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The Reaction of Aromatic Nitrile *N*-Oxides with Tetrahalo-*p*-benzoquinones

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Cycloaddition reaction of aromatic nitrile *N*-oxides, such as benzonitrile *N*-oxide, 2,4,6-trimethylbenzonitrile *N*-oxide, and 2,3,5,6-tetramethylbenzonitrile *N*-oxide, with tetrahalo-*p*-benzoquinones was studied. The reaction gave 1: 1- and/or 2: 1-adducts of a nitrile *N*-oxide and a tetrahalobenzoquinone according to the conditions, especially the mole ratios of each reactant. The 2: 1-adducts are formed *via* 1: 1-adducts, each having two stereoisomers. The structures of these adducts were determined to be dioxazole derivatives formed by the addition of nitrile *N*-oxides to the carbonyl bonds of the tetrahalobenzoquinones.

Nitrile *N*-oxide is known to be a typical 1,3-dipole and to react with many unsaturated bonds to form heterocycles.[1] In general, nitrile *N*-oxides, like other 1,3-dipoles, react with C=C double bond much faster than with C=O bond. Benzonitrile *N*-oxide reacts with styrene by 180 times faster than with its isoelectronic compound, benzaldehyde.[2] *p*-Benzoquinone and alkenyl ketones each have two different dipolarophilic functions, C=C and C=O bonds in the molecules. They give C=C addition products in the reactions with various nitrile oxides.[3] In very rare cases, however, preference for C=O addition has been reported. Some *o*-quinones gave C=O addition products. As an example, benzonitrile *N*-oxide reacts with *o*-naphthoquinone to give two isomeric 1: 1–C=O adducts, followed by the addition of nitrile *N*-oxide to the C=C and/or C=O bonds according to the first addition site.[4] Cyclobutene diones have been found to react with mesitonitrile *N*-oxide at the C=O bonds.[5] α-Azidovinyl ketones react with nitrile *N*-oxides at both C=C and C=O bonds.[6]

We have studied the reaction of aromatic nitrile *N*-oxides with tetrahalo-*p*-benzoquinones (*p*-haloanils) and found that the reaction gives dioxazole derivatives unlike the reaction with unsubstituted *p*-benzoquinone, which gives isoxazoline derivatives.[3]

Results and Discussion

Aromatic nitrile *N*-oxides, such as benzonitrile N-oxide (BNO), 2,4,6-trimethylbenzonitrile *N*-oxide (MNO), and 2,3,5,6-tetramethylbenzonitrile *N*-oxide (DNO), were allowed to react with tetrahalo-*p*-benzoquinones, such as fluoranil (FA), chloranil (CA), bromanil (BA), and iodanil (IA), in chloroform at room temperature or at elevated temperatures. Completion of the reaction was confirmed by complete comsumption of the nitrile *N*-oxide in the reaction mixture by thin layer chromatography (TLC). An equimolar reaction of MNO with CA gave a 1: 1-adduct in 93% yield and a small amount of a 2: 1-adduct in 7% yield based on MNO, the reaction in 2: 1 mole ratio giving a 2: 1-adduct. When the reaction was interrupted at an earlier stage, the 1: 1-adduct was obtained as the sole isolable product with unreacted reactants. Irrespective of solvent and temperature, 1: 1- and/or 2: 1-adducts were obtained according to the mole ratio of the reactants in more than 90% yield on the completion of the reaction. The dependence of the product composition on the reaction conditions is shown in Table 1 for the reaction of MNO with CA. When haloanil was added very slowly to a refluxing solution of a nitrile *N*-oxide, the corresponding 2: 1-adduct was obtained quantitatively without contamination of 1: 1-adduct. The condition was fulfilled by using a Soxhlet extraction apparatus. The solubility of haloanils in chloroform is sufficiently small for this procedure. The result shows that the addition reaction proceeds stepwise and irreversibly, the second addition step being much slower than the first.

The 2: 1-adduct from MNO and CA has two isomers, which differ in solubility and thermal behavior. Their elementary analyses gave the same results, the IR spectra differing slightly in finger print region. One isomer (**6a**) is almost insoluble in hexane and the other (**6b**) fairly soluble. The product mixture could be separated into **6a** and **6b** by the difference in solubility. Their ratio was always 50: 50 as shown in Table 1. This indicates that the orientation of the second addition reaction is not influenced by the mode of the first, the addition reaction occurring such a mode that only two isomers are possible for the 2: 1-adduct.

TABLE 1. DEPENDENCE OF THE PRODUCTS COMPOSITION ON THE REACTION CONDITIONS FOR THE REACTION OF MNO WITH CA

Reactants (mole ratio)	Solvent	Temp °C	Time h	Products (yield, %)	2:1-Adduct isomer ratio **6b**:**6a**
MNO/CA (1/1)	$CHCl_3$	r.t.	15	1:1-adduct(93)[a] 2:1-adduct(7)[a]	
(1.5/1)	$CHCl_3$	r.t.	18	1:1-adduct(49) 2:1-adduct(46)	
(2/1)	$CHCl_3$	r.t.	18	2:1-adduct(98)	46:54
	$CHCl_3$	reflux	11	2:1-adduct(94)	53:47
	C_6H_6	r.t.	30	2:1-adduct(93)	52:48
(2.5/1)	$CHCl_3$	r.t.	18	2:1-adduct(96)	
MNO/1:1-adduct(1/1)	$CHCl_3$	r.t.	18	2:1-adduct(86)	54:46

a) The values are calculated based on the nitrile *N*-oxide.

The IR spectra of **6a** and **6b** have very strong absorption bands in the ν_{C-O-C} region 1100—1300 cm^{-1}, but no absorption in the $\nu_{C=O}$ region 1650—1750 cm^{-1}. The mass spectra of the 1: 1-adduct (**5**) and the 2: 1-adducts (**6a** and **6b**) have molecular ion peak (M$^+$)

TABLE 2. THE REACTION PRODUCTS FROM NITRILE *N*-OXIDES AND HALOANILS

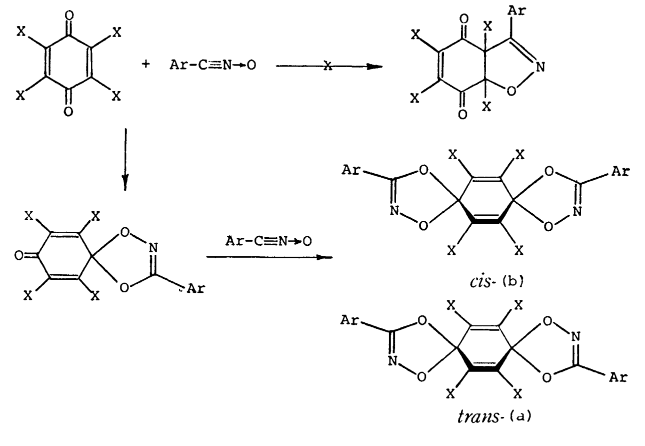
Products[a)]	Compd No.	Reactants mole ratio	React. time, h	Yield, %	Mp, °C	Found (Calcd) C	H	N	IR, $\gamma_{C=O}$ cm^{-1}	MS, *m/e*
FA·MNO	**1**	1/1	9	94	102—104	56.53 (56.31	3.49 3.25	4.34 4.10)	1700	341(M$^+$),180, 161
FA·MNO$_2$	**2**	1/2	10	95	186—190	62.39 (62.15	4.48 4.41	5.41 5.58)	—	
CA·BNO	**3**	See exp. section			162—164	42.89 (42.78	1.59 1.38	3.97 3.84)	1690	
CA·BNO$_2$	**4**	do.			218—221	49.43 (49.62	2.27 2.08	5.92 5.79)	—	486, 484, 482(M$^+$), 363, 244, 119
CA·MNO	**5**	See Table 1.			128.5—129.5	47.30 (47.21	2.65 2.72	3.43 3.44)	1715	409, 407, 405(M$^+$), 244, 161
CA·MNO$_2$	**6a**[b)]				190—194(d)	55.18	3.78	4.83	—	570, 568, 566(M$^+$), 405, 244, 161
	6b	do.			e)	54.72 (54.95	3.86 3.90	4.93 4.93)	—	
CA·DNO	**7**	1/1		93	181—183	48.27 (48.40	3.10 3.11	3.36 3.33)	1705	423, 421, 419(M$^+$), 244, 175
CA·DNO$_2$	**8**	1/2		96	168—171	56.10 (56.40	4.29 4.39	4.72 4.70)	—	
BA·MNO	**9**	1/1	15	87	140(d)	32.65 (32.86	1.70 1.90	2.12 2.39)	1695	
BA·MNO$_2$	**10**	1/2	19	93	140(d)	41.55 (41.86	3.28 2.97	3.95 3.75)	—	750, 748, 746, 744, 742(M$^+$), 581, 420
BA·DNO	**11**	1/1	15	90	140(d)	33.95 (34.09	1.96 2.19	2.13 2.34)	1695	
BA·DNO$_2$	**12**	1/2	19	92	140(d)	43.27 (43.44	3.38 3.39	3.74 3.62)	—	
JA·MNO[c)]	**13**	1/1	39	48[d)]	102—104	24.63 (24.86	1.79 1.43	2.00 1.81)	1670	
JA·MNO$_2$[c)]	**14**	1/2	40	71	186—190	33.59 (33.43	2.36 2.37	3.20 3.00)	—	

a) All the compounds were recrystallized from hexane unless otherwise stated. b) Recrystallized from chloroform. c) Recrystallized from a mixture of hexane and chloroform. d) Compound **14** was also obtained in 32% yield based on MNO. e) No apparent change was observed except for very gradual discoloration at above 160 °C, but a small endotherm was observed at 154 °C in its differential thermogram as shown in Fig. 1-(c).

at the *m/e* corresponding to their molecular weights with the peaks at M$^+$+2 and M$^+$+4 with the intensities characteristic to tetra-chlorinated compounds. They are also the composite of the fragmentation patterns of mesityl isocyanate and chloranil, except for their molecular ion peaks and the fragment ion peaks corresponding to the 1:1-adduct for the spectra of **6a** and **6b**, which gave the same fragmentation patterns. All the other addition products obtained from the reactions of the nitrile *N*-oxides and haloanils show similar spectroscopic results. Characterization data of these reaction products are summarized in Table 2. Separation of the isomers of the 2:1-adducts other than those from MNO and CA was not successful. The melting points might be those of isomer mixtures, showing fluctuation.

The results indicate that the structure of the addition products is not isoxazoline but dioxazole formed by the addition of nitrile *N*-oxides to the carbonyl bonds of haloanils as shown in the scheme.

The addition products, **5**, **6a**, and **6b**, decomposed into mesityl isocyanate and CA on heating. The isocyanate might be derived by the thermal rearrangement of MNO generated by thermal retro-addition reaction or by pyrolytic rearrangement of the dioxazoles. The precise mechanism of the decomposition should be determined by isotope labeling experiment. The



1:1-Adducts	2:1-Adducts
X=F, Ar=Ms, **1**.	X=F, Ar=Ms, **2**.
X=Cl, Ar=Ph, **3**; Ms, **5**; Du, **7**.	X=Cl, Ar=Ph, **4**; Ms, **6a** and **b**; Du, **8**.
X=Br, Ar=Ms, **9**; Du, **11**.	X=Br, Ar=Ms, **10**; Du, **12**.
X=I, Ar=Ms, **13**.	X=I, Ar=Ms, **14**.

where, Ph=C_6H_5, Ms=2,4,6-$(CH_3)_3C_6H_2$, and Du=2,3,5,6-$(CH_3)_4C_6H$.

Scheme.

decomposition temperature differed among the products (Fig. 1). The differential thermal analysis (DTA) of **6b** gives a complicated thermogram with a small endothermic peak at 154 °C and exothermic ones at 163 and 173 °C, while **6a** shows no endotherm but only an exotherm at 192 °C. Thermogravimetric analysis (TGA) of the compounds shows rapid weight decrease at the temperature at which an exotherm was observed in DTA, followed by subsequent slow decrease. The first weight loss corresponds to the weight of nitrile oxide moiety, which volatiled as isocyanate rapidly with nitrogen stream. The second slow decrease might be due to the sublimation of chloranil.

The reaction of a nitrile *N*-oxide with a C=C double bond of a haloanil would give 2-isoxazoline derivative, pyrolysis of which might result in aromatization to afford isoxazole derivative rather than degradation to a quinone and an isocyanate. The angular C–Cl bond is thought to be cleaved more easily. Thus, the result of the pyrolysis of **5** also supports the dioxazole structure of the adducts.

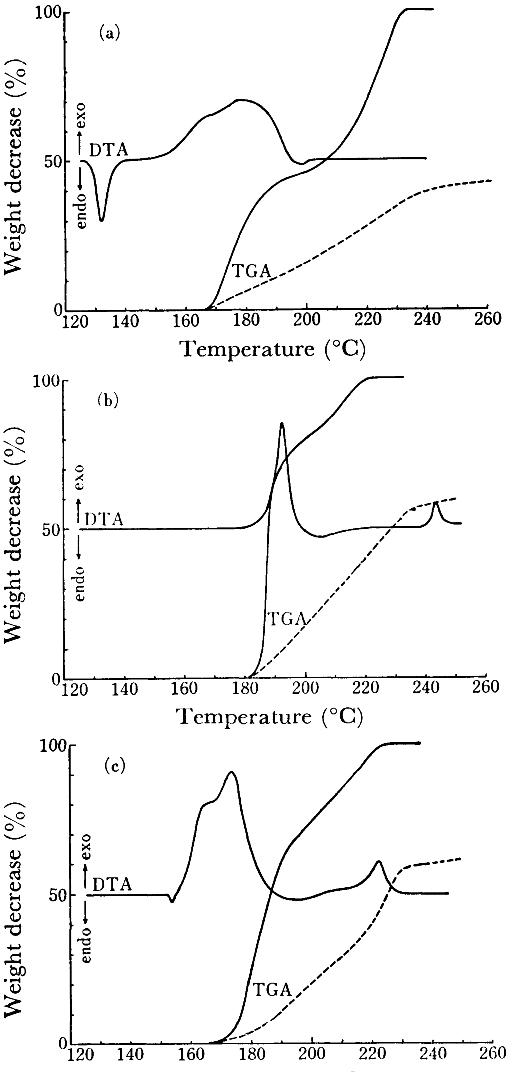


Fig. 1. Thermal analyses of the addition products of MNO with CA, (a): **5**, (b): **6a**, and (c): **6b**, under nitrogen stream (——) and under air (----). Heating rate: 5°C/min.

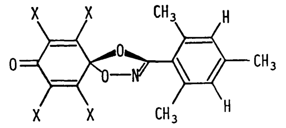
The fact that **6a** has higher melting point and is more thermally stable and less soluble in solvents than **6b** indicates that **6a** has a more symmetrical *trans* structure of the two stereoisomers.

FA, BA, and JA also reacted with MNO to give similar results, but the rate difference between the first addition and the second one differs among them. The rate difference for the reaction of MNO with IA was rather small, and thus the equimolar reaction of them gave 1: 1-(**13**) and 2: 1-adducts (**14**) in 48 and 32% yields based on MNO, respectively.

BNO and DNO also underwent similar cycloaddition with haloanils at the carbonyl sites (Table 2). In the reaction of BNO with haloanils, however, the usual *in situ* reaction process using triethylamine as an acid acceptor was not applicable because of faster reaction of the amine with haloanils. The cycloaddition was performed effectively with a solution of free BNO prepared prior to the reaction, or by heating a solution of benzhydroxamoyl chloride and a haloanil in toluene to reflux.

The PMR spectral data for the 1: 1-adducts from MNO are summarized in Table 3. The signals due to 2- and 6-methyl substituents on the mesityl radical move to down field with the change of the quinone substituents in the order of the atomic radii of halogen atoms, FA<CA<BA<JA, while the other signals due to 4-methyl and 3- and 5-hydrogens have almost the same chemical shifts. Considering the thru-space interaction of 2- and 6-methyl groups with halogens, this may also support the spiro-dioxazole structure of the adducts.

Table 3. PMR Spectral data of 1:1-adducts of MNO and haloanils, 6,7,9,10-tetrahalo-3-mesityl-2-aza-1,4-dioxaspiro[4,5]deca-2,6,9-trien-8-ones, δ (ppm) in $CDCl_3$



	MNO	X= F (**1**)	Cl (**5**)	Br (**9**)	I (**13**)
2- and 6-CH_3	2.40	2.36	2.47	2.53	2.60
4-CH_3	2.28	2.31	2.30	2.31	2.29
3- and 5-H	6.87	6.96	6.92	6.94	6.93

Addition of nitrile *N*-oxides to the carbonyl of the compounds having two potential dipolarophilic functions, C=C and C=O in the molecules is very rare. Preferential carbonyl addition in the reaction of nitrile *N*-oxides with haloanils is considered to be due to the halogen substituents on the quinones, which deactivate the reactivity of the C=C by steric hindrance and activate that of the C=O by inductive effect. This type of C=O addition is known in the reaction of diazomethane which also has a 1,3-dipole.[7] Diazomethane adds to a carbonyl group in quinones with all of the hydrogens replaced by electronegative groups. Many similarities in the modes of reaction feature were observed in 1,3-dipolar cycloaddition and Diels-Alder reactions. However, we see a distinct difference in the reactions with substituted quinones, where Diels-Alder reaction gave C=C addition products even with chloranil.[8] The reaction of diazomethane with tetramethyl-*p*-benzoquinone, however, occurs at the C=C bonds,[9] and 1,4-diphenyl-2,6-piperazinedione adds also to the C=C bond of chloranil *via* an azomethine ylide intermediacy.[10] The reactions with quinones might give clues for the elucidation of reaction mechanisms.

Experimental

All the melting points cited are uncorrected. Characterization data for the addition products from nitrile *N*-oxides and haloanils are given in Table 2.

Materials. 2,4,6-Trimethylbenzonitrile *N*-oxide and 2,3,5,6-tetramethylbenzonitrile *N*-oxide were prepared by Grundmann's procedure.[11] Commercial chloranil was purified by recrystallization from gracial acetic acid. Bromanil was prepared by the method of Jackson and Bolton[12] and recrystallized from gracial acetic acid. Iodanil was prepared from bromanil according to the procedure of Torrey and Hunder.[13]

Reaction of MNO with CA. 6,7,9,10-Tetrachloro-3-mesityl-2-aza-1,4-dioxaspiro[4, 5]deca-2,6,9-trien-8-one (5): A solution of 1.23 g (5.0 mmol) of CA and 0.18 g (5.0 mmol) of MNO in 300 ml of chloroform was stirred for 15 h at room temperature. After confirming the completion of the reaction by TLC on silica gel plate with benzene, the solvent was evaporated under vacuum. The residual solid was extracted with hot hexane to give 1.90 g (93%) of the title product as the extract, which was recrystallized from hexane.

*6, 7, 13, 14-Tetrachloro-3, 11-dimesityl-2, 10-diaza-1, 4, 9, 12-tetraoxadispiro[4,2,4,2]tetradeca-2,6,10,13-tetraene (**6a** and **6b**)*: A solution of 0.61 g (2.5 mmol) of CA and 0.81 g (5.0 mmol) of MNO in 200 ml of chloroform was heated to reflux for 11 h. The solvent was removed by evaporation under vacuum and the residue was extracted with hexane for 4 h using a Soxhlet extractor and then with chloroform for 6 h. The hexane extract (**6b**, 0.70 g, 50%) was recrystallized from hexane and 0.62 g (44%) of the chloroform extract (**6a**) from chloroform.

The same compounds were obtained by the reaction of **5** with MNO. A solution of 1.0 g (2.5 mmol) of **5** and 0.40 g (2.5 mmol) of MNO in 200 ml of chloroform was stirred for 18 h at room temperature. The reaction mixture was treated in the same manner as mentioned above to give 0.65 g (46%) of **6b** and 0.55 g (40%) of **6a**.

Reaction of BNO with CA. 6,7,9,10-Tetrachloro-3-phenyl-2-aza-1,4-dioxaspiro[4, 5]deca-2,6,9-trien-8-one (3): A solution of 0.55 g (5.0 mmol) of triethylamine in 100 ml of tetrahydrofuran (THF) was added dropwise into a solution of 0.85 g (5.0 mmol) of benzhydroxamoyl chloride in 300 ml of THF with vigorous stirring at room temperature. The mixture was stirred for 5 min, and then filtered into a solution of 1.23 g (5.0 mmol) of CA in 200 ml of THF. The solution was stirred for 10 h at room temperature. The solvent was evaporated to give tan yellow residue, which was worked up with column chromatography on silica gel (Wakogel C-100) with benzene as an eluent. The mixture was eluted in the order of diphenylfuroxan, the title compound, and chloranil. The title compound (0.88 g, 48%) was recrystallized from hexane.

The compound was also prepared by the following procedure. A solution of 1.23 g (5.0 mmol) of CA and 0.86 g (5.5 mmol) of benzhydroxamoyl chloride in 300 ml of toluene was heated to reflux for 12 h. Evolution of hydrogen chloride was observed during the course of reaction. The solvent was removed by evaporation under vacuum to give viscous tan yellow oil, which was treated in the same manner as described above to give 0.85 g (47%) of **3**.

6, 7, 13, 14-Tetrachloro-3, 11-diphenyl-2, 10-diaza-1,4,9, 12-tetraoxadispiro[4,2,4,2]tetradeca-2,6,10,13-tetraene (4): A solution of BNO prepared from 1.14 g (7.3 mmol) of benzhydroxamoyl chloride by treating with triethylamine was added into a solution of 0.82 g (3.3 mmol) of CA in THF and the mixture was stirred for 10 h. The mixture was treated in the same manner as mentioned above. Diphenylfuroxan, **3**, **4**, and CA were eluted in this order. The reaction gave 0.40 g (33%) of **3** and 0.22 g (14%) of the title compound **4**, which was recrystallized from hexane.

The compound was also prepared by the reaction of 0.82 g (3.3 mmol) of CA with 1.14 g (7.3 mmol) of benzhydroxamoyl chloride in 300 ml of toluene at refluxing temperature. The work-up of the product with column chromatography on silica gel with benzene gave 0.42 g (34%) of **3** and 0.30 g (19%) of **4**.

The Reaction of Other Haloanils with Nitrile N-*Oxides.* The reaction of other haloanils with MNO or DNO were ciarred out almost in the same manner as described in the preceding section. The results are given in Table 2.

Thermolysis of **5**. Compound **5**, 2.0 g (4.9 mmol), was placed in a sublimer and heated up to 190 °C under reduced pressure (*ca.* 1 Torr). Colorless crystals and yellow ones deposited on the condenser. The colorless part weighed 0.38 g (38%) and melted at 44—46 °C. It was shown to be mesityl isocyanate from its IR spectrum and elementary analysis (Found: C, 74.27; H, 6.77; N, 8.43%. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69%). The yellow one weighed 0.56 g (46%) and was shown to be chloranil from its melting point and IR spectrum.

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