

## A SIMPLE PHOTOSYNTHESIS OF PYRROLOINDOLOQUINONES

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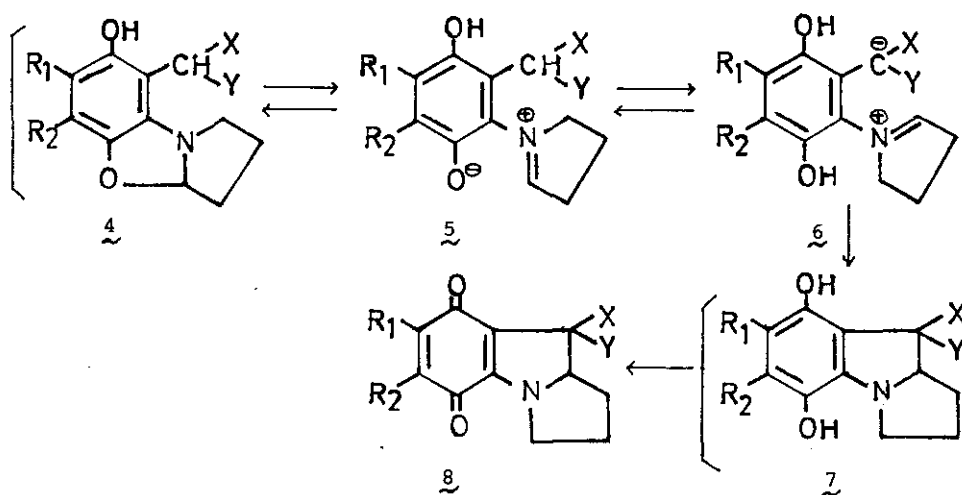
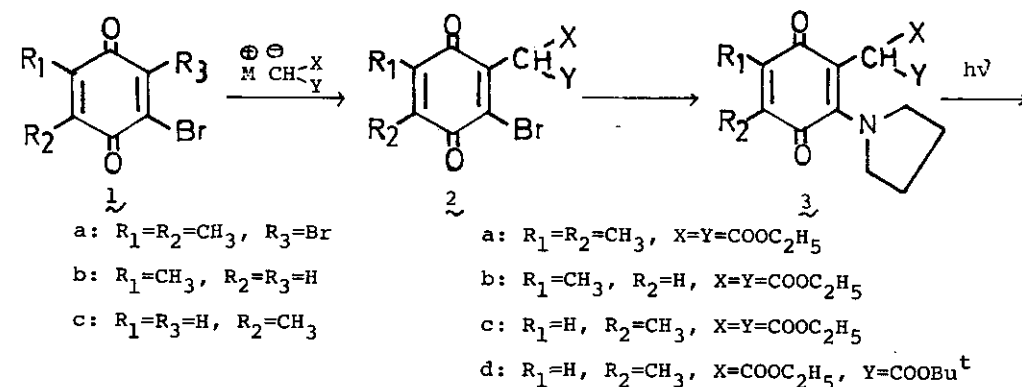
Abstract --- The improved photoreaction of pyrrolidino-1,4-benzoquinones having the active methylene groups afforded a simple and preparative route to the synthesis of pyrroloindoloquinones, which were the mother framework of mitomycins.

The pyrroloindoloquinone<sup>1</sup> has the basic structure of mitomycins and very important for their biological activities<sup>2</sup>. Recently we have reported that the photolysis of amino-1,4-naphthoquinones having the active methylene groups at the 2-position provided a preparative route to the heterocyclic quinones<sup>3</sup>. In this paper we wish to describe the improvement and application of this photo-induced reaction to newly prepared pyrrolidinobenzoquinones for the simple synthesis of pyrroloindoloquinones.

The synthetic process can be represented as shown in Scheme I. The benzoquinone 2a<sup>4</sup> was prepared easily from the substitution reaction of the dibromoquinone 1a with ethyl sodium malonate. However, 2b-d were not obtained from the corresponding quinones 1b-c under the same condition. Since it is possible for the active methylene anion to react with 1b-c at three positions (C<sub>2</sub>, C<sub>3</sub>, and C<sub>5</sub> or C<sub>6</sub>) or four positions (C<sub>2</sub>, C<sub>3</sub>, C<sub>5</sub> or C<sub>6</sub>, and methyl group<sup>5</sup>), the reaction resulted in an intractable mixture. Using the thallium malonates<sup>6</sup>, the regioselective Michael addition of these to 1b-c followed by oxidation gave the corresponding quinones 2b-d in moderate yields. On treatment with 2 equimolar amounts of pyrrolidine in chloroform, 2b-d afforded the corresponding aminoquinones 3b-d in good yields, respectively. The structures of 2 and 3, oily products, were confirmed by the analytical and spectroscopic data (IR, NMR, and MS).

The photo-induced reaction of pyrrolidinoquinones 3 was carried out as follows. A solution of 3a-c in ethanol was irradiated with a high pressure mercury lamp

through Pyrex glass. After allowing the irradiated solution 3a-c to stand for more than 3 days at room temperature, the pyrroloindoloquinones 8a-c were obtained in 47-51% yields (Method A). Secondly, an attempt to increase the yield of 8 was examined under the mild condition. The irradiated solution of 3a-c in ethanol was retained on a silica gel column for a few days, and then eluted with ethyl acetate to give 8a-c in 60-68% yields (Method B). The similar photolysis of 3d afforded the stereoisomers, 8d-(i) and 8d-(ii), due to the different substituents in a ratio of 5 : 4 after chromatography on silica gel. The stereochemistry of these isomers has not been clarified yet. The structural assignments for 8a-d were based on their analytical and spectral properties, which were in good agreement with their formulations. The results are summarized in Table I.



Scheme I

Table I. Photoreaction of Pyrrolidinoquinones 3

Compound $\underline{g}^a$	Mp ( $^{\circ}$ C)	Yield (%)		IR $\nu$ $\text{cm}^{-1}$		NMR $\delta$ ( $\text{CDCl}_3$ ) ppm		Mass $M^+$ (m/z)
		Method A	Method B	ester	C=O	bridgehead	CH <sup>b</sup>	
a	137	49	65	1740,	1715	4.81		361
b	86-88	47	60	1745,	1730	4.80		347
c	90-91	51	68	1740,	1718	4.70		347
d-(i)	109	--	34	1740,	1717	4.71		375
d-(ii)	oil	--	27	1740,	1718	4.72		375

a Recrystallized from hexane

b 1H, double doublet

This photoreaction may proceed through the following sequence: photo-insertion, ring degradation, intramolecular cyclization, and oxidation (4, 5, 6, 7, and 8) as reported previously<sup>3</sup>. Silica gel in this reaction sequence may be considered to act as acid and make promotion of 4 to dissociate to 5 and 6. Although the closure of 6 to 7 is "5-endo-trig"<sup>7</sup>, it also involves a fully conjugated  $6\pi$  electron system and this can also be viewed as a thermally allowed disrotatory electrocyclization of the Woodward-Hoffmann classification  $\pi 6s \rightarrow \pi 4s + 6s$ <sup>8</sup>.

The compounds, 8c and 8d, will be a key intermediate of the mitosene synthesis. Therefore, these conversion to mitosene are being carried out and will be reported elsewhere.

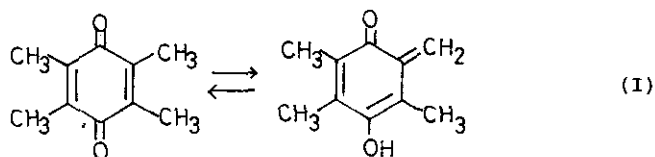
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