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Reactivities of 9-Phenylxanthylium and 9-Phenylthioxanthylium Salts in Electrophilic and Nucleophilic Reactions. III[1]

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Active methylene compounds were allowed to react with 9-phenylxanthylium perchlorate (I) and with 9-phenylthioxanthylium perchlorate (II). The products were only those that were formed by the attack of 9-position of I or II by the active methylene compound. When *t*-BuOK was used as a base, deacetylation occurred in the reaction between I and acetylacetone. When triethylamine was used as a base, expected results were obtained.

By the reaction of I or II with KCN, V or VI, in which a cyano group was introduced to 9-position, was obtained with a high yield.

The reactivities of I and II in electrophilic and nucleophilic reactions were discussed from the viewpoints of qualitative electronic theory and the theoretically calculated reaction indices. The results indicated that the contribution of the carbonium ion structure is more in I than in II and that I is more reactive than II in the nucleophilic reaction. The contribution of the onium ion structure is more in II than in I. Therefore, II is theoretically reactive than I in the electrophilic reaction. This conclusion well agrees with experimental results.

A series of studies have been performed by the present authors on 9-phenylxanthylium salt (I) and 9-phenylthioxanthylium salt (II). In this series, the electrophilic reaction[1] and the reactions of organometallic reagents[3] were studied in detail. Striking differences were found between the reactivities of I and II in these reactions.

In this report, descriptions will be made on the reactions of I and II with active methylene compounds. Discussions will also be given on the reactivities of I and II in electrophilic and nucleophilic reactions.

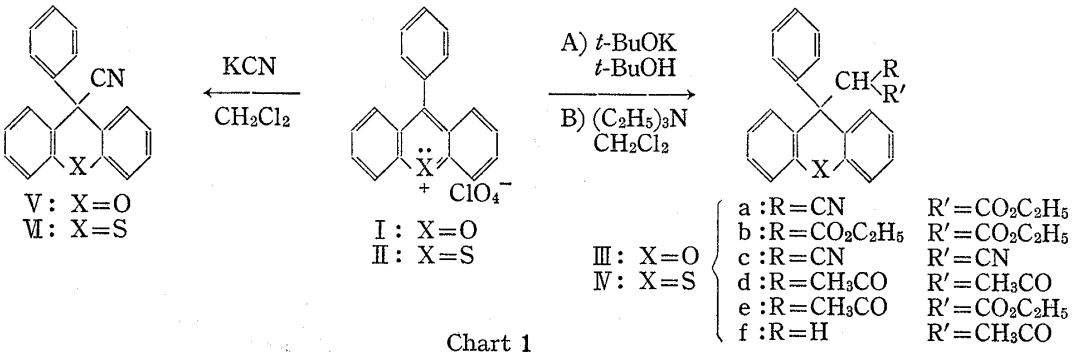


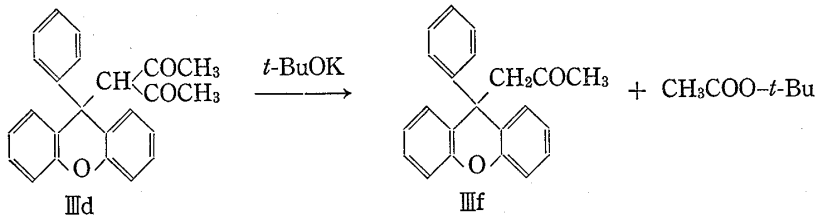
Chart 1

Reactions of Some Active Methylene Compounds with I and II

Two equivalents of an active methylene compound was allowed to react with I and II in *t*-BuOH containing *t*-BuOK as a base. The results of the reaction are shown in Table I.

1) *a*) M. Hori, T. Kataoka, K. Ohno, and T. Toyoda, *Chem. Pharm. Bull.* (Tokyo), **21**, 1272 (1973); *b*) M. Hori and T. Kataoka, *ibid.*, **21**, 1282 (1973).
2) Location: *a*) *492-36, Mitahora, Gifu*; *b*) *Juso-Nishino-cho, Higashiyodogawa-ku, Osaka.*
3) *a*) M. Hori, T. Kataoka, Y. Asahi, and E. Mizuta, *Chem. Pharm. Bull.* (Tokyo), **21**, 1318 (1973); *b*) *Idem, ibid.*, inpress.

All of these products were recrystallized from a benzene–pet. ether mixture. Colorless prisms were obtained. All the reaction products were those formed by the attack of carbon at 9-position by the active methylene compound. The yields were about 50%. However, a compound (IVe) was formed with a low yield of 5% by the reaction between II and ethyl acetoacetate. In the reaction between I and acetylacetone, 9-diacetylmethyl-9-phenylxanthene (IIId) was decomposed by the base as follows resulting in the formation of 9-acetonyl-9-phenyl-xanthene (IIIf).[4] The yield of IIIf was 76%. The structure of IIIf was determined



IIId IIIf

by the following instrumental data; IR ν_{max}^{KBr} cm^{-1}: 1705 (CO); NMR (in $CDCl_3$) τ: 6.48 (2H, singlet, CH_2), 8.27 (3H, singlet, CH_3); Mass Spectrum, *m/e*: 314 (M^+), 257 (M^+-CH_3COCH_2

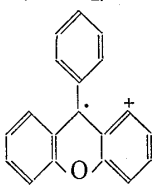
i.e.  9–phenyxanthyl).

TABLE I. Methods, Yields, Melting Points and Elemental Analyses of III and IV

Compound number	Method[a]	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
IIIa	A	50	132	$C_{24}H_{19}O_3N$	78.02	5.17	3.79	77.93	5.27	3.80
IIIb	A	50	117	$C_{26}H_{24}O_5$	74.97	5.81		75.21	5.85	
IIIc	A	78	182	$C_{22}H_{14}ON_2$	81.97	4.38	8.69	81.95	4.52	8.88[b]
IIId	B	40	170	$C_{24}H_{20}O_3$	80.88	5.66		80.84	5.78	
IIIe	B	51	108	$C_{25}H_{22}O_4$	77.69	5.74		77.54	5.85	
IIIf	A	76	139	$C_{22}H_{18}O_2$	84.05	5.77		84.29	5.86	
IVa	A	53.5	138	$C_{24}H_{19}O_2NS$	74.77	4.97	3.64	74.69	5.15	3.61
IVb	A	59	105	$C_{26}H_{24}O_4S$	72.28	5.60		72.29	5.51	
IVc	A	87	214	$C_{22}H_{14}N_2S$	78.08	4.17	8.27	78.08	4.32	8.00
IVd	B	43	146	$C_{24}H_{20}O_2S$	77.38	5.41		77.18	5.67	
IVe	A	5	117	$C_{25}H_{22}O_3S$	74.59	5.51		74.52	5.57	
	B	55								

a) A: *t*-BuOH–*t*-BuOK B: CH_2Cl_2–$(C_2H_5)_3N$

b) On heating, the sample recrystallized from benzene melted at 110°, soon became solid, and melted at 182° again. From the following analysis and NMR data, it was proved to be a one-to-one adduct of IIIc and benzene. *Anal.* Calcd. for $C_{28}H_{20}ON_2$; C, 83.97; H, 5.03; N, 7.00. Found: C, 83.88; H, 5.18; N, 6.85. The NMR spectrum exhibited an extra peak at τ 2.63 (singlet) due to the attached benzene.

Triethylamine was used instead of *t*-BuOK because the use of *t*-BuOK was accompanied by the troubles mentioned above. As a result, IIId and IVd, which are not deacetylated, were formed by the reactions with acetylacetone with yields of 40 and 43%, respectively.

4) E.S. Waight, "Rodd's Chemistry of Carbon Compounds," Vol. I, Part D, ed. by S. Coffey, Elsevier Publishing Company, Amsterdam, 1965, p. 70: $CH_3COCH_2COCH_3 \xrightarrow{NaOH} CH_3COCH_3 + CH_3COONa$

Table II. Spectral Data of III and IV

Compound Number	IR ν_{max}^{KBr} cm^{-1}	NMR (τ: $CDCl_3$)
IIIa	2230 (CN), 1749 (CO)	2.40—3.35 (13H, m, aromatic H), 5.57 (1H, s, CH), 6.15 (2H, q, J=7.0 Hz, CH_2), 9.06 (3H, t, J=7.0 Hz, CH_3)
IIIb	1760 (CO), 1730 (CO)	2.40—3.30 (13H, m, aromatic H), 5.44 (1H, s, CH), 6.05 (4H, q, J=7.0 Hz, CH_2), 8.96 (6H, t, J=7.0 Hz, CH_3)
IIIc	2220 (CN)	2.20—3.20 (13H, m, aromatic H), 5.60 (1H, s, CH)
IIId	1720 (CO), 1690 (CO)	2.55—3.14 (13H, m, aromatic H), 5.17 (1H, s, CH), 8.18 (6H, s, CH_3)
IIIe	1740 (CO), 1715 (CO), 1690 (CO)	2.35—3.20 (13H, m, aromatic H), 5.36 (1H, s, CH), 6.01 (2H, q, J=7.2 Hz, CH_2), 8.19 (3H, s, $COC\underline{H}_3$), 8.92 (3H, t, J=7.2 Hz, $CH_2C\underline{H}_3$)
IIIf	1705 (CO)	2.61—3.25 (13H, m, aromatic H), 6.48 (2H, s, CH_2), 8.27 (3H, s, CH_3)
IVa	2225 (CN), 1740 (CO)	2.30—3.30 (13H, m, aromatic H), 5.20 (1H, s, CH), 6.13 (2H, q, J=7.2 Hz, CH_2), 9.05 (3H, t, J=7.2 Hz, CH_3)
IVb	1750 (CO), 1710 (CO)	2.30—3.26 (13H, m, aromatic H), 5.12 (1H, s, CH), 6.14 (4H, q, J=7.2 Hz, CH_2), 9.02 (6H, J=7.2 Hz, CH_3)
IVc	2225 (CN)	2.20—3.25 (13H, m, aromatic H), 5.03 (1H, s, CH)
IVd	1720 (CO), 1685 (CO)	2.40—3.35 (13H, m, aromatic H), 4.72 (1H, s, CH), 8.28 (6H, s, CH_3)
IVe	1730 (CO), 1700 (CO)	2.44—3.20 (13H, m, aromatic H), 4.96 (1H, s, CH), 6.14 (2H, q, J=7.2 Hz, CH_2), 8.02 (3H, s, $COC\underline{H}_3$), 9.02 (3H, t, J=7.2 Hz, $CH_2C\underline{H}_3$)

In the reactions with ethyl acetoacetate, IIIe and IVe were produced with yields of 51 and 55%, respectively. The infrared (IR) and nuclear magnetic resonance (NMR) spectral data of IIIa—f and IVa—e are shown in Table II. Their IR spectra showed characteristic absorptions due to carbonyl and/or cyano groups. Their NMR spectra had singlet peaks at τ 4.72—5.60 due to a proton of the activated methyne groups, except for IIIf.

The reaction of I or II with KCN was also examined. An aqueous KCN solution was allowed to react with a CH_2Cl_2 solution of I or II. 9-Cyano-9-phenylxanthene (V) or 9-cyano-9-phenylthioxanthene (VI) was obtained with a high yield. Both the products were recrystallized from a benzene–pet. ether mixture to give colorless prisms.

Theoretical Consideration on the Chemical Reactivities of I and II in Electrophilic and Nucleophilic Reactions

In the preceding report,[1] the authors confirmed that II is much more reactive than I and that II is dinitrated under the condition, which mononitrates I. It was also found that the nitration of I mainly takes place at *m*-position of the phenyl group at 9-position whereas the nitration of II gives more *p*-substituents than *m*-substituents. In the present report, the reactivities of I and II in the nucleophilic reaction were studied. Chart 2 summarizes the results.

One possible factor that explains the difference in the reactivity in the electrophilic reaction is the difference in the state of π-bondings of O-C and S-C linkages. The difference in the π-bondings of O-C and S-C linkages affects the reactivity of the compounds. The examples of this effect have been found in several substitution reactions and addition reactions.[5] $-\overset{+}{\underset{\cdot\cdot}{S}}=C<$ bonding, which contains an anti-bonding, is weaker than $-\overset{+}{\underset{\cdot\cdot}{O}}=C<$ bonding, and stabilization of the former by the M-effect is less than that of the latter. Therefore, it is concluded that I is more reactive in the nucleophilic reaction than II.

On the other hand, the difference of the I-effect between I and II in the ground state is more effective than that of the M-effect in the transition state from I or II to the free ion.

5) C.C. Price and S. Oae, "Sulfur Bonding," Ronald Press, New York, pp. 9—19.

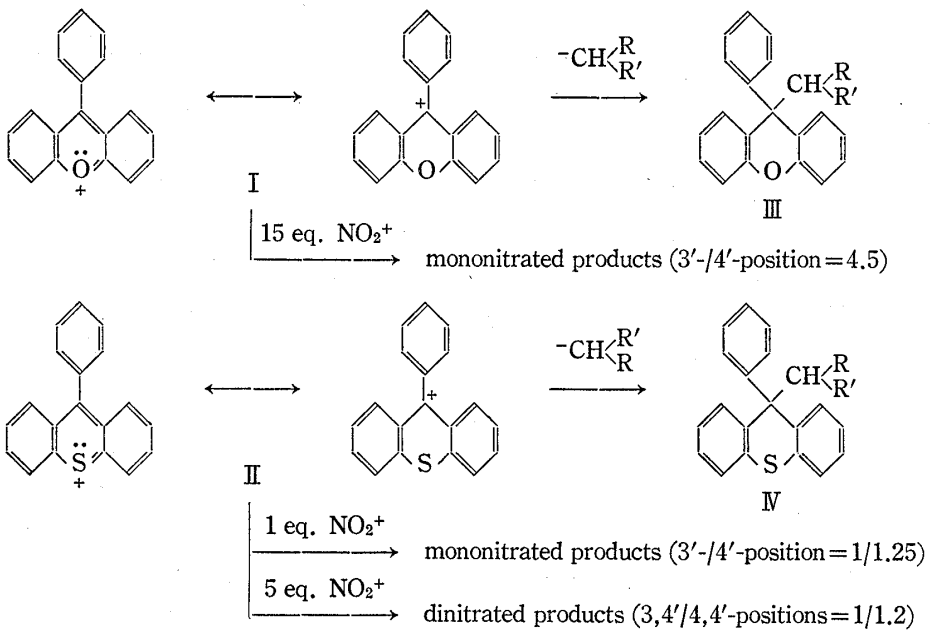
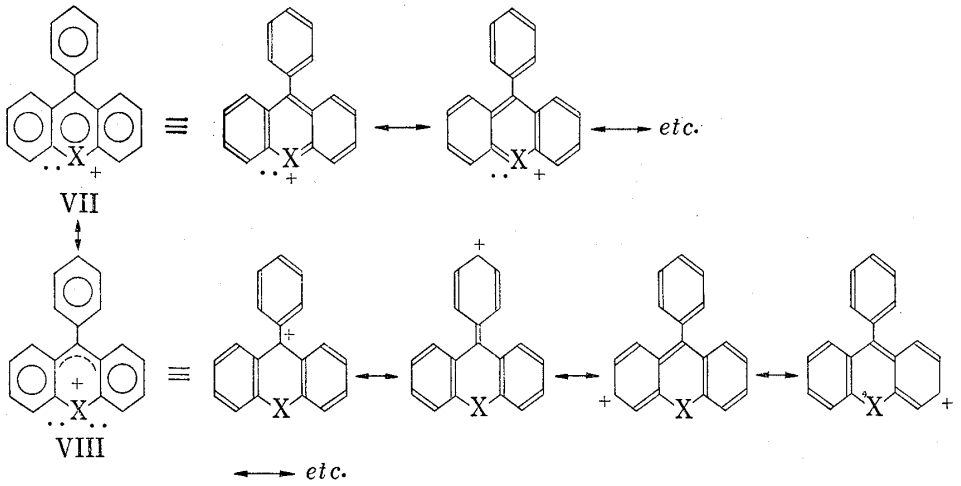


Chart 2

Namely, onium structures (VII) largely contributes in II, whereas carbonium ion structures (VIII) contributes to a large extent in I. Consequently, the former is more liable to the electrophilic reaction than the latter.

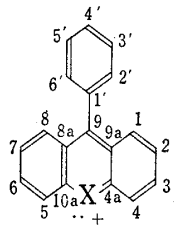


In the case of II, the through conjugation possibly affects the reaction by the 3d-orbital resonance. 3d-Orbital resonance is more effective geometrically in cyclic compounds such as thiopyrylium salt than in open chain compounds.[6] It is assumed that the positive charge of II is much more delocalized than that of the corresponding oxygen compound (I) because of the stabilization by 3d-orbital resonance.

In order to quantitatively examine the reliability of the explanation by the electronic theory, the authors calculated by the ω-technique the electron densities (Q_r)[7] and reaction indices[8] such as the frontier electron densities (f_r^N) for the nucleophilic reaction and the super delocalizabilities (S_r^E) for the electrophilic reactions. The results are shown in Table III.

6) W.G. Salmond, *Quart. Rev.* (London), **22**, 253 (1968).
7) A. Streitwieser, Jr., *J. Am. Chem. Soc.*, **82**, 4123 (1960).
8) K. Fukui, T. Yonezawa, C. Nagata, and H. Shingu, *J. Chem. Phys.*, **22**, 1433 (1954).

TABLE III. Reaction Indices of 9-Phenylxanthylium (I) and 9-Phenylthioxanthylium Salt (II) by ω-Technique



Position	I (X=O)			II (X=S)		
	Q_r	S_r^E	$f_r^{N a)}$	Q_r	S_r^E	$f_r^{N b)}$
1, 8	0.9258	0.7548	0.1824	0.9379	0.7935	0.1778
2, 7	0.9807	0.7863	0.0016	0.9875	0.8138	0.0054
3, 6	0.9188	0.6841	0.1839	0.9286	0.7022	0.1776
4, 5	**0.9823**	**0.8109**	0.0013	**0.9947**	**0.8635**	0.0078
4a, 10a	0.9560			0.9352		
8a, 9a	0.9686			0.9763		
9	**0.6997**	0.3989	**0.7325**	**0.7327**	0.4735	**0.7117**
10	1.8831		0.0660	1.7569		0.1674
1′	0.9963		0.0001	0.9993		0.0000
2′, 6′	0.9873	0.8182	0.0294	0.9972	0.8306	0.0071
3′, 5′	**0.9975**	**0.8262**	0.0000	**0.9995**	**0.8318**	0.0000
4′	**0.9869**	**0.8098**	0.0295	**0.9972**	**0.8296**	0.0071

Parameters: $\alpha_o=\alpha+2\beta$, $\alpha_{adj.}=\alpha+0.2\beta$, $\beta_{o-c}=0.6\beta$; $\alpha_s=\alpha+0.9\beta$, $\alpha_{adj.}=\alpha+0.1\beta$, $\beta_{s-c}=0.5\beta$; $\omega_r=0.55$ in $\beta_{r'}=\alpha_r\times\omega_r(P_r-Q_r)$.
Twist angles θ of $C_9-C_{1'}$ positions of I and II were estimated as *ca.* 66° and *ca.* 78° from the relation $\beta_{9-1'}=\beta\cos\theta$, respectively.
a) Energy of the lowest vacant orbital: $\varepsilon=\alpha+0.054\beta$.
b) Energy of the lowest vacant orbital: $\varepsilon=\alpha+0.004\beta$.

Table III well explains that the electrophilic reaction takes place at the positions where the Q_r and S_r^E values are large in I and II, for example at 3′,5′- and 4,5-positions, and that II is much more active than I. The results of discussion by the electronic theory mentioned before are shown by the theoretical values of S_r^E and Q_r as well as by the twist angle between the plane of the 9-phenyl group and the plane of the rest of the molecule. Namely, the results are supported by the comparison of the degree of the resonance forbidding between the 9-phenyl group and the hetero ring of I with that of II. Although II also shows large S_r^E values at 2′,6′- and 4,5-positions, it was found experimentally that these positions are not mononitrated. This result is attributable to the steric or electrostatic effect at these positions. However, the ratio of formation of the isomers obtained by mononitration and dinitration of II, namely, the ratios 3′-/4′position=1/1.25 and 3′,4-/4,4′-positions=1/1.2 do not agree with the values of S_r^E of the corresponding positions of II. More exact MO calculation, which takes the 3d-orbital of sulfur into consideration, will be made in the future.

On the other hand, the nucleophilic reaction takes place at 9-position, which shows small Q_r values, namely, the large f_r^N values for I and II. This result well agrees with the theoretical calculation. The result of theoretical calculation indicates that the reactivity of I in nucleopilic reaction is larger than that of II, but it is difficult to experimentally confirm this difference.

Now the authors are studying on the reactions of I and II with various nucleophiles other than active methylene compounds to experimentally prove the difference of reactivity in the nucleophilic reaction, which is theoretically expected.

Experimental[9]

Reaction with Active Methylene Compounds——a) A solution of the anion of active methylene compound was prepared from active methylene compound (5.5 mmole) and *t*-BuOK (2.1 g) in *t*-BuOH (50 ml) under nitrogen at 60° with stirring for 30 min. I[10] or II[11] (2 g) was added to the solution thus prepared. The reaction mixture was stirred for 3—5 hr at 60°. After evaporation of the solvent, the residue was dissolved in benzene. The benzene solution was washed with 1% HCl (100 ml), dried, and evaporated. After addition of pet. ether to the residual oil, the mixture was allowed to stand overnight. The resulting crystals were collected and recrystallized from benzene–pet. ether to give colorless prisms.

b) I or II (2 g) was added to a stirred mixture of an active methylene compound (5.5 mmole) and triethylamine (1.1 g) in CH_2Cl_2 (20 ml). The reaction mixture was stirred for a day at room temperature, and then water was added. The CH_2Cl_2 layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were dried and evaporated. The treatment of the residual oil as mentioned above gave colorless prisms.

Reactions with Potassium Cyanide——To a stirred solution of I or II (2 g) in CH_2Cl_2 (20 ml), an aqueous solution of KCN (0.4 g) in water (3 ml) was added. Reaction was continued for 30 min with stirring at room temperature. The reaction mixture was poured into water and extracted with CH_2Cl_2. The extracts were dried and evaporated. 9-Cyano-9-phenylxanthene (V) was recrystallized from benzene–pet. ether to give 0.70 g (80.0%) of colorless prisms, mp 138°. *Anal.* Calcd. for $C_{20}H_{13}ON$: C, 84.78; H, 4.62; N, 4.94. Found: C, 85.10; H, 4.95; N, 4.64. IR ν_{max}^{KBr} cm^{-1}: 2200 (CN). 9-Cyano-9-phenylthioxanthene (VI) was recrystallized from benzene–pet. ether to give 0.72 g (89.6%) of colorless prisms, mp 143°. *Anal.* Calcd. for $C_{20}H_{13}NS$: C, 80.23; H, 4.38; N, 4.84. Found: C, 80.41; H, 4.53; N, 4.75. IR ν_{max}^{KBr} cm^{-1}: 2200 (CN).

Acknowledgement The authors are indebted to Misses R. Ono and H. Konomi of Gifu College of Pharmacy for their technical assistance.

9) Melting points were measured on a Yanagimoto micromelting point apparatus and uncorrected. The NMR spectra were recorded on a Hitachi R-20B spectrometer using tetramethylsilane as an internal standard. A Hitachi EPI-S2 spectrometer was used for the IR absorption spectra.

10) R.L. Schriner and C.N. Wolf, *J. Am. Chem. Soc.*, **73**, 891 (1951).

11) C.C. Price, M. Hori, T. Parasaran, and M. Polk, *J. Am. Chem. Soc.*, **85**, 2278 (1963).