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THE CONFORMATIONAL BEHAVIOUR OF SOME DIHYDRO-1,4-THIAZINES

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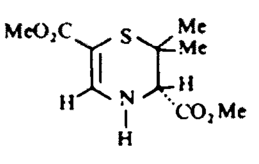
Abstract The conformational behaviour of some dihydro-1,4-thiazine derivatives has been examined by the NMR method. The results suggest that a substitutent at C-3 of these heterocycles adopts the *quasi*-axial orientation unless it is capable of forming an intramolecular hydrogen bond with the enamine hydrogen at N-4. Evidence for intramolecularly hydrogen bonded species has been obtained by IR spectroscopy

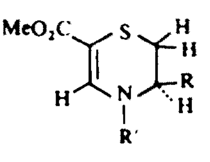
METHYL 6-α-CHLOROPENICILLANATE is readily rearranged to 3D,6-dicarbomethoxy-2,2-dimethyl-2,3-dihydro-1,4-thiazine (I) in the presence of sodium methoxide.[1] During an investigation into the reactivity of these heterocycles it was observed that the optical rotation of I showed pronounced solvent dependence. For example, in chloroform a minimum rotation of $[\alpha]_D$ −38° was observed, while higher values were obtained in acetone ($[\alpha]_D$ −183°), pyridine ($[\alpha]_D$ −238°) and methanol ($[\alpha]_D$ −258°). These rotational changes were considered to be the result of conformational changes in I. In order to examine this speculation more fully 3L,6-*dicarbomethoxy-2,3-dihydro-1,4-thiazine* (III) was prepared. Changes in the conformation of this compound should be directly measureable by NMR spectroscopy and should be reflected in changes in the coupling constants of the C-2 and C-3 protons.

6-*Carbomethoxy*-3L-*carboxy-2,3-dihydro-1,4-thiazine* (II) was obtained in 60% yield from the reaction of L-cysteine hydrochloride with sodium formylchloroacetate.[2] II was readily esterified to III with diazomethane or with methanolic hydrogen chloride. The structure of III followed from analytical and spectral considerations.

Compound III displayed large changes in its optical rotation with solvent. The smallest rotation of $[\alpha]_D$ +86° was obtained in chloroform while higher values were observed in benzene ($[\alpha]_D$ +128°), acetone ($[\alpha]_D$ +150°), methanol ($[\alpha]_D$ +154°) and pyridine ($[\alpha]_D$ +214°).

I





II: R = CO_2H, R′ = H
III: R = CO_2Me, R′ = H
IV: R = CO_2Me, R′ = D
V: R = CO NMe_2, R′ = H
VI: R = CO_2H, R′ = Me
VII: R = CO_2Me, R′ = Me
VIII: R = R′ = H

Compound III was recrystallized from deuterium oxide to give IV, whose NMR spectrum was measured in deuterochloroform, deuteroacetone, pyridine and benzene. The ABX portions of these spectra, which are shown in Fig. 1, were analysed by the method of Pople, *et al.*[3] The coupling constants calculated from these spectra are summarized in Table 1.

In deuterochloroform the AB portion of the spectrum consisted of two quartets which overlapped in such a way as to reduce the total number of peaks from eight to seven. The X portion, theoretically a sextet, did not show the two outer combination lines, and therefore appeared as a quartet.

In pyridine the AB portion showed the theoretical eight lines while the X portion simplified to a 1:2:1 triplet. Further analysis indicated that this was due to $J_{AX} = J_{BX}$.

In deuteroacetone the spectrum was considerably simplified, the AB portion appeared as a a 1:1 doublet and the X region showed a 1:2:1 triplet. This situation may arise when $J_{AX} = J_{BX}$ and $\nu_A = \nu_B$ and the spectrum is then an A_2X case. However, a five-line spectrum is also obtained if $J_{AB} \gg \frac{1}{2}(J_{AX} - J_{BX})$ and $J_{AB} \gg \nu_A - \nu_B$. This "deceptively simple" case has been discussed[4] and only the sum of J_{AX} and J_{BX} can be calculated.

In benzene the AB portion again appeared as a doublet although the higher field peak was considerably broadened; the X portion was present as a 1:2:1 triplet. This situation has been discussed by Haigh *et al.*[5]

Table 1. Coupling constants[a] (in c/s) of the ABX protons of some dihydro-1,4-thiazines

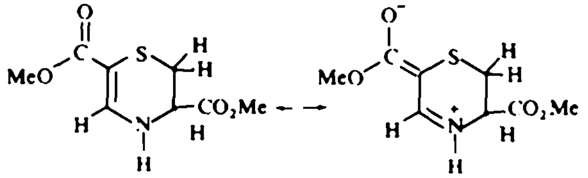
Compound	Coupling constant	$CDCl_3$	C_6H_5N	CD_3COCD_3	C_6H_6
III	J_{AB}	13·0	12·6	—	—
	J_{AX}	6·8	4·1	4·2[b]	9·4[c]
	J_{BX}	3·5	4·1	4·2[b]	
XII	J_{AB}	12·8	12·9	—	12·9
	J_{AX}	9·7	9·5	—	9·5
	J_{BX}	3·4	3·2		3·2
V	J_{AB}	12·6	12·9	–	—
	J_{AX}	9·3	9·2	-	—
	J_{BX}	3·4	3·5	-	
VII	J_{AB}	13·0	12·9	13·0	13·0
	J_{AX}	3·1	3·0	3·1	3·1
	J_{BX}	3·1	3·0	3·1	3·1

[a] The coupling constants are accurate to ±0·3 c/s.

[b] This value is calculated on the reasonable assumption that the spectrum is an A_2X case.

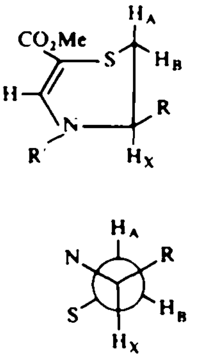
[c] This value is the sum of $J_{AX} + J_{BX}$: the broadening of the high field peak (see Fig. 1d) indicates that J_{AX} is not exactly equal to J_{BX}.

The results shown in Table 1 convincingly demonstrate that the coupling constants J_{AX} and J_{BX} of III are solvent dependent; consequently the conformation adopted by III depends upon the nature of the solvent. The vinylgous urethane present in III might be expected to display ground state conjugative stabilisation of the following type:

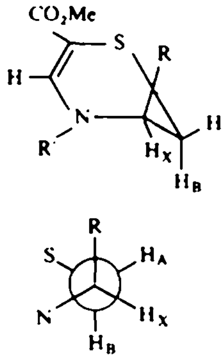


Some support for this formulation comes from IR studies which show the presence of the unsaturated ester carbonyl at 1680 cm^{-1} (in $CHCl_3$), a lower frequency than usual* and presumably indicative of such conjugation.

If the dipolar form contributes to the ground state structure of III then atoms 1,3,4,5 and 6 must be coplanar and III may exist in two extreme conformations represented by IXA and IXB. In conformation IXA the dihedral angle between H_A and H_X is ~180° and between H_B and H_X is ~60°. In IXB H_X bisects H_A and H_B and this angle is ~60°.



IXA: R = CO_2Me, R' = H
XA: R = $CONMe_2$, R' = H
XIA: R = CO_2Me, R' = Me



IXB
XB
XIB

Karplus[7] has shown that the coupling constant for two vicinal protons in a substituted ethane is a function of the dihedral angle between the two C—H planes. This relationship holds reasonably well for substituted cyclohexanes but its applicability to dihydro-1,4-thiazines remains to be demonstrated.

In order to determine the values for J_{AX} and J_{BX} in defined environments, 6L-3-*carbomethoxy-9,9-dimethyl-7-oxo-8-oxa-4-thia-1-aza-bicyclo*[4.3.0]*non-2-ene*† (XII) was prepared. This bicyclic lactone is in a fixed conformation with H_A and H_X at ~180°

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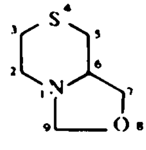
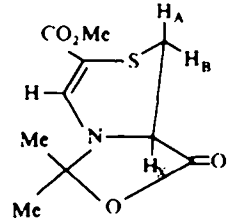
* αβ-Unsaturated carboxylic acid esters generally absorb between 1710–1720 cm^{-1}.[6]

† The parent 8-oxa-4-thia-1-aza-bicyclo[4.3.0]nonane is numbered as follows:



and H_B and H_X at ~60°, if it is assumed that the vinylgous urethane is planar (IR measurements show the unsaturated ester carbonyl at 1685 cm^{-1} in $CHCl_3$).



XII

XII was obtained in 46% yield from II and 2,2-dimethoxy propane in the presence of *p*-toluenesulphonic acid. No racemization occurred during the formation or hydrolysis of XII since optically pure II was obtained when XII was treated with one equivalent of sodium hydroxide solution.

The coupling constants for the ABX protons of XII, which are summarized in Table 1, showed no significant change with solvent. The results indicate that J_{AX} = ~9·6 c/s when H_A and H_X is ~180° and that J_{BX} = ~3·3 c/s when H_B and H_X is ~60°. It therefore appears that the Karplus equation[7] satisfactorily correlates dihedral angles and coupling constants for these heterocycles.

The values observed for J_{AX} and J_{BX} for III in pyridine and deuteroacetone (J_{AX} = J_{BX} = ~4·2 c/s) strongly suggest that in these solvents III exists largely as conformation IXB, in which the carbomethoxy group at C-3 is in a *quasi*-axial environment. The coupling constants in deuterochloroform, J_{AX} = ~6·8 c/s and J_{BX} = ~3·5 c/s, indicate that conformations IXA and IXB are approximately equally populated in this solvent. Stabilization of conformation IXA in deuterochloroform is considered to be a consequence of intramolecular hydrogen bonding between the N—H and the carbonyl oxygen of the saturated ester. In pyridine and acetone solvent molecules interact with the enamine hydrogen and destroy the intramolecular hydrogen bond; conformation IXB is then favoured. The sum of the coupling constants $J_{AX} + J_{BX}$ = ~9·4 c/s in benzene should be compared with values of ~8·4 c/s in deuteroacetone and pyridine and ~10·3 c/s in deuterochloroform. The result suggests that there is less of III present as conformation IXA in benzene than in deuterochloroform.

The intramolecular hydrogen bond formed in III is apparently not strong enough to completely stabilise conformation IXA. 3DL-N,N-*dimethylamido-6-carbomethoxy-2,3-dihydro-1,4-thiazine* (V) was therefore prepared in the hope that the more basic amide oxygen would form a stronger intramolecular hydrogen bond with the N—H; consequently V should exist mainly as conformation XA in chloroform.

Compound V was prepared in 37% yield by refluxing III with dimethylamine in methanol; the reaction was accompanied by complete racemisation of the asymmetric centre. The coupling constants for the ABX protons of V, which are summarized in Table 1, indicate that J_{AX} = ~9·3 c/s and J_{BX} = 3·5 c/s in both deuterochloroform and pyridine. This result suggests that conformation XA is predominant in both solvents and reflects the increased stability of the intramolecular hydrogen bond of V.

To further test this hypothesis 3L,6-*dicarbomethoxy-4-methyl-2,3-dihydro-1,4-thiazine* (VII) was synthesized. Intramolecular hydrogen bonding is precluded in VII and consequently the molecule should exist largely as conformation XIB in both polar and non-polar solvents. N-Methyl-L-cysteine[8] was condensed with sodium formylchloroacetate[2] in aqueous solution to give *6-carbomethoxy-3L-carboxy-4-methyl-2,3-dihydro-1,4-thiazine* (VI) in 60% yield, which gave VII after esterification with diazomethane.

The coupling constants for the ABX protons of VII are summarized in Table 1. The results show that $J_{AX} = J_{BX} = \sim 3{\cdot}1$ c/s and that the coupling constants are solvent independent. VII therefore exists as conformation XI B irrespective of solvent.

The presence of intramolecular hydrogen bonds in III and V was confirmed by IR studies on the NH stretching vibration in dilute chloroform solution. *6-Carbomethoxy-2,3-dihydro-1,4-thiazine* (VIII) was required as a model compound for these studies and it was prepared from 2-mercapto ethylamine hydrochloride and sodium formylchloroacetate[2] in 32% yield.

IR measurements on the NH stretching vibrations of VIII, III and V are shown in Fig. 2. In dilute chloroform solution (0·01M) VIII showed an absorption at 3468 cm^{-1} attributable to non-associated NH, while in more concentrated solution (0·5M) a broad peak appeared at 3365 cm^{-1} representing intermolecularly hydrogen bonded NH.

Compound III in dilute chloroform solution (0·01M) showed two peaks at 3428 and 3462 cm^{-1} in the approximate ratio of 2·5:1. The former band is due to intramolecularly hydrogen bonded species and the latter to non-associated species. The possibility that the peak at 3462 cm^{-1} was due to an overtone of the saturated ester carbonyl was excluded by measuring the N—D stretching frequency of IV. Two peaks were again observed in a similar ratio, the frequencies being lowered to 2540 and 2561 cm^{-1}. IR spectroscopy, therefore, provides direct evidence for the existence of III as an intramolecularly hydrogen bonded species (conformation IX A) and a non-associated species (conformation IX B). In concentrated chloroform solution (0·5M) a broad peak appeared at 3360 cm^{-1} representing intermolecularly hydrogen bonded species.

Compound V in dilute chloroform solution (0·01M) showed a single absorption at 3393 cm^{-1} attributable to an intramolecularly hydrogen bonded species. The frequency difference, $\Delta\nu$, between the free NH and the bonded NH is an approximate measure of the strength of the hydrogen bond.[9] In the case of III $\Delta\nu = 40$ cm^{-1} and for V $\Delta\nu = 75$ cm^{-1}, a result which suggests that the intramolecular hydrogen bond of V is approximately twice as strong as that of III.

In conclusion, therefore, it appears that a substituent at C-3 of 6-carbomethoxy-2,3-dihydro-1,4-thiazine derivatives exists preferentially in the *quasi*-axial environment. This is presumably the result of an unfavourable eclipsed interaction between a substituent in the *quasi*-equatorial position at C-3 and a substituent at N-4. In the case of III the carbomethoxyl group prefers the *quasi*-axial environment by at least 1 kcal/mole.* A substituent may be stabilised in the *quasi*-equatorial conformation if it can form an intramolecular hydrogen bond with the enamine NH.

The present results appear to be an extension of the pseudo-allylic effect first discussed by Malhotra and Johnson,[10] who pointed out that molecules with endo-

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* This assumes that conformations IX A and IX B are equally populated in chloroform and that the ratio of IX A to IX B in the more polar solvents is at least 15:85.

cyclic double bonds may possess non-bonded steric interaction between substituents R and R′. This interaction, which has been termed $A^{(1,2)}$ strain, may be relieved from XIIIA by conformational inversion to XIIIB. Malhotra *et al.*[11] have recently shown that the magnitude of this interaction when R = Me and R′ = H is approximately 0·6 kcal/mole.

Ferrier and Sankey[12] have also concluded that allylic ester groupings, present in pyranose derivatives containing an endocyclic double bond, favour the *quasi*-axial orientation. Quantitatively, this preference was found to be 0·8 kcal/mole for the acetoxy group and 1·3 kcal/mole for the benzoyloxy group.

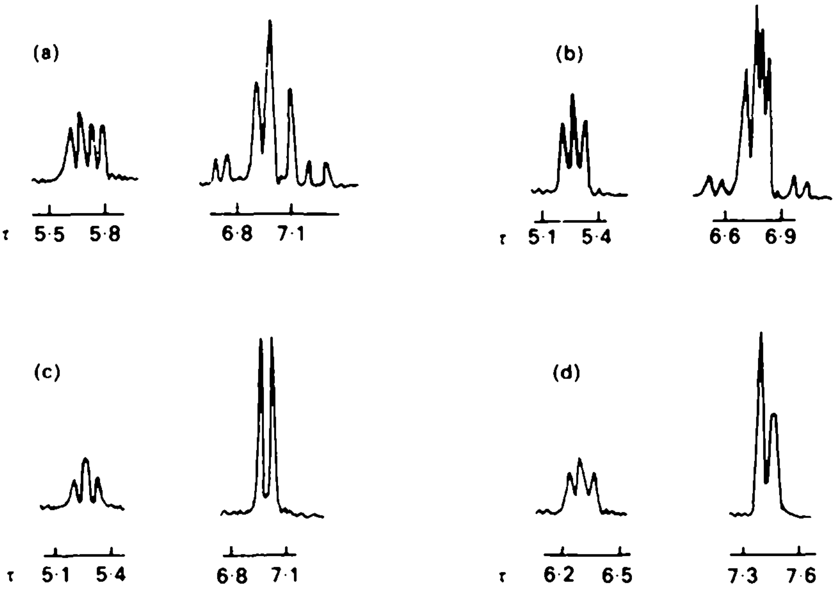

FIG. 1 NMR spectrum of 3L,6-dicarbomethoxy-2,3-dihydro-1,4-thiazine (III): ABX protons in (a) deuterochloroform, (b) pyridine, (c) deuteroacetone and (d) benzene.

EXPERIMENTAL

NMR spectra were determined in ~0·5M soln using a Perkin–Elmer R 10 spectrometer at 60 Mc/s with TMS as an internal standard. Optical rotations were measured at room temp (~20°) with a Bendix Ericson automatic polarimeter. Routine IR spectra were recorded with a Hilger and Watts Infrascan; for high resolution work a Perkin–Elmer 125 was employed. UV spectra were measured in 95% EtOH with a Unicam SP-800. Mass spectra were determined using an AEI MS 9 mass spectrometer.

3D-6-*Dicarbomethoxy-2,2-dimethyl-2,3-dihydro-1,4-thiazine* (I)

I was prepared as previously described;[1] it was recrystallized from MeOH, m.p. 164°; $[\alpha]_D$ −38° (0·53% in $CHCl_3$), −183° (2·50% in MeCOMe), −238° (2·50% in C_5H_5N) and −258° (2·50% in MeOH).

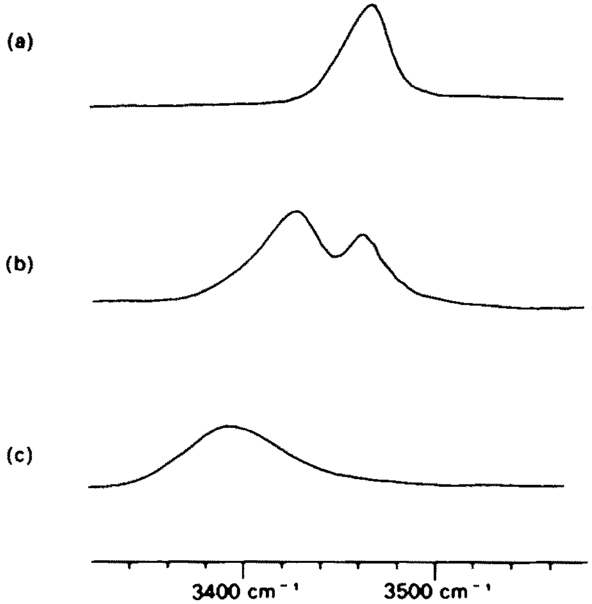

FIG. 2 IR spectra of some dihydro-1,4-thiazines. N H Stretching frequencies measured in chloroform solution (0·01 M): (a) 6-carbomethoxy-2,3-dihydro-1,4-thiazine (VIII), (b) 3L,6-dicarbomethoxy-2,3-dihydro-1,4-thiazine (III), (c) 3DL-N,N-dimethylamido-6-carbomethoxy-2,3-dihydro-1,4-thiazine (V).

6-*Carbomethoxy*-3L-*carboxy-2,3-dihydro*-1,4-*thiazine* (II)

L-Cysteine hydrochloride (0·1 mole, 15·76 g) and sodium formylchloroacetate[2] (0·1 mole, 15·84 g) were dissolved in H_2O (50 ml). The soln was left for 12 hr and II was collected by filtration (12·24 g, 60%). The material was recrystallized from H_2O containing a little MeOH, m.p. 178–180° (dec); $[\alpha]_D$ +124° (0·37% in MeOH; ν_{max}^{KBr} 3290 (NH), 1725 (CO_2H), 1660 (vinylgous urethane CO) and 1600 cm^{-1} (C═C); λ_{max}^{EtOH} 265 mμ (ε, 4000) and 312 mμ (ε, 10,700). (Found: C, 41·23; H, 4·53; N, 6·86; S, 15·93. $C_7H_9O_4NS$ requires: C, 41·38; H, 4·43; N, 6·90; S, 15·76%).

3L,6-*Dicarbomethoxy-2,3-dihydro*-1,4-*thiazine* (III)

(a) II was treated with etheral diazomethane to give III, which was recrystallized from H_2O containing a little MeOH), m p 102–104°; $[\alpha]_D$ +86° (1·06% in $CHCl_3$), +128° (0·47% in C_6H_6), +150° (1·05% in MeCOMe), +154° (0·96% in MeOH) and +214° (0·50% in C_6H_5N); ν_{max}^{KBr} 3300 (NH), 1750 (CO_2Me), 1645 (vinylgous urethane CO), 1595 (C═C) and 1530 cm^{-1} (amide II); λ_{max}^{EtOH} 265 mμ (ε, 3900) and 310 mμ (ε, 9100). The NMR spectrum ($CDCl_3$) showed a 7-line multiplet centred at τ 7·02 (2H; methylene group at C-2), singlets at τ 6·30 (3H; CO_2CH_3) and 6·20 (3H; CO_2CH_3), a quintuplet centred at τ 5·72 (1H; tertiary proton at C-3), a broadened signal at τ 4·6 (1H; NH) and a doublet centred at τ 2·39 (1H; J = 7 c/s; vinylic proton at C-5). The NH proton exchanged upon addition of D_2O to the $CDCl_3$ soln, the quintuplet simplified to a quartet and the doublet collapsed to a single line. (Found: C, 44·76; H, 5·44; N, 6·75; MW 217·0405 [mass spectrum, mol. ion]. $C_8H_{11}O_4NS$ requires: C, 44·40; H, 5·10; N, 6·45%; MW 217·0406).

(b) II (0·025 mole, 5·07 g) was dissolved in MeOH/HCl (~1N, 250 ml). After 5 hr the soln was neutralized with $NaHCO_3$ aq and extracted with $CHCl_3$(2 ×). The organic layer was washed with H_2O, dried ($MgSO_4$) and evaporated to a crystalline residue (4·45 g, 82%). The material was recrystallized from H_2O containing a little MeOH; m.p. 102–104°; $[\alpha]_D$ +87° (0·39% in $CHCl_3$).

6L-3-*Carbomethoxy*-9,9-*dimethyl*-7-*oxo*-8-*oxa*-4-*thia*-1-*aza-bicyclo*[4.3.0]*non*-2-*ene* (XII)

Compound II (0·01 mole, 2·02 g) was suspended in 2,2-dimethoxypropane (40 ml) and *p*-toluenesulphonic acid hydrate (0·01 mole, 1·90 g) was added. The suspension was stirred and a red soln formed.

After ~15 min a ppt formed which was collected by filtration and washed with ether (1·17 g, 46%). The material was recrystallized from ether containing a little $CHCl_3$, m.p. 139–140°; $[\alpha]_D$ −60° (0·26% in $CHCl_3$); $\nu_{\max}^{\mathrm{KBr}}$ 1785 (γ-lactone CO), 1690 (vinylgous urethane CO) and 1590 cm^{-1} (C=C); $\lambda_{\max}^{\mathrm{EtOH}}$ 266 mμ (ε, 3400) and 317 mμ (ε, 9200). The NMR spectrum ($CDCl_3$) showed a singlet at τ 8·29 (6H; *gem*-dimethyl group), an octuplet centred at τ 7·00 (2H; methylene group at C-5), a singlet at τ 6·18 (3H; CO_2CH_3), a quartet centred at τ 5·80 (1H; tertiary proton at C-6) and a singlet at τ 2·34 (1H; vinylic proton at C-2). (Found: C, 49·39; H, 5·35; N, 5·76; MW 243·0565 [mass spectrum, mol. ion]. $C_{10}H_{13}O_4NS$ requires: C, 49·24; H, 5·44; N, 5·71%; MW 243·0565).

3DL-N,N-*Dimethylamido-6-carbomethoxy-2,3-dihydro-1,4-thiazine* (V)

Compound II (0·05 mole, 1·01 g) was dissolved in MeOH (50 ml) and Me_2NH (~1 ml) added. The soln was refluxed for 48 hr, diluted with $CHCl_3$ and shaken with ~1N HCl. The organic layer was washed with H_2O, dried ($MgSO_4$) and evaporated to dryness. The residue was fractionated by silica gel chromatography to give V (0·43 g, 37%), which was recrystallized from EtOH containing a little $CHCl_3$, m.p. 168–170°; $\nu_{\max}^{\mathrm{KBr}}$ 3310 (NH), 1685 (vinylgous urethane CO), 1640 (amide I) and 1590 cm^{-1} (C=C); $\lambda_{\max}^{\mathrm{EtOH}}$ 268 mμ (ε, 3400) and 312 mμ (ε, 10,050). The NMR spectrum ($CDCl_3$) showed two quartets centred at τ 7·67 and 6·98 (2H; methylene group at C-2), singlets at τ 7·00 and 6·96 (6H; N,N-dimethyl group), a singlet at τ 6·33 (3H; CO_2CH_3), a sextuplet centred at τ 5·8 (1H; tertiary proton at C-3), a broadened signal at τ 4·6 (1H; NH) and a doublet centred at τ 2·83 (1H; J = 7 c/s; vinylic proton at C-5). Upon addition of D_2O to the soln the τ 4·6 signal disappeared, the sextuplet simplified to a quartet and the doublet collapsed to a single line. (Found: C, 47·09; H, 6·08; N, 12·72. $C_9H_{14}O_3N_2S$ requires: C, 46·95; H, 6·08; N, 12·17%).

6-*Carbomethoxy*-3L-*carboxy-4-methyl-2,3-dihydro-1,4-thiazine* (VI)

N-Methyl L-cysteine hydrochloride[8] (0·012 mole, 2·00 g) and sodium formylchloroacetate[2] (0·012 mole, 1·90 g) were dissolved in H_2O (10 ml). The soln was left overnight and the crystals collected (0·88 g, 60%). The material was recrystallized from H_2O, m.p. 154–156°; $\nu_{\max}^{\mathrm{KBr}}$ 1740 (CO_2H), 1655 (vinylgous urethane CO), 1605 (C=C) and 1565 cm^{-1}; $\lambda_{\max}^{\mathrm{EtOH}}$ 267 mμ (ε, 3900) and 321 mμ (ε, 12,500). (Found: C, 44·38; H, 5·16; N, 6·37. $C_8H_{11}O_4NS$ requires: C, 44·30; H, 5·07; N, 6·45%).

3L,6-*Dicarbomethoxy-4-methyl-2,3-dihydro-1,4-thiazine* (VII)

Compound VI was treated with ethereal diazomethane to give VII which was recrystallized from H_2O, m.p. 106–107°; $[\alpha]_D$ +332° (0·50% in MeCOMe); $\nu_{\max}^{\mathrm{KBr}}$ 1735 (CO_2Me), 1670 (vinylgous urethane CO) and 1605 cm^{-1} (C=C); $\lambda_{\max}^{\mathrm{EtOH}}$ 268 mμ (ε, 4070) and 320 mμ (ε, 11,900). The NMR spectrum ($CDCl_3$) showed two quartets centred at τ 7·13 and 6·71 (2H; methylene group at C-2), singlets at τ 6·95 (3H; N-Me), 6·35 (3H; CO_2Me) and 6·26 (3H; CO_2Me), a triplet at τ 5·77 (1H; tertiary proton at C-3) and a singlet at τ 2·55 (1H; vinylic proton at C-5). (Found: C, 46·91; H, 5·72; N, 5·92; S, 13·77; MW 231·0565 [mass spectrum, mol. ion]. $C_9H_{13}O_4NS$ requires: C, 46·80; H, 5·63; N, 6·06; S, 13·86%; MW 231·0565).

6-*Carbomethoxy-2,3-dihydro-1,4-thiazine* (VIII)

2-Mercaptoethylamine hydrochloride (0·001 mole, 1·136 g) and sodium formylchloroacetate[2] (0·001 mole, 1·585 g) were dissolved in H_2O (5 ml). The soln was left for 24 hr, the crystals were collected (0·56 g, 32%) and recrystallized from H_2O containing a little MeOH, m.p. 102–103°; $\nu_{\max}^{\mathrm{KBr}}$ 3320 (NH), 1655 (vinylgous urethane CO), 1600 (C=C) and 1530 cm^{-1} (amide II); $\lambda_{\max}^{\mathrm{MeOH}}$ 262 mμ (ε, 3600) and 316 mμ (ε, 11,600). The NMR spectrum ($CDCl_3$) showed a multiplet centred at τ 7·20 (2H; methylene group at C-2), a multiplet centred at τ 6·4 (2H; methylene group at C-3) which was partly obscured by a singlet at τ 6·30 (3H; CO_2CH_3), a broadened peak at τ 4·9 (1H; NH) and a doublet centred at τ 2·40 (1H; J = 7 c/s; vinylic proton at C-4). Upon addition of D_2O to the soln the τ 4·9 peak disappeared and the doublet collapsed to a single line. (Found: C, 45·22; H, 5·63; N, 8·72; MW 173·0513 [mass spectrum, mol. ion]. $C_6H_9O_2NS$ requires: C, 45·34; H, 5·67; N, 8·81%; MW 173·0510).

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