Chemical Transformations of 2,7-Di-*tert*-butylthiepine

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Selected chemical transformations of a monocyclic thiepine 2,7-di-*tert*-butylthiepine **1** have been examined. Oxidation of the thiepine **1** gave the unstable thiepine 1-oxide **3**, although further oxidation to form the thiepine 1,1-dioxide **4** did not proceed whilst *S*-methylation with methyl iodide–silver tetrafluoroborate gave rearranged aromatized compounds. In these electrophilic reactions at sulfur, the steric repulsion by two *tert*-butyl groups possibly causes the formation of the *endo*-sulfur coordinated species. Bromination gave either the ring-contracted thiophene **12**, or the thiopyran **17**, depending on the reaction conditions. The cycloaddition with tetracyanoethylene (TCNE) gave the [4 + 2] adduct **22**.

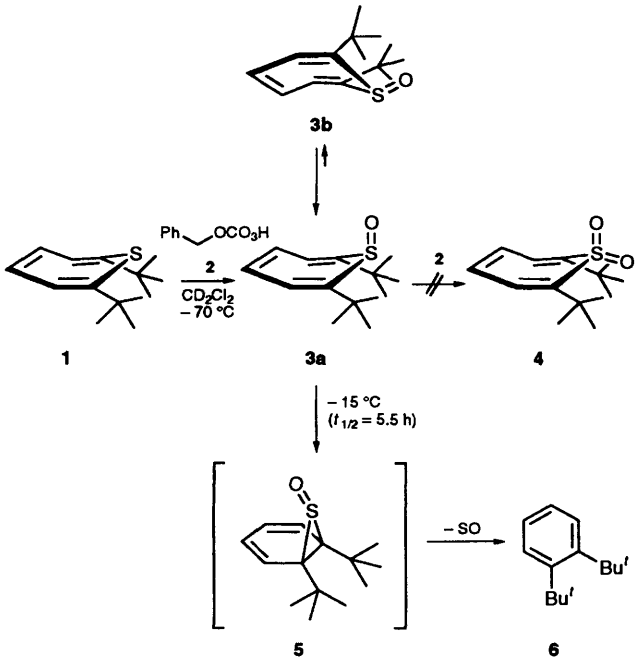
Much progress has recently been achieved in the synthesis of monocyclic thiepines.[1] The thermal instability of thiepines has been rationalized as being due to valence isomerization to form a thianorcaradiene, which is followed by an irreversible cheletropic loss of sulfur.[2] In order to help stabilize the thiepine structure, two bulky *tert*-butyl groups have been introduced at the 2,7-positions.[1b-f] Whilst most reactivity studies on thiepines have been performed on annelated thiepines,[3,4] we have previously examined several chemical transformations of a monocyclic thiepine stabilized by 2,7-*tert*-butyl groups[1d] and now report (i) oxidation of the thermally stable 2,7-*tert*-butylthiepine **1** in order to generate the hitherto unknown monocyclic thiepine 1-oxide; (ii) *S*-methylation of the thiepine **1** with methyl iodide–silver tetrafluoroborate in an attempt to generate the 1-methyl thiepinium ion; (iii) bromination of compound **1** by an electrophilic reaction at the ring carbon; and (iv) cycloaddition of compound **1** with tetracyanoethylene (TCNE) *via* a cyclic transition state.

Results and Discussion

(i) *Oxidation of* 2,7-*Di*-tert-*butylthiepine*.—Along with thiepine, both the thiepine 1-oxide and the 1,1-dioxide are of synthetic and theoretical interest. While benzothiepine 1-oxide has been synthesized and found to be thermally unstable compared to the corresponding thiepine,[3i] a monocyclic thiepine 1-oxide has not been prepared. On the other hand, thiepine 1,1-dioxides, including the parent thiepine 1,1-dioxide, are known as thermally stable compounds.[5] Even the parent thiepine 1,1-dioxide is stable at room temp ($t_{1/2}$ = *ca.* 3 h, 100 °C).[5a]

The annelated thiepines have been converted into their corresponding 1-oxide or 1,1-dioxide by treatment with *m*-chloroperbenzoic acid.[3b] Unlike these annelated thiepines, treatment of the monocyclic thiepine 2,7-di-*tert*-butyl-4-ethoxycarbonyl-5-methylthiepine,[1b,c] which is less stable than the thiepine **1**, with *m*-chloroperbenzoic acid at −78 °C, gave only a benzene derivative.[6] In order to generate a monocyclic thiepine 1-oxide, we decided to examine oxidation of the thiepine **1** with *O*-benzyl *OO*-hydrogen monoperoxycarbonate **2**, which is recommended as an alternative reagent for peroxycarboxylic acids in oxygen transfer reactions and also has the potential advantage that the reaction medium remains neutral during the oxidation.[7] To a solution of the peracid **2** (1 equiv.) in CD_2Cl_2 in an NMR tube was added the thiepine **1** (1 equiv.) in CD_2Cl_2 at −78 °C. The ^1H NMR spectrum of the solution, recorded at −70 °C, displayed signals at δ 1.24 (18 H, s) and 6.90 (4 H, AA'BB'), consistent with the structure of 2,7-di-*tert*-butylthiepine 1-oxide **3**. When the mixture was allowed to warm to −15 °C, compound **3** was gradually transformed to *o*-di-*tert*-butylbenzene **6**.[8] This conversion can be rationalized by the valence isomerization into a thianorcaradiene sulfoxide intermediate **5** followed by the rapid extrusion of SO, analogously to thiepine. The conversion was monitored at −15 °C by ^1H NMR spectroscopy and the half-life of **3** ⟶ **6** at this temperature was found to be 5.5 h. The results suggest that the thiepine 1-oxide is significantly less stable than the corresponding thiepine itself.[1d]

Further oxidation of the oxide **3** to the corresponding thiepine 1,1-dioxide **4** using the peroxycarbonate **2** was attempted. To a solution of compound **2** (2 equiv.) in CD_2Cl_2 was added the thiepine **1** (1 equiv.) in CD_2Cl_2 at −78 °C. The mixture was allowed to warm to −40 °C and ^1H NMR showed only signals for sulfoxide **3**, along with the signals due to benzyl alcohol and excess of peracid **2**. After standing at −30 °C for 113 h, warming to room temp. gave only the substituted benzene **6**. The results suggest that the sulfoxide **3** was not further oxidized to the sulfone **4**, probably because the two



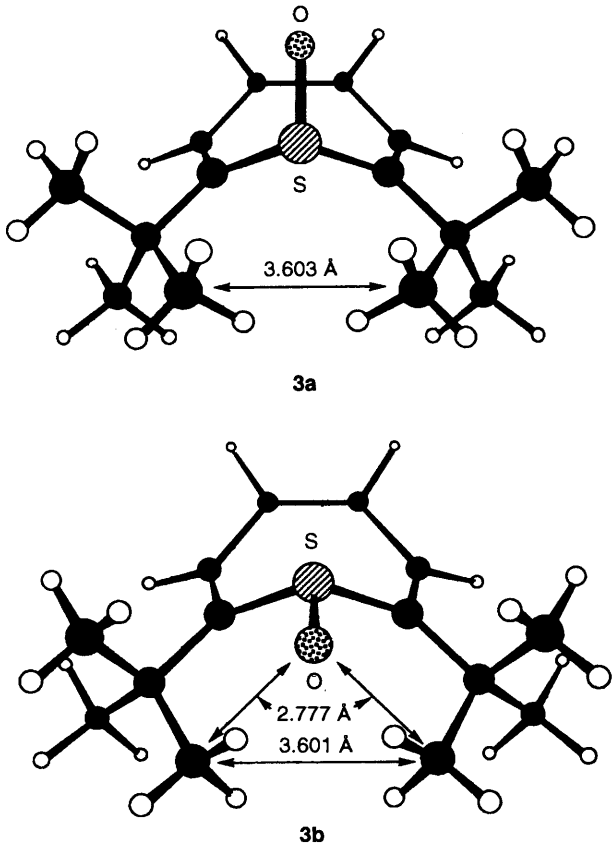


Fig. 1 The PM3-optimized structure of *endo*-sulfoxide **3a** and *exo*-sulfoxide **3b**. Structure **3a** is 3.5 kcal mol^{-1} more stable than **3b**.

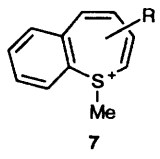
bulky *tert*-butyl groups sterically hinder the approach of the second equivalent of the peracid.

The reported X-ray structure of a stable benzothiepine 1-oxide showed a boat conformation, with the oxygen of the sulfoxide function in the *exo*(equatorial)-position.[9] However, because of steric repulsion, compound **3** may strongly prefer an *endo*(axial)-sulfoxide conformation **3a**. PM3 calculations*,[10] show that *endo*-sulfoxide **3a** is 3.5 kcal mol^{-1} more stable than *exo*-sulfoxide **3b** (Fig. 1). The shortest non-bonded atomic distances between the *tert*-butyl groups of structures **3a** and **3b** obtained by calculations are 3.603 and 3.601 Å, which are similar to that for the thiepine **1** (3.649 Å) obtained by X-ray, and are shorter than the conventional van der Waals contact between the methyl groups (4.0 Å).[1d] In **3b**, the shortest non-bonded atomic distances between *tert*-butyl groups and oxygen is 2.777 Å, which again is shorter than the van der Waals contact between the methyl group and oxygen of 3.52 Å and it is this steric repulsion which leads to the instability of structure **3b**.

(ii) *Alkylation of* 2,7-*Di*-tert-*butylthiepine with Methyl Iodide–Silver Tetrafluoroborate.*—1-Alkylthiepinium ions are, like thiepine itself, also of both synthetic and theoretical interest. No monocyclic 1-alkylthiepinium ion has so far been reported, although the annulated 1-methylbenzo[*b*]thiepinium salts **7** have been isolated.[3c]

Attempted preparation of sulfonium salts under standard conditions have been examined. To a solution of the thiepine **1** and methyl iodide in 1,2-dichloroethane was added $AgBF_4$ at room temp. and the resultant mixture was stirred overnight. The expected 2,7-di-*tert*-butyl-1-methylthiepinium fluoroborate **10** was not isolated under these reaction conditions; instead, the

* MO calculations were performed on the CONVEX C-220 computer at the Information Processing Center of Nara University of Education.



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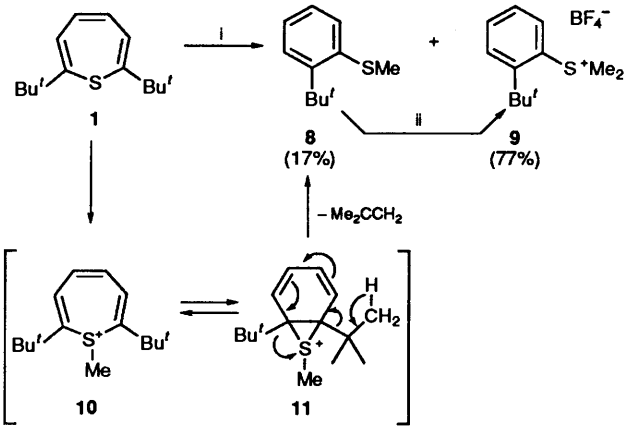
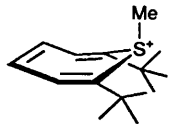
reaction was found to yield the 2-*tert*-butylphenyl methyl sulfide **8** and the *S*-methylated salt **9** in 17% and 77% yields, respectively. Under identical conditions, compound **8** was converted into the salt **9** in 75% yield. The plausible reaction mechanism for the formation of these compounds *via* the 1-methylthiepinium ion intermediate **10** and its valence isomer intermediate **11** is shown in Scheme 1. The transformation to a



Scheme 1 *Reagents and conditions:* i, MeI, $AgBF_4$, $ClCH_2CH_2Cl$, room temp.; ii, MeI, $AgBF_4$, $ClCH_2CH_2Cl$, room temp., 75%

benzene derivative is similar to the behaviour of the 1-methylbenzothiepinium salts **7** which form the naphthalene derivatives when heated.[3c] However, these salts are relatively thermally stable species compared to the corresponding benzothiepines. The results obtained here clearly suggest that the monocyclic 1-methylthiepinium ion is less stable than the corresponding thiepine **1**, which is opposite to the relative thermal stability of benzothiepine and its 1-methylbenzothiepinium ion.[1d,3c] Again, the intermediate 1-methylthiepinium ion **10** may have an *endo*(axial)-methyl conformation due to steric repulsion by the two *tert*-butyl groups. Although the structures of benzo derivatives **7** have not been determined, they probably exist in the boat conformation with an *exo*(equatorial)-methyl group, by analogy with the *exo*-oxygen in the sulfoxides. The difference in conformation is possibly responsible for the thermal instability of the 1-methylthiepinium ions.



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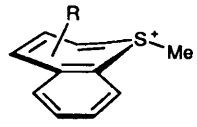

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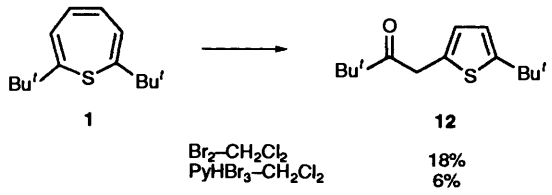
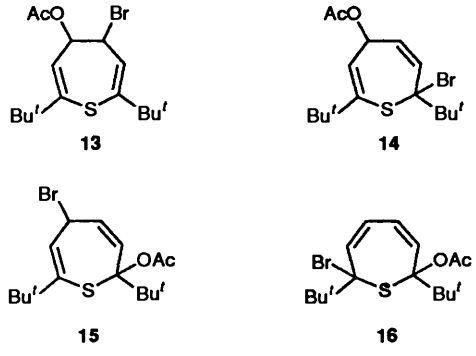
(iii) *Reaction of* 2,7-*Di*-tert-*butylthiepine with Bromine.*—Bromination of the thiepine **1** directly with bromine, or under mild conditions such as with the dioxane–bromine complex and pyridinium hydrotribromide were attempted. Reaction of thiepine **1** with bromine in CH_2Cl_2 at −78 °C followed by the usual work-up gave compound **12** as an isolable product in 18% yield. The IR spectrum (1710 cm^{-1}) clearly suggested the presence of a saturated carbonyl group. The ^1H, ^{13}C NMR, and mass spectra were consistent with the thiophene structure **12** shown below. Reaction of the thiepine **1** with pyridinium hydrotribromide in CH_2Cl_2 at room temp. followed by the usual work-up, gave a

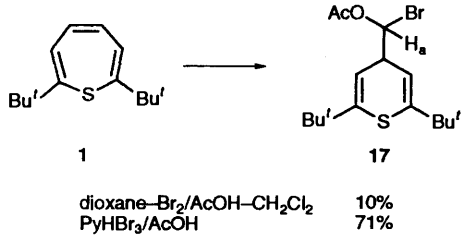


mixture of the thiophene derivative **12** in low yield along with several unidentified compounds.

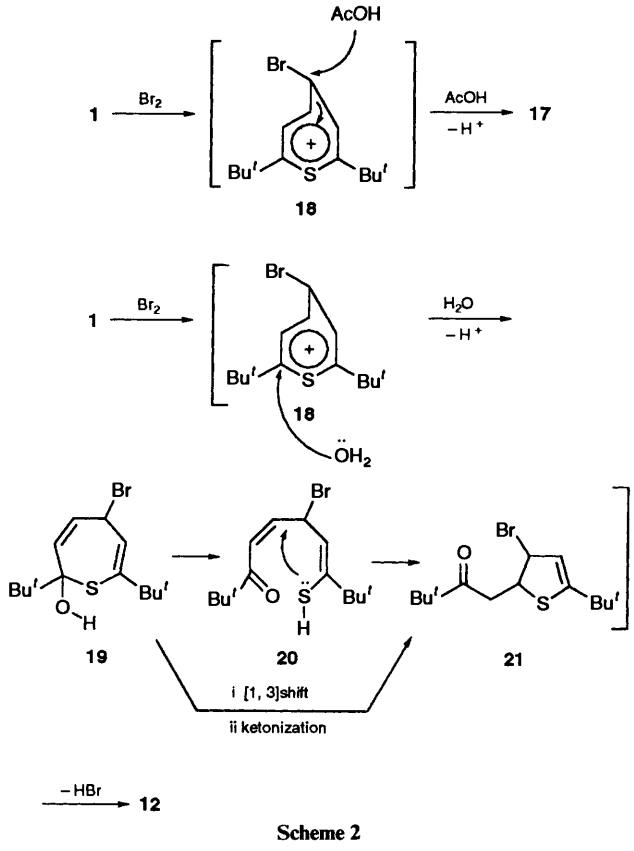
Although reaction of the thiepine **1** with a dioxane–bromine complex in CH_2Cl_2 at −78 °C gave a complex mixture, in a nucleophilic solvent (AcOH–CH_2Cl_2, 3:1) at 0 °C the bromoacetate **17** [*m/z* 360 and 362 (FD–Mass)] was obtained as an isolable product in 10% yield (the *m/z* values correspond to the molecular formula $C_{16}H_{25}BrO_2S$). The ^{1}H NMR spectra of **17** show signals due to two *tert*-butyl groups (δ 1.18 and 1.20), an acetyl group (δ 2.11), a ddd proton δ at 3.51 (ddd, *J* 7.0, 5.5 and 5.5) and three doublet protons at 5.60 (d, *J* 5.5), 5.68 (d, *J* 5.5) and 6.58 (d, *J* 7.0). The coupling pattern for the ^{1}H NMR spectra (pattern confirmed by decoupling experiments) was inconsistent with the possible dihydrothiepine derivatives **13**–**16**. However, the chemical shifts and coupling constants of



the two 1 H-doublet olefinic protons are similar to those of 4-substituted 2,6-di-*tert*-butylthiopyrans.[14] The structure of **17** can thus be assigned as a thiopyran derivative shown below. The nonequivalent signals of the ring protons can be reasonably well explained in terms of the effect of the asymmetric carbon and the low chemical shift of H_a (δ 6.58) is reasonable (for example, MeC*H*BrOAc, δ 5.80). Reaction of thiepine **1** with pyridinium hydrotribromide in AcOH at room temp. also gave compound **17** in 71% yield.



The reaction mechanism of the ring contraction from the thiepine **1** to the thiopyran **17** can be explained as follows (Scheme 2). The electrophilic bromination occurs at the 4-carbon to give a homothiopyrilium ion intermediate **18**. The 4-position for bromination and generation of a homothiopyrilium ion is analogous to protonation of the thiepine **1**.[4] In the reactions of cyclooctatetraene with chlorine or bromine, 8-halogenohomotropylium intermediates have been postulated[11] and the nucleophilic attack on the intermediate **18** by AcOH

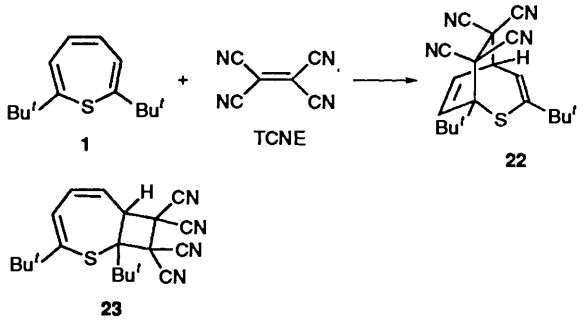


Scheme 2

would generate the thiopyran **17**. The formation in low yield of the thiophene derivative **12** can be also explained in terms of a path *via* the same intermediate **18**. Nucleophilic attack of water, which is smaller than AcOH, on the carbon adjacent to sulfur of **18** would lead to the intermediate **19**, which, as a monothiohemiacetal, might open to form a keto thiol **20**. This, followed by a Michael addition, would give the five-membered ring intermediate **21**. Another possibility is the [1,3] shift of the intermediate **19** and the subsequent ketonization to give the intermediate **21**, which could be transformed to the thiophene **12** by the loss of hydrogen bromide. Mechanistic studies of this novel bromination–ring contraction are under investigation.

(iv) *Reaction of* 2,7-*Di*-tert-*butylthiepine with TCNE.*—One of the essential characteristics of conjugated medium-ring polyenes is their capacity to undergo cycloaddition and this should be so for thiepines. Whether a sulfenyl group in the thiepine ring would have an effect on the cyclic transition state in cycloadditions is of interest and, therefore, the cycloaddition of the thiepine **1** with tetracyanoethylene (TCNE) was examined.[12] Although reactions of benzoxepine[13] and azepine derivatives[14] with TCNE gave [4 + 2] cycloadducts, the steric repulsion of *tert*-butyl groups, may promote a [2 + 2] stepwise cycloaddition in the case of the thiepine **1**. In the event, treatment of the thiepine **1** with TCNE in toluene at reflux temperature resulted only in decomposition. However, the reaction with TCNE in toluene at 60 °C under high pressure (8500 atm) for 3 days gave a 1:1 adduct, **22** (molecular formula $C_{20}H_{22}N_4S$), as the major isolable product in 46% yield (methyl acrylate was found to be inert to the reaction under the same conditions). The ^{1}H NMR spectra of compound **22** displayed two *tert*-butyl signals (δ 1.21 and 1.49), a ddd proton at 3.68 (*J* 8.8, 7.5 and 0.5) and three olefinic protons, 5.91 (d, *J* 8.8), 6.17 (dd, *J* 9.6 and 0.5) and 6.28 ppm (dd, *J* 9.6, 7.5). The ddd coupling pattern of the proton

at δ 3.68, which can be assigned to 1-H, excludes the [2 + 2] cycloadduct **23**. The ^{13}C NMR spectra of compound **22** gave 4 resonances (δ 27.5, 29.8, 39.5, 40.6) for 2 *tert*-butyl groups, 4 other sp^3 carbons (δ 39.9, 49.3, 50.9, 60.9), 4 cyano carbons (δ 111.4, 112.1, 112.5, 112.7) and 4 sp^2 carbons (109.4, 124.0, 125.8, 154.2), all of which were compatible with the [4 + 2] cycloadduct shown below. The ^{13}C NMR assignment was established by ^{13}C–^1H COSY and the long-range ^{13}C–^1H COSY spectra. The other symmetrical [4 + 2] or [2 + 2] cycloadduct can be also excluded. The same reaction occurred in acetonitrile at room temp. under atmospheric pressure over 2 weeks to give compound **22** in 49% yield.



Since the rate of this cycloaddition is dependent upon solvent polarity, the intermediate may well be a charge-transfer complex or even a zwitterion. The detailed reaction pathway is currently under investigation. Thus, a [4 + 2] cycloadduct for a thiepine has, for the first time, been obtained.[15]

Conclusions

Various chemical reactivities of a monocyclic thiepine have been examined for the first time. Electrophilic reactions at sulfur, such as the oxidation and reaction with $AgBF_4$–CH_3I, bromination by electrophilic reaction at the ring carbon and the cycloaddition with TCNE have been examined. The chemical reactivities of the monocyclic thiepine **1** observed provide new insight into thiepine chemistry. Further investigations of the reactivity of thiepines are underway in our laboratories.

Experimental

General Methods.—M.p.s were recorded using a Kofler-type hot-stage apparatus and are uncorrected. IR spectra were recorded with a JASCO A-100 instrument. NMR spectra were recorded on a JEOL JNM-GSX400, a Varian XL-100, or a JEOL JNM-PMX-60 spectrometer. For the ^1H and ^{13}C spectra, Me_4Si was used as an internal reference unless otherwise noted. Mass spectra were determined on a JEOL JMS-01SG-2 or a JEOL JMS-SX102 spectrometer. All reactions were performed under a nitrogen atmosphere.

Formation of 2,7-*Di*-tert-*butylthiepine* 1-*Oxide* **3**.—In an NMR tube containing a solution of *O*-benzyl *OO*-hydrogen monoperoxycarbonate **2**[7] (4.1 mg, 0.024 mmol) in CD_2Cl_2 (0.2 cm^3) was added the thiepine **1** (5 mg, 0.0225 mmol) in CD_2Cl_2 (0.2 cm^3) at −78 °C and the resultant solution was shaken. After 1 h, the ^1H NMR spectrum was recorded at −70 °C and the resonances due to the oxide **3** were observed amongst the signals due to benzyl alcohol; δ_H(100 MHz; CD_2Cl_2, −70 °C) *inter alia* 1.24 (18 H, s), 6.90 (4 H, 3-, 4-, 5- and 6-H).

Thermolysis of 2,7-*Di*-tert-*butylthiepine* 1-*Oxide* **3**.—The same procedure was followed as described above, except that after the addition the solution was allowed to stand at −78 °C overnight to complete the reaction. Changes in the ^1H NMR spectra of the solution were recorded at −15 °C. The ratios of the two products **3** and **6** was determined by ^1H NMR integration of *tert*-butyl protons and the half life $t_{\frac{1}{2}}$ at 15 °C was calculated to be 5.5 h.

Formation of O-*Di*-tert-*butylbenzene* **6** *from the Oxidation of the Thiepine* **1**.—To a solution of the peracid **2**[7] (33.1 mg, 0.197 mmol) in dichloromethane (3.3 cm^3) was added the thiepine **1** (20 mg, 0.090 mmol) at −78 °C and the solution was stirred for 1 h at constant temp. Evaporation of the solvent at room temp. gave the title compound **4** in 76% yield (13 mg) after column chromatography (SiO_2, hexane) as colourless crystals, m.p. 26–27.6 °C (lit.,[8c] m.p. 27–28 °C); δ_H(100 MHz; $CDCl_3$; lit.[8]) 1.56 (18 H, s), 7.12 (2 H, m) and 7.59 (2 H, m); *m/z* (70 eV) 190 (M^+).

Reaction of the Thiepine **1** *with Methyl Iodide–Silver Tetrafluoroborate to form* 2-tert-*Butylphenyl Methyl Sulfide* **8** *and the* S-*Methylated Salt* **9**.—To a solution of the thiepine **1** (50 mg, 0.225 mmol) and methyl iodide (313 mg, 2.2 mmol) in 1,2-dichloroethane (1 cm^3) was added $AgBF_4$ (49 mg, 0.25 mmol) at room temp. and the mixture was stirred overnight. The precipitate was removed by filtration and washed with dichloromethane. After evaporation of the filtrate, the residue was collected on a filter and washed with diethyl ether. Recrystallization from CH_2Cl_2–diethyl ether gave the salt **9** (49 mg, 77%) as colourless crystals, m.p. 163–164 °C; δ_H(100 MHz; CD_2Cl_2) 1.56 (9 H, s), 3.30 (6 H, s), 7.66 (3 H, m) and 8.11 (1 H, m) (Found: C, 51.0; H, 6.8. Calc. for $C_{12}H_{19}SBF_4$: C, 51.08; H, 6.79%). Concentration of the filtrate gave the free sulfonyl **8** (7 mg, 17%) as a colourless oil: δ_H(60 MHz, CCl_4) 1.47 (9 H, s), 2.43 (3 H, s) and 6.85–7.30 (4 H, m); *m/z* (70 eV) 180 (M^+).

Reaction of 2-tert-*Butylphenyl Methyl Sulfide* **8** *with Methyl Iodide–Silver Tetrafluoroborate to give the* S-*Methylated Salt* **9**.—To a solution of the sulfide **8** (6 mg, 0.033 mmol) and methyl iodide (46 mg, 0.33 mmol) in 1,2-dichloroethane (0.2 cm^3) was added $AgBF_4$ (7.2 mg, 0.037 mmol) at room temp. and the mixture was stirred overnight. The precipitate was removed by filtration and washed with dichloromethane. After removal of the solvent of the filtrate, the residue was collected and washed with diethyl ether under filtration to give the salt **9** (7 mg, 75%).

Reaction of the Thiepine **1** *with Bromine to form* 1-(5-tert-*Butyl*-2-*thienyl*)-3,3-*dimethylbutan*-2-*one* **12**.—To a solution of compound **1** (26 mg, 0.12 mmol) in dichloromethane (2 cm^3) was added dropwise a solution of bromine (24 mg, 0.15 mmol) in dichloromethane (0.08 cm^3) at −78 °C. The mixture was stirred for 2 h, allowed to warm to room temp. and then evaporated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with benzene, to give the ketone **12** (5 mg, 18%) (R_f 0.5): pale yellow oil; δ_H(400 MHz, $CDCl_3$) 1.20 (9 H, s), 1.35 (9 H, s), 3.93 (2 H, s) and 6.64 (2 H, s); δ_C(100 MHz, $CDCl_3$) 26.4, 32.5, 34.5, 37.5, 44.6, 120.7, 125.7, 132.9, 157.0 and 211.6; ν_{max}(CCl_4)/cm^{-1} 1710; *m/z* (70 eV) (relative intensity) 238 (39) and 153 (100) (Found: M^+, 238.1383. Calc. for $C_{14}H_{22}OS$: *M*, 238.1391).

Reaction of the Thiepine **1** *with Pyridinium Hydrotribromide to give the Ketone* **12**.—To a solution of the thiepine **1** (48 mg, 0.218 mmol) in dichloromethane (5 cm^3) was added pyridinium hydrotribromide (68 mg, 0.213 mmol) at room temp. The mixture was stirred overnight and then diluted with water (150 cm^3). The resultant mixture was extracted with dichloromethane and the organic phase was washed with sat. aq. NaCl, dried

(Na_2SO_4) and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (benzene–hexane, 2:1) to give the ketone **12** (3 mg, 6%) (R_f 0.3).

Reaction of the Thiepine **1** *with a Dioxane–Bromine Complex to form* 2,6-*Di*-tert-*butyl*-4H-*thiin*-4-*ylbromomethyl Acetate* **17**.—To a solution of compound **1** (51 mg, 0.23 mmol) dissolved in dichloromethane (1 cm^3) and acetic acid (3 cm^3) was added dropwise a complex of dioxane–bromine (112 mg, 0.23 mmol) as a solution in dichloromethane (5 cm^3) at 0 °C. The mixture was stirred for 1 h, diluted with further dichloromethane (20 cm^3) and then washed with 0.2 mol dm^{-3} aq. NaOH (10 cm^3 × 2), sat. aq. NH_4Cl (10 cm^3), water (10 cm^3) and sat. aq. NaCl (10 cm^3) and then dried (Na_2SO_4) and evaporated under reduced pressure. The residue was purified by column chromatography on silica (benzene) to give the acetate **17** (8 mg, 10%) (R_f 0.8) as a yellow oil; δ_H(400 MHz, $CDCl_3$) 1.18 (9 H, s), 1.20 (9 H, s), 2.11 (3 H, s), 3.51 (1 H, ddd, *J* 7.0, 5.5 and 5.5), 5.60 (1 H, d, *J* 5.5), 5.68 (1 H, d, *J* 5.5) and 6.58 (1 H, d, *J* 7.0); δ_C(100 MHz, $CDCl_3$) 20.8 (CO*Me*), 29.9 (C*Me*$_3$), 37.1 (*C*Me$_3$), 45.7 (4-C), 77.3 (*C*HBrOAc), 112.3, 112.7 (3, 5-C), 149.0, 149.5 (2, 6-C) and 168.3 (*C*O); $\nu_{max}(CCl_4)/cm^{-1}$ 1765; FD–MS 360, 362 (M^+).

Reaction of the Thiepine **1** *with Pyridinium Hydrotribromide to give the Bromo Acetate* **17**.—To a solution of the thiepine **1** (215 mg, 0.966 mmol) in acetic acid (5 cm^3) was added pyridinium hydrotribromide (305 mg, 0.954 mmol) at room temp. The mixture was stirred for 1 h and then diluted with water (300 cm^3). The resultant mixture was extracted with diethyl ether and the organic phase was washed with sat. aq. NaCl, dried (Na_2SO_4) and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane–ethyl acetate, 9:1) to give compound **17** (246 mg, 71%) R_f 0.4).

Reaction of the Thiepine **1** *with Tetracyanoethylene (TCNE) to give* 3,5-*Di*-tert-*butyl*-8,9-*tetracyano*-3-*thiabicyclo*[3.2.2]*nona*-2,6-*diene*.—(*a*) A solution of the thiepine **1** (27 mg, 0.121 mmol) and TCNE (16 mg, 0.121 mmol) in toluene (3 cm^3) was heated to 60 °C at 8500 atm in a Teflon tube for 3 days. The reaction mixture was then evaporated and the residue purified by column chromatography on silica gel (benzene) to give the [4 + 2] cycloadduct **22** (20 mg, 46%) (R_f 0.3).

(*b*) A solution of the thiepine **1** (25 mg, 0.112 mmol) and TCNE (14 mg, 0.108 mmol) in acetonitrile (5 cm^3) was stirred at room temp. for 2 weeks. The reaction mixture was then concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (benzene) to give compound **22** (19 mg, 49%) (R_f 0.3) as well as recovered starting material **1** (3 mg, 12%) (R_f 1.0). **22**: colourless plates (hexane); m.p. 132–134 °C (decomp.); δ_H(400 MHz; $CDCl_3$) 1.21 (9 H, s, C3-*Bu*^{t}), 1.49 (9 H, s, C5-*Bu*^{t}), 3.68 (1 H, ddd, *J* 8.8, 7.5 and 0.5, 1-H), 5.91 (1 H, d, *J* 8.8, 2-H), 6.17 (1 H, dd, *J* 9.6 and 0.5, 6-H) and 6.28 (1 H, dd, *J* 9.6, 7.5, 7-H) (NOE's were observed between δ 1.21 and 5.91); δ_C(100 MHz; $CDCl_3$) 27.5 (C3-C*Me*$_3$), 29.8 (C5-C*Me*$_3$), 39.5 (C5-*C*Me$_3$), 39.9 (C1), 40.6 (C5-*C*Me$_3$), 49.3 (C8), 50.9 (C9), 60.9 (C5), 109.4 (C2), 111.4 (CN), 112.1 (CN), 112.5 (CN), 112.7 (CN), 124.0 (C6), 125.8 (C7) and 154.2 (C3); *m*/*z* (70 eV) (relative intensity) 350 (12), 222 (74) and 140 (100); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 2300 (Found: C, 68.5; H, 6.4; N, 16.0; S, 9.0%. Calc. for $C_{20}H_{22}N_4S$: C, 68.54; H, 6.33; N, 15.99; S, 9.15%).

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References

1 (*a*) J. M. Hoffman Jr. and R. H. Schlessinger, *J. Am. Chem. Soc.*, 1970, **92**, 5263; (*b*) K. Nishino, S. Yano, Y. Kohashi, K. Yamamoto and I. Murata, *J. Am. Chem. Soc.*, 1979, **101**, 5059; (*c*) I. Murata, K. Nishino, S. Yano, Y. Kohashi and K. Yamamoto, *Croat. Chem. Acta*, 1980, **53**, 615. (*d*) K. Yamamoto, S. Yamazaki, Y. Kohashi, I. Murata, Y. Kai, N. Kanehisa, K. Miki and N. Kasai, *Tetrahedron Lett.*, 1982, **23**, 3195; (*e*) K. Yamamoto, S. Yamazaki, Y. Kohashi, A. Matsukawa and I. Murata, *Chem. Lett.*, 1982, 1843; (*f*) K. Yamamoto, A. Matsukawa and I. Murata, *Chem. Lett.*, 1985, 1119; (*g*) R. Gleiter, G. Krennrich, D. Cremer, K. Yamamoto and I. Murata, *J. Am. Chem. Soc.*, 1985, **107**, 6874.

2 For reviews, see: (*a*) I. Murata and K. Nakasuji, *Top. Curr. Chem.*, 1981, **97**, 33; (*b*) D. N. Reinhoudt, *Rec. Trav. Chim. Pays. Bas.*, 1982, **101**, 277.

3 For some reactions of annelated thiepines, see: (*a*) for reviews: D. R. Boyd, *Comprehensive Heterocyclic Chemistry*, 1984, Vol. 7, p. 575; (*b*) for *S*-oxidation: R. H. Schlessinger and G. S. Ponticello, *Tetrahedron Lett.*, 1968, **9**, 3017; H. Hofmann and H. Gaube, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 812; H. Hofmann and H. Djafari, *Z. Naturforsch*, 1989, **44B**, 220; (*c*) for *S*-methylation: H. Hofmann and A. Molnar, *Tetrahedron Lett.*, 1977, **18**, 1985; H. Hofmann, A. Molnar and C. Göttfert, C. *Liebigs Ann. Chem.*, 1983, 425; H. Hofmann and G. Löa, *Z. Naturforsch*, 1984, **39B**, 985; (*d*) H. Hofmann and R. Heidrich, *Z. Naturforsch*, 1982, **37B**, 1344; (*e*) H. Hofmann, H. Fischer and M. de Vries, *Z. Naturforsch*, 1990, **45B**, 1573; (*f*) S. Yamazaki, K. Okada, K. Yamamoto and I. Murata, *Chem. Lett.*, 1984, 919; (*g*) H. Hofmann and H. Djafari, *Liebigs Ann. Chem.*, 1987, 505; (*h*) H. Hofmann, C. Göttfert and H. Gaube, *Z. Naturforsch*, 1990, **45B**, 1059; (*i*) K. Nishino, S. Ishigami, Y. Tamura, K. Imagawa, Y. Ikutani and I. Murata, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1717.

4 For thermal sulfur extrusion reactions of monocyclic thiepines, see reference 1. For protonations of monocyclic thiepines, see: K. Yamamoto, S. Yamazaki, A. Matsukawa and I. Murata, *J. Chem. Soc., Chem. Commun.*, 1984, 604.

5 (*a*) W. L. Mock, *J. Am. Chem. Soc.*, 1967, **89**, 1281; H. L. Ammon and P. Watts, Jr., *J. Am. Chem. Soc.*, 1968, **90**, 4501, (*b*) H. Hofmann and H. Westernacher, *Angew. Chem., Int. Ed. Engl.*, 1966, **5**, 958; E. D. Bergmann and M. Rabinovitz, *J. Org. Chem.*, 1960, **25**, 828; H. Hofmann and H. Westernacher, *Chem. Ber.*, 1969, **102**, 205; H. Hofmann and H. Westernacher, *Angew. Chem., Int. Ed. Engl.*, 1967, **6**, 255; H. Hofmann, H. Westernacher and H. J. Haberstroh, *Chem. Ber.*, 1969, **102**, 2595; W. E. Truce and F. J. Lotspeich, *J. Am. Chem. Soc.*, 1956, **78**, 848.

6 K. Yamamoto, Y. Kohashi and I. Murata, unpublished results.

7 R. M. Coates and J. N. Williams, *J. Org. Chem.*, 1974, **39**, 3054.

8 C. Hoogzand and W. Hubel, *Angew. Chem.*, 1961, **73**, 682; E. M. Arnett, M. E. Strem, *Chem. Ind.* (London), 1961, 2008; A. W. Burgstahler and M. O. Abdel-Rahman, *J. Am. Chem. Soc.*, 1963, **85**, 173.

9 H. Hofmann, R. Böhme and E. Wilhelm, *Chem. Ber.*, 1978, **111**, 309.

10 J. J. P. Stewart, *J. Comput. Chem.*, 1989, **10**, 209, 221; J. J. P. Stewart, MOPAC, version 6, QCPE, program # 455, Indiana University, 1990, Oct.

11 G. Boche, H. Hechtl, H. Huber and R. Huisgen, *J. Am. Chem. Soc.*, 1967, **89**, 3344; R. Huisgen, G. Boche and H. Huber, *J. Am. Chem. Soc.*, 1967, **89**, 3345; R. Huisgen and J. Gasteiger, *Angew. Chem., Int. Ed. Engl.*, 1972, **11**, 1104.

12 A. J. Fataidi, *Synthesis*, 1987, 749.

13 H. Hofmann and P. Hofmann, *Liebigs Ann. Chem.*, 1975, 1571.

14 J. E. Baldwin and R. A. Smith, *J. Am. Chem. Soc.*, 1965, **87**, 4819; A. S. Kende, P. T. Izzo and J. E. Lancaster, *J. Am. Chem. Soc.*, 1965, **87**, 5044. L. A. Paquette, D. E. Kuhla, J. H. Barrett and L. M. Leichter, *J. Org. Chem.*, 1969, **34**, 2888.

15 As intermolecular cycloaddition reactions of thiepine-related compounds, [6 + 4] cycloaddition of thiepine 1,1-dioxide chromium complex has been recently reported. J. H. Rigby, H. S. Ateeq and A. C. Krueger, *Tetrahedron Lett.*, 1992, **33**, 5874. J. H. Rigby, H. S. Ateeq, N. R. Charles, S. V. Cuisiat, M. D. Ferguson, J. A. Henshilwood, A. C. Krueger, C. O. Ogbu, K. M. Short and M. J. Heeg, *J. Am. Chem. Soc.*, 1993, **115**, 1382.

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