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Protected Derivatives of (*R*)-Cysteine and (*R*)-Cysteinol

Asensio González,* and Rodolfo Lavilla*

Laboratory of Organic Chemistry, Faculty of Pharmacy, University of Barcelona, 08028 Barcelona, Spain

Juan F. Piniella, and Angel Alvarez-Larena

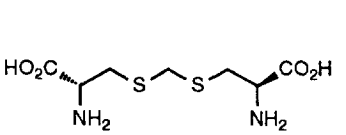
Area de Cristalografía, Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain

Abstract: The synthesis of *N, O, S* protected forms of (*R*)-cysteine and (*R*)-cysteinol as bicyclic derivatives is described. The reactivity and the preparation of substituted derivatives of these systems is also discussed.

In recent years, there has been a growing interest in the use of α-aminoacids in organic chemistry.[1] In this context, the chemistry of (*R*)-cysteine has played an important role in organic reactivity,[2] bio-organic and medicinal chemistry[3] and natural product chemistry.[4] The presence of the thiol in this aminoacid introduces difficult questions with respect to the application of well-developed synthetic methodologies which work for other aminoacids.

In this context, Seebach *et al* have recently reported a procedure for the α-alkylation of α-aminoacids without racemization. The method utilizes bicyclic chiral compounds derived from the condensation of (*S*)-proline and (*R*)-cysteine with trimethylacetaldehyde.[2c]

We wish to report here, in relation to this fruitful strategy, the synthesis of new *N,O,S* protected derivatives of (*R*)-cysteine and (*R*)-cysteinol.



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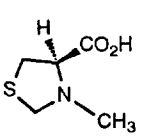

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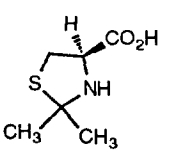

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Figure 1

Although a number of papers dealing with the reaction of cysteine with aqueous formaldehyde have been published,[5] similar studies using an organic solvent instead of water as the reaction medium, have not hitherto been reported. Ratner and Clarke described that treatment of (*R*)-cysteine hydrochloride with 1.1 moles of aqueous formaldehyde, followed by the addition of pyridine, which afforded (*R*)-thiazolidine-4-carboxylic acid.[6] Amstrong and du Vigneaud showed that combination of 2 moles of (*R*)-cysteine with 1 mole of aqueous formaldehyde in strongly acidic solution afforded djenkolic acid **1**.[7] Ando and coworkers reported that

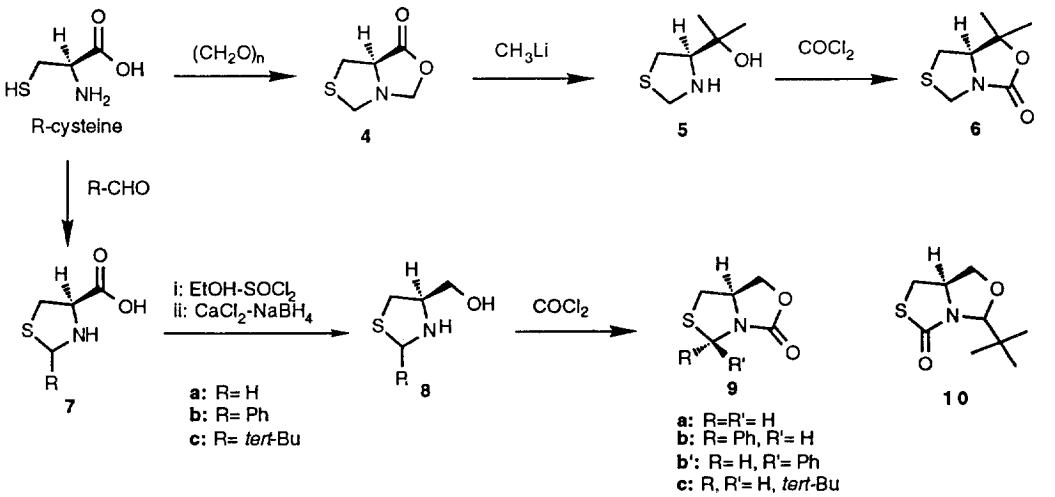
treatment of (*R*)-cysteine with excess of aqueous formaldehyde in the presence of formic acid at 100°C, provides a useful method of preparation of (*R*)-3-methylthiazolidine-4-carboxylic acid **2**.[8]

RESULTS AND DISCUSSION

We envisioned a simple procedure in which a suitable protected cysteine derivative such as (*R*)-2,2-dimethylthiazolidine-4-carboxylic acid **3**[9] would add formaldehyde and undergo a ring closure to form the full protected bicyclic derivative. Treatment of thiazolidine **3** with paraformaldehyde and a catalytic amount of *p*-toluenesulphonic acid with azeotropic removal of water using bencene as the solvent led to extensive decomposition.[10] Subsequently **3** was reacted with paraformaldehyde in dry CH_2Cl_2 in the presence of anh.$MgSO_4$ (1 week), and adduct **4** was obtained in quantitative yield. This result is not entirely unexpected, in view of the fact that thiazolidines undergo facile ring opening-ring closure reactions.[9, 11] The structure of **4** was assumed based on the ^1H- and ^{13}C-NMR spectra, and confirmed by converting (*R*)-thiazolidine-4-carboxylic acid into **4** under identical conditions. Encouraged by the successful results, we proceeded to apply the same conception to the parent α-aminoacid. (*R*)-cysteine was converted into **4** in quantitative yield in one step. Attemps to prepare **4** from (*R*)-cysteine under azeotropic removal of water were unsuccessful.

When compound **4** was treated with methyllithium in anhydrous THF, thiazolidine alcohol **5** was obtained in 40% yield. Subsequent treatment of **5** with phosgene in a dichloromethane/aqueous 2N sodium hydroxide two-phase system, afforded **6** in good yield.[12]

The synthesis of the unsubstituted parent system 1-aza-3-oxa-7-thiabicyclo[3.3.0]octan-2-one **9a** was carried out in a similar way, by reaction of thiazolidine alcohol **8a**[13] with phosgene.



Scheme 1

Although alcohol **8a** was described in the literature, neither spectroscopical nor optical rotation data were available for this substance. A set of experiments was designed to confirm the stereochemical identity of the bicyclic derivative **9a**, and to demonstrate that reduction and oxazolidinone ring formation took place without loss of stereochemical integrity, both aspects were studied. Basic hydrolysis of carbamate **9a** afforded

alcohol **8a** with the same chiroptical properties as the previously synthesized alcohol. Literature precedents showed that no epimerization takes place during the conversion of carboxylic acids to the corresponding alcohols, using the same procedure.[14] For experimental proof, ethyl (*R*)-3-methyl-1,3-thiazolidine-4-carboxylate[15] was prepared from (*R*)-3-methyl-1,3-thiazolidine-4-carboxylic acid **2**.[8] Reduction of this compound, under the same reaction conditions used before, afforded (*R*)-4-hydroxymethyl-3-methyl-1,3-thiazolidine which was characterised spectroscopically and showed the same optical rotation as reported in the literature.[16] Therefore, it can be concluded that there was no significant loss of optical purity in the transformation.

The preparation of C-8 substituted analogues was carried out following the same reaction scheme. Thus, carboxylic acids **7b**[17] and **7c**,[18] were prepared (as epimeric mixtures at C-2) according to described methods, and subsequent esterification and reduction afforded the corresponding alcohols **8b**[19] and **8c** (also as epimeric mixtures). Phosgene interaction with **8b**, afforded two stereoisomers **9b** (14%) and **9b'** (64%), after column chromatography on alumina. On the other hand, treatment of alcohol **8c** yielded only one stereoisomeric thiazolidine **9c** (73%) whose stereochemistry has not been determined and, unexpectedly, **10** (3%). Some features of this transformation deserve comment. First, the production of one isomer from (approximatively) equimolecular epimeric mixtures could be accounted for by analogy with the *N*-acylation of C-2 substitued thiazolidines.[20] Thus, a ring opening - ring closure mechanism would favor the formation of the *cis* isomer. Second, the formation of compound **10**, which has only been detected in the *tert*-butyl series, may arise from a process related to the formation of thioesters during an attempted acylation of thiazolidine alcohols.[16] The stereochemistry of cyclic compounds **9** and **10** could not be determined unambiguously by n.O.e. experiments. In order to ascertain unequivocally the stereochemistry at C-8, an X-ray crystal structure determination was performed on compound **9b'**. This compound exhibits 8*R* configuration. This stereochemistry can be established because the 5*R* configuration is known. Additional studies designed to establish the stereochemistry of thiazolidine **9c** are currently in progress and will be reported in due course.

Figure 2 shows a perspective view of the molecule with the numbering scheme. Atomic parameters are listed in Table 1 and Table 2 lists selected bond lengths and angles.

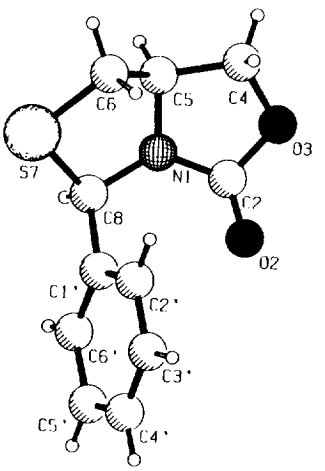


Figure 2. The Molecular Structure of (5*R*,8*R*)-8-Phenyl-1-aza-3-oxa-7-thiabicyclo[3.3.0]octan-2-one (**9b'**) as determined by X-ray Chrystallography.

Table 1. Atomic Coordinates (x 10^4) and Equivalent Isotropic Displacement Parameters (A^2 x 10^3) for **9b'**. U (eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
N(1)	9962(4)	5897(1)	6773(3)	44(1)
O(2)	13214(4)	5935(2)	9575(4)	69(1)
O(3)	13113(4)	5013(1)	6766(4)	59(1)
C(4)	11623(6)	4887(2)	4665(6)	61(1)
C(5)	9260(5)	5389(2)	4791(4)	46(1)
C(6)	8469(5)	6031(2)	2990(4)	51(1)
S(7)	6741(1)	6820(1)	4279(1)	52(1)
C(8)	8564(4)	6678(2)	7026(4)	42(1)
C(1')	10135(5)	7446(2)	7762(4)	46(1)
C(2')	11950(5)	7714(2)	6541(6)	61(1)
C(3')	13484(7)	8392(2)	7253(9)	82(1)
C(4')	13229(9)	8814(3)	9126(8)	95(1)
C(5')	11416(12)	8575(3)	10330(7)	98(2)
C(6')	9818(7)	7886(2)	9642(5)	69(1)

Table 2.. Selected Bond Lengths (Å) and Angles (deg) for **9b'**.

N(1)-C(2)	1.357(3)
N(1)-C(8)	1.456(3)
N(1)-C(5)	1.459(3)
C(2)-O(2)	1.201(4)
C(2)-O(3)	1.354(4)
O(3)-C(4)	1.445(4)
C(4)-C(5)	1.526(4)
C(5)-C(6)	1.510(4)
C(6)-S(7)	1.800(3)
S(7)-C(8)	1.855(2)
C(8)-C(1')	1.504(4)
C(2)-N(1)-C(8)	128.4(2)
C(2)-N(1)-C(5)	112.6(2)
C(8)-N(1)-C(5)	117.3(2)
O(2)-C(2)-O(3)	122.3(3)
O(2)-C(2)-N(1)	128.4(3)
O(3)-C(2)-N(1)	109.2(2)
C(2)-O(3)-C(4)	110.0(2)
O(3)-C(4)-C(5)	105.3(2)
N(1)-C(5)-C(6)	105.9(2)
N(1)-C(5)-C(4)	101.0(2)
C(6)-C(5)-C(4)	117.4(3)
C(5)-C(6)-S(7)	103.9(2)
C(6)-S(7)-C(8)	94.1(1)
N(1)-C(8)-C(1')	113.8(2)
N(1)-C(8)-S(7)	103.1(2)
C(1')-C(8)-S(7)	113.3(2)
C(6')-C(1')-C(8)	120.8(3)
C(2')-C(1')-C(8)	119.8(2)

The angle between the least-squares mean planes defined by N-1, C-2, O-3, C-4, C-5 and N-1, C-5, C-6, S-7, C-8 is 22.8°. The phenyl plane is almost perpendicular to N-1, C-5, C6, S-7, C-8 mean plane (88.7°).

To our knowledge this is the first non fused 1-aza-3-oxa-7-thiabicyclo[3.3.0]octan-2-one structure described and only three private communications[21] of polycyclic structures containing this bicyclic skeleton are listed in the Cambridge Structure Database.[22]

In conclusion, the reaction of thiazolidine aminoalcohols with phosgene represents a reliable method to obtain bicyclic derivatives of (*R*)-cysteinol[23] in homochiral form and may be understood mechanistically in terms of thiazolidine ring opening-ring closure reactions.

EXPERIMENTAL PART

General. All solvents were dried by standard methods. All reagents were of commercial quality from freshly opened containers. Prior to concentration under reduced pressure, all organic extracts were dried (Na_2SO_4). Column chromatography was carried out on Al_2O_3 (aluminum oxide, 90, neutral activity I, Merck 0.063-0.200 mm) or on SiO_2 (silica gel 60, Merck 0.063-0.200 mm) . TLC was carried out on SiO_2 (silica gel 60F 254 Merck, 0.063-0.200 mm) and the spots located with UV light or iodine vapors. Melting points were taken using a Büchi apparatus and are uncorrected. Microanalyses were performed on a Carlo-Erba 1106 analyzer by Centro de Investigación y Desarrollo (CSIC) Barcelona. ^1H and ^{13}C NMR spectra were obtained using a Varian XL-200 instrument in $CDCl_3$ with TMS as an internal reference, unless otherwise specified. IR spectra were recorded on a Perkin Elmer 1600 series FTIR. Mass spectra were determined on a Hewlett-Packard 5930A mass spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter.

(*R*)-1-Aza-3-oxa-7-thiabicyclo[3.3.0]octan-4-one (4): To a mixture of (*R*)-cysteine (3.7g, 30.5 mmol), anhydrous magnesium sulphate (4g, 33.0 mmol) in anhydrous dichloromethane (200 ml) at room temperature, paraformaldehyde (2g, 66 mmol) was added, and the suspension was stirred for 72 h. Another portion of paraformaldehyde (2g, 66 mmol) was added and stirring was continued for 96 h. The suspension was filtered through a short pad of silica-gel,and removal of the solvent under reduced pressure afforded 4.42 g (100%) of analytically pure **4**. ^1H-NMR: 5.22 (d, J=5.5 Hz, 1H, H2); 4.89 (d, J=5.5 Hz, 1H, H-2); 4.26 (d, J=11.1 Hz, 1H, H-8); 4.13 (d, J=11.1 Hz, 1H, H-8); 4.07 (dd, J=7.1 and 1.8 Hz, 1H, H-5); 3.41 (dd, J=12.1 and 1.8z, 1H, H-6); 3.24 (dd, J=12.1 and 7.1 Hz, 1H, H-6). ^{13}C-NMR: 175 .0 (C-4); 88.2 (C-2); 64.8 (C-5); 61.9 (C-8); 36.2 (C-6). IR (KBr): 1789 (C=O). MS (m/z, %): 145 (M^+, 100); 112 (15); 86 (13); 72 (28). mp 81-82°C. Anal. Calcd for $C_5H_7NO_2S$: C, 41.36; H,4.86; N, 9.65. Found: C, 41.47; H, 4.87; N, 9.64. $[\alpha]_D$ -42° (c=0.5, dichloromethane). The optical purity of this compound was secured by mild hydrolysis to (R)-thiazolidine-4-carboxylic acid with the same optical rotation as described.[6]

(*R*)-4-(1-Hydroxy-1-methylethyl)-1,3-thiazolidine (5): To a stirred solution of **4** (1.89 g, 13 mmol) in anhydrous THF (50 ml) kept at -30°C under argon atmosphere, methyllithium (24 ml, 39 mmol) was added and the solution was stirred at -30°C for 1 h and left overnight at room temperature. Saturated aqueous ammonium chloride solution (100 ml) was added and the mixture was extracted with diethyl ether (3 x 40 ml). The organic extracts, once dried and evaporated, gave a residue which was chromatographed over alumina. Elution with dichloromethane afforded **5** (0.76 g, 40%) as a colourless oil. ^1H-NMR: 4.29 ((d, J=9.5 Hz, 1H, H-2); 4.09 (d,

J=9.5 Hz, 1H, H-2); 3.01 (m, 2H, H-4 and H-5); 2.67 (t, J=11.8 Hz, 1H, H-5); 2.24 (bs, 2H, OH, NH); 1,33 (s, 3H, CH_3); 1.28 (s, 3H, CH_3). ^{13}C-NMR: 73.6 (C-4); 70.4 (C-O); 53.9 (C-2); 33.4 (C-5); 28.8 (CH_3); 27.1 (CH_3). IR (film): 3400 (O-H, N-H). MS (m/z, %): 147 (M^+, 6); 88 (100); 59 (36), 56 (33). $[\alpha]_D$ -33°C (c=0.5, dichloromethane).

(4*R*)-4-Hydroxymethyl-1,3-thiazolidines (8); General Procedure: Thionyl chloride (15 ml) was added dropwise to absolute ethanol (100 ml) kept at -10°C, under vigorous stirring. Carboxylic acids (**7**, 0.1 mol) were added in small portions, and the resulting mixtures were stirred for 4 h at 40°C. The volatiles were removed under reduced pressure, and the residue was taken in saturated aqueous sodium carbonate (250 ml) and extracted with dichloromethane (5 x 40 ml). The organic extracts, once dried and evaporated, afforded the corresponding ethyl esters which were used without further purification. Calcium chloride dihydrate (3.40g, 23.1 mmol) was dissolved in absolute ethanol (120 ml) and a solution of sodium borohydride (1.58g, 41.6 mmol) in ethanol (200 ml) was added under vigorous stirring at -20°C. After the addition was complete, stirring was continued for 20 min. A solution of carboxylic ester (50 mmol) in ethanol (50 ml) was added dropwise and the mixture stirred at -20°C for 10 h. The solution was allowed to reach room temperature, and a solution of hydrogen chloride in ethanol (25%, 10 ml) was added. The solvent was removed under reduced pressure and the residue was taken in concentrated aqueous ammonium hydroxide solution (200 ml) and extracted with dichloromethane (4 x 40 ml). Evaporation of the dried organic extracts afforded thiazolidine alcohols **8**.

8a (80%).^{1}H-NMR: 4.18 (d, J=8.5 Hz, 1H, H-2); 4.17 (d, J=8.5 Hz, 1H, H-2); 3.74 (dd, J=11.0 and 4.3 Hz, 1H, CH_2-O); 3.58 (dd, J=11.0 and 6.7 Hz, 1H, CH_2-O); 3.49 (m, 1H, H-4); 2.97 (dd, J=10.3 and 6.5 Hz, 1H, H-5); 2.70 (bs, 2H, NH and OH); 2.65 (dd, J=10.3 and 6.4 Hz, 1H, H-5). ^{13}C-NMR: 65.7 (C-4); 61.7 (CH_2O); 53.3 (C-2); 34.6 (C-5). IR (KBr): 3226 and 3175 (N-H and O-H). MS (m/z, %): 118 ($M-1^+$, 9%); 87 (39); 86 (41); 42 (100). mp 78 - 80°C (lit.[6] 79 -81°C). $[\alpha]_D$-24.0° (c=0.6, dichloromethane).

8b (75%) and **8c** (68%) were isolated as mixtures of epimers at C-2.

Oxazolidone ring formation; General Procedure: Aqueous sodium hydroxide (2M, 50 ml) was added to a solution of thiazolidine alcohol (1 mmol) in dichloromethane (50 ml). A solution of phosgene in toluene (1.93M, 2 ml) was added to the stirred solution and the mixture stirred overnight at room temperature. ***CAUTION:*** Phosgene is a highly toxic reagent with dangerous delayed effect and its use is recommended only in a well ventilated hood. The concentration of phosgene in the hood should be monitored as reported.[24] The aqueous layer was separated and extracted with dichloromethane (3 x 30 ml). The combined organic extracts, once dried and evaporated, yielded a residue which was chromatographed over alumina.

(*R*)-4,4-dimethyl-1-aza-3-oxa-7-thiabicyclo[3.3.0]octan-2-one (6). On elution with dichloromethane, compound **6** (72%) was isolated. ^{1}H-NMR: 4.86 (d, J=8.8 Hz, 1H, H-8); 4.16 (d, J=8.8 Hz, 1H, H-8); 3.72 (dd, J=9.9 and 5.9 Hz, 1H, H-5); 2.87 (dd, J=10.5 and 5.9 Hz, 1H, H-6); 2.76 (dd, J=10.5 and 9.9 Hz, 1H, H-6); 1.60 (s, 3H, CH_3); 1.49 (s, 3H, CH_3). ^{13}C-NMR: 158.2 (C-2); 79.4 (C-4); 70.9 (C-5); 47.4 (C-8); 30.8 (C-6); 28.2 (CH_3); 22.2 (CH_3). IR (KBr): 1744 (C=O). MS (m/z, %): 172 ($M-1^+$, 28); 126 (10); 81 (70), 41 (100). Mp 98 - 99°C, Anal. Calcd. for $C_7H_{11}NO_2S$: C, 48.55; H, 6.36; N, 8.09. Found: C, 48.75; H,6.48; N, 8.04. $[\alpha]_D$ -23.2° (c=0.3, MeOH).

(*R*)-1-aza-3-oxa-7-thiabicyclo[3.3.0]0ctan-2-one (9a). On elution with dichloromethane, compound **9a** (87%) was isolated. ^{1}H-NMR: 4.86 (d, J=9.0 Hz, 1H, H-8); 4.57 (dd, =9.3 and 6.9 Hz, 1H, H-4); 4.29 (dd, J=9.3 and 1.7 Hz, 1H, H-4); 4.15 (d, J=9.0 Hz, 1H, H-8); 4.10 (m, 1H, H-5); 3.15 (dd, J=10.5 and 6.4 Hz, 1H, H-6); 2.71 (dd, J=10.5 and 9.4, 1H, H-6). ^{13}C-NMR: 159.2 (C-2); 66.6 (C-4); 61.4 (C-5); 47.7 (C-8); 34.3 (C-6). IR (NaCl): 1753 (C=O). MS (m/z, %): 145 (M^+, 42); 130 (52); 99 (28); 55 (100). Anal.Calcd. for $C_5H_7NO_2S$: C, 41.38; H, 4.83: N, 9.65. Found: C, 41.37; H, 4.97; N, 9.59. $[\alpha]_D$ +3.2° (c=0.25, dichloromethane).

(5*R*, 8*S*)-8-Phenyl-1-aza-3-oxa-7-thiabicyclo[3.3.0]octan-2-one (9b). On elution with hexanes - dichloromethane (1:9), compound **9b** (14%) was isolated. ^{1}H-NMR: 7.42-7.25 (m, 5H, ArH); 5.65 (s, 1H, H-8); 4.58 (m, 1H, H-5); 4.46 (dd, J=8.8 and 7.6 Hz, 1H, H4); 4.18 (dd, J=8.8 and 7.0 Hz, 1H, H-4); 3.09 (m, 2H, H-6). ^{13}C-NMR: 152.9 (C=O); 136.4 (C-1 Phe); 128.6 (C-3 and C-5 Phe); 128.2 (C-2 and C-6 Phe); 127.5 (C-4 Phe); 66.3 (C-4); 64.4 (C-5); 62.7 (C-8); 34.3 (C-6). IR (KBr): 1743 (C=O). MS (m/z,%): 221 (M^+, 52); 162 (46); 129 (31); 104 (86). Mp 120 - 121°C. Anal. Calcd. for $C_{11}H_{11}NO_2S$: C, 59.73; H, 4.98; N, 6.33. Found, C, 59.49; H, 4.84; N, 6.25. $[\alpha]_D$ +48.7°(c=0.55, dichloromethane).

(5*R*, 8*R*)-8-Phenyl-1-aza-3-oxa-7-thiabicyclo[3.3.0]octan-2-one (9b'). On elution with dichloromethane, compound **9b'** (64%) was isolated. ^{1}H-NMR: 7.45 - 7.30 (m, 5H, ArH); 6.30 (s, 1H, H-8); 4.62 (dd, J=9.5 and 6.5 Hz, 1H, H-4); 4.34 - 4.29 (m, 2H, H-4 and H-5); 3.27 (, J=10.0 Hz and 5,5 Hz, 1H, H-6); 2.93 (t, J=10 Hz, 1H, H-6). ^{13}C-NMR: 159.0 (C-2); 140.2 (C-1 Phe); 128.6 (C-3 and C-5 Phe); 128.2 (C-2 and C-6 Phe); 126.1 (C-4 Phe); 66.7 (C-4); 65.2 (C-8); 61.7 (C-5); 31.2 (C-6). IR (KBr): 1740 (C=O). MS (m/z, %): 221 (M^+, 24); 162 (20); 121 (26); 104 (100). mp 90 - 92°C. $[\alpha]_D$ -235° (c= 0.3, MeOH).

Crystal data for compound **9b'**: $C_{11}H_{11}NO_2S$, M=221.27, monoclinic, space group $P2_1$ (No. 4), a = 5.494 (2) Å, b = 15.525 (2) Å, c= 6.159 (2) Ä, β = 98.03 (2)° (from least squares fitting of setting angles for 25 reflections 10.2 ≤θ≤14.1°), V = 520.2 Å^3, Z = 2, D_c = 1.413 g cm^{-3}, μ = 2.9 cm^{-1}; radiation: graphite monochromated Mo-Kα (λ = 0.71069 Å), colourless prismatic crystal 0.54 x 0.40 x 0.22 mm.

Data Collection and Processing: Data were collected on an Enraf Nonius CAD4 in ω-2θ scan, T = 293K, data collection range 2 < 2θ <50° (−6≤ h ≤6, 0 ≤ k ≤ 18, 0 ≤ 1≤ 7). 950 unique reflections of which 925 were observed (I > 2σ (I)). No significant variation in intensity of one standard reflection was observed.

Structure Solution and Refinement: The structure was solved by direct methods using the SHELXS-86 program.[25] Full matrix least-squares refinement on F^2 for all reflections was carried out using the SHELXL-93 program,[26] number of variables : 138, hydrogen atoms fixed at calculated positions, two overall isotropic temperature factors used for them (one for phenyl hydrogens and another one for aliphatic hydrogens). R(F) = 0.0273, $R_W(F^2)$ = 0.0730 for the observed reflections.

(5*R*)-8-*tert*-Butyl-1-aza-3-oxa-7-thiabicyclo[3.3.0]octan-2-one (9c). On elution with hexanes - dichloromethane (2:8), compound **9c** (73%) was isolated. ^{1}H-NMR: 4.54 (s, 1H, H-8); 4.37 (t, J=8.0 Hz, 1H, H-4); 4.32 (m, 1H, H-5); 4.07 (dd, J=8.0 and 5.5 Hz, 1H, H-4); 2.95 (dd, J=10.5 and 6.0 Hz, 1H, H-6); 2.76 (t, J=10.5, 1H, H6); 1.21 (s, 9H, CH_3). ^{13}C-NMR: 73.1 (C-8); 66.0 (C-4); 65.6 (C-5); 35.4 (C-C7); 32.7 (C-6); 27.7 (CH_3), (C-2 not seen). IR (KBr): 1750 (C=O). MS (m/z, %): 201 (M^+, 15%); 144 (100); 130 (23); 100 (26). Mp 67 - 68°C. Anal. Calcd. for $C_9H_{15}NO_2S$: C, 53.73; H, 7.46; N, 6.96. Found: C, 53.56; H, 7.62; N, 6.88. $[\alpha]_D$ -10.8° (c=0.31, MeOH).

(5R)-2-*tert*-Butyl-1-aza-3-oxa-7-thiabicyclo[3.3.0]octan-8-one (10). On elution with dichlorometane, compound **10** (3%) was obtained. ^{1}H-NMR: 4.95 (s, 1H, H2); 4.20 (m, 1H, H-5); 4.08 (dd, J=7.7 and 5.8 Hz, 1H, H-4); 3.61 (dd, J=11.5 and 8.7 Hz, 1H, H-6); 3.48 (dd, J=9.8 and 7.7 Hz, 1H, H-4); 3.19 (dd, J=11.5 and 2.5 Hz, 1H, H-6); 0.95 (S, 9H, CH_3). ^{13}C-NMR: 175.8 (C-8); 98.0 (C-2); 68.8 (C-4); 59.8 (C-5); 36.2 (C-C2); 29.7 (C-6); 24.9 (CH_3). IR ($CHCl_3$): 1685 (C=O).MS (m/z, %): 144(28); 116 (17); 83 (42).

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