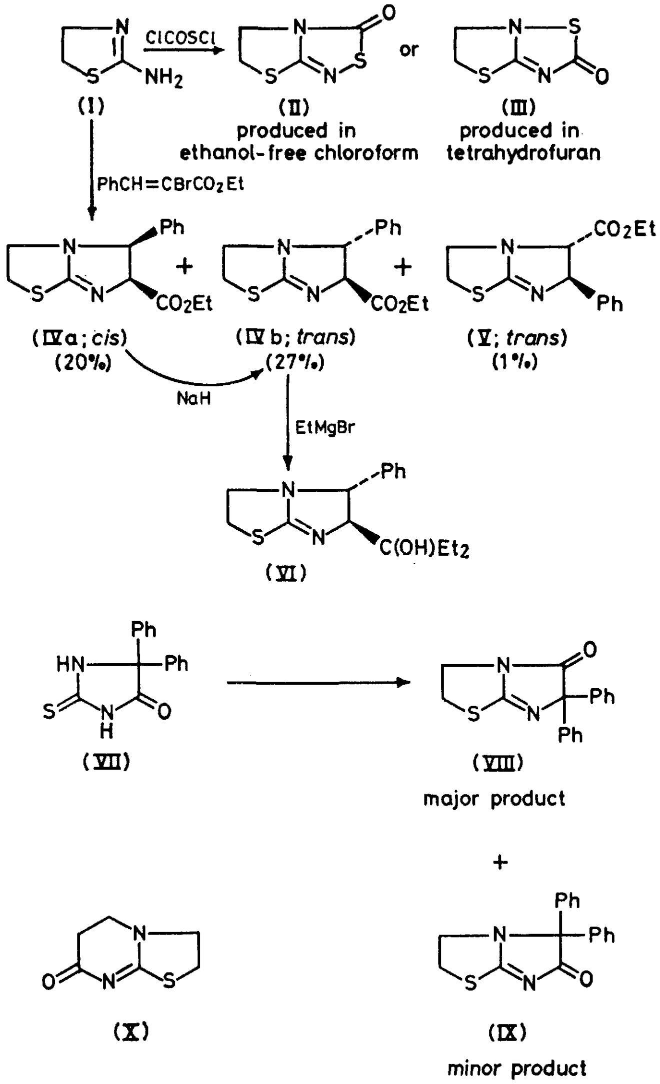
The Structures of the Products of Three Condensation Reactions. Crystal and Molecular Structures of 5,6-Dihydrothiazolo[2,3-*c*][1,2,4]thiadiazol-3-one, 6β-(1-Ethyl-1-hydroxypropyl)-5α-phenyl-2,3,5,6-tetrahydro-imidazo[2,1-*b*]thiazole, and 5,5-Diphenyl-2,3-dihydroimidazo[2,1-*b*]thiazol-6(5*H*)-one

By **A. Forbes Cameron,** * **Ian R. Cameron,** and **Fergus D. Duncanson,** Department of Chemistry, University of Glasgow, Glasgow G12 8QQ

The crystal and molecular structures of the title compounds, (II), (VI), and (IX), respectively, have been determined from diffractometer data [962 reflexions for (II), 1 563 for (VI), and 2 579 for (IX)] and have been refined by least-squares calculations to final *R* values of 0.024, 0.058, and 0.045, respectively. Crystals of (II) and (IX) are monoclinic, space group $P2_1/c$, with $Z = 4$. For (II), $a = 7.379$, $b = 14.587$, $c = 5.804$ Å, $\beta = 102.3°$, while for (IX), $a = 9.289$, $b = 14.754$, $c = 10.945$ Å, $\beta = 103.5°$. Crystals of (VI) are orthorhombic, space group $P2_12_12_1$, with $Z = 4$ and $a = 13.695$, $b = 10.581$, $c = 11.261$ Å. The analyses of (II) and (VI) have resolved structural ambiguities surrounding the several products of the respective condensation reactions by which they were produced. The analysis of (IX), a product of an analogous condensation reaction, was undertaken because of the unusual spectroscopic properties of the compound.

THE condensation of chloroformylsulphur chloride with 2-aminothiazoline (I) has been shown to yield two isomeric products when carried out in different solvents (ethanol-free chloroform or tetrahydrofuran) in the presence of triethylamine.[1] Although these products were clearly (II) and (III), it did not prove possible to distinguish unambiguously between these two isomers using i.r. spectroscopic methods on the basis of an expected difference in the stretching frequencies of the carbonyl functions in (II) (unconjugated) and (III) (conjugated). Our analysis of the product from the reaction carried out in ethanol-free chloroform has confirmed structure (II) for this isomer. Hence the product of the reaction in tetrahydrofuran is (III). Thus (III) is formed when the reaction is carried out in a proton-acceptor solvent, tetrahydrofuran, which is capable of solvating the exocyclic amino-group of (I), whereas (II) is formed in the proton-donor solvent, chloroform, which would tend to solvate the tertiary amine group of (I), leaving the exocyclic amine group free to react. It is therefore plausible to speculate that in both reactions the kinetically controlled step is attack on the sulphur atom by the available (solvent-controlled) amino-group, with subsequent rapid cyclisation preventing thermodynamic control of the product.



In another condensation reaction of 2-aminothiazoline, reaction with a mixture of the two geometrical isomers of ethyl α-bromocinnamate in ethyl acetate yielded a mixture of products from which three geometrical isomers could be isolated. While the *cis*- or *trans*-arrangements of the ring substituents in the three products could be clearly distinguished by n.m.r. spectroscopic evidence, chemical evidence indicated, but not unambiguously, that the possible relative structures of the isomers were (IVa) (*cis*-isomer; 20% yield), (IVb) (*trans*-isomer; 27% yield), and (V) (*trans*-isomer; 1%

yield). Moreover, the *cis*-isomer [tentatively (IVa)] could be converted readily by a catalytic amount of sodium hydride in dioxan into the *trans*-isomer [tentatively (IVb)], while further reaction of the latter isomer with excess of ethylmagnesium bromide yielded the *trans*-alcohol [tentatively (VI)].[2,3] By undertaking a crystal structure analysis of this *trans*-alcohol, we have confirmed that it possesses structure (VI). The structures of isomers (IVa), (IVb), and (V) are thus also confirmed.

In a reaction analogous to those mentioned above, the condensation of 5,5-diphenyl-2-thiohydantoin (VII) with ethylene dibromide yielded two isomeric products. Whilst the major product could be fully characterised as (VIII) by conventional spectroscopic techniques, and it was hence expected that the minor product was (IX), nevertheless certain spectroscopic features of the latter compound seemed to be inconsistent with the spectra observed for similar conjugated systems. In particular the C=O (1 725 cm^{-1}) and C=N (1 495 cm^{-1}) stretching frequencies are respectively higher and lower than corresponding values in similar systems [*e.g.* 1 676 and 1 542 cm^{-1} in (X)].[4] *X*-Ray analysis of (IX) was therefore undertaken to confirm the proposed structure, and also in an effort to identify any features of the molecular geometry which could possibly correlate with the unusual spectra.

EXPERIMENTAL

Crystal Data.—5,6-Dihydrothiazolo[2,3-*c*][1,2,4]thiadiazol-3-one (II), $C_4H_4N_2OS_2$, $M = 160.2$. Monoclinic, $a = 7.379(1)$, $b = 14.587(2)$, $c = 5.804(1)$ Å, $\beta = 102.3(1)°$, $U = 610.3$ Å^3, $D_m = 1.68$, $Z = 4$, $D_c = 1.71$, $F(000) = 328$. Space group $P2_1/c$. Mo-K_α radiation, $\lambda = 0.710\,7$ Å, μ(Mo-K_α) $= 7.50$ cm^{-1}.

6β-(1-Ethyl-1-hydroxypropyl)-5α-phenyl-2,3,5,6-tetrahydroimidazo[2,1-*b*]thiazole (VI), $C_{16}H_{22}N_2OS$, $M = 290.4$. Orthorhombic, $a = 13.695(2)$, $b = 10.581(2)$, $c = 11.261(2)$ Å, $U = 1\,631.8$ Å^3, $D_m = 1.20$, $Z = 4$, $D_c = 1.19$, $F(000) = 624$. Space group $P2_12_12_1$. Mo-K_α radiation, $\lambda = 0.710\,7$ Å, μ(Mo-K_α) $= 1.99$ cm^{-1}.

5,5-Diphenyl-2,3,dihydroimidazo[2,1-*b*]thiazol-6(5*H*)-one (IX), $C_{17}H_{14}N_2OS$, $M = 294.3$. Monoclinic, $a = 9.289(1)$, $b = 14.754(2)$, $c = 10.945(1)$ Å, $\beta = 103.5(2)°$, $U = 1\,452.6$ Å^3, $D_m = 1.36$, $Z = 4$, $D_c = 1.34$, $F(000) = 616$. Space group $P2_1/c$. Mo-K_α radiation, $\lambda = 0.710\,7$ Å, μ(Mo-K_α) $= 2.23$ cm^{-1}.

Structure Determinations and Refinements.—Small crystals of each of the three title compounds were exposed to graphite-monochromated Mo-K_α radiation on a Hilger and Watts Y290 diffractometer, and using the θ,ω-scan technique, the intensities ($I \geqslant 2\sigma_I$, $\sigma_I = \sqrt{I + B_1 + B_2}$) of 962 independent reflexions (2θ 0—60°), of 1 563 independent reflexions (2θ 0—50°), and of 2 579 independent reflexions (2θ 0—60°), were measured for (II), (VI), and (IX), respectively. All intensities were corrected for Lorentz and polarisation factors, but absorption effects were ignored. The three structures were resolved by direct methods using programs incorporated either in the *X*-RAY 72 [(II) and (IX)] or MULTAN [(VI)] suites of programs, and were refined by least-squares calculations which for (II) converged when R was 0.024, and for (VI) and (IX) converged when R was 0.058 and 0.045, respectively. In each case the data were weighed according to $w = x.y$ [$x = (\sin\theta)/B$ if $\sin\theta \leqslant B$, else $x = 1$; $y = C/|F_o|$ if $|F_o| \geqslant C$, else $y = 1$]. The final values of B in the three refinements were 0.45 for (II) and (IX), and 0.50 for (VI), while the final values of C were 8.0 for (II) and 10.0 for (VI) and (IX). Hydrogen atom positions were determined for (II) and (IX) from difference syntheses, and were refined in later cycles. For (VI), positions were calculated for hydrogen atoms, which were then included as fixed contributors in subsequent cycles.

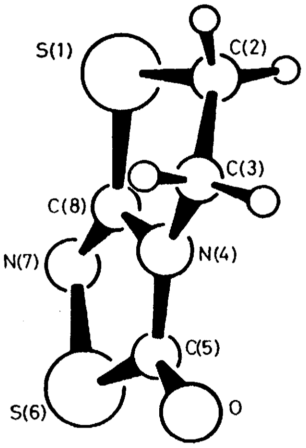


FIGURE 1 A view of one molecule of (II) defining the atomic numbering. Hydrogen atoms are numbered as the atoms to which they are bonded

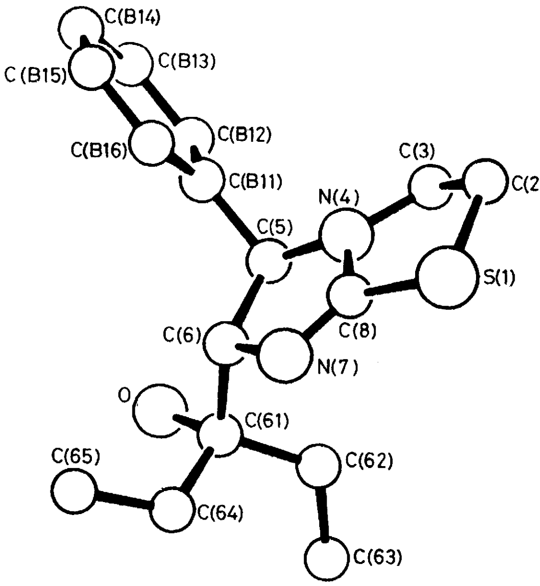


FIGURE 2 A view of one molecule of (VI) defining the atomic numbering. Hydrogen atoms are numbered as the atoms to which they are bonded

Final fractional co-ordinates are given in Tables 1—3 for (II), (VI), and (IX), respectively, while the molecular geometries of all three compounds are presented in Table 4.

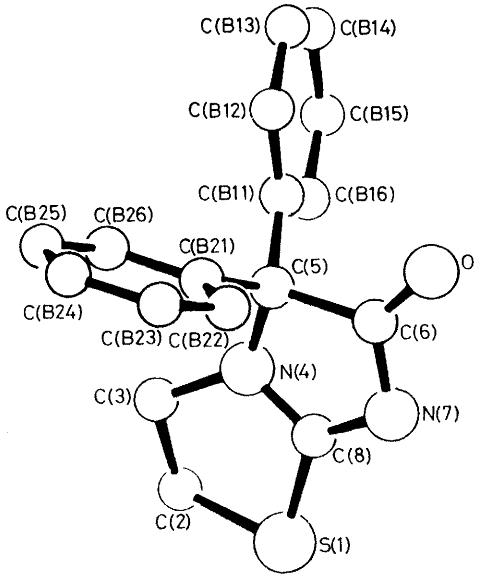


FIGURE 3 A view of one molecule of (IX) defining the atomic numbering. Hydrogen atoms are numbered as the atoms to which they are bonded

TABLE 1

Atomic co-ordinates for (II) (× 10^3 for H, × 10^5 for other atoms)

	x/a	y/b	z/c
S(1)	90 010(5)	16 025(3)	3 759(8)
C(2)	90 679(24)	7 705(13)	27 574(32)
C(3)	72 043(23)	8 310(13)	34 847(29)
N(4)	58 803(17)	10 794(8)	13 266(22)
C(5)	39 829(22)	10 762(11)	9 097(29)
S(6)	32 740(6)	16 698(3)	−18 077(7)
N(7)	54 608(19)	18 892(10)	−21 392(24)
C(8)	65 824(21)	15 454(10)	−3 446(27)
O	30 219(17)	7 305(10)	21 274(24)
H(21)	928(3)	16(2)	207(4)
H(22)	1 007(3)	91(2)	404(4)
H(31)	692(3)	27(2)	402(4)
H(32)	718(3)	131(2)	464(4)

TABLE 2

Atomic co-ordinates for (VI) (× 10^5 for S, × 10^4 for other atoms)

	x/a	y/b	z/c
S(1)	790(9)	31 120(12)	79 885(11)
C(2)	−367(4)	1 826(6)	7 042(6)
C(3)	207(4)	1 867(6)	5 919(5)
N(4)	1 118(3)	2 476(4)	6 179(4)
C(5)	1 941(4)	2 779(4)	5 406(4)
C(6)	2 428(3)	3 889(4)	6 116(4)
N(7)	1 824(3)	4 083(3)	7 194(3)
C(8)	1 113(3)	3 300(4)	7 103(6)
C(61)	2 537(4)	5 131(5)	5 400(4)
C(62)	1 526(4)	5 622(5)	5 008(5)
C(63)	1 485(6)	6 891(8)	4 373(7)
C(64)	3 069(5)	6 125(5)	6 158(6)
C(65)	4 075(6)	5 804(7)	6 571(8)
O	3 143(3)	4 763(4)	4 431(3)
C(B11)	2 593(4)	1 638(4)	5 228(4)
C(B12)	2 683(5)	1 082(6)	4 104(6)
C(B13)	3 271(5)	30(7)	3 965(7)
C(B14)	3 767(5)	−475(6)	4 916(9)
C(B15)	3 679(5)	50(6)	6 018(7)
C(B16)	3 095(5)	1 109(5)	6 178(5)

Views of the three molecules and definitions of the atomic numbering are shown in Figures 1—3.

Structure factors are in Supplementary Publication No. SUP 23011 (46 pp.).*

TABLE 3

Atomic co-ordinates for (IX) (× 10^5 for S, × 10^4 for C, N, O, and × 10^3 for H)

	x/a	y/b	z/c
S(1)	345(6)	34 992(3)	−14 384(6)
C(2)	1 124(3)	4 471(2)	−1 714(2)
C(3)	2 229(2)	4 672(1)	−478(2)
N(4)	2 479(2)	3 808(1)	167(1)
C(5)	3 415(2)	3 553(1)	1 393(2)
C(6)	2 716(2)	2 593(1)	1 517(2)
N(7)	1 462(2)	2 466(1)	564(2)
C(8)	1 390(2)	3 195(1)	−141(2)
O	3 238(2)	2 057(1)	2 341(2)
C(B11)	5 031(2)	3 436(1)	1 348(2)
C(B12)	6 141(2)	3 507(2)	2 443(2)
C(B13)	7 606(2)	3 342(2)	2 418(2)
C(B14)	7 981(2)	3 103(2)	1 314(2)
C(B15)	6 878(3)	3 033(2)	218(2)
C(B16)	5 407(2)	3 194(1)	231(2)
C(B21)	3 179(2)	4 211(1)	2 408(2)
C(B22)	2 350(3)	3 975(2)	3 260(2)
C(B23)	2 101(3)	4 608(2)	4 139(2)
C(B24)	2 662(4)	5 470(2)	4 153(2)
C(B25)	3 502(3)	5 713(2)	3 308(3)
C(B26)	3 767(3)	5 086(2)	2 443(2)
H(21)	158(2)	432(2)	−227(2)
H(22)	49(2)	496(2)	−203(2)
H(31)	183(2)	510(2)	−4(2)
H(32)	310(2)	489(2)	−62(2)
H(B12)	588(2)	368(2)	321(2)
H(B13)	840(2)	340(2)	316(2)
H(B14)	902(2)	294(2)	132(2)
H(B15)	713(2)	286(2)	−56(2)
H(B16)	463(2)	313(2)	−53(2)
H(B22)	196(2)	341(2)	331(2)
H(B23)	144(2)	438(2)	469(2)
H(B24)	241(2)	593(2)	480(2)
H(B25)	400(2)	635(2)	330(2)
H(B26)	440(2)	524(2)	191(2)

TABLE 4

Interatomic distances (Å) and angles (°)

(a) Bonded distances

	(II)	(VI)	(IX)
S(1)–C(2)	1.832(2)	1.834(6)	1.820(3)
C(2)–C(3)	1.525(3)	1.490(9)	1.525(3)
C(3)–N(4)	1.460(2)	1.434(7)	1.450(3)
N(4)–C(5)	1.369(2)	1.460(7)	1.468(2)
C(5)–S(6) or C(6)	1.777(2)	1.570(6)	1.577(3)
C(6) or S(6)–N(7)	1.696(2)	1.483(6)	1.383(3)
N(7)–C(8)	1.286(2)	1.283(6)	1.317(3)
C(8)–S(1)	1.746(2)	1.744(4)	1.723(2)
C(8)–N(4)	1.373(2)	1.358(6)	1.340(2)
C(5)–O	1.213(2)		
C(6)–O			1.213(3)
C(5)–C(B11)		1.515(7)	1.523(2)
C(5)–C(B21)			1.529(3)
C(6)–C(61)		1.549(7)	
C(61)–C(62)		1.543(8)	
C(61)–C(64)		1.538(8)	
C(61)–O		1.425(6)	
C(62)–C(63)		1.522(10)	
C(64)–C(65)		1.493(11)	
C(B11)–C(B12)		1.401(8)	1.391(3)

---

* For details of Supplementary Publications see Notice to Authors No. 7 in *J. Chem. Soc., Perkin Trans. 2*, 1979, Index Issue.

TABLE 4 (*continued*)

(a) Bonded distances

	(II)	(VI)	(IX)
C(B12)–C(B13)		1.383(10)	1.389(3)
C(B13)–C(B14)		1.376(12)	1.379(3)
C(B14)–C(B15)		1.365(12)	1.387(3)
C(B15)–C(B16)		1.388(9)	1.390(3)
C(B16)–C(B11)		1.389(8)	1.394(3)
C(B21)–C(B22)			1.385(3)
C(B22)–C(B23)			1.398(4)
C(B23)–C(B24)			1.373(4)
C(B24)–C(B25)			1.388(4)
C(B25)–C(B26)			1.386(3)
C(B26)–C(B21)			1.398(3)

(b) Interbond angles

	(II)	(VI)	(IX)
C(2)–S(1)–C(8)	90.61(8)	91.3(2)	90.9(1)
S(1)–C(2)–C(3)	106.84(10)	107.2(4)	107.0(1)
C(2)–C(3)–N(4)	104.76(12)	107.4(5)	105.0(2)
O(3)–N(4)–C(5)	128.51(11)	130.4(4)	121.6(2)
C(3)–N(4)–C(8)	116.39(11)	116.1(4)	116.4(2)
C(5)–N(4)–C(8)	113.74(11)	108.7(4)	108.0(1)
N(4)–C(5)–S(6) or C(6)	104.56(8)	100.9(4)	98.1(1)
C(5)–C(6) or S(6)–N(7)	94.91(8)	106.5(3)	110.4(2)
C(6) or S(6)–N(7)–C(8)	107.35(7)	105.6(3)	104.4(2)
S(1)–C(8)–N(4)	112.02(7)	111.7(3)	113.3(1)
S(1)–C(8)–N(7)	128.59(7)	130.1(3)	128.6(2)
N(4)–C(8)–N(7)	119.37(11)	118.2(4)	118.2(2)
N(4)–C(5)–O	126.99(9)		
S(6)–C(5)–O	128.44(8)		
N(4)–C(5)–C(B11)		111.0(4)	112.2(1)
C(6)–C(5)–C(B11)		114.4(4)	109.3(1)
N(4)–C(5)–C(B21)			110.2(1)
C(6)–C(5)–C(B21)			112.2(1)
C(B11)–C(5)–C(B21)			113.9(1)
C(5)–C(6)–O			123.3(2)
N(7)–C(6)–O			126.3(2)
C(5)–C(6)–C(61)		114.3(4)	
N(7)–C(6)–C(61)		111.2(3)	
C(6)–C(61)–O		102.9(4)	
C(6)–C(61)–C(62)		110.4(4)	
C(6)–C(61)–C(64)		109.7(4)	
C(62)–C(61)–C(64)		110.7(4)	
C(62)–C(61)–O		113.3(4)	
C(64)–C(61)–O		109.6(5)	
C(61)–C(62)–C(63)		117.7(5)	
C(61)–C(64)–C(65)		117.0(5)	
C(5)–C(B11)–C(B12)		120.4(5)	120.1(2)
C(5)–C(B11)–C(B16)		120.7(4)	120.5(2)
C(B11)–C(B12)–C(B13)		119.4(6)	120.2(2)
C(B12)–C(B13)–C(B14)		120.8(7)	120.7(2)
C(B13)–C(B14)–C(B15)		120.4(6)	119.3(2)
C(B14)–C(B15)–C(B16)		119.8(7)	120.6(2)
C(B15)–C(B16)–C(B11)		120.7(5)	120.0(2)
C(B16)–C(B11)–C(B12)		118.9(5)	119.2(2)
C(5)–C(B21)–C(B22)			121.7(2)
C(5)–C(B21)–C(B26)			119.0(2)
C(B21)–C(B22)–C(B23)			120.2(2)
C(B22)–C(B23)–C(B24)			120.2(3)
C(B23)–C(B24)–C(B25)			120.1(3)
C(B24)–C(B25)–C(B26)			120.0(3)
C(B25)–C(B26)–B(B21)			120.3(3)
C(B26)–C(B21)–C(B22)			119.2(2)

(c) Selected torsion angles

	(II)	(VI)	(IX)
S(1)–C(2)–C(3)–N(4)	31.3(2)	24.4(6)	27.8(2)
C(2)–C(3)–N(4)–C(8)	−26.0(2)	−26.6(6)	−25.1(2)
C(3)–N(4)–C(8)–S(1)	7.8(2)	15.6(5)	10.1(2)
N(4)–C(8)–S(1)–C(2)	10.6(1)	0.3(4)	7.0(2)
C(8)–S(1)–C(2)–C(3)	−24.6(1)	−14.5(4)	−20.5(2)
N(4)–C(5)–C(6) or S(6)–N(7)	−1.2(1)	−0.3(4)	−8.0(2)
C(5)–C(6) or S(6)–N(7)–C(8)	−0.4(1)	−2.6(5)	3.8(2)
C(6) or S(6)–N(7)–C(8)–N(4)	1.9(2)	5.0(5)	2.8(2)
N(7)–C(8)–N(4)–C(5)	−3.1(2)	−5.4(6)	−8.6(2)
C(8)–N(4)–C(5)–C(6) or S(6)	2.4(2)	2.9(5)	9.1(2)

TABLE 4 (*continued*)

(d) Intermolecular distances $\leqslant 3.45$ Å for (II)

	(II)	(VI)	(IX)
$C(3) \cdots N(7^{I})$	3.44(1)	$B(4) \cdots N(7^{V})$	3.12(1)
$O \cdots S(1^{II})$	3.19(1)	$C(5) \cdots N(7^{V})$	3.28(1)
$O \cdots C(2^{II})$	3.02(1)	$N(7) \cdots N(7^{V})$	3.41(1)
$N(4) \cdots C(5^{III})$	3.41(1)	$C(8) \cdots N(7^{V})$	3.16(1)
$O \cdots C(3^{IV})$	3.45(1)		

Roman superscripts refer to the following equivalent positions relative to a molecule at (*x*, *y*, *z*)

I $x, y, 1 + z$
II $-1 + x, y, z$
III $1 - x, -y, -z$
IV $1 - x, -y, 1 - z$
V $x, \frac{1}{2} - y, \frac{1}{2} + z$

DISCUSSION

Although the individual analyses were undertaken to provide solutions to different problems, fortuitously the three molecules proved to possess similar fused heterocyclic ring systems. It is therefore of some interest to compare and to contrast the three molecular geometries.

Two features are common to all three molecules, the fused dihydrothiazole ring system and the central unsaturated S(1)N(4)N(7)C(8) group. In each molecule the latter group of atoms is strictly planar, with dimensions which suggest delocalisation in particular within the N(4)C(8)N(7) portion. The shortest value for the N(4)–C(8) bond [1.340(2) Å] and the longest value for the N(7)–C(8) bond [1.317(3) Å] are both observed in (IX). This feature, together with the length of the N(7)–C(6) bond [1.383(2) Å] in the same molecule, suggests only limited involvement of the 6-carbonyl group in the pattern of delocalisation within molecules of (IX). In this context we note that the spectroscopic features of (IX), the C=O (1 725 cm^{-1}) and C=N (1 495 cm^{-1}) stretching frequencies, were considered anomalous in the expectation of more complete delocalisation such as that observed in systems such as (X).

Whereas the dihydrothiazole rings of (II) and of (IX) adopt similar and irregular half-chair conformations, defined by the torsion angles in Table 4, the corresponding ring in (VI) adopts a fairly regular envelope conformation in which C(3) is the out-of-plane atom. However, an examination of both fused and unfused dihydrothiazole systems which have been reported recently,[5-11] reveals that both conformations are represented in these examples, while two possess fairly planar conformations. Moreover, there does not appear to be any obvious structural feature in either the present or the earlier examples which may be associated with this range of conformational possibilities.

The thiadiazolone ring of (II) deviates little from planarity, there being a very slight tendency towards a shallow envelope conformation in which N(4) is the unique atom. Whereas the imidazole ring of (VI) also forms a very shallow envelope conformation in which C(8) is the unique atom, the imidazoline ring of (IX) deviates rather more from planarity, adopting a shallow and irregular half-chair form defined by the torsion angles in Table 4.

The shortest intermolecular contacts are observed in the crystal structure of (II), a feature which probably results from the lack of bulky substituents and the consequent close packing of the molecules, which is reflected in the relatively higher density of this example. Otherwise, intermolecular distances correspond to, or are greater than the relevant van der Waals' radii.

We thank Mr. P. J. Taylor and Drs. van den Broek, Hesp, and Turner of Imperial Chemical Industries Limited, Pharmaceuticals Division, who brought these problems to our attention, provided crystals, and participated in many interesting discussions.

[0/1542 *Received*, 8*th October*, 1980]

REFERENCES

[1] D. Baldwin and P. van den Broek, *J. Chem. Soc., Perkin Trans. 2*, 1975, 375.

[2] P. J. Taylor and R. W. Turner, personal communication.

[3] R. Bayles, P. W. R. Caulkett, T. P. Seden, and R. W. Turner, *Tetrahedron Lett.*, 1975, 4587.

[4] B. Hesp and P. J. Taylor, unpublished results and personal communication.

[5] A. Kálmán and Gy. Argay, *Cryst. Struct. Commun.*, 1978, **7**, 659.

[6] Gy. Argay and A. Kálmán, *Acta Crystallogr. B*, 1977, **33**, 106.

[7] Gy. Argay, A. Kálmán, A. Nahlovski, and B. Ribar, *Acta Crystallogr. B*, 1975, **31**, 1956.

[8] Gy. Argay and A. Kálmán, *Acta Crystallogr. B*, 1975, **31**, 1961.

[9] Gy. Argay, A. Kálmán, G. Tóth, and L. Tóldy, *Tetrahedron Lett.*, 1972, 3179.

[10] C. Rømming, *Acta Chem. Scand. Ser. A*, 1975, **29**, 282.

[11] A. L. Spek, *Cryst. Struct. Commun.*, 1972, **1**, 309.