143.4, 140.9, 136.5, 134.5, 131.0, 130.9, 128.55, 128.46, 125.8, 124.8, 121.2, 120.9, 96.7; MS (EI) *m/z* 436 (M^+). Anal. Calcd for $C_{22}H_{10}S_5$: C, 60.51; H, 2.77; S, 36.72. Found C, 60.64; H, 2.71; S, 36.80.
9. **4**: colorless needles (hexane), mp 243-247 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 7.0 Hz, 4H), 7.63 (d, *J* = 8.1 Hz, 4H), 7.55 (dd, *J* = 7.0, 8.1 Hz, 4H), 1.92 (s, 6H); ^{13}C NMR (100.6 MHz, CD_2Cl_2): δ 145.0, 135.4, 128.9, 124.9, 124.9, 121.1, 77.0, 16.0; MS *m/z* 370 (M^+). Anal. Calcd for $C_{24}H_{18}S_2$: C, 77.80; H, 4.90. Found: C, 77.75; H, 4.87.
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11. Single crystals of **2** were obtained by recrystallization from a mixture of $CHCl_3$ and CS_2. Crystal data for **2**: $C_{22}H_{12}S_5$, M_r = 436.67, 0.22 x 0.16 x 0.14 mm, monoclinic, space group *C* 2/*c*, *a* = 25.54(1), *b* = 9.880(2), *c* = 16.43(1) Å, β = 114.77(3)°, *V* = 3782.9(28) $Å^3$, ρ_{calc} = 1.54 Mgm^{-3}, *T* = 298 K, *Z* = 8, *R* = 0.041, *Rw* = 0.051, GOF = 2.39.
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13. Much longer C(1)-C(2) bond would be required in the trithiolane **3**, if it formed.
14. **7**: colorless crystals (hexane), mp 150 °C (dec); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88-7.84 (m, 3H), 7.78-7.73 (m, 4H), 7.69-7.57 (m, 4H), 7.47-7.41 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$, 233 K): δ 143.49, 143.47, 140.9, 140.0, 139.1, 138.8, 136.3, 134.7, 130.6, 129.6, 129.3, 129.1, 128.82, 128.75, 128.4, 127.5, 125.1, 124.7, 121.5, 121.3, 121.12, 121.10, 96.5, 96.0; MS (FAB) *m/Z* 513 ($[M+1]^+$). **8**: colorless crystals (hexane), mp 144 °C (dec); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02-7.97 (m, 4H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.63-7.52 (m, 8H), 7.48-7.44 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, 233 K): δ 143.6, 142.7, 140.8, 139.0, 138.1, 136.7, 134.4, 130.9, 129.7, 129.5, 128.9, 128.7, 128.6, 128.4, 127.4, 126.0, 123.8, 121.36, 121.34, 121.2, 121.0, 96.5, 96.1; MS (FAB) *m/Z* 513 ($[M+1]^+$). Elemental analyses were performed on a mixture of two conformers **7** and **8**. Anal. Calcd for $C_{28}H_{16}S_5$: C, 65.59; H, 3.15. Found: C,65.83; H, 3.13.
15. Single crystals of **8** were obtained by recrystallization from a mixture of hexane and CS_2 at -40 °C: these crystals included one CS_2 molecule in each formula unit. Crystal data for **8**•CS_2: $C_{29}H_{16}S_7$, M_r = 588.91, crystal dimensions 0.12 x 0.04 x 0.04 mm, triclinic, space group *P*1, *a* = 8.611(4), *b* = 10.779(8), *c* = 15.269(9) Å, α = 99.45(4), β = 100.38(4), γ = 110.12(4)°, *V* = 1269.1(13) $Å^3$, ρ_{calc} = 1.54 Mgm^{-3}, *T* = 153 K, *Z* = 2, *R* = 0.089, *Rw* = 0.096, GOF = 3.09.
16. Details of the isomerization will be discussed in a full paper.