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The Crystal and Molecular Structures of Acetone Semicarbazone and Benzaldehyde Semicarbazone

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The crystal and molecular structures of acetone semicarbazone, ASC, and benzaldehyde semicarbazone, BSC, have been determined by X-ray diffraction techniques. Both compounds form colorless, monoclinic crystals, with space group $P2_1/c$ and $Z=4$; $a=7{\cdot}488$ (1), $b=9{\cdot}672$ (1), $c=8{\cdot}691$ (1) Å, and $\beta=103{\cdot}38$ (1)° for ASC and $a=11{\cdot}985$ (1), $b=5{\cdot}484$ (1), $c=12{\cdot}963$ (2) Å, and $\beta=102{\cdot}27$ (1)° for BSC. The intensity data were measured with a computer-controlled diffractometer using Cu $K\alpha$ radiation. The structures were determined by symbolic addition procedures and Fourier syntheses and refined by full-matrix least-squares methods. The final R was 0·044 for 735 observed reflections used for ASC and 0·044 for 897 reflections for BSC. The bond distances in the two molecules are very similar, with only small differences which may be related to the nature of the parent aldehyde or ketone. One striking difference is that the C=O is *cis* to the N–NH bond in ASC but *trans* in BSC. The *trans* conformation is usually found in the thiosemicarbazones. The hydrogen-bonding pattern in the two structures is also different, a consequence of the difference in the conformation of the two molecules.

Introduction

The condensation of ketones and aldehydes with semicarbazide or thiosemicarbazide yields semicarbazones and thiosemicarbazones. Although Gertler (1946) reported that some semicarbazones were toxic to certain insects, the majority of the semicarbazones are void of any useful biological activity. In contrast, the thiosemicarbazones have a wide range of biological activities which are dependent on the parent aldehyde or ketone. As an extension of our studies on thiosemicarbazones (Palenik, Rendle & Carter, 1974, and references therein), we decided to investigate two semicarbazones for a comparison of electronic and steric effects between these two classes of compounds. Acetone semicarbazone, henceforth ASC, was chosen as an example of an alkyl derivative with no possible interaction between the side chain and the alkyl groups. In addition, the crystal structure of the corresponding thio derivative, acetone thiosemicarbazone, has been determined by Palenik, Rendle & Carter (1974). Benzaldehyde semicarbazone, BSC, was chosen as an example of an aryl derivative where an interaction between the side chain and the benzene ring could exist. Our studies of ASC and BSC demonstrate that ASC and BSC have identical bond lengths in the side chain, indicating that the side chain has little effect on the electronic structure of the semicarbazone group.

Experimental

Acetone semicarbazone, $(CH_3)_2CNNHC(NH_2)O$, m.p. 187–88°, and benzaldehyde semicarbazone, $C_6H_5CHNNHC(NH_2)O$, m.p. 222–224°C, were prepared by reacting acetone or benzaldehyde with semicarbazide hydrochloride in ethanol, in the presence of a small amount of sodium acetate. Clear, plate-like crystals were obtained by recrystallization from hot ethanol. Preliminary Weissenberg photographs indicated that both compounds crystallized with monoclinic symmetry. The systematic absences of $h0l$ if $l=2n+1$ and $0k0$ if $k=2n+1$ indicated that the most probable space group for both compounds was $P2_1/c$ (C_{2h}^5).

The data collection for both compounds was virtually identical. A crystal mounted on the end of a glass fiber was used for the intensity measurements. The unit-cell dimensions were determined by a least-squares procedure using the $2\theta, \omega, \varphi$, and χ values determined for 15 reflections measured with Cu $K\alpha$ radiation ($\lambda=1{\cdot}5418$ Å) and a Syntex $P\bar{1}$ diffractometer. The crystal sizes, cell dimensions and other pertinent data are given in Table 1. The intensity data were measured with a computer-controlled Syntex $P\bar{1}$ diffractometer with Cu radiation ($\lambda_1=1{\cdot}54051$ and $\lambda_2=1{\cdot}54434$ Å) and a take-off angle of about 4°. All the independent reflections with $2\theta\le110$ were measured with a variable rate θ–2θ scan technique. A 0·8° scan at 24° min^{-1} was made across the α_1 peak and the accumulated counts were used to calculate a scan rate for measuring the peak. If the accumulated counts were less than 150, the slowest scan speed of 1° min^{-1} was used to measure the peak; if the counts were greater than 1500, the fastest speed of 24° min^{-1} was selected. For values between these two limits, a linear interpolation was used to calculate the scan speed. Background counts were taken at the beginning and end of each scan for a time equal to one-half of the total scan time. A 0·5 mil nickel foil was placed over the counter window. Only those reflections for which $I\ge n\sigma(I)$ where $n=1{\cdot}5$ for ASC and 1·3 for BSC were used in the analysis. If $I<n\sigma(I)$, the value of I was replaced by $n\sigma(I)$ and flagged with a minus sign. A small correction (maximum 9% for ASC and 1% for BSC) was applied to reflect

the changes in four standard reflections which were measured after every 96 reflections. These data were reduced to a set of structure amplitudes on an arbitrary scale in the usual manner.

Structure determination and refinement

The signs of the larger E values (124 for ASC and 162 for BSC) were determined by the symbolic addition method using the computer programs *FAME-MAGIC-LINK-SYMPL* developed by Dewar, Stone & Fleischer (1966). In both cases all the non-hydrogen atoms were easily located in an E map computed from the signed E values. A structure factor–Fourier synthesis calculation was used to confirm the validity of our model and to refine the atomic parameters. Three full-matrix least-squares cycles of refinement were carried out with individual isotropic thermal parameters. The choice of the terminal N(3) and O atoms was made by refining both possible models and comparing thermal parameters, bond distances and R values. The correct model gave an R, usual residual, of 0·14 for ASC and 0·13 for BSC at this point. Three least-squares cycles, using anisotropic thermal parameters, reduced R to 0·09 for ASC and 0·09 for BSC. A difference Fourier synthesis was used to locate all the hydrogen atoms in both molecules. Three final least-squares cycles in which the heavy atoms were refined anisotropically and the hydrogen atoms isotropically reduced R to 0·044 for both ASC and BSC. In the last cycle the shifts were all less than 0·5 of an extimated standard deviation so that the refinement was terminated. The final parameters for ASC are given in Tables 2 and 3, with the final parameters for BSC in Tables 4 and 5.*

Table 1. *Crystal data for acetone semicarbazone (ASC) and benzaldehyde semicarbazone (BSC)*

	ASC	BSC
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$
a(Å)	7·488 (1)	11·985 (1)
b	9·672 (1)	5·464 (1)
c	8·691 (1)	12·963 (2)
β(°)	103·38 (1)	102·27 (1)
V (Å^3)	612·4	829·5
Z	4	4
D_c (g cm^{-3})	1·246	1·306
D_m (g cm^{-3})	1·25	1·29
Crystal size (mm)	0·36 × 0·36 × 0·17	0·20 × 0·19 × 0·14
μ(Cu $K\alpha$) (cm^{-1})	7·85	7·57
Number of unique reflections	767	1039
Number of observed reflections	735	897

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* Tables of observed and calculated structure factors for ASC and BSC have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30509 (11 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. *Final atomic coordinates and thermal parameters* (× 10^4) *of non-hydrogen atoms and their estimated standard deviations in parentheses for acetone semicarbazone*

The temperature factor is of the form $\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+\beta_{12}hk+\beta_{13}hl+\beta_{23}kl)]$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
O	5967 (2)	1633 (1)	−0562 (1)	289 (4)	94 (2)	70 (2)	−63 (4)	109 (4)	−31 (3)
N(1)	7210 (2)	4141 (2)	0553 (2)	182 (4)	82 (2)	90 (3)	−3 (4)	67 (5)	2 (4)
N(2)	7093 (2)	3037 (2)	1541 (2)	211 (4)	87 (2)	64 (3)	−35 (4)	69 (5)	−18 (4)
N(3)	5889 (3)	0934 (2)	1895 (2)	281 (5)	98 (2)	72 (3)	−82 (5)	91 (6)	−9 (4)
C(1)	6281 (3)	1850 (2)	0884 (2)	163 (4)	81 (3)	72 (3)	5 (5)	66 (5)	−11 (4)
C(2)	8049 (3)	5218 (2)	1204 (2)	158 (4)	82 (3)	121 (3)	−6 (5)	85 (6)	−28 (4)
C(3)	8968 (4)	5345 (3)	2924 (3)	249 (6)	136 (4)	143 (4)	−126 (8)	37 (8)	−73 (6)
C(4)	8143 (4)	6435 (3)	0168 (4)	281 (7)	88 (3)	196 (5)	−30 (8)	106 (9)	8 (6)

Table 3. *Final atomic coordinates and thermal parameters* (× 10^4) *of non-hydrogen atoms and their estimated standard deviations in parentheses for benzaldehyde semicarbazone*

The temperature factor is of the form $\exp[-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+\beta_{12}hk+\beta_{13}hl+\beta_{23}kl)]$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
O	5037 (1)	1010 (3)	6369 (1)	92 (2)	323 (8)	35 (1)	73 (6)	−4 (2)	37 (5)
N(1)	3285 (2)	4366 (4)	4360 (1)	71 (2)	289 (8)	37 (1)	44 (6)	6 (2)	26 (5)
N(2)	3969 (2)	2516 (4)	4867 (1)	87 (2)	315 (8)	32 (1)	94 (7)	0 (2)	4 (5)
N(3)	4096 (2)	4611 (4)	6426 (2)	90 (2)	343 (9)	34 (1)	46 (7)	10 (3)	−26 (6)
C(1)	4407 (2)	2673 (5)	5931 (2)	63 (2)	301 (11)	34 (2)	−41 (8)	16 (3)	20 (7)
C(2)	3013 (2)	4183 (5)	3355 (2)	65 (2)	297 (10)	39 (2)	29 (8)	9 (3)	9 (7)
C(3)	2261 (2)	5969 (4)	2712 (2)	58 (2)	311 (10)	41 (2)	7 (8)	16 (3)	34 (7)
C(4)	1911 (2)	5563 (6)	1630 (2)	79 (2)	429 (13)	40 (2)	68 (10)	11 (3)	43 (8)
C(5)	1167 (2)	7172 (6)	1005 (2)	93 (2)	556 (15)	48 (2)	72 (10)	3 (3)	92 (9)
C(6)	769 (2)	9178 (6)	1452 (2)	86 (3)	460 (14)	77 (2)	69 (11)	2 (4)	154 (10)
C(7)	1106 (2)	9625 (6)	2519 (2)	83 (3)	332 (12)	87 (3)	75 (10)	30 (4)	50 (9)
C(8)	1855 (2)	8014 (5)	3147 (2)	76 (2)	332 (11)	52 (2)	18 (8)	21 (3)	22 (8)

The quantity minimized in the least-squares calculations was $\sum w(|F_o|-|F_c|)^2$ where the weights were as follows:

$$\begin{aligned} w &= F_o/F_{\min} && \text{if } F_o < F_{\min} \\ w &= 1 && \text{if } F_{\min} \le F_o \le 4F_{\min} \\ w &= 4F_{\min}/F_o && \text{if } F_o > 4F_{\min} \end{aligned}$$

Table 4. *Positional parameters* ($\times 10^3$) *and their estimated standard deviations in parentheses for the hydrogen atoms in acetone semicarbazone*

The hydrogen atom is given followed by the atom to which it is bonded and the bond distance (in Å).

Atom [bonded to]	Distance	x	y	z	B(Å^2)
H(1)[N(2)]	0·81	701 (4)	317 (3)	244 (4)	1·5 (7)
H(2)[N(3)]	0·85	602 (4)	111 (3)	287 (4)	0·5 (8)
H(3)[N(3)]	0·94	537 (4)	008 (4)	151 (4)	1·8 (7)
H(4)[C(3)]	0·96	815 (5)	532 (4)	363 (4)	7·6 (8)
H(5)[C(3)]	1·02	979 (5)	611 (4)	314 (4)	4·3 (8)
H(6)[C(3)]	0·96	974 (5)	448 (4)	326 (4)	7·5 (8)
H(7)[C(4)]	1·02	944 (5)	676 (3)	022 (4)	4·6 (8)
H(8)[C(4)]	0·91	762 (5)	717 (4)	056 (4)	3·9 (9)
H(9)[C(4)]	1·01	753 (5)	627 (4)	−098 (5)	3·6 (9)

Table 5. *Positional parameters* ($\times 10^3$) *and their estimated standard deviations in parentheses for the hydrogen atoms in benzaldehyde semicarbazone*

The hydrogen atoms is given followed by the atom to which it is bonded and the bond distance (in Å).

Atom [bonded to]	Distance	x	y	z	B(Å^2)
H(1)[N(2)]	0·88	425 (3)	139 (6)	451 (2)	1·6 (7)
H(2)[N(3)]	0·88	444 (3)	493 (6)	708 (3)	2·1 (8)
H(3)[N(3)]	0·94	366 (3)	586 (6)	604 (2)	2·5 (8)
H(4)[C(4)]	0·95	219 (3)	417 (6)	132 (2)	1·6 (8)
H(5)[C(5)]	1·00	094 (3)	682 (6)	023 (3)	3·4 (8)
H(6)[C(6)]	0·90	027 (3)	1018 (7)	104 (3)	2·6 (8)
H(7)[C(7)]	0·95	085 (3)	1099 (7)	286 (3)	3·1 (9)
H(8)[C(8)]	0·95	208 (2)	827 (6)	388 (2)	1·2 (7)
H(9)[C(2)]	0·97	330 (2)	284 (6)	299 (2)	1·6 (7)

and where $F_{\min}$ was 2·0 for ASC and 4·0 for BSC. The scattering factors for all atoms were taken from Hanson, Herman, Lea & Skillman (1964).

Discussion

The atomic numbering, bond distances and angles for ASC are given in Fig. 1, with the corresponding information for BSC in Fig. 2. One striking difference between the two molecules is the conformation around the C(1)–N(2) bond. In ASC the C–O is *cis* to N(1)–N(2) which is similar to the configuration in semicarbazide hydrochloride reported by Nardelli, Fava &

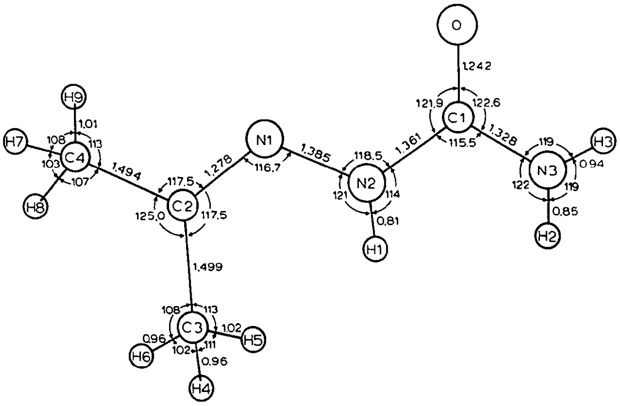

Fig. 1. Atomic numbering, bond distances and angles in acetone semicarbazone. The angles H(4)–C(3)–C(2) of 115°, H(5)–C(3)H(6) of 107°, H(7)–C(4)–C(2) of 114°, and H(8)–C(4)–H(9) of 111° were not included for clarity. The estimated standard deviations are 0·002 Å for C(1)–O and N(1)–N(2) and 0·003 Å for the remaining heavy atom distances, 0·04 Å for distances involving the hydrogen atoms, 0·2° for the heavy atom angles and 3° for angles involving the hydrogen atoms.

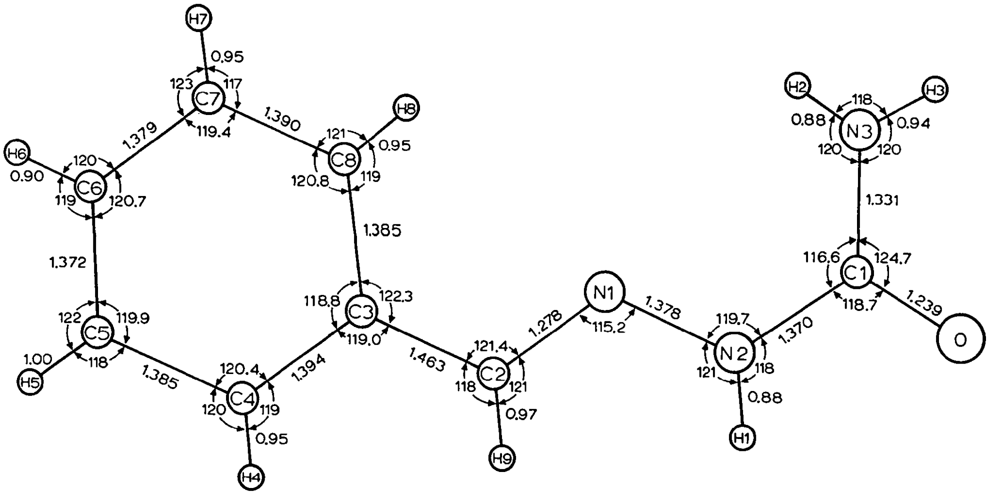

Fig. 2. Atomic numbering, bond distances and angles in benzaldehyde semicarbazone. The estimated standard deviations are: 0·004 Å for the C–C distances and 0·3° for the C–C–C angles in the benzene ring; 0·003 Å for the distances and 0·2° for the angles of the other heavy atoms; 0·03 Å for the distances and 2° for the angles involving the hydrogen atoms.

Giraldi (1965). However, in BSC the C–O is *trans* to N(1)–N(2) which is the configuration found in all the uncomplexed thiosemicarbazones (Palenik, Rendle & Carter, 1974) and in 2-formylpyridine selenosemicarbazone by Conde, López-Castro & Márquez (1972). In the thiosemicarbazones the *trans* configuration would reduce steric interactions between S and N(1); however, with the smaller oxygen atom, presumably both configurations have about the same energy. The final configuration must be dependent to some extent on the hydrogen-bonding patterns observed in the crystalline solid, see below.

A second striking feature of the two molecules is the similarity in the molecular dimensions in the side chain. The distances in the side chains of ASC and BSC have been tabulated in Table 6 together with the dimensions reported in other closely related compounds. The differences between the C(1)–O, C(1)–N(3), N(1)–N(2) and N(1)–C(1) bonds in ASC and BSC are not significant, while the difference between the C(1)–N(2) bonds is possibly significant ($t_0 = 2{\cdot}50$), using the criteria given by Cruickshank & Robertson (1953). The average C(1)–N(2) distance of 1·365 Å is not significantly different from the value of 1·382 (16) Å reported for the corresponding bond in semicarbazide hydrochloride by Nardelli, Fava & Giraldi (1965) but is significantly longer than the values of 1·350 (2) and 1·349 (2) Å found in carbohydrazide by Domiano, Pellinghelli & Tiripicchio (1972). However, these changes appear to be a direct function of the groups attached to N(2) and

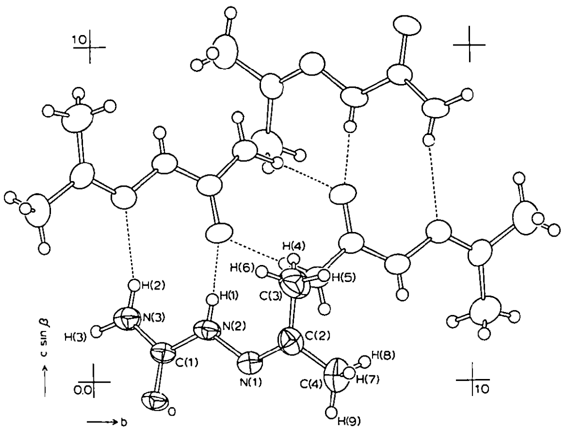

Fig. 3. The structure of acetone semicarbazone as viewed down the *a* axis. The dotted lines represent possible hydrogen bonds.

Table 7. *Least-squares planes for acetone semicarbazone ASC, and benzaldehyde semicarbazone, BSC*

Deviations (Å × 10^3) in bold-face type indicate the atoms which were used to define the plane

	ASC		BSC		
	1	2	3	4	5
O	371	**3**	**5**	**−3**	−278
N(1)	**2**	−272	**10**	35	−168
N(2)	−41	**2**	**−15**	**−2**	−248
N(3)	−281	**2**	**−5**	**−2**	−187
C(1)	23	**−7**	**5**	**7**	−229
C(2)	**−5**	−199	127	161	−55
C(3)	**1**	211	125	172	**−3**
C(4)	**1**	−530	135	192	**1**
C(5)			86	155	**2**
C(6)			26	97	**−2**
C(7)			22	83	0
C(8)			74	122	2

Parameters of planes

Equation of the plane is in the form: deviation (Å) $= lX + mY + nZ - p$ where X, Y, Z are the coordinates of the atom in Å referred to **a**, **b** and **c** sin *β*.

$l(\times 10^4)$	9019	9030	8528	8491	8296
$m(\times 10^4)$	−3488	−4167	4962	5000	5343
$n(\times 10^4)$	−1828	1046	−1626	−1704	−1623
p(Å)	3·376	3·426	2·608	2·539	2·816

Table 6. *A comparison of the distances found in semicarbazones and related compounds*

Compound	C(2)–N(1)	N(1)–N(2)	N(2)–C(1)	C(1)–O	C(1)–N(3)
ASC	1·278 (3)	1·385 (2)	1·361 (3)	1·242 (2)	1·328 (3)
BSC	1·278 (3)	1·378 (3)	1·370 (3)	1·239 (3)	1·331 (3)
CBH		1·416 (2)	1·350 (2)	1·242 (2)	
		1·417 (3)	1·349 (2)		
LMI		1·395 (4)	1·328 (6)	1·223 (5)	
HMI		1·416 (4)	1·329 (4)	1·226 (3)	
SCH		1·411 (14)	1·382 (16)	1·238 (16)	1·311 (18)
TSC		1·411 (2)	1·326 (2)	*	1·316 (3)
ATSC	1·286 (7)	1·398 (6)	1·342 (6)	*	1·344 (6)
Urea			1·351 (7)	1·243 (6)	

* contains a C–S rather than a C–O bond.

ASC: acetone semicarbazone (this work).

BSC: benzaldehyde semicarbazone (this work).

CBH: carbohydrazide (Domiano, Pellinghelli & Tiripicchio, 1972).

LMI: the low-melting isomer; HMI: the high-melting isomer of methylfuroxan carbohydrazide (Calleri, Chiari, Germain & Viterbo, 1973).

SCH: semicarbazide hydrochloride (Nardelli, Fava & Giraldi, 1965).

TSC: thiosemicarbazide (Andreetti, Domiano, Gasparri, Nardelli & Sgarabotto, 1970).

ATSC: acetone thiosemicarbazone (Palenik, Rendle & Carter, 1974).

Urea: Worsham, Levy & Peterson (1957).

N(3). If we start with urea, where Worsham, Levy & Peterson (1957) found that C–O was 1·243 (6) and C–N was 1·351 (7) Å, we can follow the changes with substitution on N(2) and N(3). First of all, the C–O distance is not significantly changed in semicarbazide hydrochloride [1·238 (16) Å] or in ASC [1·242 (2) Å] or in BSC [1·239 (3) Å]. The constant nature of C–O in these compounds is not surprising since the changes are taking place on the nitrogen atoms. We see that replacing one hydrogen on N(2) by either an $-\mathrm{NH}_3^+$ as in semicarbazide hydrochloride, or by $(\mathrm{CH}_3)_2\mathrm{C{=}N}$– as in ASC, or $(\mathrm{C}_6\mathrm{H}_5)\mathrm{HC{=}N}$ as in BSC causes an increase in C(1)–N(2) bond length compared to the value in urea. The corresponding C(1)–N(3) bond distance decreases to maintain approximately the same electron density around C(1). The symmetrical substitution as in carbohydrazide gives us molecular dimensions comparable to those in urea. These changes can be rationalized either in terms of a delocalized system involving N(1), N(2), C(1) and N(2) or else in terms of a redistribution of *s*-character on substitution following the arguments of Bent (1961). The latter arguments might by preferred since the molecules are not strictly planar (see Table 7) as might be anticipated for a delocalized system.

In both ASC and BSC the C(2)–N(1) distance of 1·278 (3) is somewhat longer than a pure C–N double bond but is in good agreement with the corresponding value of 1·286 (7) Å found in acetone thiosemicarbazone by Palenik, Rendle & Carter (1974). Since no delocalization is possible with the methyl groups on ASC, the lengthening of C(2)–N(1) must involve an interaction with the chain. The inclusion of resonance forms which lengthen C(2)–N(1) and shorten N(1)–N(2) argues for a delocalized system as discussed above. Although neither ASC or BSC are strictly planar (see Table 7), the deviations from planarity do not preclude a delocalized system. The deviations from planarity are probably steric in origin since the BSC molecule is more nearly planar. For example, N(1) is 0·272 Å out of the N(2)–C(1)–O–N(3) plane in ASC but is only 0·035 Å from the corresponding plane in BSC. The group in BSC is planar as expected.

Both ASC and BSC are hydrogen-bonded in the solid state although the hydrogen-bonding patterns are different in the two cases. Packing diagrams which also give the thermal ellipsoids are shown in Fig. 3 for ASC and Fig. 4 for BSC, with the hydrogen bonds indicated by broken lines. The dimensions of the hydrogen bonds are summarized in Table 8. We see that although both molecules have three hydrogen atoms capable of hydrogen bonding, only in ASC are all three utilized in hydrogen bonding. The use of all three hydrogen atoms for hydrogen-bonding in ASC must be related to the *cis* configuration since in BSC and in the thiosemicarbazones, only three of the hydrogen atoms capable of hydrogen bonding actually do so. In ASC the molecules are hydrogen-bonded across a center of symmetry in a dimer-like unit. The dimer units are joined by two hydrogen bonds involving N(3)–H(2) and N(2)–H(1) into infinite sheets. In BSC there is also a hydrogen bond across a center of symmetry, a feature invariably found in both semicarbazones and thiosemicarbazones. The dimer units are now connected into infinite sheets *via* N(3)–H(2)···O hydrogen bonds.

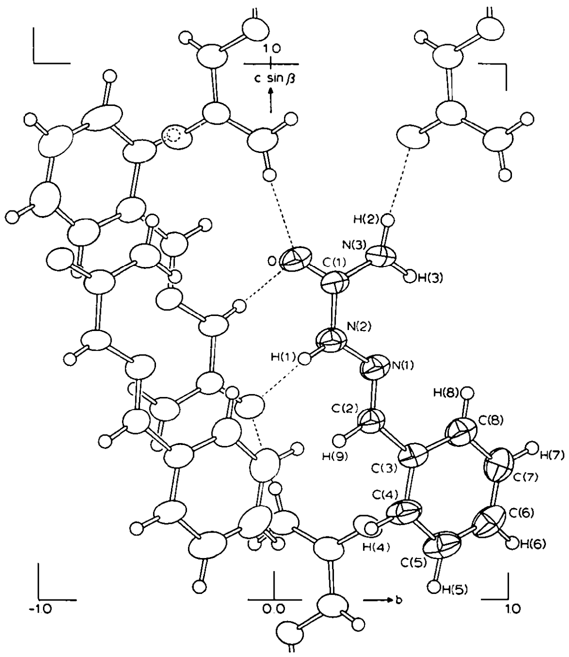

Fig. 4. The structure of benzaldehyde semicarbazone as viewed down the *a* axis. The dotted lines represent possible hydrogen bonds.

Table 8. *Hydrogen bonds*

D–H···*A*	Position of *A*	*D*–H	H···*A*	*D*···*A*	∠*D*–H···*A*	∠H–*D*···*A*
Acetone semicarbazone						
N(2)–H(1)···O	$x, \frac{1}{2}-y, \frac{1}{2}+z$	0·81 Å	2·07 Å	2·852 Å	162°	13°
N(3)–H(2)···N(1)	$x, \frac{1}{2}-y, \frac{1}{2}+z$	0·85	2·31	3·104	156	17
N(3)–H(3)···O	$1-x, -y, -z$	0·94	2·01	2·949	174	4
Benzaldehyde semicarbazone						
N(2)–H(1)···O	$1-x, -y, 1-z$	0·88	2·04	2·917	176	3
N(3)–H(2)···O	$1-x, \frac{1}{2}+y, \frac{3}{2}-z$	0·88	2·06	2·928	169	8

The reason for the difference in biological activity between semicarbazones and thiosemicarbazones is open to speculation. The sulfur analogs do appear to interact strongly with aryl groups which does not appear to be the case with semicarbazones. Presumably the difference in electronegativity of sulfur *versus* oxygen can account for the more extensive delocalization in the sulfur case. The resulting lower electron density on the sulfur atom makes certain thiosemicarbazones less susceptible to oxidation. Therefore, the thiosemicarbazone is not as easily reduced by metal ions and forms more stable chelates. In semicarbazones the smaller, more electronegative oxygen atom does not allow as stable a chelate to form as in the sulfur analogs. This hypothesis suggests that the biological activity of thiosemicarbazones is intimately connected with their chelating ability, an accepted fact in many instances [see Palenik, Rendle & Carter (1974) for a more extensive discussion].

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The Crystal and Molecular Structure of Δ^6-6-Azidobetamethasone-21-acetate

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Crystals of the title steroid are monoclinic with $a=8\cdot065$ (2), $b=11\cdot173$ (2), $c=15\cdot337$ (3) Å, $\beta=102\cdot67$ (3)°, $Z=2$, space group $P2_1$. The structure was determined by direct methods from diffractometer data and refined by least-squares methods to a final R of 0·042 for 1662 independent reflexions. The B, C and D rings are *trans*-fused. Ring A is planar, and the conformation of rings B, C and D are half-chair, chair and half-chair respectively. The molecules are linked by 'head-to-tail' hydrogen bonds between the C(17) hydroxy group and the C(3) keto group.

Introduction

The Δ^6-6-azido moiety influences the biological activity of the progestagen and corticoid series. Recent articles (Duax, Wolff & Weeks, 1973; Teutsch, Weber, Page, Shapiro, Herzog, Neri & Collins, 1973) emphasize the importance of correlating activity with three-dimensional structure. Data on the synthesis and biological activity of this compound are given by Green *et al.* (1974).

Experimental

The crystals as supplied by Dr M. J. Green of the Schering corporation had been grown by slow evaporation of an acetone solution. This procedure gave crystals containing one molecule of acetone per molecule of steroid (as determined by n.m.r. spectroscopy). Microanalysis yielded the following results.

	%C	%H	%N
Found	61·09	6·42	7·71
Calculated for $C_{24}H_{28}FO_6N_3.CH_3COCH_3$	61·00	6·45	7·91

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