Synthesis of 1- and 2-(2-Quinolyl)azulenes by the Friedländer Reaction of Acetylazulenes

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Dedicated to the memory of Professor Nicholas Alexandrou

1-Acetylazulene and 3-methyl-, 3-ethyl-, and 3-propyl-substituted 1-acetylazulenes were prepared by the reaction of 3-acetyl-2*H*-cyclohepta[*b*]furan-2-one with *in situ* generated enamines from aldehydes and amines. These four 1-acetylazulenes reacted with 2-aminobenzaldehyde and its 4,5-dimethoxy- and 4,5-methylenedioxy-substituted derivatives in the presence of sodium ethoxide to afford twelve 1-(2-quinolyl)azulenes. In a similar manner, three 2-(2-quinolyl)azulenes were also prepared from 2-acetylazulene.

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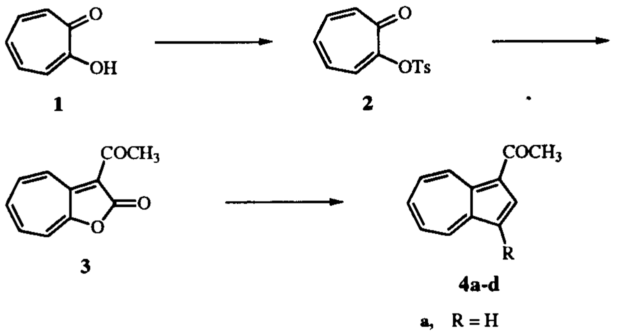
A number of alkyl-substituted azulenes, such as guaiazulene, chamazulene, vetivazulene, *etc.*, have been isolated from natural sources. However, little is known about azulenes possessing a carbocyclic or heterocyclic ring as the side-chain, except for 1- [1], 2- [2], 4- [3], 5- [4], and 6-phenylazulene [5], 4-(1-naphthyl)- [6] and 5-(2-naphthyl)-azulene [7], and 5-(2-quinolyl)azulene [8]. Details for the last azulene have not been clarified. Here, we describe the synthesis of azulenes having a quinoline ring as the side-chain at the 1- or 2-position by the Friedländer reaction of 1-and 2-acetylazulenes with 2-aminobenzaldehydes.

Results and Discussion.

Synthesis of 1- and 2-Acetylazulenes.

It has been reported that 1-acetylazulene was prepared from azulene by Friedel-Crafts type acylation using acetic anhydride in the presence of aluminum chloride or tin(IV) chloride [9] and by Vilsmeier-Haack type reaction using *N,N*-dimethylacetamide and phosphorus oxychloride [10]. Among many synthetic methods for azulenes [11], a method using the reaction of 2*H*-cyclohepta[*b*]furan-2-one with enamines is very useful for 1-substituted azulenes [12]. In this enamine method, it was found that the yields of the azulene derivatives are good on the reaction with enamines derived from cycloalkanonones or acylic carbonyl compounds having long chains, but fairly low on the reaction with enamines derived from carbonyl compounds having short chains. In addition, the use of enamines generated *in situ* from carbonyl compounds and amines is synthetically very convenient.

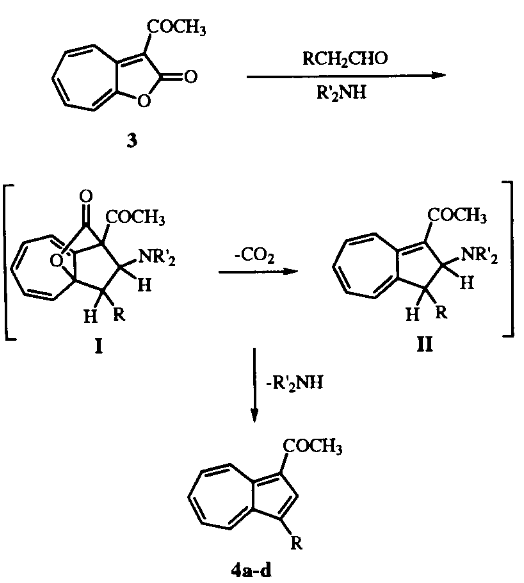
Scheme 1



a, R = H
b, R = CH_3
c, R = CH_2CH_3
d, R = $CH_2CH_2CH_3$

When the reaction of 3-acetyl-2*H*-cyclohepta[*b*]furan-2-one (**3**) [13] with *in situ* generated enamine from acetaldehyde and morpholine was carried out under refluxing condition, no azulene was isolated. Then, the reaction of **3** with acetaldehyde in the presence of diethylamine under refluxing for 3 hours without solvent gave 1-acetylazulene (**4a**) [9] as a violet oil in 49% yield. The strucutre was identified with ^{1}H and ^{13}C nmr spectral data. On the other hand, the reactions with propionaldehyde, butyraldehyde, and valeraldehyde took place in the presence of morpholine to give 1-acetyl-3-methyl- (**4b**), -3-ethyl- (**4c**), and -3-propylazulene (**4d**) in 18, 24, and 18% yield, respectively. However, the reactions with isobutyraldehyde and isovaleraldehyde gave no prduct and compound **3** was recovered. This might be due to the steric disadvantage in the intermediates **I** and **II** (Scheme 2).

Scheme 2

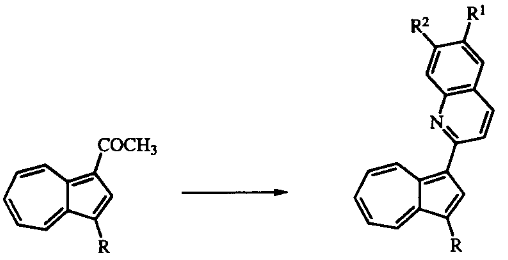


On the other hand, 2-acetylazulene (**6**) was obtained from 2*H*-cyclohepta[*b*]furan-2-one *via* 2-formylazulene [14]. Details will be published elsewhere by one (K.F.) of us.

Synthesis of 1- and 2-(2-Quinolyl)azulenes.

The Friedländer reaction is a very useful method for the synthesis of the quinoline skeleton. When a solution of 1-acetylazulene (**4a**) and 1.2 molar equivalents of 2-aminobenzaldehyde in the presence of 2.0 molar equivalents of sodium ethoxide in absolute ethanol was refluxed for 50 hours, 1-(2-quinolyl)azulene (**5aa**) was obtained as greenish blue crystals, mp 88-89°, in 26% yield. The structure was confirmed by the spectral data. The reactions of 1-acetyl-3-methyl-, -3-ethyl-, and -3-propylazulene **4b-d** with 2-aminobenzaldehyde were carried out under refluxing for 12, 7, and 7 hours to afford the corresponding 3-methyl-, 3-ethyl-, and 3-propyl-1-(2-quinolyl)azulenes **5ab-ad** in 30, 52, and 31% yield, respectively. In a similar manner, compounds **4a-d** reacted with 2-amino-4,5-dimethoxy- and -4,5-methylenedioxybenzaldehyde gave eight 1-(2-quinolyl)azulenes **5ba-cd** in 15-52% yields.

Scheme 3



4a-d

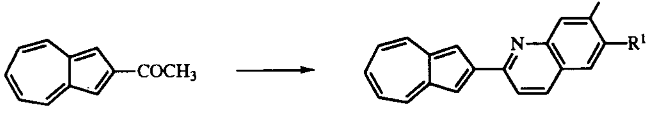
a, $R = H$
b, $R = CH_3$
c, $R = CH_2CH_3$
d, $R = CH_2CH_2CH_3$

5aa-dc

aa, $R = R^1 = R^2 = H$
ab, $R = CH_3, R^1 = R^2 = H$
ac, $R = CH_2CH_3, R^1 = R^2 = H$
ad, $R = CH_2CH_2CH_3, R^1 = R^2 = H$
ba, $R = H, R^1 = R^2 = OCH_3$
bb, $R = CH_3, R^1 = R^2 = OCH_3$
bc, $R = CH_2CH_3, R^1 = R^2 = OCH_3$
bd, $R = CH_2CH_2CH_3, R^1 = R^2 = OCH_3$
ca, $R = H, R^1 - R^2 = OCH_2O$
cb, $R = CH_3, R^1 - R^2 = OCH_2O$
cc, $R = CH_2CH_3, R^1 - R^2 = OCH_2O$
cd, $R = CH_2CH_2CH_3, R^1 - R^2 = OCH_2O$

The positional isomers, 2-(2-quinolyl)azulenes **7a-c**, were also obtained by refluxing an ethanolic solution of 2-acetylazulene (**6**) and 2-aminobenzaldehyde and its 4,5-dimethoxy- and 4,5-methylenedioxy derivatives in the presence of sodium ethoxide in 56-83% yields.

Scheme 4



6

7a-c

a, $R^1 = R^2 = H$
b, $R^1 = R^2 = OCH_3$
c, $R^1 - R^2 = OCH_2O$

Spectroscopic Aspects of 1- and 2-(2-Quinolyl)azulenes.

Twelve 1-(2-quinolyl)- **5aa-cd** and three 2-(2-quinolyl)-azulenes **7a-c** were prepared, as described above. Azulenes are blue-colored compounds which are formally bicyclo[5.3.0]decapentaene system. This non-alternant 10π aromatic system exhibits physically and chemically specific properties which are very different from those of isomeric colorless alternant naphthalenes.

The chemical shifts in the ^1H nmr spectrum of azulene itself are closely related to the charge distribution and reported as δ 7.30 for 1- and 3-H, 7.81 for 2-H, 8.23 for 4- and 8-H, 7.05 for 5- and 7-H, and 7.45 for 6-H [11]. In the spectrum of 1-(2-quinolyl)azulene (**5aa**), the signal for the 8-H proton was observed at δ 9.97. This value is at a very much lower field in comparison with that for the 4- and 8-H protons of azulene itself. This most likely is caused by the anisotropic ring current effect of the quinoline ring at the 1-position. The low field shift of the 8-H proton was observed in other 1-(2-quinolyl)azulenes **5ab-cd**. On the other hand, in the ^1H nmr spectrum of 2-(2-quinolyl)azulene (**7a**), the quinoline ring caused the low field shift of the 1- and 3-H protons to δ 8.07 in a similar effect. The spectra of the compounds **7b-c** also showed the same shift.

The electronic spectrum of azulene shows characteristic fine structure at the visible region (λ 450-750 nm). The uv and visible spectra of 1- and 2-(2-quinolyl)azulenes **5aa-cd** and **7a-c** also show absorption bands at λ 450-750 nm. In these spectra, however, the fine structure disappeared and broad absorption bands were observed. The visible maximum bands at λ 591 (log ε 2.38), 635 (2.38), and 694 nm (2.05) for 2-(2-quinolyl)azulene (**7a**) was observed at a longer wavelength region than the maximum bands at λ 575 (log ε 2.72) and 623 nm (2.07, sh) of 1-(2-quinolyl)azulene (**5aa**). This difference is attributed to steric inhibition of the coplanarity of the quinoline ring with the azulene system. In comparison with 2-(2-quinolyl)azulenes **7a-c**, 1-(2-quinolyl)azulenes **5aa-cd** exhibit a lack of coplanarity by interference of the quinoline ring with the hydrogen atom at the 8-positon. In the spectra of 1- and 2-(2-quinolyl)azulenes **5aa-cd** and **7a-c**, the uv absorption bands at λ 360-440 nm was also observed differently from spectra of both azulene and quinoline. The appearance of these bands suggested a π-π interaction between two ring systems, the azulene and quinoline.

EXPERIMENTAL

Measurements.

All melting points were determined with a Yanagimoto MP S-2 apparatus and are uncorrected. The ir spectra were taken on a JASCO A-102 spectrophotometer and the uv spectra on a Hitachi U-3210 and U-4000 spectrophotometer. The nmr spectra were recorded with a JEOL JNM-EX 90 spectrometer (90 MHz for ^{1}H and 22.5 MHz for ^{13}C). The mass spectra were measured on a JEOL JMS-01-SG spectrometer.

Materials.

3-Acetyl-2*H*-cyclohepta[*b*]furan-2-one (**3**) was prepared from tropolone (**1**) *via* 2-tosyloxytropone (**2**) in the literature method [13]. The following benzaldehydes were obtained by the reduction of the corresponding 2-nitrobenzaldehydes according to the literature procedures: 2-aminobenzaldehyde [15], 2-amino-4,5-dimethoxybenzaldehyde [16], and 2-amino-4,5-methylenedioxybenzaldehyde [17].

1-Acetylazulene (**4a**).

A mixture of 3-acetyl-2*H*-cyclohepta[*b*]furan-2-one (**3**) (565 mg, 3.0 mmoles), acetaldehyde (1.33 g, 30 mmoles), and diethylamine (15 ml) was gently refluxed for 3 hours. After removal of the excess of the aldehyde and the amine under reduced pressure, the residue was chromatographed on an activated alumina column (200 mesh, 10 g) with ethyl acetate. The violet fraction was concentrated and rechromatographed on three Wakogel B-10 plates (30 x 30 cm) with ethyl acetate to afford 1-acetylazulene (**4a**) in a yield of 250 mg (49%) as a violet oil [9]; ^{1}H nmr (deuteriochloroform): δ 2.61 (3H, s, CH_3), 7.09 (1H, d, J = 4.3 Hz, 3-H), 7.16-7.46 (3H, m), 8.10 (1H, d, J = 4.3 Hz, 2-H), 8.24 (1H, d, J = 9.5 Hz, 4-H), 9.78 (1H, d, J = 9.4 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 28.5 (CH_3), 117.2 (=CH-), 124.4 (=C<), 126.7 (=CH-), 128.5 (=CH-), 137.9 (=CH-), 138.6 (=CH-), 138.8 (=CH-), 139.3 (=C<), 140.0 (=CH-), 144.3 (=C<), 194.5 (C=O).

1-Acetyl-3-alkylazalenes **4b-d**.

To a solution of 3-acetyl-2*H*-cyclohepta[*b*]furan-2-one (**3**) (188 mg, 1.0 mmole) in ethanol (5 ml) was added aldehyde (3.0 mmoles) and morpholine (260 mg, 3.0 mmoles). The mixture was heated under refluxing for 7 hours. After removal of the solvent, the residue was chromatographed on a Wakogel C-200 column (10 g) with hexane-diethyl ether (9:1) and rechromatographed on a Wakogel B-10 plate (30 x 30 cm) with chloroform to give 1-acetyl-3-alkylazulenes **4b-d**.

1-Acetyl-3-methylazulene (**4b**).

This compound was obtained from the reaction using propionaldehyde in a yield of 33 mg (18%) as a violet oil; ir (chloroform): ν max 1662 cm^{-1} (C=O); uv (methanol): λ max 218 (log ε 4.12), 239 (4.08), 269 (3.93), 309 (4.29), 395 (3.76), 558 nm (2.51); ^{1}H nmr (deuteriochloroform): δ 2.53 (3H, s, CH_3), 2.64 (3H, s, $COCH_3$), 7.18-7.79 (3H, m, 5-,6-,7-H), 8.01 (1H, s, 2-H), 8.23 (1H, d, J = 10.0 Hz, 4-H), 9.72 (1H, dd, J = 9.7, 1.3 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 12.3 (CH_3), 28.9 (*C*O-CH_3), 123.0 (=C<), 125.2 (=C<), 125.8 (=CH-), 128.4 (=CH-), 135.1 (=CH-), 138.5 (=CH-), 138.9 (=CH-), 140.1 (=C<), 141.1 (=CH-), 141.5 (=C<), 194.8 (C=O); ms: m/z (%) 184 (M^+, 54), 169 (100).

Anal. Calcd. for $C_{13}H_{12}O$: M_r^+, 184.0889. Found: M_r^+, 184.0890.

1-Acetyl-3-ethylazulene (**4c**).

This compound was obtained from the reaction using butyraldehyde in a yield of 48 mg (24%) as violet plates, mp 51-54°; ir (chloroform): ν max 1662 cm^{-1} (C=O); uv (methanol): λ max 217 (log ε 4.20), 236 (4.18), 269 (4.02), 309 (4.37), 400 (3.85), 551 nm (2.59); ^{1}H nmr (deuteriochloroform): δ 1.40 (3H, t, J = 7.5 Hz, CH_3), 2.70 (3H, s, $COCH_3$), 2.95 (2H, q, J = 7.5 Hz, CH_2), 7.26-7.74 (3H, m, 5-, 6-, 7-H), 8.14 (1H, s, 2-H), 8.38 (1H, d, J = 10.0 Hz, 4-H), 9.79 (1H, dd, J = 9.8, 1.5 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 15.1 (CH_3), 20.1 (CH_2), 29.2 (*C*O-CH_3), 123.4 (=C<), 126.1 (=CH-), 128.7 (=CH-), 132.2 (=C<), 135.0 (=CH-), 139.0 (=CH-), 139.2 (=CH-), 139.5 (=CH-), 140.4 (=C<), 140.9 (=C<), 195.2 (C=O); ms: m/z (%) 198 (M^+, 38), 183 (100).

Anal. Calcd. for $C_{14}H_{14}O$: M_r^+, 198.1045. Found: M_r^+, 198.1041.

1-Acetyl-3-propylazulene (**4d**).

This compound was obtained from the reaction using valeraldehyde in a yield of 38 mg (18%) as a violet oil; ir (chloroform): ν max 1662 cm^{-1} (C=O); uv (methanol): λ max 216 (log ε 4.27), 237 (4.20), 268 (4.05), 309 (4.42), 398 (3.89), 553 nm (2.53); ^{1}H nmr (deuteriochloroform): δ 1.00 (3H, t, J = 7.3 Hz, CH_3), 1.64-1.89 (2H, m, β-CH_2), 2.68 (3H, s, $COCH_3$), 2.95 (2H, t, J = 7.2 Hz, α-CH_2), 7.33-7.60 (3H, m, 5-,6-,7-H), 8.10 (1H, s, 2-H), 8.35 (1H, d, J = 9.8 Hz, 4-H), 9.77 (1H, dd, J = 9.7, 1.5 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 14.1 (CH_3), 24.1 (α-CH_2), 29.0 (β-CH_2), 29.1 (*C*O-CH_3), 123.2 (=C<), 125.9 (=CH-), 128.5 (=CH-), 130.5 (=C<), 135.0 (=CH-), 138.7 (=CH-), 139.1 (=CH-), 140.2 (=CH-), 140.3 (=C<), 141.2 (=C<), 195.0 (C=O); ms: m/z: (%) 212 (M^+, 35), 197 (13), 183 (100), 140 (17).

Anal. Calcd. for $C_{15}H_{16}O$: M_r^+, 212.1202. Found: M_r^+, 212.1178.

3-Alkyl-1-(2-quinolyl)azalenes **5aa-dc**.

To a solution of 1-acetyl-3-alkylazulenes **4a-d** (1.0 mmole) and 2-aminobenzaldehyde (1.2 mmoles) in absolute ethanol

(4 ml) was added a sodium ethoxide solution, prepared from sodium (46 mg) and absolute ethanol (6 ml). This solution was refluxed for 7-57 hours. After diluting with water, the mixture was neutralized with 2*M* hydrochloric acid and extracted with chloroform. The extract was dried over sodium sulfate. The evaporation residue was chromatographed on a Wakogel B-10 plate (30 x 30 cm) with chloroform to afford 3-alkyl-1-(2-quinolyl)azulenes **5aa-dc**.

1-(2-Quinolyl)azulene (**5aa**).

This compound was obtained from the reaction of **4a** with 2-aminobenzaldehyde under refluxing for 50 hours in a yield of 66 mg (26%) as greenish blue crystals (from hexane), mp 88-89°; uv (methanol): λ max 219 (log ε 4.21), 234 (4.20), 286 (4.17), 327 (3.68), 393 (3.91), 575 (2.22), 623 nm (2.07, sh); ^{1}H nmr (deuteriochloroform): δ 7.12-7.94 (7H, m), 7.89 (1H, d, J = 8.6 Hz, 4'-H), 8.16 (1H, d. J = 8.6 Hz, 3'-H), 8.11-8.44 (3H, m), 9.97 (1H, d, J = 9.7 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 117.9 (=CH-), 121.7 (=CH-), 124.5 (=CH-), 125.4 (=CH-), 125.8 (=CH-), 126.1 (=C<), 127.4 (=CH-), 127.6 (=C<), 129.2 (=CH-), 129.3 (=CH-), 135.9 (=CH-), 137.1 (=C<), 137.3 (=CH-), 137.5 (=CH-), 138.5 (=CH-), 138.7 (=CH-), 143.6 (=C<), 148.3 (=C<), 156.4 (=C<); ms: m/z (%) 255 (M$^+$, 60), 254 (100), 253 (17), 178 (18), 177 (22), 127 (22).

Anal. Calcd. for $C_{19}H_{13}N$: C, 89.38; H, 5.13; N, 5.49; M$_r$$^+$, 255.1049. Found: C, 89.43; H, 5.08; N, 5.72; M$_r$$^+$, 255.1069.

3-Methyl-1-(2-quinolyl)azulene (**5ab**).

This compound was obtained from the reaction of **4b** with 2-aminobenzaldehyde under refluxing for 12 hours in a yield of 81 mg (30%) as greenish blue plates (from hexane), mp 115-119°; uv (methanol): λ max 223 (log ε 4.50), 239 (4.48), 288 (4.43), 402 (4.18), 600 nm (2.55); ^{1}H nmr (deuteriochloroform): δ 2.64 (3H, s, CH$_3$), 6.98-7.66 (7H, m), 7.77 (1H, d, J = 8.5 Hz, 4'-H), 8.03 (1H, d, J = 8.5 Hz, 3'-H), 8.13 (1H, s, 2-H), 8.19 (1H, d, J = 10.1 Hz, 4-H), 9.82 (1H, d, J = 9.9 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 12.7 (CH$_3$), 121.9 (=CH-), 123.1 (=CH-), 125.1 (=CH-), 125.3 (=CH-), 125.7 (=C<), 125.9 (=C<), 126.1 (=C<), 127.4 (=CH-), 129.2 (=CH-), 129.3 (=CH-), 134.4 (=CH-), 135.8 (=CH-), 137.3 (=C<), 137.9 (=CH-), 138.3 (=CH-), 138.6 (=CH-), 140.1 (=C<), 148.4 (=C<), 156.4 (=C<); ms: m/z (%) 269 (M$^+$, 80), 268 (100), 254 (66).

Anal. Calcd. for $C_{20}H_{15}N$: C, 89.18; H, 5.61; N, 5.20; M$_r$$^+$, 269.1205. Found: C, 89.08; H, 5.81; N, 5.23; M$_r$$^+$, 269.1185.

3-Ethyl-1-(2-quinolyl)azulene (**5ac**).

This compound was obtained from the reaction of **4c** with 2-aminobenzaldehyde under refluxing for 7 hours in a yield of 147 mg (52%) as a greenish blue oil; uv (methanol): λ max 228 (log ε 4.59), 288 (4.55), 403 (4.25), 595 nm (2.68); ^{1}H nmr (deuteriochloroform): δ 1.41 (3H, t, J = 7.2 Hz, CH$_3$), 3.05 (2H, J = 7.2 Hz, CH$_2$), 6.95-7.63 (7H, m), 7.81 (1H, d, J = 8.5 Hz, 4'-H), 8.02 (1H, d, J = 8.5 Hz, 3'-H), 8.20 (1H, s, 2-H), 8.21 (1H, d, J = 10.0 Hz, 4-H), 9.80 (1H, d, J = 9.9 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 15.4 (CH$_3$), 20.2 (CH$_2$), 121.8 (=CH-), 123.1 (=CH-), 125.0 (=CH-), 125.3 (=CH-), 126.1 (=C< x 2), 127.3 (=CH-), 129.1 (=CH-), 129.2 (=CH-), 132.4 (=C<), 133.9 (=CH-), 135.7 (=CH-), 136.5 (=CH-), 137.3 (=C<), 137.9 (=CH-), 138.5 (=CH-), 139.2 (=C<), 148.4 (=C<), 156.3 (=C<); ms: m/z (%) 283 (M$^+$, 98), 268 (100), 254 (64), 133 (39), 127 (5).

Anal. Calcd. for $C_{21}H_{17}N$: M$_r$$^+$, 283.1362. Found: M$_r$$^+$, 283.1368.

3-Propyl-1-(2-quinolyl)azulene (**5ad**).

This compound was obtained from the reaction of **4d** with 2-aminobenzaldehyde under refluxing for 7 hours in a yield of 92 mg (31%) as a greenish blue oil; uv (methanol): λ max 223 (log ε 4.34), 241 (4.33), 290 (4.27), 402 (4.00), 600 nm (2.34); ^{1}H nmr (deuteriochloroform): δ 1.02 (3H, t, J = 7.1 Hz, CH$_3$), 1.53-2.13 (2H, m, β-CH$_2$), 3.07 (2H, t, J = 7.2 Hz, α-CH$_2$), 7.02-8.14 (9H, m), 7.85 (1H, d, J = 8.6 Hz, 4'-H), 8.11 (1H, d, J = 8.6 Hz, 3'-H), 9.80 (1H, d, J = 9.9 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 14.3 (CH$_3$), 24.5 (β-CH$_2$), 29.4 (α-CH$_2$), 122.0 (=CH-), 123.1 (=CH-), 125.1 (=CH-), 125.4 (=CH-), 126.2 (=C< x 2), 127.4 (=CH-), 129.2 (=CH-), 129.3 (=CH-), 131.0 (=C<), 134.2 (=CH-), 135.9 (=CH-), 137.4 (=C<), 137.5 (=CH-), 137.9 (=CH-), 138.6 (=CH-), 139.7 (=C<), 148.5 (=C<), 156.5 (=C<); ms: m/z (%) 297 (M$^+$, 52), 282 (7), 268 (100), 254 (21), 133 (31).

Anal. Calcd. for $C_{22}H_{19}N$: M$_r$$^+$, 297.1518. Found: M$_r$$^+$, 297.1472.

1-(6,7-Dimethoxyquinol-2-yl)azulene (**5ba**).

This compound was obtained from the reaction of **4a** with 2-amino-4,5-dimethoxybenzaldehyde under refluxing for 54 hours in a yield of 160 mg (51%) as greenish blue crystals (from hexane-ethyl acetate), mp 149-150°; uv (methanol): λ max 212 (log ε 4.23), 228 (4.33), 286 (4.23), 350 (3.78), 392 (4.01), 582 (2.24), 634 nm (2.07); ^{1}H nmr (deuteriochloroform): δ 3.94 (3H, s, OCH$_3$), 4.03 (3H, s, OCH$_3$), 6.95 (1H, s, 5'-H), 7.14-7.42 (4H, m), 7.51 (1H, s, 8'-H), 7.68 (1H, d, J = 8.5 Hz, 4'-H), 7.92 (1H, d, J = 8.5 Hz, 3'-H), 8.29-8.40 (2H, m), 9.82 (1H, d, J = 9.8 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 55.8 (OCH$_3$), 55.9 (OCH$_3$), 105.1 (=CH-), 108.1 (=CH-), 117.7 (=CH-), 120.0 (=CH-), 121.4 (=C<), 124.0 (=CH-), 125.2 (=CH-), 128.1 (=C<), 134.2 (=CH-), 136.5 (=C<), 137.0 (=CH-), 137.3 (=CH-), 138.0 (=CH-), 138.4 (=CH-), 143.2 (=C<), 145.1 (=C<), 148.9 (=C<), 152.2 (=C<), 154.3 (=C<); ms: m/z (%) 315 (M$^+$, 100), 314 (86), 299 (13), 298 (25), 270 (12), 157 (12).

Anal. Calcd. for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44; M$_r$$^+$, 315.1260. Found: C, 79.68; H, 5.41; N, 4.58; M$_r$$^+$, 315.1267.

3-Methyl-1-(6,7-dimethoxyquinol-2-yl)azulene (**5bb**).

This compound was obtained from the reaction of **4b** with 2-amino-4,5-dimethoxybenzaldehyde under refluxing for 24 hours in a yield of 99 mg (30%) as greenish blue crystals (from hexane), mp 165-167°; uv (methanol): λ max 288 (log ε 4.55), 346 (4.16), 400 (4.32), 610 nm (2.62); ^{1}H nmr (deuteriochloroform): δ 2.68 (3H, s, CH$_3$), 3.98 (3H, s, OCH$_3$), 4.05 (3H, s, OCH$_3$), 6.99 (1H, s, 5'-H), 7.15 (1H, dd, J = 10.1, 10.0 Hz, 5-H), 7.28 (1H, dd, J = 10.2, 10.0 Hz, 7-H), 7.51 (1H, s, 8'-H), 7.53 (1H, dd, J = 10.0, 10.0 Hz, 6-H), 7.68 (1H, d, J = 8.6 Hz, 4'-H), 7.95 (1H, d, J = 8.6 Hz, 3'-H), 8.16 (1H, s, 2-H), 8.21 (1H, d, J = 10.2 Hz, 4-H), 9.63 (1H, d, J = 9.9 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 12.7 (CH$_3$), 56.0 (OCH$_3$), 56.1 (OCH$_3$), 105.2 (=CH-), 108.3 (=CH-), 120.3 (=CH-), 121.5 (=C<), 122.7 (=CH-), 124.6 (=CH-), 125.6 (=C<), 126.6 (=C<), 134.2 (=CH-), 134.3 (=C<), 136.8 (=CH-), 137.5 (=CH-), 138.2 (=CH-), 138.4 (=CH-), 139.7 (=C<), 145.3 (=C<), 149.1 (=C<), 152.3 (=C<), 154.4 (=C<); ms: m/z (%) 329 (M$^+$, 100), 314 (56), 298 (10).

Anal. Calcd. for $C_{22}H_{19}NO_2$: N, 4.25; M$_r$$^+$, 329.1417. Found: N, 4.24; M$_r$$^+$, 329.1362.

3-Ethyl-1-(6,7-dimethoxyquinol-2-yl)azulene (**5bc**).

This compound was obtained from the reaction of **4c** with 2-amino-4,5-dimethoxybenzaldehyde under refluxing for 8 hours in a yield of 110 mg (32%) as greenish blue crystals (from hexane), mp 141-144°; uv (methanol): λ max 215 (log ε 4.48), 231 (4.51), 289 (4.42), 342 (4.01), 399 (4.20), 603 nm (2.47); ^{1}H nmr (deuteriochloroform): δ 1.44 (3H, t, J = 7.6 Hz, CH_3), 2.98 (2H, q, J = 7.6 Hz, CH_2), 4.00 (3H, s, OCH_3), 4.06 (3H, s, OCH_3), 7.03 (1H, s, 5'-H), 7.17 (1H, dd, J = 10.0, 10.0 Hz, 5-H), 7.29 (1H, dd, J = 10.0, 10.0 Hz, 7-H), 7.52 (1H, s, 8'-H), 7.54 (1H, dd, J = 10.0, 10.0 Hz, 6-H), 7.73 (1H, d, J = 8.4 Hz, 4'-H), 7.99 (1H, d, J = 8.4 Hz, 3'-H), 8.23 (1H, s, 2-H), 8.28 (1H, d, J = 10.0 Hz, 4-H), 9.62 (1H, d, J = 10.0 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 15.5 (CH_3), 20.3 (CH_2), 56.0 (OCH_3), 56.1 (OCH_3), 105.2 (=CH-), 108.2 (=CH-), 120.3 (=CH-), 121.5 (=C<), 122.7 (=CH-), 124.5 (=CH-), 126.8 (=C<), 132.4 (=C<), 133.8 (=CH-), 134.2 (=CH-), 136.5 (=CH-), 136.8 (=CH-), 137.5 (=CH-), 138.4 (=CH-), 138.8 (=C<), 145.3 (=C<), 149.1 (=C<), 152.3 (=C<), 154.5 (=C<); ms: m/z (%) 343 (M^+, 100), 328 (55), 315 (14), 314 (54), 312 (23), 284 (11), 254 (12).

Anal. Calcd. for $C_{23}H_{21}NO_2$: C, 80.44; H, 6.16; N, 4.08; M_r^+, 343.1573. Found: C, 79.97; H, 6.14; N, 3.93; M_r^+, 343.1601.

3-Propyl-1-(6,7-dimethoxyquinol-2-yl)azulene (**5bd**).

This compound was obtained from the reaction of **4d** with 2-amino-4,5-dimethoxybenzaldehyde under refluxing for 7 hours in a yield of 111 mg (31%) as greenish blue crystals (from hexane), mp 111-113°; uv (methanol): λ max 289 (log ε 4.54), 347 (4.16), 400 (4.32), 608 nm (2.61); ^{1}H nmr (deuteriochloroform): δ 1.01 (3H, t, J = 7.1 Hz, CH_3), 1.53-2.10 (2H, m, β-CH_2), 3.06 (2H, m, α-CH_2), 3.97 (3H, s, OCH_3), 4.05 (3H, s, OCH_3), 6.99 (1H, s, 5'-H), 7.15 (1H, d, J = 10.0, 9.7 Hz, 5-H), 7.27 (1H, dd, J = 10.0, 9.7 Hz, 7-H), 7.48 (1H, dd, J = 10.0, 10.0 Hz, 6-H), 7.52 (1H, s, 8'-H), 7.70 (1H, d, J = 8.4 Hz, 4'-H), 7.95 (1H, d, J = 8.4 Hz, 3'-H), 8.19 (1H, s, 2-H), 8.28 (1H, d, J = 9.7 Hz, 4-H), 9.64 (1H, d, J = 9.7 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 14.3 (CH_3), 24.5 (β-CH_2), 29.4 (α-CH_2), 56.0 (OCH_3), 56.1 (OCH_3), 105.2 (=CH-), 108.3 (=CH-), 120.3 (=CH-), 121.5 (=C<), 122.7 (=CH-), 124.5 (=CH-), 126.8 (=C<), 130.9 (=C<), 134.0 (=CH-), 134.2 (=CH-), 136.9 (=C<), 137.2 (=CH-), 137.5 (=CH-), 138.4 (=CH-), 139.3 (=C<), 145.3 (=C<), 149.1 (=C<), 152.3 (=C<), 154.5 (=C<); ms: m/z (%) 357 (M^+, 82), 328 (100), 315 (14), 314 (19), 283 (7), 164 (12), 127 (6).

Anal. Calcd. for $C_{24}H_{23}NO_2$: N, 3.92; M_r^+, 357.1730. Found: N, 3.85; M_r^+, 357.1735.

1-(6,7-Methylenedioxyquinol-2-yl)azulene (**5ca**).

This compound was obtained from the reaction of **4a** with 2-amino-4,5-methylenedioxybenzaldehyde under refluxing for 57 hours in a yield of 45 mg (15%) as greenish blue crystals (from hexane), mp 147-148°; uv (methanol): λ max 212 (log ε 4.21), 232 (4.29), 283 (4.16), 301 (4.05), 340 (3.74), 392 (3.98), 632 nm (2.02); ^{1}H nmr (deuteriochloroform): δ 6.06 (2H, s, OCH_2O), 7.02 (1H, s, 5'-H), 7.48 (1H, s, 8'-H), 7.23-7.55 (4H, m), 7.71 (1H, d, J = 8.5 Hz, 4'-H), 7.95 (1H, d, J = 8.5 Hz, 3'-H), 8.29-8.40 (2H, m), 9.81 (1H, d, J = 9.7 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 101.5 (CH_2), 102.7 (=CH-), 105.9 (=CH-), 117.8 (=CH-), 120.1 (=CH-), 122.8 (=C<), 124.2 (=CH-), 125.4 (=CH-), 127.9 (=C<), 134.9 (=CH-), 136.7 (=C<), 137.1 (=CH-), 137.4 (=CH-), 138.3 (=CH-), 138.6 (=CH-), 143.4 (=C<), 146.5 (=C<), 147.1 (=C<), 150.5 (=C<), 154.5 (=C<); ms: m/z (%) 299 (M^+, 80), 298 (100), 240 (15), 155 (20), 120 (17).

Anal. Calcd. for $C_{20}H_{13}NO_2$: C, 80.25; H, 4.38; N, 4.68; M_r^+, 299.0947. Found: C, 79.86; H, 4.44; N, 4.55; M_r^+, 299.0912.

3-Methyl-1-(6,7-methylenedioxyquinol-2-yl)azulene (**5cb**).

This compound was obtained from the reaction of **4b** with 2-amino-4,5-methylenedioxybenzaldehyde under refluxing for 20 hours in a yield of 113 mg (36%) as greenish blue crystals (from hexane), mp 150-151°, uv (methanol): λ max 215 (log ε 4.26), 236 (4.31), 288 (4.20), 346 (3.80), 398 (3.98), 605 nm (2.27); ^{1}H nmr (deuteriochloroform): δ 2.68 (3H, s, CH_3), 6.06 (2H, s, OCH_2O), 7.01 (1H, s, 5'-H), 7.09 (3H, m, 5-,6-,7-H), 7.47 (1H, s, 8'-H), 7.68 (1H, d, J = 8.5 Hz, 4'-H), 7.93 (1H, d, J = 3'-H), 8.15 (1H, s, 2-H), 8.21 (1H, d, J = 10.0 Hz, 4-H), 9.65 (1H, d, J = 9.7 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 12.7 (CH_3), 101.5 (OCH_2O), 102.7 (=CH-), 106.0 (=CH-), 120.2 (=CH-), 122.7 (=C<), 122.8 (=CH-), 124.6 (=CH-), 125.7 (=C<), 126.3 (=C<), 134.3 (=CH-), 134.8 (=CH-), 136.9 (=C<), 137.6 (=CH-), 138.2 (=CH-), 138.5 (=CH-), 139.9 (=C<), 146.6 (=C<), 147.1 (=C<), 150.6 (=C<), 154.5 (=C<); ms: m/z (%) 313 (M^+, 100), 298 (67), 254 (14), 252 (9), 127 (12).

Anal. Calcd. for $C_{21}H_{15}NO_2$: N, 4.47; M_r^+, 313.1104. Found: N, 4.25; M_r^+, 313.1141.

3-Ethyl-1-(6,7-methylenedioxyquinol-2-yl)azulene (**5cc**).

This compound was obtained from the reaction of **4c** with 2-amino-4,5-methylenedioxybenzaldehyde under refluxing for 8 hours in a yield of 124 mg (38%) as greenish blue crystals (from hexane), mp 138-140°; uv (methanol): λ max 217 (log ε 4.44), 234 (4.48), 283 (4.37), 346 (3.80), 347 (3.98), 400 (4.18), 604 nm (2.45); ^{1}H nmr (deuteriochloroform): δ 1.42 (3H, t, J = 7.6 Hz, CH_3), 3.10 (2H, q, J = 7.6 Hz, CH_2), 6.04 (2H, s, OCH_2O), 6.99 (1H, s, 5'-H), 7.10-7.55 (3H, m, 5-,6-,7-H), 7.47 (1H, s, 8'-H), 7.68 (1H, d, J = 8.5 Hz, 4'-H), 7.92 (1H, d, J = 8.5 Hz, 3'-H), 8.20 (1H, s, 2-H), 8.27 (1H, d, J = 10.0 Hz, 4-H), 9.64 (1H, d, J = 10.0 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 15.5 (CH_3), 20.3 (CH_2), 101.5 (OCH_2O), 102.7 (=CH-), 106.0 (=CH-), 120.2 (=CH-), 122.8 (=CH-), 124.6 (=CH-), 126.5 (=C< x 2), 132.5 (=C<), 133.9 (=CH-), 134.8 (=CH-), 136.5 (=CH-), 136.9 (=C<), 137.7 (=CH-), 138.5 (=CH-), 138.9 (=C<), 146.6 (=C<), 147.1 (=C<), 150.5 (=C<), 154.5 (=C<); ms: m/z (%) 327 (M^+, 100), 312 (80), 298 (50), 252 (8), 155 (24), 127 (11).

Anal. Calcd. for $C_{22}H_{17}NO_2$: N, 4.28; M_r^+, 327.1260. Found: N, 3.99; M_r^+, 327.1230.

3-Propyl-1-(6,7-methylenedioxyquinol-2-yl)azulene (**5cd**).

This compound was obtained from the reaction of **4d** with 2-amino-4,5-methylenedioxybenzaldehyde under refluxing for 8 hours in a yield of 119 mg (35%) as greenish blue crystals (from hexane), mp 116-118°; uv (methanol): λ max 217 (log ε 4.44), 234 (4.48), 283 (4.37), 347 (3.98), 400 (4.18), 604 nm (2.45); ^{1}H nmr (deuteriochloroform): δ 1.01 (3H, t, J = 7.0 Hz, CH_3), 1.50-2.13 (2H, m, β-CH_2), 3.05 (2H, t, J = 7.2 Hz, α-CH_2), 6.03 (2H, s, OCH_2O), 6.99 (1H, s, 5'-H), 7.10-7.55 (3H, m, 5-,6-,7-H), 7.47 (1H, s, 8'-H), 7.67 (1H, d, J = 8.6 Hz, 4'-H), 7.92 (1H, d, J = 8.6 Hz, 3'-H), 8.17 (1H, s, 2-H), 8.27 (1H, d, J = 9.7 Hz, 4-H), 9.65 (1H, d, J = 9.9 Hz, 8-H); ^{13}C nmr (deuteriochloroform): δ 14.2 (CH_3), 24.5 (β-CH_2), 29.3 (α-CH_2), 101.4 (OCH_2O), 102.7 (=CH-), 105.9 (=CH-), 120.2 (=CH-), 122.7 (=CH-), 124.6 (=CH-), 126.4 (=C< x 2), 130.8 (=C<), 134.0 (=CH-), 134.8 (=CH-), 136.9 (=C<), 137.2 (=CH-), 137.6 (=CH-), 138.4 (=CH-), 139.3 (=C<), 146.5 (=C<), 147.0 (=C<), 150.5 (=C<), 154.5 (=C<); ms: m/z (%) 341 (M^+, 59), 312 (100), 298 (12), 252 (9), 155 (14), 127 (10).

Anal. Calcd. for $C_{23}H_{19}NO_2$: N, 4.10; M_r^+, 341.1417. Found: N, 3.95; M_r^+, 341.1432.

2-(2-Quinolyl)azulenes **7a**-**c**.

To a solution of 2-acetylazulene (**6**) (170 mg, 1.0 mmole) and a 2-aminobenzaldehyde (3.0 mmoles) in absolute ethanol (6 ml) was added a sodium ethoxide solution, prepared from sodium (92 mg, 4.0 mmoles) and absolute ethanol (4 ml). This mixed solution was refluxed for 6 hours. The mixture was diluted with water, neutralized with 2*M* hydrochloric acid, and extracted with chloroform. After drying over sodium sulfate, the extract was concentrated and chromatographed on a Wakogel B-10 plate (30 x 30 cm) with chloroform to give 2-(2-quinolyl)azulenes **7a**-**c**.

2-(2-Quinolyl)azulene (**7a**).

This compound was obtained from the reaction with 2-aminobenzaldehyde in a yield of 143 mg (56%) as blue crystals (from hexane), mp 214-216°; uv (methanol): λ max 208 (log ε 4.08), 243 (3.80), 285 (4.29), 303 (4.13), 315 (4.17), 374 (3.88), 393 (3.87), 591 (2.38), 635 (2.38), 694 nm (2.05); ^{1}H nmr (deuteriochloroform): δ 7.15 (2H, dd, J = 10.0, 9.7 Hz, 5-,7-H), 7.46-8.04 (5H, m), 8.07 (2H, s, 1-,3-H), 8.09 (1H, d, J = 8.5 Hz, 4'-H), 8.22 (1H, d, J = 8.5 Hz, 3'-H), 8.38 (2H, d, J = 9.7 Hz, 4-,8-H); ^{13}C nmr (deuteriochloroform): δ 116.3 (=CH-), 120.5 (=CH-), 121.2 (=C<), 123.8 (=CH-), 126.4 (=CH-), 127.5 (=CH-), 127.6 (=CH-), 129.6 (=CH-), 129.9 (=CH-), 136.4 (=CH-), 137.8 (=CH-), 141.3 (=C<), 148.8 (=C<), 149.2 (=C<), 154.8 (=C<); ms: m/z (%) 255 (M^+, 100).

Anal. Calcd. for $C_{19}H_{13}N$: C, 89.38; H, 5.13; N, 5.49; M_r^+, 255.1049. Found: C, 89.50; H, 5.21; N, 5.30; M_r^+, 255.1041.

2-(6,7-Dimethoxyquinol-2-yl)azulene (**7b**).

This compound was obtained from the reaction with 2-amino-4,5-dimethoxybenzaldehyde in a yield of 261 mg (83%) as greenish blue crystals (from hexane), mp 219-220°; uv (methanol): λ max 224 (log ε 4.32), 283 (4.57), 308 (4.24), 322 (4.26), 388 (4.23), 404 (4.17), 586 (2.43), 629 (2.42), 689 nm (2.08); ^{1}H nmr (deuteriochloroform): δ 3.93 (3H, s, OCH_3), 4.04 (3H, s, OCH_3), 6.92 (1H, s, 5'-H), 7.08 (2H, dd, J = 10.0, 9.4 Hz, 5-,7-H), 7.38 (1H, dd, J = 10.0, 10.0 Hz, 6-H), 7.51 (2H, s, 1-,3-H), 7.82 (1H, d, J = 8.5 Hz, 4'-H), 7.98 (1H, s, 8'-H), 8.02 (1H, d, J = 8.5 Hz, 3'-H), 8.29 (2H, d, J = 9.4 Hz, 4-,8-H); ^{13}C nmr (deuteriochloroform): δ 55.9 (OCH_3), 56.1 (OCH_3), 105.2 (=CH-), 108.5 (=CH-), 115.9 (=CH-), 118.8 (=CH-), 123.2 (=C<), 123.7 (=CH- x 2), 134.5 (=CH-), 137.2 (=CH-), 141.2 (=C<), 145.7 (=C<), 149.5 (=C<), 149.8 (=C<), 150.8 (=C<), 152.5 (=C<); ms: m/z (%) 315 (M^+, 100), 272 (11).

Anal. Calcd. for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44; M_r^+, 315.1260. Found: C, 79.63; H, 5.36; N, 4.45; M_r^+, 315.1283.

2-(6,7-Methylenedioxyquinol-2-yl)azulene (**7c**).

This compound was obtained from the reaction with 2-amino-4,5-methylenedioxybenzaldehyde in a yield of 188 mg (63%) as greenish blue crystals (from hexane), mp 234-235°; uv (methanol): λ max 222 (log ε 4.27), 281 (4.45), 306 (4.18), 321 (4.18), 387 (4.21), 404 (4.14), 588 (2.39), 631 (2.44), 690 nm (2.10); ^{1}H nmr (deuteriochloroform): δ 6.11 (2H, s, CH_2), 7.06 (1H, s, 5'-H), 7.20 (2H, dd, J = 10.0, 9.7 Hz, 5-,7-H), 7.50 (2H, s, 1-,3-H), 7.51 (1H, dd, J = 10.0, 10.0 Hz, 6-H), 7.95 (1H, d, J = 8.5 Hz, 4'-H), 7.99 (1H, s, 8'-H), 8.04 (1H, d, J = 8.5 Hz, 3'-H), 8.36 (2H, d, J = 9.7 Hz, 4-,8-H); ^{13}C nmr (deuteriochloroform): δ 101.7 (CH_2), 102.7 (=CH-), 106.4 (=CH-), 115.9 (=CH-), 118.8 (=CH-), 123.7 (=CH- x 2), 124.6 (=C<), 135.2 (=CH-), 137.3 (=C<), 137.4 (=CH-), 141.3 (=C<), 145.0 (=C<), 149.2 (=C<), 150.9 (=C<), 152.7 (=C<); ms: m/z (%) 299 (M^+, 100), 240 (20).

Anal. Calcd. for $C_{20}H_{13}NO_2$: C, 80.25; H, 4.38; N, 4.68; M_r^+, 299.0947. Found: C, 79.82; H, 4.50; N, 4.54; M_r^+, 299.0915.

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