STUDIES ON
SYNTHESES OF NOVEL HETEROCYCLES
BY USE OF TRINITROQUINOLONE

トリニトロキノロンを用いた
新規な複素環化合物の合成に関する研究

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2006

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Preface

The studies presented in this thesis have been carried out under the guidance of Professor Kiyomi Kakiuchi at Nara Institute of Science and Technology during 2004-2006 and Professor Masahiro Ariga and Associate Professor Nagatoshi Nishiwaki at Osaka Kyoiku University during 1997-1998 and 2002-2006.

This thesis deals with effective and convenient methodologies for functionalization of the 1-methyl-2-quinolone skeleton using high reactivity of 1-methyl-3,6,8-trinitro-2-quinolone. The results and findings obtained through this work are expected to develop the chemistry of both quinolone and nitro compounds. In the present work, new unnatural 1-methyl-2-quinolone derivatives were synthesized, which enables the preparation of more versatile quinolone derivatives. This basic work will contribute to development of novel functional materials containing 1-methyl-2-quinolone framework.

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March 2006

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General Introduction

Numerous natural products have been isolated, and their structural determination and total syntheses have been performed as one of the main parts of organic chemistry. These compounds are classified, on the basis of their structural features, into alkaroids, terpenes, steroids, sugars, flavonoids, polyketides, aromatics and so on. Because most natural products have biological activity, they have been used for medicinal or agricultural purposes. Furthermore, most natural products contain heterocyclic frameworks, which developed heterocyclic chemistry together with chemistry of natural products.

To discover novel biologically active compounds, it is necessary to evaluate profiles of versatile organic or inorganic compounds that are obtained by chemical syntheses. From this viewpoint, it is highly important to find a useful scaffold leading to various kinds of compounds, which enables the construction of a new chemical library for medicinal chemistry. In addition, there is a need to develop a new methodology for direct functionalization of heterocyclic compounds with easy experimental manipulations under mild conditions.

The 1-methyl-2-quinolone skeleton is often found in more than 300 quinoline alkaloids that are mainly isolated from the Rutaceae family of plants.[1-17] Naturally occurring 1-methyl-2-quinolone derivatives are of current research interest because they show a wide range of biological activities,[6,18] such as cytotoxic,[19] antiparasitic[20] and antitumor[21] activities, and many of theses derivatives are functionalized at the 3-position[6] and/or the 4-position[18-21] of the 1-methyl-2-quinolone skeleton. In pharmacological and physiological chemistry, recent attention has been paid to synthesis of novel unnatural 1-methyl-2-quinolone derivatives for construction of a highly valuable library of

compounds.[22-35]
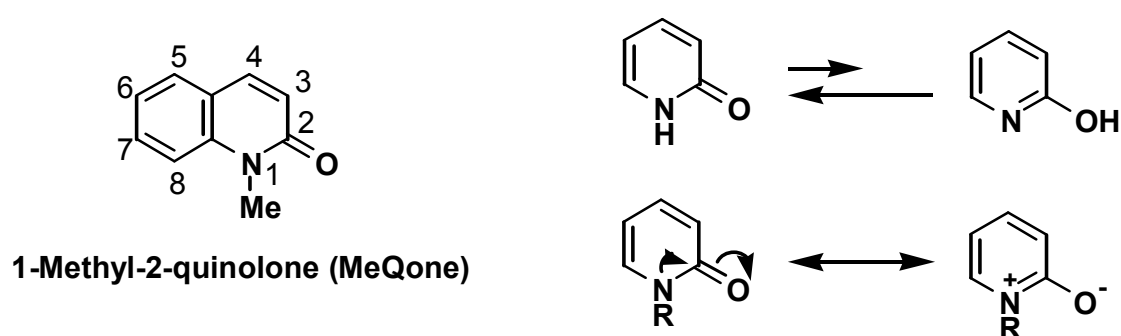
Figure 1. Tautomeric and Resonance Structures of 2-Pyridones

The 1-methyl-2-quinolone skeleton is composed of the pyridone moiety and the benzene skeleton. Because *N*-unsubstituted 2-pyridone has the tautomeric structures, 2-pyridone and 2-pyridinol, it reveals aromaticity. Although *N*-substituted pyridine does not have tautomeric structures, it also shows some aromaticity due to the contribution of the resonance structures illustrated in Figure 1.[36] Hence, all 1-methyl-2-quinolone derivatives should be treated as aromatic compounds.

The aromatic property of the quinolone ring prevents a nucleophilic functionalization[37-39], and an electrophilic functionalization[40-42] is also difficult because the ring nitrogen and the adjacent carbonyl group decrease the electron density of the whole quinolone ring. Thus, the functionalization of the 1-methyl-2-quinolone skeleton has not been easily achieved,[43, 44] and there is a high demand to develop facile methods for chemical modification. In general, the 1-methyl-2-quinolone ring is often activated by electron-donating hydroxyl[45-52] or amino[53] groups for introduction of a new substituent at the adjacent position, and then a construction of a new ring on the pyridone ring is performed by condensation between these substituents.[54-62] This methodology is

used for synthesizing both natural and unnatural 1-methyl-2-quinolone derivatives, however, it sometimes needs multi-step reactions for pre-introduction of the activating group.

On the other hand, Fujita and co-workers employed electron-withdrawing groups for activation of the 1-methyl-2-quinolone framework.[63]　They used 1-methyl-2-quinolone derivatives having an electron-withdrawing group at the 3- or the 4-positions, which underwent Diels-Alder reactions[64] with electron-rich dienes (Scheme 1).[65]　Although this methodology enables the C-C bond formations simultaneously at the 3- and 4-positions of 1-methyl-2-quinolone, several problems should be overcome such as severe reaction conditions and low yields of cycloadducts.

90 ℃, 10 kbar, **0-78 %**
160-200 ℃, atmospheric, **5-98 %**

EWG = electron-withdrawing group
EDG = electron-donating group
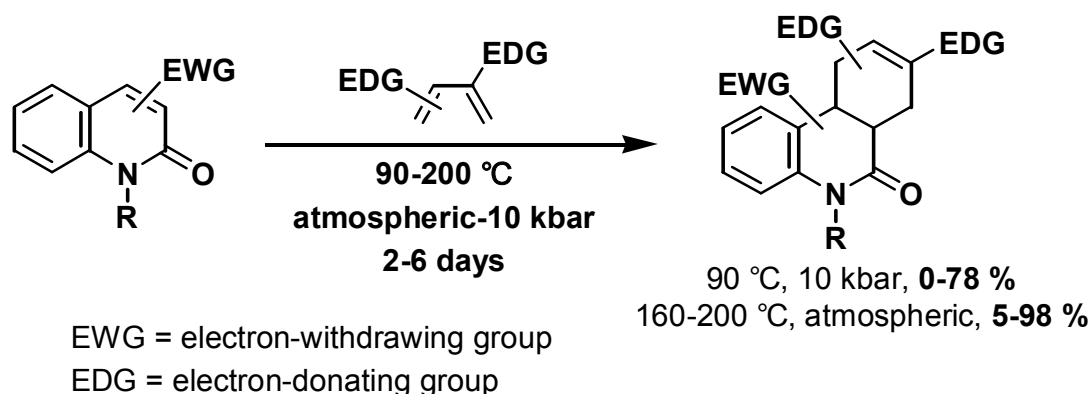
Scheme 1. Diels-Alder Reaction of 1-Methyl 3- or 4-Substituted 2-Quinolone

Meanwhile, our research group has paid attention to 1-methyl-2-quinolone derivatives activated by nitro groups. 1-Methyl-3,6,8-trinitro-2-quinolone (**TNQ-Me**) is readily prepared by nitration of 1-methyl-2-quinolone (**MeQone**) with fuming nitric acid.　When **TNQ-Me** is allowed to react with 1,3-dicarbonyl compounds in the presence of triethylamine

(NEt$_3$) in ethanol (EtOH), regioselective C-C bond formation proceeds at the 4-position accompanied by loss of a nitro group at the 3-position, which is called *cine*-substitution (Scheme 2).[66] However, reactions of **TNQ-Me** with other nucleophiles have not been studied at all.   I believe that the present *cine*-substitution will be an effective method for regioselective introduction of various functionalities to the 1-methyl-2-quinolone skeleton.   Furthermore, modification at the 6- and the 8-positions is possible via diazotization because nitroquinolones are readily reduced to aminoquinolones chemoselectively.[58] Therefore, **TNQ-Me** should be an excellent scaffold for the construction of extensive libraries consisting of various unnatural 1-methyl-2-quinolone derivatives.
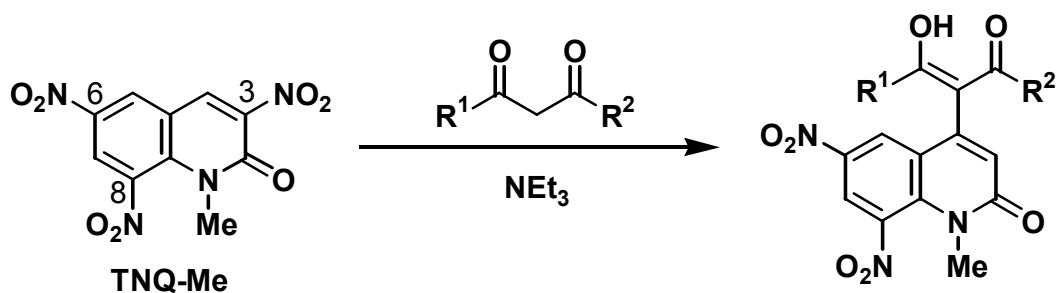
Scheme 2. *cine*-Substitution of **TNQ-Me**

In the present work, I studied methods of synthesizing various kinds of unnatural 1-methyl-2-quinolone derivatives starting from **TNQ-Me**. Furthermore, a study on the relationship between structure and reactivity of nitroquinolones was performed.   In Chapter 1, the electrophilicity of **TNQ-Me** is estimated upon treatment with amines, and C-N bond formation on the 1-methyl-2-quinolone skeleton is attempted.   In Chapter 2, introduction of the acylmethyl group is performed by conducting *cine*-substitution with enamine or

ketone. Electrophilic arylation is noted in Chapter 3, in which **TNQ-Me** is allowed to react with phenoxides. In Chapter 4, I consider the reasons why **TNQ-Me** shows high reactivity from the viewpoint of steric hindrance between the 1-methyl and the 8-nitro groups. Chapter 5 deals with cycloaddition of **TNQ-Me** leading to polycyclic quinolones, in which **TNQ-Me** behaves as both heterodiene and dienophile in the same reaction system.

CHAPTER 1.   Effective C-N Bond Formation and Dimerization
of the 1-Methyl-2-quinolone Skeleton

1-1. Introduction

1-Methyl-3,6,8-trinitro-2-quinolone (**TNQ-Me**) has been shown to have high reactivity, which causes the *cine*-substitution to afford 4-substituted 6,8-dinitro-2-quinolone upon treatment with 1,3-dicarbonyl compounds under basic conditions.[66]   This reaction is a useful protocol for regioselective functionalization of the 1-methyl-2-quinolone skeleton at the 4-position accompanied by the C-C bond formation.   It is reasonable to believe that the C-N bond formation will be possible when amines are employed as the nucleophile.

In this chapter, reactions of **TNQ-Me** with amines were performed to introduce amino groups at the 4-position regioselectively.   If the *cine*-substitution proceeds similarly to the reaction with 1,3-dicarbonyl compounds, the useful precursors for novel unnatural 1-methyl-2-quinolone derivatives will be obtained as the resultant products.[25a-d, 18b, 33, 37, 38a-b, 39, 60, 67] Because conventional strategies for construction of the aminoquinolone framework[37, 38a,b, 39, 58, 60, 67, 68] require multi-step reactions, the present C-N bond formation will afford a new methodology for direct introduction of an amino group into the methylquinolone framework in a single step.

1-2. Results and Discussion
## 1-2-1. Reactions of TNQ-Me with Primary Amines
a) Formation of Ammonium Dihydroquinolone-3-nitronate

As the first stage, the reaction of **TNQ-Me** with primary amines was

studied.   In the present study, it was necessary to employ highly polar solvents for dissolving **TNQ-Me**.   In addition, less nucleophilic and aprotic solvents should be used to avoid competitive side reactions.   Among several kinds of polar solvents, acetonitrile was found to be the most suitable solvent because it has the lowest boiling point, making it easier to use.

When propylamine was added to a solution of **TNQ-Me** in acetonitrile at room temperature, the solution immediately turned to reddish yellow and precipitates appeared after several minutes.   In the ^{1}H NMR of the product, three singlet signals were observed at 2.96, 8.40 and, 8.56 ppm respectively, however the other signals were significantly broadened.   The chemical shifts and the integral values for each signal indicate that two equivalents of propylamine reacted with **TNQ-Me**, one of which formed ammonium ion.   On the basis of these facts and other information, the product was determined to be propylammonium 4-propylaminoquinolone-3-nitronate **3b**.

A plausible mechanism for the formation of nitronate **3b** is illustrated in Scheme 3.   The first propylamine adds at the highly electrophilic 4-position of **TNQ-Me** to give an adduct intermediate **1b**, and then the intramolecular proton transfer affords dihydroquinolone **2b**.   Since the hydrogen at the 3-position (H_a) is highly acidic, deprotonation by the second amine occurs easily and leads to ammonium salt **3b**.   As another route, direct conversion from **1b** to **3b** is also possible.

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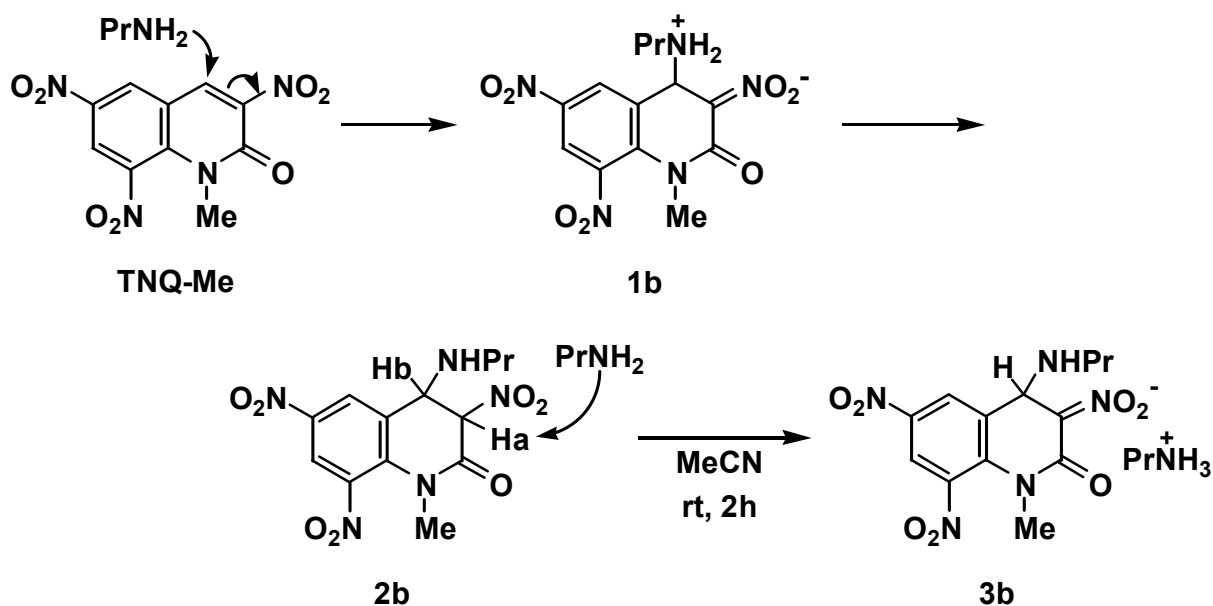
Scheme 3. A Plausible Mechanism for Formation of **3b**

This reaction was applied to other primary amines. Methylamine and butylamine readily reacted with **TNQ-Me** to furnish ammonium salt **3a** and **3c** in excellent yields. Even though sterically hindered amines, such as isopropylamine, isobutylamine, *sec*-butylamine, *tert*-butylamine and benzylamine were used, corresponding ammonium salts **3d-h** were obtained in good yields, respectively (Table 1). Versatile alkylamino groups could be introduced at the 4-position of **TNQ-Me**. This reaction is a new regioselective functionalization method accompanied by the C-N bond formation.

Table 1. Preparation of Ammonium Salt **3**
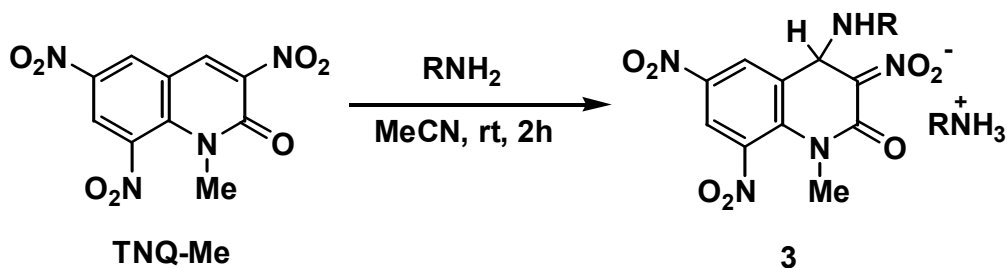
R	Product	Yield / %
Me	**3a**	91
Pr	**3b**	71
Bu	**3c**	quant
i-Pr	**3d**	79
i-Bu	**3e**	74
sec-Bu	**3f**	56
tert-Bu	**3g**	74
PhCH$_2$	**3h**	79

b) Synthesis of 4-Aminoquinolone

In the last section, ammonium nitronates **3** were isolated. In order to use these compounds for further functionalization, it is necessary to aromatize the pyridone ring. In this section, the reactions of **TNQ-Me** with amines were conducted at elevated temperature to eliminate nitrous acid.

When **TNQ-Me** was treated with propylamine under reflux conditions, 6,8-dinitro-1-methyl-4-propylamino-2-quinolone (**4b**), a *cine*-substitution product, was obtained despite in 36% yield (Table 2). Isobutylamino derivative **4e** was also prepared in 29% yield in a similar way. On the other hand, **4f** and **4g** were not formed in cases of more bulky amines such as *sec*-butylamine and *tert*-butylamine.

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Table 2. Preparation of *cine*-Substitution Product **4**
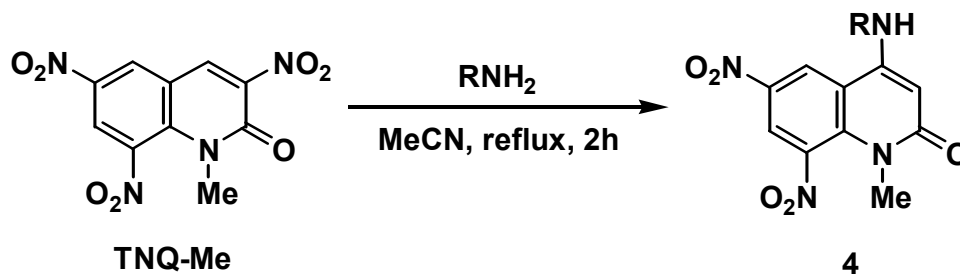
R	Product	Yield / %
Pr	**4b**	36
i-Bu	**4e**	29
sec-Bu	**4f**	0
tert-Bu	**4g**	0

At room temperature, the deprotonation at the 3-position of dihydroquinolone intermediate **2** by the second amine easily occurs leading to ammonium salt **3** with equilibrium between dihydroquinolone **2** and ammonium salt **3** (Scheme 4, path a). On the other hand, at elevated temperatures the *cine*-substituted quinolones **4b** and **4e** are produced by the elimination of nitrous acid from the 3- and the 4-positions (Scheme 4, path b), in which the second molecule of the amine might enable the deprotonation of H_b at the 4-position, and aromatization of the pyridone ring might proceed accompanied by the elimination of nitrous acid. On the contrary, sterically hindered alkylamino groups might prevent deprotonation at the geminal position (H_b), nevertheless the reactions are conducted at elevated temperatures. Thus, the reverse reaction might proceed preferably to cause the elimination of substrate from Meisenheimer complex **1**, recovering **TNQ-Me**. In the cases of *sec*-butylamine and *tert*-butylamine, it was speculated that these amines added to **TNQ-Me** generating Meisenheimer

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complexes **1** in situ which were confirmed by discoloration of the reaction solution to reddish yellow.
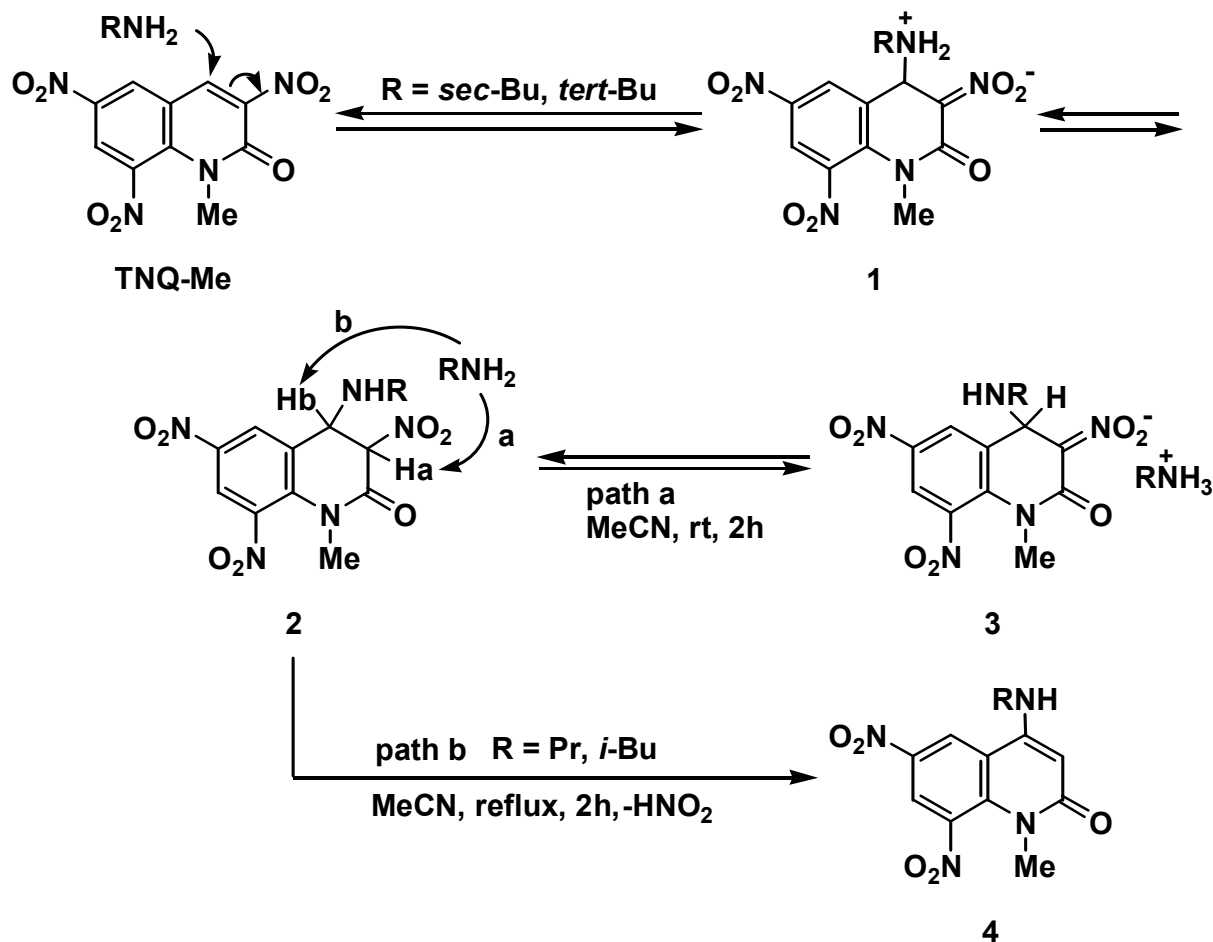
Scheme 4. A Plausible Mechanism for Formation of **4**

1-2-2. Reactions of TNQ-Me with Tertiary Amine

a) Denitration and Dimerization of TNQ-Me

As a result of investigation of how **TNQ-Me** reacts with primary amines, both electrophilicity and high reactivity of **TNQ-Me** resulted were obtained. In the present section, less nucleophilic tertiary amines were employed instead of primary ones.

When **TNQ-Me** was allowed to react with tributylamine at room

temperature, 3,4'-bis(1,2-dihydro-6,8-dinitro-1-methyl-2-oxoquinolyl) (**5**) and 6,8-dinitro-1-methyl-2-quinolone (**6,8-DNQ**) were afforded in 81% and 6% yields, respectively (Table 3). In the ^{1}H NMR of dimer **5**, two singlet signals were observed, at 7.06 and 8.56 ppm, in addition to two pairs of doublets (H5, H7, H5' and H7' protons) and two singlets (*N*-methyl groups). This observation revealed that a couple of 1,2-dihydro-6,8-dinitro-1-methyl-2-oxoquinolyl groups were connected at the 3- and the 4'-positions. Analytical and other spectral data (IR, MS, ^{13}C NMR) also supported this dimeric structure. The structure of **6,8-DNQ** was confirmed by comparison of spectral data with those of an authentic sample.[69, 70]

Isolated dimer **5** is stable under heated conditions (at 60 °C, in the presence of tributylamine), and no conversion to **6,8-DNQ** was observed. Furthermore, **6,8-DNQ** and tributylamine caused no coupling reaction at room temperature. Since interconversion between **5** and **6,8-DNQ** did not occurred, these products were formed in different pathways.

The ratio of products (**5** / **6,8-DNQ**) varied with the reaction conditions, as summarized in Table 3. In each case, **TNQ-Me** was quantitatively consumed with no byproducts being detected except for entry 3 condition, and **6,8-DNQ** was predominantly formed under heated conditions (entry 3). Dilution revealed significant efficiency in prevention of the dimerization, and **6,8-DNQ** was afforded in a good yield (entries 5 and 6).

When **MeQone** is nitrated by nitric acid, the nitro groups are introduced in the order of 6- > 3- ≧ 8-positions, which results in formation of four nitrated 1-methyl-2-quinolones, namely 6-nitro, 3,6-dinitro, 6,8-dinitro and 3,6,8-trinitroquinolones.[69] Because the separation of these quinolones is troublesome due to their similar physical properties, it is not effective to prepare

6,8-DNQ directly by nitration of **MeQone**. From this viewpoint, the present regioselective denitration reaction of **TNQ-Me** is concluded to be an effective route affording **6,8-DNQ** because **TNQ-Me** is prepared in an excellent yield from **MeQone**.

Table 3. Reactions of **TNQ-Me** with NBu$_3$ under Various Conditions
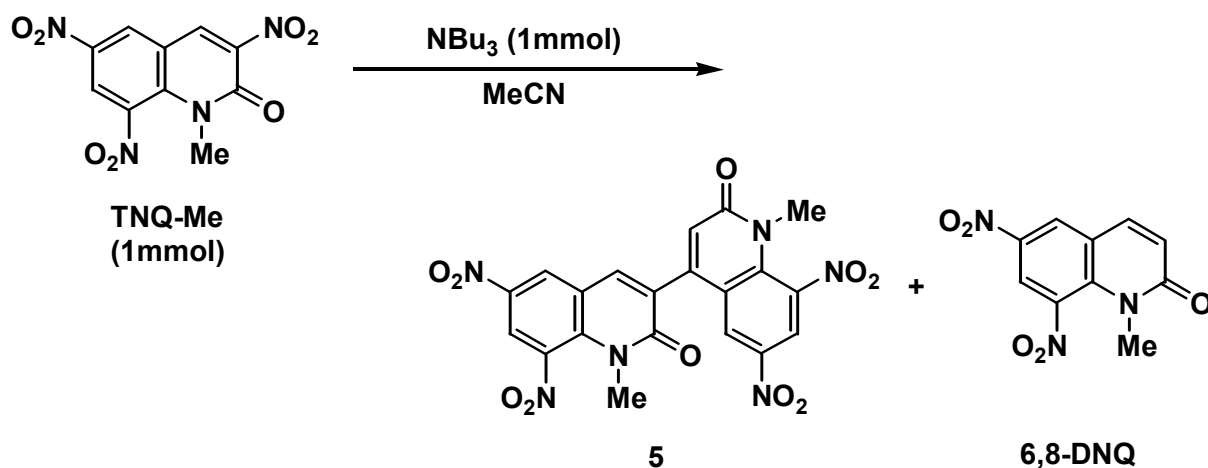
| Entry	Temp. (°C)	Solv. (mL)	Time (d)	5 / 6,8-DNQ[a,b]	Yield (%)[c] 5[b]	Yield (%)[c] 6,8-DNQ
1	rt	10	7	88 / 12	81	6
2	60	10	1	63 / 37		
3	80	10	1	40 / 60[d]		
4	rt	50	7	82 / 18		
5	60	30	1	25 / 75		
6	60	50	1	25 / 75	20	58

a) Determined by ^{1}H NMR, b) Based on **TNQ-Me**, c) Isolated yield,
d) Reaction mixture was somewhat complicated.

b) Studies on the Reaction with Several Kinds of Tertiary Aliphatic Amines

Four kinds of tertiary amines with three of the same alkyl chains were employed, and each reaction mixture was monitored with ^{1}H NMR. In the

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aromatic region, no other signals were observed other than those of **TNQ-Me** and dimer **5**.   Among the amines, there were large differences in reactivity (Figure.2, Table 4, entries 1-3).   The faster reaction rates were in the longer alkyl chains. Specifically, dimerization proceeded at a faster rate in the case of tributylamine than in the cases of tripropylamine and triethylamine.   To the contrary, trimethylamine and tribenzylamine caused no change at all on **TNQ-Me** (entries 4 and 5).   These results show the length of alkyl groups is an important factor for the reactivity of **TNQ-Me** in dimerization.
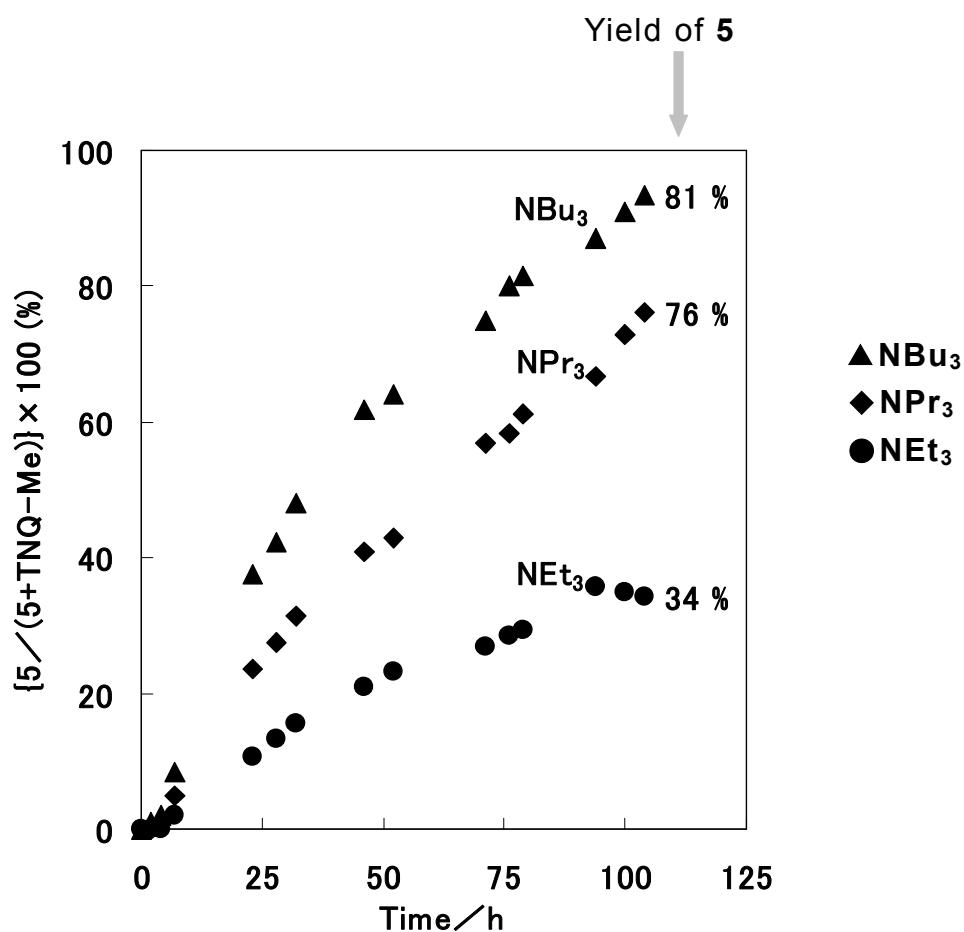
Figure 2. Comparison of Reaction Rates Using Three Amine Homologs

In   order   to   study   this   tendency   in   detail,   alkyldimethylamines

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($NRMe_2$) having only one longer alkyl chain were employed for the following reactions. Butyldimethylamine ($NBuMe_2$) and other $NRMe_2$ underwent dimerization to provide dimer **5**, however, the reaction rates became considerably low (entries 6-9). To our surprise, the reaction of dibutylmethylamine (NBu_2Me) proceeded as effectively as that of tributylamine (NBu_3) (entry 10). Hence, more than two long alkyl chains are found to be necessary for the effective formation of dimmer product **5**.

Table 4. Reaction of **TNQ-Me** with Various Trialkylamines

$$TNQ\text{-}Me \ + \ R^1NR^2_2 \ \xrightarrow[\text{rt, 7d}]{\text{MeCN}} \ 5 \ + \ 6,8\text{-}DNQ \ + \ TNQ\text{-}Me$$

Entry	R^1	R^2	Yield (%) [a]		
			5	**6,8-DNQ**	**TNQ-Me**
1	Bu	Bu	81	6	13
2[b]	Pr	Pr	76	ND	24
3[b]	Et	Et	34	ND	48
4	Me	Me	0	0	quant.
5	PhCH$_2$	PhCH$_2$	0	0	quant.
6	Bu	Me	18	0	82
7	Pentyl	Me	22	0	78
8	*i*-Pentyl	Me	19	0	81
9	Hexyl	Me	31	0	69
10	Me	Bu	79	14	7

a) Determined by ^{1}H NMR, b) 4 days

c) Study on the Mechanism

Since it is well known that trialkylamine ($NR^1R^2R^3$) often behaves as

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the single electron donor in photochemistry,[71] the possibility of single electron transfer was investigated. Dimer **5** and **6,8-DNQ** were both obtained in two cases, in the dark and under UV irradiation. Therefore the present reaction is unrelated to light. The presence of the electron acceptor, anthracene or benzophenone, had no influence on the reaction. Furthermore, **TNQ-Me** was intact to be recovered when metal (sodium, magnesium) and copper(I) salts are used instead of amine. In these experiments, no evidence of single electron transfer from amine to **TNQ-Me** was obtained.

Analysis of byproducts is one of the useful methods for examination of the mechanism. However, it was difficult to separate the products because they each had similar properties. Nevertheless, various trials revealed that *N*-nitrosodibutylamine (**10c**) could be isolated with column chromatography on silica gel. The spectral data of **10c** conforms to those of the authentic sample prepared by nitrosoation of dibutylamine with nitrous acid.[72] Taking this fact into consideration, a plausible mechanism for formation of **6,8-DNQ** is proposed as illustrated in Scheme 3. Tributylamine adds at the electron deficient 4-position of **TNQ-Me** leading to zwitter ion **6c**, from which *β*-elimination proceeds which results in the release of 1-butene to afford dihydroquinolone **7c**. Under heated conditions, **6,8-DNQ** is formed by elimination of both dibutylamino and nitro groups as dibutylnitroamine. When dihydroquinolone **7c** is converted to zwitter ion **8c** by proton transfer from the 3-position to the adjacent dibutylamino group, **8c** reacts with unreacted **TNQ-Me** to cause *cine*-substitution, giving dimer **5** via dihydroquinolone adduct **9c**. Steric hindrance of dimeric adduct **9c** assists in the elimination of nitrous acid and nitroamine, and its bulkiness also prevents further oligomerization. Nitrosoamine **10c** is considered to be a reduced product of nitroamine by nitrous acid. There is also a possibility

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that **10c** is formed by nitrosoation of dibutylamine which is derived from **8c** under equilibrium.

The structure-reactivity relationship of amines is rationalized as follows. The key step of the present reaction is the intramolecular prototropy of zwitter ion **6c** accompanied by elimination of an alkyl chain on the amino group as the alkene (Scheme 5, from **6c** to **7c**). Since trimethylamine and tribenzylamine have no β-hydrogen, only elimination of tertiary amine from the adduct proceeds to give **TNQ-Me** again. In the cases of alkyldimethylamines, the alkyl chain avoids steric repulsion with the adjacent nitro group, and the suitable conformation for β-elimination barely occurs. On the other hand, one of the alkyl chains surely locates nearby the 3-nitro group when the amino group has more than two alkyl groups. Hence, tertiary amine should have proper steric bulk for a smooth reaction (Figure 3). The differences among the reactivities of triethyl-, tripropyl- and tributylamines support this rationalization.
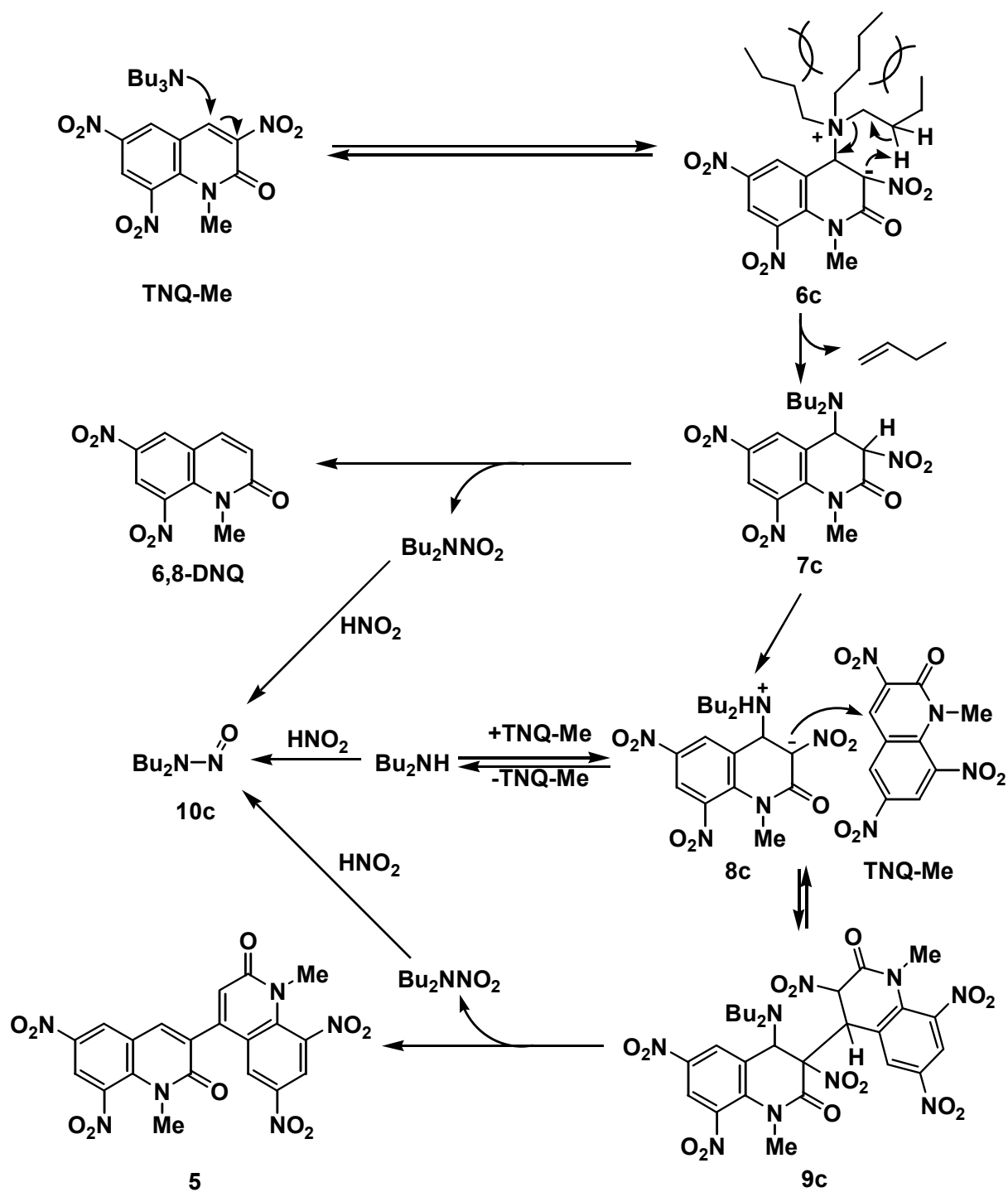
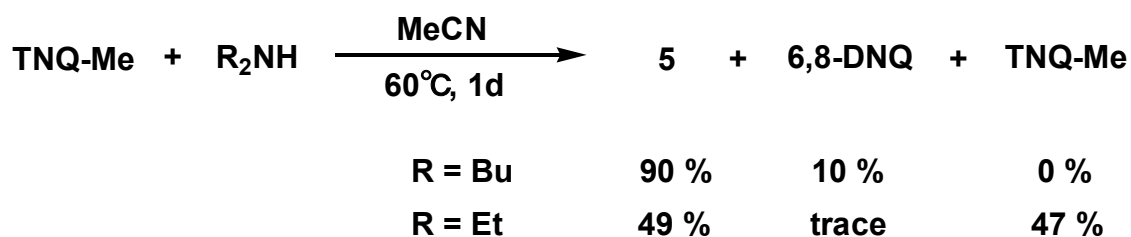**Scheme 5.** A Plausible Mechanism for Formation of **5** Promoted by NBu$_3$
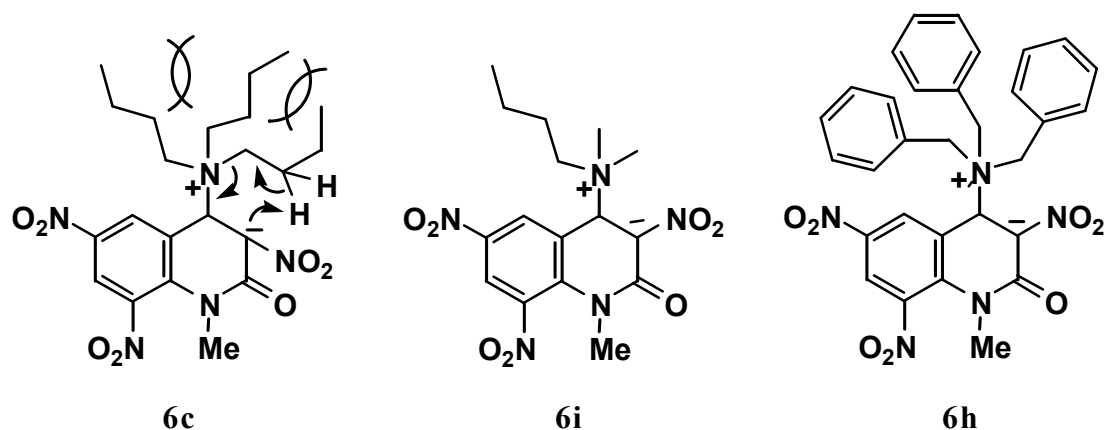
Figure 3. Proper Steric Bulk of Amino Group

1-2-3. Reaction of TNQ-Me with Secondary Amine

As noted above, the reaction of **TNQ-Me** with primary amine affords ammonium salt **3** and that with tertiary amine causes both dimerization and denitration. It is presupposed that reaction of **TNQ-Me** with secondary amine results in both of the reactivities.

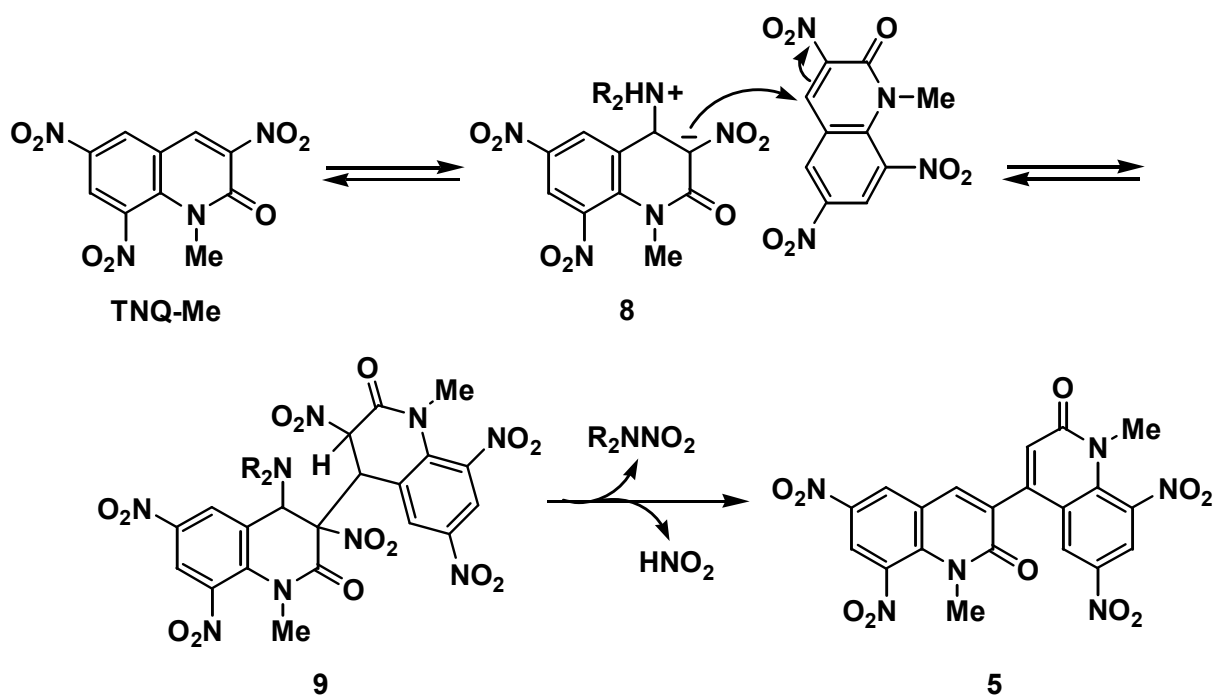### a) Reaction of TNQ-Me with Dialkylamines

The above results encouraged me to employ secondary amines instead of tertiary ones. Importantly, the dimerization of **TNQ-Me** found here was also caused by secondary amine which has two long alkyl chains (Scheme 6). In the case of dibutylamine, conversion from **TNQ-Me** to dimer **5** was smoothly performed. On the other hand, dimer **5** was obtained in a lower yield with recovery of **TNQ-Me** when diethylamine was used. It is interesting that the different chain length of alkyl groups is influential to the reactivity and even diethylamine showed higher reactivity than tertiary amine, such as dimethylbutylamine, that have a long alkyl chain.

$$\text{TNQ-Me} \quad + \quad \text{R}_2\text{NH} \quad \xrightarrow[\text{60}^\circ\text{C, 1d}]{\text{MeCN}} \quad 5 \quad + \quad \text{6,8-DNQ} \quad + \quad \text{TNQ-Me}$$

		5	6,8-DNQ	TNQ-Me
R = Bu		90 %	10 %	0 %
R = Et		49 %	trace	47 %

Scheme 6. Reaction of **TNQ-Me** with Secondary Amines

b) A Plausible Mechanism

As mentioned in the last section, the key step is the β-elimination of an alkylamino group leading to dialkylaminoquinolonium intermediate **8** in the reaction of **TNQ-Me** with tertiary amine. Then, this intermediate **8** adds another **TNQ-Me** to afford dimer **5** accompanied by elimination of nitrous acid and nitroamine (Scheme 5). In the case of secondary amine, quinolonium intermediate **8** is directly formed without the need for β-elimination of the alkyl group (Scheme 7). Since diethylamine also affords the intermediate **8**, it is rationalized that its reactivity is higher than dimethylbutylamine. Although steric hindrance of the dibutylamino group seems to be a disadvantage for addition of **8** to another **TNQ-Me** molecule, the bulkiness is thought to accelerate the elimination of nitrous acid and nitroamine from adduct **9**. Therefore, dibutylamine must have reacted with **TNQ-Me** more effectively than diethylamine to furnish dimer **5**.

**Scheme 7.** A Plausible Mechanism for Formation of **5** Promoted by R₂NH

c) The Reaction of TNQ-Me with Morpholine

In the reaction of **TNQ-Me** with secondary amines, reactivity similar that of tertiary amines was observed, leading to dimer **5** effectively. I considered that the formation of ammonium quinolone-3-nitronate **3** would be possible if bulky secondary amine had rigid structure and less basicity in order to avoid dimerization. Hence, the reaction of **TNQ-Me** with morpholine was investigated.

When **TNQ-Me** was treated with morpholine at room temperature, morpholinium salt **3j** was obtained in 67% yield, which was different from reactions of **TNQ-Me** with dibutylamine or diethylamine (Scheme 8). In order to aromatize this salt to give *cine*-substituted product, more basic triethylamine was added and the reaction mixture was heated to 75°C. The desired reaction proceeded to afford 6,8-dinitro-1-methyl-4-morpholino-2-quinolone **4j** in 67%

yield.　In a series of these reactions, neither denitration nor dimerization occurred.　This is considered to be due to moderate bulkiness of the morpholino group.　As mentioned above, use of morpholine succeeded in forming a C-N bond and introducing a dialkylamino group at the 4-position of 1-methyl-2-quinolone skeleton.
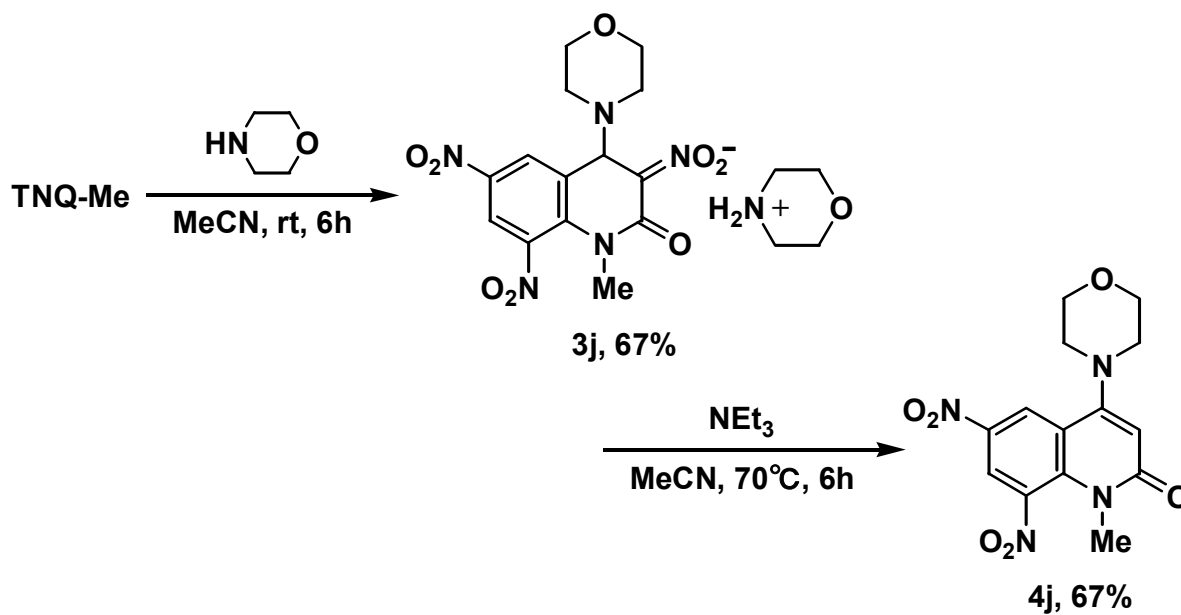

Scheme 8. Reaction of **TNQ-Me** with Morpholine

CHAPTER 2.   Syntheses of

## Unnatural 4-Acylmethyl-1-methyl-2-quinolones

2-1. Introduction

The C-C bond formation is the most fundamental protocol for construction of versatile skeletons. It is important to introduce a functional group as the substituent for further chemical transformation. Although the carbonyl group is valuable function with regard to synthetic utility, introduction of such a function into the 1-methyl-2-quinolone framework is not easy.[41, 42] In particular, direct functionalization of the pyridone moiety is rarely obtained except for a few examples[42-44, 73] because of the low reactivity caused by both the aromaticity[36] and the electron deficiency.

Friedel-Crafts reaction is the most popular procedure to achieve C-C bond formation on the aromatic ring. The acylation of 1-methyl-2-quinolone (**MeQone**) has been studied by Tomisawa.[41] When quinolone is acylated in the presence of sulfuric acid or aluminum chloride, 6-acylated 2-quinolone is obtained in a low yield together with a trace amount of 3-acylated 2-quinolone (Scheme 9).
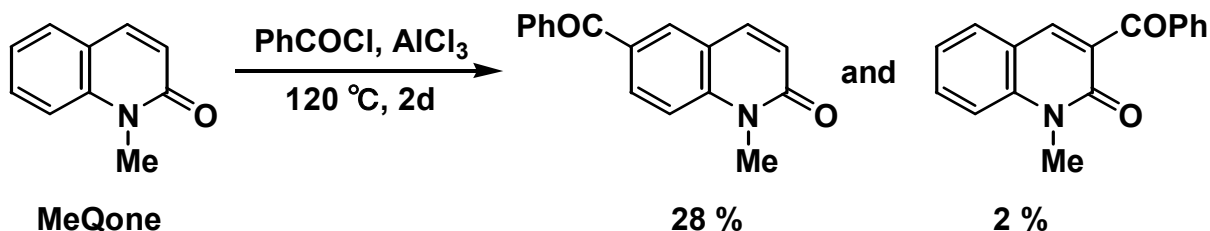

Scheme 9. Friedel-Crafts Rection of **MeQone**

On the other hand, Stadlbauer reported nucleophilic substitution of 4-chloro-1-methyl-3-nitro-2-quinolone with diethyl malonates in the presence of dipotassium carbonate,[38c] which readily proceeded to afford 4-bis(ethoxycarbonyl)methyl-1-methyl-3-nitro-2-quinolone in excellent yield (Scheme 10). It is shown to be effective to introduce both a leaving group and an activating one at the vicinal position, however multi-step synthesis of starting material is required for the present protocol.
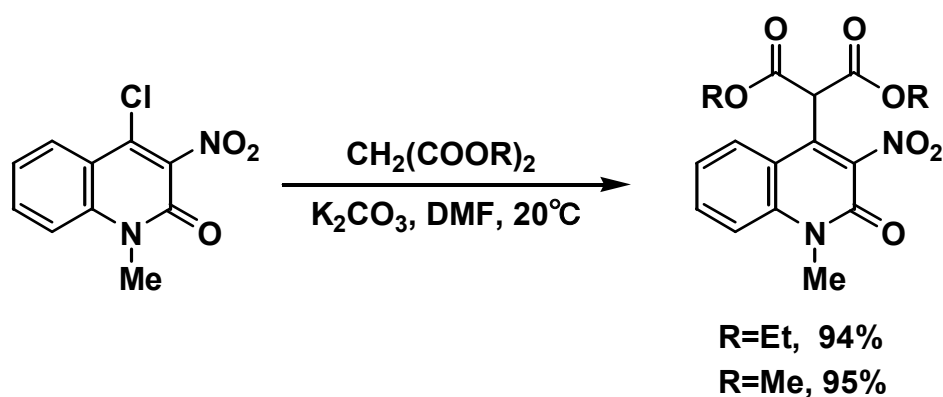
Scheme 10. Nucleophilic Substitution
of 4-Chloro-1-Methyl-2-quinolone Derivative

In light of these limitations, our attention has been paid to the high reactivity of 1-methyl-3,6,8-trinitro-2-quinolone (**TNQ-Me**). **TNQ-Me** readily reacts with 1,3-dicarbonyl compounds in the presence of triethylamine (NEt$_3$) at room temperature to form a C-C bond at the 4-position regioselectively (Scheme 11).[66] During this substitution, an adjacent nitro group at the 3-position is eliminated, called *cine*-substitution. This reaction is thought to proceed via the addition-elimination mechanism, namely nucleophilic addition of the enolate at the 4-position, to afford an adduct intermediate, and the subsequent elimination of nitrous acid accompanied by aromatization leads to *cine*-substituted products, 4-substituted 6,8-dinitro-2-quinolones.
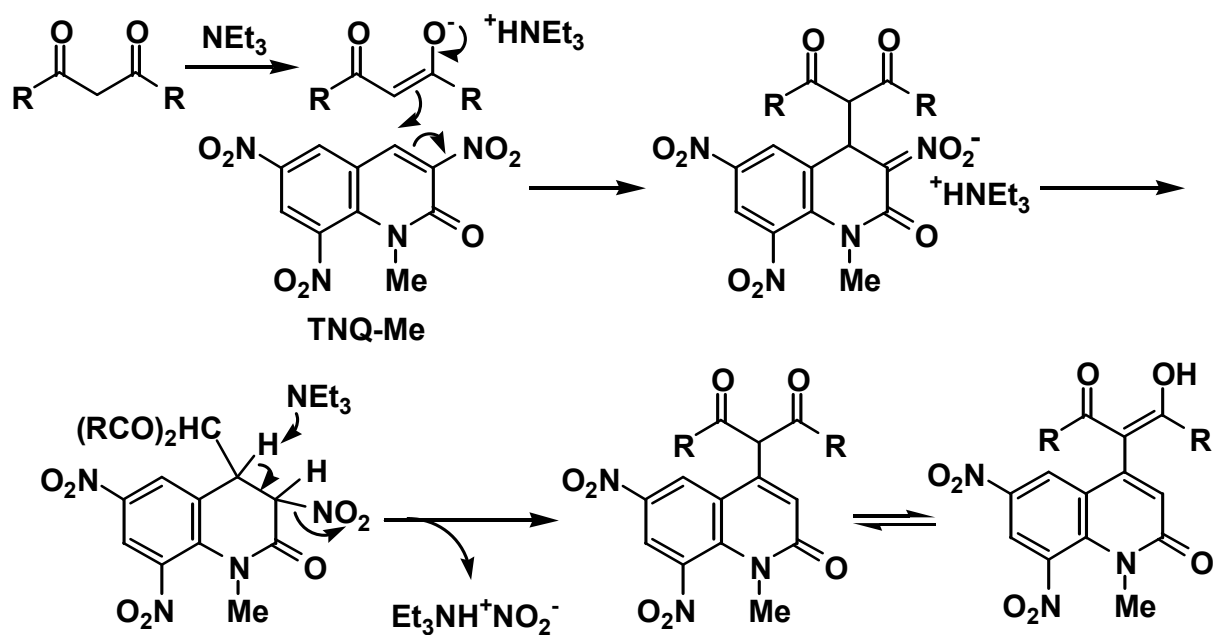
Scheme 11. *cine*-Substitution of **TNQ-Me**

This *cine*-substitution proceeds at room temperature, and only simple experimental manipulations are required. Additional benefits are that **TNQ-Me** is easily prepared by nitration of 1-methyl-2-quinolone with fuming nitric acid in high yield. These features enable the use of **TNQ-Me** as a good precursor for various kinds of 1-methyl-2-quinolone derivatives.

In this chapter, the present *cine*-substitution is applied to other nucleophiles with less reactivity, such as enamines and ketones, instead of 1,3-dicarbonyl compounds in order to improve the synthetic utility of this reaction.

2-2. Results and Discussion

2-2-1. *cine*-Substitution of TNQ-Me with Enamine

Enamines were employed as the carbon nucleophiles for *cine*-substitution of **TNQ-Me**. To a solution of **TNQ-Me** in aqueous acetonitrile,

a solution of 1-morpholino-1-phenylethene (**11a**) in acetonitrile was added at room temperature, and the mixture was stirred for 3 days. 4-Benzoylmethyl-6,8-dinitro-1-methyl-2-quinolone (**12a**) was precipitated as pale yellow powder in 37% yield during the reaction.

In the ^{1}H NMR, a singlet signal at 6.98 ppm appeared in place of the disappearance of a singlet at 9.32 ppm (Figure 4). The former signal was assigned to the proton at the 3-position, and the latter one was assigned to the proton at the 4-position, which means the substitution occurs at the 4-position accompanied by elimination of the adjacent nitro group. Besides signals in the lower field assigned to benzoyl group, a singlet signal of a methylene group was observed at 5.05 ppm. Furthermore, a couple of doublets shifted to a higher field from 9.07 and 9.24 ppm to 8.71 and 8.89 ppm, respectively. These data showed that the benzoylmethyl group was newly introduced at the 4-position of the 1-methyl-2-quinolone skeleton by *cine*-substitution. Analytical and other spectral data (IR, ^{13}C NMR) also supported this structure.
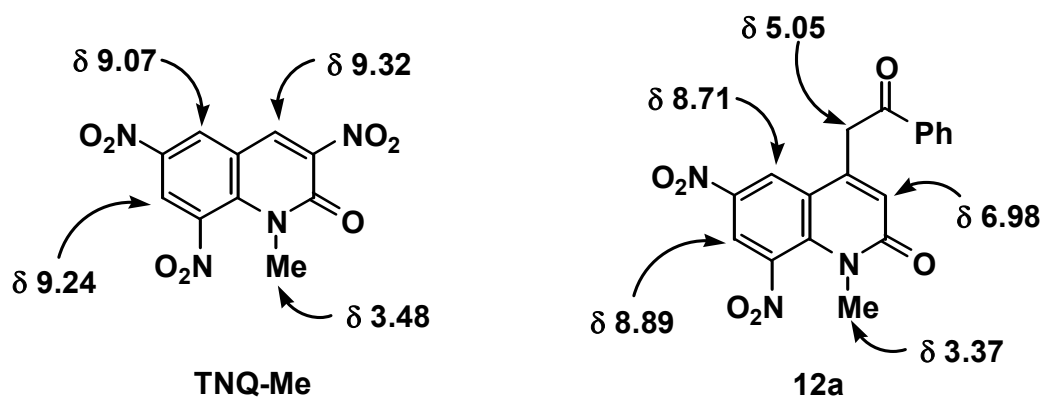

Figure 4. The Chemical Shifts of **TNQ-Me** and *cine*-Substitution Product **12a** measured by ^{1}H-NMR in DMSO-$_{d6}$

The present *cine*-substitution was found to be applicable to enamine, which was converted to a benzoylmethyl group by hydrolysis during the reaction. This result prompted me to employ other enamines for synthesis of various 4-acylmethyl-1-methyl-2-quinolones (Table 5).

When 1-morpholino-1-pheny-l,2-propene (**11b**) was employed, the substituted product **12b** was not detected, and morpholinium salt **13b** was obtained instead (entry 2). In the case of 1-morpholino-1-phenylstylene (**11c**), a similar reaction proceeded to afford morpholinium salt **13c** in an excellent yield (entry 3). Cyclic enamine **11d** also reacted with **TNQ-Me** to give corresponding salt **13d** (entry 4). These reactions were considerably affected by steric hindrance at the *β*-position of enamines, namely the presence of substituent R^2. Enamine **11e** derived from aldehyde was more reactive and lead to salt **13e** in an excellent yield within a short reaction time even though **11e** had two methyl groups at the reaction site (entry 5). In this reaction a new C-C bond was formed at the 4-position regioselectively on the methylquinolone skeleton to afford novel 4-acylmethylquinolones **12** and **13**.

When morpholinium salt **13b**, **13c**, and **13e** were treated with hydrochloric acid in acetonitrile, dihydroquinolones **14b**, **14c**, and **14e** were isolated in excellent yields (Table 6). The reverse conversion from dihydroquinolone **14** to morpholinium salt **13** was also possible upon treatment of **14** with morpholine. When equimolar amounts of morpholine was added to a solution of dihydroquinolone **14b** in deuterated chloroform, regeneration of **13b** was confirmed in the ^{1}H NMR in which the signal of the 3-position disappeared (Scheme 12, Chart 1).

Table 5. Preparation of *cine*-Substitution Product **12** and Morpholinium Salt **13**
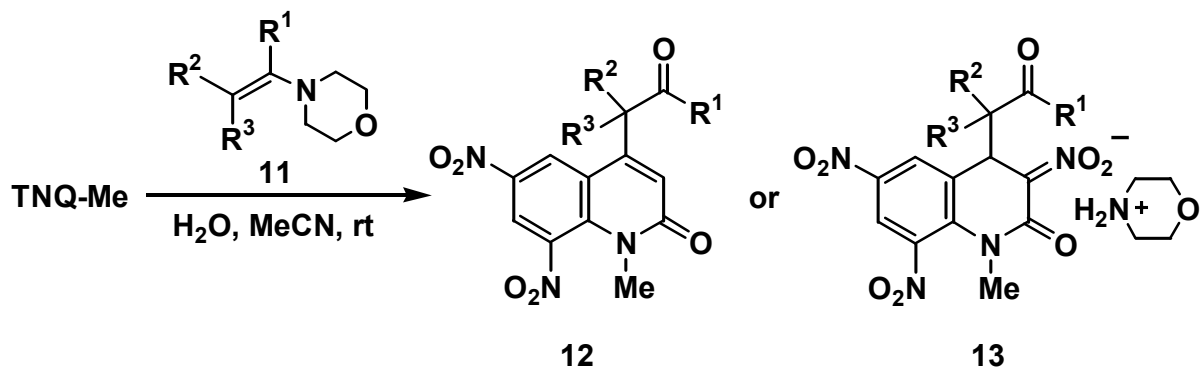
Entry	R^1	R^2	R^3	Time/d	Product	Yield/%
1	Ph	H	H	3	**12a**	37
2	Ph	Me	H	3	**13b**	43
3	Ph	Ph	H	1	**13c**	98
4	-(CH$_2$)$_3$-		H	2	**13d**	40
5	H	Me	Me	0.5	**13e**	98

Table 6. Acidification of Morpholinium Salt **13**
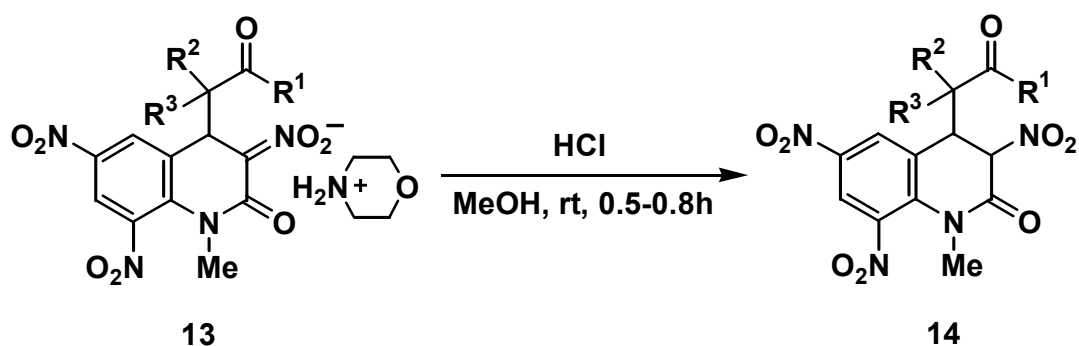
Entry	R^1	R^2	R^3	Product	Yield/%
1	Ph	Me	H	**14b**	69
2	Ph	Ph	H	**14c**	97
3	H	Me	Me	**14e**	99
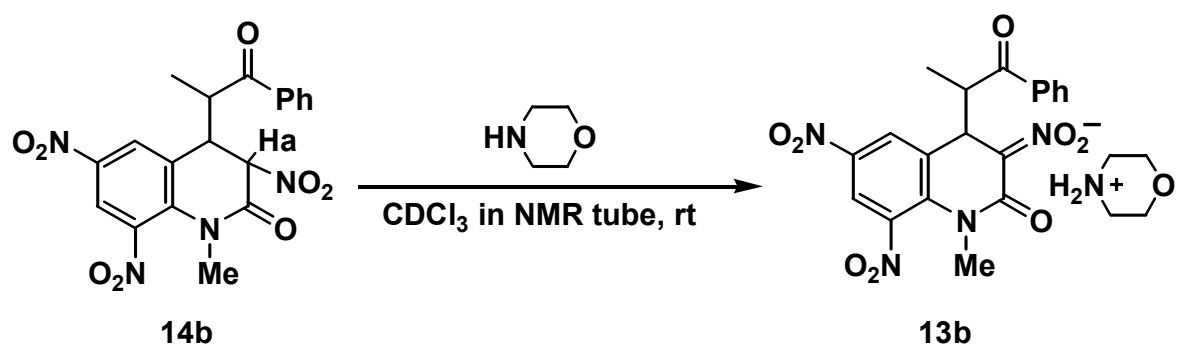
Scheme 12. The Conversion from Dihydroquinolone **14** to Morpholinium Salt **13**
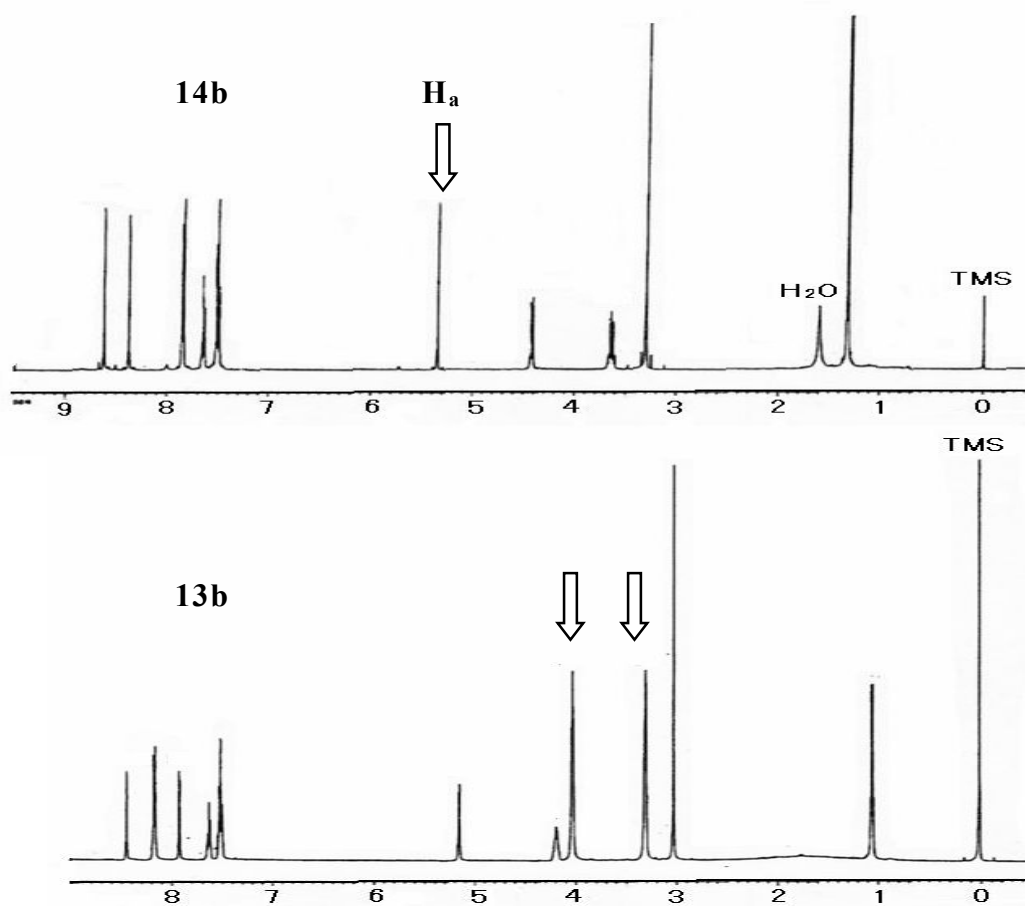
Chart 1. ^{1}H NMR spectra of **13b** and **14b** in $CDCl_3$

2-2-2. A Plausible Mechanism for the Reactions of TNQ-Me with Enamines

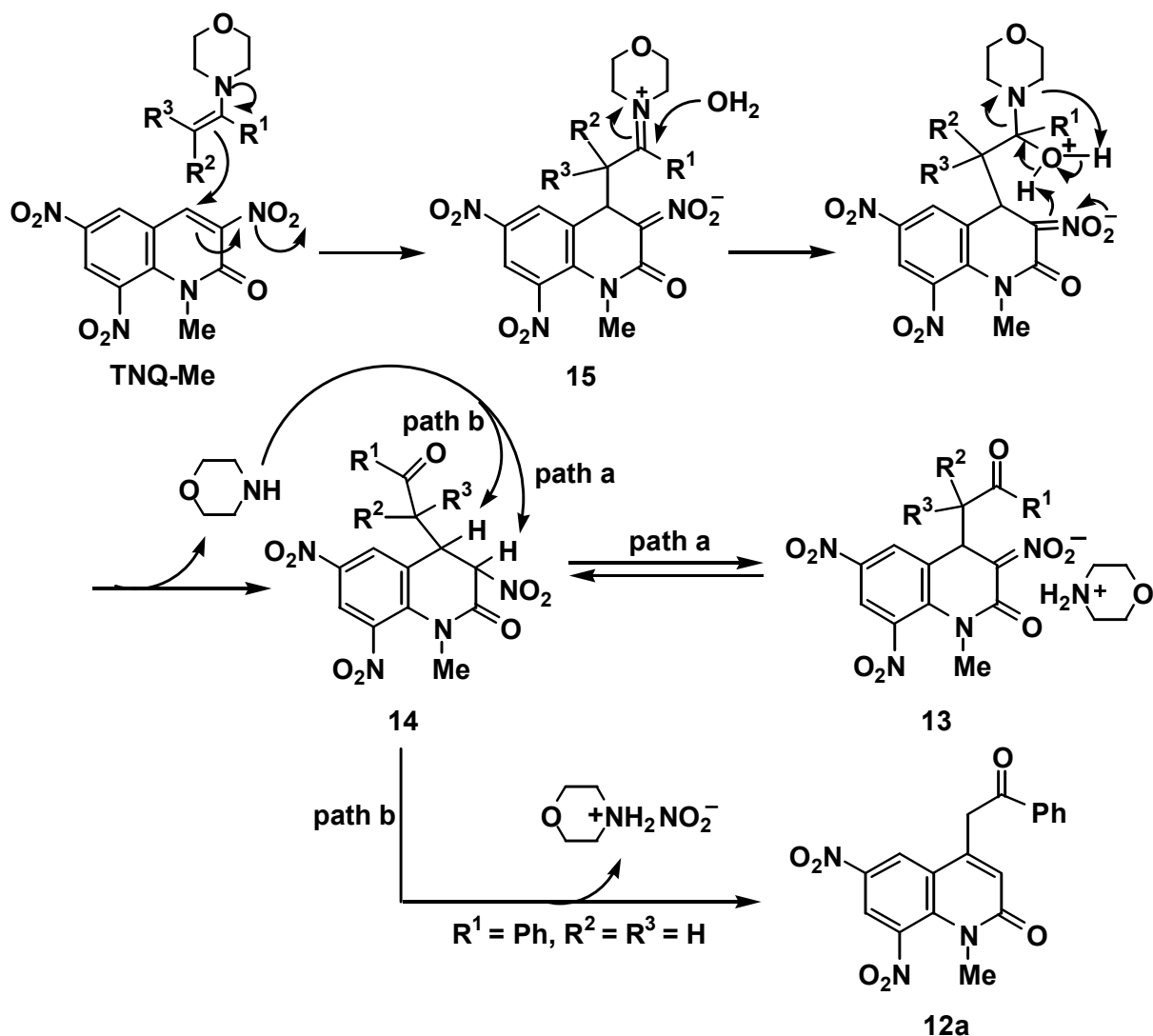A plausible mechanism for the reaction of **TNQ-Me** with enamine is illustrated in Scheme 13. The nucleophilic addition of enamine occurs at the electron deficient 4-position of **TNQ-Me** leading to Meisenheimer complex **15**, and the hydrolysis of the iminium moiety affords 3,4-dihydroquinolone **14**. During this process, morpholine is liberated, which plays an important role in the following step. There are two hydrogens that are deprotonated by morpholine in the dihydroquinolone intermediate **14**. When the acidic hydrogen at the 3-position is deprotonated, morpholinium salt **13** is formed (path a) which is interconverted with **14** under equilibrium. The deprotonation at the 4-position followed by elimination of adjacent nitro group as the nitrite ion affords *cine*-substituted product **12** (path b). The latter reaction (path b) is prevented by steric hindrance, namely this reaction proceeds only when both substituents (R^1 and R^2) are hydrogens; otherwise deprotonation at the 3-position (path a) is more likely.

Scheme 13. A Plausible Mechanism for Formation of **12** and **13**

2-2-3. Isolation of the Adduct Intermediate in *cine*-Substitution
of TNQ-Me with Enamines

In the last two sections, the reaction of **TNQ-Me** with enamine in aqueous acetonitrile in which hydrolysis of iminium moiety of adduct **15** proceeded was described. In this section, a similar reaction was carried out in anhydrous acetonitrile in order to trap adduct intermediate. Because morpholine is not liberated in this reaction, it is deduced that enaminodihydroquinolone **16** is produced from **15** via prototropy.

A solution of 1-morpholino-1-phenyl-1,2-propene (**11b**) in acetonitrile was added to a solution of **TNQ-Me** in acetonitrile on the ice bath and the resultant mixture was stirred for 2 days. After removal of the solvent, the residue was recrystallized from a mixed solvent (benzene and hexane) to afford 4-enamino-3,4-dihydroquinolone **16b** as a single isomer (Scheme 14).
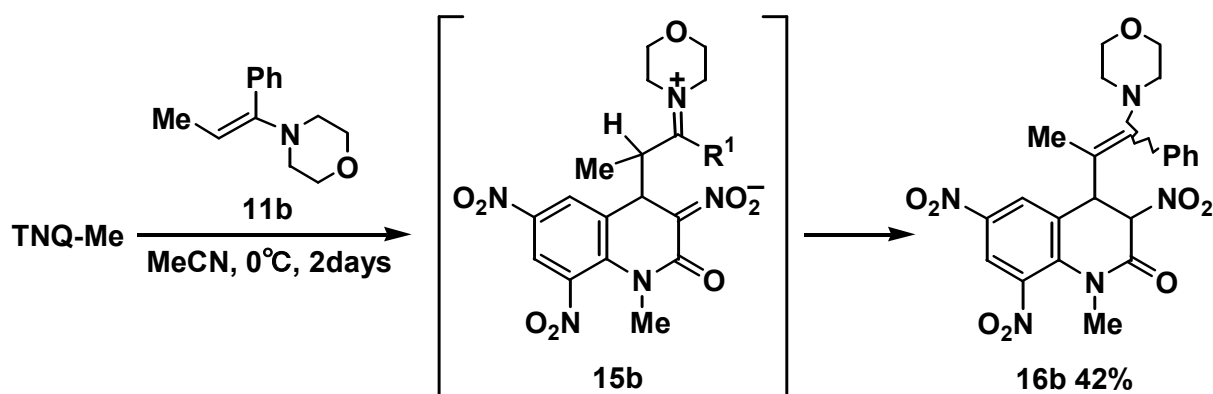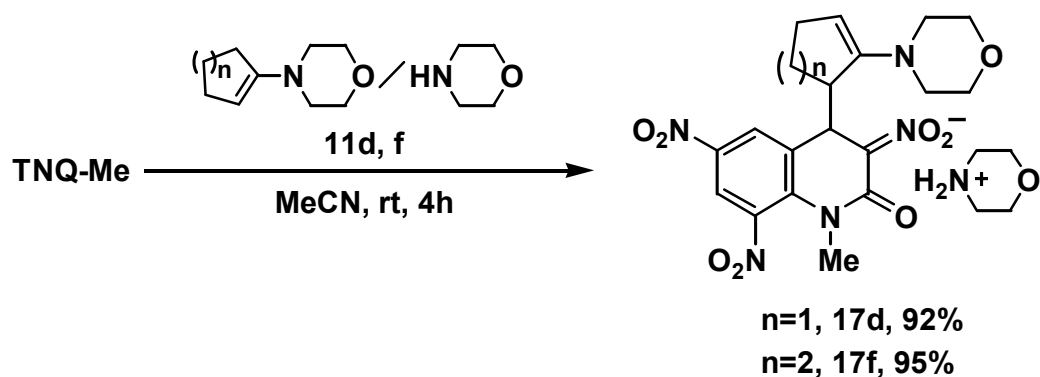

Scheme 14. Trap of Dihydroquinolone Intermadiate

In the other meantime, other enaminoquinolones has not been isolated because of easy hydrolysis of the enamine moiety. This problem was dissolved by addition of extra morpholine to the reaction mixture, and enaminoquinolones could be trapped as morpholinium salts **17**. To a solution of **TNQ-Me** in acetonitrile a solution of cyclic enamine **11d** and morpholine in acetonitrile was added at room temperature and the resultant mixture was stirred at room temperature. Morpholinium salt **17d** immediately precipitated in 92% yield (Scheme 15). In the case of enamine **11f**, effective isolation of **17f** was also successful. These results strongly support our proposed reaction mechanism, illustrated in Scheme 13.

TNQ-Me

11d, f
—————————→
MeCN, rt, 4h

n=1, 17d, 92%
n=2, 17f, 95%

Scheme 15. Trap of Dihydroquinolone Intermadiate as Morpholinium Salt

In summary, two kinds of reactivities that depend on the substituents of enamines were observed in the reactions of **TNQ-Me** with enamines in aqueous acetonitrile. Nucleophilic addition of enamine at the 4-position of **TNQ-Me** followed by hydrolysis of enamine moiety provides 4-acylmethyl-3,4-dihydroquinolone **14**. Deprotonation of **14** by morpholine at the 3-position yields morpholinium salt **13**, and that at the 4-position furnishes *cine*-substituted product **12**. Furthermore, the trap of enaminodihydroquinolone **16** was succeeded when the reaction of **TNQ-Me** with enamine was performed under unhydrous conditions.

2-2-4. *cine*-Substitution of TNQ-Me with Ketones and Aldehyde

A study of **TNQ-Me** reactions with enamines showed that **TNQ-Me** is highly electrophilic and forms a C-C bond with ease. These experimental facts prompted me to employ less nucleophilic ketones as the nucleophiles under basic conditions (Table 7, Sheme 8).

When **TNQ-Me** was treated with acetophenone **18a** in the presence of triethylamine, *cine*-substitution readily proceeded to afford 4-(benzoylmethyl)quinolone (**12a**) in an excellent yield (entry 1). Because the
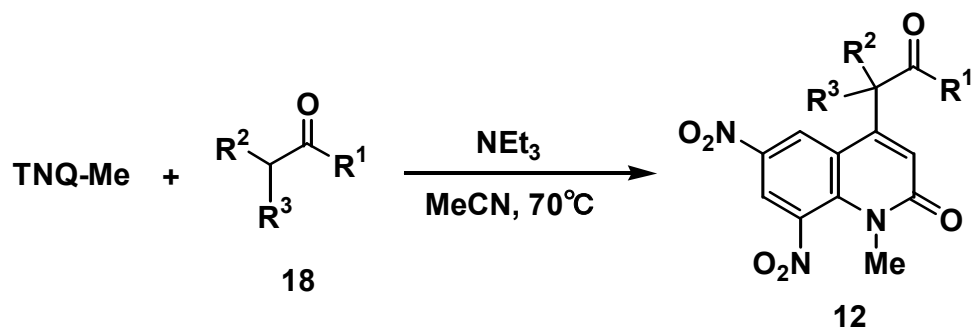
pKa value of acetophenone **18a** and the value of triethylammonium in dimethylsulfoxide are 24.7[74a] and 9.00[74b] respectively, acetophenone **18a** is not easily enolized. The nucleophilic species is considered to be enol, and triethylamine accelerates the enolization.

This reaction was applicable to other aromatic and aliphatic ketones. α-Monosubstituted acetophenones **18b** and **18c** were usable for this *cine*-substitution to provide **12b** and **12c** in good yields, respectively (entries 3, 4). However, α,α-disubstituted acetophenone **18h** was intact and **TNQ-Me** converted into 1-methyl-6,8-dinitro-2-quinolone (**6,8-DNQ)** under the same conditions (entry 5). In this case, **TNQ-Me** reacted with triethylamine, rather than the sterically hindered enol, to cause denitration as mentioned in Chapter 1. Bicyclic ketone, tetralone **18i**, also reacted with **TNQ-Me** to afford corresponding *cine*-substituted product in a moderate yield (entry 6). In addition, aliphatic ketone **18j** revealed similar reactivity to give 4-substituted dinitroquinolone **2j** effectively (entry 7).

When unsymmetrical butanone **18n** was used, thermodynamically controlled enol was more reactive than a kinetically controlled enol, and lead to **12n** as a major product (Scheme 8). Alicyclic ketones **18d** and **18f** were also found to be usable for the present reaction (entries 8 and 9). The yield of *cine*-substituted product was considerably lower in the case of 3-pentanone **18k**, in which large amounts of **6,8-DNQ** were produced as the major product (entry 10). On the other hand, aldehyde **18e** was reactive and afforded *cine*-substitution product **12e** despite the presence of two methyl groups at the reaction site (entry 11). Furthermore, the present reaction realized the introduction of hetaroylmethyl groups to the 1-methyl-2-quinolone skeleton. 2-Acetylpyridine **18l** and 2-acetylfuran **18m** reacted similarly to furnish

corresponding dihydroquinolones **12l** and **12m** (entries 12 and 13).

As mentioned in the previous sections, *cine*-substitutions of **TNQ-Me** with enamines were affected by bulkiness of nucleophiles. This is due to the bulky and rigid structure of the liberated morpholine, which can not easily deprotonate at the crowded 4-position. On the contrary, this disadvantage is overcome in cases of *cine*-substitutions of **TNQ-Me** with ketones, and various kinds of 4-acylmethyl-6,8-dinitro-1-methyl-2-quinolones **12** can be prepared in moderate to good yields. In the case of α,α-disubstituted ketone **18h**, the steric hindrance around the nucleophilic site prevents the ketone from adding to **TNQ-Me** (entry 5). The bulkiness of the acyl group (R^1CO) is also influential in this reaction. Namely, the reactivity of 3-pentanone **18k** is significantly diminished (entry 10) in comparison with 2-butanone **18n**, although the substituents at the reaction site (R^2 and R^3) are the same. Furthermore, this consideration also rationalizes the high reactivity of α,α-disubstituted aldehyde **18e** (entry 11).

Table 7. Preparation of Acylmethylquinolones **12**

	Ketones **18**				Products	
entry	R^1	R^2	R^3	Time/h	**12**	Yield/%
1	Ph	H	H	2.5	**a**	83
2	4-MeC$_6$H$_4$	H	H	2.5	**g**	59
3	Ph	Me	H	2.5	**b**	77
4	Ph	Ph	H	3.5	**c**	69
5	Ph	Me	Me	6	**h**	0[a]
6	-(o-C$_6$H$_4$)CH$_2$CH$_2$-		H	2	**i**	52
7	Me	H	H	3.5	**j**	83
8	-(CH$_2$)$_3$-		H	2	**d**	58
9	-(CH$_2$)$_4$-		H	2	**f**	82
10	Et	Me	H	4	**k**	18[a]
11	H	Me	Me	5	**e**	41
12	2-Pyridyl	H	H	2.5	**l**	74
13	2-Furyl	H	H	3	**m**	45

[a] **6,8-DNQ** was also isolated
in 41% (entry 5) and 73% (entry 10) yields, respectively.
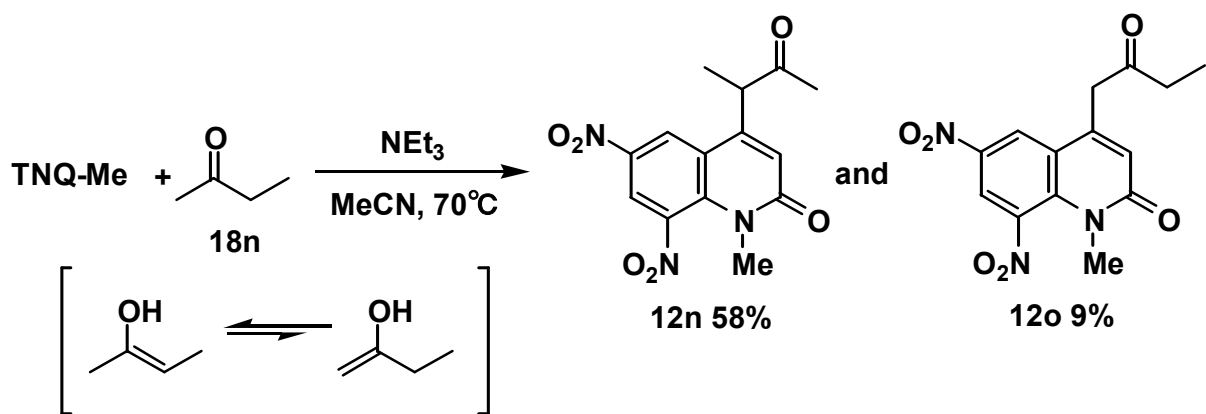
Scheme 16. Chemoselectivity of *cine*-Substitution with Butanone **18n**

In summary, ketones are usable as the nucleophile for *cine*-substitution of **TNQ-Me** leading to 4-acylmethyl-1-methyl-2-quinolone derivatives **12**, though the reaction should be conducted in the presence of triethylamine at somewhat higher temperatures. These reactions required only simple experimental manipulations, and the C-C bond formation at the 4-position was regioselectively performed. These results show this reaction would provide a new methodology for functionalization of the 1-methyl-2-quinolone skeleton.
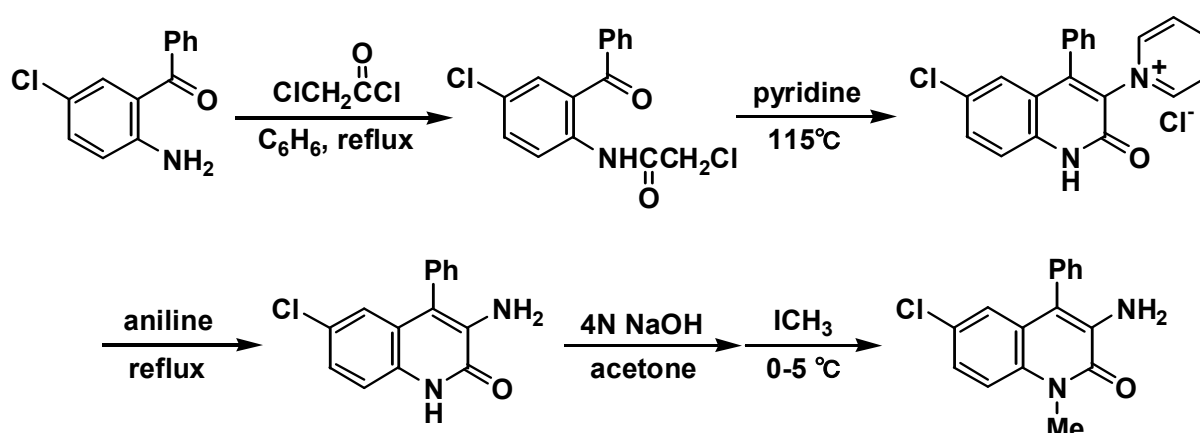
CHAPTER 3.   Syntheses of Arylated 1-Methyl-2-quinolones.

3-1. Introduction

The C-C bond formation is the most fundamental protocol for construction of versatile skeletons, however, it is difficult to introduce a carbon substituent into the 1-methyl-2-quinolone skeleton because of its low reactivity. The aromatic property of the 1-methyl-2-quinolone prevents the nucleophilic functionalization,[37-39] and the electron-deficiency also prevents electrophilic substitution.[40-42]

Arylation of 1-methyl-2-quinolone is one of the useful modifications from the viewpoint of further functionalization.   However, the direct arylation of 1-methyl-2-quinolone is more difficult than the introduction of other substituents because the introduction requires the destruction of the aromaticity of both the quinolone ring and the benzene rings.   Thus, arylated 1-methyl-2-quinolone derivatives are generally prepared by chemical transformation of benzophenone derivatives, but this methodology requires multi-steps reactions (Scheme 17).[33]

Scheme 17.   Synthesis of Arylated 1-Methyl-2-quinolone.

On the other hand, only a few examples of direct arylation of 1-methyl-2-quinolone derivatives are known. Matsumura *et al.* reported the photo coupling reaction of 3-halogeno-1-methyl-2-quinolone with aromatic or heteroaromatic compounds (Scheme 18).[22] Although this approach requires only simple manipulations, yields of arylated 1-methyl-2-quinolones are not high. Recently, Wu *et al.*[52] and Kappe *et al.*[25f] reported the effective palladium catalyzed arylation of 1-methyl-2-quinolone derivatives by use of Suzuki-Miyaura coupling reaction, respectively (Scheme 19). However the starting materials are not easily available, and severe conditions are necessary for the preparation. Thus, there is a high demand to develop effective and convenient methodologies for syntheses of arylated 1-methyl-2-quinolones.
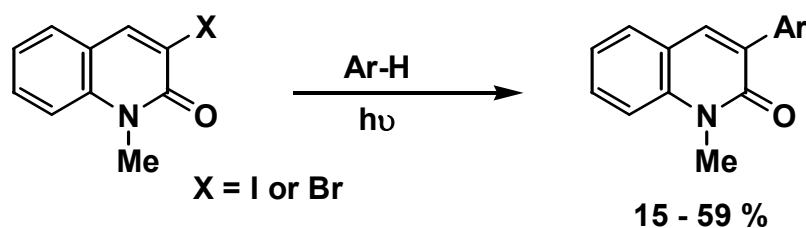
Scheme 18. Photo Coupling Reaction of 3-Halogeno-1methyl-2-quinolone.
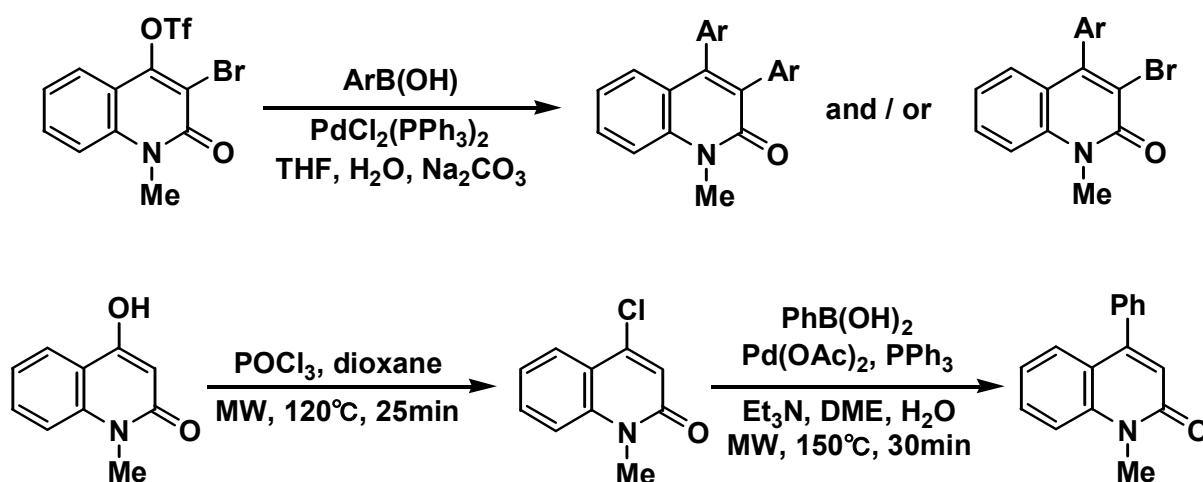
Scheme 19. Suzuki-Miyaura Reaction of 1-Methyl-2-quinolone Derivatives

39

Meanwhile, we have focused on the high reactivity of **TNQ-Me** toward nucleophiles because it provides a new methodology for C-C[66,75] and C-N[76] bond formations on the 1-methyl-2-quinolone skeleton. In previous chapters, it was demonstrated that **TNQ-Me** readily reacted with 1,3-dicarbonyl compounds[66], acylmethyl compounds,[75] and amines,[76] and various kinds of functions could be introduced at the 4-position regioselectively. These reactions are considered to proceed via the addition-elimination mechanism, namely nucleophilic addition at the 4-position affords an adduct intermediate, and the subsequent elimination of nitrous acid leads to *cine*-substitution products accompanied by aromatization (Scheme 20). In the present chapter, benzene derivatives were employed as the nucleophile in order to improve the synthetic utility of the *cine*-substitution, which realizes facile arylation of the 1-methyl-2-quinolone skeleton.
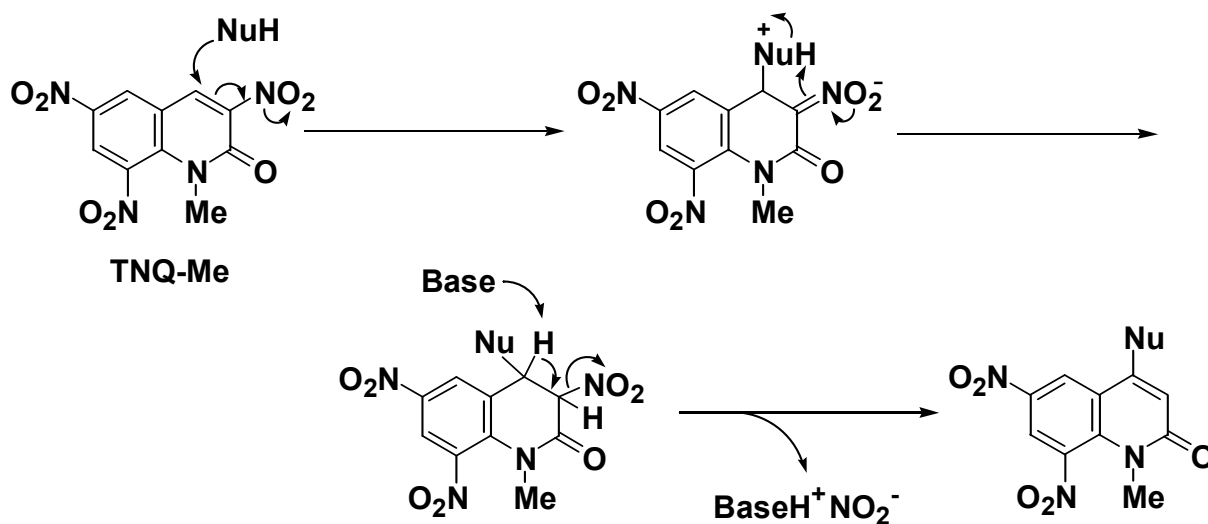
Scheme 20. *cine*-Substitution of **TNQ-Me**

3-2. Results and Discussion

3-2-1. Arylation of TNQ-Me by Use of Phenoxides

Phenoxide ions were employed as the aromatic compounds which has high nucleophilicity for *cine*-substitution of **TNQ-Me** in order to achieve the arylation of 1-methyl-2-quinolone skeleton.

To a solution of potassium phenoxide **19a** in acetonitrile, **TNQ-Me** was added and the mixture was heated to 60 ^{o}C for 3 hours (Table 8, entry 1). In the ^{1}H NMR of the product isolated after acidification of the reaction mixture, signals of the 1,2,4-trisubstituted benzene skeleton and two dinitroquinolone rings were observed. This result means the double substitution proceeded at the 2- and 4-positions of **19a**. The product was determined as 2,4-bis(quinolyl)phenol **20a** (30% yield based on **TNQ-Me**), and the mass spectrum and the elemental analysis also supported the existence of this structure. The 3-nitro group of the quinolone ring was eliminated during the substitution, namely *cine*-substitution proceeded. The yield of **20a** was improved up to 51% when the reaction was conducted for a prolonged reaction time (entry 2). In this reaction, the formation of 2,6-bis(quinolyl)phenol was not observed at all.

The double substituted product **20b** was in a good yield in the case of *o*-methylphenoxide **19b**, which was activated by an inductive electron-donating effect of *o*-methyl group (entry 3). When highly electron-rich *p*-methoxyphenoxide **19c** was used, a couple of quinolone rings were introduced at both two vicinal positions of the hydroxy group despite significant steric hindrance (entry 4). On the other hand, reactions of **TNQ-Me** with *m*-methylphenoxides **19d**, *p*-methylphenoxides **19e** and naphthoxide **19g** furnished single substitution products **22d**, **22e**, and **22g** respectively (entries 5, 6 and 8). Phenoxide **19f** derived from *p*-nitrophenol was similarly applicable to the present

reaction giving **22f** despite its low electron density (entry 7).

Table 8.   Arylation of **TNQ-Me** with Phenoxide **19**
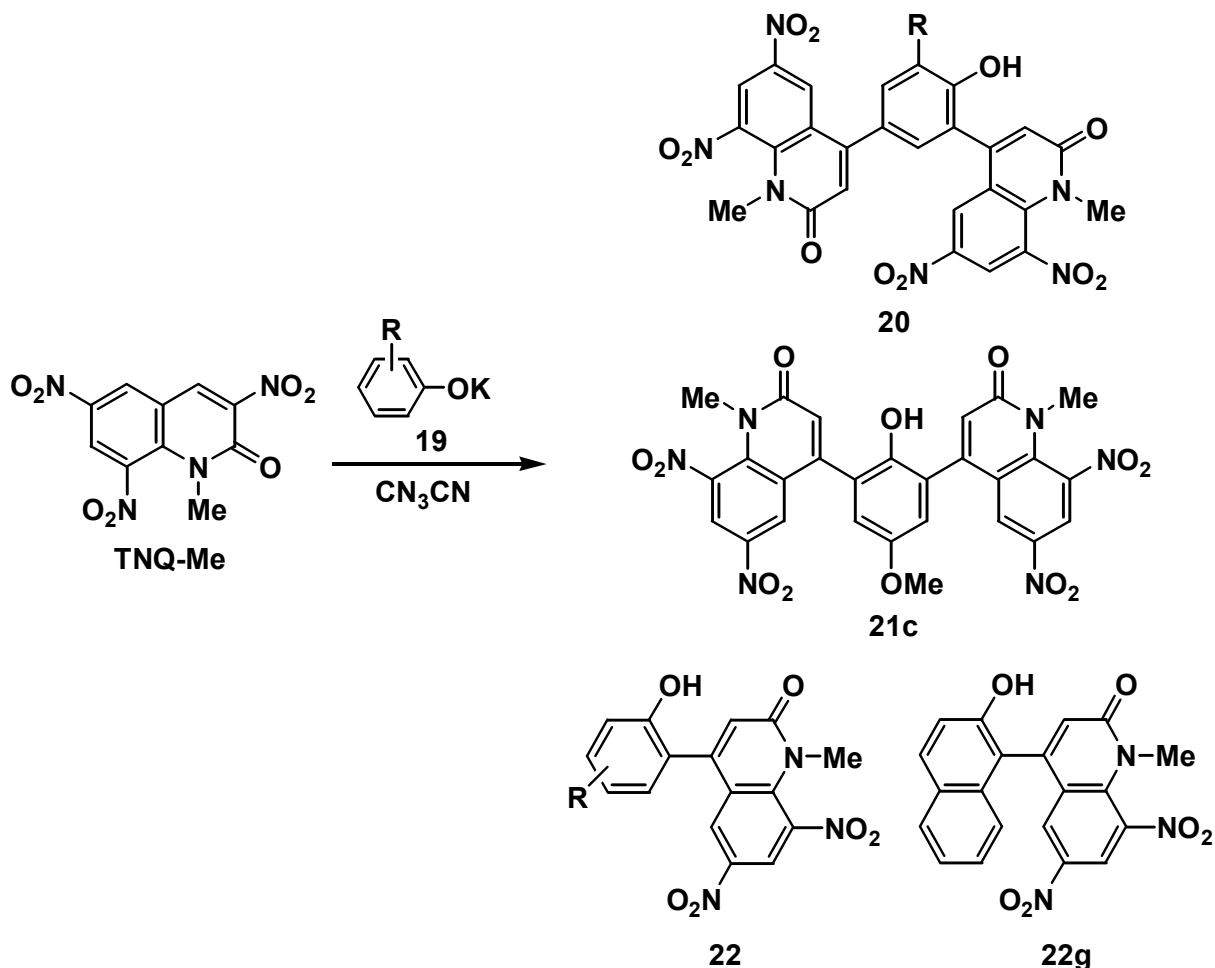
Entry	R	Temp/ °C	Time	Product	Yield/%
1	H	60	3h	**20a**	30
2	H	80	3d	**20a**	51
3	2-Me	60	3h	**20b**	91
4	4-MeO	60	3h	**21c**	67
5	3-Me	60	3h	**22d**	35
6	4-Me	80	3h	**22e**	82
7	4-NO$_2$	80	1d	**22f**	36
8	*o*-phenylene	60	3h	**22g**	75

3-2-2.　A Study on the Molar Ratio of TNQ-Me and Phenoxide 19

The role of phenoxide **19** in the present reaction was investigated by changing the molar ratio of substrates: **TNQ-Me** and **19**.

In the reaction of **TNQ-Me** with phenoxide **19b** (Table 9), no single substitution product **22b** was detected (entry 1).　Furthermore, the yield of **20b** was reduced by half without any formation of **22b** when the molar ratio of **TNQ-Me**/**19b** was changed from 1/1 to 2/1 (entry 2).　These experimental facts indicate that the second substitution proceeded much faster than the first one and half of the amount of phenoxide was consumed as the base.

Table 9.　Examination of Molar Ratio in Arylation of **TNQ-Me**
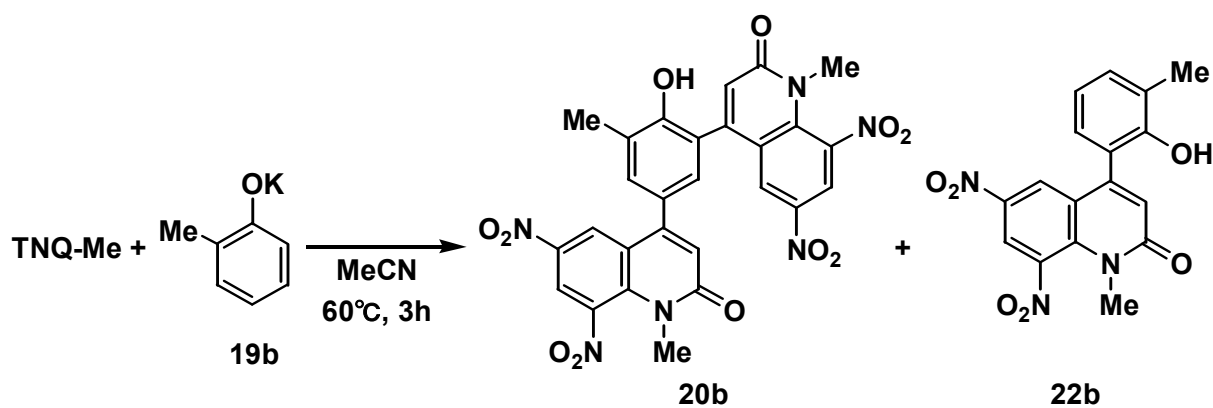
with Phenoxide **19b**

Entry	molar ratio		Yield[a] / %	
	TNQ-Me	**19b**	**20b**	**22b**
1	1	1	91	0
2	2	1	46	0

a) Based on **TNQ-Me**

3-2-3. A Plausible Mechanism

### for the Arylation of TNQ-Me with Phenoxide 19

On the basis of the results mentioned so far, a plausible mechanism for the reaction of **TNQ-Me** with phenoxide **19a** is illustrated in Scheme 21. Phenoxide **19a** adds to the 4-position of **TNQ-Me** giving adduct **23a**, and another phenoxide **19a** assists aromatization of the benzene ring, as shown by the experimental results in the last section.   In the quinolone ring, the proton transfer also occurs from the 4-position to the 3-position affording phenoxide **24a**. Since the resultant dianionic phenoxide **24a** is more reactive than **19a**, the second substitution proceeds much faster than the first one.   The final product is formed by aromatization of the quinolone ring with loss of nitrite.

The reactivity and regiochemistry of the present reaction are affected considerably by properties of the substituent on the phenoxide.   A double substitution is observed in the cases of phenoxide **19a**, 2-methylphenoxide **19b**, and 4-methoxyphenoxide **19c**.   Generally, it is very difficult to introduce more than three substituents at the successive positions on the benzene ring because of steric repulsion between substituents.   It is considered to be especially hard to introduce bulky quinolyl groups at both of the two vicinal positions of the hydroxy group.   Hence, 2,6-bis(quinolyl)phenols are not formed at all.   On the contrary, 2,6-bis(quinolyl)phenol **21c** can be prepared because the methoxy group significantly activates the benzene ring.

On the other hand, single substitution is observed in cases of 2-methyl- or 3-methylphenoxides **19d** and **19e**, though the electron density of the benzene ring is increased by the methyl group.   In these cases, the double substitution is prevented because of steric hindrance of the methyl group.   There are two reaction sites in phenoxide **19a**, the 2- and the 4-positions.   While the 4-position

is less hindered, the 2-position is considered to be highly reactive because the anionic oxygen at the vicinal position shows the electron-donating inductive effect. This consideration is supported by the fact that phenoxide **19e** afforded only 2-quinolyl derivative **22e**.
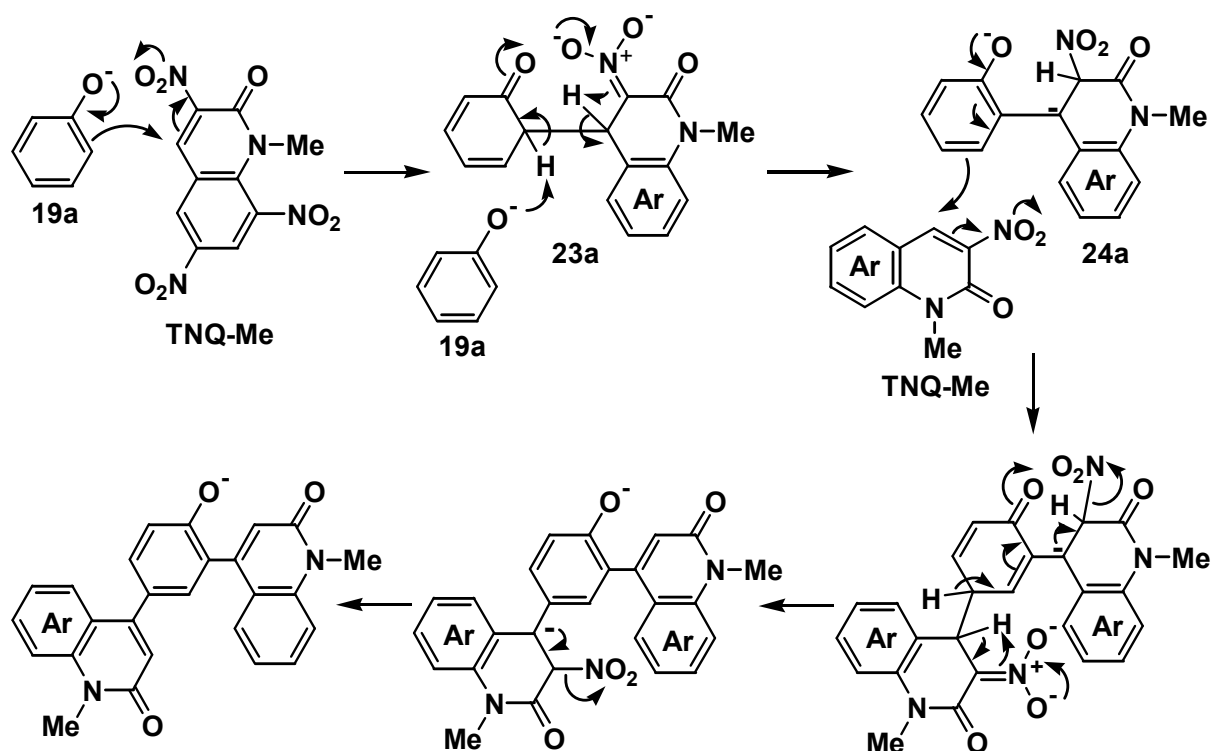
Scheme 21. A Plausible Mechanism for Formation of **20a**

The present arylation is the electrophilic substitution of phenoxides by **TNQ-Me**. This means that phenoxide having an electron-withdrawing group undergoes the substitution at the slower rate. Actually, 4-nitrophenoxide **19f** afforded single-substituted product **22f** in a lower yield. In the case of naphthoxide **19g**, only single regioisomer **22g** was obtained. This regioselectivity is explained by the stability of carbocation adduct intermediate illustrated in Scheme 22. When the 3-position of **19g** attacks the electrophile

(**TNQ-Me**), both of the two aromatic rings loose aromaticity in five resonance structures of the adduct intermediate.   On the other hand, only three resonance structures loose aromaticity when the 1-position of **19g** attacks the electrophile. Hence, the substitution at the 1-position is favored over the 3-position.
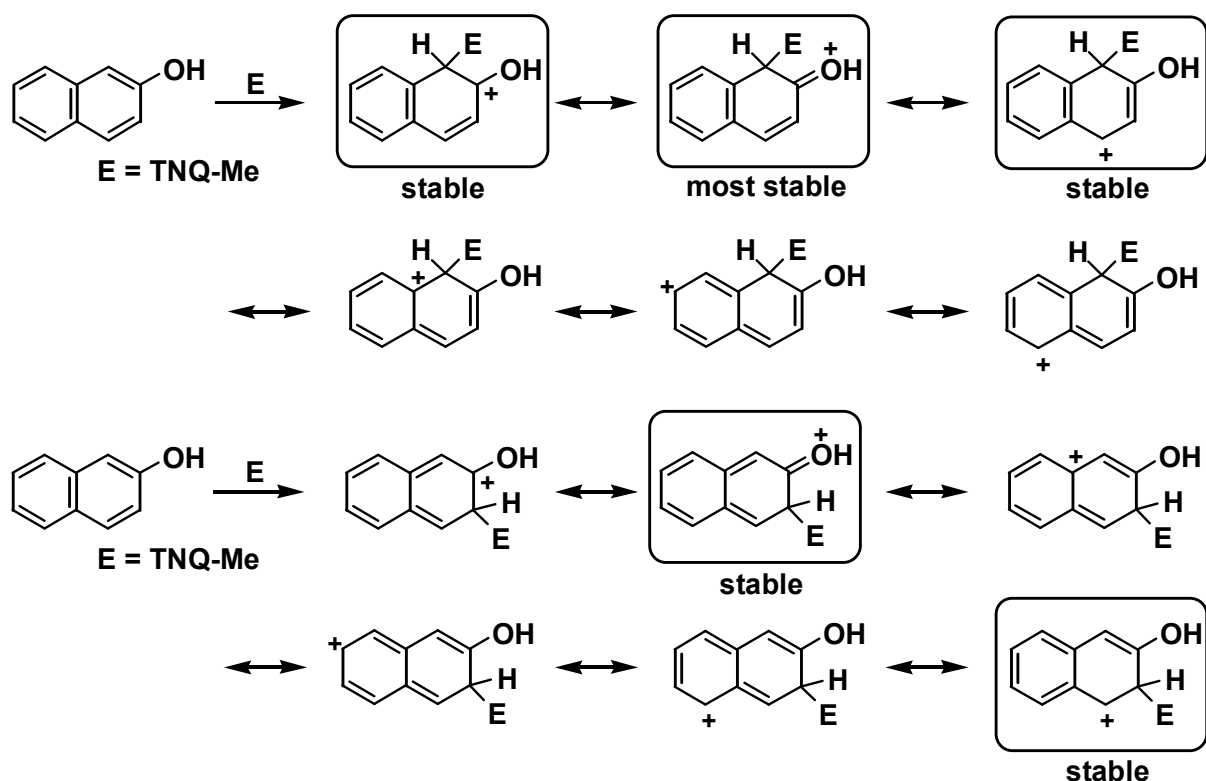
Scheme 22. Resonance structure of carbocation intermediate

3-2-3. Summary

In summary, **TNQ-Me** was found to be an excellent substrate for effective construction of an arylated 1-methyl-2-quinolone skeleton.   This *cine*-substitution enables the synthesis of several kinds of 1,2-dihydro-4-quinolylphenols, which are a new family of unnatural 1-methyl-2-quinolone derivatives.   Arylated products obtained here might be

useful for fluorescent material[33] as well as the synthetic intermediate for new drugs.[25f]

From the standpoint of the benzene ring, the present reaction can be regarded as the electrophilic arylation because 1-methyl-2-quinolone is also an aromatic compound. It is well-known that the introduction of an aryl group into the benzene ring can not be readily performed, especially because electrophilic arylation is quite difficult.[77] Hence, these experimental results also provide valuable information for benzene chemistry.

CHAPTER 4.   Studies on the Effect of the Nitro Group

4-1. Introduction

Chapters 1-3 reported the study of regioselective new-bond formations on the 1-methyl-2-quinolone skeleton by use of 1-methyl-3,6,8-trinitro-2-quinolone (**TNQ-Me**).   The results show that amines or enamines readily react with **TNQ–Me** to form a C-N[76] or a C-C[66, 75, 78] bond at the 4-position.   Introduction of the carbonyl functions is also possible when **TNQ-Me** is allowed to react with 1,3-dicarbonyl compounds[66] or ketones[75] in the presence of triethylamine.   Furthermore arylation of 1-methyl-2-quinolone derivative is achieved by treatment **TNQ-Me** with phenoxides.[78]   In a series of these reactions, *cine*-substitution is the key reaction, which proceeds via the addition-elimination mechanism.   The nucleophilic addition occurs at the 4-position of **TNQ-Me** to give 3,4-dihydro-2-quinolone derivative, and subsequent elimination of nitrous acid accompanied by aromatization furnishes 4-substituted 6,8-dinitro-1-methyl-2-quinolone (Scheme 23).[66]

As noted in the literature, it is generally difficult to functionalize the 1-methyl-2-quinolone framework nucleophilically[37-39] because of its low reactivity, and electrophilic functionalization is also difficult because the ring nitrogen and the adjacent carbonyl group reduce the electron density of the pyridine ring.[40-42]   On the contrary, **TNQ-Me** is highly reactive, which means three nitro groups activate the 1-methyl-2-qunolone ring to realize the special behavior.   In this chapter, the substituent effects of the nitro groups are studied from both electronic and steric viewpoints.
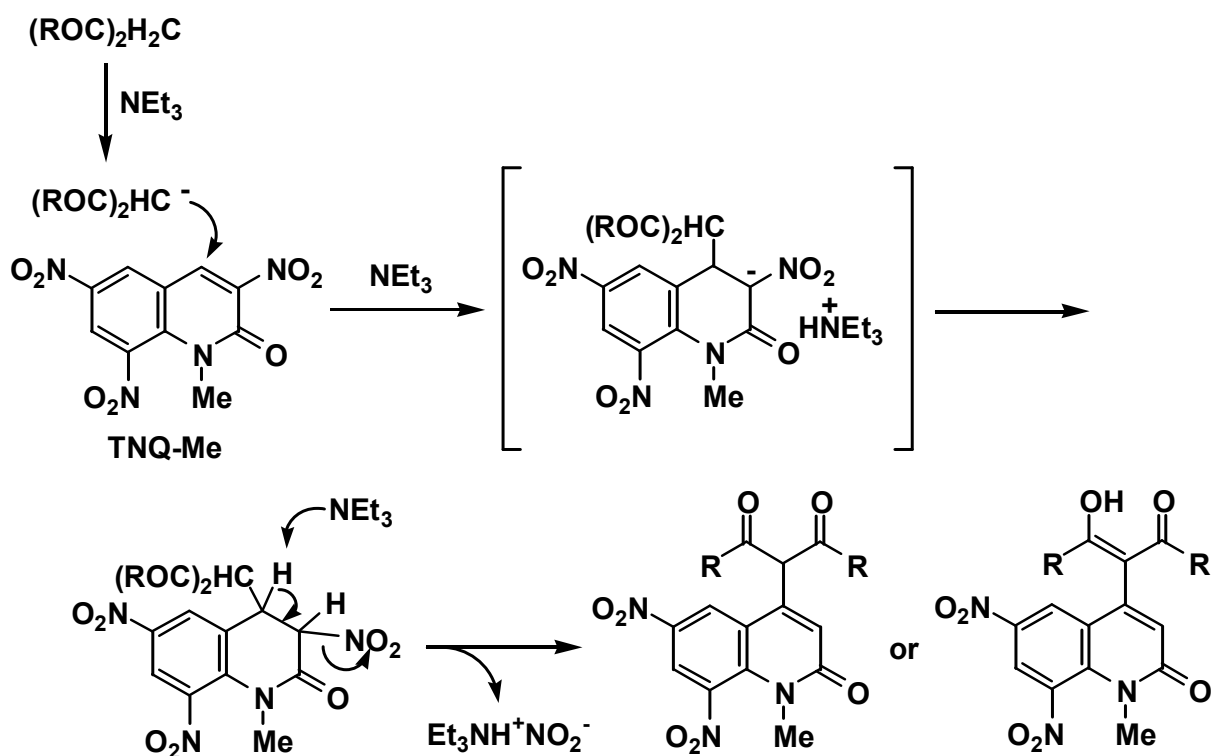
Scheme 23. *cine*-Substitution of **TNQ-Me**

4-2. Results and Discussion

4-2-1. Comparing Reactivities of Nitroquinolones

As mentioned in Chapter 1, nitration of 1-methyl-2-quinolone with nitric acid in sulfuric acid affords four kinds of nitroquinolones: 6-nitroquinolone, 6,8-dinitroquinolone, 3,6-dinitroquinolone (**DNQ-Me**) and 3,6,8-trinitroquinolone (**TNQ-Me**). In order to confirm the effect of the 8-nitro group, reactivities between the last two compounds were compared by conducting the *cine*-substitution with 2,4-pentanedione (**25**).

To a solution of **TNQ-Me** and diketone **25** in ethanol (EtOH), triethylamine (NEt₃) was added, and the mixture was stirred at room temperature for 3 hours. 4-Substituted 6,8-dinitro-2-quinolone **26**, a *cine*-substitution product, was isolated in 88 % yield after the workup (Table 10, entry 1).[66] On

the other hand, no change was observed when **DNQ-Me** was treated with **25** under the same conditions (entry 2). Furthermore **DNQ-Me** was still intact even though the reaction was conducted under reflux conditions, and only trace amounts of product **27** was detected when more basic sodium ethoxide was employed instead of NEt₃ as the base (entries 3 and 4). The yield of **27** could be improved by using *N,N*-dimethylformamide (DMF) as the solvent (entry 5), and much basic and severe reaction conditions were found to be necessary for causing *cine*-substitution of **DNQ-Me** (entry 6). These facts suggest that the nitro group at the 8-position obviously activates the 2-quinolone ring greatly though the nitro group is far from the reaction site.

Table 10. Comparison with Reactivity of Nitroquinolones
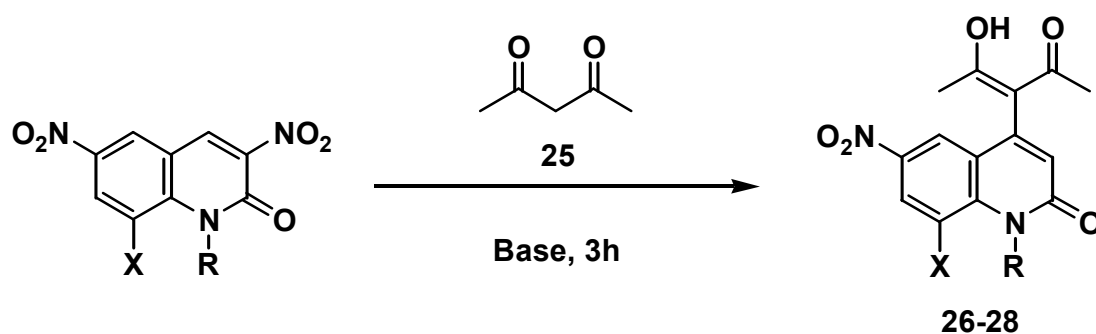
entry	Substrate			Solv.	Base	Temp. °C	Product	Yield %
	X	R						
1	NO₂	Me	**TNQ-Me**	EtOH	NEt₃	rt	**26**	88
2	H	Me	**DNQ-Me**	EtOH	NEt₃	rt	**27**	0
3	H	Me	**DNQ-Me**	EtOH	NEt₃	reflux	**27**	0
4	H	Me	**DNQ-Me**	EtOH	EtONa	rt	**27**	trace
5	H	Me	**DNQ-Me**	DMF	NEt₃	50	**27**	35
6	H	Me	**DNQ-Me**	DMF	EtONa	rt	**27**	62
7	NO₂	H	**TNQ-H**	EtOH	NEt₃	rt	**28**	0

cine-Substitution of demethylated trinitroquinolone (**TNQ-H**) was also attempted. **TNQ-H** remained intact and recovered upon treatment with **25** in the presence of NEt$_3$, against our expectation (entry 7). Therefore, both 1-methyl and 8-nitro groups are necessary for revealing these high reactivities of the 2-quinolone skeleton.
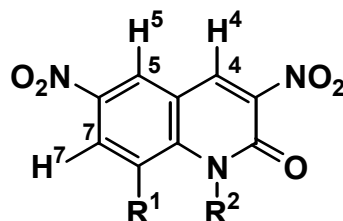

4-2-2. Electronic Effect

In the last section, both 1-methyl and 8-nitro groups were found to be necessary for the activation of the 2-quinolone skeleton. In this section, the electronic effect of the 8-nitro group was studied by measuring ^{1}H and ^{13}C NMR spectra of **TNQ-Me**, **DNQ-Me**, and **TNQ-H**. Chemical shifts of protons and carbons at the 4-, 5-, and 7-positions are shown in Table 11.

In each nitroquinolone, the proton and the carbon at the 4-position are observed at the lowest field indicating most electron deficient among the three positions, which is a result of electron-withdrawing effects of the ring nitrogen and the carbonyl group, in addition to the effect of the adjacent nitro group. Because the signal of the 4-proton of **TNQ-Me** appeared at a lower field with a 0.23 ppm difference than that of **DNQ-Me** (entries 1 and 3), the 8-nitro group somewhat diminishes the electron density at the 4-position of **TNQ-Me**. However, chemical shifts of the carbon at the 4-position are almost the same between **TNQ-Me** and **DNQ-Me** in the ^{13}C NMR (entries 5 and 6). Hence, the high activity of **TNQ-Me** cannot be completely explained by only the electronic effect of the 8-nitro group.

Though the proton at the same position of **TNQ-H** was observed at a lower field than that of **TNQ-Me** (entries 2 and 4), **TNQ-H** remained intact in the present reaction. Thus, low reactivity of **TNQ-H** might be due to the presence

of acidic *N*-hydrogen (See section 4-2-4).

Table 11. ^{1}H and ^{13}C NMR data of Nitroquinolones

entry	R^1	R^2		Chemical Shift / ppm
				H^4	H^5	H^7	C^4	C^5	C^7	Solvent.
1	NO_2	Me	**TNQ-Me**	9.32	9.07	9.24	136.4	124.8	130.4	DMSO-d_6
2	NO_2	Me	**TNQ-Me**	9.26	9.05	9.24	—	—	—	CDCl$_3$
3	H	Me	**DNQ-Me**	9.09	8.93	8.53	137.0	128.7	128.0	DMSO-d_6
4	NO_2	H	**TNQ-H**	9.44	9.26	9.22	—	—	—	CDCl$_3$

4-2-3. Steric Effect

It has been found that the 8-nitro group certainly activates the 4-position of **TNQ-Me**. In the present section, the steric effect of the nitro group is studied. It is considered that the steric repulsion between the 8-nitro and the 1-methyl groups is the main factor for activation of the 2-quinolone framework.

MOPAC (PM3) molecular orbital calculations for **TNQ-Me**, **DNQ-Me,** and **TNQ-H** were conducted (Table 12). In the cases of **DNQ-Me** and **TNQ-H**, both benzene and pyridone rings were present in almost all coplanar (entries 2 and 3). In contrast, the 8-nitro group of **TNQ-Me** has no coplanarity with the quinolone ring, which turns through 67.7° (entry 1). Furthermore, the 2-quinolone ring is torsionally strained by the steric compression of substituents

at the peri-positions, namely the 1-methyl and the 8-nitro groups.   The torsional

angle between C^8-NO_2 bond and N^1-Me one is 30.0° (entry 1).

Table 12. Calculated Dihedral Angle and Torsional Angle of 2-Quinolones

entry	X	R		∠ C^7-C^8-$C^{8'}$ C^8-NO_2 (Dihedral Angle)	∠ C^8-X N^1-R (Torsional Angle)	∠ C^2-C^3 C^6-C^7 (Torsional Angle)	∠ N^1-C^2 C^3-C^4 (Torsional Angle)
1	NO_2	Me	**TNQ-Me**	67.7°	30.0°	0.97°	8.98°
2	H	Me	**DNQ-Me**	—	0.67°	2.62°	4.45°
3	NO_2	H	**TNQ-H**	0.39°	0.04°	1.44°	—

Table 4. Torsional Angle between C^8-X Bond and N^1-R One

entry	X	R		Torsional Angle between C^8-X and N^1-R Estimated	Actual
1	NO_2	Me	**TNQ-Me**	30.0°	25.0°
2	H	Me	**DNQ-Me**	0.67°	0.90°
3	NO_2	H	**TNQ-H**	0.04°	-

In order to confirm the structural distortion of **TNQ-Me**, X-ray

analyses of **TNQ-Me** and **DNQ-Me** were performed (Figure 5, 6). The 8-NO_2

group of **TNQ-Me** turned through 55.8° (calculated value was 67.7°).   This fact

is disadvantageous for the resonance effect, thus the 8-nitro group cannot

diminish the electron density so much at the 4-position of **TNQ-Me**. And the quinolone ring of **TNQ-Me** was confirmed to be considerably strained compared with that of **DNQ-Me**. From the agreed results of X-ray analyses to calculated ones for **TNQ-Me** and **DNQ-Me**, the actual dihedral angle between the pyridone ring and the benzene ring of **TNQ-H** is also presumed to be a small.

As a result of the study on the steric effect of the substituent, the 8-nitro group significantly distorts the quinolone ring by steric repulsion with the 1-methyl group. As a result of the distortion, the pyridone ring cannot be coplanar with the benzene ring, which prevents the π-orbitals from overlapping effectively, and the aromaticity of the pyridone moiety[36] is decreased. Consequently, this structural change should be a major reason for the extremely high reactivity of **TNQ-Me**.
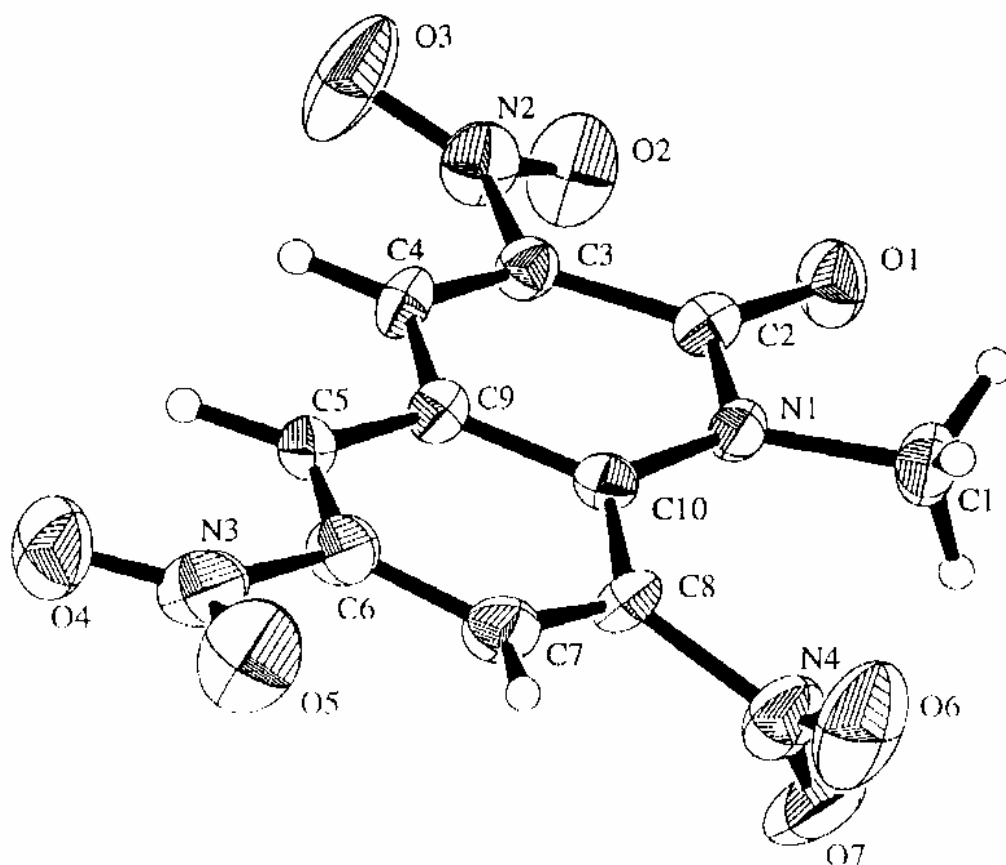
Figure 5. An ORTEP (30% probability ellipsoids) View of **TNQ-Me**
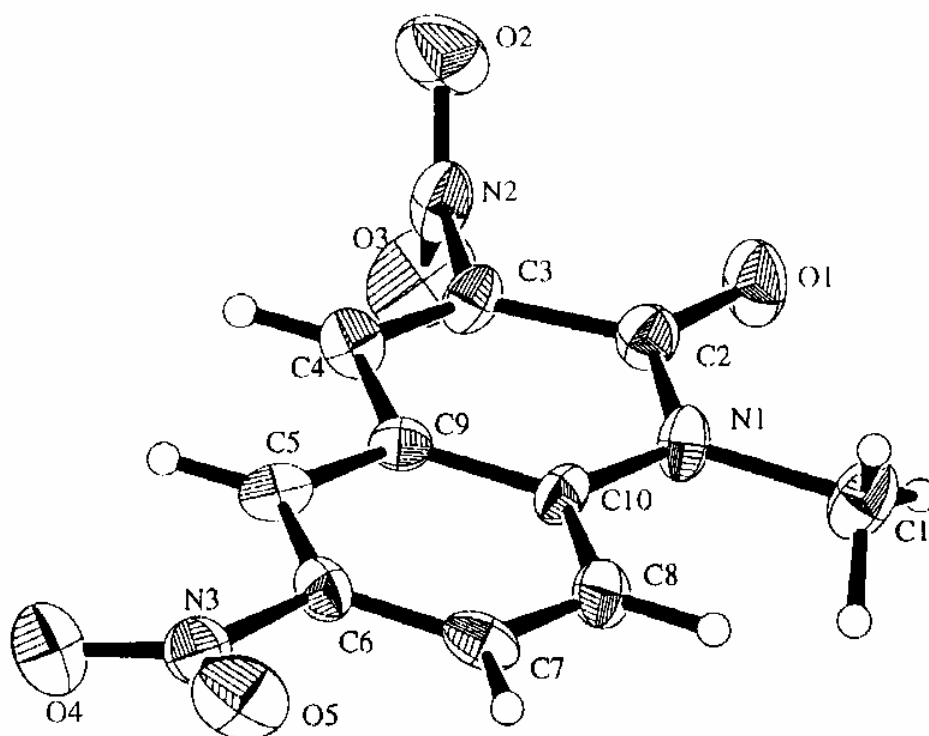
Figure 6. An ORTEP (30% probability ellipsoids) View of **DNQ-Me**

4-2-4. A Study on Low Reactivity of TNQ-H

Among three nitroquinolones, **TNQ-H** is considered to have the lowest electron density at the reaction site because the signal of the 4-hydrogen was observed at the lowest field in the ^{1}H NMR. This is due to the electron-withdrawing effect of the three nitro groups. The 8-nitro group also effectively diminishes the electron density by the resonance effect because the nitro group is coplanar with the quinolone ring. However, no reaction proceeded when **TNQ-H** was treated with 2,4-pentanedione (**25**) in the presence of NEt$_3$.

TNQ-H has tautomeric structures, the 2-quinolinol form and the 2-quinolone one. In the case of 2-pyridone, there is also tautomerism between 2-pyridone and 2-pyridinol. In the gas phase, the 2-pyridinol form preferably exists, which has been conclusively proved by IR, UV, mass spectrometric, and

photoelectron experiments.[79] In nonpolar solvents such as cyclohexane, both tautomers exist in comparable amounts.[80] However, the tautomeric equilibrium is shifted in favor of the more polar 2-pyridone form in polar solvents and in a solid state.[81] Therefore, it is considered that **TNQ-H** probably exists as a 2-quinolone form in EtOH.
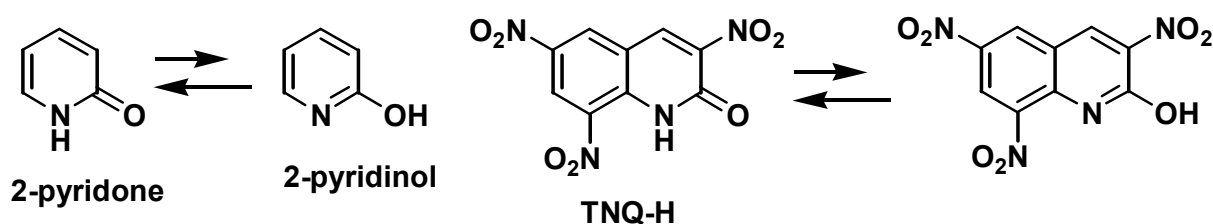
Figure 7. Tautomeric Structures of 2-Pyridones and **TNQ-H**

There are two factors that decrease the reactivity of **TNQ-H**. The first factor is the presence of an acidic *N*-hydrogen at the 1-position. The pKa values (in DMSO) of 2-pyridone and triethylammonium are 17.0^{74b} and $9.0,^{74a}$ respectively. Thus, the anionic form of 2-pyridone cannot be generated easily upon treatment of pyridone with NEt$_3$. However, the anionic **TNQ$^-$** might be generated by NEt$_3$ because nitro groups substantially improve the acidity (Scheme 24). For example, the pKa value of phenol is 18^{74b} and that of 4-nitrophenol is $10.8,^{74a}$ whose change is by the order of seven. Hence, the formation of **TNQ$^-$** prevents the nucleophilic attack of anionic 2,4-pentanedione **25**.

The second factor is the lack of distortion in the quinolone framework. Both **TNQ-H** and **DNQ-Me** are planar molecules, which show low reactivity. On the other hand, highly reactive **TNQ-Me** is distorted by steric repulsion between the 8-nitro and 1-methyl groups, as mentioned in the last section.

56

These facts suggest that distortion of the quinolone ring is important for activation.
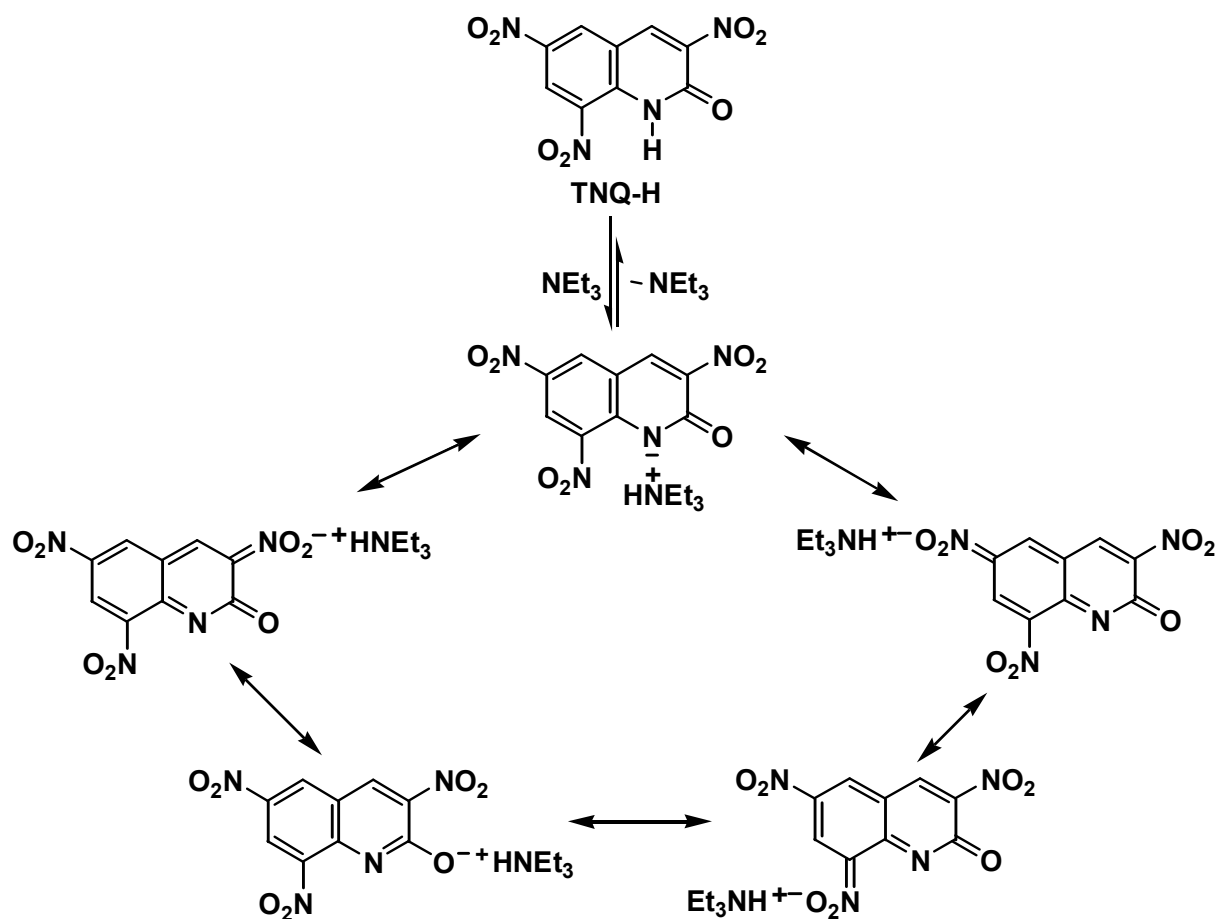
Scheme 24. Resonance Structures of TNQ-H

4-2-5. Consideration of the Effect of the Nitro Group

On the basis of the experimental results mentioned so far, I suggest a plausible reason for the remarkable activity of **TNQ-Me**. The 8-nitro group is certainly electron-withdrawing and diminishes the electron density at the 4-position of **TNQ-Me**, however, it is not so influential for the following two reasons. One is the distance between the two positions, namely the 8-nitro group locates at far from the reaction site. The other reason is the torsion of the

8-nitro group, which prevents an effective overlap of the π-orbital with those widespread on the quinolone ring. Hence, it is considered that the steric effect contributes in addition to the electronic effect to the high reactivity of **TNQ-Me**. Steric repulsion between the 8-nitro and the 1-methyl groups distorts the quinolone skeleton, in which the pyridone ring cannot be coplanar with the benzene ring. As a result of the distortion, the aromaticity of the pyridone moiety[36] is decreased and the nitroalkene property is considerably increased, which realizes high reactivity of **TNQ-Me**.

This consideration prompted me to employ 3,6-dinitroquinolone that has a bulky substituent at the 1-position and which is also sterically activated. The ethyl group could be readily introduced in a way similar to the methyl group.[82] However, several attempts to introduce more bulky substituents failed. **DNQ-Et** induced no change upon treatment with 2,4-pentanedione (**25**) in the presence of NEt$_3$ under the same conditions employed for **TNQ-Me** (Scheme 25). The most likely reason that the ethyl group was not bulky enough for activation of the quinolone skeleton by steric repulsion with a hydrogen at the 8-position.
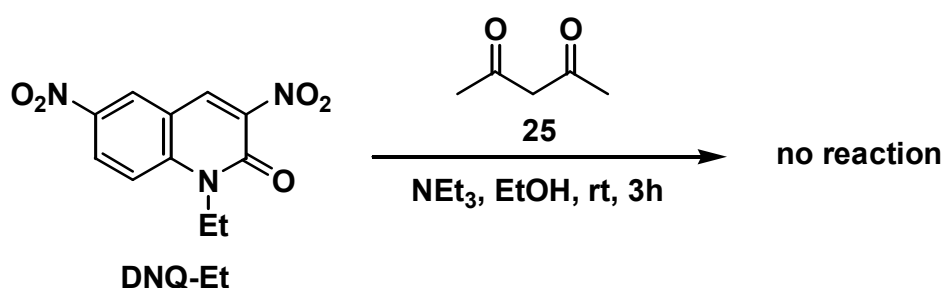
Scheme 25. Reaction of **DNQ-Et** with **25**

In conclusion, the work in this chaoter provides fundamental information about chemical behavior for 1-substituted 2-quinolone derivatives.

The steric repulsion distorts the quinolone ring, which decreases the aromaticity[36] and improves the reactivity. Because the pyridone moiety has a nitroalkene property, **TNQ-Me** could be used as electron-poor heterodiene or dienophile,[83] which is described in the next chapter.

CHAPTER 5.   Cycloaddition of 1-Methyl-3,6,8-trinitro-2-quinolone

5-1. Introduction

Cycloaddition is one of the fundamental protocols in organic syntheses for construction of a new ring from two units accompanied by formation of two bonds.   If the pyridone moiety of 1-methyl-2-quinolone is usable as a substrate for cycloaddition, it will be possible to synthesize a variety of polycyclic quinolones.   However, there are only a few examples of the cycloaddition using 1-methyl-2-quinolone derivatives[63, 65] because they are generally intact due to their aromaticity.[36]

Nagata's group reported the Diels-Alder reaction of *N*-substituted 3-phenylthio-2-quinolone with trimethylsilyloxy-1,3-butadiene in the presence of ethylaluminium dichloride at room temperature (Scheme 26).[65c]   However, this reaction suffers from limited scope of substrates.
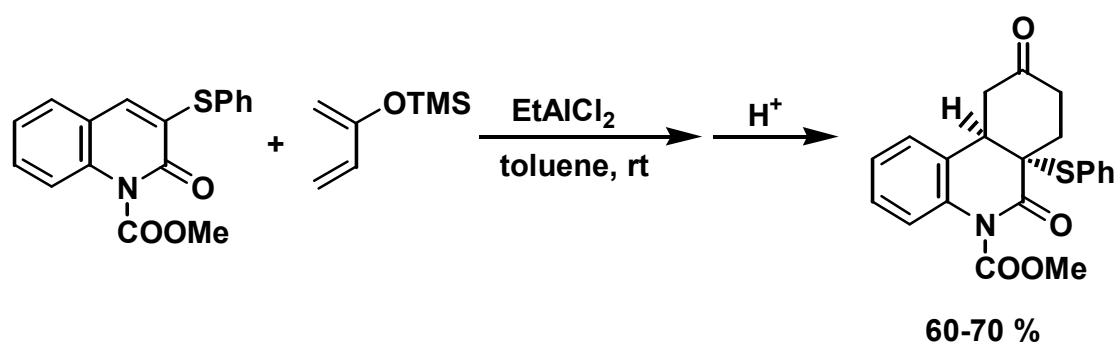
Scheme 26. Diels-Alder Reaction of *N*-substituted 3-Phenylthio-2-quinolone

Fujita succeeded in causing the cycloaddition of 1-methyl-2-quinolone by introducing an electron-withdrawing group at either the 3- or the 4-position

(Scheme 27).[63]   In this reaction, the pyridone ring behaves as an electron-poor dienophile, although severe conditions are necessary.

EWG = electron-withdrawing group
EDG = electron-donating group

90-200 ℃
atmospheric-10 kbar
2-6 days

90 ℃, 10 kbar, **0-78 %**
160-200 ℃, atmospheric, **5-98 %**
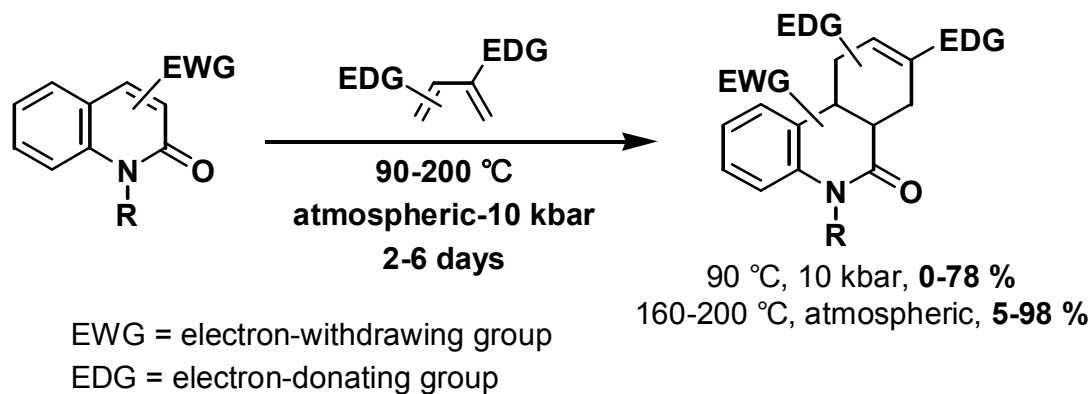
Scheme 27. Diels-Alder Reaction of 1-Methyl 3 or 4-Substituted 2-Quinolone

In the previous chapters, it was mentioned that 1-methyl-3,6,8-trinitro-2-quinolone (**TNQ-Me**) shows high reactivity. **TNQ-Me** readily undergoes *cine*-substitution upon treatment with several kinds of nucleophiles such as 1,3-dicarbonyl compounds,[66] amines,[76] enamines, ketones,[75] aldehyde[75] and phenoxides.[78]   In these reactions, the C-C or the C-N bond is regioselectively formed, which enables further functionalization of the 1-methyl-2-quinolone skeleton.   In chapter 4, it was shown that high reactivity of **TNQ-Me** is due to the increased nitroalkene property as a result of steric repulsion between the 1-methyl and the 8-nitro groups.[70]   This structural feature should allow cycloaddition even under milder conditions.

Nitroalkenes are often used for cycloaddition,[83] and they show two kinds of reactivities under different conditions.[83, 84]   When the nitro group behaves as an electron-withdrawing group, nitroalkene acts as a dienophile to

react with electron-rich diene affording cycloadducts (Scheme 28)[83, 85]. On the other hand, nitroalkene also behaves as an electron-poor heterodiene and causes cycloaddition with electron-rich dienophiles leading to cyclic nitronate (oxazine derivative), as illustrated in Scheme 29.[83, 86] There is a possibility that **TNQ-Me** also shows dual reactivities in the cycloaddition.

R^1 = H, R^2 = Me; R^1 = Me, R^2 = H,
R^1 = Me$_2$C=CHC$_2$H$_4$, R^2 = H

Ono N., 1987 [85b]
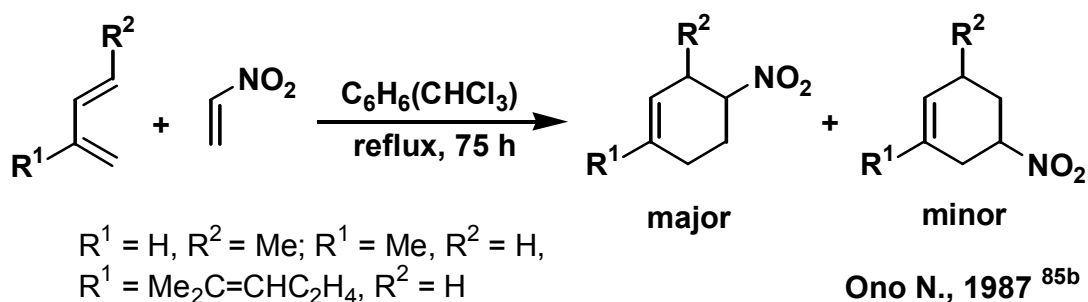
Scheme 28. Behavior of Nitroalkene as the Dienophile

Ar = *p*-NO$_2$C$_6$H$_4$
Dienophile = CH$_2$=CHOEt, 2,3-dihydrofuran, 3,4-dihydro-2H-pyran,
1-methoxycyclopentene, 1-methoxycyclohexene

Tohda Y., 1988 [86]
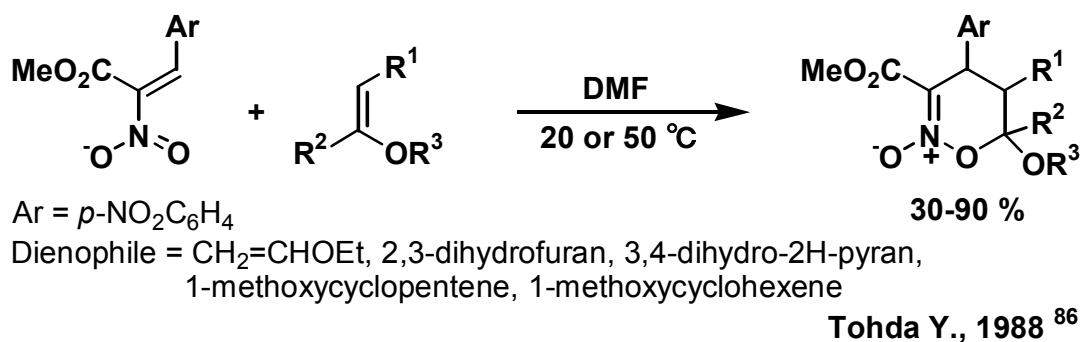
Scheme 29. Behavior of Nitroalkene as the Heterodiene

5-2. Results and Discussion

5-2-1. Diels-Alder Reactions of TNQ-Me with Dienes

Cycloaddition of **TNQ-Me** with dienes was studied in which **TNQ-Me** was regarded as an electron-poor dienophile. When cyclopentadiene was

allowed to react with **TNQ-Me** in acetonitrile under reflux, the Diels-Alder reaction proceeded to afford tetracyclic compounds **29** in moderate yield (Scheme 30).
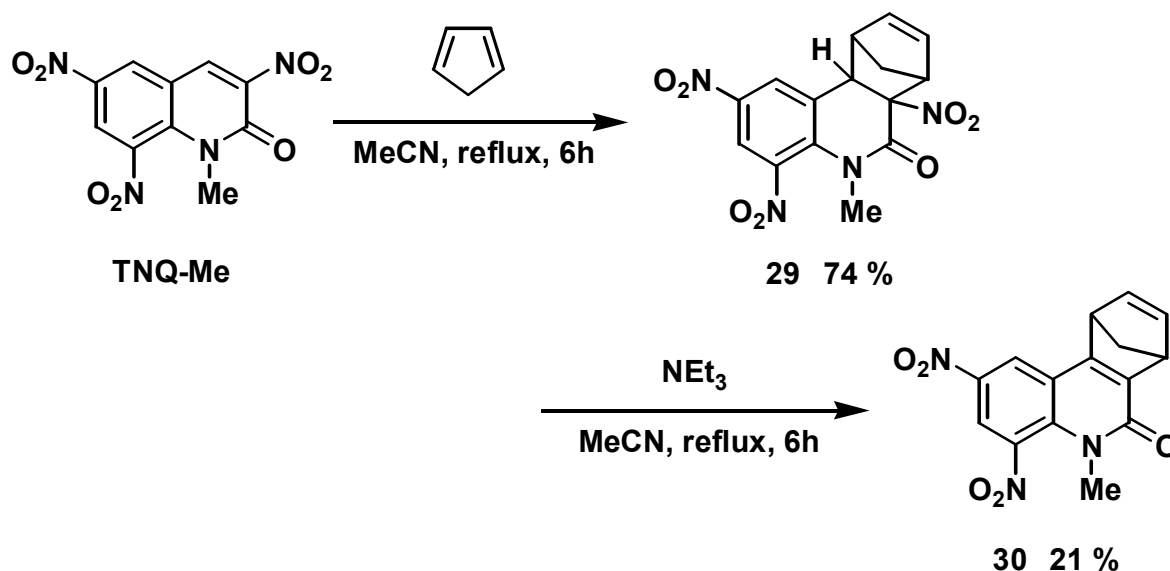
Scheme 30. Diels-Alder Reaction of **TNQ-Me** with Cyclopentadiene

In the ^{1}H-^{1}H COSY spectrum of **29**, the presence of coupling between bridgehead protons H_a and H_b was observed, which indicates that a bicyclic structure is included, and other correlations were satisfactorily confirmed. Coupling constants measurable in the ^{1}H NMR are shown in Figure 8. Since cycloadduct **29** had a 3,4-dihydroquinolone structure, nitrous acid was easily eliminated to give aromatized product **30** in 21% yield upon treatment with triethylamine in refluxing acetonitrile. In this case, the recovery of **TNQ-Me** by the NEt$_3$ promoted retro-Diels-Alder reaction was observed, which is considered to be the reaction for low yield of aromatized product **30**.
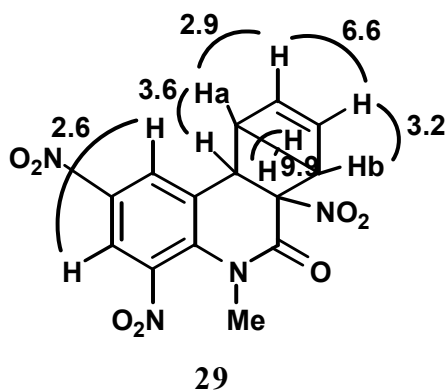
Figure 8. Measurable Coupling Constants in the ^{1}H NMR of Cycloadduct **29**

On the other hand, other reactivities were observed when **TNQ-Me** was treated with π-electron sufficient heterocycles. In the case of pyrrole, cycloadduct was not obtained and the mixture of *cine*-substitution product **31** and dihydroquinolone intermediate **32** was isolated in 56% and 19% yields, respectively (Scheme 30). Since pyrrole is an electron-rich aromatic compound, electrophilic substitution on the pyrrole ring predominantly proceeded rather than cycloaddition in which **TNQ-Me** behaved as the electrophile. Furthermore, the conversion of dihydroquinolone intermediate **32** to *cine*-substitution product was effectively performed under heated conditions in the presence of NEt$_3$. When furan was used instead of pyrrole, no reaction proceeded under the same conditions. The employed conditions were not severe enough to cause both electrophilic substitution and cycloaddition.
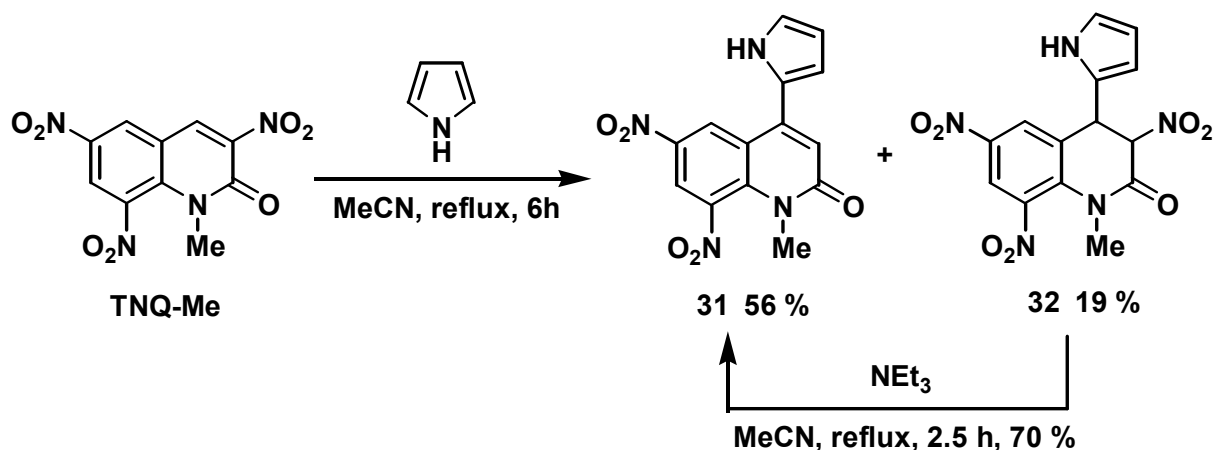
Scheme 30. Nucleophilic Substitution of **TNQ-Me** with Pyrrole

The results mentioned above prompted me to study the cycloaddition of **TNQ-Me** with dienes. The cycloaddition with heterodiene having an amino moiety is expected to assist the aromatization intramolecularly and lead to a phenanthridine derivative. When the reaction of **TNQ-Me** with hydrazone of 2-butenal was conducted, isolation of phenanthridine derivative **35** was occurred despite a low yield (Scheme 31). This reaction is initiated with tautomerism of hydrazone affording hydrazinobutadiene, subsequently this tautomer constructs a six-membered ring at the nitroalkene moiety of **TNQ-Me** by cycloaddition. During the following aromatization of cycloadduct **34**, a hydrazino group is considered to assist the elimination of nitrous acid. However, eliminated hydrazine caused side reactions yielding a complex reaction mixture.
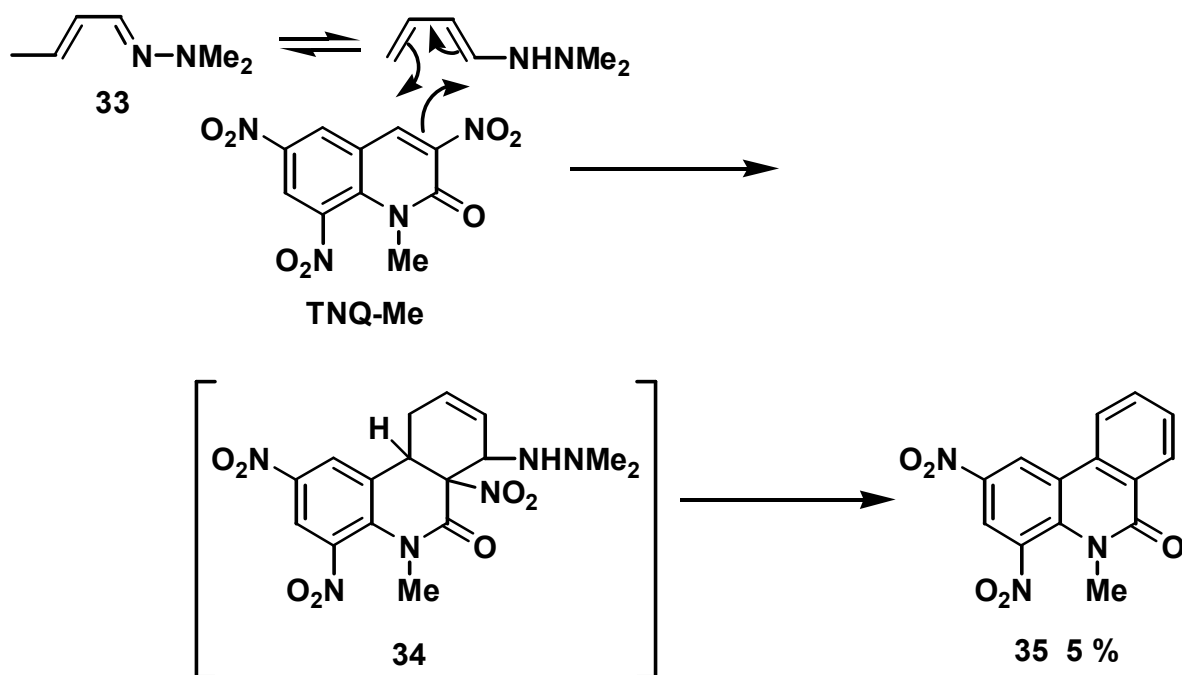
Scheme 31. Diels-Alder Reaction of **TNQ-Me** with Hydrazinobutadiene

Another kind of electron-rich heterodiene was employed. When α,β-unsaturated oxime was used with **TNQ-Me** at elevated temperature, cycloaddition proceeded yielding polycyclic diazaphenanthrene **36** in moderate yield (Scheme 32). The cycloaddition leads to an adduct intermediate from which water and nitrous acid are eliminated to afford aromatized product **36**. These experimental results reveal that **TNQ-Me** behaves as the highly reactive dienophile for cycloaddition. This fact satisfactorily agrees with our proposal that **TNQ-Me** shows a nitroalkene property rather than aromaticity.

Scheme 32. Diels-Alder Reaction of **TNQ-Me** with α,β-Unsaturated Oxime

5-2-2. Cycloaddition of TNQ-Me with Alkene

It has been shown here that **TNQ-Me** acts as dienophile leading to polycyclic azaheterocyclic compounds. In this section, the cycloaddition of **TNQ-Me** with electron-rich alkene is studied, in which **TNQ-Me** behaves as electron-poor heterodiene.

When a solution of **TNQ-Me** and ethoxyethene in acetonitrile was stirred at room temperature for 2 days, pale yellow solid was precipitated. On the basis of analytical and spectral data, the structure of the isolated product was determined as cycloadduct **37**. Because cycloadduct **37** is a cyclic nitronate, nucleophilic substitution should be possible. When a solution of nitronate **37** in methanol was heated, the ring opening reaction of **37** proceeded to afford 3,4-dihydro-4-(2,2-dialkoxyethyl)-quinolone **38a** (Scheme 33). A similar reaction also occurred giving **38b** when **37** was heated in ethanol. Aromatization of dihydroquinolones **38a** and **38b** were easily performed to afford **39a** and **39b** upon treatment with NEt$_3$. 1-Methyl-2-quinolone derivatives **39a** and **39b** were thought to be useful intermediates for syntheses of versatile 4-substituted 1-methyl-2-quinolone derivatives because the acetal function is equivalent to a formyl group. Actually, hydrolysis of **38b** proceeds to furnish **40** under acidic conditions despite low yield.

Scheme 33. Diels-Alder Reaction of **TNQ-Me** with Electron-rich Alkene

5-2-3. Dual Reactivities of TNQ-Me in the Cycloaddition

In the last two sections, it has been shown that **TNQ-Me** behaves as either dienophile or heterodiene in cycloaddition to afford polycyclic 1-methyl-2-quinolones. In general, both dual reactivities are not observed at the same time. Only one single example is found in the literature[87] which yields both products under same conditions, however nitro substituted bicyclo[2.2.2]octane is formed from cyclic nitronate via [3,3]-sigmatropic

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rearrangement (Scheme 34). I found that **TNQ-Me** shows dual reactivities in the same reaction system under mild conditions.
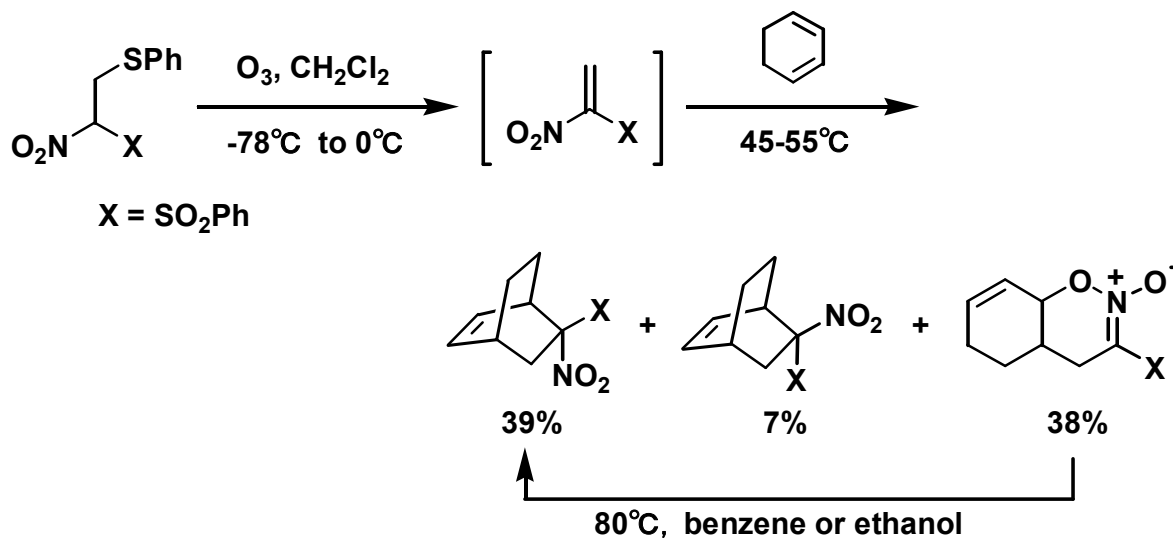
Scheme 34. Dual Behaviors of Nitroalkene in the Same Reaction System.

When the reaction of **TNQ-Me** with ethoxyethene was conducted in the presence of NEt$_3$, pale brown solid precipitated during the reaction. The elemental analysis of the product gave the empirical formula $C_{21}H_{22}N_7O_{10}$ that corresponds to the dimeric structure of **TNQ-Me** having an additional carbon with loss of one molecule of nitrous acid, and the MS spectrum also supported this result. In the ^{1}H NMR, only three kinds of signals were observed in the aromatic region, namely a couple of doublet signals appeared at 9.04 and 10.11 ppm (J = 2.3 Hz) and a singlet at 10.41 ppm, and the integral value for the latter singlet was half of those for each doublet. These facts suggest that the product has a symmetrical structure and that a new aromatic ring was formed between the two rings. Hence, the structure of the product was determined as quinolino[3,4-*b*][1,9]diazaphenanthrene derivative **41** (Scheme 35).
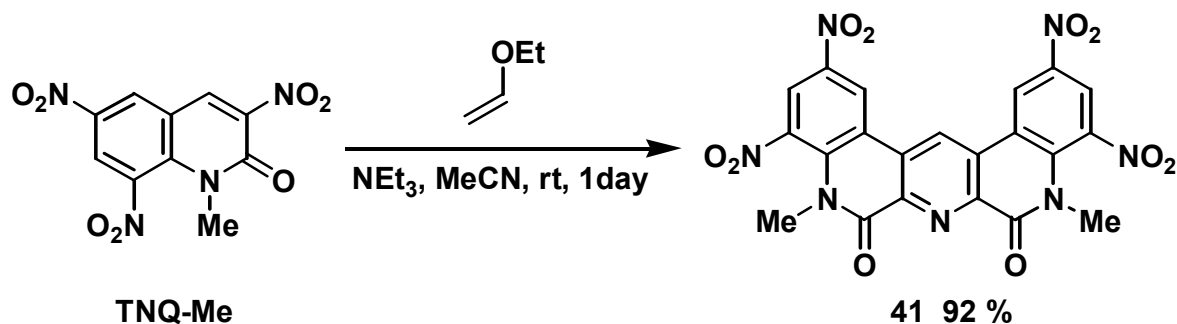
Scheme 35. Preparation of Dimeric **TNQ-Me**

A plausible mechanism for this reaction is proposed in Scheme 36. The 3- and 4-positions of **TNQ-Me** behave as an electron-poor heterodiene to cause cycloaddition with electron-rich alkene, ethoxyethene, which forms cyclic nitronate **37**. In all probabilitys NEt$_3$ accelerates the prototropy from the pyridine ring to the oxygen atom of the nitronate. Then, retro Diels-Alder reaction occurs to give α,β-unsaturated oxime **42** with a loss of ethyl formate.[84] In the ^{1}H NMR of the reaction mixture, signals of ethyl formate were actually observed. The cycloaddition with another **TNQ-Me** molecule constructs a new pyridine ring, and succeeding aromatization furnishes polycyclic product **41** together with elimination of nitrous acid and water. The experimental result that the Diels-Alder reaction of **TNQ-Me** with α,β-unsaturated oxime provided diazaphenanthrene **36**, as mentioned at section 5-2-1 (Scheme 30), also supports this proposed mechanism. In this process, the former oxime **42** behaves as an electron-rich heterodiene and the latter **TNQ-Me** behaves as an electron poor dienophile.

Nitroalkenes are widely employed for cycloaddition reactions because of their high electron deficiency and the easy chemical conversion of the nitro or the nitronate group.[83] Dual behaviors of nitroalkene, as the heterodiene and as

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the dienophile, lead to versatile skeletons.   However, both reactivities are rarely observed in the same reaction system because they usually require different conditions.

Nevertheless, dual reactivities are involved in the present reaction. Namely, the partial structure of **TNQ-Me** behaves as heterodiene to cause cycloaddition with electron-rich alkene in the initial step, and **TNQ-Me** behaves as an electron-poor dienophile to form a new pyridine ring in the last step in which **TNQ-Me** reacts with α,β-unsaturated oxime derived from cyclic nitronate **37**.   This kind of reaction has not been known to the best of our knowledge. Although further study is necessary by using other substrates, electron-rich dienophiles and dienes, this reaction is definitely the first stage for development of new methodology affording 1-methyl-2-quinolone derivatives and for new nitroalkene chemistry.
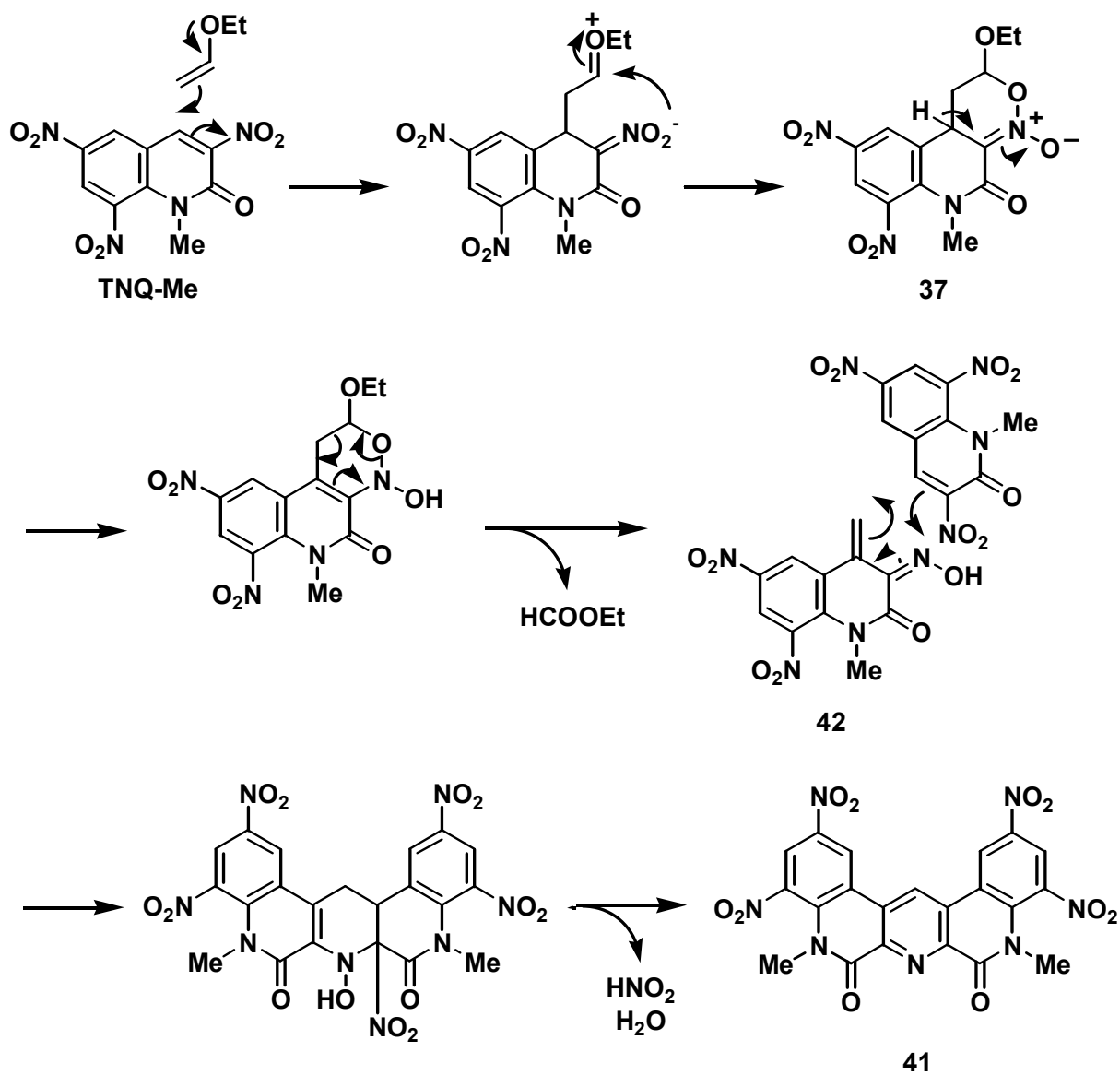
Scheme 36. A Plausible Mechanism for Formation of **41**

Conclusion

In this thesis, new functionalization methods of the 1-methyl-2-quinolone skeleton were developed utilizing 1-methyl-3,6,8-trinitro-2-quinolone (**TNQ-Me**), which shows extremely high reactivity. It was possible to employ **TNQ-Me** as a useful precursor of versatile 1-methyl-2-quinolone derivatives which were hitherto unknown in both natural and unnatural products. Furthermore, a study on the relationship between structure and reactivity of nitroquinolones was also performed. As a result, the mechanism for activation of **TNQ-Me** was clarified.

In Chapter 1, reactions of **TNQ-Me** with amines were studied. When primary amines were employed, the C-N bond formation was achieved at the 4-position of **TNQ-Me** to give *cine*-substitution products, 4-alkylamino-6,8-dinitro-1-methyl-2-quinolones **4**, and ammonium salts of 4-amioquinoline-3,4-dihydro-3-nitronic acid **3**. In addition, secondary and tertiary amines caused a coupling reaction giving a dimeric 1-methyl-2-quinolone derivative **5** under mild conditions.

In Chapter 2, acylmethylation of **TNQ-Me** was carried out for construction of a new family of 1-methyl-2-quinolones. Enamines were usable as the nucleophile to afford ammonium salts **13** of 3,4-dihydro-6,8-dinitro-2-oxoquinoline-3-nitronic acid substituted with an acylmethyl group at the 4-position. Furthermore, we succeeded in synthesizing 4-acylmethyl-1-methyl-6,8-dinitro-2-quinolones **12** effectively when **TNQ-Me** was treated with less reactive ketones or aldehyde in the presence of triethylamine. Aliphatic, aromatic, and heterocyclic ketones were applicable to this reaction to give corresponding acylmethylated quinolones.

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In Chapter 3, phenoxides were employed as a nucleophile in order to improve the synthetic utility of the *cine*-substitution of **TNQ-Me**, which realizes the easy arylation of the 1-methyl-2-quinolone skeleton. The *cine*-substitution of **TNQ-Me** with phenoxides proceeded affording 4-arylated 1-methyl-2-quinolone derivatives. This reaction is also regarded as an electrophilic arylation of the benzene ring, in which **TNQ-Me** behaved as the electrophile having aromaticity. In the cases of unsabstituted phenoxide, *o*-methylphenoxide, and highly electron-rich *p*-methoxyphenoxide, double substitution easily proceeded to provide 2,4-bis(quinolyl)phenols **20, 21c** despite steric hindrance.

In Chapter 4, reactivities of nitroquinolones were compared. While **TNQ-Me** showed high reactivity, demethylated or denitrated quinolones caused no change under the same conditions, which indicates that both the 1-methyl and the 8-nitro groups were necessary for activation of the 1-methyl-2-quinolone framework. On the basis of X-ray analyses, it was found that steric repulsion between these substituents distorted the quinolone skeleton, which diminishes the aromaticity of the pyridone moiety and increases the nitroalkene property instead. As a result, **TNQ-Me** attains considerably high reactivity.

In Chapter 5, cycloadditions of **TNQ-Me** were studied because the 3- and the 4-positions of **TNQ-Me** were found to reveal a nitroalkene property in Chapter 4. **TNQ-Me** behaved as a dienophile in reactions with 1,3-dienes or 1,3-heterodienes, and condensed 1-methyl-2-quinolones **30** and **36** were formed under mild conditions. On the other hand, **TNQ-Me** also behaved as a heterodiene to furnish cyclic nitronate **37** in the reaction with electron-rich dienophile. When the same reaction was conducted in the presence of triethylamine, quinolino[3,4-*b*][1,9]diazaphenanthrene derivative **41** was

efficiently produced. In the present reaction, **TNQ-Me** showed the dual behavior of nitroalkene, both as heterodiene and as dienophile, at the same time. These cycloadditions will provide a new stage for nitroalkene chemistry.

Although the 1-methyl-2-quinolone framework is often found in natural products and other functional materials such as medicines and luminiferous materials, syntheses of functionalized derivatives have not been easily achieved because of their aromaticity. In the present investigation, a variety of new 1-methyl-2-quinolone derivatives were synthesized from **TNQ-Me**, which is highly activated by steric repulsion between the 1-methyl and the 8-nitro groups. Furthermore, dual reactivities of nitroalkene, both as heterodiene and dienophile, were observed at the same time under mild conditions. These results contribute to the chemistry of both heterocyclic compounds and nitroalkenes.

Experimental

General

The melting points were determined on a Yanaco micro-melting-points apparatus, and were uncorrected. [1]H spectra were measured on a Bruker DPX-400 at 400 MHz and on a Hitachi R1200 at 60 MHz with TMS as an internal standard. ^{13}C NMR spectra were measured on a Bruker DPX-400 at 100 MHz with TMS as an internal standard, and assignments of signals (s, d, t and q) were made from DEPT experiments. IR spectra were recorded on a Horiba FT-200 IR spectrometer. Mass spectrum was recorded on a JEOL JMS-AX505HA. Elemental microanalyses were performed using a Yanaco MT-3 CHN corder. In some cases, satisfactory analytical data of salt **3** were not obtained because of unstable and hydroscopic properties. Methylamines and dimethylamines were prepared from corresponding amines by methylation with formaldehyde in the presence of formic acid.[88] Enamines were prepared from corresponding ketones and morpholine in the usual manner. They were distilled or recrystallized prior to use. The other reagents and solvents were commercially available and used as received. All of reactions were carried out under ambient atmosphere. Column chromatography was performed using Wakogel C-200.

Preparation of 1-methyl-3,6,8-trinitro-2-quinolone (TNQ-Me)

1-Methyl-2-quinolone[82a,b] was prepared by oxidation of 1-methylquinolinium ion using potassium ferricyanide (III) under alkaline conditions after methylation of quinoline with dimethyl sulfate. Nitration of 1-methyl-2-quinolone with fuming nitric acid (d = 1.52) afforded **TNQ-Me** in 90% yield.

Ammonium salts of 4-alkylamino-3,4-dihydro-1-methyl-3,6,8-trinitro-2-quinolone 3.

To a soltution of **TNQ-Me** (300 mg, 1 mmol) in acetonitrile (15

mL), a solution of amine (5 mmol) in acetonitrile (5 mL) was added over 5 minutes. The resultant solution was stirred at room temperature for 2 hours. The precipitated yellow solid during the reaction was collected by filtration and successively washed with small amounts of acetonitrile and hexane to afford ammonium salt **3**.

Methylammonium 3,4-dihydro-6,8-dinitro-1-methyl-4-methylamino-2-quinolone-3-nitronate (3a). Yellow powder, mp 103-111 °C (dec.). IR (KBr / cm^{-1}) 3600-3300 (br), 1659, 1603, 1539, 1524, 1338, 1215, 1074, 974; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.07 (br s, 3H), 2.40 (br s, 3H), 2.95 (s, 3H), 5.34 (br s, 1H), 5.5-6.5 (br, 4H), 8.41 (s, 1H), 8.56 (s, 1H). Anal. Calcd. for C$_{12}$H$_{16}$N$_6$O$_7$: C, 40.45; H, 4.53, N, 23. 59. Found: C, 40.42; H, 4.47; N, 23.23.

Propylammonium 3,4-dihydro-6,8-dinitro-1-methyl-4-propylamino-2-quinolone-3-nitronate (3b). Yellow powder, mp 99-107 °C (dec.). IR (KBr / cm^{-1}) 3500-3300 (br), 1653, 1608, 1537, 1338, 1221, 1072, 980; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 0.7-0.9 (br, 6H), 1.3-1.4 (br, 2H), 1.5-1.6 (br, 2H), 2.2-2.3 (br, 1H), 2.3-2.4 (br, 1H), 2.6-2.8 (br, 3H), 2.96 (s, 3H), 5.38 (br s, 1H), 4.5-7.0 (br, 3H), 8.40 (s, 1H), 8.56 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 10.9 (q), 11.7 (q), 21.1 (t), 22.7 (t), 33.8 (q), 40.9 (t), 46.2 (t), 54.8 (d), 106.8 (s), 120.5 (d), 126.7 (d), 132.7 (s), 137.1 (s), 139.2 (s), 139.5 (s), 160.0 (s). Anal. Calcd. for C$_{16}$H$_{24}$N$_6$O$_7$: C, 46.60; H, 5.87; N, 20.38. Found: C, 46.82; H, 5.60, N, 20.14.

Buthylammonium 4-buthylamino -3,4-dihydro-6,8-dinitro-1-methyl-2- quinolone-3-nitronate (3c).

The reaction was similarly conducted to the preparation of ammonium salts of 4-alkylamino-3,4-dihydro-1-methyl-3,6,8-trinitro- 2-quinolone **3** using butylamine (1 mmol) and acetonitrile (20 mL). Yellow powder, ^{1}H NMR (400 MHz, DMSO-d_6) δ = 0.7-1.0 (br, 6H), 1.2-1.7 (br, 8H), 2.8-3.6 (br, 10H), 5.2-5.6

(br, 1H), 8.3-8.7 (br, 2H). Because this salt was not stable under ambient conditions to give **TNQ** and it was too hydroscopic, only ^{1}H NMR could be measured.

Isopropylammonium **3,4-dihydro-6,8-dinitro-4-isopropylamino-1-methyl-2-quinolone-3-nitronate (3d).** Yellow powder, mp 110-120 °C (dec.). IR (KBr / cm[-1]) 3500-3300 (br), 1657, 1605, 1533, 1336, 1223, 1074, 978; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 0.5-1.5 (br, 12H), 2.7-2.8 (br, 1H), 2.9-3.0 (br, 3H), 3.0-3.2 (br, 2H), 5.1-5.3 (br, 1H), 4.5-7.0 (br, 3H), 8.2-8.3 (br, 1H), 8.5-8.6 (br, 1H). Anal. Calcd. for $C_{16}H_{24}N_6O_7$: C, 46.60; H, 5.87; N, 20.38. Found: C, 46.32; H, 5.87, N, 20.65.

Isobutylammonium **3,4-dihydro-6,8-dinitro-4-isobutylamino-1-methyl-2-quinolone-3-nitronate (3e).** Yellow powder, mp 90-110 °C (dec.). IR (KBr / cm[-1]) 3500-3300 (br), 1653, 1606, 1539, 1336, 1227, 1072, 980. Because this salt was decomposed in DMSO during the measurement, satisfactory NMR data could not be obtained. Anal. Calcd. for $C_{18}H_{28}N_6O_7$: C, 49.09; H, 6.41; N, 19.08. Found: C, 48.51; H, 6.22, N, 19.22.

***sec*-Butylammonium** **4-*sec*-butylamino-3,4-dihydro-6,8-dinitro-1-methyl-2-quinolone-3-nitronate (3f).** Yellow powder, mp 90-100 °C (dec.). IR (KBr / cm[-1]) 3500-3300 (br), 1660, 1606, 1527, 1336, 1227, 1074, 980; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 0.4-1.9 (br, 16H), 2.7-3.2 (br, 5H), 5.3-5.5 (br, 1H), 4.0-7.0 (br, 4H), 8.30 (br s, 1H), 8.56 (br s, 1H). Anal. Calcd. for $C_{18}H_{28}N_6O_7$: C, 49.09; H, 6.41; N, 19.08. Found: C, 48.66; H, 6.32, N, 19.13.

***tert*-Butylammonium** **4-*tert*-butylamino-3,4-dihydro-6,8-dinitro-1-methyl-2-quinolone-3-nitronate (3g).** Yellow powder, mp 100-120 °C (dec.). IR (KBr / cm[-1]) 3500-3300 (br), 1674, 1605, 1518, 1331, 1225, 1074, 974; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 0.4-1.9 (br, 18H), 2.7-3.9 (br, 3H), 5.51 (br s, 1H), 3.9-6.2

(br, 4H), 8.8-9.5 (br, 2H). In this case, satisfactory analytical data were not obtained because of unstable and hydroscopic properties.

Benzylammonium 4-benzylamino-3,4-dihydro-6,8-dinitro-1-methyl-2-quinolone-3-nitronate (3h). Yellow powder, mp 130-136 °C (dec.). IR (KBr / cm^{-1}) 3500-3300 (br), 1653, 1606, 1531, 1338, 1221, 1072, 982; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.6-3.3 (br, 3H), 3.3-4.4 (br, 5H), 4.7-6.8 (br, 4H), 6.8-7.7 (br, 10H), 8.8-9.6 (br, 2H). Anal. Calcd. for $C_{24}H_{24}N_6O_7$: C, 56.69; H, 4.76; N, 16.53. Found: C, 56.74; H, 4.69, N, 16.66.

4-Alkylamino-6,8-dinitro-1-methyl-2-quinolone 4. To a solution of **TNQ-Me** (300 mg, 1 mmol) in acetonitrile (15 mL), a solution of amine (5 mmol) in acetonitrile (5 mL) was added over 5 minutes. After purging with nitrogen gas, the mixture was heated under reflux for 2 hours. The precipitated yellow solid was collected by filtration after cooling down to room temperature and successively washed with small amounts of acetonitrile and hexane to afford *cine*-substituted product **4**. The filtrate was concentrated, and the residue was treated with column chromatography on silica gel to give **4** (eluted with toluene).

6,8-Dinitro-1-methyl-4-propylamino-2-quinolone (4b). Yellow needles, mp 263-268 °C (dec.). IR (KBr / cm^{-1}) 3375, 1626, 1539, 1525, 1336, 1279; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.09 (t, *J* = 7.4 Hz, 3H), 1.82 (tq, *J* = 7.4, 7.4 Hz, 2H), 3.26 (dt, *J* = 5.3, 7.4 Hz, 2H), 3.41 (s, 3H), 4.98 (br s, 1H), 5.86 (s, 1H), 8.62 (d, *J* = 2.4 Hz, 1H), 8.72 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 11.6 (q), 21.7 (t), 34.2 (q), 45.4 (t), 94.2 (d), 118.7 (s), 119.6 (d), 122.3 (d), 125.9 (s), 139.1 (s), 148.6 (s), 153.1 (s), 163.1 (s). Anal. Calcd. for $C_{13}H_{14}N_4O_5$: C, 50.98; H, 4.61; N, 18.29. Found: C, 50.87; H, 4.51, N, 18.35.

6,8-Dinitro-4-isobutylamino-1-methyl-2-quinolone (4e). Yellow needles, mp 188-189 °C (dec.). IR (KBr / cm^{-1}) 3365, 1626, 1547, 1522, 1335, 1277; ^{1}H NMR

(400 MHz, CDCl$_3$) δ = 1.07 (d, J = 6.7 Hz, 6H), 2.09 (triple septet, J = 6.7, 6.7 Hz, 1H), 3.0-3.1 (br, 2H), 3.41 (s, 3H), 5.00 (br t, 1H), 5.86 (s, 1H), 8.60 (d, J = 2.4 Hz, 1H), 8.73 (d, J = 2.4 Hz, 1H).   Anal. Calcd. for C$_{14}$H$_{16}$N$_4$O$_5$ • 1 / 2 toluene: C, 57.37; H, 5.50; N, 15.29.   Found: C, 57.44; H, 5.43, N, 15.30.

Reaction of TNQ-Me with tributylamine

To a solution of **TNQ-Me** (294 mg, 1 mmol) in acetonitrile (10 mL), tributylamine (0.24 mL, 1 mmol) was added.   After stirring at room temperature for 7 days, the mixture was concentrated under reduced pressure.   The residue was treated with column chromatography on silica gel (eluent: chloroform / ethyl acetate = 9 / 1) to afford dimer **5** (193 mg, 0.41 mmol) and **6,8-DNQ** (14 mg, 0.06 mmol).   Reactions under different conditions or with other amines were conducted similarly.

3,4'-Bis(1-methyl-6,8-dinitro-2-quinolone) (**5**).   Pale yellow powder, mp 288-291 °C (dec.). IR (Nujol / cm^{-1}) 1662, 1554, 1346; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.41 (s, 3H), 3.43 (s, 3H), 7.06 (s, 1H), 8.56 (s, 1H), 8.57 (d, J = 2.5 Hz, 1H), 8.95 (d, J = 2.5 Hz, 1H), 9.02 (d, J = 2.6 Hz, 1H), 9.10 (d, J = 2.6 Hz, 1H) ; ^{13}C NMR (100 MHz, DMSO-d_6) δ = 34.7 (q), 34.7 (q), 122.0 (s), 122.6 (d), 122.7 (d), 122.7 (d), 124.6 (s), 126.1 (s), 128.4 (d), 129.4 (s), 137.3 (s), 137.5 (s), 137.7 (s), 138.2 (s), 140.1 (d), 140.2 (d), 140.3 (s), 145.0 (s), 160.8 (s), 161.1 (s); MS (FAB) 497 (M$^+$+1). Anal. Calcd. for C$_{20}$H$_{12}$N$_6$O$_{10}$: C, 48.40; H, 2.44; N, 16.93.   Found: C, 48.50; H, 2.42, N, 17.22.

1-Methyl-6,8-dinitro-2-quinolone (6,8-DNQ).[69, 70]

^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.34 (s, 3H), 6.95 (d, J = 9.6 Hz, 1H), 8.28 (d, J = 9.6 Hz, 1H), 8.87 (d, J = 2.2 Hz, 1H), 9.02 (d, J = 2.2 Hz, 1H).

Dimerization with monitoring by ^{1}H NMR

To a solution of **TNQ-Me** (29.4 mg, 0.1 mmol) in CD$_3$CN (0.3 mL),

trialkylamine (0.1 mmol) was added, and the solution was stirred at 25 °C. The monitoring was performed with ^{1}H NMR at intervals of a few or several hours. Since no other signal than **TNQ-Me** and dimmer **5** was observed in the aromatic region, the integral ration of **5** / (**TNQ-Me+5**) could be regarded as the conversion and yield of **5**. Reactions of **TNQ-Me** with alkyldimethylamines (**NRMe$_2$**) were also conducted in a similar way.

Reaction of TNQ-Me with tributylamine in the dark and under UV irradiation.

Except for shading with aluminium foil and irradiating UV with high pressure mercury lamp, reactions were conducted in a similar way to the reaction of **TNQ-Me** with tributylamine.

Reaction of TNQ-Me with morpholine in the absence of triethylamine.

To a soltution of **TNQ-Me** (300 mg, 1 mmol) in acetonitrile (20 mL), a solution of morpholine (2.3 mmol) in acetonitrile (20 mL) was added over 5 minutes. The resultant solution was stirred at room temperature for 1.5 hours. The yellow solid precipitated during the reaction was collected by filtration and successively washed with small amounts of acetonitrile to afford morpholinium salt **3j**.

Morphorinium 3,4-dihydro-6,8-dinitro-1-methyl-4-morpholino-

2- quinolone-3-nitronate (3j). Pale yellow powder, mp >93 °C (dec.). IR (KBr / cm^{-1}) 3062, 1657, 1606, 1539, 1336 ; ^{1}H NMR (400 MHz, CD$_3$CN) δ = 2.35-2.38 (m, 2H), 2.57-2.60 (m, 2H), 3.07-3.09 (m, 2H), 3.16 (s, 3H), 3.60 (m, 4H), 3.83-3.85 (m, 4H), 5.35 (s, 1H), 5.79 (br s, 2H), 8.42 (s 1H), 8.56 (d, J = 1.6 Hz, 1H) ; Anal. Calcd. for C$_{18}$H$_{24}$N$_6$O$_9$: C, 46.15; H, 5.16; N, 17.94. Found: C, 46.56; H, 5.16, N, 18.03.

Reaction of TNQ-Me with morpholine in the presence of triethylamine.

To a soltution of **TNQ-Me** (300 mg, 1 mmol) and morpholine (4230 mg, 49 mmol) in acetonitrile (15 mL), a solution of triethylamine (220 mg, 2.2 mmol) in acetonitrile (5 mL) was added over 5 minutes.   The resultant solution was stirred at 70 °C for 6 hours.   After removal of the solvent under reduced pressure the resultant residue was treated with column chromatography on silica gel to give *cine*-substitution product **4j** (eluted with benzene).

6,8-Dinitro-1-methyl-4-morpholino-2-quinolone (**4j**).   Yellow needles, Mp 222-224 °C (dec.). IR (KBr / cm^{-1}) 3089, 1670, 1620, 1601, 1537, 1348, 1331 ; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 3.15-3.17 (m, 4H), 3.45 (s, 3H), 3.99-4.01 (m, 4H), 6.35 (s, 1H), 8.72 (d, *J* = 2.7 Hz, 1H), 8.83 (d, *J* = 2.7 Hz, 1H) ; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 34.2 (q), 52.4 (t), 52.4 (t), 66.4 (t), 66.4 (t), 109.0 (d), 120.8 (s), 122.1 (d), 123.8 (d), 138.7 (s), 139.2 (s), 139.7 (s), 157.0 (s), 162.7 (s) ; Anal. Calcd. for C$_{14}$H$_{14}$N$_4$O$_6$: C, 50.30; H, 4.22; N, 16.76.   Found: C, 49.90; H, 4.10, N, 16.55.

The reaction of TNQ-Me with enamines in the presence of water.

To a solution of **TNQ-Me** (0.28 g, 0.95 mmol) and water (0.85 g, 47.2 mmol) in acetonitrile (25 mL), was added a solution of enamine **11** (1.37 mmol) in acetonitrile (10 mL) at room temperature, and the mixture was stirred for 3 days.   Generated precipitates were collected by filtration and successively washed with a small amount of acetonitrile to afford 4-acylmethyl-6,8-dinitro-1-methyl-2-quinolone **12** or morpholinium salt **13**.

4-Benzoylmethyl-6,8-dinitro-1-methyl-2-quinolone (**12a**).   Pale yellow powder, mp 229-230 °C (dec.). IR (KBr / cm^{-1}) 1682, 1670, 1529, 1342; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ = 3.37 (s, 3H), 5.05 (s, 2H), 6.98 (s, 1H), 7.62   (dd, *J* = 7.2, 7.4 Hz, 2H), 7.73 (t, *J* = 7.4 Hz 1H), 8.13 (d, *J* = 7.2 Hz 2H), 8.71 (d, *J* = 2.5 Hz, 1H), 8.89 (d, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ = 34.4 (q), 41.8

(t), 122.2 (d), 123.6 (s), 124.9 (d), 125.1 (d), 128.4 (d), 128.4 (d), 128.7 (d), 128.7 (d), 133.7 (d), 135.9 (s), 137.6 (s), 138.7 (s), 139.9 (s), 145.5 (s), 161.2 (s), 195.9 (s). Anal. Calcd. for $C_{18}H_{13}N_3O_6$: C, 58.85; H, 3.57; N, 11.44. Found: C, 58.67; H, 3.45, N, 11.50.

Morpholinium 4-(1-benzoylethyl)-3,4-dihydro-6,8-dinitro-1-methyl-2-oxoquinoline-3-nitronate (13b). Pale yellow powder, mp 160-162 °C (dec.). IR (KBr / cm^{-1}) 1675, 1657, 1537, 1522, 1358, 1336; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.06 (d, J = 6.7 Hz, 3H), 1.2-2.5 (br, 2H), 3.03 (s, 3H), 3.2-3.4 (m, 4H), 3.9-4.1 (m, 4H), 4.2-4.3 (m, 1H), 5.16 (d, J = 3.6 Hz, 1H), 7.51 (m, 2H), 7.63 (t, J = 7.5 Hz, 1H), 7.92 (d, J = 2.2 Hz, 1H), 8.16 (d, J = 8.0 Hz, 2H), 8.44 (d, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 12.3 (q), 34.8 (q), 43.2 (d), 43.8 (t), 43.8 (t), 45.3 (d), 64.1 (t), 64.1 (t), 108.0 (s), 120.5 (d), 126.7 (d), 128.7 (d), 128.7 (d), 129.0 (d), 129.0 (d), 131.5 (s), 133.7 (d), 136.1 (s), 138.6 (s), 139.4 (s), 141.0 (s), 162.9 (s), 200.6 (s). Anal. Calcd. for $C_{23}H_{25}N_5O_9$: C, 53.59; H, 4.89; N, 13.59. Found: C, 53.39; H, 4.88, N, 13.72.

Morpholinium 4-(α-benzoylbenzyl)-3,4-dihydro-6,8-dinitro-1-methyl-2-oxoquinoline-3-nitronate (13c). Yellow powder, mp 132-133 °C (dec.). IR (KBr / cm^{-1}) 1684, 1651, 1535, 1371, 1335; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 2.31 (s, 3H), 3.26-3.29 (m, 4H), 3.96-3.99 (m, 4H), 4.97 (d, J = 2.3 Hz, 1H), 5.56 (d, J = 2.3 Hz, 1H), 6.84 (dd, J = 6.4, 3.4 Hz, 2H), 7.11-7.12 (m, 3H), 7.25-7.46 (m, 3H), 7.92 (d, J = 7.4 Hz, 2H), 8.42 (d, J = 2.6 Hz, 1H), 9.03 (d, J = 2.6 Hz, 1H); Two active protons assigned to N-hydrogens of morpholinium were not observed because of the overlap with water. ^{13}C NMR (100 MHz, CDCl$_3$) δ = 34.1 (q), 42.0 (d), 43.5 (t), 43.5 (t), 57.8 (d), 63.8 (t), 63.8 (t), 109.1 (s), 120.3 (d), 127.9 (d), 128.5 (d),128.5 (d), 128.6 (d), 128.6 (d), 128.9 (d), 128.9 (d), 129.1 (d), 129.1 (d), 129.2 (d), 131.8 (s), 133.1 (d), 135.3 (s), 135.9 (s), 138.5 (s), 139.6 (s),

141.1 (s), 162.7 (s), 198.2 (s).   Anal. Calcd. for $C_{28}H_{27}N_5O_9$: C, 58.22; H, 4.71; N, 12.13.   Found: C, 58.04; H, 4.57, N, 11.92.

Morpholinium 3,4-dihydro-6,8-dinitro-1-methyl-4-(2-oxocyclopentyl)-2-oxoquinoline-3-nitronate (13d).   Yellow powder, mp 126-128 °C (dec.). IR (KBr / cm^{-1}) 1732, 1660, 1525, 1338; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.41-1.44 (m, 1H), 1.76-1.82 (m, 1H), 1.94-2.04 (m, 3H), 2.26-2.32 (m, 1H), 2.54-2.59 (m, 1H), 3.13 (s, 3H), 3.27 (br t, *J* = 4.6 Hz, 4H), 3.98 (br t, *J* = 4.6 Hz, 4H), 5.14 (d, *J* = 4.7 Hz, 1H), 8.29 (d, *J* = 2.5 Hz, 1H), 8.49 (d, *J* = 2.5 Hz, 1H); Two active protons assigned to *N*-hydrogens of morpholinium were not observed because of the overlap with water. ^{13}C NMR (100 MHz, CDCl$_3$) δ = 20.4 (t), 26.0 (t), 34.5 (q), 38.1 (t), 39.3 (d), 43.6 (t), 43.6 (t), 53.4 (d), 64.0 (t), 64.0 (t), 108.0 (s), 120.4 (d), 126.7 (d), 132.8 (s), 138.7 (s), 139.4 (s), 141.4 (s), 162.8 (s), 217.1 (s).   Anal. Calcd. for $C_{19}H_{23}N_5O_9$: C, 49.03; H, 4.98; N, 15.05.   Found: C, 49.43; H, 5.10, N, 14.93.

Morpholinium 3,4-dihydro-4-(1,1-dimethyl-2-oxoethyl)-6,8-dinitro-1-methyl-2-oxoquinoline-3-nitronate (13e).   Yellow powder, mp 175-177 °C (dec.). IR (KBr / cm^{-1}) 1718, 1659, 1543, 1524, 1338; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.78 (s, 3H), 0.97 (s, 3H), 2.87 (s, 3H), 3.00-3.15 (m, 4H), 3.2-4.0 (br, 2H), 3.75-3.76 (m, 4H), 4.96 (s, 1H), 8.39 (s, 1H), 8.57 (s, 1H), 9.48 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 17.5 (q), 19.3 (q), 33.5 (q), 43.2 (t), 43.2 (t), 44.8 (d), 52.4 (s), 63.6 (t), 63.6 (t), 102.8 (s), 120.4 (d), 126.9 (d), 131.5 (s), 137.7 (s), 139.7 (s), 140.6 (s), 161.2 (s), 203.7 (d).   Anal. Calcd. for $C_{18}H_{23}N_5O_9$: C, 47.68; H, 5.11; N, 15.45.   Found: C, 47.55; H, 5.16, N, 15.51.

Acidification of morpholinium salt 13

To a solution of morpholinium salt **13** (1.0 mmol) in methanol (30 mL), 1 M hydrochloric acid (1.5 mL, 1.5 mmol) was added, and the mixture was stirred

for 0.5-3 days. Generated precipitates were collected by filtration and were washed with methanol (15 mL) to give dinydroquinolone **14**.

4-(1-Benzoylethyl)-3,4-dihydro-1-methyl-3,6,8-trinitro-2-quinolone (14b). White powder, mp 140.5-141.5 °C (dec.). IR (KBr / cm^{-1}) 1689, 1653, 1568, 1545, 1384; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.32 (d, J = 7.2 Hz, 1H), 3.30 (s, 3H), 3.64 (dq, J = 9.0, 7.2 Hz, 1H), 4.42 (dd, J = 9.0, 2.2 Hz, 1H), 5.34 (d, J = 2.2 Hz, 1H), 7.49-7.63 (m, 2H), 7.65 (t, J = 6.3 Hz, 1H), 7.84-7.86 (m, 2H), 8.38 (d, J = 2.6 Hz, 1H), 8.63 (d, J = 2.6 Hz, 1H); Two active protons assigned to *N*-hydrogens of morpholinium were not observed because of the overlap with water. ^{13}C NMR (100 MHz, CDCl$_3$) δ = 17.4 (q), 34.8 (q), 41.3 (d), 44.2 (d), 84.3 (d), 121.8 (d), 127.9 (d), 128.4 (d), 128.4 (d), 128.7 (s), 128.9 (s), 129.3 (d), 129.3 (d), 134.6 (d), 134.7 (s), 138.6 (s), 142.7 (s), 155.6 (s), 199.4 (s). Anal. Calcd. for C$_{19}$H$_{16}$N$_4$O$_8$: C, 53.27; H, 3.77; N, 13.08. Found: C, 52.99; H, 3.68, N, 12.90.

4-(α-Benzoylbenzyl)-3,4-dihydro-1-methyl-3,6,8-trinitro-2-quinolone (14c). White powder, mp 143-144 °C (dec.). IR (KBr / cm^{-1}) 1684, 1653, 1574, 1549, 1342; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 3.12 (s, 3H), 4.58 (d, J = 8.3, 1H), 4.86 (dd, J = 8.3, 2.0 Hz, 1H), 5.48 (d, J = 2.0 Hz, 1H), 6.93-6.95 (m, 2H), 7.23-7.26 (m, 3H), 7.35-7.39 (m, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.82-7.83 (m, 2H), 7.85 (d, J = 2.6 Hz, 1H), 8.50 (d, J = 2.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 34.5 (q), 44.3 (d), 54.5 (d), 85.0 (d), 121.4 (d), 128.4 (d), 128.5 (s), 128.6 (d), 128.9 (d), 129.0 (d), 129.3 (d), 129.8 (d), 133.5 (s), 134.2 (s), 134.9 (s), 138.5 (s), 139.8 (s), 142.3 (s), 159.3 (s), 195.2 (s). Anal. Calcd. for C$_{24}$H$_{18}$N$_4$O$_8$: C, 58.77; H, 3.70; N, 11.43. Found: C, 58.81; H, 3.70, N, 11.32.

3,4-Dihydro-4-(1,1-dimethyl-2-oxoethyl)-1-methyl-3,6,8-trinitro-2-quinolone (14e). Pale yellow needles, mp 173-175 °C (dec.). IR (KBr / cm^{-1}) 1720, 1653, 1560, 1541, 1344; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.15 (s, 3H), 1.21 (s, 3H),

3.24 (s, 3H), 4.33 (d, J = 1.6 Hz, 1H), 5.43 (d, J = 1.6 Hz, 1H), 8.35 (d, J = 2.5 Hz, 1H), 8.63 (d, J = 2.5 Hz, 1H), 9.41 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 19.7 (q), 20.2 (q), 34.8 (q), 45.8 (d), 48.2 (s), 83.7 (d), 109.3 (s), 121.9 (d), 125.9 (s), 127.5 (s), 128.9 (d), 139.2 (s), 160.0 (s), 200.8 (d). Anal. Calcd. for C$_{14}$H$_{14}$N$_4$O$_8$: C, 45.90; H, 3.85; N, 15.30. Found: C, 46.21; H, 3.84, N, 15.04.

The conversion from dihydroquinolone 14b to morpholinium salt 13b.

To a solution of dihydroquinolone **14b** (1 equiv.) in CDCl$_3$, morpholine (1.2 equiv.) was added in an NMR tube. The ^{1}H NMR analysis demonstrated that dihydroquinolone **14b** was converted to morpholinium salt **13b** quantitatively.

The reaction of TNQ-Me with enamines under anhydrous conditions.

To a solution of **TNQ-Me** (0.28 g, 0.95 mmol) in acetonitrile (19 mL), a solution of 1-morpholino-1-phenyl-1,2-propene (**11b**) (0.39 g, 1.92 mmol) in acetonitrile (11 mL) was added on the ice bath, and the resultant mixture was stirred for 2 days. After removal of the solvent, the residue was recrystallized from benzene-hexane to afford 4-enamino-3,4-dihydroquinolone **16b**.

3,4-Dihydro-1-methyl-4-(1-morpholino-1-phenyl-2-propenyl)-3,6,8-trinitro-2-oxoquinoline-3-nitronate (16b). Pale yellow needles, mp 157-158 °C (dec.). IR (KBr / cm^{-1}) 1718, 1653, 1566, 1541, 1344; ^{1}H NMR (60 MHz, CDCl$_3$) δ = 1.83 (s, 3H), 2.73 (t, J = 4.5 Hz, 4H), 3.14 (s, 3H), 3.73 (t, J = 4.5 Hz, 4H), 4.33 (d, J = 13.0 Hz, 1H), 5.56 (d, J = 13.0 Hz, 1H), 6.9-7.5 (m, 5H), 8.42 (d, J = 2.4 Hz, 1H), 8.62 (d, J = 2.4 Hz, 1H).

The trap of dihydroquinolone intermadiate as morpholinium salt 17

To a solution of **TNQ-Me** (0.60 g, 2.04 mmol) in acetonitrile (40 mL), a solution of 1-morpholino-1-cycloalkene **11** (3.95 mmol) and morpholine (0.18 g, 2.07 mmol) in acetonitrile (10 mL) was added, and the resultant mixture was

stirred at room temperature for 4 hours. Morpholinium salt **17** was precipitated as orange powder during the reaction and was collected by filtration.

Morpholimium 3,4-dihydro-6,8-dinitro-1-methyl-4-(2-morpholino-2,3-cyclopentyl)-2-oxoqui-noline-3-nitronate (17d). Orange powder, mp 149-152 °C (dec.). IR (KBr / cm^{-1}) 1647, 1535, 1333; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.14-1.22 (m, 1H), 1.27-1.32 (m, 1H), 1.73-1.83 (m, 1H), 1.95-2.02 (m, 1H), 2.92-2.95 (m, 2H), 3.13 (s, 3H), 3.26-3.29 (m, 6H), 3.45-3.46 (m, 1H), 3.92-4.00 (m, 8H), 4.60 (s, 1H), 4.68 (d, J = 3.0 Hz, 1H), 8.23 (d, J = 2.6 Hz, 1H), 8.49 (d, J = 2.6 Hz, 1H), 8.0-10.6 (br2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 24.4 (t), 29.2 (t), 35.0 (q), 41.5 (d), 43.7 (t), 43.7 (t), 46.3 (d), 48.8 (t), 48.8 (t), 64.0 (t), 64.0 (t), 67.0 (t), 67.0 (t), 104.2 (d), 109.9 (s), 120.2 (d), 128.3 (d), 130.7 (s), 137.8 (s), 139.6 (s), 140.4 (s), 150.5 (s), 162.8 (s). Anal. Calcd. for C$_{23}$H$_{30}$N$_6$O$_9$: C, 51.68; H, 5.66; N, 15.72. Found: C, 51.63; H, 5.69, N, 15.73.

Morpholimium 3,4-dihydro-6,8-dinitro-1-methyl-4-(2-morpholino-2,3-cyclohexenyl)-2-oxoquinoline-3-nitronate (17f). Orange powder, mp 143-145 °C (dec.). IR (KBr / cm^{-1}) 1653, 1539, 1333; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.95-0.98 (m, 1H), 1.16-1.25 (m, 2H), 1.61-2.00 (m, 3H), 2.60-2.75 (m, 2H), 3.11 (s, 3H), 3.00-3.30 (m, 1H), 3.17-3.30 (m, 4H), 3.31-3.51 (m, 2H), 3.80-4.03 (m, 8H), 5.05 (br t, J = 3.0 Hz, 1H), 5.16 (d, J = 3.0 Hz, 1H), 8.45 (d, J = 2.3 Hz, 1H), 8.48 (d, J = 2.3 Hz, 1H); Two active protons assigned to *N*-hydrogens of morpholinium were not observebed because of the overlap with water. ^{13}C NMR (100 MHz, CDCl$_3$) δ = 21.1 (t), 24.7 (t), 25.0 (t), 34.9 (q), 38.7 (d), 41.2 (d), 44.6 (t), 44.6 (t), 49.4 (t), 49.4 (t), 65.3 (t), 65.3 (t), 67.3 (t), 67.3 (t), 109.4 (d), 109.5 (s), 119.9 (d), 127.8 (d), 129.3 (s), 138.3 (s), 139.7 (s), 141.0 (s), 144.6 (s), 163.4 (s). Anal. Calcd. for C$_{24}$H$_{32}$N$_6$O$_9$·CH$_3$CN: C, 52.96; H, 5.98; N, 16.63. Found: C, 52.96; H, 6.10, N, 16.65.

Preparation of Acylmethylquinolones 12.

To a solution of **TNQ-Me** (0.99 mmol) and ketone (51.80 mmol) in acetonitrile (15 mL), a solution of triethylamine (0.20 g, 1.98 mmol) in acetonitrile (5 mL) was added, and the resultant mixture was extracted with chloroform (30 mL×3), and the organic layer was dried over sodium sulfate and concentrated. The residue was treated with column chromatography on silica gel to give *cine*-substitution product **12** (eluted with chloroform).

4-(1-Benzoylethyl)-6,8-dinitro-1-methyl-2-quinolone (**12b**). Pale yellow needles, mp 184-185 °C (dec.). IR (KBr / cm^{-1}) 1674, 1537, 1524, 1346; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.71 (d, J = 7.0 Hz, 3H), 3.46 (s, 3H), 5.15 (q, J = 7.0 Hz, 1H), 6.84 (s, 1H), 7.52 (dd, J = 7.4, 7.4 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.98 (d, J = 7.4 Hz, 2H), 8.70 (d, J = 2.5 Hz, 1H), 8.76 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 17.2 (q), 34.8 (q), 43.0 (d), 122.0 (d), 122.7 (d), 122.9 (s), 123.8 (d), 128.5 (d), 129.3 (d), 134.3 (d), 134.9 (s), 138.4 (s), 139.5 (s), 140.3 (s), 148.8 (s), 161.5 (s), 197.8 (s). Anal. Calcd. for C$_{19}$H$_{15}$N$_3$O$_6$·1/3H$_2$O: C, 58.92; H, 4.08; N, 10.85. Found: C, 58.52; H, 3.77, N, 11.13.

4-(α-Benzoylbenzyl)-6,8-dinitro-1-methyl-2-quinolone (**12c**). Pale yellow needles, mp 249-251 °C (dec.). IR (KBr / cm^{-1}) 1680, 1662, 1543, 1527, 1346; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 3.47 (s, 3H), 6.37 (s, 1H), 6.47 (s, 1H), 7.32-7.34 (m, 2H), 7.40-7.51 (m, 4H), 7.63 (dd, J = 7.4, 7.4 Hz, 2H), 8.01-8.03 (m, 2H), 8.57 (d, J = 2.5 Hz, 1H), 8.67 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 34.9 (q), 56.2 (d), 121.7 (d), 123.2 (d), 123.4 (s), 126.4 (d), 128.9 (d), 128.9 (d), 129.1 (d), 129.1 (d), 129.2 (d), 129.2 (d), 129.6 (d), 130.0 (d), 130.0 (d), 133.6 (s), 134.4 (d), 135.2 (s), 138.1 (s), 139.4 (s), 140.2 (s), 147.9 (s), 161.6 (s), 195.6 (s).

6,8-Dinitro-1-methyl-4-(2-oxocyclopentyl)-2-quinolone (**12d**). Pale yellow

needles, mp 169-170 °C (dec.). IR (KBr / cm^{-1}) 1738, 1674, 1539, 1520, 1335; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 2.11-2.19 (m, 1H), 2.20-2.37 (m, 2H), 2.4-2.7 (m, 3H), 3.47 (s, 3H), 3.91 (dd, J = 10.8, 8.9 Hz, 1H), 6.77 (s, 1H), 8.70 (d, J = 2.5 Hz, 1H), 8.73 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 20.7 (t), 29.3 (t), 34.9 (q), 38.3 (t), 50.9 (d), 121.9 (d), 123.7 (s), 124.8 (d), 138.2 (s), 139.2 (s), 140.1 (s), 146.2 (s), 161.7 (s), 213.3 (s). One signal was lacking because of an overlap with another signal. Anal. Calcd. for C$_{15}$H$_{13}$N$_3$O$_6$·1/4H$_2$O: C, 53.65; H, 4.05; N, 12.51. Found: C, 53.46; H, 3.82, N, 12.35.

6,8-Dinitro-1-methyl-4-(2-methyl-1-oxo-2-propyl)-2-quinolone (**12e**). Yellow powder, mp 157-159 °C (dec.). IR (KBr / cm^{-1}) 1724, 1682, 1539, 1344; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.66 (s, 6H), 3.50 (s, 3H), 7.01 (s, 1H), 8.47 (d, J = 2.3 Hz, 1H), 8.71 (d, J = 2.3 Hz, 1H), 9.73 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 23.1 (q), 23.1 (q), 35.2 (q), 51.4 (s), 121.1 (s), 121.6 (d), 124.3 (d), 125.1 (d), 128.3 (s), 138.8 (s), 139.9 (s), 149.8 (s), 161.6 (s), 200.5 (d). Anal. Calcd. for C$_{14}$H$_{13}$N$_3$O$_6$·1/3H$_2$O: C, 51.70; H, 4.23; N, 12.92. Found: C, 51.65; H, 3.98, N, 12.58.

6,8-Dinitro-1-methyl-4-(2-oxo-cyclohexyl)-2-quinolone (**12f**). Pale yellow needles, mp 229-232 °C (dec.). IR (KBr / cm^{-1}) 1703, 1668, 1531, 1344; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.86-2.01 (m, 2H), 2.11-2.22 (m, 2H), 2.31-2.35 (m, 1H), 2.40-2.44 (m, 1H), 2.67-2.71 (m, 2H), 3.48 (s, 3H), 4.10 (dd, J = 12.5, 4.8 Hz, 1H), 6.78 (s, 1H), 8.36 (d, J = 2.5 Hz, 1H), 8.69 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 25.2 (t), 27.7 (t), 32.4 (t), 34.9 (q), 42.5 (t), 52.7 (d), 121.6 (d), 123.3 (d), 123.5 (d), 123.8 (s), 138.1 (s), 139.4 (s), 140.0 (s), 147.1 (s), 161.7 (s), 207.4 (s). Anal. Calcd. for C$_{16}$H$_{15}$N$_3$O$_6$·1/4H$_2$O: C, 54.94; H, 4.47; N, 12.01. Found: C, 54.62; H, 4.20, N, 12.12.

6,8-Dinitro-1-methyl-4-{2-(4-methylphenyl)-2-oxoethyl}-2-quinolone (**12g**).

Pale yellow powder, mp 260-261 °C (dec.). IR (KBr / cm^{-1}) 1670, 1535, 1344; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.46 (s, 3H), 3.40 (s, 3H), 4.96 (s, 2H), 6.96 (s, 1H), 7.39 (d, J = 8.1 Hz, 2H), 8.02 (d, J = 8.1 Hz, 2H), 8.71 (d, J = 2.5 Hz, 1H), 8.85 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 21.2 (q), 34.3 (q), 41.7 (t), 121.8 (d), 123.6 (s), 124.9 (d), 128.4 (d), 128.4 (d), 129.1 (d), 129.1 (d), 133.2 (s), 137.4 (s), 138.5 (s), 139.7 (s), 144.1 (s), 145.2 (s), 161.0 (s), 194.9 (s). One signal was lacking because of the overlap with another signal. Anal. Calcd. for C$_{19}$H$_{15}$N$_3$O$_6$: C, 59.84; H, 3.97; N, 11.02. Found: C, 59.90; H, 3.84, N, 11.05.

4-(3,4-Benzo-2-oxocyclohexyl)-6,8-dinitro-1-methyl-2-quinolone (**12i**). Pale orange needles, mp 227-229 °C (dec.). IR (KBr / cm^{-1}) 1675, 1539, 1525, 1340; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 2.52 (dddd, J = 12.7, 4.1, 4.1, 3.8 Hz, 1H), 2.63 (dddd, J = 16.7, 12.0, 4.1 Hz, 1H), 3.44 (ddd, J = 16.7, 3.8, 4.0 Hz, 1H), 3.35 (ddd, J = 16.7, 12.0, 4.1 Hz, 1H), 3.49 (s, 3H), 4.33 (dd, J = 12.7, 4.1 Hz, 1H), 6.81 (s, 1H), 7.35-7.41 (m, 2H), 7.60 (t, J = 6.8 Hz, 1H), 8.03 (d, J = 7.6 Hz, 1H), 8.59 (d, J = 2.4 Hz, 1H), 8.70 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 27.9 (t), 29.3 (t), 35.0 (q), 50.0 (d), 121.7 (d), 123.0 (d), 124.2 (s), 124.2 (d), 127.3 (d), 128.1 (d), 129.0 (d), 131.8 (s), 134.6 (d), 138.0 (s), 139.3 (s), 140.2 (s), 143.5 (s), 148.3 (s), 161.7 (s), 194.9 (s). Anal. Calcd. for C$_{20}$H$_{15}$N$_3$O$_6$: C, 61.07; H, 3.84; N, 10.69. Found: C, 59.83; H, 3.73, N, 10.28.

6,8-Dinitro-1-methyl-4-(2-oxo-propyl)-2-quinolone (**12j**). Pale yellow needles, mp 157-158 °C (dec.). IR (KBr / cm^{-1}) 1722, 1684, 1547, 1527, 1362, 1348, 1336; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 2.43 (s, 3H), 3.49 (s, 3H), 4.06 (s, 2H), 6.79 (s, 1H), 8.47 (d, J = 2.5 Hz, 1H), 8.71 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 30.3 (q), 34.9 (q), 47.3 (t), 122.0 (d), 123.6 (s), 124.1 (d), 125.8 (d), 138.1 (s), 139.3 (s), 140.3 (s), 142.8 (s), 161.4 (s), 202.2 (s). Anal. Calcd. for C$_{13}$H$_{11}$N$_3$O$_6$: C, 51.15; H, 3.63; N, 13.76. Found: C, 51.00; H, 3.55, N, 13.71.

6,8-Dinitro-1-methyl-4-(3-oxo-2-pentyl)-2-quinolone (**12k**).   Yellow oil. IR (KBr / cm^{-1}) 1716, 1682, 1539, 1348; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.10 (t, J = 7.2 Hz, 3H), 1.63 (d, J = 7.0 Hz, 3H), 2.64 (q, J = 7.2 Hz, 2H), 3.48 (s, 3H), 4.31 (q, J = 7.0 Hz, 1H), 6.84 (s, 1H), 8.73 (s, 1H), 8.73 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 7.9 (q), 16.2 (q), 34.3 (t), 34.9 (q), 48.0 (d), 121.9 (d), 123.2 (s), 123.2 (d), 123.2 (d), 138.2 (s), 139.4 (s), 140.2 (s), 148.1 (s), 161.5 (s), 208.4 (s); As the compound **2k** was hydroscopic, satisfactory analytical data were not given.

6,8-Dinitro-1-methyl-4-{2-oxo-2-(2-pyridyl)ethyl}-2-quinolone (**12l**).   Pale orange needles, mp 201-203 °C (dec.). IR (KBr / cm^{-1}) 1695, 1680, 1538, 1340; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 3.49 (s, 3H), 4.89 (s, 2H), 6.96 (s, 1H), 7.62 (ddd, J = 7.7, 4.7, 0.9 Hz, 1H), 7.93 (ddd, J = 7.7, 7.7, 1.7 Hz, 1H), 8.08 (dd, J = 7.7, 0.9 Hz, 1H), 8.70 (d, J = 2.5 Hz, 1H), 8.83 (dd, J = 4.7, 1.7 Hz, 1H), 8.90 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 34.9 (q), 40.8 (t), 121.9 (d), 122.7 (d), 124.0 (s), 124.7 (d), 126.3 (d), 128.4 (d), 137.5 (d), 138.1 (s), 139.2 (s), 140.3 (s), 144.2 (s), 149.4 (d), 151.8 (s), 161.5 (s), 196.4 (s).   Anal. Calcd. for C$_{17}$H$_{12}$N$_4$O$_6$: C, 55.44; H, 3.28; N, 15.21.   Found: C, 55.49; H, 3.19, N, 15.15.

6,8-Dinitro-1-methyl-4-{2-oxo-2-(2-furyl)ethyl}-2-quinolone (**12m**).   Pale yellow needles, mp 212-214 °C (dec.). IR (KBr / cm^{-1}) 1670, 1541, 1335; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 3.49 (s, 3H), 4.47 (s, 2H), 6.68 (dd, J = 3.6, 1.7 Hz, 1H), 6.92 (s, 1H), 7.39 (dd, J = 3.6, 0.6, 1H), 7.73 (dd, J = 1.7, 0.6 Hz, 1H), 8.72 (d, J = 2.5 Hz, 1H), 8.73 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ = 34.4 (q), 42.0 (t), 113.4 (d), 118.9 (d), 122.0 (d), 123.8 (s), 124.5 (d), 126.3 (d), 138.1 (s), 139.2 (s), 140.3 (s), 142.8 (s), 147.5 (d), 151.6 (s), 161.4 (s), 182.9 (s).   Anal. Calcd. for C$_{16}$H$_{11}$N$_3$O$_7$: C, 53.79; H, 3.10; N, 11.76.   Found: C, 52.76; H, 2.91, N, 11.65.

6,8-Dinitro-1-methyl-4-(3-oxo-2-butyl)-2-quinolone (**12n**)   and

6,8-Dinitro-1-methyl-4-(2-oxobutyl)-2-quinolone (**12o**). These products were obtained as a mixture, and their yields were determined by ^{1}H NMR. ^{1}H NMR (400 MHz, CDCl$_3$) **12n** δ = 1.62 (d, J = 7.0 Hz, 3H), 2.27 (s, 3H), 3.45 (s, 3H), 4.23 (q, J = 7.0 Hz, 1H), 6.77 (s, 1H), 8.63 (s, 1H), 8.63 (s, 1H); **12o** δ = 1.15 (t, J = 7.0 Hz, 3H), 2.71 (q, J = 7.0 Hz, 3H), 3.45 (s, 3H), 4.03 (s, 2H), 6.71 (s, 1H), 8.63 (s, 1H), 8.63 (s, 1H).

The reaction of TNQ-Me with phenoxides.

To a solution of phenol (94 mg, 1.0 mmol) in methanol (10 mL), potassium hydroxide (56 mg, 1.0 mmol) was added, and the solution was stirred at room temperature for 1.5 hours. After removal of the solvent, the residue was dissolved into acetonitrile (10 mL), and then **TNQ-Me** (294 mg, 1.0 mmol) was added. The mixture was heated at 60 °C for 3 days. White precipitates were collected by filtration and washed with 1 M hydrochloric acid (1 mL, 1 mmol) and with water (2 mL) to afford an analytically pure product **20a** (150 mg, 0.26 mmol, 51 % yield based on **TNQ-Me**). When other phenoxides were employed, reactions were similarly conducted.

2,4-Bis(1-methyl-6,8-dinitro-2-oxo-1,2-dihydro-4-quinolyl)phenol (**20a**). White powder, Mp >300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.39 (s, 3H), 3.41 (s, 3H), 7.01 (s, 1H), 7.02 (s, 1H), 7.30 (d, J = 8.5 Hz 1H), 7.58 (d, J = 2.1 Hz, 1H), 7.67 (dd, J = 8.5, 2.1 Hz, 1H), 8.31 (d, J = 2.5 Hz, 1H), 8.59 (d, J = 2.5 Hz, 1H), 8.96 (d, J = 2.5 Hz, 1H), 8.96 (d, J = 2.5 Hz, 1H), 10.75 (s, 1H); MS (FAB): m/z = 589 (M$^+$+1, 20), 497 (60), 232 (100). Anal. Calcd. for C$_{26}$H$_{16}$N$_6$O$_{11}$: C, 53.06; H, 2.72; N, 14.29. Found: C, 52.87; H, 2.57, N, 14.02.

6-Methyl-2,4-bis(1-methyl-6,8-dinitro-2-oxo-1,2-dihydro-4-quinolyl)phenol (**20b**). White powder, mp 293-296 °C (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.39 (s, 3H), 3.39 (s, 3H), 3.42 (s, 3H), 6.97 (s, 1H), 6.99 (s, 1H), 7.38 (d, J =

2.0 Hz, 1H), 7.59 (d, J = 2.0 Hz, 1H), 8.24 (d, J = 2.5 Hz, 1H), 8.61 (d, J = 2.5 Hz, 1H), 8.95 (d, J = 2.5 Hz, 1H), 8.97 (d, J = 2.5 Hz, 1H), 9.58 (br s, 1H) ; ^{13}C NMR (100 MHz, DMSO-d_6) δ = 15.6 (q), 33.3 (q), 33.3 (q), 121.1 (d), 121.3 (d), 121.5 (s), 121.6 (s), 122.0 (s), 123.5 (d), 124.3 (s), 124.5 (d), 124.9 (d), 124.9 (d), 125.9 (s), 127.7 (s), 131.9 (d), 136.4 (d), 136.8 (s), 137.5 (s), 137.5 (s), 138.6 (s), 138.7 (s), 146.3 (s), 147.9 (s), 152.4 (s), 160.1 (s), 160.3 (s). MS (FAB): m/z = 603 (M$^+$+1, 44), 192 (100). Anal. Calcd. for $C_{27}H_{18}N_6O_{11}$: C, 53.82; H, 2.99; N, 13.95. Found: C, 53.74; H, 2.63, N, 13.94.

4-Methoxy-2,6-bis(1-methyl-6,8-dinitro-2-oxo-1,2-dihydro-4-quinolyl)phenol

(21c). Yellow granules, mp 213-215 °C (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.41 (s, 6H), 3.42 (s, 6H), 3.81 (s, 3H), 3.82 (s, 3H), 6.99 (s, 2H), 7.04 (s, 2H), 7.18 (d, J = 2.4 Hz, 4H), 8.25-8.27 (m, 4H), 8.94-8.96 (m, 5H), 9.04 (s, 1H), 8.97 (d, J = 2.5 Hz, 1H), 9.58 (br s, 1H). In the ^{1}H NMR, signals assigned for two kinds of **21c** were observed. Because a recent report states that 2-quinolone forms a complex with phenol derivatives, **21c** is considered to form a complex with another molecule of **21c**.[89] MS (FAB): m/z = 619 (M$^+$+1, 100), 238 (84). Anal. Calcd. for $(C_{27}H_{18}N_6O_{12})_2$: C, 52.44; H, 2.93; N, 13.59. Found: C, 52.43; H, 2.91, N, 13.59.

5-Methyl-2-(1-methyl-6,8-dinitro-2-oxo-1,2-dihydro-4-quinolyl)phenol (**22d**). Pale yellow powder, mp 274-285 °C (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.35 (s, 3H), 3.39 (s, 3H), 6.80 (s, 1H), 6.84 (d, J = 7.7 Hz, 1H), 6.88 (s, 1H), 7.17 (d, J = 7.7 Hz, 1H), 8.24 (d, J = 2.6 Hz, 1H), 8.91 (d, J = 2.6 Hz, 1H), 9.95 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 21.9 (q), 35.4 (q), 117.3 (d), 119.8 (s), 121.5 (d), 123.1 (d), 123.6 (s), 124.4 (d), 127.2 (d), 131.2 (d), 138.3 (s), 139.6 (s), 140.6 (s), 142.1 (s), 149.5 (s), 154.9 (s), 162.4 (s). MS (FAB): m/z = 356 (M$^+$+1, 100). Anal. Calcd. for $C_{17}H_{13}N_3O_6$: C, 57.46; H, 3.66; N, 11.83. Found: C,

57.38; H, 3.68, N, 12.08.

4-Methyl-2-(1-methyl-6,8-dinitro-2-oxo-1,2-dihydro-4-quinolyl)phenol (**22e**).
Brown oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.28 (s, 3H), 3.40 (s, 3H), 6.82 (s, 1H), 6.96 (d, J = 8.2 Hz, 1H), 7.10 (s, 1H), 7.23 (d, J = 8.2 Hz, 1H), 8.21 (d, J = 2.1 Hz, 1H), 8.92 (d, J = 2.1 Hz, 1H), 9.81 (s, 1H).   MS (FAB): m/z = 356 (M$^+$+1, 100).   The crude product was found to be pure based on NMR, however, satisfactory analytical and other spectral data were not obtained since further purification could not be performed.

2-(1-methyl-6,8-dinitro-2-oxo-1,2-dihydro-4-quinolyl)-4-nitrophenol (**22f**).
Pale yellow powder, mp >300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.42 (s, 3H), 7.01 (s, 1H), 7.24 (d, J = 9.1 Hz, 1H), 8.12 (d, J = 2.6 Hz, 1H), 8.25 (d, J = 2.9 Hz 1H), 8.35 (d, J = 9.1, 2.9 Hz, 1H), 8.94 (d, J = 2.6 Hz, 1H), 11.75 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 34.6 (q), 116.4 (d), 122.1 (s), 122.4 (s), 122.4 (d), 124.7 (d), 125.7 (d), 127.1 (d), 127.4 (s), 137.4 (d), 138.7 (s), 139.8 (s), 139.9 (s), 146.1 (s), 160.8 (s), 161.3 (s).   MS (FAB): m/z = 387 (M$^+$+1, 40), 176 (100).   Anal. Calcd. for $C_{16}H_{10}N_4O_8$: C, 49.74; H, 2.59; N, 14.51.   Found: C, 49.96; H, 2.44, N, 14.44.

1-(1-methyl-6,8-dinitro-2-oxo-1,2-dihydro-4-quinolyl)-2-naphthol (**22g**).
Yellow powder, mp 272-274 °C (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.46 (s, 3H), 6.91 (s, 1H), 7.34-7.45 (m, 4H), 7.87 (d, J = 2.6 Hz, 1H), 7.94-7.96 (m, 1H), 8.04 (d, J = 8.9 Hz, 1H), 8.92 (d, J = 2.6 Hz, 1H), 10.17 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 33.4 (q), 112.1 (s), 117.0 (d), 121.3 (d), 122.2 (d), 122.4 (d), 124.4 (s), 123.7 (d), 124.8 (d), 126.2 (d), 126.6 (s), 127.1 (d), 130.1 (s), 131.3 (s), 136.9 (s), 137.6 (s), 138.7 (s), 145.2 (s), 151.2 (s), 160.5 (s).   MS (FAB): m/z = 392 (M$^+$+1, 100).   Anal. Calcd. for $C_{20}H_{13}N_3O_6$: C, 61.38; H, 3.32; N, 10.74.   Found: C, 61.35; H, 3.11, N, 10.55.

Preparation of 3,6-dinitro-1-methyl-2-quinolone (DNQ-Me)[69, 70]

To cold 18 M sulfuric acid (8.5 mL, 306 mmol), 1-methyl-2-quinolone (1.6 g, 10 mmol) was gradually added. After gradual addition of 15 M nitric acid (16 mL, 240 mmol), the mixture was heated at 80 °C for 5 hours. The solution was cooled down to room temperature, and water (100 mL) was poured into the reaction mixture. The generated yellow precipitates (2.4 g) were collected. ^{1}H NMR (DMSO-d_6) showed this product was a mixture of four nitrated 2-quinolones (**DNQ-Me**: 41 %, 6,8-dinitro derivative: 30 %, **TNQ-Me**: 9 %, 6-nitro derivative: 19 %). Recrystallization of the mixture from benzene and successively from ethanol afforded **DNQ-Me** as yellow needles (0.52 g, 21 %).

1-Methyl-6,8-dinitro-2-quinolone: ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.34 (s, 3H), 6.95 (d, J = 9.6 Hz, 1H), 8.28 (d, J = 9.6 Hz, 1H), 8.87 (d, J = 2.2 Hz, 1H), 9.02 (d, J = 2.2 Hz, 1H).

1-Methyl-6-nitro-2-quinolone: ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.65 (s, 3H), 6.75 (d, J = 9.6 Hz, 1H), 7.68 (d, J = 9.3 Hz, 1H), 8.09 (d, J = 9.6 Hz, 1H), 8.53 (dd, J = 9.3, 2.3 Hz, 1H), 8.68 (d, J = 2.3 Hz, 1H).

1-Methyl-3,6-dinitro-2-quinolone (**DNQ-Me**). Yellow needles, Mp 256-258 °C. IR (Nujol / cm^{-1}) 1670, 1599, 1524, 1342; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.74 (s, 3H), 7.83 (d, J = 9.5 Hz, 1H), 8.53 (dd, J = 9.5, 2.0 Hz, 1H), 8.93 (d, J = 9.5 Hz, 1H), 9.09 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 31.7 (q), 117.4 (s), 117.9 (d), 128.0 (d), 128.7 (d), 137.0 (d), 141.9 (s), 143.2 (s), 145.2 (s), 154.6 (s). Anal. Calcd. for $C_{10}H_7N_3O_5$: C, 48.20; H, 2.83; N, 16.86. Found: C, 48.05; H, 2.89, N, 16.70.

Preparation of 1-ethyl-3,6-dinitro-2-quinolone (DNQ-Et) [70]

Except for the employment of diethyl sulfate in stead of dimethyl

sulfate, 1-ethyl-3,6-dinitro-2-quinolone (**DNQ-Et**) was synthesized in a way similar to the preparation of 1-methyl-6,8-dinitro-2-quinolone (**DNQ-Me**).

Preparation of 3,6,8-trinitro-2-quinolone (TNQ-H) [69, 70]

To cold 18 M sulfuric acid (2.1 g, 22 mmol), 2-quinolone (0.29 g, 2 mmol) was gradually added. After gradual addition of fuming nitric acid (d = 1.52, 1.76 g, 27 mmol), the mixture was heated at 120 °C for 7 hours. The solution was cooled down to room temperature, and water (50 mL) was poured into the reaction mixture. The generated yellow precipitates were collected and then recrystallized from benzene to afford **TNQ-H** as yellow needles (0.40 g, 1.4 mmol, 72 %).

3,6,8-trinitro-2-quinolone (TNQ-H). Yellow needles, mp 102-105 °C. ^{1}H NMR (60 MHz, CDCl$_3$) δ = 9.22 (s, 1H), 9.26 (s, 1H), 9.44 (s, 1H), 10.50 (d, J = 9.3 Hz, 1H).

cine-**Substitution of DNQ-Me.**

The sodium enolate was prepared from 2,4-pentanedione (**25**, 122 μL, 1.2 mmol) and 0.2 M NaOEt in EtOH (7.5 mL, 1.5 mmol). After removal of EtOH, the resultant enolate was dissolved in DMF (20 mL). To this solution, a solution of **DNQ-Me** (249 mg, 1.0 mmol) in DMF (20 mL) was added at room temperature over 30 minutes, and the solution color became brown. After being stirred for a further 3 hours, the mixture was quenched with 1 M HCl (1.4 mL). DMF was removed under reduced pressure, and the residue was dissolved into chloroform (50 mL). The organic layer was washed with water (60 mL x 3), dried over (MgSO$_4$), and concentrated. The residue was treated with column chromatography on silica gel to give *cine*-substitution product **27**, which was eluted with hexane-chloroform (1/1). Other *cine*-substitution of nitroquinolone with 2,4-pentanedione (**25**) was conducted in the same way.

4-(2-Hydroxy-4-oxo-2-penten-3-yl)-1-methyl-6-nitro-2-quinolone (**27**).

Yellowish brown powder, mp 230-231 °C. IR (Nujol / cm^{-1}) 1684, 1541, 1346, 1336; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.93 (s, 6H), 3.83 (s, 3H), 6.80 (s, 1H), 7.57 (d, J = 9.3 Hz, 1H), 8.41 (d, J = 2.7 Hz, 1H), 8.47 (dd, J = 9.3, 2.7 Hz, 1H), 19.92 (s, 1H). Anal. Calcd. for C$_{15}$H$_{14}$N$_2$O$_5$: C, 59.61; H, 4.66; N, 9.27. Found: C, 59.08; H, 4.53, N, 9.29.

Crystal data for TNQ-Me C$_{10}$H$_6$N$_4$O$_7$·C$_6$H$_6$, M = 372.29, orthorhombic, space group P2$_1$2$_1$2$_1$, a = 12.403 (3) Å, b = 9.150 (4) Å, c = 7.175 (1) Å, V = 1704.2 (5) Å^3, Dc = 1.451 g/cm^3, Z = 4, F(000) = 768.00, μ = 1.17 cm^{-1}. A yellow crystal of dimension 0.30 x 0.30 x 0.40 mm was sealed in a glass capillary and used for measurement at 293 K on a Rigaku AFC7R four-circle diffractometer employing graphite monochromated MoKα radiation (λ = 0.71069 Å) using the ω/2θ scan technique. The 2729 unique reflections were corrected for Lorentz and polarization effects. The structure was solved by direct methods (MITHRILL88). The final full-matrix least squares refinement, based on F using 892 reflections (I > 3.00σ (I)) and 292 parameters, converged with R = 0.039 and Rw = 0.028.

Crystal data for DNQ-Me C$_{10}$H$_7$N$_3$O$_5$, M = 249.18, orthorhombic, space group P2$_1$2$_1$2$_1$, a = 13.892 (6) Å, b = 14.97 (1) Å, c = 10.010 (9) Å, V = 2081 (2) Å^3, Dc = 1.590 g/cm^3, Z = 8, F(000) = 512.00, μ = 1.31 cm^{-1}. A yellow crystal of dimensions 0.30 x 0.30 x 0.40 mm was used for measurement at 293 K on a Rigaku AFC7R four-circle diffractometer employing graphite monochromated MoKa radiation (λ = 0.71069 Å) using the ω/2θ scan technique. The 2727 unique reflections were corrected for Lorentz and polarization effects. The structure was solved by direct methods (MITHRILL88). The final full-matrix least squares refinement, based on F using 1088 reflections (I > 3.00σ (I)) and 325 parameters, converged with R = 0.049 and Rw = 0.040.

Diels-Alder Reaction of TNQ-Me with Cyclopentadiene

To a solution of **TNQ-Me** (296 mg, 1 mmol) in acetonitrile (10 mL), a solution of cyclopentadiene (670 mg, 10 mmol) in acetonitrile (2 mL) was added, and the resultant solution was heated under reflux for 7 hours. After removal of the solvent, the residue was treated with column chromatography on silica gel to afford cycloadduct **29** as a single isomer (eluted with toluene, 270 mg, 0.74 mmol, 74 % yield).

5, 6, 6a, 10a- Tetrahydro-

7,10-methano-5-methyl-2,4,6a-trinitrophenanthridin-6-one (29). Colorless prisms, mp 163-167 °C. IR (KBr / cm^{-1}) 1695, 1556, 1541, 1531, 1340; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 2.00 (brd, J = 9.9 Hz, 1H), 2.08 (brd, J = 9.9 Hz, 1H), 3.15 (s, 3H), 3.56 (brs, 1H), 3.98 (d, J = 3.6 Hz, 1H), 4.18 (brs, 1H), 6.15 (dd, J = 6.6, 3.2 Hz, 1H), 6.20 (dd, J = 6.6, 2.9 Hz, 1H), 8.36 (d, J = 2.6 Hz, 1H), 8.51 (d, J = 2.6 Hz, 1H), ^{13}C NMR (100 MHz, CDCl$_3$) δ = 35.8 (q), 48.1 (t), 50.4 (d), 51.1 (d), 54.3 (d), 93.7 (s), 120.8 (d), 126.3 (d), 128.4 (s), 134.6 (d), 137.5 (s), 139.6 (d), 139.8 (s), 142.0 (s), 163.5 (s). Anal. Calcd. for C$_{15}$H$_{12}$N$_4$O$_7$: C, 50.01; H, 3.36; N, 15.55. Found: C, 50.01; H, 3.31, N, 15.70.

Conversion from cycloadduct 29 to aromatized product 30

To a solution of cycloadduct **29** (72 mg, 0.2 mmol) in acetonitrile (2 mL), triethylamine (59 μ L, 0.425 mmol) was added, and the mixture was heated under reflux for 12 hours. After removal of the solvent, the residue was treated with column chromatography on silica gel to give aromatized product **30** as a single isomer (eluted with toluene, 130 mg, 0.041 mmol, 21% yield).

7,10-Dihydro-7,10-methano-5-methyl-2,4-dinitrophenanthridin-6-one   (30)

Pale yellow needles, IR (KBr / cm^{-1}) 1674, 1537, 1524, 1342, ; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 2.43 (brd, J = 7.2 Hz, 1H), 2.50 (brd, J = 7.2 Hz, 1H), 3.50 (s,

3H), 4.40 (brs, 1H), 4.48 (brs, 1H), 6.94 (dd, $J = 5.0$, 3.3 Hz, 1H), 6.20 (dd, $J = 5.0$, 3.2 Hz, 1H), 8.66 (d, $J = 2.5$ Hz, 1H), 8.72 (d, $J = 2.5$ Hz, 1H), ^{13}C NMR (100 MHz, CDCl$_3$) δ = 34.6 (q), 49.3 (d), 50.3 (d), 73.5 (t), 120.8 (d), 121.6 (s), 122.6 (d), 136.0 (s), 139.2 (s), 140.1 (s), 141.0 (d), 144.7 (d), 146.2 (s), 159.6 (s), 162.7 (s). Anal. Calcd. for C$_{15}$H$_{11}$N$_3$O$_5$: C, 57.51; H, 3.54; N, 13.41. Found: C, 57.85; H, 3.61, N, 12.71.

cine-Substitution of TNQ-Me with pyrrole

To a solution of **TNQ-Me** (1 mmol) in acetonitrile (10 mL), a solution of pyrrole (10 mmol) in acetonitrile (2 mL) was added, and the resultant mixture was heated under reflux for 6 hours. In the reaction mixture, dark green precipitates were generated and were collected by filtration to give product **31**. After concentration of the filtrate, the residue was treated with column chromatography on silica gel to isolate product **32** (eluted with toluene).

6,8-Dinitro-1-methyl-4-(2-pyrrolyl)-2-quinolone (31)

Dark green needles, mp >300 °C. IR (KBr / cm^{-1}) 3248, 1653, 1533, 1346, 1333 ; ^{1}H NMR (60 MHz, DMSO-d_6) δ = 3.44 (s, 3H), 6.45 (d, $J = 2.5$ Hz, 1H), 6.79 (s, 1H), 6.93 (br s, 1H), 7.25 (br s, 1H), 9.01 (d, $J = 2.2$ Hz, 1H), 9.22 (d, $J = 2.2$, 1H), 11.91 (s, 1H), ^{13}C NMR (100 MHz, DMSO-d_6) δ = 34.3 (q), 110.3 (d), 113.3 (d), 118.1 (d), 121.5 (d), 122.3 (d), 122.9 (d), 124.4 (s), 126.2 (s), 138.4 (s), 138.6 (s), 139.7 (s), 140.6 (s), 161.3 (s). Anal. Calcd. for C$_{14}$H$_{10}$N$_4$O$_5$: C, 53.51; H, 3.21; N, 17.83. Found: C, 50.88; H, 3.07, N, 16.87.

3,4-Dihydro-1-methyl-4-(2-pyrrolyl)-3,6,8-trinitro-2-quinolone (32)

Yellow powder, mp 184-193 °C (dec.).   IR (KBr / cm^{-1}) 3421, 1709, 1572, 1543, 1342, 1288; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 3.29 (s, 3H), 5.16 (d, $J = 10.8$ Hz, 1H), 6.05 (s, 1H), 6.27 (dd, $J = 3.3$, 2.8 Hz, 1H), 6.88 (dd, $J = 2.5$, 1.3 Hz, 1H), 8.11 (dd, $J = 1.6$, 0.8 Hz, 1H), 8.37 (br s, 1H), 8.65 (d, $J = 2.4$ Hz, 1H), One

signal was lacking because of an overlap with another signal. ^{13}C NMR (100 MHz, CDCl$_3$) δ = 35.1 (q), 40.0 (d), 40.6 (d), 86.8 (d), 108.6 (d), 110.5 (d), 120.2 (d), 121.3 (d), 121.7 (d), 125.9 (s), 126.5 (s), 131.4 (s), 142.7 (s), 160.5 (s). Anal. Calcd. for C$_{14}$H$_{11}$N$_5$O$_7$: C, 46.55; H, 3.07; N, 19.39. Found: C, 47.51; H, 3.10, N, 19.15.

Diels-Alder Reaction of TNQ-Me with hydrazone of 2-butenal 33

The reaction of **TNQ-Me** with hydrazone of 2-butenal **33** was performed in a similar way to Diels-Alder Reaction of **TNQ-Me** with cyclopentadiene

5-Methyl-2,4-dinitrophenanthridin-6-one (35). Yellow plates, mp >300 °C. IR (KBr / cm^{-1}) 1678, 1541, 1527, 1352, 1336; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 3.56 (s, 3H), 7.79 (dd, J = 7.9, 7.3 Hz, 1H), 7.95 (dd, J = 8.1, 7.3 Hz, 1H), 8.36 (d, J = 8.1 Hz, 1H), 8.57 (d, J = 7.9 Hz, 1H), 8.72 (d, J = 2.5 Hz, 1H), 9.30 (d, J = 2.5 Hz, 1H). Anal. Calcd. for C$_{14}$H$_9$N$_3$O$_5$: C, 56.19; H, 3.03; N, 14.04. Found: C, 55.81; H, 3.23, N, 14.41.

Diels-Alder reaction of TNQ-Me with α, β-unsaturated oxime.

To a solution of **TNQ-Me** (294 mg, 1 mmol) in acetonitrile (10 mL), phenylstylylketoxime (289 mg, 1.3 mmol) and triethylamine (20.2 mg, 0.2 mmol) were added. After heating under reflux for 1 day, precipitated orange needles were collected by filtration to afford diazaphenanthrene **36** (185.3 mg, 0.41 mmol, 41 %).

1,9-Diaza-6,8-dinitro-2,4-diphenyl-9-methyl-10-oxo-phenanthrene (36). Orange needles; mp >300 °C. IR (KBr / cm^{-1}) 1687, 1602, 1531, 1338; ^{1}H NMR (60 MHz, CDCl$_3$) δ = 3.43 (s, 3H), 7.3-7.6 (m, 8H), 7.92 (s, 1H), 8.2-8.4 (m, 2H), 8.77 (d, J = 2.4 Hz, 1H), 10.12 (d, J = 2.4 Hz, 1H). MS (EI): m/z(%): 452 (71) (M$^+$). 421 (32), 44 (100).

Diels-Alder reaction of TNQ-Me with electron-rich alkene

To a solution of **TNQ-Me** (294 mg, 1 mmol) in acetonitrile (8 mL) ethoxyethene (360 mg, 5 mmol) was added. After stirring at room temperature for 2 days, precipitated pale yellow solid was collected by filtration, and recrystallized from acetonitrile to afford cyclic nitronate **37** (300 mg, 0.82 mmol, 82 %).

Cyclic nitronate 37. Pale yellow prism; mp 148-155 °C (dec.). IR (KBr / cm^{-1}) 1703, 1608, 1551, 1481, 1346,1142; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.11 (dd, J = 7.1, 7.1 Hz, 3H), 2.67 (ddd, J = 14.3, 5.7, 3.7 Hz, 1H), 2.85 (ddd, J = 14.3, 7.9, 3.9 Hz, 1H), 3.27 (s, 3H), 3.67 (dq, J = 9.7, 7.1 Hz, 1H), 3.95 (dq, J = 9.7, 7.1 Hz, 1H), 4.1-4.3 (br, 1H), 5.63 (dd, J = 3.9, 3.7 Hz, 1H), 8.32 (d, J = 2.4, 1H), 8.58 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) 14.5 (q), 29.6 (t), 32.9 (d), 35.0 (q), 66.2 (t), 101.9 (d), 115.6 (s), 120.9 (d), 123.4 (d), 123.8 (s), 131.0 (s), 136.2 (s), 144.5 (s), 157.8 (s). MS (FAB): m/z: 367 (M$^+$ + 1). Anal. Calcd. for C$_{14}$H$_{14}$N$_4$O$_8$: C, 45.90; H, 3.85; N, 15.30. Found: C, 46.16; H, 3.84; N, 15.31.

Ring opening reaction of cyclic nitronate 37 with alcohol

A solution of cyclic nitronate **37** (150 mg, 0.4 mmol) in methanol (5 mL) was heated under reflux for 0.5 hour, and the mixture was evaporated affording dihydroquinolone **38a** (110 mg, 0.28 mmol, 69%, single isomer). Further purification was performed by recrystallization from methanol to give **38a**. When ethanol was employed instead of methanol, the reaction was similarly conducted and lead to **38b** in 72% yield as a single isomer.

3,4-Dihydro-4-(2-ethoxy-2-methoxyethyl)-1-methyl-3,6,8-trinitro-2-quinolone (38a). Pale yellow granules; mp 137-140 °C (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.18 (dd, J = 6.9, 6.9 Hz, 3H), 1.8-2.0 (m, 2H), 3.14 (s, 3H), 3.18 (s, 3H), 3.4-3.6 (m, 2H), 4.2-4.3 (m, 1H), 4.56 (dd, J = 5.2, 5.2 Hz, 1H),

6.08 (d, J = 3.2 Hz, 1H), 8.55 (d, J = 2.4 Hz, 1H) 8.70 (d, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 15.0 (q), 30.6 (q), 33.0 (t), 34.3 (d), 37.3 (q), 52.8 (d), 61.1 (s), 85.3 (s), 100.5 (d), 121.1 (s), 127.2 (s), 130.7 (s), 137.6 (s), 142.2 (s), 160.1 (s).   MS (FAB): m/z (%): 399 (M$^+$ + 1, 20), 367 (100).   Anal. Calcd for C$_{15}$H$_{18}$N$_4$O$_9$: C, 45.23; H, 4.55; N, 14.07.   Found: C, 45.04; H, 4.50; N, 13.87.

3,4-Dihydro-4-(2,2-diethoxyethyl)-1-methyl-3,6,8-trinitro-2-quinolone   (38b)
Orange needles; mp 130-136 °C (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.03 (dd, J =6.9, 6.9 Hz, 3H), 1.16 (dd, J = 6.9, 6.9 Hz, 3H), 1.8-2.0 (m, 2H), 3.15 (s, 3H), 3.4-3.6 (m, 4H), 4.2-4.3 (m, 1H), 4.63 (dd, J = 5.2, 5.2 Hz, 1H), 6.09 (d, J = 3.2 Hz, 1H), 8.56 (d, J = 2.2 Hz, 1H), 8.70 (d, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 15.0 (q), 15.0 (q), 33.5 (t), 34.3 (d), 37.4 (q), 60.0 (t), 61.3 (t), 85.4 (d), 99.9 (d), 121.1 (d), 127.3 (d), 130.9 (s), 137.7 (s), 139.4 (s), 142.2 (s), 160.2 (s). MS (FAB): m/z(%): 412 (M$^+$, 5), 411 (10), 367 (100).   Anal. Calcd. for C$_{16}$H$_{20}$N$_4$O$_9$: C, 46.60; H, 4.88; N, 13.59. Found: C, 46.54; H, 4.97; N, 13.64.

Aromatization of 3,4-dihydro-2-quinolones 38

To a solution of 3,4-dihydro-2-quinolones **38a** (199 mg, 0.5 mmol) in acetonitrile (5 mL), triethylamine (70 μ L, 0.5 mmol) was added.   After stirring the resultant mixture at room temperature for 2 days, the mixture was concentrated under reduced pressure.   The residue was treated with column chromatography on silica gel to afford 4-substituted-6,8-dinitro-2-quinolone **39a** (eluted with CHCl$_3$ / ethyl acetate = 1 / 1, 102 mg, 0.29 mmol, 58 %).   The aromatization of **39b** was also performed in the same way.

4-(2-Ethoxy-2-methoxyethyl)-6,8-dinitro-1-methyl-2-quinolone (39a)   Orange needles, mp 98-99 °C (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.07 (dd, J = 6.9, 6.9 Hz, 3H), 3.28 (d, J = 4.9 Hz, 2H), 3.33 (s, 3H), 3.35 (s, 3H), 3.5-3.7 (m, 2H),

4.77 (t, J = 4.9 Hz, 1H), 6.90 (s, 1H), 8.91 (d, J = 2.5 Hz, 1H), 8.92 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 15.0 (q), 34.6 (q), 35.9 (t), 53.6 (q), 64.2 (t), 102.2 (d), 122.2 (d), 123.5 (s), 124.0 (s), 125.5 (d), 137.7 (s), 138.6 (s), 139.7 (s), 146.2 (s), 161.1 (s).   Anal. Calcd for $C_{15}H_{17}N_3O_7$: C, 51.28; H, 4.88; N, 11.96. Found: C, 51.24; H, 4.42; N, 11.68.

4-(2,2-Diethoxyethyl)-6,8-dinitro-1-methyl-2-quinolone (39b)   Orange needles, mp 102-104 °C (dec.); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.06(dd, J = 7.0, 7.0 Hz, 6H), 3.27 (d, J = 4.5 Hz, 2H), 3.32 (s, 3H), 3.5-3.7 (m, 4H), 4.63 (t, J = 4.5 Hz, 1H), 6.90 (s, 1H), 8.91 (d, J = 2.0 Hz, 1H), 8.96 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 15.0 (q), 34.4 (q), 33.8 (t), 61.8 (t), 101.2 (d), 122.0 (d), 123.4 (s), 124.0 (d), 125.8 (d), 137.6 (s), 138.5 (s), 139.4 (s), 146.2 (s), 161.2 (s).   Anal. Calcd for $C_{16}H_{19}N_3O_7$: C, 51.61; H, 5.21; N, 11.51. Found: C, 51.61; H, 5.24; N, 11.66.

Aromatization following Hydrolysis of

4-(2,2-diethoxyethyl)-6,8-dinitro-1-methyl-2-quinolone 38b

   To a solution of 3,4-dihydro-2-quinolone **38b** (705 mg, 1.71 mmol) in acetonitrile (10 mL), triethylamine (140 μ L, 2 mmol) was added.   After stirring the resultant mixture at room temperature for 2 days, 1 M hydrochrolic acid (2 mL, 2 mmol) was added to the mixture and continuously stirred for 1 day.   The eluate from the resultant mixture with chloroform (10 mL) was concentrated under reduced pressure to afford orange solid (85 mg).   Recrystallization of obtained orange solid afforded hydrolyzed **40** (11 mg, 0.042 mmol, 2.5 %) as yellow powder.

4-(2-hydroxyethylene)-6,8-dinitro-1-methyl-2-quinolone (40)   Yellow Powder, ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.37(s, 3H), 7.20 (d, J = 2.9 Hz, 1H), 7.36 (s, 1H), 7.69 (d, J = 2.9 Hz, 1H), 8.68 (d, J = 2.4 Hz, 1H), 9.14 (d, J = 2.4 Hz, 1H).

Diels-Alder reaction of TNQ-Me with electron-rich alkene in the presence of triethylamine.

To a solution of **TNQ-Me** (588 mg, 2 mmol) in acetonitrile (10 mL), ethoxyethene (721 mg, 10 mmol) and triethylamine (202 mg, 2 mmol) were added, and the mixture was stirred at room temperature for 1 day. During the reaction, pale yellow powder was precipitated and was collected by filtration to afford quinolino diazaphenanthrene **41** (240 mg, 0.46 mmol, 92 %). Further purification was performed by recrystallization from acetonitrile to give **12**.

5,9-Dimethyl-6,8-dioxo-2,4,10,12-tetranitroquinolino[3,4-b]1,9-diazaphenanthrene (41) Colorless needles, mp >300 °C; IR (KBr / cm^{-1}) 1705, 1695, 1608, 1538, 1463, 1346; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.48 (s, 6H), 9.02 (d, J = 2.4 Hz, 2H), 10.08 (d, J = 2.4 Hz, 2H), 10.39 (s, 1H). MS (FAB): m/z (%): 522 (M$^+$+1). Anal. Calcd. for $C_{21}H_{11}N_7O_{10}$: C, 48.37; H, 2.11; N, 18.81. Found: C, 48.04; H, 2.06; N, 18.52.

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List of Publications

1. The nitroalkene showing dual behaviors in the same reaction system

   <u>Motoki Asahara</u>, Chika Shibano, Koichi Koyama, Yasuo Tohda,

   Nagatoshi Nishiwaki, and Masahiro Ariga

   Tetrahedron Letters, **2005**, *46*, 7519-7521.

2. Electrophilic Arylation of Phenols:

    Construction of a New Family of 1-Methyl-2-quinolones

   <u>Motoki Asahara</u>, Masaki Ohtsutsumi, Mina Tamura, Nagatoshi Nishiwaki, and

   Masahiro Ariga

   Bulletin of the Chemical Society of Japan, **2005**, *78*, 2235-2237.

3. Effective C-N Bond Formation on the 1-Methyl-2-quinolone Skeleton

   <u>Motoki Asahara</u>, Moriaki Nagamatsu, Yasuo Tohda, Nagatoshi Nishiwaki, and

   Masahiro Ariga

   Arkivoc, **2005**, (i), 1-6.

4. Diels-Alder Reaction of 1-Methyl-3,6,8-trinitro-2-quinolone

   <u>Motoki Asahara</u>, Moriaki Nagamatsu, Yasuo Tohda, Nagatoshi Nishiwaki, and

   Masahiro Ariga

   Journal of Heterocyclic Chemistry, **2004**, *41*, 803-805.

5. Synthesis of Unnatural 1-Methyl-2-quinolone Derivatives

   <u>Motoki Asahara</u>, Taku Katayama, Yasuo Tohda, Nagatoshi Nishiwaki, and

   Masahiro Ariga

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6. A Nitro Group Distorting 2-Qunilone Skeleton

  Nagatoshi Nishiwaki, Chitose Tanaka, <u>Motoki Asahara</u>, Noriko Asaka,

  Yasuo Tohda, and Masahiro Ariga

  Heterocycles, **1999**, *51*, 567-574.

List of Supplementary Publications

1. *dl*-Selective Pinacol-type Coupling Using Zinc, Chlorosilane

  and Catalytic Amounts of Cp_2VCl_2 (*dl*-1,2-Dicylohexylethanediol)

    Toshikazu Hirao, Akiya Ogawa, <u>Motoki Asahara</u>, Yasuaki Muguruma, and

    Hidehiro Sakurai

    Organic Syntheses, **2004**, *81*, 26-32.

2. Highly Diastereoselective Pinacol Coupling of Secondary Aliphatic Aldehydes

  Induced by a Catalytic System Consisting of Vanadium Complex,

  Chlorosilane,and Zinc Metal

    Toshikazu Hirao, <u>Motoki Asahara</u>, Yasuaki Muguruma, and Akiya Ogawa

    Journal of Organic Chemistry, **1998**, *63*, 2812-2813.

3. Cp_2TiCl_2-Catalyzed Pinacol-Type Coupling of Aliphatic Aldehydes

  by Use of Zinc and Chlorosilane

    Toshikazu Hirao, Bunpei Hatano, <u>Motoki Asahara</u>, Yasuaki Muguruma, and

    Akiya Ogawa

    Tetrahedron Letters, **1998**, *39*, 5247-5246.

List of Supplementary Patents

1. Acylated 4-Hydroxybenzoic Acid Derivatives Having Steric Hindered Groups and Their Manufacturing Method

   Masaya Kitayama, Hiroyuki Kato, <u>Motoki Asahara</u> and Toshiki Nishino

   Jpn, Kokai Tokkyo Koho 2005-225820 (2005)

2. Liquid Crystalline Polyester Resins

   Ryuzo Ueno, Masaya Kitayama, Hiroyuki Kato, Hiroaki Terada and

   <u>Motoki Asahara</u>

   Jpn, Kokai Tokkyo Koho 2005-105232 (2005)

3. Liquid Crystalline Polymer Pellet or Manufacturing Method of

   Liquid Crystalline Polymer Compound Pellet

   Hiroyuki Kato and <u>Motoki Asahara</u>

   Jpn, Tokkyo Syutsugann 2005-161405 (2005)

4. Liquid Crystalline Polyester Resins and Their Manufacturing Method

   Hiroyuki Kato, <u>Motoki Asahara</u> and Tetsuhide Sawada

   Jpn, Tokkyo Syutsugann 2005-023415 (2005)

5. Manufacturing Method of Wholly Aromatic Liquid Crystalline Polyester Resins

   <u>Motoki Asahara</u> and Toshiki Nishino

   Jpn, Tokkyo Syutsugann 2004-294565 (2004)

6. Liquid Crystalline Polyester Resins and Their Manufacturing Method

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   Jpn, Tokkyo Syutsugann 2004-207118 (2004)

7. Liquid Crystalline Resins Containing Repeated Unit

  Consisted of 3,5-Di-tert-butyl-4-oxybenzoyl

    Masaya Kitayama, Hiroyuki Kato, <u>Motoki Asahara</u> and Toshiki Nishino

    Jpn, Tokkyo Syutsugann 2004-182484 (2004)

8. Thermotropic Liquid Crystalline Polymer

    Ryuzo Ueno, Masaya Kitayama, Kiichi Kometani, Hiroyuki Kato and

    <u>Motoki Asahara</u>

    Jpn, Kokai Tokkyo Koho 2002-371127 (2002)

9. Thermotropic Liquid Crystalline Polymer

    Ryuzo Ueno, Masaya Kitayama, Kiichi Kometani, Hiroyuki Kato and

    <u>Motoki Asahara</u>

    Jpn, Kokai Tokkyo Koho 2001-359350 (2001)

Finally, I wish to express my personal acknowledgement to my wife, son and parents for their encouragement and understanding on this work.