

티오크잔틸이온 이온과 디메돈의 반응메카니즘에 관한 연구

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Mechanistic Studies on the Reaction of Thioxanthylum Ion with Dimedone

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요 약 : 티안트렌양이온 자유라디칼의 아세토니트릴 용액에 의해 티오크잔틴이 산화되어 생성된 티오크잔틸이온 이온에 디메돈을 넣어주면 9-(4,4-dimethylcyclohexane-2,6-dionyl)thioxanthylum perchlorate (2)이 생성되나 순서를 바꾸어 넣어주면 초기에 9-(4,4-dimethylcyclohexane-2,6-dionyl)thioxanthene (1)이 생성되며 이것은 계속 반응하여 2를 만든다. 화합물 2는 물이 섞인 아세톤에서 쉽게 탈 수소화되어 9-(4,4-dimethylcyclohexane-2,6-dionylidene)thioxanthene (3)이 된다. 그러나 물이 섞인 아세토니트릴용액중에서 관찰된 219, 289, 348 nm의 isosbestic point는 3이 2와 평형상태로 존재함을 말한다. 3의 380 nm 근처에 있는 흡수띠의 위치와 강도는 용매에 따라 변하는데 이것은 용매-용질 사이의 상호작용으로 설명한다.

ABSTRACT: Addition of dimedone to thioxanthylum ion generated from the oxidation of thioxanthene by thianthrene cation radical perchlorate in acetonitrile gave 9-(4,4-dimethylcyclohexane-2,6-dionyl)thioxanthylum perchlorate (2), whereas from the reverse addition between two reactants was obtained initially 9-(4,4-dimethylcyclohexane-2,6-dionyl)thioxanthene (1), which then underwent further reaction to give 2. The compound 2 was readily deprotonated in aq acetone to give 9-(4,4-dimethylcyclohexane-2,6-dionylidene)thioxanthene (3). However, 3 turned out to be in equilibrium with 2 in which three isosbestic points at 219, 289, and 348 nm were recorded in aq acetonitrile. The intensity and the position of the maximum absorption of 3 near 380 nm vary depending on the solvents which has been explained in terms of the solvent-solute interactions.

INTRODUCTION

There are now known several methods for the preparation of thioxanthylum ion as either a crystalline salt¹ or in solution state.^{2,3} Recently, we have found that thioxanthylum ion can also be prepared from the oxidation of thioxan-

thene by thianthrene cation radical perchlorate in acetonitrile.⁴ The synthetic utility of thioxanthylum ion generated in this reaction condition has been proved from the reactions with a variety of aromatics,⁴ phosphines,⁵ and organomercurials.⁶ In the connection with the effort for exploring the utility of cation radical

in the synthetic organic chemistry, we have run the reaction of thioxanthylum ion generated, in situ, by the oxidation with thianthrene cation radical perchlorate, with dimedone which is a typical cyclic ketone with an active methylene group. Here follows a study of the identification of the products and their formation mechanism.

EXPERIMENTAL

Materials

Thioxanthene (Pfaltz and Bauer) was used without further purification. Thianthrene was synthesized by refluxing benzene and sulfur in the presence of anhydrous aluminum chloride as described in the previous report.⁵ Thianthrene cation radical perchlorate was prepared by the modified method of Rundell and Scheffer.⁷ Dimedone was obtained from Merck (Art. 6013) and used without further purification. Acetonitrile was Kanto Chemical Corporation Extra pure and purified prior to use according to the literature method.⁵ All solvents used for the column chromatography were EP grade unless otherwise specified and distilled before use.

Thin layer chromatography was carried out with Merck, Kiesel gel 60, PF₂₅₄ and chromatogram was visualized by mineral ultraviolet lamp. Column chromatography was performed with Merck, Kiesel gel 60, 70-230 ASTM mesh, 0.05-0.2 mm (Cat. No. 7734). Eluant solvents are specified in each case.

Ultraviolet spectra were obtained using Beckman 5720 UV-VIS Spectrophotometer. Infrared spectra were obtained with Perkin-Elmer Model 283 Infrared Spectrophotometer. All infrared spectra were taken using potassium bromide pellets.

¹H NMR spectra were recorded with Varian EM 360A Spectrometer and all chemical shifts

were measured in ppm relative to an internal standard TMS.

Melting points were measured using Fisher-Johnes melting point apparatus and uncorrected.

Mass spectra were taken from GC-MS LKB-9000 Spectrometer, direct inlet at 100°C, 10⁻⁷ torr, 70 eV.

Experiment

Addition of Dimedone to Thioxanthylum Ion in Acetonitrile. To the solution of 750 mg (2.38 mmol) of thianthrene cation radical perchlorate in 30 ml of acetonitrile was added 275 mg (1.38 mmol) of thioxanthene. After the color of the radical disappeared 347mg (2.47 mmol) of dimedone was added. The dark red color of the solution turned red in 24 hr. The solvent was evaporated to dryness and the residue was chromatographed on the silica gel column (2×12 cm). Elution with benzene (150 ml) gave 685 mg of a mixture of thianthrene and thioxanthene. Elution next with ether (150 ml) gave 281 mg (2.00 mmol) of crude dimedone. Subsequent elution with acetone (290 ml) gave 476 mg of a mixture of perchloric acid and red solid, which was washed with acetone to remove perchloric acid and 201mg (0.46 mmol) of red solid was obtained. The red solid was identified to be 9-(4,4-dimethylcyclohexane-2,6-dionyl)thioxanthylum perchlorate: mp 290-300° C (dec); yield 78%; UVλ_{max}^{PROH} (log ε), 226 (sh, 4.00), 247 (sh, 4.30), 281 (4.85), 381 (3.40) nm; IR (KBr) 1613 (C=O), 1100 (ClO₄⁻), 637 (ClO₄⁻) cm⁻¹; ¹H NMR (DMSO-CDCl₃) δ 1.13 (s, 6H, methyl), 2.90 (s, 4H, methylene), 7.32-8.17 (m, 9H, methine and aromatic). When 9-(4,4-dimethylcyclohexane-2,6-dionyl)thioxanthylum perchlorate was dissolved in acetone, followed by the addition of water, yellow solid appeared. It was filtered and recrystallized from a mixture of benzene and *n*-hexane. This compound was

identified to be 9-(4,4-dimethylcyclohexane-2,6-dionylidene)thioxanthene: yield 60%; mp 215.5~216.5° C; $^1\text{H NMR}$ (CDCl_3) δ 1.10 (s, 6H, methyl), 2.73 (s, 4H, methylene), 7.10-7.69 (m, 8H, aromatic); MS *m/e* (rel. intensity) 208 (32.4), 250 (67.8), 333 (86.6), 334 (100.0, M^+).

Addition of Thioxanthylum Ion to Dimedone in Acetonitrile. To the solution of 788 mg (5.62 mmol) of dimedone in 30 ml of acetonitrile at 45° was added thioxanthylum perchlorate which was obtained by mixing 553 mg (2.79 mmol) of thioxanthene with 1645 mg (5.21 mmol) of thianthrene cation radical perchlorate in 40 ml of acetonitrile. This mixture was vigorously stirred at 45° for 1 hr. The color of the solution was changed into dark red. The solvent was evaporated to dryness and the residue was chromatographed on silica gel column (2×12 cm). After the column was eluted with *n*-hexane, followed by benzene, ether fraction showing two spots (*R_f* 0.4, 0.7) on thin layer chromatogram by using chloroform as an eluant was obtained. The solvent was removed and the residue was chromatographed on silica gel column (2×11 cm). Elution with chloroform gave 537 mg (1.60 mmol) of 9-(4,4-dimethylcyclohexane 2,6-dionyl)thioxanthene; mp 203~204.5° C (aq methanol); yield 61%; UV $\lambda_{\text{max}}^{\text{EtOH}}$ (log ϵ) 271 (4.23), 250 (4.00) nm; $\lambda_{\text{max}}^{\text{CH}_3\text{CN}}$ 256, 250 (sh) nm; IR (KBr) 1570 (C=O) cm^{-1} ; $^1\text{H NMR}$ (CDCl_3 -DMSO- d_6) δ 1.19 (s, 6H, methyl), 2.45 (s, 4H, methylene), 5.28 (s, 1H, methine), 6.92-7.43 (m, 8H, aromatic), 10.49 (s, 1H, hydroxyl); MS *m/e* (rel. intensity), 165 (11.0), 197 (100.0), 198 (16.0), 199 (5.6), 252 (5.8), 303 (13.7), 336 (30.5, M^+), 337 (7.5), 338 (2.1).

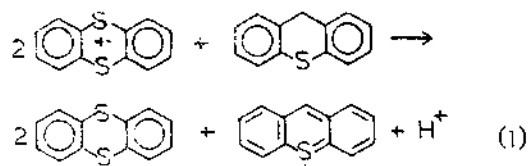
RESULTS AND DISCUSSION

Product identification. The formation of thioxanthylum ion in the oxidation reaction of thioxanthene by thianthrene cation radical perchlorate in acetonitrile seemed to occur rapidly and it remained unchanged for a long time unless no nucleophiles including water were added. Stability of thioxanthylum ion in this reaction condition is presumably due to perchloric acid generated in the process of the oxidation because cation is generally known to be stable in the acidic conditions. Reaction with a moisture, if any, resulted in the formation of thioxanthone, which was confirmed from a fluorescent spot on thin layer chromatogram as being visualized. However, the amount of it was too small to be isolated from the reaction mixture after column chromatography.

Addition of dimedone, which was slightly excess over a half mole of thianthrene cation radical perchlorate, followed by stirring vigorously did not seem to change the dark red color of the acetonitrile solution with thioxanthylum ion. After 24 hr, the solution was red. This slow observable color change does not mean slow reaction between thioxanthylum ion and dimedone (*vide infra*).

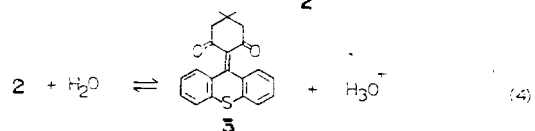
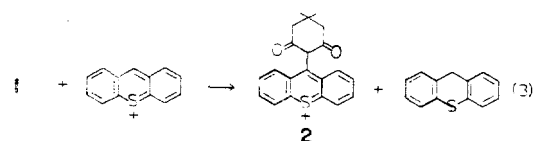
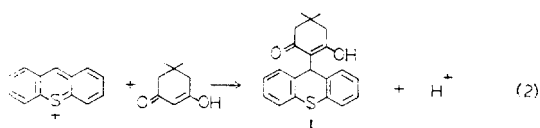
The reaction was very simple and clean. Three different fractions were collected in the chromatography in which a mixture of thianthrene and thioxanthene (685 mg), excess dimedone (281 mg), unknown were obtained from benzene, ether, and acetone, respectively. The weight of the benzene fraction of which composition can be calculated from $^1\text{H NMR}$ spectra exceeded the anticipated amounts based on the following stoichiometry by 131 mg (eq 1).

Infrared spectrum of the unknown red compound obtained from the acetone fraction sho-



wed perchlorate bands at 1100 and 637 cm^{-1} . However, it was unsuccessful to obtain a sharp melting point (decomposition) by the recrystallization. It was dissolved in acetone to give red solution but the color was slowly faded by the addition of water from which a white solid was obtained. The structure of the white solid was confirmed by IR, ^1H NMR, and mass spectral data. The following sequential pathways illustrate the observed results.

According to eq 1, thianthrene cation radical is completely reduced. Concurrently, thioxanthylum ion is generated in the solution, which



has also unreacted, excess thioxanthene. Thioxanthylum ion reacts with dimedone to give **1** which undergoes the reaction with thioxanthylum ion through a hydride transfer from **1** to thioxanthylum ion, affording **2** and thioxanthene. Therefore, overweight by 131 mg from the benzene fraction can be attributed to thioxanthene depicted in eq 3. Analogous explanation has been utilized in the hydride transfer bet-

ween 9-phenylthioxanthene and thioxanthylum ion or thioxanthene and 9-phenylthioxanthylum ion.³ The formation of **3** in the recrystallization process of **2** in aq acetone can be easily rationalized from the view point that compound **2** has not only an acidic methine proton but also a trivalent sulfur conjugated with the methine proton. This structural effect makes the proton even more acidic so that the basicity of water is strong enough for deprotonation of compound **2**.

In the meantime, compound **1** was able to be isolated from the process of reverse addition, *i.e.*, addition of acetonitrile solution of thioxanthylum ion to dimedone in acetonitrile. In order to make dimedone dissolve completely in acetonitrile, the solution temperature was maintained at 45°. Dropwise addition of the dark red solution to the concentrated dimedone solution initially resulted in colorless solution. However, the solution gradually turned to yellow, followed by pale red as the addition was continued. Therefore, the addition was stopped just before color change to pale red and thus compound **1** was obtained from the yellow solution. These series of rapid color changes during the addition suggest that the reactions between two reactants are fast although it is difficult to identify any color change from the other addition process, *i.e.*, addition of dimedone to thioxanthylum ion in acetonitrile.

UV Studies. UV spectra of **3** recorded in acetonitrile with various content of water showed three isosbestic points at 219, 289, and 348 nm (*Fig 1*).

These changes in absorption spectra indicate that compound **3** is in equilibrium with compound **2** in aq acetonitrile in which equilibrium constant depends upon the concentration of water. Since compound **3** has delocalizable π electrons in it, changes of intensity in absorp-

Table 1. UV data of 3 in various solvents.

Solvents	λ_{max} (loge) nm
CH ₃ CN ^a	225 (sh., 4.23), 251 (sh., 4.00), 265 (4.15), 297 (3.91), 378 (3.62)
<i>t</i> -BuOH ^b -CH ₃ CN (29%, v/v)	226 (sh., 4.20), 251 (sh., 4.00), 265 (4.16), 292 (3.95), 378 (3.61)
95% EtOH ^c -CH ₃ CN (29%, v/v)	251 (sh., 4.18), 262 (4.26), 291 (3.92), 378 (3.06)
MeOH ^d -CH ₃ CN(29%, v/v)	254 (4.37), 265 (4.30), 292 (3.87), 362 (2.88), 382 (2.88)
95% EtOH	250 (sh., 4.15), 265 (4.23), 291 (3.88), 380 (2.20)
<i>n</i> -Hexane ^e	226 (sh., 4.26), 251 (4.23), 262 (4.28), 286 (sh., 3.99), 360 (3.53)

The following numbers are dielectric constants which are from J.A. Riddick and W.B. Bunger, *Organic Solvents*, 3rd ed., Vol. II of A. Weissberger, Ed., *Techniques of Chemistry*, Wiley-Interscience, New York, 1970. ^a37.5(20°C) ^b12.47(25°C) ^c24.55 (25°C) ^d32.70(25°C) ^e1.88(25°C).

tions as well as peak positions are anticipated depending upon the nature of the solvents. The following Table 1 shows the absorption maxima of 3 in various solvents.

The UV spectrum shows an absorption with a shoulder at about 225 nm which starts from 242 nm in acetonitrile, 241 nm in *t*-BuOH-

CH₃CN (29%), 238 nm in EtOH-CH₃CN (29%), 237 nm in MeOH-CH₃CN(29%), 238 nm in 95% EtOH, and 240 nm in *n*-hexane. The intensity increases continually beyond 200 nm regardless of the solvents used. Of the absorption peaks, a noticeable spectral change was observed in the range of 360 to 380 nm. That is, the position of an absorption shifted to shorter wavelength with increase of nonpolarity of the solvent. In addition, the intensity of the absorption at 380 nm in ethanol diminished drastically compared with that either at 378 nm in acetonitrile or at 360 nm in hexane. These spectral changes suggest that certain canonical form of 3 among others contributes more than the others of which importance depends on the solvents used.

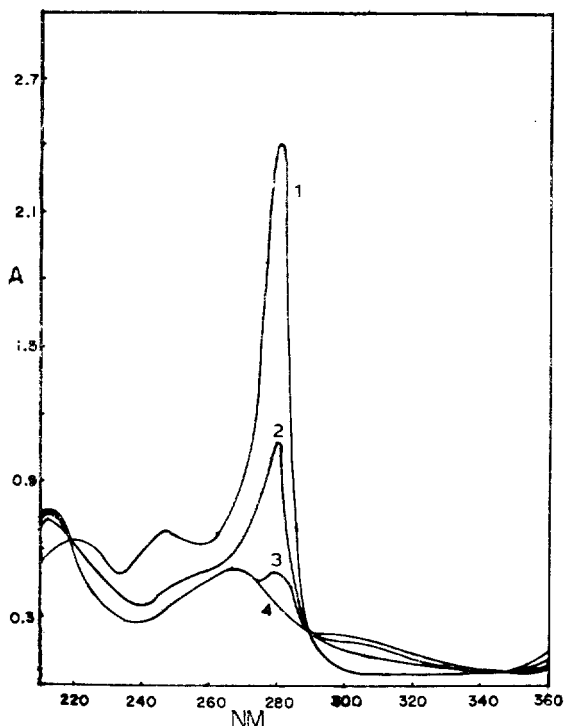
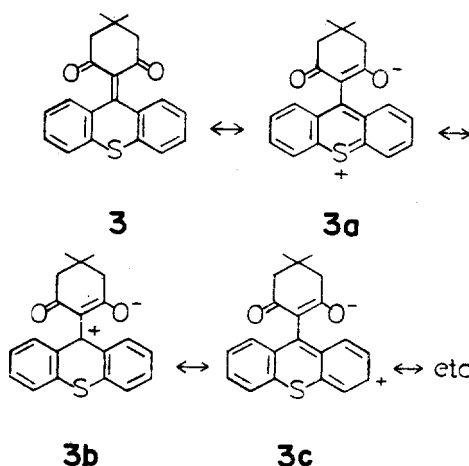
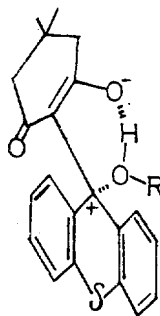


Fig. 1. Electronic absorption spectral changes of 2. 1. in dry acetonitrile. 2. in 1.6% water in acetonitrile 3. in 3.1% water in acetonitrile. 4. in 4.6% water in acetonitrile.



According to the general rule in which the more polar a solvent is the better is the polar form stabilized, Hence the polar forms, *i.e.*, **3a**, **3b**, **3c**, represent better for the compound in acetonitrile or ethanol, whereas **3** does in *n*-hexane. In fact, 9-benzylidene-thioxanthene^b which has a chromophore analogous to **3** as far as C=C bond connecting to thioxanthene ring is concerned showed an absorption at 345 nm in ethanol. Similarly, 9-phenyl- and 9-methylthioxanthylum ion¹ as well as **2** which are analogous to **3a** in the same sense as in the case of **3** showed an absorption at 383 and 375 nm in acetic acid containing 1% perchloric acid, respectively.

However, of three polar forms, **3a** is more important than others in view of the diminished intensity in hydroxy polar solvents. As can be seen in Table 1, the intensity of the absorption near 380nm decreases in the order of *t*-BuOH-CH₃CN (29%) > EtOH-CH₃CN (29%) > MeOH-CH₃CN (29%) > EtOH. If absorption is due to the contribution of **3a**, an increase in the intensity is expected in MeOH-CH₃CN system compared with EtOH-CH₃CN system. Similarly, EtOH-CH₃CN system is expected to give higher intensity than in *t*-BuOH-CH₃CN system. This is opposite to the observed results. The drastic decrease in intensity in ethanol coupled with the trend mentioned above clearly shows the participation of alcohol in stabilizing **3b** by forming hydrogen bond and interaction between the positive center and nonbonding electrons on alcoholic oxygen atom as shown below. This speculation is also supported by the intensity in *t*-BuOH-CH₃CN which is essentially the same as that in acetonitrile. In other word, *t*-BuOH is a weaker hydrogen bond doner than either ethanol or methanol and also has a bulky group so that stabilization of **3b** with *t*-BuOH by forming a six-membered



cyclization is not expected **3b** with *t*-BuOH by forming a six-membered cyclization is not expected to occur.

In MeOH-CH₃CN system, stabilization of **3b** by forming cyclization is expected to be even more accessible than in EtOH-CH₃CN system. Consequently higher intensity than in EtOH-CH₃CN is observed. It is noteworthy that two broad absorptions, *i.e.*, 362 and 382 nm, are observed only in MeOH-CH₃CN. A broad peak in other systems is believed to be overlapped peaks of the corresponding peak.

¹H NMR Studies

A prominent result in ¹H NMR data of **1**, **2** and **3** is rather large differences in chemical shift of methylene protons, *i.e.*, 2.45, 2.90, 2.73 and an observation of an enolic proton signal of **1** at 10.49 ppm. Therefore, enolic form is better representation for this compound. However, an enolic proton signal was not observed from **2**. Instead, a multiplet corresponding to 9 hydrogens was observed. So the keto form may be a proper representation for the compound **2**. The down field shift of methylene proton signal of **2** compared with that of **1** can be rationalized by the inductive electron-withdrawing effect of positive sulfur atom.

In the case of **3** in which CDCl₃ was used as a solvent because of the solubility problem, methylene proton signal appeared at 2.73 ppm which is larger value than 2.45 ppm of **1** but

smaller value than 2.90 ppm of **2**. These chemical shift differences in **3** might be somehow due to the contribution of **3a** in chloroform. This possibility warrants further study.

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