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A Photochemical Synthesis of 1,2,3,4,5,6-Hexahydro-1-benzazocine-2,6-diones from 4-Hydroxy-2-quinolones[1]

Irradiation of 4-hydroxy-2-quinolones (IVa and IVb) and their enolates in the presence of olefins provided intermolecular 2+2 addition products (V, VII, and VIII). The cycloaddition reactions were shown to be regioselective giving in all cases 1-substituted 1,2,2*a*,8*b*-tetrahydrocyclobuta[*c*]quinolin-3(4H)-ones. Base catalyzed retro aldol reaction of these cycloadducts afforded 1,2,3,4,5,6-hexahydro-1-benzazocine-2,6-diones (VI).

Keywords——photochemical synthesis; photochemical 2+2 cycloaddition; 8*b*-hydroxy-1,2,2*a*,8*b*-tetrahydrocyclobuta[*c*]quinolin-3(4H)-one; 1-benzazocine-2,6-diones; retro aldol reaction; 4-hydroxy-3-methyl-2-quinolone; regioselective cycloaddition reaction

In the previous paper of this series,[2] we reported that irradiation of 4-alkoxy-2-quinolones (I) produced intermolecular 2+2 cycloadducts (II) and their transformation to 1,2-dihydrocyclobuta[*c*]quinolin-3(4H)-ones (III) by base treatment. Replacement of the alkoxy function in II with hydroxyl group, if realized, would yield azocine derivatives by retro aldol reaction. Thus, it was of interest to investigate the photochemistry of 4-hydroxy-2-quinolones in the presence of olefins in order to obtain the 2+2 cycloadducts and examine their retro aldol reactions. The experiments along this line has led us to find a general synthetic route to 1,2,-3,4,5,6-hexahydro-1-benzazocine-2,6-diones.

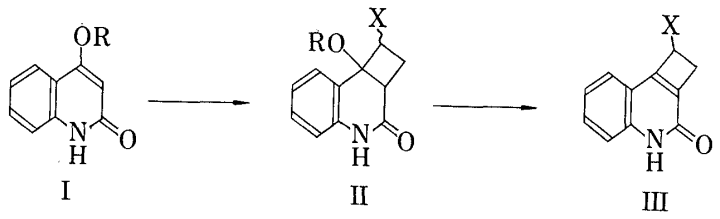


Chart 1

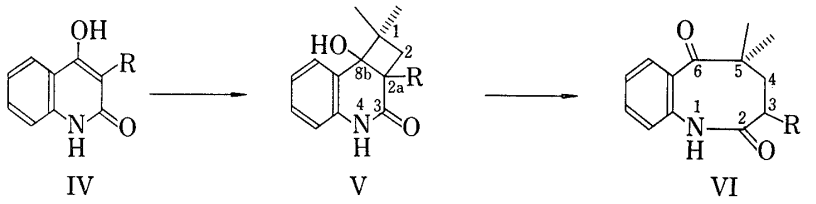
Photolysis[3] of 1.5×10^{-2} M solution of 4-hydroxy-2-quinolone (IVa) in methanol containing 1/40 volume of 30% aq. trimethylamine[4] under bubbling of isobutene yielded a cycloadduct (Va, mp 185—185.5°) and a crystalline product (X: $C_{14}H_{15}NO_2$, mp 173—174°) having an exocyclic methylene group (δ in $CDCl_3$: 5.18 d and 5.72 d; each 1H with J=1.5 Hz) in the respective yields of 60 and 6%. The structure of Va was established on the basis of combustion analysis, UV spectrum [λ_{max}^{MeOH} nm (log ε): 211 (4.42), 250.5 (4.00), 282 (3.82), and 292 sh (3.30)] which is almost the same with those of II, and finally of its PMR spectrum. Thus, the 2*a*-proton appeared as doublets of doublet (δ in $CDCl_3$: 3.64, J=11 and 9 Hz) indicating the head-to-tail structure. Refluxing of Va in methanol containing 0.1% sodium bicarbonate afforded 5,5-

1) Part IV of "Cycloadditions in Syntheses." Part III: C. Kaneko, T. Naito, and M. Ito, *Tetrahedron Lett.*, **21**, 1645 (1980).
2) C. Kaneko and T. Naito, *Chem. Pharm. Bull.*, **27**, 2254 (1979).
3) All irradiations were carried out with Toshiba 400P high-pressure mercury lamp using a Pyrex filter (λ=*ca.*$\geq$300 nm).
4) 4-Hydroxy-2-quinolone (IVa) is practically insoluble, but its enolate was found to be considerably soluble to methanol. This finding has made it possible to use IVa as a suitable starting material for the preparative photochemical experiments. Both species showed strong absorptions above 300 nm: λ_{max}^{MeOH} nm (log ε); 269 (3.86), 279 (3.85), 313 (3.76), 325 sh (3.63); the enolate (MeOH–Me_3N): 294.5 (3.92).

dimethyl-1,2,3,4,5,6-hexahydro-1-benzazocine-2,6-dione (VIa, mp 212—214°) in a quantitative yield.

Contrary to low solubility of IVa in methanol, 4-hydroxy-3-methyl-2-quinolone (IVb)[5] is soluble and hence the corresponding adduct (Vb, mp 167—167.5°) was obtained in 95% yield by irradiation in methanol as a sole product. Treatment of Vb with base as above afforded the azocine (VIb, mp 182—183°) in 89% yield. The PMR spectrum of VIb showed the presence of $CH_aH_bCH_xCH_3$ function (δ: H_a; 1.44 dd, H_b; 1.85 dd, and H_x; 2.71 ddq, with $J_{ab}=14$, $J_{ax(trans)}=9.5$, $J_{bx(cis)}=3$, and $J_{xCH_3}=6.5$ Hz) and thus, confirmed the head-to-tail structure for Vb.

In the same manner, the 2+2 cycloadducts (VIIc, d and VIIIc, d) were obtained from the reactions of IVb with mono-substituted olefins and the results are summarized in Table I.



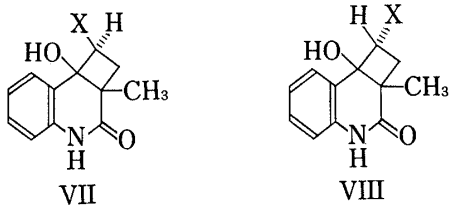
IV→VI	R
a	H
b	CH_3

Chart 2

Table I. Melting Points and Yields of VII and VIII

	VII		VIII	
c	*ca.* 265°[a]	(34%)	*ca.* 265°[a]	(52%)
d	229—230°	(48%)	271—272°	(46%)
e	105°[b]		210—211°	

a) Softened at about 190—200°.
b) Softened at about 95°.



VII, VIII	X
c	CN
d	$OCOCH_3$
e	OH

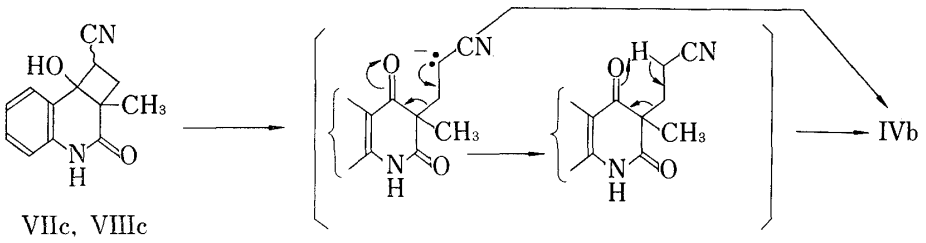
Chart 3

In melting point determination, both of VIIc and VIIIc softened at *ca.* 190—200° and melted at about 265° which was close to the melting point of IVb (mp 270°). It was verified that VIIc and VIIIc afforded IVb in almost quantitative yields by prolonged refluxing in methanol. The presence of acid prevented this reaction, while base accelerated the formation of IVb. These facts suggested that the formation of IVb occurred through 1, 8*b* bond fission followed by elimination of acrylonitrile. Hence, both VIIc and VIIIc are deduced to have

5) R.H. Baker, G.R. Lappin, and B. Riegel, *J. Am. Chem. Soc.*, **68**, 1284 (1946).

head-to-tail structure with different stereochemistry on C_1.[6] Mild hydrolyses of VIId and VIIId (reflux in 0.1% HCl–MeOH) led to isomeric dihydroxy compounds (VIIe and VIIIe) both in almost quantitative yields, both of which afforded 3-formylmethyl-3-methyl-1,2,3,4-tetrahydro-2,4-dioxoquinoline (IX, mp 140—141°) upon treatment with chromic anhydride in pyridine. The structure of IX was established from spectral data as assigned. Thus, the UV spectrum [λ_{max}^{MeOH} nm: 230, 254, 333] resembled closely with the spectrum of 3,3-tetramethylene-2,4-dioxo-1,2,3,4-tetrahydroquinoline[7] and PMR spectrum showed the presence of CH_2CHO function (δ in $CDCl_3$: 3.48 s, 2H, and 9.52 s, 1H).

The structure of X, the by-product of the cycloaddition between IVa and isobutene in methanol in the presence of base, was determined by its conversion to IVb by catalytic hydrogenation. The mechanism for the formation of X is not clear at present.



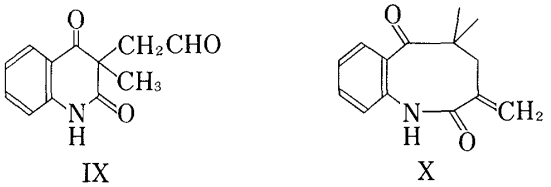


Chart 4

Our further effort will be directed toward possible extension to other ring system as well as modification of the 4-hydroxyfunction of IV in an appropriate way (*e.g.*, trialkylsilyloxy, acetoxy, *etc.*), and particularly investigation of the reactions of the cycloadducts thereby obtained.

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6) Stereochemistry at the 1-position in each isomer was determined by PMR spectroscopy. The signal of the *endo* proton appeared at the higher field than that of the *exo* proton due to the shielding of the benzene ring, *e.g.*, δ ($CDCl_3$): H_1 of VIIc; 3.43 and H_1 of VIIIc; 3.70.

7) C. Kaneko, I. Yokoe, S. Yamada, and M. Ishikawa, *Chem. Pharm. Bull.*, **17**, 1290 (1969).