Tetrahedron Vol. 41, No 3, pp. 611 to 616, 1985
Printed in Great Britain.

0040-4020/85 $3.00 + .00

OPTICAL ACTIVITY OF LACTONES AND LACTAMS—IV

CHIROPTICAL PROPERTIES OF 4-IMIDAZOLIDINONES

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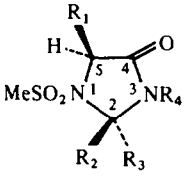
(*Received in UK* 13 *March* 1984)

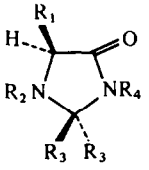
Abstract—The chiroptical properties of 4-imidazolidinones are reviewed. Several optically active compounds were obtained from amides and N-methylamides of corresponding N-acylamino acids. The origin of the two lowest energy electronic transitions is considered. The equilibrium between the two envelope conformations of heterocyclic ring was observed by means of NMR and CD spectra. The spectra of the compounds with non-protected amino group are affected by n → σ^* transition involving nitrogen lone pair.

In the preceding paper,[1] the conformational equilibria of 5-oxazolidinones, the heterocyclic analogues of γ-lactones, have been studied on the basis of their CD spectra and the sign of Cotton effect (CE) has been assigned for each conformation. The present paper reports the investigations on the less known derivatives of α-amino acids—4-imidazolidinones, which are heterocyclic analogues of γ-lactams. It seems worth examining whether the lactam sector rules[2-5] can be applied to 4-imidazolidinones and finding out a correlation between the geometry and the CE sign of these compounds. A comparison between the chiroptical properties of 4-imidazolidinones and 5-oxazolidinones, which imitate γ-lactams and γ-lactones, respectively, seems to be interesting as well.

Several optically active 4-imidazolidinones **1–8** were obtained in the acid catalyzed reaction of amides or N-methylamides of N-methylsulphonyl amino acids with aldehydes and ketones. Methylsulphonyl group was used as N-acyl for the reasons discussed previously.[1] The compounds **9–10** with the unprotected amino group were obtained by the cleavage of the corresponding 1-benzyloxycarbonyl derivatives **7–8** with hydrogen bromide in acetic acid solution.[6] The condensation of (*S*)-prolinamide with acetone gives bicyclic imidazolidinone **11**.

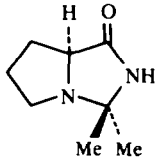
The ring geometry of 4-imidazolidinones is governed by the similar factors as in the case of 5-oxazolidinones.[1] Analogically to γ-lactams,[7] the envelope conformation with amide group C-2 and C-5 atoms in one plane and N-1 atom deviated from the ring plane is the most preferred one. The ring chirality is determined by a steric effect of bulky substituents. Thus, in the case of 1-alkylsulphonyl compounds, the A conformer with 5-substituent in an axial position is expected to be the most populated in the equilibrium.





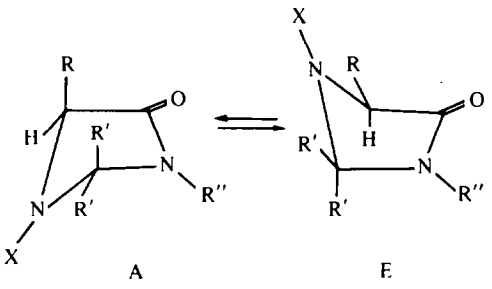
1a R_1 = Me, R_2 = R_3 = H, R_4 = Me
1b R_1 = Me, R_2 = R_3 = Me, R_4 = H
1c R_1 = Me, R_2 = R_3 = Et, R_4 = H
2 R_1 = iPr, R_2 = R_3 = H, R_4 = Me
3 R_1 = iBu, R_2 = R_3 = H, R_4 = Me
4 R_1 = CH_2Ph, R_2 = R_3 = H, R_4 = Me
5 R_1 = Ph, R_2 = R_3 = H, R_4 = Me
6a R_1 = Me, R_2 = Me, R_3 = H, R_4 = Me
6b R_1 = Me, R_2 = H, R_3 = Me, R_4 = Me

7a R_1 = Me, R_2 = $PhCH_2OCO$, R_3 = H, R_4 = Me
7b R_1 = Me, R_2 = $PhCH_2OCO$, R_3 = Me, R_4 = H
8 R_1 = CH_2Ph, R_2 = $PhCH_2OCO$, R_3 = H, R_4 = Me
9a R_1 = Me, R_2 = R_3 = H, R_4 = Me
9b R_1 = Me, R_2 = H, R_3 = Me, R_4 = H
10 R_1 = CH_2Ph, R_2 = R_3 = H, R_4 = Me



11

Scheme 1.



X=$MeSO_2$; $PhCH_2OCO$

Scheme 2.

The E conformer is disfavoured because of steric interaction of 5-substituent, occupying an equatorial position, with close 1-alkylsulphonyl group.

However, the substitution of C-2 with bulky substituents causes the increase of 1,5-transannular interactions. Hence, in such case the E conformer, in which these interactions are diminished, should contribute more to the equilibrium. The conformational similarity of 5-substituted 4-imidazolidinones and 4-substituted 5-oxazolidinones results in the resemblance of the NMR spectra of **1a–4, 7, 8** and those of corresponding 5-oxazolidinones,[1] e.g. the C-2 methylene products are unequivalent and accordingly they are manifested as AB quartet. The difference between the chemical shifts of these two protons is greater for the larger 5-substituents, as a result of a greater population of A conformer in the conformational equilibrium. However, the NMR spectra of both types of heterocycles differ considerably, since the protons attached to C-2 and C-5 of the 4-imidazolidinone ring show a long-range coupling ($^4J_{2,5}$), while the analogous protons in 5-oxazolidinones do not. Moreover, only the *trans*-arranged hydrogens exhibit the measurable values of $^4J_{2,5}$ and then the higher-field arm of the C-2 methylene AB system is split by the proton at C-5.[8] Therefore, $^4J_{2,5}$ can be applied to the easy identification of diastereoisomers; e.g. **6b** ($^4J_{2,5}$ = 2.3 Hz) is assigned as *trans*- and **6a** (no measurable $^4J_{2,5}$) is assigned as *cis*-diastereoisomer.

In phenylalanine derivatives **4** and **8** the signals of axial 2-H, for which $^4J_{2,5}$ are observed, are up-field shifted in comparison with alkyl-substituted compounds **1a–3**. It can be concluded from these results that as in the case of the corresponding 5-oxazolidinone,[1] **4** and **8** exist mainly in a folded conformation, where the phenyl ring lies directly over the heterocyclic moiety, causing anisotropic shielding of the nearby 2-H, which is *trans*-oriented to 5-H.

The chiroptical properties of 4-imidazolidinones appear to be more complicated than those of 5-oxazolidinones. The CD data of **1–6** and **9–11** are collected in Table 1. The inspection of the spectra of **1a** (Fig. 1), **2a** and **3** reveals the presence of two overlapping CD bands of opposite signs: the strong positive band near 205 nm and the negative one of moderate intensity at about 235 nm. The long-wavelength band connected with low absorption can be assigned to the $n \rightarrow \pi^*$ lactam transition; this assignment is supported by the fact that this band is red-shifted in the solvents of decreasing polarity. The nature of the short-wavelength band is difficult to explain. This transition is connected with strong absorption and, therefore, CD is not always measurable. It cannot be assigned as $\pi \rightarrow \pi^*$ transition, since it is enormously displaced to the red as compared with normal amide $\pi \rightarrow \pi^*$ bands.[9]

The possible explanation is that an exciton

Table 1. CD data for 4-imidazolidinones ([θ] in deg · mole^{-1} · cm^2; λ in nm)

Comp.	Solv.[a]	λ_{max}	[θ] · 10^{-3}	Comp.	Solv.[a]	λ_{max}	[θ] · 10^{-3}
1a	C	205	11.60	5	D	226	14.4
		240	−0.74			261	0.13[b]
	A	236.5	−0.66	6a	D	242.5	−0.08
	M	205	15.0		M	207	27.8
		235	−0.42			241	−0.03
1b	D	220	4.2	6b	C	224	2.0
	M	213	6.5		M	216	3.0
1c	C	222	1.61	9a	C	221	11.0
	M	216	7.1		M	215	12.0
2	C	235	−2.15		M[c]	215	5.97
	A	234.5	−1.23	9b	M	222	3.1
	M	208	11.0		M[c]	217	6.49
		234	−0.92				
3	D	230	−4.68	10	M[c]	216	−8.86
	M	203	14.6			227	3.24
		228	−2.69			262[b]	−0.37
4	C	217	25.6	11	C	231	−4.92
		237	−1.51			261	0.03
		259	0.07[b]		M	201	14.0
	M	216	27.9			222	−1.03
		236	−0.62			238	0.78
		259	0.10[b]			262	−0.01
					M[d]	218	8.6

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

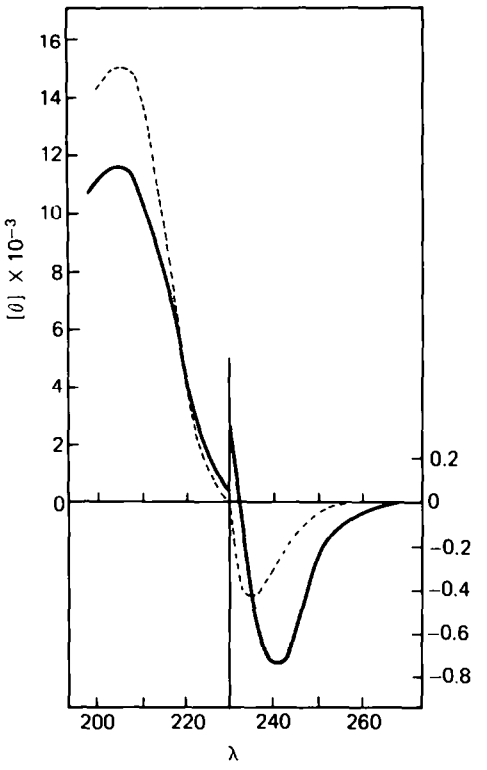


Fig. 1. Circular dichroism spectra of (*S*)-3,5-dimethyl-1-methylsulphonyl-4-imidazolidinone (**1a**) in cyclohexane–dioxane (4 : 1) (——) and methanol (-----).

coupling[10] is possible between dipole allowed $\pi \rightarrow \pi^*$ transitions in amide and sulphonamide groups; a long-wavelength part of the "couplet" formed,[5,11] which is red-shifted in respect to the isolate $\pi \rightarrow \pi^*$ excitation, is observed. The steady rigid orientation and the close space proximity of both chromophores favour this coupling.† CE corresponding to the $n \rightarrow \pi^*$ lactam transition is the most valuable for stereochemical correlations. The sector rules developed by Weigang *et al.*[3] predict a negative CD for A conformation and a positive one for E conformation of the ring (Fig. 2). It is noteworthy that these signs are opposite to those for lactones. Similar results come from the rules that are based on the ring chirality.[4] The negative CD near 235 nm for **1a**, **2**–**4**, which magnitude increases along with the increase of 5-substituent size, points to a predominance of the envelope A conformation with an axial 5-substituent, in accordance with the NMR predictions. The fact that the same results were obtained by both spectroscopic methods proves that the sector rules are still valuable for 4-imidazolidinones, in spite of a complex nature of the electronic transitions. The CD spectra of **1b** and **1c** show that the substitution of C-2 with bulky substituents causes the inversion of the CE sign. Thus, the increased 2,5-transannular interactions give rise to the predominance of the E conformer. The CE corresponding to the $n \rightarrow \pi^*$ transition is strongly affected by solvents; the polar solvents reduce considerably the negative CE and enhance the positive CE. The solvent effect reflects not only the changes of conformational equilibrium but, first of all, it alters the overlapping of oppositely signed CD bands.[14] The blue shift of the $n \rightarrow \pi^*$ transition in polar solvents increases its overlapping with strong 205 nm band and then the magnitude of the positive CD is increased and that of the negative CD is decreased (Fig. 1).

The obtained results can serve as a basis for the more complicated conformational analysis in the case of **6a** and **6b**.

No favourable conformation can be expected for *cis*-**6a**, since the diaxial form is destabilized by the 2,5-transannular interaction of axial methyls and the diequatorial form is destabilized by the interaction of N-methylsulphonyl group with neighbouring methyls as well as by the interaction of 2- and N-methyls. For this reason, only the low negative CD at 242 nm is observed, indicating a slight preference of diaxial form. In contrast, the equilibrium between the two axial-equatorial conformers can be expected for *trans*-**6b**. Both forms are characterized by equivalent interactions of methylsulphonyl group and equatorial methyls, although an additional interaction between 2- and N-methyl groups disfavours the E conformer and therefore the positive CE of moderate intensity appears in the spectrum.

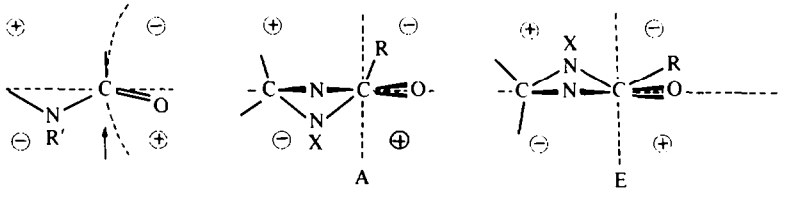
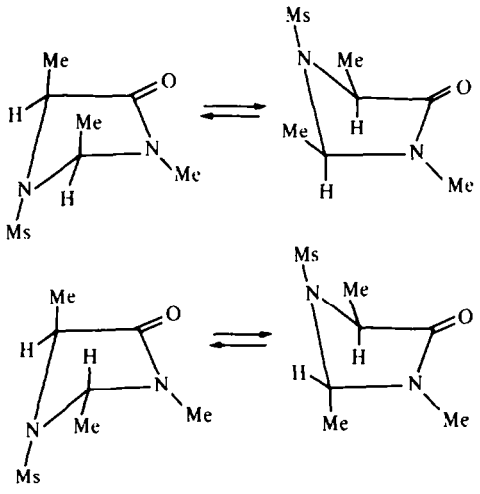


Fig. 2. The sector projections of 4-imidazolidinone conformations. The arrow shows direction of projection.

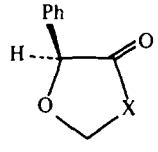
† CNDO/2-CI calculations show that the origin of both of the lowest energy transitions is more complex. In CI language,[12] the two lowest energy excited states are a combination of several singly-excited configurations that involve orbitals delocalized over the whole molecule, especially over the sulphonamide group. However, semi-empirical calculations for γ-lactams result in a simpler description since the $n \rightarrow \pi^*$ and the $\pi \rightarrow \pi^*$ excitations are almost localized in the amide chromophore.[13]

The phenylglycine derivative **5** requires some additional comments. The CD spectrum of **5** exhibits the weak CE near 260 nm of distinct vibronic structure, which corresponds to the ^1L_b transition of phenyl moiety, and the intense band at 226 nm of positive CE sign. This spectrum is very similar to that of related 5-oxazolidinone,[1] and, also to the CD of lactones and lactams (1,3-dioxolan-4-one **12** and 4-oxazolidinone **13**) derived from mandelic acid. All of them show the



Scheme 3.

same CE sign of comparable magnitude.[15] All of these compounds possess an inherently dissymmetric β, γ-unsaturated carbonyl chromophore and the CD sign of these chromophores is determined by the helicity of this arrangement.[15,16]



12 X=O
13 X=NH

Scheme 4.

The chiroptical properties of **9–11**, the compounds without 1N-sulphonyl group, were investigated for comparison with the hitherto discussed derivatives. The envelope conformation with equatorial 5-bulky substituent is expected for such compounds. This is confirmed by a strong positive CD. The protonation of amino group converts **9–10** into close analogues of the related γ-lactams. Compound **9b** is here a good example. Its CD spectrum in methanolic solution ($[\theta]_{215} \cdot 10^{-3} = 5.97$) is almost identical with the CD of (+)-3-methylpyrrolidone ($[\theta]_{217.5} \cdot 10^{-3} = 5.6$). The CD spectra of 4-imidazolidinones bearing free amino group are strongly modified by $n \rightarrow \sigma^*$ transition involving nitrogen lone pair.[17] Since the $n \rightarrow \sigma^*$ transition is observed at longer wavelengths for tertiary rather than for secondary amines,[18] this effect is the most distinct in the case of bicyclic proline derivative **11** (Fig. 3). It shows negative CE at 230 nm in cyclohexane and at 222 nm in methanol and positive CE at 261 nm and 238 nm in the same solvents,

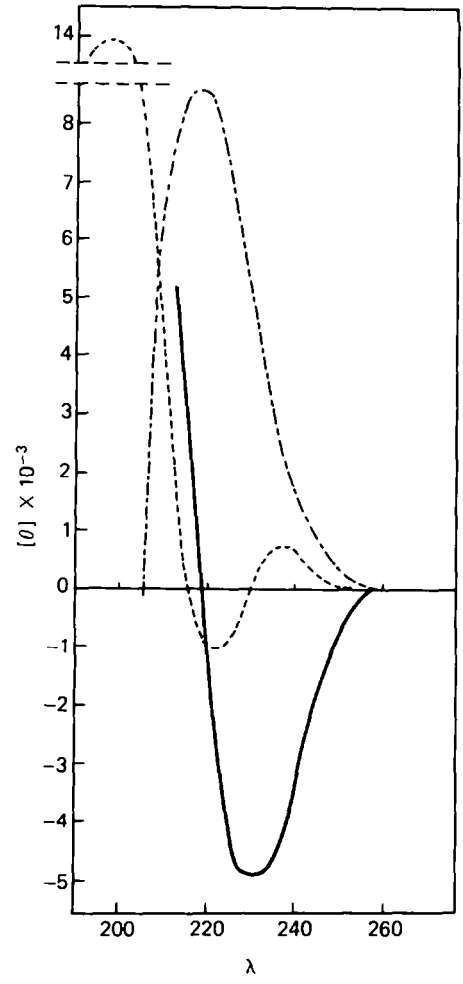


Fig. 3. Circular dichroism spectra of (*S*)-2,2 - dimethyl - 1,3 - diazabicyclo[3.3.0]octan - 4 - one (**11**) in cyclohexane–dioxane (4 : 1) (——), methanol (— —) and **11** hydrochloride in methanol (-·-·-).

respectively. The former effect is due to the $n \rightarrow \sigma^*$ transition while the latter to the $n \rightarrow \pi^*$ transition. The $n \rightarrow \sigma^*$ band disappears upon protonation of amine nitrogen and only strong positive CD corresponding to lactam $n \rightarrow \pi^*$ transition is observed.†

In conclusion, it can be stated that CD spectrometry is a valuable tool in stereochemical studies of lactones and lactams. If we assume that NX group has qualitatively similar contribution to CE sign as the CH_2 group has in the same location the Weigang sector rules can be applied and the chiroptical measurements give the results which are inaccessible by other spectroscopic methods.

EXPERIMENTAL

Spectroscopic measurements and CNDO/2-CI calculations were carried out as described previously.[1] The NMR spectra of **1a**, **2–6**, **7a** and **10** were described elsewhere.[8]

The synthesis of N-methylsulphonyl)amino acids was described in the previous paper.[1] (*S*)-Prolinamide and (*S*)-N-benzyloxycarbonylalaninamide were obtained according to the literature methods.[20,21]

(S)-N-(*Methylsulphonyl)alanine methyl ester.* (*S*)-Alanine methyl ester hydrochloride (7 g), was dissolved in 150 ml of

† Obviously, the assignment of these transitions as $n \rightarrow \pi^*$ and $n \rightarrow \sigma^*$ is not precise in the light of the overmentioned quantum mechanical calculations. The orbitals involved are delocalized over whole molecule. Especially, the overlapping of amino lone pair and amide orbitals affects the spectra of amino lactams.[13,19]

$CHCl_3$, methanesulphonyl chloride (7.7 ml) was added, the mixture was cooled to 0° and triethylamine (14.4 ml) was slowly added with stirring and cooling. The mixture was kept at 0° overnight, then washed with dil HCl, water, sat $NaHCO_3$ aq, dried ($MgSO_4$) and evaporated to dryness. The residue was crystallized from toluene/hexane to obtain 6.1 g of the product, m.p. 56–57°; NMR (δ, $CDCl_3$): 5.19 (d, 1H, SO_2NH), 4.07 (m, 1H, C<u>H</u>CH_3), 3.61 (s, 3H, CO_2Cl_3); 2.83 (s, 3H, CH_3SO_2) and 1.43 (d, 3H, CHC<u>H</u>$_3$); (Found: C, 32.97; H. 5.94; N, 7.51; $C_5H_{11}NO_4S$ requires: C, 33.15; H, 6.12; N, 7.73%).

(*S*) - N - (*Methylsulphonyl*)*alanine* - N' - *methylamide*. (*S*) - N - (Methylsulphonyl)alanine methyl ester (3.0 g) was dissolved in 33% methylamine ethanolic soln (7 ml) and left to stand overnight, after evaporation to dryness, the residue was crystallized from chloroform/hexane to obtain 3.1 g of the product, m.p. 112–113°; NMR (δ, $CDCl_3$): 6.30 (br, 1H, N<u>H</u>CH_3), 5.36 (d, 1H, SO_2NH), 3.94 (m, 1H, C<u>H</u>CH_3), 2.98 (s, 3H, CH_3SO_2), 2.86 (d, 3H, NHC<u>H</u>$_3$) and 1.45 (d, 3H, CHC<u>H</u>$_3$); (Found: C, 33.57; H, 6.77; N, 15.54; $C_5H_{12}N_2O_3S$ requires: C, 33.33; H, 6.71; N, 15.55%).

(*S*) - N - (*Methylsulphonyl*)*alaninamide*. (*S*) - N - (Methylsulphonyl)alanine methyl ester (4.0 g) was dissolved in saturated methanolic ammonia (50 ml) and left to stand overnight, then evaporated to dryness and after addition of ethyl ether the product crystallized (3.5 g); m.p. 135–137°; NMR (δ, DMSO-d_6): 7.3 and 7.1 (br, 2H, NH_2), 7.12 (d, 1H, SO_2NH), 3.80 (m, 1H, C<u>H</u>CH_3), 2.83 (s, 3H, CH_3SO_2) and 1.20 (d, 3H, CH_3CH); (Found: C, 29.21; H, 5.96; N, 17.19; $C_4H_{10}N_2O_3S$ requires: C, 28.92; H, 6.07; N, 16.86%).

(*S*) - N - (*Methylsulphonyl*)*valine* - N' - *methylamide*. (*S*) - N - (Methylsulphonyl)valine (7.0 g) was dissolved in MeOH (50 ml), cooled to 0° and $SOCl_2$ (0.5 ml) was carefully added. The mixture was left to stand overnight at room temp, then MeOH was evaporated, the residue was dissolved in ethyl ether and was washed with $NaHCO_3$ aq, dried ($MgSO_4$) and evaporated. The resultant ester was dissolved in 33% ethanolic $MeNH_2$ (10 ml) and left to stand overnight. The mixture was evaporated at reduced pressure, ethyl acetate was added, the product was filtered, washed with ethyl ether and dried — 6.5 g, m.p. 196–197°; NMR (δ, DMSO-d_6): 7.93 (q, 1H, N<u>H</u>CH_3), 7.0 (br, 1H, SO_2NH), 3.48 (d, 1H, $C_\alpha H$), 2.78 (s, 3H, SO_2CH_3), 2.59 (d, 3H, NHC<u>H</u>$_3$), 1.87 (sep, 1H) and 0.83 (d, 6H); (Found: C, 40.49; H, 7.81; N, 13.31; $C_7H_{16}N_2O_3S$ requires: C, 40.38; H, 7.75; N, 13.45%).

(*S*) - N - (*Methylsulphonyl*)*leucine* - N' - *methylamide*, obtained as above, m.p. 105–108°; (Found: C, 43.00; H, 8.09; N, 12.41; $C_8H_{18}N_2O_3S$ requires: C, 43.24; H, 8.16; N, 12.60%).

(*S*) - N - (*Methylsulphonyl*)*phenylglycine* N - *hydroxysuccinimidylester*. (*S*) - N - (Methylsulphonyl)phenylglycine (2.3 g, 10 mmol), and N-hydroxysuccinimide (1.15 g, 10 mmol) was dissolved in 20 ml THF and cooled to 0°. Then, N,N'-dicyclohexylcarbodiimide (2.1 g, 10 mmol) in 10 ml of THF was added. After 6 hr at 0° two drops of AcOH was added to the mixture, then was filtered and washed with THF. The filtrate was evaporated to dryness and crystallized from THF/hexane; 2.7 g; m.p. 168–169°; NMR (δ, DMSO-d_6): 8.63 (d, 1H, SO_2NH), 7.41 (m, 5H, C_6H_5), 5.58 (d, 1H, $C_\alpha H$), 2.87 (s, 3H, CH_3SO_2) and 2.74 (s, 4H, CH_2CH_2); (Found: C, 48.17; H, 4.53; N, 8.82; $C_{13}H_{14}N_2O_6S$ requires: C, 47.86; H, 4.33; N, 8.59%).

(*S*) - N - (*Methylsulphonyl*)*phenylglycine* N' - *methylamide*. The active ester obtained above was aminolyzed with 33% ethanolic $MeNH_2$ for 30 min at −5°; m.p. 167–169°; NMR (δ, DMSO-d_6): 8.1 (q, 1H, N<u>H</u>CH_3), 7.79 (br, 1H, SO_2NH), 7.3 (m, 5H, C_6H_5), 4.91 (s, 1H, CH), 2.63 (s, 3H, CH_3SO_2) and 2.53 (d, 3H, NHC<u>H</u>$_3$); (Found: C, 49.87; H, 5.87; N, 11.50; $C_{10}H_{14}N_2O_3S$ requires: C, 49.59; H, 5.83; N, 11.56%).

(*S*) - 3,5 - *Dimethyl* - 1 - *methylsulphonyl* - 4 - *imidazolidinone* (**1a**), (*S*) - N - (Methylsulphonyl)alanine - N' - methylamide (1.8 g), paraformaldehyde (0.6 g) and *p*-toluenesulphonic acid (0.05 g) were refluxed in benzene (100 ml) with azeotropic trapping of water. After 3 hr benzene was evaporated, toluene (50 ml) was added and the mixture was refluxed for 1 hr, then evaporated to dryness, the residue was dissolved in $CHCl_3$, washed with sat $NaHCO_3$ aq, dried ($MgSO_4$), evaporated and crystallized from benzene/hexane to obtain 1.2 g of the product, m.p. 128°; $[\alpha]_D^{20} = +63.5°$ (*c* 2, $CHCl_3$); IR (KBr): 1715 and 1698 (CO), 1340 and 1165 (SO_2); (Found: C, 37.72; H, 6.29; N, 14.40; $C_6H_{12}N_2O_3S$ requires: C, 37.50; H, 6.29; N, 14.58%).

(*S*) - 2,2,5 - *Trimethyl* - 1 - *methylsulphonyl* - 4 - *imidazolidinone* (**1b**). (*S*)-N-(Methylsulphonyl)alaninamide (1.0 g), acetone (20 ml) and *p*-toluenesulphonic acid (0.05 g) were refluxed in toluene (100 ml) for 24 hr, then concentrated at reduced pressure, the crystals were filtered off and washed with ethyl ether; 0.75 g; m.p. 217–219° (with dec.); $[\alpha]_D^{20} = +32°$ (*c* 2, MeOH); NMR (δ, DMSO-d_6): 8.71 (br, 1H, NH), 4.01 (q, 1H, CH_3C<u>H</u>), 3.03 (s, 3H, CH_3SO_2), 1.33 (d, 3H, C<u>H</u>$_3$CH), 1.57 (s, 3H) and 1.50 (s, 3H); IR (KBr): 3190 (br), 3070 (br), 1728 and 1715 (CO), 1698, 1335 and 1155 (SO_2); (Found: C, 40.52; H, 6.89; N, 13.49; $C_7H_{14}N_2O_3S$ requires: C, 40.77; H, 6.84; N, 13.59%).

(*S*) - 2,2 - *Diethyl* - 5 - *methyl* - 1 - *methylsulphonyl* - 4 - *imidazolidinone* (**1c**). (*S*)-N-(Methylsulphonyl)alaninamide (1.0 g), 3-pentanon (5 ml) and *p*-toluenesulphonic acid (0.05 g) were refluxed in toluene (50 ml) for 2 hr, then toluene was evaporated, the residue was dissolved in EtOAc, washed with $NaHCO_3$ aq, dried ($MgSO_4$), evaporated and crystallized from EtOAc to obtain 0.95 of the product; m.p. 166°; $[\alpha]_D^{20} = +11°$ (*c* 2, $CHCl_3$); NMR (δ, $CDCl_3$): 8.20 (br, 1H, NH); 4.15 (q, 1H, $C_\alpha H$), 3.0 (s, 3H, CH_3SO_2), 1.95 (m, 4H), 1.57 (d, 3H, C<u>H</u>$_3C_\alpha H$) and 0.98 (t, 6H); IR (KBr): 3210 (br), 1725 and 1715 (CO), 1696, 1360 and 1158 (SO_2); (Found: C, 46.13; H, 7.71; N, 11.97; $C_9H_{18}N_2O_3S$ requires: C, 46.15; H, 7.75; N, 11.96%).

(*S*) - 5 - *Isopropyl* - 3 - *methyl* - 1 - *methylsulphonyl* - 4 - *imidazolidinone* (**2**), was obtained as **1a**; m.p. 140° (toluene/hexane); $[\alpha]_D^{20} = +41°$ (*c* 1, $CHCl_3$); IR (KBr): 1715 and 1700 (CO), 1345 and 1165 (SO_2); (Found: C, 43.62; H, 7.35; N, 12.61; $C_8H_{16}N_2O_3S$ requires: C, 43.63; H, 7.32; N, 12.72%).

(*S*) - 5 - *Isobutyl* - 3 - *methyl* - 1 - *methylsulphonyl* - 4 - *imidazolidinone* (**3**), obtained as **1a**; m.p. 163–164° (toluene/hexane); $[\alpha]_D^{20} = +42.5°$ (*c* 2, $CHCl_3$); NMR (δ, $CDCl_3$): 4.84 and 4.64 (AB system, 2H, $J_{AB} = 8$ Hz, $^4J_{2,5} = 1.6$ Hz, CH_2), 4.09 (m, 1H, $C_\alpha H$), 2.91 (s, 3H, NCH_3), 2.87 (s, 3H, CH_3SO_2), 1.90 (m, 1H), 1.71 (d, 2H) and 0.95 (m, 6H); (Found: C, 46.50; H, 7.93; N, 12.03; $C_9H_{18}N_2O_3S$ requires: C, 46.15; H. 7.75; N, 11.96%).

(*S*) - 5 - *Benzyl* - 3 - *methyl* - 1 - *methylsulphonyl* - 4 - *imidazolidinone* (**4**), obtained as **1a**; m.p. 213–215° (toluene); $[\alpha]_D^{20} = +50.5°$ (*c* 1.5, $CHCl_3$); (Found: C, 53.92; H, 6.05; N, 10.44; $C_{12}H_{16}N_2O_3S$ requires: C, 53.73; H, 6.01; N, 10.44%).

(*S*) - 3 - *Methyl* - 1 - *methylsulphonyl* - 5 - *phenyl* - 4 - *imidazolidinone* (**5**), obtained as **1a**, m.p. 178–179° (toluene); $[\alpha]_D^{20} = +88°$ (*c* 2, dioxane); (Found: C, 51.87; H, 5.51; N, 10.92; $C_{11}H_{14}N_2O_3S$ requires: C, 51.97; H, 5.55; N, 11.02%).

(*S*) - N - *Benzyloxycarbonyl* - *alanine* - N' - *methylamide*. (*S*) - N - Benzyloxycarbonyl - alanine (4.46 g) was dissolved in MeOH (50 ml), cooled to 0° and $SOCl_2$ (0.5 ml) was carefully added. The mixture was then refluxed for 1 hr, evaporated, the residue was dissolved in ethyl ether, washed with sat $NaHCO_3$ aq, dried ($MgSO_4$) and evaporated. The resulted ester was aminolyzed with 33% ethanolic $MeNH_2$ to obtain 1.9 g of the product; m.p. 122–123° (EtOAc); NMR (δ, $CDCl_3$): 7.45 (s, 5H, C_6H_5), 6.73 (q, 1H, N<u>H</u>CH_3), 5.92 (d, 1H, CONH), 5.23 (s, 2H, CH_2Ph), 4.39 (m, 1H, CH); 2.90 (d, 3H, NHC<u>H</u>$_3$) and 1.44 (d, 3H, CHC<u>H</u>$_3$); (Found: C, 60.97; H, 6.91; N, 11.83; $C_{12}H_{16}N_2O_3$ requires: C, 61.00; H, 6.83; N, 11.86%).

(*S*) - N - *Benzyloxycarbonyl* - *phenylalanine* - N' - *methylamide*, obtained as above; m.p. 167–169°; NMR (δ, $CDCl_3$): 7.40 (s, 5H), 7.32 (s, 5H), 6.05 (br, 1H, CH_3N<u>H</u>), 5.65 (d, 1H, CONH), 5.13 (s, 2H, CH_2Ph), 4.11 (q, 1H, $C_\alpha H$), 3.11 (d, 2H, CH_2) and 2.76 (d, 3H, C<u>H</u>NH); (Found: C, 69.42; H, 6.51; N, 8.88; $C_{18}H_{20}N_2O_3$ requires: C, 69.21; H, 6.45; N, 8.97%).

(2*S*,5*S*) - *and* (2*R*,5*S*) - 2,3,5 - *Trimethyl* - 3 - *methylsulphonyl* - 4 - *imidazolidinones* (**6a** *and* **6b**). (*S*) - N - (Methylsulphonyl)alanine - N' - methylamide (2.5 g),

paraldehyde (5 ml) and *p*-toluenesulphonic acid (0.1 g) were refluxed in benzene (100 ml) with azeotropic trapping of water then washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and evaporated. From the residue *cis*-**6a** crystallized after addition of toluene. The crystals were filtered off and recrystallized from toluene to obtain 0.8 g of *cis*-**6a**; m.p. 191–192°; $[\alpha]_D^{20} = +41°$ (*c* 1.5, $CHCl_3$); (Found: C, 40.45; H, 6.73; N, 13.34; $C_7H_{14}N_2O_3S$ requires: C, 40.77; H, 6.84; N, 13.59%). The filtrate was evaporated and chromatographed on silica gel to obtain 0.5 g of the *trans*-**6b**, which was recrystallized from toluene/hexane; m.p. 75°; $[\alpha]_D^{20} = +43°$ (*c* 1, $CHCl_3$); (Found: C, 40.51; H, 7.12; N, 13.66; $C_7H_{14}N_2O_3S$ requires: C, 40.77; H, 6.84; N, 13.59%).

(*S*) - 1 - *Benzyloxycarbonyl* - 2,2,5 - *trimethyl* - 4 - *imidazolidinone* (**7b**). (*S*)-N-Benzyloxycarbonylalaninamide[20] (2.0 g), acetone (10 ml) and *p*-toluenesulphonic acid (0.05 g) were refluxed in benzene (100 ml) for 24 hr. The mixture was worked up analogously to **1c**; m.p. 107°; $[\alpha]_D^{20} = +35.5°$ (*c* 1, C_6H_6); NMR (δ, $CDCl_3$): 8.27 (br, 1H, NH), 7.25 (s, 5H, C_6H_5), 5.14 (s, 2H, CH_2Ph), 4.17 (q, 1H, CH), 1.64 (s, 6H) and 1.46 (d, 3H); (Found: C, 63.78; H, 6.91; N, 10.63; $C_{14}H_{18}N_2O_3$ requires: C, 64.11; H, 6.92; N, 10.68%).

(*S*) - 5 - *Benzyl* - 1 - *benzyloxycarbonyl* - 3 - *methyl* - 4 - *imidazolidinone* (**8**), obtained as **1a**; m.p. 124–125°, $[\alpha]_D^{20} = +152°$ (*c* 1, C_6H_6); (Found: C, 70.01; H, 6.25; N, 8.94; $C_{19}H_{20}N_2O_3$ requires: C, 70.35; H, 6.21; N, 8.64%).

(*S*) - 3,5 - *Dimethyl* - 4 - *imidazolidinone* (**9a**). (*S*) - 1 **7a**, was obtained analogously to **1a** as an oil, which was purified by column chromatography on silica gel (MN-Kiesielgel 60, 200 mesh, Macherey Nagel); NMR (δ, $CDCl_3$): 7.23 (s, 5H, C_6H_5), 5.13 (s, 2H, CH_2Ph), 4.71 and 4.65 (AB system, 2H, $J_{AB} = 6.0$ Hz, $^4J_{2,5} = 1.8$ Hz), 4.16 (m, 1H, C_aH); 2.87 (s, 3H, NCH_3) and 1.39 (d, 3H, $CHC\underline{H}_3$). The sample of **7a** (0.5 g) was dissolved in 45% hydrobromide acetic acid (3 ml), after standing for 20 min anhyd ethyl ether was added (50 ml), the precipitate was washed several times with ethyl ether and dried; free base NMR (δ, $CDCl_3$): 4.26 (s, 2H), 3.45 (q, 1H), 2.83 (s, 3H), 2.73 (s, 1H, NH) and 1.33 (d, 3H); hydrobromide m.p. 155–158° (with dec); (Found: N, 14.26; $C_5H_{11}N_2OBr$ requires: N, 14.36%).

(*S*) - 2,2,5 - *Trimethyl* - 4 - *imidazolidinone* (**9b**) was obtained from **7b** in similar manner as **9a**; NMR (δ, $CDCl_3$): 7.77 (br, 1H, CONH), 3.64 (q, 1H), 2.03 (s, 1H, NH), 1.47 (s, 3H), 1.39 (s, 3H) and 1.33 (d, 3H); IR (KBr): 3260, 3190 (br), 1715 and 1698; hydrobromide m.p. 173–175° (with decomp.); (Found: N, 13.26; $C_6H_{13}N_2OBr$ requires: N, 13.40%).

(*S*) - 5 - *Benzyl* - 3 - *methyl* - 4 - *imidazolidinone* (**10**), was obtained from **8** in similar manner as **9a**; hydrobromide m.p. 212° (with dec); IR (KBr): 2850–2650 (br), 1725 and 1718 (CO); (Found: N, 10.37; $C_{11}H_{15}N_2OBr$ requires: N, 10.33%).

(*S*) - 2,2 - *Dimethyl* - 1,3 - *diazabicyclo*[3.3.0]*octan* - 4 - *one* (**11**). (*S*)-Prolinamide[21] (0.5 g), acetone (5 ml) and *p*-toluenesulphonic acid (0.05 g) were refluxed in toluene (30 ml) for 4 hr, evaporated, dissolved in $CHCl_3$, washed with $NaHCO_3$ aq, dried ($MgSO_4$), evaporated and the residue was crystallized from toluene to obtain 0.42 g of the product; m.p. 157–158°; NMR (δ, $CDCl_3$): 7.66 (br, 1H, NH), 3.95 (m, 1H), 2.8 (m, 2H, CH_2N), 1.94 (m, 4H) and 1.43 (s, 6H); IR (KBr): 3230 (br), 1712 (CO), 1670 and 770 (br); hydrochloride m.p. 165–167° (with dec); $[\alpha]_D^{20} = -47°$ (*c* 0.5, MeOH); (Found: C, 62.27; H, 9.45; N, 18.37; $C_8H_{14}N_2O$ requires: C, 62.31; H, 9.15; N, 18.17%).

Acknowledgements—I am grateful to Drs. A. Herman, A. Tempczyk and E. Witkowska for helpful discussions, Ms. E. Gwizdała for CD measurements and Mrs. J. Skarżyńska for typing the manuscripts. I also thank Polish Academy of Sciences for partial financial support.

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