Synthesis of 1-(4-Thiazolyl)azulenes: Reactions of Bromoacetyl-substituted Azulenes with Thioamides,Thioureas, and Thiosemicarbazones

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1-(Bromoacetyl)-3-methylazulene (**1a**) and methyl 3-(bromoacetyl)azulene-1-carboxylate (**1b**) reacted with thioamides **3a**,**b** and thioureas **3c**,**d** in boiling ethanol to give the corresponding (4-thiazolyl)azulenes **4a**-**d** and **5a**-**d** in good yields, respectively. The reactions of dibromoacetyl-substituted azulene (**2**) also gave (4-thiazolyl)azulenes **5a**-**d** in lower yields and the azulene **2** was recovered. By heating compounds **5a**-**d** in 100% phosphoric acid, the ester group was eliminated to yield 1-(4-thiazolyl)azulenes **6a**-**d**. Compounds **1a**,**b** reacted with thiosemicarbazones **7a**-**f** to afford [(2-alkylidenehydrazino)thiazol-4-yl]azulenes **8a**-**f** and **9a**-**f** in moderate to high yields *via* their hydromides.

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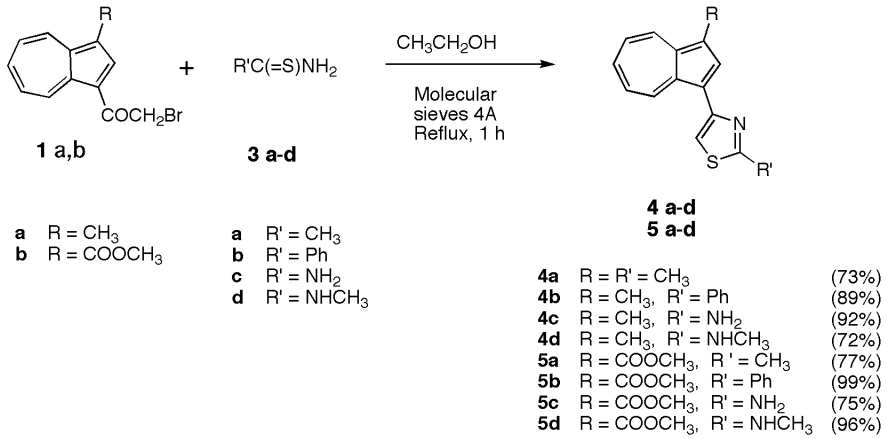
A thiazole nucleus appears frequently in a variety of biologically active compounds, such as thiamine (vitamin B_1), antibiotics penicillins (micrococcin), and many metabolic products of fungi and primitive marine animals. Recently, the thiazole ring has been identified as a central feature of a number of biologically active natural products such as patellazoles [1], cyclothiazomycin [2], mycothiazole [3], theonezolides [4], and dolabellin [5]. Predominantly, these substances are characterized as 2,4-disubstituted thiazoles, many of which are isolated from marine sources. On the other hand, many synthetic methods have been documented for the preparation of thiazoles [6]. The Hanztsch thiazole synthesis using α-haloketones was established long ago [7] and has been commonly used [8,9]. Previously, we reported that 1-(bromoacetyl)azulenes were readily obtained by the brominatin of 1-acetylazulenes with trimethylphenylammonium tribromide and are useful building blocks for the synthesis of heterocycle-substituted azulenes [10]. For example, these bromoacetyl-substituted azulenes reacted with 2-hydroxybenzaldehydes to yield 1-(2-benzofurancarbonyl)azulenes [10], while the reaction with 2-aminopyridines gave 1-(imidazo[1,2-*b*]pyrid-2-yl)azulenes [11]. In this paper, we wish to report the synthesis of a variety of thiazole-substituted azulenes by Hantzsch reaction of (bromoacetyl)azulenes with thioamides, thioureas, and thiosemicarbazones.

Results and Discussion.

Reactions with Thioamides and Thioureas.

It is a well-known fact that α-haloketones react with thioamides and related substances to give thiazole derivatives [8,9]. When a methanolic solution of 1-(bromoacetyl)-3-methylazulene (**1a**) and 1.5 molar equivalents of thioacetamide (**3a**) was refluxed for 2 hours, 1-methyl-3-(2-methylthiazol-4-yl)azulene (**4a**) was obtained as green needles, mp 85-86 °C, in 56% yield. Its structure was established by spectral data and an elemental analysis ($C_{15}H_{13}NS$), in addition to the reaction mechanism of Hantzsch reaction. In the ^1H nmr spectrum, the 5'-H proton was observed at δ 7.21 as a singlet signal. Similarly,

Scheme 1



the reactions with thiobenzamide (**3b**), thiourea (**3c**), and 1-methyl-2-thiourea (**3d**) gave the corresponding 1-methyl-3-(4-thiazolyl)azulenes **4b-d** in 57, 62, and 59% yields, respectively. When the reactions were carried out in boiling ethanol in the presence of Molecular Sieves 4A, the yields were improved to 72-92%, as shown in Scheme 1. In a similar manner, methyl 3-(bromoacetyl)azulene-1-carboxylate (**1b**) reacted with thioamides **3a**,**b** and thioureas **3c**,**d** to afford the corresponding methyl 3-(4-thiazolyl)azulene-1-carboxylates **5a-d** in high yields.

On the other hand, in the reaction of α,α-dihalogenated ketone, it was reported that the reaction of 1-(dibromoacetyl)-4-methoxybenzene with thiourea gave 2-amino-4-(4-methoxyphenyl)thiazole instead of the corresponding bromo-substituted thiazole [12]. In the case of our azulene-based substrates, the reactions of methyl 3-(dibromoacetyl)azulene-1-carboxylate (**2**) with thioacetamide (**3a**) were retarded. When the reaction was continued for 24 hours in boiling ethanol, methyl 3-(2-methyl-4-thiazolyl)azulene-1-carboxylate (**5a**) was obtained in 35% yield and the starting material (**2**) was recovered in 43% yield. Similarly, the reactions with thiobenzamide (**3b**) and 1-methyl-2-thiourea (**3d**) gave respectively thiazole-substituted azulenes **5b** (26%) and **5d** (45%). The unchanged compound **2** was isolated in 48% and 27% yields, respectively. From these results in the reactions of the α,α-dibromo ketone **2**, it might be thought that the initial attack of the thioamides and thioureas on the carbon atom bearing two bromine atoms was much more restricted by these two bulky bromine atoms than the attack on the α-monobromo ketones **1a**,**b**. Additionally, the reduction process might exist in these reactions, because the products **5a**,**b**,**d** do not contain the bromine atom. A process is not clear at the present time.

When methyl 3-(4-thiazolyl)azulene-1-carboxylates **5a-d** were heated for 15 minutes at 100 °C in 100% phosphoric acid, the ester group was eliminated and the corresponding 1-(4-thiazolyl)azulenes **6a-d** were obtained in good yields, respectively, except for **6d** (45%).

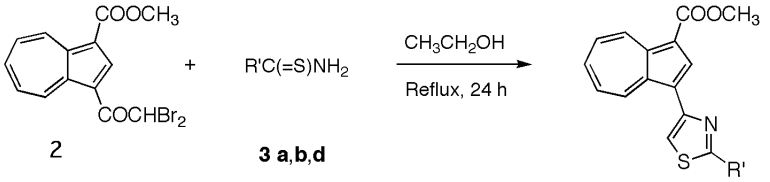
Reactions with Thiosemicarbazones.

Thiosemicarbazones have an extended thiourea-like chain. When an ethanolic solution of 1-(bromoacetyl)-3-methylazulene (**1a**) and 1.5 molar equivalents of acetone thiosemicarbazone (**7a**) was refluxed for 1 hour, 1-methyl-3-[2-(1-methylethylidenehydrazino)thiazol-4-yl]azulene hydrobromide precipitated. This hydrobromide was heated for 30 minutes in trimethyl orthoformate to afford 1-methyl-3-[2-(1-methylethylidenehydrazino)thiazol-4-yl]azulene (**8a**) as deep green needles, mp 124-125 °C, in 51% yield. Its structure was determined on the basis of spectral data as well as elemental analysis. The ir spectrum shows two characteristic absorptions at ν 2914 (NH) and 1563 cm^{-1} (C=N). In the ^1H nmr spectrum, four typical signals were observed at δ 1.96 for $=C(CH_3)_2$, 2.59 for 1-CH_3, 7.04 for 5'-H, and 10.58 for NH proton in addition to signals for azulenic protons. The reactions of 1-(bromoacetyl)azulenes **1a**,**b** with thiosemicarbazones **7a-f** also gave the corresponding 1-methyl-3-(4-thiazolyl)azulenes **8b-f** (49-90%) and methyl 3-(4-thiazolyl)azulene-1-carboxylates **9a-f** (52-98%), respectively.

Conclusion.

It was found that all the reactions of 1-(bromoacetyl)-azulenes **1a**,**b** with thioamides **3a**,**b** and thioureas **3c**,**d** were initiated by nucleophilic attack of the sulfur atom on the methylene carbon atom of the bromoacetyl group to yield azulenes having a 4-thiazolyl ring. The reactions

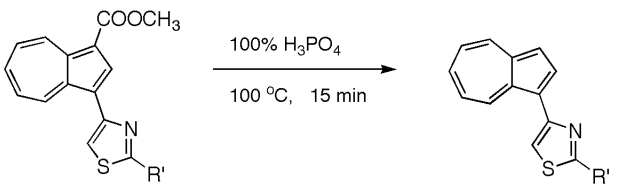
Scheme 2



a R' = CH_3
b R' = Ph
c R' = $NHCH_3$

a R' = CH_3 (35%)
b R' = Ph (26%)
c R' = $NHCH_3$ (45%)

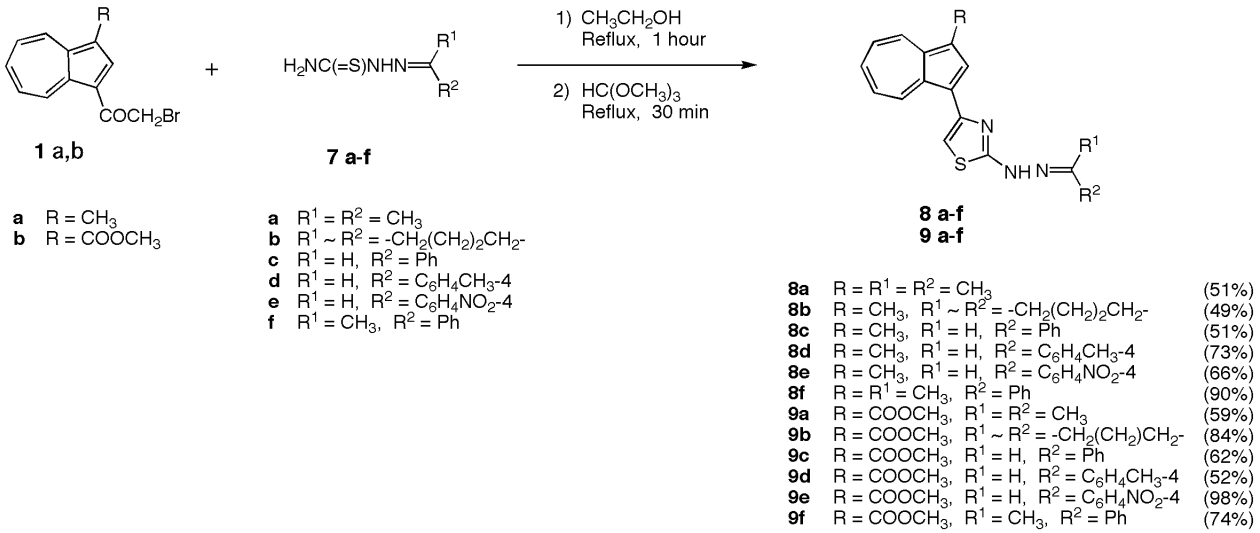
Scheme 3



a R' = CH_3
b R' = Ph
c R' = NH_2
d R' = $NHCH_3$

a R' = CH_3 (96%)
b R' = Ph (90%)
c R' = NH_2 (79%)
d R' = $NHCH_3$ (45%)

Scheme 4



a R = CH_3
b R = $COOCH_3$

a $R^1 = R^2 = CH_3$
b $R^1 \sim R^2 = -CH_2(CH_2)_2CH_2-$
c R^1 = H, R^2 = Ph
d R^1 = H, $R^2 = C_6H_4CH_3$-4
e R^1 = H, $R^2 = C_6H_4NO_2$-4
f $R^1 = CH_3$, R^2 = Ph

8a	R = $R^1 = R^2 = CH_3$	(51%)
8b	R = CH_3, $R^1 \sim R^2 = -CH_2(CH_2)_2CH_2-$	(49%)
8c	R = CH_3, R^1 = H, R^2 = Ph	(51%)
8d	R = CH_3, R^1 = H, $R^2 = C_6H_4CH_3$-4	(73%)
8e	R = CH_3, R^1 = H, $R^2 = C_6H_4NO_2$-4	(66%)
8f	R = $R^1 = CH_3$, R^2 = Ph	(90%)
9a	R = $COOCH_3$, $R^1 = R^2 = CH_3$	(59%)
9b	R = $COOCH_3$, $R^1 \sim R^2 = -CH_2(CH_2)CH_2-$	(84%)
9c	R = $COOCH_3$, R^1 = H, R^2 = Ph	(62%)
9d	R = $COOCH_3$, R^1 = H, $R^2 = C_6H_4CH_3$-4	(52%)
9e	R = $COOCH_3$, R^1 = H, $R^2 = C_6H_4NO_2$-4	(98%)
9f	R = $COOCH_3$, $R^1 = CH_3$, R^2 = Ph	(74%)

with thiosemicarbazones **7a-f** also gave the corresponding 2-(alkylidenehydrazino)thiazol-4-yl-substituted azulenes **8a-f** and **9a-f** in good yields.

EXPERIMENTAL

All the melting points were determined with a Yanagimoto MP JP-3 apparatus and are uncorrected. The ir spectra were taken on a Perkin-Elmer Pragagon 1000 spectrophotometer. The nmr spectra were recorded with a JEOL JNM-EX 300 spectrometer (300 MHz for ^1H and 75.5 MHz for ^{13}C). The ms spectra were obtained using a JEOL JMX-DX 303HF instrument. All the elemental analyses were performed at the Institute of Resource Development and analysis, Kumamoto University. Merck Kieselgel 60 and Wakogel B-10 was used for column and preparative thin layer chromatography, respectively.

Materials.

1-(Bromoacetyl)-3-methylazulene (**1a**), methyl 3-(bromoacetyl)azulene-1-carboxylate (**1b**), and methyl 3-(dibromoacetyl)azulene-1-carboxylate (**2**) were prepared according to the methods described in the literature [10].

Reactions of Bromoacetyl-substituted Azulenes **1a,b** with Thioamides **3a,b**.

General Procedure.

A solution of 1-(bromoacetyl)-3-methylazulene (**1a**) (132 mg, 0.5 mmol) or methyl 3-(bromoacetyl)azulene-1-carboxylate (**1b**) (154 mg, 0.5 mmol) and thioamide **3a,b** (0.75 mmol) in ethanol (10 ml) was refluxed for 1 hour in the presence of Molecular Sieves 4A (300 mg). The evaporation residue was chromatographed on two Wakogel B-10 plates (30 x 30 cm) with chloroform to give (4-thiazolyl)azulenes **4a,b** and **5a,b**, respectively.

1-Methyl-3-(2-methylthiazol-4-yl)azulene (**4a**).

This compound was was obtained as green needles (from benzene) in a yield of 87 mg (73%); mp 85-86 °C; ^1H nmr ($CDCl_3$): δ 2.67 (3H, s, 1-CH_3), 2.88 (3H, s, 2'-CH_3), 7.05 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.09 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.21 (1H, s, 5'-H), 7.51 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H). 8.04 (1H, s, 2-H), 8.18 (1H, d, *J* = 9.8 Hz, 8-H), 9.12 (1H, d, *J* = 9.9 Hz, 4-H); ^{13}C nmr ($CDCl_3$): δ 12.6 (3-CH_3), 19.5 (2'-CH_3), 112.0 (=CH-), 121.9 (=CH-), 122.0 (=C<), 123.0 (=CH-), 125.7 (=C<), 134.1 (=CH-), 135.3 (=C<), 136.3 (=CH-), 137.6 (=CH-), 138.2 (=CH-), 138.7 (=C<), 152.5 (=C<), 165.2 (=C<); ms (EI): *m/z* 239 (M^+, 100), 197 (32), 165 (43).

Anal. Calcd for $C_{15}H_{13}NS$: M, 239.0769; C, 75.28; H, 5.47; N, 5.85. Found: *m/z*, 239.0789; C, 75.56; H, 5.34; N, 5.69.

1-Methyl-3-(2-phenylthiazol-4-yl)azulene (**4b**).

This compound was obtained as green needles (from benzene) in a yield of 135 mg (89%); mp 43-44 °C; ^1H nmr ($CDCl_3$): δ 2.65 (3H, s, CH_3), 7.03 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.11 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.33 (1H, s, 5'-H), 7.40-7.53 (4H, m), 8.06-9.09 (3H, m), 8.15 (1H, d, *J* = 9.9 Hz, 8-H), 9.37 (1H, d, *J* = 9.9 Hz, 4-H); ^{13}C nmr ($CDCl_3$): δ 12.3 (CH_3), 112.3 (=CH-), 121.5 (=C<), 122.1 (=CH-), 123.2 (=CH-), 125.7 (=C<), 126.5 (=CH-), 128.8 (=CH-), 129.8 (=CH-), 133.9 (=C<), 134.1 (=CH-), 135.2 (=C<), 136.7 (=CH-), 137.3 (=CH-), 138.3 (=CH-), 139.0 (=C<), 153.9 (=C<), 167.2 (=C<); ms (EI): *m/z* 301 (M^+, 100), 286 (29), 197 (57), 165 (90).

Anal. Calcd for $C_{20}H_{15}NS$: M, 301.0925; C, 79.70; H, 5.02; N, 4.65. Found: *m/z*, 301.0923; C, 79.45; H, 5.01; N, 4.58.

Methyl 3-(2-Methylthiazol-4-yl)azulene-1-carboxylate (**5a**).

This compound was obtained as green needles (from benzene) in a yield of 110 mg (77%); mp 106-108 °C; ir (KBr): ν 1650 cm^{-1} (C=O); ^1H nmr ($CDCl_3$): δ 2.82 (3H, s, 2'-CH_3), 3.96 (3H, s, $COOCH_3$), 7.29 (1H, s, 5'-H), 7.48 (1H, dd, *J* = 9.8, 9.8 Hz, 5-H), 7.51 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.78 (1H, dd, *J* = 9.9. 9.8 Hz, 6-H). 8.63 (1H, s, 2-H), 9.45 (1H, d, *J* = 9.9 Hz, 4-H), 9.64 (1H, d, *J* = 9.9 Hz, 8-H); ^{13}C nmr ($CDCl_3$): δ 19.4 (2-CH_3) 51.1 (COO*C*H_3), 113.2 (=CH-), 115.7 (=C<), 122.8 (=C<), 125.7 (=CH-), 128.0 (=CH-), 138.1 (=CH-), 138.6 (=CH-), 138.7 (=C<), 139.6 (=CH-), 139.9 (=CH-), 141.9 (=C<), 151.6 (=C<), 165.4 (=C<), 165.5 (C=O); ms (EI): *m/z* 283 (M^+, 100), 252 (20), 224 (16), 183 (11), 139 (12).

Anal. Calcd for $C_{16}H_{13}NO_2S$: M, 283.0667; C, 67.82; H, 4.62; N, 4.94. Found: *m/z*, 283.0663; C, 68.02; H, 4.84; N, 4.73.

Methyl 3-(2-Phenylthiazol-4-yl)azulene-1-carboxylate (**5b**).

This compound was obtained as green needles (from benzene) in a yield of 171 mg (99%); mp 123-124 °C; ir (KBr): ν 1693 cm^{-1} (C=O); ^1H nmr ($CDCl_3$): δ 3.99 (3H, s, $COOCH_3$), 7.26 (1H, s, 5'-H), 7.46-7.52 (4H, m), 7.56 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.84 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.08-8.11 (2H, m), 8.72 (1H, s, 2-H), 9.68 (1H, d, *J* = 9.9 Hz, 4-H), 9.70 (1H, d, *J* = 9.9 Hz, 8-H); ^{13}C nmr ($CDCl_3$): δ 51.2 ($COO\mathit{C}H_3$), 113.7 (=CH-), 115.9 (=C<), 122.7 (=C<), 126.6 (=CH-), 127.8 (=CH-), 128.2 (=CH-), 129.0 (=CH-), 130.0 (=CH-), 133.8 (=C<), 138.3 (=CH-), 139.0 (=CH-), 139.7 (=CH-), 140.0 (=CH-), 140.1 (=C<), 142.2 (=C<), 153.1 (=C<), 165.7 (=C<), 167.7 (C=O); ms (EI): *m/z* 345 (M^+, 100), 314 (12), 286 (18), 211 (10), 183 (16), 139 (19).

Anal. Calcd for $C_{21}H_{15}NO_2S$: M, 345.0823; C, 73.02; H, 4.38; N, 4.06. Found: *m/z*, 345.0827; C, 72.80; H, 4.31; N, 4.15.

Reactions of Bromoacetyl-substituted Azulenes **1a,b** with Thioureas **3c,d**.

General Procedure.

A solution of 1-(bromoacetyl)-3-methylazulene (**1a**) (132 mg, 0.5 mmol) or methyl 3-(bromoacetyl)azulene-1-carboxylate (**1b**) (154 mg, 0.5 mmol) and thiourea (**3c**,**d**) (0.75 mmol) in ethanol (10 ml) was refluxed for 1 hour in the presence of Molecular Sieves 4A (300 mg). The reaction mixture was quenched with a saturated sodium hydrogencarbonate solution and extracted with ethyl acetate. The evaporation residue was chromatographed on a Kieselgel 60 column (20 g) with chloroform to give (4-thiazolyl)azulenes **4c**,**d** and **5c**,**d**, respectively.

1-Methyl-3-(2-aminothiazol-4-yl)azulene (**4c**).

This compound was obtained as green crystals (from benzene) in a yield of 110 mg (92%); mp 144-146 °C; ir (KBr): ν 3449 (NH), 3258 cm^{-1} (NH); ^1H nmr ($CDCl_3$): δ 2.60 (3H, s, CH_3), 6.87 (1H, s, 5'-H), 7.01 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.04 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.08 (2H, s, NH_2), 7.53 (1H, dd, *J* = 9.9. 9.8 Hz, 6-H), 8.05 (1H, s, 2-H), 8.17 (1H, d, *J* = 9.9 Hz, 4-H), 9.39 (1H, d, *J* = 9.9 Hz, 8-H); ^{13}C nmr ($CDCl_3$): δ 12.3 (CH_3), 101.0 (=CH-), 121.8 (=CH-), 121.9 (=CH-), 122.1 (=C<), 125.0 (=C<), 133.4 (=C<), 133.9 (=CH-), 136.7 (=CH-), 136.9 (=CH-), 138.3 (=C<), 139.5 (=CH-), 147.8 (=C<), 167.8 (=C<); ms (EI): *m/z* 240 (M^+, 100), 225 (10), 197 (13), 165 (18).

Anal. Calcd for $C_{14}H_{12}N_2S$: M, 240.0721; C, 69.97; H, 5.03; N, 11.66. Found: *m/z*, 240.0682; C, 69.77; H, 5.27; N, 11.55.

1-Methyl–3-[2-(methylamino)thiazol-4-yl]azulene (**4d**).

This compound was obtained as green crystals (from benzene) in a yield of 91 mg (72%); mp 123-126 °C; ir (KBr): ν 3364 cm^{-1} (NH); ^1H nmr ($CDCl_3$): δ 2.63 (3H, s, 1-CH_3), 2.73 (3H, s, NHCH_3), 6.54 (1H, s, 5'-H), 6.74 (1H, br, NH), 6.98 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 6.99 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.44 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 7.97 (1H, s, 2-H), 8.11 (1H, d, *J* = 9.8 Hz, 8-H), 9.03 (1H, d, *J* = 9.9 Hz, 4-H); ^{13}C nmr ($CDCl_3$): δ 12.5 (3-CH_3), 32.0 (NH$\mathit{C}H_3$), 100.4 (=CH-), 121.7 (=CH-), 122.5 (=CH-), 122.7 (=C<), 125.4 (=C<), 134.5 (=C<), 133.8 (=CH-), 136.2 (=CH-), 137.5 (=CH-), 138.0 (=CH-), 138.5 (=C<), 148.7 (=C<), 171.0 (=C<); ms (EI): *m/z* 254 (M^+, 100), 197 (26), 165 (43).

Anal. Calcd for $C_{15}H_{14}N_2S$: M, 254.0878; C, 70.83; H, 5.55; N, 11.01. Found: *m/z*, 254.0874; C, 70.71; H, 5.56; N, 10.83.

Methyl 3-(2-Aminothiazol-4-yl)azulene-1-carboxylate (**5c**).

This compound was obtained as green crystals (from benzene) in a yield of 107 mg (75%); mp 237-238 °C; ir (KBr): ν 3350 (NH), 3297 (NH), 1691 cm^{-1} (C=O); ^1H nmr ($CDCl_3$): δ 3.91 (3H, s, $COOCH_3$), 7.01 (1H, s, 5'-H), 7.19 (2H, br, NH_2), 7.57 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.62 (1H, dd, *J* = 9.8, 9.8 Hz, 7-H), 7.94 (1H, dd, *J* = 9.9. 9.8 Hz, 6-H), 8.65 (1H, s, 2-H), 9.51 (1H, d, *J* = 9.9 Hz, 4-H), 9.73 (1H, d, *J* = 9.9 Hz, 8-H); ^{13}C nmr ($CDCl_3$): δ 51.1 ($COO\mathit{C}H_3$), 102.4 (=CH-), 114.8 (=C<), 121.9 (=CH-), 123.4 (=C<), 127.3 (=CH-), 128.0 (=CH-), 137.4 (=CH-), 138.3 (=C<), 138.8 (=CH-), 139.3 (=CH-), 141.0 (=C<), 146.7 (=C<), 164.7 (=C<), 168.2 (C=O); ms (EI): *m/z* 284 (M^+, 100), 253 (23), 115 (32), 183 (18), 139 (29).

Anal. Calcd for $C_{15}H_{12}N_2O_2S$: M, 284.0619; C, 63.36; H, 4.26; N, 9.85. Found: *m/z*, 284.0642; C, 63.59; H, 4.19; N, 9.85.

Methyl 3-[2-(Methylamino)thiazol-4-yl]azulene-1-carboxylate (**5d**).

This compound was obtained as green needles (from benzene) in a yield of 143 mg (96%); mp 88-89 °C; ir (KBr): ν 3204 (NH), 1703 cm^{-1} (C=O); ^1H nmr ($CDCl_3$): δ 2.82 (3H, s, NHCH_3), 3.96 (3H, s, $COOCH_3$), 6.48 (1H, br, NH), 6.65 (1H, s, 5'-H), 7.43 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.49 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.76 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.60 (1H, s, 2-H), 9.37 (1H, d, *J* = 9.8 Hz, 4-H), 9.63 (1H, d, *J* = 9.9 Hz, 8-H); ^{13}C nmr ($CDCl_3$): δ 32.0 ($NHCH_3$), 51.1 ($COO\mathit{C}H_3$), 101.7 (=CH-), 115.6 (=C<), 123.8 (=C<), 127.1 (=CH-), 127.8 (=CH-), 138.0 (=CH-), 138.5 (=CH-), 139.6 (=CH-), 139.8 (=CH-), 139.9 (=C<), 141.8 (=C<), 148.0 (=C<), 165.7 (=C<), 171.1 (C=O); ms (EI): *m/z* 298 (M^+, 100), 267 (11), 239 (26).

Anal. Calcd for $C_{16}H_{14}N_2O_2S$: M, 298.0775; C, 64.41; H, 4.73; N, 9.39. Found: *m/z*, 298.0742; C, 64.48; H, 4.66; N, 9.18.

Reactions of Methyl 3-(Dibromoacetyl)azulene-1-carboxylate (**2**) with Thioamides **3a,b** and *N*-Methylthiourea (**3d**).

a) A solution of methyl 3-(dibromoacetyl)azulene-1-carboxylate (**2**) (77 mg, 0.2 mmol) and thioacetamide (**3a**) (23 mg, 0.3 mmol) in ethanol (10 ml) was refluxed for 24 hours. The reaction mixture was diluted with water and extracted with chloroform. The evaporation residue was chromatographed on a Kieselgel 60 column (20 g) with benzene to give methyl 3-(2-methylthiazol-4-yl)azulene-1-carboxylate (**5a**) (20 mg, 36%) and **2** (33 mg, 43%).

b) The reaction of **2** (77 mg, 0.2 mmol) and thiobenzamide (**3b**) (41 mg, 0.3 mmol) in ethanol (10 ml) was carried out and worked up, as described above, to give methyl 3-(2-phenylthiazol-4-yl)azulene-1-carboxylate (**5b**) (18 mg, 26%) and **2** (37 mg, 48%).

c) The reaction of **2** (77 mg, 0.2 mmol) and 1-methyl-2-thiourea (**3d**) (27 mg, 0.3 mmol) in ethanol (10 ml) was carried out and worked up, as described above, to give methyl 3-[2-(methylamino)thiazol-4-yl)azulene-1-carboxylate (**5d**) (27 mg, 46%) and **2** (21 mg, 27%).

Hydrolysis and Decarboxylation of Methyl 3-(4-Thiazolyl)azulene-1-carboxylates **5a-d**.

General Procedure.

A suspension of methyl 3-(4-thiazolyl)azulene-1-carboxylate **5a-d** (0.5 mmol) in 100% phosphoric acid (2.5 ml) was heated for 15 minutes at 100 °C. The reaction mixture was diluted with

water (60 ml) and extracted with chloroform. The extract was washed with water and brine, and dried over sodium sulfate. The evaporation residue was chromatographed on a Kieselgel 60 column (15 g) with chloroform to give 1-(4-thiazolyl)azulenes **6a**-**d**.

1-(2-Methylthiazol-4-yl)azulene (**6a**).

This compound was obtained as green oil in a yield of 108 mg (96%); ^{1}H nmr ($CDCl_3$): δ 2.82 (3H, s, CH_3), 7.13 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.18 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.24 (1H, s, 5'-H), 7.38 (1H, d, *J* = 4.1 Hz, 3-H), 7.58 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.18 (1H, d, *J* = 4.1 Hz, 2-H), 8.29 (1H, d, *J* = 9.9 Hz, 4-H), 9.27 (1H, d, *J* = 9.9 Hz, 8-H); ^{13}C nmr ($CDCl_3$): δ 19.4 (CH_3), 112.2 (=CH-), 117.8 (=CH-), 123.5 (=CH-), 123.6 (=C<), 123.8 (=CH-), 135.2 (=C<), 136.6 (=CH-), 136.9 (=CH-), 137.2 (=CH-), 138.3 (=CH-), 142.3 (=C<), 152.6 (=C<), 165.2 (=C<); ms (EI): *m/z* 225 (M^+, 100), 184 (95), 139 (68).

Anal. Calcd for $C_{14}H_{11}NS$: M, 225.0612. Found: *m/z*, 225.0636.

1-(2-Phenylthiazol-4-yl)azulene (**6b**).

This compound was obtained as green crystals (from benzene) in a yield of 130 mg (90%); mp 52-53 °C; ^{1}H nmr ($CDCl_3$): δ 7.11 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.23 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.35 (1H, s, 5'-H), 7.37 (1H, d, *J* = 3.9 Hz, 3-H), 7.39-7.47 (3H, m), 7.56 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.06-8.09 (2H, m), 8.21 (1H, d, *J* = 3.9 Hz, 2-H), 8.27 (1H, d, *J* = 9.9 Hz, 4-H), 9.51 (1H, d, *J* = 9.9 Hz, 8-H); ^{13}C nmr ($CDCl_3$): δ 112.6 (=CH-), 117.9 (=CH-), 123.2 (=C<), 123.6 (=CH-), 124.0 (=CH-), 126.5 (=CH-), 128.8 (=CH-), 129.8 (=CH-), 133.9 (=C<), 135.1 (=C<), 136.4 (=CH-), 137.2 (=CH-), 137.3 (=CH-), 138.4 (=CH-), 142.4 (=C<), 154.0 (=C<), 167.3 (=C<); ms (EI): *m/z* 287 (M^+, 100), 184 (97), 139 (77).

Anal. Calcd for $C_{19}H_{13}NS$: M, 287.0769; C, 79.41; H, 4.56; N, 4.87. Found: *m/z*, 287.0765; C, 79.15; H, 4.45; N, 4.91.

1-(2-Aminothiazol-4-yl)azulene (**6c**).

This compound was obtained as green crystals (from benzene) in a yield of 89 mg (79%); mp 136-137 °C; ir (KBr): ν 3425 (NH), 3256 cm^{-1} (NH); ^{1}H nmr ($CDCl_3$): δ 5.43 (2H, br, NH_2), 6.62 (1H, s, 5'-H), 7.13 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.18 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.36 (1H, d, *J* = 3.9 Hz, 3-H), 7.57 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.12 (1H, d, *J* = 3.9 Hz, 2-H), 8.28 (1H, d, *J* = 9.9 Hz, 4-H), 9.13 (1H, d, *J* = 9.9 Hz, 8-H); ^{13}C nmr ($CDCl_3$): δ 102.4 (=CH-), 117.7 (=CH-), 123.5 (=CH-), 123.5 (=CH-), 123.6 (=CH-), 123.7 (=C<), 135.2 (=C<), 136.5 (=CH-), 137.2 (=CH-), 138.3 (=CH-), 142.2 (=C<), 148.2 (=C<), 167.5 (=C<); ms (EI): *m/z* 287 (M^+, 100), 184 (97), 139 (77).

Anal. Calcd for $C_{13}H_{10}N_2S$: M, 226.0565; C, 69.00; H, 4.45; N, 12.38. Found: *m/z*, 226.0531; C, 68.87; H, 4.53; N, 12.21.

1-[2-(Methylamino)thiazol-4-yl)azulene (**6d**).

This compound was obtained as green crystals (from benzene) in a yield of 54 mg (46%); mp 105-106 °C; ir (KBr): ν3193 cm^{-1} (NH); ^{1}H nmr ($CDCl_3$): δ 2.86 (3H, s, CH_3), 6.10 (1H, br, NH), 6.63 (1H, s, 5'-H), 7.11 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.17 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.36 (1H, d, *J* = 4.1 Hz, 3-H), 7.56 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.15 (1H, d, *J* = 4.1 Hz, 2-H), 8.27 (1H, d, *J* = 9.9 Hz, 4-H), 9.23 (1H, d, *J* = 9.9 Hz, 8-H); ^{13}C nmr ($CDCl_3$): δ 32.1 (CH_3), 100.8 (=CH-), 117.6 (=CH-), 123.3 (=CH-), 123.4 (=CH-), 124.3 (=C<), 135.1 (=C<), 136.5 (=CH-), 136.9 (=CH-), 137.0 (=CH-), 138.2 (=CH-), 142.2 (=C<), 149.0 (=C<), 170.8 (=C<); ms (EI): *m/z* 240 (M^+, 38), 152 (13), 44 (100).

Anal. Calcd for $C_{14}H_{12}N_2S$: M, 240.0721; C, 69.97; H, 5.03; N, 11.66. Found: *m/z*, 240.0736; C, 69.82; H, 4.92; N, 11.85.

Reactions of 1-(Bromoacetyl)azulene **1a** with Thiosemicarbazones **7a**-**f**.

General Procedure.

A solution of 1-(bromoacetyl)azulene **1a** (132 mg, 0.5 mmol) and thiosemicarbazone **7a**-**f** (0.75 mmol) in ethanol (10 ml) was refluxed for 1 hour. The precipitate was collected and heated for 30 minutes in boiling trimethyl orthoformate (2 ml). After removal of the ortho ester under reduced pressure, the residure was washed with methanol to give 1-methyl-3-[2-(alkylidenehydrazino)thiazol-4-yl]azulenes **8a**-**f**.

1-Methyl-3-[2-(1-methylethylidenehydrazino)thiazol-4-yl]azulene (**8a**).

This compound was obtained by using acetone thiosemicarbazone (**7a**) as deep green needles in a yield of 76 mg (51%); mp 124-124 °C; ir (KBr): ν 2914 (NH), 1563 cm^{-1} (C=N); ^{1}H nmr (DMSO-d_6): δ 1.96 [6H, s, =C(CH_3)$_2$], 2.59 (3H, s, 1-CH_3), 7.03 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.04 (1H, s, 5'-H), 7.05 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.54 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.06 (1H, s, 2-H), 8.19 (1H, d, *J* = 9.9 Hz, 4-H), 9.37 (1H, d, *J* = 9.9 Hz, 8-H), 10.58 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 12.4 (3-CH_3), 17.7 (CH_3), 24.9 (CH_3), 102.7 (=CH-), 112.3 (=C<), 122.0 (=CH-), 122.1 (=CH-), 125.1 (=C<), 133.6 (=C<), 134.1 (=CH-), 136.5 (=C<), 136.9 (=CH-), 136.9 (=C<), 138.4 (=CH-), 138.6 (=C<), 149.5 (=C<), 169.6 (=C<).

Anal. Calcd for $C_{17}H_{17}N_3S$: C, 69.12; H, 5.80; N, 14.22. Found: C, 68.84; H, 5.77; N, 13.99.

1-Methyl-3-[2-(cyclopentylidenehydrazino)thiazol-4-yl]azulene (**8b**).

This compound was obtained by using cyclopentanone thiosemicarbazone (**7b**) as deep green needles in a yield of 77 mg (48%); mp 65 °C; ir (KBr): ν 2945 (NH), 1562 cm^{-1} (C=N); ^{1}H nmr (DMSO-d_6): δ 1.67-1.80 (4H, m, 3"-CH_2 + 4"- CH_2), 2.35-2.42 (4H, m, 2"-CH_2 + 5"-CH_2), 2.59 (3H, s, CH_3), 7.00-7.08 (3H, m, 5-,7-, 5'-H), 7.54 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.06 (1H, s, 2-H), 8.17 (1H, d, *J* = 9.9 Hz, 8-H), 9.37 (1H, d, *J* = 9.9 Hz, 4-H), 10.52 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 12.4 (CH_3), 24.6 (CH_2 x 2), 28.7 (CH_2), 32.8 (CH_2), 102.6 (=CH-), 111.6 (=C<), 122.0 (=CH-), 122.1 (=CH-), 125.1 (=C<), 133.6 (=C<), 134.1 (=CH-), 135.8 (=C<), 136.9 (=CH-), 138.4 (=C<), 138.6 (=CH-), 148.4 (=C<), 161.4 (=C<), 169.6 (=C<).

Anal. Calcd for $C_{19}H_{19}N_3S$: C, 70.99; H, 5.96; N, 13.07. Found: C, 70.69; H, 5.96; N, 12.93.

1-Methyl-3-[2-(benzylidenehydrazino)thiazol-4-yl]azulene (**8c**).

This compound was obtained by using benzaldehyde thiosemicarbazone (**7c**) as deep green needles in a yield of 87 mg (51%); mp 117-119 °C; ir (KBr): ν 2840 (NH), 1575 cm^{-1} (C=N); ^{1}H nmr (DMSO-d_6): δ 2.60 (3H, s, CH_3), 7.06 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.11 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.15 (1H, s, 5'-H), 7.37 –7.45 (3H, m, 3"-,4"-,5"-H), 7.56 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 7.66 (2H, d, *J* = 8.4 Hz, 2"-, 6"-H), 8.05 (1H, s, N=CH), 8.09 (1H, s, 2-H), 8.20 (1H, d, *J* = 9.6 Hz, 4-H), 9.35 (1H, d, *J* = 9.8 Hz, 8-H), 12.19 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 12.4 (CH_3), 103.1 (=CH-), 114.0 (=C<), 121.9 (=C<), 122.2 (=CH-), 122.3 (=CH-), 125.3 (=C<), 126.2 (=CH-), 128.9 (=CH-), 129.2 (=CH-), 133.7 (=C<), 134.3 (=CH-), 134.5 (=C<), 136.8 (=CH-),

137.0 (=CH-), 138.6 (=CH-), 138.7 (=C<), 141.0 (=CH-), 167.9 (=C<).

Anal. Calcd for $C_{21}H_{17}N_3S$: C, 73.44; H, 4.99; N, 12.23. Found: C, 73.01; H, 5.04; N, 11.98.

1-Methyl-3-[2-(4-methylbenzylidenehydrazino)thiazol-4-yl]azulene (**8d**).

This compound was obtained by using 4-methylbenzaldehyde thiosemicarbazone (**7d**) as deep green needles in a yield of 131 mg (73%); mp 207-209 °C; ir (KBr): ν 2837 (NH), 1570 cm^{-1} (C=N); ^1H nmr (DMSO-d_6): δ 2.31 (3H, s, 4"-CH_3), 2.60 (3H, s, 1-CH_3), 7.02-7.62 (8H, m), 8.02 (1H, s, N=CH), 8.08 (1H, s, 2-H), 8.18 (1H, d, *J* = 9.9 Hz, 8-H), 9.36 (1H, d, *J* = 9.9 Hz, 4-H), 12.11 (1H, br, NH).

Anal. Calcd for $C_{22}H_{19}N_3S$: C, 73.92; H, 5.36; N, 11.75. Found: C, 73.77; H, 5.63; N, 12.02.

1-Methyl-3-[2-(4-nitrobenzylidenehydrazino)thiazol-4-yl]azulene (**8e**).

This compound was obtained by using 4-nitrobenzaldehyde thiosemicarbazone (**7e**) as brown micro-crystals in a yield of 129 mg (66%); mp 222-224 °C; ir (KBr): ν 2873 (NH), 1563 cm^{-1} (C=N); ^1H nmr (DMSO-d_6): δ 2.60 (3H, s, CH_3), 7.07 (1H, dd, *J* = 9.8, 9.8 Hz, 7-H), 7.08 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.21 (1H, s, 5'-H), 7.57 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 7.87 (2H, d, *J* = 8.6 Hz, 2"-,6"-H), 8.08 (1H, s, 2-H), 8.12 (1H, s, N=CH), 8.20 (1H, d, *J* = 9.9 Hz, 8-H), 8.24 (2H, d, *J* = 8.6 Hz, 3"-,5"-H), 9.33 (1H, d, *J* = 9.9 Hz, 4-H), 12.59 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 12.4 (CH_3), 103.8 (=CH-), 121.6 (=C<), 122.3 (=CH-), 122.5 (=CH-), 124.2 (=CH-), 125.3 (=C<), 126.9 (=CH-), 133.8 (=C<), 134.3 (=CH-), 136.7 (=CH-), 137.0 (=CH-), 138.4 (=CH-), 138.6 (=C<), 138.8 (=C<), 139.6 (=C<), 140.9 (=C<), 147.0 (=C<), 167.4 (=C<).

Anal. Calcd for $C_{21}H_{16}N_4O_2S$: C, 64.93; H, 4.15; N, 14.42. Found: C, 64.99; H, 4.29; N, 14.12.

1-Methyl-3-[2-(1-phenylethylidenehydrazino)thiazol-4-yl]-azulene (**8f**).

This compound was obtained by using acetophenone thiosemicarbazone (**7f**) as deep green needles in a yield of 160 mg (90%); mp 149-150 °C; ir (KBr): ν 2915 (NH), 1556 cm^{-1} (C=N); ^1H nmr (DMSO-d_6): δ 2.35 (3H, s, N=CCH_3), 2.60 (3H, s, CH_3), 7.07 (2H, dd, *J* = 9.9, 9.8 Hz, 5-,7-H), 7.13 (1H, s, 5'-H), 7.37-7.44 (3H, m, 3"-,4"-,5"-H), 7.56 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 7.80 (2H, d, *J* = 6.9 Hz, 2"-,6"-H), 8.09 (1H, s, 2-H), 8.19 (1H, d, *J* = 9.9 Hz, 8-H), 9.39 (1H, d, *J* = 9.9 Hz, 4-H), 11.20 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 12.4 (3-CH_3), 14.0 (N=CCH_3), 103.5 (=CH-), 122.0 (=CH-), 122.1 (=C<), 122.3 (=CH-), 125.2 (=C<), 125.6 (=CH-), 128.4 (=CH-), 128.6 (=CH-), 133.7 (=C<), 134.2 (=CH-), 136.9 (=CH-), 137.0 (=CH-), 138.0 (=C<), 138.7 (=CH-), 146.2 (=C<), 169.5 (=C<).

Anal. Calcd for $C_{22}H_{19}N_3S$: C, 73.92; H, 5.36; N, 11.75. Found: C, 74.10; H, 5.41; N, 11.63.

Reactions of 1-(Bromoacetyl)azulene **1b** with Thiosemicarbazones **7a**-**f**.

General Procedure.

The reactions of 1-(bromoacetyl)azulene **1b** (154 mg, 0.5 mmol) and thiosemicarbazone **7a**-**f** (0.75 mmol) in ethanol (10 ml) was also carried out under reflux for 30 minutes, as described above. The precipitate was collected and heated for 30 minutes in boiling trimethyl orthoformate (2 ml). After removal of the ortho ester under reduced pressure, the residue was washed with methanol to give methyl 3-[2-(alkylidenehydrazino)thiazol-4-yl]azulene-1-carboxylates **9a**-**f**.

Methyl 3-[2-(1-Methylethylidenehydrazino)thiazol-4-yl]azulene-1-carboxylate (**9a**).

This compound was obtained by using acetone thiosemicarbazone (**9a**) as deep green needles in a yield of 100 mg (59%); mp 157-159 °C; ir (KBr): ν 2090 (NH), 1699 (C=O), 1562 cm^{-1} (C=N); ^1H nmr (DMSO-d_6): δ 1.96 [6H, s, =C(CH_3)$_2$], 3.87 (3H, s, 3-$COOCH_3$), 7.25 (1H, s, 5'-H), 7.57 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.61 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.93 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.62 (1H, s, 2-H), 9.49 (1H, d, *J* = 9.9 Hz, 4-H), 9.68 (1H, d, *J* = 9.9 Hz, 8-H), 10.66 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 17.7 (CH_3), 24.8 (CH_3), 51.1 (COO*C*H_3), 104.1 (=CH-), 114.9 (=C<), 123.4 (=C<), 127.5 (=CH-), 128.1 (=CH-), 137.5 (=CH-), 138.3 (=C<), 138.9 (=CH-), 139.2 (=CH-), 140.9 (=CH-), 141.0 (=C<), 147.1 (=C<), 149.7 (=C<), 164.7 (=C<), 169.8 (C=O).

Anal. Calcd for $C_{18}H_{17}N_3O_2S$: C, 63.70; H, 5.05; N, 12.38. Found: C, 63.52; H, 4.80; N, 12.15.

Methyl 3-[2-(Cyclopentylidenehydrazino)thiazol-4-yl]azulene-1-carboxylate (**9b**).

This compound was obtained by using cyclopentanone thiosemicarbazone (**9b**) as deep green micro-crystals in a yield of 154 mg (84%); mp 190-191 °C; ir (KBr): ν 2947 (NH), 1678 (C=O), 1568 cm^{-1} (C=N); ^1H nmr (DMSO-d_6): δ 1.67-1.81 (4H, m, 3"-CH_2 + 4"-CH_2), 2.35-2.42 (4H, m, 2"-CH_2 + 5"-CH_2), 3.87 (3H, s, $COOCH_3$), 7.25 (1H, s, 5'-H), 7.57 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.62 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.94 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.65 (1H, s, 2-H), 9.49 (1H, d, *J* = 9.9 Hz, 4-H), 9.68 (1H, d, *J* = 9.9 Hz, 8-H), 10.59 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 24.6 (CH_2 x 2), 28.7 (CH_2), 32.9 (CH_2), 51.1 (COO*C*H_3), 104.0 (=CH-), 114.9 (=C<), 123.4 (=C<), 127.5 (=CH-), 128.2 (=CH-), 137.5 (=CH-), 138.3 (=C<), 138.9 (=CH-), 139.2 (=C<), 140.9 (=CH-), 141.1 (=C<), 147.2 (=CH-), 161.6 (=C<), 164.7 (=C<), 169.6 (C=O).

Anal. Calcd for $C_{20}H_{19}N_3O_2S$: C, 65.73; H, 5.24; N, 11.50. Found: C, 65.51; H, 5.20; N, 11.31.

Methyl 3-[2-(Benzylidenehydrazino)thiazol-4-yl]azulene-1-carboxylate (**9c**).

This compound was obtained by using benzaldehyde thiosemicarbazone (**9c**) as deep green needles in a yield of 120 mg (62%); mp 175-177 °C; ir (KBr): ν 1677 (C=O), 1561 cm^{-1} (C=N); ^1H nmr (DMSO-d_6): δ 3.89 (3H, s, $COOCH_3$), 7.34 (1H, s, 5'-H), 7.36-7.74 (7H, m, 5-,7-H + Ph), 7.95 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.07 (1H, s, N=CH), 8.66 (1H, s, 2-H), 9.51 (1H, d, *J* = 9.9 Hz, 4-H), 9.35 (1H, d, *J* = 9.9 Hz, 8-H), 12.21 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 51.1 (COO*C*H_3), 104.5 (=CH-), 114.9 (=C<), 123.0 (=C<), 126.2 (=CH-), 127.6 (=CH-), 128.3 (=CH-), 128.8 (=CH-), 129.2 (=CH-), 134.4 (=C<), 137.6 (=CH-), 138.4 (=C<), 138.9 (=CH-), 139.0 (=CH-), 141.0 (=CH-), 141.1 (=C<), 141.2 (=CH-), 147.3 (=C<), 164.7 (=C<), 168.1 (C=O).

Anal. Calcd for $C_{22}H_{17}N_3O_2S$: C, 68.20; H, 4.42; N, 10.84. Found: C, 68.12; H, 4.49; N, 10.65.

Methyl 3-[2-(4-Methylbenzylidenehydrazino)thiazol-4-yl]azulene-1-carboxylate (**9d**).

This compound was obtained by using 4-methylbenzaldehyde thiosemicarbazone (**9d**) as deep green needles in a yield of 105 mg (52%); mp 193-195 °C; ir (KBr): ν 2045 (NH), 1693 (C=O), 1582 cm^{-1} (C=N); ^1H nmr (DMSO-d_6): δ 2.32 (3H, s, 4"-CH_3), 3.88 (3H, s, $COOCH_3$), 7.23 (2H, d, *J* = 7.8 Hz, 3"-,5"-H), 7.34 (1H, s, 5'-H), 7.54-7.67 (4H, m, 5-,7-,2"-,6"-H), 7.96 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.02 (1H, s, N=CH), 8.66 (1H, s, 2-H), 9.51 (1H, d, *J* = 9.8 Hz, 4-H), 9.66 (1H, d, *J* = 9.9 Hz, 8-H), 12.14 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 20.9 (4"-CH_3), 51.1 ($COOCH_3$), 104.4 (=CH-), 114.9 (=C<), 123.1 (=C<), 126.2 (=CH-), 127.5 (=CH-), 128.3 (=CH-), 129.4 (=CH-), 129.5 (=C<), 131.7 (=C<), 137.6 (=CH-), 138.3 (=C<), 138.9 (=C<), 139.0 (=CH-), 139.1 (=CH-), 141.0 (=CH-), 141.1 (=C<), 141.4 (=CH-), 164.7 (=C<), 168.1 (C=O).

Anal. Calcd for $C_{23}H_{19}N_3O_2S$: C, 68.81; H, 4.77; N, 10.47. Found: C, 68.53; H, 4.91; N, 10.25.

Methyl 3-[2-(4-Nitrobenzylidenehydrazino)thiazol-4-yl]azulene-1-carboxylate (**9e**).

This compound was obtained by using 4-nitrobenzaldehyde thiosemicarbazone (**9e**) as brown micro-crystals in a yield of 212 mg (98%); mp 254-256 °C; ir (KBr): ν 1667 (C=O), 1565 cm^{-1} (C=N); ^1H nmr (DMSO-d_6): δ 3.88 (3H, s, $COOCH_3$), 7.41 (1H, s, 5'-H), 7.59 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.64 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.85 (2H, d, *J* = 8.6 Hz, 2"-,6"-H), 7.95 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.11 (1H, s, N=CH), 8.23 (2H, d, *J* = 8.3 Hz, 3"-,5"-H), 8.64 (1H, s, 2-H), 9.50 (1H, d, *J* = 9.9 Hz, 4-H), 9.62 (1H, d, *J* = 9.9 Hz, 8-H), 12.63 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 51.1 ($COOCH_3$), 105.2 (=CH-), 115.0 (=C<), 122.8 (=C<), 124.1 (=CH-), 126.9 (=CH-), 127.6 (=CH-), 128.4 (=CH-), 130.4 (=CH-), 134.2 (=C<), 137.6 (=CH-), 138.4 (=C<), 138.6 (=CH-), 139.0 (=CH-), 140.8 (=C<), 141.0 (=CH-), 141.1 (=C<), 147.0 (=C<), 164.6 (=C<), 167.6 (C=O).

Anal. Calcd for $C_{22}H_{16}N_4O_4S$: C, 61.10; H, 3.73; N, 12.96. Found: C, 60.95; H, 3.41; N, 12.72.

Methyl 3-[2-(1-Phenylethylidenehydrazino)thiazol-4-yl]azulene-1-carboxylate (**9f**).

This compound was obtained by using acetophenone thiosemicarbazone (**9f**) as deep green needles in a yield of 149 mg (74%); mp 172-174 °C; ir (KBr): ν 2945 (NH), 1694 (C=O), 1544 cm^{-1} (C=N); ^1H nmr (DMSO-d_6): δ 2.35 (3H, s, N=CCH_3), 3.88 (3H, s, $COOCH_3$), 7.34 (1H, s, 5'-H), 7.36-7.44 (3H, m, 3"-,4"-,5"-H), 7.59 (1H, dd, *J* = 9.9, 9.8 Hz, 5-H), 7.63 (1H, dd, *J* = 9.9, 9.8 Hz, 7-H), 7.79 (2H, d, *J* = 7.5 Hz, 2"-,6"-H), 7.95 (1H, dd, *J* = 9.9, 9.8 Hz, 6-H), 8.67 (1H, s, 2-H), 9.51 (1H, d, *J* = 9.9 Hz, 4-H), 9.69 (1H, d, *J* = 9.9 Hz, 8-H), 11.26 (1H, br, NH); ^{13}C nmr (DMSO-d_6): δ 14.0 (N=CCH_3), 51.1 ($COOCH_3$), 104.9 (=CH-), 123.2 (=C<), 125.7 (=CH-), 127.6 (=CH-), 128.3 (=CH-), 128.4 (=CH-), 128.5 (=CH-), 128.7 (=CH-), 137.5 (=CH-), 137.7 (=C<), 138.3 (=C<), 139.0 (=C<), 139.1 (=CH-), 141.0 (=CH-), 141.1 (=C<), 146.4 (=C<), 164.7 (=C<), 169.7 (C=O).

Anal. Calcd for $C_{23}H_{19}N_3O_2S$: C, 68.81; H, 4.77; N, 10.47. Found: C, 68.80; H, 4.57; N, 10.52.

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