Tetrahedron Letters,Vol.28,No.34,pp 3975-3978,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

NOVEL ADDITION OF NITROALKANES TO o-QUINONES

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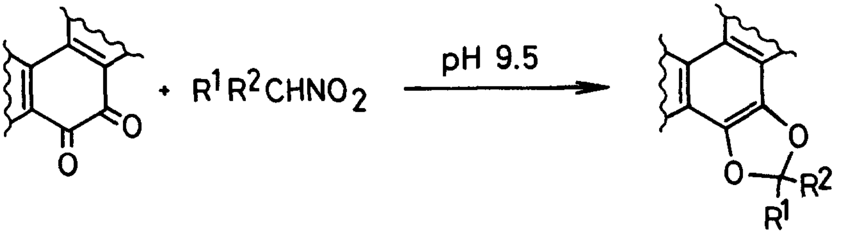
Abstract: A novel addition reaction of nitroalkanes to o-quinones is found to give 1,3-dioxole derivatives.

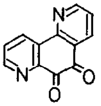
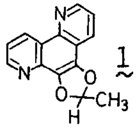
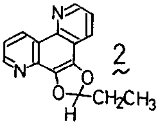
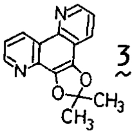
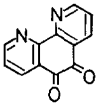
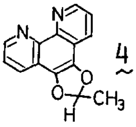
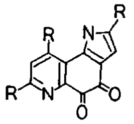
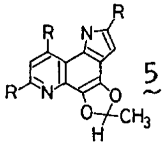
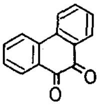
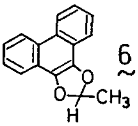
The reaction between nitroalkanes and o-quinones is very interesting in connection with the function of coenzyme PQQ (4,5-dihydro-4,5-dioxo-1H-pyrrolo[2,3-f]quinoline-2,7,9-tricarboxylic acid, Methoxatin)[1] in bacterial nitroalkane oxidases[2] where nitroalkanes are converted into aldehydes and nitrite ion by the reaction with PQQ. However, details of such a reaction has not been clarified. In this paper, we studied the reaction between nitroalkanes and several o-quinones to obtain informations about the system, and found a novel type of addition-cyclization reaction providing 1,3-dioxole derivatives (cyclic acetals) as shown in eq 1. This type of reaction between nitroalkanes and o-quinones has not been reported, and is also interesting from a viewpoint of organic chemistry.



(1)

Treatment of 1,7-phenanthroline-5,6-dione (4.8 mM) with nitroethane (0.48 M) in 0.1 M carbonate buffer (pH 9.5)-CH_3CN (1:1) at 55°C for 5 h under anaerobic conditions gave 2-methyl-1,3-dioxole derivative **1** in 88 % yield (entry 1 in Table 1). The structure of **1** was well confirmed by spectroscopic analyses.[3] This reaction was applicable to other primary and secondary nitroalkanes (entry 2 and 3) and to other o-quinones such as 1,10-phenanthroline-5,6-dione (entry 4), 2,7,9-tris(dimethylcarbamoyl) derivative of PQQ (entry 5), and phenanthraquinone (entry 6). In the case of a p-quinone (anthraquinone) and an α-diketone (benzil), on the other hand, such an addition reaction of the nitroalkane was not observed under these conditions. Hence, the present reaction is considered to be characteristic of o-quinones.

Table 1. Reaction of o-quinones and nitroalkanes

Entry	Quinone	Nitroalkane	Time(h)	Product	Yield(%)
1		$CH_3CH_2NO_2$	5	 1	88
2	"	$CH_3CH_2CH_2NO_2$	5	 2	70
3	"	$(CH_3)_2CHNO_2$	5	 3	67
4		$CH_3CH_2NO_2$	5	 4	67
5	 R=CON(CH$_3$)$_2$	$CH_3CH_2NO_2$	5	 5	53
6		$CH_3CH_2NO_2$	22	 6	60

[Quinone] = 4.8 mM, [Nitroalkane] = 0.48 M, 0.1 M Carbonate Buffer (pH 9.5)-CH_3CN (1:1), 55°C, under anaerobic conditions (N_2)

Figure 1 shows a spectral change along the progress of the reaction of 1,7-phenanthroline-5,6-dione (4.0×10^{-5}M) and nitroethane (8.0×10^{-2}M) in 0.1 M carbonate buffer (pH 9.5)-CH_3CN (1:1) at 40°C under anaerobic conditions. Absorption at 345 nm increased with proceeding of the reaction, and introduction of air to the final reaction mixture did not change the final spectrum. Inspection of the spectral change of Figure 1 points out existence of an intermediate (appearance of the absorption at 325 nm at the first stage of the reaction). The consecutive pseudo-first-order plot of Figure 2 using the appearance of absorption at 345 nm (k_{obsd}= $5.68 \times 10^{-3}s^{-1}$ and 9.93×10^{-3} s^{-1}) also indicates the change of the rate-determining steps and the existence of at least one intermediate.

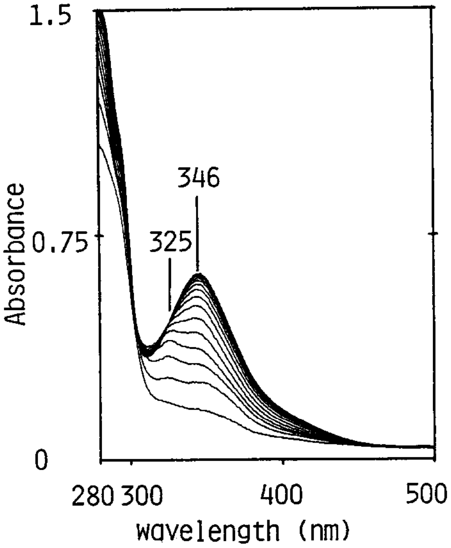


Fig. 1 Spectral change along the progress of the reaction of 1,7-phenanthroline-5,6-dione and nitroethane

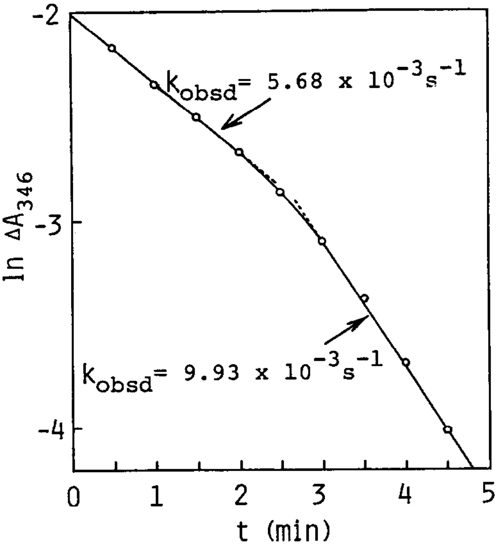
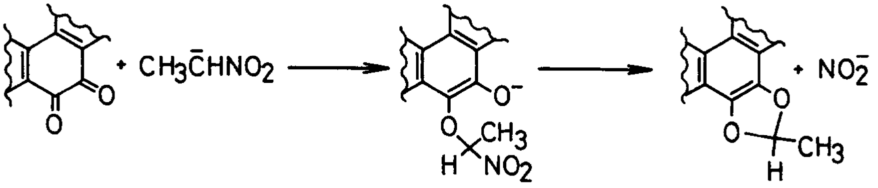


Fig. 2 Pseudo-first-order plot for the reaction of 1,7-phenanthroline-5,6-dione and nitroethane

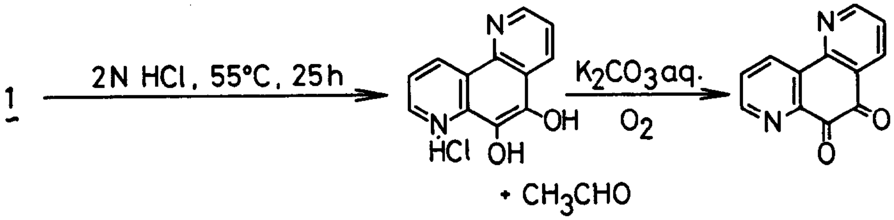


Scheme

It is known that vinylmagnesium bromide adds to carbonyl oxygen of phenanthraquinone followed by cyclization to a 1,3-dioxole derivative **6**.[4] The present reaction is considered to proceed via a similar addition intermediate. Namely, nitroethane anion formally adds to the carbonyl oxygen of the o-quinone followed by cyclization to the product as shown in Scheme. One of the possible mechanism of this abnormal addition is that involving electron transfer from nitroethane anion to the quinone and subsequent radical coupling in the solvent cage. Alternatively, a mechanism of the anion addition to the carbonyl carbon of the quinone followed by 1,2-rearrangement may be possible. In either case, the present reaction is novel as compared with well known Henry reaction (aldol type addition of nitroalkanes to carbonyl carbon).[5] Further investigations concerning the mechanism are in progress now.

Finally, hydrolysis of the dioxole product **1** (20 mg, 0.084 mmol) was performed in 2 N HCl (1 ml) at 55 °C for 24 h. 5,6-Dihydroxy-1,7-phenanthroline hydrochloride (quinol, reduced form) was obtained quantitatively and formation of acetaldehyde was confirmed by GLC (eq. 2). Furthermore, the quinone could be easily regenerated from the corresponding quinol by treating in an alkaline aqueous solution under aerobic conditions.

Consequently, the redox system between nitroethane and the quinone could be formally constructed. These results may serve elucidation of the function of PQQ in nitroalkane oxidases.



(2)

References and Notes

1. S. A. Salisbury, H. S. Forrest, W. B. T. Cruse, and O. Kennard, Nature, **280**, 843 (1979).
2. T. Kido and K. Soda, Seikagaku (in Japanese), **57**, 1065 (1985)
3. **1**: m.p.: 129 - 131 °C; I.R.(KBr): ν = 1650 cm^{-1} (C=C); ^{1}H-N.M.R.($CDCl_3$/TMS): δ = 1.94 (d, J = 5.0 Hz, 3H, CH_3), 6.74 (q, J = 5.0 Hz, 1H, $C\underline{H}CH_3$), 7.58 (dd, J = 4.5, 8.6 Hz, 1H), 7.61 (dd, J = 4.5, 8.0 Hz, 1H), 8.25 (dd, J = 2.0, 8.0 Hz, 1H), 8.95 (dd, J = 1.8, 4.5 Hz, 1H), 9.00 (dd, J = 2.0, 4.5 Hz, 1H), 9.51 (dd, J = 1.8, 8.6 Hz, 1H); ^{13}C-N.M.R.($CDCl_3$/TMS): 19.9 (CH_3), 111.1 ppm ($\underline{C}HCH_3$), and twelve aromatic carbons; M.S.: m/e = 238 (M^+).
   The m.p. and representative spectral data for other products;
   2: m.p.: 110 - 114°C; I.R. (KBr): ν = 1654 cm^{-1} (C=C); ^{1}H-N.M.R. ($CDCl_3$/TMS); δ = 1.23 (t, J = 7.5 Hz, 3H, CH_3), 2.25 (dq, J = 4.7, 7.5 Hz, 2H, CH_2), 6.58 (t, J = 4.7 Hz, 1H, $C\underline{H}CH_2CH_3$).
   3: m.p.: 129 - 132 °C; I.R. (KBr): ν = 1648 cm^{-1} (C=C), ^{1}H-N.M.R. ($CDCl_3$/TMS): δ = 1.93 (s, 6H, 2 x CH_3).
   4: m.p.: 166 - 172 °C, I.R.(KBr): ν = 1660 cm^{-1} (C=C); ^{1}H-N.M.R. ($CDCl_3$/TMS): δ = 1.90 (d, J = 5.0 Hz, 3H, CH_3), 6.67 (q, J = 5.0 Hz, 1H, $C\underline{H}CH_3$).
   5: m.p.: 244 - 248°C (dec.); I.R.(KBr): ν = 1634 cm^{-1} (C=C, $CONMe_2$); ^{1}H-N.M.R. ($CDCl_3$/TMS); δ = 1.78 (d, J = 5.1 Hz, 3H, CH_3), 6.48 (q, J = 5.1 Hz, 1H, $C\underline{H}CH_3$).
   Spectral data of **6** were identical for those of the authentic sample.[4]
4. D. Wege, Aust. J. Chem., **24**, 1531 (1971).
5. S. Patai, "The chemistry of the nitro and nitroso groups", Wiley; New York, 1969.

(Received in Japan 19 May 1987)