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New Spirans Containing a 1,5-Benzodithiepine System, Derived from Methylbenzenes. Conformational Transmission

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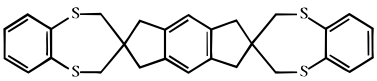
ABSTRACT



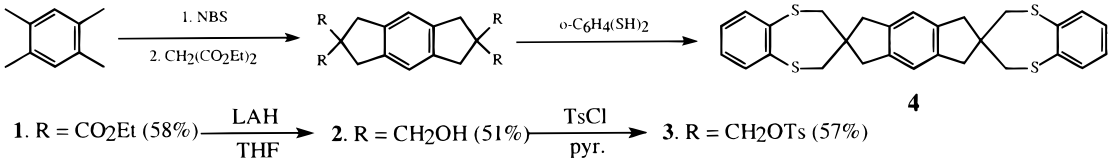
A synthesis of three new spirans, derived from methylbenzenes, containing the 1,5-benzodithiepine system is reported. X-ray structure proved the identity of model monospiran 9. In the solid and liquid state, the conformation of the seven-membered ring is chair, and the five-membered ring has the envelope conformation. The effect of conformational transmission in spirans 9 and 10 was observed. The synthesis of trispirans from hexamethylbenzene using the proposed scheme is also possible.

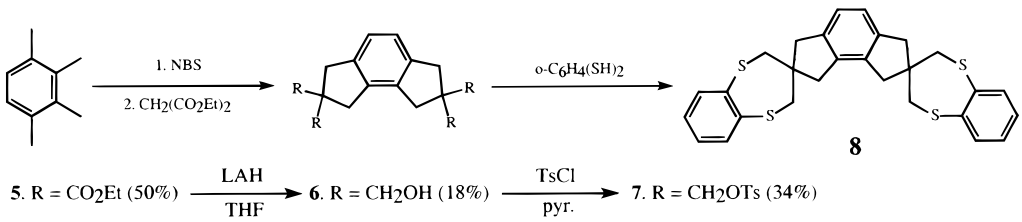
The chemistry of spirans has been studied extensively from many points of view.[1,2] Much interest has been focused on the bonding character of the central spiroatom. In the past few years many aspects of spiran chemistry have been developed such as conformational transmission,[3] spiroconjugation,[4] helical structure,[5] and photochromism.[6]

A new group of spirans are the compounds containing the 1,5-benzodithiepine system.[7]

The reaction of durene with NBS yields 1,2,4,5-tetrakis-(bromomethyl)benzene. In the reaction with ethyl malonate this compound gave ester **1**, which was reduced with $LiAlH_4$ to tetrol **2**. Finally, treatment of tosylate **3** with the sodium salt of 1,2-benzenedithiol in a sealed tube afforded dispiran **4** as a stable, high-melting compound. In the same way, from prehnitene were obtained new compounds **5**−**8**.

All the new compounds **1**-**8** were characterized by elemental analyses and spectroscopic data. Unfortunately, low solubility of spirans **4** and **8** caused such a weak intensity of NMR spectra in low temperature that the respective spectra could not be interpreted.[8] In this situation, using the method





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described above,[9] we obtained new monospiran **9**. This model spiran **9** contained the seven-membered 1,5-dithiepine ring identical with the rings in dispirans **4** and **8**.

The structure of **9** was determined from X-ray data.[10] A perspective view of the molecule **9** with the atom numbering scheme is given in Figure 1. The compound **9** belongs to

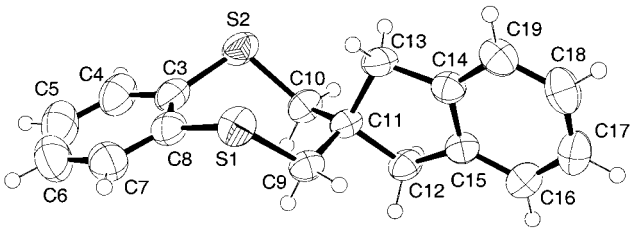

Figure 1. Molecular structure of spiran **9**.

asymmetric spirans. The spiroatom C11 joins two rings—the seven-membered ring (S1, C8, C3, S2, C10, C11, C9) containing two sulfur heteroatoms and the five-membered ring (C11, C13, C14, C15, C12). Both rings are condensed with aromatic moieties (C3, C4, C5, C6, C7, C8 and C14, C15, C16, C17, C18, C19, respectively). To visualize the complex geometry of the molecule, a continuous symmetry measure[11] (CSM) can be employed. The seven-membered heteroring has the chair conformation with a total puckering amplitude of 0.973(1) and corresponds very closely to an H-form.[12] The moiety composed of atoms numbered 1 through 13 (involving the 1,5-benzodithiepine fragment) has a near-mirror symmetry with the mirror plane passing through the spiroatom C11 and intersecting bonds C3−C8 and C5−C6. The continuous symmetry measure (CSM) has a value of 0.0186. The second moiety, C11−C19, has also a near-mirror plane symmetry with a CSM value of 0.0035. The mirror plane passes through the spiroatom C11 and intersects bonds C14−C15 and C17−C18. Both symmetry planes are inclined at an angle of 87°. The five-membered ring has an envelope conformation with the plane C12−C11−C13 inclined at an angle of 27° with the planar fragment C12−C19.

The environment of the spiroatom C11 deviates from tetrahedral symmetry: the valency angle C9−C11−C10 is 112.09°, whereas the angle C12−C11−C13 is 103.58°. Their

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(8) **Experimental Details.** Melting points (uncorrected): Boetius hot-stage microscope. IR: Bruker IFS 48. ^{1}H and ^{13}C NMR: Bruker AMX 500 (500 MHz). Chemical shifts are referenced to interal $SiMe_4$. MS: Finnigan MAT 44S (EI, 70 eV). **Dispiro[bis(2*H*-benzo[*f*]-3,4-dihydro-1,5-dithiepine-3,2′,3,6′)cyclopentano[*f*′]indan] (4).** A mixture of 60 mL of ethyl cellosolve, 0.20 g (8.8 mmol) of sodium, 0.64 g (4.4 mmol) of 1,2-benzenedithiol, and 2.00 g (2.2 mmol) of **3** in sealed tube was stirred at 130 °C for 30 h. After evaporation of the solvent, the residue was dissolved in benzene and sodium tosylate was filtered off. Product **4** was purified chromatographically on Al_2O_3 using benzene as an eluent: colorless crystals (chloroform−methanol); 132 mg (13%); mp 287−288 °C; IR (KBr) ν (cm^{-1}) = 3049, 2904 (CH_2), 1442, 751; ^{1}H NMR ($CDCl_3$) δ = 2.96 (broad s, 16H, CH_2, CH_2S), 7.03 (s, 2H, aromatic H), 7.16−7.26 (m, 4H, aromatic H), 7.46−7.59 (m, 4H, aromatic H); ^{13}C NMR ($CDCl_3$) δ = 43.6, 48.2, 52.0, 124.8, 126.4, 127.4, 133.1, 141.0; MS (EI) *m*/*z* (%) = 490 (34) M$^+$, 349 (50), 207 (94), 193 (100), 178 (43). Anal. Calcd for $C_{28}H_{26}S_4$ (490.82): C, 68.51; H, 5.35. Found: C, 68.28; H, 5.13. **Dispiro[bis(2*H*-benzo[*f*]-3,4-dihydro-1,5-dithiepine-3,2′,3,5′)cyclopentano[*e*′]indan] (8)**. Dispirane **8** was obtained analogously from **7** in 16% yield, colorless crystals (benzene), mp 206−207 °C: IR (KBr) ν (cm^{-1}) = 3044, 2901, 2835 (CH_2), 1442, 1268, 760; ^{1}H NMR ($CDCl_3$) δ = 2.97 (broad s, 16H, CH_2, CH_2S), 7.02 (s, 2H, aromatic H), 7.17−7.26 (m., 4H, aromatic H), 7.42−7.59 (m, 4H, aromatic H); ^{13}C NMR ($CDCl_3$) δ = 43.2, 44.0, 45.1, 48.6, 123.3, 127.7, 132.1, 133.5, 137.7, 139.9; MS (EI) *m*/*z* (%) = 490 (29) M$^+$, 349 (45), 207 (81), 193 (100), 178 (24). Anal. Calcd for $C_{28}H_{26}S_4$ (490.82): C, 68.51; H, 5.35. Found: C, 68.07; H, 5.25. **Spiro(2*H*-benzo[*f*]-3,4-dihydro-1,5-dithiepine-3,2′-indan) (9)**. Spirane **9** was prepared similarly by treating the ditosylate of 2,2-bis(hydroxymethylo)indan[9] with the sodium salt of 1,2-benzenedithiol: 23% yield; colorless crystals (benzene); mp 117−118 °C; IR (KBr) ν (cm^{-1}) = 2903, 2830 (CH_2), 1440, 1270, 751; ^{1}H NMR ($CDCl_3$) δ = 2.94 (broad s, 8H, CH_2, CH_2S), 7.14−7.34 (m, 6H, aromatic H), 7.57 (broad s, 2H, aromatic H); ^{13}C NMR ($CDCl_3$) δ = 43.1, 43.7, 48.4, 125.0, 126.6, 127.6, 133.4, 134.2, 141.3; MS (EI) *m*/*z* (%) = 284 (100) M$^+$, 156 (36), 153 (48), 143 (93), 129 (89). Anal. Calcd for $C_{17}H_{16}S_2$ (284.43): C, 71.79; H, 5.67. Found: C, 71.52; H, 5.76. New compounds **1**−**3** and **5**−**7** were obtained according to procedures described in ref 3. Data for new compounds **1**−**3** and **5**−**7** follows. **2,2,6,6-Tetrakis-(ethoxycarbonyl)cyclopentano[*f*]indan] (1):** colorless crystals (ethanol); yield 58%; mp 161−163 °C; IR (KBr) ν (cm^{-1}) = 2985, 2969, 2920 (CH_2, CH_3), 1725 (CO), 1283, 1054, 907; ^{1}H NMR ($CDCl_3$) δ = 1.25 (t, *J* = 7 Hz, 12H, CH_3), 3.51 (s, 8H, CH_2), 4.17/4.21 (q, *J* = 7 Hz, 8H, OCH_2), 7.01 (s, 2H, aromatic H); ^{13}C NMR ($CDCl_3$) δ = 14.0, 40.1, 60.8, 61.7, 120.0, 139.0, 171.7; MS (EI) *m*/*z* (%) = 446 (24) M$^+$, 297 (100). Anal. Calcd for $C_{24}H_{30}O_8$ (446.54): C, 64.55; H, 6.78. Found: C, 64.10; H, 6.82. **2,2,6,6-Tetrakis(hydroxymethyl)cyclopentano[*f*]indan] (2):** colorless crystals (ethanol); yield 51%; mp 274−275 °C; IR (KBr) ν (cm^{-1}) = 3314 (OH), 2937, 2832 (CH_2), 1082, 1032; ^{1}H NMR (DMSO-d_6) δ = 2.62 (s, 8H, CH_2), 3.35 (s, 8H, OCH_2), 4.60 (t, *J* = 5.0 Hz, 4H, OH), 6.91 (s, 2H, aromatic H); ^{13}C NMR (DMSO-d_6) δ = 37.1, 50.0, 64.4, 121.0, 140.2; MS (EI) *m*/*z* (%) = 278 (16) M$^+$, 193 (100). Anal. Calcd for $C_{16}H_{22}O_4$ (278.38): C, 69.03; H, 7.98. Found: C, 69.10; H, 8.20. **Tetratosylate of 2,2,6,6-tetrakis(hydroxymethyl)cyclopentano[*f*]indan] (3):** colorless crystals (acetone); yield 57%; mp 218−219 °C; IR (KBr) ν (cm^{-1}) = 2958, 2853 (CH_2, CH_3), 1358, 1178 (SO_2), 1099; ^{1}H NMR ($CDCl_3$) δ = 2.46 (s, 12H, CH_3), 2.66 (s, 8H, CH_2), 3.91 (s, 8H, OCH_2), 6.76 (s, 2H, aromatic H), 7.26−7.35 (m, 8H, aromatic H), 7.71−7.73 (m, 8H, aromatic H); ^{13}C NMR ($CDCl_3$) δ = 21.7, 37.7, 47.3, 71.1, 121.4, 127.9, 130.0, 132.4, 138.8, 145.2. Anal. Calcd for $C_{44}H_{46}O_{12}S_4$ (895.18): C, 59.03; H, 5.19. Found: C, 58.72; H, 5.31. **2,2,5,5-Tetrakis(ethoxycarbonyl)cyclopentano[*e*]indan] (5):** colorless crystals (ethanol); yield 50%; mp 82−84 °C.; IR (KBr) ν (cm^{-1}) = 2989, 2970, 2890 (CH_2, CH_3), 1739 (CO), 1258, 1065, 860; ^{1}H NMR ($CDCl_3$) δ = 1.25 (t, *J* = 7 Hz, 12H, CH_3), 3.50 (s, 4H, CH_2), 3.55 (s, 4H, CH_2), 4.18/4.22 (q, *J* = 7 Hz, 8H, OCH_2), 7.00 (s, 2H, aromatic H); ^{13}C NMR ($CDCl_3$) δ = 14.0, 38.9, 40.4, 60.5, 61.7, 122.8, 135.7, 138.9, 171.7; MS (EI) *m*/*z* (%) = 446 (19) M$^+$, 297 (100). Anal. Calcd for $C_{24}H_{30}O_8$ (446.54): C, 64.55; H, 6.78. Found: C, 64.49; H, 6.92. **2,2,5,5-Tetrakis(hydroxymethyl)cyclopentano[*e*]indan] (6):** colorless crystals (methanol); yield 18%; mp 192−193 °C; IR (KBr) ν (cm^{-1}) = 3261 (OH), 2926, 2830 (CH_2), 1090, 1023; ^{1}H NMR (DMSO-d_6) δ = 2.60 (s, 4H, CH_2), 2.69 (s, 4H, CH_2), 3.40 (s, 8H, OCH_2), 4.59 (br. s, 4H, OH), 6.93 (s, 2H, aromatic H); ^{13}C NMR (DMSO-d_6) δ = 35.9, 37.45, 49.8, 64.6, 122.3, 138.5, 140.1; MS (EI) *m*/*z* (%) = 278 (9) M$^+$, 193 (100). Anal. Calcd for $C_{16}H_{22}O_4$ (278.38): C, 69.03; H, 7.98. Found: C, 68.72; H, 8.14. **Tetratosylate of 2,2,5,5-tetrakis(hydroxymethyl)cyclopentano[*e*]indan] (7):** colorless crystals (acetone); yield 34%; mp 151−152 °C; IR (KBr) ν (cm^{-1}) = 2960, 2848 (CH_2, CH_3), 1361, 1180 (SO_2), 1100; ^{1}H NMR ($CDCl_3$) δ = 2.46 (s, 12H, CH_3), 2.57 (s, 4H, CH_2), 2.71 (s, 4H, CH_2), 3.92 (s, 8H, OCH_2), 6.85 (s, 2H, aromatic H), 7.30−7.36 (m, 8H, aromatic H), 7.68−7.73 (m, 8H, aromatic H); ^{13}C NMR ($CDCl_3$) δ = 21.7, 36.6, 38.1, 47.1, 71.2, 123.6, 127.9, 130.1, 132.3,136.2, 138.7, 145.2. Anal. Calcd for $C_{44}H_{46}O_{12}S_4$ (895.18): C, 59.03; H, 5.19. Found: C, 58.65; H, 5.44.

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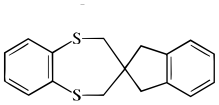
significant departure from the ideal value of 109.28° corresponds to the classic rule of Thorpe−Ingold.[13] Similar effects were observed in crystal structures of asymmetrically strained spirans containing nine-membered heterorings.[14,15] The geometry of the molecule seems to result also from the stiffness of the terminal aromatic substituents and repulsion of the sulfur atoms.

The ^{1}H NMR spectra of **4**, **8**, and **9** recorded at room temperature revealed broad singlets at $\delta = 2.96$, 2.97, and 2.94 for all methylene protons (CH_2S, CH_2), respectively. This result is probably connected with rapid inversion of the 1,5-dithiepine ring. It was supported by ^{1}H NMR measurements of the model spiran **9** at low temperatures (down to −90 °C). Then the broad singlet at $\delta = 2.94$ which was produced by methylene protons was split at low temperature and three other signals appeared at $\delta = 2.77/2.89$ (AB, $J =$ 14 Hz, CH_2S) as well as singlets at $\delta = 2.78$ and 3.42 for acyclic methylene protons. The shape of the ^{1}H NMR spectrum allowed the attribution of the *chair* conformation also in solution for the 1,5-dithiepine ring.

It seems probable that the 1,5-dithiepine rings adopt a similar conformation also in dispirans **4** and **8**. In fact, these compounds exhibit an identical configuration around the spiroatoms as in the model monospiran **9** (1,5-benzodithiepine−spiroatom−five-membered ring). A change of configuration around the spiroatom in spiran **10**[3] (1,5-benzodithiepine−spiroatom−seven-membered ring) affects the conformation of benzodithiepine.



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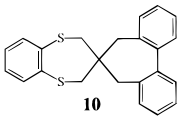

10

On the basis of 2D NMR spectra (TOCSY, NOESY), spiran **10** at −90 °C was ascribed two dominant conformations of the heterocyclic ring: *chair* and *twist-boat* with a population of 2:1.

In contrast to the ^{1}H NMR spectrum (−90 °C) of the model **9**, the spectrum of **10** is more complicated and shows the following signals: $\delta = 2.62/2.75$ (AB, $J = 14$ Hz, 2H, CH_2S), 2.71/2.96 (AB, $J = 14$ Hz, 2H, CH_2S), 1.88/3.88 (AX, $J = 12$ Hz, 2H, CH_2C), 2.10/2.36 (AB, $J = 12$ Hz, 2H, CH_2C)—when the 1,5-dithiepine ring adopts the *chair* (C) conformation—and $\delta = 2.52/3.80$ (AX, $J = 14$ Hz, 4H, CH_2S), 2.00/2.74 (AX, $J = 12$ Hz, 4H, CH_2C)—in the case of the *twist-boat* (TB) conformation.

The interconversion barrier of C-TB conformations of the 1,5-dithiepine ring at the coalescence temperature of −15 °C, calculated[16] for the AX signal at $\delta = 2.52/3.80$, is equal to 12.8 kcal/mol.

In the present authors' opinion the changes observed in the shape of NMR spectra of spirans **9** and **10** are the result of mutual interaction of both spiran components transmitted by the spiroatom, the effect of which is analogous to the well-known effect of the Barton conformational transmission.[17]

Structural consequences of the conformational transmission will be the subject of future reports. It should also be possible to develop a general route described above to obtain trispirane from hexamethylbenzene[18] and containing the 1,5-benzodithiepine system.

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