HETEROCYCLIC TAUTOMERISM. VIII.[1] X-RAY CRYSTAL STRUCTURES OF TWO SUBSTITUTED 2-METHYLENETHIAZOLIDIN-4-ONES

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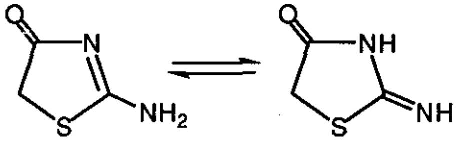
(Dedicated to Prof Alan R. Katritzky on the occassion of his 65th birthday)

Abstract - Location and refinement of the hydrogen atoms in low temperature crystal structure determinations have unambiguously established the tautomeric structures of two title compounds in the solid state. Both the carbamoyl (**3**) and benzoyl (**4**) derivatives exist as N-H tautomers with a Z-substituted exocyclic double bond. In both cases the carbonyl oxygen of the substituent is coplanar with the ring and in an s-cis conformation. The acetamide (**3a**) crystallises with two molecules in the asymmetric unit and packs with a complex network of intermolecular hydrogen bonds. Bond lengths in the benzoyl derivative (**4a**) suggest a contribution to the structure from a charged form.

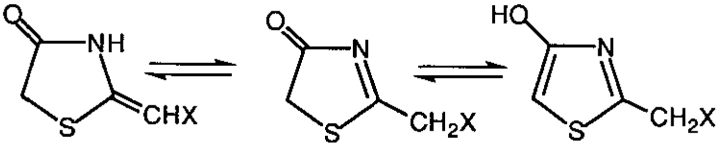
INTRODUCTION

In solution many heterocyclic compounds can exist as a number of different tautomers with the position of equilibrium often depending on the specific solvent.[2,3] In the solid state however most[4] compounds exist as a single tautomer, the structure of which can often be deduced by infrared spectroscopy. The most definitive method for the determination of the solid state structures of tautomeric compounds is low temperature X-ray crystallography with precise location and refinement of the tautomeric hydrogen atoms. For example, we recently[5] redetermined the crystal structure of 2-aminothiazol-4-one (pseudothiohydantoin) at -140 °C and showed that this compond exists as the amino tautomer (**1a**) rather than the imino tautomer (**1b**) reported in two earlier[6] room temperature crystal structure analyses. This resolved an apparent contradiction with more recent infrared studies.[7] In continuation of our studies of heterocyclic tautomerism[8] we now describe the structures of two related compounds that have been the subject of controversy as to their tautomeric structures.



(1a) **(1b)**

Reactions of activated nitriles with thioglycolate esters were first reported by Satzinger[9] to give compounds which were assigned the methylene tautomeric structures (**2a**). Subsequent work by Taylor[10] and Ceder *et al.*[11] appeared to confirm these structures and even described the isolation of geometrical isomers about the exocyclic methylene. However more recent studies[12-14] have questioned these structures and have suggested that they exist as the endocyclic tautomers (**2b**) or hydroxy tautomers (**2c**).[15] We now report the low temperature X-ray crystal structures of two such compounds, *viz* **3** (X = $CONH_2$), which has variously been assigned structures (**3a**),[10,16] (**3b**)[13] and (**3c**),[13] and **4** (X = COPh) which has been assigned structures (**4a**),[10,17] (**4b**)[14] and (**4c**).[12]



(2a) **(2b)** **(2c)**

(3) X = $CONH_2$
(4) X = COPh

RESULTS AND DISCUSSION

The thiazole derivatives (**3**) and (**4**) were prepared according to literature procedures[13,12] by reaction of thioglycolic acid with cyanoacetamide or benzoylacetonitrile and recrystallised from pyridine and ethanol respectively. X-Ray crystal structure determinations were carried out at -140 °C in order to locate and refine the tautomeric hydrogen atoms.

The acetamide derivative (**3**) crystallises in space group $P2_1/c$ with two independent molecules in the asymmetric unit. Figure 1 shows a perspective view and atom labelling of one of the molecules. The location of the hydrogen atoms from difference Fourier syntheses and their successful refinement, in combination with the bonding geometry (Table 1), unambiguously establish that **3** exists as the N-H tautomer (**3a**) as originally proposed.[10] Furthermore the structure determination shows that **3a** exists as the (*Z*)-isomer about the C(2)-C(6) double bond and that it exists in an s-cis conformation about the C(6)-C(7) bond [C(2) - C(6) - C(7) - O(7) torsional angle = -2.2° and -0.5° for the two independent molecules]. This is exactly the structure predicted by Taylor[10] on the basis of detailed infrared studies, although he claimed that this isomer exists as a hydrate.

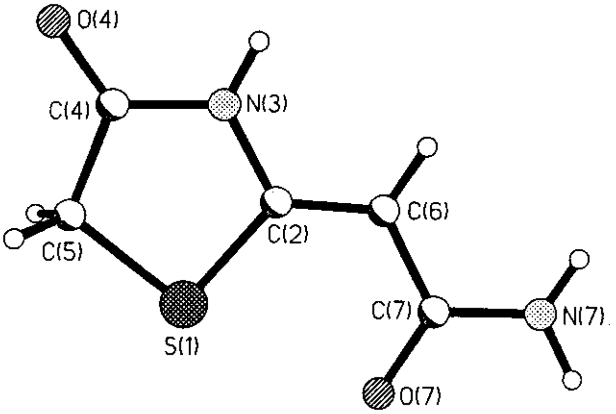


Figure 1. Perspective view and atom labelling of the crystal structure of one of the two independent molecules of **3a**.

The two independent molecules are identical in geometry within experimental error (Table 1). The molecules are planar with the maximum deviations from the meanplanes being 0.122 Å [O(4)] and 0.019 Å [N(3')]. All three NH hydrogen atoms of each molecule participate in a

Table 1. Bond lengths (Å) and angles (°).

	(3a)	(3a')	(4a)
S(1)-C(2)	1.768(2)	1.765(2)	1.754(3)
S(1)-C(5)	1.828(2)	1.825(2)	1.829(4)
C(2)-C(6)	1.364(3)	1.357(3)	1.370(5)
C(2)-N(3)	1.395(3)	1.398(3)	1.390(5)
N(3)-C(4)	1.363(3)	1.362(3)	1.380(5)
C(4)-O(4)	1.235(3)	1.235(3)	1.223(4)
C(4)-C(5)	1.515(3)	1.518(3)	1.517(5)
C(6)-C(7)	1.464(3)	1.470(3)	1.444(5)
C(7)-O(7)	1.267(3)	1.264(3)	1.253(4)
C(7)-N(7)	1.349(3)	1.345(3)	
C(7)-C(11)			1.509(5)
C(11)-C(16)			1.402(5)
C(11)-C(12)			1.407(5)
C(12)-C(13)			1.397(5)
C(13)-C(14)			1.384(5)
C(14)-C(15)			1.395(5)
C(15)-C(16)			1.402(5)
C(2)-S(1)-C(5)	91.7(1)	92.1(1)	92.4(2)
C(6)-C(2)-N(3)	121.9(2)	122.3(2)	123.1(3)
C(6)-C(2)-S(1)	127.1(2)	127.2(2)	126.0(3)
N(3)-C(2)-S(1)	111.0(2)	110.6(2)	110.9(3)
C(4)-N(3)-C(2)	117.9(2)	118.4(2)	118.2(3)
O(4)-C(4)-N(3)	123.7(2)	124.6(2)	123.7(3)
O(4)-C(4)-C(5)	124.9(2)	124.2(2)	125.5(3)
N(3)-C(4)-C(5)	111.5(2)	111.2(2)	110.7(3)
C(4)-C(5)-S(1)	107.7(2)	107.7(2)	107.3(3)
C(2)-C(6)-C(7)	120.9(2)	121.9(2)	121.0(3)
O(7)-C(7)-C(6)	120.2(2)	121.2(2)	121.7(3)
O(7)-C(7)-N(7)	121.7(2)	122.4(2)	
N(7)-C(7)-C(6)	118.1(2)	116.4(2)	
O(7)-C(7)-C(11)			119.3(3)
C(6)-C(7)-C(11)			118.9(3)
C(16)-C(11)-C(12)			118.6(4)
C(16)-C(11)-C(7)			122.0(3)
C(12)-C(11)-C(7)			119.4(3)
C(13)-C(12)-C(11)			120.5(3)
C(14)-C(13)-C(12)			120.7(4)
C(13)-C(14)-C(15)			119.4(4)
C(14)-C(15)-C(16)			120.4(3)
C(11)-C(16)-C(15)			120.4(4)

complex network of intermolecular hydrogen bonding to oxygen atoms of adjacent molecules. The O ··· N separations are in the range 2.705-3.025 Å and the N - H ··· O angles 153.5 - 169.3°. Figure 2 shows a perspective view and atom labelling of the structure of the benzoyl analogue (4) which also exists as the N-H tautomer (**4a**) and, as suggested by Taylor,[10] exists as the s-cis-(*Z*) isomer [C(2) - C(6) - C(7) - O(7) torsional angle = -6.1°]. The molecule is planar except for the phenyl ring which is inclined to the rest of the molecule at an angle of 27.2°. The NH hydrogen atom is hydrogen bonded to the benzoyl oxygen of an adjacent molecule with an O ··· N separation of 2.867 Å and an N - H ··· O angle of 160.6°.

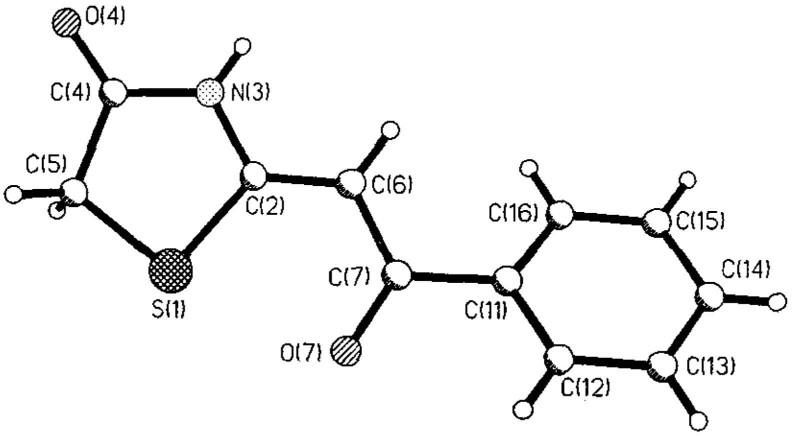
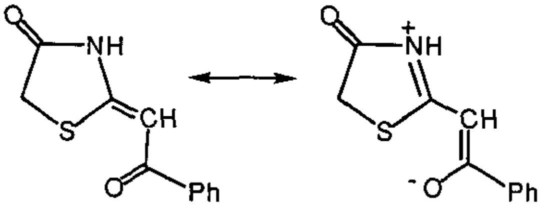


Figure 2. Perspective view and atom labelling of the crystal structure of **4 a**

Comparison of the bond lengths in the two structures with those previously reported[5] for **1a** reveals some interesting differences. In particular this shows that there is a contribution to the structure of **4a** from the polar resonance contributor (**4a'**) due to competition for the ring nitrogen lone pair from the conjugated exocyclic carbonyl group.



(4a) **(4a')**

Table 2. Atomic coordinates (x10^4) and isotropic thermal parameters (Å^{2}x10^3) for **3a** and **4a**.

(3a)	x	y	z	U_{eq}[a]
S(1)	6197(1)	2922(1)	1613(1)	33(1)
C(2)	5410(2)	1735(2)	1872(2)	29(1)
N(3)	5753(2)	745(2)	1433(2)	29(1)
C(4)	6658(2)	819(2)	975(2)	30(1)
C(5)	7035(2)	2036(2)	912(2)	32(1)
O(4)	7119(1)	-12(1)	673(2)	35(1)
C(6)	4584(2)	1728(2)	2435(2)	30(1)
C(7)	4265(2)	2774(2)	2921(2)	31(1)
N(7)	3412(2)	2717(2)	3432(2)	36(1)
O(7)	4787(2)	3698(1)	2861(2)	36(1)
S(1')	1329(1)	-925(1)	5956(1)	32(1)
C(2')	591(2)	-1557(2)	4395(2)	29(1)
N(3')	886(2)	-965(2)	3490(2)	29(1)
C(4')	1664(2)	-49(2)	3914(2)	31(1)
C(5')	2056(2)	167(2)	5359(2)	33(1)
O(4')	2013(2)	531(1)	3218(2)	35(1)
C(6')	-152(2)	-2494(2)	4063(2)	30(1)
C(7')	-456(2)	-3113(2)	5022(2)	31(1)
N(7')	-1216(2)	-4019(2)	4572(2)	35(1)
O(7')	-26(2)	-2796(1)	6201(2)	36(1)

(4a)	x	y	z	U_{eq}[a]
S(1)	8734(1)	-40(2)	9162(1)	29(1)
C(2)	8316(2)	-1080(8)	7637(3)	28(1)
N(3)	8632(2)	215(7)	6795(3)	32(1)
C(4)	9219(2)	1950(8)	7255(3)	31(1)
O(4)	9585(1)	3024(5)	6615(2)	38(1)
C(5)	9334(2)	2334(8)	8642(3)	29(1)
C(6)	7755(2)	-2924(8)	7289(3)	30(1)
C(7)	7452(2)	-4234(7)	8202(3)	29(1)
O(7)	7731(1)	-3899(5)	9346(2)	32(1)
C(11)	6794(2)	-6103(8)	7764(3)	28(1)
C(12)	6675(2)	-8036(8)	8576(3)	31(1)
C(13)	6068(2)	-9785(8)	8193(3)	33(1)
C(14)	5569(2)	-9631(8)	7015(3)	34(1)
C(15)	5679(2)	-7721(8)	6200(3)	36(1)
C(16)	6288(2)	-5960(8)	6572(3)	32(1)

[a] *Equivalent isotropic* U defined as one third of the trace of the orthogonalised U_{ij} tensor

EXPERIMENTAL

The acetamide (**3**) was prepared by reaction of cyanoacetamide with thioglycolic acid as previously reported[13] and recrystallised from pyridine. The phenacyl analogue (**4**) was prepared by reaction of benzoylacetonitrile[18] with thioglycolic acid according to the literature procedure[12] and recrystallised from ethanol.

*Crystal data for **3a** at -140 °C* : $C_5H_6N_2O_2S$, Mr = 158.18, monoclinicic, space group $P2_1/c$, a = 11.681(2), b = 11.818(1), c = 11.302(2) Å, β = 115.21(1) °, U = 1411.6(5) Å^3, F(000) = 656, Z = 8, D_c = 1.489 g cm^{-3}, μ(Mo–Kα) = 0.40 mm^{-1}, ω scans, $2\theta_{max}$ = 50°, N = 2400, 218 parameters, S = 1.00, wR(F^2) = 0.108 for all data, R = 0.042 for 2001 reflections with $I > 2\sigma(I)$.

*Crystal data for **4a** at -140 °C* : $C_{11}H_9NO_2S$, Mr = 219.25, monoclinic, space group $P2_1/c$, a = 17.907(6), b = 5.213(2), c = 11.134(4) Å, β = 105.08(4) °, U = 1003.6(6) Å^3, F(000) = 456, Z = 4, D_c = 1.451 g cm^{-3}, μ(Mo–Kα) = 0.30 mm^{-1}, ω scans, $2\theta_{max}$ = 52°, N = 1947, 149 parameters, S = 1.05, wR(F^2) = 0.1399 for all data, R = 0.053 for 1280 reflections with $I > 2\sigma(I)$.

Intensity data were collected at -140 °C with a Siemens P4s four-circle diffractometer by using monochromatized Mo Kα (λ = 0.7107 Å) radiation. The crystals used were a yellow block of dimensions 0.58 x 0.38 x 0.16 mm for **3a** and a yellow plate measuring 0.67 x 0.21 x 0.03 mm for **4a**. Cell parameters were determined by least squares refinement. Throughout data collections the intensities of three standard reflections were monitored at regular intervals and this indicated no significant crystal decomposition. The intensities were corrected for Lorentz and polarization effects but not for absorption.

The structures were solved by direct methods using SHELXTL PC,[19] and refined on F^2 using SHELXL92.[20] All non-hydrogen atoms were refined with anisotopic thermal parameters. The phenyl group hydrogen atoms of **4a** were included in calculated positions while all other hydrogens were located from difference maps and their positions refined. All hydrogens were assigned isotropic thermal parameters 1.3 times the isotropic equivalent of their carrier atoms. The functions minimised were $\Sigma w\ (F_o^2 - F_c^2)$, with $w = [\sigma^2(F_o^2) + 0.0841P^2]^{-1}$ for **3a** and $w = [\sigma^2(F_o^2) + 0.0648P^2 + 0.4269P]^{-1}$ for **4a**, where $P = [\max(F_o^2 + 2F_c^2]/3$. Final atom coordinates are listed in Table 2. Tabulations of hydrogen atom coordinates, anisotropic thermal parameters, structure factors and equations of meanplanes are available from the authors.

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