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REACTION OF 2-AMINOAZULENES WITH ALDEHYDES. ONE POT SYNTHESIS OF DIAZULENO[2,1-*b*:1,2-*e*]PYRIDINES†

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Abstract **-** Diazuleno[2,1-*b*:1,2-*e*]pyridines (**2a** and **2b**) were prepared in one pot by the reaction of 2-aminoazulene (**1a**) with paraformaldehyde or benzaldehyde in moderate yields. Bis(2-amino-3-ethoxycarbonyl-1-azulenyl)methane (**8a**) was formed by the reaction of ethyl 2-aminoazulene-1-carboxylate (**1b**) with 1/2 molar amount of paraformaldehyde. Treatment of **8a** with paraformaldehyde at room temperature afforded three heterocyclic compounds (**9**, **10**, and **11**). When 2-acetylaminoazulenes (**1c** and **1d**) were used for this reaction, bis(2-acetylamino-1-azuleny)methanes (**8b** and **8c**) were exclusively formed.

INTRODUCTION

The reaction of azulenes with aldehydes under acidic conditions leads to the formation of di(1-azulenyl)methane derivatives along with 1,3-bis(1-azulenylmethyl)azulene derivatives.[1,2] The reaction have been applied to the substituted azulenes including 2-methoxy- and 2-hydroxyazulenes, and a variety of substituted bis(1-azulenyl)methane derivatives have been obtained in high yields.[3] It has also been reported that the extremely stable carbocations with high pK_R^+ values were derived from di(1-azulenyl)phenylmethane and tri(1-azulenyl)methane derivatives.[2b,4]

A novel azulene analogue of calixarenes[5] consisting of four molecules of 2-methoxyazulene, i.e., [1.1.1.1]-2-methoxyazulenophane, has been synthesized using 2-methoxyazulenes and paraformaldehyde under acidic conditions.[3a] Our studies to prepare the calixarene derivatives from azulenes have been focused on the reaction of 2-aminoazulene derivatives with aldehydes. To the best of our knowledge, no

† Dedicated to Prof. Shô Ito on the occasion of his 77th birthday.

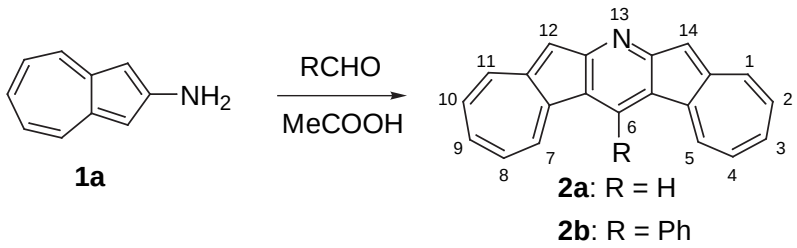
reactions of 2-aminoazulenes with aldehydes to produce di(1-azulenyl)methane derivatives have been reported hitherto.[6] We have investigated the reaction of several 2-aminoazulenes (**1a**–**d**) with aldehydes toward the synthesis of calixarene derivatives. In this paper, we will report the reaction of 2-aminoazulenes (**1a**–**d**) with aldehydes under acidic conditions.

RESULTS AND DISCUSSION

We have carried out the reaction of 2-aminoazulene (**1a**)[7] with aldehydes in acetic acid to prepare the di(1-azulenyl)methane derivatives. However, the reaction afforded diazuleno[2,1-*b*:1,2-*e*]pyridine (**2a**) as the sole product in 47% yield (Scheme 1). Synthesis of **2a** by a multi-step reaction starting from **1a** has been reported by Morita *et al*.[8] Likewise, 6-phenyldiazuleno[2,1-*b*:1,2-*e*]pyridine (**2b**) was obtained by the reaction of **1a** with benzaldehyde in 51% yield.

Scheme 2 illustrates a possible mechanism for the formation of **2a** and **2b** by the reaction of **1a** with aldehydes. Mixing of **1a** with aldehydes initially leads to the formation of **5**, because the reaction of azulenes with aldehydes has been known to give bis(1-azulenyl)methane derivatives.

Scheme 1

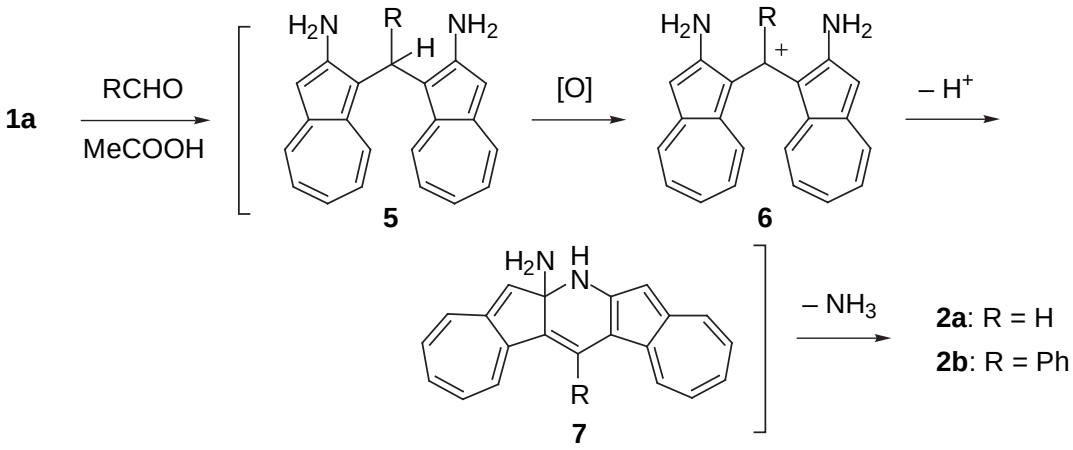


1a

2a: R = H

2b: R = Ph

Scheme 2



^{1}H NMR chemical shift of H_6 in **2a** is observed at down field (δ 9.24) compared with that of pyridine (δ 7.64). Large upfield shifts of $H_{4,8}$ and $H_{5,7}$ (δ 6.77 and 7.21, respectively) in **2b** compared with those of

2a (δ 7.21 and 8.33, respectively) are attributable to the anisotropic effect of the phenyl group at the 6 position. A remarkable difference of the vicinal coupling constants ($J_{1,2}$ = 10.8, $J_{2,3}$ = 8.3, $J_{3,4}$ = 10.8, and $J_{4,5}$ = 8.2 Hz for **2a**; $J_{1,2}$ = 10.8, $J_{2,3}$ = 8.3, $J_{3,4}$ = 10.9, and $J_{4,5}$ = 8.9 Hz for **2b**) in ^{1}H NMR spectra suggests a large bond alternation in azulene moiety. Thus, the 22π-electron periferality seems to be less important for **2a** and **2b**.

The UV–VIS spectra of **2a** and **2b** in acetonitrile are shown in Figure 1. When a drop of concentrated hydrochloric acid was added into the solutions, the color of the solutions changed from brown to deep red, which exhibited a strong absorption at 436 (log ε 5.13) and 438 (5.14) nm, respectively (Figure 2). These results indicate the formation of diazuleno[2,1-*b*:1,2-*e*]pyridiniums (**3a** and **3b**) by the protonation of **2a** and **2b**. Conjugate acids (**3a** and **3b**) are stabilized by the canonical structures **4** as shown in Chart 1.

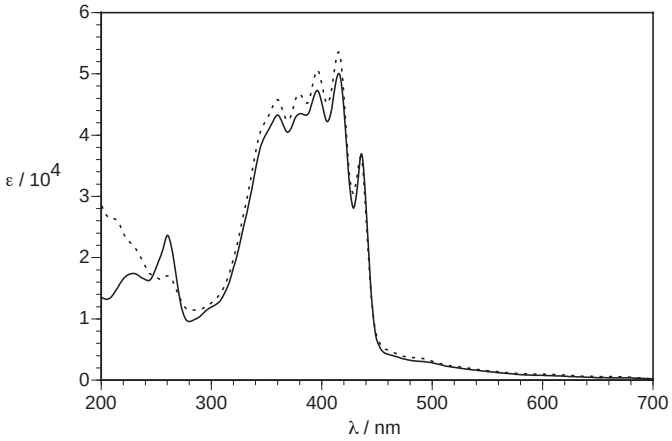


Figure 1. UV–VIS sprectra of **2a** (soild line) and **2b** (dotted line) in acetonitrile.

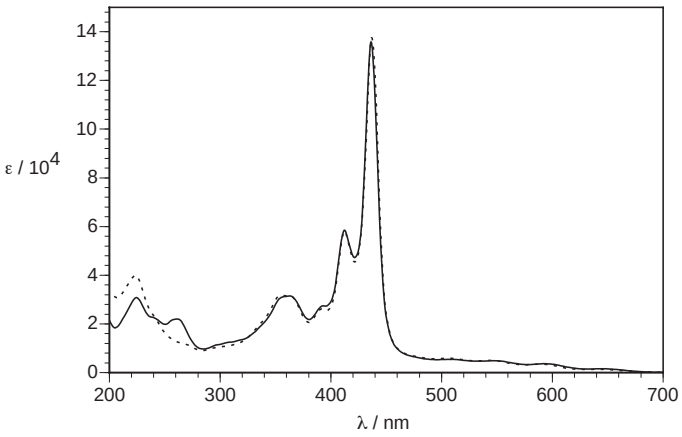
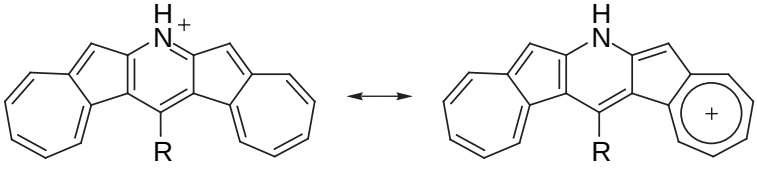


Figure 2. UV–VIS sprectra of **3a** (soild line) and **3b** (dotted line) in acetonitrile.

Chart 1



3a: R = H
3b: R = Ph

4

The pK_a values of the conjugate acids (**3a** and **3b**) were determined spectrophotometrically at 25 °C in a buffer solution prepared in 50% aqueous acetonitrile.[2b,9] The pK_a values of **3a** (7.0 ± 0.1) and **3b** (6.5 ± 0.1) are relatively high for pyridine derivatives. The larger pK_a values of **3a** and **3b** compared with that of pyridine (pK_a 5.17)[10] provide a criterion of the relatively high basicity of **2a** and **2b**. They are as large as

that of 2,6-dimethylpyridine (pK_a 6.75).[10] The protonation and the neutralization of **2a** and **2b** are completely reversible. Neutralization of the acidic solutions of **3a** and **3b** with NaOH regenerated the absorption of **2a** and **2b** in the UV–VIS region quantitatively.

We have then attempted the reaction of ethyl 2-aminoazulene-1-carboxylate (**1b**)[7] with paraformaldehyde to examine the effect of 1-ethoxycarbonyl substituent on azulene ring as shown in Scheme 3. Table 1 summarizes the results under several conditions. In contrast to the formation of **2a** and **2b**, bis(2-amino-3-ethoxycarbonyl-1-azulenyl)methane (**8a**) was formed in 87% yield using 1/2 molar amount of paraformaldehyde (entry 1). The product (**8a**) did not afford diazuleno[2,1-*b*:1,2-*e*]pyridine derivative even in refluxing acetic acid.

Scheme 3

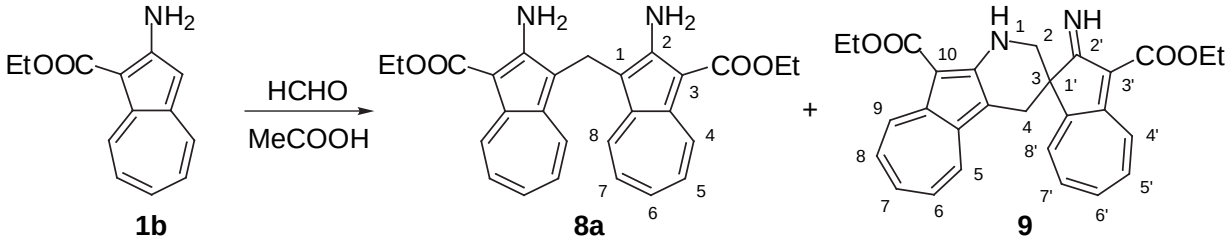


Table 1. Reaction of Ethyl 2-Amino-1-carboxylate (**1b**) with Paraformaldehyde at Room Temperature

entry	**1b** : HCHO	conditions	**8a**	**9**
1	2 : 1	20 h	87%	0%
2	1 : 1.2	20 h	0%	85%
3	1 : 1	4 h	73%	25%

Use of 1.2 molar amounts of paraformaldehyde afforded 1-aza-10-ethoxycarbonyl-1,2,3,4-tetrahydrobenz[*a*]azulene-3-spiro-1'-(3'-ethoxycarbonyl-1',2'-dihydroazulene)-2'-imine (**9**) in 85% yield instead of **8a** (entry 2). When the reaction of **1b** with the equimolar amount of paraformaldehyde was stopped at an early stage, **8a** and **9** were obtained in 73 and 25% yields, respectively (entry 3). Formation of **9** could be attributable to the further reaction from **8a** with paraformaldehyde under the conditions.

We have found that the reaction of **8a** with paraformaldehyde in acetic acid gives three heterocyclic compounds (**9**, **10**, and **11**) (Scheme 4). Table 2 summarizes the results under various conditions. The products ratio depends on the reaction conditions. Treatment of **8a** with 5-molar amount of paraformaldehyde gave **9** in 43% yield along with **10** and **11** in 21 and 26% yields, respectively (entry 2). When the reaction was stopped at an early stage (5 h), the ratio of the products (**9** and **10**) increased to 4:1

(entry 1) in comparison with that of entry 2 (**9**:**10** = 2:1). Thus, it is considered that the first step of the reaction is the formation of **9**. The yield (26%, entry 2) of **11** is increased by a prolonged reaction time (55%, entry 3) or by the addition of a large excess of paraformaldehyde (35%, entry 4). The yield (43%, entry 2) of **9** is significantly decreased by the prolonged reaction time (4%, entry 3). Thus, it is thought that only **9** reacts with an another paraformaldehyde to afford **11**. Compound (**10**) could be formed from the isomerization of **9**. Thus, **10** is the major product when a less amount of paraformaldehyde was used (entry 5).

Scheme 4

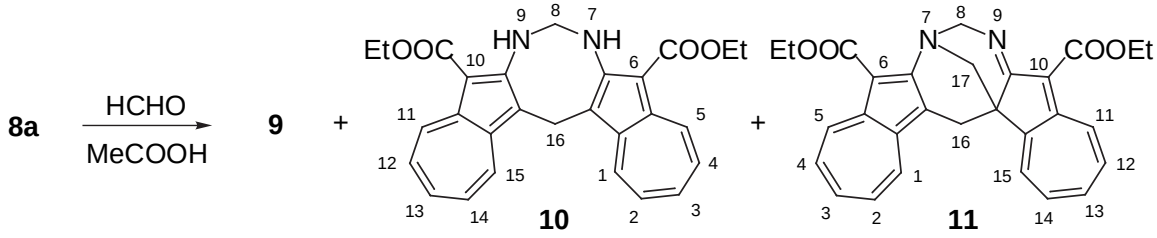


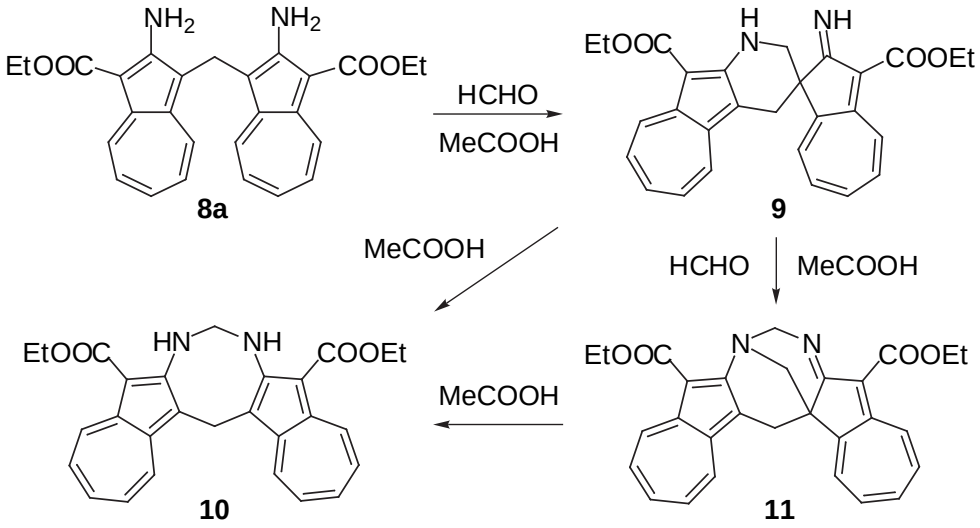
Table 2. Reaction of Bis(2-amino-1-azulenyl)methane (**8a**) with Paraformaldehyde at Room Temperature

entry	**8a** : HCHO	time	**9**[a)]	**10**	**11**[a)]
1[b)]	1 : 5	5 h	17%	4%	0%
2	1 : 5	20 h	43%	21%	26%
3	1 : 5	42 h	4%	18%	55%
4	1 : 10	21 h	29%	14%	35%
5	1 : 2	20 h	28%	43%	17%

a) The yields of the compounds (**9** and **11**) were determined by ^{1}H NMR, since **9** and **11** were decomposed significantly on repeated column chromatography. b) Starting compound (**8a**) was recovered in 54% yield.

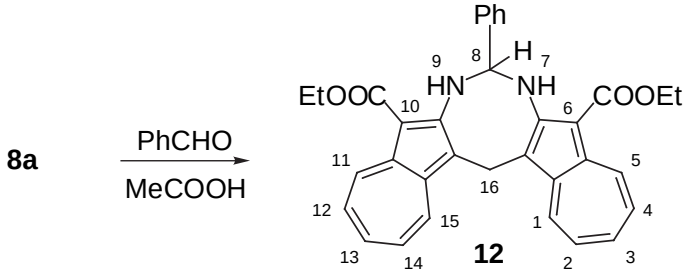
To prove the pathway of the reaction of **8a** with paraformaldehyde, we have studied the reaction of each product (**9**, **10**, and **11**) under similar conditions. Warming a solution of **9** in benzene at 50 °C in the presence of acetic acid for 2 h afforded **10** in 50% yield. Compound (**10**) was also obtained by the prolonged warming (94 h) of a solution of **11** under similar conditions in 62% yield. Compound (**9**) readily reacted with paraformaldehyde in dichloromethane in the presence of acetic acid at room temperature to give **11** in 83% yield. No reaction of **10** took place with paraformaldehyde under similar conditions. On the basis of these results, a possible pathway can be illustrated as shown in Scheme 5.

Scheme 5

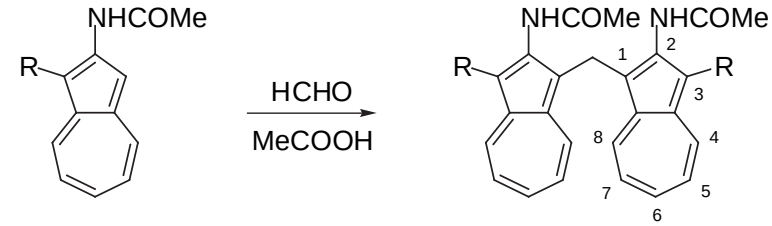


Bis(2-amino-1-azulenyl)methane (**8a**) reacted with benzaldehyde to give 6,10-diethoxycarbonyl-7,9-diaza-7,8,9,16-tetrahydro-8-phenyldiazuleno[2,3-*d*:3,2-*g*]cyclooctene (**12**) as the sole product, although the reactivity of **8a** with benzaldehyde was relatively low (Scheme 6). Prolonged refluxing for 6 days of a mixture of **8a** and benzaldehyde in benzene in the presence of acetic acid afforded **12** in 66% yield.

Scheme 6



Scheme 7



1c: R = H
1d: R = COOEt

8b: R = H
8c: R = COOEt

To examine the reactivity of azulene bearing an amino group protected with acetyl function, we have carried out the reactions of 2-acetylaminoazulenes (**1c** and **1d**)[7] with paraformaldehyde (Scheme 7). The reaction in acetic acid at room temperature for 1 day exclusively gave bis(2-acetylamino-1-

azulenyl)methanes (**8b** and **8c**) in 77 and 79% yields, respectively. The product (**8c**) remained toward the reaction with paraformaldehyde under similar conditions.

We have demonstrated that the reaction of **1a** with paraformaldehyde or benzaldehyde in acetic acid affords diazuleno[2,1-*b*:1,2-*e*]pyridines (**2a** and **2b**) in one pot. The reaction of **1b** with paraformaldehyde resulted in the formation of bis(2-amino-1-azulenyl)methane derivative (**8a**). When **1c** and **1d** were used, the reaction leads to an exclusive formation of bis(2-acetylamino-1-azulenyl)methanes (**8b** and **8c**). The reaction using 2-aminoazulenes with amino protecting group is potentially useful for the preparation of bis(2-amino-1-azulenyl)methane derivatives. Extending this methodology to produce calixarene like compounds will be a focus of future work.

EXPERIMENTAL

General. Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. MS spectra were obtained with a JEOL HX-110 or a Hitachi M-2500 instrument usually at 70 eV. IR spectra were recorded on a Shimadzu FTIR-8100M or a Hitachi 270-30 spectrophotometer and UV–VIS spectra were measured on a Hitachi U-3410 or a Hitachi 340 spectrophotometer. NMR spectra (^{1}H and ^{13}C NMR) were recorded on a JEOL JNM A500 at 500 MHz (125 MHz) or a Bruker AM 600 spectrometer at 600 MHz (150 MHz). Elemental analyses were performed at the Instrumental Analysis Center of Chemistry, Faculty of Science, Tohoku University.

Diazuleno[2,1-*b*:1,2-*e*]pyridine (2a). A solution of 2-aminoazulene (**1a**) (106 mg, 0.740 mmol) and paraformaldehyde (21 mg, 0.70 mmol) in acetic acid (3 mL) was stirred at rt for 30 h. The reaction mixture was poured into water and extracted with CH_2Cl_2. The organic layer was washed with aqueous $NaHCO_3$ solution, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (Al_2O_3, ethyl acetate) to give **2a** (49 mg, 47%). brown needles; mp 225–227 °C (decomp) (lit.,[8] 153–155 °C); MS (70 eV) m/z (rel intensity) 279 (M^+, 100); IR (KBr disk) ν_{max} 1590, 1572, 1398, 1314, 1266, 1200, 810, and 690 cm^{-1}; UV–VIS (MeCN) λ_{max}, nm (log ε) 228 (4.24), 261 (4.38), 360 (4.64), 381 (4.64), 396 (4.68), 415 (4.70), and 436 (4.57); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.24 (s, 1H, H_6), 8.33 (d, *J* = 8.2 Hz, 2H, $H_{5,7}$), 8.05 (d, *J* = 10.8 Hz, 2H, $H_{1,11}$), 7.53 (s, 2H, $H_{12,14}$), 7.27 (dd, *J* = 10.8, 8.3 Hz, 2H, $H_{3,9}$), 7.21 (dd, *J* = 10.8, 8.2 Hz, 2H, $H_{4,8}$), and 7.06 (dd, *J* = 10.8, 8.3 Hz, 2H, $H_{2,10}$); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.21 ($C_{12a,13a}$), 144.79 ($C_{11a,14a}$), 139.27 ($C_{5a,6b}$), 134.84 ($C_{1,11}$), 133.65 ($C_{3,9}$), 126.98 ($C_{4,8}$), 126.53 ($C_{2,10}$), 126.51 ($C_{5,7}$), 121.16 ($C_{5b,6a}$), 120.67 (C_6), and 116.93 ($C_{12,14}$). Anal. Calcd for $C_{21}H_{13}N\cdot 1/3H_2O$: C, 88.39; H, 4.83; N 4.91. Found: C, 88.41; H, 5.67; N, 4.77.

6-Phenyldiazuleno[2,1-*b*:1,2-*e*]pyridine (2b). The same procedure was followed, using **1a** (1.01 g, 7.05

mmol), benzaldehyde (386 mg, 3.64 mmol), and acetic acid (40 mL) at rt for 52 h afforded **2b** (645 mg, 51%). brown needles; mp 276–281 °C (decomp); MS (70 eV) m/z (rel intensity) 355 (M^+, 100); IR (KBr disk) ν_{max} 1584, 1534, 1518, 1498, 1400, 1258, 1218, 710, and 696 cm^{-1}; UV–VIS (MeCN) λ_{max}, nm (log ε) 261 (4.23), 359 (4.66), 379 (4.67), 396 (4.70), 415 (4.73), and 435 (4.56); ^1H NMR (600 MHz, $CDCl_3$) δ = 8.08 (d, *J* = 10.8 Hz, 2H, $H_{1,11}$), 7.74–7.69 (m, 3H, $H_{3',4',5'}$), 7.63 (s, 2H, $H_{12,14}$), 7.54–7.53 (m, 2H, $H_{2',6'}$), 7.21 (d, *J* = 8.9 Hz, 2H, $H_{5,7}$), 7.11 (dd, *J* = 10.9, 8.3 Hz, 2H, $H_{3,9}$), 7.00 (dd, *J* = 10.8, 8.3 Hz, 2H, $H_{2,10}$), and 6.77 (dd, *J* = 10.9, 8.9 Hz, 2H, $H_{4,8}$); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 161.19 ($C_{12a,13a}$), 145.56 ($C_{11a,14a}$), 142.88 (C_6), 139.97 ($C_{5a,6b}$), 138.18 ($C_{1'}$), 134.92 ($C_{1,11}$), 133.34 ($C_{3,9}$), 130.54 ($C_{5,7}$), 130.08 ($C_{3',5'}$), 128.76 ($C_{4'}$), 127.90 ($C_{2',6'}$), 127.24 ($C_{4,8}$), 126.31 ($C_{2,10}$), 119.03 ($C_{5b,6a}$), and 117.26 ($C_{12,14}$). Anal. Calcd for $C_{27}H_{17}N{\cdot}1/3H_2O$: C, 89.72; H, 4.93; N, 3.88. Found: C, 89.98; H, 4.93; N, 3.88.

Bis(2-amino-3-ethoxycarbonyl-1-azulenyl)methane (8a). A solution of ethyl 2-aminoazulene-1-carboxylate (**1b**) (2.33 g, 10.4 mmol) and paraformaldehyde (181 mg, 6.03 mmol) in acetic acid (55 mL) was stirred at rt for 24 h. The precipitated crystals were collected by filtration, washed with water, and dried *in vacuo*. The filtrate was diluted with CH_2Cl_2. The organic layer was worked up and combined with the precipitated crystals. The mixture was purified by column chromatography (SiO_2, 5% ethyl acetate/CH_2Cl_2) to afford **8a** (2.08 g, 87%). orange plates; mp 205–210 °C (decomp); MS (70 eV) m/z (rel intensity) 442 (M^+, 65); IR (KBr disk) ν_{max} 3460, 3416, 3348, 3320, 1666, 1642, 1618, 1604, 1520, 1434, 1256, 1238, and 1110 cm^{-1}; UV–VIS (CH_2Cl_2) λ_{max}, nm (log ε) 311 (5.01); ^1H NMR (600 MHz, $CDCl_3$) δ = 8.94 (d, *J* = 9.6 Hz, 2H, H_4), 8.06 (d, *J* = 10.7 Hz, 2H, H_8), 7.35 (dd, *J* = 10.0, 9.6 Hz, 2H, H_5), 7.29 (dd, *J* = 10.0, 9.7 Hz, 2H, H_6), 7.27 (dd, *J* = 10.7, 9.7 Hz, 2H, H_7), 6.01 (br, 4H, 2-NH_2), 4.40 (q, *J* = 7.1 Hz, 4H, 3-COOEt), 4.35 (s, 2H, CH_2), and 1.42 (t, *J* = 7.1 Hz, 6H, 3-COOEt); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 166.73 (3-COOEt), 159.31 (C_2), 142.54 (C_{3a}), 140.54 (C_{8a}), 130.93 (C_6), 129.37 (C_5), 128.55 (C_4), 127.81 (C_7), 126.60 (C_8), 110.02 (C_1), 98.12 (C_3), 59.53 (3-COOEt), 19.38 (CH_2), and 14.66 (3-COOEt). Anal. Calcd for $C_{27}H_{26}N_2O_4{\cdot}1/3H_2O$:C, 72.30; H, 5.99; N, 6.25. Found: C, 72.43; H, 6.18; N, 6.04.

1-Aza-10-ethoxycarbonyl-1,2,3,4-tetrahydrobenz[*a*]azulene-3-spiro-1'-(3'-ethoxycarbonyl-1',2'-dihydroazulene)-2'-imine (9). A solution of ethyl 2-aminoazulene-1-carboxylate (**1b**) (600 mg, 2.79 mmol) and paraformaldehyde (100 mg, 3.33 mmol) in acetic acid (9 mL) was stirred at rt for 20 h. Workup followed by recrystalization from benzene/hexane gave **9** (536 mg, 85%). red needles; mp 218–223 °C (decomp); MS (70 eV) m/z (rel intensity) 454 (M^+, 100); IR (KBr disk) ν_{max} 3440, 3388,

3312, 3290, 2980, 1686, 1654, 1586, 1562, 1528, 1458, 1436, 1376, 1258, 1220, 1208, and 1142 cm^{-1}; UV–VIS (CH_2Cl_2) λ_{max}, nm (log ε) 248 (4.43), 327 (4.78), and 402 (4.35); ^1H NMR (600 MHz, $CDCl_3$) δ = 10.06 (br, 1H, 2'-NH), 8.87 (d, *J* = 9.7 Hz, 1H, H_9), 8.23 (d, *J* = 12.0 Hz, 1H, $H_{4'}$), 7.70 (d, *J* = 9.9 Hz, 1H, H_5), 7.47 (br, 1H, H_1), 7.34 (dd, *J* = 10.0, 9.7 Hz, 1H, H_8), 7.25 (dd, *J* = 10.0, 9.3 Hz, 1H, H_7), 7.20 (dd, *J* = 9.9, 9.3 Hz, 1H, H_6), 6.78 (ddd, *J* = 12.0, 8.0, 1.0 Hz, 1H, $H_{5'}$), 6.46 (dddd, *J* = 11.0, 8.0, 0.9, 0.8 Hz, 1H, $H_{6'}$), 6.37 (dddd, *J* = 11.0, 8.5, 1.0, 0.9 Hz, 1H, $H_{7'}$), 6.22 (dd, *J* = 8.5, 0.9 Hz, 1H, $H_{8'}$), 4.47 (q, *J* = 7.1 Hz, 2H, COOEt), 4.39 (q, *J* = 7.1 Hz, 2H, COOEt), 3.69 (d, *J* = 12.7 Hz, 1H, H_2), 3.43 (d, *J* = 16.5 Hz, 1H, H_4), 3.34 (ddd, *J* = 12.7, 4.4, 1.9 Hz, 1H, H_2), 2.98 (dd, *J* = 16.5, 1.9 Hz, 1H, H_4), 1.49 (t, *J* = 7.1 Hz, 3H, COOEt), and 1.43 (t, *J* = 7.1 Hz, 3H, COOEt); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 180.05 ($C_{2'}$), 166.95 (COOEt), 165.25 (COOEt), 161.35 ($C_{3'a}$), 158.58 ($C_{8'a}$), 156.19 (C_{10}), 143.24 (C_{9a}), 140.22 (C_{4b}), 138.12 ($C_{5'}$), 135.86 ($C_{7'}$), 132.95 ($C_{6'}$), 132.04 ($C_{4'}$), 130.50 (C_7), 129.72 ($C_{8'}$), 129.19 (C_8), 128.00 (C_9), 127.50 (C_6), 127.11 (C_5), 112.60 ($C_{3'}$), 109.27 (C_{4a}), 96.44 (C_{10}), 60.23 (COOEt), 59.54 (COOEt), 50.16 (C_2), 46.15 (C_3), 30.43 (C_4), 14.78 (COOEt), and 14.40 (COOEt). Anal. Calcd for $C_{28}H_{26}N_2O_4 \cdot 1/3H_2O$: C, 73.03; H, 5.84; N, 6.08. Found: C, 73.40; H, 5.89; N, 5.88.

Reaction of Bis(2-amino-3-ethoxycarbonyl-1-azulenyl)methane (8a) with Paraformaldehyde. A solution of **8a** (443 mg, 1.00 mmol) and paraformaldehyde (300 mg, 10.0 mmol) in acetic acid (24 mL) was stirred at rt for 21 h. Workup followed by column chromatography (Al_2O_3, CH_2Cl_2 and ethyl acetate) gave 6,10-diethoxycarbonyl-7,9-diaza-7,8,9,16-tetrahydrodiazuleno[2,3-*d*:3,2-*g*]cyclooctene (**10**) (63 mg,14%), and a mixture of 1-aza-10-ethoxycarbonyl-1,2,3,4-tetrahydrobenz[*a*]azulene-3-spiro-1'-(3'-ethoxycarbonyl-1',2'-dihydroazulene)-2'-imine (**9**) and 6,10-diethoxycarbonyl-7,9-diaza-7,8,9,16-tetrahydro-7,15b-methanodiazuleno[2,3-*d*:3,2-*g*]cyclooctene (**11**) (293 mg) with a ratio of 45 (29%) : 55 (35%). These compounds (**9** and **11**) were separable by repeated column chromatography (Al_2O_3, 10 to 70% ethyl acetate/CH_2Cl_2).

10: orange needles; mp 269–271 °C (decomp); MS (70 eV) m/z (rel intensity) 454 (M^+, 100); IR (KBr disk) ν_{max} 3328, 1660, 1644, 1580, 1558, 1540, 1524, 1432, 1366, 1228, 1158, and 1128 cm^{-1}; UV–VIS (CH_2Cl_2) λ_{max}, nm (log ε) 244 (4.47), 306 (5.12), and 368 (4.27); ^1H NMR (600 MHz, $CDCl_3$) δ = 8.91 (br dd, *J* = 8.6, 7.0 Hz, 2H, $H_{7,9}$), 8.77 (d, *J* = 9.7 Hz, 2H, $H_{5,11}$), 8.20 (d, *J* = 10.4 Hz, 2H, $H_{1,15}$), 7.27 (dd, *J* = 10.4, 8.8 Hz, 2H, $H_{2,14}$), 7.26 (dd, *J* = 9.9, 9.7 Hz, 2H, $H_{4,12}$), 7.20 (dd, *J* = 9.9, 8.8 Hz, 2H, $H_{3,13}$), 6.24 (dt, *J* = 15.6, 8.6 Hz, 1H, H_8), 4.94 (d, *J* = 16.7 Hz, 1H, H_{16}), 4.76 (dt, *J* = 15.6, 7.0 Hz, 1H, H_8), 4.70 (d, *J* = 16.7 Hz, 1H, H_{16}), 4.43 (q, *J* = 7.1 Hz, 4H, 6,10-COOEt), and 1.45 (t, *J* = 7.1 Hz, 6H, 6,10-COOEt); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.45 (6,10-COOEt), 159.56 ($C_{6a,9a}$), 142.18 ($C_{5a,10a}$),

140.84 ($C_{15a,16b}$), 130.80 ($C_{3,13}$), 129.26 ($C_{4,12}$), 128.60 ($C_{5,11}$), 127.65 ($C_{2,14}$), 127.00 ($C_{1,15}$), 113.83 ($C_{15b,16a}$), 98.49 ($C_{6,10}$), 59.69 (6,10-COOEt), 52.64 (C_8), 21.84 (C_{16}), and 14.70 (6,10-COOEt). Anal. Calcd for $C_{28}H_{26}N_2O_4$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.71; H, 5.85; N, 6.11.

11: orange crystals; mp 150–153 °C; MS (70 eV) m/z (rel intensity) 466 (M^+, 42); IR (KBr disk) ν_{max} 1680, 1478, 1454, 1430, 1208, and 1200 cm^{-1}; UV–VIS (CH_2Cl_2) λ_{max}, nm (log ε) 229 (4.54), 251 (4.46), 275 (4.32), 335 (4.59), and 383 (4.34); ^1H NMR (600 MHz, $CDCl_3$) δ = 9.48 (d, *J* = 10.1 Hz, 1H, H_5), 8.01 (d, *J* = 9.8 Hz, 1H, H_1), 7.83 (d, *J* = 12.1 Hz, 1H, H_{11}), 7.62 (dd, *J* = 9.9, 9.5 Hz, 1H, H_3), 7.48 (dd, *J* = 10.1, 9.9 Hz, 1H, H_4), 7.34 (dd, *J* = 9.8, 9.5 Hz, 1H, H_2), 6.56 (ddd, *J* = 12.1, 8.0, 1.0 Hz, 1H, H_{12}), 6.44 (dddd, *J* = 11.2, 7.9, 1.0, 0.8 Hz, 1H, H_{14}), 6.35 (dddd, *J* = 11.2, 8.0, 0.9, 0.7 Hz, 1H, H_{13}), 6.15 (ddd, *J* = 7.9, 0.9 Hz, 1H, H_{15}), 5.44 (d, *J* = 18.1 Hz, 1H, H_8), 5.15 (d, *J* = 18.1 Hz, 1H, H_8), 4.60 (dq, *J* = 10.8, 7.1 Hz, 1H, COOEt), 4.40 (dq, *J* = 10.8, 7.1 Hz, 1H, COOEt), 4.29 (dq, *J* = 11.0, 7.1 Hz, 1H, COOEt), 4.23 (dq, *J* = 11.0, 7.1 Hz, 1H, COOEt), 3.56 (d, *J* = 12.3 Hz, 1H, H_{17}), 3.48 (dd, *J* = 12.3, 1.5 Hz, 1H, H_{17}), 3.33 (dd, *J* = 16.5, 1.5 Hz, 1H, H_{16}), 3.04 (d, *J* = 16.5 Hz, 1H, H_{16}), 1.49 (t, *J* = 7.1 Hz, 3H, COOEt), and 1.27 (t, *J* = 7.1 Hz, 3H, COOEt); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 168.76 (C_{9a}), 164.72 (COOEt), 164.59 (COOEt), 159.61 (C_{6a}), 159.25 (C_{15a}), 158.99 (C_{10a}), 141.95 (C_{5a}), 139.03 (C_{16b}), 136.32 (C_3), 136.02 (C_{12}), 135.54 (C_5), 133.75 (C_{14}), 132.19 (C_{13}), 131.83 (C_{11}), 131.42 (C_1), 128.37 (C_4), 126.81 (C_2), 124.91 (C_{15}), 119.17 (C_{10}), 116.44 (C_{16a}), 107.52 (C_6), 73.86 (C_8), 60.35 (COOEt), 59.83 (COOEt), 50.70 (C_{17}), 42.84 (C_{15b}), 34.09 (C_{16}), 14.54 (COOEt), and 14.34 (COOEt). Anal. Calcd for $C_{29}H_{26}N_2O_4 \cdot 1/3H_2O$: C, 73.71; H, 5.69; N, 5.93. Found: C, 73.89; H, 5.83; N, 5.80.

Reaction of 8a with Benzaldehyde. A solution of **8a** (103 mg, 0.233 mmol) and benzaldehyde (265 mg, 2.50 mmol) in acetic acid (3 mL) and benzene (20 mL) was refluxed for 6 days. Workup followed by column chromatography (Al_2O_3, CH_2Cl_2) gave 6,10-diethoxycarbonyl-7,9-diaza-7,8,9,16-tetrahydro-8-phenyldiazuleno[2,3-*d*:3,2-*g*]cyclooctene (**12**) (82 mg, 66%). orange crystals; mp 190–191 °C; MS (70 eV) m/z (rel intensity) 530 (M^+, 100); IR (KBr disk) ν_{max} 3295, 1655, 1557, 1538, 1524, 1497, 1154, and 1125 cm^{-1}; UV–VIS (CH_2Cl_2) λ_{max}, nm (log ε) 248 (4.53), 309 (5.17), and 372 (4.34); ^1H NMR (500 MHz, $CDCl_3$) δ = 9.00 (br d, *J* = 8.2 Hz, 2H, $H_{7,9}$), 8.83 (d, *J* = 9.6 Hz, 2H, $H_{5,11}$), 8.22 (d, *J* = 10.2 Hz, 2H, $H_{1,15}$), 7.80 (d, *J* = 7.3 Hz, 2H, $H_{2',6'}$), 7.55 (dd, *J* = 7.4, 7.3 Hz, 2H, $H_{3',5'}$), 7.52 (t, *J* = 8.2 Hz, 1H, H_8), 7.46 (t, *J* = 7.4 Hz, 1H, $H_{4'}$), 7.29 (dd, *J* = 10.2, 9.9 Hz, 2H, $H_{2,14}$), 7.27 (dd, *J* = 9.9, 9.6 Hz, 2H, $H_{4,12}$), 7.22 (dd, *J* = 9.9, 9.9 Hz, 2H, $H_{3,13}$), 5.03 (d, *J* = 16.7 Hz, 1H, H_{16}), 4.81 (d, *J* = 16.7 Hz, 1H, H_{16}), 4.42–4.35 (m, 4H, 6,10-COOEt), and 1.38 (t, *J* = 7.2 Hz, 6H, 6,10-COOEt); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 167.22 (6,10-COOEt), 158.75 ($C_{6a,9a}$), 142.34 ($C_{5a,10a}$), 140.97 ($C_{15a,16b}$), 139.57 ($C_{1'}$),

130.95 ($C_{3,13}$), 129.68 ($C_{3',5'}$), 129.35 ($C_{4,12}$), 129.08 ($C_{4'}$), 128.81 ($C_{5,11}$), 127.72 ($C_{2,14}$), 127.15 ($C_{1,15}$), 125.84 ($C_{2',6'}$), 113.85 ($C_{15b,16a}$), 98.73 ($C_{6,10}$), 66.126 (C_8), 59.66 (6,10-COOEt), 22.28 (C_{16}), and 14.58 (6,10-COOEt). Anal. Calcd for $C_{34}H_{30}N_2O_4$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.84; H, 5.72; N, 5.20.

Bis(2-acethylamino-1-azulenyl)methane (8b). The same procedure was followed, using 2-acethylaminoazulene (**1c**) (495 mg, 2.67 mmol), paraformaldehyde (42 mg, 1.40 mmol), and acetic acid (16 mL) at rt for 25 h afforded **8b** (396 mg, 77%). blue prisms; mp 261–263 °C (decomp); MS (70 eV) m/z (rel intensity) 382 (M^+, 44); IR (KBr disk) ν_{max} 3400, 1706, 1574, 1530, 1500, and 1238 cm^{-1}; UV–VIS (CH_2Cl_2) λ_{max}, nm (log ε) 242 (4.50), 306 (5.05), 354 (4.06), 370 (4.14), 387 (4.07), and 554 (2.68); ^1H NMR (600 MHz, DMSO-d_6) δ = 10.03 (s, 2H, 2-NHCOMe), 8.28 (d, *J* = 9.5 Hz, 2H, H_4), 8.06 (d, *J* = 9.9 Hz, 2H, H_8), 7.97 (s, 2H, H_3), 7.48 (dd, *J* = 9.8, 9.8 Hz, 2H, H_6), 7.21 (dd, *J* = 9.8, 9.5 Hz, 2H, H_5), 7.04 (dd, *J* = 9.9, 9.8 Hz, 2H, H_7), 4.97 (s, 2H, CH_2), and 2.25 (s, 6H, 2-NHCOMe); ^{13}C NMR (150 MHz, DMSO-d_6) δ = 168.70 (2-NHCOMe), 144.79 (C_2), 139.51 (C_{3a}), 134.62 (C_{8a}), 134.33 (C_6), 133.53 (C_4), 131.05 (C_8), 123.57 (C_5), 122.57 (C_7), 115.85 (C_1), 107.85 (C_3), 23.82 (2-NHCOMe), and 19.87 (CH_2). Anal. Calcd for $C_{25}H_{22}N_2O_2$: C, 78.51; H, 5.80; N, 7.32. Found: C, 78.28; H, 5.86; N; 7.25.

Bis(2-acethylamino-3-ethoxycarbonyl-1-azulenyl)methane (8c). The same procedure was followed, using ethyl 2-acethylaminoazulene-1-carboxylate (**1d**) (723 mg, 2.81 mmol), paraformaldehyde (53 mg, 1.77 mmol), and acetic acid (21 mL) at rt for 24 h afford **8c** (581 mg, 79%). purple crystals; mp 248–249 °C; MS (70 eV) m/z (rel intensity) 526 (M^+, 27); IR (KBr disk) ν_{max} 3305, 1690, 1676, 1489, 1456, 1428, 1210, and 1130 cm^{-1}; UV–VIS (CH_2Cl_2) λ_{max}, nm (log ε) 248 (4.51), 312 (4.95), and 539 (2.96); ^1H NMR (600 MHz, $CDCl_3$) δ = 9.30 (d, *J* = 9.9 Hz, 2H, H_4), 9.30 (br, 2H, 2-NHCOMe), 8.43 (d, *J* = 10.1 Hz, 2H, H_8), 7.65 (dd, *J* = 10.0, 9.5 Hz, 2H, H_6), 7.46 (dd, *J* = 10.0, 9.9 Hz, 2H, H_5), 7.35 (dd, *J* = 10.1, 9.5 Hz, 2H, H_7), 4.87 (s, 2H, CH_2), 4.42 (q, *J* = 7.1 Hz, 4H, 3-COOEt), 1.64 (s, 6H, 2-NHCOMe), and 1.45 (t, *J* = 7.1 Hz, 6H, 3-COOEt); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 168.09 (2-NHCOMe), 166.28 (3-COOEt), 146.42 (C_2), 139.92 (C_{8a}), 139.52 (C_{3a}), 137.10 (C_6), 135.24 (C_4), 134.33 (C_8), 127.89 (C_5), 126.90 (C_7), 120.75 (C_1), 106.31 (C_3), 60.17 (3-COOEt), 24.00 (CH_2), 23.64 (2-NHCOMe), and 14.52 (3-COOEt). Anal. Calcd for $C_{31}H_{30}N_2O_6 \cdot 1/3H_2O$: C, 69.91; H, 5.80; N, 5.26. Found: C, 69.97; H, 5.82; N, 5.23.

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