HIGHLY DIASTEREOSELECTIVE HETEROCYCLISATION OF N-(2-CYCLOHEXENYL)-SUBSTITUTED THIOAMIDES, THIOUREAS AND DITHIOCARBAMATES TO Δ^2-THIAZOLINE DERIVATIVES

Tadeusz S. JAGODZINSKI,[1]* Jacek G. SOŚNICKI[1] an d Mirosława KRÓLIKOWSKA[2]
[1]Department of Organic Chemistry,Technical University,
71-065 Szczecin, Aleja Piastów 42, Poland
[2]Institute of Chemical Technology and Engineering
Technical University, 60-695 Poznan, Pl. M.Skłodowskiej - Curie 2, Poland

ABSTRACT: N-(2-cyclohexenyl)-substituted thioamides, thioureas and dithiocarbamates were prepared. Their stereospecific cyclisation with the bromine-dioxane complex or iodine yielded the 2-substituted derivatives of (3a*RS*,7*SR*,7a*RS*)-7-bromo(or iodo)-3a,4,5,6,7,7a-hexahydrobenzo-thiazole, the configuration of which has been determined with the aid of 1D and 2D-NMR spectra. Stereochemistry of the heterocyclisation reaction was discussed.

INTRODUCTION

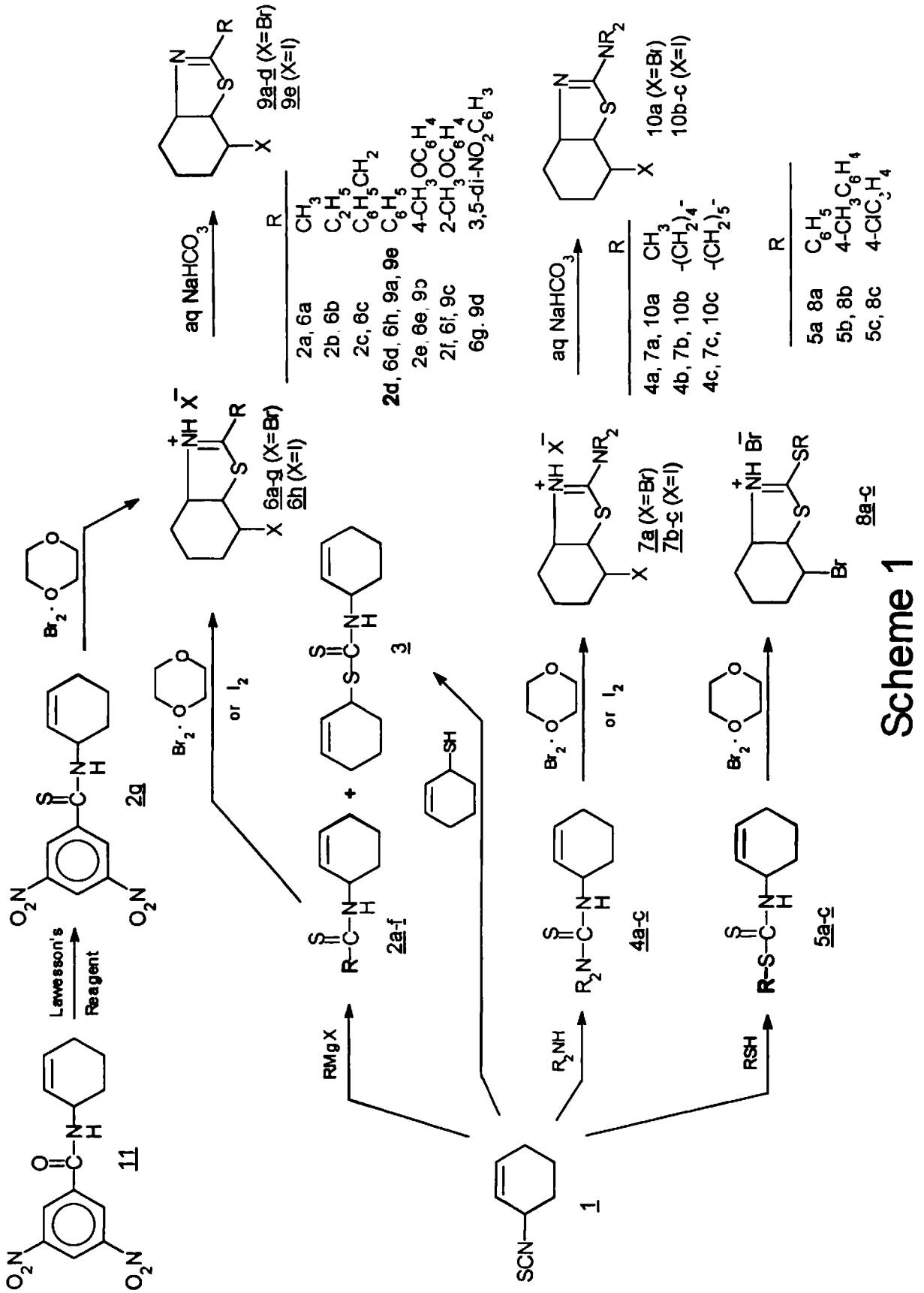
The electrophilic cyclisation of unsaturated compounds containing heteroatoms, such as nitrogen, oxygen and sulphur, is rapidly gaining importance as a method for regio- and stereoselective synthesis of heterocyclic, usually bioactive natural products (1). In particular, this concerns thioamides and their olefinic derivatives (2).

Depending on their structure, unsaturated thioamides can undergo heterocyclisation to yield derivatives of Δ^2-thiazoline (3), pyrrole (1,2) and thiophene (2). Although some elements of stereochemical investigations are to be found in most of the quoted papers, no comprehensive studies have been presented as yet.

As a continuation of our earlier investigations on the synthesis (4) and structure (5) of thioamides and Δ^2-thiazoline derivatives (6) we present now the results concerning the synthesis and stereochemistry of the heterocyclisation reaction of the N-(2-cyclohexenyl) derivatives of thioamides 2a-f, thioureas 4a-c and dithiocarbamates 5a-c.

RESULTS AND DISCUSSION

The starting thioamides 2a-f, thioureas 4a-c and dithiocarbamates 5a-c were prepared in the reaction of 2-cyclohexenyl isothiocyanate 1 with organomagnesium compounds, amines and thiophenols, respectively (Scheme 1). The configuration of the bicyclic cyclisation products was inferred from their 1D- and 2D-NMR spectra.


Lawesson's Reagent
11
2g
1
SCN
RMgX
2a-f
3
SH
R2NH
4a-c
RSH
5a-c
Br2·O
or I2
aq NaHCO3
6a-g (X=Br)
6h (X=I)
9a-d (X=Br)
9e (X=I)
R
2a, 6a CH3
2b, 6b C2H5
2c, 6c C6H5CH2
2d, 6d, 6h, 9a, 9e C6H5
2e, 6e, 9b 4-CH3OC6H4
2f, 6f, 9c 2-CH3OC6H4
6g, 9d 3,5-di-NO2C6H3
7a (X=Br)
7b-c (X=I)
10a (X=Br)
10b-c (X=I)
4a, 7a, 10a CH3
4b, 7b, 10b -(CH2)4-
4c, 7c, 10c -(CH2)5-
5a, 8a C6H5
5b, 8b 4-CH3C6H4
5c, 8c 4-ClC6H4
8a-c
Scheme 1

The thiourethane 3 was obtained in 5-20% yield as a rather unexpected by-product in all the reactions with a Grignard reagent. It was also prepared in an independent synthesis from 1 and 2-mercaptocyclohexene (Scheme 1). This suggests the formation of 2-mercaptocyclohexene as an intermediate in the reaction with Grignard reagents. Further investigations are required to confirm this. The thioamide 2g was obtained in a routine reaction of amide thiation with the Lawesson's reagent (7).

When treated with a bromine-dioxane complex in dioxane or anhydrous THF, compounds 2a-f, 2g, 4a and 5a-c readily cyclised to give, usually in high yields, the hydrobromides of the corresponding 7-bromo-3a,4,5,6,7,7a-hexahydrobenzothiazoles 6a-g, 7a, 8a-c (Scheme 1). The bromine-dioxane complex proved to be a much more convenient reagent than bromine itself, especially in small scale operations. Moreover, as a mild reagent, it cyclised thiourethanes 5a-c with no trace of their decomposition, though rupture of the thiourethane fragments in N-allylurethanes was observed earlier under the action of elemental bromine (8).

Since the thiourea derivatives 4b-c yielded under similar conditions (bromine-dioxane complex or bromine) only intractable oils, their heterocyclisation was carried out with iodine. The resulting crystalline hydroiodides of aminothiazolines 7b-c as well as the hydrobromides 6d-g, 7a were converted into free bases by the action of sodium hydrogen carbonate as reported earlier (6), 6a-c and 8a-c decomposed in an alkaline medium (9,10).

There are three methine signals in the δ 3.8-4.6 ppm range in the ^{1}H-NMR spectra of 6a-10c, but close overlapping makes unambiguous assignments difficult. Since the heterocyclisation process is capable of yielding two conformers (Fig.1), the broad singlet at 4.29 ppm that appears in the ^{1}H,^{1}H-COSY spectrum of 9a may be assigned to the equatorial proton at either carbon C3a (structure A) or C7 (structure B). The problem was solved with the aid of ^{13}C-NMR spectroscopy by comparing the chemical shift (11) of carbon atoms bonded to bromine in 9a and iodine in it's iodo-analogue 9e (Table 1). In that way we came to the following ^{13}C assignments for the heteroatom-bonded carbon atoms: =N-C (75.89 ppm), -S-C (60.70 ppm), Br-C (56.26 ppm). Consequently, it was possible to make assignments for all signals in the ^{1}H-NMR and ^{13}C-NMR spectra and to identify the compounds 6a-10c as the A conformers (Fig.1).

Table 1: ^{13}C chemical shifts (δ ppm) of compounds 9a and 9e in $CDCl_3$

carbon atom	bromo-analog 9a	iodo-analog 9e	Δδ
C-5	22.22	23.27	1.05
C-4	28.14	28.12	-0.02
C-6	35.59	35.50	-0.09
C-7	56.26	37.57	-18.69
C-7a	60.70	62.48	1.78
C-3a	75.89	75.13	-.076

The coupling constants J_{H7aH7} and J_{H3aH7a} for all 6-10 were calculated with a computer program for NMR spectra simulation (12) (Table **2**), while the Karplus equation in the Haasnoot modification (13) was used in calculating the torsion angles from the J^3_{HH} coupling constants. Some values illustrating these calculations are cited in Table **2.** All the NMR data indicate a *trans* conformation of the essentially axial H7a-H7 protons, a *cis* conformation of the H3a-H7a protons, and an equatorial position of the H3a proton; the nitrogen and sulphur atoms are *cis* to one another whereas sulphur is *trans* to the equatorial bromine atom (structure A).

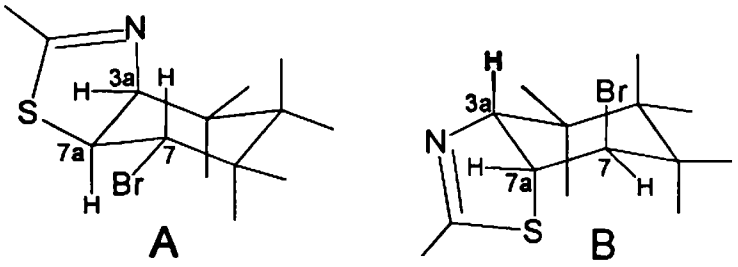
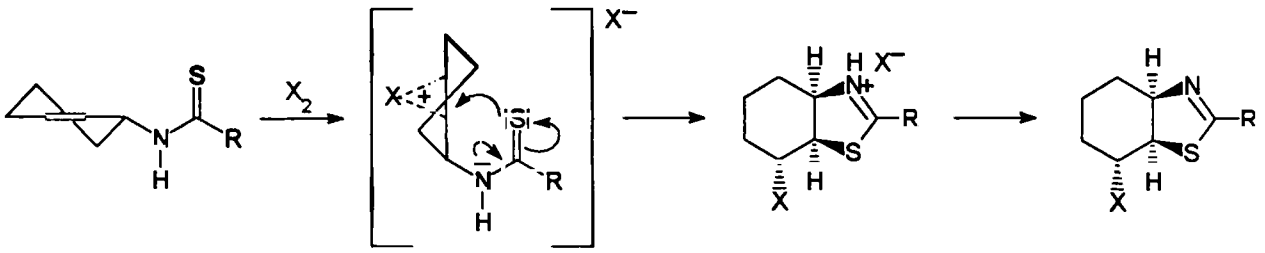


Figure 1

There is, therefore, every reason to assume that the halogen-induced (bromine, bromine-dioxane complex or iodine) conversion of the *N*-cyclohexenyl derivatives 2a-f, 2g, 4a-c and 5a-c into the corresponding hydrohalides of Δ^2-thiazoline 6a-h, 7a-c and 8a-c proceeds *via trans*-cyclisation and *cis*-annulation (Scheme 2). High stereoselectivity of the process with respect to the H3a-H7a and H7a-H7 proton pairs (Fig.1) is presumably determined by the transition state in which the donor (sulphur atom bearing electron pair) and the acceptor (the halogen) synchronously act on the *trans*-π–electrons of the cyclohexene double bond.



Scheme 2

In the transition state, the position of the H3a proton is strictly defined and the H7a and H7 protons are coplanar with the planar fragment of the cyclohexene ring. Electrophilic splitting of the double bond and heterocyclisation take place synchronously in the next stage. The H7a and H7 protons are therefore positioned *transoid* to one another, the inverse *trans*-positions being occupied by the donor and acceptor atoms, *i.e.*, by sulphur and halogen, respectively.

Table 2: The chemical shifts, coupling constants and torsion angles of methine protons H3a, H7a, H7

Comp.	δH^{3a}eq (ppm)	δH^{7a}ax (ppm)	δH^{7}ax (ppm)	$J_{H^{3a}-H^{7a}}$ (Hz)[a]	$HC_{3a}C_{7a}H$ torsion angles (deg)[b]	$J_{H^{7a}-H^{7}}$ (Hz)[a]	$HC_{7}C_{7a}H$ torsion angles (deg)[b]
6a	4.39	4.33	4.26	5.8	36.8	9.9	-159.1
6b	4.46	4.40	4.30	6.0	35.5	10.0	-159.9
6c	4.31	4.20	3.95-4.12	6.2	34.1	10.0	-159.9
6d	4.55	4.41	4.26	6.0	35.5	10.4	-163.4
6e	4.46	4.31	4.21	6.0	35.5	10.2	-161.6
6f	4.52	4.32	4.32	6.2	34.1	10.1	-160.7
6g	4.33-4.42	4.33-4.42	4.09	-c	-	9.8	-158.4
7a	4.25-4.44			-c	-	-c	-
7b	4.26	4.57	4.50	4.9	42.4	10.5	-160.4
7c	4.29	4.54	4.49	5.0	41.8	10.5	-160.4
8a	4.18	4.12	4.01	5.8	36.8	9.8	-156.3
8b	4.30	4.17	4.10	5.6	38.1	10.2	-159.8
8c	3.98-4.30			-c	-	-c	-
9a	4.27	3.90	3.89	5.6	38.1	9.5	-156.1
9b	4.27	3.82-3.94		-c	-	-c	-
9c	4.19	3.97	3.89	5.9	36.1	9.9	-159.1
9d	4.37	4.12	3.85	6.4	32.8	10.2	-161.6
9e	4.12	4.15	4.05	5.6	37.8	9.9	-155.8
10a	4.08	3.78	4.00	5.3	40.1	9.9	-159.1
10b	3.95	3.98	4.17	5.6	37.8	9.8	-155.1
10c	3.92	3.95	4.12	5.3	39.8	10.0	-156.5

a - calculated coupling constants (12) unless otherwise stated
b - torsion angles calculated for one enantiomer
c - coupling constants not determined because of signal overlap

EXPERIMENTAL PART

Melting points were determined on a digital apparatus Elektrothermal model IA9300 and are uncorrected. Infrared spectra of compounds 3, 4a-c, 5a-c, 6a-h, 7a-c, 8a-c, 9a-e, 10a-c were taken with a Specord M80 instruments in KBr pellets, of compound 1 as a film and those of compounds 2a-g, 11 in a CCl_4 solution (C=0.25 mol/dcm^3, layer thickness = 0.11mm). ^{1}H NMR spectroscopic measurements for compounds 2a-f, 3, 4a-c, 5a-c, 6a-g, 7a, 9a-d, 10a and the 1D-^{13}C NMR and 2D-^{1}H,^{1}H (COSY), ^{1}H,^{13}C (COSY) spectroscopic measurements for compound 9a were performed on a Varian Gemini 300VT apparatus (300 MHz) in $CDCl_3$ or DMSO-d_6 with TMS as internal standard. ^{1}H NMR spectroscopic measurements for compounds 1, 2g, 7b, 7c, 10b, 10c were performed on a Bruker MSL (300 MHz) spectrometer and for compound 6h on a Bruker DPX (400

MHz) spectrometer in $CDCl_3$ or DMSO-d_6 with TMS as internal standard. ^{13}C NMR spectra for compounds 1, 3, 9e were obtained on a Brucker AC (200 MHz) spectrometer using $CDCl_3$ or DMSO-d_6 with TMS as internal standard. All determined coupling constants were confirmed by computer simulation of NMR spectra using the NMRSIM 2.4 program (12). Analytical data were satisfactory (0.3% for C,N,S) for all compounds.

2-Cyclohexenyl isothiocyanate 1: Potasium thiocyanate (63 g, 0.65 mol) was dissolved in 130 cm^3 of boiling methanol and 2-bromocyclohexene was added dropwise to the hot solution. The mixture was refluxed for five hours and cooled and potassium chloride was filtered. Methanol was evaporated and the dark yellow oil was fractionally distilled under reduced pressure to yield 34 g (62%) of colourless liquid of onion-like odour, b.p. 60-62 °C/2mm. ^1H NMR ($CDCl_3$) δ 1.50-2.12 (m, 6H, $3CH_2$), 4.16-4.23 (m, 1H, SCN-CH), 5.62-5.67 (m, 1H, =CH), 5.84-5.91 (m, 1H, =CH); ^{13}C NMR δ 18.6, 24.3, 29.8, 52.1, 124.3, 130.1, 131.6; IR (film) ν(cm^{-1}) 3032, br. 2100, 1652;

***N*-(2-Cyclohexenyl)-thioamides 2a-f: General procedure.**
To an ice-cooled (0°C) dry etheral solution (THF for aryl halides, diethyl ether for alkyl halides) of the appropriate Grignard reagent prepared from 2 g (0.082 mole) of Mg turnings and 0.08 mole of appropriate halide, 10.9 g (0.078 mole) of 2-cyclohexenyl isothiocyanate 1 in 30 cm^3 of ether was added dropwise under stirring. Stirring was continued for 2 h at room temperature. The resulting product was hydrolyzed with an excess of a 15% solution of ammonium chloride in water and then extracted twice with 100 cm^3 portions of ethyl acetate. The combined organic layers were dried with $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude material was chromatographed on silica gel with hexane-ethyl acetate 4:1 to afford two products; *N*-(cyclohexenyl)-thioamides 2a-f (major fraction, yield 62-80%), *N*-(2-cyclohexenyl)-*S*-(2-cyclohexenyl)-dithiocarbamate (**3**) (minor fraction, yield 5-20%).

***N*-(2-Cyclohexenyl)-ethanethioamide 2a**
Yield 62%, crystallized from hexane-toluene, mp 61-62 °C; ^1H NMR ($CDCl_3$) δ 1.62-1.75 (m, 3H, CH_2, C<u>H</u>H), 1.95-2.10 (m, 3H, CH_2, C<u>H</u>H), 5.07 (br s, 1H, N=CH), 5.63-5.71 (m, 1H, =CH), 5.92-6.00 (m, 1H, =CH), 7.16 (br s, 1H, NH); IR (CCl_4) ν(cm^{-1}) 3400 (NH), 3364 br (NH), 3028 (=CH), 1502 (thioamide band).

***N*-(2-Cyclohexenyl)-propanethioamide 2b**
Yield 65%, crystallized from hexane-toluene, mp 49-51 °C; ^1H NMR ($CDCl_3$) δ 1.30 (t, J=7.5 Hz, 3H, CH_3), 1.59-1.76 (m, 3H, CH_2, C<u>H</u>H), 1.95-2.10 (m, 3H, CH_2, C<u>H</u>H), 2.66 (q, J=7.5 Hz, 2H, CH_2), 5.10 (br s, 1H, N-CH), 5.63-5.71 (m, 1H, =CH), 5.93-6.01(m, 1H, =CH), 7.12 (br s, 1H, NH); IR (CCl_4) ν(cm^{-1}) 3396 (NH), 3356 br (NH), 3028 (=CH), 1496 (thioamide band).

***N*-(2-Cyclohexenyl)-2-phenyletanethioamide 2c**
Yield 64.5%, crystallized from benzene, m.p 85.5-87 °C; ^1H NMR ($CDCl_3$) δ 1.39-1.71 (m, 3H, CH_2, C<u>H</u>H), 1.88-2.02 (m, 3H, CH_2, C<u>H</u>H), 4.12 (s, 2H, CH_2), 5.07 (br s, 1H, N-CH), 5.50-5.58 (m, 1H, =CH), 5.83-5.91 (m, 1H, =CH), 6.90 (br s, 1H, NH), 7.21-7.41 (m, 5H, C_6H_5); IR (CCl_4) ν(cm^{-1}) 3364 (NH), 3028 (=CH), 1506 (thioamide band).

***N*-(2-Cyclohexenyl)-phenylmethanethioamide 2d**
Yield 80%, crystallized from benzene, mp 67-68 °C; ^1H NMR ($CDCl_3$) δ 1.60-1.89 (m, 3H, CH_2, C<u>H</u>H), 2.03-2.17 (m, 3H, CH_2, C<u>H</u>H), 5.25 (br s, 1H, N-CH), 5.74-5.84 (m, 1H,=CH), 5.98-6.07 (m, 1H, =CH), 7.34-7.56 (m, 4H, C_6H_5, NH), 7.70-7.78 (m, 2H, C_6H_5); IR (CCl_4) ν(cm^{-1}) 3396 (NH), 3028 (=CH), 1500 (thioamide band).

***N*-(2-Cyclohexenyl)-4-methoxyphenylmethanethioamide 2e**
Yield 76%, crystallized from hexane-toluene, mp 99-101 °C; ^1H NMR ($CDCl_3$) δ 1.54-1.9 (m, 3H, CH_2, C<u>H</u>H), 2.03-2.16 (m, 3H, CH_2, C<u>H</u>H), 3.84 (s, 3H, CH_3-O), 5.25 (br s, 1H, N-CH), 5.73-5.82 (m, 1H, =CH), 5.98 - 6.05 (m, 1H,=CH), 6.89 (d, J=8.9 Hz, 2H, ArH), 7.40 (br s, 1H, NH), 7.77(d, J=8.9 Hz, 2H, ArH); IR (CCl_4) ν(cm^{-1}) 3400 (NH), 3028 (=CH), 1508 (thioamide band).

***N*-(2-Cyclohexenyl)-2-methoxyphenylmethanethioamide 2f**
Yield 63%, purified by column chromatography on SiO_2 with benzene, oil; ^1H NMR ($CDCl_3$) δ 1.60-1.89 (m, 3H, CH_2, CHH), 1.85-1.99 (m, 3H, CH_2, CHH), 3.90(s, 3H, CH_3), 5.31 (br s, 1H, N=CH), 5.76-5.83 (m, 1H, =CH), 5.93-6.02 (m, 1H, =CH), 6.91 (dd, J=8.4 Hz and J=1 Hz, 1H, ArH), 7.03 (td, J=7.4 Hz and J=1.0 Hz, 1H, ArH), 7.38 (ddd, J=8.4 Hz and J=7.4 Hz and J=1.8 Hz, 1H, ArH), 8.34 (dd, J=7.5 Hz and J=1.8 Hz, 1H, ArH), 9.02 (br s, 1H, NH); IR (CCl_4) ν(cm^{-1}) 3392 (NH), 3351 br (NH), 3032 (=CH), 1520 (thioamide band).

***N*-(2-Cyclohexenyl)-*S*-(2-cyclohexenyl)-dithiocarbamate 3**
To a water-cooled mixture of 2-cyclohexenyl isothiocyanate 1 2.92 g (0.021 mole) and 2-cyclohexenyl mercaptan (0.021 mole), two drops of triethylamine were added as a catalyst. The mixture was then left standing 2 days at room temperature. After which time product was purified by column chromatography on SiO_2 with benzene-hexane 4:1 and recrystallized from hexane-ethyl acetate (4:1). Yield 73%.
Compound 3 was obtained as a by-product in Grignard's reactions with 5-20% yield (Scheme 1).
Mp 72-74 °C; ^1H NMR ($CDCl_3$) δ 1.52-1.80 (m, 5H, $2CH_2$, CHH), 1.91-2.13 (m, 7H, $3CH_2$, CHH), 4.60 (br s, 1H, S-CH), 5.16 (br s, 1H, N-CH), 5.62-5.83 (m, 2H, 2=CH), 5.85-6.00 (m, 2H, 2=CH), 6.85 (br s,1H, NH); ^{13}C NMR ($CDCl_3$) δ 19.6, 19.9, 24.8, 24.9 ($4CH_2$); 28.0 (CH_2CHS); 29.4 (CH_2,CHN); 46.4 (CHS); 51.6 (CHN); 125.7, 125.8 (CH=CHCHS, CH=CHCHN); 131.7, 132.4 (CH=CHCHS, CH=CHCHN); 196.3 (C=S). IR (KBr) ν(cm^{-1}) 3208, 3024, 1498.

***N*-(2-Cyclohexenyl)-3,5-dinitrophenylmethaneamide 11:** 2.5-Dinitrobenzoyl chloride (9.22 g 0.04 mole) was added in small portions to a water-cooled and stirred solution of 3.78 g (0.039 mole) of 2-cyclohexenyl amine and 4.25 g (0.042 mole) of triethylamine in 75 cm^3 dioxane. Stirring was continued for 2 hours at room temperature and the mixture was then left standing over night. The crystals of triethylamine hydrochloride were filtered off and the filtrate was passed through a 10 cm thick layer of neutral Al_2O_3. The solvent was removed *in vacuo* and the crude solid product was crystallised from water-ethanol to yield 8.7g (75%). Mp 182-184 °C; IR (CCl_4) ν(cm^{-1}) 3292 (NH), 1644 (C=O).

***N*-(2-Cyclohexenyl)-3,5-dinitrophenylmethanethioamide 2g:** N-(2-cyclohexenyl)-3,5-dinitrophenylmethaneamide 2g 4.01 g (0.0138 mole) was heated under reflux with Lawesson's reagent 8.4 g (0.02 mole) in dry THF (70 cm^3) for 5 hours. Evaporation of the solvent and chromatography (SiO_2; dichloromethane-hexane 4:1 afforded 3.5 g (83% yield). Mp 126-128 °C; ^1H NMR ($CDCl_3$) δ 1.55-1.92 (m, 3H, CH_2, CHH), 2.05-2.20 (m, 3H, CH_2, CHH), 5.02 (br s, 1H, N=CH), 5.75-5.83 (m, 1H, =CH), 6.05-6.12 (m, 1H, =CH), 7.70 (br s, 1H, NH), 8.84 (d, J=2.0 Hz, 2H, ArH), 9.07 (t, J=2.0 Hz, 1H, ArH); IR (CCl_4) ν(cm^{-1}) 3380 (NH), 3028 (=CH), 1502 (thioamide band).

***N*^{1}-(2-Cyclohexenyl)-*N*^{2},*N*^{2}-dialkylthiourea 4a-c. General procedure**
2-Cyclohexenyl isothiocyanate 1 3.28 g (0.0236 mole) was added dropwise to a water-cooled constantly stirred solution of appropriate dialkylamine (0.024 mole) in ethanol (40 cm^3). Stirring was continued for 1 hour at room temperature. The material after evaporation of the solvent was purified by column chromatography on Al_2O_3 with $CHCl_3$, solidified products were recrystallized from hexane-toluene.
***N*^{1}-(2-Cyclohexenyl)-*N*^{2},*N*^{2}-dimethylthiourea 4a**
Yield 90%,purified by column chromatography on Al_2O_3 with $CHCl_3$, oil;^1H NMR ($CDCl_3$) δ 1.57-1.72 (m, 3H, CH_2, CHH), 1.90-2.07 (m, 3H, CH_2, CHH), 3.26 (s, 6H, $2CH_3$), 5.00-5.10 (br s, 1H, N-CH), 5.24 (br d, 1H, NH), 5.63-5.67 (m, 1H, =CH), 5.82-5.86 (m, 1H, =CH); IR (KBr) ν(cm^{-1}) 3436 (NH), 3028 (=CH), 1518 (thioamide band).
***N*-(2-Cyclohexenyl)-1-pyrrolidinecarboxthioamide 4b**
Yield 96%, crystallized from hexane-toluene, mp 84-86 °C; ^1H NMR ($CDCl_3$) δ 1.55-1.78 (m, 4H,

$2CH_2$), 1.90-2.18 (m, 6H, $3CH_2$), 3.60 (br s, 4H, $2N\text{-}CH_2$), 5.09 (br s, 2H, NH, N-CH), 5.64-5.73 (m, 1H, =CH), 5.84-5.92 (m, 1H, =CH); IR (KBr) $\nu(cm^{-1})$ 3428 (NH), 3028 (=CH), 1520 (thioamide band).

***N*-(2-Cyclohexenyl)-1-piperidinecarboxthioamide 4c**

Yield 95%, crystallized from hexane-toluene, mp 86-87 °C; ^1H NMR ($CDCl_3$) δ 1.55-1.78 (m, 9H, $4CH_2$, CHH), 3.70-3.84 (m, 4H, $2N\text{-}CH_2$), 5.11 (br s, 1H, N-CH), 5.35 (br d, 1H, NH), 5.66-5.74 (m, 1H,=CH), 5.85-5.92 (m, 1H, =CH): IR (KBr) $\nu(cm^{-1})$ 3436 (NH), 3028 (=CH), 1512 (thioamide band).

S-Aryl-*N*-(2-cyclohexenyl)-dithiocarbamates 5a-c. General procedure

To a water-cooled mixture of 2-cyclohexenyl isothiocyanate 1 2.92 g (0.021 mole) and thiophenol (0.021 mole), two drops of triethylamine were added as a catalyst. The mixture was then left standing 1 day at room temperature. After which time solidified product was recrystallized.

***N*-(2-Cyclohexenyl)-*S*-phenyldithiocarbamate 5a**

Yield 95%, crystallized from heptane-toluene, mp 80-82 °C; ^1H NMR ($CDCl_3$) δ 1.30-1.46 (m, 1H, CHH), 1.41-1.48 (m, 2H, CH_2), 1.82-1.98 (m, 3H, CH_2, CHH), 5.05 (br s, 1H, N-CH), 5.49-5.54 (m, 1H, =CH), 5.80-5.85 (m, 1H, =CH), 6.47 (br s, 1H, NH), 7.45-7.62(m, 5H, C_6H_5); IR (KBr) $\nu(cm^{-1})$ 3364 (NH), 3032 (=CH), 1482 (thioamide band).

***N*-(2-Cyclohexenyl)-*S*-4-methoxyphenyldithiocarbamate 5b**

Yield 94%, crystallized from hexane-toluene, mp 73-75 °C; ^1H NMR ($CDCl_3$) δ 1.32-1.47 (m, 1H, CHH), 1.48-1.68 (m, 2H, CH_2), 1.85-2.00 (m, 3H, CH_2, CHH), 3.78 (s, 3H, CH_3-O), 5.05 (br s, 1H, N-CH), 5.47-5.54 (m,1H,=CH), 5.81-5.90 (m, 1H, =CH), 6.54 (br d, 1H, NH), 7.00 (d, J=8.9 Hz, 2H, ArH), 7.48 (d, J=8.9 Hz, 2H, ArH); IR (KBr) $\nu(cm^{-1})$ 3360 (NH), 3028 (=CH), 1482 (thioamide band).

***N*-(2-Cyclohexenyl)-*S*-4-chlorophenyldithiocarbamate 5c**

Yield 83%, crystallized from hexane-toluene, mp 75.5-77.5 °C;^1H NMR ($CDCl_3$) δ 1.36-1.49 (m, 1H, CHH), 1.50-1.71 (m, 2H, CH_2), 1.87-2.03 (m, 3H, CH_2, CHH), 5.05 (br s, 1H, N-CH), 5.49-5.57 (m, 1H,=CH), 5.85-5.93 (m, 1H, =CH), 6.50 (br d, 1H, NH), 7.45-7.53 (m, 4H, ArH); IR (KBr) $\nu(cm^{-1})$ 3372 (NH), 3028 (=CH), 1476 (thioamide band).

The cyclization reaction of 2a-g, 4a-c, 5a-c. General procedure.

The bromine-dioxane complex (14) (2.48 g, 0.01 mole) was added in small portions to the water-cooled and agitated solution of 0.01 mole of *N*-(2-cyclohexenyl) derivatives 2a-g, 4a, 5a-c in 25 cm^3 dioxane or dry THF. After 2-3 h the crystals were filtered off and recrystallized from nitromethane or ethanol. The same procedure was applied using iodine instead of the bromine-dioxane complex in the reaction with 2d, 4b, 4c. (3a*RS*,7*RS*,7a*RS*)-2-aryl(or 2-(*N*,*N*-dialkyl))-7-bromo-(iodo)-3a,4,5,6,7,7a-hexa-hydrobenzothiazole hydrobromide 6d-g or (hydroiodide) 6h, 7b-c (0.005 mole) was shaken with solution of 0.5 g (0.006 mole) $NaHCO_3$ in 30 cm^3 of water. The aqueous solution was extracted twice with 50 cm^3 portions of ethyl acetate. The solid material left upon evaporation of the solvent was recrystallized or purified by column chromatography.

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-methyl-3a,4,5,6,7,7a-hexahydrobenzothiazole hydrobromide 6a

Yield 68%, crystallized from nitromethane, mp 196 °C (dec.); ^1H NMR (DMSO-d_6) δ 1.43 (qt, J=13.2 Hz and J=ca 3.3 Hz, 1H, H^5ax), 1.63-1.92 (m, 3H, H^4ax, H^5eq, H^6ax), 2.15 (br d, 1H, H^6eq), 2.42 (br d, 1H, H^4eq), 2.50 (br s, 3H, CH_3), 4.26 (ddd, $J_H{}^7{}_{ax}H^6{}_{ax}$=11.2 Hz and $J_H{}^7{}_{ax}H^7{}^a{}_{ax}$=9.9 Hz and $J_H{}^7{}_{ax}H^6{}_{eq}$=4.0 Hz, 1H, H^7ax), 4.33 (dd, $J_H{}^7{}^a{}_{ax}H^7{}_{ax}$=9.9 Hz and $J_H{}^7{}^a{}_{ax}H^3{}^a{}_{eq}$=5.8 Hz, 1H, $H^{7a}ax$), 4.39 (br s, 1H, $H^{3a}eq$), 5.53 (br s, 1H, NH); IR (KBr) $\nu(cm^{-1})$ 2622 br $(NH)^+$, 1610 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-ethyl-3a,4,5,6,7,7a-hexahydrobenzothiazole hydrobromide 6b

Yield 55%, crystallized from ethanol, mp 161-163 °C; ^1H NMR (DMSO-d_6) δ 1.22 (t, J=7.5 Hz, 3H, CH_3), 1.47 (qt, J=13.3 Hz and J= ca 2.4 Hz, 1H, H^5ax), 1.64-1.72 (m, 3H, H^4ax, H^5eq, H^6ax), 2.15 (br d, 1H, H^6eq), 2.29 (br d, 1H, H^4eq), 2.98 (qd, J=7.5 Hz and J=1.5 Hz, 2H, CH_2), 4.30 (ddd, $J_H{}^7{}_{ax}H^6{}_{ax}$=11.4 Hz and $J_H{}^7{}_{ax}H^7{}^a{}_{ax}$=10.0 Hz and $J_H{}^7{}_{ax}H^6{}_{eq}$=4.2 Hz, 1H, H^7ax), 4.40 (dd, $J_H{}^7{}^a{}_{ax}H^7{}_{ax}$=10.0 Hz and $J_H{}^7{}^a{}_{ax}H^3{}^a{}_{eq}$=6.0 Hz, 1H, $H^{7a}ax$), 4.46 (br s, 1H, $H^{3a}eq$), 5.01 (br s, 1H, NH); IR (KBr) $\nu(cm^{-1})$ 2684 br $(NH)^+$, 1592 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-phenylmethyl-3a,4,5,6,7,7a-hexahydrobenzothiazole hydrobromide 6c: Yield 48%, crystallized from ethanol, mp 170-172 °C; ^{1}H NMR (DMSO-d_6) δ 1.44 (qt, J=13.2 Hz and J=ca 2.5 Hz, 1H, H^5ax), 1.63-1.89 (m, 3H, H^4ax, H^5eq, H^6ax), 2.14 (br d, 1H, H^6eq), 2.29 (br d, 1H, H^4eq), 3.95-4.12 (m, 4H, NH, Ar-CH_2, H^{7a}ax), 4.20 (dd, $J_H{}^{7a}{}_{ax}H^{7}{}_{ax}$=10.0 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=6.2 Hz, 1H, H^{7a}ax), 4.31 (br s, 1H, H^{3a}eq), 7.28-7.42 (m, 5H, C_6H_5); IR (KBr) ν(cm^{-1}) 2592 br (NH)$^+$, 1596 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-phenyl-3a,4,5,6,7,7a-hexahydrobenzothiazole hydrobromide 6d Yield 90%, crystallized from nitromethane, mp 185-186 °C; ^{1}H NMR (DMSO-d_6) δ 1.51 (qt, J=13.2 Hz and J=ca 2.6 Hz, 1H, H^5ax), 1.66-1.99 (m, 3H, H^4ax, H^5eq, H^6ax), 2.18 (br d, 1H, H^6eq), 2.49 (br d, 1H, H^4eq), 4.26 (ddd, $J_H{}^{7}{}_{ax}H^{6}{}_{ax}$=11.3 Hz and $J_H{}^{7}{}_{ax}H^{7a}{}_{ax}$=10.4 Hz and $J_H{}^{7}{}_{ax}H^{6}{}_{eq}$=4.2 Hz, 1H, H^7ax), 4.41 (dd, $J_H{}^{7a}{}_{ax}H^{7}{}_{ax}$=10.4 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=6.0 Hz, 1H, H^{7a}ax), 4.55 (br s, 1H, H^{3a}eq), 5.11 (br s, 1H, NH), 7.61 (t, J=7.3 Hz, 2H, C_6H_5), 7.73 (t, 7.4 Hz, 1H, C_6H_5), 7.97 (d, J=7.4 Hz, 2H, C_6H_5); IR (KBr) ν(cm^{-1}) 2676 br (NH)$^+$, 1568 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-phenyl-3a,4,5,6,7,7a-hexahydrobenzothiazole 9a
Yield 80%, crystallized from hexane, mp 79-81 °C; ^{1}H NMR ($CDCl_3$) δ 1,58 (qt, J=13.0 Hz and J=ca 3.0 Hz, 1H, H^5ax), 1.70-1.90 (m, 3H, H^4ax, H^5eq, H^6ax), 2.25 (br d, 1H, H^6eq), 2.60 (br d, 1H, H^4eq), 3.89 (ddd, $J_H{}^{7}{}_{ax}H^{6}{}_{ax}$=12.0 Hz and $J_H{}^{7}{}_{ax}H^{7a}{}_{ax}$=9.5 Hz and $J_H{}^{7}{}_{ax}H^{6}{}_{eq}$=4.4 Hz, 1H, H^7ax), 3.90 (dd, $J_H{}^{7a}{}_{ax}H^{7}{}_{ax}$=9.5 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=5.6 Hz, 1H, H^{7a}ax), 4.27 (br s, 1H, H^{3a} eq), 7.36-7.50 (m, 3H, ArH), 7.83-7.89 (m, 2H, ArH); IR (KBr) ν(cm^{-1}) 1592 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(4-methoxyphenyl)-3a,4,5,6,7,7a-hexahydrobenzothiazole hydrobromide 6e: Yield 94%, crystallized from nitromethane, mp 182 °C (dec.);^{1}H NMR (DMSO-d_6) δ 1.49 (qt, J=13.2 Hz and J=ca 2.5 Hz, 1H, H^5ax), 1.62-1.96 (m, 3H, H^4ax, H^5eq, H^6ax), 2.17 (br d, 1H, H^6eq), 2.43 (br d, 1H, H^4eq), 3.87 (s, 3H, O-CH_3), 4.21 (ddd, $J_H{}^{7}{}_{ax}H^{6}{}_{ax}$=11.0 Hz and $J_H{}^{7}{}_{ax}H^{7a}{}_{ax}$=10.2 Hz and $J_H{}^{7}{}_{ax}H^{6}{}_{eq}$=4.3 Hz, 1H, H^7ax), 4.25 (br s, 1H, NH), 4.31 (dd, $J_H{}^{7a}{}_{ax}H^{7}{}_{ax}$=10.2 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=6.0 Hz, 1H, H^{7a}ax), 4.46 (br s, 1H, H^{3a}eq), 7.13 (d, J=9 Hz, 2H, ArH), 7.91 (d, J=9 Hz, 2H, ArH); IR (KBr) ν(cm^{-1}) 2690 br (NH)$^+$, 1575 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(4-methoxyphenyl)-3a,4,5,6,7,7a-hexahydrobenzothiazole 9b
Yield 94%, crystallized from hexane, mp 90-91 °C; ^{1}H NMR ($CDCl_3$) δ 1,59 (qt, J=13.1 Hz and J=ca 2.9 Hz, 1H, H^5ax), 1.70-1.90 (m, 3H, H^4ax, H^5eq, H^6ax), 2.26 (br d, 1H, H^6eq), 2.62 (br d, 1H, H^4eq), 3.82-3.94 (m, 5H, CH_3, H^7ax, H^{7a}ax), 4.27 (br s, 1H, H^{3a}eq), 6.9 (d, J=9.0 Hz, 2H,ArH), 7.81 (d, J=9.0 Hz, 2H, ArH); IR (KBr) ν(cm^{-1}) 1588 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(2-methoxyphenyl)-3a,4,5,6,7,7a-hexahydrobenzothiazole hydrobromide 6f: Yield 72%, crystallized from nitromethane, mp 177-179 °C; ^{1}H NMR (DMSO-d_6) δ 1.55 (qt, J=13.0 Hz and J=ca 2.0 Hz, 1H, H^5ax), 1.66-1.97 (m, 3H, H^4ax, H^5eq, H^6ax), 2.17 (br d, 1H, H^6eq), 2.48 (br d, 1H, H^4eq), 4.00 (s, 3H, O-CH_3), 4.32 (dd, $J_H{}^{7a}{}_{ax}H^{7}{}_{ax}$=10.1 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=6.2 Hz, 1H, H^{7a}ax), 4.32 (ddd, $J_H{}^{7}{}_{ax}H^{6}{}_{ax}$=11.8 Hz and $J_H{}^{7}{}_{ax}H^{7a}{}_{ax}$=10.1 Hz and $J_H{}^{7}{}_{ax}H^{6}{}_{eq}$=4.2 Hz, 1H, H^7ax), 4.52 (br s, 1H, H^{3a}eq), 4.75 (br s, 1H, NH), 7.20 (t, J=7.7 Hz, 1H, ArH), 7.35 (d, J=8.4 Hz, 1H, ArH), 7.77 (ddd, J=8.4 Hz and J=7.7 Hz and J=1.5 Hz, 1H, ArH), 8.05 (dd, J=7.7 Hz and J=1.5 Hz, 1H, ArH); IR (KBr) ν(cm^{-1}) 2580 br (NH)$^+$, 1556 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(2-methoxyphenyl)-3a,4,5,6,7,7a-hexahydrobenzothiazole 9c
Yield 97%, crystallized from hexane, mp 83-85 °C; ^{1}H NMR ($CDCl_3$) δ 1,59 (qt, J=12.9 Hz and J=ca 2.9 Hz, 1H, H^5ax), 1.70-1.90 (m, 3H, H^4ax, H^5eq, H^6ax), 2.27 (br d, 1H, H^6eq), 2.61 (br d, 1H, H^4eq), 3.79 (dd, $J_H{}^{7a}{}_{ax}H^{7}{}_{ax}$=9.9 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=5.8 Hz, 1H, H^{7a}ax), 3.89 (ddd, $J_H{}^{7}{}_{ax}H^{6}{}_{ax}$=12.0 Hz and $J_H{}^{7}{}_{ax}H^{7a}{}_{ax}$=9.9 Hz and $J_H{}^{7}{}_{ax}H^{6}{}_{eq}$=4.2 Hz, 1H, H^7ax), 3.90 (s, 3H, CH_3), 4.19 (br s, 1H, H^{3a}eq), 6.96 (d, J=8.4 Hz, 1H, ArH), 7.00 (t, J=7.6 Hz, 1H, ArH), 7.40 (ddd, J=8.4 Hz and J=7.6 Hz and J=1.8 Hz, 1H, ArH), 7.85 (dd, J=7.6 Hz and J=1.8 Hz, 1H, ArH); IR (KBr) ν(cm^{-1}) 1588 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(3,5-dinitrophenyl)-3a,4,5,6,7,7a-hexahydrobenzothiazole hydrobromide 6g: Yield 95%, crystallized from nitromethane, mp 206 °C (dec.); ^{1}H NMR (DMSO-d_6) δ 1.45 (qt, J=13.2 Hz and J=ca 2.4 Hz, 1H, H^5ax), 1.65-1.98 (m, 3H, H^4ax, H^5eq, H^6ax), 2.16 (br d, 1H, H^6eq), 2.53 (br d, 1H, H^4eq), 4.09 (ddd, $J_H{}^{7}{}_{ax}H^{6}{}_{ax}$=11.8 Hz and $J_H{}^{7}{}_{ax}H^{7a}{}_{ax}$=9.8 Hz and

$J_H{}^7{}_{ax}H^6{}_{eq}$=4.4 Hz, 1H, H^7ax), 4.33-4.42 (m, 2H, H^{7a}ax, H^{3a}eq), 4.70 (br s, 1H, NH), 8.78 (d, J=2 Hz, 2H, ArH), 8.96 (t, J=2 Hz, 1H, ArH); IR (KBr) ν(cm^{-1}) 2597 br $(NH)^+$, 1539 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(3,5-dinitrophenyl)-3a,4,5,6,7,7a-hexahydrobenzothiazole 9d

Yield 76%, crystallized from hexane, mp 130-131 °C; ^{1}H NMR ($CDCl_3$) δ 1,75 (qt, J=13.3 Hz and J=ca 2.9 Hz, 1H, H^5ax). 1.77-1.98 (m, 3H, H^4ax, H^5eq, H^6ax), 2.31 (br d, 1H, H^6eq), 2.68 (br d, 1H, H^4eq), 3.85 (ddd, $J_H{}^7{}_{ax}H^6{}_{ax}$=12.0 Hz and $J_H{}^7{}_{ax}H^{7a}{}_{ax}$=10.2 Hz and $J_H{}^7{}_{ax}H^6{}_{eq}$=4.3 Hz, 1H, H^7ax), 4.12 (dd, $J_H{}^{7a}{}_{ax}H^7{}_{ax}$=10.2 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=6.4 Hz, 1H, H^{7a}ax), 4.37 (br s, 1H, H^{3a} eq), 9.00 (d, J=2.0 Hz, 2H, ArH), 9.14 (t, J=2.0 Hz, 1H, ArH); IR (KBr) ν(cm^{-1}) 1540 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(dimethylamino)-3a,4,5,6,7,7a-hexahydrobenzothiazole hydrobromide 7a: Yield 60%, crystallized from nitromethane, mp 169 °C (dec.); ^{1}H NMR (DMSO-d_6) δ 1.45-1.90 (m, 4H, H^4ax, H^5ax, H^5eq, H^6ax), 2.15-2.32 (m, 2H, H^4eq, H^6eq), 3.23 (s, 6H, $2CH_3$), 3.38 (br s, 1H, NH), 4.25-4.44 (m, 3H, H^{3a}eq, H^7ax, H^{7a}ax); IR (KBr) ν(cm^{-1}) 2890 br $(NH)^+$, 1636 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(dimethylamino)-3a,4,5,6,7,7a-hexahydrobenzothiazole 10a

Yield 62%, crystallized from hexane, mp 71-72 °C; ^{1}H NMR ($CDCl_3$) δ 1.56-1.88 (m, 4H, H^4ax, H^5ax, H^5eq, H^6ax), 2.21-2.42 (m, 2H, H^4eq, H^6eq), 3.00 (s, 6H, CH_3), 3.78 (dd, $J_H{}^{7a}{}_{ax}H^7{}_{ax}$=9.9 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=5.3 Hz, 1H, H^{7a}ax), 4.00 (ddd, $J_H{}^7{}_{ax}H^6{}_{ax}$=11.5 Hz and $J_H{}^7{}_{ax}H^{7a}{}_{ax}$=9.9 Hz and $J_H{}^7{}_{ax}H^6{}_{eq}$=4.3 Hz, 1H, H^7ax), 4.08 (br s, 1H, H^{3a}eq); IR (KBr) ν(cm^{-1}) 1610 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(phenylthio)-3a,4,5,6,7,7a-hexahydrobenzothiazole hydrobromide 8a: Yield 70%, crystallized from nitromethane, mp 182 °C (dec.); ^{1}H NMR (DMSO-d_6) δ 1.40 (qt, J=13.4 Hz and J=ca 3.3 Hz, 1H, H^5ax), 1.57-1.82 (m, 3H, H^4ax, H^5eq, H^6ax), 2.13 (br d, 1H, H^6eq), 2.25 (br d, 1H, H^4eq), 4.01 (ddd, $J_H{}^7{}_{ax}H^6{}_{ax}$=11.3 Hz and $J_H{}^7{}_{ax}H^{7a}{}_{ax}$=9.8 Hz and $J_H{}^7{}_{ax}H^6{}_{eq}$=4.2 Hz, 1H, H^7ax), 4.12 (dd, $J_H{}^{7a}{}_{ax}H^7{}_{ax}$=9.8 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=5.8 Hz, 1H, H^{7a}ax), 4.18 (br s, 1H, H^{3a}eq), 6.42 (br s, 1H, NH), 7.45-7.55 (m, 3H, ArH), 7.64-7.70 (m, 2H, ArH); IR (KBr) ν(cm^{-1}) 2570 br $(NH)^+$, 1546 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(4-methoxyphenylthio)-3a,4,5,6,7,7a-hexahydrobenzothiazole hydrobromide 8b: Yield 75%, crystallized from nitromethane, mp 172-174 °C; ^{1}H NMR (DMSO-d_6) δ 1.43 (qt, J=13.2 Hz and J=ca 2.5 Hz, 1H, H^5ax), 1.58-1.85 (m, 3H, H^4ax, H^5eq, H^6ax), 2.13 (br d, 1H, H^6eq), 2.24 (br d, 1H, H^4eq), 3.83 (s, 3H, O-CH_3), 4.10 (ddd, $J_H{}^7{}_{ax}H^6{}_{ax}$=12.0 Hz and $J_H{}^7{}_{ax}H^{7a}{}_{ax}$=10.2 Hz and $J_H{}^7{}_{ax}H^6{}_{eq}$=4.4 Hz, 1H, H^7ax), 4.17 (dd, $J_H{}^{7a}{}_{ax}H^7{}_{ax}$=10.2 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=5.6 Hz, 1H, H^{7a}ax), 4.30 (br s, 1H, H^{3a}eq), 5.05 (br s, 1H, NH), 7.08 (d, J=8.6 Hz, 2H, ArH), 7.62 (d, J=8.6 Hz, 2H, ArH); IR (KBr) ν(cm^{-1}) 2620 br $(NH)^+$, 1526 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Bromo-2-(4-chlorophenylthio)-3a,4,5,6,7,7a-hexaydrobenzothiaole hydrobromide 8c: Yield 84%, crystallized from nitromethane, mp 182 °C (dec.); ^{1}H NMR (DMSO-d_6) δ 1.39 (qt, J=12.9 Hz and J=ca 2.6 Hz, 1H, H^5ax), 1.56-1.83 (m, 3H, H^4ax, H^5eq, H^6ax), 2.12 (br d, 1H, H^6eq), 2.25 (br d, 1H, H^4eq), 3.98-4.30 (m, 4H, NH, H^{3a}eq, H^7ax, H^{7a}ax), 7.56 (d, J=8.4 Hz, 2H, ArH), 7.69 (d, J=8.4 Hz, 2H,ArH); IR (KBr) ν(cm^{-1}) 2560 br $(NH)^+$, 1536 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Iodo-2-phenyl-3a,4,5,6,7,7a-hexahydrobenzothiazole hydroiodide 6h

Yield 40%, crystallized from nitromethane, mp 204-206 °C; ^{1}H NMR (DMSO-d_6) δ 1.43 (qt, J=13.0 Hz and J=ca 3.1 Hz, 1H, H^5ax), 1.49-1.57 (m, 1H, H^5eq), 1.86-2.03 (m, 2H, H^4ax, H^6ax), 2.22 (br d, 1H, H^6eq), 2.48 (br d, 1H, H^4eq), 3.68 (br s, 1H, NH), 4.17 (ddd, $J_H{}^7{}_{ax}H^6{}_{ax}$=11.9 Hz and $J_H{}^7{}_{ax}H^{7a}{}_{ax}$=10.7 Hz and $J_H{}^7{}_{ax}H^6{}_{eq}$=4.2 Hz, 1H, H^7ax), 4.25 (br s, 1H, H^{3a}eq), 4.48 (dd, $J_H{}^{7a}{}_{ax}H^7{}_{ax}$=10.7 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=6.1 Hz, 1H, H^{7a}ax), 7.56 (t, J=7.3 Hz, 2H, C_6H_5), 7.66 (t, 7.4 Hz, 1H, C_6H_5), 7.87 (d, J=7.2 Hz, 2H, C_6H_5); IR (KBr) ν(cm^{-1}) 2925 br $(NH)^+$, 1626 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Iodo-2-phenyl-3a,4,5,6,7,7a-hexahydrobenzothiazole 9e

Yield 85%, crystallized from hexane, mp 120-123 °C; ^{1}H NMR ($CDCl_3$) δ 1.42-1.72 (m, 2H, CHH, CHH), 1.82-2.07 (m, 2H, CHH, CHH), 2.33 (br d, 1H, H^6eq), 2.69 (br d, 1H, H^4eq), 4.05 (ddd, $J_H{}^7{}_{ax}H^6{}_{ax}$=11.7 Hz and $J_H{}^7{}_{ax}H^{7a}{}_{ax}$=9.9 Hz and $J_H{}^7{}_{ax}H^6{}_{eq}$=4.0 Hz, 1H, H^7ax), 4.12 (br s, 1H, H^{3a}eq), 4.15 (dd, $J_H{}^{7a}{}_{ax}H^7{}_{ax}$=9.9 Hz and $J_H{}^{7a}{}_{ax}H^{3a}{}_{eq}$=5.6 Hz, 1H, H^{7a}ax), 7.37-7.51 (m, 3H, C_6H_5), 7.86 (dd, J=8.3 Hz and J=1.4 Hz, 2H, C_6H_5); IR (KBr) ν(cm^{-1}) 1592 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Iodo-2-(1-pyrrolidinyl)-3a,4,5,6,7,7a-hexahydrobenzothiazole hydroiodide 7b: Yield 82%, crystallized from nitromethane, mp 188-190 °C; ^{1}H NMR (DMSO-d_6) δ

1.52-1.65 (m, 2H, CHH, CHH), 1.80-2.17 (m, 6H, $2CH_2$, CHH, CHH,), 2.26-242 (m, 2H, H^6eq, H^4eq), 3.43 (br s, 1H, NH), 3.65 (br s, 4H, 2N-CH_2), 4.26 (br s, 1H, $H^{3a}eq$), 4.50 (ddd, $J_H{}^7ax H^6ax$=12.0 Hz and $J_H{}^7ax H^{7a}ax$=10.5 Hz and $J_H{}^7ax H^6eq$=4.0 Hz, 1H, H^7ax), 4.57 (dd, $J_H{}^{7a}ax H^7ax$=10.5 Hz and $J_H{}^{7a}ax H^{3a}eq$=4.9 Hz, 1H, $H^{7a}ax$); IR (KBr) ν(cm^{-1}) 2596 br $(NH)^+$, 1582 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Iodo-2-(1-pyrrolidinyl)-3a,4,5,6,7,7a-hexahydrobenzothiazole 10b

Yield 70%, crystallized from hexane, mp 66.5-68.5 °C; ^1H NMR ($CDCl_3$) δ 1.40-1.75 (m,4H, H^4ax, H^5ax, H^5eq, H^6ax), 1.83-2.03 (m, 4H, $2CH_2$), 2.31 (br d, 1H, H^6eq), 2.42 (br d, 1H,H^4eq), 3.30-3.52 (m, 4H, 2N-CH_2), 3.95 (br s, 1H, $H^{3a}eq$), 3.98 (dd, $J_H{}^{7a}ax H^7ax$=9.8 Hz and $J_H{}^{7a}ax H^{3a}eq$=5.6 Hz, 1H, $H^{7a}ax$), 4.17 (ddd, $J_H{}^7ax H^6ax$=12.0 Hz and $J_H{}^7ax H^{7a}ax$=9.8 Hz and $J_H{}^7ax H^6eq$=4.2 Hz, 1H, H^7ax); IR (KBr) ν(cm^{-1}) 1592 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Iodo-2-(1-piperidinyl)-3a,4,5,6,7,7a-hexahydrobenzothiazole hydroiodide 7c: Yield 82%, crystallized from nitromethane, mp 164-165 °C; ^1H NMR (DMSO-d_6) δ 1.50-1.97 (m, 9H, $2CH_2$, CHH, H^4ax, H^5ax, H^5eq, H^6ax), 1.97-2.15 (m, 1H, CHH), 2.24-2.43 (m, 2H, H^6eq, H^4eq), 3.44 (br s, 1H, NH), 3.68 (br s, 4H, 2N-CH_2), 4.29 (br s, 1H, $H^{3a}eq$), 4.49 (ddd, $J_H{}^7ax H^6ax$=12.0 Hz and $J_H{}^7ax H^{7a}ax$=10.5 Hz and $J_H{}^7ax H^6eq$=4 0 Hz, 1H, H^7ax), 4.54 (dd, $J_H{}^{7a}ax H^7ax$=10.5 Hz and $J_H{}^{7a}ax H^{3a}eq$=5 0 Hz, 1H, $H^{7a}ax$); IR (KBr) ν(cm^{-1}) ca 3000 br $(NH)^+$, 1632 (C=N).

(3a*RS*,7*RS*,7a*RS*)-7-Iodo-2-(1-piperidinyl)-3a,4,5,6,7,7a-hexahydrobenzothiazole 10c

Yield 62%, purified on silica gel column with ethyl acetate as eluent, oil; ^1H NMR ($CDCl_3$) δ 1.40-1.75 (m, 9H, H^4ax, H^5ax, H^5eq, H^6ax, CHH, $2CH_2$), 1.90 (qd, J=12.0 Hz and J=3.5 Hz, 1H, CHH), 2.31 (br d, 1H, H^6eq), 2.39 (br d, 1H, H^4eq), 3.31-3.45 (br s, 4H, 2N-CH_2), 3.92 (br s, 1H, $H^{3a}eq$), 3.95 (dd, $J_H{}^{7a}ax H^7ax$=10.0 Hz and $J_H{}^{7a}ax H^{3a}eq$=5.3 Hz, 1H, $H^{7a}ax$), 4.12 (ddd, $J_H{}^7ax H^6ax$=12.1 Hz and $J_H{}^7ax H^{7a}ax$=9.9 Hz and $J_H{}^7ax H^6eq$=4.2 Hz, 1H, H^7ax); IR (KBr) ν(cm^{-1}) 1604 (C=N).

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