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THE NOVEL OXIDATION OF 1-ALKYLAZULENES TO 1-ACYLAZULENES WITH DDQ

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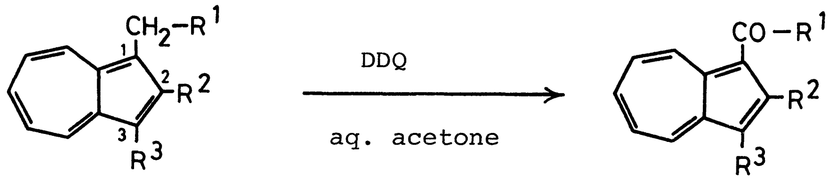
The α-methylene group of 1-alkylazulene side-chain is readily oxidized to carbonyl by treatment with DDQ in aq. acetone or dioxane. The reaction provides a convenient method for the conversion of 1-alkylazulenes (1) into 1-acylazulenes (2).

Since the azulene nucleus is sensitive to oxidation reagents, such as chromic acid, nitric acid, and permanganate,$^{1)}$ the conversion of alkyl side-chain in azulenes into functional group by oxidation is very difficult, thus little is known about examples of such a conversion by direct oxidation, except that guaiazulene yields a small amount of 1-formyl- and 1-carboxy-7-isopropyl-4-methylazulene on treatment with selenium dioxide or potassium permanganate.$^{1,2)}$ We now report that the α-methylene group of alkyl side-chain at C-1 of azulenes is readily oxidized to carbonyl by treatment with DDQ in aq. acetone or dioxane, thus providing a convenient method for the conversion of 1-alkylazulenes (1) into 1-acylazulenes (2).

When a solution of 1,2-tetramethylenazulene (1a)$^{3)}$ (364 mg, 2 mmol) in acetone (50 ml) containing 10% of water was treated with DDQ (998 mg, 4.4 mmol) at room temperature, the initial blue solution soon became red in color. After being stirred for 5 min., the solution was passed through a short column of alumina to remove the resulting hydroquinone, diluted with water, and extracted with benzene. The extract was purified by column chromatography (alumina; benzene) to give 1,2-(1-oxotetramethylen)azulene (2a)$^{4)}$ in 97% yield. In a similar manner, some 1,2-polymethylenazulenes (1b-1j) and 1-alkylazulenes (1k-1n)$^{3)}$ were oxidized to the corresponding 1-acylazulenes (2b-2n)$^{4)}$ in respective excellent yields (Table 1). Similar results were also obtained by use of aq. dioxane instead of aq. acetone as the solvent. The results show that the α-methylene group of alkyl side-chain at C-1 of azulenes is readily oxidized with DDQ to carbonyl although the oxidation is retarded or does not proceed in the case of 1-alkylazulenes (1i, 1j, and 1p) which possess an electron-withdrawing trifluoroacetyl or nitro substituent at C-3. In contrast, the alkyl side-chain at C-2 of azulenes was not oxidized with DDQ under the same conditions.



(1) (2)

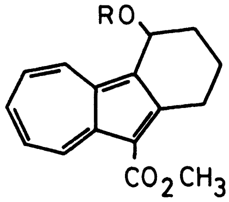
Table 1. The oxidation of 1-alkylazulenes (1) to 1-acylazulenes (2) with DDQ in aq. acetone at room temperature

Alkylazulene (1)				Reaction time (min.)	Product (2)				
	R^1	R^2	R^3			Crystal form[a)]	Mp (°C)	Yield (%)	$\nu_{C=O}$ cm^{-1}
1a	$-(CH_2)_3-$		H	5	2a	rvn	96-97	97	1630
1b	$-(CH_2)_4-$		H	5	2b	vp	69-70	93	1630
1c	$-(CH_2)_5-$		H	5	2c	vp	61-62	92	1614
1d	$-(CH_2)_2-$		CO_2CH_3	10	2d	ron	200-201	86	1672, 1694
1e	$-(CH_2)_3-$		CO_2CH_3	15	2e	rn	145-146	98	1640, 1682
1f	$-(CH_2)_4-$		CO_2CH_3	30	2f	rn	82-83	91	1638, 1688
1g	$-(CH_2)_5-$		CO_2CH_3	45	2g	rvn	85-86	93	1625, 1700
1h	$-(CH_2)_3-$		CN	30	2h	rn	152-153	93	1645
1i	$-(CH_2)_3-$		$COCF_3$	150	2i	ron	127-128	87	1645, 1660
1j	$-(CH_2)_4-$		NO_2	1680	2j	ron	123-124	80	1650
1k	CH_3	H	H	5	2k	rv	oil[6)]	59	1635
1m	CH_3	H	CO_2CH_3	15	2m	rvn	120-121	89	1648, 1700
1n	H	C_2H_5	CO_2CH_3	10	2n	rp	111-112	90	1644, 1695
1p	H	C_2H_5	$COCF_3$	-[b)]					

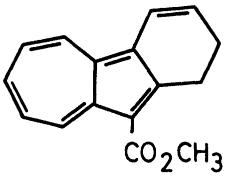
a) vp: violet prisms, rvn: reddish violet needles, rn: red needles, ron: reddish orange needles, rv: reddish violet, rp: red prisms.

b) No reaction under reflux.

When treated with 1.2 molar equivalent of DDQ in aq. acetone at room temperature, 1e gave an alcohol (3) [violet needles, mp 141-142°C, IR (KBr): ν_{OH} 3480 cm^{-1}] in 9% as well as 2e (55%) and 1e (32%). The alcohol, 3, gave 2e in a quantitative yield on treatment with DDQ. These facts suggest that 3 should be an intermetiate in the oxidation of the methylene group of 1e to carbonyl with DDQ. Further, 1e, when treated with DDQ in dioxane containing methanol, gave a mixture of three products, from which were isolated methyl 1,2-dihydrobenz[a]azulene-10-carboxylate (4) [dark green scales, mp 85-86°C] and methyl 4-methoxybenz[a]azulene-10-carboxylate (5) [dark green prisms, mp 105-106°C] by column chromatography (alumina; benzene). The third product was assumed to be a methoxyl derivative (6) by an nmr examination, although it could not be isolated because of its instability to be changed into 4 upon chromatography. A similar treatment of 1f with DDQ in dioxane-methanol yielded a didehydro compound (7) [blue oil] and a methoxyl derivative (8) [violet oil] in respective 32 and 39% yields.



(3): R=H
(6): R=CH_3



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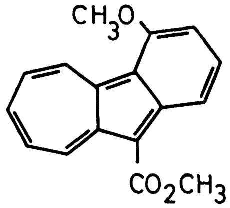

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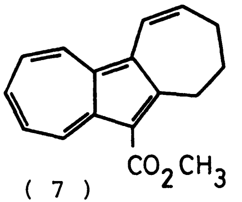

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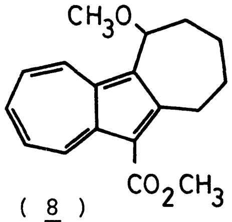

(8)

On the basis of the above-mentioned findings, the oxidation of 1-alkylazulenes (1) with DDQ is explained by a reaction mechanism involving a cationic (A) and a hydroxylic intermediate (B) (Chart 1). The hydride ion is abstracted with DDQ from the α-methylene of alkyl side-chain at C-1 of 1 to give the cation (A); the hydride abstraction is facilitated by delocalization of charge in the resulting cation (A), attributable to a large contribution of a resonance form of 1-alkylidenazulenium ion (A'). The existence of the cation (A) is supported by the fact that the cation of such a type is known to be formed from 1-(1-hydroxyalkyl)azulenes under an acidic condition.7) The presence of a strongly electron-withdrawing substituent at C-3 of 1 affects to depress delocalization of charge in the cation (A), so nitro and trifluoroacetyl derivatives (1i, 1j, and 1p) resist to oxidation with DDQ. In aq. acetone or dioxane the nucleophilic addition of water to the cation (A) yields the alcohol (B), which is further oxidized with DDQ to 1-acylazulenes (2). On the other hand, in dioxane-methanol the cation (A) affords the didehydro compounds (4 and 7) by deprotonation and the methoxyl derivatives (6 and 8) by nucleophilic addition of methanol, respectively. The failure of 2-alkylazulenes to undergo oxidation with DDQ is probably due to the reason that extensive delocalization of charge is precluded in the cation (C) which would be formed by abstraction of hydride ion from the α-methylene of alkyl side-chain at C-2, because of a lack of alkylidenazulenium ion-type resonance contribution.

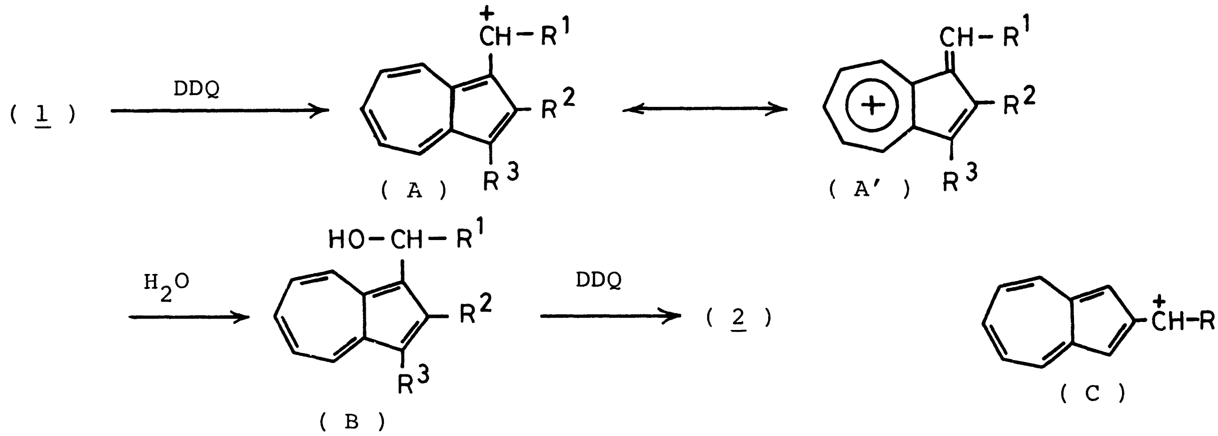

Chart 1. The reaction mechanism for the oxidation of 1-alkylazulenes (1) to 1-acylazulenes (2) with DDQ

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REFERENCES AND NOTES

* To whom correspondence should be addressed.
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