

**DIMERIZATION AND DENITRATION OF  
1-METHYL-3,6,8-TRINITRO-2-QUINOLONE**

Nagatoshi Nishiwaki,<sup>a</sup> Mayumi Azuma,<sup>a</sup> Chitose Tanaka,<sup>a</sup> Noriko Asaka,<sup>b</sup>  
Makoto Shoda,<sup>c</sup> Yasuo Tohda,<sup>c</sup> and Masahiro Ariga\*<sup>a</sup>

<sup>a</sup> Department of Chemistry, Osaka Kyoiku University,

<sup>b</sup> Center for Instrumental Analysis, Osaka Kyoiku University,

<sup>c</sup> Division of Natural Science, Osaka Kyoiku University,

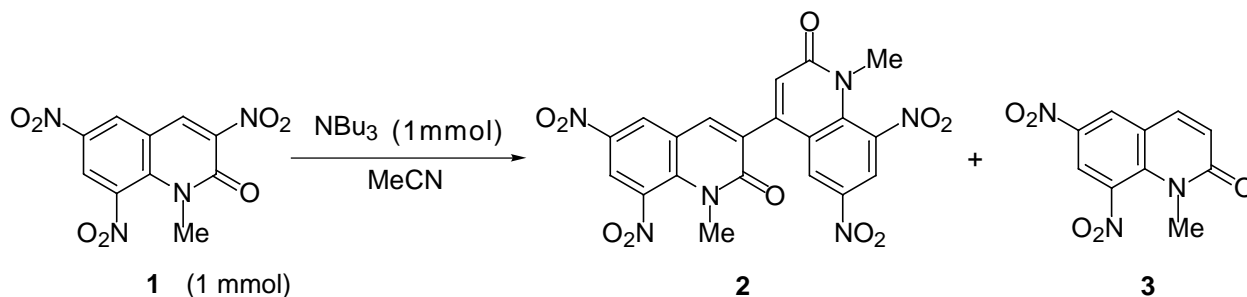
Asahigaoka 4-698-1, Kashiwara, Osaka 582-8582, Japan

**Abstract** - The reaction of 1-methyl-3,6,8-trinitro-2-quinolone (**1**) with tertiary amine caused dimerization and denitration. Dimerization predominantly proceeded at room temperature, and denitration mainly occurred under heated conditions.

A great number of quinoline alkaloids have been isolated, and determination of their structures and syntheses have been performed. Among them, alkaloids having the 1-methyl-2-quinolone (MeQone) skeleton form a large family.<sup>1-3</sup> From a viewpoint of biochemical interest, it is highly required to synthesize novel MeQone derivatives and to develop facile method for functionalizing MeQone.

1-Methyl-3,6,8-trinitro-2-quinolone (**1**) showed interesting chemical behaviors. *cine*-Substitution brought about the regioselective C-C bond formation at the 4-position.<sup>4</sup> It was also found that the nitro group at the 8-position sterically activated the quinolone ring.<sup>5</sup> In this communication, we would like to show a novel reactivity of **1**, dimerization and denitration, observed in the reaction with tertiary amines.

Trinitroquinolone (**1**) was stirred with NBU<sub>3</sub> at room temperature in MeCN for 7 days. Concentration of the



Temp. /°C	Solv./mL	Time/d	Ratio of <b>2/3</b> <sup>a</sup>	Isolated Yield/%	
				<b>2</b> <sup>b</sup>	<b>3</b>
25	10	7	88/12	81	6
60	10	1	63/37		
80	10	1	40/60 <sup>c</sup>		
60	50	1	25/75	20	58

<sup>a</sup> Determined by <sup>1</sup>H NMR. <sup>b</sup> Based on **1**. <sup>c</sup> A small amount of by-products was formed.

reaction mixture followed by column chromatography gave 3,4'-bis(1-methyl-6,8-dinitro-2-quinolone) (**2**) in 81 %. In the  $^1\text{H}$  NMR of **2**, two singlets were observed at 7.06 and 8.56 ppm in addition to two pairs of doublets (H5, H7, H5' and H7' hydrogens). This fact revealed that a couple of 6,8-dinitroquinolones was connected at the 3- and 4'-positions. Other spectral and analytical data supported this dimeric structure.<sup>6</sup> Several other tertiary amines were employed instead of  $\text{NBu}_3$ . To a solution of quinolone (**1**) (0.1 mmol) in  $\text{CD}_3\text{CN}$  (0.3 mL), amine (0.1 mmol) was added, and the reaction mixture was monitored with  $^1\text{H}$  NMR for 7 days. In each case, signals other than those of **1** and **2** were not observed in the aromatic region. Considerable differences of reactivity between amines appeared. No reaction proceeded in the reaction of **1** with  $\text{NMe}_3$  and  $\text{NBu}_3$ . When  $\text{NEt}_3$  and  $\text{NPr}_3$  were used, dimer (**2**) was produced in 34 % and 76 % yields, but these reactions were much slower than the case of  $\text{NBu}_3$  (93 %). Although the role of amines has not been clarified, the longer carbon chain caused more positive effect.

Dinitroquinolone (**3**) became the major product under heated conditions. Dilution of the reaction mixture to avoid the intermolecular coupling reaction increased the ratio of **3**. Since isolated **2** and **3** did not interconvert on treatment with  $\text{NBu}_3$  in  $\text{MeCN}$ , one was not an intermediate of the other. It seems that dimer (**2**) is kinetically controlled product, and **3** is thermodynamically controlled product.

The present denitration newly established the preparative method for 6,8-dinitroquinolone (**3**) in cooperation with trinitration of MeQone.<sup>4</sup> This method is superior to the direct preparation from MeQone by the nitration with 15 M  $\text{HNO}_3$  and 18 M  $\text{H}_2\text{SO}_4$  (in 30 % yield), which suffers from troublesome isolation from the mixture with by-products.<sup>5</sup> As a result, the former procedure furnished dinitroquinolone (**3**) in a higher yield (53 % based on MeQone) with simple manipulations.

Two kinds of methods for modification of the MeQone skeleton were provided.

## REFERENCES AND NOTES

- Alkaloids containing MeQone: (a) M. F. Grundon, 'The Alkaloids: Quinoline Alkaloids Related to Anthranic Acid,' Vol. 32, Academic Press, London, 1988, p. 341; (b) N. Atta-ur-Rahman, M. I. Sultane, P. M. Choudhary, and M. R. Khan, *J. Nat. Prod.*, 1998, **61**, 713; (c) I.-S. Chen, I.-W. Tsai, C.-M. Teng, J.-J. Chen, Y.-L. Chang, F.-N. Ko, M.-C. Lu, and J. M. Pezzuto, *Phytochemistry*, 1997, **46**, 525; (d) G. Brader, M. Bacher, H. Greger, and O. Hofer, *Phytochemistry*, 1996, **42**, 881.
- Functionalization of MeQone: (a) K. C. Majumdar, A. K. Kundu, and P. Biswas, *Heterocycles*, 1999, **51**, 471; (b) Y. Tagawa, T. Kawaoka, and Y. Goto, *J. Heterocycl. Chem.*, 1997, **34**, 1677; (c) A. E. Täubl, and W. Stadlbauer, *J. Heterocycl. Chem.*, 1997, **34**, 989; (d) H. Suginome, Y. Kajizuka, M. Suzuki, H. Senboku, and K. Kobayashi, *Heterocycles*, 1994, **37**, 283.
- Dimeric quinoline alkaloids containing MeQone: (a) J.-H. Ye, K.-Q. Ling, Y. Zhang, N. Li, and J.-H. Xu, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2017. (b) S. A. Barr, C. F. Neville, M. F. Grundon, D. R. Boyd, J. F. Malone, and T. A. Evance, *J. Chem. Soc., Perkin Trans. 1*, 1995, 445; (c) I.-S. Chen, S.-J. Wu, Y.-C. Lin, I.-L. Tsai, H. Seki, F.-N. Ko, and C.-M. Teng, *Phytochemistry*, 1997, **46**, 525.
- N. Nishiwaki, A. Tanaka, M. Uchida, Y. Tohda, and M. Ariga, *Bull. Chem. Soc. Jpn.*, 1996, **69**, 1377. Nitration of MeQone with fuming  $\text{HNO}_3$  ( $d = 1.52$ ) afforded trinitroquinolone (**1**) in 90 % yield.
- N. Nishiwaki, C. Tanaka, M. Asahara, N. Asaka, Y. Tohda, and M. Ariga, *Heterocycles*, 1999, **51**, 567. 3,6-Dinitroquinolone (41 %), 6-nitroquinolone (19 %) and **1** (9 %) were produced together with **3**.
- 2**; Pale yellow powder (eluted with  $\text{CHCl}_3$ ); mp 288-291 °C (decomp); IR (Nujol /  $\text{cm}^{-1}$ ) 1662, 1554, 1346;  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ , TMS)  $\delta$  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);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$  / ppm) 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 ( $\text{M}^+ + 1$ ). Anal. Calcd for  $\text{C}_{20}\text{H}_{12}\text{N}_6\text{O}_{10}$ : C: 48.40, H: 2.44, N: 16.93. Found; C: 48.50, H: 2.42, N: 17.22.