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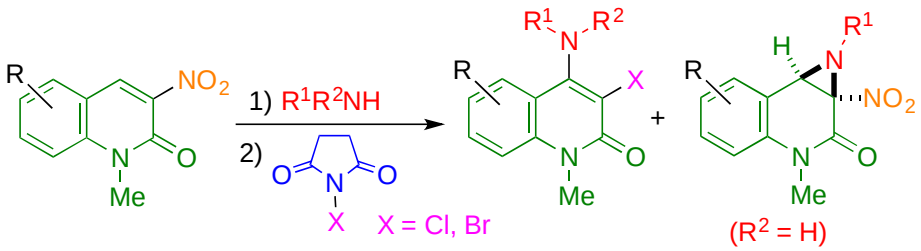
Graphical Abstract



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Direct Amino-halogenation and Aziridination of the 2-Quinolone Framework by Sequential Treatment of 3-Nitro-2-quinolone with Amine and *N*-halosuccinimide

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Keywords: amination • aziridination • halogenation •imidation•quinolone

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ABSTRACT: The sequential treatment of 3-nitro-2-quinolones with amines and *N*-halosuccinimides under mild conditions facilitated the direct amino-halogenation and aziridination at the 4- and 3-positions of the 2-quinolone framework. The selectivity of the functionalization was influenced by the electronic properties of the substituents on the benzene moiety of the nitroquinolone. The electron-withdrawing nitro group promoted the amino-halogenation, and replacement of the nitro group with a halogen or hydrogen markedly increased the selectivity of the aziridination. Moreover, a succinimide group instead of an alkylamino group was introduced at the 4-position, affording the masked form of the 4-amino-3-chloro-2-quinolone derivative. Furthermore, the prepared bis-functionalized quinolones were subjected to Suzuki-Miyaura coupling reaction, ring opening, and hydrazinolysis to afford differently functionalized quinolones.

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1. Introduction

4-Aminated 2-quinolones have garnered considerable attention owing to their various applications in medicinal chemistry. For example, 4-aminated 6-thiazolyl-2-quinolones are potent CD38 inhibitors for the treatment of metabolic syndrome (Figure 1, a).[1] Recently, the design, synthesis, and evaluation of new acetylcholinesterase inhibitors combining 4-amino-2-quinolone rings and benzylpiperidino groups joined by a carboxamide fragment was described (Figure 1, b).[2] In addition, 4-amino-2-quinolones possessing benzimidazole rings at the 3-position have been found to serve as a novel class of receptor tyrosine kinase inhibitors for the treatment of cancer (Figure 1, c).[3] Furthermore, 4-aminated 3-phenyl-2-quinolones have been reported to be *N*-methyl-D-aspartate receptor antagonists with anticonvulsant activities (Figure 1, d).[4]

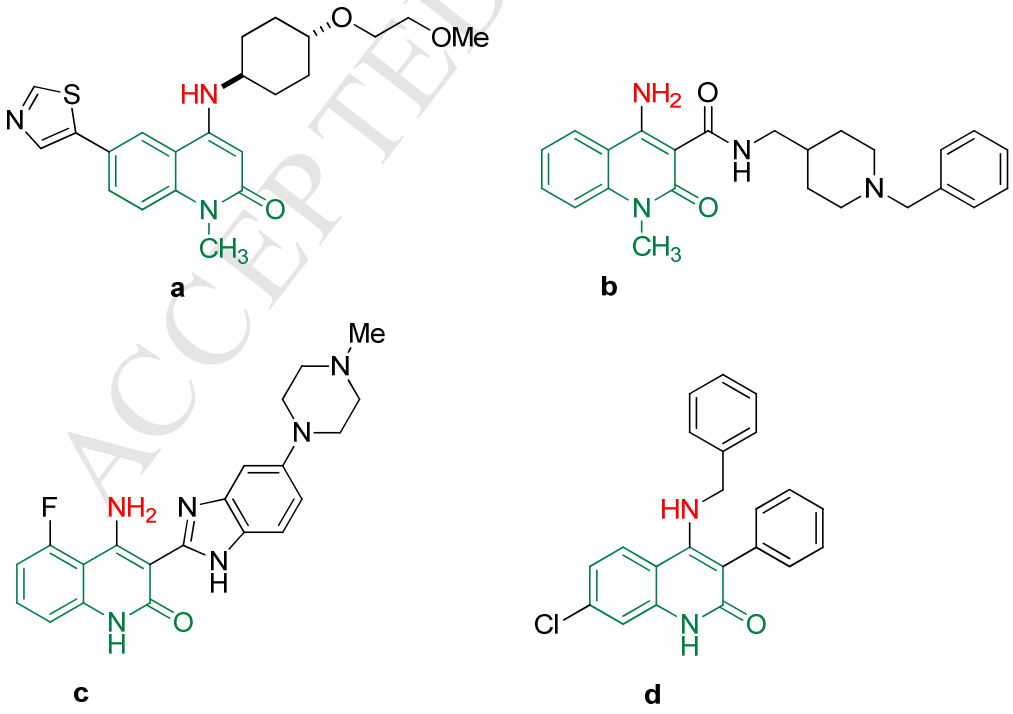


Fig. 1. Examples of bioactive compounds based on the 4-aminated 2-quinolones

Despite these significant applications, 2-quinolones are inert because of their inherent aromaticity, which prevents their direct amination.[5] Hence, conventional strategies for the preparation of such scaffolds involve the construction of heterocyclic rings through cumbersome multistep reaction sequences, some of which involve expensive reagents, harsh reaction conditions and low yields.[4,6] As an alternative approach, 4-aminated 2-quinolones can be also synthesized by chemical conversion from the 4-hydroxy[4,7] or 4-chloro[1,2,8] derivatives. Therefore, the direct and practical amination of the 2-quinolone framework is strongly demanded.

A nitro group is one of the most important functional groups in organic syntheses because of its strong electron-withdrawing ability to activate the scaffold, facilitating the reaction with nucleophilic reagents.[9] Moreover, a nitro group serves not only as a precursor of versatile functionalities but also as a good leaving group.[10] Inspired by these properties of nitro group, we have found that 3-nitrated 1-methyl-2-quinolones (**MeQone**s) are highly reactive in direct C-C/C-O bond formation at the 4-position with carbon nucleophiles[11,12] and alkoxy anions,[13] respectively.

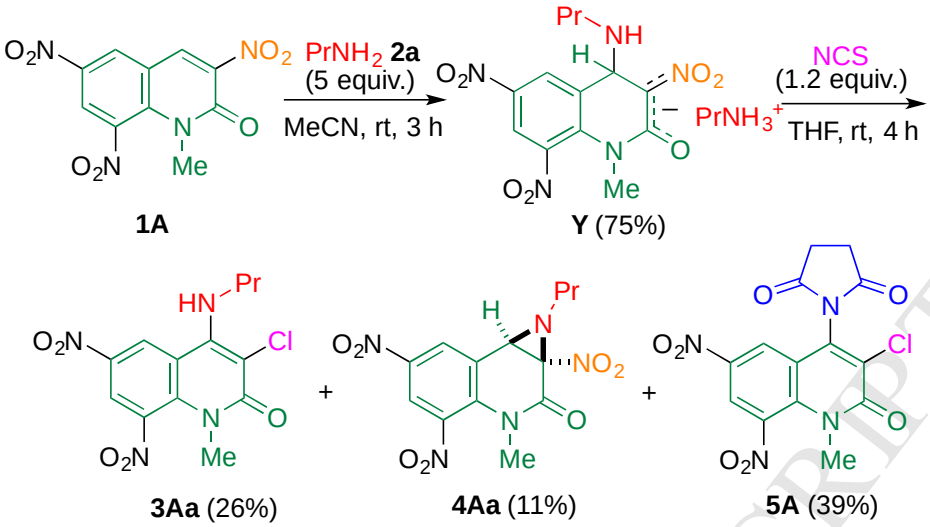
Interested in these results and with the aim of achieving versatile functionalization of the 2-quinolone framework, we decided to investigate direct C-N bond formation at the 4-position of the **MeQone** framework upon treatment of 3-nitrated **MeQone**s with amines, in which an electrophile is necessary to trap the anionic adduct intermediate because a heteronucleophile is easily eliminated even though it adds to quinolone framework.[14] We focused on

the halogenation because the hitherto unknown 4-aminated and 3-halogenated 2-quinolones compose a novel class of 2-quinolones with potentially interesting and valuable bioactivities, and will surely serve as key intermediates for constructing a library of versatile 2-quinolones.

2. **Results and discussion**

To evaluate the potential for vicinal functionalization, trinitro-2-quinolone **1A** was chosen as a model substrate. Initially, a Meisenheimer complex **Y** was synthesized by treating **1A** with excess propylamine **2a**; subsequent reaction with *N*-chlorosuccinimide (NCS) gave the amino-chlorinated product **3Aa** in 26% yield, thus confirming the feasibility of the introduction of vicinal amino and halo groups onto the 2-quinolone framework (Scheme 1). The *N*-propylaziridine ring fused compound **4Aa** was obtained in 11% yield, of which the structure was definitely confirmed by X-ray diffraction of single crystal of **4Fa**,[15] an analogue of **4Aa** (Figure 2). To the best of our knowledge, there is very few report about the aziridination on the **MeQone** framework.[16] Therefore, our investigation will facilitate efficient access to functionalized quinolones. Moreover, the imido-chlorinated product **5A**, which was formed through the reaction of **1A** with NCS and a succinimide anion,[13] was obtained in 39% yield, indicating that regeneration of **1A** from **Y** proceeded under equlibrium.

In order to gain insight into the mechanism of the reaction, a control experiment involving a radical scavenger was performed.[17] The addition of TEMPO had a slight influence on the reaction, but did not completely inhibit the reaction, thus suggesting that radical intermediates were not involved in the process (See Supplementary data).



Scheme 1. Reaction of Meisenheimer complex **Y** with NCS

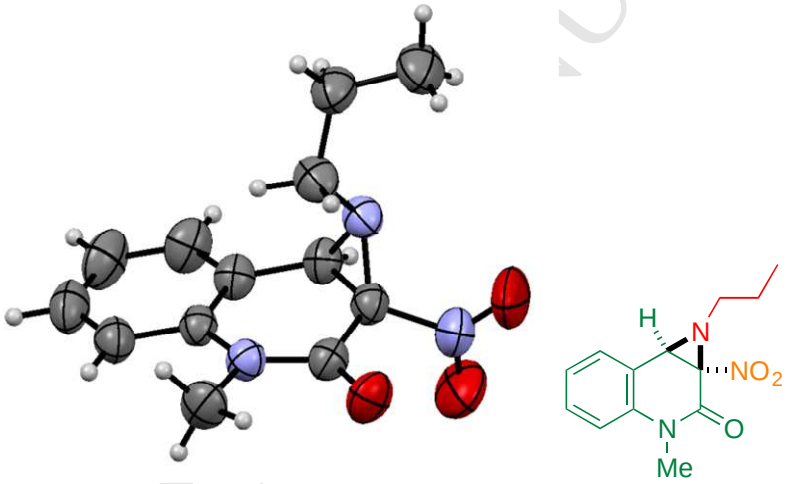
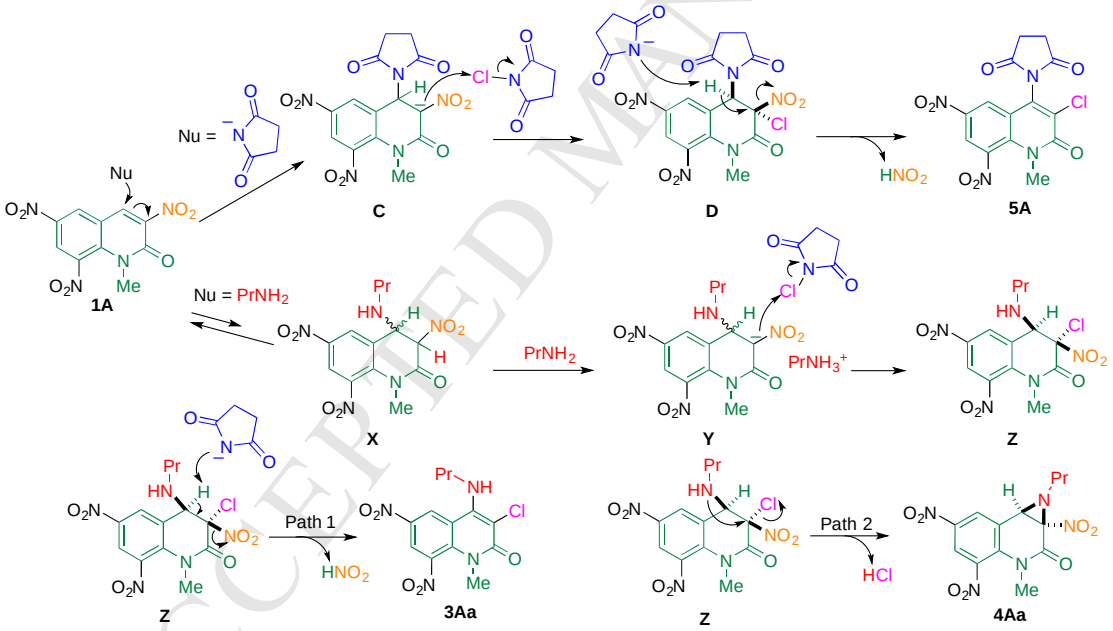


Fig. 2. Structure of **4Fa** from X-ray diffraction analysis (the thermal ellipsoid plots are drawn at 50% probability level)

Based on the aforementioned results, it was postulated that the amine attacks the 4-position of **1A** to give dihydroquinolone **X** (Scheme 2). As a result of deprotonation at the 3-position by another amine, a Meisenheimer complex **Y** is formed. The reaction of **Y** with NCS facilitates chlorination at the 3-position by nucleophilic substitution, whereby NCS approaches from the *trans* direction to avoid the steric

hindrance of the propylamino group, thus affording intermediate **Z**.[18] Hence, the base-promoted rearomatization takes place via the preferred bimolecular antiperiplanar elimination, which leads to the formation of amino-halogenated product **3Aa**. Meanwhile, the intramolecular substitution of the chloro group by the adjacent amino group can occur to form the *N*-propylaziridine ring at the 3- and 4-positions, affording product **4Aa**.[16,19] Additionally, **1A** was regenerated under equilibrium from **X** and then underwent a nucleophilic addition with the succinimide anion followed by chlorination and rearomatization, delivering imido-chlorinated product **5A**.[13]

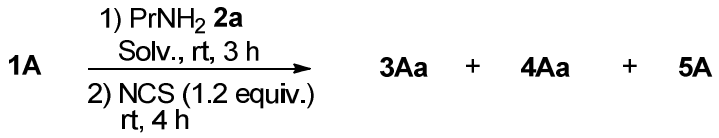


Scheme 2. A plausible mechanism for formation of **3Aa**, **4Aa** and **5A**

In order to enhance the practicality of the method, we attempted to carry out the reaction in a one-pot, two-step fashion using trinitroquinolone **1A**, propylamine **2a**, and NCS as model substrates (Table 1). After a solution of **1A** and **2a** was stirred at

room temperature for 3 h, NCS was added, and the resulting mixture was stirred at room temperature for 4 h. We tested a variety of solvents in the presence of 2.5 equiv. of **2a** in order to find the optimal conditions (Table 1). The conversion of **1A** into amino-chlorinated product **3Aa** did not work well in the ethanol or dichloromethane, as imido-chlorinated product **5A** was the major product in these two solvents (entries 1 and 2). The Meisenheimer complex **Y** is considered to be more solvated with ethanol than **C** by forming hydrogen bonds, which might prevent the approach of NCS. Thus, polar aprotic solvents (MeCN, DMF and THF) were more suitable for the amino-chlorination, and the yield was improved to 45% when THF was used (entries 3–5). In these cases, **4Aa** was obtained as well. Next, a larger amount of **2a** was added to promote the conversion of **1A**, giving **3Aa** in 62% yield without concomitant formation of **5A**. **4Aa** decomposed into other compounds in this process (entry 6), as confirmed by the reaction of **4Aa** with propylamine **2a** (See Supplementary data). However, low temperatures did not further improve the yield (entry 7). This is presumably due to the incomplete conversion of **1A** to **X**, which also underwent the competitive reaction of **1A** with the succinimide anion. Meanwhile, the decomposition of **4Aa** was suppressed at low temperature. Thus, the reaction conditions utilized in entry 6 were determined to be optimal.

Table 1 Conditions screening for aminochlorination



Entry	Solvent	$PrNH_2$ (Equiv.)	Yield (%)		
			3Aa	**4Aa**	**5A**
1	EtOH	2.5	11	5	48
2	CH_2Cl_2	2.5	14	12	34
3	MeCN	2.5	31	11	16
4	DMF	2.5	39	15	3
5	THF	2.5	45	10	19
6	THF	3.0	62	trace	0
7[a]	THF	3.0	37	13	21

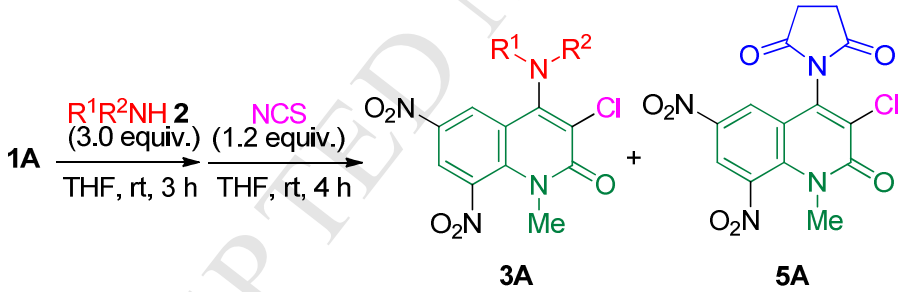
[a]The reaction was conducted at -20 □.

With the optimized reaction conditions in hand, we surveyed the scope of amines **2** (Table 2). Reactions of **1A** with various aliphatic primary amines **2b–f** afforded the corresponding vicinally amino-chlorinated compounds **3Ab–f** in moderate to good yields (entries 1–5); however, **4** was not observed. Alicyclic amines such as piperidine **2g** and morpholine **2h** worked well (entries 6 and 7). Moreover, anilines **2i-m** were also examined. Several functional groups, such as butyl, methoxy and iodo groups on the benzene ring were tolerated, and a larger amount of aniline **2i** promoted the conversion of **1A** (entry 8). However, only a trace amount of **3Am** was detected in the case of 4-nitroaniline **2m** owing to the strong electron-withdrawing effect of the nitro group (entry 12). Due to the steric hindrance preventing the approach of NCS, the target product was not formed in the presence of diethylamine **2n**, and only a trace amount of the desired product was observed in the reaction with *N*-methylaniline **2o**

(entries 13 and 14). In some cases, the succinimide anion was produced under basic condition, and underwent imido-chlorination to furnish **5A** (entries 2, 7 and 13).

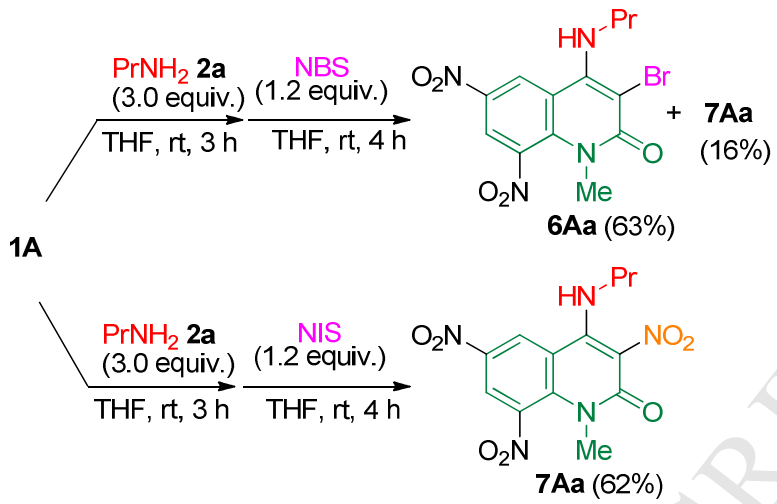
In order to expand the scope of the protocol, two other *N*-halosuccinimides, NBS and NIS, were also employed (Scheme 3). The bromo-amination proceeded smoothly to give **6Aa** in 63% yield. Notably, 4-aminated trinitroquinolone **7Aa** was also obtained in 16% yield, which was presumably due to the higher leaving ability of bromide than chloride. **7Aa** was obtained in 62% yield without the iodo-aminated product in the reaction using NIS.

Table 2 Study on amine scope



Entry	R^1	R^2		Yield (%)	
				3A	**5A**
1	*i*-Bu	H	**b**	70	0
2	*sec*-Bu	H	**c**	49	26
3	$HOCH_2CH_2$	H	**d**	56	0
4	Allyl	H	**e**	35	0
5	Benzyl	H	**f**	54	0
6	$-(CH_2)_4-$		**g**	48	0
7	$-CH_2CH_2OCH_2CH_2-$		**h**	62	3
8	Ph	H	**i**	41 (54[a])	0
9	4-BuC_6H_4	H	**j**	41	0
10	4-$MeOC_6H_4$	H	**k**	37	0
11	4-IC_6H_4	H	**l**	62[a]	0
12	4-$NO_2C_6H_4$	H	**m**	trace	0
13	Et	Et	**n**	0	27
14	Ph	Me	**o**	trace	0

[a]5 equiv. of amine was used.

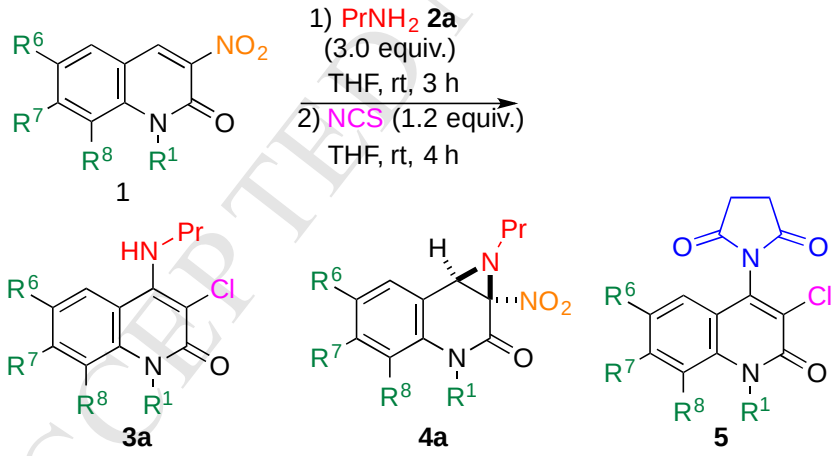


Scheme 3. The reaction invoving NBS and NIS

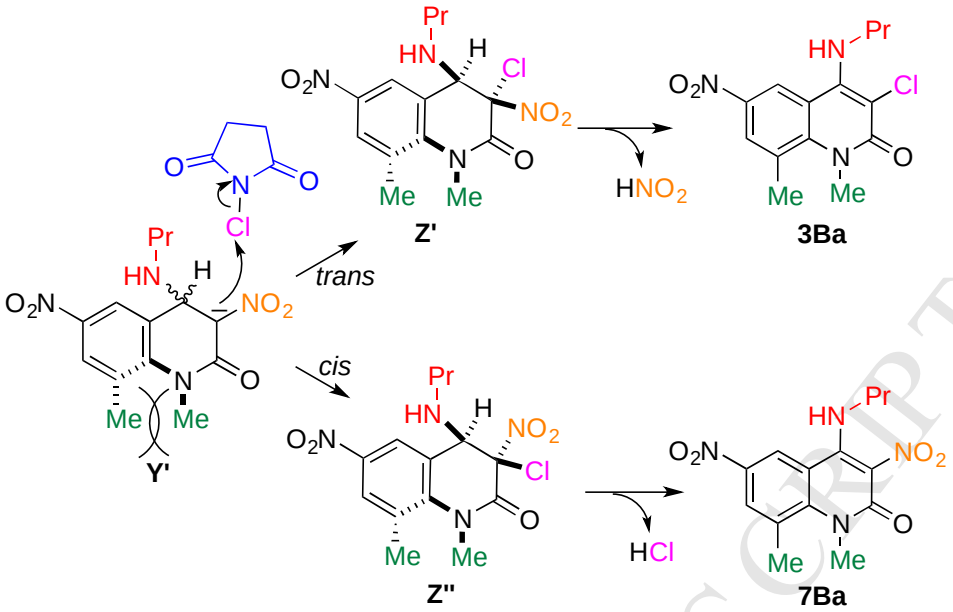
Next, 3-nitrated **MeQone**s with different substituents on the benzene ring were further investigated. As indicated in Table 3, a reduction in the number of nitro groups on the benzene ring had a negative impact on the formation of amino-chlorinated product **3**. When the 8-nitro group was replaced with a methyl group or hydrogen atom, **3Ba** and **3Ca** were furnished in 13% yield (entries 1 and 2). Interestingly, the reaction involving **1B** afforded 3-nitro-4-propylamino substituted product **7Ba**, an analogue of **7Aa**, in 21% yield. This might be due to the steric repulsion between the 1-methyl and the 8-methyl groups, leading to the torsional strain in the 2-quinolone ring;[12] accordingly, NCS could approach the carbanion **Y'** from the *cis* direction (Scheme 4). Consequently, the elimination of nitrous acid together with hydrogen chloride resulted in the formation of 3-chlorinated and 3-nitrated products (**3Ba** and **7Ba**) simultaneously (Scheme 4). Moreover, a nitro group with a bromo atom or hydrogen atom on the benzene ring markedly decreased the selectivity of the formation of **3** (entries 3–5). On the other hand, in these reactions, the

N-propylaziridine ring fused compounds **4Ba–4Fa** were obtained as the major products in moderate to good yields. These aziridines were stable while **4Aa** easily decomposed because **4Aa**, activated by the electron-withdrawing nitro group at the 8-position, was easily attacked by nucleophiles. Indeed, **4Fa** caused no change even though it was heated with propylamine at 60 °C for 12 hours. The reaction did not proceed in the case of 3-nitrated **MeQone** with two electron-donating groups on the benzene ring (entry 6). Additionally, the methyl group was not crucial for the aziridine formation, and **4Ha** was obtained in 61% yield in the reaction using **1H** (entry 7).

Table 3 Reactions of 3-nitrated **MeQone**s with **2a** and NCS



Entry	1					Yield (%)		
	R^1	R^6	R^7	R^8		**3a**	**4a**	**5**
1	Me	NO_2	H	Me	**B**	13	21	trace
2	Me	NO_2	H	H	**C**	13	49	7
3[a]	Me	Br	H	H	**D**	trace	68	0
4[a]	Me	H	Br	H	**E**	0	65	0
5[a]	Me	H	H	H	**F**	0	71	0
6[a]	Me	MeO	MeO	H	**G**	0	0	0
7[a]	H	H	H	H	**H**	0	61	0



Scheme 4. Steric repulsion between *peri*-substituents affording **7**

Based on the aforementioned results, the selective formation of **3** and **4** was attributed to the electronic effects of the substituents on the benzene ring. As depicted in Scheme 3, the intermediate **Z** likely played a very important role in this reaction, and the benzylic hydrogen atom in the 4-position determined the direct halo-amination or aziridination of the **MeQone** framework. Although **Z** was not detected during the reaction, we could indirectly characterize the electronic properties of the 4-H on nitroquinolone **1** and the resultant aziridine **4** by ^{1}H NMR analysis (Table 4).

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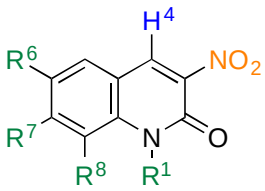
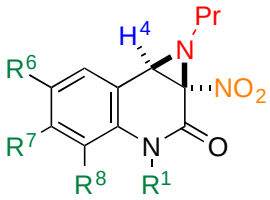
Table 4 Chemical shift of H^4 of **1** and **4a** in ^1H NMR spectra



1



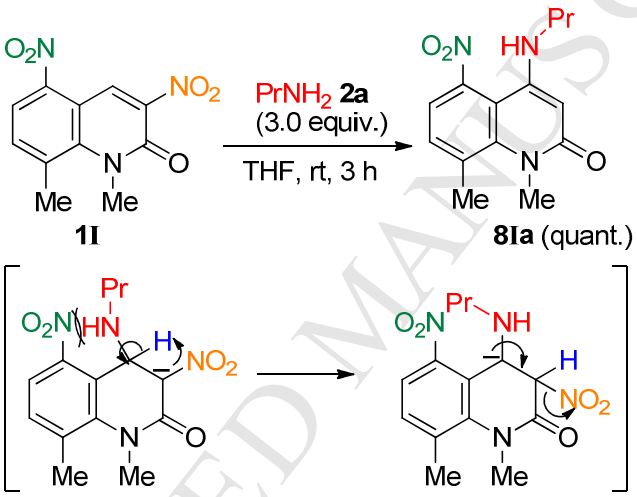
4a

R^1	R^6	R^7	R^8		Chemical shift of H^4 (ppm)	
					1	**4a**
Me	NO_2	H	NO_2	**A**	9.26	4.32
Me	NO_2	H	H	**C**	9.13	4.22
Me	H	H	H	**F**	8.90	4.12
Me	MeO	MeO	H	**G**	8.82	—
H	H	H	H	**H**	8.93	4.16

As described previously, more nitro groups led to lower field, indicating that the electron density at the 4-position decreased owing to the nitro group on the benzene ring through the electron-withdrawing effect, thus increasing the acidity of the benzylic proton (Table 4).[20] As a result, a nitrous acid is easily eliminated via an antiperiplanar elimination, leading to the formation of amino-halogenated product **3** (Scheme 2, Path 1). In contrast, the hydrogen atom becomes less acidic in the presence of weaker electron-withdrawing groups such as bromo atoms or in the absence of electron-withdrawing groups, thus resulting in an intramolecular substitution to form an aziridine ring (Scheme 2, Path 2). On the other hand, when electron-donating groups such as methoxy were introduced on the aromatic ring, the electron density was significantly increased, thus preventing the nucleophilic addition at the 4-position of the **MeQone** system.

Interestingly, when 1,8-dimethyl-3,5-dinitro-2-quinolone (**1I**) was employed

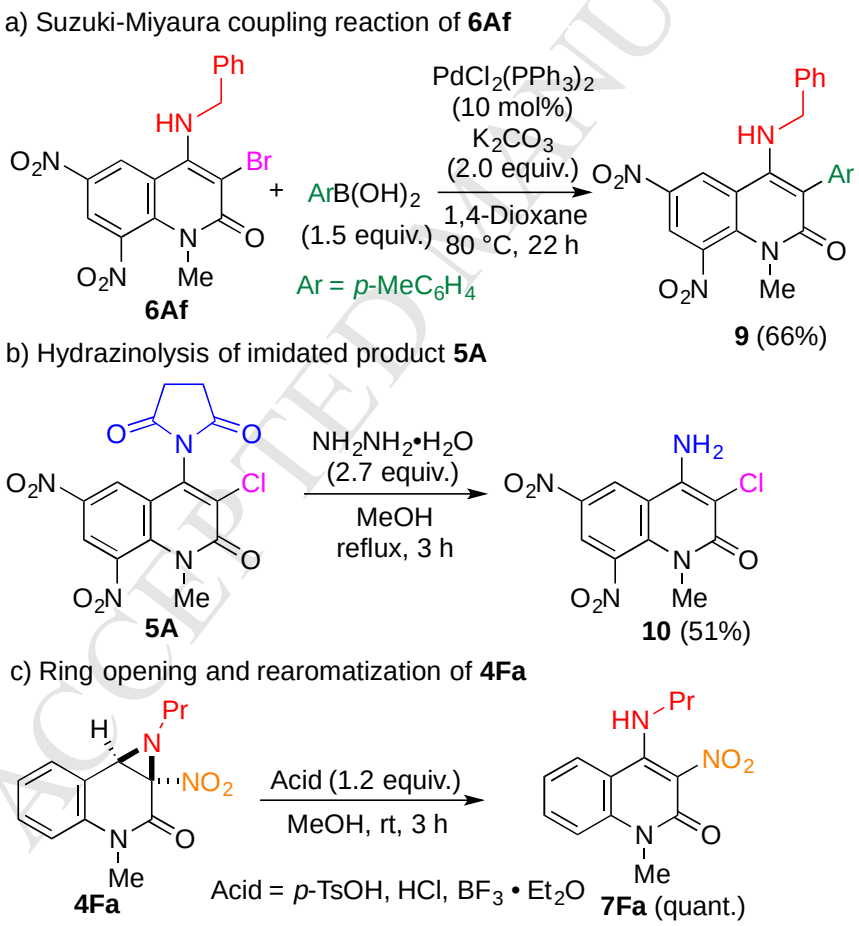
under the same conditions, *cine*-substituted product **8Ia** was obtained without **3Ia** or **4Ia**. In this reaction, addition of a propylamine **2a** afforded the Meisenheimer complex; however, it was not stable due to the steric repulsion of the *peri*-substituent (Scheme 5). Therefore, proton transfer to the 3-position likely releasing this repulsion and facilitating the elimination of the nitrite ion accompanied by aromatization to afford *cine*-substituted product **8Ia**.



Scheme 5. Reaction of 3,5-dinitroquinolone **1I** with propylamine **2a**

Finally, to illustrate the synthetic utility of the developed protocol, the conversion of the resulting products into other useful synthetic building blocks was investigated. Using the present method, benzylamino-brominated compound **6Af** was synthesized in 55% yield, and was subjected to Suzuki-Miyaura coupling,[21] as **MeQone**s with an benzylamino group and an aryl group in the vicinal positions are known *N*-methyl-D-aspartate receptor antagonists.[4] When **3Af** and **6Af** were reacted with 4-methylphenylboronic acid in the presence of a palladium catalyst, 3-arylated **9** was

successfully obtained in 27% and 66% yields, respectively, indicating that the higher reactivity of C-Br than C-Cl bond facilitated the transformation (Scheme 6, a). Furthermore, imido-chlorinated product **5A** is a masked form of an aminated quinolone, and the hydrazinolysis of the imidated ring introduced an unsubstituted amino group at the 4-position (Scheme 6, b). Compound **4Fa** underwent a ring-opening reaction followed by rearomatization in the presence of an acid, leading to vicinally amino-nitrated MeQone **7Fa** in quantitative yield (Scheme 6, c).



Scheme 6. Conversion of **6Af**, **5A** and **4Fa** into other useful building blocks

3. Conclusion

In conclusion, an operationally simple protocol for the direct 4-amination and 3-halogenation of **MeQone** was developed by treatment of 3-nitrated **MeQone**s with amines followed by addition of *N*-halosuccinimides under mild conditions. The vicinally functionalized **MeQone**s will serve as key synthetic intermediates for a versatile library of **MeQone**s, as demonstrated through the palladium-catalyzed arylation at the 3-position. Meanwhile, we found that aziridination occurred at the 3- and 4-positions of the **MeQone** framework through intramolecular substitution. The selectivity between vicinal amino-halogenation and aziridination was associated with the electronic properties of the substituents on the benzene ring. Moreover, imido-chlorination proceeded in some cases, leading to 4-imidated product, a masked form of the 4-aminoquinolone. Further investigations focused on the ring opening of the aziridine ring are currently in progress, and may facilitate the efficient and practical functionalization of **MeQone**s.

4. Experimental

4.1. General information

The melting points were determined on SRS-Optimelt Automated Melting Point System, and are uncorrected. All the reagents and solvents were commercially available and used as received. The ^{1}H NMR spectra were measured on a Bruker Ascend-400 at 400 MHz with tetramethylsilane 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 high-resolution mass spectra were measured on an AB SCIEX Triple TOF^{TM} 4600. X-ray diffraction was conducted on a Rigaku AFC7R diffractometer with graphite monochromatized Mo-K radiation. The IR spectra were recorded on a JASCO FT/IR-4200 spectrometer.

4.2. General procedure for the preparation of 3-nitrated quinolones

1-Methyl-2-quinolone was prepared from quinoline by methylation with Me_2SO_4 followed by oxidation with $K_3[Fe(CN)_6]$ under alkaline conditions. Nitration of 1-methyl-2-quinolone with fuming HNO_3 afforded trinitroquinolone **1A** in 86% total yield.[22] Other dinitroquinolones **1B**, **1C** and **1I** were also prepared in a similar way except for using milder reaction conditions in the nitration step.[12a]

Mononitrated quinolones **1D–H** were successfully synthesized using 2-nitrobenzaldehyde as the starting material via sequential reduction using Fe/HCl,[23] condensation with ethyl nitroacetate,[24] intramolecular cyclization,[24] and methylation with iodomethane.[25]

4.3. Reaction of trinitroquinolone 1A with propylamine 2a

To a solution of trinitroquinolone **1A** (100.0 mg, 0.34 mmol) in acetonitrile (2.5 mL), propylamine **2a** (102.5 mg, 1.70 mmol) was added at room temperature. When amine was added, yellowish solid immediately precipitated. After stirring for 3 h, the Meisenheimer complex **Y** was collected by filtration as a yellow solid (105.1 mg, 0.26 mmol, 75%);[26] Since this salt was not stable under ambient conditions to give **TNQ** and it was too hydroscopic, only ^{1}H NMR could be measured, and satisfactory analytical data were not obtained despite several attempts. In the ^{1}H NMR of **Y** using

DMSO-d_6 as the solvent, the signals were considerably broadened, and the decomposition of **Y** into **TNQ** and propylamine **2a** was observed in $CDCl_3$.

4.4. General procedure for amino-halogenation and aziridination of the 2-quinolone framework

To a solution of 3-nitrated quinolones **1** (100.0 mg) in THF (1.0 mL), amine **2** (3.0 equiv.) was added, and the resultant mixture was stirred at room temperature for 3 h. Then, a solution of *N*-halosuccinimide (1.2 equiv.) in THF (0.5 mL) was added, and the resultant mixture was stirred at room temperature for further 4 h. The solvent was evaporated to afford a reaction mixture as a yellow residue, from which amino-halogenated and aziridine fused quinolone, **3** and **4**, were isolated through SiO_2 column chromatography (eluted with CH_2Cl_2).

*4.4.1. 3-Chloro-1-methyl-6,8-dinitro-4-(propylamino)-2-quinolone (**3Aa**)*

Yellow solid (71.2 mg, 0.21 mmol, 62%); R_f = 0.44 (CH_2Cl_2); mp 131−133 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.07 (t, *J* = 7.2 Hz, 3H), 1.79 (tq, *J* = 7.2, 7.2 Hz, 2H), 3.50 (s, 3H), 3.55 (dt, *J* = 6.8, 7.2 Hz, 2H), 4.86 (br s, 1H), 8.73 (d, *J* = 2.4 Hz, 1H), 8.96 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.2 (CH_3), 24.8 (CH_2), 35.4 (CH_3), 51.0 (CH_2), 110.2 (C), 118.9 (C), 121.8 (CH), 124.0 (CH), 136.7 (C), 139.1 (C), 139.5 (C), 149.0 (C), 158.4 (C); IR: ν (cm^{-1}) 3372, 1645, 1537, 1531; HRMS (ESI) Calcd for $C_{13}H_{14}ClN_4O_5$ [$(M+H)^+$]: 341.0647, found 341.0647.

*4.4.2. 3-Chloro-1-methyl-4-(2-methylpropylamino)-6,8-dinitro-2-quinolone (**3Ab**)*

Yellow solid (83.5 mg, 0.24 mmol, 70%); R_f = 0.44 (CH_2Cl_2); mp 122−123 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.07 (d, *J* = 6.8 Hz, 6H), 1.97 (triple septet, *J* = 6.8, 6.8 Hz, 1H), 3.38 (dd, *J* = 6.8, 6.8 Hz, 2H), 3.50 (s, 3H), 4.89 (br s, 1H), 8.73 (d, *J* = 2.4

Hz, 1H), 8.95 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 20.0 (CH_3), 30.5 (CH), 35.4 (CH_3), 56.9 (CH_2), 110.1 (C), 118.8 (C), 121.8 (CH), 124.1 (CH), 136.7 (C), 139.1 (C), 139.4 (C), 149.2 (C), 158.3 (C); IR: ν (cm^{-1}) 3343, 1645, 1537, 1531; HRMS (ESI) Calcd for $C_{14}H_{16}ClN_4O_5$ [$(M+H)^+$]: 355.0804, found 355.0802.

*4.4.3. 4-(2-Butylamino)-3-chloro-1-methyl-6,8-dinitro-2-quinolone (**3Ac**)*

Yellow solid (58.2 mg, 0.16 mmol, 49%); R_f = 0.51 (CH_2Cl_2); mp 153−155 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.08 (t, *J* = 7.2 Hz, 3H), 1.34 (d, *J* = 6.4 Hz, 3H), 1.65-1.78 (m, 2H), 3.51 (s, 3H), 3.67−3.74 (m, 1H), 4.46 (d, *J* = 10.0 Hz, 1H), 8.72 (d, *J* = 2.4 Hz, 1H), 8.93 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 10.5 (CH_3), 21.9 (CH_3), 31.6 (CH_2), 35.4 (CH_3), 57.1 (CH), 112.7 (C), 119.4 (C), 121.8 (CH), 124.0 (CH), 136.5 (C), 139.2 (C), 139.7 (C), 148.9 (C), 158.4 (C); IR: ν (cm^{-1}) 3345, 1667, 1537, 1531; HRMS (ESI) Calcd for $C_{14}H_{16}ClN_4O_5$ [$(M+H)^+$]: 355.0804, found 355.0814.

*4.4.4. 3-Chloro-4-(2-hydroxyethylamino)-1-methyl-6,8-dinitro-2-quinolone (**3Ad**)*

Yellow solid (64.4 mg, 0.19 mmol, 56%); R_f = 0.35 (CH_2Cl_2/MeOH = 20:1); mp 125−128 °C; ^{1}H NMR (CD_3CN, 400 MHz) δ = 3.40 (s, 3H), 3.71−3.74 (m, 4H), 5.59 (br s, 1H), 8.76 (d, *J* = 2.4 Hz, 1H), 9.06 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (CD_3CN, 100 MHz) δ = 34.8 (CH_3), 49.5 (CH_2), 60.8 (CH_2), 107.9 (C), 119.3 (C), 121.8 (CH), 123.5 (CH), 136.7 (C), 138.6 (C), 139.5 (C), 148.6 (C), 158.6 (C); IR: ν (cm^{-1}) 3352, 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{12}H_{12}ClN_4O_6$ [$(M+H)^+$]: 343.0440, found 343.0427.

*4.4.5. 3-Chloro-1-methyl-6,8-dinitro-4-(2-propenylamino)-2-quinolone (**3Ae**)*

Yellow solid (39.9 mg, 0.12 mmol, 35%); R_f = 0.14 (CH_2Cl_2); mp 148−149 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 3.51 (s, 3H), 4.16 (dd, *J* = 5.3, 5.3 Hz, 2H), 4.96 (br s, 1H), 5.38 (dd, *J* = 0.8, 10.2 Hz, 1H), 5.49 (dd, *J* = 0.8, 17.0 Hz, 1H), 6.03 (ddt, *J* = 5.3, 10.2, 17.0 Hz, 1H), 8.73 (d, *J* = 2.4 Hz, 1H), 8.95 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 35.5 (CH_3), 51.0 (CH_2), 111.1 (C), 118.5 (CH_2), 118.7 (C), 121.9 (CH), 123.9 (CH), 133.7 (CH), 136.6 (C), 139.2 (C), 139.7 (C), 148.8 (C), 158.4 (C); IR: ν (cm^{-1}) 3360, 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{13}H_{12}ClN_4O_5$ [$(M+H)^+$]: 339.0491, found 339.0500.

*4.4.6. 4-(Benzylamino)-3-chloro-1-methyl-6,8-dinitro-2-quinolone (**3Af**)*

Yellow solid (70.0 mg, 0.18 mmol, 54%); R_f = 0.40 (CH_2Cl_2); mp 178−179 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 3.50 (s, 3H), 4.73 (d, *J* = 6.0 Hz, 2H), 5.21 (t, *J* = 6.0 Hz, 1H), 7.36−7.43 (m, 5H), 8.72 (d, *J* = 2.4 Hz, 1H), 8.99 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 35.5 (CH_3), 52.9 (CH_2), 111.1 (C), 118.8 (C), 121.9 (CH), 123.9 (CH), 127.4 (CH), 128.6 (CH), 129.3 (CH), 136.6 (C), 137.3 (C), 139.2 (C), 139.6 (C), 148.6 (C), 158.4 (C); IR: ν (cm^{-1}) 3360, 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{17}H_{14}ClN_4O_5$ [$(M+H)^+$]: 389.0647, found 389.0643.

*4.4.7. 3-Chloro-1-methyl-6,8-dinitro-4-piperidino-2-quinolone (**3Ag**)*

Yellow solid (59.8 mg, 0.16 mmol, 48%); R_f = 0.40 (CH_2Cl_2); mp 181−183 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.78−1.85 (m, 6H), 3.2−3.4 (m, 4H), 3.50 (s, 3H), 8.71 (d, *J* = 2.4 Hz, 1H), 9.07 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 23.9 (CH_2), 26.5 (CH_2), 35.8 (CH_3), 52.1 (CH_2), 121.5 (C), 121.8 (CH), 124.0 (C), 124.4

(CH), 136.4 (C), 139.1 (C), 140.4 (C), 152.1 (C), 160.0 (C); IR: ν (cm^{-1}) 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{15}H_{15}ClN_4NaO_5$ [$(M+Na)^+$]: 389.0623, found 389.0609.

*4.4.8. 3-Chloro-1-methyl-4-morpholino-6,8-dinitro-2-quinolone (**3Ah**)*

Yellow solid (76.9 mg, 0.21 mmol, 62%); R_f = 0.09 (CH_2Cl_2); mp 248−250 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 3.35−3.37 (m, 7H), 3.85 (t, *J* = 4.4 Hz, 4H), 8.94 (d, *J* = 2.4 Hz, 1H), 8.98 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ = 35.7 (CH_3), 50.1 (CH_2), 66.7 (CH_2), 120.7 (C), 122.4 (CH), 122.8 (C), 124.2 (CH), 136.2 (C), 138.7 (C), 140.2 (C), 150.7 (C), 159.4 (C); IR: ν (cm^{-1}) 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{14}H_{13}ClN_4NaO_6$ [$(M+Na)^+$]: 391.0416, found 391.0422.

*4.4.9. 3-Chloro-1-methyl-6,8-dinitro-4-phenylamino-2-quinolone (**3Ai**)*

Yellow solid (68.5 mg, 0.18 mmol, 54%); R_f = 0.24 (CH_2Cl_2); mp 199−201 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 3.56 (s, 3H), 6.72 (br s, 1H), 6.99 (d, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.35 (dd, *J* = 7.6, 7.6 Hz, 2H), 8.58 (d, *J* = 2.4 Hz, 1H), 8.63 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 35.7 (CH_3), 114.9 (C), 118.6 (C), 121.6 (CH), 121.7 (CH), 125.1 (CH), 125.5 (CH), 130.1 (CH), 136.5 (C), 139.3 (C), 139.6 (C), 141.1 (C), 144.1 (C), 158.6 (C); IR: ν (cm^{-1}) 3341, 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{16}H_{11}ClN_4NaO_5$ [$(M+Na)^+$]: 397.0310, found 397.0314.

*4.4.10. 4-(4-Butylphenylamino)-3-chloro-1-methyl-6,8-dinitro-2-quinolone (**3Aj**)*

Yellow solid (58.9 mg, 0.14 mmol, 41%); R_f = 0.50 (CH_2Cl_2); mp 109−110 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 0.92 (t, *J* = 7.6 Hz, 3H), 1.33 (tq, *J* = 7.6, 7.6 Hz, 2H), 1.58 (tt, *J* = 7.6, 7.6 Hz, 2H), 2.60 (t, *J* = 7.6 Hz, 3H), 3.55 (s, 3H), 6.72 (s, 1H), 6.93

(d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 8.57 (d, *J* = 2.8 Hz, 1H), 8.61 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 13.9 (CH_3), 22.1 (CH_2), 33.4 (CH_2), 35.0 (CH_2), 35.7 (CH_3), 113.6 (C), 118.4 (C), 121.6 (CH), 122.3 (CH), 125.3 (CH), 130.1 (CH), 136.6 (C), 138.6 (C), 139.2 (C), 139.4 (C), 140.9 (C), 144.5 (C), 158.6 (C); IR: ν (cm^{-1}) 3352, 1667, 1537, 1531; HRMS (ESI) Calcd for $C_{20}H_{20}ClN_4O_5$ [$(M+H)^+$]: 431.1117, found 431.1115.

*4.4.11. 3-Chloro-4-(4-methoxyphenylamino)-1-methyl-6,8-dinitro-2-quinolone (**3Ak**)*

Yellow solid (50.7 mg, 0.13 mmol, 37%); R_f = 0.36 (CH_2Cl_2); mp 100−102 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 3.54 (s, 3H), 3.81 (s, 3H), 6.69 (s, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 8.59 (d, *J* = 2.8 Hz, 1H), 8.61 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 35.7 (CH_3), 55.6 (CH_3), 112.7 (C), 115.4 (CH), 118.3 (C), 121.6 (CH), 124.5 (CH), 125.2 (CH), 133.8 (C), 136.7 (C), 139.2 (C), 139.3 (C), 144.8 (C), 158.0 (C), 158.5 (C); IR: ν (cm^{-1}) 3354, 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{17}H_{14}ClN_4O_6$ [$(M+H)^+$]: 405.0596, found 405.0604.

*4.4.12. 3-Chloro-4-(4-iodophenylamino)-1-methyl-6,8-dinitro-2-quinolone (**3Al**)*

Yellow solid (104.7 mg, 0.21 mmol, 62%); R_f = 0.39 (CH_2Cl_2); mp 135−137°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 3.57 (s, 3H), 6.56 (s, 1H), 6.71 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 8.59 (d, *J* = 2.4 Hz, 1H), 8.66 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 35.8 (CH_3), 88.4 (C), 116.7 (C), 118.8 (C), 121.9 (CH), 122.6 (CH), 124.7 (CH), 136.3 (C), 139.0 (CH), 139.4 (C), 139.9 (C), 141.1 (C), 143.4 (C), 158.5 (C); IR: ν (cm^{-1}) 3306, 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{16}H_{10}ClIN_4NaO_5$ [$(M+Na)^+$]: 522.9277, found 522.9259.

*4.4.13. 3-Chloro-1,8-dimethyl-6-nitro-4-(propylamino)-2-quinolone (**3Ba**)*

Yellow solid (15.1 mg, 0.05 mmol, 13%); R_f = 0.27 (CH_2Cl_2); mp 156−158 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.04 (t, *J* = 7.2 Hz, 3H), 1.74 (tq, *J* = 7.2, 7.2 Hz, 2H), 2.76 (s, 3H), 3.41 (t, *J* = 7.2 Hz, 2H), 3.81 (s, 3H), 4.67 (br s, 1H), 8.18 (d, *J* = 2.4 Hz, 1H), 8.62 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.2 (CH_3), 24.1 (CH_3), 24.8 (CH_2), 38.0 (CH_3), 50.9 (CH_2), 109.3 (C), 117.5 (C), 119.4 (CH), 127.2 (C), 128.5 (CH), 141.4 (C), 144.4 (C), 150.1 (C), 160.5 (C); IR: ν (cm^{-1}) 3372, 1651, 1599, 1574; HRMS (ESI) Calcd for $C_{14}H_{16}ClN_3NaO_3$ [$(M+Na)^+$]: 332.0772, found 332.0768.

*4.4.14. 3-Chloro-1-methyl-6-nitro-4-(propylamino)-2-quinolone (***3Ca***)*

Yellow solid (15.3 mg, 0.05 mmol, 13%); R_f = 0.18 (CH_2Cl_2); mp 217−219 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.06 (t, *J* = 7.2 Hz, 3H), 1.76 (tq, *J* = 7.2, 7.2 Hz, 2H), 3.58 (dt, *J* = 6.0, 7.2 Hz, 2H), 3.79 (s, 3H), 4.76 (br s, 1H), 7.46 (d, *J* = 9.6 Hz, 1H), 8.39 (dd, *J* = 2.4, 9.6 Hz, 1H), 8.84 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.2 (CH_3), 24.8 (CH_2), 31.0 (CH_3), 50.8 (CH_2), 109.3 (C), 115.3 (C), 115.4 (CH), 121.6 (CH), 125.0 (CH), 141.5 (C), 142.5 (C), 149.4 (C), 158.3 (C); IR: ν (cm^{-1}) 3337, 1643, 1557, 1550; HRMS (ESI) Calcd for $C_{13}H_{15}ClN_3O_3$ [$(M+H)^+$]: 296.0797 found 296.0806.

*4.4.15. 1a,2,3,7b-Tetrahydro-3-methyl-1a,4,6-trinitro-2-oxo-1-propyl-1H-azirino [2,3-c]quinoline (**4Aa**)*

Yellow oil (17.6 mg, 0.05 mmol, 15%); R_f = 0.67 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 0.93 (t, *J* = 7.2 Hz, 3H), 1.56 (ddq, *J* = 7.2, 7.2, 7.2 Hz, 2H), 2.11 (dt, *J* =

6.8, 7.2 Hz, 1H), 2.33 (dt, *J* = 6.8, 7.2 Hz, 1H), 3.39 (s, 3H), 4.32 (s, 1H), 8.58 (d, *J* = 2.8 Hz, 1H), 8.68 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ = 11.2 (CH_3), 21.9 (CH_2), 35.4 (CH_3), 46.8 (CH), 47.4 (CH_2), 77.7 (C), 119.8 (C), 122.7 (CH), 129.1 (CH), 136.9 (C), 139.2 (C), 141.8 (C), 160.1 (C); IR: ν (cm^{-1}) 1694, 1543, 1537; HRMS (ESI) Calcd for $C_{13}H_{12}N_5O_7$ [$(M-H)^-$]: 350.0742, found 350.0759.

*4.4.16. 1a,2,3,7b-Tetrahydro-3,4-dimethyl-1a,6-dinitro-2-oxo-1-propyl-1H-azirino[2,3-c]quinoline (**4Ba**)*

Pale yellow solid (24.4 mg, 0.08 mmol, 21%); R_f = 0.61 (CH_2Cl_2); mp 159−160 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 0.84 (t, *J* = 7.2 Hz, 3H), 1.43 (ddq, *J* = 7.2, 7.2, 7.2 Hz, 2H), 1.95 (dt, *J* = 5.6, 7.2 Hz, 1H), 2.31 (dt, *J* = 5.6, 7.2 Hz, 1H), 2.67 (s, 3H), 3.58 (s, 3H), 4.77 (s, 1H), 8.26 (d, *J* = 2.8 Hz, 1H), 8.42 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ = 11.3 (CH_3), 22.0 (CH_2), 22.7 (CH_3), 37.3 (CH_3), 47.2 (CH_2), 47.3 (CH), 77.9 (C), 117.4 (C), 124.0 (CH), 129.1 (C), 129.5 (CH), 142.8 (C), 144.2 (C), 161.1 (C); IR: ν (cm^{-1}) 1682, 1562, 1524; HRMS (ESI) Calcd for $C_{14}H_{16}N_4NaO_5$ [$(M+Na)^+$]: 343.1013, found 343.1014.

*4.4.17. 1a,2,3,7b-Tetrahydro-3-methyl-1a,6-dinitro-2-oxo-1-propyl-1H-azirino [2,3-c]quinoline (**4Ca**)*

Pale yellow solid (60.2 mg, 0.20 mmol, 49%); R_f = 0.60 (CH_2Cl_2); mp 144−145 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 0.90 (t, *J* = 7.2 Hz, 3H), 1.55 (ddq, *J* = 6.8, 6.8, 7.2 Hz, 2H), 2.02 (dt, *J* = 5.2, 6.8 Hz, 1H), 2.30 (dt, *J* = 5.2, 6.8 Hz, 1H), 3.62 (s, 3H), 4.22 (s, 1H), 7.33 (d, *J* = 9.2 Hz, 1H), 8.39 (dd, *J* = 2.4, 9.2 Hz, 1H), 8.43 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ = 11.3 (CH_3), 21.9 (CH_2), 30.4 (CH_3),

46.5 (CH), 46.9 (CH_2), 78.2 (C), 115.4 (C), 117.0 (CH), 125.8 (CH), 126.3 (CH), 142.7 (C), 142.8 (C), 158.7 (C); IR: ν (cm^{-1}) 1682, 1562, 1526; HRMS (ESI) Calcd for $C_{13}H_{14}N_4NaO_5$ [$(M+Na)^+$]: 329.0856, found 329.0855.

*4.4.18. 6-Bromo-1a,2,3,7b-tetrahydro-3-methyl-1a-nitro-2-oxo-1-propyl-1H-azirino[2,3-c]quinoline (**4Da**)*

White solid (81.2 mg, 0.24 mmol, 68%); R_f = 0.69 (CH_2Cl_2); mp 171−172 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 0.89 (t, *J* = 7.2 Hz, 3H), 1.54 (ddq, *J* = 7.2, 7.2, 7.2 Hz, 2H), 2.00 (dt, *J* = 5.2, 7.2 Hz, 1H), 2.28 (dt, *J* = 5.2, 7.2 Hz, 1H), 3.53 (s, 3H), 4.05 (s, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 7.60−7.63 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.5 (CH_3), 22.4 (CH_2), 29.9 (CH_3), 47.4 (CH), 47.7 (CH_2), 77.8 (C), 116.5 (CH), 116.6 (C), 116.9 (C), 133.3 (CH), 133.6 (CH), 137.3 (C), 158.4 (C); IR: ν (cm^{-1}) 1667, 1562, 1557; HRMS (ESI) Calcd for $C_{13}H_{13}BrN_3O_3$ [$(M-H)^-$]: 338.0146, found 338.0160.

*4.4.19. 5-Bromo-1a,2,3,7b-tetrahydro-3-methyl-1a-nitro-2-oxo-1-propyl-1H-azirino[2,3-c]quinoline (**4Ea**)*

Pale yellow solid (77.6 mg, 0.23 mmol, 65%); R_f = 0.73 (CH_2Cl_2); mp 120−122 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 0.88 (t, *J* = 7.2 Hz, 3H), 1.52 (ddq, *J* = 7.2, 7.2, 7.2 Hz, 2H), 1.96 (dt, *J* = 5.2, 7.2 Hz, 1H), 2.30 (dt, *J* = 5.2, 7.2 Hz, 1H), 3.53 (s, 3H), 4.08 (s, 1H), 7.32−7.37 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.5 (CH_3), 22.4 (CH_2), 29.9 (CH_3), 47.6 (CH_2), 47.7 (CH), 77.8 (C), 113.5 (C), 118.1 (CH), 124.6 (C), 127.0 (CH), 132.0 (CH), 139.3 (C), 158.6 (C); IR: ν (cm^{-1}) 1678, 1597, 1562; HRMS (ESI) Calcd for $C_{13}H_{13}BrN_3O_3$ [$(M-H)^-$]: 338.0146, found 338.0159.

*4.4.20. 1a,2,3,7b-Tetrahydro-3-methyl-1a-nitro-2-oxo-1-propyl-1H-azirino[2,3-c] quinoline (**4Fa**)*

Pale yellow solid (89.8 mg, 0.34 mmol, 71%); R_f = 0.55 (CH_2Cl_2); mp 98−100 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 0.86 (t, *J* = 7.2 Hz, 3H), 1.52 (ddq, *J* = 7.2, 7.2, 7.2 Hz, 2H), 1.95 (dt, *J* = 5.2, 7.2 Hz, 1H), 2.31 (dt, *J* = 5.2, 7.2 Hz, 1H), 3.55 (s, 3H), 4.12 (s, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 1H), 7.50-7.54 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.5 (CH_3), 22.4 (CH_2), 29.8 (CH_3), 47.5 (CH_2), 48.2 (CH), 78.2 (C), 114.5 (C), 114.8 (CH), 124.1 (CH), 130.7 (CH), 130.8 (CH), 138.1 (C), 158.7 (C); IR: ν (cm^{-1}) 1668, 1562, 1557; HRMS (ESI) Calcd for $C_{13}H_{15}N_3NaO_3$ [$(M+Na)^+$]: 284.1006, found 284.1012.

*4.4.21. 1a,2,3,7b-Tetrahydro-1a-nitro-2-oxo-1-propyl-1H-azirino[2,3-c]quinoline (**4Ha**)*

Yellow solid (78.1 mg, 0.32 mmol, 61%); R_f = 0.18 (CH_2Cl_2); mp 122−123 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 0.89 (t, *J* = 7.2 Hz, 3H), 1.56 (ddq, *J* = 7.2, 7.2, 7.2 Hz, 2H), 2.08 (dt, *J* = 5.2, 7.2 Hz, 1H), 2.44 (dt, *J* = 5.2, 7.2 Hz, 1H), 4.16 (s, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 7.22 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.44 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.5 (CH_3), 22.4 (CH_2), 47.6 (CH_2), 49.1 (CH), 77.9 (C), 113.6 (C), 116.3 (CH), 124.7 (CH), 130.2 (CH), 130.7 (CH), 135.4 (C), 160.3 (C); IR: ν (cm^{-1}) 1681, 1562, 1557; HRMS (ESI) Calcd for $C_{12}H_{13}N_3NaO_3$ [$(M+Na)^+$]: 270.0849, found 270.0843.

*4.4.22. 3-Chloro-1-methyl-6,8-dinitro-4-(2,5-dioxopyrrolidino)-2-quinolone (**5A**)*

Yellow solid (61.2 mg, 0.16 mmol, 48%). R_f = 0.10 (CH_2Cl_2); mp 294−297 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 3.05−3.23 (m, 4H), 3.52 (s, 3H), 8.98 (d, *J* = 2.4 Hz, 1H), 9.04 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ = 29.6 (CH_2), 36.4 (CH_3), 120.2 (C), 123.4 (CH), 124.1 (CH), 128.9 (C), 135.5 (C), 137.3 (C), 139.0 (C), 141.3 (C), 157.8 (C), 175.3 (C); IR: ν (cm^{-1}) 1682, 1537, 1531; HRMS (ESI) Calcd for $C_{14}H_{10}ClN_4O_7$ [$(M+H)^+$]: 381.0233, found 381.0238.

*4.4.23. 3-Chloro-1-methyl-6,8-dinitro-4-(2,5-dioxopyrrolidino)-2-quinolone (**5C**)*

Yellow powder (8.9 mg, 0.03 mmol, 7%); R_f = 0.48 (CH_2Cl_2/MeOH = 20/1); mp 283−285 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 2.98−3.19 (m, 4H), 3.83 (s, 3H), 7.92 (d, *J* = 9.2 Hz, 1H), 8.50 (dd, *J* = 2.8, 9.2 Hz, 1H), 8.64 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ = 29.5 (CH_2), 31.8 (CH_3), 116.8 (C), 117.4 (CH), 120.7 (CH), 126.2 (CH), 127.7 (C), 137.4 (C), 141.7 (C), 142.7 (C), 157.0 (C), 175.4 (C); IR: ν (cm-1) 1651, 1537, 1520; HRMS (ESI) Calcd for $C_{14}H_{11}ClN_3O_5$ [$(M+H)^+$]: 336.0382, found 336.0387.

*4.4.24. 3-Bromo-1-methyl-6,8-dinitro-4-(propylamino)-2-quinolone (**6Aa**)*

Yellow solid (81.8 mg, 0.21 mmol, 63%); R_f = 0.35 (ethyl acetate/hexane = 1/2); mp 213-215 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.06 (t, *J* = 7.2 Hz, 3H), 1.66 (tq, *J* = 7.2, 7.2 Hz, 2H), 3.49−3.53 (m, 5H), 4.89 (br s, 1H), 8.73 (d, *J* = 2.4 Hz, 1H), 8.96 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ = 11.2 (CH_3), 24.8 (CH_2), 35.7 (CH_3), 51.5 (CH_2), 103.0 (C), 118.6 (C), 122.0 (CH), 124.3 (CH), 137.2 (C), 139.1

(C), 139.4 (C), 151.3 (C), 158.5 (C); IR: ν (cm^{-1}) 3374, 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{13}H_{12}BrN_4O_5$ [$(M-H)^-$]: 382.9997, found 383.0007.

*4.4.25. 4-(Benzylamino)-3-bromo-1-methyl-6,8-dinitro-2-quinolone (**6Af**)*

Yellow solid (79.8 mg, 0.19 mmol, 55%); R_f = 0.45 (CH_2Cl_2); mp 134−136 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 3.51 (s, 3H), 4.69 (d, *J* = 6.4 Hz, 2H), 5.26 (t, *J* = 6.4 Hz, 1H), 7.34−7.44 (m, 5H), 8.73 (d, *J* = 2.4 Hz, 1H), 8.99 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 35.8 (CH_3), 53.2 (CH_2), 104.1 (C), 118.6 (C), 122.0 (CH), 124.2 (CH), 127.4 (CH), 128.6 (CH), 129.3 (CH), 137.1 (C), 137.2 (C), 139.1 (C), 139.5 (C), 150.9 (C), 158.5 (C); IR: ν (cm^{-1}) 3352, 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{17}H_{14}BrN_4O_5$ [$(M+H)^+$]: 433.0142, found 433.0160.

*4.4.26. 1-Methyl-3,6,8-trinitro-4-(propylamino)-2-quinolone (**7Aa**)*

Yellow solid (73.0 mg, 0.21 mmol, 62%); R_f = 0.10 (CH_2Cl_2); mp 184−187 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.07 (t, *J* = 7.2 Hz, 3H), 1.85 (tq, *J* = 7.2, 7.2 Hz, 2H), 3.43 (s, 3H), 3.56 (dt, *J* = 6.8, 7.2 Hz, 2H), 7.69 (br s, 1H), 8.81 (d, *J* = 2.4 Hz, 1H), 9.04 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.1 (CH_3), 23.8 (CH_2), 35.0 (CH_3), 48.9 (CH_2), 117.9 (C), 122.7 (C), 124.0 (CH), 124.5 (CH), 138.4 (C), 139.3 (C), 139.6 (C), 146.2 (C), 156.2 (C); IR: ν (cm^{-1}) 3343, 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{13}H_{14}N_5O_7$ [$(M+H)^+$]: 352.0888, found 352.0904.

*4.4.27. 1,8-Dimethyl-3,6-dinitro-4-(propylamino)-2-quinolone (**7Ba**)*

Yellow solid (25.2 mg, 0.08 mmol, 21%); R_f = 0.17 (CH_2Cl_2); mp 208−210 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.07 (t, *J* = 7.2 Hz, 3H), 1.84 (tq, *J* = 7.2, 7.2 Hz, 2H), 2.72 (s, 3H), 3.61 (dt, *J* = 5.2, 7.2 Hz, 2H), 3.70 (s, 3H), 8.06 (br s, 1H), 8.27 (d, *J* =

2.4 Hz, 1H), 8.67 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.2 (CH_3), 23.7 (CH_3), 23.9 (CH_2), 37.6 (CH_3), 49.2 (CH_2), 116.3 (C), 119.8 (CH), 121.9 (C), 128.4 (C), 130.7 (CH), 141.6 (C), 145.9 (C), 149.0 (C), 158.1 (C); IR: ν (cm^{-1}) 3331, 1643, 1524, 1518; HRMS (ESI) Calcd for $C_{14}H_{16}N_4NaO_5$ [$(M+Na)^+$]: 343.1013, found 343.1022.

4.5. *cine*-Substitution of 1,8-dimethyl-3,5-dinitro-2-quinolone (1I)

To a solution of **1I** (70.0 mg, 0.27 mmol) in THF (1.0 mL) was added propylamine **2a** (47.2 mg, 0.80 mmol), and the resultant mixture was stirred at room temperature for 3 h. Then, the solvent was evaporated to afford a reaction mixture **8Ia** as a yellow solid (75.5 mg, 0.27 mmol, quant.); R_f = 0.27 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 0.97 (t, *J* = 7.2 Hz, 3H), 1.67 (tq, *J* = 7.2, 7.2 Hz, 2H), 2.59 (s, 3H), 3.41 (dt, *J* = 5.6, 7.2 Hz, 2H), 3.77 (s, 3H), 6.60 (d, *J* = 9.6 Hz, 1H), 7.82 (br s, 1H), 7.96 (d, *J* = 9.6 Hz, 1H), 8.04 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.3 (CH_3), 23.2 (CH_3), 24.9 (CH_2), 36.9 (CH_3), 54.0 (CH_2), 113.7 (C), 117.0 (C), 117.9 (CH), 131.0 (CH), 131.1 (C), 136.6 (CH), 146.0 (C), 149.0 (C), 163.9 (C); IR: ν (cm^{-1}) 3300, 1651, 1580, 1574; HRMS (ESI) Calcd for $C_{14}H_{18}N_3O_3$ [$(M+H)^+$]: 276.1343, found 276.1339.

4.6. Suzuki-Miyaura coupling reaction of benzylamino-brominated 6Af

To a solution of **6Af** (63.0 mg, 0.15 mmol) in 1,4-dioxane (2.0 mL), were added *p*-$MeC_6H_4B(OH)_2$ (29.7 mg, 0.22 mmol), $Pd(PPh_3)_2Cl_2$ (10.2 mg, 0.01 mmol) and K_2CO_3 (40.3 mg, 0.29 mmol). Then, the resultant mixture was heated at 80 °C for 22 h. After the mixture was filtrated, the solvent was evaporated to afford a reaction mixture as a yellow residue, from which arylated product **9** was isolated by SiO_2 column chromatography (eluted with ethyl acetate/hexane = 1/5) as a yellow solid

(42.4 mg, 0.10 mmol, 66%); R_f = 0.29 (ethyl acetate/hexane = 1/5); mp 143−145 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 2.38 (s, 3H), 3.46 (s, 3H), 4.22 (d, *J* = 6.4 Hz, 2H), 4.57 (t, *J* = 6.4 Hz, 1H), 7.10−7.13 (m, 4H), 7.23 (d, *J* = 7.6 Hz, 2H), 7.31−7.32 (m, 3H), 8.72 (d, *J* = 2.4 Hz, 1H), 8.92 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 20.3 (CH_3), 33.8 (CH_3), 51.9 (CH_2), 116.8 (C), 119.4 (C), 120.7 (CH), 122.4 (CH), 126.5 (CH), 127.1 (CH), 128.0 (CH), 128.5 (C), 128.7 (CH), 129.1 (CH), 136.5 (C), 137.0 (C), 137.5 (C), 137.8 (C), 138.3 (C), 147.8 (C), 161.4 (C); IR: ν (cm^{-1}) 3352, 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{24}H_{21}N_4O_5$ [$(M+H)^+$]: 445.1507, found 445.1505.

4.7. Hydrazinolysis of 5A

To a solution of **5A** (50.0 mg, 0.13 mmol) in MeOH (2.0 mL), NH_2NH_2•H_2O (17.8 mg, 0.36 mmol) was added, and the resultant mixture was heated at 70 °C for 3 h. Then, the solvent was evaporated to afford a reaction mixture as a yellow solid. After the solid was washed by water (5 mL × 1), 4-aminoquinolone **10** was isolated through filtration as a yellow solid (20.0 mg, 0.07 mmol, 51%); R_f = 0.36 (CH_2Cl_2/MeOH = 10/1); mp > 300 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 3.29 (s, 3H), 7.54 (br s, 2H), 8.89 (d, *J* = 2.0 Hz, 1H), 9.35 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (DMSO-d_6, 400 MHz) δ = 35.1 (CH_3), 99.8 (C), 117.2 (C), 122.5 (CH), 123.2 (CH), 136.5 (C), 138.5 (C), 139.7 (C), 147.1 (C), 158.2 (C); IR: ν (cm^{-1}) 1651, 1537, 1531; HRMS (ESI) Calcd for $C_{10}H_8ClN_4O_5$ [$(M+H)^+$]: 299.0178, found 299.0172.

4.8. Acid-catalyzed ring-opening of aziridine ring

To a solution of **4Fa** (38.5 mg, 0.15 mmol) in MeOH (0.5 mL), acid (*p*-TsOH•H_2O or 1 N HCl aq. or BF_3•Et_2O, 0.18 mmol, 1.2 equiv.) was added, and

the resultant mixture was stirred at room temperature for 3 h. Then, the solvent was evaporated to afford a mixture as a yellow residue, from which vicinally amino-nitrated product **7Fa** was isolated by SiO_2 column chromatography (eluted with CH_2Cl_2) as a yellow solid (38.5 mg, 0.15 mmol, quant.); R_f = 0.60 (CH_2Cl_2); mp 121−122 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.00 (t, *J* = 7.2 Hz, 3H), 1.69 (tq, *J* = 7.2, 7.2 Hz, 2H), 3.11 (dt, *J* = 5.6, 7.2 Hz, 2H), 3.80 (s, 3H), 6.09 (br s, 1H), 7.27−7.30 (m, 1H), 7.33−7.40 (m, 2H), 7.48 (dd, *J* = 0.8, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 11.3 (CH_3), 23.2 (CH_2), 31.1 (CH_3), 45.0 (CH_2), 114.3 (CH), 115.5 (C), 120.3 (CH), 124.1 (CH), 126.4 (CH), 128.2 (C), 129.6 (C), 131.2 (C), 158.9 (C); IR: ν (cm^{-1}) 3312, 1651, 1574, 1557; HRMS (ESI) Calcd for $C_{13}H_{16}N_3O_3$ [$(M+H)^+$]: 262.1186, found 262.1195.

Supplementary data

Control experiments; characterization data including copies of ^{1}H and ^{13}C NMR spectra; cif files of X-ray single crystal structure. This material is available free of charge via the Internet at http://dx.doi.org.

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