

Yukio Ikemi

Department of Chemistry, College of Liberal Arts and Sciences, Kyoto University,
Kyoto 606, Japan

Received May 11, 1989

Diphenylcyclopropenethione undergoes nucleophilic attack by pyridinium disubstituted ylides **1a-1e** to produce the corresponding 2-pyranthione **3a**, 2-pyrone **4a** or **4c**, thiopyran-2-one **6a**, **6b**, **6d** or **6e**, and/or 5*H*-thieno[3,2-*b*]thiopyran **5a**.

J. Heterocyclic Chem., **27**, 1597 (1990).

Cyclopropenes and related compounds are of great interest as synthetic reagents and reports regarding their use are growing steadily [1,2]. Pyridinium monosubstituted methylides and pyridinium imines react usually as nucleophiles with diphenylcyclopropenone and diphenylcyclopropenethione to give the 2-pyrone, thiopyran-2-one, and/or 1,3-oxazine, derivatives [3]. However, little is known on the reaction of cycloimmonium disubstituted ylides with cyclopropenones and cyclopropenethiones. We report in full detail on the reaction of pyridinium disubstituted ylides with diphenylcyclopropenethione [4].

Reaction of pyridinium bis(methoxycarbonyl)methylide (**1a**) with diphenylcyclopropenethione (**2**, DPPS) in acetonitrile was performed with stirring at room temperature for 3 days. Upon chromatography of the reaction products on silica gel and/or tlc, were isolated the three products that proved 3,4-diphenyl-5-methoxycarbonyl-6-methoxypyran-2-thione (**3a**, 12%), 4,5-diphenyl-3-methoxycarbonyl-6-methylthio-2-pyrone (**4a**, 47%), and 5,5-bis(methoxycarbonyl)-2,3,6,7-tetraphenyl-5*H*-thieno[3,2-*b*]thiopyran (**5a**, 5%).

The structures of these compounds were determined based upon their ¹H and ¹³C nmr, ir, uv, mass spectroscopic and elementary analysis. The 2-pyranthione **3a** exhibited two methyl resonances of the methoxy and the methoxycarbonyl that absorbed at 3.53, 3.55 (singlet, 3H) in the ¹H nmr spectrum and a carbonyl stretch at 1725 cm⁻¹, a thiocarbonyl stretch at 1105 cm⁻¹ in the ir spectrum. The mass spectrum showed a parent ion at *m/z* 352 (M⁺). Compound **4a** had an almost identical mass spectrum, with the

major ion at *m/z* 324, 305 corresponding to the carbonyl, and the methylthione fragments and molecular ion at *m/z* 352 (M⁺). The ir spectrum showed a carbonyl of lactone at 1705 cm⁻¹.

5,5-Bis(methoxycarbonyl)-2,3,6,7-tetraphenyl-5*H*-thieno[3,2-*b*]thiopyran (**5a**) showed a stretch of the carbonyl at 1725 cm⁻¹ and a stretch of the ester's C-O at 1230 cm⁻¹. The ¹³C nmr spectrum exhibited only 10 sp² carbon atoms unattached to H along with 6 resonances corresponding to sp² carbon atoms attached to H. The mass spectrum showed the molecular ion (*m/z* 574), and fragments at 515 and 456 due to the successive loss of two methoxycarbonyl groups.

In contrast, the reaction of **1a** with DPPS **2** in such a polar protic solvent as methanol at room temperature gave 6-methoxy-5-methoxycarbonyl-3,4-diphenylthiopyran-2-one (**6a**) in 40% yield. The thiopyran-2-one **6a** showed a carbonyl stretch at 1723 cm⁻¹ and a carbonyl stretch of lactone at 1625 cm⁻¹. The ¹H nmr exhibited two methyl resonances of the methoxy and the methoxycarbonyl that absorbed at 3.35, 4.03 (singlet, 3H) and the mass spectrum also showed the molecular ion (*m/z* 352). It is noted that two molecules of **2** are incorporated in **5a** and that the 2-pyrone, presumably formed by methyl shift, is the major product in acetonitrile. Pyridinium bis(ethoxycarbonyl)methylide (**1b**) reacted with DPPS **2** in acetonitrile at room temperature. A tlc analysis of the reaction mixture (silica/dichloromethane) indicated the two main spots, but attempts to isolate another component of the products by

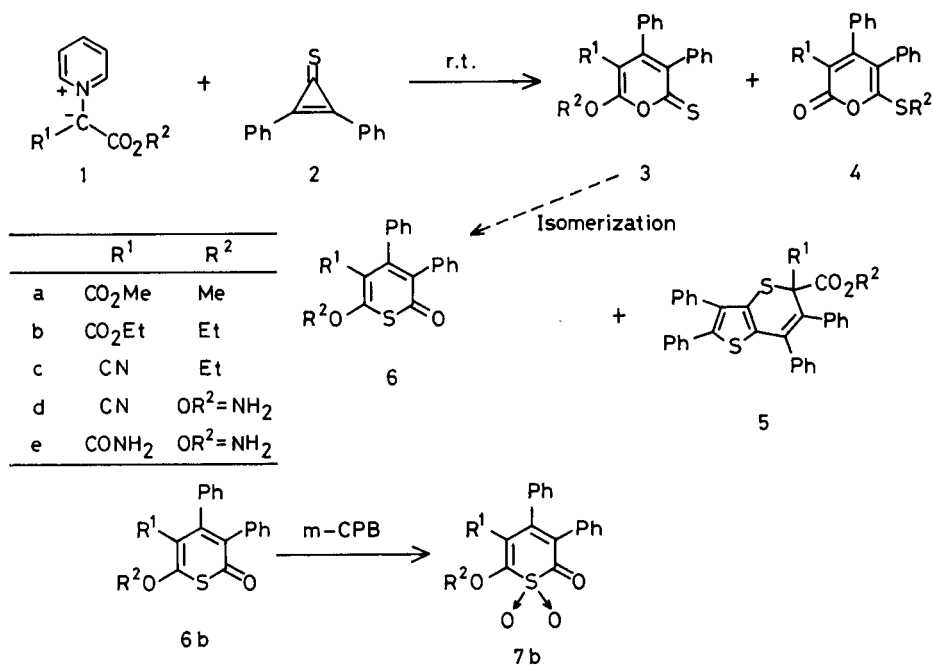
Table
Reaction of Pyridinium Disubstituted Methylide (**1**) with Diphenylcyclopropenethione

	Ylide		Solvent	Temperature	Day	Product	mp(°C)	Yield (%)
	R ¹	R ²						
1a	CO ₂ CH ₃	CH ₃	CH ₃ CN	rt	3	3a 4a 5a	182-183 139-141 198-199	12 47 5
1a	CO ₂ CH ₃	CH ₃	CH ₃ OH	rt	3	6a	180-181	40
1b	CO ₂ C ₂ H ₅	C ₂ H ₅	CH ₃ CN	rt	12	6b	134-136	55
1c	CN	C ₂ H ₅	CH ₃ CN	rt	1	4c	207-209	18
1d	CN	OR ² =NH ₂	CH ₃ OH	rt	7	6d	160-162	56
1e	CONH ₂	OR ² =NH ₂	DMF	rt	1	6e	216-218	21

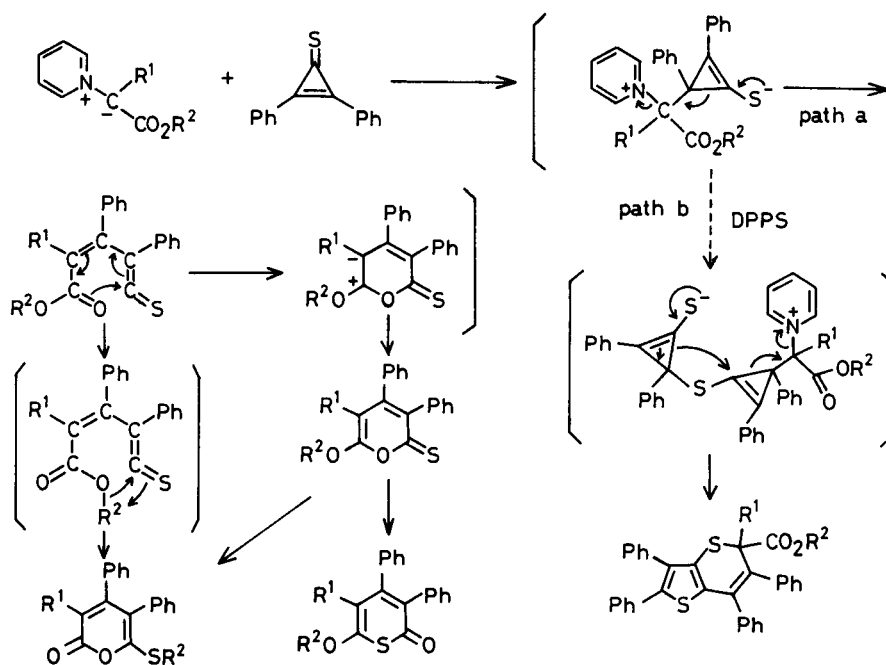
rapid preparative tlc failed, this compound isomerizing to 6-ethoxy-5-ethoxycarbonyl-3,4-diphenylthiopyran-2-one (**6b**, yellow crystals, 55% yield). The mobile compound is presumably the 2-pyranthione **3b**. Thermal isomerization of thiones to thiopyran-2-one is known [5].

The thiopyran-2-one **6b** was oxidized on treatment with *m*-chloroperbenzoic acid to give 6-ethoxy-5-ethoxycarbonyl-3,4-diphenylthiopyran-2-one 1,1-dioxide (**7b**). In a similar reaction of pyridinium cyano(ethoxycarbonyl)methylide **1c** with DPPS **2**, 3-cyano-6-ethylthio-4,5-diphenyl-2-

Scheme 1



Scheme 2



pyrone (**4c**) was obtained in 18% yield, whereas pyridinium cyanocarbonylmethylide (**1d**) with DPPS **2** afforded a 56% yield of the 6-amino-5-cyano-3,4-diphenylthiopyran-2-one (**6d**).

Likewise, pyridinium bis(carbamoyl)methylide (**1e**) generated *in situ* from the corresponding quaternary salt, underwent addition reaction to DPPS **2** to give 6-amino-5-carbamoyl-3,4-diphenylthiopyran-2-one (**6e**) in 21% yield. Compound **6e** showed the N-H stretch of the primary amide at 3500 and 3400 cm^{-1} along with the carbonyl stretch at 1640 cm^{-1} in the ir spectrum. The mass spectrum exhibited a molecular ion (M^+) at m/z 322. These reactions can be rationalized as shown in the Scheme 1.

The first step involves a nucleophilic attack of the ylide to DPPS **2** to form the thioketene intermediate, which cyclizes either to the 2-pyranthione or the 2-pyrone (path a), depending on the solvents and substituents, though the reason for these different modes of cyclizations is not clear. Rearrangement of the 2-pyranthione to the thiopyran-2-one is presumably catalysed by pyridine ejected during the reaction and by a trace of acid and silica gel during work up.

The formation of 5*H*-thieno[3,2-*b*]thiopyran **5a** can be readily rationalized by consideration of path b in Scheme 2 below.

EXPERIMENTAL

General.

Melting points were taken on a Yanagimoto micro melting point apparatus and uncorrected. The ir spectra were obtained on a Jasco IR-G spectrometer. The ^1H nmr spectra were measured on a JEOL JNM-60HL instrument. The ^{13}C nmr spectra were recorded a JEOL FX-60 or FX-90Q pulsed Fourier-transform spectrometer operating at 15.035 MHz and 22.49 MHz, respectively. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. Partial proton decoupling was used to distinguish between individual carbon atoms. Mass spectra were obtained on a JEOL 01SG-2 mass spectrometer. Thin-layer chromatography (tlc) and column chromatography were performed on Kieselgel 60 HF₂₅₄ (Merck) and Wakogel C-100 (149-420 μ) as the stationary phase, respectively. Acetonitrile and methanol were distilled and then dried with molecular sieves (5 Å). The pyridinium methylides **1a-1e** were prepared according to the method of Kobayashi *et al* [6].

3,4-Diphenyl-5-methoxycarbonyl-6-methoxy-pyran-2-thione (**3a**), 4,5-Diphenyl-3-methoxycarbonyl-6-methylthio-2-pyrone (**4a**) and 5,5-Bismethoxycarbonyl-2,3,6,7-tetra-phenyl-5*H*-thieno[3,2-*b*]thiopyran (**5a**).

A mixture of pyridinium bis(methoxycarbonyl)methylide (**1a**) (0.839 g, 4 mmoles) and DPPS **2** (0.901 g, 4 mmoles) in acetonitrile (20 ml) was stirred at room temperature for 3 days. The solvent was removed *in vacuo* and the residue was chromatographed on silica. Elution with hexane, hexane-benzene (1:1), benzene, dichloromethane and benzene-acetone (20:1) gave crude **5a** and a

mixture of **3a** and **4a**. Silica gel chromatography of the mixture of successive elution with hexane-dichloromethane (10:1 and 5:1) and dichloromethane gave **4a** and a mixture of **3a** and **4a**, from which **3a** was isolated by tlc [Kieselgel 60 HF₂₅₄ (Merck)] with dichloromethane. The compounds **4a** and **5a** were purified by recrystallization from methanol and hexane, respectively.

Compound **3a**.

This compound was obtained as yellow crystals (0.169 g), mp 182-183°; ms: [m/z] 352 (M^+); ir (potassium bromide): ν max 1725 and 1105 cm^{-1} ; uv (dichloromethane): λ max 418 sh, 364 sh, 302, and 230 nm ($\log \epsilon$ 4.22, 4.26, 4.47, and 4.62); ^1H nmr (deuteriochloroform): δ 3.53 (s, 3H), 3.55 (s, 3H), 7.15-7.45 (m, 10H); ^{13}C nmr (deuteriochloroform): δ 53.0 (bs, CH₃), 125.4 (s, C-6), 128.1, 128.6, 129.0, 129.2, 129.4, 129.7, 130.5 (each d, Ar-C with H), 136.1, 137.5, 151.7 (each s, C-3,4,5), 165.2 (s, C-2), and 167.1 (s, CO).

Anal. Calcd. for C₂₀H₁₆O₄S: C, 68.16; H, 4.58. Found: C, 68.11; H, 4.94.

Compound **4a**.

This compound was obtained as yellow crystals (0.664 g), mp 139-141°; ms: [m/z] 352 (M^+), 324 ($M^+\text{-CO}$), and 305 ($M^+\text{-SCH}_3$); ir (potassium bromide): ν max 1740 and 1705 cm^{-1} ; uv (dichloromethane): λ max 370 and 260 nm ($\log \epsilon$ 4.71 and 4.72); ^1H nmr (deuteriochloroform): δ 2.58 (s, 3H), 3.57 (s, 3H), and 6.9-7.4 (m, 10H); ^{13}C nmr (deuteriochloroform): δ 13.7 (q, -SCH₃), 52.3 (q, -CH₃), 112.8 (s, C-6), 117.2 (s, C-4), 127.7, 128.1, 130.8 (each d, Ar-sp²C with H), 132.6, 134.8, (each s, Ar-sp²C without H), 156.7 (s, C-5), 158.9 (s, C-3), 163.4 (s, C-2), and 165.0 (s, CO).

Anal. Calcd. for C₂₀H₁₆O₄S: C, 68.16; H, 4.58. Found: C, 67.99; H, 4.60.

Compound **5a**.

This compound was obtained as yellow crystals (0.115 g), mp 198-199°; ms: [m/z] 574 (M^+), 515 ($M^+\text{-CO}_2\text{CH}_3$) and 456 ($M^+\text{-CO}_2\text{CH}_3 \times 2$); ir (potassium bromide): ν max 1725 and 1230 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.53 (bs, 3H \times 2) and 6.8-7.4 (m, 20H); ^{13}C nmr (deuteriochloroform): δ 53.5 (q, -OCH₃ \times 2), 66.1 (s, C-5), 125.9 (s, C-6), 127.2, 130.4, 133.3, 134.6 (each s, Ar-sp²C without H), 127.8, 128.3, 128.6, 128.8, 129.9, 130.6 (each d, Ar-sp²C with H), 134.7 (s, C-7), 135.7 (s, C-7a), 137.3 (s, C-2), 139.0 (s, C-3), 140.1 (s, C-3a) and 168.9 (s, CO).

Anal. Calcd. for C₃₅H₂₆O₄S₂: C, 73.14; H, 4.56. Found: C, 72.92; H, 4.39.

6-Methoxy-5-methoxycarbonyl-3,4-diphenylthiopyran-2-one (**6a**).

A mixture of pyridinium bis(methoxycarbonyl)methylide (**1a**) (0.339 g, 1.6 mmoles) and DPPS **2** (0.444 g, 2 mmoles) in methanol (20 ml) was stirred at room temperature for 3 days. The solvent was evaporated and the residue was chromatographed on silica. Successive elution with benzene, dichloromethane and benzene-acetone (10:1) gave the crude compound **6a**, which was recrystallized from petroleum ether to give **6a** as yellow crystals (0.229 g), mp 180-181°; ms: [m/z] 352 (M^+); ir (potassium bromide): ν max 1723 and 1625 cm^{-1} ; ^1H nmr (deuteriochloroform): δ 3.35 (s, 3H), 4.03 (s, 3H), 6.8-7.4 (m, 10H).

Anal. Calcd. for C₂₀H₁₆O₄S: C, 68.16; H, 4.57. Found: C, 68.41; H, 4.66.

6-Ethoxy-5-ethoxycarbonyl-3,4-diphenylthiopyran-2-one (**6b**).

A mixture of pyridinium bis(ethoxycarbonyl)methylide (**1b**) (0.948 g, 4 mmoles) and DPPS **2** (0.888 g, 4 mmoles) in acetonitrile (20 ml) was stirred at room temperature for 12 days. After removal of precipitated material, the filtrate was concentrated and chromatographed on silica gel. Successive elution with hexane, benzene and benzene-dichloromethane gave the compound **6b** (0.840 g) as yellow crystals; mp 134-136°C; ms: [m/z] 380 (M⁺) and 352 (M⁺-CO); ir (potassium bromide): ν max 1725, 1695 and 1610 cm⁻¹; ¹H nmr (deuteriochloroform): δ 0.95 (t, 3H, J = 7 Hz), 1.12 (t, 3H, J = 8 Hz), 4.02 (q, 2H, J = 7 Hz), 4.05 (q, 2H, J = 8 Hz) and 7.1-7.5 (m, 10H, ArH).

Anal. Calcd. for C₂₂H₂₀O₄S: C, 69.45; H, 5.30. Found: C, 69.36; H, 5.32.

6-Ethoxy-5-ethoxycarbonyl-3,4-diphenylthiopyran-2-one 1,1-Dioxide (**7b**).

A solution of the thiopyran-2-one **6b** (0.114 g, 0.2 mmole) and *m*-chloroperbenzoic acid (0.172 g, 1 mmole) in dichloromethane (5 ml) was stirred at room temperature for 1 day. The insoluble *m*-chlorobenzoic acid was removed by filtration and washed with dichloromethane. The combined filtrate was washed with 10% sodium carbonate solution, dried (Drierite), and evaporated to give the compound **7b** as colorless crystals (0.098 g), mp 196-197°C; ms: [m/z] 412 (M⁺); ir (potassium bromide): ν max 1730, 1700 and 1315 cm⁻¹; ¹H nmr (deuteriochloroform): δ 0.92, 0.98, 1.10 and 1.20 (each t, 6H, J = 7 Hz), 4.05, 4.09 and 4.21 (each q, 4H, J = 7 Hz), and 7.2-7.9 (m, 10H, ArH).

Anal. Calcd. for C₂₂H₂₀O₆S: C, 64.06; H, 4.89. Found: C, 64.13; H, 4.79.

3-Cyano-6-ethylthio-4,5-diphenyl-2-pyrone (**4c**).

A mixture of pyridinium cyano(ethoxycarbonyl)methylide (**1c**) (0.158 g, 1 mmole) and DPPS **2** (0.333 g, 1.5 mmoles) in acetonitrile (10 ml) was stirred at room temperature for 1 day. After removal of the precipitated material, the filtrate was chromatographed on silica. Elution with dichloromethane gave the crude compound **4c**, which was crystallized from ethyl alcohol to give **4c** as yellow crystals (0.050 g), mp 207-209°C; ms: [m/z] 333 (M⁺), 304 (M⁺-CO), 272 (M⁺-SC₂H₅) and 216 (Ph₂C₄N); ir (potassium bromide): ν max 2250, 1735 and 1720 cm⁻¹; ¹H nmr (deuteriochloroform): δ 1.32 (t, 3H, J = 7.5 Hz), 3.09 (q, 2H, J = 7.5 Hz) and 6.6-7.4 (m, 10H, ArH).

Anal. Calcd. for C₂₀H₁₅NO₂S: C, 72.05; H, 4.59; N, 4.20. Found: C, 72.20; H, 4.59; N, 4.02.

6-Amino-5-cyano-3,4-diphenylthiopyran-2-one (**6d**).

A mixture of pyridinium carbamoylcyanomethylide (**1d**) (0.644

g, 4 mmoles) and DPPS **2** (0.888 g, 4 mmoles) in methanol (20 ml) was stirred at room temperature for 7 days. After the solvent was evaporated, the residue was dissolved in dichloromethane and the insoluble solid was filtered off. The filtrate was subjected to chromatography on silica. Elution with dichloromethane gave the compound **6d** (0.651 g) as yellow crystals, mp 160-162°C; ms: [m/z] 304 (M⁺), 278 (M⁺-CN); ir (potassium bromide): ν max 3270, 2460 and 1630 cm⁻¹; ¹H nmr (deuteriodimethylsulfoxide): δ 7.4-7.9 (m, 10H, ArH), NH₂ signal was not observed.

Anal. Calcd. for C₁₈H₁₂N₂OS: C, 71.03; H, 3.97; N, 9.20. Found: C, 71.04; H, 4.08; N, 9.08.

6-Amino-5-carbamoyl-3,4-diphenylthiopyran-2-one (**6e**).

To a solution of the hydrobromide salt of bis(carbamoyl)methylide (**1e**) (1.3 g, 5 mmoles) in DMF (10 ml) was added solid potassium carbonate (0.7 g). After the solution turned orange, was added a solution of DPPS **2** (1.11 g, 5 mmoles) in DMF (5 ml) and stirred at room temperature for 1 day. The solvent was evaporated and the residue was treated with dichloromethane. The insoluble solid was filtered off and the filtrate was concentrated and chromatographed over silica. Elution with benzene, dichloromethane and benzene-ethyl acetate gave the compound **6e** as yellow crystals (0.346 g), mp 216-218°C; ms: [m/z] 322 (M⁺); ir (potassium bromide): ν max 3500, 3400 and 1640 cm⁻¹; ¹H nmr (deuteriodimethyl sulfoxide): δ 7.4-7.9 (m, 10H, ArH), NH₂ signal was not observed.

Anal. Calcd. for C₁₈H₁₄N₂O₂S: C, 67.06; H, 4.38; N, 8.69. Found: C, 66.95; H, 4.33; N, 8.61.

Acknowledgments.

The author wishes to thank Professors K. Matsumoto (Kyoto University) and T. Uchida (Fukui University) for their helpful discussions and encouragement through this work. Thanks are also due to Miss Y. Yagi and Mr. H. Tahara for their assistance.

REFERENCES AND NOTES

- [1] Review: M. L. Deem, *Synthesis*, 701 (1982).
- [2] Recent examples: T. Eicher and D. Krause, *Synthesis*, 899 (1986); H. Yoshida, H. Sano, M. Kato, T. Ogata, and K. Matsumoto, *Bull. Chem. Soc. Japan*, **59**, 2833 (1986) and references cited.
- [3] K. T. Potts and J. S. Baum, *Chem. Rev.*, **74**, 189 (1974).
- [4] A preliminary communication: K. Matsumoto and Y. Ikemi, *Heterocycles*, **14**, 1445 (1980).
- [5] W. V. Turnur and W. H. Pirkle, *J. Org. Chem.*, **39**, 1935 (1974); W. H. Pirkle, H. Seto, and W. V. Turnur, *J. Am. Chem. Soc.*, **92**, 6984 (1970).
- [6] Y. Kobayashi, T. Kutsuma, K. Morinaga, M. Fujita, and Y. Hanzawa, *Chem. Pharm. Bull.*, **18**, 2489 (1970).