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OPTICAL ACTIVITY OF LACTONES AND LACTAMS—III

CIRCULAR DICHROISM SPECTRA OF 5-OXAZOLIDINONES

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Abstract—The synthesis and the chiroptical properties of several 5-oxazolidinones derived from α-amino acids are reported. The existence of an equilibrium between the two enantiomeric envelope conformations of 5-membered ring has been inferred from CD and NMR spectra. In a few cases the small contribution of the planar ring conformation to the equilibrium is proposed. The nature of the lowest energy transition and the usefulness of the Weigang lactone sector rule for Cotton effect sign predictions are discussed on the basis of CNDO/2-CI calculations.

In the previous papers,[1] the chiroptical properties of 1,3-dioxolan-4-ones and 4-oxazolidinones, heterocyclic analogues of γ-lactones and γ-lactams, derived from α-hydroxy acids, have been investigated. Several sector rules determining the sign of the Cotton effect (CE) for the lowest energy $n \rightarrow \pi^*$ electronic transition have been tested.

The present studies deal with 5-oxazolidinones and 4-imidazolidinones,[2] lactones and lactams, respectively, derived from α-amino acids. This research was aimed to analyze the conformational equilibria of 5-oxazolidinones on the basis of their CD curves.

The CD spectra of several 3-(toluene-4-sulphonyl)-5-oxazolidinones were measured previously by Satsumabayashi *et al.*[3] However these authors could not observe the CD due to $n \rightarrow \pi^*$ lactone transition, as this band was masked by strong aromatic ^1L_a transition of toluene-4-sulphonamide moiety. To avoid such an undesirable effect, alkylsulphonyl groups which do not exhibit any absorption maxima above 180 nm,[4] were chosen as N-acyl groups in these studies.

Synthesis. 5-Oxazolidinones with an unequivocal absolute configuration are easily available in the acid catalyzed reaction of N-acylamino acids with aldehydes.[5] Several optically active compounds (**1–5**) were obtained from N-methylsulphonyl amino acids and paraformaldehyde. The same reaction with acetaldehyde as a substrate gave a mixture of the diastereoisomers **6a** and **6b**, which were separated by fractional crystallization and by column chromatography.

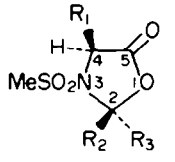
The synthesis of N-t-butylsulphonyl compounds met some difficulties, since trimethylmethanesulphonyl chloride is an unstable compound and it does not acylate an amino group.[6] The compounds **7** and **8** were obtained in the several step synthesis: the corresponding amino acid esters were acylated with trimethylmethanesulphinyl chloride and the resultant sulphinylamides were then oxidized with $KMnO_4$ to give the esters **9a, b**. The esters **9a, b** were smoothly hydrolyzed to the N-t-butylsulphonylamino acids **10a, b**, which were converted into 5-oxazolidinones in the usual manner.

For comparison, the bicyclic 5-oxazolidinone **11** without N-sulphonyl group was obtained as a single product in the condensation of (S)-proline with chloral. The stereochemistry of **11** appears to be analogous to **12**, the compound obtained recently by Seebach *et al.*[7] The geometry at C-2 of **11** was deduced from NOE experiment.†

NMR spectra. NMR data of several 5-oxazolidinones are collected in Table 1. The characteristic feature of these spectra is a nonequivalence of C-2 methylene protons, which are manifested as an AB quartet.

The five-membered ring in γ-lactones is known to occur in an envelope conformation, in which O=C—O group and the two α- and γ-C atoms are lying in one plane and β-atom is deviated from the ring plane, as it was shown by X-ray and NMR studies.[8] Since 5-oxazolidinones are the heterocyclic analogues of γ-lactones, the similar geometry of the ring is expected for both types of compounds. The ring chirality is determined by a steric effect of bulky substituents.

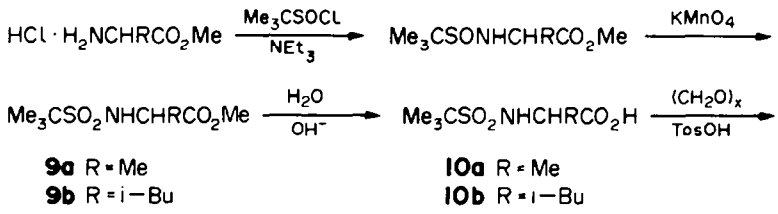
A conformation with a bulky 4-substituent in an axial position is the most preferred one; in such case, the unfavourable steric interaction of 4-substituent with alkylsulphonyl group is diminished. The sulphonylamino group deshields near protons and



1 R_1=Me, R_2=R_3=H
2 R_1=i—Pr, R_2=R_3=H
3 R_1=i—Bu, R_2=R_3=H
4 R_1=CH_2Ph, R_2=R_3=H
5 R_1=Ph, R_2=R_3=H
6a R_1=Me, R_2=Me, R_3=H
6b R_1=Me, R_2=H, R_3=Me

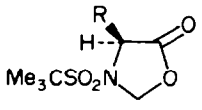
Scheme 1.

† Double irradiation of —$CHCCl_3$ proton produces 20% enhancement of the signal of one of the two —CH_2N— protons. From this result, it was inferred that —CCl_3 group is on *exo*-face in a *cis*-relationship with bridgehead hydrogen, since in this configuration —$CHCCl_3$ and —NCH_2— hydrogens are close.



9a R = Me
9b R = i—Bu

10a R = Me
10b R = i—Bu



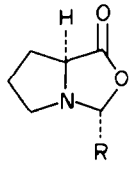
7 R = Me
8 R = i—Bu

Scheme 2.

therefore the equatorial protons are observed at lower field than the axial ones. As a result of the increased population of A conformer the difference between the chemical shifts of C-2 hydrogens grows for the compounds with bulky 4-substituent (*cf.* **1** and **2**) or for those with bulky N-alkylsulphonyl group (*cf.* **1** and **8**). The phenylalanine derivative **4** seems to be an interesting case. The signal of an axial proton at C-2 is shifted up-field by about 1 ppm, as compound with the signals of the corresponding protons in 4-alkyl substituted 5-oxazolidinones. This effect can be attributed to the formation of the folded conformation in which the phenyl ring lies directly over the heterocycle moiety and, thus causes the anisotropic shielding of the nearby C-2 hydrogen.

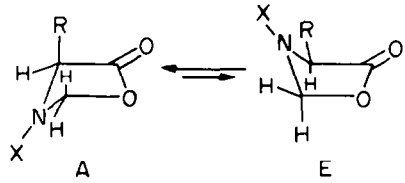
Such a folding is the result of an interaction between the permanent dipole of heterocycle and the induced dipole in the phenyl ring; this geometry is a common feature of benzyl-substituted heterocyclic derivatives such as 2,5-piperazinediones,[9] hydantoins,[10] and 4-oxazolidinones.[1]

The above considerations neglected another potentially important factor, namely the influence of sulphonamide nitrogen inversion and rotation around S—N bond on the conformational equilibria and on the spectra of 5-oxazolidinones. However, X-ray[11] and electron diffraction studies[12] revealed that sulphonamide N-atom is only 0.27 Å away from the plane of the three neighbouring atoms, whereas the distance 0.51 Å is expected for pyramidal configuration. The p



11 R = CCl_3
12 R = CMe_3

Scheme 3.

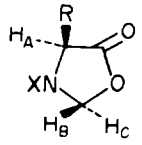


A E

X = $MeSO_2$; Me_3CSO_2

Scheme 4.

Table 1. ^{1}H-NMR data for 5-oxazolidinones.[a]



Comp.	R	X	δH_A[b]	δH_B	δH_C	J_{BC}	δH
1	Me	$MeSO_2$	4.31 (q)	5.30	5.57	6.0	3.0
2	i-Pr	$MeSO_2$	4.03 (d)	5.21	5.66	6.9	2.97
3	i-Bu	$MeSO_2$	4.22 (t)	5.21	5.61	7.6	2.95
4	CH_2Ph	$MeSO_2$	4.57 (t)	4.46	5.50	6.8	2.74
5	Ph	$MeSO_2$	5.29 (s)	5.28	5.71	6.0	2.87
7	Me	Me_3CSO_2	4.57 (q)	5.17	5.70	4.8	1.43
8	i-Bu	Me_3CSO_2	4.57 (t)	5.13	5.73	6.3	1.40
13	Me	$PhCH_2OCO$	4.36 (q)	5.33	5.53	4.4	5.24, 7.41

[a] Recorded in $CDCl_3$; δ (ppm); J (Hz).
[b] q = quartet, d = doublet, t = triplet, s = singlet.

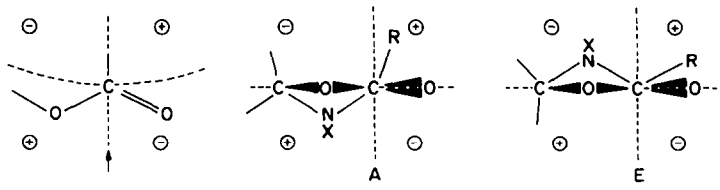
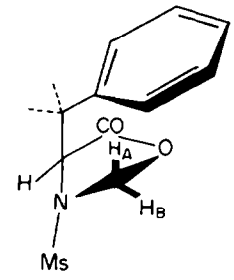


Fig. 1. The sector projections of 5-oxazolidinone conformations. The arrow shows direction of projection.

character of nitrogen lone pair calculated for this geometry amounts to 93%, whereas the corresponding values for sp^2 and sp^3 hydridization amount to 100% and 75%, respectively.[10] Recent X-ray crystalographic studies on $(PhSO_2)_2NH$ showed that N-atom is almost purely sp^2 and planar.[13] The effect of nitrogen inversion and S—N rotation on NMR spectra was studied for several types of sulphonamides.[14] Lambert *et al.*[15] found that the magnitude of the barrier to nitrogen inversion in N-tosylazetidine was extremely low (6.2 kcal/mol at −170°, about 3 kcal/mol lower than for the corresponding N-methyl compound) and that



Scheme 5.

the S—N rotation was rapid in the NMR time scale. They also postulated that these phenomena would not be observed for larger ring-sulphonamides. Therefore the assumption that the sulphonamide group is planar on average in time seems to be a justified simplification for the purpose of conformational analysis. The close analogy between NMR spectra of **3** and N-benzyloxycarbonyl derivative **13** supports the validity of this assumption.

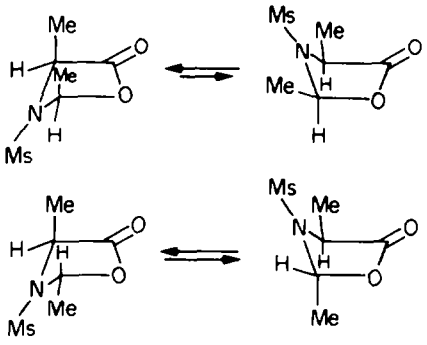
Circular dichroism spectra. Chiroptical properties are extremely sensitive to stereochemical changes thus the CD spectra should provide a more detailed picture of 5-oxazolidinone conformational equilibria than NMR. In the previous paper[1] of this series, it was shown that the best correlation between CD corresponding to the $n \rightarrow \pi^*$ transition and lactone stereochemistry is given by Weigang *et al.*'s[16,17] sector rule. If we assume that the NX group has an effect qualitatively similar to that of CH_2 in the same location, this rule predicts a positive CE sign for A and a negative for E conformation of 5-oxazolidinones (Fig. 1). According to the Snatzke doctrine of spheres,[18] it was assumed that the contribution of chiral ring to the magnitude of CE outweighs the contribution of alkyl substituent. The CD data of **1–11** are presented in Table 2. The strong positive CD band near 215 nm (Fig. 2) suggests the predominance of an envelope A conformation with an axial 4-substituent for **1–4** and **7, 8** in accordance with NMR predictions. The magnitude of this band is augmented with the increase of the size of 4-substituent (*cf.* **1–2**) and the size of 3-alkylsulphonyl group (*cf.* **1–7** and **3–8**), since the enhancement of substituent bulkiness results in the predominance of A conformer. The solvation of sulphonamide group enhances its steric interactions with substituents. Hence, this effect is probably responsible for the increase of intensity of positive CE caused by polar solvents.

These observations can be applied to the

Table 2. CD data for 5-oxazolidinones ($[\theta]$ in deg · $mole^{-1}$ · cm^2; λ in nm)

Comp.	Solv.[a]	λ_{max}	$[\theta] \cdot 10^{-3}$	Comp.	Solv.[a]	λ_{max}	$[\theta] \cdot 10^{-3}$
1	C	216	3.5	4	C	210	17.9
		255	−0.02			263	−0.12[b]
	A	213	4.0		A	212	12.3
		253	−0.006			253	0.10[b]
	M	213.5	4.03	5	C	223	12.2
		254	−0.006			257	−0.13[b]
2	C	218	4.03	6a	C	214	5.97
		256	−0.014		M	212.5	6.12
	A	216.5	4.95	6b	C	215	−1.39
		255	−0.006		M	215	−0.55
	M	217	4.97	7	C	215	4.69
		256	−0.005		A	215	4.9
3	C	214	1.54		M	215	4.9
		243	−0.23				
	A	213	2.5	8	C	216.5	4.79
		243	−0.16		A	216.5	4.25
	M	212	2.55		M	217	4.21
		243	−0.14	11	C	228.5	−15.2

[a] C = cyclohexane–dioxane (4:1), A = acetonitrile, M = methanol.
[b] The highest intensity vibronic band.



Scheme 6.

differentation of diastereoisomers **6a** and **6b**. Strong interactions between two methyl and methylsulphonyl groups lead to the predominance of a diaxial conformer of *cis*-diastereoisomer.

The strong positive CD, which is only slightly solvent-dependent, indicates that *cis*-**6a** exists in a solution as an almost pure diaxial conformer. Yet, two nearly equivalent axial-equatorial conformers are expected in equilibrium for the *trans*-diastereoisomer.† The weak negative CD exhibited by *trans*-**6b** points to the slight predominance of the form with 4-substituent in an axial position. It reflects probably the known tendency of substituents to eclipse a carbonyl group.[19] The above examples illustrate the advantage of CD over NMR spectroscopy in such correlations, since **6a** and **6b** show essentially the same chemical shifts for all corresponding protons.

The thorough analysis of CD spectra of **1**–**3** shows that the additional negative CD band of low intensity for **1** and **2** and of moderate intensity for **3** is present at $n \rightarrow \pi^*$ region (Fig. 2). The attempts to find out the origin of this band come across some difficulties. It is obvious that the presence of the strong positive CE near 215 nm is responsible for the red shifting of this long-wavelength band to about 250 nm. It was shown,[20] that a close proximity of oppositely signed CE affected the position and the magnitude of CD maxima. The long-wavelength negative CE appears to be affected by conformational equilibria, since its intensity is solvent- and substituent-dependent. It seems unlikely that E conformation is responsible for this CE since the ring E is a mirror image of the ring A, thus both conformers should absorb at the same wavelength (*cf.* the spectra of **6a** and **6b**); the presence of E conformer in an equilibrium is manifested only by the decrease of the intensity of 215 nm band. The negative CE is the most distinct in the CD spectrum of **3** where there is a strong interaction of the bulky 4-axial substituent with the 2-axial hydrogen and is absent from the spectra of **7** and **8**; where there is an interaction between the bulky 3- and 4-substituents. This indicates that the third conformation, more crowded than A, is responsible for the long-wavelength CE. This may be the planar or near planar conformation which is more crowded than A

† The relative thermodynamic instability of *trans*-**6b** over *cis*-**6a** originates from the destabilization of steric interactions between methyl and methylsulphonyl groups and is manifested in the condensation reaction which leads to the almost pure *cis*-**6a** diastereoisomer.

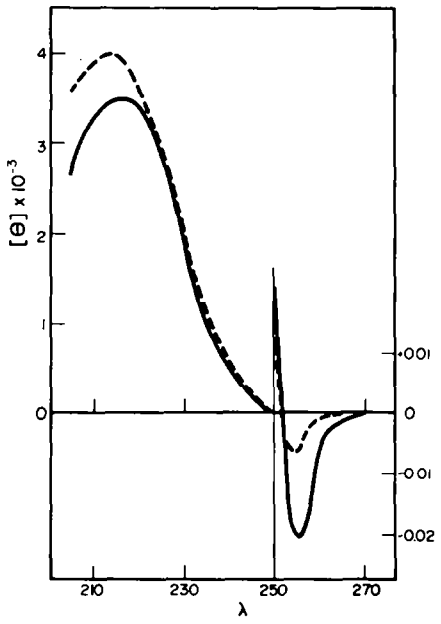
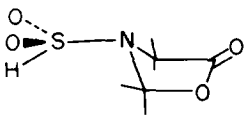
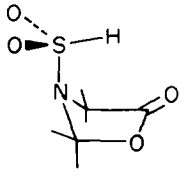
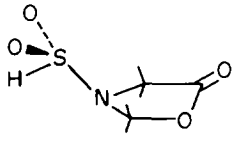


Fig. 2. Circular dichroism spectra of (S)-4-methyl-3-methylsulphonyl-5-oxazolidinone (**1**) in cyclohexane–dioxane (4:1) (——) and methanol (----).

and E, yet it diminishes 2,4-diacial interactions. It is noteworthy that a similar tendency is the characteristic feature of 1,3-dioxolan-4-ones, which were investigated earlier.[1] CNDO/2-CI calculations for several structures presented in Table 3 confirm this assignment. The calculated $n \rightarrow \pi^*$ transition energy has the lowest value for the planar conformation. However, it is confusing that according to the Weigang sector rule positive CD sign for the planar conformation is predicted. Obviously, the planar ring does not contribute to CE sign but vicinal effects of substituents are responsible for positive contribution to CE. Quantum mechanical calculations offer a reasonable explanation. INDO[21] and CNDO/2[1] calculations for various types of lactones show that the lowest energy $n \rightarrow \pi^*$ transition is almost localized in the ester group. However, the present CNDO/2-CI calculations for 5-oxazolidinones show that the presence of nitrogen atom in the heterocycle causes the extensive mixing of single-excited configurations and thus it is difficult to characterize the lowest energy transition in terms of one-electron excitations between specific pairs of orbitals. This transition may be better characterized as a combination of several transitions in chromophore extended to a whole molecule, especially to the nitrogen atom. Similar conclusion comes from Richardson *et al.*[22] semiempirical calculations for α-amino acids and from experimental results for amino lactones.[23] Moreover, the interaction between CO π^* orbital and the amino lone pair orbital is known to affect the electronic spectra of α-substituted ketones.[24] This is probably the reason why the Weigang lactone sector rule predicts the correct sign for a chiral ring contribution but it fails for smaller vicinal effects of substituents.

The hitherto discussed compounds were N-acylated species. It seems to be interesting to compare these derivatives with the analogous compounds lacking N-

Table 3. CNDO/2-CI results.[a]

Form[b]	E_t	ΔE	μ
	−121.2981	6.56	4.76
	−121.2969	6.45	1.19
	−121.3009	6.37	2.17

[a] E_t = total energy in a.u.; ΔE = transition energy in eV; μ = dipole moment in D.

[b] The dihedral angle C5, 01, C2, N3 was assumed 24° for envelope conformations, the geometry of sulphonamide group according to ref. 12.

sulphonyl group. Since 5-oxazolidinones exhibit properties of active esters,[4] the proline derivative **11** was chosen to avoid the self-condensation reaction. The CD spectrum of **11** shows the strong negative CE near 220 nm. This result indicates the predominance of E conformation of oxazolidinone ring. The strong magnitude of CE is probably due to the close in energy $n \rightarrow \sigma^*$ transitions involving nitrogen and chlorine lone pairs.[25]

EXPERIMENTAL

CD spectra were recorded on a JASCO J-20 spectropolarimeter. Methanolic solutions of 5-oxazolidinones were freshly prepared before measurement to avoid slow solvolysis reaction. NMR spectra were taken with a Varian EM-260A (60 MHz) spectrometer with TMS as an internal standard. IR spectra were measured with a Zeiss IR-10 spectrometer. Trimethylmethanesulphonyl chloride was freshly prepared and used without further purification.[26] The CNDO/2-CI calculations were performed for geometries derived from X-ray[8] and electron diffraction data.[12] The standard parameterization[27] with 3d orbitals and limited CI was used for 27 singly excited configurations.

(*S*)-N-(*Methylsulphonyl*)*alanine*, obtained by acylation of (*S*)-alanine with methanesulphonyl chloride, m.p. 63–65° ($CHCl_3$ form); $[\alpha]_D^{20} = -25.6°$ (*c* 2, AcOEt); NMR (δ, DMSO-d_6): 9.64 (br, 1H, CO_2H), 7.51 (d, 1H, SO_2NH), 4.01 (q, 1H, $C\underline{H}CH_3$), 2.99 (s, 3H, CH_3SO_2) and 1.31 (d, 3H, $CHC\underline{H}_3$); (Found: C, 28.64; H, 5.61; N, 8.31; $C_4H_9NO_4S$ requires: C, 28.75; H, 5.43; N, 8.38); *cyclohexylammonium salt*, m.p. 134–135°; (Found: C, 45.35; H, 8.30; N, 10.47; $C_{10}H_{22}N_2O_4S$ requires: C, 45.10; H, 8.33; N, (10.52%).

(*S*)-N-(*Methylsulphonyl*)*valine*, obtained as above, oil, NMR (δ, $CDCl_3$): 10.13 (s, 1H, CO_2H), 5.53 (d, 1H, SO_2NH), 3.97 (dd, 1H, $C_\alpha H$), 2.93 (s, 3H, CH_3SO_2), 2.14 (m, 1H, $C_\beta H$), 0.97 (d, 3H) and 0.83 (d, 3H); *cyclohexylammonium salt*, m.p. 181–183°; (Found: C, 48.92; H, 8.93; N, 9.59; $C_{12}H_{26}N_2O_4S$ requires: C, 48.97; H, 8.90; N, 9.52%).

(*S*)-N-(*Methylsulphonyl*)*phenylalanine*, obtained as above, m.p. 104–105°; $[\alpha]_D^{20} = -21.9°$ (*c* 2, MeOH); (Found: C, 49.28; H, 5.39; N, 5.65; $C_{10}H_{13}NO_4S$ requires: C, 49.38; H, 5.39; N, 5.76%).

(*S*)-N-(*Methylsulphonyl*)*phenylglycine*, obtained as above, m.p. 126–127°; $[\alpha]_D^{20} = +128.3°$ (*c* 2, MeOH); (Found: C, 47.10; H, 4.82; N, 6.05; $C_9H_{11}NO_4S$ requires: C, 47.17; H, 4.84; N, 6.11%).

(*S*)-N-(t-*Butylsulphonyl*)*alanine methyl ester* (**9a**). (*S*)-Alanine methyl ester hydrochloride (7.0 g) was dissolved in $CHCl_3$ (100 ml) and trimethylmethanesulphinyl chloride (7.7 g) was added, after cooling to 0° Et_3N (15.0 ml) was slowly added with stirring and cooling. The mixture was stirred for 15 min, then it was washed with dil HCl, water and $NaHCO_3$ aq, dried ($MgSO_4$) and evaporated. The residue was dissolved in acetone (100 ml) and sat $KMnO_4$ soln was added slowly until the $KMnO_4$ colour persisted, then the soln was filtered and acetone was evaporated at reduced pressure. The resulted sulphonamide was extracted with $CHCl_3$, dried ($MgSO_4$), $CHCl_3$ was evaporated and residue was crystallized from toluene/hexane to obtain 8.5 g of the product; m.p. 68°; NMR (δ, CCl_4): 5.14 (d, 1H, SO_2NH), 4.06 (m, 1H, $CH_3C\underline{H}$); 3.77 (s, 3H, CO_2CH_3); 1.47 (d, 3H, $C\underline{H}_3CH$) and 1.36 (s, 9H, $C(CH_3)_3$); IR (KBr): 3325 (SO_2NH), 1740 (CO_2Me), 1320 and 1130 (SO_2); (Found: C, 43.03; H, 7.94; N, 6.29; $C_8H_{17}NO_4S$ requires: C, 43.05; H, 7.68; N, 6.27%).

(*S*)-N-(t-*Butylsulphonyl*)*leucine methyl ester* (**9b**), obtained as **9a**; m.p. 59° (hexane); NMR (δ, CCl_4): 5.17 (d, SO_2NH, 1H), 3.97 (m, 1H, $C\underline{H}NH$), 3.74 (s, 3H, CO_2CH_3), 1.33 (s, 9H, $C(CH_3)_3$); IR (KBr): 3300 (SO_2NH), (CO_2CH_3), 1310 and 1133 (SO_2); (Found: C, 50.04; H, 9.07; N, 5.30; $C_{11}H_{23}NO_4S$ requires: C, 49.80; H, 8.74; N, 5.28%).

(*S*)-N-(t-*Butylsulphonyl*)*alanine* (**10a**). **9a** (4.46 g) was dissolved in MeOH (50 ml) and after cooling to 0° 10% NaOH aq (10 ml) was added. After 1 hr at 0°, MeOH was evaporated, the mixture was extracted with ethyl ether and aqueous phase was acidified with dil H_2SO_4. The product was extracted with ethyl ether and after drying ($MgSO_4$) and evaporation of ether it was crystallized from EtOAc/hexane to obtain 3.1 g of crystals; m.p. 162–164°; $[\alpha]_D^{20} = -23.5°$ (*c* 2, MeOH); NMR (δ, $CDCl_3$): 8.13 (br, 1H, CO_2H), 4.87 (d, 1H, SO_2NH), 4.17 (m, 1H, $CH_3C\underline{H}$), 1.50 (d, 3H, $CHC\underline{H}_3$) and 1.36 (s, 9H, $C(CH_3)_3$);

(Found: C, 40.12; H, 7.49; N, 6.65; $C_7H_{15}NO_4S$ requires: C, 40.19; H, 7.23; N, 6.70%).

(*S*)-N-(t-*Butylsulphonyl*)*leucine* (**10b**), obtained as **10a**, m.p. 98° (toluene/hexane); $[\alpha]_D^{20} = -28.5°$ (*c* 2, $CHCl_3$); NMR (δ, $CDCl_3$): 9.6 (s, 1H, CO_2H), 5.04 (d, 1H, SO_2NH), 4,03 (m, 1H, $C_\alpha H$), 1.30 (s, 9H); (Found: C, 47.72; H, 8.26; N, 5.53; $C_{10}H_{21}NO_4S$ requires: C. 47.80; H, 8.42; N, 5.57%).

(*S*)-4-*Methyl*-3-*methylsulphonyl*-5-*oxazolidinone* (**1**). (*S*)-N-(Methylsulphonyl)alanine (1.4 g), paraformaldehyde (0.6 g) and *p*-toluenesulphonic acid (0.05 g) were refluxed for 1 hr in $CHCl_3$ (150 ml) with azeotropic trapping of water. The mixture was washed with $NaHCO_3$ aq, dried ($MgSO_4$) and evaporated. The residue was crystallized from toluene to obtain 1.2 g of the product; m.p. 86°; $[\alpha]_D^{20} = +145°$ (*c* 2, $CHCl_3$); NMR (δ, $CDCl_3$): 5.57 and 5.30 (AB system, 2H, NCH_2O), 4.31 (q, 1H, $CH_3C\underline{H}$), 3.0 (s, CH_3SO_2) and 1.61 (d, 3H, $C\underline{H}_3CH$); IR (KBr): 1808 and 1794 (CO), 1332 (SO_2); IR ($CHCl_3$): 1812 (CO); (Found: C, 33.59, H, 4.95; N, 7.77; $C_5H_9NO_4S$ requires: C, 33.53; H, 5.06; N, 7.82%).

(*S*)-4-*Isopropyl*-3-*methylsulphonyl*-5-*oxazolidinone* (**2**), obtained as **1** but the condensation reaction was carried out in benzene, m.p. 56° (benzene/hexane), $[\alpha]_D^{20} = +125°$ (*c* 1, $CHCl_3$); (Found: C, 40.62; H, 6.23; N, 6.75; $C_7H_{13}NO_4S$ requires: C, 40.58; H, 6.32; N, 6.76%).

(*S*)-4-*Isobutyl*-3-*methylsulphonyl*-5-*oxazolidinone* (**3**), obtained as **2**; m.p. 51–52° (toluene/hexane); $[\alpha]_D^{20} = +103°$ (*c* 2, $CHCl_3$), (lit.[28] m.p. 49–50°; $[\alpha]_D^{20} = +102.5°$ (*c* 2, $CHCl_3$)).

(*S*)-4-*Benzyl*-3-*methylsulphonyl*-5-*oxazolidinone* (**4**), obtained as **2**, m.p. 106° (toluene/hexane); $[\alpha]_D^{20} = +108°$ (*c* 1, $CHCl_3$); (Found: C, 51.37; H, 5.31; N, 5.17; $C_{11}H_{13}NO_4S$ requires: C, 51.77; H, 5.13; N, 5.49%).

(*S*)-4-*Phenyl*-3-*methylsulphonyl*-5-*oxazolidinone* (**5**), obtained as **2**, m.p. 125° (toluene/hexane); $[\alpha]_D^{20} = +172°$ (*c* 1.5, $CHCl_3$); (Found: C, 50.02; H, 4.61; N, 5.89; $C_{10}H_{11}NO_4S$ requires: C, 49.80; H, 4.60; N, 5.81%).

(2*S*,4*S*)- and (2*R*,4*S*)-2,4-*Dimethyl*-3-*methylsulphonyl*-5-*oxazolidinones* (**6a** and **6b**). (*S*)-N-(Methylsulphonyl)alanine (3.3 g), paraldehyde (30 ml) and *p*-toluenesulphonic acid (0.1 g) were refluxed in $CHCl_3$ (100 ml) for 6 hr with azeotropic trapping of water. The mixture was then washed with $NaHCO_3$ aq, dried ($MgSO_4$) and evaporated. The residue was crystallized from toluene to obtain 2.4 g of *cis*-**6a**, m.p. 126°; $[\alpha]_D^{20} = +69.5°$ (*c* 2, $CHCl_3$); NMR (δ, $CDCl_3$): 5.70 (q, J = 5.5 Hz, 1H, $C\underline{H}CH_3$), 4.21 (q, J = 7.2 Hz, 1H, $C_\alpha\underline{H}CH_3$), 2.96 (s, 3H, CH_3SO_2), 1.63 (d, J = 5.5 Hz, 3H, $CHC\underline{H}_3$) and 1.58 (d, J = 7.2 Hz, 3H, $C_\alpha HC\underline{H}_3$); (Found: C, 37.46; H, 5.71; N, 7.18; $C_6H_{11}NO_4S$ requires: C, 37.31; H, 5.74; N, 7.25%). The mother liquor from crystallization was evaporated and chromatographed on silica gel to obtain 0.15 g of *trans*-**6b**; m.p. 58–60° (toluene/hexane); NMR (δ, $CDCl_3$): 5.72 (q, J = 5.5 Hz, 1H, $C\underline{H}CH_3$), 4.21 (q, J = 7.2 Hz, 1H, $C_\alpha\underline{H}CH_3$), 3.03 (s, 3H, CH_3SO_2), 1.68 (d, J = 5.5 Hz, 3H, $CHC\underline{H}_3$) and 1.64 (d, J = 7.2 Hz, 3H, $C_\alpha HC\underline{H}_3$); (Found: C, 37.05; H, 5.89; N, 7.12; $C_6H_{11}NO_4S$ requires C, 37.31; H, 5.74; N, 7.25%).

(*S*)-4-*Methyl*-3-t-*butylsulphonyl*-5-*oxazolidinone* (**7**), obtained from **10a** in similar manner as **2**; m.p. 91° (toluene/hexane); $[\alpha]_D^{20} = +101°$ (*c* 1.5, $CHCl_3$); IR (KBr): 1808 and 1705 (CO), 1332 and 1145 (SO_2); IR (CCl_4): 1820 (CO); (Found: C, 43.36; H, 7.02; N, 6.33; $C_8H_{15}NO_4S$ requires: C, 43.44; H, 6.83; N, 6.33).

(*S*)-4-*Isobutyl*-3-t-*butylsulphonyl*-5-*oxazolidinone* (**8**), obtained from **10b** in similar manner as **2**, m.p. 75° (toluene/hexane); $[\alpha]_D^{20} = +102°$ (*c* 1, $CHCl_3$); IR (KBr): 1812 and 1802 (CO), 1330 and 1130 (SO_2); (Found: C, 50.10; H, 8.25; N, 5.83; $C_{11}H_{21}NO_4S$ requires: C, 50.18; H, 8.04; N, 5.32%).

(2*R*,5*S*)-2-*Trichloromethyl*-1-*aza*-3-*oxabicyclo*[3.3.0]*octan*-4-*one* (**11**). (*S*)-Proline (1.7 g), chloral hydrate (4.0 g) and DMSO (10 ml) were refluxed in benzene (50 ml) with azeotropic trapping of water for 2 hr. The mixture was washed several times with $NaHCO_3$ aq, dried ($MgSO_4$), decolorized with silica gel and evaporated to dryness. The residue was crystallized from toluene/hexane to obtain 2.2 g of the product; m.p. 108° (lit.[29] m.p. 110°); $[\alpha]_D^{20} = +33°$ (*c* 2, C_6H_6); NMR (δ, CCl_4): 5.05 (s, 1H, $CHCCl_3$), 4.00 (t, 1H, $C_\alpha H$), 3.40 (m, 1H, CH_2N), 3.23 (m, 1H, CH_2N) and 2.0 (m, 4H); IR (CCl_4): 1822 (CO); (Found: C, 33.97; H, 3.28; N, 5.44; $C_4H_8NO_2Cl_3$ requires: C, 34.38; H, 3.30; N, 5.73%).

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