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# THE SYNTHESIS AND SOME PROPERTIES OF 2,6-DIHYDROXYAZULENE

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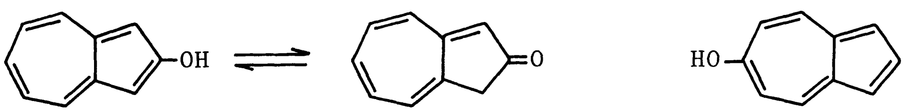
2,6-Dihydroxyazulene (3) is synthesized and it is shown that 3 exists in the solvent-dependent keto-enol tautomerism: thus, in acetone or DMSO 3 exists in the enol-type of 2,6-dihydroxyazulene (3a), whereas in chloroform 3 exists in the diketone-type of 1,3-dihydroazulene-2,6-dione [4,5-(2-oxotrimethylene)tropone] (3b).

There is considerable interest in the keto-enol tautomerism on hydroxyazulenes and such a phenomenon is known about some monohydroxyazulenes. As described in our previous paper,[1] it has been shown that 2-hydroxyazulene (1) exists in the solvent-dependent, tautomeric mixture of the enol-type of 2-hydroxyazulene (1a) and the keto-type of 2(1H)-azulenone (1b), whereas 6-hydroxyazulene (2) exists in the enol form.[2] Further, it is known that 6-hydroxy-4,8-dimethylazulene exists in the enol form,[3] 3-hydroxyguaiazulene exists only in the keto form,[4] and 2-hydroxyguaiazulene exists in the solvent-dependent, keto-enol tautomeric mixture.[5] However, none of dihydroxy- and polyhydroxyazulenes, for which a number of position isomers would be expected, have been obtained. We now wish to report the synthesis of 2,6-dihydroxyazulene (3) together with some of its chemical and physical properties.




1a 1b 2

Diethyl 2,6-dihydroxyazulene-1,3-dicarboxylate (4),[6] prepared from diethyl 2-diazo-6(2H)-oxoazulene-1,3-dicarboxylate[7] by photochemical decomposition in acetic acid, was used as the starting material for synthesizing 3. Deethoxycarbonylation of 4 took place upon heating with 48% hydrobromic acid or 100% phosphoric acid, giving a mixture of 2,6-dihydroxyazulene, 3, and some other deethoxycarbonylation products. Although the isolation of 3 from the mixture was difficult as such, it was accomplished by chromatography (silica gel; benzene) after acetylation, thus affording 2,6-diacetoxyazulene (5) [violet needles, mp 142-143°C], ethyl 2,6-diacetoxyazulene-1-carboxylate (6a) [red needles, mp 136-137°C], ethyl 6-acetoxy-2-hydroxyazulene-1-carboxylate (6b) [orange needles, mp 102-103°C], 6-acetoxy-2-ethoxyazulene (7) [red scales, mp 151-152°C], and the 1,2'-biazulenyl derivative (8) [yellowish green needles, mp 145-146°C].[8] The yields of the products varied with the reaction conditions (Table 1); thus the desired compound, 5, was isolated in a maximal yield of 57%.

Table 1. Deethoxycarbonylation of 4 by treatment with hydrobromic acid or phosphoric acid

| Reaction Condition | | | Yield of Product[a] (%) | | | | |
|---|---|---|---|---|---|---|---|
| Reagent | Temp. (°C) | Time (min.) | 5 | 6a | 6b | 7 | 8 |
| 48% HBr-HOAc | 100 | 15 | 18 | 12 | 31 | - | - |
| 48% HBr-HOAc | 100 | 60 | 57 | - | - | - | 17 |
| 100% $H_3PO_4$ | 100 | 60 | trace | 36 | 19 | 21 | - |

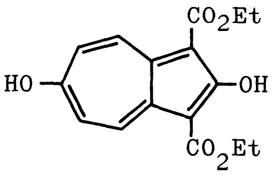
a) The products were isolated by chromatography after acetylation.

The parent 2,6-dihydroxyazulene, 3, was obtained as reddish orange needles, mp blackened at about 175-185°C, in a 92% yield by treatment of 5 with 100% phosphoric acid at room temperature for 2 hr, followed by dilution with water and extraction with ethyl acetate. The compound, 3, is not so stable that it is gradually converted into a slightly soluble, brown substance at room temperature. The compound, 3, gave 2,6-diacetoxyazulene, 5, by acetylation with acetic anhydride and gave 2,6-dimethoxyazulene (9) [red scales, mp 159-160°C] by methylation with diazomethane in ethyl acetate.

The uv and nmr spectra of 3 vary with the different kinds of solvents (Fig. 1 and Table 2). The uv spectrum of 3 in dimethyl sulfoxide shows a curve typical of azulene; however, the uv spectrum in chloroform is quite different from that in dimethyl sulfoxide and similar to that of tropone. Further, the nmr spectrum of 3 in acetone-$d_6$ shows a pattern similar to that of 2,6-dimethoxyazulene, 9, in $CDCl_3$; however, the spectrum of 3 in $CDCl_3$ reveals a singlet at $\delta$ 3.54 ppm, which gradually disappears on addition of $D_2O$, and a pair of AB type doublets at $\delta$ 6.99 and

7.10 ppm (J=12.5 Hz), corresponding to the methylene and the tropone ring protons, respectively. These findings indicate the existence of the solvent-dependent, keto-enol tautomerism in 3: thus, in acetone or dimethyl sulfoxide 3 exists in the enol-type of 2,6-dihydroxyazulene (3a), whereas in chloroform 3 exists in the diketone-type of 1,3-dihydroazulene-2,6-dione [4,5-(2-oxotrimethylene)tropone] (3b). The ir spectrum also supports that in chloroform 3 exists in the diketone form, 3b (Table 2).

The 1,2'-biazulenyl derivative, 8, which is obtained from 4 upon heating with hydrobromic acid followed by acetylation, is assumed to be formed by the acid-catalyzed condensation of two molecules of the resulting 3, namely 3b, and this is confirmed by the fact that the same compound, 8, is obtained from 3 upon heating with hydrobromic acid, followed by acetylation.

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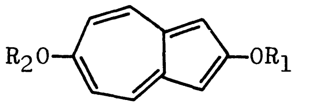
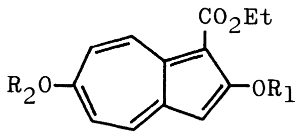



5: $R_1=R_2=COCH_3$

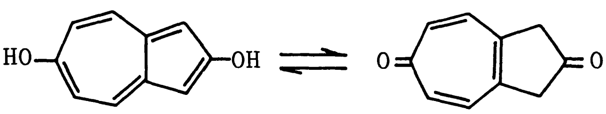
7: $R_1=C_2H_5$; $R_2=COCH_3$

9: $R_1=R_2=CH_3$




6a: $R_1=R_2=COCH_3$

6b: $R_1=H$; $R_2=COCH_3$




3a 3b

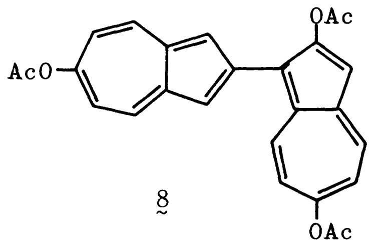



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Table 2. The spectral data of 2,6-dihydroxyazulene, 3

ir: $\nu_{max}$(KBr) 3200~2500 (broad), 1762 (w), 1740 (w), 1640 (m), 1600 (s), 1580 (s), 1500~1460 (broad, vs), 1430~1390 (broad, vs), 1325 (s), 1240 (vs), 1155 (s), 1065 (s), 880 (m), 750 (m), and 688 (s) $cm^{-1}$.

$\nu_{max}$($CHCl_3$) 1766 (s, C=O), 1627 (s, tropone), and 1572 (s, tropone) $cm^{-1}$.

uv: $\lambda_{max}$(DMSO) 298 nm (log ε 4.83), 337 (3.95), 374 (3.77), 391 (3.82), and 454 (3.08).

$\lambda_{max}$($CHCl_3$) 315 nm (log ε 4.10) and 322 (4.10).

nmr: δ (acetone-$d_6$) 6.67 (s, 2H, H-1,3), 6.86 (d, J=11.0 Hz, 2H, H-5,7), 7.87 (d, J=11.0 Hz, 2H, H-4,8), and 8.97 (bs, 2H, OH) ppm [60 MHz].

δ ($CDCl_3$) 3.54 (s, 4H, H-1,1,3,3), 6.99 (d, J=12.5 Hz, 2H, H-4,8 or 5,7), and 7.10 (d, J=12.5 Hz, 2H, H-4,8 or 5,7) ppm [100 MHz].

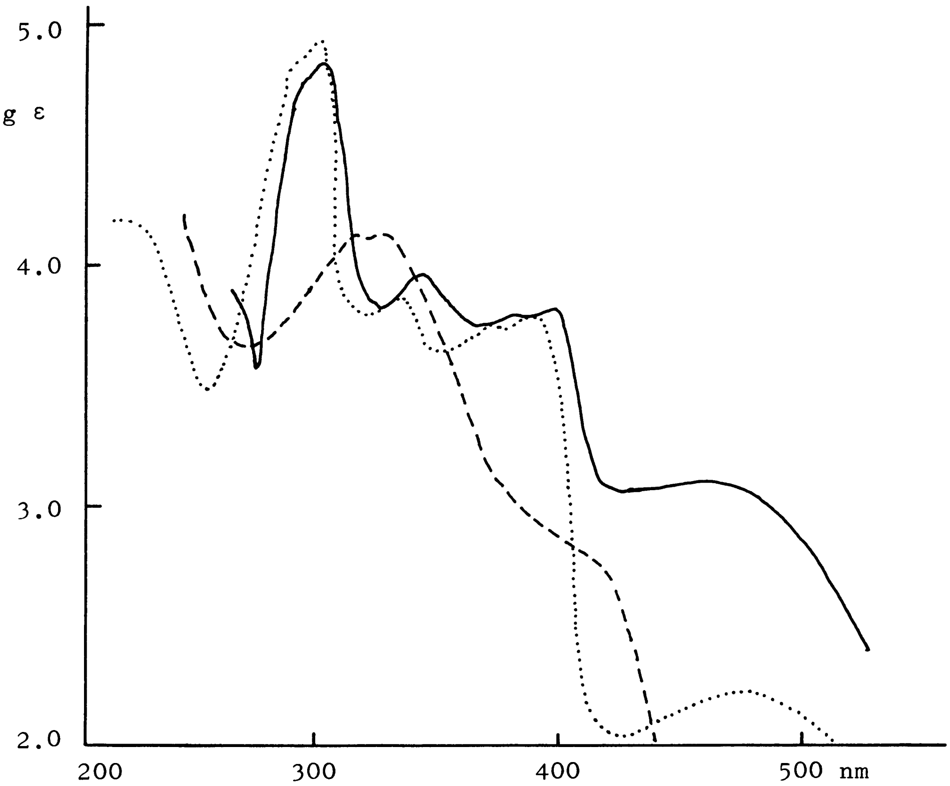


Fig.1. The uv spectra of 2,6-dihydroxyazulene (3) in dimethyl sulfoxide ( ———— ) and in chloroform ( ---------- ), and 2,6-dimethoxyazulene (9) in methanol ( ·········· ).

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REFERENCES AND NOTES

* To whom correspondence should be addressed.


1) K. Takase, T. Asao, Y. Takagi, and T. Nozoe, J. Chem. Soc., Chem. Commun., 1968, 368.

2) Reexamination of the nmr spectra of 6-hydroxyazulene (2) shows that in acetone-$d_6$ it exists only in the enol-type of 2, whereas in $CDCl_3$ it exists in the tautomeric mixture (2.2 : 1) of the enol-type of 2 and the keto-type of 6(1H)-azulenone [δ 3.57 (bs, $C\underline{H}_2$) ppm].

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