groups of the dicyanomethylide moiety), *viz* this group is removed from the $C(CN)_2$ moiety [the C(1)—C(2)—C(3)—C(4) and C(2)—C(3)—C(4)—O torsion angles are -170.9 (3) and -157.8 (3)° respectively]. The conformation of molecule (I) in the crystal is fixed both by the extended conjugation system and by shortened non-bonded contacts. Thus a considerable change of conformation in solution seems quite improbable.

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Structure of 4-(3-Chlorophenyl)thiosemicarbazide

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Abstract. $C_7H_8ClN_3S$, $M_r = 201.67$, monoclinic, $P2_1/c$, $a = 6.914$ (5), $b = 4.304$ (4), $c = 30.306$ (3) Å, $\beta = 94.66$ (3)°, $V = 899.0$ (1) Å^3, $Z = 4$, $D_m = 1.54$, $D_x = 1.490$ Mg m^{-3}, λ(Cu $K\alpha$) = 1.5418 Å, $\mu = 5.54$ mm^{-1}, $F(000) = 416$, $T = 298$ K, final $R = 0.048$ for 1219 observed reflections. The S and terminal hydrazinic N atoms are in a *trans* conformation. As a result of the σ-electron-withdrawing effect of the Cl atom at the *meta* position in the phenyl ring with respect to the thiosemicarbazide chain, the net negative charge on the terminal N atom decreases compared to the *p*-chloro and *p*-methoxy derivatives. The antibacterial activity of the compound is also lowered.

Introduction. The biological activities possessed by thiosemicarbazides and thiosemicarbazones arise from their reductive capacity and their ability to

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form complexes with metal ions (Sorkin, Roth & Erlenmeyer, 1952; Kirschner, Wei, Francis & Bergman, 1966). Only the S and terminal hydrazinic N atoms are actively involved in binding the metal ions. Depending on the metal ion and the particular derivative of the ligand, one or both of these atoms can coordinate. Substituents at various points in the ligand framework alter the extent and the nature of biological activities of the product by virtue of their electronic effect, stereochemical effects, *etc.* Since the activity of these compounds is related to reductive and metal-chelating properties, substituents which improve the electron-donating capacity of the donor atoms, S and N(3), are expected to raise their activities. Nandi, Chaudhuri, Mazumdar & Ghosh (1984*a*) showed that the *in vitro* antibacterial activity of 4-(4-chlorophenyl)thiosemicarbazide increased significantly over that of 4-phenylthiosemicarbazide owing to electron enrichment in the thiosemicarbazide side chain caused by the presence of the Cl atom in the phenyl ring at a position *para* to the side

chain. Similarly, the electron-releasing methoxy group at the same position resulted in electron enrichment in the side chain (Chattopadhyay, Banerjee, Mazumdar, Ghosh & Kuroda, 1987). It was also found that the antibacterial activity of different substituted 4-phenylthiosemicarbazides and their metal complexes varies with the nature of the substituents in the phenyl ring (Ghosh, Ray, Bandyopadhyay & Guha, 1987).

The Cl atom at a position *meta* to the thiosemicarbazide chain is expected to exert a σ-electron-withdrawing effect leading to a decrease in electron density in the thiosemicarbazide chain.

Crystal structure analysis of the title compound was undertaken with a view to understanding the effect of the substitution on the structure and charge-density distribution in the molecule. The *in vitro* antibacterial activity of the ligand was determined against *Escherichia coli*. The atomic charge densities have been calculated by the CNDO/2 method (Pople & Beveridge, 1970).

Experimental. *Determination of antibacterial activity. In vitro* growth-inhibitory activity of three ligands was determined against *E. coli* 10536 in a medium of nutrient broth (Difco) by the serial dilution technique. The lowest concentration of a compound which resulted in the complete inhibition of visible bacterial growth was recorded as the minimum inhibitory concentration (MIC) of the compound.

Colourless needle-shaped crystals (from ethanol); density by flotation (benzene–bromoform); crystal size: $0.25 \times 0.20 \times 0.22$ mm; $P2_1/c$; Enraf–Nonius CAD-4 diffractometer; graphite-monochromated Cu $K\alpha$ radiation; cell parameters refined from 25 2θ angles ($12 < 2\theta < 30°$), $-7 \le h \le 7$, $0 \le k \le 5$, $0 \le l \le 34$, 1773 unique reflections ($3 < 2\theta < 130°$), 1219 observed reflections [$I > 2.5\sigma(I)$], intensities corrected for Lp, absorption ignored; $\omega/2\theta$ scan mode, scan angle ($0.85 + 0.15\tan\theta)°$, scan aperture ($2.50 + 0.85\tan\theta$) mm, maximum scan time 100 s, three

Fig. 1. Atom-labelling scheme for 4-(3-chlorophenyl)thiosemi-carbazide.

orientation control reflections (300, 020, 0,0,10) monitored every 200 reflections, intensities of three reflections ($\bar{2},0,10$, 0,0,18, 115) checked every hour of exposure; no significant deterioration of intensity; structure solved by direct methods (*MULTAN*78; Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978); full-matrix least-squares refinement on F for non-H atoms with anisotropic thermal parameters (*SHELX*76; Sheldrick, 1976); six H atoms located from difference syntheses; further refinement with isotropic temperature factors for the H atoms; two H atoms fixed in calculated positions, with fixed isotropic temperature factor 0.05 Å^2; $R = 0.044$, $wR = 0.048$, $S = 2.54$, $w = 8.9/(\sigma^2|F_o| + |F_o|^2)$, $\Delta/\sigma < 0.2$, $\Delta\rho$ excursions 0.16 e Å^{-3}, atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV).

Discussion. Fig. 1 shows the atom-labelling scheme. Fractional atomic coordinates and bond distances and angles are listed in Tables 1 and 2 respectively.*

The MIC of the compound was found to be $0.20 \,\mu M$ ml^{-1}. The MIC values for 4-phenyl-thiosemicarbazide and 4-(4-chlorophenyl)thiosemi-carbazide were 0.33 and $0.13 \,\mu M$ ml^{-1} respectively.

The thiosemicarbazide moiety is planar with the S and terminal hydrazinic N(3) atoms in a *trans* conformation with respect to the C(7)—N(2) bond. N(1) and N(3) lie *cis* to each other and as a result favour an intramolecular hydrogen-bond-like contact [N(1)···N(3) 2.604 (4), N(3)···H(N1) 2.13 (3), N(1)—H(N1) 0.83 (4) Å, N(1)—H(N1)···N(3) 117 (3)°]. This intramolecular contact resulting in the formation of a five-membered ring seems to be a common feature of similar crystal structures (Chattopadhyay, Mazumdar, Banerjee & Sheldrick, 1989, and references therein). The mean plane of the thiosemicarbazide chain makes an angle of 125.11 (9)° with the plane of the phenyl ring. N(1) deviates by 0.094 (3) Å from the ring plane. The C(1)—N(1)—C(7)—N(2) torsion angle of -178.0 (3)° suggests that the molecule is in an overall extended conformation. The C(1)—N(1) bond length is comparable to those in various similar derivatives. Other bonds in the side chain also have lengths comparable to those in various 4-phenyl-thiosemicarbazide derivatives (Nandi *et al.*, 1984*a,b*; Chattopadhyay *et al.*, 1987) except the N(2)—N(3) bond, which is considerably shorter in the present structure [1.404 (4) Å] than in 4-phenylthiosemi-
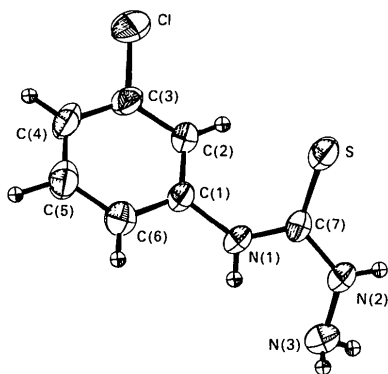
Table 1. *Fractional atomic coordinates and equivalent isotropic temperature factors with e.s.d.'s in parentheses*

$$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i{}^*a_j{}^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}(Å²)
S	0·7579 (1)	0·3675 (2)	0·54456 (3)	0·0559 (3)
Cl	0·3751 (1)	−0·3205 (3)	0·66261 (3)	0·0664 (4)
N(1)	0·0052 (4)	0·1064 (8)	0·6072 (1)	0·055 (1)
N(2)	1·1210 (4)	0·1985 (8)	0·5413 (1)	0·058 (1)
N(3)	1·2970 (4)	0·0673 (12)	0·5582 (1)	0·071 (1)
C(1)	0·8758 (4)	0·0812 (8)	0·6413 (1)	0·044 (1)
C(2)	0·7033 (4)	−0·0776 (8)	0·6347 (1)	0·044 (1)
C(3)	0·5919 (4)	−0·1110 (8)	0·6700 (1)	0·043 (1)
C(4)	0·6474 (5)	0·0061 (9)	0·7112 (1)	0·050 (1)
C(5)	0·8184 (5)	0·1628 (9)	0·7172 (1)	0·058 (1)
C(6)	0·9358 (5)	0·2014 (9)	0·6826 (1)	0·055 (1)
C(7)	0·9693 (4)	0·2145 (8)	0·5661 (1)	0·045 (1)

Table 2. *Bond distances* (Å), *bond angles* (°) *and selected torsion angles* (°) *with e.s.d.'s in parentheses*

S—C(7)	1·685 (3)	C(1)—C(2)	1·375 (4)
Cl—C(3)	1·748 (3)	C(2)—C(3)	1·376 (4)
N(1)—C(1)	1·425 (4)	C(3)—C(4)	1·372 (4)
N(1)—C(7)	1·334 (4)	C(4)—C(5)	1·360 (5)
N(2)—N(3)	1·400 (4)	C(5)—C(6)	1·387 (5)
N(2)—C(7)	1·341 (4)	C(6)—C(1)	1·386 (4)
C(1)—N(1)—C(7)	128·6 (3)	Cl—C(3)—C(4)	118·7 (2)
N(3)—N(2)—C(7)	120·8 (3)	C(3)—C(4)—C(5)	118·6 (3)
N(1)—C(1)—C(6)	117·8 (3)	C(4)—C(5)—C(6)	120·9 (3)
N(1)—C(1)—C(2)	121·4 (3)	C(1)—C(6)—C(5)	119·2 (3)
C(2)—C(1)—C(6)	120·6 (3)	N(1)—C(7)—N(2)	114·3 (3)
C(1)—C(2)—C(3)	118·2 (3)	S—C(7)—N(1)	126·0 (3)
Cl—C(3)—C(2)	118·9 (2)	S—C(7)—N(2)	119·7 (2)
C(2)—C(3)—C(4)	122·4 (3)		
N(3)—N(2)—C(7)—S	−178·8 (3)	N(3)—N(2)—C(7)—N(1)	2·1 (5)
C(1)—C(2)—C(3)—Cl	−178·4 (2)	Cl—C(3)—C(4)—C(5)	178·5 (3)
C(7)—N(1)—C(1)—C(2)	55·2 (5)	C(7)—N(1)—C(1)—C(6)	−129·6 (4)

carbazide [1·431 (6) Å] (Kálmán, Argay & Czugler, 1972).

The C(7)—S bond distance [1·685 (3) Å] indicates that the molecule is in the thione tautomeric form (Nandi *et al.*, 1984*a*).

The C(3)—Cl bond length [1·748 (3) Å] is similar to the C(phenyl)—Cl bond length in 4-(4-chloro-phenyl)thiosemicarbazide [1·749 (3), 1·751 (3) Å]. The Cl atom deviates by 0·046 (1) Å from the plane of the phenyl ring and accepts a hydrogen bond from the N(1) atom of a neighbouring molecule. This N—H···Cl hydrogen bond, although weak, is notable because a covalently bonded Cl atom only rarely accepts a hydrogen bond (Pauling, 1960). In the present structure, the H···Cl distance of 2·74 (4) Å is shorter than the sum of the van der Waals radii (Taylor & Kennard, 1982) of these atoms (2·95 Å), thereby suggesting the existence of the hydrogen bond [N(1)—H(N1) 0·83 (4), N(1)···Cl 3·470 (4) Å, N(1)—H(N1)···Cl 147 (3)°].

The average carbon–carbon bond length in the phenyl ring is 1·376 (4) Å. The angle *ipso* to the Cl

atom is increased by 2·4° from the sp^2 value; this may be attributed to the σ-electron-withdrawing effect of the Cl atom (Domenicano, Vaciago & Coulson, 1975).

The crystal structure is stabilized by a network of hydrogen bonds. The molecules form hydrogen-bonded dimers through N(2)—H(N2)···S hydrogen bonds across centres of symmetry [N(2)···S 3·364 (4), H(N2)···S 2·68 (4), N(2)—H(N2) 0·81 (4) Å, N(2)—H(N2)···S 144 (4)°]. These dimers are linked into infinite chains along *a* through N(1)—H(N1)···Cl and N(3)—H(N3)1···S hydrogen bonds between molecules separated by an *a* translation [N(3)···S 3·494 (4), H(N3)1···S 2·75 (5), N(3)—H(N3)1 0·95 (5) Å, N(3)—H(N3)1···S 136 (3)°]. A view of the crystal packing down the *b* axis (Fig. 2) shows the hydrogen-bonding pattern.

Structure–activity correlation studies on substituted 1-formylisoquinoline thiosemicarbazones revealed that while the introduction of electron-withdrawing substituents in the ring resulted in the reduction of antineoplastic activity, electron-releasing groups caused enhancement of the activity (Agrawal, Booth & Sartorelli, 1968; Agrawal, Cushley, McMurray & Sartorelli, 1970). In the present structure the Cl atom exerts a σ-electron-withdrawing effect and the net negative charge on the terminal hydrazinic N atom decreases compared with those in the 4-chlorophenyl and 4-methoxyphenyl derivatives (Table 3). The *in vitro* growth-inhibitory activity of the compound is also lowered compared with these derivatives. Since other
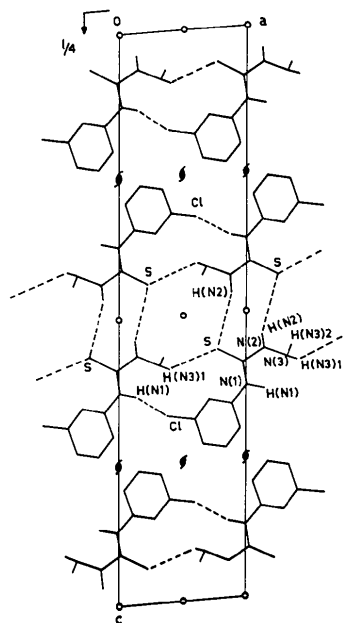

Fig. 2. A view of the crystal packing down the *b* axis.

Table 3. *Charge-density distribution calculated by the CNDO/2 method*

Cl	−0·17	C(2)	−0·03
S	−0·45	C(3)	−0·11
N(1)	−0·17	C(4)	−0·01
N(2)	−0·11	C(5)	−0·03
N(3)	−0·15	C(6)	−0·05
C(1)	0·15	C(7)	0·27

factors like solubility, steric effects and so on also play critical roles in determining the activity of a particular compound, no specific comment about this can be made.

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Structure of
(2R)-2-[(1S,2R,3S)-3-Hydroxy-2-methylcyclopentyl]-6-methyl-6-heptenoic Acid

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Abstract. $C_{14}H_{24}O_3$, $M_r = 240·3$, triclinic, $P\bar{1}$, $a = 8·532$ (1), $b = 8·596$ (1), $c = 10·425$ (3) Å, $\alpha = 100·89$ (1), $\beta = 100·11$ (1), $\gamma = 104·18$ (2)°, $V = 707·9$ (5) Å³, $Z = 2$, $D_x = 1·127$ Mg m⁻³, Mo $K\alpha$, $\lambda = 0·71070$ Å, $\mu = 0·053$ mm⁻¹, $F(000) = 264$, $T = 294$ K, $R = 0·049$, $wR = 0·053$ for 938 significant reflections. X-ray diffraction analysis clearly shows a *cis* stereochemistry for the title compound obtained when the reducing agent of the corresponding cyclopentanone is L-selectride.

Introduction. The stereochemistry of nucleophilic reagent addition on 2-alkyl- and 3-alkylcyclopentanones (Morrison & Mosher, 1971; Brown & Dickason, 1970; Richer & Belanger, 1966) showed that substituents in position 2 have a stronger influence on the addition stereochemistry than substit-

uents in position 3. In connection with a total synthesis of (1S,2S)-dihydroxycholecalciferol, J. Ficini & I. Daoust-Maleval (personal communication, not yet published) had to reduce the cyclopentanone (1). Reduction by sodium borohydride led to a mixture of both isomers (3) and (4), but the use of a more bulky reducing agent such as L-selectride [LiB(*sec*-Bu)₃H] was assumed, from NMR results, to lead to the *cis* isomer.

(1)	(2)	(3)	(4)
	NaBH₄	60%	40%
	LiB(sec-Bu)₃H	0%	100%