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(3a*R*,6*R*)-3,3,6-Trimethyl-3,3a,4,5,6,7-hexahydro-2*H*-indazole-2-carbothioamide

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Keywords: crystal structure; indazole; carbothioamide; thiosemicarbazide; N—H···N hydrogen bonds; N—H···S hydrogen bonds.

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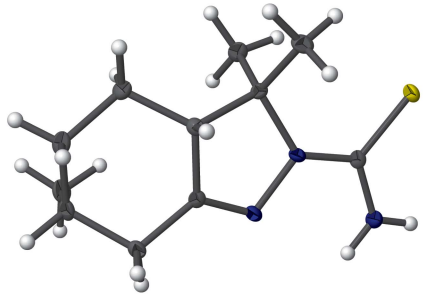
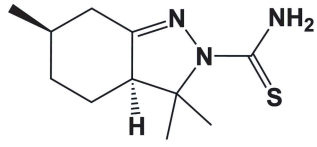
Structural data: full structural data are available from iucrdata.iucr.org

The title compound, $C_{11}H_{19}N_3S$, was prepared by the reaction of (*R*)-pulegone with thiosemicarbazide in acidic medium, using ethanol as solvent. The molecule is built up from fused six and five-membered rings. The six-membered ring adopts a chair conformation, while the five-membered ring displays an envelope conformation with the dimethyl-substituted C atom as the flap. The dihedral angle between the mean planes of the two rings is 20.35 (6)°. In the crystal, molecules are linked by N—H···N and N—H···S hydrogen bonds into chains running parallel to [100].

3D view



Chemical scheme



Structure description

In recent years, the synthesis of heterocyclic systems containing nitrogen has attracted great interest because of their broad spectrum of pharmacological activities. In particular, indazole is a crucial heterocyclic skeleton present in a wide variety of drugs, many natural products and biologically active compounds (Gautam *et al.*, 2015). Compounds containing the indazole skeleton are known to display a broad spectrum of potent pharmacological activities including anti-inflammatory (Rosati *et al.*, 2007), antidepressant (Bailey *et al.*, 1985), anticancer (De Lena *et al.*, 2001), antituberculosis (Guo *et al.*, 2010) and antimicrobial activities (Ali *et al.*, 2012). The therapeutic usefulness of these heterocyclic systems prompted us to prepare a new substituted 2*H*-indazole from a naturally occurring monoterpene. The title compound (3a*R*,6*R*)-3,3,6-trimethyl-3,3a,4,5,6,7-hexahydro-2*H*-indazole-2-carbothioamide was prepared by the reaction of (*R*)-pulegone with thiosemicarbazide in acidic medium, using ethanol as solvent. The

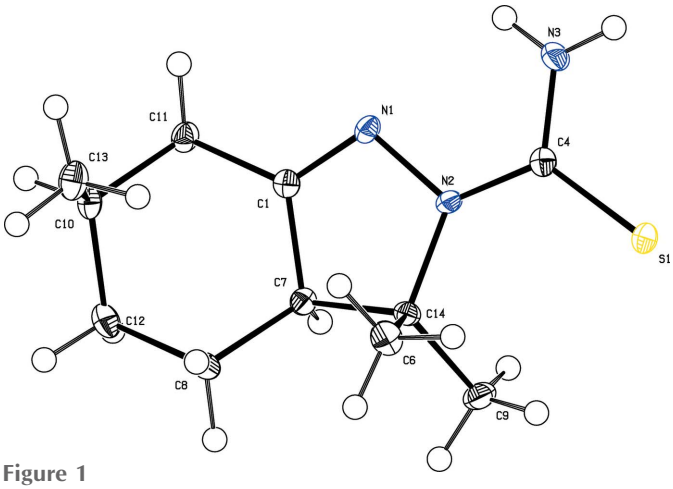


Figure 1
Molecular structure of the title compound, with atom labelling. Displacement ellipsoids are drawn at the 30% probability level. Labels very small

resulting product obtained as diastereomeric mixture, was then crystallized from ethanol to give the new compound as white monocrystals.

The title molecule, Fig. 1, contains a fused ring system and a carbothioamide group as a substituent to the pyrazolidine ring. The six-membered ring (C1/C7/C8/C19—C12) has a chair conformation as indicated by puckering parameters Q_T = 0.5218 (16) Å, θ = 16.11 (18) and $\varphi 2$ = 199.40 (16)°. The pyrazolidine ring (N1/N2/C1/C7/C14) adopts an envelope conformation with atom C14 as the flap; deviating by 0.341 (1) Å from the mean plane through the other four atoms in the ring.

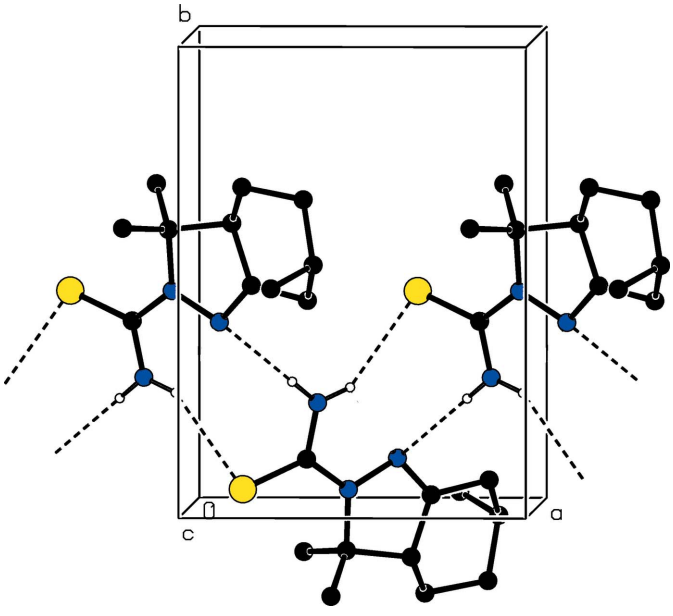


Figure 2
Partial crystal packing view along the *c* axis of the title compound. The N—H···N and N—H···S hydrogen bonds (dashed lines; Table 1) indicate the formation of a chain parallel to the *a* axis. H atoms not involved in hydrogen bonding have been omitted for clarity.

Table 1
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3*B*···N1^{i}	0.86	2.37	3.230 (3)	176
N3—H3*A*···S1^{ii}	0.86	2.70	3.442 (3)	146

Symmetry codes: (i) $x-\frac{1}{2}, -y+\frac{1}{2}, -z+1$; (ii) $x+\frac{1}{2}, -y+\frac{1}{2}, -z+1$.

In the crystal, molecules are linked by N—H···N and N—H···S hydrogen bonds into chains running parallel to [100] (Table 1 and Fig. 2).

Owing to the presence of the S atom, the absolute configuration could be fully confirmed, by refining the Flack parameter (Parsons *et al.*, 2013), as C3a(*R*) and C6(*R*).

Synthesis and crystallization

A hot ethanolic solution containing equimolar quantities of thiosemicarbazide and (*R*)-pulegone with a few drops of concentrated HCl was heated under reflux. The progress of the reaction was monitored by TLC. After the completion of the reaction, the solvent was evaporated under reduced pressure and the crude product was purified by chromatography on silica gel (230–400 mesh) using hexane/ethyl acetate (95:5) as eluent. The pure indazolic product was obtained in 64% yield as a diastereomeric mixture. Slow evaporation from

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{11}H_{19}N_3S$
M_r	225.35
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	100
a, *b*, *c* (Å)	7.957 (5), 10.796 (5), 13.673 (5)
V (Å^3)	1174.6 (10)
Z	4
Radiation type	Cu *K*α
μ (mm^{-1})	2.21
Crystal size (mm)	0.24 × 0.2 × 0.15
Data collection	
Diffractometer	Bruker APEXII CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2009)
T_{min}, T_{max}	0.618, 0.718
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	17550, 2315, 2270
R_{int}	0.027
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.618
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.021, 0.054, 1.06
No. of reflections	2315
No. of parameters	140
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.22, −0.17
Absolute structure	Parsons *et al.* (2013), 972 Friedel pairs
Absolute structure parameter	0.028 (12)

Computer programs: *APEX2* and *SAINT* (Bruker, 2009), *SHELXS97* and *SHELXL97* (Sheldrick, 2008), *PLATON* (Spek, 2009) and *publCIF* (Westrip, 2010).

an ethanolic solution of the title compound gave crystals of the title compound, suitable for X-ray crystallographic analysis.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

Acknowledgements

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full crystallographic data

IUCrData (2016). **1**, x160573 [doi:10.1107/S2414314616005733]

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Crystal data

$C_{11}H_{19}N_3S$
M_r = 225.35
Orthorhombic, $P2_12_12_1$
a = 7.957 (5) Å
b = 10.796 (5) Å
c = 13.673 (5) Å
V = 1174.6 (10) Å^3
Z = 4
$F(000)$ = 488
D_x = 1.274 Mg m^{-3}
Cu $K\alpha$ radiation, λ = 1.5418 Å
Cell parameters from 17550 reflections
θ = 5.2–72.9°
μ = 2.21 mm^{-1}
T = 100 K
Prismatic, colourless
0.24 × 0.2 × 0.15 mm

Data collection

Bruker APEXII CCD diffractometer
Radiation source: microsource
Multi-layer mirror monochromator
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2009)
T_{min} = 0.618, T_{max} = 0.718
17550 measured reflections
2315 independent reflections
2270 reflections with $I > 2\sigma(I)$
R_{int} = 0.027
θ_{max} = 72.2°, θ_{min} = 5.2°
h = −9→9
k = −12→13
l = −16→16

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.021
$wR(F^2)$ = 0.054
S = 1.06
2315 reflections
140 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0309P)^2 + 0.2126P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}
Absolute structure: Parsons *et al.* (2013), 972 Friedel pairs
Absolute structure parameter: 0.028 (12)

Special details

Geometry. All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.15695 (3)	0.04077 (2)	0.529496 (19)	0.01460 (8)
C1	0.68856 (13)	0.02162 (11)	0.35481 (8)	0.0111 (2)
N2	0.45543 (12)	0.03660 (9)	0.43699 (7)	0.01126 (18)
N1	0.59405 (12)	0.10135 (9)	0.39659 (7)	0.01179 (19)
C4	0.33782 (15)	0.10291 (10)	0.48530 (7)	0.0117 (2)
N3	0.37036 (13)	0.22324 (9)	0.49959 (7)	0.0167 (2)
H3A	0.4626	0.2548	0.4784	0.020*
H3B	0.2990	0.2690	0.5300	0.020*
C6	0.31991 (15)	−0.10083 (12)	0.31667 (9)	0.0171 (2)
H6A	0.2100	−0.0815	0.3413	0.026*
H6B	0.3194	−0.1827	0.2893	0.026*
H6C	0.3503	−0.0421	0.2670	0.026*
C7	0.63141 (14)	−0.10999 (10)	0.36496 (8)	0.0117 (2)
H7	0.6947	−0.1462	0.4194	0.014*
C8	0.66596 (16)	−0.19039 (10)	0.27468 (9)	0.0168 (2)
H8A	0.5851	−0.1713	0.2238	0.020*
H8B	0.6542	−0.2772	0.2916	0.020*
C9	0.40770 (15)	−0.18861 (10)	0.48000 (9)	0.0167 (2)
H9A	0.4661	−0.1662	0.5388	0.025*
H9B	0.4432	−0.2695	0.4593	0.025*
H9C	0.2889	−0.1894	0.4922	0.025*
C10	0.87482 (14)	−0.02785 (11)	0.21395 (8)	0.0148 (2)
H10	0.9909	−0.0184	0.1912	0.018*
C11	0.85262 (14)	0.05119 (10)	0.30711 (8)	0.0137 (2)
H11A	0.9439	0.0344	0.3523	0.016*
H11B	0.8561	0.1384	0.2902	0.016*
C12	0.84475 (17)	−0.16553 (11)	0.23718 (9)	0.0176 (2)
H12A	0.8640	−0.2141	0.1786	0.021*
H12B	0.9250	−0.1922	0.2862	0.021*
C13	0.75792 (16)	0.01904 (12)	0.13366 (9)	0.0191 (3)
H13A	0.7674	−0.0336	0.0773	0.029*
H13B	0.7887	0.1021	0.1162	0.029*
H13C	0.6441	0.0181	0.1569	0.029*
C14	0.44718 (14)	−0.09470 (10)	0.40007 (8)	0.0116 (2)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.01105 (13)	0.01600 (13)	0.01675 (13)	−0.00067 (11)	0.00364 (10)	−0.00051 (11)
C1	0.0114 (5)	0.0133 (5)	0.0086 (5)	0.0002 (4)	−0.0023 (4)	0.0002 (4)
N2	0.0104 (4)	0.0093 (4)	0.0141 (4)	−0.0019 (4)	0.0017 (3)	0.0004 (4)
N1	0.0098 (4)	0.0138 (4)	0.0118 (4)	−0.0025 (4)	0.0008 (3)	0.0007 (4)
C4	0.0118 (5)	0.0136 (5)	0.0098 (5)	0.0015 (4)	−0.0011 (4)	0.0013 (4)
N3	0.0140 (5)	0.0134 (5)	0.0228 (5)	0.0001 (4)	0.0053 (4)	−0.0047 (4)
C6	0.0134 (6)	0.0202 (6)	0.0178 (5)	0.0002 (5)	−0.0018 (5)	−0.0035 (5)
C7	0.0105 (5)	0.0121 (5)	0.0125 (5)	0.0008 (4)	0.0001 (4)	0.0012 (4)
C8	0.0183 (6)	0.0123 (5)	0.0197 (5)	0.0000 (5)	0.0035 (5)	−0.0034 (4)
C9	0.0172 (5)	0.0128 (5)	0.0200 (6)	−0.0022 (4)	0.0020 (5)	0.0034 (5)
C10	0.0108 (5)	0.0195 (6)	0.0141 (5)	0.0014 (5)	0.0029 (4)	−0.0009 (5)
C11	0.0100 (5)	0.0164 (5)	0.0148 (5)	−0.0015 (5)	0.0007 (4)	−0.0004 (4)
C12	0.0163 (6)	0.0175 (5)	0.0189 (5)	0.0045 (5)	0.0032 (5)	−0.0029 (4)
C13	0.0182 (6)	0.0260 (7)	0.0131 (5)	0.0003 (5)	0.0011 (4)	0.0014 (5)
C14	0.0120 (5)	0.0093 (5)	0.0134 (5)	0.0002 (4)	0.0002 (4)	−0.0010 (4)

Geometric parameters (Å, º)

S1—C4	1.6990 (14)	C8—H8A	0.9700
C1—N1	1.2778 (16)	C8—H8B	0.9700
C1—C11	1.4938 (16)	C9—C14	1.5235 (16)
C1—C7	1.4983 (16)	C9—H9A	0.9600
N2—C4	1.3507 (15)	C9—H9B	0.9600
N2—N1	1.4180 (14)	C9—H9C	0.9600
N2—C14	1.5062 (15)	C10—C13	1.5254 (16)
C4—N3	1.3390 (15)	C10—C12	1.5387 (18)
N3—H3A	0.8600	C10—C11	1.5433 (15)
N3—H3B	0.8600	C10—H10	0.9800
C6—C14	1.5265 (17)	C11—H11A	0.9700
C6—H6A	0.9600	C11—H11B	0.9700
C6—H6B	0.9600	C12—H12A	0.9700
C6—H6C	0.9600	C12—H12B	0.9700
C7—C8	1.5339 (15)	C13—H13A	0.9600
C7—C14	1.5513 (17)	C13—H13B	0.9600
C7—H7	0.9800	C13—H13C	0.9600
C8—C12	1.5358 (19)		
N1—C1—C11	124.44 (11)	C14—C9—H9C	109.5
N1—C1—C7	114.76 (10)	H9A—C9—H9C	109.5
C11—C1—C7	120.55 (10)	H9B—C9—H9C	109.5
C4—N2—N1	117.92 (10)	C13—C10—C12	111.98 (10)
C4—N2—C14	129.24 (9)	C13—C10—C11	109.92 (10)
N1—N2—C14	111.55 (8)	C12—C10—C11	110.24 (9)
C1—N1—N2	107.45 (10)	C13—C10—H10	108.2
N3—C4—N2	116.85 (10)	C12—C10—H10	108.2

N3—C4—S1	119.67 (9)	C11—C10—H10	108.2
N2—C4—S1	123.47 (9)	C1—C11—C10	110.02 (9)
C4—N3—H3A	120.0	C1—C11—H11A	109.7
C4—N3—H3B	120.0	C10—C11—H11A	109.7
H3A—N3—H3B	120.0	C1—C11—H11B	109.7
C14—C6—H6A	109.5	C10—C11—H11B	109.7
C14—C6—H6B	109.5	H11A—C11—H11B	108.2
H6A—C6—H6B	109.5	C8—C12—C10	112.45 (10)
C14—C6—H6C	109.5	C8—C12—H12A	109.1
H6A—C6—H6C	109.5	C10—C12—H12A	109.1
H6B—C6—H6C	109.5	C8—C12—H12B	109.1
C1—C7—C8	114.07 (9)	C10—C12—H12B	109.1
C1—C7—C14	102.39 (9)	H12A—C12—H12B	107.8
C8—C7—C14	118.59 (10)	C10—C13—H13A	109.5
C1—C7—H7	107.0	C10—C13—H13B	109.5
C8—C7—H7	107.0	H13A—C13—H13B	109.5
C14—C7—H7	107.0	C10—C13—H13C	109.5
C7—C8—C12	109.62 (10)	H13A—C13—H13C	109.5
C7—C8—H8A	109.7	H13B—C13—H13C	109.5
C12—C8—H8A	109.7	N2—C14—C9	113.26 (9)
C7—C8—H8B	109.7	N2—C14—C6	108.67 (9)
C12—C8—H8B	109.7	C9—C14—C6	111.73 (10)
H8A—C8—H8B	108.2	N2—C14—C7	99.36 (8)
C14—C9—H9A	109.5	C9—C14—C7	110.25 (9)
C14—C9—H9B	109.5	C6—C14—C7	113.02 (10)
H9A—C9—H9B	109.5		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3*B*···N1^{i}	0.86	2.37	3.230 (3)	176
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Symmetry codes: (i) $x-1/2, -y+1/2, -z+1$; (ii) $x+1/2, -y+1/2, -z+1$.