Reactive 2-Quinolones Dearomatized by Steric Repulsion between 1-Methyl and 8-Substited Groups

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Reactive 2-Quinolones Dearomatized by Steric Repulsion between 1-Methyl and 8-Substited Groups

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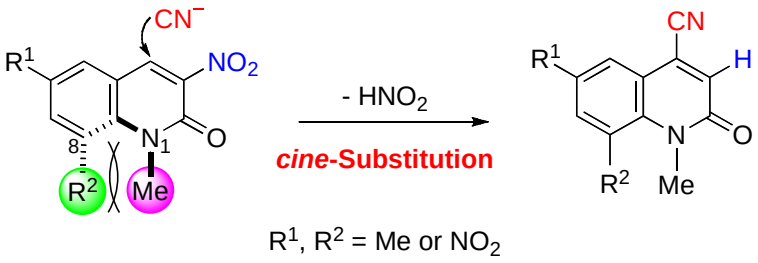


Abstract

Usual 1-methyl-2-quinolone (**MeQone**) derivatives are not reactive because of aromatic property in the heterocyclic ring. On the other hand, 8-substituted **MeQones** have been proved to be highly reactive, which is caused by steric repulsion between the 1-methyl and the 8-substituted groups. When 1-methyl-3,6,8-trinitro-2-quinolone was treated with potassium (or trimethylsilyl) cyanide, cyanation proceeded at the 4-position regioselectively as a result of *cine*-substitution. This reaction is initiated with addition of cyanide species, and the cyanoquinolone is formed by the protonation of the resultant anionic intermediate followed by elimination of nitrous acid. The high reactivity was maintained even when one of the nitro groups on the benzene moiety was replaced by a methyl group, which afforded corresponding *cine*-substituted products upon treatment with potassium cyanide.

Introduction

A *Rutaceae* family, commonly known as *Citrus*, reveals high commercial value because of wide consumption in the world. The family is quite large, including approximately 160 genera and 1900 species with great diversity in morphological characters. The *Rutaceae* family plays an important role to supply extraordinary array of phytochemicals such as limonoids, flavonoids, coumarins, alkaloids, volatile oils, and so on.[1] Furthermore, quinolone alkaloids have been extensively studied by using various synthetic techniques, and various medicinal properties have been reported, such as antitumor activity,[2] antianemia activity,[3] antikinetoplastid activity,[4] antimicrobial activity,[5] antibacterial activity,[6] dipeptidyl peptidase IV inhibition,[7] chymase inhibition,[8] and so on.

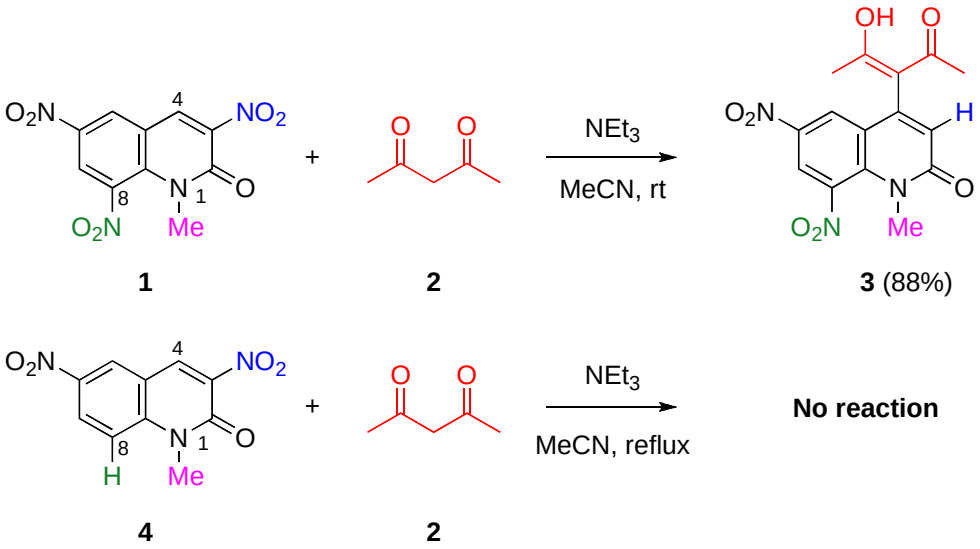
The 1-methyl-2-quinolone (**MeQone**) framework is a fundamental partial structure of these biologically active compounds. Naturally occurring **MeQone** derivatives have attracted many researchers' interest, and their isolations, structural determinations, total syntheses, and modifications have been important subjects over the past decades. In addition, unnatural **MeQone** derivatives have also attracted much attention recently because of their latent pharmacological and physiological activities. However, the functionalization of the **MeQone** skeleton is not easily performed due to the aromatic

property of the pyridone moiety; the development of facile methods for the functionalization of the **MeQone** framework is still challenging.[9]

On the other hand, we have found that 1-methyl-3,6,8-trinitro-2-quinolone (**1**) exhibited extraordinary high reactivity compared with other **MeQone** derivatives. Indeed, the functionalization of the **MeQone** framework was easily performed by *cine*-substitution or cycloaddition.[10] Among three nitro groups, the 8-nitro group was found to be essential for the activation of the quinolone **1**. The *cine*-substitution proceeded efficiently to afford 4-functionalized 6,8-dinitro-2-quinolone (**3)** upon treatment of the quinolone **1** with 2,4-pentanedione (**2**) in the presence of triethylamine at room temperature.[11] To the contrary, 1-methyl-3,6-dinitro-2-quinolone (**4**) caused no change even at an elevated temperature (Scheme 1).[12] The quite different reactivity between the quinolones **1** and **4** cannot be rationalized by only electron-withdrawing effect of the 8-nitro group, because it is far from the reaction site (the 4-position). Hence, we suppose the high reactivity of the quinolone **1** is caused by steric repulsion between the 1-methyl and the 8-nitro groups, by which the coplanarity of the pyridone moiety and the benzene ring is disturbed. Indeed, X-ray analysis indicated that the dihedral angle between the N_1-Me and C_8-R^8 bonds was 25^o (Figure 1) while the corresponding angle of **4** was 0.9^o.[12] As a result of disturbing the

coplanarity, the pyridone moiety serves as an activated nitroalkene rather than an aromatic species.[13] This hypothesis prompted us to study the sterical activation of the **MeQone** framework sterically by a substituent at the 8-position.

Scheme 1. *cine*-Substitution of Nitrated 1-Methyl-2-quinolones with 2,4-Pentanedione



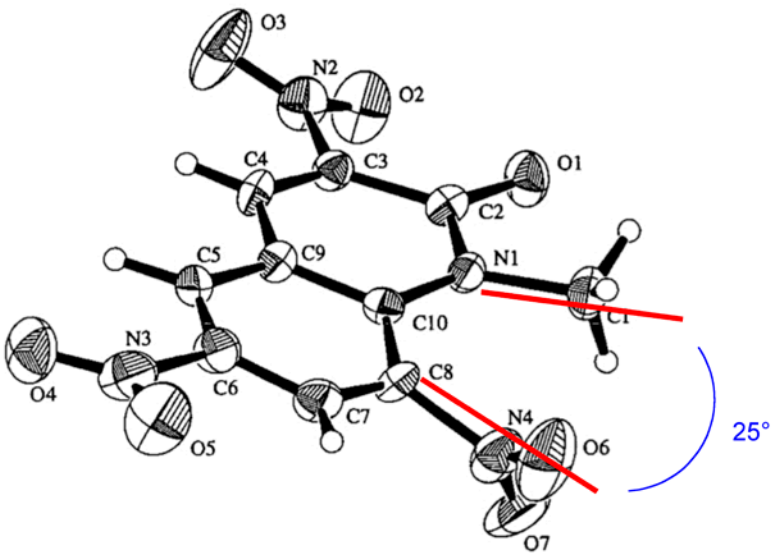


Figure 1. ORTEP (30% probability ellipsoids) view of the quinolone **1**.[12]

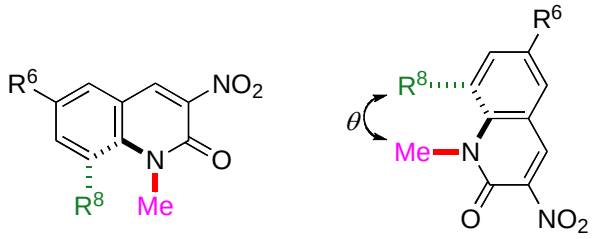
Results and Discussion

1. Prediction of Steric Distortion by DFT Calculation

In order to predict the reactivity of **MeQone** derivatives, the dihedral angles between the N_1-Me and C_8-R^8 bonds were estimated by DFT calculations (Table 1). When the R^8 group at the 8-position is hydrogen (Compound **4**), the benzene and pyridone moieties are almost coplanar. On the other hand, when the 8-position is substituted by a methyl or nitro group (**5** and **6**), the 2-quinolone ring is torsionally strained by the steric compression of the 1-methyl and 8-methyl/nitro groups. As a result, 1,6-dimethyl-3,8-dinitro-2-quinolone (**5**)

and 1,8-dimethyl-3,6-dinitro-2-quinolone (**6**) are considered to surely reveal high reactivity as well as the trinitroquinolone **1**.

Table 1. Dihedral Angles between the N_1-Me and C_8-R^8 Bonds



Compound	R^6	R^8	Dihedral angles θ[a]
1	NO_2	NO_2	29.0°
4	NO_2	H	1.5°
5	Me	NO_2	29.2°
6	NO_2	Me	30.9°

[a] Estimated by DFT calculations using B3LYP/6-31+G (d,p)

2. Preparation of Nitroquinolones

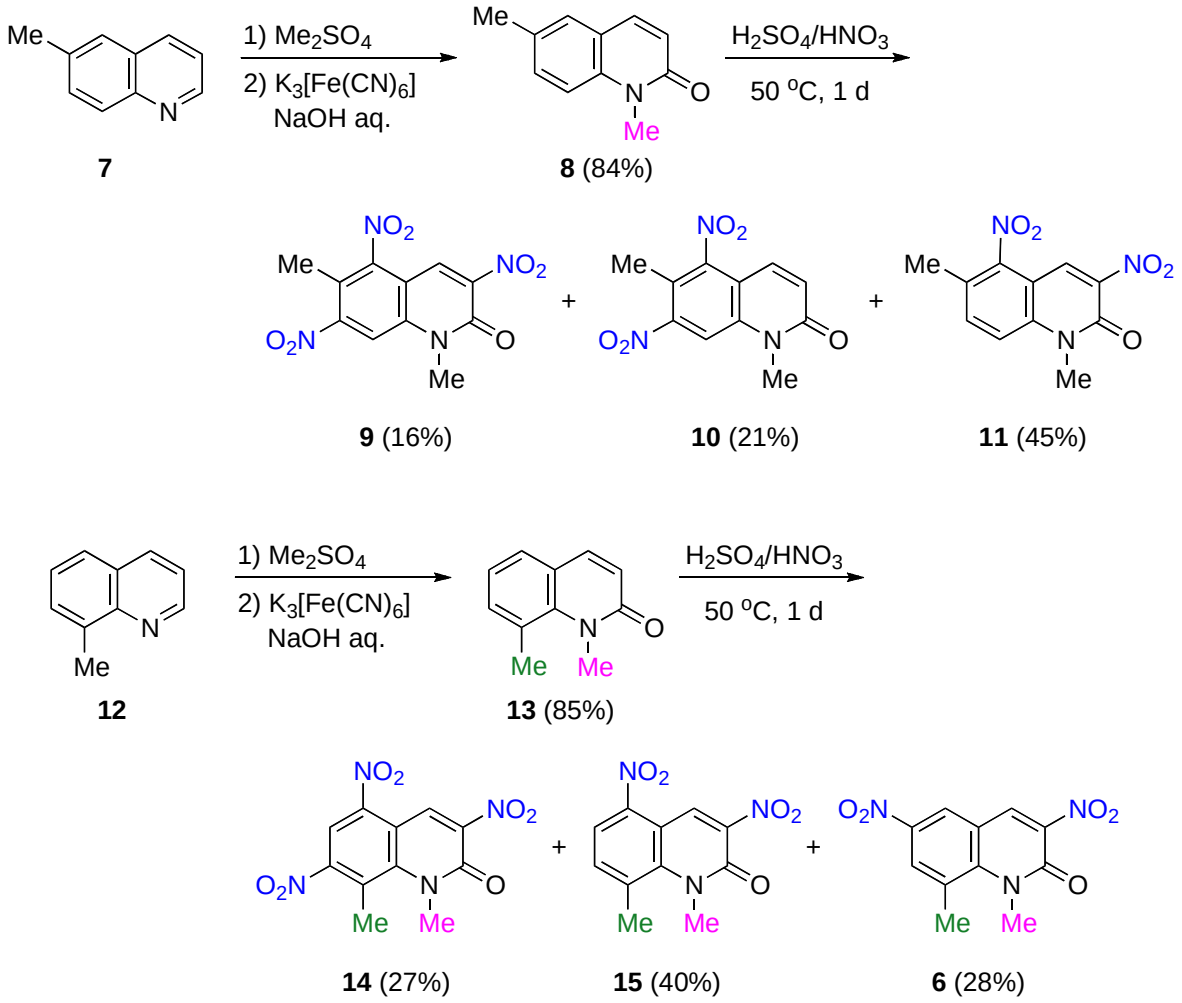
Firstly, synthetic methods for the nitrated dimethyl-2-quinolones **5** and **6** were studied (Scheme 2). The starting dimethyl-2-quinolones, 1,6-dimethyl-2-quinolone (**8**)[14] and 1,8-dimethyl-2-quinolone (**13**),[14] were prepared from the commercially available methylquinolines **7** and **12** according to the synthetic method reported for 1-methyl-2-quinolone.[15a] In fact, when 1,6-dimethyl-2-quinolone (**8**) was nitrated, the nitro

groups were mainly introduced at the 5 and 7-positions as well as at the 3-position, in which the electro-donating 6-methyl group serves as an *ortho*-directing group.

Thus, 1,6-dimethyl-3,5,7-trinitro-2-quinolone (**9**), 1,6-dimethyl-5,7-dinitro-2-quinolone (**10**), and 1,6-dimethyl-3,5-dinitro-2-quinolone (**11**) were obtained without any detection of the desired 3,8-dinitroquinolone **5**.

In the case of the nitration of 1,8-dimethyl-2-quinolone (**13**), 8-methyl group served as a stronger *ortho*, *para*-directing group than the acylamino group (the ring nitrogen) to afford 1,8-dimethyl-3,5,7-trinitro-2-quinolone (**14**), 1,8-dimethyl-3,5-dinitro-2-quinolone (**15**) as the products. In the present reaction, the acylamino group also served as a *para*-directing group to give the desired 1,8-dimethyl-3,6-dinitro-2-quinolone (**6**) in 28% yield.

Scheme 2. Preparation of Dimethyl-dinitro-2-quinolones

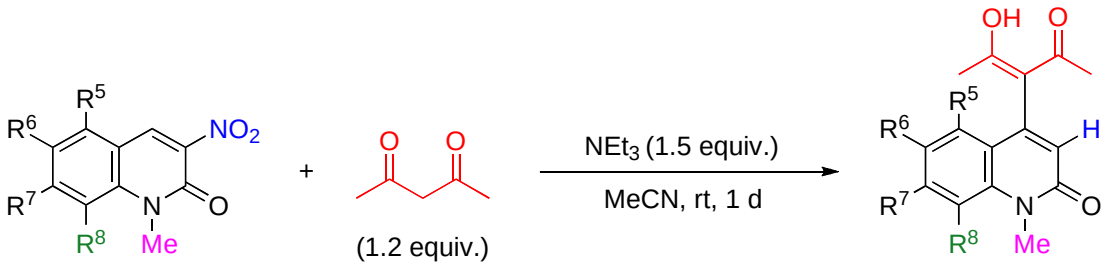


3. *cine*-Substitution Using 2,4-Pentanedione (2)

The obtained nitroquinolones **9**, **14**, **15**, and **6** were subjected to the reactions with 2,4-pentanedione (**2**) in the presence of triethylamine. While the 3,6,8-trinitroquinolone **1** efficiently underwent the *cine*-substitution, neither trinitroquinolones **9** nor **14** caused no

reaction (Table 2, entries 1-3) under the same conditions. In the case of the dinitroquinolone **15**, the corresponding product **18** was not detected (entry 4).

Table 2. *cine*-Substitution of Nitro-1,8-dimethyl-2-quinolones with 2,4-Pentanedione



Entry	R^5	R^6	R^7	R^8	Nitroquinolone	Product	Yield/%
1	H	NO_2	H	NO_2	**1**	**3**	88
2	NO_2	Me	NO_2	H	**9**	**16**	0
3	NO_2	H	NO_2	Me	**14**	**17**	0
4	NO_2	H	H	Me	**15**	**18**	0
5	H	NO_2	H	Me	**6**	**19**	92

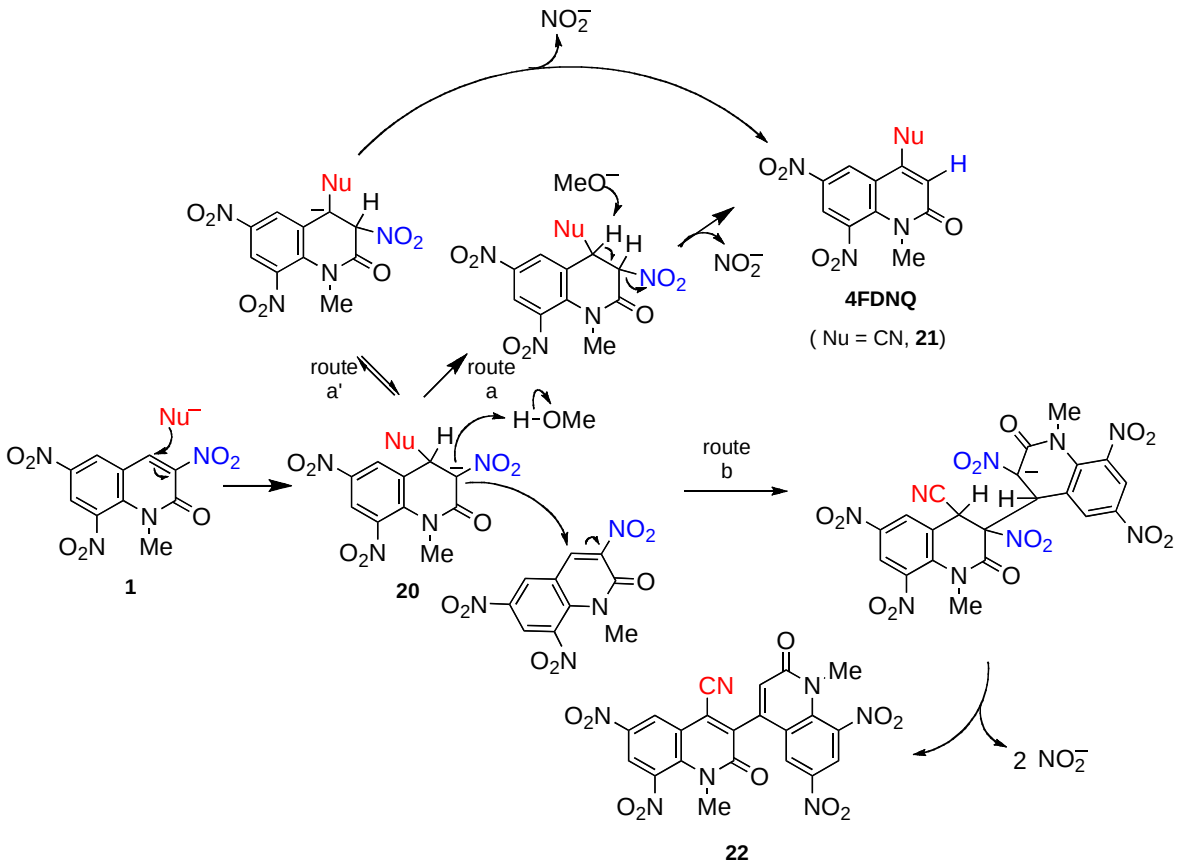
It is noteworthy that *cine*-substitution efficiently proceeded to afford **19** in 92% yield when the substrate **6** was employed, which has only two nitro groups (entry 5). This experimental fact strongly supports our hypothesis; the steric repulsion between two methyl groups activates the **MeQone** framework. However, the quinolones **14** and **15** did not undergo the *cine*-substitution despite the presence of a methyl group at the 8-position, in

which the *peri*-substituent (R^5) might prevent the approach of the bulky enolate of **2** to the 4-position.

4. Cyanation of the Trinitroquinolone 1

In order to estimate the activating effect of the steric repulsion between the substituents at the 1- and 8-positions, it is necessary to employ a small nucleophile instead of a bulky enolate of **2** to avoid the steric hindrance of a substituent at the 5-position. From this viewpoint, cyanide was employed as a nucleophile. When a solution of potassium cyanide in methanol was added to a solution of the quinolone **1** in acetonitrile, and heated at 60 °C for 2 hours, a complex mixture was obtained, from which two products, the 4-cyano-2-quinolone derivative **21** and the dimeric product **22** were isolated.

Scheme 3. A Plausible Reaction Mechanism for the Formation of 21 and 22



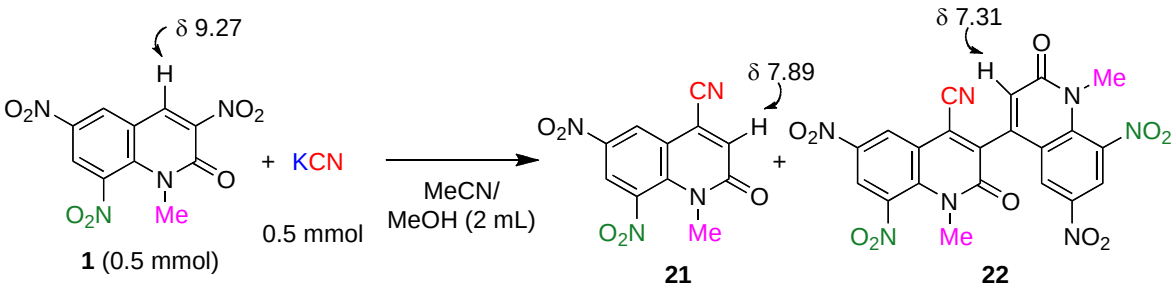
A plausible mechanism for the formation of these products is illustrated in Scheme 3. The reaction is initiated with the nucleophilic attack of cyanide (Nu = CN) at the 4-position of the quinolone **1**. The cyanoquinolone **21** is afforded when the resultant anion **20** is protonated, followed by the elimination of a nitrous acid molecule (Scheme 3, route a). Another route is also acceptable, which involves a proton migration followed by

elimination of nitrite anion (route a'). On the other hand, the dimeric product **22** is formed when the intermediate anion **20** attacks another molecule of the quinolone **1**, and the pyridone moieties aromatize accompanied by the elimination of nitrous acid molecules (route b). Although this kind of dimerization was observed in the reaction of the quinolone **1** with tertiary amines,[16] this is the first example to isolate a dimer in the reaction with *C*-nucleophiles. The strongly electron-withdrawing ability of the carbonyl and nitro groups is considered to stabilize the anionic intermediate **20.**

The reaction conditions were optimized as shown in Table 3. The reaction temperature was found to be a crucial factor for the present reaction. When the temperature was lowered to 0 °C, the total yield of **21** and **22** increased up to 94% (the yield of **21** was increased up to 80%), accompanied with the simplification of the reaction mixture (entries 2-4). On the other hand, a longer reaction time did not affect the yields of **21** and **22** (entry 5). Next, the control of the reaction routes (routes a and b) was attempted by changing the volume of the solvent. When the reaction was conducted under concentrated conditions, many signals other than those of **21** and **22** were observed in the reaction mixture without considerable change in the ratio of **21/22** (entry 6). Moreover, dilution was not so effective for avoiding the dimerization (entry 7). The solvent effect for the reaction was also investigated; when

H_2O was employed as the solvent for dissolving potassium cyanide, many by-products were observed (entry 8). Hence, methanol was found to be a more suitable solvent dissoluble of potassium cyanide, which was somewhat influential for inhibiting the side reactions during the whole reaction process.

Table 3. Optimization of Reaction Conditions

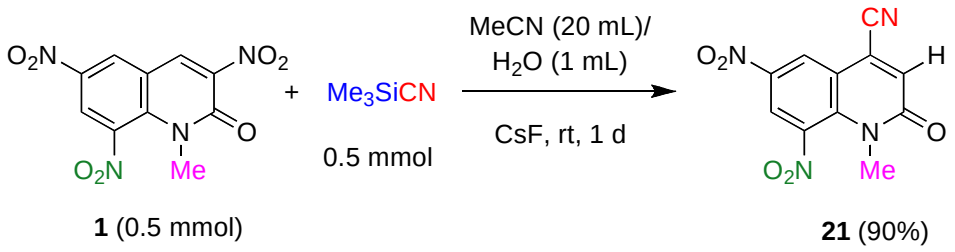


Entry	Temp. /°C	Solv. /mL	Time /h	Yield/%		Total yield/%	Recovery of **1**/%
				21	**22**		
1	60	20	2	63	9	72	7
2	rt	20	2	73	7	80	7
3	0	20	2	80	14	94	6
4	-20	20	2	78	10	88	11
5	0	20	4	69	9	78	6
6	0	10	2	71	7	78	9
7	0	50	2	62	7	69	8
8[b]	0	20	2	73	14	87	9

[a]Determined by ^{1}H NMR based on **1**. [b]H_2O was used as the solvent in order to completely dissolve KCN.

Finally, in order to investigate the cation effect of cyanide compounds, trimethylsilyl cyanide/cesium fluoride was employed instead of potassium cyanide. To our expectation, the formation of the dimer **22** was not observed, and the yield of **21** dramatically increased up to 90%, when the reaction was conducted at room temperature for 1 d (Scheme 4). We suppose that the anionic intermediate **20** is trapped by a trimethylsilyl group to afford a stable enolate intermediate, which prevents the nucleophilic attack of the intermediate **20** to another molecule of the quinolone **1**.

Scheme 4. *cine*-Substitution of Quinolone 1 with Trimethylsilyl Cyanide



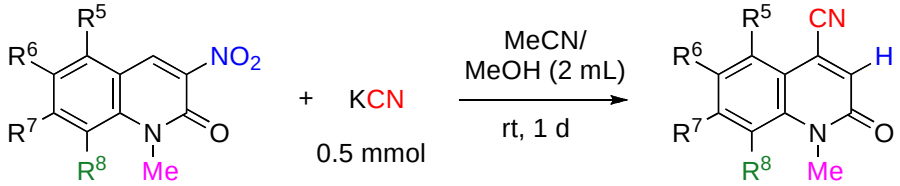
1 (0.5 mmol) **21** (90%)

While known cyanation methods require multi-step reactions,[17] the present method enables the cyanation through a shorter synthetic route, which will be a useful synthetic tool for constructing a library of versatile **MeQone** derivatives by the chemical conversion of the cyano and nitro functions.

5. Estimation of the Steric Activation Using the Cyanation

The cyanation reactions of nitrated 1,8-dimethyl-2-quinolones using potassium cyanide were investigated because of smaller size than that of trimethylsilyl cyanide (Table 4). Although the 3,5,7-trinitroquinolone **14** caused no change upon treatment with 2,4-pentanedione (**2**), the reaction with potassium cyanide efficiently proceeded to afford the *cine*-substituted product, 4-cyanoquinolone **23**, in 83% yield (entry 2). The cyanation also took place even when the 3,5-dinitroquinolone **15** was employed (entry 3). Furthermore, the 3,6-dinitroquinolone **6** revealed high reactivity to undergo the *cine*-substitution quantitatively (entry 4). These results strongly support our consideration that the steric repulsion between 1-methyl and 8-methyl groups activated the **MeQone** by disturbing the coplanarity (entries 3 and 4).

Table 4. *cine*-Substitution of Nitro-1,8-dimethyl-2-quinolones with Potassium Cyanide



Entry	R^5	R^6	R^7	R^8	Nitroquinolone	Product	Yield/%
1	H	NO_2	H	NO_2	**1**	**3**	73
2	NO_2	H	NO_2	Me	**14**	**23**	83
3	NO_2	H	H	Me	**15**	**24**	47
4	H	NO_2	H	Me	**6**	**25**	quant.

Conclusion

We have developed a simple method for the cyanation of the 3-nitro-8-substituted **MeQones**. When the 8-position was substituted with a nitro group, *cine*-substitution and dimerization easily proceeded under mild reaction conditions to afford the cyanoquinolones **21** and **22**. The reaction could be used for estimating the activation degree of the **MeQone** framework. As a result, the presence of an 8-substituent was found to be crucial for causing the *cine*-substitution, which activated the **MeQone** framework by steric repulsion with the 1-methyl group. These results should be valuable information for the functionalization of the **MeQone** framework by activating sterically, and are helpful for finding new biologically active compounds.

Experimental

General

The melting points were determined on a Yanaco micro-melting-points apparatus, and were uncorrected. All the reagents and solvents were commercially available and used as received. TLC was performed using Merck silica gel 60 F254, and column chromatography was performed using silica gel 60 (Nacalai Tesque, spherical neutral, 150 μm). The ^{1}H NMR spectra were measured on a Bruker Ascend-400 at 400 MHz with TMS as an internal standard. The ^{13}C NMR spectra were measured on a Bruker Ascend-400 at 100 MHz, and assignments of ^{13}C NMR spectra were performed by DEPT experiments. The IR spectra were recorded on a JASCO FT/IR-4200 spectrometer. The mass spectra and the high resolution mass spectra were measured on a JEOL JMS-DX303HF or JEOL-JMS-700 MStation.

Nitration of 1,6-Dimethyl-2-quinolone

To cold 18 M H_2SO_4 (11.1 mL, 200 mmol), the quinolone **8** (1.7 g, 10 mmol) was gradually added and then 15 M HNO_3 (23.3 mL, 350 mmol) was added gradually. The resultant mixture was heated at 50 °C for 1 d. After cooling down to room temperature, H_2O (30 mL) was poured into the reaction mixture. The generated yellow precipitate (2.6 g)

was collected with filtration. Further purification was performed by recrystallization or column chromatography on silica gel. The nitration of the 1,8-dimethyl-2-quinolone **13** was conducted in a similar manner.

1,6-Dimethyl-3,5,7-trinitroquinolin-2(1*H*)-one (9). Eluted with hexane/ethyl acetate = 8/2; 493 mg, 16% yield; yellow solid; mp 189−191 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.42 (s, 3H), 3.40 (s, 3H), 8.53 (s, 1H), 8.68 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.9 (CH_3), 34.2 (CH_3), 111.2 (C), 124.2 (C), 127.1 (CH), 131.7 (C), 131.7 (CH), 138.5 (C), 141.4 (C), 148.8 (C), 152.7 (CO); MS (EI, 70 eV) *m/z* = 308 (M^+, 3), 220 (25), 191 (36), 115 (100), 105 (55); HRMS (EI, magnetic field) Calcd for $C_{11}H_8N_4O_7$ 308.0393, found 308.0393.

1,6-Dimethyl-5,7-dinitroquinolin-2(1*H*)-one (10). Eluted with hexane/ethyl acetate = 7/3; 553 mg, 21% yield; yellow solid; mp 112−115 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.37 (s, 3H), 3.33 (s, 3H), 6.92 (d, J = 10.0 Hz, 1H), 7.74 (d, J = 10.0 Hz, 1H), 8.32 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 15.6 (CH_3), 34.0 (CH_3), 114.6 (C), 123.2 (C), 125.3 (CH), 129.7 (CH), 131.8 (CH), 132.3 (C), 139.3 (C), 149.2 (C), 160.8 (CO); MS (EI, 70 eV) *m/z* = 263 (M^+, 100), 233 (30), 173 (45); HRMS (EI, magnetic field) Calcd for $C_{11}H_9N_3O_5$ 263.0542, found 263.0542.

1,6-Dimethyl-3,5-dinitroquinolin-2(1*H*)-one (11). 1.18 g, 45% yield; yellow needles; recrystallized from MeCN; mp 259−261 °C; ^{1}H NMR (400 MHz, CD_3CN) δ 2.44 (s, 3H), 3.78 (s, 3H), 7.72 (d, J = 9.2 Hz, 1H), 7.81 (d, J = 9.2 Hz, 1H), 8.31 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 16.4 (CH_3), 30.9 (CH_3), 108.7 (C), 118.7 (CH), 124.8 (C), 128.3 (CH), 136.5 (CH), 139.2 (C), 142.1 (C), 148.2 (C), 152.9 (CO); MS (EI, 70 eV) *m/z* = 263 (M^+, 38), 142 (41), 115 (57), 69 (100); HRMS (EI, magnetic field) Calcd for $C_{11}H_9N_3O_5$ 263.0542, found 263.0537.

1,8-Dimethyl-3,5,7-trinitroquinolin-2(1*H*)-one (14). Eluted with hexane/ethyl acetate = 3/7; 862 mg, 27% yield; yellow solid; mp 188−190 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.85 (s, 3H), 3.82 (s, 3H), 8.53 (s, 1H), 8.60 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.2 (CH_3), 37.7 (CH_3), 111.0 (C), 127.9 (CH), 131.3 (C), 131.6 (CH), 133.2 (C), 140.7 (C), 142.8 (C), 145.9 (C), 154.9 (CO); MS (EI, 70 eV) *m/z* = 308 (M^+, 10), 130 (29), 101 (32), 75 (46), 69 (100); HRMS (EI, magnetic field) Calcd for $C_{11}H_8N_4O_7$ 308.0393, found 308.0395.

1,8-Dimethyl-3,5-dinitroquinolin-2(1*H*)-one (15). Eluted with hexane/ethyl acetate = 3/7; 1.05 g, 40% yield; yellow solid; mp 216−219 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.84 (s, 3H), 3.78 (s, 3H), 6.92 (d, J = 9.6 Hz, 1H), 7.66 (d, J = 9.6 Hz, 1H), 8.39 (s, 1H); ^{13}C NMR

(100 MHz, DMSO-d_6) δ 23.4 (CH_3), 36.4 (CH_3), 113.2 (C), 125.6 (CH), 129.5 (CH), 129.9 (C), 131.8 (C), 131.8 (CH), 140.0 (C), 146.0 (C), 162.1 (CO); MS (EI, 70 eV) *m/z* = 263 (M^+, 100), 159 (28), 130 (20), 75 (17); HRMS (EI, magnetic field) Calcd for $C_{11}H_9N_3O_5$ 263.0542, found 263.0541.

1,8-Dimethyl-3,6-dinitroquinolin-2(1*H*)-one (6). Eluted with hexane/ethyl acetate = 7/3; 737 mg, 28% yield; yellow solid; mp 236−238 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.84 (s, 3H), 3.85 (s, 3H), 8.42 (d, J = 2.8 Hz, 1H), 8.80 (d, J = 2.8 Hz, 1H), 9.09 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.2 (CH_3), 37.0 (CH_3), 118.4 (C), 125.2 (CH), 128.4 (C), 131.1 (CH), 136. 7 (CH), 140.3 (C), 142.0 (C), 146.0 (C), 155.4 (CO); MS (EI, 70 eV) *m/z* = 263 (M^+, 95), 210 (58), 193 (53), 142 (80), 117 (100); HRMS (EI, magnetic field) Calcd for $C_{11}H_9N_3O_5$ 263.0542, found 263.0541.

***cine*-Substitution Using 2,4-Pentanedione (2)**

To a solution of 1,8-dimethyl-3,6-dinitro-2-quinolone (**6,** 132 mg, 0.5 mmol) and 2,4-pentanedione (**2**, 61mg, 0.6 mmol) in acetonitrile (20 mL), 0.025 M solution of triethylamine (30 mL, 0.75 mmol) was added at room temperature over 30 min and the solution color turned to brown. The reaction mixture was stirred for a further 1 d. After concentration, the reaction mixture was dissolved into $CHCl_3$ (20 mL) and washed with

H_2O (20 mL) to remove Et_3NHNO_2. The organic layer was dried over ($MgSO_4$), and concentrated to get residue. Then, the residue was purified by recrystallization with hexane to afford *cine*-substituted product **19** (145 mg, 0.46 mmol, 92% yield).

(*Z*)-4-(2-Hydroxy-4-oxopent-2-en-3-yl)-1,8-dimethyl-6-nitroquinolin-2(1*H*)-one (19). orange solid; mp 192−194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (s, 6H), 2.85 (s, 3H), 3.89 (s, 3H), 6.75 (s, 1H), 8.24 (d, J = 2.4 Hz, 1H), 8.25 (d, J = 2.4 Hz, 1H), 16.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.9 ($2CH_3$), 24.3 (CH_3), 37.1 (CH_3), 109.0 (C), 120.2 (CH), 122.8 (C), 125.9 (CH), 127.2 (C), 129.6 (CH), 142.3 (C), 146.0 (C), 146.4 (C), 164.0 (CO), 190.7 (CO); MS (EI, 70 eV) *m/z* = 316 (M^+, 100), 263 (75); HRMS (EI, magnetic field) Calcd for $C_{16}H_{16}N_2O_5$ 316.1059, found 316.1062.

General Procedure for Synthesis of 21 and 22

To a solution of 1-methyl-3,6,8-trinitro-2-quinolone (**1**)[15] (147 mg, 0.5 mmol) in acetonitrile (20 mL) was added potassium cyanide (33 mg, 0.5 mmol) at 60 °C, and the mixture was stirred for 2 h. Then, the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel to afford the *cine*-substituted product **21** (eluted with hexane/ethyl acetate = 7/3, 87 mg, 0.315 mmol, 63%) and the dimeric product

22 (eluted with hexane/ethyl acetate = 1/1, 12 mg, 0.023 mmol, 9% based on **1**), respectively.

1-Methyl-6,8-dinitro-2-oxo-1,2-dihydroquinoline-4-carbonitrile (21). Yellow powder; mp 168−171 °C; IR (KBr) 2247 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.37 (s, 3H), 7.89 (s, 1H), 8.70 (d, J = 2.4 Hz, 1H), 9.07 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 34.8 (CH_3), 113.6 (CN), 119.4 (C), 121.7 (C), 123.6 (CH), 124.7 (CH), 132.3 (CH), 137.2 (C), 138.7 (C), 140.5 (C), 160.1 (CO); MS (EI, 70 eV) *m/z* = 274 (M^+, 68), 244 (100), 182 (63), 127 (61); HRMS (EI, magnetic field) Calcd for $C_{11}H_6N_4O_5$ 274.0338, found 274.0337.

1,1'-Dimethyl-6,6',8,8'-tetranitro-2,2'-dioxo-1,1',2,2'-tetrahydro-3,4'-biquinoline-4 -carbonitrile (22). Reddish brown oil; IR (KBr) 2240 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.45 (s, 3H), 3.46 (s, 3H), 7.31 (s, 1H), 8.79 (d, J = 2.4 Hz, 1H), 8.81 (d, J = 2.4 Hz, 1H), 8.97 (d, J = 2.4 Hz, 1H), 9.18 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 34.9 (CH_3), 35.5 (CH_3), 112.8 (CN), 119.9 (C), 121.1 (C), 122.6 (C), 123.2 (CH), 124.1 (CH), 125.3 (CH), 125.8 (CH), 125.9 (CH), 136.9 (C), 137.4 (C), 137.5 (C), 138.7 (C), 138.9 (C), 140.7 (C), 140.8 (C), 142.7 (C), 159.6 (CO), 160.8 (CO); MS (EI, 70

eV) *m/z* = 521 (M^+, 95), 491 (100); HRMS (EI, magnetic field) Calcd for $C_{21}H_{11}N_7O_{10}$ 521.0567, found 521.0560.

Cyanation of Trinitroquinolone 1 using Trimethylsilyl Cyanide

To a solution of 1-methyl-3,6,8-trinitro-2-quinolone (**1**)[17] (147 mg, 0.5 mmol) and trimethylsilyl cyanide (50 mg, 05 mmol) in acetonitrile (20 mL), caesium fluoride (76 mg, 0.5 mmol) in 1 mL H_2O was added at room temperature, and the mixture was stirred for 1 d and concentrated. Then, the residue was detected by ^{1}H NMR, and the yield of *cine*-substituted product **21** was calculated with internal standard ($Cl_2CHCHCl_2$).

Cyanation of Nitroquinolones using Potassium Cyanide

1,8-Dimethyl-5,7-dinitro-2-oxo-1,2-dihydroquinoline-4-carbonitrile (23).

To a solution of 1,8-dimethyl-3,5,7-trinitro-2-quinolone (**14**, 154 mg, 0.5 mmol) in acetonitrile (15 mL) was added potassium cyanide (33 mg, 0.5 mmol in 2 mL MeOH) at room temperature, and the mixture was stirred for 1 d. Then, the reaction mixture was filtrated, and the filtrate was concentrated under reduced pressure. The residue was recrystallized with MeOH to afford *cine*-substituted product **23** (119 mg, 0.41 mmol, 83% yield). Red solid; mp 221−223 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.78 (s, 3H), 3.69 (s, 3H), 7.86 (s, 1H), 8.50 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.2 (CH_3), 38.1 (CH_3),

108.3 (CN), 112.0 (C), 115.6 (C), 130.7 (CH), 131.0 (C), 133.6 (C), 136.4 (CH), 138.3 (C), 146.8 (C), 160.1 (CO); MS (EI, 70 eV) *m/z* = 288 (M^+, 40), 184 (100); HRMS (EI, magnetic field) Calcd for $C_{12}H_8N_4O_5$ 288.0495, found 288.0494.

1,8-Dimethyl-5-nitro-2-oxo-1,2-dihydroquinoline-4-carbonitrile (24).

To a solution of 1,8-dimethyl-3,5-dinitro-2-quinolone (**15**, 132 mg, 0.5 mmol) in acetonitrile (15 mL) was added KCN (33 mg, 0.5 mmol in 2 mL MeOH) at room temperature, and the mixture was stirred for 1 d. Then, the solution was concentrated under reduced pressure, and purified with column chromatography to afford *cine*-substituted product **24** (eluted with hexane/ethyl acetate = 3/7, 57 mg, 0.24 mmol, 47% yield). Yellow solid; mp 215−217 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.86 (s, 3H), 3.77 (s, 3H), 7.02 (d, J = 9.6 Hz, 1H), 8.17 (d, J = 9.6 Hz, 1H), 8.42 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.7 (CH_3), 36.4 (CH_3), 113.4 (CN), 119.2 (C), 123.0 (C), 125.4 (CH), 129.2 (C), 129.7 (CH), 132.3 (C), 135.6 (CH), 145.1 (C), 162.3 (CO); MS (EI, 70 eV) *m/z* = 243 (M^+, 53), 197 (62), 169 (100), 142 (67); HRMS (EI, magnetic field) Calcd for $C_{12}H_9N_3O_3$ 243.0644, found 243.0639.

1,8-Dimethyl-6-nitro-2-oxo-1,2-dihydroquinoline-4-carbonitrile (25).

To a solution of 1,8-dimethyl-3,6-dinitro-2-quinolone (**6**, 132 mg, 0.5 mmol) in acetonitrile (15 mL) was added KCN (33 mg, 0.5 mmol in 2 mL MeOH) at room temperature, and the mixture was stirred for 1 d. Then, the solution was concentrated under reduced pressure. Pure *cine*-substituted product **25** (166 mg, 0.5 mmol, quant.) was obtained without further purification without any detectable of by-products. Brown solid; mp 197−198 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.84 (s, 3H), 3.79 (s, 3H), 7.66 (s, 1H), 8.39 (d, J = 2.4 Hz, 1H), 8.41 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.3 (CH_3), 36.8 (CH_3), 114.3 (CN), 117.8 (C), 119.4 (CH), 122.0 (C), 128.8 (C), 129.8 (CH), 130.7 (CH), 141.6 (C), 145.2 (C), 161.2 (CO); MS (EI, 70 eV) *m/z* = 243 (M^+, 100), 228 (35), 169 (40); HRMS (EI, magnetic field) Calcd for $C_{12}H_9N_3O_3$ 243.0644, found 243.0637.

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Supporting Information Statement

Supporting Information. Table of atom coordinates and absolute energies for DFT calculations, ^{1}H NMR and ^{13}C NMR spectra of compounds **6**, **8-11**, **13-15**, **19**, and **21-25** are available.

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