Synthesis of 2-Formylazulene and Its Derivatives by Oxidative Cleavage of 2-Styrylazulenes

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(Received April 24, 1980)

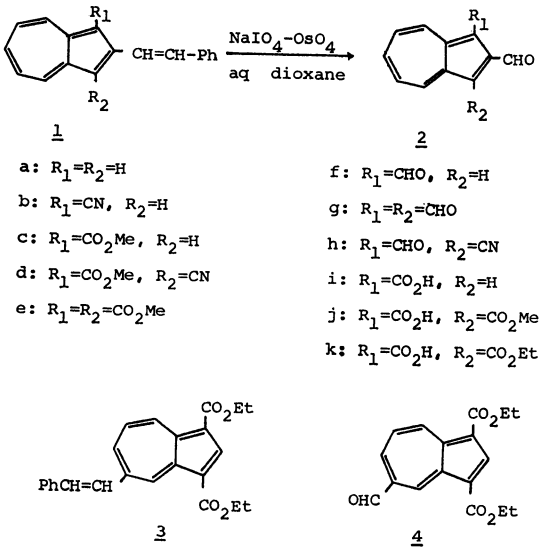
2-Formylazulene and its derivatives were prepared by the oxidative cleavage of styrylazulenes with $NaIO_4$–OsO_4. 1,2-Diformyl-, 1,2,3-triformylazulenes, and 5-formylazulene derivative were also synthesized. The reaction of dimethyl 2-methylazulene-1,3-dicarboxylate with *p*-nitroso-*N*,*N*-dimethylaniline in the presence of NaOR (R=Me or Et) gave the corresponding 3-alkoxycarbonyl-2-[*p*-(dimethylamino)phenyliminomethyl]-azulene-1-carboxylic acids followed by hydrolysis with hydrochloric acid to give 3-alkoxycarbonyl-2-formylazulene-1-carboxylic acids. Acetylation of 2-formylazulene-1-carboxylic acids with acetic anhydride gave five membered lactol acetates.

Formylazulenes are useful for synthesizing various azulene derivatives because of their functional formyl groups. Of five possible positional isomers, 1-formylazulene and its derivatives were easily obtained by formylation of azulenes according to the Vilsmeier-Haack method,[1-3] Gatterman reaction,[4] and with use of triethyl orthoformate–tetrafluoroboric acid[5] or perchloric acid,[6] the properties of which have been investigated.[1,2,7] The oxidation of some 1-methylazulenes with selenium dioxide or potassium permanganate also gave 1-formylazulenes.[8,9] However, preparation of the other isomeric formylazulenes is difficult. Sato[10] reported that 2-formylazulene is derived from 2-cyanoazulene by hydrolysis, esterification, reduction with lithium aluminum hydride, and subsequent oxidation of the resulting alcohol with manganese dioxide.

Arnold and Pahls[11] reported that 6-formyl-4,8-dimethylazulene is obtained from ethyl 4,8-dimethylazulene-6-carboxylate by reduction with lithium aluminum hydride, followed by oxidation by means of the Kröhnke-Karrer method. Hafner and Moritz[12] reported that the formylation of some 1,3-dialkylazulenes by the Vilsmeier-Haack method gives 2-formyl- and 5-formyl derivatives, together with 1-formylazulenes. The oxime of 6-formylazulene derivative was obtained by treatment of diethyl 2-amino-6-methylazulene-1,3-dicarboxylate with isopentyl nitrite.[13] This paper describes a useful method of synthesizing 2-formylazulene and its derivatives by oxidative cleavage of 2-styrylazulenes obtained by the condensation of 2-methylazulene derivative with benzaldehyde in good yields.[14]

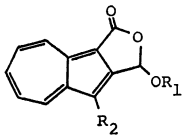
Results and Discussion

The Lemieux-Johnson oxidation[15] is effective for oxidative cleavage of the ethylenic linkage of 2-styrylazulenes. Thus, on treatment with sodium periodate in aq dioxane in the presence of a catalytic amount of osmium tetroxide, 2-styrylazulenes (**1a**—**j**) gave the corresponding 2-formylazulenes (**2a**—**j**), respectively. A lower yield (13%) of the parent 2-formylazulene (**2a**) may be due to its instability: it changes into a brown, hardly soluble substance on being heated or allowed to stand for a long time. The other 2-formylazulene derivatives, having substituents at the 1-(and 3-)positions, are stable and were obtained in good yields.



Scheme 1.

1,2-Diformyl[16] and 1,2,3-triformylazulenes (**2f,g,h**), not obtained by formylation of 2-formylazulenes (**2a,b,f**) by means of the Vilsmeier-Haack method, were obtained, in a similar manner, from 1-formyl- and 1,3-diformyl-2-styrylazulenes (**1f,g,h**) which were prepared by formylation of 2-styrylazulenes. The Lemieux-Johnson oxidation could be applied to the synthesis of not only 2-formylazulenes but also 5-formylazulenes. Thus, treatment of diethyl 5-styrylazulene-1,3-dicarboxylate (**3**) obtained by condensation of diethyl 5-methylazulene-1,3-dicarboxylate[17] and benzaldehyde with sodium periodate–osmium tetroxide afforded diethyl 5-formylazulene-1,3-dicarboxylate (**4**). The IR spectra (KBr) of 2-formylazulenes show absorptions corresponding to $\nu_{C=O}$ of the 2-formyl groups within the range 1672—1701 cm^{-1} in somewhat lower frequency region than that (1708—1699 cm^{-1})[18] of benzaldehydes; that of 1-formylazulenes appear in a lower frequency region 1610—1650 cm^{-1}.[7b,8] The electronic spectra of 2-formylazulenes conform to the extended Plattner rule.[19] The NMR spectra of 2-formylazulenes, as expected, show a singlet due to the formyl proton at δ 10—11 ppm, as well as signals due to the other protons. 2-Formylazulenes easily gave carbonyl derivatives, such as oximes and hydrazones, and were converted into the corresponding alcohols or carboxylic acids by reduction



5a: R_1=R_2=H

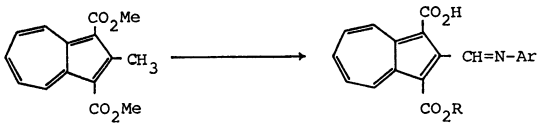
5b: R_1=H, R_2=CO_2Me

6a: R_1=COMe, R_2=CO_2Me

6b: R_1= COMe, R_2=CO_2Et

Fig. 1.

with sodium borohydride or oxidation with silver oxide, respectively. 2-Formylazulene-1-carboxylic acids (**2i,j**) possess a structure analogous to that of *o*-formylbenzoic acid which undergoes cyclization easily into the lactol, and existing as a mixture of ring-chain tautomers, the acid and lactol (13 : 87) in dioxane.[20] In the case of **2i** and **2j**, however, the ring tautomers (**5a,b**) could not be detected by either IR (KBr, $CHCl_3$) or NMR ($CDCl_3$), **2i** and **2j** exist predominantly in the acid chain structure. This can be explained by resonance stabilization of the formyl group at position 2 and also by the larger bond angle between two substituents in **2i** and **2j** than in *o*-formylbenzoic acid. On the other hand, the acetylation of **2j** gave a lactol acetate (**6a**), whose structure was established on the basis of spectral data. The IR (KBr) shows an absorption at 1767 cm^{-1} due to the five-membered lactone, and the NMR spectrum ($CDCl_3$) shows singlets at δ 2.20 ($COCH_3$), 3.90 (OCH_3), and 7.78 ppm (methine), as well as signals due to the ring protons at δ 7.6—8.3 (3H,m), 9.10 (1H, bd), and 9.90 ppm (1H, bd).



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8a: R=Me, Ar=p-$(Me)_2NC_6H_5$-

8b: R=Et, Ar=p-$(Me)_2NC_6H_5$-

Scheme 2.

Reactive methyl or methylene groups are convertible into carbonyl groups by condensation with *p*-nitroso-*N,N*-dimethylaniline (**NDA**)[21] and subsequent hydrolysis of the resulting Shiff base. Such a reaction was carried out for synthesizing 2-formylazulenes from 2-methylazulene derivatives directly. The reaction of dimethyl 2-methylazulene-1,3-dicarboxylate (**7**) with **NDA** proceeded easily in the presence of sodium methoxide or ethoxide to give condensation products **8a** and **8b**. Hydrolysis of non-purified **8a** with acid gave an acidic compound identical with **2j**. **8a** could not be isolated in a pure form since it was easily hydrolyzed to **2j**; **8b** was isolated in pure form. Hydrolysis of **8b** gave 3-ethoxycarbonyl-2-formylazulene-1-carboxylic acid (**2k**). Acetylation of **2k** gave a lactol acetate (**6b**). The structures of **8b**, **2k**, and **6b** were established on the basis of spectral data (IR and NMR).

The fact that **8b** is acidic enough to be soluble in aq $NaHCO_3$ solution also supports the half ester structure of **8b**. The mechanism of the formation of the half ester **8b** is assumed to be similar to that of the formation of the half ester of 2-styrylazulene-1,3-dicarboxylic acid by condensation of **7** and benzaldehyde.[14]

Experimental

All melting points were determined in a capillary and are uncorrected. Electronic spectra were measured on a Hitachi EPS-3 spectrometer, and IR spectra on a Shimadzu IR-27 infracord, and NMR spectra on a Varian A-60 spectrometer in $CDCl_3$ containing TMS.

General Procedure for the Oxidation of 2-Styrylazulenes to 2-Formylazulenes. Finely ground $NaIO_4$ (2—4 molar equivalents) was added in portions to a stirred solution of 2-styrylazulenes and OsO_4 (1—2% by weight) dissolved in aq dioxane (dioxane : H_2O=7 : 3) at room temp over a period of 30—60 min. Stirring was continued for 4—8 h. The reaction mixture was diluted with water and extracted with $CHCl_3$, the extract being washed with H_2O and dried over Na_2SO_4. After evaporation of the solvent the residue was chromatographed over a silica-gel column and eluted with benzene. The first colorless effluent gave benzaldehyde, the second and third colored portions giving 2-styrylazulenes and 2-formylazulenes, respectively.

2-Formylazulene (2a). 2-Styrylazulene (**1a**) (460 mg, 2 mmol) was treated according to the general procedure to give **1a** (30 mg) and **2a** (40 mg, 13% yield) as blue scales (from cyclohexane), mp 62—63 °C (reported[10] mp 63 °C); IR (KBr): 1675 cm^{-1}; $\lambda_{max}^{cyclohexane}$ 244 nm (log ε 4.23), 275 sh (4.50), 288 (4.69), 296 (4.70), 335 (3.68), 346 (3.72), 360 (3.80), 613 (2.61), 664 (2.19); NMR ($CDCl_3$): δ 7.13 (br t, J=10 Hz, H-5,7), 7.67 (br t, J=10 Hz, H-6), 7.70 (s, H-1,3), 8.42 (br d, J=10 Hz, H-4,8), 10.37 (s, CHO). Found: C, 84.63; H, 5.23%. Calcd for $C_{11}H_8O$: C, 84.59; H, 5.16%.

Phenylhydrazone: Green needles (from benzene), mp 197 °C. Found: C, 82.63; H, 5.80; N, 11.08%. Calcd for $C_{17}H_{14}N_2$: C, 82.90; H, 5.73; N, 11.37%.

1-Cyano-2-formylazulene (2b). 1-Cyano-2-styrylazulene (**1b**) (2.25 g, 10 mmol) was treated according to the general procedure to give **1b** (340 mg) and **2b** (1.17 g, 75% yield) as green needles (from benzene), mp 184—185 °C; IR (KBr): 1686, 2217 cm^{-1}; λ_{max}^{MeOH} 233 nm (log ε 4.25), 287 (4.57), 298 (4.79), 345 (3.69), 362 (3.64); NMR ($CDCl_3$): δ 7.2—7.8 (m, H-5,7), 7.96 (br t, J=9 Hz, H-6), 8.58 (br t, J=11 Hz, H-4), 8.78 (br d, J=11 Hz, H-8), 10.48 (s, CHO). Found: C, 79.59; H, 3.80; N, 7.60%. Calcd for $C_{12}H_7ON$: C, 79.55; H, 3.89; N, 7.73%.

Oxime: Brown blue crystals (from $CHCl_3$), mp 264—266 °C. Found: 73.78; H, 3.66; N, 13.92%. Calcd for $C_{12}H_8O_2N_2$: C, 73.46; H, 4.11; N, 14.28%.

Hydrazone: Green crystals (from benzene), mp over 300 °C. Found: C, 73.78; H, 4.46; N, 21.00%. Calcd for $C_{12}H_9N_3$: C, 73.83; H, 4.65; N, 21.53%.

p-*(Dimethylamino)phenylimino Derivative*: Reddish brown crystals (from benzene–cyclohexane), mp 194—196 °C. Found: C, 79.89; H, 5.58; N, 13.88%. Calcd for $C_{20}H_{17}N_3$: C, 80.24; H, 5.72; N, 14.04%.

Methyl 2-Formylazulene-1-carboxylate (2c). Methyl 2-styrylazulene-1-carboxylate (**1c**) (1.30 g, 4.5 mmol) was treated in the usual way to give **1c** (130 mg) and **2c** (560 mg, 64% yield) as green needles (from ethanol), mp 119—120 °C; IR (KBr): 1701, 1678 cm^{-1}; λ_{max}^{MeOH} 238 nm (log ε 4.32), 291

(4.61), 301 (4.68), 335 sh (3.79), 350 (3.84), 369 (3.75), 573 (2.98), 606 (3.02), 650 sh (2.70); NMR ($CDCl_3$): δ 3.98 (s, OCH_3), 7.2—7.6 (m, H-5, 7), 7.63 (s, H-3), 7.83 (tm, J=9 Hz, H-6), 8.47 (br d, J=10 Hz, H-4), 9.62 (br d, J=10 Hz, H-8), 10.92 (s, CHO). Found: C, 72.90; H, 4.82%. Calcd for $C_{13}H_{10}O_3$: C, 72.89; H, 4.71%.

Methyl 3-Cyano-2-formylazulene-1-carboxylate (2d). Methyl 3-cyano-2-styrylazulene-1-carboxylate (**1d**) (3.13 g, 10 mmol) was treated in the usual way to give **1d** (1.02 g) and **2d** (1.29 g, 80% yield) as reddish violet needles (from MeOH), mp 221—223 °C; IR (KBr): 2865, 2219, 1698, 1678, 1115, 1064 cm^{-1}; λ_{max}^{MeOH} 235 nm (log ε 4.55), 267 (4.34), 293 (4.63), 303 (4.73), 340 (3.90), 367 (3.89). Found: C, 70.22; H, 3.82; N, 5.79%. Calcd for $C_{14}H_9O_3N$: C, 70.29; H, 3.79; N, 5.86%.

Dimethyl 2-Formylazulene-1,3-dicarboxylate (2e). Dimethyl 2-styrylazulene-1,3-dicarboxylate (**1e**) (1.38 g, 4 mmol) was treated in the usual way to give **1e** (120 mg) and **2e** (810 mg, 82% yield) as red needles (from MeOH), mp 167—168 °C; IR (KBr): 2865, 1698, 1215, 1192, 1088, 1064 cm^{-1}; λ_{max}^{MeOH} 234 nm (log ε 4.53), 275 sh (4.43), 292 (4.62), 302 (4.70), 340 (3.89), 368 (4.00); $\lambda_{max}^{CHCl_3}$ 525 nm (log ε 2.97); NMR ($CDCl_3$): δ 3.92 (s, 2 OCH_3), 7.5—8.1 (m, H-5—7), 9.73 (dm, J=10 Hz, H-4,8), 10.75 (s, CHO). Found: C, 66.34; H, 4.50%. Calcd for $C_{15}H_{12}O_5$: C, 66.17; H, 4.44%.

1,2-Diformylazulene (2f). 1-Formyl-2-styrylazulene (**1f**) (1.03 g, 4 mmol) was treated in a similar manner to that above to give **2f** (660 mg, 90% yield) as bluish green needles (from cyclohexane), mp 155—156 °C; IR (KBr): 1672, 1643 cm^{-1}; $\lambda_{max}^{chloroform}$ 290 nm (log ε 4.48), 315 (4.60), 325 (4.57), 350 (4.08), 370 (4.08), 390 (4.04), 540 (2.63), 600 (2.94), 640 sh (2.75); NMR ($CDCl_3$): δ 7.3—8.3 (m, H-5—7), 7.83 (s, H-3), 8.75 (br d, J=10 Hz, H-4), 9.87 (br d, J=10 Hz, H-8), 10.87 (s, CHO), 11.00 (s, CHO). Found: C, 78.22; H, 4.39%. Calcd for $C_{12}H_8O_2$: C, 78.25; H, 4.38%.

1,2,3-Triformylazulene (2g). 1,3-Diformyl-2-styrylazulene (**1g**) (600 mg, 2.1 mmol) was treated in the usual way to give **2g** (380 mg, 86% yield) as reddish violet needles (from $CHCl_3$), mp 242—243 °C; IR (KBr): 1689, 1658 cm^{-1}; $\lambda_{max}^{chloroform}$ 304 nm (log ε 4.64), 315 (4.66), 351 (3.98), 377 (3.84), 560 (3.14); NMR ($CDCl_3$): 8.05 (t, J=9 Hz, H-5—7), 8.33 (t, J=9 Hz, H-6), 9.90 (d, J=9 Hz, H-4,8), 10.75 (s, 2 CHO), 11.13 (s, CHO on C-2). Found: C, 73.58; H, 3.69%. Calcd for $C_{13}H_8O_3$: C, 73.58; H, 3.80%.

1-Cyano-2,3-diformylazulene (2h). 1-Cyano-3-formyl-2-styrylazulene (**1h**) (1.42 g, 5 mmol) was treated in the usual way to give **2g** (920 mg, 88% yield) as reddish violet needles (from $CHCl_3$), mp 242—245 °C; IR (KBr): 2212, 1692, 1661 cm^{-1}; $\lambda_{max}^{chloroform}$ 303 nm (log ε 4.64), 312 (4.64), 350 (3.98), 377 (3.84), 570 (3.18); NMR ($CDCl_3$): δ 7.8—8.3 (m, H-5—7), 9.05 (dm, J=10 Hz, H-4), 10.07 (dm, J=10 Hz, H-8), 10.85 (s, CHO), 10.92 (s, CHO). Found: C, 74.48; H, 3.46; N, 6.69%. Calcd for $C_{13}H_7O_2N$: C, 74.64; H, 3.37; N, 6.70%.

2-Formylazulene-1-carboxylic Acid (2i). 2-Styrylazulene-1-carboxylic acid (**1i**) (280 mg, 1 mmol) was treated according to the general procedure to give **2i** (90 mg, 44% yield) as blue needles (from ethanol), mp above 300 °C; IR (KBr): 3200—2857, 1672, 1640 cm^{-1}; $\lambda_{max}^{dichloromethane}$ 308 nm (log ε 4.54), 355 (3.98), 610 (2.99); NMR ($CDCl_3$+DMSO-d_6 (2 : 1)): δ 7.3—8.2 (m, H-5—7), 7.73 (s, H-3), 8.63 (br d, J=10 Hz, H-4), 9.83 (br d, J=10 Hz, H-8), 11.00 (s, CHO). Found: C, 71.82; H, 4.11%. Calcd for $C_{12}H_8O_3$: C, 71.99; H, 4.03%.

2-Formyl-3-(methoxycarbonyl)azulene-1-carboxylic Acid (2j). 3-Methoxycarbonyl-2-styrylazulene-1-carboxylic acid (**1j**) (405 mg, 1.2 mmol) was treated according to the general procedure. Crystals obtained on dilution with water were collected to give **2j** (205 mg, 65% yield) as red prisms (from MeOH), mp 242—245 °C; IR (KBr): 3030—2857, 1701, 1658, 1221, 1092 cm^{-1}. Found: C, 64.82; H, 3.78%. Calcd for $C_{14}H_{10}O_5$: C, 65.12; H, 3.90%.

Diethyl 5-Formylazulene-1,3-dicarboxylate (4). Diethyl 5-styrylazulene-1,3-dicarboxylate (**3**) (100 mg, 0.27 mmol) was treated according to the general procedure to give **4** (52 mg, 64.9% yield) as red needles (from ethanol), mp 137—138 °C; IR (KBr): 1700 sh, 1690, 1205, 1025 cm^{-1}; $\lambda_{max}^{chloroform}$ 275 nm (log ε 4.39), 308 (4.53), 333 (4.11), 406 (4.23), 520 (3.13); NMR ($CDCl_3$): δ 1.47 and 1.49 (t, J=7.0 Hz, 2 OCH_2CH_3), 4.45 and 4.48 (q, J=7.0 Hz, 2 OCH_2CH_3), 7.82 (t, J=10 Hz, H-7), 8.48 (dt, J=1.5 and 10 Hz, H-6), 8.83 (s, H-2), 9.83 (dd, J=1.5 and 10 Hz, H-8), 10.15 (d, J=1.5 Hz, H-4), 10.20 (s, CHO). Found: C, 66.40; H, 4.40%. Calcd for $C_{15}H_{12}O_5$: C, 66.17; H, 4.44%.

1-Formyl-2-styrylazulene (1f). $POCl_3$ (320 mg) was added to a stirred solution of 2-styrylazulene (**1a**) (480 mg, 2 mmol) in DMF (5 ml) under ice-cooling. After being stirred for 30 min, the mixture was poured into ice-water (200 ml) containing 1 M KOH solution (10 ml). The product was extracted with $CHCl_3$, washed with water and dried over Na_2SO_4. The solvent was evaporated and the residue was chromatogtaphed over an alumina column and eluted with benzene. Recrystallization from cyclohexane gave **1f** (500 mg, 93% yield) as reddish violet needles, mp 125—127 °C; IR (KBr): 2762, 1626, 1610sh, 979 cm^{-1}; $\lambda_{max}^{dichloromethane}$ 345 nm (log ε 4.67), 365sh (4.58), 405 (4.02); NMR ($CDCl_3$): δ 7.0—7.8 (10 H, m, H-5—7, CH=CH–, and C_6H_5), 7.97 (s, H-3). 8.30 (complex d. J=9,Hz, H-4), 9.33 (complex d. J=10 Hz, H-8), 10.73 (s, CHO). Found: C, 88.10; H, 5.38%. Calcd for $C_{19}H_{14}O$: C, 88.34; H, 5.46%.

1,3-Diformyl-2-styrylazulene (1g). A solution of **1f** (510 mg, 2 mmol) in DMF (15 ml) was treated with $POCl_3$ (530 mg) in a manner similar to that described above. Recrystallization from benzene gave **1g** (540 mg, 95% yield) as red needles, mp 174—175 °C; IR (KBr): 1660—1620 (br), 979 cm^{-1}; $\lambda_{max}^{dichloromethane}$ 317 nm (log ε 4.59), 340 (4.59), 500 (2.80): NMR ($CDCl_3$): δ 6.93 (d, J=8.0 Hz, =CH–), 7.2—8.0 (m, H-5—7 and C_6H_5), 7.97 (d, J=8.0 Hz, =CH–), 9.7—9.9 (m, H-4, 8), 10.48 (s, 2 CHO). Found: C, 83.71; H, 4.81%. Calcd for $C_{20}H_{14}O_2$: C, 83.90; H, 4.93%.

1-Cyano-3-formyl-2-styrylazulene (1h). A solution of 1-cyano-2-styrylazulene (**1b**) (1.90 g, 6.7 mmol) in DMF (50 ml) was treated with $POCl_3$ (2 ml) in a similar manner to that described above. Recrystallization of the crude product from benzene gave **1h** (1.96 g, 93% yield) as red needles, mp 222—224 °C; IR (KBr): 2203, 1645, 1613, 952 cm^{-1}; NMR ($CDCl_3$): δ 7.27—8.03 (10 H, m, H-5—7, and protons of styryl group), 8.60—8.83 (m, H-4), 9.57—9.80 (m, H-8), 10.67 (s, CHO). Found: C, 84.86; H, 4.77; N, 4.85%. Calcd for $C_{20}H_{13}NO$: C, 84.78; H, 4.63; N, 4.94%.

Reduction of 2f with $NaBH_4$. To a stirred solution of **2f** (50 mg) in dioxane (2 ml) was added a solution of $NaBH_4$ (6 mg) in MeOH (1 ml) at room temp. After being stirred for 5 min, acetic acid was added in order to decompose excess $NaBH_4$. The reaction mixture was diluted with water and extracted with chloroform. The extract was washed with water and dried (Na_2SO_4). The solvent was evaporated and the residue was chromatographed (silica gel) and eluted with chloroform to give 40 mg of 1-formyl-2-(hydroxymethyl)-azulene as red needles, mp 117—118 °C (from ethanol); IR (KBr); 3400, 1621 cm^{-1}; $\lambda_{max}^{dichloromethane}$ 265 nm (log ε 4.24), 269 (4.29), 315 (4.85), 365 (4.10), 3.80 (4.22), 514 (2.69); NMR ($CDCl_3$): δ 5.13 (s, CH_2OH), 6.2 (br s, OH), 7.32 (s, H-3), 7.38—7.90 (m, H-5—7), 8.45 (br d, J=10 Hz,

H-4), 9.05 (br d, J=10 Hz, H-8), 10.60 (s, C<u>H</u>O). MS: *m/e* (rel intensity), 186 (M^+, 100), 168 (M^+—CO, 28), 157 (48), 139 (42).

1-Cyano-2-(hydroxymethyl)azulene was obtained by the reduction of **2b** with $NaBH_4$ in 93% yield in a similar manner to that described above, violet needles, mp 124—125 °C (from cyclohexane–dichloromethane); IR (KBr): 3460, 2200 cm^{-1}; NMR ($CDCl_3$): δ 2.37 (br s, OH), 5.17 (s, C<u>H</u>$_2$OH), 7.32 (s, H-3), 7.2—7.9 (m, H-5—7), 7.33 (d, J=9 Hz, H-4), 8.50 (d, J=9 Hz, H-8). MS (25 eV, at 120 °C): *m/e* (rel intensity), 183 (M^+, 83), 167 (83), 166 (100%).

Oxidation of 2b with Ag_2O. To a stirred solution of **2b** (205 mg) in ethanol (5 ml) was added freshly prepared Ag_2O (650 mg). After being stirred for 5 h, the mixture was diluted with water. The resulting crystals were collected and dissolved in a 1 M $NaHCO_3$ solution. The solusion was shaken with benzene and acidified with 6 M HCl to give crystals. Recrystallization from ethanol gave 1-cyanoazulene-2-carboxylic acid (86 mg, 38% yield) as dark green crystals, mp over 300 °C; IR (KBr): 2860 (br), 2217, 1686, 926 cm^{-1}. Found: C, 72.79; H, 3.68; N, 6.96%. Calcd for $C_{12}H_7O_2N$: 73.09; H, 3.58; N, 7.10%.

Diethyl 5-Styrylazulene-1,3-dicarboxylate (3). A mixture of 1.0 g (3.5 mmol) of diethyl 5-methylazulene-1,3-dicarboxylate[17] and 1.86 g (17.5 mmol) of benzaldehyde in a sodium ethoxide solution prepared from 403 mg (17.5 matom) of sodium and 50 ml of anhydrous ethanol was stirred at room temp for 4 d. The reaction mixture was diluted with water and acidified with dilute HCl and then extracted with chloroform. After evaporation of the solvent from the organic extract the residue was chromatographed (alumina, benzene) to give 114 mg of the unreacted diethyl 5-methylazulene-1,3-dicarboxylate from the first effluent and 116 mg (8.9%) of **3** from the second effluent as red needles (from ethanol); mp 127—128 °C (lit,[22] 122.5—123 °C); IR (KBr): 1690—1670 (br), 1200, 950 cm^{-1}; NMR ($CDCl_3$): δ 1.46 and 1.48 (t, J=7.0 Hz, 2 OCH$_2$C<u>H</u>$_3$), 4.48 and 4.50 (q, J=7.0 Hz, 2 OC<u>H</u>$_2$CH$_3$), 7.3—7.7 (m, C$_6$<u>H</u>$_5$), 7.76 (t, J=10 Hz, H-7), 8.23 (dd, J=10, 2 Hz, H-6), 8.93 (s, H-2), 9.76 (d, J=10 Hz, H-8), 10.30 (d, J=2 Hz, H-4). Found: C, 76.59; H, 6.18%. Calcd for $C_{24}H_{22}O_4$: C, 76.98; H, 5.92%. From the third effluent with chloroform, 380 mg (27.7%) of diethyl 5-(2-hydroxy-2-phenylethyl)azulene-1,3-dicarboxylate was obtained as reddish violet needles (from ethanol), mp 159.5—161 °C; IR (KBr): 3450, 1690, 1660, 770, 750 cm^{-1}; NMR ($CDCl_3$): δ 1.41 (t, J=7.0 Hz, 2 OCH$_2$C<u>H</u>$_3$), 2.65 (br s, OH), 3.30 (d, J=6.5 Hz, CH(OH)C<u>H</u>$_2$), 4.35 and 4.40 (q, J=7.0 Hz, 2 OC<u>H</u>$_2$CH$_3$), 5.50 (t, J=6.5 Hz, C<u>H</u>(OH)CH$_2$), 7.28 (br s, C$_6$H$_5$), 7.50 (t, J=9.0 Hz, H-7), 7.73 (br d, J=9.0 Hz, H-6), 8.75 (s, H-2), 9.41 (dd, J=9.0, 2 Hz, H-8), 9.75 (d, J=2 Hz, H-4). Found: C, 73.52; H, 6.35%. Calcd for $C_{24}H_{24}O_5$: C, 73.47; H, 6.16%.

Dehydration of Diethyl 5-(2-Hydroxy-2-phenylethyl)azulene-1,3-dicarboxylate. A mixture of 100 mg of diethyl 5-(2-hydroxy-2-phenylethyl)azulene-1,3-dicarboxylate, $POCl_3$ (3 ml), and pyridine (5 ml) was allowed to stand at room temp for 18 h. The reaction mixture was diluted with water and extracted with ether. The extracts were washed with dilute HCl and dried (Na_2SO_4) and worked up to give 93 mg (98% yield) of **3**.

The Lactol Acetate (6a). A drop of concd H_2SO_4 was added to a suspension of **2j** (100 mg) in Ac_2O (2 ml). After being stirred at room temp for 20 min, the mixture was diluted with water and extracted with $CHCl_3$, the extract being washed with water and dired (Na_2SO_4). The solvent was evaporated and the residue dissolved in benzene and passed through a short alumina column. Recrystallization from benzene gave **6a** (85 mg) as red needles, mp 220—222 °C; IR (KBr): 1767, 1706 cm^{-1}; λ_{max}^{MeOH} 234 nm (log ε 4.73), 271 (4.66), 300 (4.87), 327 (3.93), 355 (4.09), 367 (4.17), 492 (2.96); NMR ($CDCl_3$): δ 2.20 ($COCH_3$), 3.90 (OCH_3), 7.78 (methine), 7.6—8.3 (3H, m), 9.10 (1H, br d), 9.90 (1H, br d). Found: C, 64.37; H, 4.32%. Calcd for $C_{16}H_{12}O_6$: C, 64.00; H, 4.03%.

The Lactol Acetate (6b). The acid **2k** (50 mg) was treated with Ac_2O–concd H_2SO_4 in a silimar manner to that described above. Recrystallization from benzene gave **6b** (40 mg) as red needles, mp 198—200 °C; IR (KBr): 1770, 1701 cm^{-1}; λ_{max}^{MeOH} 235 nm (log ε 4.72), 271 (4.66), 292 (4.76), 301 (4.84), 326 (3.90), 355 (4.09), 368 (4.18). Found: C, 69.61, H, 4.28%. Calcd for $C_{17}H_{14}O_6$: C, 64.96; H, 4.49%.

Reaction of Dimethyl 2-Methylazulene-1,3-dicarboxylate (7) with p-Nitiroso-N,N-dimethylaniline (NDA). *a) In MeOH*: To a stirred solution of NaOMe were added 102 mg (0.39 mmol) of **7** and 100 mg (0.67 mmol) of NDA at room temp. After being stirred for 12 h, the reaction mixture was diluted with water and left to stand for 5 h. The precipitate formed was collected by filtration and chromatographed (silica gel, C_6H_6) to give 12 mg of **7**. The filtrate was acidified with 6 M HCl to give precipitate which was collected by filtration to give 60 mg of **2j** as red crystals.

b) In EtOH: 500 mg (3.3 mmol) of NDA was added to a stirred solution of NaOEt prepared from 150 mg of Na and anhydrous EtOH (3 ml). After being stirred for 12 h, the reaction mixture was diluted with water and extracted with chloroform. The organic layer was washed with water, dried (Na_2SO_4), and concentrated to a small volume. The residue was chromatographed (silica gel) to give 40 mg of **7** from the fraction eluted with C_6H_6. From the fraction eluted with chloroform 400 mg (53% yield) of **8b** was obtained as reddish brown needles; mp 228—229 °C (from benzene). IR (KBr): 1669, 1616, 1587, 813 cm^{-1}; λ_{max}^{MeOH} 239 nm (log ε 4.51), 308 (4.49), 540 (4.25); NMR ($CDCl_3$): δ 1.52 (t, J=7.0 Hz, OCH$_2$C<u>H</u>$_3$), 2.97 (s, N(C<u>H</u>$_3$)$_2$), 4.55 (q, J=7.0 Hz, OC<u>H</u>$_2$CH$_3$), 6.67 (2H, d, J=9.5 Hz, =NC$_6$<u>H</u>$_4$N(Me)$_2$), 7.45 (2H, d, J=9.5 Hz, =NC$_6$<u>H</u>$_4$N(Me)$_2$), 7.5—8.0 (m, H-5—7), 9.48 (br d, J=10 Hz, H-8), 9.70 (s, COOH), 10.50 (dm, J=10 Hz, H-4). Found: C, 70.94; H, 5.75; N, 7.23%. Calcd for $C_{23}H_{22}O_4N_2$: C, 70.75; H, 5.68; N, 7.18%.

3-Ethoxycarbonyl-2-formylazulene-1-carboxylic Acid (2k). A solution of 100 mg of **8b** and 6 M HCl (2 drops) in EtOH (10 ml) was heated at 80 °C for 15 min. The mixture was diluted with water and extracted with chloroform. The organic layer was worked up to give 35 mg of **2k** as red needles, mp 222—223 °C (from benzene). IR (KBr): 3030—2778, 1706, 1654, 1212, 1088, 901 cm^{-1}. Found: C, 65.80; H, 4.43%. Calcd for $C_{15}H_{12}O_5$: C, 66.17; H, 4.44%.

The present work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture.

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