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A simple synthesis of azuleno[1,2-*c*]thiophenes by reactions of 1-acyl-2-(bromomethyl)azulenes with thioamides

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Azuleno[1,2-*c*]thiophenes are obtained by using simple method from 1-acyl-2-(bromomethyl)azulene prepared from acylation and bromination of 2-methylazulene in good yields.

Keywords: Acylation, bromination, synthesis, azulene, azulenothiophene

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Azulenothiophenes, which are polycyclic aromatic compounds containing a thiophene ring, are of interest in the physical properties and chemical behaviours. All three isomers of azulenothiophenes, which are condensed with thiophene ring at the 1,2-position of azulene are known. Of these isomers, azuleno[1,2-*b*] thiophenes have been synthesized by several methods[1]. Azuleno[2,1-*b*]thiophenes are readily obtained by reacting 2-chloroazulene derivatives with ethyl mercaptoacetate in a few steps in good yield[2,3]. On the other hand, the first synthesis of azuleno[1,2-*c*]thiophenes were accomplished by reacting 3-methoxy-carbonyl-2*H*-cyclohepta[*b*] furan-2-one with morpholino enamine of 3-oxotetrahydrothiophene followed by dehydrogenation in poor yield[1c].

In the chemistry of thiophene-fused heterocycles, it became necessary to synthesize thieno[3,4-*b*]indole and theno[3,4-*b*]furan for biological evalution[4].

On the other hard, these 14π-reaction systems as heteroaromatic intermediates are of practical importance as dienophiles for the region and stereocontrolled anelation of aromatic system and has been applied to efficient syntheses of alkaloids, steroids, and terpenes[5a,5b].

In this paper, a simple method for synthesis of 2-substituted azuleno[1,2-*c*]thiophenes using 2-methylazulenes as stating materials was developed.

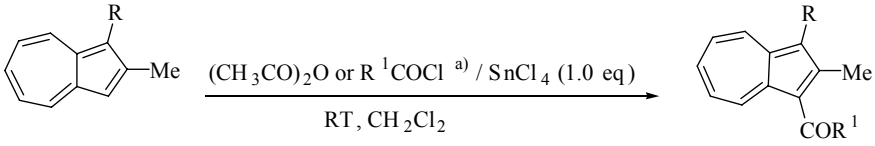
Results and Discussion

Synthesis of 1-acyl-2-methylazulenes. Although 1-acyl-2-methylazulenes have been synthesized by the Friedel-Crafts acylation of 2-methylazulenes **1a**,**b** using acyl chloride, 1-acetyl-2-methylazulenes **2a**,**b** (ref. 2) were prepared using acetic anhydride and stannic chloride in dichloromethane in the yields of 91% and 84% respectively (**Table I**, Entries 1 and 2). Further acylation of **1a**,**b** with acyl chloride under these conditions gave the corresponding 1-acyl-2-methylazulenes **2c**,**d**,**g**,**h** in high yields (Entries 3,4,7,8). However, the reaction using benzoyl chloride gave **2e**,**f** in the yields of 70 and 59% respectively, and the starting materials, 2-methylazulenes **1a**,**b**, were recovered (Entries 5, 6).

Bromination of 1-acyl-2-methylazulenes with NBS. The 1-acyl-2-(bromomethyl)azulenes **3a-h** were synthesized by bromination of 1-acyl-2-methylazulenes **2a-h** with *N*-bromosuccinimide (NBS) in the presence of benzoyl peroxide (BOP). The results are listed in **Table II**.

The reactions were carried out in refluxing carbon tetrachloride in the presence of BOP in a molar ratio of 1:1.2. Methyl 2-methyl-1-propionylazulene-3-carboxylate **2c** was reacted with NBS and in the presence of BOP to give methyl 2-(bromomethyl)-1-propionylazulene-3-carboxylate **3c**, methyl 1-bromo-

Table I — Preparation of 1-acyl-2-methylazulenes

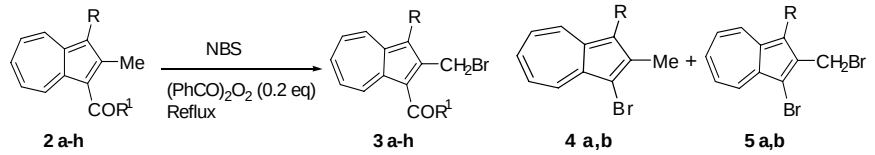


1 a,b **2 a-h**

Entry	R	Reagent	Time (hr)	Yield (%)[b]	Recov (%)
1	**1a** COOMe	$(MeCO)_2O$	2	**2a** 91	
2	**1b** CN	$(MeCO)_2O$	2	**2b** 84	
3	**1a** COOMe	E_tCOCl	12	**2c** 93	
4	**1b** CN	E_tCOCl	12	**2d** 92	
5	**1a** COOMe	PhCOCl	12	**2e** 70	**1a** 27
6	**1b** CN	PhCOCl	12	**2f** 59	**1b** 34
7	**1a** COOMe	PhCH=CHCOCl	1	**2g** 89	
8	**1b** CN	PhCH=CHCOCl	1	**2h** 95	

[a]The reactions were carried out in a 1:2 molar ratio for **1**:R'COCl.
[b] The yield was given for chromagraphically purified material based on **1**.

Table II — Bromination of 1-acyl-2-methylazulenes by NBS



2 a-h **3 a-h** **4 a,b** **5 a,b**

Entry	R	R^1	Molar ratio[a]	Solvent	Time (hr)	Product Yield(%)[b] **3**	**4**	**5**
1	**2a** COOMe	Me	1:2	C_6H_6	0.5	**3a** 76	**4a** 7	**5a** 6
2	**2b** CN	Me	1:2	CCl_4	6	**3b** 78	**4b** 2	**5b** 7
3	**2c** COOMe	Et	1:1.2	CCl_4	2	**3c** 61	**4a** 2	**5a** 22
4	**2d** CN	Et	1:1.2	CCl_4	2	**3d** 59	**4b** 10	**5b** 20
5	**2e** COOMe	Ph	1:1.2	CCl_4	4	**3e** 88		**5b** 4
6	**2f** CN	Ph	1:1.2	CCl_4	4	**3f** 90		
7	**2g** COOMe	CH=CHPh	1:1.2	CCl_4	12	**3g** 76		
8	**2h** CN	CH=CHPh	1:1.2	CCl_4	12	**3h** 64		

[a] **2**:NBS.
[b] The yield was given for chromagraphically purified material based on **2**.

2-methylazulene **4a** and methyl 1-bromo-2-(bromomethyl)azulene-3-carboxylate **5a** in a 61, 2 and 22% yield, respectively (Entry 3). The 3-cyano-2-(bromomethyl)-1-propionyl-azulene **3d** was prepared under a similar condition from 3-cyano-2-methyl-1-propionyl-azulene **2d** in a 59% yield. Furthermore, the deacylated products, 1-bromo-3-cyano-2-methyl-azulene **4b** and 1-bromo-2-(bromomethyl)-3-cyano-azulene **5b**, were also isolated in 10 and 20% yields, respectively (Entry 4). Similarly, 1-acyl-2-(bromomethyl)azulenes **3e-h** were prepared in moderate to high yields (Entries 5-8).

Reactions of 1-acyl-2-(bromomethyl)azulenes with thioamides: **Synthesis of azuleno[1,2-*c*]thiophenes**. The reaction of methyl 1-acetyl-2-(bromomethyl)azulene-3-carboxylate **3a** with thioacetamide **6a** (1.5 mole) under refluxing in ethanol for 1 hr to give methyl 2-methylazuleno[1,2-*c*]thiophene-8-carboxylate **7a** in 88% yield (**Table III**, Entry 1). The structure was confirmed by the spectral data. The IR spectrum showed an ester group at 1682 cm^{-1}. In the ^1H NMR spectrum, a singlet peak for the 2-methyl group at δ 2.80, a singlet peak for the methoxy-carbonyl group at δ 3.94, and three seven-membered

ring protons at 6.87-6.99, 7.56-7.64 and 8.81-8.88 were observed. A singlet peak at δ 7.14 was assigned to 9-H for the thiophene ring.

The reaction with thiobenzamide **6b** for the product **7a** was also given (Entry 2). 8-cyano-2-methylazuleno [1,2-*c*]thiophene **7b** was prepared by reacting 1-acetyl-2-(bromomethyl)-3-cyano-azulene **3b** with thioacetamide in an 92% yield (Entry 3). In a similar manner, 8-cyano or methoxycarbonyl-substituted azuleno[1,2-*c*] thiophene derivatives **7c-h** were obtained by reacting 1-acyl-2-(bromomethyl)azulenes **3c-h** with thioacetamide in high yields (Entries 4-9).

Experimental Section

All melting points were determined with a Yanaco MP JP-3 apparatus and were uncorrected. The IR spectra were measured on a JASCO A-102 IR spectrophotometer. The NMR spectra were recorded with a JEOL JNM-EX 300 spectrometer (300 MHz for ^{1}H and 75.5 MHz for ^{13}C).

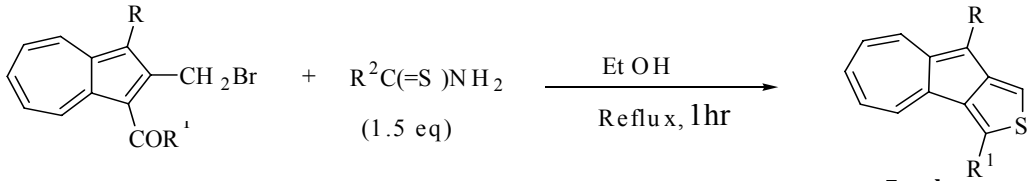
Methyl 2-methylazulene-1-carboxylate **1a** (ref. 3), 3-cyano-2-methylazulene **1b** (ref. 6), methyl 1-acetyl-2-methylazulene-3-carboxylate **2a** (ref. 2) and 1-acetyl-3-cyano-2-methylazulene **2b** (ref. 2) were prepared according to the methods described in the literature.

Preparation of 1-acyl 2-methylazulenes 2c-2h. A solution of 2-methylazulene-1-carboxylate **1a** (100 mg, 0.5 mmole), stannic chloride (156 mg, 0.6 mmole) and acyl chloride (55 mg, 0.6 mmole) in dry dichloro methane (10 mL) was stirred for 12 hr at room temperature. It was then shaken thoroughly with water (50 mL). In this process, the blue solution turned to red. The mixture was extracted with benzene. The residue remaining after removal of the solvent from the combined extracts was chromatographed on silica gel column with benzene to give 1-acyl 2-methylazulenes **2c-2h**.

Methyl 2-methyl-1-propionylazulene-3-carboxylate 2c: Red needles (from benzene, 93%); m.p.73-74°C; IR(KBr): 1681 (C=O), 1645 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.28 (3H, t, *J* = 7.5 Hz, CH_2CH_3), 2.95 (3H, s, CH_3), 2.92 (2H, q, *J* = 7.5 Hz, CH_2CH_3), 4.00 (3H, s, $COOCH_3$), 7.60 (1H, dd, *J* = 10.2, 9.6 Hz, 5- or 7-H), 7.63 (1H, dd, *J* = 10.2, 9.6 Hz, 7- or 5-H), 7.82 (1H, t, *J* = 9.6 Hz, 6-H), 9.01 (1H, d, *J* = 9.9 Hz, 8-H), 9.49 (1H, d, *J* = 10.2 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 8.9 (CH_2CH_3), 17.2 (CH_3), 37.9 (CH_2CH_3), 51.2 ($COOCH_3$), 116.2 (=C<), 128.8 (=C<), 129.8 (=CH-), 130.0 (=CH-), 136.7 (=CH-), 137.2 (=CH-), 139.1 (=CH-), 141.5 (=C<), 142.5 (=C<), 152.3 (=C<), 166.4 (C=O), 203.3 (C=O); Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.76; H, 6.43%.

3-Cyano-2-methyl-1-propionylazulene 2d: Red needles (from benzene, 92%); m.p.109-10℃; IR (KBr): 2185 (CN), 1648 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ 1.29 (3H, t, *J* = 7.5 Hz, CH_2CH_3), 2.96 (3H, s, CH_3), 3.00 (2H, q, *J* = 7.5 Hz, CH_2CH_3), 7.72 (1H, dd, *J* = 10.2, 9.6 Hz, 5- or 7-H), 7.75 (1H, dd, *J* = 10.2, 10.2 Hz, 7- or 5-H), 7.94 (1H, t, *J* = 9.6 Hz, 6-H), 8.63 (1H, d, *J* = 9.9 Hz, 8-H), 9.51 (1H, d, *J* = 10.2 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 8.5 (CH_2CH_3),

Table III — New synthetic method of azuleno[1,2-*c*]thiophenes



3 a-h **6 a, b** **7 a-h**

Entry	Substrate **3**		Reagent **6**	**7** Yield(%)[a]
	R	R^1	R^2	
1	COOMe	Me	Me	**a** 88
2	COOMe	Me	Ph	**a** 75
3	CN	Me	Me	**b** 92
4	COOMe	Et	Me	**c** 79
5	CN	Et	Me	**d** 95
6	COOMe	Ph	Me	**e** 89
7	CN	Ph	Me	**f** 76
8	COOMe	PhCH=CH	Me	**g** 62
9	CN	PhCH=CH	Me	**h 73**

[a]The yield was given for chromagraphically purified material based on **3**.

17.4 (CH_3), 37.7 (CH_2CH_3), 100.1 (=C<), 116.4 (=C<), 126.0 (=C<), 130.2 (=CH-), 131.9 (=CH-), 136.1 (=C<), 139.2 (=CH-), 139.8 (=CH-), 140.3 (=C<), 142.2 (=CH-), 144.6 (=C<), 153.5 (CN), 203.3 (C=O); Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.80; H, 6.00; N, 6.45%.

Methyl 1-benzoyl-2-methylazulene-3-carboxylate 2e: Red needles (from benzene, 70%); m.p. 95-96°C; IR (KBr): 1691 (C=O), 1641 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 2.63 (3H, s, CH_3), 3.98 (3H, $COOCH_3$), 7.43 (2H, dd, *J* = 7.8, 7.8 Hz, 3'-,5'-H), 7.46 (1H, dd, *J* = 9.9, 9.9 Hz, 5- or 7-H), 7.56 (1H, t, *J* = 7.5, 7.5 Hz, 4'-H), 7.63 (1H, t, *J* = 9.9 Hz, 6-H), 7.74-7.80 (3H, m, 2'-,6'- and 5- or 7-H), 8.57 (1H, d, *J* = 9.9 Hz, 8-H), 9.61 (1H, d, *J* = 9.9 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 17.4 (CH_3), 51.1 ($COOCH_3$), 115.6 (=C<), 128.4 (=CH-), 129.3 (=CH-), 129.6 (=CH-), 129.7 (=CH-), 132.7 (=CH-), 136.2 (=CH-), 137.3 (=CH-), 138.9 (=CH-), 140.0 (=C<), 142.2 (=C<), 142.6 (=C<), 153.7 (=C<), 166.3 (C=O), 195.3 (C=O); Anal. Calcd for $C_{20}H_{16}O_3$: C, 78.93; H, 5.30. Found: C, 78.65; H, 5.00%.

1-Benzoyl-3-cyano-2-methylazulene 2f: Red needles (from benzene, 59%); m.p.121-22°C; IR (KBr): 2205 (CN), 1627 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 2.54 (3H, s, CH_3), 7.48 (2H, dd, *J* = 6.9, 6.6 Hz, 3'-,5'-H), 7.61 (1H, t, *J* = 8.1, 6.9 Hz, 4'-H), 7.62 (1H, dd, *J* = 1.5, 10.2 Hz, 5- or 7-H), 7.71 (1H, dd, *J* = 9.9, 9.0 Hz, 7- or 5-H), 7.75 (2H, d, *J* = 7.8 Hz, 2',6'-H), 7.91 (1H, t, *J* = 9.9 Hz, 6-H), 8.57 (1H, d, *J* = 9.9 Hz, 8-H), 9.61 (1H, d, *J* = 9.9 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 16.0 (CH_3), 99.2 (=C<), 116.2 (=C<), 126.5 (=C<), 128.6 (=CH-), 129.5 (=CH-), 129.7 (=CH-), 130.5 (=CH-), 132.9 (=CH-), 135.9 (=CH-), 137.7 (=CH-), 139.8 (=C<), 140.0 (=CH-), 141.9 (=C<), 144.4 (=C<), 154.4 (CN), 193.7 (C=O); Anal. Calcd for $C_{19}H_{13}NO$: C, 84.11; H, 4.83; N, 5.16. Found: C, 83.78; H, 4.75; N, 5.38%.

Methyl 1-cinnamoyl-2-methylazulene-3-carboxylate 2g: Red needles (from benzene, 89%); m.p.98-99°C; IR (KBr): 1680 (C=O), 1656 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 2.92 (3H, s, CH_3), 3.97 (3H, s, $COOCH_3$), 7.21 (1H, d, *J* = 15.9 Hz, 3'-H), 7.31-7.33 (3H, m, 3"-,4"-,5"-H), 7.45-7.59 (4H, m, 5-,7-,2"-,6"-H), 7.50 (1H, d, *J* = 15.9 Hz, 2'-H), 7.73 (1H, t, *J* = 9.6 Hz, 6-H), 8.87 (1H, d, *J* = 9.9 Hz, 8-H), 9.51 (1H, d, *J* = 9.9 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 17.3 (CH_3), 51.1 ($COOCH_3$), 115.8 (=C<), 128.2 (=C<), 129.3 (=CH-), 128.3 (=CH-), 128.6 (=CH-), 128.9 (=CH-), 129.7 (=CH-), 129.8 (=CH-), 130.4 (=CH-), 134.7 (=C<), 136.3 (=CH-), 137.3 (=CH-), 139.0 (=CH-), 141.9 (=C<), 142.7 (=C<), 143.9 (=C<), 153.2 (=C<), 166.3 (1-C=O), 192.3 (3-C=O); Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 80.26; H, 5.30%.

1-Cinnamoyl-3-cyano-2-methylazulene 2h: Red needles (from benzene, 95%); m.p.96-97°C; IR (KBr): 2209 (CN), 1643 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 2.90 (3H, s, CH_3), 7.43 (1H, d, *J* = 15.6 Hz, 3'-H), 7.40-7.43 (3H, m, 3"-,4"-,5"-H), 7.58-7.61 (2H, m, 2"-,6"-H), 7.64 (1H, d, *J* = 15.6 Hz, 2'-H), 7.69 (2H, dd, *J* = 9.9, 9.9 Hz, 5-, 7-H), 7.92 (1H, t, *J* = 9.6 Hz, 6-H), 8.61 (1H, d, *J* = 9.9 Hz, 8-H), 9.10 (1H, d, *J* = 9.9 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 16.4 (CH_3), 99.5 (=C<), 116.3 (=C<), 127.3 (=CH-), 127.5 (=CH-), 128.4 (=CH-), 129.0 (=CH-), 129.9 (=CH-), 130.6 (=CH-), 131.0 (=CH-), 134.6 (=C<), 136.0 (=CH-), 138.1 (=CH-), 140.1 (=CH-), 141.8 (=C<), 144.1 (=CH-), 144.5 (=C<), 153.7 (CN), 189.8 (C=O); Anal. Calcd for $C_{21}H_{15}NO$: C, 84.82; H, 5.09; N, 4.71. Found: C, 84.59; H, 5.01; N, 4.70%.

Bromination of 1-acyl-2-methylazulenes 2c-h. **General procedure**. A solution of 1-acyl-2-methylazulene **2c-h** (0.5 mmole) in carbon tetrachloride(20 mL) containing finely powdered *N*-bromosuccinimide (NBS,0.6-1.0 mmole) and dibenzoyl peroxide (10 mg) was refluxed for 2-12 hr. After cooling, the reaction mixture was diluted with water and extracted with dichloromethane. The extract was dried over sodium sulfate and evporated *in vacuo* to leave a residue which was chromatographed on a silica gel column with benzene as eluent to give 1-acyl-2-(bromomethyl)azulenes **3a-h**, 1-bromo-2-methylazulene **4a**,**b** and 1-bromo-2-(bromomethyl) azulene **5a**,**b**.

Methyl 1-acetyl-2-(bromomethyl)azulene-3-carboxylate 3a: Violet needles (from benzene); m.p.85-86°C (lit.[2] m.p. 85-86°C).

Methyl 1-bromo-2-methylazulene-3-carboxylate 4a: Violet needles (benzene); m.p. 88-89°C; (lit.[2] m.p.88-89°C).

Methyl 1-bromo-2-(bromomethyl)azulene-3-carboxylate 5a: Violet needles (benzene); m.p. 99-101°C; (lit.[2] m.p.99-01°C).

1-Acetyl-2-bromomethyl-3-cyano-azulene 3b: Violet needles (benzene); m.p.129°C (dec); (lit.[2] m.p.129°C).

1-Bromo-3-cyano-2-methylazulene 4b: Blue crystals, m.p.154-56°C (lit.[2] m.p.154-56°C).

1-Bromo-2-(bromomethyl)-3-cyano-azulene 8b: Blue crystals, m.p.125-27°C (lit.[2] m.p.125-27°C).

Methyl 2-(Bromomethyl)-1-propionylazulene-3-carboxylate (3c): Violet needles (benzene); m.p.90-91°C; IR (KBr): 1692 (C=O), 1644 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.32 (3H, t, *J* = 7.2 Hz, CH_2CH_3), 3.13 (2H, q, *J* = 7.2 Hz, CH_2CH_3), 4.04 (3H, s, $COOCH_3$), 5.29 (2H, s, CH_2Br), 7.59 (1H, dd, *J* = 9.9, 9.6 Hz, 5- or 7-H), 7.64 (1H, dd, *J* = 10.2, 9.9 Hz, 7- or 5-H), 7.86 (1H, t, *J* = 9.6 Hz, 6-H), 8.90 (1H, d, *J* = 9.9 Hz, 8-H), 9.60 (1H, d, *J* = 10.2 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 8.9 (CH_2CH_3), 25.4 (CH_2CH_3), 37.9 (CH_2Br), 51.5 ($COOCH_3$), 114.8 (=C<), 128.3 (=C<), 129.9 (=CH-), 130.1 (=CH-), 138.0 (=CH-), 139.6 (=CH-), 140.8 (=CH-), 140.9 (=C<), 142.2 (=C<), 148.4 (=C<), 165.4 (C=O); 202.7 (C=O). Anal. Calcd for $C_{16}H_{15}BrO_3$: C, 57.44; H, 4.26. Found: C, 57.34; H, 4.50 %.

2-(Bromomethyl)-3-cyano-1-propionylazulene 3d: Violet needles (benzene); m.p.162-64°C; IR (KBr): 2212 (CN), 1643 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.33 (3H, t, *J* = 7.2 Hz, CH_2CH_3), 3.17 (2H, q, *J* = 7.2 Hz, CH_2CH_3), 5.06 (2H, s, CH_2Br), 7.76 (1H, dd, *J* = 9.9, 9.0 Hz, 5- or 7-H), 7.78 (1H, dd, *J* = 10.2, 9.6 Hz, 7- or 5-H), 8.02 (1H, t, *J* = 9.6 Hz, 6-H), 8.72 (1H, d, *J* = 10.5 Hz, 8-H), 9.37 (1H, d, *J* = 10.5 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 8.6 (CH_2CH_3), 23.8 (CH_2CH_3), 37.1 (CH_2Br), 99.1 (=C<), 115.1 (=C<), 125.6 (=CH-), 130.5 (=CH-), 131.7 (=CH-), 138.1 (=C<), 140.8 (=CH-), 141.4 (=C<), 141.9 (=CH-), 144.2 (=C<), 149.8 (CN), 199.6 (C=O); Anal. Calcd for $C_{15}H_{12}BrNO$: C, 59.62; H, 4.00; N, 4.64. Found: C, 59.69; H, 4.13; N, 4.72 %.

Methyl 1-benzoyl-2-(bromomethyl)azulene-3-carboxylate 3e: Violet needles (benzene); m.p.125-26°C; IR (KBr): 1693 (C=O), 1640 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 4.05 (3H, s, $COOCH_3$), 5.15 (2H, s, CH_2Br), 7.43 (1H, dd, *J* = 9.9, 8.4 Hz, 5- or 7-H), 7.47 (2H, d, *J* = 7.8 Hz, 3'-,5'-H), 7.60 (1H, t, *J* = 7.5 Hz, 4'-H), 7.68 (1H, t, *J* = 9.9 Hz, 6-H), 7.79 (1H, d, *J* = 8.1 Hz, 2'-,or 6'-H), 7.80 (1H, d, *J* = 8.1 Hz, 6'- or 2'-H), 7.84 (1H, dd, *J* = 9.9, 9.6 Hz, 7- or 5-H), 8.37 (1H, d, *J* = 9.3 Hz, 8-H), 9.68 (1H, d, *J* = 10.5 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 24.8 (CH_2Br), 51.6 ($COOCH_3$), 115.0 (=C<), 127.2 (=C<), 128.3 (=CH-), 128.6 (=CH-), 129.3 (=CH-), 129.9 (=CH-), 130.1 (=CH-), 133.2 (=CH-), 138.4 (=CH-), 139.7 (=CH-), 139.8 (=CH-), 140.7 (=CH-), 141.6 (=C<), 142.3 (=C<), 150.4 (=C<), 165.4 (C=O), 194.5 (C=O); Anal. Calcd for $C_{20}H_{15}BrO_3$: C, 62.68; H, 3.94. Found: C, 61.94; H, 4.00 %.

1-Benzonyl-2-(bromomethyl)-3-cyanoazulene 3f: Violet needles (benzene); m.p.159-61°C; IR (KBr): 2212 (C=O), 1631 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 4.81 (2H, s, CH_2Br), 7.45 (1H, dd, *J* = 7.8, 7.2 Hz, 3'- or 5'-H), 7.52 (1H, dd, *J* = 7.2, 6.6 Hz, 5'- or 3'-H), 7.57 (1H, dd, *J* = 9.6, 9.0 Hz, 5- or 7-H), 7.64 (1H, t, *J* = 7.8 Hz, 4'-H), 7.74 (1H, dd, *J* = 9.9, 9.9 Hz, 5- or 7-H), 7.79 (1H, d, *J* = 7.8 Hz, 6'- or 2'-H), 7.80 (1H, d, *J* = 7.5, Hz, 6'- or 2'-H), 7.96 (1H, t, *J* = 9.9 Hz, 6-H), 8.55 (1H, d, *J* = 9.3 Hz, 8-H), 8.75 (1H, d, *J* = 9.9 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 22.7 (CH_2Br), 98.6 (=C<), 115.1 (=C<), 126.0 (=C<), 128.8 (=CH-),129.7 (=CH-), 130.1 (=CH-), 130.5 (=CH-), 133.4 (=CH-), 138.2 (=CH-), 139.4 (=C<), 139.7 (=CH-), 141.3 (=C<), 141.7 (=CH-), 144.1 (=C<), 151.2 (CN), 192.9 (C=O); Anal. Calcd for $C_{19}H_{12}BrNO$: C, 65.16; H, 3.45; N, 4.00. Found: C, 65.12; H, 3.28; N, 4.08 %.

Methyl 2-bromomethyl-1-cinnamoylazulene-3-carboxylate 3g: Reddish-violet needles (benzene); m.p. 161-62°C; IR (KBr): 1692 (C=O), 1646 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 4.05 (3H, s, $COOCH_3$), 5.01 (2H, s, CH_2Br), 7.39-7.41 (3H, m, 3"-,4"-,5"-H), 7.54 (1H, d, *J* = 15.9 Hz, 3'-H), 7.63-7.70 (4H, m, 5-, 7-,2"-,6"-H), 7.69 (1H, d, *J* = 15.9 Hz, 2'-H), 7.87 (1H, t, *J* = 9.6 Hz, 6-H), 8.97 (1H, d, *J* = 9.6 Hz, 8-H), 9.66 (1H, d, *J* = 9.3 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 26.0 (CH_2Br), 51.5 ($COOCH_3$), 114.7 (=C<), 127.5 (=CH-), 128.1 (=C<),128.7 (=CH-), 128.9 (=CH-), 130.1 (=CH-), 130.3 (=CH-), 130.6 (=CH-), 134.6 (=C<), 138.9 (=CH-), 139.7 (=CH-), 140.9 (=CH-), 141.6 (=C<), 142.6 (=C<), 144.9 (=CH-), 148.7 (=C<), 165.4 ($COOCH_3$), 191.1 (C=O); Anal. Calcd for $C_{22}H_{17}BrO_3$: C, 64.56; H, 4.19. Found: C, 64.68; H, 4.34 %.

2-(Bromomethyl)-1-cinnamoyl-3-cyanoazulene 3h: Violet needles (benzene); m.p.154-56°C; IR (KBr): 2211(CN), 1649 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 5.03 (2H, s, CH_2Br), 7.4-7.45 (3H, m, 3"-, 4"-,5"-H), 7.54 (1H, d, *J* = 15.6 Hz, 3'-H), 7.66-7.69 (2H, m, 2"-,6"-H), 7.75 (1H, d, *J* = 15.6 Hz, 2'-H), 7.74-7.80 (2H, m, 5-,7-H), 8.02 (1H, t, *J* = 9.9 Hz, 6-H), 8.75 (1H, d, *J* = 9.9 Hz, 8-H), 9.18 (1H, d, *J* = 9.6 Hz, 4-H); ^{13}C NMR ($CDCl_3$): δ 23.6 (CH_2Br), 98.6 (=C<), 115.1 (=C<), 126.6 (=CH-), 126.7 (=C<), 128.7 (=CH-), 129.0 (=CH-), 130.3 (=CH-), 130.8 (=CH-), 131.3 (=CH-), 134.4 (=C<), 137.9 (=CH-), 140.4 (=CH-), 141.2 (=C<), 141.9 (=CH-), 144.3 (=C<), 145.1 (=CH-), 149.5 (CN), 188.9 (C=O); Anal. Calcd for $C_{21}H_{14}BrNO$: C, 67.04; H, 3.75; N, 3.72. Found: C, 67.23; H, 3.98; N, 3.87 %.

Reaction of 1-acyl-2-(bromomethyl)azulenes 3a-h with thioamides.**General procedure**. To a solution of 1-acyl-2-(bromomethyl)azulenes **3a-h** (0.3 mmole) in absolute ethanol (10 mL) were added thioacetamide **6a** (34 mg, 0.45 mmole). The mixture was heated under refluxing for 1 hr. The mixture was quenched with water (10 mL) and extracted with chloroform (2 × 10 mL). The extract was dried over sodium sulfate and the concentrated residue was purified on a Wakogel C-200 column with benzene as an eluent to give the products **7a-h**.

Methyl 2-methylazuleno[1,2-*c*]thiophene-8-carboxylate 7a: Greenish-yellow needles (benzene); m.p. 142-44°C; IR (KBr): 1682 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 2.82 (3H, s, CH_3), 3.94 (3H, s, $COOCH_3$), 6.87-6.99 (3H, m, 4-,5-,6-H), 7.14 (1H, s, 9-H), 7.56-7.64 (1H, m, 3-H), 8.81-8.88 (1H, m, 7-H); ^{13}C NMR ($CDCl_3$): δ 14.8 (CH_3), 51.0 ($COOCH_3$), 105.7 (=CH-), 110.0 (=C<), 129.1 (=CH-), 130.4 (=CH-), 130.5 (=CH-), 133.4 (=C<), 134.0 (=CH-), 134.5 (=C<), 134.8(=CH-), 140.0 (=C<), 145.2 (=C<), 151.7 (=C<), 166.0 (C=O); Anal. Calcd for $C_{15}H_{12}O_2S$: C, 70.28; H, 4.72. Found: C, 70.38; H, 4.77 %.

8-Cyano-2-methylazuleno[1,2-*c*]thiophene 7b: Greenish-yellow needles (benzene); m.p.163-64°C; IR (KBr): 2196 cm^{-1} (CN); ^1H NMR ($CDCl_3$): δ 2.82 (3H, s, CH_3), 6.82-6.92 (2H, m, 4-,6-H), 6.93-6.97 (1H, m, 5-H), 6.96 (1H, s, 9-H), 7.52-7.55 (1H, m, 3-H), 7.65 (1H, d, *J* = 10.5 Hz, 7-H); ^{13}C NMR ($CDCl_3$): δ 14.7 (CH_3), 91.3 (=C<), 103.8 (=CH-), 128.9 (=CH-), 130.1 (=CH-), 130.8 (=CH-), 133.4 (=CH-), 133.8 (=C<), 134.2 (=C<), 135.0 (=C<), 138.2 (=C<), 143.6 (=C<), 154.5 (CN); Anal. Calcd for $C_{14}H_9NS$: C, 75.30; H, 4.06; N, 6.27. Found: C, 75.08; H, 4.02; N, 6.33 %.

Methyl 2-ethylazuleno[1,2-*c*]thiophene-8-carboxylate 7c: Greenish-yellow needles (benzene); m.p. 104-05°C; IR (KBr): 1688 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 1.47 (3H, t, *J* = 7.5 Hz, CH_2CH_3), 3.23 (2H, q, *J* = 7.5 Hz, CH_2CH_3), 3.95 (3H, s, $COOCH_3$), 6.91-6.97 (3H, m, 4-,5-,6-H), 7.20 (1H, s, 9-H), 7.60-7.65 (1H, m, 3-H), 8.84-8.91 (1H, m, 7-H); ^{13}C NMR ($CDCl_3$): δ 14.4 (CH_2CH_3), 23.0 (CH_2CH_3), 51.0 ($COOCH_3$), 105.7 (=CH-), 110.3 (=C<), 129.1 (=CH-), 130.3 (=CH-), 130.4 (=CH-), 133.6 (=C<), 134.0 (=CH-), 134.8 (=C<), 139.9 (=CH-), 141.7 (=C<), 145.4 (=C<), 151.7 (=C<), 166.0 (C=O); Anal. Calcd for $C_{16}H_{14}O_2S$: C, 71.08; H, 5.22. Found: C, 71.02; H, 5.21 %.

8-Cyano-2-ethylazuleno[1,2-*c*]thiophene 7d: Black needles (benzene); m.p. 124-25°C; IR (KBr): 2196 cm^{-1} (CN); ^1H NMR ($CDCl_3$): δ 1.46 (3H, t, *J* = 7.5, CH_2CH_3), 3.18 (2H, q, *J* = 7.5 Hz, CH_2CH_3), 6.65-6.89 (2H, m, 4-,6-H), 6.90-6.94 (1H, m, 5-H), 6.96 (1H, s, 9-H), 7.46-7.51 (1H, m, 3-H), 7.61 (1H, d, *J* = 9.9 Hz, 7-H); ^{13}C NMR ($CDCl_3$): δ 14.3 (CH_2CH_3), 22.8 (CH_2CH_3), 91.4 (=C<), 103.7 (=CH-), 116.9 (=C<), 128.9 (=CH-), 129.9 (=CH-), 130.7 (=CH-), 133.1 (=CH-), 133.2 (=C<), 133.7 (=CH-), 137.9 (=C<), 143.2 (=C<), 143.6 (=C<), 154.3 (CN); Anal. Calcd for $C_{15}H_{11}NS$: C, 75.91; H, 4.67; N, 5.90. Found: C, 76.20; H, 4.41; N, 6.14 %.

Methyl 2-phenylazuleno[1,2-*c*]thiophene-8-carboxylate 7e: Black needles (benzene); m.p.118-19°C; IR (KBr): 1672 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 3.96 (3H, s, $COOCH_3$), 6.71-6.78 (1H, m), 6.91-6.97 (2H, m), 7.41-7.49 (3H, m, 4-,5-,6-H), 7.46 (1H, d, *J* = 2.1 Hz, 9-H), 7.65 (1H, d, *J* = 8.1 Hz, 2'- or 6'-H), 7.66 (1H, d, *J* = 8.1 Hz, 6'- or 2'-H), 7.97 (1H, d, *J* = 8.7 Hz, 3-H), 8.91-8.95 (1H, m, 7-H); ^{13}C NMR ($CDCl_3$): δ 51.1 ($COOCH_3$), 109.3 (=CH-), 109.9 (=CH-), 128.1 (=CH-), 128.5 (=CH-), 128.9 (=CH-), 129.4 (=CH-), 130.2 (=CH-), 130.6 (=CH-), 133.8 (=C<), 133.9 (=C<), 135.2 (=CH-), 137.4 (=C<), 139.1 (=C<), 145.8 (=C<), 151.8 (=C<), 165.9 (C=O); Anal. Calcd for $C_{20}H_{14}O_2S$: C, 75.44; H, 4.43. Found: C, 75.63; H, 4.21 %.

8-Cyano-2-phenylazuleno[1,2-*c*]thiophene 7f: Black needles (benzene); m.p.178-79°C; IR (KBr): 2198 cm^{-1} (CN); ^1H NMR ($CDCl_3$): δ 6.79 (1H, t, *J* = 9.9 Hz, 5-H), 6.91 (1H, dd, *J* = 9.9, 9.6 Hz, 4-H), 6.97 (1H, dd, *J* = 9.9, 9.6 Hz, 7-H), 7.27 (1H, d, *J* = 0.9 Hz, 9-H), 7.45-7.53 (3H, m, 3'-,4'-,5'-H), 7.66 (1H, d, *J* = 8.4 Hz, 2'- or 6'-H), 7.67 (1H, d, *J* = 8.1 Hz, 6'- or 2'-H), 7.77 (1H, d, *J* = 9.9 Hz, 3-H), 7.89 (1H, d, *J* = 8.7 Hz, 7-H); ^{13}C NMR ($CDCl_3$): δ 91.3 (=C<), 107.2 (=CH-), 116.8 (=C<), 128.1 (=CH-), 128.9 (=CH-), 129.1 (=CH-), 129.3 (=CH-), 130.2 (=CH-), 130.6 (=CH-), 133.1 (=C<), 133.4 (=C<), 133.8 (=CH-), 134.9 (=CH-), 137.4 (=C<), 138.9 (=C<), 144.2 (=C<), 154.6 (CN); Anal. Calcd for $C_{19}H_{11}NS$: C, 79.97; H, 3.86; N, 4.91. Found: C, 79.83; H, 3.85; N, 5.06 %.

Methyl 2-styrylazuleno[1,2-*c*]thiophene-8-carboxylate 7g: Greenish-yellow needles (benzene); m.p. 152-53°C; IR (KBr): 1689 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 3.94 (3H, s, $COOCH_3$), 6.95-6.70 (3H, m, 4-,5-,6-H), 7.17 (1H, d, *J* = 15.6 Hz, 3′-H), 7.30 (1H, s, 9-H), 7.32-7.42 (3H, m, 3"-,4"-,5"-H), 7.54 (2H, d, *J* = 7.2 Hz, 2"-,6"-H), 7.71 (1H, d, *J* = 15.6

Hz, 2'-H), 7.86 (1H, d, *J* = 9.3 Hz, 3-H), 8.88 (1H, d, *J* = 10.2 Hz, 7-H); ^{13}C NMR ($CDCl_3$): δ 51.1 ($COOCH_3$), 108.2 (=CH-), 109.9 (=CH-), 120.1 (=CH-), 126.7 (=CH-), 128.2 (=CH-), 128.8 (=CH-), 130.4 (=CH-), 130.7 (=CH-), 131.6 (=CH-), 134.7 (=C<), 134.9 (=CH-), 135.2 (=CH-), 136.3 (=C<), 136.7 (=C<), 139.9 (=C<), 145.7 (=C<), 151.9 (=C<), 165.8 (C=O); Anal. Calcd for $C_{22}H_{16}O_2S$: C, 76.72; H, 4.68. Found: C, 76.68; H, 4.72 %.

8-Cyano-2-styrylazuleno[1,2-*c*]thiophene 7h: Greenish-yellow needles (benzene); m.p.186-87℃; IR (KBr): 2198 cm^{-1} (CN); ^{1}H NMR ($CDCl_3$): δ 6.81-6.88 (1H, m, 5-H), 6.93-6.96 (2H, m, 4-,6-H), 7.03 (1H, s, 9-H), 7.14 (1H, d, *J* = 15.6 Hz, 3'-H), 7.32 (1H, t, *J* = 7.2, 7.2 Hz, 4"-H), 7.39 (2H, dd, *J* = 7.5, 6.9 Hz, 3"-,5"-H), 7.51 (2H, d, *J* = 7.2 Hz, 2"-,6"-H), 7.57 (1H, d, *J* = 15.6 Hz, 2'-H), 7.63 (1H, d, *J* = 11.8 Hz, 3-H), 7.65-7.69 (1H, m, 7-H); ^{13}C NMR ($CDCl_3$): δ 91.3 (=C<), 105.6 (=CH-), 116.6 (=C<), 119.2 (=CH-), 126.8 (=CH-), 128.5 (=CH-), 128.9 (=CH-), 130.0 (=CH-), 130.3 (=CH-), 130.7 (=CH-), 132.6 (=CH-), 133.6 (=CH-), 134.0 (=C<), 134.6 (=CH-), 136.3 (=C<), 137.7 (=C<), 138.1 (=C<), 144.1 (=C<), 154.6 (CN); Anal. Calcd for $C_{21}H_{13}NS$: C, 80.99; H, 4.21; N, 4.50. Found: 80.72; H, 4.18; N, 4.44 %.

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