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Stopped-Flow Kinetics of the Formation and Decomposition of 2,4- and 4,4-Disubstituted Meisenheimer Complexes in the Reaction of 4-Piperidino-1,3-dinitrophenanthrene with Potassium Methoxide in Dimethyl Sulfoxide-Methanol[1)]

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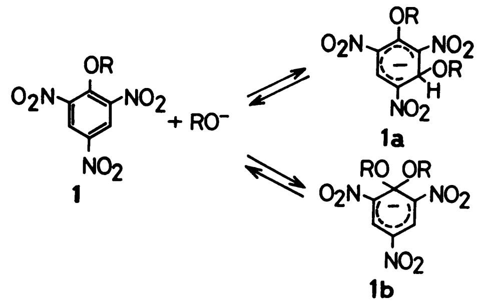
The formation of 2,4-disubstituted anionic σ complex, followed by the formation of 4,4-disubstituted one was confirmed by means of absorption and NMR spectra in the reaction of 4-piperidino-1,3-dinitrophenanthrene with potassium methoxide in DMSO-CH_3OH. The rates and activation parameters were determined by kinetic studies using stopped-flow and conventional spectrophotometers. It was found, compared with the previous results on the naphthalene system that the presence of H^5 of the title compound affects the rates differently.

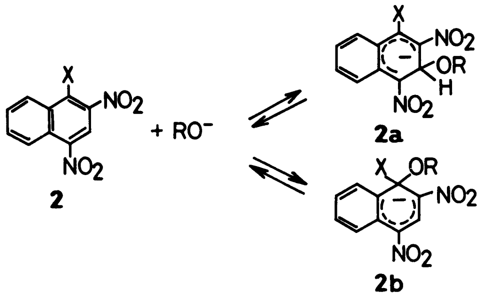
Many Jackson-Meisenheimer complexes (anionic σ complex) have been prepared by nucleophilic attack on polynitroaromatic compounds (Eqs. 1a and 1b), in



(1a)

(1b)

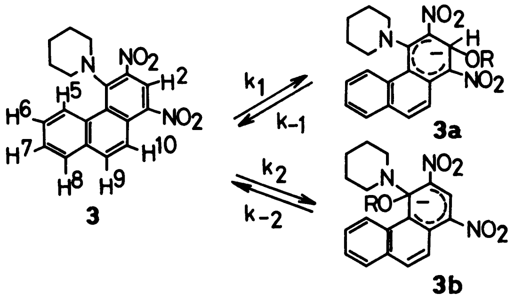
which at first **1a** (R: alkyl; hereafter called 1,3-disubstituted complex) is formed (kinetically controlled), subsequently rearranging into **1b** (hereafter called 1,1-disubstituted complex) (thermodynamically controlled.)[2)] Although many 1,3-disubstituted anionic σ complexes such as **1a** have been identified in the benzene or heteroaromatic systems, only a few ones such as **2a** (1,3-disubstituted complex) have been found in the naphthalene system (Eqs. 2a and 2b).[3–5)] The fact that **2a** (X; alkoxyl) is difficult to confirm in the reactions of **2** (X; alkoxyl) with alkoxide ions can be ascribed to its less stability than **1a**, mainly because the presence of nitro group para to the reaction site (C-3) stabilizes **1a** to much greater extent.[2)]



(2a)

(2b)

On the other hand, in the reactions with various nucleophiles, especially amines, the steric effects exerted by the structures of substrates or bulkiness of nucleophiles on the reaction mechanism have attracted much attention.[6–9)] In order to elucidate the effect of the structure of a substrate on the reaction rate, therefore, at first, we tried the reaction of 4-piperidino-1,3-dinitrophenanthrene (**3**) with potassium methoxide (CH_3OK) in DMSO-CH_3OH (90:10 v/v) (Eqs. 3a and 3b). We patterned the present experiments on those of the previous work.[5)]



(3a)

(3b)

This paper reports the stopped-flow kinetics of the formation of 2,4-disubstituted complex (**3a**) and of its decomposition or the formation of 4,4-disubstituted complex (**3b**), corresponding to **1b** and **2b**, and the comparison of the results with those for the naphthalene systems.[5)]

Results

General Features. Upon addition of excess CH_3OK to a DMSO-CH_3OH solution of **3**, Curve b appeared instantly, and then changed into Curve c at a relatively slow rate (Fig. 1), where the former could be attributed to **3a**, and the latter to **3b**.[4–7)] The results indicate that the reaction consists of the two seperate stages, i.e., the first rapid formation of **3a** and the second relatively slow decomposition of **3a** or the formation of **3b**.

NMR technique is expected to be useful for

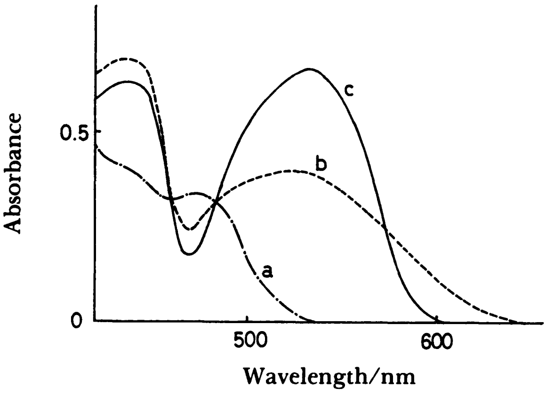
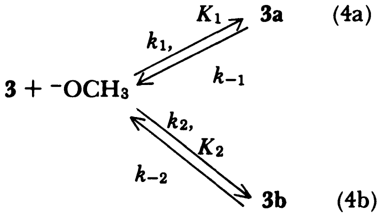


Fig. 1. Spectral change relevant to the reaction of 4-piperidino-1,3-dinitrophenanthrene (**3**) with CH_3OK in DMSO-CH_3OH (90:10, v/v); (a) **3** (3.87×10^{-5} M [M=mol dm^{-3}]) at room temperature; (b) just after addition of CH_3OK (2.95×10^{-2}); (c) 60 min.

elucidating the assignment mentioned above. Just after addition of methanolic CH_3OK (1.40×10^{-4} mol) to a DMSO-CH_3OH solution (0.5 ml) of **3** (1.40×10^{-4} mol), the solution turned red, suggesting the formation of a complex. Just upon addition of CH_3OK, H^2 sharp singlet (δ 8.25) of **3** shifted to δ 6.25, with a small singlet at δ 9.23, attributed to H^2 of **3b**, indicating the formation of **3a** (Eq. 3a) (sweep time 20 cps). This upfield shift is well-known to be characteristic of 2,4-disubstituted complex such as **3a**, corresponding to **2a** (1,3-disubstituted complex).[2] The H^2 singlet (δ 9.23) of **3b** increased in strength at the expense of the singlet at δ 6.25, which disappeared in 60 min. These results support the reaction path as shown in Eqs. 3a and 3b very well. It can be expected, therefore, that the separate kinetics of formation and decomposition of **3a** is possible.

Kinetics. Let us rewrite Eqs. 3a and 3b in a form convenient for quantitative discussion as Eq. 4. In the



(4a)

(4b)

$$K_1=\frac{k_1}{k_{-1}},\quad K_2=\frac{k_2}{k_2}$$

kinetics on Stage I, Stage II can be neglected, since the former reaction is completed in several thousandths seconds, making contamination by the latter negligible from considering the time scale of reaction.

Stage I. The pseudo-first-order rate constant, k_ψ, for the attainment of an equilibrium is the sum of forward and reverse components.[8,9] Therefore, the following expression should hold:

$$k_\psi = k_1([^-OCH_3]+[\mathbf{3}])+k_{-1} \tag{5}$$

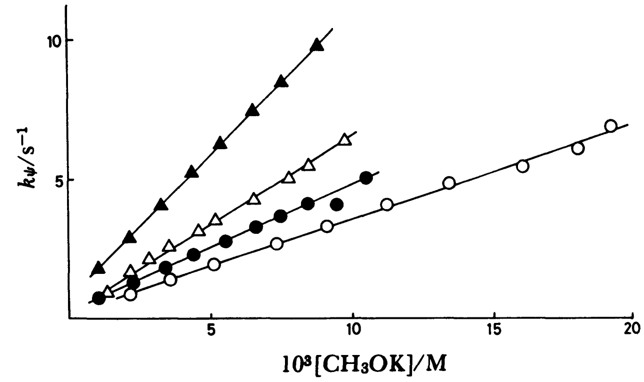


Fig. 2. Relationship between k_ψ and [CH_3OK] in Stage I; $[\mathbf{3}]_0$ 1.53×10^{-4} M; μ 0.05 M ($KClO_4$); ○ 25 °C; ● 30 °C; △ 35 °C; ▲ 45 °C.

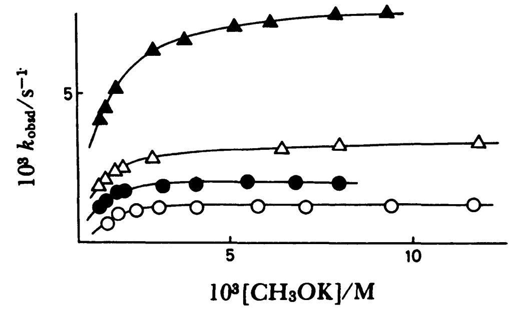


Fig. 3. Relationship between k_{obsd} and [CH_3OK] in Stage II; $[\mathbf{3}]_0$ 1.99—6.00×10^{-5} M; μ 0.05 M ($KClO_4$); ○ 25 °C; ● 30 °C; △ 35 °C; ▲ 45 °C.

Under the usual conditions ($[^-OCH_3]\gg[\mathbf{3}]$), Eq. 5 is simplified to

$$k_\psi = k_1[^-OCH_3]+k_{-1} \tag{6}$$

As a result, dependence of k_ψ on [$^-OCH_3$] would afford a linear relationship, and k_1 and k_{-1} are estimated from the slope and the intercept, respectively. The results in Fig. 2 are compatible with Eq. 6. Although the k_1 value can be exactly estimated from the slope, the k_{-1} one is very small relative to k_1, and has a large error. As a result, the k_{-1} value was calculated by the method described in the following paragraph.

Stage II. In considering the kinetics on Stage II, Stage I can be dealt with as a mobile equilibrium, lying almost entirely on the right under the conditions. Putting $[\mathbf{3}]_{st}=[\mathbf{3}]+[\mathbf{3a}]$ and K_1 the equilibrium constant for Stage I reaction, one obtains the following expression.

$$k_{obsd} = k_{-2}+\frac{k_2[^-OCH_3]}{1+K_1[^-OCH_3]}, \tag{7}$$

where k_{obsd} is the pseudo-first-order rate coefficient for Stage II reaction, and k_2 and k_{-2} are the rate coefficients for forward and reverse reactions. Consequently, de-

Table 1. Rate and Equilibrium Constants for Stages I and II at Various Reaction Temperatures

Temp	k_1	k_{-1}	$10^{-3}\,K_1$[a]	k_2	$10^5\,k_{-2}$	$10^{-5}\,K_2$[b]
°C	$M^{-1}\,s^{-1}$[c]	s^{-1}	M^{-1}[c]	$M^{-1}\,s^{-1}$[c]	s^{-1}	M^{-1}[c]
25	349± 8	0.16±0.05	2.18±0.73	2.90±0.06	1.24±0.03	2.33±0.01
30	437±12	0.24±0.03	1.82±0.27	4.06±0.07	1.50±0.04	2.70±0.01
35	576±16	0.36±0.02	1.60±0.13	5.63±0.11	2.66±0.11	2.49±0.02
45	973±27	0.77±0.04	1.26±0.01	10.5 ±0.22	7.90±0.33	1.32±0.02

a) $K_1=k_1/k_{-1}$. b) $K_2=k_2/k_{-2}$. c) $M^{-1}=dm^3\,mol^{-1}$.

pendence of k_{obsd} on [$^-OCH_3$] would afford a curvilinear relationship (convex upward), in which the curve would not pass through the origin (Fig. 3).

The exact k_2, k_{-2}, and k_1 values were estimated in the following way. First, k_1, k_{-1}, and K_1 ($=k_1/k_{-1}$) are obtained from the slope and intercept (Fig. 2), although k_{-1} has some extent of error. Second, in the plateau (Fig. 3) $K_1[^-OCH_3]\gg 1$, so the following relationship holds. In Eq. 8 it is clear from the previous work[5)] that $k_2/k_1 \gg k_{-2}$.

$$k_{obsd} = k_{-2} + \frac{k_2}{K_1} \qquad (8)$$

As a result, k_2 can be calculated by using the K_1 value obtained just above. Once k_2 and K_1 are estimated, k_{-2} can be calculated from Eq. 7 by using appropriate experimental values of k_{obsd} and methoxide concentration. Third, by substituting these values into Eq. 7 as initial values and using a nonlinear least squares method (Gauss-Newton Method), the optimum K_1, k_2, and k_{-2} values can be obtained, which are listed in Table 1.

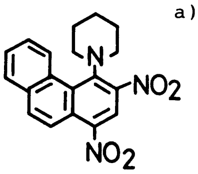
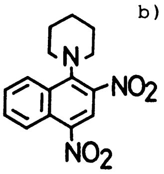
From K_1 and k_1, k_{-1} can be estimated (Table 1). Calculated k_ψ and k_{obsd} obtained by substituting the values in Table 1 into Eqs. 6 and 7 are in agreement with the observed ones almost within <2% in almost all runs.

The rate and equilibrium constants and activation parameters, obtained by the Arrhenius plot are summarized in Table 2, together with those for the naphthalene system.[5)]

Discussion

Stage I. The k_1 value is smaller for the phenanthrene system than for the naphthalene one, depending on $\Delta S_1^{\ddagger}$ rather than $\Delta H_1^{\ddagger}$. Such a result would stem from the following steric reason. When a methoxide ion attack C-2 of **3** or C-3 of **2**, the negative charge donated by the ion is delocalized over the ring to a larger extent for the phenanthrene system than the naphthalene one, which is reflected on $\Delta H_1^{\ddagger}$. This delocalization, however, would make $\Delta S_1^{\ddagger}$ decrease for the phenanthrene system as follows: both ortho-nitro groups to the reaction site could assume coplanarity to the ring upon delocalization, since the negative charge donated by the ion ($^-OCH_3$) delocalizes especially over these two nitro groups in the transition state of k_1 step.[6,7,10)] The coplanarity of 3-nitro group of **3** would make the steric interference among 3-nitro, 4-piperidino, and H^5 groups severer than that of 2-nitro group of **2** would do among 2-nitro, 1-piperidino, and H^8 groups, and make the piperidyl ring almost perpendicular to the phenanthrene one, resulting in less freedom.

Table 2. Rate and Equilibrium Constants and Activation Parameters[a)]
(1 cal_{th} = 4.184 J)

	 a) **3**	 b) **2**
$k_1/M^{-1}\,s^{-1}$[c,d)]	349±8	480±35
k_{-1}/s^{-1}[c)]	0.16±0.05	1.04±0.11
K_1[c)]	2180±730	460±80
$\Delta H_1^{\ddagger}/kcal_{th}\,mol^{-1}$	9.6±0.7	11.5±2.3
$\Delta S_1^{\ddagger}/cal_{th}\,K^{-1}$	−14.8±2.5	−7.1±5.3
$\Delta H_{-1}^{\ddagger}/kcal_{th}\,mol^{-1}$	14.2±2.6	13.5±3.6
$\Delta S_{-1}^{\ddagger}/cal_{th}\,K^{-1}$	−11.5±5.3	−10.9±9.2
$\Delta H^0/kcal\,mol^{-1}$[e)]	−4.6±1.2	−2.0±5.9
$\Delta S^0/cal_{th}\,K^{-1}$[e)]	−3.3±2.0	3.8±14.5
$k_2/M^{-1}\,s^{-1}$[c)]	2.90±0.06	2.53±0.29
k_{-2}/s^{-1}[c,d)]	1.24±0.03×10⁻⁵	1.80±1.31×10⁻⁴
$\Delta H_2^{\ddagger}/kcal_{th}\,mol^{-1}$	11.5±2.2	12.2±2.5
$\Delta S_2^{\ddagger}/kcal_{th}\,K^{-1}$	−17.0±12.3	−15.4±10.2
$\Delta H_{-2}^{\ddagger}/kcal_{th}\,mol^{-1}$	20.6±5.1	27.2±7.2
$\Delta S_{-2}^{\ddagger}/cal_{th}\,K^{-1}$	−40±4.2	−15.8±1.5

a) Activation parameters at 25 °C. b) Cited from Ref. 5. c) Cited from Table 1. d) $M^{-1}=dm^3\,mol^{-1}$. e) $\Delta H^0 = \Delta H_1^{\ddagger} - \Delta H_{-1}^{\ddagger}$; $\Delta S^0 = \Delta S_1^{\ddagger} - \Delta S_{-1}^{\ddagger}$.

In k_{-1} step, both $\Delta H_{-1}^{\ddagger}$ and $\Delta S_{-1}^{\ddagger}$ are slightly unfavorable for the phenanthrene system, since **3a** is more stable by ca. 0.5 kcal mol⁻¹ ($\Delta\Delta G^0=\Delta\Delta H^0-T\Delta\Delta S^0$) than **2a** owing to more extensive delocalization and, as a result, the reverse reaction is unfavorable. The fact the ΔG^0 is −3.6 and −3.1 kcal mol⁻¹ for **3a** and **2a** respectively is very interesting indicating that **3a** and **2a** are more stable than **3** and **2** ($\Delta G^0=\Delta H^0-T\Delta S^0$), respectively.

Stage II. The k_2 value is larger for the phenanthrene system than for the naphthalene one, depending on

$\Delta H^{\ddagger}_{2}$ rather than $\Delta H^{\ddagger}_{2}$. The $\Delta\Delta H^{\ddagger}_{2}$ value ($=\Delta H^{\ddagger}_{2}$ for **2** $-\Delta H^{\ddagger}_{2}$ for **3**) is 0.7 kcal mol^{-1}, which makes k_2 for **3** ca. 3.3 times larger than k_2 for **2**, whereas the observed ratio is ca. 1.1 (Table 2). As a result, it can be seen that $\Delta S^{\ddagger}_{2}$ for **3** unfavorably affects k_2 to make the rate ratio of ca. 3.3 depending on $\Delta H^{\ddagger}_{2}$ reduce to ca. 1.1, although the $\Delta S^{\ddagger}_{2}$ values have large errors. In the transition state of k_2 step for the phenanthrene system, H^5 protrudes over between the piperidino and methoxyl (nucleophile) groups, and consequently the steric interference among H^5, piperidino, and 3-nitro groups would be relieved to some extent, compared with the transformation of **2** to **2b**, which is expected to lower the potential energy barrier between the reactants and transition state. This effect, however, would decrease $\Delta S^{\ddagger}_{2}$ to a larger extent for the phenanthrene system. In addition, delocalization of the negative charge donated by a methoxide ion is more extensive for the phenanthrene system than for the naphthalene one, and the larger resonance inhibition between the unshared electron pair on the piperidino nitrogen and the phenanthrene ring would make the nucleophilic attack on C-4 of a methoxide ion easier than for the naphthalene system. These effects would lower $\Delta H^{\ddagger}_{2}$ for the phenanthrene system.

Although the k_{-2} values can not be rigorously discussed because of large error in the case of **2**, they can be said to be much less smaller than the k_2 ones for the two systems. The large K_2 values indicate that **3b** and **2b** are very stable, compared with the reactants.

In conclusion it is found that H^5 of **3** exerts steric interference to the reaction site indirectly (Stage I) or directly (Stage II) in the reaction of 4-piperidino-1,3-dinitrophenanthrene (**3**) with $KOCH_3$ in DMSO–CH_3OH (9:1 v/v), which is very different from the fimilar reaction of the naphthalene analogue.

Experimental

NMR spectra were recorded on a Varian A-60D spectrometer and UV-VIS absorption spectra on a Hitachi Model 200-10 spectrophotometer.

Materials. 4-Piperidino-1,3-dinitrophenanthrene (**3**) was prepared from 4-chloro-1,3-dinitrophenanthrene (CDNP) and piperidine according to the method described previously.[11] The compound (CDNP) was prepared from 1,3-dinitro-4-phenanthrol, *p*-toluenesulfonyl chloride, and *N*,*N*-diethylaniline according to the method described previously.[10] Commercial dimethyl sulfoxide and methanol were purified according to the method described previously.[5] Commercial potassium perchlorate of special grade was used without further purification to keep the ionic strenght at 0.05 mol l^{-1} in rate measurements.

Rate Measurement. As regards the kinetics of formation of 2,4-disubstituted complex, an increase in the absorbance at 532 nm due to the complex was followed in order to estimate the apparent rate constants (k_ψ) with a thermostatted stopped-flow spectrophotometer (Otsuka Denshi Co.). In order to estimate k_{obsd}, a decrease in the absorbance at 600 nm due to 2,4-disubstituted complex was followed with a thermostatted Hitachi Model 200-10 spectrophotometer.

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