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SYNTHESIS OF METHYL 1,5- AND 1,7-AZULENEQUINONE-3-CARBOXYLATES

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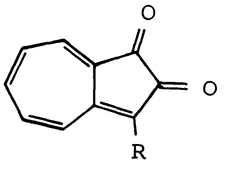
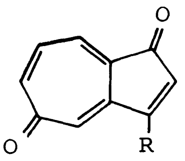
Methyl 1,5- and 1,7-azulenequinone-3-carboxylates were synthesized by oxidation of methyl 3-acetoxy-7-methoxy- and 3-acetoxy-5-methoxyazulene-1-carboxylates with ceric ammonium nitrate, respectively.

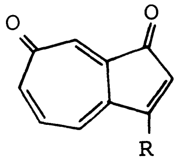
Although the chemistry of quinone(1) and azulenes(2) has a long and colorful history and several reports of highly annelated azulenequinones have appeared,(3) no simple azulenequinone, one of the non-benzenoid quinones, had been known until we reported the synthesis of 1,2-azulenequinones (1).(4) Non-annelated 2,6-azulenequinone derivatives(5) have been synthesized but isolated only in a form of dimer. Recently, a theoretical prognosis of azulenequinones has been reported.(6) We now report the synthesis of 1,5- (2b) and 1,7-azulenequinone derivatives (3b) as the first example of simple extended azulenequinones.



1a: R=H
1b: R=CO_2Et
1c: R=CN



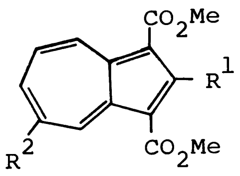
2a: R=H
2b: R=CO_2Me



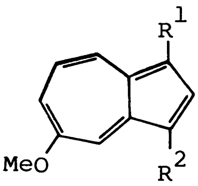
3a: R=H
3b: R=CO_2Me

A 5-chloroazulene derivative (4) was synthesized by application of the azulene synthesis reaction(7) of troponoid with an active methylene compound in the presence of base. The reaction of 5-chloro-2-tosyloxytropone(8) with methyl cyanoacetate in the presence of MeONa in anhydrous MeOH led to 4 [orange, mp 176-177.5 °C] in 80% yield. Smooth deamination of 4 to dimethyl 5-chloroazulene-1,3-dicarboxylate (5) [red, mp 185.5-186 °C] was achieved in 90% yield by diazotization with isopentyl nitrite and sulfuric acid in the presence of hydroquinone.(7a,9)

Methoxylation of 5 succeeded by a modification of the reaction of 6-haloazulenes[10] with nucleophilic reagents. Heating of 5 with NaOMe-MeOH in anhydrous benzene gave a 5-methoxyazulene derivative (6) [red, mp 195-197 °C] in 90% yield. Half demethoxycarbonylation[11a] of the diester 6 with 100% phosphoric acid[7,11] (90 °C, 10 m) nicely gave a mixture (1:1) of the monoesters, methyl 5- (7) [green, mp 66.5-67 °C] and 7-methoxyazulene-1-carboxylates (8) [green, mp 65.5-66 °C] in 70% yield which could be separated by a column chromatography (silica gel, benzene). To date only benzoyloxylation[3,9b,12] of azulenes with benzoyl peroxide has been known as a method for direct acyloxylation of azulenes, but, sometimes, the yield was low. Therefore, lead tetraacetate (LTA) was employed herein as an acetoxylation reagent. Treatment of 8 with 3 eq. of LTA in PhH-pyridine-DMSO afforded methyl 3-acetoxy-7-methoxyazulene-1-carboxylate (9) [green, mp 129-130 °C] in 75% yield. In a like fashion, acetoxylation of 7 led to methyl 3-acetoxy-5-methoxyazulene-1-carboxylate (10) [green, mp 133-134 °C] in 60% yield.



4: $R^1=NH_2$, $R^2=Cl$
5: $R^1=H$, $R^2=Cl$
6: $R^1=H$, $R^2=OMe$



7: $R^1=CO_2Me$, $R^2=H$
8: $R^1=H$, $R^2=CO_2Me$
9: $R^1=OAc$, $R^2=CO_2Me$
10: $R^1=CO_2Me$, $R^2=OAc$

Structural assignment of all the intermediates and detail of the reaction sequence will be discussed elsewhere. Finally, direct oxidation of dihydroxyazulene derivatives 9 and 10 with ceric ammonium nitrate[13] gave methyl 1,5- (2b) [yellow needles, mp 141-142 °C (dec)] and 1,7-azulenequinone-3-carboxylates (3b) [yellow needles, mp 137-138 °C (dec)], in 71 and 73% yields, respectively. The individual structural assignment rests on the spectral data (IR, UV, MS, and NMR) and the following chemical evidence. Reductive acetylation of 2b and 3b with Zn-AcOH-Ac_2O afforded methyl 3,7- (11) [green, mp 126-128 °C] and 3,5-diacetoxyazulene-1-carboxylates (12) [green, mp 136-137 °C] in 25 and 40% yields, respectively. The mass spectra of 2b and 3b show the corresponding molecular ion peak at m/e 216.[14] The IR spectra of these quinones show three main bands in the carbonyl region [2b (KBr): 1725sh, 1711, 1648, and 1590 cm^{-1}; 3b (KBr): 1724sh, 1711, 1641, and 1590 cm^{-1}] due to the characteristic absorption of tropone[15] and the unsaturated 5-membered cyclic ketone with methoxycarbonyl group. The electronic spectra (Fig. 1) of quinones (2b and 3b) have three absorption bands in the region of 220

Table 1. ^{1}H-NMR Data of 2b, 3b, 11, and 12 (at 200 MHz, in $CDCl_3$, chemical shift in δppm from TMS)

compound	ring protons[a]						others	
	H-2	H-4	H-5	H-6	H-7	H-8	CO_2CH_3	$OCOCH_3$
2b	7.09	7.81		7.03	7.19	7.43	3.98	
3b	7.02	7.83	7.20	6.95		7.35	3.99	
11	8.24	9.41		7.53	7.27	8.29	3.92	2.38 and 2.43
12	8.32	9.58	7.51	7.46		8.10	3.93	2.38 and 2.42

a) The numbering of 11 and 12 corresponds to those of 2b and 3b, respectively.

Table 2. ^{13}C-NMR Data[16)] of 2b and 3b (at 50.3 MHz, in $CDCl_3$, chemical shift in δppm from TMS)

compound	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_{3a}	C_{8a}
2b	192.2	138.2	152.2	134.7	187.2	144.6	134.1	130.1	142.2	136.1
3b	193.6	135.5	152.7	128.6	135.9	140.8	187.6	135.0	140.5	136.6

Table 3. Half-wave Potentials of 2b, 3b, and 1b (V vs SCE)

	E_1	E_2
2b	-0.54	
3b	-0.50	
1b[a)]	-0.40	-1.00

a) Ref. 4).

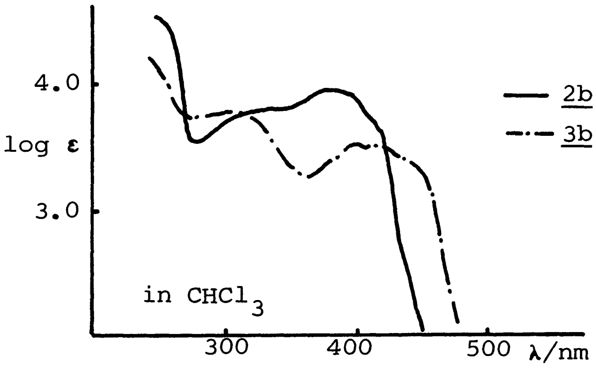


Fig. 1. UV spectra of 2b and 3b.

—500 nm. The colors of these quinones are due to the long-wavelength absorptions (2b: 372, 390, and 414sh nm; 3b: 376sh, 403, and 423 nm in chloroform).

In the ^{1}H-NMR spectra (Table 1) of 2b and 3b, the ring protons appear upper field than those of the corresponding dihydroxyazulene derivatives (11 and 12) and the chemical shifts of H-6 and H-7 of 2b (H-6 and H-5 for 3b) are similar to those of H-2 (δ 6.93) and H-3 (δ 7.31) of tropone.[17)] In the ^{13}C-NMR data (Table 2), the order of the average shifts[18)] (149.1 for 2b; 148.6 for 3b) of the ring carbons agree with those of the polarographic half-wave potentials[19)] (Table 3) which were determined in an anhydrous MeCN (at 25 °C, dropping-mercury electrode to SCE, supporting electrolyte 0.1 M NEt_4ClO_4). These potentials (E_1) parallel with the decreasing order of the LUMO energies[6)] of the corresponding parent azulenequinones (-0.63, -0.66, and -0.70 eV for 2a, 3a, and 1a, respectively).

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19) We thank Dr. Y. Kato of Tohoku Univ. for the measurement of polarographic data.

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