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

Motoki Asahara, Moriaki Nagamatsu, Yasuo Tohda, Nagatoshi Nishiwaki* and Masahiro Ariga*

Department of Chemistry, Osaka Kyoiku University, Asahigaoka 4-698-1, Kashiwara, Osaka 582-8582, Japan

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1-Methyl-3,6,8-trinitro-2-quinolone (**1**) behaved as the dienophile in Diels-Alder reactions with dienes. When cyclopentadiene was used, cycloadduct **4** was obtained, which was then aromatized on treatment with triethylamine. In the reaction of **1** with hydrazone of 2-butenal, phenanthridine derivative **7** was produced.

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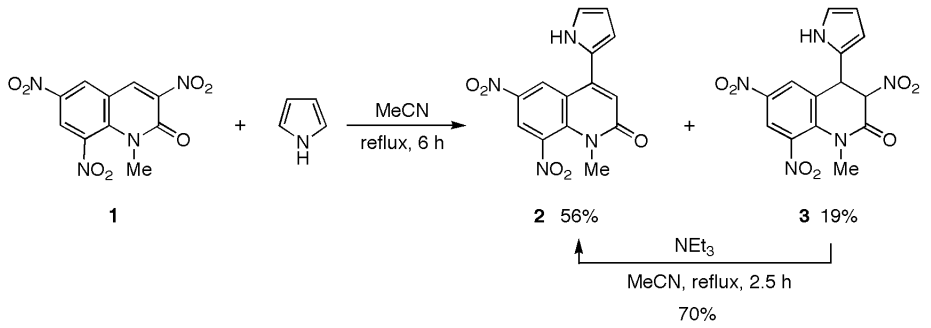
The 1-methyl-2-quinolone (MeQone) skeleton is often seen as the partial structure of quinoline alkaloids isolated from the Rutaceae family, and their structural determination and total syntheses are still active areas of research [1-5]. From the viewpoint of biological and pharmacological interests, syntheses of unnatural compounds possessing the MeQone skeleton are also important projects [6-10], however, direct functionalization of MeQone is not always easy because of its low reactivity. Recently, Fujita and coworkers reported the Diels-Alder reactions of quinolone derivatives having an electron-withdrawing group at the 3- or 4-positions [11-13]. In these reactions, relatively severe reaction conditions are required.

In our previous study, 1-methyl-3,6,8-trinitro-2-quinolone (**1**) has been shown to be highly reactive because of steric repulsion between the 1-methyl and the 8-nitro groups [14]. Namely, the pyridone ring of **1** shows rather nitroalkene property than aromaticity [15], and it is actually reactive compared with other quinolone derivatives. Upon treatment of quinolone **1** with tertiary amine, dimerization proceeds at room temperature and denitration occurs at elevated temperature [16]. When quinolone **1** is reacted with 1,3-dicarbonyl compounds in the presence of triethylamine, substitution at the 4-position accompanied by elimination of the 3-nitro group proceeds, which is well known as *cine*-substitution [17]. On the basis of these experimental results, we considered it is possible to use trinitroquinolone **1** as the dienophile for cycloaddition with dienes.

Reactions of trinitroquinolone **1** with π-electron sufficient heterocyles were conducted. To a solution of quinolone **1** (1 mmol) in acetonitrile (10 mL), was added a solution of pyrrole (10 mmol) in acetonitrile (2 mL), 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 **2** in 56% yield. After concentration of the filtrate, the residue was treated with column chromatography on silica gel to isolate product **3** in 19% yield (eluted with toluene). In the ^{1}H nmr of **2**, a singlet signal appeared at δ 6.79, and signals assigned for the pyrrole ring were also observed in the aromatic region. These data showed compound **2** was *cine*-substituted product, and product **3** was determined as dihydroquinolone by spectral and analytical data. Isolated **3** was readily aromatized on treatment with triethylamine to give **2** in 70% yield (Scheme 1). When furan was used instead of pyrrole, no reaction proceeded under the same conditions.

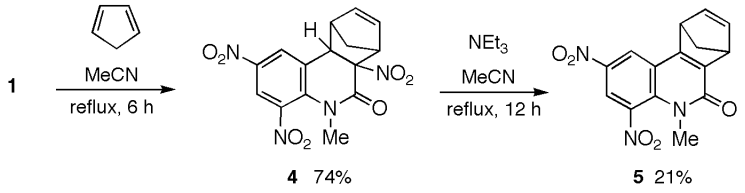
Scheme 1



On the other hand, cycloaddition proceeded to afford tetracyclic compounds **4** in 74% yield when cyclopentadiene was employed as the dienophile (Scheme 2). In the ^{1}H-^{1}H COSY spectrum of **4**, the presence of coupling between H_a and H_b was observed, and other correlations were satisfactorily confirmed. Coupling constants measurable in the ^{1}H nmr were shown in Figure 1. Since cycloadduct **4** had dihydroquinolone structure, nitrous acid

was easily eliminated similar to the case of **3** giving aromatized product **5** in 21% yield upon treatment with triethylamine in refluxing acetonitrile.

Scheme 2



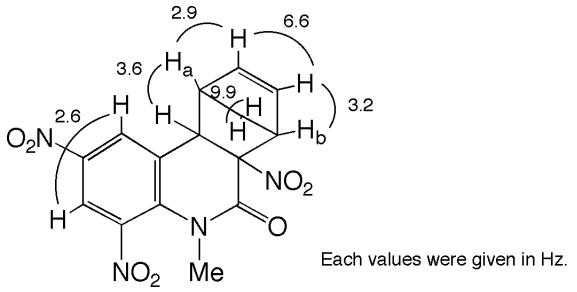
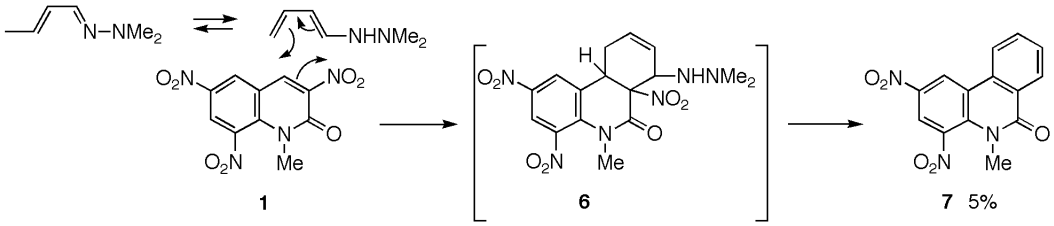


Figure 1 Coupling constants measureble in the ^{1}H nmr

The results mentioned above prompted us to study the cycloaddition of quinolone **1** with diene having an amino moiety, which is expected to assist the aromatization intramolecularly, and leading to phenanthridine derivative. When the reaction of quinolone **1** with hydrazone of 2-butenal was conducted, phenanthridine derivative **7** was isolated despite a low yield. This reaction is initiated with tautomerism of hydrazone affording hydrazinobutadiene, and then this tautomer constructs a six membered ring at the nitroalkene moiety of **1**. During the following aromatization of cycloadduct **6**, hydrazino group is considered to assist the elimination of nitrous acid (Scheme 3).

Scheme 3



In summary, novel reactivity of trinitroquinolone **1** was revealed. The 8-nitro group promotes nitroalkene property of the 3- and 4-positions, and the 3-nitro group diminishes the electron density at this moiety. As a result, both activating effects cause Diels-Alder reaction under milder conditions to furnish unnatural MeQone derivatives, which provides a new methodology for quinolone chemistry.

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. ^{1}H nmr and ^{13}C nmr spectra were measured on a Bruker DPX-400 at 400 MHz and at 100 MHz with TMS as an internal standard. ^{13}C nmr assignment (s,d,t and q) were made from dept experiments. Ir spectra were recorded on a Horiba FT-200 IR spectrometer. Elemental microanalyses were performed using a Yanaco MT-3 CHN corder.

General Procedure.

To a solution of trinitroquinolone **1** (296 mg, 1 mmol) in acetonitrile (10 mL), was added a solution of cyclopentadiene (0.67 g, 10 mmol) in acetonitrile (2 mL), and the resultant solution was heated under reflux for 7 hours. After removal of solvent, the residue was treated with column chromatography on silica gel to afford cycloadduct **4** (eluted with toluene, 270 mg, 0.74 mmol, 74% yield). The reaction of **1** with hydrazone of 2-butenal was performed in a similar way.

To a solution of cycloadduct **4** (72 mg, 0.2 mmol) in acetonitrile (2 mL), triethylamine (59 μL, 0.425 mmol) was added, and the mixture was heated under reflux for 12 hours. After removal of solvent, the residue was treated with column chromatography on silica gel to give aromatized product **5** (eluted with toluene, 130 mg, 0.041 mmol, 21% yield).

5,6,6a,10a-Tetrahydro-7,10-methano-5-methyl-2,4,6a-trinitrophenanthridin-6-one (**4**).

This compound was obtained as colorless prisms in 74% yield; mp 163-167 °C (dec.); ir (potassium bromide): ν 1695, 1556, 1541, 1531, 1340 cm^{-1}; ^{1}H nmr (400 MHz, deuteriochloroform):

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, deuteriochloroform): 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: $C_{15}H_{12}N_4O_7$: C, 50.01; H, 3.36; N, 15.55. Found: C, 50.01; H, 3.31; N, 15.70

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

This compound was obtained as pale yellow needles in 21% yield; ir (potassium bromide): ν 1674, 1537, 1524, 1342 cm^{-1}; ^{1}H nmr (400 MHz, deuteriochloroform): 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, deuteriochloroform): 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: $C_{15}H_{11}N_3O_5$: C, 57.51; H, 3.54; N, 13.41. Found: C, 57.85; H, 3.61; N, 12.71.

5-Methyl-2,4-dinitrophenanthridin-6-one (**7**).

This compound was obtained as yellow plates in 5% yield; mp >300 °C; ir (potassium bromide): ν 1678, 1541, 1527, 1352, 1336 cm^{-1}; ^{1}H nmr (400 MHz, deuteriochloroform): 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: $C_{14}H_9N_3O_5$: C, 56.19; H, 3.03; N, 14.04. Found: C, 55.81; H, 3.23; N, 14.41.

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