Studies on β-Lactams. Part 46.[1] Synthesis of Nine-membered Heterocycles *via* β-Lactams

By **Ajay K. Bose, William A. Hoffman III,** and **Maghar S. Manhas,*** Department of Chemistry and Chemical Engineering, Stevens Institute of Technology, Hoboken, New Jersey 07030, U.S.A.

Benzothiazepinones and benzoxazepinones were converted into thioamides and then into cyclic thioimidates, which were annelated to give β-lactams by treatment with an acid chloride and a weak base. Reactions of these homologues of cepham and penam with periodate led to rearrangement to 1,4-thiazonine and 1,4-oxazonine derivatives.

MONOCYCLIC and polycyclic β-lactams with a variety of substituents are available by a number of synthetic methods. Furthermore, β-lactams undergo rearrangements involving cleavage of various bonds of the four-membered ring system.[2] We have taken advantage of such cleavage reactions in a route to some nine-membered heterocycles. Our interest in the preparation of β-alkylthio-β-lactams as potential antibiotics led to the examination of compounds in which the β-lactam ring is fused to a seven-membered heterocycle. This paper is concerned with the synthesis of such compounds and their ring expansion reactions.

The starting material for the synthesis of compounds of the type (I) was a benzoxazepinone (IV), obtained from a chroman-4-one (III) *via* a Schmidt reaction. As discussed by Huckle *et al.*[3] and Sidhu *et al.*,[4] the reaction proceeds well in the desired direction affording the product (IV) in satisfactory yields. When the same reaction was applied to thiochroman-4-ones (V), however, a 1 : 1 mixture of isomers, (VI) and (VII), was formed.

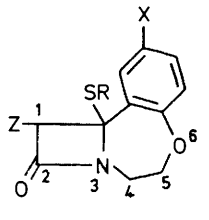
[1] Part 45, A. K. Bose, S. G. Amin, J. C. Kapur, and M. S. Manhas, *J.C.S. Perkin I*, 1976, 2193.

[2] M. S. Manhas and A. K. Bose, 'Beta-lactams, Natural and Synthetic,' Wiley–Interscience, New York, 1971, part I, ch. 3.

[3] D. Huckle, I. M. Lockhart, and M. Wright, *J. Chem. Soc.* (*C*), 1965, 1137.

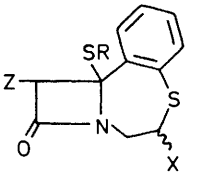
[4] G. S. Sidhu, G. Thyagarajan, and U. T. Bhalerao, *J. Chem. Soc.* (*C*), 1966, 969.

The 1,5-benzothiazepinone (VI) was prepared independently by a Beckmann rearrangement to confirm its



(I)

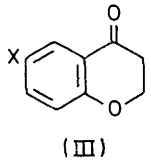
a ; X=H , R=Me , Z=OMe
b ; X=H , R=Me , Z=N_3
c ; X=H , R=Me , Z=OPh
d ; X=H , R=Et , Z=N_3
e ; X=H , R=Pr^i , Z=OMe
f ; X=H , R=Pr^i , Z=N_3
g ; X=Cl , R=Me , Z=OMe
h ; X=Cl , R=Me , Z=N_3
i ; X=Cl , R=Et , Z=OMe
j ; X=Cl , R=Et , Z=N_3
k ; X=Cl , R=Pr^i , Z=OMe
l ; X=Cl , R=Pr^i , Z=N_3
m ; X=Cl , R=Me , Z=N_3(1−Me)



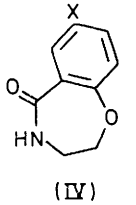
(II)

a ; X=H , R=Me , Z=OMe
b ; X=H , R=Me , Z=N_3
c ; X=H , R=Pr^i , Z=OMe
d ; X=H , R=Pr^i , Z=N_3
e ; X=OMe , R=Me , Z=OPh

structure. Although fractional crystallization was capable of separating (VI) and (VII), the process was inefficient. Therefore, an alternative method, the



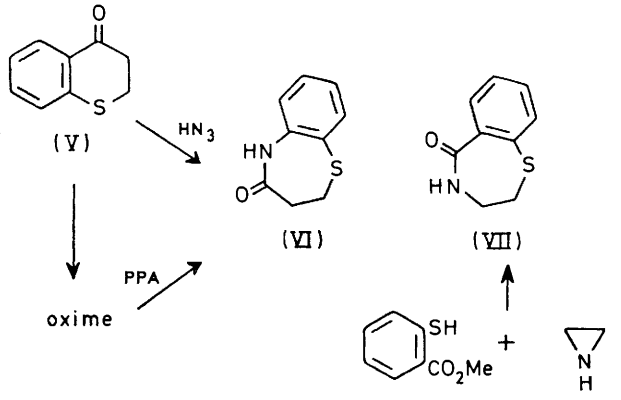
(III)



(IV)

a; X=H
b; X=Cl

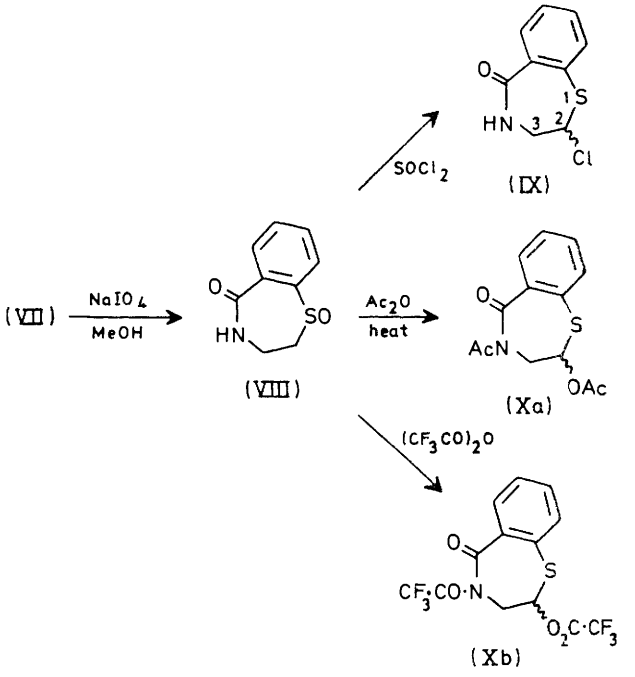
reaction of aziridine with methyl 2-mercaptobenzoate in methanol [5] was used to obtain the desired isomer (VII).



[5] F. Jakob and P. Schlack, *Chem. Ber.*, 1963, **96**, 88.
[6] M. Uskokovic, G. Grethe, J. Iacobelli, and W. Wenner, *J. Org. Chem.*, 1965, **30**, 3111.

The benzothiazepinone (VII) was oxidized with sodium periodate [6] to produce the sulphoxide (VIII) in good yield. The presence of the sulphoxide allowed substituents to be introduced on the aliphatic portion of the molecule. For example, thionyl chloride [7] in cold methylene chloride reacted with (VIII) to produce the α-chloro-sulphide (IX). Reactions of (VIII) with refluxing acetic anhydride and with trifluoroacetic anhydride produced the *N*-acyl products (Xa and b) *via* Pummerer rearrangement.

To be of further use, compounds (Xa and b) needed to be hydrolysed selectively, leaving the acyloxy-group intact. A variety of conditions were employed which either effected no change, or complete deacylation.

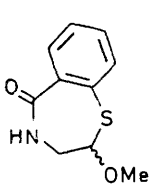


However the α-chloro-sulphide (IX) was conveniently converted by silver oxide in methanol into the useful α-methoxy-sulphide (XI). The ^1H n.m.r. spectra of compounds (IX)—(XI) exhibit a C-2 proton signal at lower field than its expected position, but this can be explained on the basis of a fairly rigid ring conformation which holds the C-2 proton near the deshielding region of the aromatic ring. The C-3 protons (adjacent to N) are non-equivalent, and one of these is also deshielded because of the conformation.

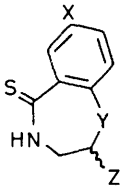
Conversion of the amides (IVa and b), (VII), and (XI) into the corresponding thioamides proceeded in good yield with 1 equiv. of phosphorus pentasulphide in refluxing pyridine.[8] The thioamides each could be obtained in either of two interconvertible crystal forms, depending on the solvent used for recrystallization; no differences were noted in their subsequent reactions in solution.

[7] L. H. Sternbach, H. Lehr, E. Reeder, T. Hayes, and N. Steiger, *J. Org. Chem.*, 1965, **30**, 2812.
[8] A. K. Bose and J. L. Fahey, *J. Org. Chem.*, 1974, **39**, 115.

The methyl thioimidates (XVa and b), (XVIa), and (XVII) were easily prepared from the thioamides with

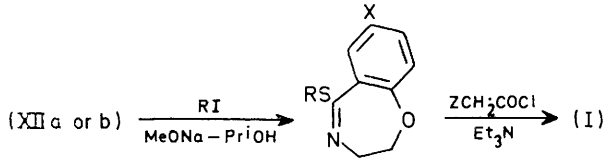


(XI)



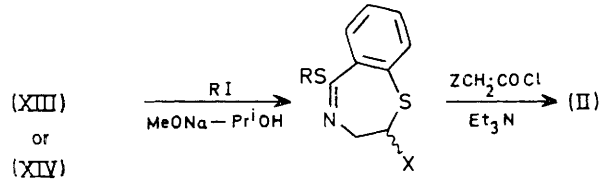
(XII) a; Y=O, X=H, Z=H
b; Y=O, X=Cl, Z=H
(XIII) Y=S, X=H, Z=H
(XIV) Y=S, X=H, Z=OMe

methyl iodide in refluxing tetrahydrofuran; the hydroiodide salt precipitated from the hot solution in a high state of purity. It was important that the thioamide itself should be pure for the formation of the methyl thioimidate hydroiodide to occur with ease. The formation of the ethyl thioimidates (XVc and d) and (XVIb) was even more sensitive to the purity of the thioamide, and these were prepared by treating the sodium salt of the thioamide with ethyl iodide in refluxing propan-2-ol.



(XV)

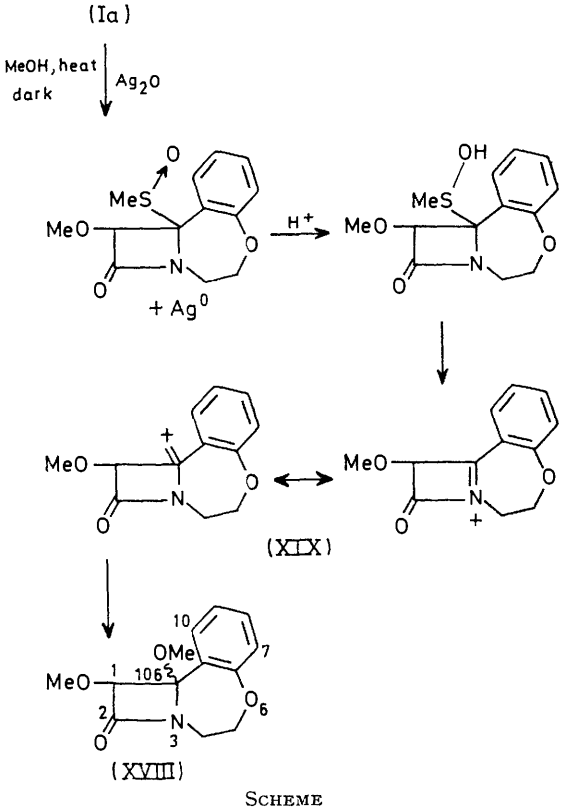
a; X=H, R=Me
b; X=Cl, R=Me
c; X=H, R=Et
d; X=Cl, R=Et
e; X=H, R=Pr^i
f; X=Cl, R=Pr^i



(XVI) a; X=H, R=Me
b; X=H, R=Pr^i
(XVII) X=OMe, R=Me

When the alkyl thioimidates (XV), (XVI), and (XVII) were treated with a substituted acetyl chloride in anhydrous methylene chloride in the presence of triethylamine as proton scavenger, β-lactams were obtained in 30—65% yield as single isomers. Good yields of the azido-derivatives were assisted by high dilution of the added azidoacetyl chloride in anhydrous methylene chloride, slow addition below room temperature, and exclusion of light.

Several laboratories have reported replacement of methylthio-groups at the 6- or 7-position of various penicillin or cephalosporin derivatives by use of mercury(II) acetate,[9] chlorine,[10] t-butyl hypochlorite in methanol,[11] and t-butyl hypochlorite with lithium methoxide.[12] We have found that a similar reaction can be accomplished with silver oxide or silver carbonate in refluxing dry methanol. When one of the new β-lactams (Ia) was treated under these conditions in the dark, the replacement occurred, producing (XVIII) in *ca.* 30% yield.[13]

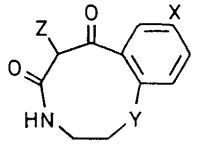


SCHEME

In the absence of *X*-ray analysis it is difficult to prove conclusively the stereochemistry of the β-lactams (I) and (II) because of the multi-substitution at the asymmetric centres. Irrespective of the configuration of the alkylthio-β-lactam (I) or (II), the illustrated mechanistic pathway (see Scheme) suggests that (XVIII) should be a mixture of 10b-epimeric azetobenzoxazepinones formed through an intermediate resonance-stabilized carbocation (XIX).[14]

[9] W. A. Slusarchyk, H. E. Applegate, P. Funke, W. Koster, M. S. Puar, M. Young, and J. E. Dolfini, *J. Org. Chem.*, 1973, **38**, 943.
[10] W. A. Spitzer and T. Goodson, *Tetrahedron Letters*, 1973, 273.
[11] J. E. Baldwin, F. J. Urban, R. D. G. Cooper, and F. L. Jose, *J. Amer. Chem. Soc.*, 1973, **95**, 2401.
[12] G. A. Koppel and R. E. Koehler, *J. Amer. Chem. Soc.*, 1973, **95**, 2403.
[13] (*a*) A. K. Bose, J. C. Kapur, S. G. Amin, and M. S. Manhas, *Tetrahedron Letters*, 1974, 1917; (*b*) A. K. Bose, B. Dayal, J. C. Kapur, B. Lal, and M. S. Manhas, *ibid.*, p. 3135.
[14] G. V. Kaiser, C. W. Ashbrook, and J. E. Baldwin, *J. Amer. Chem. Soc.*, 1971, **93**, 2342.

When several of the new β-lactams were treated with periodate in aqueous propan-2-ol, the alkythio-group was again oxidized, and again the sulphoxide rearranged to the carbocation (XIX). Attack by water produced the corresponding hydroxy-β-lactam. Although isolation was possible in some cases, all eventually rearranged to benzoxazoninediones (XXa—d). The ring sulphur atom in (IIa) is not oxidized under these conditions. This ring expansion reaction readily provides medium-sized heterocyclic systems which are otherwise not easily accessible.



a; X=H, Y=O, Z=OMe
b; X=H, Y=O, Z=N_3
c; X=Cl, Y=O, Z=OMe
d; X=H, Y=S, Z=OMe

(XX)

In the light of our previous work [15] some of the azido-β-lactams described here should be convenient starting materials for synthesis of the corresponding α-amido-β-lactams. We have shown [16] that the angular thioalkyl group can be replaced by hydrogen with retention of configuration by using Raney Ni for hydrogenolysis. It should therefore be possible to convert compounds of type (I) into *cis*-β-lactams.

EXPERIMENTAL

M.p.s were taken for samples in open capillary tubes (Mel-Temp apparatus). I.r. spectra were taken with a Perkin-Elmer IR 247 instrument. ^{1}H N.m.r. spectra were taken with a Varian A-60 or a Perkin-Elmer R-12 instrument (tetramethylsilane as internal standard). ^{13}C N.m.r. spectra were obtained by Dr. P. R. Srinivasan, Department of Chemistry and Chemical Engineering, Stevens Institute, with a Bruker HFX-90 spectrometer. Mass spectra were obtained with a Perkin-Elmer RMU spectrometer. Elemental analyses were determined by A. Bernhardt, West Germany.

3,4-Dihydro-1,4-benzoxazepin-5(2*H*)-one (IVa) and its 7-chloro-derivative (IVb) were prepared by the method of Sidhu and his co-workers.[4]

Reaction of Thiochroman-4-one (V) *with Hydrogen Azide.*—A mixture of thiochroman-4-one (V) (10 g, 61 mmol) and sodium azide (8 g, 122 mmol) in 10% ether–benzene (250 ml) was cooled to 0 °C and kept at that temperature during the cautious addition of sulphuric acid (20 ml, 360 mmol). The stirred solution was allowed to reach room temperature, and left overnight. The reaction was quenched with water, and the organic layer separated, dried, and evaporated, leaving crystals (7.1 g, 70%). Recrystallization from chloroform–hexane, with cooling and scratching, gave a crystalline solid, m.p. 161—162°. N.m.r. showed this to be a mixture of 3,4-dihydro-1,4-benzothiazepin-5(2*H*)-one (VII) and 2,3-dihydro-1,5-benzothiazepin-4(5*H*)-one (VI). Fractional crystallization from chloroform–hexane gave the product (VI) (80%) as the less soluble ingredient. Recrystallization from 50% aqueous ethanol afforded pure material, m.p. 218—219° (lit.,[17] 216—217°). The mother liquor was allowed to evaporate, and the residue recrystallized from acetone to give the product, m.p. 192—196° (lit.,[5] 194—196°).

3,4-*Dihydro*-1,4-*benzothiazepin*-5(2H)-*one* 1-*Oxide* (VIII).—A mixture of the benzothiazepinone (VII) (20 g, 112 mmol) and aqueous 0.5M-sodium periodate (240 ml) in methanol (220 ml) was stirred at room temperature overnight. The solid was filtered off and the aqueous phase extracted with chloroform (7 × 150 ml). The dried chloroform extract was evaporated, leaving a white solid (16 g, 74%). Recrystallization from acetonitrile gave the oxide (VIII) (14.5 g, 67%), m.p. 233—234°, $\nu_{max.}$ (Nujol) 3 150, 1 625, 1 220, 1 055, 1 020, 980, 860, and 740 cm^{-1}.

2-*Chloro*-3,4-*dihydro*-1,4-*benzothiazepin*-5(2H)-*one* (IX).—Under dry conditions, the sulphoxide (VIII) (2.5 g) was dissolved in a solution containing thionyl chloride (10 ml) and methylene chloride (50 ml). Within about 15 min a white precipitate separated. The slurry was stirred for another 15 min, and poured into ice–water (500 ml) containing potassium hydroxide (20 g). The methylene chloride layer was separated and the aqueous layer extracted with methylene chloride (2 × 150 ml). The combined organic layers were dried and evaporated, leaving fluffy *needles* (2.4 g, 86%), m.p. 163—165°; $\nu_{max.}$ (Nujol) 3 170, 1 660, 1 200, 1 160, 950, 780, and 740 cm^{-1}; δ ($CDCl_3$) 7.6 (5 H, m), 5.6 (1 H, dd), and 3.5 (2 H, m).

3,4-*Dihydro*-2-*methoxy*-1,4-*benzothiazepin*-5(2H)-*one* (XI).—Freshly prepared silver oxide, obtained from methanolic solutions of silver nitrate (2.3 g, 14 mmol) and potassium hydroxide (0.5 g, 7 mmol), was suspended in anhydrous methanol (75 ml). To the suspension was added the chlorobenzothiazepinone (IX) (1.5 g, 7 mmol) in methanol (150 ml). The mixture was stirred at room temperature, overnight, in the dark, then filtered through Hi-Flo Supercel. Evaporation left an oil which solidified on cooling, and was recrystallized from propan-2-ol to give the *product* (XI) (1.0 g, 67%), m.p. 142—144°; $\nu_{max.}$ (Nujol) 3 200, 3 050, 1 645, 1 300, 1 185, 1 160, 1 100, 1 080, 1 055, 1 040, 950, and 740 cm^{-1}; δ ($CDCl_3$) 8.2 (1 H, m), 7.45 (4 H, m), 5.05 (1 H, dd), 3.47 (3 H, s), and 3.3 (2 H m) (Found: C, 57.3; H, 5.2; N, 6.7; S, 15.45. $C_{10}H_{11}NO_2S$ requires C, 57.4; H, 5.3; N, 6.7; S, 15.3%).

TABLE 1

Thioimidate hydroiodides

Compd. †	M.p. (°C)	Yield (%)
(XVa)	156—158	71
(XVb)	195—197	65
(XVc)	115—117	47
(XVd)		60
(XVd) [19]	(Oil)	90 *
(XVe)	(Oil)	100 *
(XVf)	(Oil)	100
(XVIa)	204—208	75
(XVII)	183—185	6

* Isolated as free bases. † All the compounds were characterized by spectral data.

Reactions of the Sulphoxide (VIII) *with Acetic Anhydride and with Trifluoroacetic Anhydride.*—Refluxing (VIII) for 1½ h in acetic anhydride, followed by quenching with

[15] A. K. Bose, B. Anjaneyulu, S. K. Bhattacharya, and M. S. Manhas, *Tetrahedron*, 1967, **23**, 4769.

[16] A. K. Bose, M. S. Manhas, J. S. Chib, H. P. S. Chawla, and B. Dayal, *J. Org. Chem.*, 1974, **39**, 2877.

[17] W. H. Mills and J. B. Whitworth, *J. Chem. Soc.*, 1927, 2738.

water, afforded the *N*-acyl acetate (Xa), which was air-dried; m.p. 104—106°; $\nu_{max.}$ (Nujol) 1 745, 1 680, 1 445, 1 270, 1 250, 1 205, 1 020, 980, and 960 cm^{-1}; δ ($CDCl_3$) 7.55 (4 H, m), 6.3 (1 H, dd), 4.75 (1 H, dd), 3.25 (1 H, dd), 2.7 (3 H, s), and 2.1 (3 H, s). A similar reaction with trifluoroacetic anhydride produced the analogue (Xb); $\nu_{max.}$ (Nujol) 1 780, 1 730, 1 700, 1 220, 1 170, 1 140, 1 025, 960, 925, and 750 cm^{-1}; δ ($CDCl_3$) 7.6 (4 H, m), 6.45 (1 H, dd), 4.85 (1 H, dd), and 3.6 (1 H, m).

General Procedures for Thioamide Formation.—(*A*) A mixture of the amide and phosphorus pentasulphide (0.2 mol. equiv.) was refluxed in pyridine for 1—3 h. The mixture was decanted into about 3 times its volume of warm water. On cooling the product separated and was recrystallized from aqueous ethanol.

(*B*) After refluxing as in (*A*), the solution was poured into sufficient 20% hydrochloric acid to neutralize the pyridine, and extracted several times with chloroform. The dried organic layer was then evaporated, and the crude product recrystallized from chloroform–hexane.

3,4-Dihydro-1,4-benzoxazepine-5(2*H*)-thione (XIIa), prepared from (IVa) (3.2 g) and phosphorus pentasulphide (1.0 g) in 62% yield (2.2 g), had m.p. 100—102° (lit.,[18] 101—103°). Its 7-chloro-derivative (XIII), prepared similarly from (VII) in 62—80% yield, had m.p. 197—199° (lit.,[19] 198°). 3,4-Dihydro-2-methoxy-1,4-benzothiazepine-5(2*H*)-thione (XIV) was synthesized from (XI) in 75% yield; m.p. 128—130°; $\nu_{max.}$ (Nujol) 3 150, 1 650, 1 250, 1 100, 1 060, 1 040, 1 005, 950, 770, and 740 cm^{-1}.

Preparation of Thioimidates.—(*A*) The thioamide was dissolved in the minimum volume of tetrahydrofuran (THF), and methyl or ethyl iodide, in 10% excess, was added in one portion. The solution was then refluxed for at least 30 min; the product precipitated from the hot THF. After cooling to room temperature, the product was filtered off and washed with a small volume of THF followed by ether. Air-dried material was used without further purification.

(*B*) The thioamide was dissolved in propan-2-ol (25 ml per g) and treated with sodium methoxide (1 mol. equiv.). Ethyl or isopropyl iodide (1 mol. equiv.) was added in one portion and the solution was stirred at room temperature,

TABLE 2

β-Lactams

Compd.	Yield (%)	M.p. (°C)	$\nu_{max.}$/cm^{-1}	δ ($CDCl_3$)	% Reqd. / % Found C	H	N	S
(Ia)	53	118—120	1 750, 1 300, 1 215, 1 105	7.2 (4 H, m), 4.75 (1 H, s), 4.05 (4 H, m), 3.8 (3 H, s)	58.85	5.7	5.3	12.1
(Ib)	65	138—140	2 100, 1 755, 1 260, 1 210	7.15 (4 H, m), 5.05 (1 H, s), 4.0 (4 H, m), 2.1 (3 H, s)	52.15 52.2	4.4 4.2	20.3 20.3	11.6 11.6
(Ic)	40	(Oil)	1 765, 1 490, 1 240, 1 210	7.2 (9 H, m), 5.5 (1 H, s), 4.0 (5 H, m), 2.2 (3 H, s)	(Single spot on t.l.c. in 3 systems)			
(Id)	56	79—80	2 100, 1 765, 1 480, 1 210	7.15 (4 H, m), 5.0 (1 H, s), 4.0 (4 H, m), 2.55 (2 H, q), 1.2 (3 H, t)	53.75 53.7	4.85 4.75	19.3 19.2	11.05 10.9
(Ie)	89	94—97	1 760, 1 290, 1 255, 1 200	7.15 (4 H, m), 4.8 (1 H, s), 3.95 (5 H, m), 3.8 (3 H, s), 1.25 (6 H, q)				
(If)	65	63—65	2 100, 1 760, 1 260, 1 205	7.15 (4 H, m), 5.0 (1 H, s), 4.05 (4 H, m), 2.97 (1 H, m), 1.2 (6 H, q)				
(Ig)	44	163—164	1 755, 1 295, 1 260, 1 205	7.1 (3 H, m), 4.75 (1 H, s), 3.9 (4 H, m), 3.8 (3 H, s), 2.2 (3 H, s)	52.1 52.65	4.7 4.6	4.65 4.6	10.7 10.65
(Ih)	63	162—164	2 100, 1 760, 1 480, 1 200	7.5 (3 H, m), 5.0 (1 H, s), 3.9 (4 H, m), 2.2 (3 H, s)	46.4 46.6	3.55 3.65	18.05 18.3	10.3 10.4
(Ii)	43	118.5—119.5	1 750, 1 290, 1 255, 1 210	7.1 (3 H, m), 4.75 (1 H, s), 3.9 (4 H, m), 3.8 (3 H, s), 2.75 (2 H, q), 1.2 (3 H, t)	53.6 53.4	5.15 5.35	4.65 4.45	10.2 10.0
(Ij)	50	88—90	2 090, 1 760, 1 255, 1 205	7.1 (3 H, m), 4.95 (1 H, s), 3.9 (4 H, m), 2.8 (2 H, q), 1.2 (3 H, t)	48.05 48.4	4.05 4.25	17.25 17.5	9.85 9.9
(Ik)	51	110—112	1 750, 1 290, 1 255, 1 215	7.1 (3 H, m), 4.75 (1 H, s), 3.8 (5 H, m), 3.8 (3 H, s), 1.3 (6 H, q)	54.95 55.5	5.5 5.45	4.25 4.5	9.8 9.75
(Im)	30	144—145	2 090, 1 760, 1 260, 1 200	7.1 (3 H, m), 3.9 (4 H, m), 2.2 (3 H, s), 1.2 (3 H, s)	48.05 48.35	4.05 3.95	17.25 16.55	9.85 9.55
(IIa)	65	134—135	1 760, 1 430, 1 390, 1 215	7.28 (4 H, m), 4.8 (1 H, s), 3.8 (3 H, s), 3.65 (4 H, m), 2.16 (3 H, s)				
(IIb)	50	166—168	2 100, 1 755, 1 270, 1 210	7.35 (4 H, m), 5.1 (1 H, s), 3.6 (4 H, m), 2.1 (3 H, s)	49.3 49.65	4.15 4.2	19.15 19.6	21.95
(IIc)	39	84—85	1 735, 1 295, 1 220, 1 030	7.3 (4 H, m), 4.8 (1 H, s), 3.8 (3 H, s), 3.7 (5 H, m), 1.3 (6 H, q)	58.2 58.2	6.2 6.1	4.55 4.5	20.75 20.55
(IId)	30	89.5—90.5	2 095, 1 760, 1 260, 1 215	7.3 (4 H, m), 5.0 (1 H, s), 3.6 (5 H, m), 1.2 (6 H, q)	52.45 51.8	5.05 4.85	17.5 17.2	20.0 19.8
(IIe)	80	(Oil)	1 760, 1 590, 1 485, 1 430	7.25 (9 H, m), 5.5 (1 H, s), 4.75 (1 H, m), 3.6 (2 H, m), 3.5 (3 H, s), 2.2 (3 H, s)				

[18] L. I. Barsky and W. L. Bencze, *J. Medicin. Chem.*, 1971, **14**, 40.

[19] K. H. Wunsch and A. Ehlers, *Chem. Ber.*, 1969, **102**, 1869.

under nitrogen, for 1 h, then was refluxed for 2½—4 h. The cooled mixture was then poured into two volumes of water, and extracted with three portions of chloroform. The dried extracts were evaporated, and the residue was either used directly or distilled. No spectral difference was found between undistilled and distilled material, although in one case the distilled material crystallized. Method (*B*) is the higher yielding of the two; (*A*) is the more convenient.

2,3-*Dihydro*-5-*isopropylthio*-1,4-*benzothiazepine* (XVIb) was prepared by procedure (*B*) as an oily liquid (30%), b.p. 180 °C at 30 mmHg, which solidified to a crystalline solid, m.p. 57—59°; $\nu_{max.}$ (neat) 2 925, 2 850, 1 590, 1 450, 1 420, 1 360, 1 280, 1 205, 1 150, 940, and 720 cm^{-1}; δ ($CDCl_3$): 7.35 (4 H, m), 3.9 (1 H, m), 3.5 (4 H, m), 1.35 (6 H, d) (Found: C, 60.6; H, 6.15; N, 5.7; S, 26.85. $C_{12}H_{15}NS_2$ requires C, 60.7; H, 6.35; N, 5.9; S, 27.05%).

Chromatography was rarely needed, but when used, it was performed with a Florisil column and benzene as eluant.

Analytical and spectral data are given in Table 2.

1,4,5,10b-*Tetrahydro*-1,10b-*dimethoxyazeto*[1,2-d][1,4]-*benzoxazepin*-2-*one* (XVIII).—A solution of the β-lactam (Ia) (100 mg) in dry methanol (100 ml) was treated with freshly prepared silver carbonate (0.2 g), and the mixture refluxed overnight in the dark. A silver mirror was produced. The mixture was filtered through Celite, and the methanol removed under reduced pressure, leaving an oil. The total product was subjected to preparative t.l.c. (5% acetone–chloroform; 1½ h). Six bands were visible under u.v. light; the fourth contained the title compound (M^+ 249) (60 mg, 60%), and a small amount of a dimer (M^+ 496). Compound (XVIII) was a 1 : 1 mixture of epimers, obtained as an oil; $\nu_{max.}$ (neat) 2 950, 1 760, 1 490, 1 445, 1 395, 1 300, 1 215, 1 055, 1 040, 780, and 760 cm^{-1}; δ ($CDCl_3$): 7.2 (4 H, m), 4.8 (1 H, d), 3.95 (4 H, m), 3.8 (1.5 H, s), 3.47 (1.5 H, s), and 3.4 (3 H, s).

TABLE 3

3,4-Dihydro-1,4-benzoxazonine-5,7(2*H*,6*H*)-diones

Compd.	Yield (%)	M.p (°C)	$\nu_{max.}$/cm^{-1}	δ ($CDCl_3$)	% Reqd. / % Found C	H	N
(XXa)	15	211—213	3 300, 1 700, 1 675, 1 530	7.45 (5 H, m), 5.9 (1 H, s), 4.0 (4 H, m), 3.5 (3 H, s)	(*m/e* 235)		
(XXb)	25	167 (decomp.)	3 275, 2 100, 1 680, 1 620	7.45 (5 H, m), 5.85 (1 H, s), 4.05 (4 H, m)	53.65 / 53.6	4.1 / 4.15	22.75
(XXc)	30	167—169	3 300, 1 680, 1 650, 1 580	7.45 (5 H, m), 5.95 (1 H, s), 4.05 (4 H, m)	53.25 / 53.1	4.45 / 4.5	5.15 / 5.1

The thioimidates (XV), (XVI), and (XVII) were also synthesized as described above and were characterized spectroscopically as free bases or hydroiodides. These imidates were used without further purification. M.p.s and yields are given in Table 1.

General Synthesis of β-*Lactams* (I) *and* (II).—Under anhydrous conditions, a 0.1—0.2M-solution of the alkyl thioimidate in anhydrous methylene chloride (10—20 mmol per 100 ml) was treated with 1 mol. equiv. (an additional mol. equiv. if the hydriodide was used) of triethylamine. To the stirred solution was then added, dropwise, a solution of the acetyl chloride (1 mol. equiv.) in anhydrous methylene chloride (50 ml) (1—2 h). After stirring at room temperature overnight, the solution was washed with water, 20% hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and water. After drying ($MgSO_4$) the organic layer was evaporated to give an oil, which solidified, and was recrystallized from the solvent named (Table 2).

General Procedure for Oxidation of β-*Lactams* (I).—A suspension of the β-lactam (1 mmol) in propan-2-ol (20 ml) was treated with aqueous 0.5M-sodium periodate (2 ml, 1 mmol). After 1 h the solid was filtered off (Celite), and the filtrate evaporated. Recrystallization of the residue from propan-2-ol afforded the *benzoxazonines* (XXa—c). The same product (XXc) was isolated from each of the β-lactams (1g), 1i), and (1k). Analytical and spectral data are summarized in Table 3. Similarly compound (IIa) was converted into (XXd).

We thank the Stevens Institute of Technology for research facilities and financial assistance (to W. A. H.).

[6/816 *Received*, 26*th April*, 1976]