[Chem. Pharm. Bull. 15(11)1796~1799(1967)]

UDC 615.41-014.4-011:577.16:541.486

231. Shun-ichi Hata, Koji Mizuno, and Suiichi Tomioka*1 : Effects of Electron Donors on the Photodecomposition of Menadione in Aqueous Solution.*2,3 II.*4 Stability of Menadione in Aqueous Solution of Electron Donors.

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The photodecomposition of menadione in aqueous electron donor solutions were studied. As a result of these measurements, it was found that menadione was stabilized in the presence of various electron donors.

Therefore, the relationships between the rate of stabilization and the various constants related to the complex formation which is due to the mutual reaction of electrons between menadione and various electron donors seemed to play an important role in stabilization of menadione.

(Received June 2, 1966)

In a previous paper,*4 it was reported that various electron donors formed molecular complexes with menadione in aqueous systems, and that the resulted menadione complex might suppress the photodecomposition.

It was found that menadione was stabilized with the electron donors used to a certain extents. In this paper, the relationships between the rate of stabilization and various constants related to the complex formation were described.

Experimental

Materials——Menadione and various electron donors used in this paper were the same as described in Part I in this series of study.

Measurement of Stability——Sample solutions were prepared by dissolving a certain amount of menadione and the compound added in phosphate buffer ($N/15$) of pH 7.0, and put them in colorless 5 ml. ampules to test the acceleration experiment. The concentration of menadione and the compound added are indicated in the figure. Substitution with innert gas, such as nitrogen gas, was omitted in this experiment. The acceleration experiment was carried out by the irradiation of two 20 W. fluorescent chemical lamps with the wave length of 360 ± 50 mμ. The sample is placed at a distance of 20 cm. from the light source, and temperature rise of the sample was controlled by circulating cooling water at 20~25°. The quantitative determination of menadione was carried out by ethyl cyanoacetate method.[1]

Results and Discussion

The absorption spectra of menadione after the irradiation in the presence or absence of the complexing agents were shown in Fig. 1. Menadione, without any electron donors, is colored remarkably, while the absorption spectra of menadione with an electron donor are not changed in every case, and so the photodecomposition is thought to be suppressed.

Then the effects of electron donor concentrations on the stability of menadione were examined. The rate of residual menadione at various concentrations of several electron

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*3 A preliminary report of this study has appeared in This Bulletin, **13**, 96 (1965).

*4 Part I : This Bulletin, **15**, 1791 (1967).

1) Shu-yuan Yeh, A. Wiese : Drug Standards, **26**, 22 (1958).

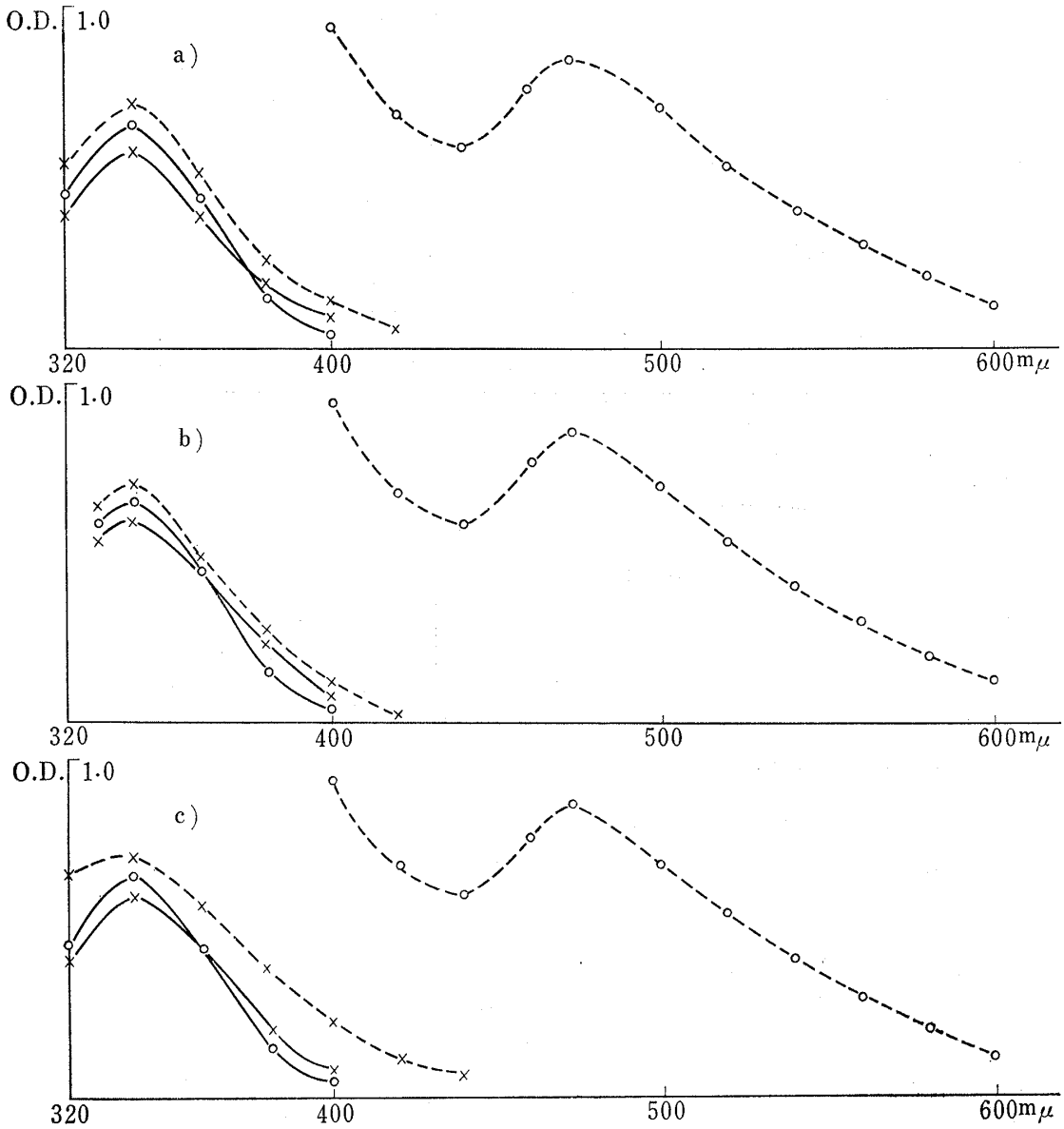

Fig. 1. The Absorption Spectra of Menadione after Irradiation (45 min.) in pH 7.0 Phosphate Buffer
a) Caffeine ($2.06\times10^{-2}M$/L.) b) Salicylic acid (Na salt) ($2.50\times10^{-2}M$/L.) c) Nicotinamide ($3.26\times10^{-1}M$/L.)
——— Before irradiation - - - - - - After irradiation ○ Menadione ($6.97\times10^{-4}M$/L.) × Compound added

donors are shown in Fig. 2. These results show that the stability of menadione increases remarkably as the concentration of electron donor is increased. From the above observations, it is apparent that various electron donors which forms molecular complexes with menadione suppresses the photodecomposition of menadione to a certain extents.

Therefore, the rate of stabilization was compared with the decomposition rate of menadione as shown in Fig. 3. The concentrations of menadione and various electron donors are shown in the figure. It can be considered that the decomposition rate of menadione with and without electron donors may follow to a pseudo-first order, and on this assumption, the rate constant of decomposition and the rate of stabilization were determined as tabulated in Table I. From these results, the relationships between the rate of stabilization and various constants related to the complex formation, as shown in a previous report,*[4] were discussed. The results thus obtained are shown in Fig. 4, 5 and 6. As expected the elevation of the free energy change or the enthalpy change in

Table I. Rate Constant of Decomposition and Rate of Stabilization

Compound added	k (min^{-1})	$\frac{k'-k}{k'} \times 100(\%)$
—	0.004721 (k')	—
β-Hydroxynaphthoic acid	0.001078	77.2
Salicylic acid (Na salt)	0.001336	71.7
Caffeine	0.002198	53.4
Theophylline	0.002016	57.3
Ethyl aminobenzoate	0.001873	60.3
Nicotinamide	0.002599	44.9
Dehydroacetic acid (Na salt)	0.002471	47.7
Theobromine	0.002661	43.6

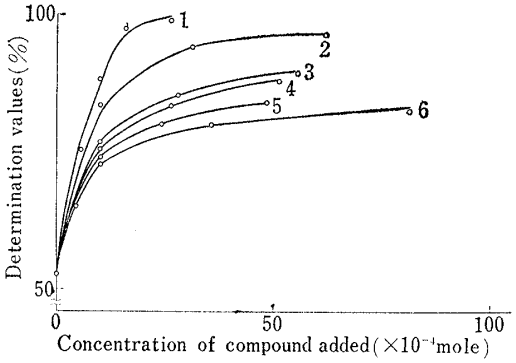

Fig. 2. Effects of Compounds added on the Stability of Menadione ($7.58 \times 10^{-4}M$/L.) in pH 7.0 Phosphate Buffer (Irradiation : 60 min.)

1 : β-Hydroxynaphthoic acid
2 : Salicylic acid (Na salt)
3 : Theophyline
4 : Caffeine
5 : Dehydroacetic acid (Na salt)
6 : Nicotinamide

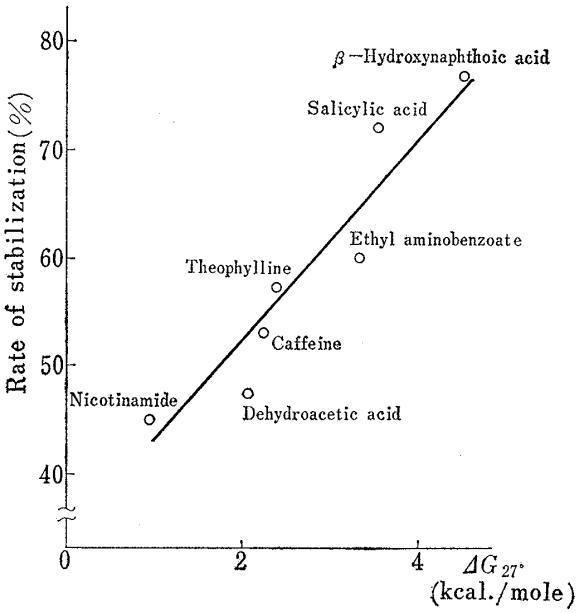

Fig. 4. Relation between Apparent Free Energy Change ($\Delta G_{27}°$) and Rate of Stabilization

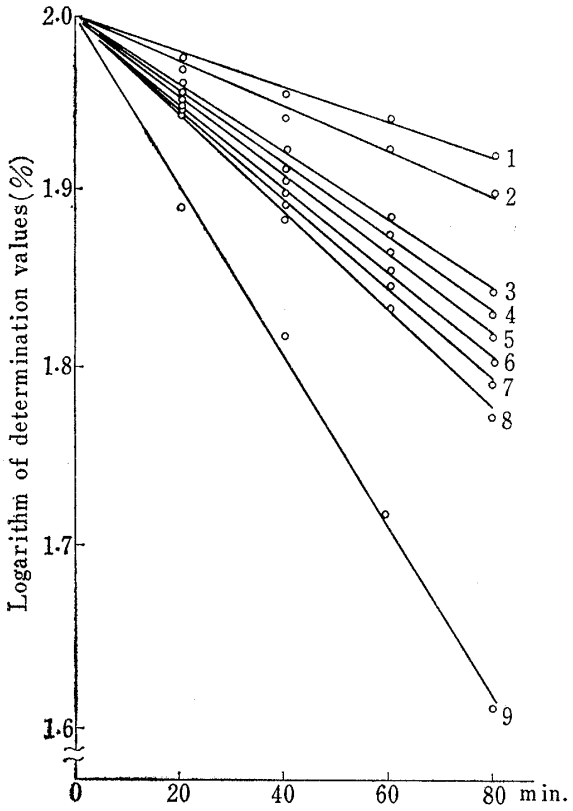

Fig. 3. Decomposition Rate of Menadione ($7.58 \times 10^{-4}M$/L.) when Various Compounds ($10 \times 10^{-4}M$/L.) are added

1 : β-Hydroxynaphthoic acid
2 : Salicylic acid (Na salt)
3 : Ethyl aminobenzoate
4 : Theophylline
5 : Caffeine
6 : Dehydroacetic acid
7 : Nicotinamide
8 : Theobromine
9 : Menadione only

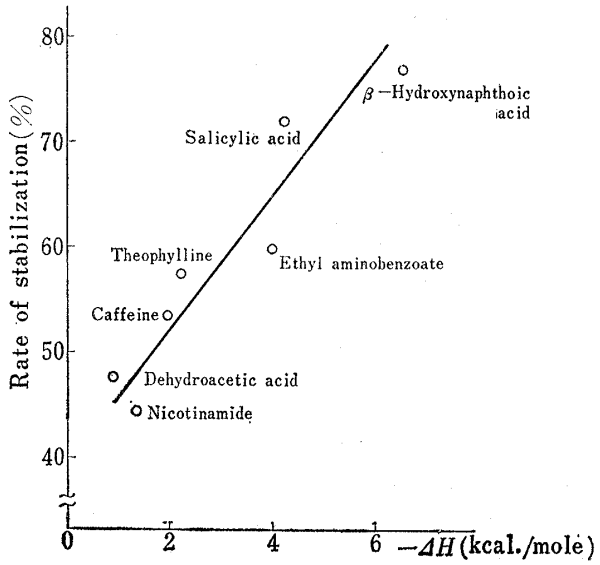

Fig. 5. Relation between Apparent Bond Energy (ΔH) and Rate of Stabilization

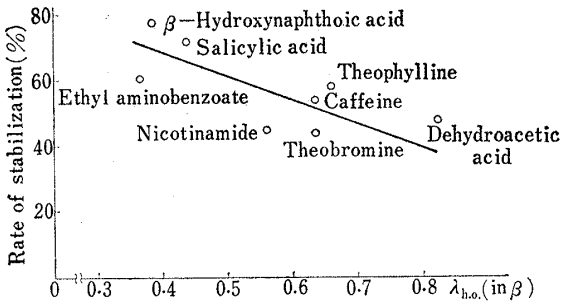

Fig. 6. Relation between Rate of Stabilization and $\lambda_{h.o.}$

complex formation enhanced the rate of stabilization. In addition, Fig. 6. shows that stability of menadione tends to be increased by the addition of better electron donors.

Therefore, it might tentatively be concluded that stability of menadione in aqueous electron donor solutions are dependent to charge transfer complex formation.