A SIMPLEST ISOLABLE MONOCYCLIC THIEPIN. SYNTHESIS, STRUCTURE, AND THERMAL STABILITY OF 2,7-DI-*tert*-BUTYLTHIEPIN¹

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Summary: As an example of a simplest isolable monocyclic thiepin, 2,7-di-tert-butylthiepin (2) has been synthesized from 2,6-di-tert-butylthiopyrylium salt, and the thermal properties together with the X-ray crystal structure of **2** have been examined.

In general simple thiepins are known to be thermally unstable owing to ready sulfur extrusion.² Consequently, almost all thiepins known to date are heavily substituted and/or highly annelated derivatives.² In view of the widely accepted mechanism for the sulfur extrusion process which involves valence isomerization of the thiepin ring to its corresponding thianorcaradiene (benzene episulfide) isomer followed by irreversible loss of sulfur³ it might be feasible that a simple monocyclic thiepin can be prepared if the energy difference between the ground state of the thiepin form and the thianorcaradiene form were reasonably large.^{4,5} This situation might be realized by introduction of two bulky groups at 2- and 7-positions of the thiepin ring so that these groups force the nonbonding interaction in corresponding thianorcaradiene structure (B) to be large and hence the thiepin structure (A) will be favored. Actually, 2,7-di-tert-buty1-4-



ethoxycarbonyl-5-methylthiepin $(1)^4$ has recently been synthesized by us as a first example of stable monocyclic thiepin.⁵ Nevertheless, the thiepin 1 is still a highly substituted derivative. Although we believe that a remarkable thermal stability of 1 is originated primarily from the presence of two *tert*-butyl groups, there is a controversy⁶ that the ethoxycarbonyl group also plays an important role in the thermal stability of 1 by diminishing the anti-aromaticity.⁷ To remove this ambiguity we have prepared 2,7-di-*tert*-butylthiepin. To our knowledge this is a first report not only on the synthesis of a thiepin stabilized soley by steric effect but also on the X-ray molecular structure determination⁸ of a fundamental thiepin skeleton.

In view of the substantial thermal stability of 1,⁴ the decision was made to construct the thiepin skeleton of 2 by solvolytic ring expansion reaction of an appropriate precursor 6 in the final stage of the synthetic sequence.⁹ To this end, 4-hydroxymethyl-2,6-di-tert-butyl-4H-

thiopyran (5) was prepared from the known 2,6-di-*tert*-butylthiopyrylium salt (3)⁴ via a carbinyl carbanion equivalent.¹⁰ The cation salt 3 was treated with ethoxyethyloxymethyllithium¹⁰ prepared in situ from (ethoxyethyloxymethyl)tributylstannane and butyllithium (THF, -78°C, overnight), and the resulting thiopyran 4^{11} was hydrolyzed (PPTS¹²/MeOH, reflux, 2 h) to give the carbinol 5^{13} in 79% yield from 3. With the preparation of the key intermediate 5 thus achieved, the carbinol was converted to the mesylate 6^{14} (CH₃SO₂Cl/Et₃N/CH₂Cl₂, -10°C, 15 min, 86% yield), which was solvolyzed directly to the thiepin 2. Thus, treatment of 6 with acetic anhydride and sodium acetate in glacial acetic acid at 90°C for 5 h gave 2 after usual workup followed by silica gel column chromatography (hexane) in 29% yield.



2,7-Di-*tert*-butylthiepin (2) showed the following characteristics: stable pale yellow plates, mp 36-36.5°C (recrystallized from methanol); MS, m/z 222.1446 (M⁺) calcd for C₁₄H₂₂S 222.1441; ¹H NMR (100-MHz, in CDCl₃)¹⁵ δ 1.23 (s, 18H), 6.27 (s, 4H); ¹³C NMR (22.5-MHz, in CDCl₃) δ 30.6 (C(CH₃)₃, 39.9 (C(CH₃)₃), 127.7, 132.9, (C₃, C₄, C₅, and C₆), 151.1 (C₂, C₇); UV (cyclohexane) λ_{max} 226 (log ε 4.02), 252 (3.35), 362 nm (2.51).

The evidence for the thiepin structure 2 was further substantiated by X-ray crystallographic analysis (vide post) and thermal sulfur extrusion reaction. The thermolysis of 2 in benzene- d_6 in the presence of an equimolar amount of triphenylphosphine at 110°C for 42 h (monitored by ¹H NMR) gave *o*-di-*tert*-butylbenzene¹⁶ quantitatively. It is interesting to note that, in the absence of triphenylphosphine, the thiepin 2 was quite stable in decalin- d_{18} at 130°C for 20 h. Its half-life under these conditions is about 195 h.¹⁷ The dramatic difference in thermal stability between 1^{18} and 2 still remains unexplored at the present stage.

As a means of evaluating the extent of bond alternation in **2** the vicinal coupling constants of the ring $(J_{3,4} = J_{5,6} = 5.5 \text{ Hz} \text{ and } J_{4,5} = 10.6 \text{ Hz})$ provided by the analysis¹⁹ of the 360-MHz NMR spectrum in decalin- d_{18} , which showed, unlike 100-MHz spectrum, a well resolved AA'BB'-system at δ 6.10 (H-4 and 5) and 6.16 ppm (H-3 and 6),²⁰ were used. These coupling constants were found to be strongly alternating and to be in close agreement with those of the nonplanar seven-membered trienes.²¹

The X-ray crystal structure analysis of **2** has been carried out by using the diffractometer data collected at $-50^{\circ}C$.²² The ORTEP picture (Figure 1)²⁵ indicates the non-crystallographic mirror symmetry of the molecule passing through the S atom and the center of the C(4)-C(5) bond. The thiepin ring takes a boat form. The dihedral angles between the base plane [C(2), C(3), C(6), C(7)] and the bow [S, C(2), C(7)] and stern [C(3), C(4), C(5), C(6)] planes are 49.6° and 28.0°, respectively. The bond alternation is clearly observed in the C(2) to C(7) skeleton (Figure 2). The C(2)-C(3), C(4)-C(5) and C(6)-C(7) distances are those of double bond while the C(3)-C(4) and C(5)-C(6) are approximately equal to the C(sp²)-C(sp²) single bond. The shortest non-bonded



FIGURE 1. Molecular structure of **2**. Thermal ellipsoids are drawn at the 20% probability level.



FIGURE 2. Selected bond distances and angles in **2**. The e.s.d.'s of C-S and C-C distances are 0.006 and 0.008 -0.010 Å, respectively.

atomic distance between the *tert*-butyl groups [C(13)...C(23)] is 3.649(10) Å, which is shorter than the conventional van der Waals contact between the methyl groups of 4.0 Å. The steric repulsion between these methyl groups may strongly restrict the C(2)...C(7) distance from shortening in the expected thianorcaradiene intermediate formation through the sulfur extrusion reaction.

In summary, we have prepared the first example of a simple monocyclic thiepin derivative and demonstrated that it possessed substantial thermal stability arising from the nonbonding interaction between two *tert*-butyl groups at 2- and 7-positions. We are continuing to explore the interesting chemistry of 2 and the results will be reported in due course.

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- 3.71 (d, 2H, J =4.3 Hz), 5.55 (d, 2H, J=6.0 Hz). 14) 6: Colorless oil, MS m/z 318 (M⁺); ¹H NMR (100-MHz, CDCl₃) δ 1.19 (s, 18H), 2.98 (s, 3H), 3.18-3.43 (m, 1H), 4.17 (d, 2H, J=5.3 Hz), 5.55 (d, 2H, J=7.0 Hz).
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