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*hedron Lett.*, **28**, 4575 (1987); (b) J. S. Cha, S. Y. Oh, K. W. Lee, M. S. Yoon, J. C. Lee and J. E. Kim, *Bull. Korean Chem. Soc.*, **9**, 48 (1988). (c) J. S. Cha, J. E. Kim, M. S. Yoon and Y. S. Kim, *Tetrahedron Lett.*, **28**, 6231 (1987).

4. Although the role of pyridine in this reduction is not clear, we believe that pyridine behaves as a coordinator to the boron atom of **1** resulted in a borane-pyridine complex which inhibits the hydride attack from LAH to the carbonyl carbon.

## Evidence of Radical Ion Pair for Singlet Oxygen Reaction of Bilirubin and Related Oxopyrromethenes. Oxidation Potential of Bilirubin and Related Oxopyrromethenes

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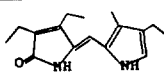
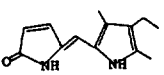
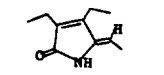
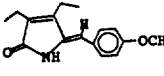
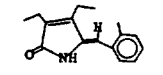
The phototherapy for treating neonatal jaundice is used since the caused bilirubin IX- $\alpha$  (BR) in the human body is destroyed by light illumination<sup>1-3</sup>. BR is destroyed by photo-reaction under aerobic or anaerobic conditions. Photooxygenation of BR in the presence of a sensitizer, rose bengal, gave methylvinyl maleimide, hematinic acid and two propen-dyopents<sup>4-5</sup>. The oxomonopyrromethenes (**6**, **7**, **8**, see table 1) resisted dye-sensitized photooxygenation; whereas oxodipyrrromethenes (**1**, **2**, see Table 1) and mesobilirubin (MBR) reacted with singlet oxygen (<sup>1</sup>O<sub>2</sub>) to give products from cleavage of exocyclic enamide double bonds<sup>6</sup>. Kinetic study showed that highly substituted oxodipyrrromethenes are more reactive toward <sup>1</sup>O<sub>2</sub><sup>6</sup>. Thus radical ion mechanism<sup>6</sup> was suggested for singlet oxygen reaction of BR and BR-related compounds.

In this work singlet oxygen reaction rate (<sup>1</sup>O<sub>2</sub> generated by the thermal method) and oxidation potential of BR and BR-related enamines (mainly oxopyrromethenes) were measured as evidences for radical ion pair mechanism in the singlet oxygen reaction of the enamine derivatives (BR and BR-related substrates).

Khan and Kasha<sup>7</sup> reported that <sup>1</sup>O<sub>2</sub> is generated by reaction of NaOCl with H<sub>2</sub>O<sub>2</sub>. BR and BR-related substrates (1 mg) was dissolved in 5 ml of methanol. The solution (1 ml) was taken in 3 ml UV cuvette and 1 ml of 30% H<sub>2</sub>O<sub>2</sub> and 0.2 ml of NaOCl solution (effective chlorine 10%) were added. The percent change of the absorbance of BR and BR-related substrates were measured within 3 min reaction time. They are summarized in Table 1. MBR, BR and oxodipyrrromethenes (**1,2**) are reactive; whereas BV and oxomonopyrromethenes (**6,7,8**) are unreactive toward <sup>1</sup>O<sub>2</sub> generated chemically. For comparison, K<sub>R</sub> values, reaction rate constant of enamine substrates from ref. 6 was also given in the table. The same reactivity tendency of BR and BR-related substrates is shown for <sup>1</sup>O<sub>2</sub> generated photochemically or thermally.

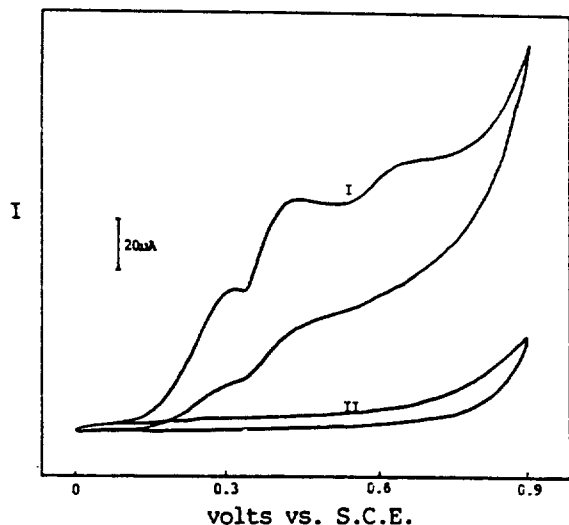
Cyclic voltammograms of BR and BR-related substrates

**Table 1.** Reaction Rate Constants and Percent Absorbance Changes of Bilirubin and Its Model Compounds with <sup>1</sup>O<sub>2</sub> Generated by Photochemical and Thermal Methods, Respectively. Oxidation Potential of Bilirubin and Its Model Compounds

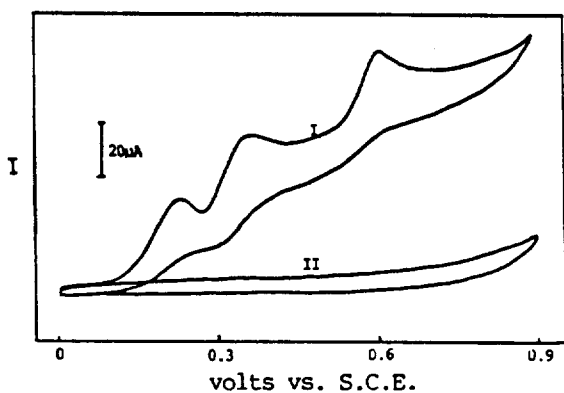
Bilirubin and its model compounds	% change of absorbance in 3 min <sup>b</sup>	K <sub>R</sub> (× 10 <sup>9</sup> M <sup>-1</sup> S <sup>-1</sup> ) <sup>c</sup>	Oxidation potential vs. S.C.E. (volt)
 <b>1</b>	37.2%	1.4 1.0 <sup>a</sup>	0.24
 <b>2</b>	43.9%	0.1	0.32
Mesobilirubin IX-a (MBR) <b>3</b>	60.8%	0.79 <sup>a</sup>	0.24, 0.37 0.60
Bilirubin IX-a (BR) <b>4</b>	33.1% <sup>a</sup>	0.28 <sup>a</sup>	0.32, 0.44 0.64
Biliverdin IX-a (BV) <b>5</b>	0%	0.0024	0.34, 0.60
 <b>6</b>	0%	0	0.80
 <b>7</b>	0%	0	0.98, 1.06
 <b>8</b>	0%	0	1.07, 1.12

<sup>a</sup> With 0.2% vol. conc. NH<sub>4</sub>OH. <sup>b</sup> In methanol. <sup>c</sup> Taken from ref. 6. in methanol.

were measured within 0~+1.2 volt vs. Saturated Calomel Electrode (SCE) with polarographic analyzer and universal



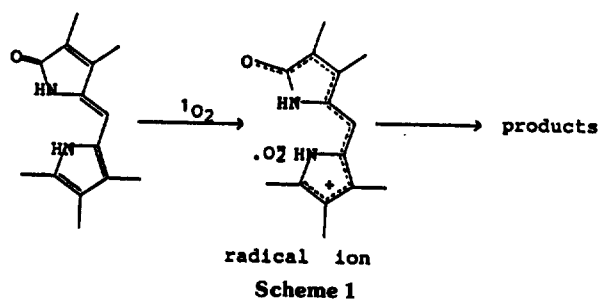
**Figure 1.** The cyclic voltammogram of  $4.5 \times 10^{-4}$ M bilirubin(I) and residual current(II) in 0.1M tetraethylammonium perchlorate in DMF solution at 25 °C. Voltage scan rate; 2 mV/sec.



**Figure 2.** The cyclic voltammogram of  $4.5 \times 10^{-4}$ M meso-bilirubin(I) and residual current(II) in 0.1M tetraethylammonium perchlorate in DMF solution at 25 °C. Voltage scan rate; 2 mV/sec.

programmer as shown in Figure 1 and 2. In Figure 1, the cyclic voltammogram of  $4.5 \times 10^{-4}$ M BR(I) and residual current(II) in 0.1M tetraethylammonium perchlorate (supporting electrolyte) in DMF solution at 25 °C is shown. The oxidation peak potentials of BR, which are 0.32, 0.44 and 0.64 volt vs. SCE respectively could be observed. It is an irreversible wave since no re-reduction wave is shown. These results are different from that of Norman<sup>8</sup> in DMF solvent (0.6 and 0.8 volt vs. SCE), but the same as that of Longhi<sup>9</sup>

(0.35-0.40, 0.58-0.60, and 0.72-0.73 volt vs. SCE). The small differences in the oxidation peak potentials are due to the different working electrode (Glassy Carbon electrode in this work). The cyclic voltammogram of MBR is shown in Figure 2. Three oxidation peaks of MBR (0.24, 0.37, and 0.60 volt vs. SCE) which are lower oxidation potentials than BR were observed in Figure 2. The oxidation potential of BR and BR-related substrates are given in Table 1. The more reactive oxodipyrromethenes (1,2), MBR, and BR toward  $^1\text{O}_2$  have low oxidation potentials. The easier MBR and oxodipyrromethenes are oxidized, the easier cation radicals are formed with  $^1\text{O}_2$  (see Scheme 1). Electron poor enamides (6, 7 and 8) which are unreactive toward  $^1\text{O}_2$  have high oxidation potential. The pyrrolinone moiety of the oxomonopyrromethenes destabilizes the intermediate, cation radical in the  $^1\text{O}_2$  reaction.



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