Synthesis and Stereochemistry of rac.-*trans*-Tetrahydro-6-hydroxy-7-(4-methoxyphenyl)-1,4-thiazepin-5(2*H*)-one

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The base catalyzed reaction of 2-aminoethanethiol (**3**) with *trans*-3-(*p*-methoxyphenyl)glycidate (**4**) gave a mixture of isomeric lactams **5** and **6**, and in addition, a by-product **7**. The structures of these isomers were proven by X-ray crystallography. The data revealed that both isomers adopt the chair conformation in the solid state and the size of the heterocyclic ring in compound **5** is a six- and in compound **6** is a seven-membered ring.

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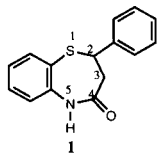
The 2-phenyl-1,5-benzothiazepinone ring system **1** is a common structural moiety present in several pharmacologically effective compounds [1]. The first synthesis of 2-phenyl-2,3-dihydro-1,5-benzothiazepin-4(5*H*)-one (**1**) by the reaction of 2-aminothiophenol with cinnamic acid was reported by Mills *et al.* [2]. Later, Kugita *et al.* [3] synthesized the 3-hydroxy derivatives of **1** by condensation of 2-nitrophenol with arylglycidic esters and cyclization to the 1,5-benzothiazepinone derivatives.



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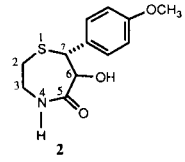

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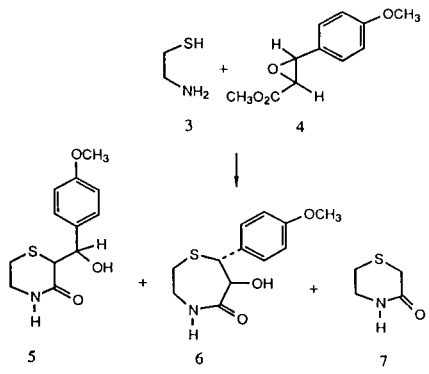
In this connection, we have recently examined the base catalyzed reaction of 2-aminoethanethiol (**3**) with *trans*-3-(*p*-methoxyphenyl)glycidate (**4**) [4] as a potential route to rac.-*trans*-tetrahydro-6-hydroxy-7-(4-methoxyphenyl)-1,4-thiazepin-5(2*H*)-one (**2**) [5]. The synthetic route to **2** is outlined in Scheme 1.

Scheme 1



Reaction of 2-aminoethanethiol (**3**) with *trans*-3-(*p*-methoxyphenyl)glycidate (**4**) [4] in methanol in the presence of sodium methoxide at room temperature gave a mixture of isomeric lactams **5** and **6** and an additional by-product **7**. The minor isomer **5** which crystallized after 17 hours at room temperature was isolated by filtration (mp 143-145°). After stirring the filtrate an additional 72 hours, the major isomer **6** was separated by filtration as a crystalline solid and obtained in pure form by recrystallization (mp 168-170°). Tentatively, structures **5** (mp 143-145°) and **6** (mp 168-170°) respectively, were assigned to these isomers. Conclusive identification of the isomers by spectroscopic methods proved to be difficult. Isomers **5** and **6** had similar ir, uv and ms spectra. The ^{1}H nmr spectrum of **5** (deuteriochloroform) features a one-proton broad triplet at δ 8.03 due to the N*H* proton, an AA'BB' pattern at δ 7.29, 6.87 (J = 8.5 Hz) for the four aromatic protons, a one-proton doublet at 5.55 (J = 3.5 Hz) due to the *H*OCH proton, and a one-proton doublet of doublets at 5.03 (J = 3.5 and 6.5 Hz) which can be assigned to the HOC*H* proton. Furthermore, this compound shows a one-proton doublet at δ 3.77 (J = 6.5 Hz) due to the C*H*S proton, a three-proton singlet at 3.75 for the methoxy protons, a two-proton multiplet at 3.20 for the NCH_2 protons and a two-proton multiplet at 2.57, 2.22 for the SCH_2 protons. On the other hand, the ^{1}H nmr spectrum (deuteriodimethyl sulfoxide) of **6** showed a one-proton broad triplet at δ 8.36 due to the N*H* proton, and AA'BB' pattern at 7.26, 6.84 (J = 8.5 Hz) for the four aromatic protons, a one-proton doublet at 4.58 (J = 9.5 Hz) due to the *H*OCH proton, and a one-proton doublet of doublets at 4.75 (J = 9.5 and 7.0 Hz) which can be assigned to the CH(OH)C*H* proton. The other signals are a three-proton singlet at δ 3.74 for the aromatic methoxy protons, a two-proton multiplet at 3.57 due to the NCH_2 protons and a two-proton multiplet at 2.68 due to the CH_2S protons. Thus, analysis of ^{1}H nmr spectra suggested that compound **6** could possess a structure resembling that of **5** but the data was insufficiently characteristic to allow definitive structure assignments. Conclusive proof of structure of **5** was obtained by single crystal X-ray analysis (Figure 1) [6]. Assignment of structure and stereochemistry required conversion of **6** to the dimethylaminoethyl derivative **8** [7] which was suitable for X-ray crystallographic analysis. The X-ray crystallographic structure of **8** (Figure 2) revealed that in the solid state the thiazepinone ring has the slightly twisted-chair confor-

mation with the C-6 hydroxyl and the C-7 aryl groups in *trans* orientation [5].

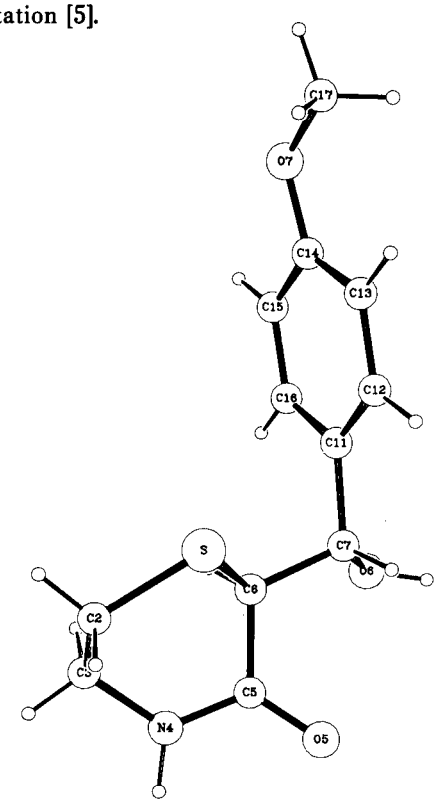


Figure 1. Structure of compound **5** as determined by X-ray analysis.

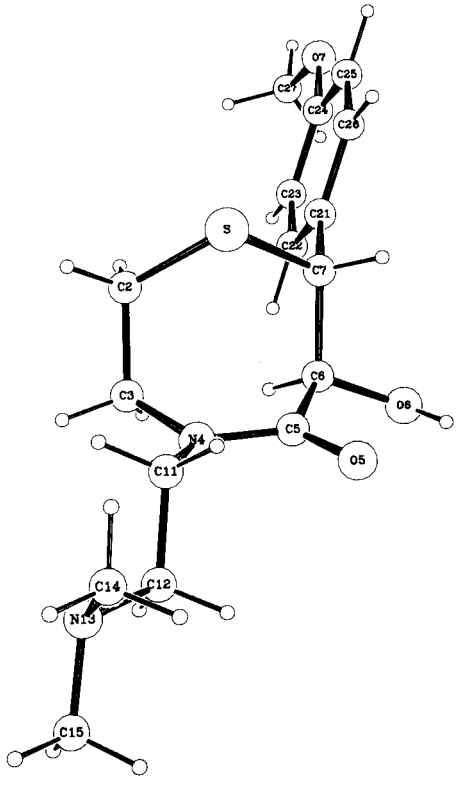


Figure 2. Structure of compound **8** as determined by X-ray analysis.

On the basis of the results described above the most likely stereochemical course of the reaction is outlined in Scheme 2. It is well documented that the stereochemistry of 3-(*p*-methoxyphenyl)glycidate (**4**) prepared by the Darzens reaction is *trans* [8]. Furthermore, ring opening of oxirans by nucleophiles under basic conditions is generally considered to proceed *via* an S_{N2}-type of mechanism with inversion of configuration [9]. Accordingly, the mechanism of the reaction outlined above has been rationalized in terms of the intermediacy of **9** and **10**, formed by the initial nucleophilic epoxide opening with the 2-aminoethanethiol anion **3**, followed by cyclization *in situ* to provide **5** and **6**, respectively.

Scheme 2

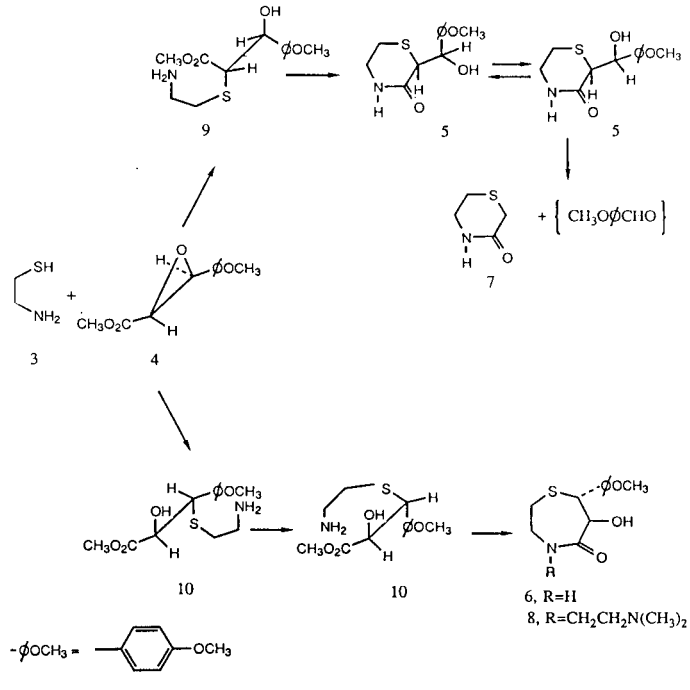


Table I

Crystal Data and Intensity Collections for **5** and **8**

Compound	**5**	**8**
Formula	$C_{12}H_{15}N0_3S$	$C_{16}H_{24}N_20_3S$
Mw	253.32	324.44
Crystal system	monoclinic	triclinic
Space group	$P2_1/a$	$P\bar{1}$
Cell constants		
a (Å)	12.619(3)	7.566(2)
b (Å)	8.583(2)	9.975(2)
c (Å)	12.204(3)	12.166(2)
α (°)		67.48(1)
β (°)	115.26(1)	83.23(2)
γ (°)		83.20(2)
V (Å^3)	1195.4	839.6
Z	4	2
D_{calc} (g cm^{-3})	1.407	1.283
μ(CuKα) (cm^{-1})	23.2	17.8
Crystal size (mm)	0.12 x 0.20 x 0.25	0.14 x 0.25 x 0.30
T (°C)	23	23
Maximum θ (°)	48	57
No. of unique reflections	1118	2252
No. of observed reflections [$I > 2.5\sigma(I)$]	996	2068
No. of variables	154	199
R	0.033	0.047
R_w	0.039	0.060
Largest peak of final difference map	0.2	0.4

Table II. Final Atomic Parameters and Equivalent Isotropic Thermal Parameters for 5 and 8 (with Standard Deviations in Parentheses)

Compound 5

Atom	X	Y	Z	Beqv
S	0.0528(1)	0.8014(1)	0.1703(1)	3.64(2)
O(5)	0.2110(2)	0.7656(2)	-0.0172(2)	3.20(6)
O(6)	0.3020(2)	0.5130(2)	0.1706(2)	3.26(6)
O(7)	0.0906(2)	0.3191(3)	0.5368(2)	4.28(6)
N(4)	0.2212(2)	0.9786(3)	0.0956(2)	3.22(7)
C(2)	0.0780(3)	1.0100(4)	0.1801(3)	3.64(9)
C(3)	0.1995(3)	1.0508(4)	0.1921(3)	3.49(9)
C(5)	0.2103(3)	0.8260(4)	0.0747(3)	2.58(8)
C(6)	0.1918(3)	0.7344(3)	0.1714(3)	2.51(8)
C(7)	0.1881(3)	0.5588(4)	0.1575(3)	2.71(8)
C(11)	0.1588(3)	0.4824(3)	0.2528(3)	2.35(8)
C(12)	0.0524(3)	0.4142(4)	0.2283(3)	2.98(8)
C(13)	0.0255(3)	0.3557(4)	0.3198(3)	3.12(9)
C(14)	0.1071(3)	0.3651(4)	0.4376(3)	3.00(9)
C(15)	0.2163(3)	0.4294(4)	0.4644(3)	3.54(9)
C(16)	0.2406(3)	0.4875(4)	0.3730(3)	3.22(9)
C(17)	-0.0186(3)	0.2493(4)	0.5161(3)	5.20(11)
HO(6)	0.295	0.432	0.119	4.00
HN(4)	0.244	1.043	0.046	4.00
H(2)A	0.018	1.060	0.105	4.00
H(2)B	0.069	1.051	0.252	4.00
H(3)A	0.206	1.166	0.188	4.00
H(3)B	0.259	1.012	0.272	4.00
H(6)	0.257	0.761	0.252	3.00
H(7)	0.128	0.529	0.075	3.00
H(12)	-0.008	0.406	0.142	3.50
H(13)	-0.053	0.307	0.299	3.50
H(15)	0.277	0.433	0.550	4.00
H(16)	0.320	0.535	0.393	3.50
H(17)A	-0.019	0.221	0.595	6.00
H(17)B	-0.030	0.153	0.466	6.00
H(17)C	-0.084	0.324	0.472	6.00

Compound 8

Atom	X	Y	Z	Beqv
S	0.7686(1)	0.1246(1)	0.4345(1)	4.99(2)
O(5)	0.6423(2)	0.1477(2)	0.7312(2)	4.43(5)
O(6)	0.3886(2)	0.3280(2)	0.5897(2)	3.43(4)
O(7)	0.2190(3)	0.4700(2)	0.0250(2)	5.10(5)
N(4)	0.8670(3)	0.2552(2)	0.5977(2)	3.40(5)
N(13)	1.2245(3)	0.1596(2)	0.8058(2)	3.46(5)
C(2)	0.9088(4)	0.2714(5)	0.3856(3)	6.33(10)
C(3)	0.9246(4)	0.3425(3)	0.4752(3)	4.72(7)
C(5)	0.6929(3)	0.2291(3)	0.6316(2)	3.12(6)
C(6)	0.5598(3)	0.3052(3)	0.5370(2)	2.84(5)
C(7)	0.5513(3)	0.2138(3)	0.4610(2)	3.22(6)
C(11)	1.0010(3)	0.1576(3)	0.6745(3)	3.70(6)
C(12)	1.0438(3)	0.2104(3)	0.7692(2)	3.65(6)
C(14)	1.2515(4)	0.0016(4)	0.8581(3)	5.19(8)
C(15)	1.2659(5)	0.2217(4)	0.8896(3)	5.63(9)
C(21)	0.4586(3)	0.2899(3)	0.3465(2)	3.00(6)
C(22)	0.4349(4)	0.4391(3)	0.2905(3)	3.90(6)
C(23)	0.3550(4)	0.5048(3)	0.1826(3)	4.09(7)
C(24)	0.2977(3)	0.4187(3)	0.1306(2)	3.58(6)
C(25)	0.3197(4)	0.2688(3)	0.1862(2)	3.86(7)
C(26)	0.3982(4)	0.2066(3)	0.2918(2)	3.52(6)
C(27)	0.2029(5)	0.6230(4)	-0.0392(3)	5.43(8)
HO(6)	0.365	0.257	0.661	4.00
H(2)A	1.032	0.234	0.365	7.00
H(2)B	0.861	0.348	0.312	7.00
H(3)A	1.053	0.361	0.472	4.50
H(3)B	0.850	0.437	0.451	4.50
H(6)	0.603	0.402	0.484	3.00
H(7)	0.476	0.133	0.511	3.50
H(11)A	1.113	0.150	0.624	4.50
H(11)B	0.955	0.059	0.715	4.50
H(12)A	1.032	0.319	0.736	4.00
H(12)B	0.957	0.173	0.841	4.00
H(14)A	1.166	-0.036	0.930	5.00
H(14)B	1.377	-0.028	0.882	5.00
H(14)C	1.230	-0.040	0.798	5.00
H(15)A	1.182	0.188	0.963	6.50
H(15)B	1.252	0.331	0.852	6.50
H(15)C	1.391	0.189	0.911	6.50
H(22)	0.476	0.502	0.328	4.00
H(23)	0.340	0.613	0.143	4.00
H(25)	0.278	0.205	0.149	4.00
H(26)	0.413	0.098	0.331	4.00
H(27)A	0.144	0.645	-0.114	6.00
H(27)B	0.324	0.660	-0.060	6.00
H(27)C	0.130	0.671	0.011	6.00

Furthermore, the structure of a small amount of the by-product **7** isolated from the concentrated filtrate of **6** by preparative tlc was determined on the basis of its spectroscopic data. Its mass spectrum exhibits the molecular ion peak as required at m/e 117 and the infrared spectrum showed an NH absorption at 3415 cm^{-1} and amide carbonyl absorption at 1617 cm^{-1}. The ^1H nmr spectrum (deuteriochloroform) was in complete agreement with structure **7** and features a one-proton broad absorption at δ 7.22 for the N*H* proton, a two-proton multiplet at 3.62 for the CH_2N protons, a two-proton singlet at 3.30 for the COCH_2-S protons and a two-proton multiplet at 2.82 for the CH_2S protons. Moreover, the ^{13}C nmr spectrum of **7** showed in particular the amide carbonyl singlet at δ 168.4. The formation of this compound presumably resulted from the competing base catalyzed retro-aldol reaction of **5** (Scheme 2).

Finally, alkylation of **6** with 2-dimethylaminoethyl chloride in dimethyl sulfoxide in the presence of sodium hydride gave **8**, which on treatment with hydrogen chloride (anhydrous) in ethyl acetate afforded the corresponding hydrochloride salt.

Table III. Bond Lengths (Å) for 5 and 8 (with Standard Deviations in Parentheses)

Compound 5

Bond	Lengh	Bond	Length
S - C(2)	1.813(4)	C(5)- C(6)	1.516(5)
S - C(6)	1.841(4)	C(6)- C(7)	1.516(4)
O(5)- C(5)	1.240(4)	C(7)-C(11)	1.513(5)
O(6)- C(7)	1.432(4)	C(11)-C(12)	1.375(5)
O(7)-C(14)	1.371(5)	C(11)-C(16)	1.388(4)
O(7)-C(17)	1.423(5)	C(12)-C(13)	1.391(6)
N(4)- C(3)	1.457(5)	C(13)-C(14)	1.368(4)
N(4)- C(5)	1.329(4)	C(14)-C(15)	1.388(5)
C(2)- C(3)	1.517(6)	C(15)-C(16)	1.371(6)

Compound 8

Bond	Lengh	Bond	Length
S - C(2)	1.781(4)	C(2)- C(3)	1.534(6)
S - C(7)	1.829(3)	C(5)- C(6)	1.528(4)
O(5)- C(5)	1.219(3)	C(6)- C(7)	1.537(5)
O(6)- C(6)	1.410(3)	C(7)-C(21)	1.517(4)
O(7)-C(24)	1.368(3)	C(11)-C(12)	1.518(5)
O(7)-C(27)	1.421(4)	C(21)-C(22)	1.378(4)
N(4)- C(3)	1.453(3)	C(21)-C(26)	1.388(5)
N(4)- C(5)	1.358(3)	C(22)-C(23)	1.398(4)
N(4)-C(11)	1.464(3)	C(23)-C(24)	1.376(5)
N(13)-C(12)	1.460(3)	C(24)-C(25)	1.383(4)
N(13)-C(14)	1.455(4)	C(25)-C(26)	1.368(4)
N(13)-C(15)	1.458(5)		

Table IV. Bond Angles (°) for 5 and 8 (with Standard Deviations in Parentheses)

Compound 5

Bond	Angle	Bond	Angle
C(2)- S - C(6)	99.6(2)	O(6)- C(7)-C(11)	111.0(2)
C(14)- O(7)-C(17)	117.7(2)	C(6)- C(7)-C(11)	110.5(3)
C(3)- N(4)- C(5)	122.2(3)	C(7)-C(11)-C(12)	123.6(2)
S - C(2)- C(3)	112.1(2)	C(7)-C(11)-C(16)	118.9(3)
N(4)- C(3)- C(2)	110.7(2)	C(12)-C(11)-C(16)	117.4(3)
O(5)- C(5)- N(4)	123.0(3)	C(11)-C(12)-C(13)	121.9(3)
O(5)- C(5)- C(6)	123.4(3)	C(12)-C(13)-C(14)	119.3(3)
N(4)- C(5)- C(6)	113.6(3)	O(7)-C(14)-C(13)	125.5(3)
S - C(6)- C(5)	107.1(2)	O(7)-C(14)-C(15)	114.6(3)
S - C(6)- C(7)	109.0(2)	C(13)-C(14)-C(15)	119.8(4)
C(5)- C(6)- C(7)	115.9(3)	C(14)-C(15)-C(16)	119.8(3)
O(6)- C(7)- C(6)	106.2(3)	C(11)-C(16)-C(15)	121.6(3)

Compound 8

Bond	Angle	Bond	Angle
C(2)- S - C(7)	101.9(2)	S - C(7)- C(6)	112.7(2)
C(24)- O(7)-C(27)	117.9(3)	S - C(7)-C(21)	111.6(2)
C(3)- N(4)- C(5)	121.3(2)	C(6)- C(7)-C(21)	115.8(2)
C(3)- N(4)-C(11)	118.3(2)	N(4)-C(11)-C(12)	112.5(2)
C(5)- N(4)-C(11)	117.5(2)	N(13)-C(12)-C(11)	111.8(2)
C(12)-N(13)-C(14)	112.5(2)	C(7)-C(21)-C(22)	123.6(3)
C(12)-N(13)-C(15)	110.3(2)	C(7)-C(21)-C(26)	119.1(2)
C(14)-N(13)-C(15)	110.0(2)	C(22)-C(21)-C(26)	117.2(2)
S - C(2)- C(3)	116.1(2)	C(21)-C(22)-C(23)	121.8(3)
N(4)- C(3)- C(2)	114.2(3)	C(22)-C(23)-C(24)	119.3(2)
O(5)- C(5)- N(4)	122.8(2)	O(7)-C(24)-C(23)	124.8(2)
O(5)- C(5)- C(6)	120.5(2)	O(7)-C(24)-C(25)	115.7(3)
N(4)- C(5)- C(6)	116.7(2)	C(23)-C(24)-C(25)	119.5(3)
O(6)- C(6)- C(5)	111.2(2)	C(24)-C(25)-C(26)	120.2(3)
O(6)- C(6)- C(7)	110.2(2)	C(21)-C(26)-C(25)	121.9(2)
C(5)- C(6)- C(7)	109.7(2)		

EXPERIMENTAL

Melting points were taken in capillary tubes with a Thomas Hoover melting point apparatus and are uncorrected. Ultraviolet spectra were measured in 95% ethanol with a Carey Model 14 spectrophotometer. Infrared spectra were determined with a Beckman Model IR-9 spectrophotometer. Nuclear magnetic resonance spectra were measured with a Varian A-60 or HA-100 spectrometer and recorded in δ values with deuteriochloroform or dimethyl sulfoxide-d_6 as the solvent and tetramethylsilane as an internal reference. The proton signals are designated as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Mass spectra (70 eV, direct inlet system) were determined with a CEC type 21110 spectrometer. Crystallographic data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, 0-20 scans, pulse-height discrimination).

rac.-Dihydro-2-[hydroxy(4-methoxyphenyl)methyl]-2*H*-1,4-thiazin-3(4*H*)one (**5**), rac.-*trans*-Tetrahydro-6-hydroxy-7-(4-methoxyphenyl)-1,4-thiazepin-5(2*H*)-one (**6**) and 4*H*-2,3,5,6-Tetrahydro[1,3]-thiazin-3-one (**7**).

To a solution of sodium methoxide [from 1.4 g of sodium (0.54 g atom) in 100 ml of methanol] was added 6.06 g (0.053 mole) of 2-aminoethanethiol hydrochloride (**3**) and the mixture was heated at reflux for 45 minutes. It was chilled in an ice-bath and filtered. To the filtrate 10.2 g (0.049 mole) of *trans*-3-(*p*-methoxyphenyl)-glycidate (**4**) was added and the solution was stirred at room temperature for 17 hours. The minor isomer **5**, which crystallized out from the solution, was isolated by filtration to give 3.5 g (28%) of white crystalls, mp 143-145°; ir (chloroform): 3420, 3400 (NH), 1664 (lactam CO), 1615, 1587, 1517 cm^{-1}; uv (ethanol): λ max 226 mμ (ε 11960), 267 shoulder (1000), 274 (1275), 280 (1100); ^1H nmr (deuteriochloroform): δ 8.03 (s, 1H, NH), 7.29, 6.87 (AA'BB', J = 8.5 Hz, 4H, ArH), 5.55 (d, J = 3.5 Hz, 1H, HOC*H*), 5.03 (d, d, J = 3.5 and 6.5 Hz, 1H, HOC*H*), 3.77 (d, J = 6.5 Hz, 1H, CHS), 3.75 (s, 3H, OCH_3), 3.20 (m, 2H, NCH_2), 2.57, 2.22 (m, 2H, SCH_2); ms: (70 eV) m/e 253 (M^+).

Anal. Calcd. for $C_{12}H_{15}NO_3S$: C, 56.91; H, 5.97; N, 5.53. Found: C, 56.68; H, 5.86; N, 5.50.

The filtrate, after removal of **5**, was stirred at room temperature for an additional 72 hours and the solids were separated by filtration. The crude product was recrystallized from ethyl acetate to give 4.5 g (36%) of **6** as a white solid, mp 168-170°; ir (chloroform): 3415 (NH), 1670 (lactam CO), 1613, 1514 cm^{-1}; uv (ethanol): λ max 229 mμ (ε, 12250), 276 (1330), 283 (1178), 331 (398); ^1H nmr (DMSO-d_6): δ 8.36 (t, 1H, NH), 7.26, 6.84 (AA'BB', J = 8.5 Hz, 4H, ArH), 4.58 (d, J = 9.5 Hz, 1H, *H*OCH), 4.75 (d, d, J = 9.5 and 7.0 Hz, 1H, HOC*H*), 3.84 (d, J = 9.5 Hz, 1H, CH(OH)C*H*), 3.74 (s, 3H, OCH_3), 3.57 (m, 2H, NCH_2), 2.68 (m, 2H, CH_2S); ms: (70 eV) 253 (M^+).

Anal. Calcd. for $C_{12}H_{15}NO_3S$: C, 56.91; H, 5.97; N, 5.53. Found: C, 56.67; H, 5.91; N, 5.49.

Evaporation of the filtrate, after removal of **6**, yielded 1.2 g of a residue. A portion (0.2 g) of this mixture was chromatographed by preparative tlc on 0.5 mm silica gel plates (a 70:10:0.4, v/v mixture chloroform, methanol and ammonium hydroxide was used as eluent). Extraction of the most intense band (R_f 0.52) afforded crude **7** as a yellow solid which after recrystallization from ethyl acetate gave 0.023 g of pure 3-thiamorpholone **7** mp 89-90° (reported mp 90-91° [12]).

rac.-*trans*-Tetrahydro-6-hydroxy-4-[2-(dimethylamino)ethyl]-7-(4-methoxyphenyl)-1,4-thiazepin-5(2*H*)-one Hydrochloride (**8**).

A suspension of sodium hydride (0.4 g of 50% dispersion in mineral oil, 0.008 mole) in 40 ml dry dimethyl sulfoxide under nitrogen was heated at 70° for one hour and cooled to room temperatue. To the mixture 1.5 g (0.006 mole) of rac.-*trans*-tetrahydro-6-hydroxy-7-(4-methoxyphenyl)-1,4-thiazepin-5(2*H*)-one (**6**) was added then stirred at room temperature for one hour and treated dropwise with a solution of 1.1 g (0.008 mole) of 2-dimethylaminoethyl chloride in 15 ml of dimethyl sulfoxide. After heating at 50° for 1.5 hours, the mixture was poured onto ice-water and the aqueous suspension was extracted with ethyl acetate (3 x 40 ml). The combined ethyl acetate solutions were extracted with 2*N* hydrochloric acid (120 ml). The cooled acidic solution was made basic with 10*N* sodium hydroxide and extracted with ethyl acetate (4 x 40 ml). The organic extracts were dried (magnesium sulfate) and removal of the solvent under reduced pressure gave 1.5 g (79%) of the crude base **8**, which, after treatment with hydrogen chloride (anhydrous) in ethanol, and recrystallization from ethanol afforded 1.0 g (47%) of **8** HCl as a white solid, mp 196-198°; ir (potassium bromide): 3420, 3310 (OH), 2660, 2575, 2470 (NH^+), 1643 (lactam CO) cm^{-1}; uv (ethanol): λ max 229 mμ (ε 1400), 277 (2600), 283 (2450).

Anal. Calcd. for $C_{16}H_{24}N_2O_3S$·HCl: C, 53.25; H, 6.98; N, 7.76. Found: C, 53.38; H, 6.76; N, 7.75.

A sample of the **8**·HCl in water was treated with dilute sodium hydroxide and the aqueous suspension was extracted with ethyl acetate. The organic solutions were dried (magnesium sulfate) and removal of the solvent gave the crude base, which after recrystallization from ether-ethyl acetate afforded the pure base **8** as a yellow solid, mp 90-91°; ir (chloroform): 3400 (OH), 1645 (lactam CO) cm^{-1}; uv (ethanol): λ max 227 mμ (ε 13580), 276 (1350), 283 (1200).

Anal. Calcd. for $C_{16}H_{24}N_2O_3S$: C, 59.23; H, 7.46; N, 8.63. Found: C, 59.00; H, 7.38; N, 8.55.

Crystal Data and Structure Determination.

Details of the crystal data for compounds **5** and **8** are summarized in Table 1. The intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, ω 20 scans, pulse-height discrimination). The structures were solved by a multiple-solution procedure [10] and were refined by full-matrix least squares. In the final refinement, the nonhydrogen atoms were refined anisotropically; the hydrogen atoms were included in structure-factor calculations, but their parameters were not refined.

The final atomic coordinates and equivalent isotropic temperature factors are given in Table II. Bond lengths and bond angles are listed in Tables III and IV.

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[5] *Trans* nomenclature in this work refers to the relative orientation of the aryl and hydroxyl groups.

[6] Crystals from **5** suitable for X-ray analysis were obtained by recrystallization from ethyl acetate.

[7] Crystals from **8** suitable for X-ray analysis were obtained by recrystallization from ethyl acetate.

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