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# An Account of the Site- and Regio-selectivity in the Reaction of Nitrile Oxides with Substituted *p*-Benzoquinones by Frontier Molecular Orbital Theory

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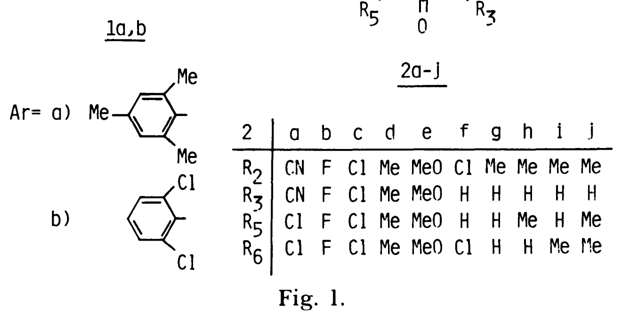
The 1,3-dipolar cycloaddition reactions of nitrile oxides with substituted *p*-benzoquinones are discussed in terms of Frontier Molecular Orbital (FMO) theory. The calculation is carried out by *ab initio* Self Consistent Field (SCF) method with STO-3G basis set. The site- and regio-selectivities in the reactions are correlated with two types of FMO interactions. Some predictions have been confirmed by experimental results.

Frontier Molecular Orbital (FMO) theory is widely used to explain or predict the reactivities and the selectivities in the organic reactions. In the field of cycloaddition reactions, such as Diels-Alder and 1,3-dipolar cycloaddition reactions, it is a powerful tool to study and account for the reactions.[1—6] By applying FMO theory to cycloaddition reactions, Sustmann has classified them into three groups.[7]

We reported before[8—11] the 1,3-dipolar cycloaddition reactions of nitrile oxides with various *p*-benzoquinones, which have two kinds of potentially reactive sites, one is the carbon–oxygen double bond and the other the carbon–carbon double bond. Depending on the number, pattern, combination and kind of the substituents of the quinones, two different types of the adducts were obtained in the reactions. One is the C=O addition product, *i.e.* spiro[1, 4, 2]dioxazole derivative and the other is the C=C addition product, *i.e.* isoxazoline derivative. We tried to account for the site-selectivity and reactivity of the quinones, and also the regio-selectivity in the C=C addition reactions in terms of FMO theory. This paper describes the calculation of the energy levels of FMO's and the coefficients of FMO's on the atoms of nitrile oxides and substituted *p*-benzoquinones, and correlates the experimental results with the calculation.

## Results and Discussion

The following were studied: nitrile oxides: 2,4,6-trimethylbenzonitrile oxide (**1a**) and 2,6-dichlorobenzonitrile oxide (**1b**); quinones: 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (**2a**), tetrafluoro-*p*-benzoquinone (**2b**), tetrachloro-*p*-benzoquinone (**2c**), tetramethyl-*p*-benzoquinone (**2d**), tetramethoxy-*p*-benzoquinone (**2e**), 2,6-dichloro-*p*-benzoquinone (**2f**), 2-methyl-*p*-benzoquinone (**2g**), 2,5-dimethyl-*p*-benzoquinone (**2h**), and 2,6-dimethyl-*p*-benzoquinone (**2i**), 2,5,6-trimethyl-*p*-benzoquinone (**2j**). The structures are shown in Fig. 1. The reactions of **1a** with **2a—f** has been known to give 1,4,2-dioxazole derivatives through C=O addition and those with **2g—i** isoxazoline derivatives through C=C addition. The reactions of **1b** gave similar results, except with **2d—f** as will be discussed later. This kind of site-selectivity and the orientation of the addition (regio-selectivity in C=C addition) are to be accounted for and predicted.



| 2 | a | b | c | d | e | f | g | h | i | j |
|---|---|---|---|---|---|---|---|---|---|---|
| $R_2$ | CN | F | Cl | Me | MeO | Cl | Me | Me | Me | Me |
| $R_3$ | CN | F | Cl | Me | MeO | H | H | H | H | H |
| $R_5$ | Cl | F | Cl | Me | MeO | H | H | Me | H | Me |
| $R_6$ | Cl | F | Cl | Me | MeO | Cl | H | H | Me | Me |

Fig. 1.

*Ab Initio SCF Calculation.* The FMO calculations on nitrile oxides, not only fulminic acid but also aromatic nitrile oxides, by semiempirical methods have been reported.[1,5] The calculation by nonempirical method has been reported only for fulminic acid[12] and no calculations for aromatic nitrile oxides have been reported as far as we know.

On the other hand, the calculations for several *p*-benzoquinones by *ab initio* method have been reported by Rozemboom *et al.*,[13] though only the one for 2-methyl-*p*-benzoquinone is available for our study. We calculated the FMO's of nitrile oxides and substituted *p*-benzoquinones by *ab initio* SCF method with STO-3G basis set.[14]

The calculation for nitrile oxides were carried out using the bond lengths (in nm) 0.1436 for C–C, 0.1147 for C–N, and 0.1243 for N–O, which are the averaged values of the X-ray results for 4-methoxy-2,6-dimethyl- and 4-bromo-2,6-dimethylbenzonitrile oxides.[15] Other geometries used are standard ones given by Pople and Gordon.[16] The methyl substituents of **1a** can have various conformations. We computed the energies for several representative conformations of the methyl groups and selected and used the most stable one for the FMO calculation. When one hydrogen of the methyl group is placed in the same plane as the aromatic nucleus of the nitrile oxides, the energy of FMO's does not exceed that of the most stable conformation by more than 0.1 eV.

The energy values and coefficient magnitudes of FMO's of nitrile oxides are given in Table 1, together with the negative values of the ionization potential (experimentally estimated HOMO energies).[12,17,18] The orderings of the calculated HOMO energy and the experimentally estimated ones are the same. Our calculation on fulminic acid gave nearly the same energy values as the one (HOMO −7.69 eV) reported by *ab initio* method. From fulminic acid to **1b**, the

TABLE 1. ENERGY LEVELS AND COEFFICIENTS OF FMO OF NITRILE OXIDES

| Nitrile oxide | FMO | ε/eV | | Cα[b)] | C | N | O |
|---|---|---|---|---|---|---|---|
| | | Calcd | Exptl[a)] | | | | |
| HCNO | LUMO | 8.66 | | — | 0.82 | −0.80 | 0.43 |
| | HOMO | −7.61 | −10.83 | — | 0.54 | 0.14 | −0.84 |
| phCNO | LUMO | 5.33 | | 0.53 | 0.27 | −0.42 | 0.29 |
| | HOMO | −6.42 | −8.96 | −0.26 | 0.44 | 0.20 | −0.72 |
| **1a** | LUMO | 5.58 | | 0.50 | 0.27 | −0.42 | 0.28 |
| | HOMO | −6.12 | −8.35 | −0.32 | 0.41 | 0.21 | −0.69 |
| **1b** | LUMO | 4.43 | | 0.55 | 0.22 | −0.40 | 0.29 |
| | HOMO | −6.89 | — | −0.24 | 0.46 | 0.18 | −0.73 |

a) These are the negative values of the ionization potentials. b) This carbon connects with the dipole moiety.

calculated values well reflect the substituent effect. The phenyl group of benzonitrile oxide, which is a conjugative group, raises HOMO energy and lowers LUMO energy. Substitution on benzonitrile oxide with methyl groups, which are electron-releasing groups, raise both HOMO and LUMO energies; the increase in HOMO is larger than that of LUMO (**1a**). Chlorine atoms lower both HOMO and LUMO energies. The decrease in LUMO is larger than that of HOMO as a result of mixing of electron-withdrawing and -releasing natures (**1b**). Furthermore, inspection of Table 1 reveals that the nodal positions and the ordering of the magnitudes of the atomic orbital coefficients are preserved in all four calculated nitrile oxides.

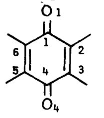
The results of the calculations of the substituted *p*-benzoquinones are listed in Table 2. The geometries of quinones, *p*-benzoquinone, **2a**, **2b**, **2c**, and **2f** are those of X-ray results.[19)] In the cases of methyl- and methoxy-substituted quinones, such as **2d**, **2e**, **2g**, **2h**, **2i**, and **2j**, the methyl group can take various conformations. The conformation of methyl group of **2g** used for the calculation is the same one as reported by Rozemboom *et al.*[13)] and those for **2d**, **2e**, **2h**, **2i**, and **2j** are the most stable ones estimated by computation in the same way as in the case of **1a**. The geometries of quinone moieties of **2g**, **2h**, **2i**, and **2j** are derived from that of *p*-benzoquinone,[19)] and those of **2d** and **2e** are X-ray results.[20)] The electron affinities of these quinones[21)] are also listed in Table 2. The tendency is in good accordance with that of the calculated values. The substituent effects to FMO's energies are also reasonable.

Our calculation values and those reported by Rozemboom *et al.*[13)] for *p*-benzoquinone and 2-methyl-

TABLE 2. ENERGY LEVELS AND COEFFICIENTS OF FMO OF SUBSTITUTED *p*-BENZOQUINONES

| Quinone | FMO | ε/eV | | $C_1$ | $C_2$ | $C_3$ | $C_4$ | $C_5$ | $C_6$ | $O_1$ | $O_4$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Calcd | Exptl[a)] | | | | | | | | |
| *p*-Benzo-quinone | LUMO | 3.74 | −1.91 | −0.30 | −0.34 | 0.34 | 0.30 | 0.34 | −0.34 | 0.49 | −0.49 |
| | HOMO | −8.23 | | 0.20 | −0.34 | −0.34 | 0.20 | −0.34 | −0.34 | 0.44 | 0.44 |
| **2a** | LUMO | 1.61 | −3.07 | −0.24 | −0.25 | 0.25 | 0.24 | 0.43 | −0.43 | 0.44 | −0.44 |
| | HOMO | −9.34 | | 0.10 | −0.45 | −0.45 | 0.10 | −0.12 | −0.12 | 0.30 | 0.30 |
| **2b** | LUMO | 3.02 | −2.45[b)] | −0.32 | −0.31 | 0.31 | 0.32 | 0.31 | −0.31 | 0.50 | −0.50 |
| | HOMO | −8.30 | | 0.13 | −0.33 | −0.33 | 0.13 | −0.33 | −0.33 | 0.39 | 0.39 |
| **2c** | LUMO | 2.21 | −2.49 | −0.28 | −0.35 | 0.35 | 0.28 | 0.35 | −0.35 | 0.48 | −0.48 |
| | HOMO | −9.40 | | 0.12 | −0.32 | −0.32 | 0.12 | −0.32 | −0.32 | 0.34 | 0.34 |
| **2d** | LUMO | 4.20 | −1.66 | −0.32 | −0.33 | 0.33 | 0.32 | 0.33 | −0.33 | 0.48 | −0.48 |
| | HOMO | −7.44 | | 0.16 | −0.35 | −0.35 | 0.16 | −0.35 | −0.35 | 0.42 | 0.42 |
| **2e** | LUMO | 4.24 | | −0.36 | −0.30 | 0.28 | 0.36 | 0.30 | −0.28 | 0.48 | −0.48 |
| | HOMO | −6.08 | | 0.05 | −0.30 | −0.32 | 0.05 | −0.30 | −0.32 | 0.32 | 0.32 |
| **2f** | LUMO | 2.78 | −2.77 | −0.30 | −0.34 | 0.34 | 0.28 | 0.34 | −0.34 | 0.49 | −0.48 |
| | HOMO | −8.83 | | 0.13 | −0.31 | −0.33 | 0.18 | −0.33 | −0.31 | 0.35 | 0.42 |
| **2g** | LUMO | 3.85 | −1.83 | −0.32 | −0.33 | 0.32 | 0.30 | 0.35 | −0.34 | 0.50 | −0.48 |
| | HOMO | −8.03 | | 0.17 | −0.38 | −0.41 | 0.20 | −0.28 | −0.28 | 0.42 | 0.45 |
| **2h** | LUMO | 3.97 | −1.78 | −0.31 | −0.34 | 0.32 | 0.31 | 0.34 | 0.32 | 0.49 | −0.49 |
| | HOMO | −7.89 | | 0.18 | −0.33 | −0.36 | 0.18 | −0.33 | −0.36 | 0.43 | 0.43 |
| **2i** | LUMO | 3.96 | −1.66 | −0.33 | −0.33 | 0.33 | 0.29 | 0.33 | −0.33 | 0.50 | −0.48 |
| | HOMO | −7.88 | | 0.16 | −0.34 | −0.35 | 0.20 | −0.35 | −0.34 | 0.41 | 0.45 |
| **2j** | LUMO | 4.06 | −1.74[b)] | −0.31 | −0.33 | 0.34 | 0.32 | 0.31 | −0.32 | 0.48 | −0.49 |
| | HOMO | −7.70 | | 0.17 | −0.28 | −0.26 | 0.15 | −0.41 | −0.41 | 0.43 | 0.41 |

a) The values are the negatives of the average of the EA's determined from reduction potentials and charge-transfer spectra except **2b** and **2j**. b) The values are the negatives of EA's determined from reduction potentials. c) The numbering of the atoms is the following:



*p*-benzoquinone are nearly the same, the difference is due to the difference in the geometry of the quinone moiety which was employed.

*C=O Addition.* Figure 2 shows the FMO energy levels of the nitrile oxides and the quinones. The quinones **2a**—**f**, which have been found to undergo C=O addition with **1a**, have very low LUMO energy values, except for **2d** and **2e**. The energy difference between the HOMO of **1a** and the LUMO of the quinones is smaller than that between the LUMO of **1a** and the HOMO of the quinones by more than about 5 eV, except in the cases of **2d** and **2e**. This energetical analysis clearly suggests that the HOMO (nitrile oxide)-LUMO (quinone) interaction is the governing factor of C=O addition. This suggests that the reactions of **1b** with **2a**—**c** give C=O adducts; this is indeed the case. The reactions of **1b** with **2d**—**f** will be discussed later.

The kinetic data of these reactions also supports this suggestion. Reaction rate constants measured by a UV method at 20 °C⁽¹⁰⁾ (Table 3) show that quinone **2a**, which has the lowest LUMO energy value, reacts most rapidly, and also that the rate in the reactions of **1b** with **2a**—**c** is always slower than that of **1a** with the corresponding quinones. This is reflecting the fact that **1b** has a lower HOMO energy value than **1a** by 0.65 eV.

*C=C Addition.* The quinones **2g**—**j** have been known to undergo C=C addition with **1a**, and their FMO energy levels are higher than those of quinones **2a**—**f**, except **2d** and **2e**, as shown in Fig 1. In addition, *p*-benzoquinone, which has been reported to undergo C=C addition with benzonitrile oxide,[22] has nearly the same FMO levels as the quinones **2g**—**j** and was confirmed to undergo C=C addition with **1a** and **1b** as described in the Experimental section. The energy differences between the two possible interactions are far smaller than those in the cases mentioned in the preceding section and are less than 3.9 eV with **1a** and less than 2.0 eV with **1b**. The participation of LUMO(nitrile oxide)-HOMO(quinone) interaction is considered to become important to some extent in these reactions.

The reaction rate constants were also measured as shown in Table 3. Contrary to the C=O addition, the reaction rate of the C=C addition of **1b** with **2h**—**j** is shown to be always faster than the corresponding one of **1a**. This indicates that the orbital interactions exerted different effects from those in C=O addition. We should take note of not only the decrease of the HOMO level of **1b** but also that of the LUMO level. As mentioned above, the decrease of the HOMO level of **1b** is only 0.65 eV, but that of the LUMO level is 1.09 eV. Because of this large decrease in LUMO of **1b**, the ener-

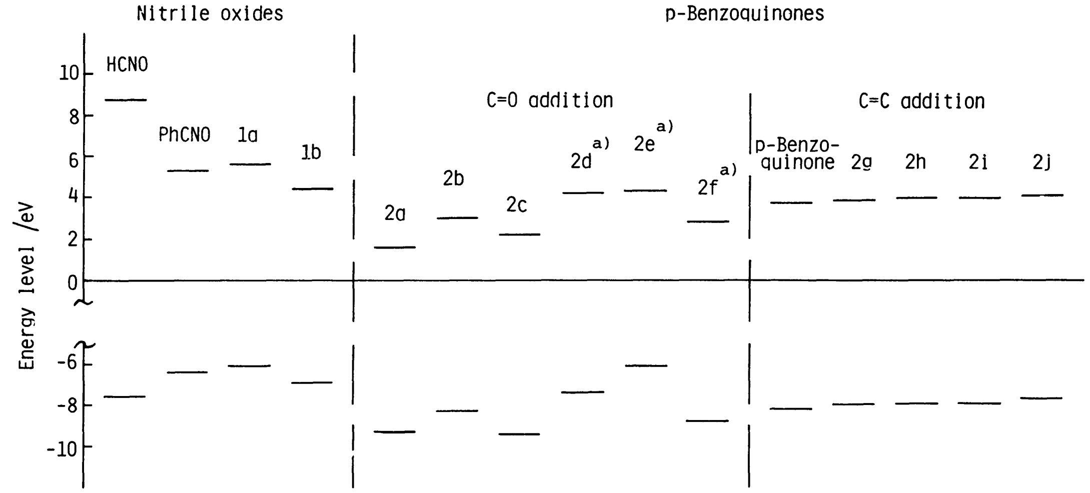


Fig. 2. Energy levles of HOMO and LUMO of nitrile oxides and substituted *p*-benzoquinones calculated by *ab initio* SCF method with STO-3G basis set.
a) The reaction with la gives C=O adduct.

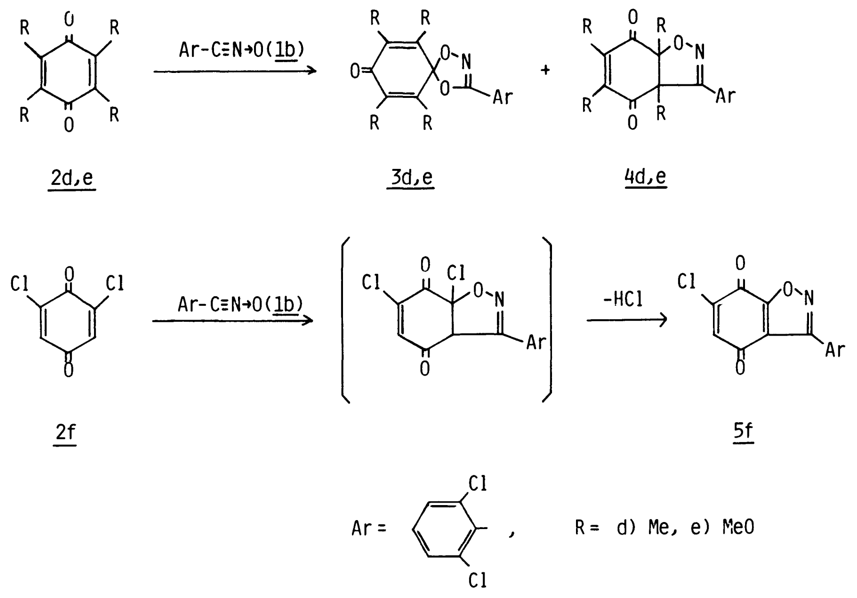
Table 3. Rate constants for the reactions of nitrile oxides with quinones

| Quinone | Solvent | $k$/l mol$^{-1}$ s$^{-1}$ With **1a**$^{a)}$ | $k$/l mol$^{-1}$ s$^{-1}$ With **1b** | Mode |
|---|---|---|---|---|
| **2a** | $CHCl_3$ | 3.52 | $5.98\times10^{-2}$ | C=O |
| | $C_6H_6$ | $5.60\times10^{-1}$ | $3.60\times10^{-3}$ | |
| **2b** | $CHCl_3$ | $5.18\times10^{-2}$ | $1.15\times10^{-3}$ | C=O |
| **2c** | $CHCl_3$ | $1.59\times10^{-2}$ | $7.09\times10^{-4}$ | C=O |
| **2h** | $CHCl_3$ | $4.77\times10^{-4}$ | $2.36\times10^{-3}$ | C=C |
| | $C_6H_6$ | $9.30\times10^{-4}$ | $4.94\times10^{-3}$ | |
| **2i** | $CHCl_3$ | $1.33\times10^{-3}$ | $4.50\times10^{-3}$ | C=C |
| | $C_6H_6$ | $1.50\times10^{-3}$ | $5.26\times10^{-3}$ | |
| **2j** | $C_6H_6$ | $4.35\times10^{-4}$ | $2.60\times10^{-3}$ | C=C |

a) The values for **2a**—**c** measured in $CHCl_3$ are reported ones.⁽¹⁰⁾

TABLE 4. THE ENERGY DIFFERENCE BETWEEN LUMO(NITRILE OXIDES)–HOMO(QUINONES) AND HOMO(NITRILE OXIDES)–LUMO(QUINONES) INTERACTION

| | **2a** | **2b** | **2c** | **2d** | **2e** | **2f** | *p*-Benzoquinone | **2g** | **2h** | **2i** | **2j** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1a** | 7.19 | 4.74 | 6.65 | 2.70 | 1.30 | 5.51 | 3.90 | 3.64 | 3.38 | 3.38 | 3.10 |
| **1b** | 5.27 | 2.82 | 4.73 | 0.78 | −0.62 | 3.59 | 2.03 | 1.72 | 1.46 | 1.46 | 1.18 |



Scheme 1.

gy gain by LUMO (**1b**)–HOMO (quinone) interaction overcomes the energy loss by the HOMO (**1b**)–LUMO (quinone) interaction. This result suggests that in the reactions giving C=C adducts LUMO (nitrile oxide)–HOMO (quinone) interaction is more significant than the opposite interaction. Usually *p*-benzoquinones are thought to be electron acceptor and known to form CT complexes with many electron donors. The reactivity and selectivity of the reactions involving *p*-benzoquinones are known to be dominated by the interaction of LUMO of quinones and HOMO of nucleophiles or dienes. But in the reactions discussed here, HOMO of quinones participates in the reactions to some extent, and quinones appear to behave as if electron donors.

We show in Table 4 the energy difference between LUMO (nitrile oxide)–HOMO (quinone) and HOMO (nitrile oxide)–LUMO (quinone) interaction. The results with **1a** shows that, if the energy difference is larger than 5 eV, C=O addition will occur, and if the energy difference is less than 4 eV, C=C addition will occur, except for the cases of **2d** and **2e**. This energetical analysis predicts that the reaction of **1b** with **2f** will give C=C adduct because the energy difference is less than 4 eV. Moreover it is expected that the reaction pattern of **1b** with **2d** and **2e** will be different from that of **1a**.

In fact, **1b** underwent C=C addition with **2f** and not C=O addition. As shown in Scheme 1, isoxazoloquinone **5f** was formed in the reaction *via* C=C addition and subsequent dehydrochlorination. The structure of the product **5f** was determined by spectral data; the characterization is described in the Experimental section.

The reactions of **1b** with **2d** and **2e** were also found to proceed in a different mode from those of **1a**. Compound **1b** underwent both C=C and C=O additions with **2d** and **2e**. The results are shown in Scheme 2. The characterization of the adducts is also described in the Experimental section. Though the yields were low, the reactions were clean and no other products were detected. This is the first case of the isolation of C=C adducts in the reactions of nitrile oxides with tetrasubstituted *p*-benzoquinones and of the competitive reactions of C=C and C=O additions. Compound **2d** has FMO levels very close to those of the quinones **2g—j**, while **2e** has very close LUMO to those of **2g—j**, but a much higher HOMO level. The energy difference between the two possible interactions of **1b** with **2d** is less than 1 eV. For tetrasubstituted *p*-benzoquinones, the steric hindrance cannot be neglected. Actually, tetrafluoro-*p*-benzoquinone (**2b**) underwent only C=O addition with **1b** despite the energy difference being smaller than 4 eV. The reaction of tetramethoxy-*p*-benzoquinone (**2e**) is not clearly understood by considering the steric effect only. The higher orbital interactions involving methoxy groups may have to be considered in the interpretation of the experimental result, for which further study is needed.

*Accounts for the Selectivity.* In the 1,3-dipolar cycloaddition reactions, the square of the products of the coefficients of the interacting atoms and resonance integral (CaCbβab) should be taken into consideration, as discussed by Houk.[1] But such an approach to rationalize the site-selectivity may be applicable only for the specific addition to a bond among the same kinds of unsaturated bonds, and not among the different kinds of unsaturated bonds. Furthermore there are many factors which cannot be neglected: for example, Coulombic repulsion, and we cannot exactly estimate the extent of the importance of the factors.

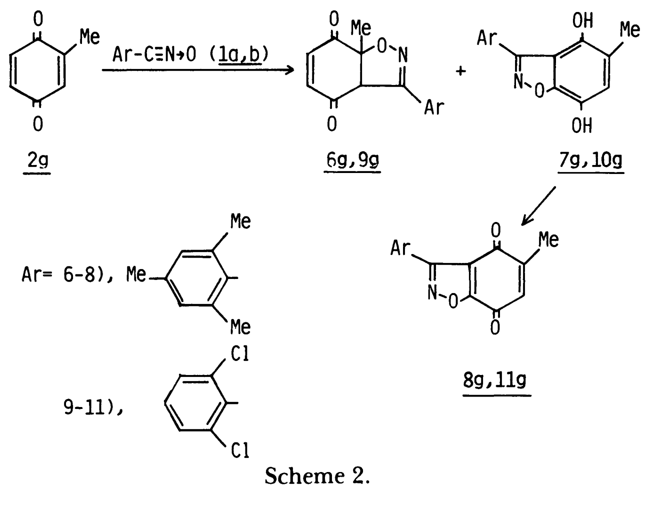
In the reactions giving C=O adducts, which is considered to be chiefly governed by the HOMO (nitrile oxide)–LUMO (quinone) interaction, Coulombic repulsion is thought to play a significant role. The regioselectivity of the C=O addition is clearly influenced by Coulombic repulsion but not by the overlap of the orbitals.

2,6-Dichloro-*p*-benzoquinone (**2f**) has two different C=O sites and undergoes C=O addition onto the carbonyl group of chlorine-substituted side exclusively.[9] This site-selectivity among the two C=O addition sites has been interpreted in terms of LFER theory.[10] This can also be treated by considering the primary interactions in FMO theory, *i.e.* comparison in the sum of the square of the product of the coefficients of interacting atoms and resonance integral $(C_CC_O\beta_{CO})$[1] for two possible interaction shows that the value for the addition to the substituted side (2.41) is larger than that to the unsubstituted side (2.20).

The reactions giving C=C adducts are thought to be governed chiefly by the LUMO(nitrile oxide)–HOMO (quinone) interaction. Considering this interaction, one notes that the coefficients on the carbon atom are nearly equal in **1a** or less in **1b** than those on the terminal oxygen atom. But by taking into consideration the secondary orbital interaction with the $\alpha$-carbon connecting with the nitrile oxide moiety,[5,23] regio-selectivity can be explained.

For the purpose of the study of the selectivities of the reactions, we tried the reactions of nitrile oxides with 2-methyl-*p*-benzoquinone (**2g**), which has two types of carbon–carbon double bond. The C=C adduct added on the methyl-substituted side was isolated in the reactions and the formation of the adduct added on the other side was only suggested.[11] Here we could confirm the formation of the two C=C adducts by derivating the latter to the corresponding isoxazoloquinone (**8g** or **11g**) by oxidation, as shown in Scheme 2. The characterization of the adducts will be described in the Experimental section.

The quinone **2g** has a larger coefficient magnitude on the carbon atoms of the methyl-substituted C=C bond. The most efficient overlap of the orbitals of interacting atoms leads to the products **6g** or **9g**. The interaction leading to products **7g** or **10g** has not so efficient an overlap, and the yields of **6g** and **9g** are thought to become much larger than those of **7g** and **10g**. In fact, the yield of **6g** or **9g** is larger but not so much, which is thought to be due to the steric effect of the methyl group. In the reactions with 2,5,6-trimethyl-*p*-benzoquinone (**2j**), the cycloaddition occurred onto only the less hindered side,[11] though the coefficients of HOMOs' of the carbon atoms at the hindered side are larger than those at the less hindered side.



Scheme 2.

The orientation of the C=C addition with quinones **2f—j**[11] is in accordance with the theory that the most efficient overlap of the interacting orbitals includes secondary orbital interaction of LUMO of nitrile oxides with HOMO of quinones, as mentioned before.

In conclusion we can classify the substituted *p*-benzoquinones into two groups: One is a group giving C=O adducts, the reaction of which is chiefly governed by HOMO (nitrile oxide)–LUMO (quinone) interaction, and the other is that giving C=C adducts, the reaction of which is chiefly governed by LUMO (nitrile oxide)–HOMO (quinone) interaction. The borderline-energy-difference between two interactions may be about 4 eV, having some exceptions. Some quinones such as **2d** and **2e** gave both C=C and C=O adducts competitively in the reactions with **1b**.

## Experimental

Melting points were measured using a micro-melting-point-measuring apparatus (Yazawa Co., Ltd.) and are uncorrected. Column chromatography was conducted on silica gel (Wako gel C-200) with benzene as an eluent. IR spectra were recorded with a JASCO IRA-1 spectrophotometer. UV spectra were recorded with a JASCO UVIDEC-505 spectrophotometer. $^1$H NMR spectra were measured in CDCl$_3$ with a JEOL JMN-MH 100 spectrometer, and chemical shifts are reported in ppm from internal tetramethylsilane. Mass spectra were recorded with a Hitachi RMU-7L high resolution mass spectrometer.

*Materials.* 2,4,6-Trimethylbenzonitrile oxide (**1a**) and 2,6-dichlorobenzonitrile oxide (**1b**) were prepared by the method of Grundmann.[24] *p*-Benzoquinone, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (**2a**), tetrafluoro-*p*-benzoquinone (**2b**), tetrachloro-*p*-benzoquinone (**2c**), tetramethyl-*p*-benzoquinone (**2d**), and 2-methyl-*p*-benzoquinone (**2g**) were commercially obtained and were used after recrystallization. Tetramethoxy-*p*-benzoquinone (**2e**) was prepared by the method of Robinson and Vasey.[25] 2,5-Dimethyl-*p*-benzoquinone (**2h**), 2,6-dimethyl-*p*-benzoquinone (**2i**), and 2,5,6-trimethyl-*p*-benzoquinone (**2j**) were prepared by the method described in the previous paper.[11]

*Reactions of 2,4,6-Trimethylbenzonitrile Oxide (**1a**) and 2,6-Dichlorobenzonitrile Oxide (**1b**) with* p*-Benzoquinone.* A solution of 0.806 g (5 mmol) of **1a** and 1.081 g (10 mmol) of *p*-benzoquinone in 100 ml benzene was stirred for 3 d at room temperature. Solvent was then evaporated under reduced pressure, and the residue was subjected to column chromatography. 3-(2,4,6-Trimethylphenyl)-1,2-benzisoxazole-4,7-dione (0.853 g 64%) was obtained and the recrystallization was carried out from benzene–hexane. Mp 130—132 °C. IR (KBr) 1670 and 1680 cm$^{-1}$ ($\nu_{C=O}$). $^1$H NMR (CDCl$_3$) $\delta$=2.07 (s, 6H, mesityl *o*-methyl), 2.35 (s, 3H, mesityl *p*-methyl), 6.74 (d, 1H, olefinic), 6.89 (d, 1H, olefinic), and 6.96 (s, 2H, aromatic).

Found: C, 71.79; H, 4.80; N, 5.49%. Calcd for $C_{16}H_{13}N_1O_3$: C, 71.65; H, 4.89; N, 5.22%.

The reaction of 2,6-dichlorobenzonitrile oxide (**1b**) with *p*-benzoquinone was conducted and worked up in a similar manner. 3-(2,6-dichlorophenyl)-1,2-benzisoxazole-4,7-dione (73%). Mp 178—180 °C. IR (KBr) 1670 and 1680 cm$^{-1}$ ($\nu_{C=O}$) $^1$H NMR ($CDCl_3$) $\delta=6.78$ (d, 1H, olefinic), 6.87 (d, 1H, olefinic), and 7.42 (s, 3H, aromatic).

Found: C, 52.89; H, 1.53; N, 4.70%. Calcd for $C_{13}H_5N_1O_3Cl_2$: C, 53.09; H, 1.71; N, 4.76%.

*Reaction of 2,6-Dichlorobenzonitrile Oxide (1b) with Tetramethyl-p-benzoquinone (2d).* A solution of 0.503 g (3 mmol) of **1b** and 0.574 g (3 mmol) of **2d** in 60 ml of benzene was stirred for about one month at room temperature. The solvent was evaporated under reduced pressure, and the residue was worked up with column chromatography. The first fraction gave a mixture of starting materials and **3d**. The residue was recrystallized from benzene–hexane to give 3-(2,6-dichlorophenyl)-6,7,9,10-tetramethyl-2-aza-1,4-dioxaspiro[4.5]deca-2,6,9-trien-8-one (**3d**), (0.14 g 13%). Mp 204—205 °C. IR (KBr) 1665 cm$^{-1}$ ($\nu_{C=O}$)$^1$H NMR ($CDCl_3$) $\delta=1.97$ (s, 6H, methyl), 2.24 (s, 6H, methyl), and 7.47 (s, 3H, aromatic). $M^+$ (351.0361) was observed as a very weak signal, and fragment ion peaks at $m/z$ 186.9574 and 164.0841 arising from the starting component (*i. e.* the nitrile oxide and the quinone) were very intensive in the mass spectrum. The fragmentation pattern is characteristic of C=O adducts.

Found: C, 58.03; H, 4.31; N, 3.92%; $M^+$, 351.0361. Calcd for $C_{17}H_{15}N_1O_3Cl_2$: C, 57.97; H, 4.29; N, 3.98%; $M^+$, 351.0431.

The second fraction gave yellow needles of 3-(2,6-dichlorophenyl)-3a,5,6,7a-tetramethyl-3a,7a-dihydro-1,2-benzisoxazole-4,7-dione (**4d**), (0.14 g 13%), which was recrystallized from benzene–hexane. Mp 135—136 °C. IR (KBr) 1670 and 1710 cm$^{-1}$ ($\nu_{C=O}$)$^1$H NMR ($CDCl_3$) $\delta=1.53$ (s, 3H, methyl), 1.59 (s, 3H, methyl), 1.97 (s, 3H, methyl), 2.07 (s, 3H, methyl), and 7.31 (s, 3H, aromatic). $M^+$ was not observed but characteristic fragmentation of the C=C adducts, which was the elimination of angular methyl and CO, was observed in the mass spectrum.

Found: C, 57.84; H, 4.38; N, 3.91%. Calcd for $C_{17}H_{15}N_1O_3Cl_2$: C, 57.97; H, 4.29; N, 3.98%.

*Reaction of 2,6-Dichlorobenzonitrile Oxide (1b) with Tetramethoxy-p-benzoquinone (2e).* The reaction was conducted and worked up in the same manner as the above. The second fraction gave 3-(2,6-dichlorophenyl)-3a,5,6,7a-tetramethoxy-3a,7a-dihydro-1,2-benzisoxazole-4,7-dione (**4e**), (27%). Mp 174—176 °C. IR (KBr) 1685 and 1700 cm$^{-1}$ ($\nu_{C=O}$) $^1$H NMR ($CDCl_3$) $\delta=3.27$ (s, 3H, methoxyl methyl), 3.84 (s, 3H, methoxyl methyl), 4.04 (s, 3H, methoxyl methyl), 4.06 (s, 3H, methoxyl methyl), and 7.31 (s, 3H, aromatic).

Found: C, 48.85; H, 3.65; N, 3.34%; $M^+$, 415.0302. Calcd for $C_{17}H_{15}N_1O_7Cl_2$: C, 49.06; H, 3.63; N, 3.37%; $M^+$, 415.0227.

The third fraction gave 3-(2,6-dichlorophenyl)-6,7,9,10-tetramethoxy-2-aza-1,4-dioxaspiro[4.5]deca-2,6,9-trien-8-one (**3e**), (13%). Mp 163—164 °C. IR (KBr) 1650 cm$^{-1}$ ($\nu_{C=O}$)$^1$H NMR ($CDCl_3$) $\delta=3.70$ (s, 6H, methoxyl methyl), 4.12 (s, 6H, methoxyl methyl), and 7.38 (s, 3H, aromatic). $M^+$ was not observed, but fragment ion peaks at $m/z$ 186.9576 and 288.0625 arising from the starting component (*i.e.* the nitrile oxide and the quinone) were very intense in the mass spectrum.

Found: C, 49.12; H, 3.62; N, 3.42%. Calcd for $C_{17}H_{15}N_1O_7Cl_2$: C, 49.06; H, 3.63; N, 3.37%.

*Reaction of 2,6-Dichlorobenzonitrile Oxide (1b) with 2,6-Dichloro-p-benzoquinone (2f).* A solution of 0.94 g (5 mmol) of **1b** and 0.885 g (5 mmol) of **2f** in 100 ml benzene was stirred for 3d at room temperature. Then the solvent was evaporated under reduced pressure. The residue was worked up with column chromatography. The first fraction gave 3-(2,3-dichlorophenyl)-6-chloro-1,2-benzisoxazole-4,7-dione (**5f**), (1.14 g 63%), which was recrystallized from hexane. Mp 142—145 °C. IR (KBr) 1680 and 1700 cm$^{-1}$ ($\nu_{C=O}$)$^1$H NMR ($CDCl_3$) $\delta=7.05$ (s,1H, olefinic), and 7.46 (s, 3H, aromatic). The mass spectrum shows the elimination of CO from the parent ion, which is a characteristic pattern of C=C adduct.

Found: C, 47.48; H, 1.19; N, 4.53%. Calcd for $C_{13}H_4N_1O_3Cl_3$: C, 47.53; H, 1.22; N, 4.26%.

*Reaction of 2,4,6-Trimethylbenzonitrile Oxide (1a) with 2-Methyl-p-benzoquinone (2g).* A solution of **1a** 0.805 g (5 mmol) and **2g** 0.61 g (5 mmol) in 100 ml of benzene was stirred for about one week at room temperature. The solvent was evaporated under reduced pressure, and the residue was subjected to column chromatography. The first fraction gave the mixture of **1a** and **2g**. The second fraction gave the yellow crystals of 3-mesityl-7a-methyl-3a,7a-dihydro-1,2-benzisoxazole-4,7-dione (**6g**), (0.48 g 34%), which was recrystallized from benzene–hexane. Mp 137—139 °C. IR (KBr) 1680 and 1700 cm$^{-1}$ ($\nu_{C=O}$) $^1$H NMR ($CDCl_3$) $\delta=1.62$ (s, 3H, angular methyl), 2.16—2.43 (m, 9H, mesityl methyl), 4.30 (s, 1H, angular methine), 6.72 (d, 1H, olefinic), 6.94 (d, 1H, olefinic), and 6.84 (s, 2H, aromatic).

Found: C, 72.02; H, 6.15; N, 5.17%. Calcd for $C_{17}H_{17}N_1O_3$: C, 72.07; H, 6.04; N, 4.94%.

The third fraction gave a glassy mass which was assumed to be 3-mesityl-5-methyl-1,2-benzoisoxazole-4,7-diol (**7g**), which can not be isolated as a pure state, from its IR spectrum ($\nu_{OH}$ at about 3200 cm$^{-1}$). Oxidation of **7g** was conducted with sodium dichromate in the presence of sulfuric acid in benzene–water mixture with vigorous stirring. The reaction mixture was extracted from benzene. The extract was dried over anhydrous sodium sulfate. Evaporation of the solvent gave 3-mesityl-5-methyl-1,2-benzisoxazole-4,7-dione (**8g**), (0.28 g 20%). The recrystallization was carried out from benzene–hexane. Mp 139—141 °C. IR (KBr) 1670 and 1680 cm$^{-1}$ ($\nu_{C=O}$) $^1$H NMR ($CDCl_3$) $\delta=2.12$ (s, 6H, mesityl *o*-methyl), 2.24 (s, 3H, methyl), 2.37 (s, 3H, mesityl *p*-methyl), 6.65 (s, 1H, olefinic), and 7.00 (s, 2H, aromatic).

Found: C, 72.96; H, 5.55; N, 4.55%. $M^+$, 281.1084. Calcd for $C_{17}H_{15}N_1O_3$: C, 72.58; H, 5.37; N, 4.98%. $M^+$, 281.1053.

*The Reaction of 2,6-Dichlorobenzonitrile Oxide (1b) with 2-Methyl-p-benzoquinone (2g).* The reaction was conducted and worked up in the same manner as the above.

3-(2,6-Dichlorophenyl)-7a-methyl-3a,7a-dihydro-1,2-benzisoxazole-4,7-dione (**9g**), (47%). Mp 175—177 °C. IR (KBr) 1680 and 1700 cm$^{-1}$ ($\nu_{C=O}$) $^1$H NMR ($CDCl_3$) $\delta=1.77$ (s, 3H, angular methyl), 4.51 (s, 1H, angular methine), 6.89 (d, 1H, olefinic), 7.06 (d, 1H, olefinic), and 7.42 (s, 3H, aromatic).

Fonud: C, 54.41; H, 2.87; N, 4.90%. Calcd for $C_{14}H_9N_1O_3Cl_2$: C, 54.22; H, 2.92; N, 4.52%.

3-(2,6-dichlorophenyl)-5-methyl-1,2-benzisoxazole-4,7-dione (**11g**), (31%). Mp 215—217 °C. IR (KBr) 1680 and 1685 cm$^{-3}$ ($\nu_{C=O}$). $^1$H NMR ($CDCl_3$) $\delta=2.14$ (s, 3H, methyl), 6.71 (s, 1H, olefinic), and 7.43 (s, 3H, aromatic).

Found: C, 54.98; H, 2.13; N, 4.63%; $M^+$, 306.9720. Calcd for $C_{14}H_7N_1O_3Cl_2$: C, 54.54; H, 2.29; N, 4.55%; $M^+$, 306.9804.

*The Reactions of 1b with 2a—c*: The reaction was carried out using 2.5 mmol of each reactant in chloroform at room temperature for 1 d and worked up in the same manner as the above. The product of each reaction follows. The reaction gave exclusively spiro[1,4,2]dioxazole derivatives.

6,7-Dichloro-9,10-dicyano-3-(2,6-dichlorophenyl)-2-aza-1,4-dioxaspiro[4.5]deca-2,6,9-trien-8-one. Yield 77%. Mp 172—174 °C. IR (KBr) 1700 cm$^{-1}$ ($\nu_{C=O}$). Found: C, 43.61; H, 0.79; N, 9.86%. Calcd for $C_{15}H_3N_3O_3Cl_4$: C, 43.41; H, 0.73; N, 10.12%.

6,7,9,10-Tetrafluoro-3-(2,6-dichlorophenyl)-2-aza-1,4-dioxaspiro[4.5]deca-2,6,9-trien-8-one. Yield 92%. Mp 148—150 °C. IR (KBr) 1700 cm$^{-1}$ ($\nu_{C=O}$). Found: C, 42.70; H, 0.71; N, 3.96%. Calcd for $C_{13}H_3N_1O_3Cl_2F_4$: C, 42.42; H, 0.82; N, 3.81%.

6,7,9,10-Tetrachloro-3-(2,6-dichlorophenyl)-2-aza-1,4-dioxaspiro[4.5]deca-2,6,9-trien-8-one. Yield 88%. Mp 165—167 °C. IR (KBr) 1695 cm$^{-1}$ ($\nu_{C=O}$). Found: C, 36.34; H, 0.57; N, 3.34%. Cacld for $C_{13}H_3N_1O_3Cl_6$: C, 35.99; H, 0.70; N, 3.23%.

*Kinetic Study.* The reaction rate constants were measured by UV method at 20 °C.[10] As the solvent, benzene and chloroform were used. Equimolar portions of the solutions of a nitrile oxide and a quinone were placed in a quartz cell for UV measurement and the progress of the reaction was followed by the spectral change at the absorption maximum of the quinone or of the adduct formed. The concentration of the reactants was about (2—4)×10$^{-3}$ mol l$^{-1}$ in C=O addition reactions and about (1—3)×10$^{-2}$ mol l$^{-1}$ in C=C addition reactions.

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