mL of H_2O. The mandelic acid was isolated again as above. The two portions of crude acid were combined and recrystallized from benzene to afford 585 mg (3.8 mmol, 71%) of (−)-mandelic acid; $[\alpha]_D$ −152.2° (*c* 0.0472, H_2O); optical purity 99.3%. An additional 126 mg (0.83 mmol) of acid was obtained by concentrating and cooling of the mother liquor. The optical purity of this material was 85.7% ($[\alpha]_D$ −130.5°).

Acknowledgment. This research was supported by grants from the National Institutes of Health (Grant No. GM 21925) and the Robert A. Welch Foundation (Grant No. F-626).

Registry No. 1 (isomer 1), 86748-47-2; 1 (isomer 2), 19939-69-6; 2 (isomer 1), 86748-48-3; 2 (isomer 2), 86748-49-4; 3 (isomer 1), 86748-50-7; 3 (isomer 2), 86748-51-8; 4 (isomer 1), 86748-52-9; 4 (isomer 2), 86766-02-1; 5 (isomer 1), 86748-53-0; 5 (isomer 2), 86783-90-6; 6 (isomer 1), 86748-54-1; 6 (isomer 2), 86748-55-2; 7 (isomer 1), 86748-56-3; 7 (isomer 2), 86748-57-4; NaSH, 16721-80-5; H_2S, 7783-06-4; *dl*-2,5-hexanediol, 38484-56-9; *meso*-2,5-hexanediol, 38484-55-8; (−)-mandelic acid, 611-71-2; D-(−)-*O*-acetylmandelic acid, 51019-43-3; *l*-menthol, 2216-51-5; 4-(dimethylamino)pyridine, 1122-58-3; dicyclohexylcarbodiimide, 538-75-0; *l*-menthyl D-(−)-*O*-acetylmandelate, 26171-76-6; *l*-menthyl D-(−)-mandelate, 25926-70-9; (±)-2-octanol, 4128-31-8; (2*R*,5*R*)-2,5-hexanediol, 17299-07-9.

Penicillin–Cephalosporin Conversion. 8.[1] Synthesis of 2,3′-Dithio-Substituted Cephalosporin via Electrolytic Chlorination of Thiazoline–Azetidinone

Sigeru Torii,* Hideo Tanaka, Takashi Siroi, and Michio Sasaoka

Department of Industrial Chemistry, School of Engineering, Okayama University, Okayama 700, Japan

Received February 25, 1983

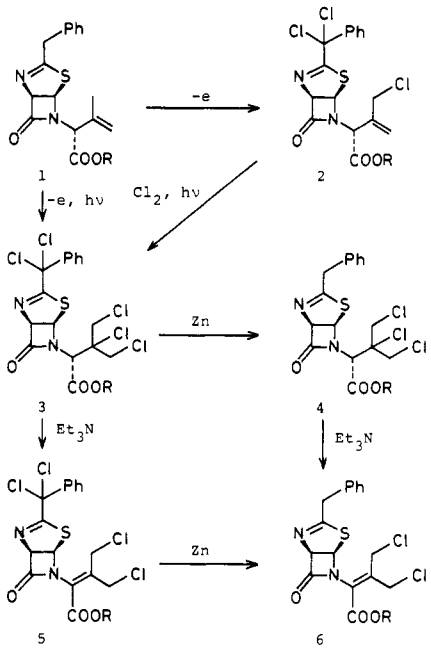
Recently, thiazoline–azetidinones **1**, derived from natural penicillin, have played an important role in penicillin–cephalosporin conversion chemistry.[2] In preceding papers, we disclosed an efficient ene-type chlorination of **1**, providing useful trichloride intermediates **2**[3] which leads directly to the corresponding 3′-thio-substituted cephalosporins.[4] As an extension of this work, we described here a straightforward route to 2,3′-dithio-substituted cephalosporins **9**[5] starting from compound **1** which undergoes electrolytic chlorination to give pentachloride **3** and subsequent intramolecular recyclization into **9** via dichloride **6** (Schemes I and II).

The electrochemical chlorination of **1** was carried out in a manner similar to that reported in the preceding paper.[3] As expected, the chlorination in an aqueous NaCl–H_2SO_4–$CHCl_3$ system gave trichloride **2** in 80% yield after passage of 15 F/mol of electricity. Without isolation, continued electrolysis under irradiation with a 750-W halogen lamp afforded pentachloride **3** in 50% overall yield after an additional 5 F/mol of electricity was passed. The successful conversion of **2** to **3** was achieved by treatment with chlorine in CH_2Cl_2 under illumination for 10 min (90% yield).

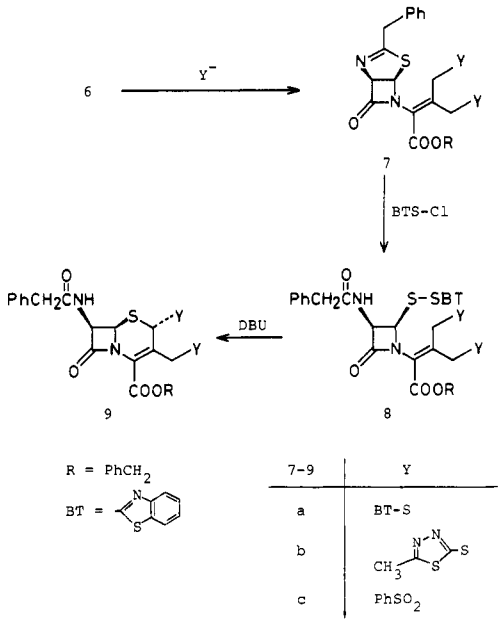
The conversion of **3** to the dichloride **6** was performed by the reduction of the geminal chlorine atoms with 2 equiv of zinc powder in acetic acid–CH_2Cl_2 solution, giving **4** (96%) and subsequent dehydrochlorination with triethylamine in CH_2Cl_2 (86%). The dichloride **6** was also obtained by the dehydrochlorination followed by the reduction of tetrachloride **5** (73% overall yield).

One direct route from **6** to the desired derivatives **9** would be hydrolytic ring opening of the thiazoline moiety followed by the intramolecular nucleophilic replacement of the allylic chlorine atom with the leaving thiol group, leading to 3′-chlorocephalosporin **9** (C(2) Y = H; C(3′) Y

Scheme I



Scheme II



(1) Part 7: Torii, S.; Tanaka, H.; Siroi, T.; Madono, T.; Saitoh, N.; Sasaoka, M.; Nokami, J. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1285.

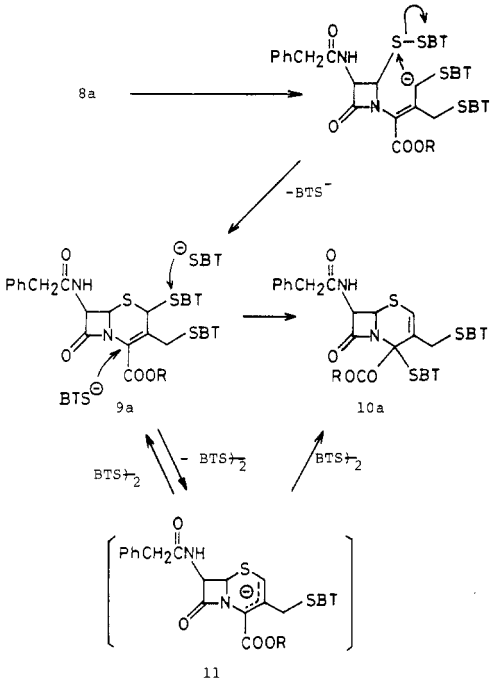
(2) (a) Torii, S.; Tanaka, H.; Sasaoka, M.; Saitoh, N.; Siroi, T.; Nokami, J. *Bull. Soc. Chim. Belg.* **1982**, *91*, 951. (b) "Topics in Antibiotic Chemistry"; Ed. Sammes, R. G., Ed.; Ellis Horwood: Chichester, 1980; Vol. 4. (c) Uyeo, S.; Aoki, T.; Itani, H.; Tsuji, T.; Nagata, W. *Heterocycles* **1978**, *10*, 99. (d) Nakatsuka, S.; Tanino, H.; Kishi, Y. *J. Am. Chem. Soc.* **1975**, *97*, 5008. (e) Franceschi, G.; Fogrio, M.; Masi, P.; Suarato, A.; Palamidessi, G.; Bernardi, L.; Arcamone, F.; Cainelli, G. *J. Am. Chem. Soc.* **1977**, *99*, 248.

(3) Torii, S.; Tanaka, H.; Saitoh, N.; Siroi, T.; Sasaoka, M.; Nokami, J. *Tetrahedron Lett.* **1981**, *22*, 3193.

(4) Torii, S.; Tanaka, H.; Sasaoka, M.; Saitoh, N.; Siroi, T.; Nokami, J. *Tetrahedron Lett.* **1982**, *23*, 2495.

(5) (a) Applegate, E. H.; Cimarusti, C. M.; Dolfini, J. E.; Funke, P. T.; Koster, W. H.; Puar, M. S.; Slusarchyk, W. A.; Young, M. G. *J. Org. Chem.* **1979**, *44*, 811. (b) Slusarchyk, W. A.; Applegate, H. E.; Cimarusti, C. M.; Dolfini, J. E.; Funke, P. T.; Puar, M. S. *J. Am. Chem. Soc.* **1978**, *100*, 1886.

Scheme III



= Cl).[6] First, we investigated this possibility by using various acids, but all attempts on this line failed. Finally, we found the three-step conversion of **6** to **9** outlined in Scheme II. Displacement of the allylic chlorine atoms of **6** with thiolates or benzenesulfinate proceeded smoothly to give **7a** (Y = 2-benzothiazolylthio, 68%), **7b** (Y = 2-methyl-1,3,4-thiadiazol-5-ylthio, 77%), and **7c** (Y = phenylsulfonyl, 60%), respectively. The hydrolytic ring opening of the thiazoline moiety of **7** was performed in 58–80% yields by treatment with 2-benzothiazolesulfenyl chloride (BTS-Cl) in aqueous HCl–dioxane.[4] Treatment of the disulfide **8a** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in tetrahydrofuran (THF) at −78 °C for 30 min afforded the desired 2,3′-bis(2-benzothiazolylthio)-substituted Δ^3-cephem **9a** along with Δ^2 isomer **10a** in 73% yield (**9a**/**10a**, 88/12). The ratio of **9a** to **10a** varied depending upon the temperature employed. Thus, higher temperature, e.g., at room temperature, facilitated the formation of the Δ^2 isomer **10a**, yielding a mixture of **9a** and **10a** (33:67). The isomerization of **9a** to **10a** took place when the compound **9a** was treated with 2-mercaptobenzothiazole and DBU in THF at −78 °C for 30 min, affording a mixture of **9a** and **10a** (70:30). These results suggest that the initial ring closure of **8a** affords **9a**, which, in turn, isomerizes to **10a** in the basic media (Scheme III). Thus, the leaving thiolate (BTS^-) would attack the C(4) position and/or the C(2)-benzothiazol-2-ylthio moiety,[7] affording **10a** and/or **11** and disulfide (BTS–SBT), the latter of which would collapse back to **9a** or give **10a**.[5a]

In a similar manner, **9b** (Y = 2-methyl-1,3,4-thiadiazol-5-ylthio) and **9c** (Y = phenylsulfonyl)[8] were prepared from **8b** and **8c** in 51–55% yields, respectively.

(6) Kishi and co-workers have reported a similar cyclization leading to 3′-bromo-7-methoxycephalosporin, though the product decomposed under these conditions (see ref 2d).

(7) Grossert, J. S.; Dubey, P. K. *J. Chem. Soc., Chem. Commun.* **1982**, 1183.

(8) The stereochemistry of the C(2) substituents was tentatively assigned as α by comparison of their ^{1}H NMR spectra with those of the corresponding sulfoxide derived from **9c** by treatment with *m*-chloroperbenzoic acid: ^{1}H NMR ($CDCl_3$) δ 3.63 (s, 2 H), 4.44 (d, 1 H, J = 14.7 Hz), 4.96 (s, 2 H), 5.23 (d, 1 H, J = 4.6 Hz), 5.28 (d, 1 H, J = 14.7 Hz), 6.21 (dd, 1 H, J = 4.6, 10 Hz), 6.54 (d, 1 H, J = 10 Hz), 6.56 (s, 1 H), 7.26 (s, 5 H), 7.36 (s, 5 H), 7.1–8.0 (m, 10 H) (see ref 5a).

Experimental Section

All melting points are uncorrected. IR spectra were determined with a JASCO Model IRA-1 grating spectrometer. ^{1}H NMR spectra were obtained with a Hitachi R-24 spectrometer (60 MHz) and/or a JEOL MX-100 spectrometer (100 MHz), and chemical shifts (δ) are expressed in parts per million downfield from internal Me_4Si with the coupling constants (J) given in hertz. Field-desorption mass spectra were performed on a Hitachi M-80 mass spectrometer. Elemental analyses were performed in our laboratory.

Benzyl 3-(Chloromethyl)-3,4-dichloro-2-[3-(phenyldichloromethyl)-7-oxo-4-thia-2,6-diazabicyclo[3.2.0]hept-2-en-6-yl]butanoate (3). Procedure A. A stirred mixture of **1** (382 mg, 0.94 mmol), NaCl (20 g), and concentrated H_2SO_4 (1.4 mL) in H_2O (60 mL) and $CHCl_3$ (40 mL) was electrolyzed in an undivided cell[9] fitted with two platinum electrodes (3 × 4 cm^2) at a constant current density (10 mA/cm^2) at room temperature. After passage of 15 F/mol of electricity, concentrated H_2SO_4 (1 mL) was added and then the electrolysis was continued under irradiation with a 750 W halogen lamp (Kondo Sylvania Ltd.). After passage of an additional 5 F/mol of electricity, the organic phase was separated, washed with brine, dried (Na_2SO_4), and concetrated in vacuo. The residue was chromatographed (SiO_2; hexane–AcOEt, 5:1) to give **3**: 273 mg (50%); mp 84–85 °C (from ether); IR ($CHCl_3$) 1782, 1743, 1604 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.88 (s, 2 H), 4.10 (s, 2 H), 5.17 (s, 1 H), 5.21 (s, 2 H), 6.04 (d, 1 H, J = 4.2 Hz), 6.21 (d, 1 H, J = 4.2 Hz), 7.1–7.9 (m, 10 H); FDMS, m/z 583 (M^+ + 5), 581 (M^+ + 3), 579 (M^+ + 1). Anal. Calcd for $C_{23}H_{19}Cl_5N_2O_3S$: C, 47.57; H, 3.30. Found: C, 47.85; H, 3.41.

Procedure B. To a stirred solution of **2**[4] (403 mg, 0.79 mmol) in CH_2Cl_2 (10 mL) was added a 0.8 M solution of Cl_2 in CCl_4 (5 mL, 4 mmol) at room temperature. The solution was irradiated for 10 min by using a 750-W halogen lamp (Kondo Sylvania Ltd.). After removal of the solvents, the residue was chromatographed (SiO_2; hexane–AcOEt, 8:1) to give **3** (450 mg, 98%) whose spectral data were identical with those described above.

Benzyl 2-(3-Benzyl-7-oxo-4-thia-2,6-diazabicyclo[3.2.0]-hept-2-en-6-yl)-4-chloro-3-(chloromethyl)-2-butenoate (6). Procedure A (3 → 4 → 6). A mixture of **3** (569 mg, 0.98 mmol) and zinc powder (141 mg, 2.16 mmol) in CH_2Cl_2 (5 mL) and AcOH (0.5 mL) was vigorously stirred for 30 min at 0 °C. The reaction mixture was diluted with ether and worked up in the usual manner to give the crude products, which were chromatographed (SiO_2; hexane–AcOEt, 4:1) to yield **4**: 482 mg (96%); IR ($CHCl_3$) 1773, 1740, 1613, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.78 (br s, 2 H), 3.84 (d, 1 H, J = 12 Hz), 3.96 (d, 1 H, J = 12 Hz), 4.10 (s, 2 H), 5.09 (s, 1 H), 5.16 (s, 2 H), 5.87 (d, 1 H, J = 4.5 Hz), 6.02 (d, 1 H, J = 4.5 Hz), 7.20 (s, 5 H), 7.30 (s, 5 H). Anal. Calcd for $C_{23}H_{21}Cl_3N_2O_3S$: C, 53.97; H, 4.14. Found: C, 54.18; H, 4.15.

A mixture of **4** (420 mg, 0.82 mmol) in CH_2Cl_2 (5 mL) containing Et_3N (0.23 mL, 1.65 mmol) was stirred for 2 h at 5–15 °C. The reaction mixture was worked up and chromatographed (SiO_2; hexane–AcOEt, 5:1) to yield **6** (335 mg, 86%) as an oil: IR ($CHCl_3$) 1775, 1725, 1613, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.79 (br s, 2 H), 4.10 (s, 2 H), 4.62 (s, 2 H), 5.23 (s, 2 H), 5.75 (d, 1 H, J = 4.5 Hz), 5.97 (d, 1 H, J = 4.5 Hz), 7.22 (s, 5 H), 7.33 (s, 5 H). Anal. Calcd for $C_{23}H_{20}Cl_2N_2O_3S$: C, 58.11; H, 4.24. Found: C, 58.30; H, 4.45.

Procedure B (3 → 5 → 6). A mixture of **3** (87 mg, 0.15 mmol) in CH_2Cl_2 (2 mL) containing Et_3N (0.1 mL, 0.7 mmol) was stirred for 1.5 h at room temperature. The usual workup followed by column chromatography (SiO_2; hexane–AcOEt, 4:1) afforded **5**: 78 mg (96%); oil; IR ($CHCl_3$) 1780, 1722, 1601, 1450 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.94 (d, 1 H, J = 11 Hz), 4.16 (d, 1 H, J = 11 Hz), 4.48 (d, 1 H, J = 12 Hz), 4.70 (d, 1 H, J = 12 Hz), 5.08 (d, 1 H, J = 11 Hz), 5.30 (d, 1 H, J = 11 Hz), 5.77 (d, 1 H, J = 4.5 Hz), 6.02 (d, 1 H, J = 4.5 Hz), 7.1–7.9 (m, 10 H).

A mixture of **5** (35 mg, 0.064 mmol) and zinc powder (8.5 mg, 0.13 mmol) in CH_2Cl_2 (1 mL) and AcOH (0.3 mL) was vigorously stirred for 30 min at 5 °C. The mixture was worked up and chromatographed (SiO_2; hexane–AcOEt, 5:1) to give **6** (23 mg, 76%) whose spectral data were identical with those described above.

(9) The electrolysis cell was similar to that described previously: Torii, S.; Tanaka, H.; Mishima, K. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1575.

Reaction of 6 with Sodium 2-Benzothiazolethiolate. To a solution of **6** (72 mg, 0.15 mmol) in acetone (2 mL) was added sodium 2-benzothiazolethiolate (62 mg, 0.33 mmol) at 0–5 °C. After being stirred for 1 h at this temperature the reaction mixture was worked up and chromatographed (SiO_2; hexane–AcOEt, 5:1) to give **7a** (75 mg, 68%) as a colorless foam: IR ($CHCl_3$) 1775, 1717, 1609, 1452 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.74 (br s, 2 H), 4.33 (br s, 2 H), 4.68 (d, 1 H, J = 13.5 Hz), 4.79 (d, 1 H, J = 13.5 Hz), 5.22 (s, 2 H), 5.79 (d, 1 H, J = 4.5 Hz), 5.94 (d, 1 H, J = 4.5 Hz), 7.16 (s, 5 H), 7.33 (s, 5 H), 7.2–7.8 (m, 8 H); FDMS, m/z 737 (M^+ + 1). Anal. Calcd for $C_{37}H_{28}N_4O_3S_5$: C, 60.30; H, 3.83. Found: C, 60.56; H, 3.99.

Reaction of 6 with 5-Mercapto-2-methyl-1,3,4-thiadiazole. To a solution of **6** (72 mg, 0.15 mmol) and 5-mercapto-2-methyl-1,3,4-thiadiazole (37 mg, 2.1 mmol) in *N,N*-dimethylformamido (DMF, 1 mL) was added Et_3N (43 μL, 2.0 mmol) at −10 °C. After being stirred for 1 h the mixture was worked up and chromatographed (SiO_2; benzene–AcOEt, 3:1), affording **7b**: 79 mg, (7[illegible]; colorless foam; IR ($CHCl_3$) 1773, 1716, 1610, 1596 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.66 (s, 3 H), 2.69 (s, 3 H), 3.76 (br s, 2 H), 4.15 (s, 2 H), 4.50 (d, 1 H, J = 14 Hz), 4.67 (d, 1 H, J = 14 Hz), 5.20 (s, 2 H), 5.78 (d, 1 H, J = 4.5 Hz), 5.90 (d, 1 H, J = 4.5 Hz), 7.19 (s, 5 H), 7.31 (s, 5 H); FDMS, m/z 667 (M^+ + 1). Anal. Calcd for $C_{29}H_{26}N_5O_3S_5$: C, 52.23; H, 3.93. Found: C, 52.23; H, 3.75.

Reaction of 6 with Sodium Benzenesulfinate. A solution of **6** (100 mg, 0.21 mmol) and sodium benzenesulfinate (86 mg, 0.52 mmol) in DMF (2 mL) was stirred for 1.5 h at 80 °C. The mixture was worked up and chromatographed (SiO_2; benzene–AcOEt, 8:1) to give **7c**: 87 mg (60%); colorless foam; IR ($CHCl_3$) 1768, 1720, 1606, 1597 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.58 (d, 1 H, J = 16 Hz), 3.85 (d, 1 H, J = 16 Hz), 4.37 (s, 2 H), 4.67 (d, 1 H, J = 14 Hz), 4.81 (d, 1 H, J = 14 Hz), 4.91 (d, 1 H, J = 12 Hz), 4.98 (d, 1 H, J = 12 Hz), 5.63 (d, 1 H, J = 4.5 Hz), 5.82 (d, 1 H, J = 4.5 Hz), 7.1–7.9 (m, 20 H). Anal. Calcd for $C_{35}H_{30}N_2O_7S_3$: C, 61.20; H, 4.40. Found: C, 60.96; H, 4.51.

Ring Opening of the Thiazoline Moiety of 7 with 2-Benzothiazolesulfenyl Chloride. A solution of **7a** (98 mg, 0.13 mmol) in dioxane (3 mL) and 5% HCl (0.3 mL) was stirred at room temperature for 30 min. To this solution was added a solution of 2-benzothiazolesulfenyl chloride prepared from 2-benzothiazolyl disulfide (106 mg, 0.32 mmol) and Cl_2 (0.8 M Cl_2/CCl_4, 0.4 mL, 0.32 mmol) in dioxane (5 mL). After being stirred for 30 min at room temperature, the mixture was passed through a silica gel column with AcOEt. The eluate was concentrated in vacuo, and the residue was chromatographed (SiO_2; benzene–AcOEt, 2:1) to give **8a**: 93 mg (75%); colorless foam; IR ($CHCl_3$) 3390, 1778, 1712, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.56 (br s, 2 H), 4.68 (d, 1 H, J = 13 Hz), 4.68 (d, 1 H, J = 14 Hz), 4.86 (d, 1 H, J = 14 Hz), 4.90 (d, 1 H, J = 12 Hz), 4.98 (dd, 1 H, J = 5, 8 Hz), 5.08 (d, 1 H, J = 13 Hz), 5.08 (d, 1 H, J = 12 Hz), 5.48 (d, 1 H, J = 5 Hz), 6.62 (d, 1 H, J = 8 Hz), 7.10 (s, 5 H), 7.23 (s, 5 H), 7.0–7.9 (m, 12 H); FDMS, m/z 920 (M^+ + 1). Anal. Calcd for $C_{44}H_{33}N_5O_4S_7$: C, 57.43; H, 3.61. Found: C, 57.58; H, 3.64.

Similarly, the disulfides **8b** and **8c** were prepared from **7b** and **7c** in 80% and 58% yields, respectively. The spectral data are as follows.

Compound **8b**: IR ($CHCl_3$) 3400, 1777, 1717, 1683 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.70 (br s, 6 H), 3.75 (br s, 2 H), 4.50 (d, 1 H, J = 13 Hz), 4.50 (d, 1 H, J = 14 Hz), 4.73 (d, 1 H, J = 13 Hz), 4.87 (d, 1 H, J = 14 Hz), 4.98 (d, 1 H, J = 12 Hz), 5.13 (d, 1 H, J = 12 Hz), 5.4–5.6 (m, 2 H), 7.10 (s, 5 H), 7.1–7.9 (m, 10 H); FDMS, m/z 850 (M^+ + 1). Anal. Calcd for $C_{36}H_{31}N_7O_4S_7$: C, 50.86; H, 3.67. Found: C, 50.92; H, 3.96.

Compound **8c**: IR ($CHCl_3$) 3380, 1777, 1717, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.63 (br s, 2 H), 4.11 (d, 1 H, J = 15 Hz), 4.55–5.14 (m, 5 H), 5.32 (d, 1 H, J = 5 Hz), 5.38 (d, 1 H, J = 14 Hz), 6.57 (d, 1 H, J = 8 Hz), 7.1–8.0 (m, 24 H). Anal. Calcd for $C_{42}H_{35}N_3O_8S_5$: C, 57.98; H, 4.05. Found: C, 58.08; H, 3.91.

Cyclyzation of 8 to 9. To a stirred solution of **8a** (56 mg, 0.06 mmol) in THF (2 mL) was added DBU (20 μL, 0.13 mmol) at −78 °C, and the stirring was continued for 30 min at this temperature. After being quenched with concentrated HCl and diluted with AcOEt, the mixture was worked up and chromatographed (SiO_2; benzene–AcOEt, 20:1) to give **9a** (29 mg, 64%) as a colorless foam (R_f 0.42; benzene–AcOEt, 4:1) and **10a** (4 mg, 9%) as a colorless foam (R_f 0.65; benzene–AcOEt, 4:1).

Compound **9a**: IR ($CHCl_3$) 3380, 1782, 1740, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.37 (br s, 2 H), 4.50 (d, 1 H, J = 14 Hz), 4.85 (d, 1 H, J = 14 Hz), 5.22 (s, 2 H), 5.29 (d, 1 H, J = 4 Hz), 5.60 (dd, 1 H, J = 4, 9 Hz), 5.72 (s, 1 H), 6.48 (d, 1 H, J = 9 Hz), 7.00 (s, 5 H), 7.30 (s, 5 H), 7.1–8.0 (m, 8 H); FDMS, m/z 753 (M^+ + 1). Anal. Calcd for $C_{37}H_{28}N_4O_4S_5$: C, 59.02; H, 3.75. Found: C, 58.92; H, 3.96.

Compound **10a**: IR ($CHCl_3$) 3380, 1789, 1727, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.60 (br s, 2 H), 4.34 (d, 1 H, J = 14 Hz), 4.94 (d, 1 H, J = 14 Hz), 5.23 (d, 1 H, J = 4.5 Hz), 5.34 (s, 2 H), 6.03 (dd, 1 H, J = 4.5, 9 Hz), 6.44 (d, 1 H, J = 9 Hz), 6.67 (s, 1 H), 7.23 (s, 5 H), 7.36 (s, 5 H), 7.1–7.9 (m, 8 H); FDMS, m/z 753 (M^+ + 1). Anal. Calcd for $C_{37}H_{28}N_4O_4S_5$: C, 59.02; H, 3.75. Found: C, 59.07; H, 4.02.

In a similar manner, **9b** and **9c** were prepared from **8b** and **8c** in 51% and 55% yields, respectively. The spectral data are as follows.

Compound **9b** (Y = 2-methyl-1,3,4-thiadiazol-5-ylthio): IR ($CHCl_3$) 3390, 1783, 1746, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.68 (s, 3 H), 2.76 (s, 3 H), 3.54 (br s, 2 H), 4.61 (d, 1 H, J = 13.4 Hz), 4.39 (d, 1 H, J = 13.4 Hz), 5.10 (d, 1 H, J = 4.1 Hz), 5.21 (s, 3 H), 5.54 (dd, 1 H, J = 4.1, 8.1 Hz), 6.28 (d, 1 H, J = 8.1 Hz), 7.26 (s, 5 H), 7.33 (m, 5 H). Anal. Calcd for $C_{29}H_{26}N_6O_4S_5$: C, 51.01; H, 3.84. Found: C, 50.92; H, 3.63.

Compound **9c** (Y = SO_2Ph): IR ($CHCl_3$) 3370, 1789, 1722, 1683 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.63 (br s, 2 H), 4.77 (d, 1 H, J = 14.4 Hz), 5.05 (s, 2 H), 5.22 (d, 1 H, J = 14.4 Hz), 5.7–5.9 (m, 2 H), 5.90 (s, 1 H), 7.26 (s, 5 H), 7.2–8.1 (m, 16 H). Anal. Calcd for $C_{35}H_{30}N_2O_8S_3$: C, 59.81; H, 4.30. Found: C, 59.74; H, 4.41.

Registry No. **1**, 86832-59-9; **2**, 86832-60-2; **3**, 86832-61-3; **4**, 86832-62-4; **5**, 86833-34-3; **6**, 86832-63-5; **7a**, 86766-47-4; **7b**, 86766-48-5; **7c**, 86766-49-6; **8a**, 86766-50-9; **8b**, 86784-84-1; **8c**, 86766-51-0; **9a**, 86766-52-1; **9b**, 86766-53-2; **9c**, 86766-54-3; **10a**, 86784-85-2; sodium 2-benzothiazolethiolate, 2492-26-4; 5-mercapto-2-methyl-1,3,4-thiadiazole, 29490-19-5; sodium benzenesulfinate, 873-55-2; 2-benzothiazolesulfenyl chloride, 33405-92-4.

Reaction of Methyl 4-Bromocrotonate with Lithium Ester Enolates: Direct S_N2 Displacement vs. Michael-Initiated Ring Closure

Pirote Prempree, Shuleewan Radviroongit, and Yodhathai Thebtaranonth*

Department of Chemistry, Faculty of Science, Mahidol University, Bangkok 10400, Thailand

Received October 13, 1982

Nucleophilic conjugate addition to an α,β-unsaturated carbonyl compound producing an enolate which subsequently undergoes an intramolecular ring closure has made a considerable impact on organic synthesis strategies.[1] This type of reaction has been termed MIRC (Michael-initiated ring closure) by Little, who showed that three- and five- to seven-membered carbocycles can be formed by this method.[2]

Thus the diester **1** was found to smoothly undergo the MIRC-type of reaction to give **3**[3] and the reaction was

(1) (a) Posner, G. H.; Mallamo, J. P.; Black, A. Y. *Tetrahedron* **1981**, *37*, 3921. (b) Cooke, M. P., Jr. *Tetrahedron Lett.* **1979**, 2199. (c) Chang, Y. H.; Pinnick, H. W. *J. Org. Chem.* **1978**, *43*, 373. (d) Posner, G. H.; Sterling, J. J.; Whitten, C. E.; Lentz, C. M.; Brunelle, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 107.

(2) Little, R. D.; Dawson, J. R. *Tetrahedron Lett.* **1980**, *21*, 2609.

(3) (a) Kolsaker, P.; Storesund, H. J. *J. Chem. Soc., Chem. Commun.* **1972**, 375. (b) Torii, S.; Tanaka, H.; Nagai, Y. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2825. (c) De Vos, M. J.; Krief, A. *Tetrahedron Lett.* **1979**, 1891. (d) Verhe, R.; Courtheyn, D.; De Kimpe, N.; De Buyck, L.; Thierie, R.; Van Caenegem, L.; Schamp, N. *Org. Prep. Proced. Int.* **1981**, *13*, 13. (e) Nugent, S. T.; Baizer, M. M.; Little, R. D. *Tetrahedron Lett.* **1982**, *23*, 1339.

0022-3263/83/1948-3553$01.50/0