solution of Cl_2 and a 0.10 M solution of **3a, 3b,** or **3c** in CCl_4. The tube was placed in the probe of a Varian A-60A spectrometer held at 2 °C. The relative intensities of the aromatic protons vs. the benzylic protons in the products were compared by integration. Under these conditions the time required for 40% reaction was 3, 55, and 1440 min for **3a, 3b,** and **3c,** respectively. This gives a relative rate of chlorination of 460:17:1.

***N*-Azetidinyltriphenylphosphonium iodide (10)** was prepared in several steps from acrolein as follows. A solution of β-azidopropionaldehyde (prepared from 17.2 g of acrolein)[11] in ether was added with ice bath cooling to a stirred solution of 5 g of $NaBH_4$ in 30 ml of H_2O at such a rate that the temperature remained below 20 °C. After 10 min the aqueous phase was saturated with NaCl and the ether separated, dried ($MgSO_4$), and removed in vacuo giving 17.5 g (65% based on acrolein) of 3-azido-1-propanol. This product was added dropwise to 12 g of $SOCl_2$ in 15 ml of pentane. Removal of the solvent and distillation gave 9.25 g (58%) of 1-azido-3-chloropropane: bp 51 °C (15 mm); NMR τ 6.2–6.7 (overlapping triplets, 4, J = 7 Hz) and 8.0 (quintet, 4, J = 7 Hz). Treatment of 23.8 g of this material with 60 g of NaI in 500 ml of 2-butanone at reflux for 15 h gave, after water–pentane workup, 33 g (78%) of 1-azido-3-iodopropane: bp 83–84 °C (15 mm); NMR τ 6.7 (overlapping triplets, J = 7 Hz) and 8.0 (m, 2). When 5.4 g of this material was refluxed with 6.55 g of triphenylphosphine in 150 ml of hexane for 3 h, after cooling and filtration 5.4 g (49%) of **10** was obtained, mp 157–161 °C. The analytical sample was obtained by recrystallization from absolute ethanol/2-propanol and had mp 162–165 °C after drying at 65 °C (20 mm); NMR τ 2.0–2.5 (m, 15), 5.7 (m, 4, J_{P-H} = 4.0, J_{H-H} = 7.5 Hz), and 6.8–7.6 (m, 2, J_{PNCCH} = 4.5, J_{H-H} = 7.5 Hz).

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Registry No.—**3a,** 27356-57-6; **3b,** 27278-93-9; **3c,** 58503-29-0; **3d,** 30271-50-2; **3e,** 27278-92-8; **3f,** 58503-30-3; **3g,** 27356-56-5; **3h,** 58503-31-4; **3j,** 58503-32-5; **3k,** 58503-33-6; **3l,** 58503-34-7; **3m,** 58503-35-8; **4a,** 58503-36-9; **4b,** 58503-37-0; **4c,** 58503-38-1; **4d,** 58503-39-2; **4e,** 58503-40-5; **4f,** 58503-41-6; **4g,** 58503-42-7; **4h,** 58503-43-8; **4i,** 58503-44-9; **5a,** 58503-45-0; **5b,** 58503-46-1; **5d,** 58503-47-2; **5e,** 58503-48-3; **5f,** 58503-49-4; **5g,** 58503-50-7; **5h,** 58503-51-8; **5i,** 58503-52-9; **10,** 58503-53-0; **10** pentavalent form, 58503-54-1; *threo*-1-azido-1-phenyl-2-iodopropone, 58503-55-2; trimethyl phosphite, 121-45-9; 1-azido-2-iodo-3,3-dimethylbutane, 58503-56-3; 2-azido-1-iodo-2-methylpropane, 58503-57-4; 2-azido-3-iodo-2,3-dimethylbutane, 58503-58-5; *erythro*-4-azido-3-iodo-2,2-dimethylpentane, 16717-75-2; *cis*-4,4-dimethyl-2-pentene, 26232-98-4; *threo*-4-azido-3-iodo-2,2-dimethylpentane, 58503-59-6; β-azidopropionaldehyde, 58503-60-9; 1-azido-3-chloropropane, 58503-61-0; 1-azido-3-iodopropane, 58503-62-1.

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Synthesis of 3-Hydroxy-, 3-Chloro-, and 3-Methoxy-3-cephems from Penicillins via 4-Dithio-2-azetidinone Intermediates[1]

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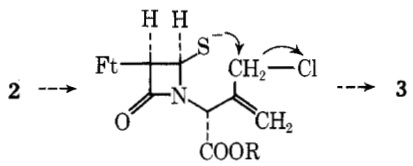
Cyclization of monocyclic dithioazetidinone **2** to 3-methylene cepham **3** with potassium iodide was accomplished. A key intermediate **3** after ozonolysis afforded 3-hydroxy-3-cephem **5,** which in turn was treated with phosphorus trichloride in dimethylformamide to give 3-chloro-3-cephem **6.** From the reaction of the enol **5** with diazomethane the corresponding 3-methoxy-3-cephem **7** was obtained. Preparation of compounds **3, 5, 6,** and **7** from **2** and **4** is significant since it represents the first synthesis of directly 3-substituted cephalosporins from penicillins.

Recently a new series of potent cephalosporin antibiotics having halo and methoxy groups attached directly to the 3 position of the 3-cephem ring system have been discovered.[2] These antibiotics were synthesized from various cephalosporanic acids, in which the 3-acetoxymethyl group was converted to 3-methylene cephams.[3] The latter compounds were ozonized to the 3-hydroxy-3-cephems and converted to 3-methoxy- and 3-chloro-3-cephems by standard methods. While this synthetic scheme led directly to 3-substituted cephalosporins, there still existed a need to prepare these antibiotics more economically from penicillins. For this reason we sought a shorter synthesis from readily available penicillins.

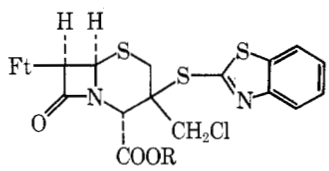
It seemed to us that a key intermediate, 3-methylene cepham **3,** might be synthesized from a monocyclic azetidinone **2.** The desired 4-benzothiazol-2′-yldithio-2-azetidinone (**2**) was prepared from 2β-chloromethylpenam 1-(*R*)-sulfoxide (**1**) by refluxing with 2-mercaptobenzothiazole in benzene for 30–50 min according to the method described by Kamiya and co-workers.[4] The first transformations attempted on compound **2** centered at the allylic halide position. However, **2** did not react with silver nitrate in acetone at room temperature even after prolonged refluxing (24 h) with an excess of silver salt. Nucleophilic displacement of the allylic chloride in **2** with sodium thiocyanate in refluxing acetone for 20 h also did not succeed. This was surprising since we had expected the allyl halide to be very reactive. Our attention was then turned to reduction of the disulfide linkage in **2.** We believed that reduction should give an intermediate having a mercapto group, and hopefully after nucleophilic displacement as depicted by A, the desired 3-methylene cepham **3** would be formed. However, reduction with (a) stannous chloride in THF, (b) sodium cyanoborohydride in methanol/dimethylformamide



A

at pH 4.0, and (c) hydrogen over palladium on carbon in methanol/tetrahydrofuran at room temperature for 1 h resulted only in minor degradation of the starting material. After all these unsuccessful reductions we decided to try oxidation of the disulfide bond. Oxidation with *m*-chloroperbenzoic acid in methylene chloride, even when the reaction was carried out at room temperature for prolonged periods of time, resulted in a complete recovery of the starting material.

In view of the rather peculiar reactivity encountered with this compound, we reexamined the proposed structure for **2.** One possible structure is the following:



B

Therefore, ^{13}C magnetic resonance studies were carried out in order to verify the structure. ^{13}C NMR spectroscopy provided a simple way of choosing between **2** and B. The spectrum of **2a** showed five resonances typical of sp^3 carbons: a methylene resonance (45.6 ppm), an *O*-methyl resonance (52.7 ppm), and three methine resonances (55.1, 59.1, and 76.3 ppm). Clearly such a result is not consistent with B.

The successful ring closure of compound **2** to desired key intermediate **3** was finally achieved with potassium iodide. Refluxing of **2** in acetone in the presence of potassium iodide for 40 h resulted in ring closure to **3** in 30–52% yield. Upon ozonolysis compound **3** was converted to the 3-hydroxy-3-cephem **5,** which was also prepared by cyclization of **4** with potassium iodide. Treatment of **5** with phosphorus trichloride in dimethylformamide for 1 h at room temperature gave the desired 3-chlorocephem **6** in good yield. 3-Methoxycephem **7** was obtained by treating 3-enol cephem **5** with diazomethane in methylene chloride.

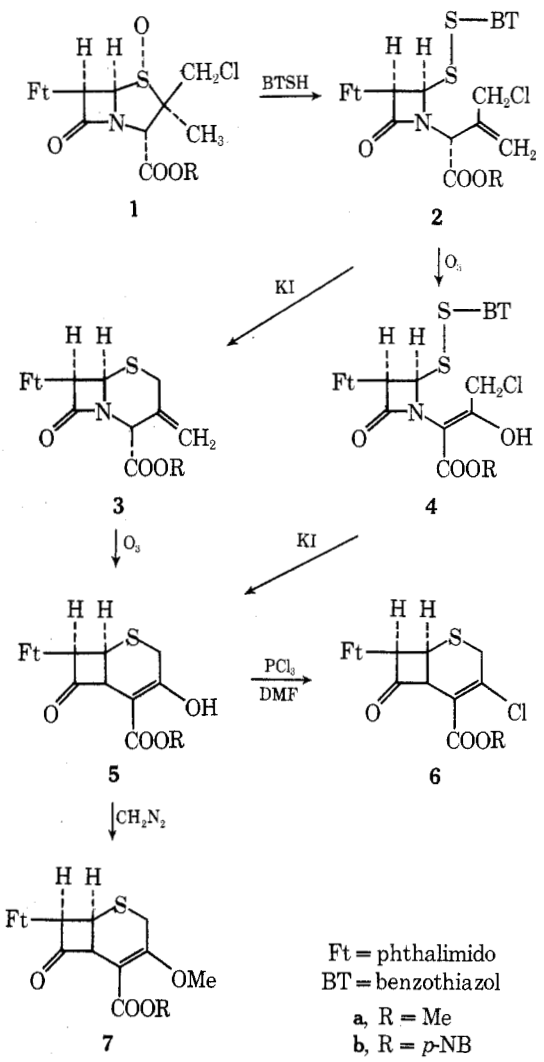
The cyclization of **2** to **3** is significant since it represents the first conversion of penicillins into a key intermediate for the synthesis of 3-substituted cephalosporins.

Experimental Section[5]

4-(2′-Benzothiazolyldithio)-3-phthalimido-1-(1′-methoxycarbonyl-2′-chloromethylprop-2′-enyl)-azetidin-2-one (2a). To 200 ml of methylene chloride was added 11.2 g (28.4 mmol) of methyl 6-phthalimido-2β-chloromethyl-2α-methylpenam-3-carboxylate.[6] Methylene chloride (100 ml) containing 5.68 g (28.4 mmol) of *m*-chloroperbenzoic acid was added, and the resulting mixture was stirred for 1 h at ice bath temperature. The reaction mixture was then washed successively with 50 ml of 5% aqueous sodium sulfite, twice with 50 ml of 5% sodium bicarbonate, 100 ml of water, and 100 ml of brine. The mixture was then dried over magnesium sulfate and evaporated to give 11.54 g (28.1mmmol) of methyl 6-phthalimido-2β-chloromethyl-2α-methylpenam-3-carboxylate 1α-oxide (**1a**): NMR ($CDCl_3$) δ 1.41 (s, 3, CH_3), 3.81 (s, 3, OCH_3), 4.14 (s, 2, CH_2Cl), 4.92 (s, 1, H3), 4.96 (d, 1, J = 4.5 Hz), 5.93 (d, 1, J = 4.5 Hz), and 7.81 (m, 4 ArH).

To 150 ml of benzene were added 11.54 g (28.1 mmol) of methyl 6-phthalimido-2β-chloromethyl-2α-methylpenam-3-carboxylate 1α-oxide and 4.7 g (28.1 mmol) of 2-mercaptobenzothiazole. The mixture was heated to reflux for 30 min, and then evaporated to give the title compound as a light yellow foam: NMR ($CDCl_3$) δ 3.81 (s, 3, OCH_3), 4.3 and 4.5 (AB q, 2, CH_2Cl, J = 12 Hz), 5.43 (s, 1), 5.53 (s, 1), 5.65 (s, 1), 5.98 (s, 2, azetidinone H), and 7.81 (m, 4 ArH).

Chart I



Anal. Calcd for $C_{24}H_{18}ClN_3O_5S_3$: C, 51.47; H, 3.24; N, 7.50; S, 17.18. Found: C, 51.40; H, 3.21; N, 7.55; S, 17.09.

4-(2′-Benzothiazolyldithio)-3-phthalimido-1-[1′-(*p*-nitrobenzyloxycarbonyl)-2′-chloromethylprop-2′-enyl]azetidin-2-one (2b). To 200 ml of methylene chloride was added 6.45 g (12 mmol) of *p*-nitrobenzyl 6-phthalimido-2β-chloromethyl-2α-methylpenam-3-carboxylate.[6] An insoluble portion of approximately 100–200 mg was filtered off, and 2.4 g (12 mmol) of *m*-chloroperbenzoic acid was added. The mixture was stirred for about 30 min and then washed successively with aqueous sodium bicarbonate and aqueous sodium chloride. The mixture was dried over magnesium sulfate and evaporated. The residue was dissolved in a mixture of 10 ml of methylene chloride and 3 ml of cyclohexane. The insolubles were filtered off, and the solvent was evaporated to give 5.6 g of *p*-nitrobenzyl 6-phthalimido-2β-chloromethyl-2α-methylpenam-3-carboxylate 1α-oxide (**1b**): NMR ($CDCl_3$) δ 1.42 (s, 3, CH_3), 4.38 (s, 2, CH_2Cl), 5.08 (s, 1, C_3 H), 5.1 (d, 1, J = 5 Hz), 5.4 (s, 2, CH_2 of *p*-NB), 6.05 (d, 1, J = 5 Hz), and 7.5–8.4 (m, 8 ArH).

A mixture of 5.32 g (10 mmol) of *p*-nitrobenzyl 6-phthalimido-2β-chloromethyl-2α-methylpenam-3-carboxylate 1α-oxide and 1.7 g (10 mmol) of 2-mercaptobenzothiazole in 100 ml of benzene was refluxed for 50 min, and the resulting clear, warm solution was transferred to another flask and allowed to crystallize overnight. Crystals (4.5 g, 66%) of the title compound were collected by filtration and shown by TLC to be one spot material: mp 204–205 °C dec; NMR ($CDCl_3$) δ 4.23 and 4.5 (AB q, 2, CH_2Cl, J = 12 Hz), 5.3 (s, 1), 5.33 (s, 2, CH_2 of *p*-NB), 5.5 (s, 1), 5.6 (s, 1), 5.75 (d, 1, J = 4.5 Hz), 5.85 (d, 1, J = 4.5 Hz), and 7.4–8.3 (m, 8 ArH); ir (KBr) 1790, 1778, 1750, and 1720 cm^{-1}.

Anal. Calcd for $C_{30}H_{21}ClN_4O_7S_3$: C, 52.90; H, 3.11; Cl, 5.20; S, 14.12; O, 16.44. Found: C, 53.11; H, 3.08; Cl, 5.29; S, 14.42; O, 16.11.

Methyl 7-Phthalimido-3-methylenecepham-4-carboxylate (3a). To a solution of 1.12 g (2 mmol) of 4-(2′-benzothiazolyldithio)-3-phthalimido-1-(1′-methoxycarbonyl-2′-chloromethylprop-2′-

enyl)azetidin-2-one in 75 ml of acetone was added 0.50 g (3 mmol) of potassium iodide. The mixture was refluxed for 3 days, after which TLC of the reaction mixture showed a spot indicative of unreacted starting material. An additional 0.5 g of potassium iodide was added and refluxing was continued for an additional 1 day. The mixture was evaporated to dryness, and the residue was taken up in 50 ml of ethyl acetate. The ethyl acetate solution was washed successively with 20 ml of 0.1 N sodium bisulfite solution, 25 ml of water, and 25 ml of brine. The ethyl acetate solution was then dried over sodium sulfate and evaporated to give 1.05 g of the title compound as a tan foam. Recrystallization from ethyl acetate gave colorless crystals: mp 194–196.5 °C dec; $[\alpha]^{25}D$ +179°; NMR ($CDCl_3$) δ 3.38 and 3.63 (AB q, 2, J = 14 Hz), 3.80 (s, 3), 5.32 (m, 3), 5.46 (d, 1, J = 4.5 Hz), 5.67 (d, 1, J = 4.5 Hz), 7.83 (m, 4); mass spectrum m/e 358, 330, 299, 272, 187, 172, ir ($CHCl_3$) 1790, 1775, 1725 cm^{-1}.

Anal. Calcd for $C_{17}H_{14}N_2O_5S$ (358.37): C, 56.98; H, 3.94; N, 7.82; O, 22.32; S, 8.95. Found: C, 56.79; H, 4.04; N, 7.74; O, 22.18; S, 8.95.

p-Nitrobenzyl 7-Phthalimido-3-methylenecepham-4-carboxylate (3b). A mixture of 1.3 g of 4-(2′-benzothiazolyldithio)-3-phthalimido-1-[1′-(p-nitrobenzyloxycarbonyl)-2′-chloromethylprop-2′-enyl]azetidin-2-one and 400 mg of potassium iodide in 70 ml of acetone was refluxed, and a TLC of the reaction mixture after 19 h of reflux indicated that approximately one-half of the starting material remained. Refluxing was continued for a total of 44 h, after which time a TLC of the reaction mixture indicated the absence of starting material. The solution was evaporated, and the residue was dissolved in ethyl acetate. The ethyl acetate solution was washed successively with aqueous sodium thiosulfate, water aqueous sodium bicarbonate, and aqueous sodium chloride. The ethyl acetate solution then was dried over magnesium sulfate and evaporated to give a solid residue. The residue was dissolved in 5 ml of toluene after which crystallization began to occur, and 200 mg of the title compound was collected by filtration and recrystallized from a mixture of 5 ml of benzene and 2 ml of chloroform. Crystals of the title compound were collected and again were recrystallized from a mixture of 4 ml of benzene and 3 ml of chloroform.

The toluene filtrate was evaporated, and the residue (650 mg) was chromatographed over a silica gel column (1.5 × 30 cm) and eluted with a 9:1 mixture of toluene and ethyl acetate to obtain an additional 300 mg of the title compound, total yield 52%. A sample for analysis was recrystallized from methylene chloride and cyclohexane. Colorless rosettes melted at 194–196 °C; $[\alpha]^{25}D$ +139° (in $CHCl_3$); mass spectrum m/e 479, 451, 433, 293, 187; NMR ($CDCl_3$) δ 3.3 and 3.62 (AB q, 2, CH_2S, J = 14 Hz), 5.37 (s, 5 H), 5.43 (d, 1, J = 4.5 Hz), 5.62 (d, 1, J = 4.5 Hz), and 7.4–8.3 Hz (m, 8 ArH).

Anal. Calcd for $C_{23}H_{17}N_3O_7S$: C, 57.62; H, 3.57; N, 8.76; S, 6.69. Found: C, 57.37; H, 3.72; N, 8.87; S, 6.79.

Methyl 7-Phthalimido-3-chloro-3-cephem-4-carboxylate (6a). Methyl 7-phthalimido-3-methylenecepham-4-carboxylate (7.5 g, 21 mmol) was dissolved in 300 ml of methylene chloride and cooled in a dry ice–acetone bath. A stream of oxygen containing ozone was passed through the cold solution until a light blue color was seen. Oxygen was then passed through to discharge the color followed by sulfur dioxide for 2 min. The solution was then allowed to warm to room temperature and dried ($MgSO_4$). The solvent was removed in vacuo giving 7.68 g of a light yellow foam of methyl 7-phthalimido-3-hydroxy-3-cephem-4-carboxylate (**5a**). This material was then dissolved in 60 ml of dry N,N-dimethylformamide and 2.8 ml (1.5 equiv) of phosphorus trichloride was added. After 1 h the crude product was poured onto a mixture of 100 ml of ethyl acetate and 100 ml of water. The layers were then separated and the lower layer washed with 1 N hydrochloric acid (2 × 100 ml), water (2 × 100 ml), and brine (1 × 100 ml) and dried ($MgSO_4$). Evaporation in vacuo gave 4.3 g of a light yellow foam. Chromatography over silica gel gave 1.76 g of methyl 7-phthalimido-3-chloro-3-cephem-4-carboxylate. Recrystallization from acetone gave colorless needles: mp 193–195 °C; NMR ($CDCl_3$) δ 3.47 and 3.96 (AB q, 2, J = 17 Hz), 3.87 (s, 3), 5.20 (d, 1, J = 4.5 Hz), 5.80 (d, 1, J = 4.5 Hz), 7.83 (m, 4); mass spectrum m/e 378, 350, 291, 230, 192, 187.

Anal. Calcd for $C_{16}H_{11}N_2O_5SCl$ (378.78): C, 50.73; H, 2.93; N, 7.40; O, 21.12; S, 8.46; Cl, 9.36. Found: C, 50.99; H, 3.13; N, 7.16; O, 20.91; S, 8.19; Cl, 9.20.

p-Nitrobenzyl 3-Chloro-3-cephem-4-carboxylate (6b). A solution of 350 mg of p-nitrobenzyl 7-phthalimido-3-methylenecepham-4-carboxylate in 100 ml of chloroform was prepared and cooled in a dry ice–acetone bath. Ozone was then passed through the mixture for 2–3 min until the color of the mixture turned blue. Sulfur dioxide gas was passed through the solution for about 2 min, and magnesium sulfate was then added to the solution. The solution was brought to room temperature and filtered. The filtrate was evaporated to give 270 mg of p-nitrobenzyl 7-phthalimido-3-hydroxy-3-cephem-4-carboxylate (**5b**) as a colorless solid: NMR ($CDCl_3$) δ 2.95 and 4.02 (AB q, 2, CH_2S, J = 15 Hz), 5.25 (d, 1, J = 4.5 Hz), 5.4 (s, 2, CH_2 of p-NB), 5.76 (d, 1, J = 4.5 Hz), and 7.6–8.3 Hz (m, 8 ArH).

This material was dissolved in 5 ml of dry DMF and 0.1 ml of phosphorus trichloride was added. After usual workup the crude product was purified by chromatography over silica gel. A sample for analysis was recrystallized from methylene chloride and cyclohexane: NMR ($CDCl_3$) δ 3.5 and 3.9 (AB q, 2, J = 16 Hz, CH_2S), 5.24 (d, 1, J = 5 Hz), 5.47 (s, 2, CH_2 of p = NB), 5.97 (d, 1, J = 5 Hz), 7.5–8.4 Hz (8 ArH).

Anal. Calcd for $C_{22}H_{14}N_3O_7SCl$: C, 52.86; H, 2.82; N, 8.41; S, 6.41; Cl, 7.09. Found: C, 52.60; H, 3.03; N, 8.29; S, 6.14; Cl, 7.26.

Methyl 7-Phthalimido-3-methoxy-3-cephem-4-carboxylate (7a). A solution of 1.12 g (2 mmol) of 4-(2′-benzothiazolyldithio)-3-phthalimido-1-(1′-methoxycarbonyl-2′-chloromethylprop-2′-enyl)-azetidin-2-one in 100 ml of CH_2Cl_2 was cooled in an acetone–dry ice bath and ozone was introduced into this solution from a generator for 5 min. In order to reduce the formed ozonide sulfur dioxide gas was passed through the solution for 2 min. The mixture was then warmed to room temperature and was washed with water and brine. After drying over $MgSO_4$, the solvent was evaporated to give 870 mg of compound **4a:** NMR ($CDCl_3$) δ 3.75 (s, 3, OCH_3), 4.45 and 4.75 (AB q, 2, CH_2Cl, J = 12 Hz), 5.70 (d, 1, J = 5 Hz), and 5.92 (d, 1, J = 5 Hz).

Anal. Calcd for $C_{23}H_{16}ClN_3O_6S_3$: C, 49.15; H, 2.87; N, 7.48; O, 17.08. Found: C, 49.58; H, 3.29; N, 7.21; O, 16.89.

A solution of 870 mg of 4-(2′-benzothiazolyldithio)-3-phthalimido-1-(1′-methoxycarbonyl-2′-oxo-3′-chloropropyl)azetidin-2-one (**4a**) and 500 mg of potassium iodide in 40 ml of acetone was refluxed for 20 h. The solvent was evaporated, and the residue was dissolved in a mixture of 50 ml of ethyl acetate and 10 ml of water. The ethyl acetate extract was washed with 10 ml of brine and dried over $MgSO_4$. The solvent was evaporated to give methyl 7-phthalimido-3-hydroxy-3-cephem-4-carboxylate (**5a**): NMR ($CDCl_3$) δ 2.93 and 4.07 (AB q, 2, CH_2S, J = 15 Hz), 3.8 (s, 3, OCH_3), 5.22 (d, 1, J = 4.5 Hz), 5.75 (d, 1, J = 4.5 Hz), and 7.8 (m, 4, ArH).

To a solution of 460 mg of **5a** in 10 ml of methylene chloride, an ethereal solution of diazomethane (ca. 5 mmol) was added at 0–5 °C and stirred for 35 min. The excess of diazomethane was treated with acetic acid, the solvent evaporated, and the crude product purified by chromatography over silica gel (toluene–ethyl acetate, 9:1). Fractions 78–101 contained 220 mg of **7a,** which was recrystallized from 1.0 ml of methylene chloride and 1.0 ml of cyclohexane, giving needles: mp 236–237 °C; $[\alpha]^{25}D$ −40.3° (Me_2SO); mass spectrum m/e 374, 346, 331, 315, 287, and 255; NMR ($CDCl_3$) δ 3.15 and 3.97 (AB q, 2, J = 15 Hz, C_2 H), 3.8 (s, 3, OMe), 3.95 (s, 3, OMe), 5.18 (d, 1, J = 4.5 Hz, azetidinone H), 5.7 (d, 1, J = 4.5 Hz, azetidinone H), and 7.8 (m, 4, ArH).

Anal. Calcd for $C_{17}H_{14}N_2O_6S$: C, 54.54; H, 3.77; N, 7.48; O, 25.64; S, 8.56. Found: C, 54.35; H, 3.92; N, 7.21; O, 25.42; S, 8.34.

p-Nitrobenzyl 7-Phthalimido-3-methoxy-3-cephem-4-carboxylate (7b). A solution of 650 mg of 4-(2′-benzothiazolyldithio)-3-phthalimido-1-[1′-(p-nitrobenzyloxycarbonyl)-2′-chloromethylprop-2′-enyl]azetidin-2-one (**3b**) and 100 ml of CH_2Cl_2 was cooled in an acetone–dry ice bath, and ozone was introduced until a blue color appeared (3–5 min). Sulfur dioxide gas then was passed through the solution for 2 min and the mixture was warmed to room temperature. The mixture was then washed with water and a brine solution. After drying over $MgSO_4$, the solvent was evaporated to yield **4b.**

A mixture of 465 mg of **4b,** 350 mg of potassium iodide, and 30 ml of acetone was refluxed for 21 h. The solvent was evaporated, and the residue dissolved in ethyl acetate and washed with brine. The solution was dried ($MgSO_4$) and the solvent evaporated to give **5b** as a colorless foam: NMR ($CDCl_3$) δ 2.95 and 4.02 (AB q, 2, CH_2S, J = 15 Hz), 5.25 (d, 1, J = 4.5 Hz), 5.4 (s, 2, CH_2 of pNB), 5.76 (d, 1, J = 4.5 Hz), and 7.6–8.3 (m, 8 ArH).

The colorless foam was dissolved in 10 ml of dichloromethane and treated with an excess of an ethereal diazomethane for 30 min at room temperature. The solvent was removed in vacuo and the crude product chromatographed by preparative TLC (silica gel; toluene–ethyl acetate, 7:3). The extracted material (110 mg) was recrystallized from acetone–ether. Colorless crystals of **7b** melted at 205–206 °C dec; NMR ($CDCl_3$) δ 3.3 and 4.0 (AB q, 2, C_2H, J = 15 Hz), 4.0 (s, 3, OCH_3), 5.28 (d, 1, J = 4.5 Hz), 5.78 (d, 1, J = 4.5 Hz), and 7.5–8.35 (m, 9 ArH); $[\alpha]^{25}D$ −18.1°.

Anal. Calcd for $C_{23}H_{17}N_3O_8S$: C, 55.76; H, 3.46; H, 8.48; O, 25.83; S, 6.47. Found: C, 55.51; H, 3.50; N, 8.23; O, 25.61; S, 6.19.

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Registry No.—**1a**, 51416-11-6; **1b**, 58735-17-4; **2a**, 58735-18-5; **2b**, 58735-19-6; **3a**, 58735-20-9; **3b**, 58735-21-0; **4a**, 58735-22-1; **4b**, 58735-23-2; **5a**, 58735-24-3; **5b**, 58735-25-4; **6a**, 58735-26-5; **6b**, 58735-27-6; **7a**, 58735-28-7; **7b**, 58735-29-8; methyl 6-phthalimido-2β-chloromethyl-2α-methylpenam-3-carboxylate, 51415-59-9; 2-mercaptobenzothiazole, 149-30-4; *p*-nitrobenzyl 6-phthalimido-2β-chloromethyl-2α-methylpenam-3-carboxylate, 56446-37-8.

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Photochemical Reaction of 4-Diphenylmethylene-4*H*-thiopyrans

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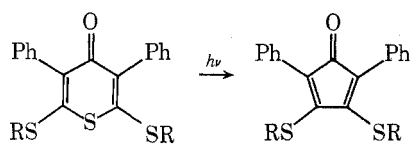
Ultraviolet irradiation of 4-diphenylmethylene-2,6-bis(methylthio)-3,5-diphenyl-4*H*-thiopyran affords 2-diphenylmethylene-4,5-bis(methylthio)-3,6-diphenyl-2*H*-thiopyran via the triplet state of the former. Photolysis of 4-diphenylmethylene-4*H*-thiopyran, 4-diphenylmethylene-2,6-bis(methylthio)-3,5-dimethyl-4*H*-thiopyran, and 4-diphenylmethylene-3,5-diphenyl-4*H*-thiopyran resulted in the recovery of the starting materials. All of these 4-diphenylmethylene-4*H*-thiopyrans fluoresce at room temperature, but do not phosphoresce at 77 K.

The photochemistry of 4-thiopyrones has been the subject of study in this and other laboratories. Under the influence of ultraviolet light, unhindered 4*H*-thiopyran-4-ones undergo dimerization,[2] whereas hindered 4*H*-thiopyran-4-ones lead to elimination of sulfur atom.[3] In this photochemical rearrangement of 2,6-bis(alkylthio)-3,5-diphenyl-4*H*-thiopyran-4-ones (**1**) to 3,4-bis(alkylthio)-2,5-diphenylcyclopentadienones (**2**), evidence in favor of the mechanism

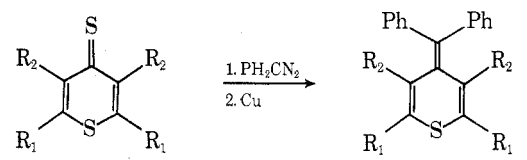


1 **2**

involving its n,π* triplet state was given.[3] It seemed of considerable import to inspect the photochemistry of a system lacking n,π* excitation but having a similar π system. Such a molecule would have available only π,π* excited state and its photochemistry would define the behavior of these states. Accordingly the diphenylmethylene analogues were selected for the present study. Specifically, 4-diphenylmethylene-2,6-bis(methylthio)-3,5-diphenyl-4*H*-thiopyran was chosen for study of the photochemical reaction in detail.[4]

Results and Discussion

4-Diphenylmethylene-4*H*-thiopyrans (**3–6**) were most conveniently prepared by the reaction of corresponding 4*H*-thiopyran-4-thiones (**7–10**) with diphenyldiazomethane, followed by treatment with copper powder according to the established procedure.[5,6] The structure assigned to 4-diphenylmethylene-4*H*-thiopyrans rests on their elemental analysis and spectral data. Their mass spectra showed an intense peak correspondent with their parent ion. The ir spectra exhibited a stretching vibration of the exocyclic double bond at 1605–1620 cm^{-1}. The NMR spectra of **3** and **4** showed the equivalent thiomethyl protons at δ 2.2–2.3 and those of **5** and



7, R_1 = SMe; R_2 = Ph
8, R_1 = SMe; R_2 = Me
9, R_1 = R_2 = H
10, R_1 = H; R_2 = Ph

3, R_1 = SMe; R_2 = Ph
4, R_1 = SMe; R_2 = Me
5, R_1 = R_2 = H
6, R_1 = H; R_2 = Ph

6 displayed the olefinic protons at δ 6.2–6.9. These spectral data were in complete agreement with the structure and are given in the Experimental Section.

Irradiation of 4-diphenylmethylene-2,6-bis(methylthio)-3,5-diphenyl-4*H*-thiopyran (**3**) in benzene with a medium-pressure mercury lamp through a Pyrex filter gave an almost quantitative yield of a product isomeric with the starting material. This is assigned structure **11** on the basis of chemical reaction outlined in Scheme I. Photooxygenation of the photoproduct yielded 4,5-bis(methylthio)-3,6-diphenyl-2*H*-thiopyran-2-one (**12**). Upon addition to Li–$EtNH_2$ the photoproduct was desulfurized[7] to give 3,6-diphenyl-2*H*-thiopyran-2-one (**13**),[8,9] identical with an authentic sample[11,12] in ir and NMR spectra. The irradiation of **3** in methylene chloride under similar conditions also afforded **11** in excellent yield.

Irradiation of **4** or **5** or **6** in benzene with a medium-pressure mercury lamp equipped with a Pyrex filter or a 313–436-nm solution filter[13] produced no reaction. Prolonged irradiation of **4**, **5**, or **6** also resulted in the recovery of the starting materials. When photolysis was sensitized by acetophenone which absorbed more than 95% of the incident light, **5** was also recovered unchanged.

Ultraviolet absorption spectra of the 4-diphenylmethylene-4*H*-thiopyran in ethanol are given in Figure 1, which shows two broad intense bands at 230–240 and 340–380 nm, whereas the corresponding 4*H*-thiopyran-4-ones exhibit two