Some Electrophilic Substitution Reactions of 2-Hydroxyazulene Derivatives[1]

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The bromination, chlorination, and nitration of 1,3-disubstituted 2-hydroxyazulenes were investigated. Bromination by bromine or NBS afforded 1-bromoazulan-2-one derivatives as kinetically-controlled products and 6-bromo-2-hydroxyazulene derivatives as thermodynamically-controlled products. Chlorination by NCS gave 1-chloroazulan-2-one derivatives, while that by chlorine afforded further chlorine addition products. Nitration afforded a mixture of 1-nitroazulan-2-one and 6-nitro-2-hydroxyazulene derivatives. The ultraviolet, infrared, and NMR spectra of the products were discussed.

It has been established[2,3] that the electrophilic substitutions of azulenes occur at the 1 and 3 positions; positions which coincide with the calculated positions[4] thought to have the highest electron density by theoretical considerations, and that the 5, 7, and 2 positions, with the next higher electron density, undergo the reaction in the case of 1,3-disubstituted azulenes.[5]

However, 1,3-disubstituted azulenes with strongly electron-releasing groups, such as an amino or a methylamino group, at the 2-position have been known to undergo facile bromination at the 6-position,[6] and 1,3-dicyano-2-hydroxy-5-isopropylazulene have also been known to afford 6,8-dibromo derivative by bromination.[7] These facts indicate that the strongly electron-releasing group at the 2-position governs the substitution at the 4, 6, and 8 positions.

In the present research, some electrophilic substitutions of 1,3-disubstituted 2-hydroxyazulenes were investigated; the results will be reported herein.

The bromination of diethyl 2-hydroxyazulene-1,3-dicarboxylate (I)[8] with 1.5 molar equivalents of bromine in acetic acid in the presence of sodium acetate afforded a reddish pink solid (II). When the solid was dissolved in ethanol, it gradually turned yellow; from it 90% of the starting azulene (I) and 5.5% of yellow needles (III) (mp 163 °C) were then obtained. Compound III, corresponding to the monobromide of I, shows an ultraviolet spectrum (Fig. 1) similar to that of I; its infrared spectrum displays an out-of-plane deformation band due to adjacent two hydrogens at 830 cm^{-1}. Furthermore, the NMR spectrum of III shows two doublets with the same coupling constant (J=11.8 Hz) at δ 7.86 and 8.93, each corresponding to two protons. These data clearly show that Compound III is diethyl 6-bromo-2-hydroxyazulene-1,3-dicarboxylate.

When the reddish pink solid (II) was washed with ether and then recrystallized from benzene–petroleum ether, a pure specimen of II was obtained as reddish prisms (mp 129 °C) in a yield of 68%. Compound II was also obtained by the reaction of I and NBS in CCl_4 in a 75% yield. Elemental analyses show that Compound II is also a monobromide of I; its UV spectrum (Fig. 1) is completely different from that of I or III, but rather similar to those of 1-oxaazulan-2-one (1*H*-1-oxaazulene-2-one) derivatives[9] or 8,8-dicyanoheptafulvene[10] in methanol.

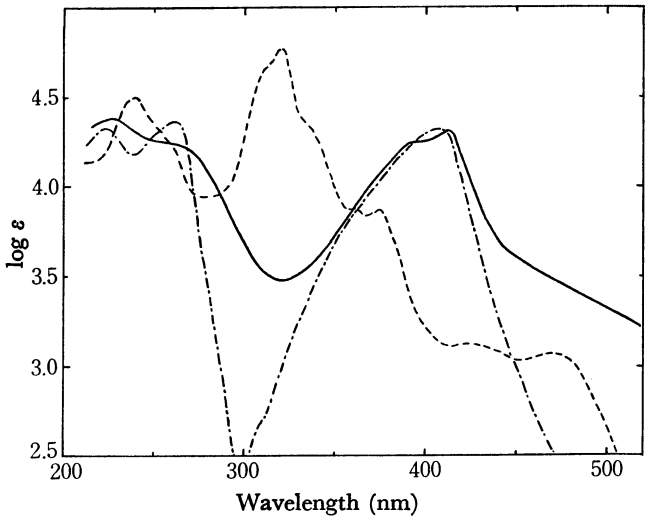

Fig. 1. UV spectra of II (——), III (----), and ethyl 1-oxa-2-oxo-azulane-3-carboxylate (—·—) in methanol.

The IR spectrum of II shows carbonyl bands at 1749 and 1689 cm^{-1}; the former one is comparable to that of 1-oxaazulan-2-one.[9] The NMR spectrum of II exhibits signals at δ 8.40 (bd, J=12 Hz, Ha), 6.7—7.2 (m, Hb–He), 4.31 (q), 4.20 (q), 1.36 (t), and 1.1 (t). From the above data, it is clear that II is diethyl 1-bromo-2-oxo-azulane-1,3-dicarboxylate (diethyl 1*H*-1,2-dihydro-1-bromo-2-oxoazulene-1,3-dicarboxylate), with a heptafulvenoid chromophore. The formation of II can be explained by considering that Compound I reacts as a β-keto ester form (Ia) under the present reaction conditions. The reactivity is similar to that of β-naphthol.[11]

It has been found that 2-hydroxyazulene (IV) exists in the enol form (IV) in methanol and in the keto form, 1,2-dihydroazulene-2-one (IVa), in $CHCl_3$ or water, and that the IR of 2-hydroxyazulene in KBr disk does not show any carbonyl band.[12] Meanwhile, Nozoe *et al.* have reported, in their azulene synthesis from the reactive troponoids with active methylene compounds, that there are three principal interme-

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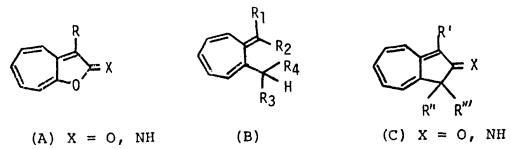


(A) X = O, NH (B) (C) X = O, NH

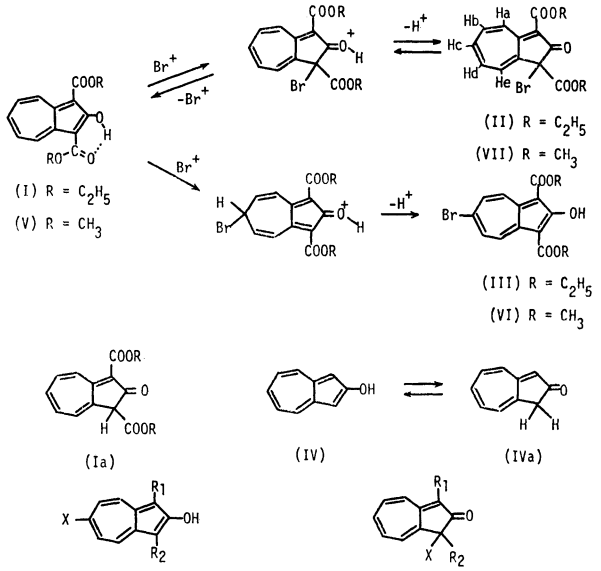
diates: "oxaazulanone" (A), "heptafulvene" (B), and "azulanone" (C).[13] However, the B and C intermediates are so unstable in the basic reaction conditions that they could not be isolated. Compound II is the first example of stable azulanone type compound obtained from azulene derivatives, and from the above view points, it is of interest to investigate the properties of II and the similar compounds obtained below.

Compound II is unstable to protic solvents, especially to bases, and in these solvents II liberates the bromine cation, which can easily be detected by the iodine-starch test, to give mainly I and a small amount of III at room temperature. Even on standing in air, II is gradually decomposed, presumably by moisture, to give I and III. Compound II immediately gave the sodium salt of hydroxyazulene (I) by the action of a sodium hydroxide solution, while the reaction with potassium iodide in acetone afforded potassium salt of I. The reaction of II with 2,4-dinitrophenylhydrazine or hydrazine yielded I and the hydrazine salt of I respectively.

On the other hand, the heating of II in DMF at 90 °C afforded 55% of I and 45% of III. When II was heated in DMF at 90 °C in the presence of an equimolar amount of dimethyl 2-hydroxyazulene-1,3-dicarboxylate (V),[10] dimethyl 6-bromo-2-hydroxyazulene-1,3-dicarboxylate (VI) (mp 210 °C) was obtained besides I, III, and V by intermolecular reaction. Therefore, it is clear that the bromination of I afforded at first the 1-bromo derivative (II) as a kinetically controlled product; then it afforded the 6-bromo derivative (III) as a thermodynamically controlled product under more severe reaction conditions. For the purpose of the direct synthesis of III, the bromination of I at an elevated temperature was attempted. Thus, the action of bromine on I in acetic acid–sodium acetate or in DMF–sodium acetate at 100 °C afforded III in yields of 45 and 70% respectively, besides I.

The bromination of the dimethyl ester (V) by bromine in $CHCl_3$ in the presence of sodium acetate at room temperature afforded 1-bromo compound (VII) as reddish prisms (mp 136 °C), whose UV and IR spectra are very similar to those of Compound II. When the reaction was carried out in DMF in the presence of sodium acetate and then the mixture was left standing at room temperature for 10 hr, the 6-bromo derivative (VI) was obtained in a 76% yield. Compound VI was also obtained by heating VII in DMF.

Similarly, the bromination of ethyl 1-cyano-2-hydroxyazulene-3-carboxylate (VIII)[13] with bromine in acetic acid–sodium acetate or with NBS in benzene afforded ethyl 1-bromo-3-cyano-2-oxo-azulane-1-carboxylate (IX) (mp 109 °C); the bromination of VIII in acetic acid–sodium acetate at 100 °C afforded ethyl 6-bromo-3-cyano-2-hydroxyazulene-1-carboxylate (X) (mp 207 °C).



(I) R = C_2H_5
(V) R = CH_3
(II) R = C_2H_5
(VII) R = CH_3
(III) R = C_2H_5
(VI) R = CH_3

(Ia) (IV) (IVa)

(VIII) X = H, R_1 = CN, R_2 = $COOC_2H_5$
(X) X = Br, R_1 = CN, R_2 = $COOC_2H_5$
(XI) X = H, R_1 = R_2 = CN
(XIII) X = Br, R_1 = R_2 = CN
(XV) X = R_1 = H, R_2 = $COOC_2H_5$
(XVI) X = H, R_1 = Br, R_2 = $COOC_2H_5$
(XXIV) X = NO_2, R_1 = R_2 = $COOC_2H_5$
(XXVI) X = NO_2, R_1 = CN, R_2 = $COOC_2H_5$
(XXIX) X = CN, R_1 = R_2 = $COOC_2H_5$

(IX) X = Br, R_1 = CN, R_2 = $COOC_2H_5$
(XII) X = Br, R_1 = R_2 = CN
(XVIII) X = Cl, R_1 = R_2 = $COOC_2H_5$
(XIX) X = Cl, R_1 = R_2 = $COOCH_3$
(XX) X = Cl, R_1 = CN, R_2 = $COOC_2H_5$
(XXIII) X = NO_2, R_1 = R_2 = $COOC_2H_5$
(XXV) X = NO_2, R_1 = CN, R_2 = $COOC_2H_5$
(XXX) X = $CONH_2$, R_1 = R_2 = $COOC_2H_5$

The bromination of 1,3-dicyano-2-hydroxyazulene (XI)[13] by bromine in $CHCl_3$ in the presence of sodium acetate at room temperature afforded a reddish oily product (XII), which did not crystallize and which could not be purified because of its instability. The IR of XII exhibits a strong carbonyl band at 1724 cm^{-1} and a weak cyano band at 2215 cm^{-1}. The UV of XII shows a curve similar to that of II, with maxima at 290, 406, and 425 nm. From these data, the oil is assumed to be 1-bromo-1,3-dicyanoazulan-2-one (XII). When the solution of the oil (XII) in $CHCl_3$ was allowed to stand at room temperature for 30 min, it turned yellow and 50% of the 6-bromo-1,3-dicyano-2-hydroxyazulene (XIII) was obtained, besides XI. The structure of XIII was determined by means of the spectroscopic data.

When a solution of XI, 1.5 molar equivalents of bromine, and sodium acetate in acetic acid was allowed to stand at room temperature for 1 hr, the 6-bromo derivative (XIII) was obtained in a yield of 67% besides an unidentified yellowish-brown mixture. The reaction of XI with 3 molar equivalents of bromine in acetic acid in the presence of sodium acetate afforded 4,6,8-tribromo-1,3-dicyano-2-hydroxyazulene (XIV) besides XIII and an unidentified brown solid.

On the bromination of ethyl 2-hydroxyazulene-1-carboxylate (XV),[8] the unsubstituted 3-position was exclusively attacked, and ethyl 3-bromo-2-hydroxyazulene-1-carboxylate (XVI) was obtained in a good yield.

When the 6-bromo compound (III) was further

treated with NBS in benzene, the solution turned red, and the UV of the solution showed a curve similar to that of 1-bromide (II); therefore, the 1,6-dibromo compound (XVII) seems to be formed. However, the working-up of the solution afforded only the starting compound (III), and no XVII or 4,6-dibromo derivative could be isolated; such unreactivity may due to a steric interaction of ethoxycarbonyl groups at the 1 and 3 positions to the peri-position of the nucleus.

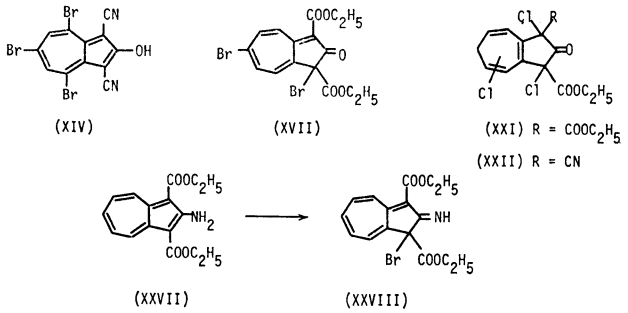
The reactions of I, V, and VIII with *N*-chlorosuccinimide (NCS) in benzene afforded three 1-chloro derivatives, XVIII (mp 98 °C), XIX (mp 161 °C), and XX (mp 132 °C), in good yields. The structures of these products were determined by their spectroscopic properties. These compounds are more stable than the corresponding bromides (II and VII), and do not change easily on standing in the air.

The reaction of I and VIII with chlorine in CCl_4 afforded two pale yellow oils (XXI and XXII respectively). The results of the analyses of these products almost accord with those of trichloride of the starting compounds, and their UV maxima appear only at 261 nm in both compounds. The IR of XXI displays bands at 1790 and 1767 cm^{-1}, while that of XXII shows them at 2205 (vw), 1975, and 1767 cm^{-1}. From these data, the structures of the compounds can tentatively be assigned as is shown in the figure. Compound XXI is quite stable; however, XXII gradually changes when allowed to stand at room temperature and gives a reddish solid, from which the 1-chloro compound (XX) is subsequently isolated in a 50% yield.

The nitration of I with concentrated nitric acid in acetic acid was carried out, and two kinds of mononitro derivatives, were isolated. One consisted of brown needles (XXIV) (41% yield), while the other consisted of reddish crystals (XXIII) with a low melting point (36% yield). Compound XXIV was determined to be diethyl 2-hydroxy-6-nitroazulene-1,3-dicarboxylate from its spectroscopic data; the UV is similar to those of azulenes, and the NMR in $CDCl_3$ shows A_2B_2-type doublets at δ 9.48 and 8.43, with the same coupling constant (J=12 Hz). From the similarity of UV and IR spectra of XXIII to those of II, Compound XXIII is assumed to be diethyl 1-nitro-2-oxo-azulane-1,3-dicarboxylate.

A similar nitration of VIII afforded 6-nitro derivative (XXVI) as brown crystals in a 39% yield and 1-nitro derivative (XXV) as reddish crystals in a 42% yield. In these nitrations of I and VIII, reddish powders were obtained in 10—15% yields; however, attempts to purify them were not successful.

As has been mentioned at the beginning, diethyl 2-aminoazulene-1,3-dicarboxylate (XXVII) undergoes a facile bromination by bromine at the 6-position in a $CHCl_3$ solution to give orange crystals with UV maxima at 473, 410, 332, 320, and 245 nm.[6] The UV spectrum of a solution of XXVII and NBS in benzene displays maxima at 395 and 375 nm characteristic of heptafulvene chromophore, therefore, the 1-bromoazulan-2-imine derivative (XXVIII) must be formed in the solution. However, the compound could not be isolated.



In order to synthesize the model compound (C; R′=R″=$COOC_2H_5$, R‴=CN or $CONH_2$) of the "azulanone" intermediate in the azulene synthesis,[13] the reaction of II with cyanogen bromide or urea was attempted. The reaction of silver salt of I with cyanogen bromide afforded II, III, and a small amount of a compound assumed to be diethyl 6-cyano-2-hydroxyazulene-1,3-dicarboxylate (XXIX). On the heating of I with urea in acetic acid in the presence of a few drops of sulfuric acid, reddish orange needles, which were assumed to be diethyl 1-carbamoyl-2-oxo-azulan-2-one-1,3-dicarboxylate (XXX), were obtained once in a 5% yield; also the starting azulene was recovered. However, the structure and the reactivity of XXX were not clarified because of the lack of a sample.

Experimental***

Bromination of Diethyl 2-Hydroxyazulene-1,3-dicarboxylate (I). (a) To a stirred solution of I (1 g) and sodium acetate (427 mg) in acetic acid (10 ml), a solution of bromine (834 mg) in acetic acid was added at room temperature. The solution turned deep red. After 2 hr, a 40 ml portion of water was added, thus giving a reddish oil, which was subsequently solidified by allowing to stand. The reddish pink solid that resulted was washed with ether, and 870 mg (68%) of reddish crystals were obtained. Recrystallization from benzene–petroleum ether gave II as reddish needles; mp 128—129 °C.

Found: C, 52.66; H, 4.29; Br, 22.00%. Calcd for $C_{16}H_{15}O_5Br$: C, 52.32; H, 4.12; Br, 21.76%.

λ_{max}^{MeOH} nm (log ε); 228 (4.39), 260 (4.24), 395 (4.24) and 414 (4.31).

By treating the filtrate with sodium hydroxide, sodium salt of I was recovered in a 25% yield.

(b) NBS (354 mg) was added to a stirred solution of I (500 mg) and sodium acetate in benzene (20 ml). After 15 min, the solvent was removed until the volume was about 10 ml, and then succinimide was removed by filtration. The filtrate was further condensed to about 5 ml, and petroleum ether was added to give reddish crystals (495 mg, 79%), which were subsequently washed with petroleum ether and recrystallized from benzene–petroleum ether to give red needles (mp 128—129 °C), whose infrared spectrum was superimposable upon that of II obtained by Procedure (a).

(c) A solution of I (1 g), sodium acetate (427 mg), and bromine (894 mg) in acetic acid was warmed on a water bath for 2 hr; then it was allowed to stand overnight at room temperature. The precipitate was filtered to give 490 mg

*** All melting points are uncorrected.

of yellow crystals; when water was then added to the filtrate to yield a reddish oil which was subsequently crystallized by the addition of ethanol, 80 mg of the same yellow crystals and 500 mg of the starting materials were obtained. The combined product was then recrystallized from ethanol to give III as yellow needles (470 mg, 73%); mp 162—163 °C

Found: C, 52.44; H, 4.32%. Calcd for $C_{16}H_{15}O_5Br$: C, 52.32; H, 4.12%.

λ_{max}^{MeOH} nm (log ε); 240 (4.50), 263^{sh} (4.23), 313^{sh} (4.67), 322 (4.78), 360 (3.87), 375 (3.87), 420 (3.13) and 470 (3.07).

$\lambda_{max}^{MeOH-0.1N\ NaOH}$nm (log ε); 247 (4.42), 275 (3.99), 320^{sh} (4.60), 334 (4.73), 420 (3.77) and 490 (3.72).

Methyl Ether: Methyl ether was obtained by the reaction of III with diazomethane; reddish orange needles; mp 124—125 °C.

Found: C, 53.39; H, 4.80%. Calcd for $C_{17}H_{17}O_5Br$: C, 53.55; H, 4.50%.

Ethyl Ether: Ethyl ether was obtained by the reaction of III with diazoethane; reddish orange needles; mp 109—110 °C.

Found: C, 54.53; H, 4.70%. Calcd for $C_{18}H_{19}O_5Br$: C, 54.71; H, 4.85%.

(d) A solution of I (200 mg), sodium acetate (85 mg), and bromine (166 mg) in dimethyl formamide (4 ml) was allowed to stand at room temperature for 2 days. When water (15 ml) was then added, 245 mg solid was obtained. The fractional recrystallization of the solid afforded 175 mg (68%) of III and 50 mg of I.

Thermal Reaction of Diethyl 1-Bromo-2-oxo-azulan-2-one-1,3-dicarboxylate (II). A solution of II (100 mg) in DMF (2 ml) was heated at 100 °C for 3 hr. When water was then added and the precipitate was fractionally recrystallized from ethanol, 45 mg (45%) of III and 40 mg (50%) of I were obtained.

Reaction of II and Dimethyl 2-Hydroxyazulene-1,3-dicarboxylate (V). A solution of II (200 mg) and V (142 mg) in DMF (6 ml) was heated at 100 °C for 3 hr. The crystals (80 mg) which were precipitated out were recrystallized from ethyl acetate to give 75 mg (40%) of pale yellow needles (mp 210 °C). The crystals were identified as dimethyl 6-bromo-2-hydroxyazulene-1,3-dicarboxylate (VI) by a mixed-melting-point comparison and by a comparison of the infrared spectra. The filtrate of the reaction was diluted with water and extracted with chloroform. When the extract was then evaporated, 215 mg of crystals were obtained. The crystals were proved to be a mixture of I, V, and a small amount of III by separation using thin-layer chromatography on silica gel.

Bromination of Dimethyl 2-Hydroxyazulene-1,3-dicarboxylate (V). (a) To a stirred solution of V (100 mg) and sodium acetate (42 mg) in chloroform (5 ml), a solution of bromine (80 mg) in chloroform was added at room temperature. After 15 min, the inorganic substance thus precipitated was filtered off, and to the filtrate petroleum ether was added to obtain reddish crystals. The crystals were then recrystallized from $CHCl_3$–petroleum ether to give VII as reddish prisms (25 mg); mp 136 °C.

Found: C, 49.49; H, 3.24%. Calcd for $C_{14}H_{11}O_5Br$: C, 49.60; H, 3.27%.

λ_{max}^{MeOH} nm (log ε); 227 (4.38), 270^{sh} (4.21), 395^{sh} (4.20) and 415 (4.26).

The treatment of the filtrate with sodium hydroxide afforded 70 mg of a sodium salt of V.

(b) A solution of V (200 mg), sodium acetate (77 mg), and bromine (148 mg) in DMF (5 ml) was allowed to stand at room temperature for 12 hr. Water (20 ml) was then added, and the crystals thus precipitated were washed with methanol and recrystallized from ethyl acetate to give VI (200 mg, 76%) as pale yellow needles; mp 210 °C.

Found: C, 49.39; H, 3.34%. Calcd for $C_{14}H_{11}O_5Br$: C, 49.60; H, 3.27%.

λ_{max}^{MeOH} nm (log ε); 240 (4.52), 264^{sh} (4.27), 310^{sh} (4.65), 321 (4.77), 335^{sh} (4.47), 374 (4.28), 420 (3.48) and 470 (3.30).

$\lambda_{max}^{MeOH-0.1N\ NaOH}$ nm (log ε); 247 (4.50), 280^{sh} (4.14), 325^{sh} (4.70), 333 (4.76), 415 (4.28) and 488 (4.18).

Bromination of Ethyl 3-Cyano-2-hydroxyazulene-1-carboxylate (VIII). (a) To a suspended solution of VIII (200 mg) and sodium acetate (88 mg) in acetic acid (20 ml) was added a solution of bromine (162 mg) in acetic acid at room temperature. After the solution had been stirred for 30 min, water (30 ml) was added and the solution was extracted with benzene. The extract was dried, the solvent was removed to a small volume, and petroleum ether was added to give reddish crystals (175 mg, 66%). Subsequent recrystallization from benzene–petroleum ether afforded ethyl 1-bromo-3-cyano-2-oxo-azulane-1-carboxylate (IX) as reddish prisms; mp 109 °C.

Found: C, 52.41; H, 3.15; N, 4.69; Br, 25.02%. Calcd for $C_{14}H_{10}O_3NBr$: C, 52.54; H, 3.40; N, 4.38; Br, 24.97%.

λ_{max}^{MeOH} nm (log ε); 225 (4.27), 258 (4.15), 395 (4.19) and 417 (4.25).

When the combined filtrates were treated with a sodium hydroxide solution, 55 mg of the sodium salt of VIII were recovered.

(b) To a stirred solution of VIII (500 mg) in benzene (25 ml), NBS (445 mg) was added at room temperature. After 20 min, the solvent was removed to about 10 ml and the precipitated succinimide was filtered off. A large amount of petroleum ether was then added to the filtrate, and 630 mg (95%) of reddish crystals were obtained. Recrystallization from benzene–petroleum ether afforded IX as reddish prisms; their infrared spectrum was superimposable on that of IX obtained by Procedure (a).

(c) A solution of VIII (300 mg), sodium acetate (154 mg), and bromine (298 mg) in acetic acid (15 ml) was heated at 100 °C for 3 hr. After the solution had stood overnight, 300 mg of crystals were obtained; they were recrystallized from ethyl acetate to give ethyl 6-bromo-3-cyano-2-hydroxyazulene-1-carboxylate (X) (230 mg, 60%) as yellow needles; mp 206—207 °C. From the combined filtrate, VIII (60 mg) and X (20 mg) were obtained.

Found: C, 52.21; H, 3.30; N, 4.07%. Calcd for $C_{14}H_{10}O_3NBr$: C, 52.54; H, 3.40; N, 4.38%.

λ_{max}^{MeOH} nm (log ε); 235 (4.54), 315^{sh} (4.74), 319 (4.82), 375 (3.93) and 450 (2.95).

$\lambda_{max}^{MeOH-0.1N\ NaOH}$nm (log ε); 247 (4.50), 270^{sh} (3.86), 320^{sh} (4.69), 332 (4.79), 422 (3.95) and 485 (3.77).

Bromination of 1,3-Dicyano-2-hydroxyazulene (XI). (a) To a suspended solution of XI (200 mg) and sodium acetate (127 mg) in $CHCl_3$ (10 ml), a solution of bromine (248 mg) in $CHCl_3$ was added. After 15 min, the precipitate was filtered off, a 50 ml portion of petroleum ether was added to the filtrate, and a reddish oil (200 mg, 70%) was obtained by decantation. The oil could not be crystallized or purified. A solution of the oil in $CHCl_3$ showed UV maxima at 290, 406, and 425 nm. The precipitate obtained from the reaction mixture was identified as a mixture of XI and the 6-bromo derivative (XIII) by a comparison of the infrared spectra.

(b) Bromine (620 mg) was added to a suspension of XI (500 mg) and sodium acetate (317 mg) in acetic acid (10 ml) at room temperature. After 1 hr, the crystals which were precipitated out were filtered and 470 mg of yellow crystals were obtained; these crystals were recrystallized from ethanol

to give 6-bromo-1,3-dicyano-2-hydroxyazulene (XIII) as yellow crystals; mp over 300 °C.

Found: C, 52.74; H, 2.02; N, 9.97%. Calcd for $C_{12}H_5ON_2Br$: C, 52.79; H, 1.85; N, 10.26%.

λ_{max}^{MeOH} nm (log ε); 228 (4.54), 250^{sh} (4.18), 315 (4.78), 328 (4.88), 426 (3.91) and 473 (3.63).

The filtrate obtained from the reaction mixture was diluted with water; a reddish brown solid, which could not be purified, was thus obtained.

(c) To a stirred suspension of XI (500 mg) and sodium acetate (640 mg) in acetic acid (15 ml), bromine (1.24 g) was added at room temperature. The suspension turned deep red, and yellow crystals began to precipitate after 20 min. After 3 hr, the crystals (480 mg) were filtered out and recrystallized from DMF to give 1,3-dicyano-2-hydroxy-4,6,8-tribromoazulene (XIV) (290 mg, 25%) as orange yellow crystals; mp over 300 °C.

Found: C, 32.47; H, 0.67; N, 5.87%. Calcd for $C_{12}H_3ON_2Br_3$: C, 33.43; H, 0.70; N, 6.50%.

λ_{max}^{MeOH} nm; 227, 283, 325, 338 and 440.

From the filtrate of the recrystallization, the 6-bromo derivative (XIII) (150 mg) was obtained. When water was then added to the filtrate of the reaction mixture, 410 mg of a reddish brown solid was obtained.

Ethyl 3-Bromo-2-hydroxyazulene-1-carboxylate (XVI). A solution of ethyl 2-hydroxyazulene-1-carboxylate (XV) (100 mg) and NBS (100 mg) in CCl_4 (4 ml) was gently heated for 20 min. Working up as usual sebsequently afforded XVI (110 mg) as deep orange needles; mp 106—107 °C after recrystallization from ethanol.

Found: C, 53.34; H, 3.82%, Calcd for $C_{13}H_{11}O_3Br$: C, 52.93; H, 3.76%.

λ_{max}^{MeOH} nm (log ε); 247 (4.36), 320 (4.53), 375 (3.75), 390^{sh} (3.77) and 408 (3.81).

$\lambda_{max}^{MeOH-0.1N\ NaOH}$nm (log ε); 245 (4.36), 320 (4.58), 369 (4.76) and 407 (3.70).

Chlorination of Diethyl 2-Hydroxyazulene-1,3-dicarboxylate (I), (a) A solution of I (250 mg), NCS (150 mg), and sodium acetate (100 mg) in $CHCl_3$ (10 ml) was gently heated for 30 min. The resulting reddish solution was washed with water, dried over anhydrous sodium sulfate, and chromatographed on silica gel column, using $CHCl_3$ as the solvent, to give 230 mg of reddish crystals. Subsequent recrystallization from benzene–cyclohexane afforded diethyl 1-chloroazulan-2-one-1,3-dicarboxylate (XVIII) as reddish prisms; mp 97—98 °C.

Found: C, 59.33; H, 4.60%. Calcd for $C_{16}H_{15}O_5Cl$: C, 59.54; H, 4.69%.

λ_{max}^{MeOH} nm (log ε); 225 (4.40), 258 (4.25), 395 (4.26) and 414 (4.30).

(b) To a stirred solution of I (250 mg) in $CHCl_3$, two molar equivalents of a solution of chlorine in CCl_4 were slowly added under gentle heating. The solution first turned red and then pale yellow. The solvent was then removed to give a pale yellow oil (XXI) which could not be purified further.

Found: C, 47.52; H, 3.81%. Calcd for $C_{16}H_{15}O_5Cl_3$: C, 48.85; H, 3.86%.

Dimethyl 1-Chloro-2-oxo-azulane-1,3-dicarboxylate (XIX). By the reaction of dimethyl 2-hydroxyazulene-1,3-dicarboxylate (V) with NCS, XIX was obtained in an 80% yield as reddish prisms (from benzene–cyclohexane); mp 160—161 °C.

Found: C, 57.49; H, 3.83%. Calcd for $C_{14}H_{11}O_5Cl$: C, 57.06; H, 3.76%.

λ_{max}^{MeOH} nm (log ε); 225 (4.38), 265 (4.20), 395 (4.25) and 415 (4.30).

Chlorination of Ethyl 3-Cyano-2-hydroxyazulene-1-carboxylate (VIII). (a) The reaction of VIII with NCS afforded ethyl 1-chloro-3-cyano-2-oxo-azulane-1-carboxylate (XX) as reddish prisms (from benzene–cyclohexane); mp 131—132 °C.

Found: C, 60.97; H, 3.95; N, 5.28%. Calcd for $C_{14}H_{10}O_3NCl$: C, 61.00; H, 3.95; N, 5.08%.

λ_{max}^{MeOH} nm (log ε); 222 (4.38), 255 (4.30), 395 (4.28) and 416 (4.31).

(b) To a solution of VIII (300 mg) in $CHCl_3$ (5 ml), a solution of chlorine in CCl_4 was added. The solution became pale yellow. The solvent was then removed to give a pale yellow oily product, which was assumed to be trichloride (XXII); however, it could not be purified. The oil was gradually decomposed to give a reddish solid. When a part (180 mg) of the solid was dissolved in $CHCl_3$ and chromatographed on silica gel, a compound (91 mg) (mp 132 °C) was obtained whose IR was superimposable upon that of XX obtained by Method (a).

Nitration of Diethyl 2-Hydroxyazulene-1,3-dicarboxylate (I). To a stirred solution of I (1 g) in acetic acid (10 ml), concentrated nitric acid (5 ml) was added at room temperature. A small amount of the solution was then placed in a test tube and heated until the solution turned deep red. The solution was then added to the original reaction mixture, and the mixture was stirred at room temperature. The mixture thereupon turned deep red; then it was cooled with ice. After 10 min, water (3 ml) was added and the precipitate was filtered and washed with ethanol to give 410 mg of brown crystals. The filtrate was diluted with water (50 ml) and extracted with $CHCl_3$. The extract was dried and chromatographed on silica gel, using $CHCl_3$ as the solvent. From the first effluent, 100 mg of the starting azulene (I) was obtained; the second effluent gave 420 mg of a reddish oil, which could not be crystallized or purified completely. The compound was considered to be diethyl 1-nitro-2-oxo-azulane-1,3-dicarboxylate (XXIII) from the analytical results and the UV spectrum.

Found: C, 58.01; H, 4.90; N, 3.98%. Calcd for $C_{16}H_{15}O_7N$: C, 57.66; H, 4.54; N, 4.20%.

λ_{max}^{MeOH} nm; 225, 256, 395, and 416.

From the third effluent, 70 mg of brown crystals were obtained. The combined brown crystals (480 mg) were recrystallized from ethyl acetate to give diethyl 2-hydroxy-6-nitroazulene-1,3-dicarboxylate (XXIV) as brown needles; mp 219—220 °C.

Found: C, 57.44; H, 4.64; N, 4.13%. Calcd for $C_{16}H_{15}O_7N$: C, 57.66; H, 4.54; N, 4.20%.

λ_{max}^{MeOH} nm (log ε); 247 (4.54), 328 (4.64), 342 (4.59), 370 (3.98), 385 (3.95), 408 (3.92) and 465 (4.22).

$\lambda_{max}^{MeOH-0.1N\ NaOH}$nm (log ε); 243 (4.50), 342 (4.55), 382 (3.96), 405 (3.92) and 487 (4.41).

From the last effluent of the chromatography using ethanol as the solvent, 105 mg of a deep red powder were obtained.

Methyl Ether of XXIV: The methylation of XXIV with diazomethane afforded methyl ether as brownish green needles; mp 143.5—144.5 °C (from ethyl acetate).

Found: C, 58.47; H, 4.54; N, 4.25%. Calcd for $C_{17}H_{17}O_7N$: C, 58.79; H, 4.93; N, 4.03%.

λ_{max}^{MeOH} nm (log ε); 247 (4.49), 318 (4.78), 374 (3.84), 390 (3.86), 406 (3.89) and 470 (3.24).

Ethyl Ether of XXIV: Ethyl ether was obtained by the reaction of XXIV with diazoethane; green needles; mp 106—107 °C (from ethyl acetate).

Found: C, 60.23; H, 5.31%. Calcd for $C_{18}H_{19}O_7N$: C, 59.83; H, 5.30%.

Nitration of Ethyl 3-Cyano-2-hydroxyazulene-1-carboxylate (VIII). A solution of VIII (600 mg) and concentrated nitric acid (10 ml) in acetic acid (20 ml) was gently heated until a

reddish color appeared. When the solution was cooled and water was added 175 mg of brown crystals was obtained. The filtrate was then worked up as in the case of the nitration of I; 220 mg of reddish crystals (XXV), 100 mg of brown crystals, and 84 mg of a reddish powder were thus obtained. The reddish crystals (XXV) showed a mp of 105—108 °C and UV maxima at 225, 257, 397 and 417 nm, but they could not be purified further.

Found: C, 59.20; H, 3.60; N, 9.56%. Calcd for $C_{14}H_{10}O_5N_2$: C, 58.74; H, 3.52; N, 9.79%.

The combined brown crystals (275 mg) were recrystallized from ethyl acetate to give ethyl 3-cyano-2-hydroxy-6-nitroazulene-1-carboxylate (XXVI) as brown needles; mp 231—232 °C.

Found: C, 59.12; H, 3.38; N, 9.57%. Calcd for $C_{14}H_{10}O_5N_2$: C, 58.74; H, 3.52; N, 9.79%.

λ_{max}^{MeOH} nm (log ε); 236 (4.56), 325 (4.65), 340^{sh} (4.63), 370 (4.10), 385 (4.10) and 468 (4.16).

$\lambda_{max}^{MeOH-0.1N\ NaOH}$nm (log ε); 233 (4.55); 327 (4.51), 338 (4.54), 380 (4.02) and 476 (4.34).

Reaction of Silver Salt of I with Cyanogen Bromide. Silver salt of I was obtained by the reaction of I with silver oxide in ethanol and was used after drying under reduced pressure. To a stirred solution of silver salt of I (396 mg) in DMF (4 ml) at 100 °C, cyanogen bromide (400 mg) was added, whereupon the solution immediately turned red. After 30 min, the precipitated silver bromide was filtered off and washed with $CHCl_3$; the solvent was then removed under reduced pressure to leave a reddish oily product. A solution of the oil in $CHCl_3$ was chromatographed on silica gel. The crystals obtained from the reddish effluent was fractionally recrystallized from $CHCl_3$–petroleum ether; 120 mg of II, 20 mg of III, and 55 mg of reddish needles (XXIX) (mp 128—130 °C) were thus obtained.

Found: C, 64.95; H, 4.78; N, 4.19%. Calcd for $C_{17}H_{15}O_5N$: C, 65.23; H, 4.83; N, 4.48%.

λ_{max}^{MeOH} nm; 237, 262, 301, 312, and 410.

IR (KBr disk); 2242 and 1690 cm^{-1}.

NMR ($CDCl_3$); δ 1.52 (t), 4.53 (q), 7.92 (2H, d, J=8.6 Hz) and 10.03 (2H, d, J=8.6 Hz).

Reaction of I with Urea. A solution of I (400 mg) and urea (250 mg) in acetic acid (5 ml) was heated at *ca.* 90 °C for 4 hr in the presence of 5 drops of concentrated sulfuric acid. The solution was then diluted with water and extracted with $CHCl_3$, after which the extract was dried and chromatographed on a silica gel column. From the first effluent, 130 mg of the starting azulene (I) was recovered; the next effluent afforded 50 mg of a reddish oil, which was crystallized from benzene–petroleum ether, and also 10 mg of XXX as reddish-orange needles (mp 154—155 °C) was obtained (from benzene–petroleum ether).

Found: C, 63.55; H, 5.51%. Calcd for $C_{17}H_{17}O_6N$: C, 61.63; H, 5.17%.

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