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Preparation, characterization, and cycloaddition reaction of the heterocumulenes attached directly to azulenes. An efficient strategy for the preparation of azulene-substituted heterocycles

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Abstract—Preparation and cycloaddition reaction of novel azulene-substituted *N*-sulfinylamines **1** and **2** are reported. The influence of the –N═S═O group on the UV–vis and NMR spectra of the azulene ring to which it is bonded is discussed. X-ray crystal analysis of **1** revealed the *syn*-configuration and the twisted structure of the *N*-sulfinylamine moiety. The synthetic utility of **1** and **2** have been explored by the cycloaddition reaction to afford novel azulene-substituted heterocycles under high-pressure conditions. We also described herein the synthesis and some properties of related 2-azulenylisothiocyanate.

1. Introduction

Azulene ($C_{10}H_8$) has attracted the interest of many research groups due to its unusual properties. Especially, the compound shows beautiful deep blue color and has a tendency to stabilize cations, as well as anions, owing to its remarkable polarizability. The preparation of the azulene derivatives is extensively studied since the development of excellent synthetic methods for azulene nucleus in the 1950's.[1] Functionalized heterocycles have become important in recent years for the application to the functional and biologically active substance.[2] The heterocycles substituted by azulene moiety could be utilized to construct advanced materials for electronic and photonic applications, because substitution of the azulene provide a new electrochemical property to the systems owing to the polarizability.[3] Cycloaddition reactions of the heterocumulenes provide a simple route to heterocycles, which are often quite difficult to synthesize by other synthetic methods.[4] To our knowledge, a few azulene-substituted heterocumulenes have been appeared in the literature, e.g. 2-, 5-, and 6-azulenyl azides,[5] 1-azulenyl nitrones,[6] and di(1-azulenyl)thioketone *S*-oxide.[7] However, there are some deficiencies of knowledge concerning the heterocumulenes directly attached to the azulene systems. Therefore, we have decided to explore the preparation of the novel azulene-substituted heterocumulenes and the application to the cycloaddition reaction for the synthesis of various azulene-substituted heterocycles. *N*-Sulphinylamines (R–N═S═O) are highly reactive substances and their properties, preparation, and chemistry have been extensively studied.[8] The *N*-sulphinylamines are excellent reagents for the cycloaddition reactions, which are able to lead to four-, five-, and six-membered heterocycles. Therefore, we have initiated a research program to examine the synthesis and the cycloaddition reaction of *N*-sulfinylamines bearing the azulenyl substituent adjacent to the heterocumulene function. In this paper, we report the synthesis of novel *N*-sulfinyl-2- and 6-azulenylamines (**1** and **2**) and the cycloaddition reaction with 2,3-dimethyl-1,3-butadiene under high-pressure conditions. Furthermore, we report herein the synthesis and some properties of related 2-azulenylisothiocyanate (**3**) (Chart 1). These studies will make up the deficiency of the heterocumulenes in the chemistry of azulene and direct to the development of new methodologies for the synthesis of various azulene-substituted heterocycles.

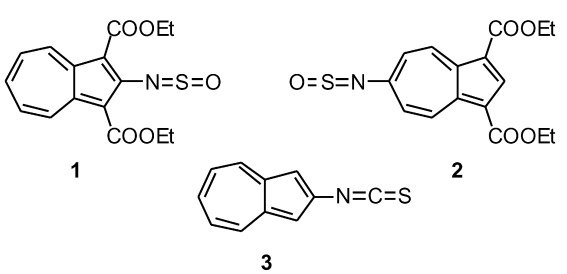

Chart 1.

Keywords: azulene; *N*-sulfinylamine; isothiocyanate; high-pressure cycloaddition; redox behavior.

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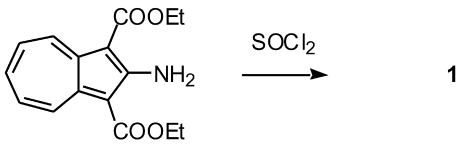
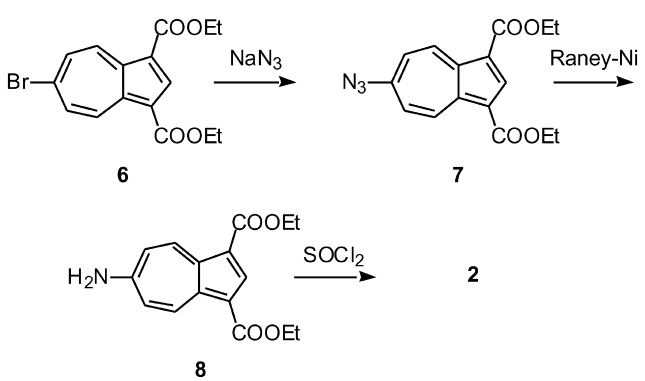
2. Results and discussion

A wide range of *N*-sulphinylamines was prepared by heating the corresponding amines with thionyl chloride in dry benzene. However, the similar reaction using the parent 2-azulenylamine (**4**)[9] did not afford the desired *N*-sulfinyl-2-azulenylamine because of the high reactivity of the azulene system with thionyl chloride at 1- and 3-positions.[10] We found that the treatment of diethyl 2- and 6-aminoazulene-1,3-dicarboxylates (**5**[9] and **8**[11]), in which the reactive 1,3-positions are protected by two ester groups, with thionyl chloride in dry toluene at room temperature afforded the first azulene-substituted *N*-sulfinylamines **1** and **2** in high yields (Schemes 1 and 2). The preparation of the starting amine **8** is reported by the reaction of diethyl 6-bromoazulene-1,3-dicarboxylate (**6**) with sodium azide in DMSO.[11b] However, we could not obtained the amine **8** directly by the reaction of **6** with sodium azide in DMSO, but the reaction afforded the azide **7** in 92% yield. The amine **8** could be obtained by the Raney-Ni reduction of **7** in 93% yield as outlined in Scheme 2. The *N*-sulfinylamines **1** and **2** were purified by recrystallization from dry toluene and fully characterized by spectroscopy including the X-ray crystallographic analysis in the case of **1**, although **1** and **2** are highly moisture sensitive compounds to reproduce the starting amines **5** and **8**.

UV–vis spectra of **1** and **2** and those of related amines **5** and **8** and diethyl azulene-1,3-dicarboxylate (**9**) in dichloromethane are shown in Figures 1 and 2. The absorption maximum of **1** and **2** in visible region showed a consistent bathochromic shift on changing $-NH_2$ to $-N{=}S{=}O$, although magnitude of the shifts was rather different (Table 1). The longest absorption maximum in **2** exhibited appreciable bathochromic shift by 48 nm as compared with that of **9**. However, that in **1** was little influenced by the $-N{=}S{=}O$ group at the 2-position. The absorption maxima of azulenes in the visible region follow a simple but remarkable pattern known as Plattner's rule.[12] According to the rule, substitution on the 2- and 6-positions in azulenes is



Scheme 1.



Scheme 2.

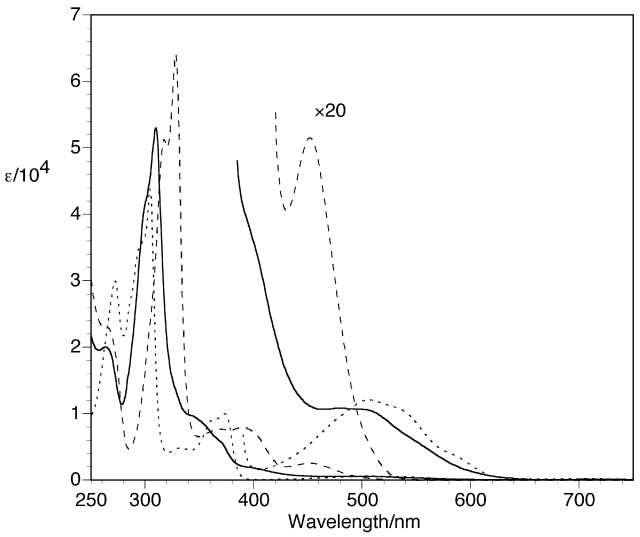


Figure 1. UV–vis spectra of **1** (continuous line), **5** (broken line), and **9** (dotted line) in dichloromethane.

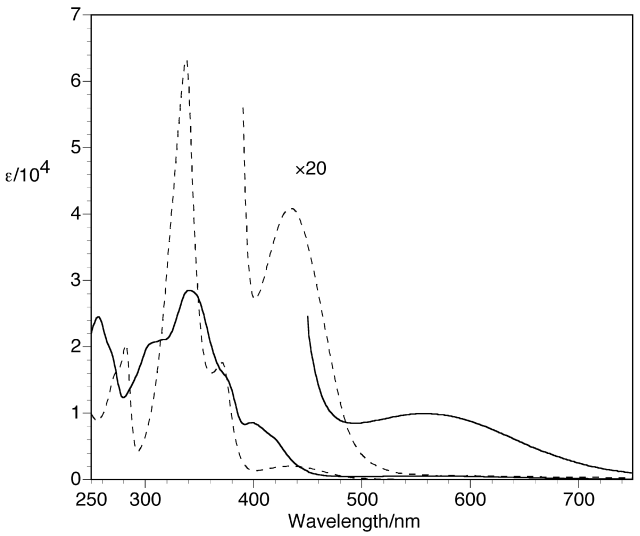


Figure 2. UV–vis spectra of **2** (continuous line) and **8** (broken line) in dichloromethane.

expected to show similar tendency toward the shift of the transition. Therefore, these results suggest that the $-N{=}S{=}O$ group in **1** has non-planar structure due to the steric effect of the neighboring two ester groups to reduce the conjugation, whereas that in **2** is efficiently conjugated with the azulene ring. Indeed, the twisted structure in **1** was revealed by X-ray crystallographic analysis.

Table 1. Absorption maximum and coefficient in visible region of **1**–**3**, **5**, **8**, **9**, and **18**

Sample	2-Subst.	6-Subst.	1,3-Subst.	λ_{max}, nm (log ε)
1	$N{=}S{=}O$	H	COOEt	507 sh (2.72)
2	H	$N{=}S{=}O$	COOEt	553 (2.69)
5	NH_2	H	COOEt	453 (3.41)
8	H	NH_2	COOEt	433 (3.31)
9	H	H	COOEt	505 (2.78)
3	$N{=}C{=}S$	H	H	557 (2.66)
18	H	H	H	576 (2.51)

Table 2. ^{1}H NMR data of **1**–**3**, **5**, **8**, **9**, and **18** (δ in ppm and J in Hz)

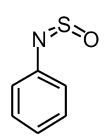
Sample	2-H	4,8-H	5,7-H	6-H	Coupling constants	1,3-COOEt or 1,3-H	Ref.
1	–	9.70	7.77	7.93	$J_{4,5}$=10.3 Hz, $J_{5,6}$=9.7 Hz	4.46, 1.46 (J=7.1 Hz)	
2	8.79	9.62	7.95	–	$J_{4,5}$=11.2 Hz	4.44, 1.46 (J=7.1 Hz)	
5	7.79 (NH_2)	9.13	7.53	7.42	$J_{4,5}$=10.0 Hz, $J_{5,6}$=9.8 Hz	4.46, 1.48 (J=7.1 Hz)	
8	8.34	9.42	6.88	5.09 (NH_2)	$J_{4,5}$=11.4 Hz	4.38, 1.42 (J=7.1 Hz)	
9	8.85	9.80	7.75	7.97	$J_{4,5}$=10.1 Hz, $J_{5,6}$=9.8 Hz	4.44, 1.46 (J=7.1 Hz)	
3	–	8.22	7.24	7.58	$J_{4,5}$=9.9 Hz, $J_{5,6}$=9.9 Hz	7.15	
18	7.81	8.23	7.05	7.45	$J_{4,5}$=9.5 Hz, $J_{5,6}$=10.0 Hz	7.30	[1]

Table 3. ^{13}C NMR data of **1**–**3**, **5**, **8**, **9**, and **18** (δ in ppm)

Sample	C-1,3	C-2	C-3a,8a	C-4,8	C-5,7	C-6	Other signals	Ref.
1	107.1	149.8	142.8	138.8	131.8	140.0	164.0 (s), 60.7 (t), 14.3 (q)	
2	117.7	144.5	143.0	137.6	127.3	150.4	164.4 (s), 60.3 (t), 14.5 (q)	
5	99.8	162.4	146.1	131.4	132.6	132.8	166.5 (s), 59.8 (t), 14.6 (q)	
8	116.1	136.2	137.3	139.8	116.4	159.3	165.7 (s), 59.6 (t), 14.6 (q)	
9	116.2	143.6	144.0	139.2	130.6	140.6	165.0 (s), 60.0 (t), 14.6 (q)	
3	113.2	135.7 Or 135.6	139.3	136.7	125.0	137.5	135.6 or 135.7 (2-N=C=S)	
18	118.1	136.9	140.2	136.4	122.6	137.1	–	[1]

The influence of the –N=S=O group on the NMR spectra of the azulene ring to which it is bonded was investigated (Tables 2 and 3). As expected by the substituent effect of N=S=O function in monosubstituted benzene,[13] the compound **1** exhibited a consistent upfield shift in the *ipso*-carbon signal and also downfield shift in C-1 and C-3 signals on changing $-NH_2$ to –N=S=O. The chemical shift of **1** in the *ipso*-carbon is rather close to that of **9**. Changing $-NH_2$ to –N=S=O at C-6 position also caused significant shielding of the *ipso*-carbon (C-3), as well as significant deshielding at C-5 and C-7 in the ^{13}C NMR spectra and also deshielding at the H-5 and H-7 signals in ^{1}H NMR spectra. However, the chemical shift of **2** in the *ipso*-carbon is observed at almost middle position between those of **8** and **9**. In the case of monosubstituted benzene, the chemical shift of Ph–N=S=O (**10**) in the *ipso*-carbon is rather close to that of aniline, compared with that of benzene. Therefore, the influence of the N=S=O moiety at 6-position to the azulene ring could be concluded to be much greater than that at 2-position in analogy with the results on UV–vis spectra.

The crystal structure of **1** was determined by X-ray diffraction analysis. Suitable crystals for X-ray structure determination were obtained by slow evaporation of the solution in dichloromethane/hexane. The *N*-sulphinylamine **1** crystallizes in a monoclinic cell, space group $P\bar{1}$ and Z=4. The ORTEP drawing is shown in Figure 3. The molecule exhibits two independent molecules. Each molecules has *syn* configuration with the respect to the S=O double bond and the C–N single bond, as similar to those for all the



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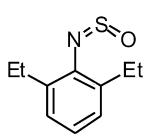

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Chart 2.

R–N=S=O compounds reported so far.[8a] The bond lengths and angles of the–N=S=O group in **1** are almost identical with those of Ph–N=S=O (**10**) and 2,6-Et_2Ph–N=S=O (**11**) reported previously (Chart 2).[14] The dihedral angles between the–N=S=O group and the plane of each azulene ring in each molecule of **1** are 81° and 89°, respectively, while **10** has fully planar *syn* configuration. Ethyl substituents in both *ortho* positions in **11** were reported to twist the–N=S=O group by 53.3° from the planar structure. Estimates by R. M. Romano et al. using ab initio calculations of **10** are that the deviations of the planarity are energetically more favorable than change in the configuration of the–N=S=O group.[8a] Therefore, the twisted structure of the–N=S=O group in **1** should be concluded by the steric interaction between the–N=S=O group and 1,3-diethoxycarbonyl groups, although there is a significant difference of the rotational angles between those of **1** and **11**.

The [4+2] cycloaddition is widely studied by the reaction of *N*-sulfinylamines.[13] The products formed in these reactions of **1** and **2** with 1,3-butadiene are azulene-substituted 6*H*-2,3-dihydro-1,2-thiazine 1-oxides. However, the newly prepared *N*-sulphinylazulenylamines **1** and **2** did not easily underwent thermal cycloaddition with 2,3-dimethylbuta-1,3-diene (**12**) to give the cycloadducts **13** and **14**. The cycloaddition of **2** with **12** under atmospheric pressure required prolonged heating in refluxing toluene and the yield of the desired cycloadduct **14** was poor (29%). However, we found that the high-pressure (10 kbar) reaction[15] of **1** and **2** with a large excess of **12** in dichloromethane at 40°C and subsequent chromatographic purification of the reaction mixture on silica gel afforded the desired [4+2] cycloadducts **13** and **14** in 66 and 77% yields, respectively (Schemes 3 and 4). The adducts **13** and **14** were single pure products and could be fully characterized as Diels–Alder adducts with **12**.

Ring-opening reactions of the 6*H*-2,3-dihydro-1,2-thiazine 1-oxides are known and this could be used in the synthesis

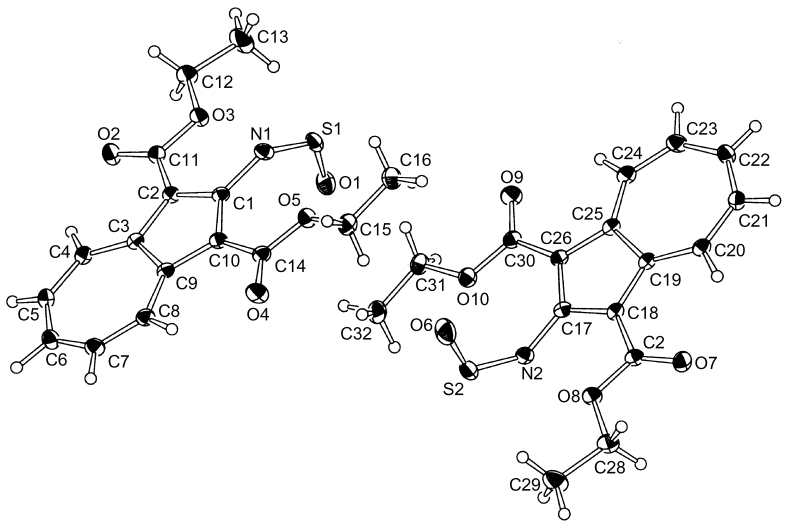
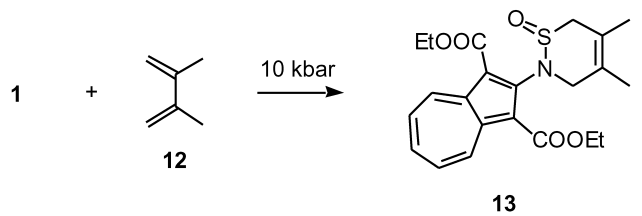


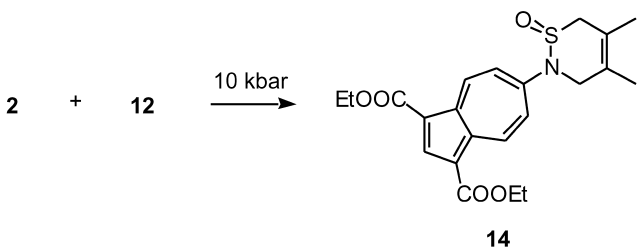
Figure 3. ORTEP drawing of two independent molecules of **1** in the crystalline state along with the numbering scheme. Thermal ellipsoids are drawn at the 30% probability level. The two molecules exhibit slight difference in their conformations. Selected bond lengths (Å) and angles (deg). For **I**: C1–N1=1.401(3), N1–S1=1.499(2), S1–O1=1.453(2), C1–N1–S1=129.5(2), N1–S1–O1=119.6(1). For **II**: C17–N2=1.395(3), N2–S2=1.495(2), S2–O6=1.448(2), C17–N2–S2=132.8(2), N2–S2–O6=120.0(1).

of 4-amino-2-butene-1-sulfinate derivatives.[16] The cycloadducts **13** and **14** also reacted with ethanol in chloroform in the presence of hydrochloric acid to afford the 4-amino-2-butene-1-sulfinate derivatives **15** and **16** in 98% and 83% yields, respectively, along with **17** in the case of the reaction of **14** (Schemes 5 and 6).

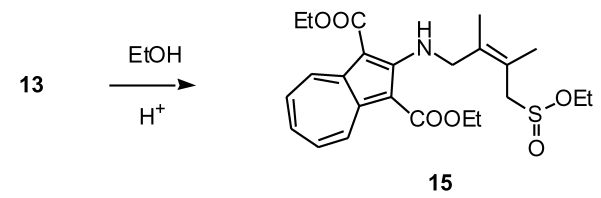
The cumultative double bond systems in isothiocyanate also show enhanced reactivity in cycloaddition reactions.[17] We have also focussed the synthesis of the azulene-substituted isothiocyanate. We found that the treatment of 2-aminoazulene (**4**) with carbon disulfide in dry toluene in the presence of triethylamine and the following reaction with phosphorus oxychloride in the presence of triethylamine afforded the desired 2-azulenyl isothiocyanate (**3**), although the yield was poor (Scheme 7). When the reaction was carried out using the diethyl 2-aminoazulene-1,3-dicarboxylate (**5**), the desired isothiocyanates could not be obtained under the similar reaction conditions. The results might be a consequence of the low reactivity of the amine **5** with carbon disulfide. Although the *N*-sulfinylamines are highly moisture sensitive compounds, the isothiocyanate **3** was stable compound and purified by column chromatography on silica gel. Satisfactory microanalysis also could be



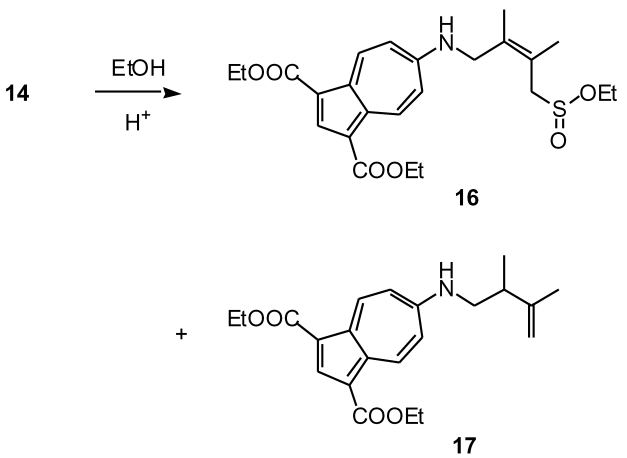
Scheme 3.



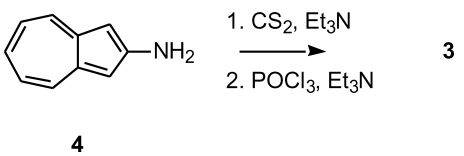
Scheme 4.



Scheme 5.



Scheme 6.



Scheme 7.

obtained as described in Section 4. The characteristic absorption of N═C═S function of **3** was observed on the IR spectra at 2164 and 2128 cm^{-1}. The absorption maximum of **3** in visible region showed a slight hypsochromic shift by 19 nm as compared with that of parent azulene (**18**) (Table 1). As expected by the substituent effect of N═C═S function in monosubstituted benzene,[18] compound **3** did not exhibit significant chemical shift difference in the *ipso*-carbon and also C-1 and C-3 signals with those of **18** (Tables 2 and 3).

To clarify the electrochemical property of the azulene-substituted heterocycles the redox behavior of the adducts **13** and **14** was examined by cyclic voltammetry (CV) and differential pulse voltammetry (DPV) and compared with those of the corresponding aminoazulenes **5** and **8**. Redox potentials (in volts vs Ag/Ag^{+}) of **5**, **8**, **13**, and **14** measured by CV and DPV are summarized in Table 4. The reduction wave of **13** and **14** are shown in Figure 4. Electrochemical reduction of aminoazulenes **5** and **8** exhibited an irreversible wave at −1.85 V and −1.90 V, respectively, upon CV due to the formation of radical anions. The less negative reduction potential of **5**, compared with that of **8**, indicates the slightly higher electron affinity of 2-amino derivative **5**. Compounds **13** and **14** showed an irreversible reduction wave at −1.48 V and −1.42 V, respectively, upon CV. The reduction potentials of **13** and **14** are less negative by 0.37 V and 0.48 V, respectively, as compared with those of aminoazulenes **5** and **8** due to the stabilization of the reduction state by the resonance effect of amine function with S═O group in the attached heterocycle moiety. The larger potential difference in **8** and **14**, compared with that in **5** and **13**, is correspond to the larger effect of the formation of a heterocycle in 6-amino derivative **8**. The larger effect in **14** could be explained by the existence of the formal cyclopentadienide substructure in the resonance form, which should stabilize the reduction state more effectively by push–pull effect, as illustrated in Scheme 8, in addition to the slightly low electron affinity of **8**.

The electrochemical oxidation of **13** and **14** showed an irreversible wave at +1.12 and +1.13 V, respectively, due to the oxidation of an azulene ring to give radical cationic species. The more positive oxidation potentials of **13** and **14** by 0.17–0.23 V than those of **5** and **8** exhibited the destabilization of the radical cationic state by the heterocycles. However, the potential differences in the electrochemical oxidation are less than those in the reduction. Thus, the attachment of the heterocyle unit with azulene increases the amphoteric properties (Table 4).

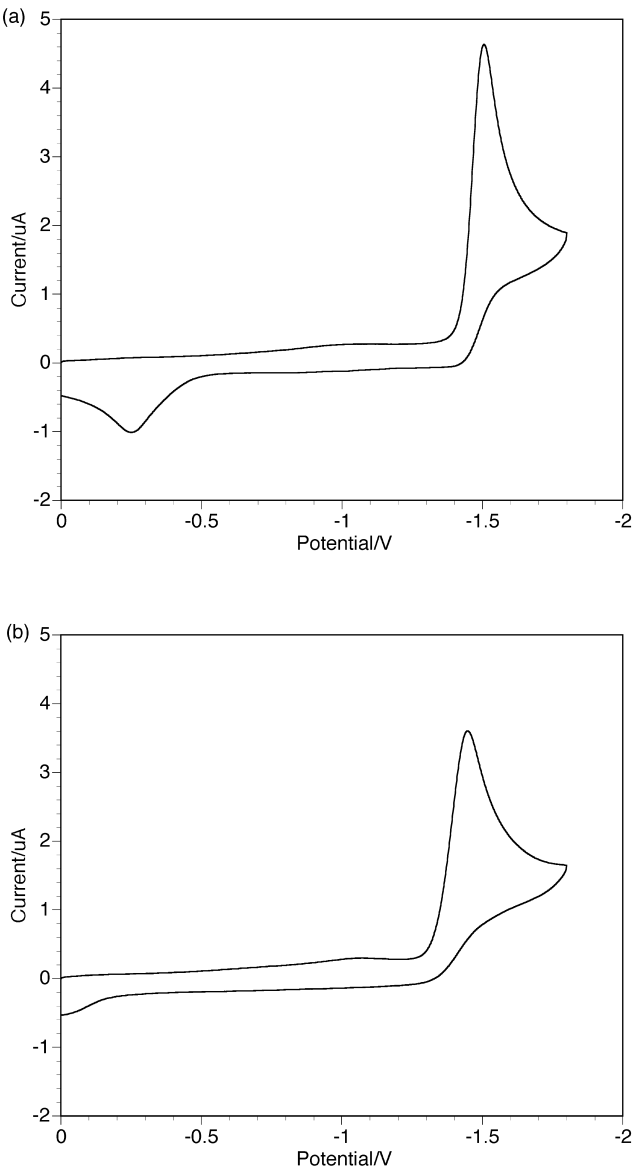


Figure 4. Cyclic voltammograms of (a) **13** and (b) **14** (1 mM) in PhCN containing Et_4NClO_4 (0.1 M) as a supporting electrolyte; scan rate, 100 mV/s.

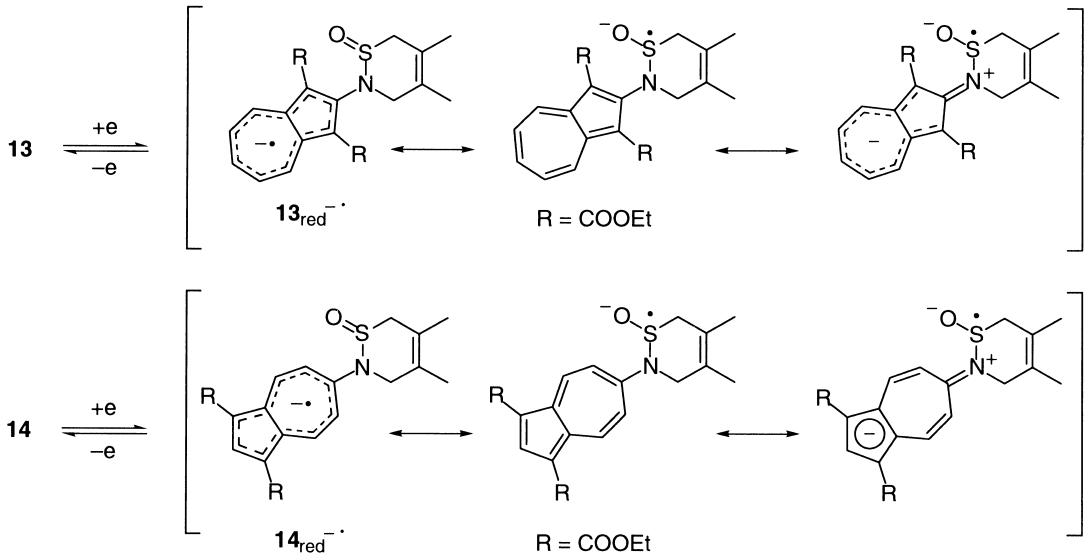
Table 4. Redox potentials of the compounds **5**, **8**, **13**, and **14**

Sample	E_1^{ox}	E_2^{ox}	E_3^{ox}	E_1^{red}	$E_1^{ox}-E_1^{red}$
5	0.95	1.08	1.79	−1.85	2.80
	(0.92)	(1.06)	(1.71)	(−1.82)	(2.74)
8	0.90			−1.90	2.80
	(0.87)			(−1.88)	(2.75)
13	1.12	1.52		−1.48	2.60
	(1.08)	(1.47)		(−1.45)	(2.53)
14	1.13	1.78		−1.42	2.55
	(1.11)	(1.72)		(−1.39)	(2.50)

The redox potentials were measured by CV and DPV (in parentheses) (0.1 M Et_4NClO_4 in benzonitrile, Pt electrode, scan rate=100 mV/s, and Fc/Fc^{+}=+0.15 V). All of the waves are irreversible. In the case of CV, E_{ox} and E_{red} values were calculated as E_{pa} (anodic peak potential) −0.03 and E_{pc} (cathodic peak potential)+0.03 V, respectively.

3. Conclusions

In conclusion, the results described above demonstrate that azulene-substituted *N*-sulfinylamines **1** and **2** are prepared conveniently by the reaction of the corresponding amines with thionyl chloride in high yields. We could also obtain 2-azulenyl isothiocyanate (**3**), although the yield was poor. A possible use of the *N*-sulfinylamines **1** and **2** as dienophile partners in heterocycloaddition reactions was investigated. The S═N bond of *N*-sulphinylamines participates the [4+2] cycloadditions with 1,3-dienes. The redox behavior of the azulene-substituted heterocycles **13** and **14** was also examined by CV, which revealed the stabilization of the reduction state and increasing the amphoteric properties of



Scheme 8.

azulene ring as compared with those of aminoazulenes **5** and **8**. Apart from the cycloaddition that we have examined, a number of other reactions are also known for the heterocumulenes. This study shows the potential utility of the novel heterocumulenes substituted directly by azulene for the preparation of azulene-substituted heterocycles.

4. Experimental

4.1. General

Melting points were determined on a Yanagimoto micro melting point apparatus MP-S3 and are uncorrected. Mass spectra were obtained with a Hitachi M-2500 instrument usually at 70 eV. IR and UV spectra were measured on a Shimadzu FTIR-8100M and a Hitachi U-3410 spectrophotometers, respectively. ^{1}H NMR spectra (^{13}C NMR spectra) were recorded on a JEOL GSX 400 at 400 MHz (100 MHz), a JEOL A500 at 500 MHz (125 MHz) or a Bruker AM 600 spectrometer at 600 MHz (150 MHz). Gel permeation chromatography (GPC) was performed on a TSKgel G2000H$_6$. Elemental analyses were performed at the Instrumental Analysis Center of Chemistry, Faculty of Science, Tohoku University.

4.1.1. *N*-Sulfinyl-1,3-bis(ethoxycarbonyl)-2-azulenylamine (1). To a solution of **5** (1.46 g, 5.08 mmol) in dry benzene (50 ml) was added thionyl chloride (2.00 g, 16.8 mmol). The resulting mixture was refluxed for 3 d under an Ar atmosphere. After the solvent was removed under reduced pressure, the residue was purified by recrystallization from toluene/hexane to afford **1** (1.60 g, 94%): red prisms; mp 96–98°C; MS (70 eV) *m/z* (relative intensity) 333 (M$^+$, 100%) and 288 (M$^+$−OEt, 56); IR (KBr disk) ν_{max} 1682 (C=O), 1443, 1433, 1300, 1183, and 1148 cm^{-1}; UV–vis (CH_2Cl_2) λ_{max} 239 (log ε 4.49), 263 (4.30), 302 sh (4.63), 311 (4.73), 343 sh (3.98), 367 sh (3.78), 390 sh (3.31), 482 sh (2.73), 507 sh (2.72), and 555 sh (2.43) nm. Anal. Calcd for $C_{16}H_{15}NO_5S$: C, 57.65; H, 4.54; N, 4.20; S, 9.62. Found: C, 57.95; H, 4.69; N, 4.27; S, 9.41.

4.1.2. Diethyl 6-azidoazulene-1,3-dicarboxylate (7). A mixture of **6** (3.15 g, 8.97 mmol) and sodium azide (1.19 g, 18.3 mmol) in DMSO (300 ml) was heated at 70°C for 1.5 h under an Ar atmosphere. The reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on Al_2O_3 with CH_2Cl_2 to afford **7** (2.59 g, 92%): deep red powder; mp 150.5–152°C decomp.; MS (70 eV) *m/z* (relative intensity) 313 (M$^+$, 96%), 285 (M$^+$−N$_2$, 49), 229 (M$^+$−N$_2$−2Et+2H, 43), and 212 (M$^+$−N$_2$−COOEt, 100); IR (KBr disk) ν_{max} 2110 (N$_3$), 1682 (C=O), 1580, 1431, 1391, 1279, 1266, and 1204 cm^{-1}; UV–vis (CH_2Cl_2) λ_{max} 268 sh (log ε 4.12), 278 (4.17), 327 sh (4.75), 334 (4.76), 368 sh (4.18), 374 (4.20), 500 (2.92), 540 sh (2.76), and 579 sh (2.30) nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ=9.54 (d, J=11.2 Hz, 2H, H-4,8), 8.63 (s, 1H, H-2), 7.21 (d, J=11.2 Hz, 2H, H-5,7), 4.42 (q, J=7.1 Hz, 4H, 1,3-COOEt), and 1.45 (t, J=7.0 Hz, 6H, 1,3-COOEt); ^{13}C NMR (100 MHz, $CDCl_3$) δ=164.7 (s, 1,3-COOEt), 152.1 (C-6), 141.4 (C-2), 140.7 (C-3a,8a), 138.1 (C-4,8), 120.7 (C-5,7), 117.4 (C-1,3), 60.1 (t, 1,3-COOEt), and 14.5 (q, 1,3-COOEt). Anal. Calcd for $C_{16}H_{15}N_3O_4$: C, 61.34; H, 4.83; N, 13.41. Found: C, 61.16; H, 4.90; N, 13.16.

4.1.3. Diethyl 6-aminoazulene-1,3-dicarboxylate (8). To a solution of **7** (1.69 g, 5.39 mmol) in THF (30 ml) was added a mixture of 25 ml of 15% NaOH solution and 15 g of ice. At 1 h intervals, 588, 572, 889, and 638 mg portions of Raney nickel–aluminum alloy were added to the resulting suspension with vigorous stirring. The suspension was poured into CH_2Cl_2 (100 ml) and the nickel was removed by filtration. The organic layer was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with CH_2Cl_2 and ethyl acetate to afford **8** (1.44 g, 93%): yellow crystals; mp 232–235°C [lit.[11a] mp 236–237°C].

4.1.4. *N*-Sulfinyl-1,3-bis(ethoxycarbonyl)-6-azulenylamine (2). The same procedure used for the prepartion of **1** was adopted. The reaction of **8** (115 mg, 0.400 mmol) with thionyl chloride (267 mg, 2.24 mmol) in dry benzene (20 ml) for 1 d afforded **2** (128 mg, 96%): brown crystals; mp 108.5–110°C; MS (70 eV) *m/z* (relative intensity) 333 (M^+, 100%) and 288 (M^+-OEt, 53); IR (KBr disk) ν_{max} 1678 (C=O), 1651 (C=O), 1431, 1387, 1204, 1171, and 1048 cm^{-1}; UV–vis (CH_2Cl_2) λ_{max} 257 (log ε 4.39), 270 sh (4.28), 311 sh (4.32), 315 sh (4.32), 340 (4.45), 372 sh (4.20), 399 (3.93), 417 sh (3.81), and 553 (2.69) nm. HRMS calcd for $C_{16}H_{15}NO_5S$, 333.0665; found 333.0666. Anal. Calcd for $C_{16}H_{15}NO_5S$: C, 57.65; H, 4.54; N, 4.20; S, 9.62. Found: C, 57.84; H, 4.73; N, 4.23; S, 9.37.

4.1.5. 2-[1,3-Bis(ethoxycarbonyl)-2-azulenyl]-4,5-dimethyl-6*H*-2,3-dihydro-1,2-thiazine 1-oxide (13). A teflon vessel (9.1 ml) was filled with **1** (507 mg, 1.52 mmol), **12** (626 mg, 7.62 mmol), and CH_2Cl_2. The mixture was left at 10 kbar (40°C) for 3 d. After the solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel with 5% ethyl acetate/CH_2Cl_2 and 70% ethyl acetate/CH_2Cl_2 to afford **5** (110 mg, 25%) and **13** (414 mg, 66%): orange needles; mp 126–128°C; MS (70 eV) *m/z* (relative intensity) 415 (M^+, 7%), 367 (M^+-SO, 40), and 333 ($M^+-C_6H_{10}$, 100); IR (KBr disk) ν_{max} 1700 (C=O), 1673 (C=O), 1460, 1433, 1196, and 1086 cm^{-1}; UV–vis (CH_2Cl_2) λ_{max} 271 (log ε 4.27), 305 sh (4.42), 323 (4.51), 362 sh (3.81), 391 sh (3.64), and 505 (2.65) nm; ^1H NMR (400 MHz, $CDCl_3$) δ=9.27 (dd, J=10.7, 1.1 Hz, 2H, H-4′,8′), 7.82 (tt, J=9.7, 1.1 Hz, 1H, H-6′), 7.65 (dd, J=10.7, 9.7 Hz, 2H, H-5′,7′), 4.54 (d, J=16.3 Hz, 1H, H-3), 4.47 (dq, J=10.8, 7.1 Hz, 2H, 1′,3′-COOEt), 4.44 (dq, J=10.8, 7.1 Hz, 2H, 1′,3′-COOEt), 3.98 (d, J=15.7 Hz, 1H, H-6), 3.68 (d, J=16.3 Hz, 1H, H-3), 3.15 (d, J=15.7 Hz, 1H, H-6), 1.87 (s, 3H, 5-Me), 1.79 (s, 3H, 4-Me), and 1.43 (t, J=7.1 Hz, 6H, 1′,3′-COOEt); ^{13}C NMR (100 MHz, $CDCl_3$) δ=165.2 (s, 1′,3′-COOEt), 154.0 (C-2′), 141.3 (C-3′a,8′a), 138.9 (C-6′), 137.3 (C-4′,8′), 130.3 (C-5′,7′), 124.4 (C-5), 115.6 (C-4), 112.9 (C-1′,3′), 60.8 (t, 1′,3′-COOEt), 54.5 (C-6), 48.8 (C-3), 20.1 (5-Me), 17.1 (4-Me), and 14.4 (q, 1′,3′-COOEt). Anal. Calcd for $C_{22}H_{25}NO_5S$: C, 63.60; H, 6.06; N, 3.37; S, 7.72. Found: C, 63.56; H, 6.15; N, 3.32; S, 7.51.

4.1.6. 6-[1,3-Bis(ethoxycarbonyl)-6-azulenyl]-4,5-dimethyl-6*H*-2,3-dihydro-1,2-thiazine 1-oxide (14). The same procedure used for the preparation of **13** was adopted. The high-pressure reaction of **2** (561 mg, 1.68 mmol) with **12** (643 mg, 7.83 mmol) in a teflon vessel (9.1 ml) for 2 d afforded **14** (539 mg, 77%). The reaction of **2** (95 mg, 0.28 mmol) with **12** (244 mg, 2.97 mmol) in refluxing toluene (15 ml) for 21 h under an Ar atmosphere afforded **8** (45 mg, 55%) and **14** (34 mg, 29%): red crystals; mp 163–164°C; MS (70 eV) *m/z* (relative intensity) 415 (M^+, 18%), 333 ($M^+-C_6H_{10}$, 100), and 288 ($M^+-C_6H_{10}-OEt$, 47); IR (KBr disk) ν_{max} 1694 (C=O), 1435, 1198, and 1053 cm^{-1}; UV–vis (CH_2Cl_2) λ_{max} 259 sh (log ε 4.14), 270 (4.21), 280 (4.18), 337 (4.74), 372 (4.28), and 474 (2.99) nm; ^1H NMR (400 MHz, $CDCl_3$) δ=9.64 (d, J=11.5 Hz, 2H, H-4′,8′), 8.66 (s, 1H, H-2′), 7.47 (d, J=11.5 Hz, 2H, H-5′,7′), 4.42 (q, J=7.2 Hz, 4H, 1′,3′-COOEt), 4.37 (d, J=16.0 Hz, 1H, H-3), 3.80 (d, J=16.0 Hz, 1H, H-3), 3.77 (d, J=16.1 Hz, 1H, H-6), 3.33 (d, J=16.1 Hz, 1H, H-6), 1.88 (s, 6H, 4-Me and 5-Me), and 1.45 (t, J=7.2 Hz, 6H, 1′,3′-COOEt); ^{13}C NMR (100 MHz, $CDCl_3$) δ=165.0 (s, 1′,3′-COOEt), 156.7 (C-6′), 141.3 (C-2′), 140.6 (C-3′a,8′a), 138.1 (C-4′,8′), 124.3 (C-5), 122.6 (C-5′,7′), 116.9 (C-1′,3′), 115.4 (C-4), 60.0 (t, 1′,3′-COOEt), 55.1 (C-6), 46.5 (C-3), 19.6 (5-Me), 17.4 (4-Me), and 14.5 (q, 1′,3′-COOEt). Anal. Calcd for $C_{22}H_{25}NO_5S$: C, 63.60; H, 6.06; N, 3.37; S, 7.72. Found: C, 63.86; H, 6.31; N, 3.32; S, 7.81.

4.1.7. Ethyl 4-[1,3-bis(ethoxycarbonyl)-2-azulenylamino]-2,3-dimethyl-2-butene-1-sulfinate (15). To a solution of **13** (86 mg, 0.21 mmol) in $CHCl_3$ (10 ml) and ethanol (5 ml) was added two drops of conc HCl. The color of the solution immediately changed from red to orange. The reaction mixture was poured into water. The organic layer was separated, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with ethyl acetate to afford **15** (94 mg, 98%): yellow crystals; mp 50.5–52°C; MS (70 eV) *m/z* (relative intensity) 461 (M^+, 3%), 368 (M^+-SO_2Et, 100), 367 (M^+-HSO_2Et, 54), and 276 ($M^+-SO_2Et-2OEt$, 82); IR (KBr disk) ν_{max} 3028 (m, NH), 1684 (C=O), 1653 (C=O), 1638 (C=O), 1559, 1524, 1163, and 1132 cm^{-1}; UV–vis (CH_2Cl_2) λ_{max} 255 (log ε 4.35), 285 (4.33), 320 sh (4.68), 329 (4.75), 380 sh (3.96), 414 (4.04), and 456 sh (3.38) nm; ^1H NMR (600 MHz, $CDCl_3$) δ=8.90 (br, 2H, H-4′,8′), 8.21 (br s, 1H, 4-NH), 7.48 (dd, J=10.1, 9.9 Hz, 2H, H-5′,7′), 7.39 (t, J=9.8 Hz, 1H, H-6′), 4.45 (q, J=7.2 Hz, 4H, 1′,3′-COOEt), 4.13 (dq, J=10.1, 7.1 Hz, 1H, 1-SO_2Et), 4.10 (d, J=14.2 Hz, 1H, H-4), 4.06 (dq, J=10.1, 7.1 Hz, 1H, 1-SO_2Et), 4.05 (d, J=14.2 Hz, 1H, H-4), 3.70 (d, J=13.2 Hz, 1H, H-1), 3.60 (d, J=13.2 Hz, 1H, H-1), 1.87 (s, 3H, 2-Me), 1.81 (s, 3H, 3-Me), 1.46 (t, J=7.2 Hz, 6H, 1′,3′-COOEt), and 1.32 (t, J=7.1 Hz, 3H, 1-SO_2Et); ^{13}C NMR (150 MHz, $CDCl_3$) δ=166.7 (br s, 1′,3′-COOEt), 160.5 (C-2′), 145.0 (br, C-3′a,8′a), 134.1 (C-3), 132.5 (C-6′), 131.7 (C-5′,7′), 130.4 (br, C-4′,8′), 122.3 (C-2), 101.8 (br, C-1′,3′), 65.0 (t, 1-SO_2Et), 63.1 (C-1), 60.2 (t, 1′,3′-COOEt), 50.4 (C-4), 20.7 (2-Me), 17.7 (3-Me), 15.9 (q, 1-SO_2Et), and 14.6 (q, 1′,3′-COOEt). Anal. Calcd for $C_{24}H_{31}NO_6S$: C, 62.45; H, 6.77; N, 3.03; S, 6.95. Found: C, 62.29; H, 6.60; N, 3.15; S, 6.85.

4.1.8. Ethyl 4-[1,3-bis(ethoxycarbonyl)-6-azulenylamino]-2,3-dimethyl-2-butene-1-sulfinate (16). The same procedure used for the preparation of **15** was adopted. The reaction of **14** (312 mg, 0.752 mmol) with 8 drops of conc HCl in $CHCl_3$ (30 ml) and ethanol (15 ml) afforded **16** (288 mg, 83%) and **17** (24 mg, 9%).

4.1.9. Ethyl 4-[1,3-bis(ethoxycarbonyl)-6-azulenylamino]-2,3-dimethyl-2-butene-1-sulfinate (16). Yellow crystals; mp 92–94.5°C; MS (70 eV) *m/z* (relative intensity) 461 (M^+, 31%), 368 (M^+-SO_2Et, 86), 367 (M^+-HSO_2Et, 100), and 322 ($M^+-HSO_2Et-OEt$, 40); IR (KBr disk) ν_{max} 3337 (m, NH), 1678 (C=O), 1667 (C=O), 1595, 1584, 1435, 1383, 1215, and 1198 cm^{-1}; UV–vis (CH_2Cl_2) λ_{max} 256 (log ε 4.21), 276 (4.24), 286 (4.31), 344 (4.84), 374 sh (4.40), 391 sh (4.18), and 426 (3.67) nm; ^1H NMR (400 MHz, $CDCl_3$) δ=9.31 (d, J=11.1 Hz, 2H, H-4′,8′), 8.25 (s, 1H, H-2′), 6.79 (d, J=11.1 Hz, 2H, H-5′,7′), 6.67 (br

s, 1H, 4-NH), 4.36 (q, J=7.1 Hz, 4H, 1′,3′-COOEt), 4.18 (dq, J=10.0, 7.1 Hz, 1H, 1-SO_2Et), 4.10 (dq, J=10.0, 7.1 Hz, 1H, 1-SO_2Et), 3.93 (dd, J=13.4, 2.9 Hz, 1H, H-4), 3.82 (dd, J=13.4, 5.9 Hz, 1H, H-4), 3.71 (d, J=13.0 Hz, 1H, H-1), 3.54 (d, J=13.0 Hz, 1H, H-1), 1.88 (s, 6H, 2-Me and 3-Me), 1.41 (t, J=7.1 Hz, 6H, 1′,3′-COOEt), and 1.35 (t, J=7.1 Hz, 3H, 1-SO_2Et); ^{13}C NMR (100 MHz, $CDCl_3$) δ=165.8 (s, 1′,3′-COOEt), 160.0 (C-6′), 139.0 (br, C-4′,8′), 136.0 (C-3′a,8′a), 134.9 (C-2′), 134.2 (C-3), 123.6 (C-2), 115.5 (C-1′,3′), 65.8 (t, 1-SO_2Et), 62.9 (C-1), 59.4 (t, 1′,3′-COOEt), 46.3 (C-4), 20.1 (2-Me), 19.5 (3-Me), 15.9 (q, 1-SO_2Et), and 14.6 (q, 1′,3′-COOEt). HRMS calcd for $C_{24}H_{31}NO_6S$, 461.1867; found 461.1856. Anal. Calcd for $C_{24}H_{31}NO_6S$: C, 62.45; H, 6.77; N, 3.03; S, 6.95. Found: C, 62.08; H, 6.60; N, 3.03; S, 6.66.

4.1.10. Diethyl 6-(2,3-dimethyl-3-butenyl)azulene-1,3-dicarboxylate (17). Yellow needles; mp 112–113.5°C; MS (70 eV) m/z (relative intensity) 369 (M^+, 53%) and 300 ($M^+-C_5H_9$, 100); IR (KBr disk) ν_{max} 3347 (m, NH), 1661 (C=O), 1595, 1435, 1418, 1383, 1200, 1154, and 1046 cm^{-1}; UV–vis (CH_2Cl_2) λ_{max} 256 (log ε 4.05), 276 (4.10), 285 (4.19), 344 (4.79), 375 (4.32), 390 sh (4.07), and 429 (3.57) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ=9.35 (d, J=11.6 Hz, 2H, H-4′,8′), 8.28 (s, 1H, H-2′), 6.73 (d, J=11.6 Hz, 2H, H-5′,7′), 5.22 (dd, J=5.5, 4.4 Hz, 1H, NH), 4.97 (m, 1H, H-4), 4.92 (m, 1H, H-4), 4.37 (q, J=7.1 Hz, 4H, 1′,3′-COOEt), 3.29 (ddd, J=12.5, 5.5, 5.5 Hz, 1H, H-1), 3.19 (ddd, J=12.5, 9.2, 4.4 Hz, 1H, H-1), 2.61 (m, 1H, H-2), 1.72 (m, 3H, 3-Me), 1.42 (t, J=7.1 Hz, 6H, 1′,3′-COOEt), and 1.18 (d, J=7.0 Hz, 3H, 2-Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ=165.8 (s, 1′,3′-COOEt), 159.2 (C-6′), 146.0 (C-3), 139.2 (C-4′,8′), 136.2 (C-3′a,8′a), 135.3 (C-2′), 115.8 (C-1′,3′), 114-115 (br, C-5′,7′), 113.4 (C-4), 59.5 (t, 1′,3′-COOEt), 46.7 (C-1), 40.6 (C-2), 18.3 (3-Me), 17.3 (2-Me), and 14.6 (q, 1′,3′-COOEt). Anal. Calcd for $C_{22}H_{27}NO_4\cdot 1/3H_2O$: C, 70.38; H, 7.43; N, 3.73. Found: C, 70.57; H, 7.36; N, 3.83.

4.1.11. 2-Azulenylisothiocyanate (3). To a solution of **4** (153 mg, 1.07 mmol) in CS_2 (15 ml) was added triethylamine (153 mg, 1.51 mmol). The resulting mixture was stirred at room temperature for 24 h under an Ar atmosphere. After the solvent was removed under reduced pressure, the residue was diluted by triethylamine (213 mg, 2.10 mmol) and dry CH_2Cl_2 (20 ml). To the resulting mixture was added $POCl_3$ (170 mg, 1.11 mmol) at 0°C and the resulting mixture was stirred at room temperature for 24 h under an Ar atmosphere. The reaction mixture was poured into 3% $NaHCO_3$ solution and the organic layer was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with 80% CH_2Cl_2/hexane to afford **3** (28 mg, 14%): purple crystals; mp 74–75°C; MS (70 eV) m/z (relative intensity) 185 (M^+, 100%); IR (KBr disk) ν_{max} 2164 (N=C=S), 2128 (N=C=S), 1406, and 785 cm^{-1}; UV–vis (CH_2Cl_2) λ_{max} 247 sh (log ε 4.31), 258 (4.40), 295 (4.79), 306 (4.91), 333 sh (3.65), 347 sh (3.86), 362 (4.14), 379 (4.35), 513 sh (2.46), 557 (2.66), 591 (2.65), and 642 sh (2.29) nm. Anal. Calcd for $C_{11}H_7NS$: C, 71.32; H, 3.81; N, 7.56; S, 17.31. Found: C, 71.22; H, 3.89; N, 7.55; S, 17.40.

4.1.12. X-Ray crystallographic data for 1. Data and diffraction parameters were obtained for a crystal with dimension 0.30×0.25×0.20 mm^3 using a Rigaku/MSC mercury CCD diffractometer with Mo Kα radiation (λ=0.71069 Å) at −123°C. Crystal system: monoclinic. Space group: P$\bar{1}$. Unit cell dimensions: a=8.4252(9) Å, b=10.8822(7) Å, c=18.139(2) Å, α=82.095(3)°, β=76.437(3)°, γ=78.602(1)°, V=1577.5(3) $Å^3$, Z=4. D_{calcd}=1.404 g cm^{-3}. μ (Mo Kα)=2.30 cm^{-1}. F (000)=696. 2θ range for data collection=0.0–59.7°. Number of measured reflections=10588. Independent reflections=6268 (R_{int}=0.016). Final R=0.043, R_w=0.047 for 4830 observed reflections ($I_0>3\sigma(I_0)$). Parameters=415. GOF=1.70. $\Delta\rho_{max}$ and $\Delta\rho_{min}$ are 0.17 and −0.18 e^- $Å^{-3}$, respectively. Refinement method: full-matrix least-squares. All calculations were performed using software package of Molecular Structure Corporation (Crystal Structure Analysis Package, Molecular Structure Corporation, 1985 and 1999).

Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 196832. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

References

1. Zeller, K.-P. In *Houben-Weyl; Methoden der Organischen Chemie*; Georg Thieme: Stuttgart, 1985; Vol. V/2c, pp 127–418.
2. See, e.g.: (a) Ohshiro, Y. *Yuki Gosei Kagaku Kaishi* **1995**, *53*, 846–857. (b) Katritzky, A. R.; Rees, C. W. *Comprehensive Heterocyclic Chemistry*; Pergamon: Oxford, 1984; Vol. 1–8.
3. (a) Ito, S.; Inabe, H.; Okujima, T.; Morita, N.; Watanabe, M.; Harada, H.; Imafuku, K. *J. Org. Chem.* **2001**, *66*, 7090–7101. (b) Ito, S.; Inabe, H.; Okujima, T.; Morita, N.; Watanabe, M.; Harada, N.; Imafuku, K. *Tetrahedron Lett.* **2001**, *42*, 1085–1089. (c) Ito, S.; Inabe, H.; Okujima, T.; Morita, N.; Watanabe, M.; Imafuku, K. *Tetrahedron Lett.* **2000**, *41*, 8343–8347.
4. Ulrich, H. *Cycloaddition Reactios of Heterocumulenes*; Academic: New York, 1967.
5. (a) Huang, T. H.; Morita, T.; Lin, B. B.; Lin, Y. S. *J. Chin. Chem. Soc., (Taipei)* **1994**, *41*, 199–203. (b) Horino, H.; Toda, T. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1212–1215. (c) Nozoe, T.; Horino, H.; Toda, T. *Tetrahedron Lett.* **1967**, 5349–5353. (d) Nitta, M.; Iino, Y.; Mori, S.; Takayasu, T. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1001–1007. (e) Nitta, M.; Iino, Y.; Sugiyama, T.; Akaogi, A. *Tetrahedron Lett.* **1993**, *34*, 831–834. (f) Hafner, K.; Patzelt, H.; Kaiser, H. *Liebigs Ann. Chem.* **1962**, *656*, 24–33.
6. (a) Becker, D. A. *J. Am. Chem. Soc.* **1996**, *118*, 905–906. (b) Becker, D. A.; Natero, R.; Echegoyen, L.; Lawson, R. C. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1289–1292.
7. Asao, T. *Pure Appl. Chem.* **1990**, *62*, 507–512.
8. See, e. g.: (a) Romano, R. M.; Della Védova, C. O. *J. Mol. Struct.* **2000**, *522*, 1–26. (b) Johnson, C. R. *Compr. Org. Chem.*; Pergamon: Oxford, 1979; Vol. 3. pp 241–246.

9. Nozoe, T.; Seto, S.; Matsumura, S.; Murase, Y. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1179–1188.
10. Replogle, L. L.; Peters, G. C.; Maynard, J. R. *J. Org. Chem.* **1969**, *34*, 2022–2024.
11. (a) Nozoe, T.; Takase, K.; Tada, M. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 1006–1009. (b) Nozoe, T.; Takase, K.; Tada, M. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 247–251. (c) Nozoe, T.; Takase, K. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1948–1951.
12. Heilbronner, E. In *Non-Benzenoid Aromatic Compounds*; Ginsburg, D., Ed.; Interscience: New York, 1959; pp 171–276.
13. Butler, R. N.; O'Halloran, G. A.; Burke, L. A. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1855–1989.
14. Romano, R. M.; Della Védova, C. O.; Boese, R. *J. Mol. Struct.* **1999**, *475*, 1–4.
15. Bell, S. I.; Weinreb, S. M. *Tetrahedron Lett.* **1988**, *34*, 4233–4236.
16. (a) Wucherpfenning, W. *Justus Liebigs Ann. Chem.* **1971**, *746*, 16–27. (b) Kresze, G.; Rössert, M. *Liebigs Ann. Chem.* **1981**, 58–64.
17. See, e.g.: (a) Mukerjee, A. K.; Ashare, R. *Chem. Rev.* **1991**, *91*, 1–24. (b) L'abbé, G. *Synthesis* **1987**, 525–531.
18. Ewing, D. F. *Org. Magn. Reson.* **1979**, *12*, 499–524.