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A New Rearrangement Reaction of 2-Methylthiolated Cephem Derivatives*

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A new rearrangement reaction of some 2-methylthiocephem derivatives to an oxazolone compound (**2**) is described.

In our preceding paper,[2] it was reported that treatment of 3-cephem compounds with lithium diisopropylamide followed by reaction of the resulting anions with methyl methanethiosulfonate resulted in the formation of 4-methylthio-2-cephems, while analogous treatment of 3-cephem-1-oxides gave 2-methylthiolated compounds. In the course of this study, it was found that some 2-methylthio compounds thereby synthesized are labile and, on treatment with acid or base, formed new rearrangement products containing neither the β-lactam nor the dihydrothiazine ring system. This paper describes structural elucidation of these products and related features of this rearrangement.

Methyl 7β-benzamido-3-methyl-2α-methylthio-3-cephem-4-carboxylate-1β-oxide (**1**), whose synthesis was reported earlier,[2] was treated with acetic acid in the presence of potassium acetate at 70°, giving a red-colored product (**2**) in 53% yield. Elementary analysis of **2** and a molecular ion peak at *m/e* 376 in the mass spectrum confer a molecular formula of $C_{17}H_{16}O_4N_2S_2$ on **2**, indicating that **2** is a rearrangement product formed with the removal of one equivalent of water from **1**. Compound **2** formed a mono-N-acetyl derivative as will be mentioned later and the nuclear magnetic resonance (NMR) spectrum of **2** observed in d_6-dimethyl sulfoxide shows a broad absorption at 9.9 ppm due to a hydrogen bonded amino group which exchanges with tetradeuteroacetic acid. The infrared spectrum shows characteristic absorption at 1795 (shoulder), 1770, 1660, and 1590 cm^{-1} (Nujol mull) which is compatible with those of the forgoing reports,[3] and shows the presence of a substituted alkylidene azlactone moiety. Major mass fragmentation peaks include *m/e* 313 due to M^+-$COOCH_3$ and 285 due to M^+-$CSSCH_3$ which also suggest the presence of not only an ester group but also of a newly-formed methyl dithioate group in **2**. Further, the ultraviolet spectrum exhibits an extended chromophore at 460, 352, 311, and 242 mμ. Based on these facts, it was concluded that compound **2** is a derivative of 2-phenyl-4-aminomethylene-5-oxazolone as shown in the Chart.

In spite of homogeneity of the rearrangement product (**2**) which was revealed on thin-layer chromatography with several solvent systems, the NMR spectrum indicated that the product **2** is a mixture of two isomeric compounds. Although the NMR spectrum in deuteriochloroform exhibits absorptions due to three kinds of methyl protons at 2.27, 2.66 and 3.98 ppm as singlets respectively, one olefinic proton appears as two singlets at 6.96 and 7.20 ppm in a ratio of 1:3. This fact indicates that compound **2** is a 1:3 mixture of two closely related geometrical isomers. Acetylation of **2** with acetyl chloride in pyridine gave an isomeric mixture of acetates (**3**) which was separated by chromatography to a minor amorphous acetate and a major crystalline acetate as described in the experimental section.

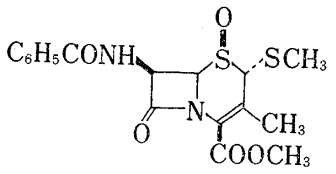
* Dedicated to the memory of Prof. Eiji Ochiai.

1) Location: *Hiromachi, Shinagawa-ku, Tokyo.*

2) A. Yoshida, S. Oida, and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **23**, 2507 (1975).

3) S. Kukolja, R.D.G. Cooper, and R.B. Morin, *Tetrahedron Letters*, **1969**, 3381; S. Wolfe, C. Ferrari, and W.S. Lee, *ibid.*, **1969**, 3385; H. Bundgaard and H.R. Angelo, *ibid.*, **1974**, 3001.

Moreover, the same acetate mixture was obtained on treatment of the sulfoxide (**1**) with acetic anhydride in pyridine at 55°. Benzoates of the azlactone (**2**) were found as an unseparable mixture.



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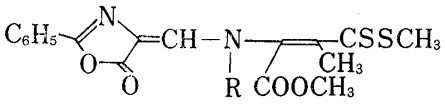
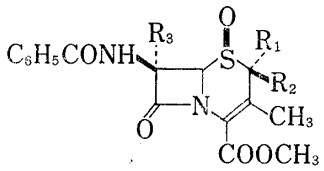
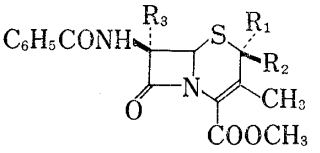


2 : R=H
3 : R=$COCH_3$



4 : $R_1=R_2=R_3=SCH_3$
5 : $R_1=R_2=SCH_3$, $R_3=H$
11 : $R_1=R_3=SCH_3$, $R_2=H$



6 : $R_1=R_2=R_3=SCH_3$
7 : $R_1=R_2=SCH_3$, $R_3=H$
12 : $R_1=R_3=SCH_3$, $R_2=H$
13 : $R_1=H$, $R_2=R_3=SCH_3$

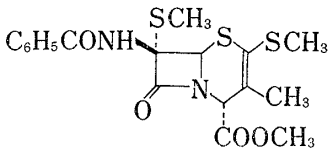


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Chart 1

On the other hand, it was found that not only a 2-methylthio sulfoxide like **1** but also some sulfides undergo such a rearrangement to the same azlactone (**2**) under basic conditions. Methyl 7β-benzamido-3-methyl-2,2,7α-trimethylthio-3-cephem-1-oxide (**4**) and its 2,2-dimethylthio analog[2] (**5**) were reduced with acetyl chloride and potassium iodide in N,N-dimethylformamide, giving the corresponding sulfides (**6** and **7**) respectively. Either of these sulfides (**6** or **7**) on treatment with 2.4 equivalents of lithium diisopropylamide in tetrahydrofuran at −78° affords the same azlactone (**2**) which proved identical with the sample obtained as above.

Similar to the foregoing criticism on the penicillin-penicillenate rearrangement,[4] formation of the azlactone (**2**) would involve an attack of the amide side chain on the β-lactam carbonyl group with simultaneous or subsequent cleavage of S—C-6 bond; however, the following pathways might be also plausible. As shown below, formation of **2** from the sulfoxide (**1**) would be illustrated as an initial bond cleavage between S-1 and C-6 by a β-elimination and successive dehydration of the resulting sulfenic acid intermediate (**8**) to give a dithioic ester (**9**). Ring formation takes place *via* an intramolecular attack of the C-7 amide oxygen at the labile azetinone carbonyl in **9**. In the base-catalysed formation of the azlactone (**2**) from the sulfide (**6** or **7**), the initial step would be interpreted as carbanion formation at C-7 by abstraction of the 7α-methylthio group or 7α-proton with base and the formed carbanion (**10**) would undergo ring opening and simultaneous demethylthiolation, giving the same dithioic ester intermediate (**9**).

Moreover, reduction of a 2α,7α-dimethylthio analog[2] (**11**) gave a 2α,7α-dimethylthio sulfide (**12**) and its 2β,7α-dimethylthio isomer (**13**) in a ratio of 1 : 3.[5] Treatment of the major sulfide (**13**) with lithium diisopropylamide under the same conditions, only giving a trace of the azlactone (**2**). In this case main product was found to be a 2-methylthio-2-cephem compound (**14**).

4) M.A. Schartz, *J. Pharm. Sci.*, **54**, 472 (1965); H. Bundgaard, *ibid.*, **60**, 1273 (1971).
5) Similar to some examples described previously,[2] the 2β-methylthio sulfide (**13**) was labile towards base and, on treatment with 1,4-diazabicyclo[2.2.2]octane, gave a mixture of its 2α-methylthio isomer (**12**) and the 2-cephem (**14**) in a ratio of 1 : 4.5.

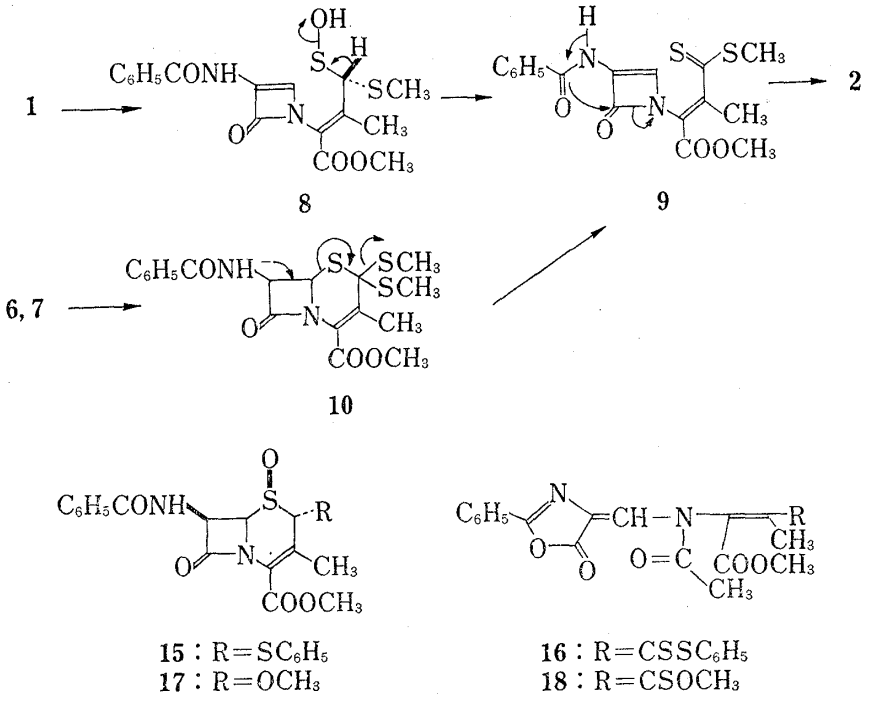

Chart 2

Finally we would like to mention some application of this rearrangement reaction to other examples. A 2α-phenylthio sulfoxide (**15**) whose preparation was reported previously[2] was treated with acetic anhydride in pyridine to give an isomeric mixture of the corresponding N-acetyl phenyl dithioates (**16**) in 57% yield. A 2α-methoxy sulfoxide (**17**) was prepared by 2-methoxylation of methyl 7β-benzamido-3-methyl-3-cephem-4-carboxylate according to a modification of the Spry's method[6] and successive 1-oxidation. Analogous reaction of **17** with acetic anhydride resulted in a formation of a methyl thioic O-ester (**18**).

In penicillins, rearrangements of acylamino-β-lactams into azlactones with opening of thiazolidine rings commonly occur as shown in a formation of reactive penicillenates which has been implicated as a factor in penicillin allergy[7]; however, no example of analogous reaction in cephalosporins has previously been reported. Consequently, these results are not only of interest as providing the first example of the rearrangement reaction but also in view of possible haptens formation in cephalosporins.

Experimental

Melting points are not corrected. IR spectra were recorded on a JASCO A-2 or Perkin-Elmer Model 225 spectrometer, UV spectra on a Cary 14 (Serial No. 1258) or a Cary 118c (Serial No. 103) spectrometer, NMR spectra on a Hitachi Perkin-Elmer R-24 (60 MHz), and mass spectra on a JEOL-01SG mass spectrometer. Thin-layer chromatography (TLC) was performed on TLC-plates, Silica gel F_{254} precoated, layer thickness 0.25 mm (E. Merck) and spots were visualized by UV-irradiation or by spraying with vanadic acid-sulfuric acid followed by heating or with iodine. Columns for ordinary chromatography were prepared with Wakogel C-200 (Wako Pure Chemical Industries, Ltd.) and plates for preparative TLC with Silica gel $60F_{254}$ (E. Merck). Solvents were removed by a rotary flash evaporator at diminished pressure and usually at 15—35°. The abbreviations used are as follows: s, singlet; d, doublet; q, quartet; br, broad; sh, shoulder.

Methyl 7β-Benzamido-3-methyl-2,2,7α-trimethylthio-3-cephem-4-carboxylate (**6**)——To an ice-cold solution of 385 mg of methyl 7β-benzamido-3-methyl-2,2,7α-trimethylthio-3-cephem-4-carboxylate-1-oxide[2] (**4**) and 526 mg of KI in 2 ml of DMF was added dropwise 248 mg of AcCl with stirring. After stirring for 4 hr at room temperature, the mixture was poured onto an ice-cold dil. $K_2S_2O_5$ and extracted with AcOEt.

6) D.O. Spry, *Tetrahedron Letters.*, **1972**, 3717.
7) E.P. Abraham, "Topics in Pharmaceutical Sciences," D. Perlman, Ed., Vol. 1, Wiley (Interscience), N.Y., 1968, p. 25.

The extract was washed with dil. $NaHCO_3$ and with H_2O, dried and evaporated. Preparative TLC of the residue with benzene–AcOEt (6: 1, v/v) gave 271 mg of **6**, mp 180.5—182°, prisms (from benzene–AcOEt). IR ν_{max}^{Nujol} cm^{-1}: 3350, 1783, 1724, 1667, 1500, 782, 718. NMR ($CDCl_3$) δ ppm: 2.00 (3H, s), 2.21 (3H, s), 2.30 (3H, s), 2.36 (3H, s), 3.78 (3H, s), 5.25 (1H, s). *Anal.* Calcd. for $C_{19}H_{22}O_4N_2S_4$: C, 48.49; H, 4.71; N, 5.95; S, 27.25. Found: C, 48.82; H, 4.70; N, 5.65; S, 26.92.

Methyl 7β-Benzamido-3-methyl-2,2-dimethylthio-3-cephem-4-carboxylate (7)——As described above, 202 mg of AcCl was added to an ice-cold solution of 283 mg of methyl 7β-benzamido-3-methyl-2,2-dimethylthio-3-cephem-4-carboxylate-1-oxide[2] (**5**) and 427 mg of KI in 4 ml of DMF and the mixture was stirred for 5 hr. Purification of the product by chromatography gave 212 mg of **7** as a foam. IR ν_{max}^{Nujol} cm^{-1}: 3300, 1782, 1727, 1655, 1598, 1523, 780, 759, 708. NMR ($CDCl_3$) δ ppm: 2.04 (3H, s), 2.23 (3H, s), 2.28 (3H, s), 3.83 (3H, s), 5.24 (1H, d, J=5 Hz), 5.94 (1H, q, J=5,9 Hz). Mass Spectrum *m/e*: 424 (M^+, $C_{18}H_{20}O_4N_2S_3$).

Formation of the Azlactone 2 and Its Acetate 3——i) A stirred mixture of 300 mg of methyl 7β-benzamido-3-methyl-2α-methylthio-3-cephem-4-carboxylate-1-oxide[2] (**1**), 285 mg of KOAc, and 7 ml of AcOH was warmed at 70° for 1 hr and then evaporated *in vacuo*. The residue was dissolved in $CHCl_3$, washed with dil. $NaHCO_3$ and with H_2O, and dried. Evaporation of the solvent left a colored crystalline mass which was recrystallized from AcOEt to 152 mg (53%) of **2**, mp 160.5—162° (decomp.), red-colored needles. IR ν_{max}^{Nujol} cm^{-1}: 1795 (sh), 1770, 1736, 1660, 1590, 1578, 864, 692. UV λ_{max}^{EtOH} nm (ε): 242 (11500), 311 (17900), 352 (19300), 460 (11000). NMR (d_6-DMSO) δ ppm: 2.15 and 2.30 (3H, s, *ca.* 3: 1), 2.70 (3H, s), 3.55 and 3.81 (3H, s, *ca.* 3: 1), 9.9 (1H, br. s, disappeared by addition of CD_3COOD); ($CDCl_3$) δ ppm: 2.27 (3H, s), 2.66 (3H, s), 3.98 (3H, s), 6.96 and 7.20 (1H, s, *ca.* 1: 3). *Anal.* Calcd. for $C_{17}H_{16}O_4N_2S_2$: C, 54.24; H, 4.28; N, 7.44; S, 17.03. Found: C, 54.23; H, 4.23; N, 7.65; S, 17.38.

To an ice-cold solution of 150 mg of **2** in 4 ml of pyridine was added dropwise 52 mg of AcCl and the mixture was stirred for 1.5 hr and evaporated *in vacuo*. The residue was dissolved in AcOEt and washed with 10% dil. $KHSO_4$ and with H_2O and dried. Evaporation of the solvent and preparative TLC of the residue gave 16 mg (10%) of a syrupy acetate I and 112 mg (67%) of a crystalline acetate II, mp 172—173°, prisms (from MeOH–acetone). IR $\nu_{max}^{CHCl_3}$ cm^{-1} for I,: 1787, 1754, 1724, 1660, 1602, 1000, 891; for II: 1793, 1758, 1722, 1662, 1602, 1000, 890. UV λ_{max}^{EtOH} nm (ε): for I: 252 (15200), 323 (27900), 346 (30200), 363 (23200); for II: 252 (15300), 327 (30800), 345 (31700), 362 (24200). NMR ($CDCl_3$) δ ppm for I: 2.26 (3H, s), 2.56 (3H, s), 2.67 (3H, s), 3.72 (3H, s); for II: 2.07 (3H, s), 2.28 (3H, s), 2.79 (3H, s), 3.64 (3H, s), 8.26 (1H, s). Mass Spectrum *m/e* for I and II: 418 (M^+, $C_{19}H_{18}O_5N_2S_2$). *Anal.* Calcd. for $C_{19}H_{18}O_5N_2S_2$: C, 54.53; H, 4.34; N, 6.69; S, 15.32. Found: for II: C, 54.69; H, 4.24; N, 6.50; S, 15.70.

Benzoylation of 150 mg of **2** in 4 ml of pyridine with 120 mg of benzoyl chloride in the usual manner gave 176 mg of a benzoate mixture, mp 185—188°, prisms (from MeOH–acetone), whose separation by TLC was not successful. IR ν_{max}^{Nujol} cm^{-1}: 3090, 1795, 1734, 1695, 1660, 1620, 1600, 1567. NMR ($CDCl_3$) δ ppm: 2.00 and 2.58 (3H, s, *ca.* 2: 1), 2.64 (3H, s), 3.62 and 3.75 (3H, s, *ca.* 2: 1). Mass Spectrum *m/e*: 480 (M^+, $C_{24}H_{20}O_5N_2S_2$). *Anal.* Calcd. for $C_{24}H_{20}O_5N_2S_2$: C, 60.00; H, 4.20; N, 5.83; S, 13.32. Found: C, 60.18; H, 4.07; N, 5.93; S, 13.25.

ii) A mixture of 200 mg of **1**, 4 ml of pyridine, and 0.6 ml of Ac_2O was warmed at 60° for 3.5 hr and then evaporated *in vacuo*. The residue was dissolved in AcOEt and washed with H_2O, dried and evaporated. Preparative TLC of the residue with benzene–AcOEt (20: 1, v/v) gave 27 mg (13%) of the acetate I, and 76 mg (36%) of the acetate II.

iii) To a stirred solution of 101 mg (2.4 eq.) of diisopropylamine in 15 ml of THF was added 0.5 ml (2.4 eq.) of 20% *n*-butyllithium hexane solution (E. Merck) at 0° and, after 5 min stirring at 0°, 196 mg of **6** and 0.5 ml of hexamethylphosphoramide was added at −78°. Stirring was maintained for 2 hr at −30° and further for 1 hr at −10°. After cooling at −78° again, 200 mg of AcOH was added slowly and the mixture was poured onto an ice-water and extracted with AcOEt. The extract was washed with dil. $NaHCO_3$ and with H_2O, dried and evaporated. Purification of the residue by chromatography over 10 g of silica gel with benzene–AcOEt (50: 1, v/v) gave 54 mg (34%) of **2** as needles.

iv) To a lithium diisopropylamide solution prepared from 55 mg of diisopropylamine, 0.1 ml of 20% *n*-butyllithium hexane solution in 10 ml of THF was added 100 mg of **7** and 1 ml of hexamethylphosphoramide. Work-up in the same way as described above and chromatography of the product gave 29 mg (33%) of **2**.

Methyl 7β-Benzamido-3-methyl-2α,7α-dimethylthio-3-cephem-4-carboxylate (12) and Its 2β,7α-Dimethylthio Isomer (13)——Similar to the case of the preparation of **6**, 400 mg of methyl 7β-benzamido-3-methyl-2α,7α-dimethylthio-3-cephem-4-carboxylate-1-oxide[2] (**11**) was treated with 664 mg of KI and 315 mg of AcCl. Work-up of the product including preparative TLC gave 74 mg (19%) of **12** as a foam and 230 mg (61%) of **13** as prisms, mp 164.5—167° (from EtOH–hexane). IR ν_{max}^{Nujol} cm^{-1} for **12**: 3330, 1802, 1764, 1732, 1668, 1512, 768; for **13**: 3340, 1772, 1723, 1672, 1507, 723. NMR ($CDCl_3$) δ ppm for **12**: 2.19 (3H, s), 2.27 (3H, s), 2.38 (3H, s), 3.80 (3H, s), 4.26 (1H, s), 5.37 (1H, s); for **13**: 1.92 (3H, s), 2.39 (6H, s), 3.78 (3H, s), 4.09 (1H, s), 5.32 (1H, s). Mass Spectrum *m/e* for **12** and **13**: 424 (M^+, $C_{18}H_{20}O_4N_2S_3$). *Anal.* Calcd. for $C_{18}H_{20}O_4N_2S_3$ 0.52 CCl_4[8]: C, 43.98; H, 3.98; N, 5.54; S, 19.01; Cl, 14.85. Found: for **12**: C, 44.10; H, 3.86; N, 5.55;

8) Contaminated with the extraction solvent.

S, 19.18; Cl, 14.98. *Anal.* Calcd. for $C_{18}H_{20}O_4N_2S_3$: C, 50.92; H, 4.75; N, 6.60; S, 22.66. Found for **13**: C, 51.14; H, 4.58; N, 6.28; S, 22.72.

Treatment of 13 with Base——To a stirred solution of lithium diisopropylamide prepared from 186 mg of diisopropylamine and 0.9 ml of 20% *n*-butyllithium hexane solution in 20 ml of THF was added a solution of 260 mg of **13** in 5 ml of THF at −78°. After addition of 1 ml of hexamethylphosphoramide, the mixture was treated as described earlier. The product was purified by preparative TLC, giving 232 mg of methyl 7β-benzamido-3-methyl-2,7α-dimethylthio-2-cephem-4-carboxylate (**14**), needles, mp 138—139° (from AcOEt–hexane), along with 3 mg of **2**. IR ν_{max}^{Nujol} cm^{-1}: 3320, 1790, 1780, 1743, 1735, 1654, 1640, 1521. NMR ($CDCl_3$) δ ppm: 2.06 (3H, s), 2.20 (3H, s), 2.32 (3H, s), 3.79 (3H, s), 4.84 (1H, br. s), 5.43 (1H, s). Mass Spectrum *m/e*: 424 (M^+, $C_{18}H_{20}O_4N_2S_3$).

Formation of the Azlactone Acetate 16——Treatment of 100 mg of methyl 7-benzamido-3-methyl-2α-phenylthio-3-cephem-4-carboxylate-1-oxide[2] (**15**) with 160 mg of Ac_2O in 1 ml of pyridine at 55° for 2 hr and purification of the product (**16**) by preparative TLC afforded 20 mg (19%) of an azlactone acetate I, mp 182—183.5°, prisms (from $CHCl_3$–MeOH), and 40 mg (38%) of its isomeric azlactone acetate II, mp 149—150°, prisms (from $CHCl_3$–MeOH). IR ν_{max}^{Nujol} cm^{-1} for I: 1798, 1759, 1731, 1712, 1670, 1492, 1197, 881; for II: 1793, 1758, 1732, 1708, 1663, 1490, 1192, 880. UV λ_{max}^{EtOH} nm (ε) for I: 333 (28600), 346 (31100), 363 (23000); for II: 330 (31800), 345 (33600), 363 (23900). NMR ($CDCl_3$) δ ppm for I: 2.26 (3H, s), 2.75 (3H, s), 3.77 (3H, s), 8.12 (1H, s); for II: 2.16 (3H, s), 2.26 (3H, s), 3.73 (3H, s), 7.50 (5H, s), 8.18 (1H, s). Mass Spectrum *m/e* for I and II: 480 (M^+). *Anal.* Calcd. for $C_{24}H_{20}O_5N_2S_2$: C, 59.98; H, 4.20; N, 5.83; S, 13.34. Found for II: C, 59.81; H, 4.04; N, 5.79; S, 13.32.

Methyl 7β-Benzamido-2α-methoxy-3-methyl-3-cephem-4-carboxylate-1-oxide (**17**)——To a solution of 332 mg of methyl 7β-benzamido-3-methyl-3-cephem-4-carboxylate[2] in a mixture of 15 ml of MeOH and 10 ml of CH_2Cl_2 was added 120 mg of *t*-butyl hypochlorite in one portion with cooling and stirring and the mixture was stirred for 1 hr. Then, the mixture was poured onto a mixture of CH_2Cl_2 and aq. $CaCl_2$. The organic layer was separated, washed with dil. $NaHCO_3$ and with H_2O, dried and evaporated *in vacuo*. The residue was charged on 15 g of silica gel and eluted with $CHCl_3$ containing AcOEt gradient-wise. Thus, 126 mg (35%) of a 2α-methoxy derivative was obtained as needles (from $CHCl_3$–AcOEt), mp 193—194.5° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3290, 1780, 1735, 1650, 1536, 1083, 942. NMR (d_6-DMSO) δ ppm: 1.88 (3H s), 3.25 (3H, s), 3.76 (3H, s), 4.95 (1H, d, J=5 Hz), 5.01 (1H, s), 5.81 (1H, q, J=5, 7.5 Hz), 9.31 (1H, d, J=7.5 Hz). Mass Spectrum *m/e*: 362 (M^+, $C_{17}H_{18}O_5N_2S$). *Anal.* Calcd. for $C_{17}H_{18}O_5N_2S$ 0.03 $CHCl_3$: C, 55.89; H, 4.97; N, 7.65; S, 8.76. Found: C, 55.90; H, 4.77; N, 7.49; S, 8.82.

To an ice-cold solution of 100 mg of the 2α-methoxy sulfide thereby obtained in 5 ml of $CHCl_3$ was added 60 mg of *m*-chloroperbenzoic acid (85% purity, Aztec Chemicals) in portions and the mixture was stirred for 1 hr with cooling. After dilution with $CHCl_3$, the mixture was washed with dil. $NaHCO_3$ and with H_2O, dried and concentrated. The concentrate was diluted with EtOH and was evaporated slowly *in vacuo*, giving 84 mg of **17** as needles, mp 140—141°. Yield, 81%. IR ν_{max}^{Nujol} cm^{-1}, 3310, 1782, 1733, 1652, 1537, 1088, 709. NMR ($CDCl_3$) δ ppm: 2.13 (3H, s), 3.59 (3H, s), 3.80 (3H, s), 4.46 (1H, s), 4.53 (1H, d, J=5 Hz), 6.23 (1H, q, J=5, 10 Hz).

Formation of the Azlactone Acetate 18——Treatment of 100 mg of **17** with 0.2 ml of Ac_2O and 2 ml of pyridine at 60° for 1.5 hr and work-up in the usual manner afforded 12 mg (11%) of one of the acetates (**18**) as plates (from EtOH–hexane), mp 157—158°. IR ν_{max}^{Nujol} cm^{-1}: 1796, 1732, 1722, 1667, 1193, 880, 698. NMR ($CDCl_3$) δ ppm: 1.99 (3H, s), 2.18 (3H, s), 3.62 (3H, s), 4.22 (3H, s), 8.11 (1H, s). Mass Spectrum *m/e*: 402 (M^+, $C_{19}H_{18}O_6N_2S$).