quantitatively analyzed by GC–MS.

The mercurous trifluoroacetate $Hg_2(O_2CCF_3)_2$ which crystallized directly from dichloromethane in 90% yield was analyzed directly. Anal. Calcd for $HgO_2C_2F_3$: C, 7.66; F, 18.17. Found:[45] C, 7.91; F, 18.41. Mp 281–285 °C.

Quantum yield was determined by ferrioxalate actinometry[46] using light from a 500-W Eimac Xe lamp through interference filters (vide supra). The constant light intensity of this system was established by serially irradiating identical tubes for varying lengths of time. Typically the $Fe(Phen)_3^{3+}$ absorbance at λ 516 nm increased as follows with time (s): 0.48 (10), 0.83 (20), 1.23 (30), 1.72 (40), 1.83 (45). This shows a linear relationship of 0.15 einstein s^{-1} with a correlation coefficient of 0.9978.

Deuterium labeling studies were carried out with HMB-d_{18} and protio trifluoroacetic acid. Analysis of the products by GC–MS (Hewlett-Packard 5890-5790 B) showed the following cracking pattern for recovered HMB-d_{18}, m/z (relative intensity): 181 (6), 180 (50), 179 (10), 178 (4), 163 (11), 162 (100), 161 (18), 160 (1), 146 (3). These data compare with those of starting HMB-d_{18} of m/z (relative intensity) 181 (6), 180 (49), 179 (7), 178 (3), 163 (12), 162 (100), 161 (12), and 146 (2) and of the all protio-HMB of m/z (relative intensity) 163 (5), 162 (40), 161 (5), 148 (11), 147 (100), and 145 (2). The pentamethylbenzyl trifluoroacetate from the CT photochemistry of HMB-d_{18} showed the following mass spectrum, m/z (relative intensity): 292 (9), 291 (58), 290 (7), 179 (11), 178 (80), 177 (26), 176 (100), 175 (35). This compares with that derived from the all protio analogue, m/z (relative intensity): 275 (9), 274 (49), 162 (12), 161 (94), 160 (100), 148 (2), 147 (6), 146 (4), 145 (24). Thus the HMB-d_{18} recovered from the photolysis showed no evidence of proton exchange. However a comparison of the mass spectrum of the benzylic ester shows fragment ions with m/z 176 (100) and 178 (80) which are considered to be equivalent to 160 (100) and 161 (94) in the all protio analogue. Additional ions with m/z 175 (35) and 177 (26) can be accounted for if one of the 17 deuterium atoms has been replaced with a proton, i.e., $C_{14}D_{16}HF_3O_2$.

(45) Analysis performed by Galbraith Laboratories, Knoxville, TN.
(46) Calvert, J. G.; Pitts, J. N., Jr. *Photochemistry*; Wiley: New York, 1966.

Acknowledgment. We thank Halocarbon Products, Inc., for a generous supply of trifluoroacetic acid, Dr. J. C. Huffman for the X-ray structure in Figure 2, and the National Science Foundation and Robert A. Welch Foundation for financial support.

Registry No. HMB, 87-85-4; HgT_2, 13257-51-7; [HMB,HgT_2], 77001-38-8; Hg, 7439-97-6; ^{199}Hg, 14191-87-8; $HMB^{\bullet+}$, 34473-51-3; mercurous trifluoroacetate, 2923-15-1; pentamethylbenzyl trifluoroacetate, 35843-80-2.

Supplementary Material Available: Tables of the final atomic coordinates, bond lengths, bond angles, and anisotropic thermal parameters for the mercury(II) trifluoroacetate and hexamethylbenzene EDA complex (6 pages). Ordering information is given on any current masthead page.

Oxidation Studies on β-Lactam Antibiotics. The 6-(Diacylamino)penicillins

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Received August 6, 1985

The oxidation of the 6-(diacylamino)penicillins is a convenient, high yield route to the pencillin 1α-sulfoxides. The yield of the 1α-sulfoxide is dependent on the solvent, the temperature, the C-3 ester function, and the substituent at the C-2 position. The 6-(diacylamino)penicillin 1α-sulfoxides are readily converted to the penicillin 1α-sulfoxides on treatment with zinc and ammonium acetate.

The Morin rearrangements[1] of penicillin sulfoxides, **1**, to the desacetoxycephalosporins, **3**, has been shown to proceed via the azetidinone sulfenic acids, **2**.[2] This sigmatropic reaction is completely stereospecific, a proton from the C-2 methyl group cis to the sulfoxide S–O bond being abstracted to form the sulfenic acid, **2**. (See Scheme I.)

While unimportant in the case of penicillins (in which the *gem*-dimethyl groups are equivalent), this factor becomes significant in the case of the 2-(substituted-methyl)penicillins and the 2β-isomers, **4** (Scheme II), which are readily available.[3]

The 2β-(substituted-methyl)penicillin 1β-sulfoxides, **5**, are the major products formed by oxidation of compounds **4** (in which the C-6 substituent is an amide group) by the usual oxidants. This preferential formation of the 1β-sulfoxides, **5**, is explained by steric approach control, in which the amide proton bonds to the oxidant and, hence, directs the oxidation from the hindered β-face.[4] The thermolysis of these 2β-(substituted-methyl)penam 1β-sulfoxides, **5**, generates the vinylic azetidinone sulfenic acids, **6**.[5]

Table I. Percent α-Isomer[a,b] as a Function of Temperature[c]

substrate	reaction temp (°C)		
	−20 to −15	0	25
11a	44	58	76
11d	75	100	100

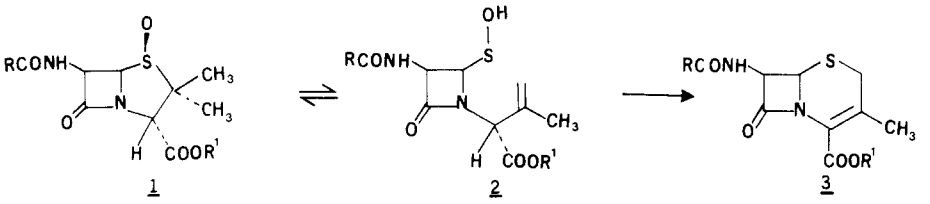
[a] Figures represent the average of three separate experiments. [b] Percent α-isomer is given on the basis of NMR; rest β-isomer formed. [c] Conditions: MCPBA/CH_2Cl_2/30 min.

(1) Morin, R. B.; Jackson, B. G.; Mueller, R. A.; Lavagnion, E. R.; Scanlon, W. B.; Andrews, S. L. *J. Am. Chem. Soc.* **1963**, *85*, 1896; **1969**, *91*, 1401.
(2) Cooper, R. D. G.; Spry, D. O. "Cephalosporin and Penicillin: Chemistry and Biology"; Flynn, E. H., Ed.; Academic Press: New York, 1972; 183–254.
(3) Kamiya, T.; Teraji, T.; Saito, Y.; Hashimoto, M.; Nakaguchi, O.; Oku, T. *Tetrahedron Lett.* **1973**, 3001.
(4) Cooper, R. D. G.; De marco, P. V.; Cheng, J. C.; Jones, N. D. *J. Am. Chem. Soc.* **1969**, *91*, 1408.
(5) Micetich, R. G., unpublished work.

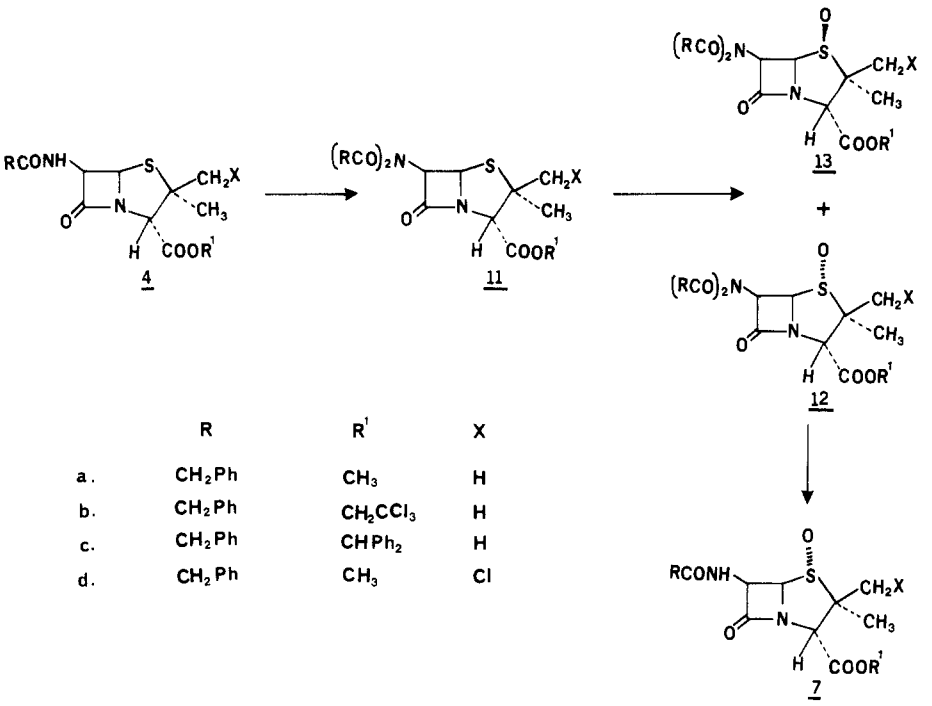
† University of Alberta.
‡ Ayerst Laboratories.

0022-3263/86/1951-1811$01.50/0

Scheme I



Scheme II



	R	R'	X
a.	CH_2Ph	CH_3	H
b.	CH_2Ph	CH_2CCl_3	H
c.	CH_2Ph	$CHPh_2$	H
d.	CH_2Ph	CH_3	Cl

In contrast, thermolysis of the 2β-(substituted-methyl)penam 1α-sulfoxides, **7**, generate the allylic azetidinone sulfenic acids, **8**[6] and these compounds have been utilized to prepare the 3-(substituted-methyl)cephams, **9a**, 3-methylenecephams, **9b**, and 2,2-bis(halomethyl)penams, **10**.[6,7]

The use of oxidants such as iodobenzene dichloride[8] or ozone[9] produces a mixture of the penam 1α-sulfoxides and penam 1β-sulfoxides, and chromatography is necessary for separation. Those penicillins (or cephalosporins) in which the C-6 (or C-7) substituent lacks any NH proton produce the 1α-sulfoxides as the major product on oxidation. Thus 6-phthalimidopenicillins,[10] the *N*-nitrosopenicillins,[11] cephalosporin Schiff bases,[12] and 6-isocyanatocephalosporins[12] all produce the 1α-sulfoxides as the major products on oxidation. However, the 6-methoxyimidopenicillins[13] and 6,6-dihydropenicillins,[14] both types of compounds lacking a C-6 NH proton, produce the 1β-sulfoxides as the major products with peracids.

We have found that the 6-(diacylamino)penicillins, **11** (Scheme III),[15] provide a very useful route to the penicillin 1α-sulfoxides, **12** and **7**. In this case the ratio of the 1α-sulfoxide, **12**, to 1β-sulfoxide, **13**, formed in the oxidation step, is influenced by the solvent, the C-3 ester group, the temperature of the reaction, and the substituent X in the case of the 2β-(substituted-methyl)penicillins, **4**.

The 6-(diacylamino)penicillins, **11**[15] (Table I), required as starting material, were prepared by converting the 6-amidopenicillins, **4**, to the respective 6-chloroimines by using PCl_5 and pyridine. Reaction with the sodium salt of the acid gave the desired 6-(diacylamino)penams, **11**. These compounds on oxidation with peracids under appropriate conditions gave the 1α-sulfoxides, **12**, almost exclusively. These 6-(diacylamino)penicillin 1α-sulfoxides, **12**, on treatment with zinc and ammonium acetate gave the 6-amidopenicillin 1α-sulfoxides, **7**.

Results and Discussion

The oxidation of methyl 6-(bis(phenylacetyl)amino)-penicillanate, **11a**, with *m*-CPBA in dichloromethane at 0 °C gave a mixture (58:42) of the 1α-, **12a**, and the 1β-

(6) Uyeo, S.; Aoki, T.; Itani, H.; Tsuji, T.; Nagata, W. *Heterocycles* **1978**, *10*, 99.
(7) Spry, D. O.; *Chem. Commun.* **1973**, 259. Kukolja, S.; Lammert, S. R.; Gleissner, M. R. B.; Ellis, A. I. *J. Am. Chem. Soc.* **1976**, *98*, 5040. Koppel, G. A.; Kinnick, M. D.; Nummy, L. J. *J. Am. Chem. Soc.* **1977**, *99*, 2822. Koppel, G. A.; McShane, L. J. *J. Am. Chem. Soc.* **1978**, *100*, 288.
(8) Barton, D. H. R.; Comer, F.; Sammes, P. G. *J. Am. Chem. Soc.* **1969**, *91*, 1529.
(9) Spry, D. O. *J. Org. Chem.* **1972**, *37*, 793.
(10) Cooper, R. D. G.; De marco, P. V.; Spry, D. O. *J. Am. Chem. Soc.* **1969**, *91*, 1528.
(11) Uyeo, S.; Aoki, T.; Itani, H.; Tsuji, T.; Nagata, W. *Heterocycles* **1978**, *11*, 305.
(12) De Koning, J. J.; Marx, A. F.; Poot, M. M.; Smid, P. M.; Verweij, J. "Recent Advances in the Chemistry of β-Lactam Antibiotics"; Elks, J., Ed.; The Chemical Society: UK, 1976; p 171.
(13) Micetich, R. G.; Singh, R. *Heterocycles* **1985**, *23*, 1445.
(14) Hall, T. W.; Maiti, S. N.; Micetich, R. G.; Spevak, P.; Yamabe, S.; Ishida, N.; Kajitani, M.; Tanaka, M.; Yamasaki, T. "Recent Advances in Chemistry of β-Lactam Antibiotics"; Brown, A. G., Roberts, S. M., Eds.; The Chemical Society: UK, 1985; 242.
(15) Oszczapowiez, I. B.; Cieslak, J. *Rocez. Chem.* **1971**, *45*, 111; Chem. Abstr. **1971**, *75*, 5784.

Scheme III

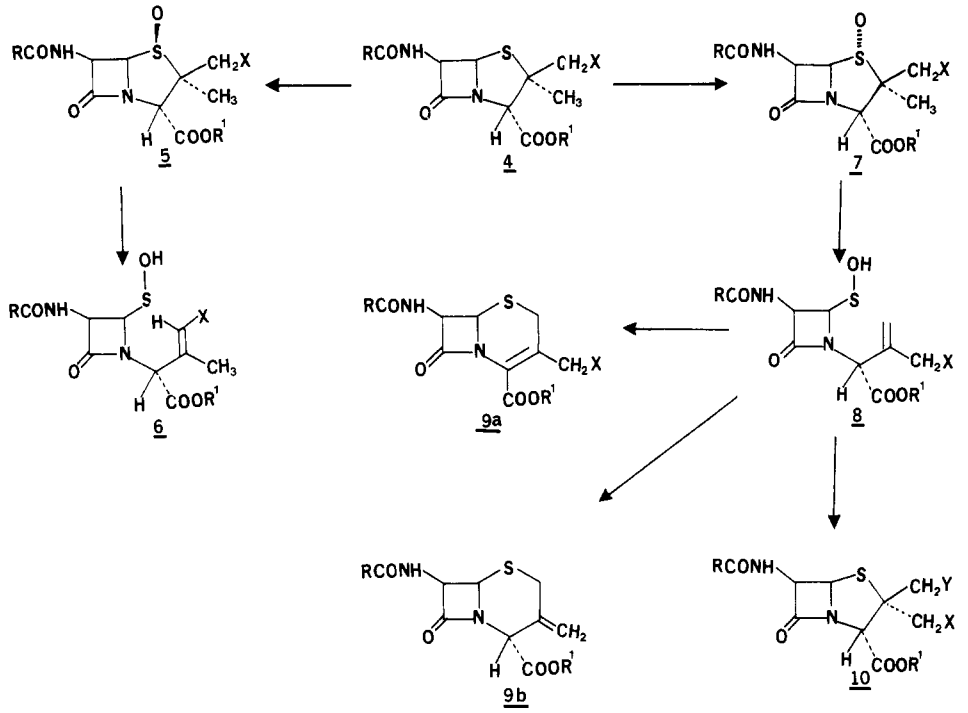


Table II. Percent α-Isomer[a,b] as a Function of Solvent, Ester Group, C_2-Substituent, and Oxidant[d]

	solvent							
substrate	$ClCH_2CH_2Cl$	CH_2Cl_2	$CHCl_3$	CCl_4	HCOOMe	AcOEt	PhH	PhMe
11a	72	76 (58[c])	52	95	75	95	98 (94[c])	96
11b		57					100	
11c		43					100	
11d		100					100	

[a] The figures represent the average of three separate experiments. [b] Percent α-isomer is given on the basis of NMR, the remaining portion is the β-isomer. [c] In this case the oxidant is H_2O_2/AcOH [d] Conditions: MCPBA([c]H_2O_2/AcOH)/25 °C/30 min ([c]24 h).

sulfoxide, **13a**, which was separated by silica gel column gradient elution chromatography using hexane and ethyl acetate. The stereochemical assignment for the sulfoxides was made from their ^1H NMR spectra (solvent induced shifts).[4,16]

The ratio of the 1α-sulfoxide, **12a**, to 1β-sulfoxide, **13a**, in this oxidation varied considerably with temperature. (See Table I.) This ratio was determined from the ^1H NMR spectrum of the crude reaction product, the integration of the signals of the 2-CH_3 and 3-CH, providing a measure of the concentrations of the 1α- and 1β-sulfoxides. In the two compounds, **11a** and **11d**, investigated, under otherwise identical conditions, there was a significant increase in the 1α-sulfoxide content with an increase in temperature. Thus with **11a**, the 1α-sulfoxide content rose from 44% at a temperature of −15 to −20 °C to 76% at 25 °C. This is the first time, as far as we know, that such an effect has been observed in these oxidations.

A possible explanation for the results in Table I is a temperature-dependent isomerization of the β-sulfoxide to the more stable α-product. However, we found that the α-sulfoxide, **12a**, is stable to thermolysis in benzene (for 1.5 h); the β-sulfoxide, **13a**, is partially decomposed (15–20%) after heating in benzene (1.5 h), but there is no evidence in the ^1H NMR spectrum of the product for the formation of the α-sulfoxide in this reaction, so the above suggestion for our observed results (Table I) appears unlikely.

Besides temperature, we found that the solvent, the C-3 ester group, the C-2 substituent of compounds **11**, and the oxidant used also affected the ratio of the 1α-, **12**, and 1β-sulfoxides, **13**, formed. These data are summarized in Table II.

In the case of chlorinated solvents the yield of the 1α-sulfoxide, **12a**, varied from a low of 52% for chloroform to a high of 95% for carbon tetrachloride; with esters such as methyl formate the yield of **12a** was 75%, while ethyl acetate gave 95% and hydrocarbon solvents (benzene and toluene) gave about 98% yields. There is, hence, a considerable variation with changes in solvent, and as far as we know, this is also the first time that such an effect has been observed. With an increase in the steric bulk of the ester function there is an increase in the proportion of the 1β-sulfoxide formed, and this effect is more dramatic in halogenated solvents such as methylene chloride than in hydrocarbon solvents. Substitution of the C-2 β-methyl group as in compound **11d** (X = Cl) results in increased yields of the 1α-sulfoxide, **12d** (X = Cl) – (100%).

The ratio of the α-sulfoxide **12** and β-sulfoxide **13** formed in these oxidations is also affected by the presence of impurities in compound **11**. The results described in this paper are based on the purified (by silica gel chromatography), colorless compounds **11**.

These observations can be explained by the formation of complexes of compound **11** (solutes) with the solvent. This concept has been utilized by Ledall to explain the ^1H NMR solvent shifts of dimethyl sulfoxide,[17] and by Cooper

(16) De marco, P. V.; Nagarajan, R. "Cephalosporin and Penicillin: Chemistry and Biology"; Flynn, E. H. Ed.; Academic Press: New York, 1972; p 353 and references cited therein.

(17) Leddal, T. *Tetrahedron Lett.* **1968**, 1683.

Table III. Physical Constants and Spectroscopic Data of (Diacylamino)penicillins 11, S-Oxides 12, and (Monoacylamino)penicillins 1α-S-Oxides 7

compd	yield,[a] %	IR (KBr) cm^{-1}	NMR ($CDCl_3$ δ ppm)	EIMS m$^+$ calcd	EIMS m$^+$ found
11a	36	2992, 1784, 1748, 1715, 1682	1.40 (s, 3 H), 1.60 (s, 3 H), 3.76 (s, 3 H), 3.97 and 4.09 (ABq, J = 16.5 Hz, 4 H), 4.50 (s, 1 H), 5.20 (d, J = 3.66 Hz, 1 H), 5.42 (d, J = 3.66 Hz, 1 H), 7.14 (m, 4 H), 7.30 (m, 6 H)	$C_{25}H_{26}N_2O_5S$ (466.1593)	$C_{17}H_{20}N_2O_4S$ (348.1144)
11b	40	2971, 1782, 1758, 1716, 1680	1.50 (s, 3 H), 1.66 (s, 3 H), 3.97 and 4.09 (ABq, J = 16.9 Hz, 4 H), 4.64 (s, 1 H), 4.70 and 4.86 (ABq, J = 11.8 Hz, 2 H), 5.22 (d, J = 4.22 Hz, 1 H), 5.35 (d, J = 4.22 Hz, 1 H), 7.18 (7, 4 H), 7.32 (m, 6 H)	$C_{26}H_{25}N_2O_5SCl_3$ (584.0510)	$C_{18}H_{19}N_2O_4SCl_3$ (466.0134)
11c	42	2992, 1782, 1743, 1712, 1681	1.20 (s, 3 H), 1.60 (s, 3 H), 3.98 and 4.09 (ABq, J = 15.8 Hz, 4 H), 4.60 (s, 1 H), 5.22 (d, J = 4.16 Hz, 1 H), 5.44 (d, J = 4.16 Hz, 1 H), 6.98 (S, 1 H), 7.18 (7, 4 H), 7.32 (m, 16 H)	$C_{37}H_{34}N_2O_5S$ (618.2177)	$C_{29}H_{28}N_2O_4S$ (500.1770)
11d	59	2992, 1785, 1746, 1716, 1680	1.50 (s, 3 H), 3.52 and 3.84 (ABq, J = 12 Hz, 2 H), 3.76 (s, 3 H), 3.97 and 4.09 (ABq, J = 17 Hz, 4 H), 4.98 (s, 1 H), 5.16 (d, J = 4.0 Hz, 1 H), 5.40 (d, J = 4.0 Hz, 1 H), 7.18 (m, 4 H), 7.30 (m, 6 H)	$C_{25}H_{25}N_2O_5SCl$ (500.1203)	$C_{17}H_{19}N_2O_4SCl$ (382.0754)
12a	67	2992, 1797, 1741, 1694	1.20 (s, 3 H), 1.72 (s, 3 H), 3.82 (s, 3 H), 4.08 and 4.14 (ABq, J = 17.24 Hz, 4 H), 4.30 (d, J = 4.30 Hz, 1 H), 4.52 (S, 1 H), 5.38 (d, J = 4.30 Hz, 1 H), 7.18 (m, 4 H), 7.34 (m, 6 H)	$C_{25}H_{26}N_2O_6S$ (482.1542)	$C_{17}H_{18}N_2O_4S$ (346.0988)
12b	65	2992, 1799, 1766, 1726, 1688	1.28 (s, 3 H), 1.76 (s, 3 H), 4.08 and 4.14 (ABq, J = 16.2 Hz, 4 H), 4.26 (d, J = 4.23 Hz, 1 H), 4.64 (s, 1 H), 4.66 and 4.98 (ABq, J = 12.3 Hz, 2 H), 5.38 (d, J = 4.23 Hz, 1 H), 7.16 (m, 4 H), 7.36 (m, 6 H)	$C_{26}H_{25}N_2O_6SCl_3$ (600.0459)	$C_{18}H_{17}N_2O_4SCl_3$ (463.9916)
12c	52	2997, 1797, 1743, 1692	0.94 (s, 3 H), 1.66 (s, 3 H), 4.04 and 4.10 (ABq, J = 15.8 Hz, 4 H), 4.20 (d, J = 4.12 Hz, 1 H), 4.60 (s, 1 H), 5.34 (d, J = 4.12 Hz, 1 H), 7.00 (s, 1 H), 7.14 (m, 4 H), 7.38 (m, 16 H)	$C_{37}H_{34}N_2O_6S$ (634.2126)	$C_{29}H_{26}N_2O_4S$ (498.1613)
12d	66	2992, 1799, 1744, 1693	1.36 (s, 3 H), 3.83 (s, 3 H), 4.05 and 4.13 (ABq, J = 11.9 Hz, 2 H), 4.14 (s, 4 H), 4.40 (d, J = 4.75 Hz, 1 H), 4.72 (s, 1 H), 5.46 (d, J = 4.75 Hz, 1 H), 7.16 (m, 4 H), 7.36 (m, 6 H)	$C_{25}H_{25}N_2O_6SCl$ (516.1152)	$C_{17}H_{17}N_2O_4SCl$ (380.0598)
7a	60	3279, 3000, 1796, 1753, 1672	1.28 (s, 3 H), 1.64 (s, 3 H), 3.60 (s, 2 H), 3.80 (s, 3 H), 4.40 (s, 1 H), 4.68 (d, J = 4.0 Hz, 1 H), 5.12 (q, J_1 = 7.8 Hz, J_2 = 4 Hz, 1 H), 7.15 (d, J = 7.8 Hz, 1 H), 7.30 (m, 5 H)	$C_{17}H_{20}N_2O_5S$[c]	nd[e]
7c	63	3287, 3033, 1795, 1749, 1670	1.04 (s, 3 H), 1.62 (s, 3 H), 3.62 (s, 2 H), 4.52 (s, 1 H), 4.66 (d, J = 4.2 Hz, 1 H), 5.24 (q, J_1 = 7.5 Hz, J_2 = 4.2 Hz, 1 H), 6.74 (d, J = 7.5 Hz, 1 H), 7.00 (s, 1 H), 7.36 (m, 15 H)	$C_{29}H_{20}N_2O_5S$	nd[e]
7d	43	3312, 2984, 1794, 1748, 1667	1.40 (s, 3 H), 3.60 (s, 2 H), 3.84 (s, 3 H), 4.08 and 4.12 (ABq, J = 12.5 Hz, 2 H), 4.76 (d, J = 4.30 Hz, 1 H), 4.78 (s, 1 H), 5.12 (q, J_1 = 7.30 Hz, J_2 = 4.30 Hz, 1 H), 7.30 (m, 6 H)	$C_{17}H_{19}N_2O_5SCl$[d]	nd[e]

[a] All the compounds are foams. The yields reported are affter purification by column chromatography. [b] In the case of the sulfides the significant ion represents m$^+$ ($-C_6H_5CHCO$), while in case of the sulfoxides this is m$^+$ ($-C_6H_5CH_2COOH$). [c] Reference 8. [d] Reference 11. [e] Not done.

and co-workers to confirm the structures of penicillin 1α- and 1β-sulfoxides from the solvent induced ^{1}H NMR shift values.[4] It appears probable that in the case of compounds **11**, solvates are formed in which the solvent binds to the hindered β-face. The variation in product composition with solvent is probably due to a difference in the "stability" of these solvates or upon the relative orientation of the solute and solvent molecule in the solvate. The effect of temperature could again be due to a change in the relative orientation of the solvate and solvent molecule in the solvate.

Experimental Section

NMR spectra were recorded on a Bruker AM-300 spectrometer; chemical shifts are reported as δ values relative to tetramethylsilane as internal standard. IR spectra were recorded on a Nicolet DX-FTIR spectrophotometer.

General Procedure. Synthesis of 6β-(Bis(phenylacetyl)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2α-carboxylate Esters (11). A mixture of the ester benzylpenicillin (24.5 mmol) and pyridine (100 mmol) in benzene (60 mL) was cooled in an ice bath, and PCl_5 (25 mmol) was added in portions over a period of 10 min. After stirring at ice temperature for 1 h, the precipitate formed was filtered and washed with benzene. The combined filtrates were washed in sequence with ice cold aqueous $NaHCO_3$, brine, H_2O, aqueous $CuSO_4$, and brine, then dried over Na_2SO_4, and concentrated to give the 6-(chloroimino)penicillin as a brown foam. The crude product was dissolved in anhydrous toluene (150 mL), and sodium phenylacetate (24.5 mmol) was added. The mixture was stirred at 55–60 °C under nitrogen for 1.5 h. The reaction mixture was concentrated, and the residue was taken up in ethyl acetate. The solution was washed with ice cold $NaHCO_3$ and water, dried over Na_2SO_4, filtered, and concentrated to give the crude product as a pale brown foam. Gradient elution chromatography on silica gel using ethyl acetate/hexane gave the title compound and also some of the ester of benzylpenicillin (20–25%). The physical constants and spectroscopic data of these compounds (**11a–d**) are summarized in Table III.

Oxidation of 6β-(Bis(phenylacetyl)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2α-carboxylate Esters with *m*-Chloroperbenzoic Acid. *m*-Chloroperbenzoic acid (2.5 mmol) was added to a well-stirred solution of **11** (2.5 mmol) in benzene (50 mL) at room temperature. After 30 min, the TLC showed no starting material. The reaction mixture was washed successively with aqueous 5% sodium bisulfite, ice cold saturated $NaHCO_3$, water, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated to give the crude product as

a light yellow foam. Purification by gradient elution chromatography on silica gel using ethyl acetate/hexane as eluants gave the pure compounds. The physical constants and spectroscopic data of compounds (**12a-d**) are summarized in Table III.

Methyl 6β-(Phenylacetamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2α-carboxylate 1α-*S*-Oxide (7a). Zn (2.0 g) was added to a solution of **12a** (1.0 g) in THF (15 mL), followed by 1 M aqueous ammonium acetate (5 mL) under stirring at room temperature. After 2 h stirring at this temperature, the reaction mixture was filtered through Celite, and the filtrate was washed with water, diluted HCl, and brine solution successively. The organic phase was dried over Na_2SO_4 and concentrated, and the residue was chromatographed over silica gel by using ethyl acetate/dichlomethane (35:65) as eluant. The title compound was obtained as a white foam. Similarly, compounds **7c** and **7d** were prepared. The data for compounds (**7a**, **7c**, and **7d**) are summarized in Table III.

Acknowledgment. We thank the Alberta Heritage Foundation for Medical Research (AHFMR) for the award of a PDF to R.S.

Stereoselective Synthesis, Structural Studies, and Hydrolysis of Tricyclic Alkoxysulfonium Salts

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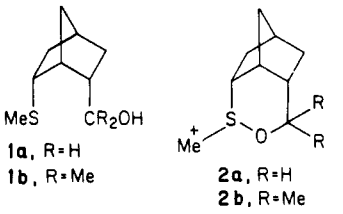
Received August 13, 1985

The crystal and molecular structure of endo tertiary alcohol **1b** determined by X-ray crystallographic techniques is reported. The molecule crystallizes in the space group $P2_1/n$ with a = 14.628 (7) Å, b = 5.648 (1) Å, c = 14.973 (8) Å, β = 113.78 (4)°, Z = 4. This structure features an unsymmetrical contra twist of the norbornyl skeleton and an intramolecular hydrogen bond between the sulfur atom and hydroxyl group with a very short distance of 3.119 Å. IR spectroscopic studies provide evidence for this intramolecular hydrogen bond in dilute solutions of endo tertiary alcohol **1b** but not in endo primary alcohol **1a**. Treatment of endo primary alcohol **1a** and endo tertiary alcohol **1b** with *tert*-butyl hypochlorite followed by mercury(II) chloride provides the corresponding alkoxysulfonium salts **2a** and **2b**, respectively. The crystal and molecular structures of these salts were determined by single-crystal X-ray studies. These salts crystallize in the space groups $P2_1/c$ and $P\bar{1}$, respectively, with a = 10.152 (3) Å, b = 11.857 (4) Å, c = 12.087 (3) Å, β = 97.98 (2)°, Z = 4, and a = 8.416 (3) Å, b = 9.678 (3) Å, c = 10.688 (4) Å, β = 87.72 (3)°, Z = 2, respectively. Both structures feature short S–O bond lengths of 1.58 (1) Å and 1.587 (4) Å, respectively, and large S–O–C (8) bond angles of 121.2 (9)° and 124.0 (3)°, respectively. Base hydrolysis of these salts produces the corresponding sulfoxides **11a** and **11b** by nucleophilic attack by hydroxide ion on sulfur.

Introduction

Alkoxysulfonium salts, $(RR^1SOR^2)^+ X^-$, are intermediates in several important reactions. Oxidation of alcohols,[1] halides, and *p*-toluenesulfonates[2] to aldehydes and ketones with dimethyl sulfoxide and related reactions[3] proceed via alkoxysulfonium salts. Neighboring-group participation by sulfoxide groups in the solvolysis of halides and sulfonates[4] and protonation of medium-sized ring keto sulfoxides[5] results in the formation of alkoxysulfonium salts. Our[6] and others[7] studies on the oxidation of sulfides with suitably disposed alcohol moieties reveal the generation of alkoxysulfonium salts. Such neighboring-group participation has important consequences such as the unusually low potential for oxidation of endo primary alcohol **1a**.[8] In addition, pulse radiolysis studies[9] on endo tertiary



alcohol **1b** show stabilization of the corresponding one-electron oxidation products which is ascribed to neighboring-group participation by the alcohol moiety.

Despite the importance of alkoxysulfonium salts only one detailed structure study had been communicated[10] prior to our initial report.[6] This paper presents the full details on the preparation and X-ray crystal structure study of alkoxysulfonium salt **2a** and similar studies on

(1) Moffat, J. G. In "Oxidation"; Augustine, R. L., Trecker, D. J., Eds; Dekker: New York, 1971; pp 1–64. Albright, J. D. *J. Org. Chem.* **1974**, *39*, 1977.

(2) Kornblum, N.; Jones, W. J.; Anderson, G. J. *J. Am. Chem. Soc.* **1959**, *81*, 4113. Ganem, B.; Boeckman, R. K., Jr., *Tetrahedron Lett.* **1974**, 917.

(3) Corey, E. J.; Kim, C. U. *J. Am. Chem. Soc.* **1972**, *94*, 7586. Corey, E. J.; Kim, C. U; Takeda, M. *Tetrahedron Lett.* **1972**, 4339. Corey, E. J.; Kim, C. U. *Ibid.* **1973**, 919. Corey, E. J.; Kim, C. U. *Ibid.* **1974**, 287. McCormick, J. P. *Ibid.* **1974**, 1701. Barton, D. H. R.; Forbes, C. P. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1614.

(4) Hogeveen, H.; Maccagnani, G.; Montanari, F. *Boll. Sci. Fac. Chim. Ind. Bologna* **1963**, *21*, 257; *Chem. Abstr.* **1964**, *60*, 10511e. Ghersetti, S.; Hogeveen, H.; Maccagnani, G.; Montanari, F.; Taddel, F. *J. Chem. Soc.*, **1963**, 3718. Montanari, F.; Daniel, R.; Hogeveen, H.; Maccagnani, G. *Tetrahedron Lett.* **1964**, 2685. Jones, D. N.; Saeed, M. A. *Proc. Chem. Soc. (London)* **1964**, 81. Martin, J. C.; Uebel, J. J. *J. Am. Chem. Soc.* **1964**, *86*, 2939. Buck, K. W.; Foster, A. B.: Perry, A. R.; Webber, J. M. *J. Chem. Soc., Chem. Commun.* **1965**, 433. Cinquini, M.; Colonna, S.; Montanari, F. *Tetrahedron Lett.* **1966**, 3181. Hogeveen, H.; Maccagnani, G.; Montanari, F. *J. Chem. Soc. C* **1966**, 1585. Cinquini, M.; Colonna, S.; Montanari, F. *Ibid.* **1967**, 1213. Foster, A. B.; Hasan, Q. H.; Hawkins, D. R.; Webber, J. M. *J. Chem. Soc., Chem. Commun.* **1968**, 1084. Jones, D. N.; Green, M. J.: Saeed, M. A.; Whitehouse, R. D. *J. Chem. Soc. C*, **1968**, 1362.

(5) Leonard, N. J.; Johnson, C. R. *J. Am. Chem. Soc.* **1962**, *84*, 3701. Leonard, N. J.; Rippie, W. L. *J. Org. Chem.* **1963**, *28*, 1957.

(6) Glass, R. S.; Setzer, W. N.: Prabhu, U. D. G.; Wilson, G. S. *Tetrahedron Lett.* **1982**, *23*, 2335.

(7) Kline, J.; Stollar, H. *Tetrahedron* **1974**, *30*, 2541. Hirschon, A. S.; Doi, J. T.; Musker, W. K. *J. Am. Chem. Soc.* **1982**, *104*, 725.

(8) Glass, R. S.; Duchek, J. R.; Klug, J. T.; Wilson G. S. *J. Am. Chem. Soc.* **1977**, *99*, 7349.

(9) Glass, R. S.; Hojjatie, M.; Wilson, G. S.; Mahling, S.; Göbl, M.; Asmus, K.-D. *J. Am. Chem. Soc.* **1984**, *106*, 5382.

(10) Hirschon, A. S.; Beller, J. D.; Olmstead, M. M.; Doi, J. T.; Musker, W. K. *Tetrahedron Lett.* **1981**, *22*, 1195.

0022-3263/86/1951-1815$01.50/0