8-CH), 6.77 (1 H, s, ArH), 6.85 (1 H, s, ArH); MS, m/z 329 (M^+). Anal. Calcd for $C_{20}H_{27}NO_3 \cdot 0.1H_2O$: C, 72.52; H, 8.28; N, 4.23. Found: C, 72.43; H, 8.50; N, 3.95.

7,8-Dehydro-2,3-dimethoxy-17-methylmorphinan (34). To a stirred solution of **33** (65 mg, 0.198 mmol) in liquid NH_3 (30 mL) was added sodium metal (35 mg, 1.5 mmol), the mixture was stirred for a further 10 min at −78 °C and treated with methanol (5 mL), and then NH_3 was removed by warming. The residue was extracted with methylene chloride, and the extract was washed with water, dried over Na_2SO_4, and evaporated to give the residue, which was subjected to column chromatography on silica gel. Elution with methanol–chloroform (1:9, v/v) afforded the morphinan **34** (46 mg, 78%) as a gum: IR ($CHCl_3$) 1600 cm^{-1}; ^1H NMR δ 2.45 (3 H, s, NMe), 3.88 (6 H, s, 2 OMe), 5.52 (2 H, s, 7-H, 8-H), 6.60 (1 H, s, ArH), 6.76 (1 H, s, ArH); MS, m/z 299 (M^+); exact mass calcd for $C_{19}H_{25}NO_2$ 299.1886, found 299.1887.

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Registry No. **1**, 70779-48-5; **2**, 66336-47-8; **3**, 110416-98-3; **4**, 110416-99-4; **5**, 110417-00-0; **6**, 110417-01-1; **7**, 110417-02-2; **8**, 110417-03-3; **9**, 110417-04-4; **10**, 110417-05-5; **11**, 110417-06-6; **12**, 110417-07-7; **13**, 79214-95-2; **14**, 110417-08-8; **15**, 6023-73-0; **16**, 34603-52-6; **17**, 110417-09-9; **18**, 110417-10-2; **19**, 110417-11-3; **20**, 110417-12-4; **21**, 110417-13-5; **22**, 110417-14-6; **23**, 110417-15-7; **24**, 110417-16-8; **25**, 110417-17-9; **26**, 110417-18-0; *cis*-**27**, 110417-19-1; *trans*-**27**, 110417-27-1; **28**, 110417-20-4; **29**, 110417-21-5; **30**, 110417-22-6; **31**, 110417-23-7; **32**, 110417-24-8; **33**, 110417-25-9; **34**, 110417-26-0; α-chloroacrylonitrile, 920-37-6; lithium divinylcuprate, 22903-99-7.

Ring Contraction Reactions of Dihydro- and Tetrahydrothiazepines to Isothiazolone Derivatives under Pummerer Conditions

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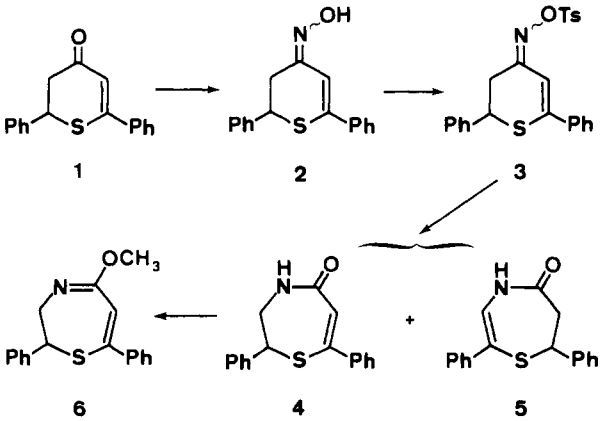
2,7-Diphenyl-5-oxo-2,3,4,5-tetrahydro-1,4-thiazepine (**4**) and 2,7-diphenyl-5-oxo-4,5,6,7-tetrahydro-1,4-thiazepine (**5**) were prepared from 2,3-dihydro-2,6-diphenyl-4*H*-thiopyran-4-one (**1**) through its *O*-tosyloxime (a mixture of syn and anti isomers) followed by Beckmann rearrangement (triethylamine in 70% aqueous dioxane). Upon Pummerer reaction (sodium acetate in acetic anhydride), 2,7-diphenyl-5-methoxy-2,3-dihydro-1,4-thiazepine 1-oxide (**7**), obtained from **4** through methylation by trimethyloxonium tetrafluoroborate followed by *m*-chloroperbenzoic acid oxidation, afforded 3-oxo-5-phenyl-(*Z*)-*N*-styrylisothiazole (**8**) quantitatively which on heating isomerized to the *E* isomer (**9**). The sulfoxide **10** derived from **4** also reacted with sodium acetate in acetic anhydride to give **9** along with 2-acetoxy-4,5-diphenylpyridine (**11**). On the other hand, when treated with trifluoroacetic anhydride in dichloromethane, the sulfoxide **10** gave *N*-[2-(trifluoroacetoxy)-2-phenylethyl]-3-oxoisothiazole (**17**) in good yield. The mechanisms of these ring contractions, **7** → **8** and **10** → **17**, which involve a common bicyclic intermediate (C), are suggested.

In general, conjugated seven-membered sulfur heterocycles such as thiepines[2] and thiazepines[3] are thermally unstable owing to their ready sulfur extrusion. It has already been demonstrated that the instability of these heterocycles can be largely overcome by introducing two bulky groups at both neighbors of the sulfur atom.[4] Recently we have reported the first synthesis of a stable monocyclic 1,4-thiazepine, 2,7-di-*tert*-butyl-5-methoxy-1,4-thiazepine,[5] utilizing the stabilizing effect of two *tert*-butyl groups. Prior to this success we had occasion to examine the 2,7-diphenyl-1,4-thiazepine system. In the course of this study we have found new ring contraction reactions of some dihydro- and tetrahydro-1,4-thiazepine derivatives.

Scheme I



Reaction of 2,3-dihydro-2,6-diphenyl-4*H*-thiopyran-4-one (**1**)[6] with hydroxylamine gave a mixture of the oximes

(1) Current address: Department of Chemistry, Nara University of Education, Takabatake-cho, Nara 630, Japan.

(2) For reviews, see: (a) Field, L.; Tuleen, D. L.; Traynelis, V. J. In *Seven-Membered Heterocyclic Compounds Containing Oxygen and Sulfur*; Rosowsky, A., Ed.; Wiley-Interscience: New York, 1972; Chapters X and XI. (b) Murata, I.; Nakasuji, K. *Top. Curr. Chem.* **1981**, *97*, 33. (c) Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas.* **1982**, *101*, 277. (d) Eisner, U.; Krishnamurthy, U. *Int. J. Sulfur Chem.* **1971**, *6*, 267. (e) Reid, D. H. *Org. Compd. Sulphur, Selenium, Tellurium*, **1970**, *1*, 358; **1973**, *2*, 545; **1977**, *4*, 332.

(3) For a review, see: Wuensch, K. H.; Ehlers, A. *Z. Chem.* **1970**, *10*, 361.

(4) (a) Hoffman, J., Jr.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 5263. (b) Nishino, K.; Yano, S.; Kohashi, Y.; Yamamoto, K.; Murata, I. *J. Am. Chem. Soc.* **1979**, *101*, 5059. (c) Murata, I.; Nishino, K.; Yano, S.; Kohashi, Y.; Yamamoto, K. *Croat. Chem. Acta* **1980**, *53*, 615. (d) Yamamoto, K.; Yamazaki, S.; Kohashi, Y.; Murata, I.; Kai, Y.; Kanehisa, N.; Miki, M.; Kasai, N. *Tetrahedron Lett.* **1982**, *23*, 3195.

(5) Yamamoto, K.; Yamazaki, S.; Osedo, H.; Murata, I. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 635.

(6) Chen, C. H.; Reynolds, G. A.; Van Allan, J. A. *J. Org. Chem.* **1977**, *42*, 2777.

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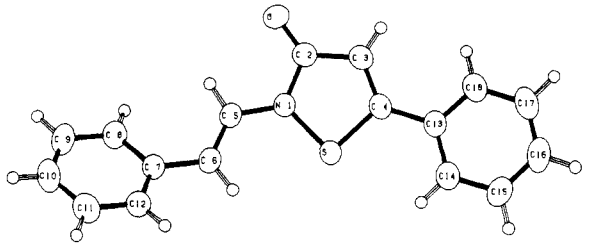
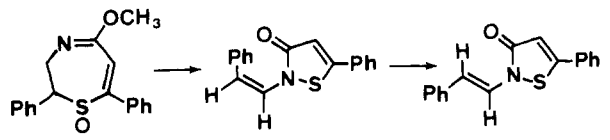


Figure 1. ORTEP drawing of 9.

Scheme II



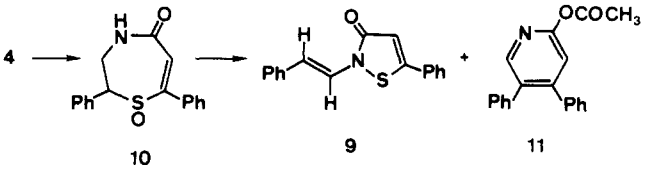
7 8 9

2. The mixture was converted into the tosylates **3** which underwent Beckmann rearrangement in 70% aqueous dioxane with triethylamine to give a mixture of seven-membered lactams. The mixture could be separated by column chromatography on silica gel into 2,7-diphenyl-5-oxo-2,3,4,5-tetrahydro-1,4-thiazepine (**4**) and 2,7-diphenyl-5-oxo-4,5,6,7-tetrahydro-1,4-thiazepine (**5**) in 37% and 15% yield, respectively (Scheme I). The 100-MHz ^{1}H NMR and IR spectra of **4** and **5** clearly distinguish the site of the double bonds. For example, the vinyl proton in **4** (δ 6.19) appears further upfield than that in **5** (δ 6.70) and is weakly coupled (^4J = 1.5 Hz) to its N–H proton. In contrast, the vinyl proton in **5** features a large spin interaction (^3J = 4.0 Hz) that is compatible with its vicinal relationship to the N–H proton. Furthermore, carbonyl stretching frequencies of **4** (1620 cm^{-1}) and **5** (1665 cm^{-1}) clearly indicate the existence of an α,β-unsaturated carbonyl moiety in **4**.

In order to introduce a second double bond, **4** was treated with trimethyloxonium tetrafluoroborate in dichloromethane to give 2,7-diphenyl-5-methoxy-2,3-dihydro-1,4-thiazepine (**6**) in 77% yield. Contrary to our expectation,[7] Pummerer reaction (NaOAc in Ac_2O) of the sulfoxide **7**, derived from **6** in 94% yield by *m*-chloroperbenzoic acid (MCPBA) oxidation in dichloromethane, resulted in the quantitative formation of a product with composition $C_{17}H_{13}NOS$, which is assigned structure **8** on the basis of NMR spectra (Scheme II). The ^{1}H NMR spectra of **8** definitely shows the absence of the methoxy group and the presence of a β-substituted styryl grouping as exemplified by an AB quartet at δ 6.19 and 7.03 with J_{AB} = 9.3 Hz, suggesting a *Z* arrangement of the α,β-vinyl protons. Furthermore, the IR spectrum of **8** strongly suggests the existence of an amide linkage. On heating, **8** was quantitatively isomerized to **9**. The spectral data of **9** are quite similar to those of **8** except for the chemical shifts (δ 6.37 and 7.84) and the coupling constant (J = 14.5 Hz) of the styryl AB quartet. This spectral and thermal behavior can reasonably be explained by the conversion of **8** → **9** as *Z* → *E* isomerization of the *N*-styryl function. In addition, the ^{13}C NMR spectra of **8** and **9** are in harmony with the postulated structures of 3-oxo-5-phenyl-(*Z*)-*N*-styrylisothiazole (**8**) and its *E* isomer **9**, respectively. The structure of **9** was finally confirmed by X-ray diffraction (Figure 1).

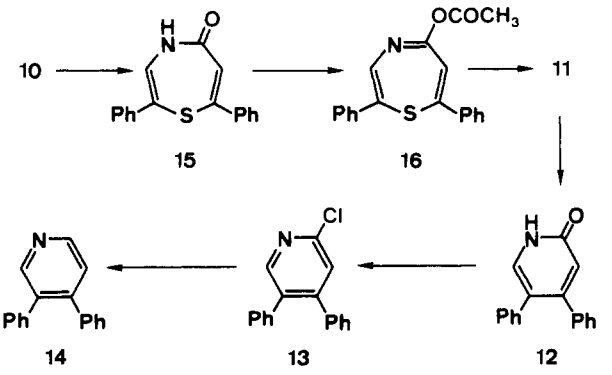
(7) One might expect that the Pummerer reaction of **7** will produce 4,5-diphenyl-2-methoxypyridine through 2,7-diphenyl-5-methoxy-1,4-thiazepine as a thermally labile initial product.

Scheme III



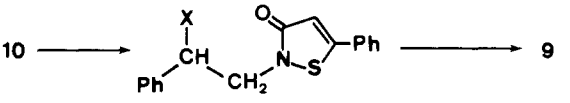
10 9 11

Scheme IV



15 16 10 11 14 13 12

Scheme V



17, X = $OCOCF_3$

18, X = OH

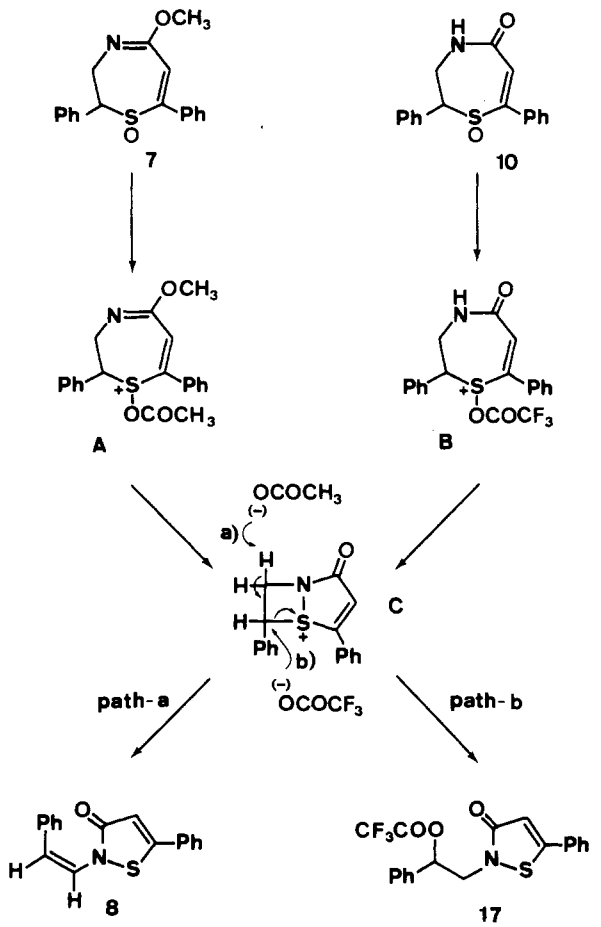
19, X = OMs

Similar ring contraction reactions were also observed during the Pummerer reaction of the sulfoxide **10** derived from **4** by MCPBA oxidation (Scheme III). On treatment with sodium acetate in acetic anhdyride, the sulfoxide **10** gave 2-acetoxy-4,5-diphenylpyridine (**11**) as a major product (68%) along with the aforementioned rearrangement product **9** as a minor product (6%). The structure of **11** was deduced from its spectral data and finally confirmed by hydrolysis to the pyridone **12** and further conversion via the 2-chloropyridine **13** to the known 3,4-diphenylpyridine (**14**)[8] (Scheme IV). The formation of pyridine derivative **11** could reasonably be rationalized by the initial formation of 2,7-diphenyl-5-oxo-4,5-dihydro-1,4-thiazepine (**15**) followed by lactim fixation to form 5-acetoxy-2,7-diphenyl-1,4-thiazepine (**16**) as a thermally labile intermediate which underwent sulfur extrusion to give **11**.

On the other hand, when treating the sulfoxide **10** with trifluoroacetic anhydride in dichloromethane, the compound **17** is obtained in 92% yield as the sole product instead of **8**. The MS (*m/z* 393, M$^+$) and IR spectra (1780 cm^{-1} (CF_3CO) and 1630 cm^{-1} (-N–CO-)) of **17** suggest that **17** resulted from the addition of trifluoroacetoxy group to **10** with some skeletal rearrangement. The ^{1}H NMR spectrum of **17** is similar to those of **8** and **9** except for the lack of an AB quartet due to their styryl protons. Instead, a typical ABX pattern of signals at δ 4.05, 4.32, and 6.16 with J_{AB} = 14.9, J_{AX} = 8.3, and J_{BX} = 4.0 Hz emerged. From these special features together with the fact that both **17** and **8** are formed under the Pummerer reaction conditions, the structure of **17** may be assigned as 3-oxo-5-

(8) (a) Westphal, O.; Feix, G.; Joos, A. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 74. (b) Mortimer, P. I. *Aust. J. Chem.* **1968**, *21*, 467.

Scheme VI



phenyl-*N*-[2-(trifluoroacetoxy)-2-phenylethyl]isothiazole (17), which was finally confirmed by the chemical transformation into 9 according to the reaction sequence, 17 → 18 (KOH/MeOH), 18 → 19 (CH_3SO_2Cl/Et_3N), and 19 → 9 (NaI then DBU/THF), as shown in Scheme V.

Unlike the sulfoxides 7 and 10, when the corresponding sulfoxide derived from 5 was subjected to Pummerer reaction (trifluoroacetic anhydride in dichloromethane or trimethylsilyl iodide and diisopropylethylamine[9] in dichloromethane), only an ill-defined complex mixture resulted.

The formation of 8 and 17 can be interpreted as follows (Scheme VI). In the first steps of these reactions, the addition of acetate and trifluoroacetate on 7 and 10 leads to the acyloxy sulfides (A) and (B), respectively.[10] We postulate that the rearrangements of A and B can occur through the common bicyclic intermediate (C) as a result of the intramolecular transannular bond formation between N and S atoms.[11] An acetate ion (hard base), liberated from the sulfonium ion (A), abstracts a proton from the methylene carbon atom adjacent to the nitrogen atom to produce the (*Z*)-*N*-styryl derivative 8 (path a), whereas the less hard but more nucleophilic trifluoroacetate ion, generated from (B), attacks preferentially at the benzylic carbon atom to afford 17 (path b). This mechanism represents a good example of the competition between elimination (path a) and substitution (path b).

(9) Miller, R. D.; McKean, D. R. *Tetrahedron Lett.* **1983**, *24*, 2619.
(10) For the mechanism of Pummerer reactions, see: Oae, S. In *Organic Chemistry of Sulfur*; Oae, S., Ed.; Plenum Press: New York and London, 1977; pp 406–412.
(11) Leonard, N. J.; Wilson, G. E., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 5307.

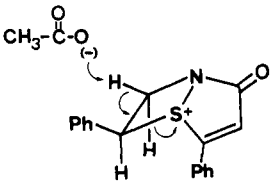


Figure 2.

The high directionality of the reaction courses, path a and b, depending on acetate ion and trifluoroacetate ion, respectively, is also demonstrated in the aforementioned reaction of 10 with sodium acetate in acetic anhydride. The formation of 9 in this reaction is most likely rationalized in terms of the intermediate C which is converted to 9 through 8 by means of a proton abstraction (path a) concomitant with thermal *Z,E* isomerization under the reaction conditions.

Molecular models show that in the stable conformations of A and B favorable for transannular bond formation, the phenyl group located at the sp^3 C atom may occupy a pseudoequatorial position. This means that the bicyclic intermediate C possesses the structure shown in Figure 2 and its enantiomeric form. Thus the pseudoequatorial hydrogen should be removed by the less hindered approach of the acetate ion. Hence, the predominant formation of the *Z* isomer 8 can be justified.

To conclude, it should be noted that the Pummerer reaction of 10 reported in this paper contrasts strikingly with that of 2,7-di-*tert*-butyl-5-oxo-2,3,4,5-tetrahydro-1,4-thiazepine 1-oxide,[5] which reacted smoothly under the same reaction conditions to give the desired diene without rearrangement. A meaningful rationale about the difference in *tert*-butyl vs. phenyl substitutents in this Pummerer reaction must await further study.

Experimental Section

General Methods. Melting points were uncorrected. IR spectra were recorded with a JASCO A-100 spectrophotometer. ^1H NMR spectra were recorded in $CDCl_3$ on either Varian XL-100 NMR or JEOL-JNM-PMX-60 NMR spectrometers. ^{13}C NMR spectra were taken on JEOL FX-90Q spectrometer. All chemical shifts are reported in δ units downfield from Me_4Si, and the *J* values are given in hertz. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra were determined on a JEOL JMS-01SG-2 spectrometer and UV/vis spectra were measured with a Hitachi 340 recording spectrophotometer. All reactions were carried out under a nitrogen atmosphere. Tetrahydrofuran (THF) was distilled over sodium benzophenone ketyl and dichloromethane and hexane were distilled from CaH_2 before use. Column chromatography separations were performed on silica gel deactivated with 5% water. Sodium sulfate was used as a drying agent.

***syn*- and *anti*-2,6-Diphenyl-2,3-dihydro-4*H*-thiopyran-4-one Oximes (2).** A solution of NaOH (2.71 g, 67.7 mmol) in 9.87 mL of water was added dropwise with stirring at 0 °C to a mixture of 2,6-diphenyl-2,3-dihydro-4*H*-thiopyran-4-one (1) (9 g, 33.8 mmol) and hydroxylamine hydrochloride (4.73 g, 67.7 mmol) in 150 mL of 80% aqueous ethanol. The mixture was refluxed for 1 h and the solution was concentrated in vacuo. After the addition of water the mixture was extracted with CH_2Cl_2, and the extract was washed with water and dried. Removal of the solvent gave a mixture of the syn and anti oxime isomers 2 (9.20 g, 97%) as colorless crystals, mp 166–168 °C (recrystallized from benzene): ^1H NMR (100 MHz) δ 2.82 (dd, *J* = 12.9, 17.0 Hz, 1 H), 3.74 (dd, *J* = 3.2, 17.0 Hz, 1 H), 4.43 (dd, *J* = 3.2, 12.9 Hz, 1 H), 6.71 (s, 1 H), 7.17–7.69 (m, 10 H), 8.64 (br s, 1 H); IR (KBr) 3250, 1580 cm^{-1}; MS, *m/z* 281 (M^+).

Anal. Calcd for $C_{17}H_{15}NOS$: C, 72.57; H, 5.37; N, 4.98; S, 11.39. Found: C, 72.43; H, 5.34; N, 4.93; S, 11.27.

***syn*- and *anti*-2,6-Diphenyl-2,3-dihydro-4*H*-thiopyran-4-one *O*-Tosyloximes (3).** To a solution of 2 (7.0 g, 24.9 mmol) in pyridine (14 mL) and CH_2Cl_2 (64 mL) was added *p*-toluene-

sulfonyl chloride (5.34 g, 27.9 mmol) at room temperature, and the mixture was stirred overnight. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined extracts were washed with 2 N aqueous HCl and saturated aqueous $NaHCO_3$ solution and dried. Removal of the solvent gave crude **3** (11.0 g, quantitative) as colorless solid: ^1H NMR (60 MHz) δ 2.40 (s, 3 H), 2.67–3.07 (m, 1 H), 3.63 (dd, J = 4.0, 16.0 Hz, 1 H), 4.35 (dd, J = 4.0, 14.0 Hz, 1H), 6.57 (s, 1 H), 7.23–7.53 (m, 14 H).

2,7-Diphenyl-5-oxo-2,3,4,5-tetrahydro-1,4-thiazepine (4) and 2,7-Diphenyl-5-oxo-4,5,6,7-tetrahydro-1,4-thiazepine (5). A solution of the crude tosylate **3** (11.23 g, 25.8 mmol) and triethylamine (7.53 mL) in 560 mL of 70% aqueous dioxane was stirred at 80 °C for 6 h. The solution was concentrated in vacuo and the residue was diluted with water, extracted with CH_2Cl_2, and dried. Removal of the solvent and separation by column chromatography on silica gel with chloroform–ether (1:1) gave **5** (1.18 g, 15%) as less polar product (R_f 0.6 on Al_2O_3 TLC, ether) and **4** (2.56 g, 37%) as more polar product (R_f 0.4 on Al_2O_3 TLC, ether). **4**: colorless crystals, mp 160–161 °C (recrystallized from ethyl acetate); ^1H NMR (100 MHz) δ 3.81 (ddd, J = 3, 7, 15.0 Hz, 1 H), 3.92 (ddd, J = 6.0, 7.5, 15.0 Hz, 1 H), 4.68 (dd, J = 3.0, 7.5 Hz, 1 H), 6.29 (d, J = 1.5 Hz, 1 H), 7.23–7.37 (m, 9 H), 7.47–7.62 (m, 2 H); IR (KBr), 1620, 1655 cm^{-1}; MS, m/z 281 (M^+).

Anal. Calcd for $C_{17}H_{15}NOS$: C, 72.57; H, 5.37; N, 4.98; S, 11.39. Found: C, 72.52; H, 5.34; N, 4.96; S, 11.27.

5: colorless crystals, mp 166–167 °C (recrystallized from ethyl acetate); ^1H NMR (100 MHz) δ 3.04 (dd, J = 4.3, 13.0 Hz, 1 H), 3.34 (dd, J = 10.3, 13.0 Hz, 1 H), 4.95 (dd, J = 4.3, 10.3 Hz, 1 H), 6.70 (d, J = 4.0 Hz, 1 H), 7.17–7.51 (m, 10 H), 7.81 (br s, 1 H); IR (KBr) 1665, 1615 cm^{-1}; MS, m/z 281 (M^+).

Anal. Calcd for $C_{17}H_{15}NOS$: C, 72.57; H, 5.37; N, 4.98; S, 11.39. Found: C, 72.42; H, 5.36; N, 5.05; S, 11.38.

2,7-Diphenyl-5-methoxy-2,3-dihydro-1,4-thiazepine (6). To a solution of **4** (2.01 g, 7.15 mmol) in CH_2Cl_2 (71.5 mL) was added trimethyloxonium tetrafluoroborate (1.41 g, 9.47 mmol). The resulting solution was stirred at room temperature overnight and quenched with aqueous K_2CO_3 solution. The mixture was extracted with CH_2Cl_2 and the extracts were dried. The solvent was removed in vacuo and the residue was chromatographed on silica gel, eluting with chloroform–ether (1:1), to give **6** (1.62 g, 77%) as a viscous pale yellow oil, bp 100 °C/4 Torr: ^1H NMR (100 MHz) δ 3.64 (s, 3 H), 4.07–4.46 (m, 2 H), 4.61 (dd, J = 3.0, 6.8 Hz, 1 H), 6.15 (s, 1 H), 7.20–7.57 (m, 10 H); ^{13}C NMR (22.5, MHz) δ 53.0, 55.0, 56.2, 116.2, 127.5, 127.9, 128.0, 128.5, 128.9, 129.5, 140.3, 140.6, 151.4, 161.6; IR (neat) 1650, 1590 cm^{-1}; MS, m/z 295 (M^+).

Anal. Calcd for $C_{18}H_{17}NOS$: C, 73.19; H, 5.80; N, 4.74; S, 10.85. Found: C, 73.05; H, 5.82; N, 4.78; S, 10.56.

2,7-Diphenyl-5-methoxy-2,3-dihydro-1,4-thiazepine 1-Oxide (7). To a solution of **6** (693 mg, 2.35 mmol) in CH_2Cl_2 (31 mL) was added a solution of MCPBA (80%, 507 mg, 2.35 mmol) in 12 mL of CH_2Cl_2. After being stirred at 0 °C for 1 h, the solution was washed with 5% $NaHSO_3$ solution and saturated aqueous $NaHCO_3$ solution and then dried. The solvent was removed and the residue was chromatographed on silica gel, eluting with chloroform–ether (1:1), to give **7** (687 mg, 94%) as a pale yellow oil: ^1H NMR (100 MHz) δ 3.82 (s, 3 H), 4.01–4.27 (m, 2 H), 4.64 (t, J = 5.3 Hz, 1 H), 6.46 (s, 1 H), 7.24–7.55 (m, 10 H); IR (neat) 1640 cm^{-1}; MS, m/z 311 (M^+).

3-Oxo-5-phenyl-(*Z*)-*N*-styrylisothiazole (8) from Pummerer Reaction of 7. A mixture of **7** (423 mg, 1.36 mmol) and sodium acetate (423 mg, 5.15 mmol) in acetic anhydride (3.9 mL) was heated under reflux for 1 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel, eluting with chloroform–ether (1:1), to give **8** quantitatively as pale yellow crystals, mp 119–120 °C (recrystallized from ethyl acetate): ^1H NMR (100 MHz) δ 6.19 (d, J = 9.3 Hz, 1 H), 6.34 (s, 1 H), 7.03 (d, J = 9.3 Hz, 1 H), 7.22–7.44 (m, 10 H); ^{13}C NMR (22.5 MHz) δ 108.5, 117.3, 122.5, 125.9, 128.2, 128.5, 129.3, 129.4, 129.6, 131.2, 133.9, 157.7, 169.3; IR (KBr) 1660, 1640 cm^{-1}; MS, m/z 279 (M^+).

Anal. Calcd for $C_{17}H_{13}NOS$: C, 73.09; H, 4.69; N, 5.01; S, 11.48. Found: C, 72.92; H, 4.67; N, 4.97; S, 11.31.

3-Oxo-5-phenyl-(*E*)-*N*-styrylisothiazole (9): Thermal Isomerization of 8 into 9. The crystals of **8** were heated without solvent at 140 °C for 8 h. After cooling to room temperature, the solidified product was recrystallized from benzene to give **9** as yellow crystals, mp 154–154.5 °C: ^1H NMR (100 MHz) δ 6.37 (d, J = 14.5 Hz, 1 H), 6.51 (s, 1 H), 7.23–7.57 (m, 10 H), 7.84 (d, J = 14.5 Hz, 1 H); ^{13}C NMR (22.5 MHz) δ 110.2, 115.0, 112.2, 125.8, 125.9, 127.3, 128.7, 129.4, 129.7, 131.4,135.1, 155.9, 166.9; IR (KBr) 1660, 1630 cm^{-1}; UV (cyclohexane) λ_{max} nm (log ϵ) 276 (4.26), 294 (4.18), 302 (4.16), 324 (sh, 3.98), 358 (4.05); MS, m/z 279 (M^+).

Anal. Calcd for $C_{17}H_{13}NOS$: C, 73.09; H, 4.69; N, 5.01; S, 11.48. Found: C, 72.96; H, 4.71; N, 5.00; S, 11.45.

2,7-Diphenyl-5-oxo-2,3,4,5-tetrahydro-1,4-thiazepine 1-Oxide (10). To a solution of **4** (151 mg, 0.536 mmol) in CH_2Cl_2 (7.2 mL) was added dropwise with stirring at 0 °C a solution of MCPBA (116 mg, 0.536 mmol) in CH_2Cl_2 (2.8 mL). After further stirring at 0 °C for 1 h, the solution was washed with 5% aqueous $NaHSO_3$ and saturated aqueous $NaHCO_3$ solution, dried, and concentrated to give crude **10** (162 mg, 100%) as colorless crystals, mp 214–215 °C (recrystallized from $CHCl_3$): ^1H NMR (100 MHz) δ 4.08 (t, J = 7.0 Hz, 2 H), 5.12 (t, J = 7.0 Hz, 1 H), 6.92 (s, 1 H), 7.27–7.62 (m, 10 H), 7.97 (br s, 1 H); IR (KBr) 1655 cm^{-1}; MS, m/z 297 (M^+).

Anal. Calcd for $C_{17}H_{15}NO_2S$: C, 68.66; H, 5.08; N, 4.71; S, 10.78. Found: C, 68.13; H, 4.98; N, 4.71; S, 11.00.

Pummerer Reaction of 10 with Sodium Acetate in Acetic Anhydride. Formation of 2-Acetoxy-4,5-diphenylpyridine (11) and 3-Oxo-5-phenyl-(*E*)-*N*-styrylisothiazole (9). A mixture of **10** (563 mg, 1.89 mmol) and sodium acetate (563 mg, 6.86 mmol) in acetic anhydride (5.5 mL) was heated under reflux for 1 h. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel, eluting with benzene–ether (6:1), to afford 2-acetoxy-4,5-diphenylpyridine (**11**) (373 mg, 68%) as a brown oil together with **9** (32 mg, 6%). **11**: ^1H NMR (100 MHz) δ 2.34 (s, 3 H), 7.02–7.24 (m, 11 H), 8.34 (s, 1 H); IR ($CHCl_3$) 1760, 1700, 1595 cm^{-1}; MS, m/z 289 (M^+).

4,5-Diphenyl-2-pyridone (12). A solution of **11** (864 mg, 2.99 mmol) and potassium hydroxide (334 mg, 5.96 mmol) in 118 mL of methanol containing 0.72 mL of water was stirred at room temperature for 3 h. The solution was concentrated under reduced pressure and the residue was diluted with water and extracted with CH_2Cl_2. The extracts were dried and concentrated to give **12** (567 mg, 76.8%) as pale yellow crystals, mp 219–220 °C (recrystallized from ethanol): ^1H NMR (100 MHz) δ 6.62 (s, 1 H), 6.89–7.30 (m, 11 H), 7.42 (s, 1 H); IR (KBr) 1650 cm^{-1}; MS, m/z 247 (M^+).

Anal. Calcd for $C_{17}H_{13}NO$: C, 82.57; H, 5.30; N, 5.66. Found: C, 82.17; H, 5.34; N, 5.69.

2-Chloro-4,5-diphenylpyridine (13). A mixture of **12** (400 mg, 1.62 mmol) and phosphoryl chloride (5.5 mL) was refluxed for 5.3 h. The reaction mixture was poured onto ice and extracted with CH_2Cl_2. The extracts were washed with water and saturated aqueous $NaHCO_3$ solution and dried. The solvent was removed and the residue was chromatographed on silica gel, eluting with $CHCl_3$, to give **13** (87 mg, 20%) as pale yellow crystals, mp 113–114 °C (recrystallized from ethanol): ^1H NMR (100 MHz) δ 6.86–7.30 (m, 11 H), 8.30 (s, 1 H); IR (KBr) 1580 cm^{-1}; MS, m/z 265, 267 (M^+).

Anal. Calcd for $C_{17}H_{12}NCl$: C, 76.84; H, 4.55; N, 5.27; Cl, 13.38. Found: C, 76.47; H, 4.63; N, 5.27; Cl, 13.34.

3,4-Diphenylpyridine (14). A solution of **13** (58.8 mg, 0.22 mmol) and potassium hydroxide (67.7 mg, 1.21 mmol) in 5.9 mL of methanol containing 20 mg of 5% Pd/C was hydrogenated at room temperature for 16 h. After filtration of the catalyst and evaporation of the solvent, the residue was extracted with CH_2Cl_2. The extracts were washed with water and dried. Removal of the solvent gave **14** (40.6 mg, 79.2%) as colorless crystals, mp 113–114 °C (recrystallized from ethanol) (lit.[8a] mp 112 °C; lit.[8b] mp 114 °C): ^1H NMR (100 MHz) δ 7.02–7.24 (m, 11 H), 8.54 (d, J = 4.4 Hz, 1 H), 8.56 (s, 1 H); IR (KBr) 1580 cm^{-1}; UV (ethanol) λ_{max} nm (ϵ) 235 (19 200), 280 (sh, 6000); MS, m/z 231 (M^+).

Anal. Calcd for $C_{17}H_{13}N$: C, 88.28; H, 5.66; N, 6.06. Found: C, 87.91; H, 5.70; N, 5.98.

Pummerer Reaction of 10 with Trifluoroacetic Anhydride. Formation of 3-Oxo-5-phenyl-*N*-[2-(trifluoroacetoxy)-2-phenylethyl]isothiazole (17). To a mixture of **10** (1.09 g, 3.68 mmol) in CH_2Cl_2 (49 mL) was added trifluoroacetic anhydride (1.03 mL, 7.36 mmol) at 0 °C. The mixture was stirred at room

temperature overnight. The excess trifluoroacetic anhydride and the solvent were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and the solution was washed with saturated aqueous $NaHCO_3$ solution, dried, and concentrated to give **17** (1.33 g, 92%) as a colorless oil: ^1H NMR (100 MHz) δ 4.05 (dd, J = 8.3, 14.9 Hz, 1 H), 4.33 (dd, J = 4.0, 14.9 Hz, 1 H), 6.16 (dd, J = 4.0, 8.3 Hz, 1 H), 6.38 (s, 1 H), 7.28-7.40 (m, 10 H); IR ($CHCl_3$) 1780, 1635 cm^{-1}; MS, m/z 393 (M^+).

Transformation of 17 into 9. A solution of **17** (2.15 g, 5.47 mmol), potassium hydroxide (611 mg, 10.9 mmol), and water (1.32 mL) in methanol (215 mL) was stirred at room temperature for 3 h. The solution was concentrated under reduced pressure and the residue was diluted with water, extracted with CH_2Cl_2, and dried. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel, eluting with chloroform-ether (1:1), to give *N*-(2-hydroxy-2-phenylethyl)-5-phenylisothiazol-3-one (**18**) (984 mg, 60.6%) as colorless crystals, mp 171-171.5 °C (recrystallized from ethyl acetate): ^1H NMR (90 MHz) δ 3.86 (dd, J = 7.8, 14.6 Hz, 1 H), 4.16 (dd, J = 3.3, 14.6 Hz, 1 H), 4.54 (br s, 1 H), 5.01-5.14 (m, 1 H), 6.40 (s, 1 H), 7.23-7.54 (m, 10 H); IR (KBr) 3240, 1625 cm^{-1}; MS, m/z 297 (M^+).

Anal. Calcd for $C_{17}H_{15}NO_2S$: C, 68.66; H, 5.08; N, 4.71; S, 10.78. Found: C, 68.42; H, 5.08; N, 4.69: S, 10.91.

The product **18** (2.26 g, 7.63 mmol) thus obtained was stirred in 87 mL of CH_2Cl_2 with 1.58 mL of triethylamine and 0.64 mL of methanesulfonyl chloride for 1 h at 0 °C and then 20 min at room temperature. The reaction mixture was extracted with CH_2Cl_2 and the extracts were washed with water and dried. The solvent was removed and the residue was chromatographed on silica gel, eluting with chloroform-ether (1:1), to give *N*-[2-[(methylsulfonyl)oxy]-2-phenylethyl]-3-oxo-5-phenylisothiazole (**19**) (3 g, 100%) as an oil: ^1H NMR (60 MHz) δ 2.73 (s, 3 H), 4.05-4.23 (m, 2 H), 5.83 (dd, J = 5.0, 8.0 Hz, 1 H), 6.38 (s, 1 H), 7.33 (narrow m, 10 H).

The product **19** (974 mg, 2.60 mmol) was mixed with sodium iodide (1.0 g, 6.62 mmol) and dry acetone (26.5 mL), and stirred at 4 °C for 67 h. Following evaporation of the acetone and dilution of the remaining residue with chloroform, the insoluble solid was filtered and washed with chloroform. The combined chloroform layer was concentrated under reduced pressure and the residue was dissolved in 21.1 mL of THF at 0 °C. To the solution was added DBU (1.53 g, 10.20 mmol) in 21 mL of THF. The mixture was stirred for 2 h at room temperature and extracted with CH_2Cl_2, and the extracts were washed with 2 N HCl and saturated aqueous $NaHCO_3$ solution and dried. The solvent was removed and the residue was chromatographed on silica gel, eluting with chloroform-ether (1:1), to afford (*E*)-*N*-styryl-5-phenylisothiazol-3-one (**9**) (419 mg, 58%) as yellow crystals, mp 154-154.5 °C. The melting point and all spectral data are in full agreement with those of **9** described previously.

Single-Crystal X-ray Diffraction Analysis of (*E*)-*N*-Styryl-5-phenyl-3-oxoisothiazole (9). The crystal data for **9** are as follows: triclinic; space group $P\bar{1}$; a = 7.847 (1), b = 14.242 (3), and c = 6.331 (1) Å, α = 90.23 (1)°, β = 100.35 (1)°, γ = 102.23 (1)°, V = 679.4 (2) Å^3, Z = 2. The empirical formula is $C_{17}H_{13}NOS$, molecular weight is 279.35, and calculated density is 1.37 g cm^{-3}. The three-dimensional X-ray data were collected by using a crystal with dimensions 0.3 × 0.3 × 0.4 mm by the use of graphite-monochromated Mo Kα radiation (λ = 0.71069 Å) on a Syntex R3 automatic diffractometer up to a maximum 2θ of 55.0°. Of 3114 total unique reflections, 2710 were considered observed at the level of ($|F_o| > 3\sigma|F_o|$). Data were corrected for Lorentz and polarization effect in the usual way but not for absorption as the linear absorption coefficient is small enough [(Mo Kα) = 2.3 cm^{-1}]. The structure was solved by the direct method (MULTAN78) and refined anisotropically by full-matrix least-squares. All the hydrogen atoms, located on a difference Fourier map, were included in the final part of the refinement with the isotropic temperature factors. The final unweighted residual index (R) was 0.040 for non-zero reflections, and the weighted R_w was 0.039, the weighting scheme of which is $w = [a|F_o|^2 + b|F_o| + c]$ with a = 0.0012, b = -0.0191, c = 0.1677. There is no feature greater than 0.21 e A^{-3} on the final difference Fourier map. All the calculations were done on a HITAC M-200H computer of the Hiroshima University by using the structure analysis program system UNICS.[12]

Registry No. **1**, 60839-95-4; **2** (isomer 1), 110567-82-3; **2** (isomer 2), 110567-83-4; **3** (isomer 1), 110567-84-5; **3** (isomer 2), 110567-85-6; **4**, 110567-87-8; **5**, 110567-86-7; **5** (*S*-monooxide), 110567-99-2; **6**, 110567-88-9; **7**, 110567-89-0; **8**, 110567-90-3; **9**, 110567-91-4; **10**, 110567-92-5; **11**, 110567-93-6; **12**, 110567-94-7; **13**, 110567-95-8; **14**, 5216-04-6; **17**, 110567-96-9; **18**, 110567-97-0; **19**, 110567-98-1.

Supplementary Material Available: Tables of fractional coordinates, anisotropic thermal parameters, interatomic distances, and interatomic angles for **9** (4 pages). Ordering information is given on any current masthead page.

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Synthesis of Naturally Occurring Bithiophenes: A Photochemical Approach

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A photochemical approach to the synthesis of six naturally occurring bithiophenes is described. The irradiation of 5-iodo-2-thiophenecarbaldehyde (**3**) in the presence of 2-bromothiophene (**4**) or 2-methylthiophene (**15**) furnishes 5-bromo- (**5**) and 5-methyl-2,2′-bithiophene-5′-carbaldehyde (**16**) in 99 and 69% yields respectively. Compounds **5** and **16** are used in the synthesis of 5-(1-propynyl)-2,2′-bithiophene-5′-methanol (**7**), 5′-propynyl-2,2′-bithiophene-5-carbaldehyde (**8**), 5-ethynyl-5′-(1-propynyl)-2,2′-bithiophene (**9**), 5-ethenyl-5′-(1-propynyl)-2,2′-bithiophene (**11**), 5′-[(isovaleryloxy)methyl]-5-[4-(isovaleryloxy)but-1-ynyl]-2,2′-bithiophene (**14**), and 5-methyl-5′-[1-(buta-1,3-dienyl)]-2,2′-bithiophene (**17**) through known reactions. In particular, the most important synthetic methodology used is an alkynylation procedure accomplished in the presence of Pd(0) in phase-transfer conditions.

Introduction

Recently, we reported that the irradiation of 3- and 5-halogenothiophenecarbaldehydes or 3- and 5-halogenothiopheneketones **1** in benzene solution furnished good yields of the corresponding phenyl derivatives **2**.[1]

We also reported that the irradiation could be performed in thiophene solution to give the corresponding bithienyl

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