endo-**9-Azabicyclo[3.3.1]nonan-3-ol** (**3**).—Compound **2** (2 g) dissolved in acetic acid (20 ml) was hydrogenated over 10% PtO_2 on charcoal at atmospheric pressure and room temperature for 12 hr. The product obtained following the usual work-up (1.1 gr) was crystallized from chloroform, mp 104° (lit.[7] 102–104°).

3,7-Bis[9-(9-azabicyclo[3.3.1]nonan-3-one)]cyclooctanone (**4**).—To a solution of 2,7-cyclooctadien-1-one (6 g) in methanol (20 ml) was added slowly while stirring a 10% NH_3 in MeOH solution (20 ml), and the mixture was allowed to stand at room temperature until no more dienone could be detected by ir. The methanol was concentrated and the residue filtered to give 3 g of **4**: mp 190° (acetone); ir ν_{max}^{KBr} 2920, 1700, 1280, 1225, 1200, 1150, 1115, 1055, 1010, 950, 845 cm^{-1}; nmr δ 3.60 (m, 4 H), 3.33 (m, 2 H), 2.10–3.00 (m, 12 H), 1.40–2.10 (m, 18 H); mass spectrum *m/e* (rel intensity) 400 (10), 382 (15), 262 (30), 242 (25), 218 (40), 178 (100). *Anal.* Calcd for $C_{24}H_{36}O_3N_2$: C, 71.96; H, 9.06; N, 6.99. Found: C, 72.20; H, 9.06; N, 6.57.

endo-**9-Acetyl-9-azabicyclo[3.3.1]nonan-3-yl Acetate** (**5**).—To a solution of compound **3** (1 g) in pyridine (10 ml) was added acetic anhydride (1 ml), and the solution was left at room temperature overnight. Following the usual work-up compound **5** (1.5 g) was obtained: mp 99–100° (hexane); ir $\nu_{max}^{CHCl_3}$ 1730, 1640, 1030, 800 cm^{-1}; mass spectrum *m/e* (rel intensity) 222 (35, $M\cdot^+$), 210 (10), 182 (20), 166 (28), 165 (30), 124 (100). *Anal.* Calcd for $C_{12}H_{19}NO_3$: C, 64.06; H, 8.50; N, 6.21. Found: C, 64.15; H, 8.48; N, 6.06.

endo-**9-Acetyl-9-azabicyclo[3.3.1]nonan-3-ol** (**6**).—Compound **5** (1 g) was left overnight in a 1% KOH–MeOH solution (20 ml). After neutralization by the addition of 10% HCl in MeOH solution (2 ml), the solvent was evaporated, the residue dissolved in chloroform, and the chloroform washed with water dried (Na_2SO_4) and evaporated. The white solid thus obtained was crystallized from hexane yielding **6** (700 mg): mp 128° (lit.[7] 128–129°); ir ν_{max}^{neat} 3320, 1600, 1020, 1050 cm^{-1}.

2-Acetyl-2-aza-6-oxaadamantane (**7**) **and 9-Acetyl-9-azabicyclo[3.3.1]nonan-3-one** (**8**).—A mixture of dry benzene (120 ml), lead tetraacetate (12 g, dried over P_2O_5 at 0.1 mm), and $CaCO_3$ (6 g, dried over P_2O_5) was heated for 15 min at reflux. Compound **6** (2 g) dissolved in benzene (100 ml) and iodine (5.2 g) was then added and refluxing was continued for 3 hr. The cooled solution was filtered and the filtrate washed with 10% aqueous $Na_2S_2O_3$ (30 ml) and water (15 ml). After the solution was dried and evaporated, the residue was chromatographed on a silica gel column. The first compound which was eluted with 3% MeOH–CH_2Cl_2 was compound **8** (500 mg): mp 115° (hexane); ir ν_{max}^{neat} 1630, 1185, 1100, 1050, 1020, 1000, 980, 950, 860, 780 cm^{-1}; mass spectrum *m/e* (rel intensity) 181 (16, $M\cdot^+$), 153 (8), 138 (16), 124 (8), 96 (100). *Anal.* Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.39; N, 7.72. Found: C, 66.13; H, 8.29; N, 7.68. The second compound which was eluted with 5% MeOH–CH_2Cl_2 was **7** (700 mg): mp 86–87° (hexane); nmr δ 4.10–4.30 (1 H), 4.90–5.10 (1 H), 4.10–4.30 (2 H), 1.6–2.3 (8 H), 2.08 (s, $NCOCH_3$); ir ν_{max}^{neat} 1640, 1060, 1020, 1000, 970, 950, 860, 780 cm^{-1}; mass spectrum *m/e* (rel intensity) 181 (100, $M\cdot^+$), 166 (5), 138 (30), 124 (35), 111 (50). *Anal.* Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.39; N, 7.72. Found: C, 66.20; H, 8.26; N, 8.85.

9-Phenyl-9-azabicyclo[3.3.1]nonan-3-one (**9**).—Following the same procedure as described for **1**, the addition of aniline (0.9 g) to 2,7-cyclooctadien-1-one (1.1 g) at 50° yielded compound **9** (1.2 g): bp 160–162° (0.1 mm); mp 70° (MeOH, lit.[10] 62–64°); ir ν_{max}^{KBr} 3605, 1700, 1600, 1115, 910, 740 cm^{-1}.

endo-**9-Phenyl-9-azabicyclo[3.3.1]nonan-3-ol** (**10**).—Reduction of compound **9** (1 g) under the same conditions as described for the reduction of **1** to give **2** yielded compound **10** (900 mg): mp 98° (benzene–hexane); ir ν_{max}^{KBr} 3220, 1600, 1060, 1025, 910, 730 cm^{-1}. *Anal.* Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.45; H, 8.90; N, 6.55.

9-Azabicyclo[3.3.1]nonan-3-one (**12**).—Compound **1** (1 g) dissolved in methanol (25 ml) was hydrogenated over 5% palladium on charcoal at room temperature and atmospheric pressure for 48 hr in the presence of calalylic amounts of $HClO_4$. After the usual work-up compound **12** (500 mg) was obtained, identical in all respects with the one described in the literature.[7]

9-Benzoyl-9-azabicyclo[3.3.1]nonan-3-one (**11**).—To a solution of **12** (150 mg) in pyridine (2 ml) freshly distilled benzoyl chloride (0.3 ml) was added at 0°. After 4 hr the reaction mixture was poured on ice water and worked up in the usual way. The crude product was chromatographed on an Al_2O_3 column to give compound **11** (80 mg): mp 84–85° (benzene-hexane); ir ν_{max}^{neat} 3030, 1710, 1630, 1600 cm^{-1}; mass spectrum *m/e* (rel intensity) 243 (22, $M\cdot^+$), 138 (45, $C_8H_{12}NO\cdot^+$), 105 (100, $C_6H_5CO\cdot^+$).

Registry No.—**1**, 2291-58-9; **2**, 36079-66-0; **3**, 36079-67-1; **4**, 36146-86-8; **5**, 36079-68-2; **6**, 36079-69-3; **7**, 36146-87-9; **8**, 36146-88-0; **9**, 27092-81-5; **10**, 36079-70-6; **11**, 36146-90-4; **12**, 4390-39-0; 2-aza-6-oxaadamantane, 19557-29-0.

Epimerization of *cis*-4-Amino-5-phenyl-3-isothiazolidinone 1,1-Dioxide and Its 4-*N*-Acetyl Derivative

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Received June 23, 1972

The synthesis of *cis*- and *trans*-4-amino-5-phenyl-3-isothiazolidinone 1,1-dioxide (**3** and **5**) *via* methanolysis of the corresponding 4-acetamido derivatives **1** and **6** and base-catalyzed ring closure is described. Both **1** and **3** undergo rapid and irreversible base-catalyzed epimerizations to **6** and **5**, respectively. These results require reversal of tentative configurational assignments for **1** and **6**.

Recently we reported the synthesis of *cis*- and *trans*-4-acetamido-5-phenyl-3-isothiazolidinone 1,1-dioxide (**1** and **6**) and their rearrangement to 4-benzylidine-2-methyl-2-oxazolin-5-one (**4**) in acetic anhydride–pyridine.[1] We now described the transformation of **1** and **6** to the corresponding 4-amino derivatives **3** and **5**; these are cyclic analogs of phenylalanine, and the first 4-amino-3-isothiazolidinone 1,1-dioxides to be isolated and characterized.[2] During this work it was found that **1** and **3** can be readily epimerized to **6** and **5**, respectively; this result requires reversal of our tentative configurational assignments for **1** and **6**.[3]

Methanolysis of **1** and **6** gave the corresponding 3-sulfamyl phenylalanine methyl esters **2** and **7**; the yield of **7** was consistently low, partly because the crude material was always contaminated with some of the *N*-acetyl derivative **9**, the initial methanolysis product.

(1) J. C. Howard, *J. Org. Chem.*, **36**, 1073 (1971).

(2) The synthesis of 4-amino-3-isothiazolidinone 1,1-dioxide has been reported, but it was characterized only as the silver salt and benzoyl derivative: H. Baganz and G. Dransch, *Chem. Ber.*, **93**, 784 (1960).

(3) These were assigned (ref 1) on the basis of their nmr coupling constants, $J_{4,5}$ = 10.6 (cis) and 7.7 Hz (trans) in pyridine-d_5, but with the caveat that such assignments were valid only in the absence of substituent electronegativity effects, which in the case of **1** and **6** are unknown. The new assignments are based on relative stabilities and are less subject to uncertainty.

TABLE I

RATE CONSTANTS FOR THE BASE-CATALYZED EPIMERIZATION OF 1 AND 3[a]

Compd	Concn, $M \cdot 10^4$	Base: Type	Base: Concn, M	Temp, °C	k_1,[b] $sec^{-1} \cdot 10^2$	k_2, M^{-1} sec^{-1}
1	1.88	H_2O–NaOH	0.100	20.3	1.32	0.132
1	1.90	H_2O–NaOH	0.100	24.8	1.93	0.193
1	1.87	H_2O–NaOH	0.100	29.1	2.89	0.289
1	1.86	H_2O–NaOH	0.050	37.6	2.44	0.488
1	1.99	CH_3OH–CH_3ONa	0.195	24.8	0.231	0.0118
3	1.835	H_2O–NaOH	0.200	20.3	0.376	0.0188
3	1.835	H_2O–NaOH	0.100	24.8	0.297	0.0297
3	1.835	H_2O–NaOH	0.150	24.8	0.468	0.0312
3	1.835	H_2O–NaOH	0.200	24.8	0.577	0.0289
3	1.835	H_2O–NaOH	0.250	24.8	0.741	0.0296
3	1.835	H_2O–NaOH	0.200	29.1	0.825	0.0413
3	1.790	H_2O–NaOH	0.100	37.6	0.774	0.0774

[a] All reaction mixtures except those in CH_3OH–CH_3ONa were made up to ionic strength 1.00 with KCl. [b] Average of two runs, reproducibility ±3%. Activation parameters: 1, $\Delta H^{\pm} = 13.1$ kcal mol^{-1}, $\Delta S^{\pm} = -18.0$ cal mol^{-1} deg^{-1}; 3, $\Delta H^{\pm} = 14.1$ kcal mol^{-1}, $\Delta S^{\pm} = -18.4$ cal mol^{-1} deg^{-1}.

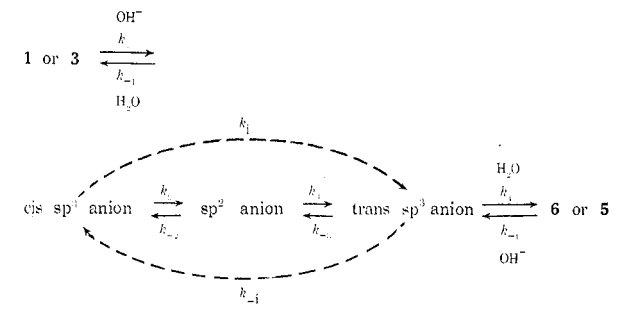
The ring closure reactions of **2**, **7**, and **9** proceeded rapidly with 1 equiv of sodium hydroxide to form in good yield **3**, **5**, and **6**, respectively.

The inner salt character of **3** and **5** was evidenced by their high decomposition points, insolubility in nonpolar solvents, infrared spectra (presence of $-NH_3^+$ and carboxylate bands), and titration data. The pK_1 (proton gained) was too low to be measured in water at the maximum solubility of **3**, but pK_1' values of 2.00 and 2.29, respectively, were obtained for **3** and **5** in 50% ethanol. These are similar to the "proton lost" values of **1** (2.21) and **6** (2.47).[1] Under the same conditions saccharin (**8**), which has a similar acidic function, gave a pK' value of 2.43. The pK_2 values of 5.86 and 6.16 for **3** and **5** reflect the large base-weakening effect of the sulfonyl group; for comparison, under the same conditions the pK_2 for phenylalanine was 9.16.

On one occasion the ring closure of **2** gave **5** instead of the expected **3**; this was found to be the effect of a slight excess of base. Further investigation revealed that in alkaline solution both **1** and **3** epimerized readily and irreversibly to **6** and **5**, respectively. We have investigated the kinetics of these two reactions at four temperatures and varying hydroxide ion concentrations. The rates were followed by recording the increase in absorbance which occurs at 223 nm during the reactions. The results (Table I) showed the epimerizations to be second order overall and first order with respect to substrate and hydroxide ion. The larger rate constant for the epimerization of **1** is considered to be a result of the electron-withdrawing capability of the *N*-acetyl group; the similar value of $\Delta S^{\pm}$ for **1** and **3** would appear to be inconsistent with a marked steric effect.

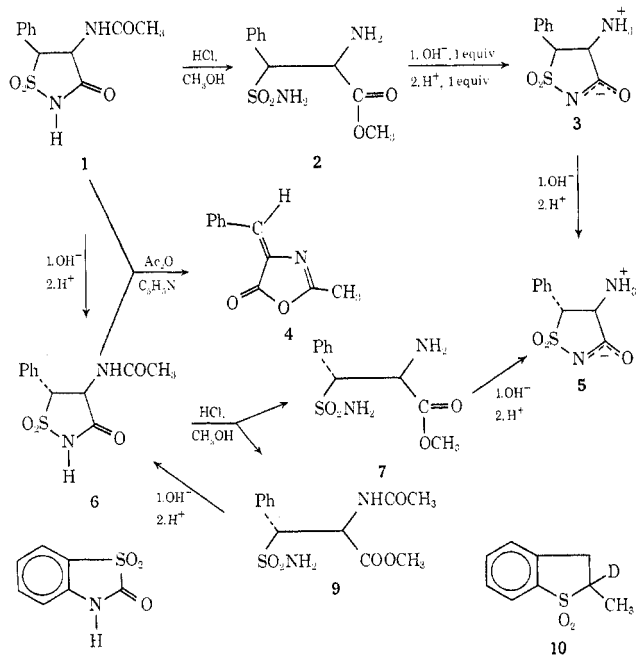
The driving force behind these epimerizations is almost certainly the release from crowding experienced by the α-sulfonyl carbanions[4] as they proceed from the cis to the less restrictive trans isomers. This may take place directly, by inversion of the cis sp^3 anion, or indirectly *via* formation of the sp^2 planar anion, which is then protonated exclusively from the side opposite to the original location of the proton.

Since α-sulfonyl carbanions are the conjugate bases



of very weak acids,[5] it can be assumed that k_{-1} [H_2O] $\gg$ k_1 [OH^-] and k_4 [H_2O] $\gg$ k_{-4} [OH^-]. In addition, the observed irreversibility of the epimerizations requires that k_1 (or $k_2 + k_3$) be much larger than k_{-i} (or $k_{-2} + k_{-3}$).

The large rate-accelerating effect of the phenyl group, previously noted for other α-sulfonyl systems,[6,7]



(4) For a discussion of α-sulfonyl carbanions see D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, pp 105–113, and ref 6–8.

(5) The pK of dibenzyl sulfone is ~22: F. G. Bordwell, R. H. Imes, and E. C. Steiner, *J. Amer. Chem. Soc.*, **89**, 3905 (1957).

(6) F. G. Bordwell, D. D. Phillips, and J. M. Williams, Jr., *ibid.*, **90**, 426 (1968).

(7) L. A. Paquette, J. P. Freeman, and M. J. Wyvratt, *ibid.*, **93**, 3216 (1971).

becomes apparent when the 300-sec half-time for the epimerization of **1** in methanol–sodium methoxide (0.195 *M*) at 24.8° is compared with the 11.5 hr required for 64.6% racemization of the nonbenzylic α-sulfonyl carbanion from 2-deuterio-2-methyl-2,3-dihydrothiophene 1,1-dioxide (**10**) in methanol–sodium methoxide (0.16 *M*) at 76.2°.[8]

It would appear that **1** and **6**, since they are water soluble and differ strikingly from their epimers in uv and nmr absorbance, have distinct advantages as model compounds for the study of α-sulfonyl carbanions. At present we do not plan more experiments in this area.

Experimental Section

Elemental microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Melting points were taken on a calibrated Mel-Temp apparatus. The ir spectra were determined with a Perkin-Elmer 137-B spectrophotometer, and nmr spectra were determined by W. W. Simons of Sadtler Research Laboratories, Philadelphia, Pa., on a Varian A-60A spectrometer using TMS as an internal standard. Dissociation constants were measured at 24 ± 3° by methods previously described.[1]

Rate Determinations.—These were carried out in a Cary 14 spectrophotometer in thermostated cells (temperature variation ±0.05°). The reference cell contained the desired concentration of NaOH adjusted with KCl to constant ionic strength (μ = 1.00). The sample cell contained 2.60 ml of NaOH–KCl solution appropriately constituted to give the same hydroxide ion concentration and ionic strength as the reference cell at 2.80 ml total volume (in reactions carried out in methanol standard CH_3ONa but no KCl was used). After thermal equilibration (20 min), 0.200 ml of stock solution (2×10^{-3} *M*) of **1** or **3** was added at zero time. The increase in absorbance at 223 nm was recorded for at least two and generally three half-times and the infinity absorbance was measured after ten half-times. Scans made at this time gave spectra identical with those of the products **6** or **5** under the same conditions. First-order constants were obtained from semilog plots of $A_\infty - A_t$ *vs* time and second-order constants by dividing these by the hydroxide ion concentration. Runs were made in duplicate, and excellent pseudo-first-order behavior was observed; rate constants were reproducible to within ±3%. Values for E_{act} were calculated from the least-squares slopes of plots of log k_2 *vs.* $1/T$; $\Delta H^{\pm}$ and $\Delta S^{\pm}$ were calculated from k_2 and E_{act} values by the usual equations.[9]

***threo*-3-Sulfamyl Phenylalanine Methyl Ester (2).**—Anhydrous HCl was added to 10 g (37 mmol) of *cis*-4-acetamido-5-phenyl-3-isothiazolidinone 1,1-dioxide[1] (**1**, previously identified[1] as trans) in 170 ml of methanol. After saturation the solution was refluxed for 3 hr and stored overnight at 25°. After chilling briefly, the precipitated hydrochloride salt was collected, washed with methanol–ether, dried at 25° (11 g), and stirred into 25 ml of 10% Na_2CO_3. The precipitate was collected, washed with water, and dried *in vacuo* at 25°, 6.5 g (59%), mp 156–157° dec; recrystallization from methanol raised the melting point to 158–160° dec; p*K* (proton gained) = 4.90; ir (mineral oil) 3350, 3200 (–NH_2), 1750 cm^{-1} (s, C=O).

Anal. Calcd for $C_{10}H_{14}N_2O_4S$: C, 46.51; H, 5.46; N, 10.85; S, 12.41. Found: C, 46.46; H, 5.61; N, 10.70; S, 12.66.

***cis*-4-Amino-5-phenyl-3-isothiazolidinone 1,1-Dioxide (3).**—To 2.5 g (10 mmol) of **2** was added over a 10-min period 10 ml of 1.0 *N* NaOH. After a total of 17 min the cloudy solution was filtered and 10 ml of 1.0 *N* HCl was added. The pH was adjusted to 4 with NaOH and the mixture was stored for 0.5 hr at 0°. The crystals were collected, washed with 1–2 ml of H_2O, and dried at 100°, 1.64 g (72%), mp 235–240° dec. Recrystallization from H_2O gave a hydrate which was dehydrated *in vacuo* at 80°: pK_1' (50% EtOH) = 2.00 (proton gained), pK_2 = 5.86 (proton lost); ir (mineral oil) 2700, 1900 (NH_3^+), 1580 cm^{-1} (s, COO^-); nmr (DMSO-d_6) AB quartet δ 4.50, 4.75 (J = 8 Hz, 2 H, $C_{4,5}$ protons), 7.4 (s, 5 H, phenyl); nmr (TFA-*d*) 5.65 (s, 2 H, $C_{4,5}$ protons), 7.5 (m, 5 H, phenyl); uv max (pH 9.0) $\lambda_{max}^{0.05\ M\ Tris}$ 2700 nm (ε 259), 2635 (351), 2570 (306); for **1**, $\lambda_{max}^{0.05\ M\ Tris}$ 2700 nm (ε 246), 2630 (346), 2570 (302).

Anal. Calcd for $C_9H_{10}N_2O_3S$: C, 47.78; H, 4.46; N, 12.38; S, 14.17. Found: C, 47.75; H, 4.36; N, 12.36; S, 14.39.

Epimerization of 3.—To 203 mg (0.90 mmol) of **3** was added 2 ml of 0.50 *N* NaOH. After 30 min, 1.0 ml of 1.0 *N* HCl was added; the solution was stored at 4°, and the crystals were collected and dried at 100°, 129 mg (63%). The filtrate was evaporated to dryness *in vacuo*, 71 mg. Each fraction gave an ir spectrum virtually identical with that of **5** prepared from **7**.

***erythro*-*N*-Acetyl-3-sulfamyl Phenylalanine Methyl Ester (9).**—Anhydrous HCl was added to 2.0 g (7.5 mmol) of *trans* 4-acetamido-5-phenyl-3-isothiazolidinone 1,1-dioxide[1] (**6**, previously identified[1] as cis) in 50 ml of methanol over a 15-min period. The hot solution was stored at 25° for 20 min and then evaporated *in vacuo*. To the residue was added 25 ml of 0.6 *M* $NaHCO_3$ (pH 7–8). The precipitate was collected, washed with water, and dried *in vacuo*, 1.1 g (49%), mp 147–150° dec. Recrystallization from 3 ml of methanol raised the melting point to 150–151° dec; ir (mineral oil) 3550, 3450, 3300, 3200 (–NH), 1730 (s, ester C=O), 1675 cm^{-1} (s, amide C=O).

Anal. Calcd for $C_{12}H_{16}N_2O_5S$: C, 47.99; H, 5.37; N, 9.33; S, 10.68. Found: C, 47.87; H, 5.35; N, 9.55; S, 10.92.

***erythro*-3-Sulfamyl Phenylalanine Methyl Ester (7).**—To 50 ml of methanol saturated with anhydrous HCl was added 3.0 g (11.2 mmol) of **6**. The solution was refluxed for 2 hr and evaporated *in vacuo* to a gum, to which was added 30 ml of 0.6 *M* $NaHCO_3$ (pH 8). The cloudy solution was evaporated to 15 ml, decolorized with Darco, and stored overnight at 4°. The precipitate was collected, washed with water, and dried at 25°, 1.25 g. The ir spectrum showed the product to be mainly **7** but with some contamination by **9**. Several recrystallizations from methanol afforded pure **7**: mp 154–155 dec; p*K* (proton gained) = 4.81; ir (mineral oil) 3400, 3300, 3250 (NH), 1710 cm^{-1} (s, ester C=O).

Anal. Calcd for $C_{10}H_{14}N_2O_4S$: C, 46.51; H, 5.46; N, 10.85; S, 12.41. Found: C, 46.36; H, 5.41; N, 10.72; S, 12.53.

***trans*-4-Amino-5-phenyl-3-isothiazolidinone 1,1-Dioxide (5).**—To 582 mg (2.25 mmol) of **3** was added 2.20 ml of 1.0 *N* NaOH. The solution was heated to 50° for 10 min, 2.20 ml 1.0 *N* HCl was added, and the mixture was chilled. The crystals were collected and washed with a little H_2O: 360 mg (71%), mp 246–248° dec. Recrystallization from H_2O raised the melting point to 258–260° dec. Neither ir nor nmr spectra showed any evidence of the cis epimer [pK_1 (50% EtOH) = 2.29, pK_2 = 6.15]: ir (mineral oil) 2500, 1950, 1630 (s, NH_3^+), 1590 cm^{-1} (s, COO^-); nmr (DMSO-d_6) 4.56 (s, 2 H, $C_{4,5}$ protons), 7.45 (s, 5 H, phenyl); nmr (TFA-*d*) AB quartet δ 5.60 and 5.40 (J = 11 Hz, 2 H, $C_{4,5}$ protons), 7.6 (s, 5 H, phenyl); uv max (pH 9.0) $\lambda_{max}^{0.05\ M\ Tris}$ 269 nm (ε 158), 263 (237), 259 (271); for **2**, $\lambda_{max}^{0.05\ M\ Tris}$ 270 nm (ε 174), 263 (254), 259 (286).

Anal. Calcd for $C_9H_{10}N_2O_3S$: C, 47.78; H, 4.46; N, 12.38; S, 14.17. Found: C, 47.86; H, 4.32; N, 12.37; S, 14.05.

Synthesis of 6 from 9.—To 225 mg (0.75 mmol) of **9** was added 0.75 ml of 1 *N* NaOH. The solution was filtered from some cloudiness and after 15 min strongly acidified with HCl and chilled. The crystals were collected and dried, 111 mg (53%) mp 223–225°. The ir spectrum showed no evidence of the cis epimer.

Epimerization of 1.—To 57 mg (0.21 mmol) of **1** was added 1.0 ml of 1.0 *N* NaOH. After 6 min at 25° 0.5 ml of 12 *N* HCl was added and the solution was chilled and filtered. The crystals were washed with a little H_2O and dried *in vacuo* at 80°, 44 mg (77%); the ir spectrum was identical with that of **6**.[1]

Registry No.—**1**, 36529-48-3; **2**, 36529-49-4; **3**, 36529-50-7; **5**, 36529-51-8; **6**, 36529-52-9; **7**, 36529-53-0; **9**, 36529-54-1.

Acknowledgment.—We are grateful to the National Science Foundation for Grants GB 4043 and GB 7267, which made this work possible.

(8) D. J. Cram and T. A. Whitney, *J. Amer. Chem. Soc.*, **89**, 4651 (1967).

(9) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, pp 605–607.