Friary, J. Posler, and M. A. Schwartz, *J. Org. Chem.*, **33**, 712 (1968).
(17) (a) E. Wenkert and B. G. Jackson, *J. Am. Chem. Soc.*, **81**, 5601 (1959); (b) T. A. Spencer, T. D. Weaver, M. A. Schwartz, W. J. Greco, Jr., and J. L. Smith, *Chem. Ind. (London)*, 577 (1964).
(18) L. Velluz, J. Valls, and G. Nomine, *Angew. Chem., Int. Ed. Engl.*, **4**, 181 (1965).
(19) R. M. Coates and J. E. Shaw, *J. Org. Chem.*, **35**, 2597 (1970).
(20) This reaction must be conducted in a well-ventilated hood; the chemist should wear rubber gloves during the workup because both hexamethylphosphoric triamide and chloromethyl methyl ether are carcinogens.
(21) We are grateful to Professor R. M. Carman for providing an authentic sample of (±)-methyl callitrisate.
(22) M. E. Kuehne, *J. Am. Chem. Soc.*, **83**, 1493 (1961).
(23) We are grateful to Professor S. R. Wilson, Indiana University, for providing generous samples of 7-methoxy-2-tetralone and tricyclic enone **9B**.
(24) L. H. Briggs, R. C. Cambie, and J. L. Hoare, *Tetrahedron*, **7**, 262 (1959). *O*-Methyl methyl podocarpate was prepared from (+)-podocarpic acid (Aldrich 11,979-2) by esterification with ethereal diazomethane followed by alkylation using methyl iodide and anhydrous potassium carbonate in refluxing acetone for 18 h.
(25) P. A. Bartlett and W. S. Johnson, *Tetrahedron Lett.*, 4459 (1970).
(26) (a) For examples of alkylation of unhindered exocyclic enolate anions see H. O. House and T. M. Bare, *J. Org. Chem.*, **33**, 943 (1968); R. E. Ireland and L. N. Mander, *ibid.*, **32**, 689 (1967); **34**, 142 (1969); (b) For an example of alkylation of a hindered exocyclic enolate anion see F. E. Ziegler and J. A. Kloek, *Tetrahedron Lett.*, 315 (1974).
(27) Prepared by Mr. P. S. Chu in our laboratory from methyl hydrogen malonate, isopropylmagnesium chloride, and 3-methoxypropanoyl chloride in 70% yield according to the procedure of R. E. Ireland and J. A. Marshall, *J. Am. Chem. Soc.*, **81**, 2907 (1959).
(28) C. H. Heathcock and J. E. Ellis, *Chem. Commun.*, 1474 (1971); J. E. Ellis, J. S. Dutcher, and C. H. Heathcock, *Synth. Commun.*, **4**, 71 (1974); I. N. Nazarov and S. I. Zavyalov, *Zh. Obshch. Khim.*, **23**, 1703 (1953); *J. Gen. Chem. USSR (Engl. Transl.)*, **23**, 1793 (1953).
(29) R. L. Augustine, "Catalytic Hydrogenation", Marcel Dekker, New York, N.Y., 1965, pp 11–14.
(30) Z. G. Hajos, R. A. Micheli, D. R. Parrish, and E. P. Oliveto, *J. Org. Chem.*, **32**, 3008 (1967); Z. G. Hajos and D. R. Parrish, *ibid.*, **38**, 3239 (1973).
(31) D. Caine, *Org. React.*, **23**, 1–258 (1976); G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, **86**, 1761 (1964).
(32) L. F. Fieser and J. E. Herz, *J. Am. Chem. Soc.*, **75**, 121 (1953); S. K. Pradham, G. Subrahmanyam, and H. J. Ringlod, *J. Org. Chem.*, **32**, 3004 (1967).
(33) K. Adank, H. A. Pfenninger, W. G. Stoll, and M. Viscontini, *Helv. Chim. Acta*, **46**, 1030 (1963); S. B. Kadin, *J. Org. Chem.*, **31**, 620 (1966).
(34) W. L. Dilling and R. A. Plepys, *J. Org. Chem.*, **35**, 2971 (1970).
(35) M. F. Semmelhack and R. D. Stauffer, *J. Org. Chem.*, **40**, 3619 (1975).
(36) Aldrich Chemical Co., Milwaukee, Wis., Catalog No. Z10,046-3.
(37) W. S. Johnson and W. P. Schneider, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 132.
(38) R. L. Augustine, "Oxidation", Vol. 1, Marcel Dekker, New York, N.Y., 1969, p 222.

Rearrangements of Penicillin Sulfoxides. 1

Abraham Nudelman[1] and Ronald J. McCaully

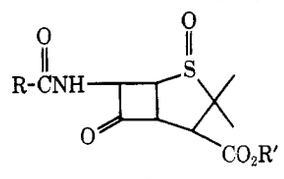
Wyeth Laboratories, Inc., Radnor, Pennsylvania 19087

Received February 3, 1977

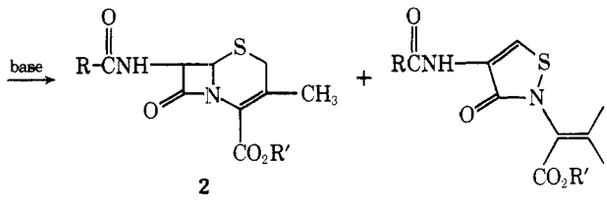
Penicillin sulfoxides are converted to 3-halo-3-methylcepham-4-carboxylic acid esters or the corresponding cephem derivatives by heating the penicillin sulfoxide precursor in the polyhaloalkane solvent in the presence of an equimolar amount of a neutral or basic catalyst, respectively. Basic catalysts such as pyridine or 4-picoline afford cephem derivatives, whereas the quaternary ammonium salts bring about the formation of 3-halocepham derivatives.

Several recent articles have reported the conversion of penicillins into cephalosporins by treatment of penicillin sulfoxides with reagents such as anhydrides,[2] acids,[3] diazo compounds–amine hydrochlorides,[4] 2-mercaptobenzothiazole followed by halogenation and dimethylformamide treatment,[5] thionyl chloride–triethylamine,[6] and trimethylchlorosilane–α-picoline.[7]

The present paper describes a novel, convenient process for the conversion of penicillin sulfoxides to a variety of cephalosporin derivatives. Most of the reported reactions, whereby the expansion of penicillin sulfoxides to ceph systems have been carried out, have involved acidic reagents. It was speculated that the reaction should also proceed under basic conditions. For this purpose, sulfoxide **1** was treated with a number of basic reagents in a variety of solvents. The desired deacetoxycephem **2** was indeed obtained in certain instances; however, in most cases the major or only product was the known[2,8] isothiazole **3** (Table I).



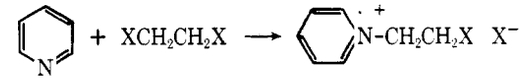
1



2 **3**

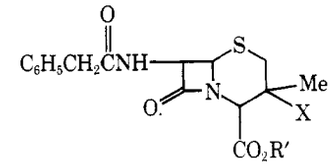
R = $C_6H_5CH_2$-, R′ = *p*-$NO_2C_6H_4CH_2$-

The best yields of cephem **2** were obtained in the presence of pyridine in 1,2-dichloroethane. The reaction was then repeated with various molar ratios of pyridine:sulfoxide **1**, ranging from trace amounts to very large molar excesses of base. The best results were obtained when 2 mol of pyridine/mol of sulfoxide **1** was used. In the presence of a large excess of pyridine, the quaternary salt **4a** precipitated out of solution



4a, X = Cl
b, X = Br

in crystalline form and it was found that this salt was a better catalyst for the rearrangement than pyridine itself. In 1,2-dichloroethane in the presence of 1 to 2 mol of salt **4a**/mol of sulfoxide **1**, the only detectable product obtained was a novel cephalosporin, which was subsequently shown to be cepham **5a**.[10]



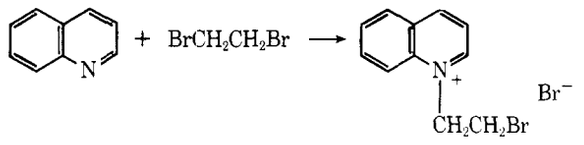
5a, X = Cl
b, X = Br

Table I. Rearrangement of Penicillin 1 to Cephem 2 and Isothiazole 3

Catalyst	Solvent	Product
Imidazole	1,2-Dichloroethane	Only **3**
N-Methylimidazole	1,2-Dichloroethane	Only **3**
4-Picoline	1,2-Dichloroethane	1:1 mixture of 2:3
Pyridine	Acetonitrile	Only **3**
Pyridine	Dioxane	Only **3**
Pyridine	Trichloroethylene	**3** quantitative yield
Pyridine	1,2-Dichloroethane	Mostly **2**
Pyridine	Chloroform	No reaction
Pyridine	*n*-Butyl chloride	No reaction
	1,2-Dichloroethane	No reaction

The catalytic effect of salt **4a** was further substantiated by the formation of cepham **5a** when the reaction was carried out in solvents where pyridine failed to produce ceph products. (Table II).

Other quaternary ammonium salts such as tetramethylammonium chloride or *N*-ethylpyridinium bromide failed to effect the penicillin–cephalosporin rearrangement. The reaction proceeded with *N*-(2-bromoethyl)pyridinium bromide[9] (**4b**) as well as with the corresponding chloro analogue to give the corresponding 3-bromocepham **5b** (X–Br). Similar results were obtained with the quinolinium salt **6**. The halogen

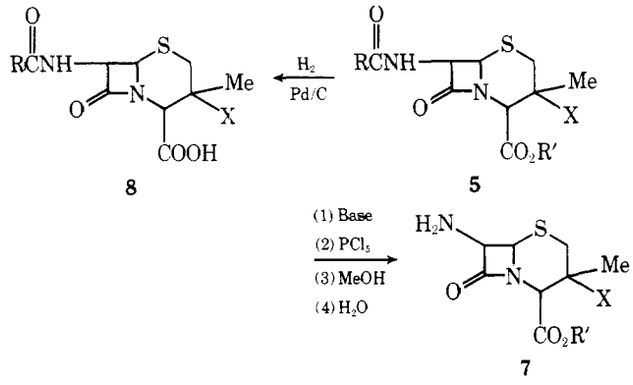


6

component of the salt used and the solvent had to be the same, otherwise halogen exchange took place, and chloro cepham **5a** was obtained when salt **4b** was used in 1,2-dichloroethane.

The attempted displacement of the 3-halo group in cepham **5** by silver acetate resulted in the formation of cephem **2**. The most efficient reagent found for the dehydrohalogenation reaction was 1,5-diazabicylo[4.3.0]non-5-ene (DBN) where an almost quantitative yield of cephem **2** was obtained.

Hydrogenolysis of **5** afforded the corresponding free acids **8**. Removal of the amido side chain was accomplished by a variation of the imino ether cleavage reaction.[12]



8 **5** **7**

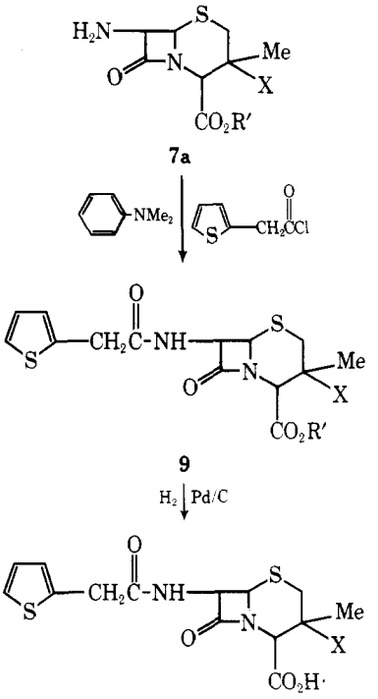
The preferred base for this cleavage reaction was *N*,*N*-dimethylaniline. Other bases, such as pyridine, caused a large degree of dehydrohalogenation.

The amine **7** was successfully reacylated, and the *p*-nitrobenzyl protecting group was easily removed by hydrogenation. No evidence of dehydrohalogenation was observed during the catalytic hydrogenolysis.

The NMR spectra of **8** and **10** indicated that the 3-halo group and the 4-H appear cis to each other.[10]

Table II. Rearrangement of Penicillin 1 to Cepham 5a in the Presence of Salt 4

Solvent	Product
1,2-Dichloroethane	Only **5**
Trichloroethylene	3:2 ratio of **3**:**5**
Acetonitrile	Only **5** (low yield)
Nitromethane	Only **5**
Dimethylacetamide	Only **5** (low yield)
Dioxane (95 °C)	No reaction
Dioxane (reflux)	Only **5** (low yield)



7a **9** **10**

R′ = *p*-$CH_2C_6H_4NO_2$

X = Cl

Discussion

The mechanism of the penicillin sulfoxide–cephalosporin rearrangement has been shown[2] to involve sulfenic acid intermediates, which, in turn, have been trapped by a variety of reagents.[11]

The unique characteristics of the haloethylpyridinium (and quinolinium) halide catalyst in effecting the rearrangement has led to the mechanism suggested in Scheme I.

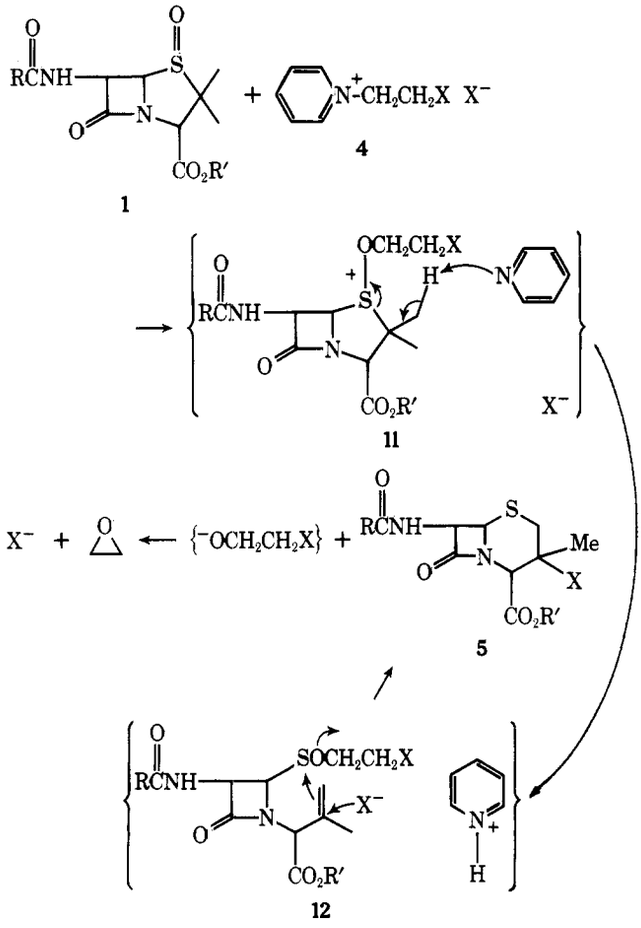
All attempts to isolate or identify 2-chloroethanol by vapor-phase chromatography proved futile. Under the reaction conditions, a further breakdown of **13** into ethylene oxide **14** and halide ion may occur, and the oxide **14** probably evaporated or decomposed. By the proposed mechanism, no free base is present for any length of time, and dehydrohalogenation of **5** does not occur. In the presence of free bases, the reaction may proceed by two alternative paths, A and B, leading to the formation of cephem **2** or isomer **3** (Scheme II).

Experimental Section

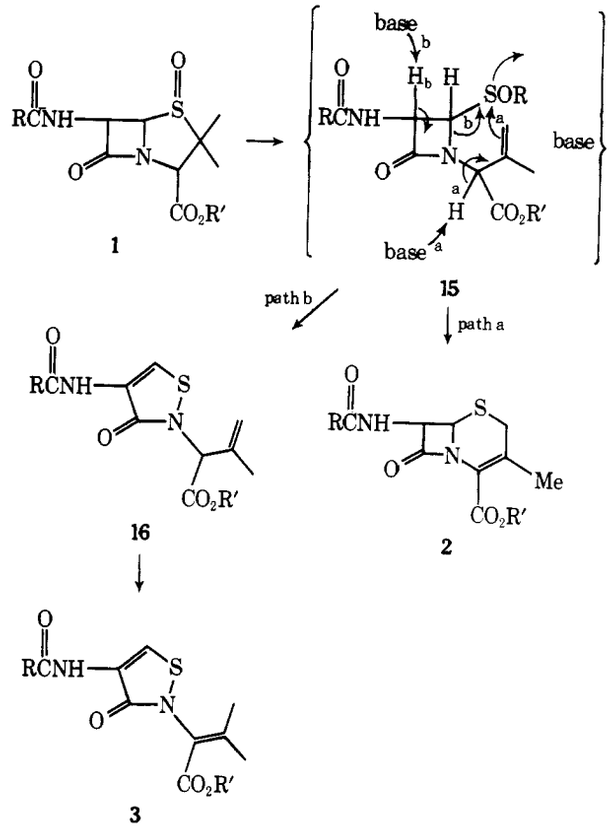
The course of the rearrangement reaction was followed by thin-layer chromatography on silica gel plates. A 10:7 1,2-dichloroethane:ether eluent solution gave excellent separation of penicillin, cephalosporins, and isothiazole components of the reactions. In some cases, the products of the reaction were not isolated and only a qualitative estimate of product composition is reported (Tables I and II) as detected by the thin-layer chromatography.

1-(2-Chloroethyl)pyridinium Chloride (4a). A solution of pyr-

Scheme I



Scheme II



idine (100 g, 1.25 mol) in 800 mL of 1,2-dichloroethane was refluxed for 72 h. The white crystalline material which formed was filtered, washed repeatedly with fresh 1,2-dichloroethane, and dried: collected 200 g (89% yield); NMR (D_2O) ppm (δ), 4.3 (t, 3), 5.6 (t, 3), 8.1–9.3 (m, 5).

1-(2-Bromoethyl)quinolinium Bromide (6). A solution of quinoline (20 mL) in 200 mL of 1,2-dibromoethane was heated under nitrogen at 70 °C for 18 h. The crystalline solid was filtered, washed with dichloromethane, and recrystallized from methanol–ether: collected 32 g (65% yield); mp 205–207 °C; NMR (D_2O) 4.22 (t, 2), 5.63 (t, 2), 7.8–8.6 (m, 5), 9.1–9.6 (m, 3).

3-Chloro-3-methyl-8-oxo-7-(2-phenylacetamido)-5-thia-1-azabicyclo[4.2.0]octane-2-carboxylic Acid *p*-Nitrobenzyl Ester (5a). To a solution of 6-(2-phenylacetamido)penicillanic acid *p*-nitrobenzyl ester 1-oxide (1) (5 g, 10.3 mmol) in 2.4 L of dry 1,2-dichloroethane was added 1-(2-chloroethyl)pyridinium chloride (3.8 g, 21.3 mmol). The mixture was heated to reflux for 21 h; it was then concentrated to 500 mL, washed with water, treated with charcoal, dried, and flash evaporated. The residual oil was dissolved in dichloromethane and the solution obtained was added to pentane. A light yellow solid was obtained (4.3 g, 83% yield), which was further recrystallized from dichloromethane–pentane: mp 134–136 °C; NMR ($DCCl_3$) ppm (δ), 1.63 (s, 3, 3-methyl), 3.12 (ABq, δ 0.925 ppm, J = 15 Hz, 2-CH_2), 3.68 (s, 2, CH_2CO) 4.80 (s, 1, 4-H), 5.16 (d, 1, 6 H), 5.30 (s, 2, OCH_2), 5.68 (q, 1, 7 H), 6.6 (d, 1, NH) 7.30 (s, 5, C_6H_5), 7.95 (ABq, δ 0.75 ppm, J = 9 Hz, *p*-$NO_2C_6H_4$).

Anal. Calcd for $C_{23}H_{22}ClN_3O_6S$ (mol wt 503.96): C, 54.81, H. 4.40; N, 8.34; Cl, 7.04; S, 6.36. Found: C, 54.42; H, 4.59; N, 7.95; Cl, 7.08; S, 6.49.

3-Bromo-3-methyl-8-oxo-7-(2-phenylacetamido)-5-thia-1-azabicyclo[4.2.0]octane-2-carboxylic Acid *p*-Nitrobenzyl Ester (5b). Method I. To a solution of 6-(2-phenylacetamido)penicillanic acid *p*-nitrobenzyl ester 1-oxide (1 g, 2.06 mmol) in 100 mL of dry 1,2-dibromoethane was added 1-(2-bromoethyl)pyridinium bromide (1.13 g, 4.2 mmol). The mixture was heated at 90 °C for 10 h. The solvent was flash evaporated, and the residue was chromatographed on 25 g of silica gel which was eluted with ether. The residue obtained after evaporation of the eluent was crystallized from dichloromethane–pentane to give 300 mg (26.4% yield) of the title compound: mp 136–137.5 °C; NMR (Me_2SO-d_6) ppm (δ), 1.81 (s, 3, 3-CH_3), 3.1 (ABq, δ 0.775 ppm, J = 15 Hz, 2-CH_2), 3.62 (s, 2 CH_2CO), 4.86 (s, 1, 4-H), 5.23 (d, 1, 6 H), 5.70 (s, 2, OCH_2), 5.60 (q, 1, 7 H), 6.57 (d, 1 NH), 7.32 (s, 5, C_6H_5), 7.90 (ABq, δ 0.725 ppm, J = 9 Hz, *p*-$NO_2C_6H_4$). Anal. Calcd for $C_{23}H_{22}BrN_3O_6S$ (mol wt 548.45): C, 50.37; H, 4.04; N, 7.66; Br, 14.57. Found: C, 51.20; H, 4.15; N, 7.76; Br, 14.67.

The NMR spectrum indicated a small amount of dehydrohalogenated product which accounts for the high C analysis.

Method II. To a solution of 6-(2-phenylacetamido)penicillanic acid *p*-nitrobenzyl ester 1-oxide (2.42 g, 5 mmol) in 150 mL of 1,2-dibromethane was added 1-(2-bromoethyl)quinolinium bromide (1.6 g, 5 mmol). The mixture was heated for 16 h at 85 °C. The solvent was washed with water, mixed with charcoal, dried over magnesium sulfate, and flash evaporated to an oil which was chromatographed on 40 g of silica gel eluted with ether. The desired product crystallized in the eluent: collected 1.32 g (48% yield); melting point and NMR identical with those described in method I. Anal. Found: C, 50.80; H, 4.02; N, 7.69.

3-Chloro-3-methyl-8-oxo-7-(2-phenylacetamido)-5-thia-1-azabicyclo[4.2.0]octane-2-carboxylic Acid (8a). 3-Chloro-3-methyl-8-oxo-7-(2-phenylacetamido-5-thia-1-azabicyclo[4.2.0]octane-2-carboxylic acid *p*-nitrobenzyl ester (1.06 g, 2.1 mmol) was hydrogenated in 60 mL of ethyl acetate over 1 g of 10% palladium on charcoal. The catalyst was filtered and washed with ethyl acetate. The filtrate was extracted with ice-cold saturated sodium bicarbonate (100 mL). The aqueous phase was covered with fresh ethyl acetate (100 mL) and was acidified with concentrated hydrochloric acid to pH 1.5. The organic phase was separated, dried, and flash concentrated to a total of 10 mL. The residual solution was added to pentane to give 475 mg (61% yield) of the desired acid, which did not melt, but slowly decomposed above 90 °C: NMR (Me_2SO-d_6) ppm (δ), 1.75 (s, 3, CH_3), 3.32 (ABq, δ 0.975 ppm, J = 14.2 Hz, 2-CH_2), 3.63 (s, 2, $CH_2C{=}O$) 4.55 (s, 1, 4-H), 5.22 (s, 1, 6 H), 5.51 (q, 1, 7 H), 7.34 (s, 5, C_6H_5), 9.1 (d, 1, NH).

Anal. Calcd for $C_{16}H_{17}ClN_2O_4S$ (mol wt 368.81): C, 52.10; H. 4.65; N, 7.60; Cl, 9.60; S, 8.70. Found: C, 52.00; H, 4.60; N, 7.48; Cl, 9.29; S, 8.29.

3-Bromo-3-methyl-8-oxo-7-(2-phenylacetamido)-5-thia-1-azabicyclo[4.2.0]octane-2-carboxylic Acid (8b). The title compound was prepared in 65% yield from the *p*-nitrobenzyl ester by the same procedure as that described for **8a**: NMR ($DCCl_3$) ppm (δ), 1.83 (s, 3, CH_3), 3.18 (ABq, δ 0.875 ppm, J = 15 Hz, 2-CH_2), 3.70 (s, 2, $CH_2C{=}O$) 4.81 (s, 1, 4 H), 5.28 (s, 1, 6 H), 5.60 (q, 1, 6 H), 6.85 (exchangeable protons) 7.40 (s, 5, C_6H_5).

3-Methyl-8-oxo-7-(phenylacetamido)-5-thia-1-azabicyclo-

[4.2.0]oct-2-ene-2-carboxylic Acid *p*-Nitrobenzyl Ester, 2. To a solution of 6-(2-phenylacetamido)penicillanic acid *p*-nitrobenzyl ester 1-oxide (1.2 g, 2.47 mmol) in 100 mL of 1,2-dichloroethane was added pyridine (200 mg, 2.47 mmol). The solution was heated to reflux for 29 h, it was then washed with dilute hydrochloric acid and water, treated with charcoal, dried, and flash evaporated. The residual oil was chromatographed on 25 g of silica gel using 2:1 diethyl ether, dichloromethane as eluents. Evaporation of the combined eluents gave 0.51 g (45% yield) of the title compound, **2**, melting point and NMR identical to the literature values,[2b] and 0.26 g (22% yield) of the known isomer α-isopropylidene-3-oxo-4-(2-phenylacetamido)-4-isothiazoline-2-acetic acid *p*-nitrobenzyl ester (**3**).

When this reaction was carried out under the same conditions as method I, but replacing the pyridine by other amines such as picolines, lutidine, quinoline, etc., larger amounts of the isothiazoline isomer and small amounts of the title compound were isolated.

Dehydrohalogenation of 5a. To a solution of **5a** (1 g, 2 mmol) in 25 mL of acetone was added 1,5-diazabicyclo[4.3.0]non-5-ene (247 mg, 2 mmol); the purple solution was stirred for 15 min, and was added to water. A solid precipitated which was filtered, dissolved in dichloromethane, dried over magnesium sulfate, treated with charcoal, and evaporated to a solid, 800 mg (86.5% yield), whose NMR spectrum was identical with that of compound **2** obtained by method I.

7-Amino-3-chloro-3-methyl-8-oxo-5-thia-1-azabicyclo-[4.2.0]octane-2-carboxylic Acid *p*-Nitrobenzyl Ester (7a). To an ice-cold solution of 3-chloro-3-methyl-8-oxo-7-(2-phenylacetamido)-5-thia-1-azabicyclo[4.2.0]octane-2-carboxylic acid *p*-nitrobenzyl ester (5.04 g, 10 mmol) in 100 mL of dichloromethane were added in rapid succession phosphorus pentachloride (3.1 g, 15 mmol) and *N,N*-dimethylaniline (1.8 g, 15 mmol). The mixture was stirred at 0 °C for 15 min and at 25 °C for 3 h, then 30 mL of absolute methyl alcohol was added and the solution was further stirred for 1 h. The solvent was flash evaporated. To the residue were added 25 mL of ethyl acetate and 30 mL of water, and the mixture was stirred thoroughly. The crystalline solid thus obtained was filtered and air-dried to give 2.75 g (65.2% yield) of product, which decomposed above 160 °C: NMR (Me_2SO-d_6) ppm (δ), 1.74 (s, 3, 3-CH_3), 3.38 (ABq, δ 0.45 ppm, J = 14.5 Hz, 2-CH_2), 4.92 (s, 1, 4 H), 5.0 (d, 1, 6 H), 5.34 (d, 1, 7 H), 5.51 (s, 2, CO_2CH_2), 8.05 (ABq, δ 0.525 ppm, J = 7.5 Hz, *p*-$NO_2C_6H_4$).

Anal. Calcd for $C_{15}H_{16}N_3ClO_5S$·HCL·0.5H_2O: C, 41.77; H, 4.21; N, 9.74. Found: C, 41.54; H, 4.11; N, 9.80.

3-Chloro-3-methyl-8-oxo-7-[2-(2-thienylacetamido)]-5-thia-1-azabicyclo[4.2.0]octane-2-carboxylic Acid *p*-Nitrobenzyl Ester (9a). To a mixture of 7-amino-3-chloro-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]octane-2-carboxylic acid *p*-nitrobenzyl ester hydrochloride (1.05 g, 2.5 mmol), and 2-thienylacetyl chloride (0.4 g, 2.5 mmol) in 50 mL of dichloromethane, *N,N*-dimethylaniline (0.61 g 5 mmol) was added. The mixture was stirred at 0 °C for 1 h and was then washed with ice-cold 1 N hydrochloric acid and ice-cold water. The organic phase was dried, decolorized with charcoal, concentrated to 10 mL, and added to vigorously stirred pentane. The product, 1.04 g (86% yield), was obtained as a white powder which decomposed at ~70 °C. NMR (Me_2SO-d_6 ppm (δ) 1.69 (s, 3, 3-CH_3), 3.28 (Abq, δ, 0.575 ppm, J = 16 Hz, 2-CH_2), 3.85 (s, 2, CH_2CO), 4.86 (s, 1, 4 H), 5.25 (d, 1, 6 H), 5.42 (s, 2, CO_2CH_2), 5.53 (d, 1, 7 H) and 7.0 (m, 2), and 7.4 (m, 1, 2-thienyl) and 8.04 (ABq, δ 0.575 ppm, J = 8 Hz, *p*-$NO_2C_6H_4$).

Anal. Calcd for $C_{21}H_{20}N_3ClO_6S_2$: C, 49.46; H, 3.95; N, 8.24. Found: C, 49.43; H, 3.92; N, 8.01.

3-Chloro-3-methyl-8-oxo-7-[2-(2-thienylacetamido)]-5-thia-1-azabicyclo[4.2.0]octane-2-carboxylic Acid (10a). The title compound was prepared from the ester **9a** by the same procedure as that described in the preparation of **8a**. The product obtained in 70% yield decomposed above 80 °C: NMR ($DCCl_3$) ppm (δ), 1.73 (s, 3, 3-CH_3), 3.20 (ABq, 1.0 ppm, J = 14.5 Hz, 2-CH_2), 3.88 (s, 2, CH_2CO) 4.70 (s, 1, 4-H), 5.26 (d, 1, 6-H), 5.60 (d, 1, 7 H), 7.0 (m, 2) and 7.3 (m, 1, 2-thienyl).

Anal. Calcd for $C_{14}H_{15}N_2ClO_4S_2$: C, 44.85; H, 4.03; N, 7.47. Found: C, 44.59; H, 4.19; N, 7.14.

Registry No.—**1**, 29124-80-9; **2**, 34104-27-3; **3**, 58681-34-8; **4a**, 7041-27-2; **5a**, 58865-64-8; **5b**, 58844-04-5; **6**, 58844-03-4; **7a** HCl, 62532-97-2; **8a**, 58844-05-6; **8b**, 58844-06-7; **9a**, 58844-07-8; **10a**, 58844-08-9; pyridine, 110-86-1; 1,2-dichloroethane, 75-09-2; quinoline, 91-22-5; 1,2-dibromoethane, 106-93-4; *N,N*-dimethylaniline, 121-69-7; 2-thienylacetyl chloride, 39098-97-0.

References and Notes

(1) Address correspondence to this author at the Weizmann Institute of Science, Rehovot, Israel, Department of Organic Chemistry.
(2) (a) R. B. Morin, B. G. Jackson, R. A. Mueller, E. R. Lavagnino, W. B. Scanlon, and S. L. Andrews, *J. Am. Chem. Soc.*, **91**, 1401 (1969); (b) D. H. R. Barton, F. Comer, D. G. T. Creig, P. G. Sammes, C. M. Cooper, G. Hewitt, and W. G. E. Underwood, *J. Chem. Soc., C*, 3540 (1971).
(3) W. J. Gottstein, P. F. Misco, and L. C. Cheney, *J. Org. Chem.*, **37**, 2765 (1972).
(4) M. Numata, Y. Imashiro, I. Minamida, and M. Yamaoka, *Tetrahedron Lett.*, 5097 (1972).
(5) T. Kamiya, T. Teraji, Y. Saito, M. Hashimoto, O. Nakaguchi, and T. Oku, *Tetrahedron Lett.*, 3001 (1973).
(6) S. Kukolja, S. R. Lammert, M. R. Gleissner, and A. I. Ellis, *J. Am. Chem. Soc.*, **97**, 3192 (1975).
(7) J. J. de Koning, H. J. Kooreman, H. S. Tan, and J. Verweij, *J. Org. Chem.*, **40**, 1346 (1975).
(8) M. Fukumura, N. Hamma, and T. Nakagome, *Tetrahedron Lett.*, 4123 (1975).
(9) J. D. Barnhurst, *J. Org. Chem.*, **26**, 4520 (1961).
(10) S. Kukolja, N. D. Jones, M. O. Cheney, T. A. Elzey, M. R. Gleissner, J. W. Paschal, and D. E. Dorman, *J. Org. Chem.*, **40**, 2388 (1975).
(11) See Penicillin and Cephalosporin Sulfoxides Section: (a) A. Nudelman, *Int. J. Sulfur Chem., Part B*, **7**, 241 (1975); (b) *Phosphorous Sulfur*, **2**, 51 (1976).
(12) B. Fechtig, H. Peter, H. Bickel, and E. Vischer, *Helv. Chim. Acta*, **57**, 1108 (1969).