hydroxyl group is crucial in modifying an *N*-methylacridinium nucleus as an NAD^+ model oxidant. The excellent yields and turnover nature suggest that Ac^+OH would provide further interesting redox chemistry.

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Registry No. Benzenemethanol, 100-51-6; cyclohexanol, 108-93-0; benzaldehyde, 100-52-7; cyclohexanone, 108-94-1; benzylamine, 100-46-9; benzaldehyde 2,4-DNP, 1157-84-2; aniline, 62-53-3; 2-chloro-4-methoxybenzoic acid, 21971-21-1; 5-methoxydiphenylamine-2-carboxylic acid, 19218-83-8; 3-methoxyacridone, 61736-68-3; 3-methoxyacridine, 23043-46-1; 3-methoxy-*N*-methylacridinium iodide, 75874-18-9; benzylidenebenzylamine, 780-25-6; AcOH, 77081-04-0; AcHOH, 77081-05-1.

Frontier Molecular Orbital Theory of Substituent Effects on Regioselectivities of Nucleophilic Additions and Cycloadditions to Benzoquinones and Naphthoquinones

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Experimental data on nucleophilic additions and cycloadditions of unsymmetrical electron-rich dienes to substituted benzoquinones and naphthoquinones have been used to derive generalizations about the preferred site of nucleophilic attack on donor-substituted, acceptor-substituted, and conjugatively substituted species. SCF ab initio molecular orbital calculations have been carried out on examples of all of these species with the STO-3G basis set. Where known, the experimentally preferred site of attack by nucleophiles is that position having the largest LUMO coefficient, unless a donor group is attached to that position. In cases where experimental data are unavailable, predictions as to the most reactive position of the quinone toward nucleophiles are made. Frontier molecular orbital (FMO) theory parallels resonance theory arguments used to explain regioselectivity but provides predictions for relative rates of attack at all carbons of the quinones.

Diels–Alder reactions involving cycloadditions of dienes to quinones have been valuable in elegant syntheses of many natural products. Cycloadditions to *p*-benzoquinones have been the cornerstones of syntheses of steroids,[2] cortisone,[3] reserpine, yohimbine, estrone, and terramycin,[4] among others. Corey's achievement of the stereospecific total synthesis of gibberellic acid is a recent demonstration of the utility of a regioselective Diels–Alder cycloaddition involving a substituted benzoquinone.[5]

Recent interest in quinone cycloadditions has intensified due to the feverish activity directed at the synthesis of anthracycline antibiotics such as adriamycin and daunomycin, two molecules of this class which are effective in cancer chemotherapy.[6-15] Synthetic approaches to these and related anthraquinones have been developed on the basis of Diels–Alder cycloadditions to naphthoquinones or anthraquinones,[6-16] and as a fringe benefit, much information has been accumulated about the regioselectivities of these cycloadditions. A resonance theory model has been developed to rationalize these results.[7] We have also recently elucidated the regioselectivity of cycloadditions to the substituted double bond of methoxybenzoquinones and methoxynaphthoquinones.[17] We report here a systematic investigation of the influence of substituents upon the shapes of the frontier molecular orbitals of benzoquinones and naphthoquinones. Because the majority of cycloadditions and additions to quinones involve electron-rich species (nucleophiles), we concentrate attention on substituent effects on the low-lying vacant molecular orbitals of the quinones. The lowest unoccupied molecular orbitals (LUMOs) of the quinones can be used in the context of frontier molecular orbital (FMO) theory to explain the orientation of nucleophilic additions and cycloadditions to unsymmetrical benzoquinones and naphthoquinones.[18] Predictions have also been made for

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(2) Woodward, R. B.; Sondheimer, F.; Taub, D.; Heusler, K.; McLamore, W. M. *J. Am. Chem. Soc.* **1951**, *73*, 2403, 3546, 3548; **1952**, *74*, 4223.

(3) Sarett, L. H.; Arth, G. E.; Lukes, R. M.; Beyler, B. M.; Poos, G. I.; Johns, W. F.; Constantin, J. M. *J. Am. Chem. Soc.* **1952**, *74*, 4974.

(4) For a summary of these and others, see: Anand, N.; Bindra, J. S.; Ranganathan, S. "Art in Organic Synthesis"; Holden-Day: San Francisco, 1970.

(5) Corey, E. J.; Danheiser, R. L.; Chandrasekan, S.; Siret, P.; Keck, G. E.; Gras, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 8031. Corey, E. J.; Danheiser, R. L.; Chandrasekan, S.; Keck, G. E.; Gopalan, B.; Larsen, S. D.; Siret, P.; Gras, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 8034.

(6) Kelly, T. R.; Gillard, J. W.; Goerner, R. N., Jr.; Lyding, J. M. *J. Am. Chem. Soc.* **1977**, *99*, 5513.

(7) (a) Kelly, T. R.; Goerner, R. N., Jr.; Gillard, J. W.; Prazak, B. K. *Tetrahedron Lett.* **1976**, 3869. (b) Kelly, T. R.; Gillard, J. W.; Goerner, R. N., Jr. *Ibid.* **1976**, 3873. (c) Kelly, T. R. *Ibid.* **1978**, 1387. (d) Kelly, T. R.; Montury, M. *Ibid.* **1978**, 4309. (e) Kelly, T. R.; Montury, J. *Ibid.* **1978**, 4311.

(8) Farina, F.; Prados, P. *Tetrahedron Lett.* **1979**, 477 and references therein.

(9) Boeckman, R. K., Jr.; Dolak, T. M.; Culos, K. O. *J. Am. Chem. Soc.* **1978**, *100*, 7098.

(10) Grandmaison, J.-L.; Brassard, P. *J. Org. Chem.* **1978**, *43*, 1435.

(11) Lee, E. W.; Martinez, A. P.; Smith, T. H.; Henry, D. W. *J. Org. Chem.* **1976**, *41*, 2296.

(12) Wiseman, J. R.; French, N. I.; Hallmark, R. K.; Chiong, K. G. *Tetrahedron Lett.* **1978**, 3765.

(13) (a) Kende, A. S.; Tsay, T.-G.; Mills, J. E. *J. Am. Chem. Soc.* **1976**, *98*, 1967. (b) Kende, A. S.; Curran, D. P.; Tsay, T.-G.; Mills, J. E. *Tetrahedron Lett.* **1977**, 3537.

(14) Jung, M. E.; Lowe, J. A. *J. Org. Chem.* **1977**, *42*, 2371.

(15) Krohn, K.; Tolkiehn, K. *Tetrahedron Lett.* **1978**, 4023.

(16) Garland, R. B.; Palmer, J. A.; Schulz, J. A.; Sollman, P. B.; Pappo, R. *Tetrahedron Lett.* **1978**, 3669.

(17) Tegmo-Larsson, I.-M.; Rozeboom, M. D.; Rondan, N. G.; Houk, K. N. *Tetrahedron Lett.*, in press.

0022-3263/81/1946-2338$01.25/0

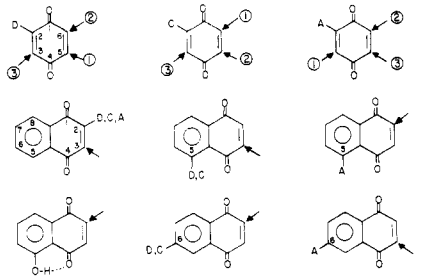


Figure 1. Summary of sites of attack of nucleophiles on substituted benzoquinones and naphthoquinones: D = donor; A = acceptor; C = conjugating substituent. When several positions can be attacked, position 1 is the most reactive, position 2 is next, etc.

the regioselectivities of some cycloadditions for which no experimental data are available. This method of prediction is compared to the resonance theory method.

Summary of Experimental Data on Regioselectivities of Nucleophilic Additions and Cycloadditions to Quinones

Figure 1 summarizes the position of attack of nucleophiles, or of the most nucleophilic terminus of a diene or 1,3-dipole, on various positions of benzoquinones and naphthoquinones substituted by donors, conjugating groups, or acceptors. Juglone (5-hydroxynaphthoquinone), although formally a donor-substituted naphthoquinone, is a special case, so that the reactions of this compound have been summarized separately. Finley has provided an excellent general survey of additions and cycloadditions to quinones.[19] In Figure 1 we have attempted to summarize results of kinetic control, although examples of thermodynamic control through adduct rearrangement occasionally have been shown to occur. The origin of the generalizations made in Figure 1 will be discussed only briefly here, with special attention to ambiguous cases. Finley's review[19] can be consulted for greater detail.

Donor-Substituted Benzoquinones. There are many examples of the attack of nucleophiles at the 5-position of donor-substituted benzoquinones.[19] For example, 2,5-disubstituted quinones are formed readily by attack of nucleophiles such as alcohols and amines on benzoquinones. Fewer data are available on the relative reactivities of the 3- and 6-positions. However, in a study we will refer to repeatedly, Wilgus et al. found that 1-phenyl-5-mercaptotetrazole (HPMT) gives only 5-PMT adducts with methoxybenzoquinone, but reactions of HPMT with alkylbenzoquinones give both 5- and 6-adducts, with the former predominating.[20] Hegedus and co-workers reported that methylbenzoquinone gives 5-, 6-, and 3-adducts in a ratio of 4.2:3.2:1 with π-allylnickel complexes, a reaction thought to involve electron-transfer processes.[21] We deduce the order of reactivity shown in Figure 1, with the regioselectivity determined by the electron-donating power of the substituent. The 2-position is apparently least reactive in 2-donor-substituted benzoquinones.[17] Similar regioselectivity is observed in Diels–Alder reactions of electron-rich (nucleophilic) dienes with donor-substituted benzoquinones.[17,22]

A recent report by Drew, Griffiths, and King apparently does not fit these generalizations.[23] These authors found that 2,6-dimethoxybenzoquinone reacts with methylamine thermally to give 2-methoxy-6-(methylamino)benzoquinone, whereas photochemical reaction gives 2,6-dimethoxy-3-(methylamino)benzoquinone. The thermal reaction gives a product which results from attack at one position of methoxy substitution and at position 6 relative to the other. It is conceivable that the thermal addition step is reversible, giving the final product which arises from an intermediate which can lose methanol.

Conjugatively Substituted Benzoquinones. Few data are available on additions or cycloadditions to this type of benzoquinone, although Wilgus et al. reported that HPMT adds to phenylbenzoquinone to give 6- and 5-adducts in a ratio of 4.6:1.[20] We deduce that the preferential order of attack is C-6 > C-5 > C-3, but on the basis of only this single experiment.

Acceptor-Substituted Benzoquinones. Nucleophiles and the nucleophilic termini of dienes prefer to add to the 3-position of these species.[19] With acetylbenzoquinone, a small amount of addition to C-6 is also found for HPMT,[20] so that the order C-3 $\gg$ C-6 > C-5 is proposed, precisely opposite that obtained for donors.

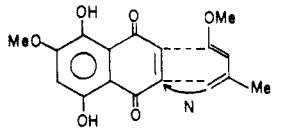
2-Substituted Naphthoquinones. Most examples of these reactions involve attack of nucleophiles at the unsubstituted (3-position) carbon of the quinone ring.[19] We have recently found this orientation experimentally for some Diels–Alder cycloadditions of electron-rich naphthoquinones.[17] Substitutions of good leaving groups may occur, although even these reactions could involve initial attack at the unsubstituted carbon and rearrangement ultimately to form the thermodynamically more stable compound.

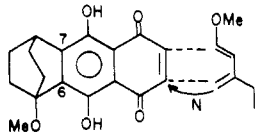
Aromatic-Ring-Substituted Naphthoquinones. Our deductions here are based on relatively few examples. Nucleophilic additions and Diels–Alder cycloadditions to juglone and many other 5-substituted naphthoquinones have been studied. Nucleophiles and the nucleophilic termini of dienes usually add to C-2 juglone,[5-7,13,14,21,22,24-26] although sulfur nucleophiles are found to add to the 3-position.[27] This has been suggested to involve radical attack, although product isomerization (thermodynamic control) may be a more serious problem. The electron-rich diene 1,4-dimethoxy-2-methylbutadiene also gives a slight preference for the "wrong" regioisomer,[9] but the weak electron donation by methyl may be overridden by steric hindrance or by an unusual preferred conformation of one of the methoxy groups in this molecule. The generally preferred attack at C-2 of juglone is usually considered to arise by direct activation of the C-4 carbonyl by intramolecular hydrogen bonding.[6,24]

Oda et al. have reported that 5-nitronaphthoquinone undergoes Diels–Alder reactions with piperylene and isoprene such that the more nucleophilic termini of these dienes attack C-2 of the quinone.[29]

(18) PMO theory has been applied to thermal and photochemical cycloadditions of *o*-quinones. Herndon, W. C.; Giles, W. B. *J. Chem. Soc., Chem. Commun.* **1969**, 497.
(19) Finley, K. T. In "The Chemistry of the Quinonoid Compounds"; Patai, S., Ed.; Wiley: New York, 1974; Part 2, Chapter 17.
(20) Wilgus, H. S., III; Frauenglass, F.; Jones, E. T.; Porter, R. F.; Gates, J. W., Jr. *J. Org. Chem.* **1964**, *29*, 594.
(21) Hegedus, L. S. *J. Organomet. Chem. Libr.* **1976**, *1*, 329 and references therein.
(22) Bohlmann, F.; Mathar, W.; Schwarz, H. *Chem. Ber.* **1977**, *110*, 2028. Tou, J. S.; Reusch, W. *J. Org. Chem.* **1980**, *45*, 5012. Kozikowski, A. P.; Sugiyama, K. *Tetrahedron Lett.* **1980**, 4597.
(23) Drew, S. M.; Griffiths, J.; King, A. J. *J. Chem. Soc., Chem. Commun.* **1979**, 1037.
(24) Birch, A. J.; Dowell, V. H. *Tetrahedron Lett.* **1970**, 3467.
(25) (a) Trost, B. M.; Ippen, J.; Vladuchick, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 8116. (b) Manning, W. B. *Tetrahedron Lett.* **1979**, 1661.
(26) Manning, W. B.; Kelly, T. P.; Muschik, G. M. *Tetrahedron Lett.* **1980**, 2629.
(27) MacLeod, J. W.; Thomson, R. H. *J. Org. Chem.* **1960**, *25*, 36 and references therein.
(28) Pratt, Y. T. *J. Org. Chem.* **1962**, *27*, 3905.

We are aware of only a few cases of nucleophilic additions to 6-donor-substituted naphthoquinones. The 6-methyl compound experiences attack by amines at C-2,[19] and the two Diels–Alder reactions indicated below are also examples of this type. In the first case, there is a slight (3:1) preference for attack as shown, while in the second, a 4:1 preference is exhibited.[6c] In the latter case, the 7-substituent is expected to be more electron donating than the 6-substituent due to the inductive electron withdrawal by the methoxy group. Manning has recently reported a 1.5:1 preference for attack of the unsubstituted terminus of styrene on C-2 of 6-methoxynaphthoquinone.[25b]

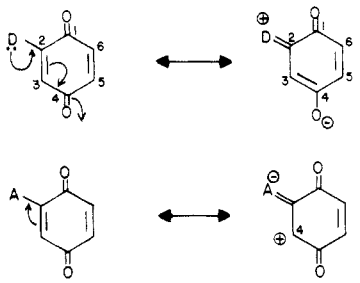




Finally, we know of no examples of nucleophilic additions to naphthoquinones substituted at C-6 by either purely conjugating or electron-withdrawing groups. The deduction given in Figure 1 is based merely on the reasonable notion that donors and acceptors will have opposite effects, as they do at the 5-position.

Previous Rationalizations of Regioselectivity

Resonance theory arguments have been used to rationalize the site of attack by nucleophiles on quinones[30] and the regioselectivity of Diels–Alder reactions of unsymmetrical dienes with substituted quinones.[6,7] As indicated below, donor substituents selectively diminish the elec-



tron-withdrawing ability of one of the quinone carbonyls through resonance, so that attack of a nucleophile occurs β to the other, more electron-deficient carbonyl.[6] Electron-withdrawing substituents activate the β-position by resonance. This type of reasoning may be applied to explain the effects of 5- and 6-position donor or acceptor substituents on naphthoquinone reactivities.

Thus, resonance theory arguments perform brilliantly in rationalization of the influence of donor substituents on remote unsubstituted bonds and of acceptor substituents on bonds to which they are attached. However, the influence of conjugating substituents, which can enter into both donor and acceptor resonance, or of donors on substituted bonds and acceptors on remote bonds, is not so obvious. In the case of attack on substituted bonds, the resonance structure shown would appear to favor attack at the substituted carbon (C-2), whereas experimental results seem to favor the attack of nucleophiles at C-2 over C-3 (see, however, the Drew et al. work cited above).[23] Alternatively, one can use qualitative arguments such as used by Kelly: since a donor substituent at C-2 diminishes the electron-withdrawing effect of the C-4 carbonyl, C-3 is activated more than C-2. Fleming has rationalized the orientation of attack on species such as citraconic anhydride and methylbenzoquinones in similar terms, predicting that the LUMOs of the donor-substituted double bond of these species will reflect this polarization.[31] In fact, the calculated LUMOs do not.[32] Similarly, it is not clear from resonance theory how an acceptor at C-2 should influence the reactivities of C-5 and C-6.

Nevertheless, the resonance theory rationalization of regioselectivity is quite useful for donor-substituted quinones and for conjugatively substituted quinones, assuming that the conjugating substituent acts as a donor. Furthermore, if carried out in a complete (valence bond) fashion, resonance theory should give static reactivity predictions identical with those obtained from molecular orbital calculations. As we will show, however, MO theory in the FMO approximation can predict simultaneously the relative reactivities of all positions of a substituted quinone.

Frontier Molecular Orbital Based Treatments of Nucleophilic Reactivity

According to the frontier molecular orbital treatment of chemical reactivity,[31,33-36] the rate and site of reactivity of a molecule with a nucleophile is dominated by the interaction of the LUMO of the molecule in question with the HOMO of the nucleophile. The closer they are in energy, the more strongly these orbitals will interact and the faster the reaction will be. The overlap of these orbitals will be greatest when the nucleophile interacts at the site of largest LUMO coefficient, so that this is the predicted site of nucleophilic attack. Similarly, the most nucleophilic terminus of a diene is that with the larger terminal HOMO coefficient, and this terminus should become attached to the site of largest LUMO coefficient, even if the reaction is concerted.[35]

The previous paragraph describes a relationship between calculated quantities and reactivities, but there is also a relationship between experimentally measured quantities and the site of attack. The hyperfine couplings observed in ESR spectra of the radical anion of a molecule are related to the site of reaction of nucleophiles on the neutral molecule.[34a] This is because the hyperfine couplings are related to the spin densities at a given site through the McConnell equation, and the spin densities at each site are, in turn, related to the coefficients of the singly occupied orbital of the radical anion. This singly occupied orbital of the radical anion is the LUMO of the neutral molecule. Thus, the site of largest hyperfine coupling in the radical anion is also the site of attack of a nucleophile on the neutral molecule.

(29) Oda, N.; Kobayashi, K.; Ueda, T.; Ito, I. *Chem. Pharm. Bull.* **1978**, *26*, 2578.
(30) Thomson, R. H. *J. Org. Chem.* **1951**, *16*, 1082.
(31) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley-Interscience: New York, 1976.
(32) Houk, K. N.; Domelsmith, L. N.; Strozier, R. W.; Patterson, R. T. *J. Am. Chem. Soc.* **1978**, *100*, 6531.
(33) Fukui, K. *Fortschr. Chem. Forsch.* **1970**, *15*, 1 and references therein.
(34) (a) Epiotis, N. D.; Cherry, W. *J. Am. Chem. Soc.* **1976**, *98*, 5432. (b) Epiotis, W. D. "Theory of Organic Reactions"; Springer-Verling: West Berlin, 1978.
(35) Houk, K. N. *Acc. Chem. Res.* **1975**, *8*, 361. Houk, K. N. In Marchand, A. P.; Lehr, R. E. "Pericyclic Reactions"; Academic Press: New York, 1977; Vol. 2.
(36) (a) Klopman, G., Ed. "Chemical Reactivity and Reaction Paths"; Wiley-Interscience: New York, 1974, Chapter 4. Hudson, R. F. *Ibid.*, Chapter 5.

Table I. Frontier π Molecular Orbitals (STO-3G) of Benzoquinone and 2-Substituted Benzoquinones[a]

	HOMO					LUMO				
benzoquinone	ϵ	C_2	C_3	C_5	C_6	ϵ	C_2	$-C_3$	$-C_5$	C_6
parent	−8.14	0.34	0.34	0.34	0.34	3.82	0.33	0.33	0.33	0.33
2-methyl	−7.97	0.38	0.40	0.29	0.29	3.91	0.33	0.32	0.34	0.33
2-hydroxy	−7.71	0.40	0.52	0.12	0.14	3.69	0.31	0.30	0.36	0.33
2-methoxy	−7.44	0.36	0.54	0.12	0.13	3.96	0.32	0.28	0.36	0.34
2-formyl	−8.24	0.37	0.38	0.29	0.29	3.38	0.34	0.41	0.27	0.29
2-vinyl	−7.32	0.37	0.48	0.09	0.10	3.72	0.34	0.37	0.30	0.30

[a] Geometries were the same as those for benzoquinone,[32] except that substituents in standard geometries (Pople, J. A.; Gordon, M. *J. Am. Chem. Soc.* **1967**, *89*, 4253) were substituted for one hydrogen. Additional fixed parameters: methyl dihedral angle $C_3C_2CH = 0°$; hydroxy dihedral angle $C_3C_2OH = 180°$; MeO dihedral angle $C_3C_2OC = 0°$; $C_3C_2O = 124°$; $C_2OC = 118°$; formyl dihedral angle $C_3C_2CO = 0°$; vinyl dihedral angle $C_3C_2CC = 0°$. ϵ's are orbital energies (eV), and C's are coefficients at the indicated atom.

In some cases of nucleophilic attack, electron transfer from a nucleophile to a substrate of high electron affinity may occur first, followed by combination of the radical anion and radical cation at the sites of greatest spin density in the two. In orbital terms, this union will occur at the sites of the largest singly occupied MO (SOMO) density, which also corresponds to the site of greatest spin density. Either the two-electron- or the one-electron-transfer mechanisms should lead, according to these ideas, to attack of a nucleophile at the site of largest LUMO coefficient. The quantities of interest to theoretical predictions of reactivity and regioselectivity are, then, the LUMO coefficients and orbital energies. These are given for the quinones in the next section.

Molecular Orbitals of Quinones: STO-3G Computational Results and Perturbation Rationalizations of LUMO Polarizations

We have carried out calculations on various quinones by both semiempirical and ab initio methods. The ordering of the high-lying filled and low-lying vacant π orbitals is generally the same in these calculations. Furthermore, the substituent effects on the LUMO shapes are sufficiently large so that all of the computational methods give qualitatively similar results about the order of coefficient magnitudes at ring carbons. Only ab initio calculations with the minimal (STO-3G) basis set[37] are reported here.

Benzoquinones. Some π orbitals of benzoquinone are summarized in Figure 2. The geometry used is Trotter's X-ray crystallographic structure.[38] Orbitals shapes are only shown for the four π orbitals which are heavily concentrated on the CC double bonds. Both of the filled orbitals shown are π_{CC} bonding orbitals, and both of the vacant orbitals are π^*_{CC} antibonding orbitals. For the occupied orbitals, negatives of experimental ionization potentials[39] are shown for comparison with predicted orbital energies. There is considerable disagreement as to the correct assignment of the first four ionization potentials of benzoquinone, since two oxygen lone-pair and two π ionization potentials are intermingled in two structured bands between 10 and 11 eV in the photoelectron spectrum.[39] We are interested mainly in the π orbitals, however, and there is agreement that the b_{3u} orbital is higher in energy than the b_{1g}. The first electron affinity (EA) of

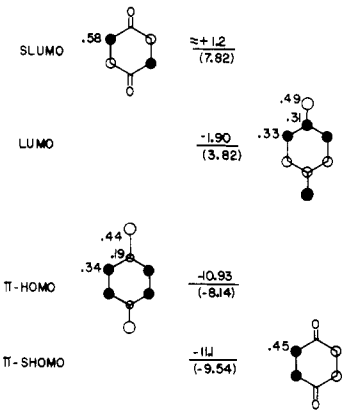


Figure 2. STO-3G π orbital shapes and energies (in electron volts, below line). Energies above lines are negatives of experimental IPs and estimated electron affinities.

benzoquinone is about 1.90 eV,[40] and the negative of this EA is also given in the figure as the LUMO energy. The electron affinity corresponding to addition of an electron to the SLUMO has been estimated in the following way: ethylene, which has as experimental EA of −1.78 eV,[41] has a calculated LUMO energy of 8.68 eV, according to STO-3G. This is less than 1 eV above the energy calculated for the SLUMO of benzoquinone, so that the second EA of benzoquinone should be only slightly less negative than that of ethylene. We crudely estimate that the second EA of benzoquinone is 0.6 eV higher than that of ethylene.

The LUMO of benzoquinone is lowered in energy to a large extent because it is of the correct symmetry to mix substantially with the carbonyl π^* orbitals. Whereas the SLUMO and the π-SHOMO are lowered in energy only by inductive effects, the π-HOMO is lowered in energy both by mixing with the π^* orbitals of the carbonyl, and by the inductive effect of the carbonyls; however, these effects are partially counteracted by energy raising due to mixture of the π_{CC} orbitals with lower lying π orbitals of the carbonyl groups. As a point of reference, benzoquinone is a more electron-deficient species than fumaronitrile (IP $\simeq$ 11.15 eV; EA = 0.7 eV)[42] as assessed by the EA.

Upon monosubstitution of benzoquinone, the symmetry of benzoquinone is reduced, and mixing of the four π orbitals with each other, and with substituent orbitals, occurs. The STO-3G orbital energies and coefficients for several substituted benzoquinones are given in Table I. Standard substituent geometries were used,[43] except for

(37) Hehre, W. J.; Lathan, W. D.; Ditchfield, R.; Newton, M. D.; Pople, J. A. "Gaussian 70"; Quantum Chemistry Program Exchange: No. 236, Indiana University, Bloomington, IN. Hehre, W. J.; Stewart, R. F.; Pople, J. A. *J. Chem. Phys.* **1969**, *51*, 2657.
(38) Trotter, J. *Acta Crystallogr.* **1960**, *13*, 86.
(39) (a) Dougherty, D.; McGlynn, S. P. *J. Am. Chem. Soc.* **1977**, *99*, 3234. (b) Over a dozen studies of the photoelectron spectra of benzoquinones have been reported and are referred to in : Bigelow, R. W. *J. Chem. Phys.* **1978**, *68*, 5086.
(40) This is the average of the EAs determined from reduction potentials and charge-transfer spectra: Chen, E. M.; Wentworth, W. E. *J. Chem. Phys.* **1975**, *63*, 3183.
(41) Jordan, K. D.; Burrow, P. D. *Acc. Chem. Res.* **1978**, *11*, 341.
(42) Houk, K. N.; Munchausen, L. L. *J. Am. Chem. Soc.* **1976**, *98*, 937.

methoxy, where normal aromatic methoxy angles were used. When several substituent conformations are possible, computations were performed to determine the most stable.

For the three donor substituents, Me, OH, and MeO, polarization of the LUMO gives coefficients of unsubstituted ring carbons in the order $C_5 > C_6 \gtrsim C_3$. The differences in coefficient magnitudes are small but of the same order of magnitude as those which produce high regioselectivity in simpler examples.[35] According to perturbation theory, the selectivity for attack at various positions is proportional to the difference in the square of the coefficients at different positions.

The LUMO polarization of donor-substituted benzoquinones is borne out by ESR spectra of the radical anions of benzoquinones, in which the LUMO of the neutral compound becomes singly occupied. The hyperfine couplings due to various protons, which reflect the odd electron spin density at the attached carbons, are 2.70, 2.44, and 1.95 G for positions 5, 6, and 3, respectively, of methylbenzoquinone in Me_2SO[44] and 4.98, 1.34, and 0.60 G for hydroxybenzoquinone in aqueous base.[45] For comparison, benzoquinone has all four a_H's equal to 2.42 G in Me_2SO.[44] The hyperfine couplings in the donor-substituted benzoquinones correspond to the order of LUMO coefficients for the neutral species.

The HOMOs of the donor-substituted species are polarized ($C_3 > C_6 \gtrsim C_5$) oppositely to the LUMO and are increased in energy in the order expected for increased electron donation: H < Me < OH < OMe. This order holds for the LUMO energies as well, except that hydroxybenzoquinone has a lower LUMO energy than benzoquinone, due to the weak intramolecular hydrogen bond between the hydroxyl proton and the C-1 carbonyl oxygen.

The formyl group, an electron acceptor, causes precisely the opposite order of LUMO coefficient magnitudes, $C_3 > C_6 > C_5$, from that caused by the donor but the same order of HOMO coefficients. This latter effect is a result of some π electron donation by the π_{CO} orbital.[35] Both the HOMO and LUMO are, however, lowered in energy by the acceptor.

The vinyl group has mixed behavior, giving coefficient magnitudes in the order $C_3 > C_6 \gtrsim C_5$ in the LUMO, reflecting behavior somewhat more like that expected of an acceptor than of a donor. The HOMO is strongly polarized in the same direction as that found for the other substituents. The HOMO is raised in energy, and the LUMO is lowered, the usual effect of a conjugating substituent.[35]

The origin of these polarizations can be understood by applications of perturbation theory,[46] diagrammed for the donor case in an unavoidedly complex fashion in Figure 3. Substituents will cause greatest mixing of those orbitals which are closest in energy and have the largest coefficients at the site of perturbation. A donor causes higher energy orbitals to mix into lower ones in a negative fashion at the site of substitution and vice versa. Acceptors cause exactly the opposite mixing.[46] Starting with the effect of a donor substituent, one sees that the SLUMO will be mixed into the LUMO in a negative fashion, and this will cause the LUMO no longer to be evenly distributed over the two double bonds; this mixing polarizes the LUMO toward the unsubstituted double bond. Mixing of the SHOMO into

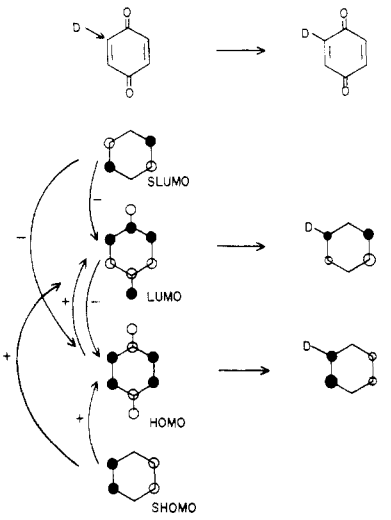


Figure 3. Orbital mixing caused by a donor substituent. The plus and minus signs indicate that the orbital at the origin of the arrow is mixed into the orbital at the point of the arrow in a plus or a minus fashion, respectively, at the site of donor substitution.

the HOMO has the opposite effect on the HOMO; that is, the HOMO becomes concentrated at the substituted double bond. These vacant–vacant and filled–filled mixings cause "side-to-side" polarization but do not alter the position of C-2 relative to C-3 or C-5 relative to C-6. Second, the donor causes the HOMO and SHOMO to be mixed into the LUMO in a positive fashion, and this causes the LUMO coefficient at C-2 to be increased at the expense of that at C-3. Since the HOMO and SHOMO are of nearly the same energy, the SHOMO, which has larger coefficients at carbon than the HOMO, dominates the polarization at the unsubstituted double bond, since the coefficient at C-5 increases in magnitude at the expense of that at C-6. Both the LUMO and SLUMO are mixed in a negative fashion into the HOMO, causing the opposite polarization.

An acceptor reverses these trends for the LUMO, so that the LUMO becomes concentrated on the substituted double bond, C_3 grows, and C_5 becomes greater than C_6. The HOMO of 2-formylbenzoquinone is very much like that of a donor-substituted species because the formyl group can act as a donor through its π_{CO} orbital.

The vinyl group exhibits its usual dual behavior; the LUMO is polarized as expected for an acceptor, but the coefficients at C-5 and C-6 are identical. The HOMO is polarized as expected for a donor substituent.

Although we will return to this part in more detail, there is an obvious correspondence between the LUMO coefficient magnitudes and the preferential site of attack by nucleophiles for both donor- and acceptor-substituted benzoquinones. The calculated results for the vinyl compound do not agree with the results for the single experiment cited earlier,[20] but we suspect that conjugating substituents in general may give regiochemical results ranging from those expected for a donor ($C_5 > C_6 > C_3$) to those expected for an acceptor ($C_3 > C_6 > C_5$), depending upon the exact nature of the conjugating group.

Naphthoquinones. The geometry used for naphthoquinone and its derivatives in the calculations was essentially that of benzoquinone to which standard hexagonal benzene (all r_{CC} = 1.40 Å) was fused.[47,48] Four of the 12

(43) Pople, J. A.; Jordan, M. S. *J. Am. Chem. Soc.* **1967**, *89*, 4253.
(44) Stone, E. W.; Maki, A. H. *J. Chem. Phys.* **1962**, *36*, 1944.
(45) Ashworth, P.; Dixon, W. T. *J. Chem. Soc., Perkin Trans. 2* **1972**, 1130.
(46) Libit, L.; Hoffmann, R. *J. Am. Chem. Soc.* **1974**, *96*, 1370. Santiago, C.; McAlduff, E. J.; Houk, K. N.; Snow, R. A.; Paquette, L. A. *Ibid.* **1978**, *100*, 6149 and references therein.
(47) The X-ray crystal structure of 1,4-naphthoquinone indicates that the bond lengths of the benzo ring vary from 1.38 to 1.11 Å: Gaultier, J.; Hauw, C. *Acta Crystallogr.* **1965**, *18*, 179.

Table II. π Frontier Orbitals of Naphthoquinones (STO-3G)[a]

1,4-naphthoquinone	THOMO			HOMO (or SHOMO)			LUMO			TLUMO		
	ϵ	C_2	C_3	ϵ	C_2	C_3	ϵ	C_2	$-C_3$	ϵ	C_2	$-C_3$
parent	−8.78	0.51	0.51	−7.53	0.18	0.18	4.15	0.33	0.33	7.08	0.48	0.48
2-methyl	−8.46	0.48	0.51	−7.46	0.21	0.22	4.23	0.33	0.32	7.17	0.48	0.47
2-hydroxy	−8.09	0.29	0.40	−7.44	0.33	0.41	4.03	0.30	0.30	7.10	0.48	0.45
2-methoxy	−7.90	0.21	0.35	−7.22	0.32	0.46	4.28	0.31	0.28	7.26	0.49	0.45
2-formyl	−8.66	0.46	0.48	−7.67	0.19	0.19	3.70	0.35	0.42	6.18	0.14	0.35
2-vinyl	−7.76	0.16	0.22	−7.16	0.34	0.44	4.03	0.35	0.38	6.45	0.26	0.42
5-methyl	−8.75	0.51	0.51	−7.47	0.16	0.17	4.19	0.33	0.33	7.13	0.49	0.48
5-hydroxy (*anti*-OH)	−8.78	0.49	0.49	−7.59[b]	0.22	0.22	4.19	0.31	0.33	7.01	0.48	0.48
5-methoxy	−8.70	0.49	0.49	−7.49[b]	0.21	0.21	4.28	0.31	0.33	7.12	0.49	0.48
5-formyl ($\perp$)	−9.03	0.51	0.51	−7.83[b]	0.14	0.13	3.81	0.34	0.31	6.86	0.48	0.48
5-hydroxy (*syn*-OH)	−9.04	0.51	0.52	−7.82[b]	0.14	0.15	3.80	0.35	0.32	6.89	0.49	0.48
5-vinyl ($\perp$)	−8.77	0.50	0.50	−7.51	0.18	0.18	4.17	0.33	0.33	7.09	0.48	0.48
6-methyl	−8.66	0.51	0.51	−7.31	0.13	0.14	4.21	0.34	0.33	7.13	0.48	0.48
6-hydroxy	−8.68	0.49	0.50	−7.97[b]	0.15	0.12	4.12	0.34	0.33	7.11	0.49	0.47
6-methoxy	−8.55	0.48	0.50	−7.86[b]	0.15	0.11	4.21	0.35	0.33	7.23	0.49	0.47
6-formyl	−8.86	0.50	0.50	−7.59	0.15	0.15	3.82	0.28	0.29	6.41	0.29	0.40
6-vinyl	−8.52	0.46	0.48	−7.75[b]	0.15	0.12	4.10	0.31	0.31	6.72	0.33	0.43

[a] Substituent geometries and dihedral angles for the 2-substituents were the same as those described in the footnote to Table I. The 5-methylnaphthoquinone with $C_{10}C_5CH = 180°$ is 5.9 kcal/mol more stable than the 0° rotamer; the 5-methoxy is anti; the 5-formyl and 5-vinyl substituents are perpendicular and are 1.2 and 3.1 kcal/mol, respectively, more stable than the anti planar conformers. The 6-methyl group has essentially no barrier to rotation; the 6-OH and 6-vinyl are anti, and the 6-formyl is syn. [b] This is the SHOMO but corresponds in shape to the benzoquinone HOMO. The SHOMO is nearly degenerate.

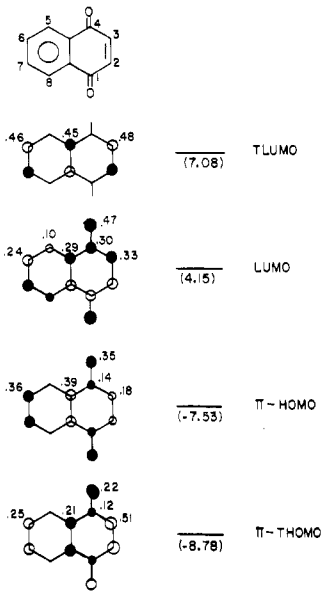
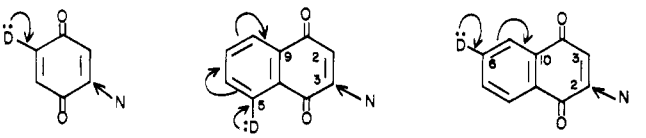


Figure 4. Some STO-3G π MOs of 1,4-naphthoquinone. Only coefficients greater than 0.10 are shown.

π orbitals of naphthoquinone are shown in Figure 4. The π-HOMO and π-THOMO both resemble the π-HOMO of benzoquinone, since the benzo fusion splits the latter into two orbitals. The π-SHOMO is essentially a pure benzene orbital which is of the wrong symmetry to interact with the high-lying occupied π orbital of benzoquinone. The same pattern is observed in the lowest three vacant orbitals. Because the THOMO and TLUMO have the greatest density on the reactive C_2C_3 bond, we have considered the effect of substituents on these orbitals as well as on the HOMO and LUMO. In general, the HOMO and THOMO are polarized in the same direction as are the LUMO and TLUMO. In the following discussion we will refer to "HOMO" and "LUMO" when, in fact, we are taking into account both relevant filled or both relevant vacant orbitals. The calculations are summarized in Table II. Standard substituent geometries were again used, and the orbitals are given for the rotamer with the lowest energy, except for *anti*-5-hydroxynaphthoquinone.

A substituent at the 2-position of naphthoquinone has the same effect as that substituent has on the benzoquinone double bond to which it is directly attached. The donor substituents raise all orbital energies in the order Me < OH < OMe, except that the 2-OH again lowers the energy of the naphthoquinone LUMO and TLUMO. Formyl lowers both the HOMO and LUMO, while vinyl compresses the HOMO–LUMO gap.

Except for *syn*-5-OH, substituents at the 5-position have the same effect as substituents attached directly to the benzoquinone nucleus at what would be considered the 9-position of naphthoquinone (i.e., meta to the substituent), except that the polarization by the 5-Me is too small to be observed when only two significant figures are given. The structures below show the analogy between a resonance donor at the 2-position of benzoquinone and at the 5-position of naphthoquinone.[7] Similarly, a substituent at the 6-position is equivalent to a substituent directly attached to the benzoquinone at the 10-position of naphthoquinone.



Donors at C-5 cause a small increase of the C-3 coefficient in the vacant orbital, while 5-formyl increases C_2. The influence of vinyl is again too small to be noted here. Donors at the 6-position increase the C-2 coefficients of the vacant orbitals, and the effect is slightly larger than that caused by donors at C-5. The 6-formyl and 6-vinyl substituents increase C_3 in the vacant orbitals. In a few cases, described in the footnotes to Table II, the order of occupied orbitals is altered due to large substituent effects on the π-SHOMO, the nearly pure benzene orbital.

Juglone (5-hydroxynaphthoquinone) is a special case in nucleophilic additions and cycloadditions,[7] as described

(48) Semiempirical calculations on all of the isomeric naphthoquinones and azuloquinones have been reported elsewhere: Scott, L. T.; Rozeboom, M. D.; Houk, K. W.; Fukunaga, T.; Lindner, H. J.; Hafner, K. *J. Am. Chem. Soc.* **1980**, *102*, 5169.

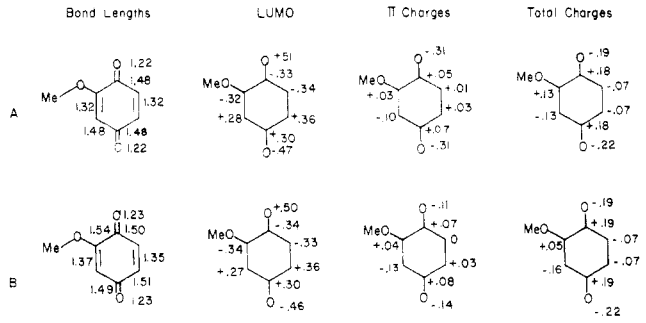


Figure 5. Geometries, LUMO coefficients, and π and total charges of standard (A) and partially optimized (B) methoxybenzoquinone.

earlier. When the hydroxy group is constrained to the anti conformation, where hydrogen bonding with the peri carbonyl is impossible, then hydroxy behaves as a donor, as reflected by the orbital coefficients and energies particularly of the vacant orbitals. However, in the more stable *syn*-5-hydroxynaphthoquinone, which has an OH···O=C hydrogen bond, the hydroxy substituent acts as an acceptor, due to electrostatic interaction between the partially positive proton and the carbonyl. The π orbitals in Table II are all stabilized by the *syn*-5-OH, and the LUMO is strongly polarized with the larger coefficient at C-2.

Relationships between Frontier Molecular Orbitals, Resonance Theory, and Regioselectivity of Nucleophilic Attack on Benzoquinones and Naphthoquinones

Having described the FMOs of substituted benzoquinones and naphthoquinones, we turn to applications of these FMO generalizations for understanding and predicting regioselectivities of nucleophilic additions and cycloadditions.

The polarizations of the LUMOs of substituted benzoquinones and naphthoquinones mainly parallel nucleophilic reactivity; the site with the largest LUMO coefficient is the position most rapidly attacked by nucleophiles or by the more nucleophilic terminus of electron-rich dienes. The only exception to this involves the site of donor substitution, which is always less reactive than would be predicted on the basis of LUMO coefficients. We have suggested earlier that these sites are deactivated due to secondary orbital interactions which occur between the nucleophile HOMO and the substituent contribution to the LUMO upon attack on this position.[17,32] That is, direct repulsive interactions between the attacking nucleophile and the substituent diminish the reactivity of the substituted site.

For reasons of economy, our calculations utilized standard quinone geometries. In order to explore the significance of substituents on geometries and coefficients, we have investigated 2-methoxybenzoquinone somewhat more thoroughly. Figure 5A shows the standard geometry of 2-methoxybenzoquinone, along with the corresponding LUMO coefficients and π and total charges. We fully optimized this structure by MINDO/3 and using this result optimized the carbonyl CO bond lengths using STO-3G, since these lengths are systematically different by MINDO/3 and STO-3G. This optimization lengthens the C-2,C-3 and shortens the C-3,C-4 bond lengths, in agreement with expectation based on resonance electron donation by the methoxy group. Furthermore, there is an increase in the LUMO polarization and charge separation with π-charge donation to the C-4 carbonyl group, as suggested by resonance theory.

As described earlier, the extent of charge-transfer stabilization upon interaction of a nucleophile HOMO with the quinone LUMO at any position is proportional to the square of the coefficient at that position. At the 5-, 6-, and 3-positions, the LUMO coefficients squared are 0.13, 0.11, and 0.08, in the same order as the order of attack by nucleophiles generalized earlier. Upon interaction with a nucleophile, the geometrical distortions and coefficient polarizations will further increase to maximize bonding and minimize antibonding in the partially occupied LUMO.[48] This is undoubtedly the origin of the large difference in a_H's in the radical anions of substituted benzoquinones.

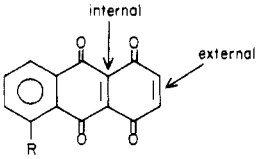
Finally, we can compare the FMO regioselectivity rationalizations and predictions with those made by resonance theory. First, inspection of Figure 5 shows that the LUMO coefficients are largest at the site of greatest partial positive π charge, whereas small LUMO coefficients are present at sites of largest partial negative charge. This is no accident, since the substituent causes charge polarization in part by inducing mixing of the quinone filled and vacant orbitals. For example, the methoxy substituent causes the LUMO to mix into the HOMO in a negative fashion at C-2, and this increases both the HOMO coefficients and the π charges at C-3 and C-5, at the expense of those at C-2 and C-6. SLUMO mixing into the HOMO increases both the HOMO coefficients and the π charges at C-3 and C-6 at the expense of those at C-2 and C-5. The latter effect dominates, leading to the HOMO coefficients and charges shown in Figure 5. Although the π and total charges are a sum of all filled orbital charges, there is a qualitative correspondence between a large HOMO coefficient, a small LUMO coefficient, and a large π charge, and vice versa.

Resonance theory arguments give predictions of π charges in reactants and then postulate that nucleophilic attack occurs at the site of highest partial positive charge. FMO predictions are based on LUMO coefficients. In these molecules, there is a parallel between these, so either may be considered to be a reliable rule of thumb.

Frontier Orbital Insights into Various Unsolved Problems and Anomalies

Some additional problems have arisen in the field of cycloadditions of benzoquinones and naphthoquinones. In order to provide some additional insight into this synthetically important areas, we have carried out some additional calculations which are described in this section.

Internal vs. External Cycloaddition to Diquinones. Kelly and others have reported competition between attack on the internal and external double bonds of quinizarin diquinone, shown below, and its derivatives.[7a,11,13] Buta-



diene, acetoxybutadiene, 2,4-hexadiene, and anthracene are representative of the dienes which add primarily at the external double bond, while 1-methoxybutadiene, isoprene, 1-methoxy-3-(trimethylsiloxy)butadiene, and 5-methoxy-2,4-pentadiene are representative of dienes which add to the internal double bond.[7a,11,13,49,50] Kende et al. have

(49) For an extensive list, see ref 7a and 11.
(50) Altman, J.; Cohen, E.; Maymon, T.; Peterson, J. B.; Reshef, N.; Ginsburg, D. *Tetrahedron* **1969**, *25*, 5115.

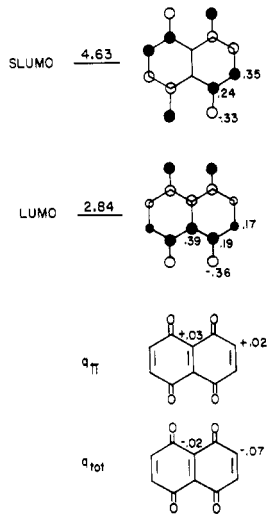


Figure 6. LUMO, SLUMO, and charges of 1,4,5,8-naphthodiquinone.

proposed an explanation for these phenomena.[13a] An explanation related to that of Kende is supported by the LUMO, the SLUMO, and the charges of a simple model diquinone shown in Figure 6. The LUMO of the molecule is more heavily concentrated on the internal double bond, while there is a node through these carbons in the SLUMO. Furthermore, the internal double bond is more positive (q_π) or less negative (q_{tot}) than the external one. Both the concentration of the LUMO on the internal double bond and the more positive character of this region of the molecule should direct electron-rich dienes to the internal bond. For a very electron-rich diene, the HOMO^d–LUMO^q (d = diene and q = quinone) interaction [which is proportional to $1/(IP^d - EA^q)$] will be much larger than the HOMO^d–SLUMO^q interaction, leading to a large preference for attack at the internal double bond. For a less electron-rich diene, the two aforementioned interactions will not be greatly different, and little selectivity should be observed. Superimposed on this is the fact that attack at the internal double bond should be sterically unfavorable with respect to attack at the external double bond. A rough pattern of selectivity can be discerned: electron-rich dienes prefer to attack the internal double bond, while less electron-rich dienes are less selective or add to the external double bond. Steric hindrance, especially 1-substitution or 1,4-disubstitution, causes attack at the external double bond.

Reversal of Regioselectivity by Catalysts. While enhancement of the regioselectivity of Diels–Alder reactions by Lewis acid catalysts is a well-understood phenomenon,[51] there are several curious examples of reversals of regioselectivity in the Lewis acid catalysis of juglone derivatives. While we cannot offer a completely general explanation of all these phenomena, we have uncovered several points of interest relevant to these data. One particularly intriguing type of reversal of regioselectivity upon catalysis occurs with dienes having both alkoxy and thioalkoxy substituents. For example, the dienes shown in Figure 7 add to juglone with low (2:1 to 3:1) regioselectivity in the sense shown.[25a,52,53] However, BF_3 catalysis

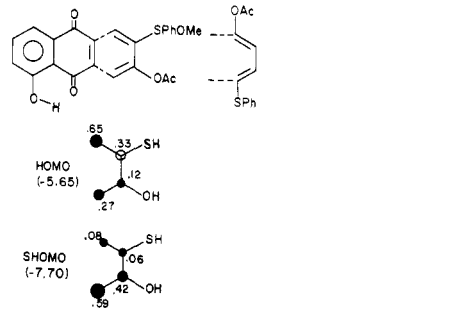


Figure 7. Regioselectivity of *O,S*-diene cycloaddition to juglone and frontier MOs (STO-3G) of a model diene.

gives the opposite regioisomers in both of these cases. The regioselectivities of the uncatalyzed reactions are readily rationalized by using the frontier molecular orbitals calculated for the model diene shown at the bottom of Figure 7. Clearly, the high-lying S lone pair has made the terminus conjugated with S a more nucleophilic site, due to the high HOMO coefficient at this position. The enormous differences in terminal coefficients exaggerate the difference in nucleophilicites of the two sites, since there are three additional occupied π orbitals not too much lower in energy than the HOMO. The obtention of the opposite regioisomer with BF_3 catalysis cannot be rationalized on the basis of simple lowering of the quinone LUMO upon complexation, since this should *increase* FMO control. Instead, we suggest that a zwitterionic intermediate is formed reversibly, with oxygen better able to stabilize the allyl cation formed from the diene moiety than sulfur. The other reasonable possibility would involve coordination of BF_3 with sulfur, which would reverse the diene HOMO polarization; this, however, should be accompanied by a decrease in reactivity. Trost et al. suggested that the thermal reaction was diradical in character, while the catalyzed reaction was zwitterionic, or that the Lewis acid coordinates the diene acetoxy groups.[25a,52]

Conclusion

We have shown how the frontier orbitals of benzoquinones and naphthoquinones are influenced by substituents and how the LUMO coefficients of these species are related to the regioselectivity of attack by nucleophiles and nucleophilic dienes. The frontier orbital and resonance theory predictors are parallel in this series. The most important general result of this work is the prediction that substituent effects can be transmitted through many bonds, a prediction which has clear synthetic applications.

Acknowledgment. We are grateful to the National Institutes of Health for financial support of this research, to Professors T. Ross Kelly, R. K. Boeckman, Jr., and Alan P. Kozikowski for enlightening discussions, and to a referee for valuable critical comments.

Registry No. Benzoquinone, 106-51-4; 2-methylbenzoquinone, 553-97-9; 2-hydroxybenzoquinone, 2474-72-8; 2-methoxybenzoquinone, 2880-58-2; 2-formylbenzoquinone, 26172-03-2; 2-vinylbenzoquinone, 51985-12-7; 1,4-naphthoquinone, 130-15-4; 2-methyl-1,4-naphthoquinone, 58-27-5; 2-hydroxy-1,4-naphthoquinone, 83-72-7; 2-methoxy-1,4-naphthoquinone, 2348-82-5; 2-formyl-1,4-naphthoquinone, 76916-86-4; 2-vinyl-1,4-naphthoquinone, 76916-87-5; 5-methyl-1,4-naphthoquinone, 571-63-1; 5-hydroxy-1,4-naphthoquinone, 481-39-0; 5-methoxy-1,4-naphthoquinone, 4923-61-9; 5-formyl-1,4-naphthoquinone, 76916-88-6; 5-vinyl-1,4-naphthoquinone, 76916-89-7; 6-methyl-1,4-naphthoquinone, 605-93-6; 6-hydroxy-1,4-naphthoquinone, 4923-53-9; 6-methoxy-1,4-naphthoquinone, 29263-68-1; 6-formyl-1,4-naphthoquinone, 76916-90-0; 6-vinyl-1,4-naphthoquinone, 76916-91-1; 1,4,5,8-naphthodiquinone, 23077-93-2.

(51) Houk, K. N.; Strozier, R. W. *J. Am. Chem. Soc.* **1973**, *95*, 4094.
(52) Trost, B. M.; Bridges, A. J. *J. Am. Chem. Soc.* **1976**, *98*, 5017.
(53) Earlier results on catalyzed reversals of regioselectivity in cycloadditions to quinones can be found in: Stojanac, Z.; Dickinson, R. A.; Stojanac, N.; Woznow, R. J.; Valenta, Z. *Can. J. Chem.* **1975**, *53*, 616.