References and Notes

(1) Weitl, F. L.; Raymond, K. N.; Smith, W. L.; Howard, T. R. *J. Am. Chem. Soc.* **1978**, *100*, 1170–1172.
(2) Hurd, C. D.; Botteron, D. G. *J. Org. Chem.* **1946**, *11*, 207–214.
(3) Fishman-Goldenberg, V.; Spoerri, P. E. *Anal. Chem.* **1959**, *31*, 1735.
(4) Hines, J. W., Jr.; Stammy, C. H. *J. Med. Chem.* **1977**, *20*, 965–967.
(5) Ghosh, N.; Sarkar, D. *J. Indian Chem. Soc.* **1968**, *45*, 550–551; **1969**, *46*, 528–530; **1970**, *47*, 562–566, 723–725.
(6) Smith, W. L.; Raymond, K. N. *J. Inorg. Nucl. Chem.* **1979**, *41*, 1431–1436.
(7) (a) Berman, H.; Kim, S.-H. *Acta Crystallogr.* **1967**, *23*, 180–181. (b) Larsen, I. K.; Jerslev, B. *Acta Chem. Scand.* **1966**, *20*, 983–991.
(8) Bracher, B. H.; Small, R. W. H *Acta Crystallogr., Sect. B* **1970**, *26*, 1705–1709.
(9) Göttlicher, S.; Ochsenreiter, P. *Chem. Ber.* **1974**, *107*, 391–397.
(10) Larsen, I. K. *Acta Crystallogr., Sect. B.* **1978**, *34*, 962–964.
(11) Orville-Thomas, W. J.; Parsons, A. E. *J. Mol. Spectrosc.* **1958**, *2*, 203–212.
(12) Göttlicher, S.; Ochsenreiter, P. *Chem. Ber.* **1974**, *107*, 398–413.
(13) Larsen, I. K. *Acta Chem. Scand.* **1971**, *25*, 2409–2420.
(14) Kjaer, A.; Larsen, I. K.; Siversten, P. *Acta Chem. Scand., Ser. B* **1977**, *31*, 415–423.
(15) Smith, W. L.; Raymond, K. N., in preparation.
(16) Programs used by the PDP 8/E were written by Enraf-Nonius Corp.
(17) A maximum of 90 s was used to scan a reflection through a variable scan angle of $0.6 + 0.14 \tan\theta$, where θ was calculated using $(\lambda_{K\alpha_1} + \lambda_{K\alpha_2})/2$. The background was estimated by extending the scan 25% on each side. An aperture with a variable width of $2.0 + \tan\theta$ mm and a height of 4 mm was located 173 mm from the crystal. An attenuator was employed when the intensity exceeded 5×10^4 Hz. The orientation was checked every 250 reflections and recalculated if any of the setting angles changed more than 0.1%. Three intensity standards were measured every 7200 s.
(18) Abu-Dari, K.; Ekstrand, J. D.; Freyberg, D. P.; Raymond, K. N. *Inorg. Chem.* **1979**, *18*, 108–112.
(19) Templeton, L. K.; Templeton, D. K. "American Crystallographic Association Proceedings," Ser. 2, Vol. 1; 1973; p 143.
(20) Baker, E. C.; Brown, L. D.; Raymond, K. N. *Inorg. Chem.* **1975**, *14*, 1376–1379.
(21) Machine computations were performed on a CDC 7600 computer using, in addition to locally written programs, Zalkin's FORDAP Fourier program; Ibers' NUCLS group least-squares version of the Busing–Levy ORFLS; ORFFE, a function and error program by Busing and Levy; Johnson's ORTEP, a thermal ellipsoid plot program; MULTAN, a program series for direct-methods phase determination by Germain, Main, and Woolfson.
(22) The function minimized in all refinements is $\sum w(|F_o| - |F_c|)^2$ where $w = 4F_o^2/\sigma^2(F_o^2)$.
(23) Definitions of indicators are $R = \sum||F_o| - |F_c||/\sum|F_o|$, $R_w = [\sum w(|F_o| - |F_c|)^2/\sum wF_o^2]$, and the error in an observation of unit weight $= [\sum w(|F_o| - |F_c|)^2/(N_o - N_v)]^{1/2}$, where N_o is the number of observations and N_v is the number of refined variables.
(24) "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, England, 1974; Vol. IV.
(25) Zachariasen, W. H. *Acta Crystallogr., Sect. A* **1968**, *24*, 212–216.
(26) Hamilton, W. C. *Acta Crystallogr.* **1965**, *18*, 502–510.
(27) "Tables of Interatomic Distances and Configurations in Molecules and Ions," *Chem. Soc., Spec. Publ., Suppl. 1956–1959* **1965**, *No. 18*.
(28) Housty, J.; Hospital, M. *Acta Crystallogr.* **1966**, *21*, 553–559.
(29) Hospital, M.; Housty, J. *Acta Crystallogr.* **1966**, *20*, 626–630.
(30) Hospital, M. *Acta Crystallogr., Sect. B* **1971**, *27*, 484–494.
(31) Smith, W. L.; Ekstrand, J. D.; Raymond, K. N. *J. Am. Chem. Soc.* **1978**, *100*, 3539–3544.
(32) Busing, W. R.; Levy, H. A. *Acta Crystallogr.* **1964**, *17*, 142–146.
(33) $\bar{x} = 1/n \sum x_i$; $\sigma_{(\bar{x})} = [\sum(x_i - \bar{x})^2/n(n-1)]^{1/2}$.
(34) Hamilton, W. C. *Annu. Rev. Phys. Chem.* **1962**, *13*, 19–40.
(35) Dyer, J. R. "Application of Absorption Spectroscopy of Organic Compounds"; Prentice-Hall: Englewood Cliffs, N.J., 1965; p 35.
(36) Price, B. J.; Sutherland, I. O. *Chem. Commun.* **1967**, 1070–1071.
(37) Hadži, D.; Prevoršek, D. *Spectrochim. Acta* **1957**, *10*, 38–51.
(38) Exner, O. *Collect. Czech. Chem. Commun.* **1965**, *30*, 652–663.

A Molecular Orbital Study of the Benzene Oxide–Oxepin Valence Isomerization

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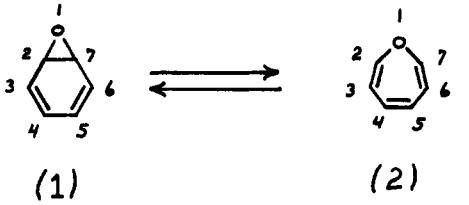
Abstract: Theoretical calculations on the valence isomerization of various substituted benzene oxides (**1**) to the corresponding oxepins (**2**) have been carried out using ab initio self-consistent-field and semiempirical (MINDO/3) molecular orbital theory. The MINDO/3 calculations successfully reproduce the known substituent effects at ring positions X_2 and X_3 and give a reasonable estimate of the activation energy for **1** → **2**. Several predictions are made concerning the effect of other substituents on the benzene oxide–oxepin equilibrium. Additionally, some substitution patterns are suggested which may "drive" the equilibrium completely toward either the oxepin or benzene oxide isomers. We also present calculated structures for benzene oxide and oxepin (C_6H_6O) and compare them with the structures of ethylene oxide (C_2H_4O), benzenimine (C_6H_6NH), and norcaradiene ($C_6H_6CH_2$).

Introduction

The epoxidation of planar aromatic hydrocarbons yields molecules with structures similar to **1**. These arene oxides are generally unstable species which may isomerize to give oxepins (**2**) or phenols, or may suffer nucleophilic attack. The first successful synthesis of the simplest arene oxide, benzene oxide (**1**), occurred some 14 years ago.[2] Since then, many structural analogues of **1** including molecules with different substituents at ring positions 2, 3, and 4 and molecules which replace -O- by -NX- and -CXX'- have been synthesized and characterized.[3] Particularly well studied has been the valence isomerization **1** ⇄ **2**. One of the aspects of these studies which is especially interesting relates to the effect of ring substitution on the position of the benzene oxide–oxepin equilibrium.



(1) (2)

Substitution at position 2 (X_2) favors oxepin while substitution at position 3 (X_3) favors benzene oxide relative to the parent compound $X_2 = X_3 = H$.

We have become interested in elucidating the underlying electronic causes of this substituent effect and wish to present here the results of our analysis. We discuss not only the effect

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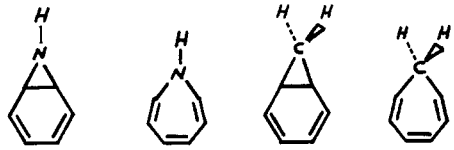
Table I. Ethylene Oxide Structure[a]

coordinate	exptl[b]	MINDO/3	STO-3G[c]
R(C-C)	1.472	1.447	1.483
R(C-O)	1.436	1.389	1.433
R(C-H)	1.082	1.114	1.088
θ(H-C-H)	116.7	107.4	114.5
θ(H_2C-C)[d]	159.4	160.3	155.3

[a] Distances in ångstroms and angles in degrees; C_{2v} symmetry assumed. [b] Reference 9. [b] Reference 10. [d] This is the angle between the C-C axis and the bisector of the H-C-H angle.

on the benzene oxide–oxepin equilibrium of changing a given substituent from one ring position to another, but also the relative stabilizing effect of a wide range of different substituents. Is it possible, for example, to suggest substituent patterns which will shift the equilibrium far toward either the oxide or oxepin isomers? In addition, the activation energies for **1** ⇄ **2** are known to be rather low. Do the substituents markedly alter these activation energies? Possibly, one could design a substituted arene oxide which is thermodynamically unstable with respect to isomerization to oxepin but which is nonetheless kinetically locked into the arene oxide tautomer. Finally, we wish to compare the structure and electronic properties of **1** and **2** with the related isoelectronic species benzenimine (**3**), azepin (**4**), norcaradiene (**5**), and cycloheptatriene (**6**).



(3) (4) (5) (6)

Methods of Calculation

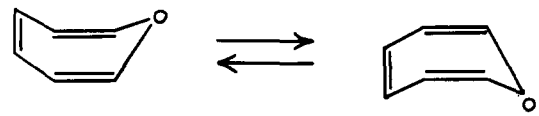
Both ab initio and semiempirical self-consistent-field molecular orbital theory were used to determine molecular equilibrium geometries, relative energies of isomers, activation energies for isomerization, bond orders, and charge densities. The ab initio SCF-MO calculations were done using the GAUSSIAN 70 computer program written by Pople and coworkers,[4-6] and Dewar's MINDO/3 program[7-8] was used for the semiempirical molecular orbital calculations. All geometry optimizations with the GAUSSIAN 70 program were done with the STO-3G basis set. A few selected calculations were also done at the 4-31G level to check the basis-set dependence of our results.

Results and Discussion

Structural Studies of Benzene Oxide and Oxepin. The difficulty of isolating benzene oxide and oxepin from their isomers has precluded the detailed determination of their structures. Since these molecules may be intermediates in many reactions of importance in organic and biochemistry, the determination of their structures using molecular orbital theory seems appropriate. We have used both the MINDO/3 and ab initio SCF molecular orbital methods described above to accomplish this. In order to assess the capability of our computational procedures to accurately determine the structures of epoxides, we began this portion of our study by first calculating the structure of a simple epoxide, ethylene oxide, whose structure is known.

A summary of these calculations is reported in Table I. Both molecular orbital procedures agree closely with the experimental structure, although the ab initio calculations seem to consistently do better than MINDO/3 in predicting bond lengths.

We have used both MINDO/3 and ab initio SCF-MO methods to determine the equilibrium geometries of both benzene oxide and its valence tautomer oxepin. The optimizations were done assuming most C-H bond lengths equal to 1.09 Å and a single plane of symmetry passing through the oxygen atom and bisecting the opposite C-C bond. The calculated structures are presented in Table II and the coordinates optimized are explicitly indicated by an asterisk. Of particular interest is the degree of nonplanarity in the ring. Vogel and Günther[2] have suggested from their NMR studies of substituted (2,7-dimethyl) and unsubstituted oxepins that the parent oxepin assumes the boat-like structure shown in **7**. The



(7)

MINDO/3 studies confirm this, although the degree of nonplanarity is calculated to be exceedingly small. That MINDO/3 should predict a more flattened ring conformation than is actually observed is consistent with the results of other MINDO/3 calculations on heterocyclic systems. We have shown in a separate study that this molecular orbital method consistently underestimates the degree of nonplanarity of rings.[11] The ab initio calculations with a STO-3G basis set appear to fail on this point and predict that the planar conformation of oxepin is preferred. However, this could be due to the fact that we did not *completely* optimize this structure with ab initio techniques. The preference shown by oxepin for a planar or near-planar structure in these calculations is probably indicative of a very low barrier to inversion of the boat forms shown in **7**. Benzene oxide, on the other hand, is calculated by both methods to be highly nonplanar as shown in structure **8**. Both methods predict that the epoxide ring makes

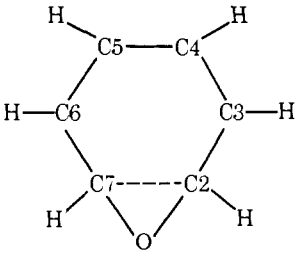
(8)

an angle of 73° with respect to the benzene ring. The alternating long and short C-C bonds around the ring in benzene oxide and oxepin are consistent with the alternating single and double bonds shown in the valence-bond structures **1** and **2** and argue against a high degree of aromaticity in these systems. In fact, we have some evidence that the degree of homoaromaticity in the benzene oxide system is small. If we compare the MINDO/3 calculated C-C bond lengths of 1,3-butadiene[12] with the corresponding bond distances in benzene oxide, one observes no shortening of the C4-C5 (formally single) bond relative to butadiene (1.463 vs. 1.464 Å) and only a small lengthening of the C5-C6 and C4-C3 (double) bonds (1.361 vs. 1.330 Å). Later in this report, we note that the degree of nonplanarity of benzene oxide and benzenimine (**11**) is substantially greater (73° in both molecules) than in the isoelectronic norcaradiene (**9**) (62°). This may be due to a net stabilizing interaction between the oxygen and nitrogen lone pairs and the butadienoid π system. Such an interaction would be impossible with norcaradiene.

Politzer and Daiker[13] have carried out extensive geometry optimization calculations on benzene oxide using ab initio SCF-MO theory with a STO-5G basis set and have found an equilibrium geometry very close to our own.

Benzene Oxide–Oxepin Isomerization Energies. Vogel and Günther[2] have determined the enthalpy of isomerization for the reaction **1** → **2** in a nonpolar solvent system by measuring

Table II. Calculated Equilibrium Geometries of Benzene Oxide and Oxepin[a]



coordinates	MINDO/3 benzene oxide	MINDO/3 oxepin	ab initio benzene oxide	ab initio oxepin
		Bond Lengths (Å)		
C5-C4	1.463*	1.349*	1.480	1.332*
C5-C6 = C4-C3	1.361*	1.471*	1.340	1.440*
C6-C7 = C3-C2	1.484*	1.345*	1.536*	1.284*
C7-C2	1.512*	2.416*	1.520*	2.478*
C7-O = C2-O	1.393*	1.333*	1.450*	1.434*
C5-H5 = C4-H4	1.09	1.09	1.09	1.09
C6-H6 = C3-H3	1.09	1.09	1.09	1.09
C7-H7 = C2-H2	1.09	1.09	1.083	1.083
		Bond Angles (deg)		
C4-C5-C6 = C5-C4-C3	121.4*	126.8*	122.4	128.0
C5-C6-C7 = C4-C3-C2	121.1*	128.1*	120.6*	127.9*
C6-C7-O = C3-C2-O	117.6*	129.9*	117.1*	134.3*
C6-C7-C2 = C3-C2-C7	117.5*	105.0*	117.0*	104.1*
C7-O-C2	65.8*	130.0*	63.2*	119.6*
C4-C5-H5 = C5-C4-H4	117.5*	119.0*	118.8	118.8
C5-C6-H6 = C4-C3-H3	121.5*	115.9*	119.8	119.8
O-C7-H7 = O-C2-H2	114.8*	106.7*	114.9*	106.5*
		Dihedral Angles[b] (deg)		
C3-C4-C5-C6	0.0	0.0	0.0	0.0
C4-C5-C6-C7	358.1*	357.6*	0.0	0.0*
C5-C4-C3-C2	1.9*	2.4*	0.0	0.0*
C5-C6-C7-C2	1.9*	2.0*	0.0	0.0*
C4-C3-C2-C7	358.1*	358.0*	0.0	0.0*
C5-C6-C7-O	296.6*	359.0*	293.6*	0.0*
C4-C3-C2-O	63.4*	1.0*	66.4*	0.0*
C3-C4-C5-H5	180.0	180.0	180.0	180.0
C6-C5-C4-H4	180.0	180.0	180.0	180.0
C4-C5-C6-H6	173.3*	177.6*	180.0	180.0*
C5-C4-C3-H3	186.7*	182.4*	180.0	180.0*
C2-O-C7-H7	247.2*	186.4*	249.5*	180.0*
C7-O-C2-H2	112.7*	173.6*	110.5*	180.0*
α[c]	73.4*	2.3*	73.3*	0.0*
β[d]	1.9*	0.9*	0.0	0.0*
calcd dipole moments, D	2.03	0.38	1.51	0.76
calcd energies[e]	−0.23	−1.93	−301.682 48	−301.647 64

[a] C_s symmetry was assumed for both molecules during the optimizations. The coordinates which have been optimized are indicated by an asterisk. [b] The following convention is used in defining the dihedral angles: for the four atoms A-B-C-D, one looks along the C-B axis from C toward B. One then rotates the A-B bond *clockwise* about the B-C axis until it eclipses the C-D bond. The angle of rotation is the dihedral angle. Negative angles correspond to counterclockwise rotations. [c] This is the angle the C7-O-C2 plane makes with the C6-C7-C2-C3 plane. Positive angles mean the C7-O-C2 plane is tilted toward the reader. [d] This is the angle between the C5-C4-C6-C3 and the C6-C7-C2-C3 planes. Positive angles mean C5-C4-C6-C3 is tilted toward the reader when C6-C7-C2-C3 is constrained to lie in the plane of the paper. [e] MINDO/3 energies are heats of formation expressed in kcal/mol. The ab initio energies are in hartrees and represent the calculated total electronic energy of the molecule.

the temperature dependence of the equilibrium constant. They report a value of +1.7 kcal/mol. The entropy change was also determined and permitted a calculation of the Gibbs free energy, which is reported to be −1.3 kcal/mol at room temperature. Changing to more polar solvents, however, shifts the equilibrium toward benzene oxide (more positive ΔG) and suggests a larger dipole moment for benzene oxide than for oxepin. Since the dipole moments for these species have not been measured, we decided to compute them quantum mechanically and the results are shown in Table II. Both MINDO/3 and ab initio MO (STO-3G basis set) theory predict benzene oxide to be much more polar than oxepin in agreement with our expectations. For benzene oxide, the value appears to be in the range 1.5-2.0 D. Since the STO-3G basis set often leads to dipole moments which are too small while the 4-31G basis often overestimates them,[14,15] it seems likely that the dipole moment of benzene oxide is greater than 1.5 D. For oxepin, in addition to MINDO/3 and ab initio MO (STO-3G) dipole moments, we were also able to calculate a value for the dipole moment using the 4-31G basis set. MINDO/3 gives 0.38 D while ab initio MO theory with the STO-3G and 4-31G bases gives 0.76 and 1.36 D, respectively. Because of the previously noted tendency for the STO-3G basis to underestimate polarity and for the 4-31G basis to overestimate it, we believe the true dipole moment for oxepin to lie in the range 0.76-1.36 D.

If the polarity of the solvent is decreased, we expect that the enthalpy of isomerization **1** → **2** would be less than +1.7

Table III. Calculated MINDO/3 and Ab Initio (STO-3G) Energies for Some Substituted Benzene Oxides and Oxepins

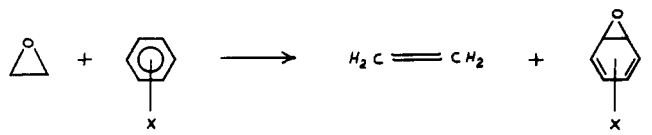
MINDO/3[a,b]				
benzene oxide	$\Delta H_f°$, kcal/mol	oxepin	$\Delta H_f°$, kcal/mol	$\Delta(\Delta H_f°)$, kcal/mol
3-aminobenzene oxide	−10.83	3-aminooxepin	−4.86	+5.97
3-hydroxybenzene oxide	−54.90	3-hydroxyoxepin	−49.60	+5.30
3-nitrobenzene oxide	−19.15	3-nitrooxepin	−15.49	+3.66
3-fluorobenzene oxide	−49.63	3-fluorooxepin	−48.46	+1.17
2-nitrobenzene oxide	−14.06	2-nitrooxepin	−13.15	+0.91
3-methylbenzene oxide	−4.09	3-methyloxepin	−3.55	+0.54
4-aminobenzene oxide	−10.32	4-aminooxepin	−9.98	+0.34
4-methylbenzene oxide	−3.58	4-methyloxepin	−3.62	−0.04
benzene oxide[d]	−0.23	oxepin	−1.93	−1.70
4-nitrobenzene oxide	−18.63	4-nitrooxepin	−20.85	−2.22
4-fluorobenzene oxide	−50.06	4-fluorooxepin	−53.33	−3.27
2-fluorobenzene oxide	−54.57	2-fluorooxepin	−60.53	−5.96
2-methylbenzene oxide	−3.35	2-methyloxepin	−11.48	−8.13
2-cyanobenzene oxide	+19.32	2-cyanooxepin	+10.65	−8.67
2-aminobenzene oxide	−8.89	2-aminooxepin	−18.37	−9.48
2,7-dimethylbenzene oxide	−3.14	2,7-dimethyloxepin	−20.72	−17.58

Ab Initio (STO-3G)[c]				
benzene oxide	E, hartrees	oxepin	E, hartrees	ΔE, kcal/mol
3-methylbenzene oxide	−340.266 03	3-methyloxepin	−340.226 80	+24.62
4-methylbenzene oxide	−340.266 90	4-methyloxepin	−340.229 27	+23.61
2-methylbenzene oxide	−340.268 25	2-methyloxepin	−340.233 27	+21.95
benzene oxide	−301.682 48	oxepin	−301.647 64	+21.86
4-aminobenzene oxide	−355.992 72	4-aminooxepin	−355.958 53	+21.45
4-nitrobenzene oxide	−502.382 13	4-nitrooxepin	−502.349 14	+20.70

[a] The MINDO/3 calculations on benzene oxide and oxepin involved complete geometry optimizations consistent with the maintenance of a plane of symmetry passing through oxygen and fixed C–H bond lengths (1.09 Å). With the substituted benzene oxides and oxepins, MINDO/3 was used to optimize *only* the geometry of the substituent. The optimized benzene oxide or oxepin coordinates were used for the remainder of the molecule. [b] The isomerizations presented in this table are in order of increasing preference for oxepin (increasing exothermicity). [c] A large-scale (but not full) geometry optimization at the STO-3G level was carried out on benzene oxide and oxepin. The degrees of freedom optimized are shown in Table II by asterisks. No further optimizations were performed on the substituted benzene oxides and oxepins. Standard geometries are assumed for the substituent. [d] For the sake of comparison, the MINDO/3 heat of formation for phenol (with partial geometry optimization) is −28.27 kcal/mol, indicating that this is the thermodynamically preferred isomer vis-à-vis benzene oxide and oxepin.

kcal/mol, and, unless there is an opposing shift in ΔS, one should observe a shift in the equilibrium toward oxepin. Similarly, in the gas phase ΔH should be less than +1.7 kcal/mol. Our molecular orbital calculations correspond to the gas-phase reaction and our calculated energies of **1**, **2**, and various substituted benzene oxides and oxepins are presented in Table III. MINDO/3 predicts an enthalpy of isomerization of −1.7 kcal/mol, in good agreement with our expectations. The ab initio SCF-MO calculations with the STO-3G basis give a very different and unexpected isomerization energy, ΔE = +21.9 kcal/mol. We have also done this calculation using the 4-31G basis and obtain a ΔE of −7.6 kcal/mol. Since the STO-3G basis set is known to yield significantly poorer estimates of reaction energies than the 4-31G basis for nonisodesmic[16] reactions,[17] it is likely that the MINDO/3 and 4-31G results provide the more reliable approximations to the actual gas-phase benzene oxide → oxepin isomerization energy. Furthermore, since MINDO/3 has been reported to overestimate the stability of epoxide rings, it is likely that the 4-31G calculated isomerization energy of −7.6 kcal/mol is the more accurate value.

The relative stabilities of various arene oxides can be compared by computing the energies of the reaction shown below. We have done such a calculation with MINDO/3 using fully optimized geometries only for the case X = H and find that ΔH = +17 kcal/mol. This ΔH is consistent with the relative resonance stabilities of reactant (benzene) and products ("butadiene" + ethylene).



Substituent Effects on the Benzene Oxide–Oxepin Equilibrium. A large number of substituted benzene oxide–oxepin systems have been synthesized and, in several cases, the relative amounts of the two valence isomers have been determined. Briefly, one finds that relative to the **1** ⇄ **2** parent system:

(1) Methyl substitution at the 2 position shifts the equilibrium toward oxepin. As mentioned previously, Vogel and Günther[2] report a $\Delta H°$ of +1.7 kcal/mol for **1** → **2**. For the 2-methyl system, $\Delta H°$ drops to +0.4 ± 0.2, in a nonpolar solvent, indicating an increased preference for the oxepin. The equilibrium between the two isomers is rapid with measured Arrhenius activation energies of 9.2 kcal/mol for oxide → oxepin and 8.7 kcal/mol for the reverse reaction. Replacing methyl with acetyl in the 2 position shifts the equilibrium markedly toward oxepin.

(2) 2,7-Dimethylbenzene oxide–oxepin is almost entirely in the oxepin form (<5% oxide).[2]

(3) Methyl substitution at the 3 position shifts the equilibrium toward the oxide, although there are still detectable amounts of the oxepin isomer.[3] Also, substitution in the 3 position with chloro and $-CO_2C(CH_3)_3$ favors the oxide.

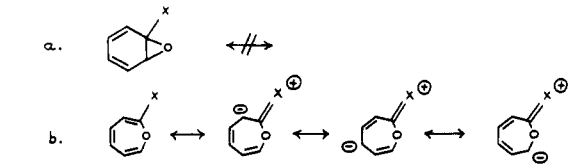
(4) 4-Methyl substitution enhances the contribution of the oxepin tautomer but both isomers exist in detectable amounts at equilibrium.

(5) 4,5-Dimethyl substitution strongly favors the oxide isomer. However, replacement of each methyl by $-C(O)OCH_3$ yields a system in which oxide and oxepin exist in roughly equal concentrations.

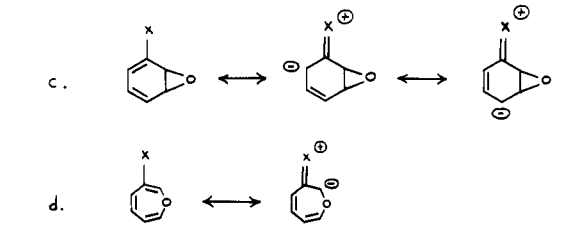
Since a great deal of effort has gone into the synthesis of these and other substituted benzene oxides–oxepins, it is of some interest to try to understand how the substitution pattern affects the oxide–oxepin equilibrium. Specifically, we wish to know why 2 substitution normally favors oxepin and why 3

Scheme I. Low-Energy Resonance Structures for π-Electron Donors

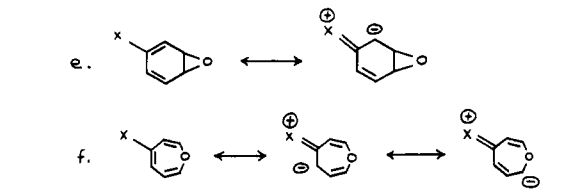
Substitution in the 2 Position:



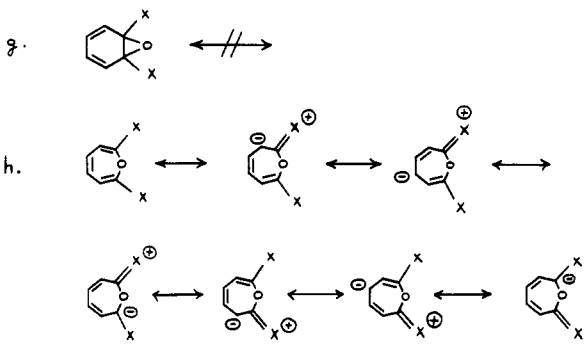
Substitution in the 3 Position:



Substitution at the 4 Position:



Substitution in the 2,7 Position:



substitution favors oxide. We also wish to determine the generality of these observations by studying, theoretically, the effects of other substituents on the isomerization.

We have thus carried out MINDO/3 and ab initio SCF-MO (STO-3G basis) calculations on a number of substituted benzene oxides and oxepins and the computed energies of these molecules are presented in Table III. In order to test the reliability of our methods, we first compare our methyl substituent effects with those summarized above. MINDO/3 predicts the isomerization energies for the 2-, 3-, and 4-methyl system to be −8.13, +0.54, and −0.04 kcal/mol, respectively, compared with −1.70 kcal/mol for the parent system. Thus, this method correctly predicts that 2-methyl substitution favors oxepin and 3-methyl substitution favors the oxide. It incorrectly predicts the effect of 4-methyl substitution, although it is consistent with the observation that 4,5-dimethyl substitution favors the oxide. The disubstituted species 2,7-dimethyloxepin is correctly predicted to be much more stable than the corresponding oxide. That is, the stabilizing effect of two methyl groups appears to be about twice that of one. The ab initio calculations with the STO-3G basis do poorly in this test. Thus, all three methyl substitution patterns are predicted to favor the oxide.

The methyl substituent effect is probably most simply explained in terms of valence bond resonance structures involving the π electrons (Scheme I). The methyl group can act as a π-electron donor to a π system via hyperconjugation involving the methyl C–H bonds. When methyl is attached at the 2 position of benzene oxide, it is not able to conjugate with the π system in the ring. We can write only one important energy-lowering resonance structure for this species, Ia. However, when methyl is attached in the 2 position of oxepin, hyperconjugation with the ring π system is possible and four resonance structures can be written, Ib. We would correctly predict that substitution of a π-electron donor in the 2 position would stabilize oxepin relative to oxide. Resonance structures Ic and Id show the effect of placing a π-electron donor (such as methyl) in the 3 position. Three energy-lowering resonance structures can be written for the substituted oxide while only two can be written for the oxepin. Therefore, we conclude that 3-methyl substitution favors oxide over oxepin, in agreement with observation. Since the difference in the number of valence-bond structures that can be written for this case is small (two vs. three), we would expect this substituent effect to be small. In the case of 2 substitution, however, the difference in the number of resonance structures is large (one vs. four) and we expect the effect of the substituent on the equilibrium to be more pronounced. Our MINDO/3 calculations support this prediction. Recall that $\Delta H°$ for the parent system is calculated to be −1.70 kcal/mol. Methyl substitution at the 2 position shifts the equilibrium ($\Delta H°$) 6.43 kcal/mol farther toward oxepin. Substitution in the 3 position, however, only shifts $\Delta H°$ 2.24 kcal/mol in the direction of the oxide. Vogel and Günther[2] have measured quantitatively the effect of 2-methyl substitution on the enthalpy of isomerization [$\Delta H°$(parent) = +1.7 kcal/mol, $\Delta H°$(2-methyl) = +0.4 kcal/mol] but unfortunately there is no comparable study of 3-methyl substitution against which we can check our prediction.

The important energy-lowering resonance structures for the 4-methyl system are shown in Ie–If. The oxepin affords the greatest delocalization of the substituent electrons undergoing hyperconjugation with the ring and we, therefore, expect the equilibrium to shift away from the oxide. This is observed experimentally[3] but our MINDO/3 calculations fail to reproduce this effect. Instead, they predict a very small stabilization of the oxide isomer. Substitution in both the 2 and 7 positions is predicted on the basis of Ig–Ih to shift the equilibrium strongly toward oxepin. Both MINDO/3 and the experimental studies done on this system confirm this.

We have carried out MINDO/3 calculations on a variety of other substituted benzene oxides and oxepins in order to probe the effect of various substituent patterns on the oxide-oxepin equilibrium. To our knowledge, none of these systems has yet been synthesized and, therefore, they constitute a prediction of what might be found. We have chosen substituents which are both π-electron donors (-CH_3, -NH_2, -F, -OH) and π-electron acceptors (-CN, -NO_2). Table III shows that substitution of any ligand, which is capable of conjugating with the ring, at the 3 position favors oxide. This is true of both π-electron donors (-CH_3, -NH_2, -F, -OH) and acceptors (-NO_2). Substitution at the 4 position has little effect with MINDO/3 predicting that some substituents shift the equilibrium toward oxepin (-NO_2, -F) and others toward oxide (-NH_2, -CH_3). Substitution at the 2 position strongly favors oxide except for -NO_2. It may be that 2-nitro substitution is particularly unfavorable for oxepin because of the nearness of the ring oxygen to the substituent oxygen in this isomer relative to benzene oxide. Note that 2-cyano, which is also a π acceptor, does not show this anomalous behavior, presumably because it is more distant from the ring oxygen.

Scheme II contains valence bond resonance structures for various substituted benzene oxides and oxepins in which the substituent is viewed as a π-electron acceptor. Thus, Scheme II serves as the complement of Scheme I. Comparison of Schemes I and II shows that all the conclusions concerning the relative stabilization of benzene oxide and oxepin via conjugation with π-donating substituents also apply to π acceptors. As pointed out above, the MINDO/3 calculations reported

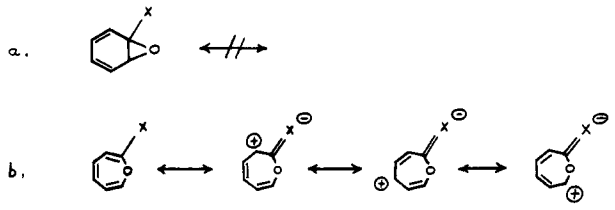
Table IV. MINDO/3 Calculated Activation Energies for Some Valence Isomerizations

bicyclic species	ΔH_f, kcal/mol	activation energy for →	transition state ΔH_f, kcal/mol	activation energy for ←	ΔH_f, kcal/mol	monocyclic species
benzene oxide[a]	−0.23	12.37	12.14[a]	14.07	−1.93	oxepin[a]
2,7-dimethylbenzene oxide[b]	−3.14	5.62	2.48[b]	23.20	−20.72	2,7-dimethyloxepin[b]
norcaradiene[a]	47.99	10.92	58.91[a]	23.06	35.85	cycloheptatriene[a]
2-methylnorcaradiene[c]	52.77	8.80	61.57[c]	25.21	36.36	2-methylcycloheptatriene[c]
benzenimine[a]	50.60	14.32	64.92[a]	22.81	42.11	azepin[a]

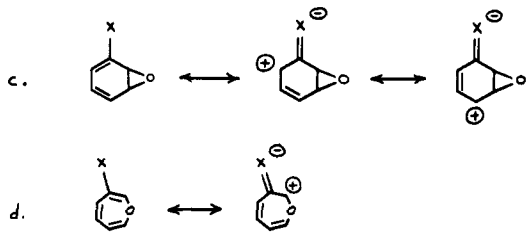
[a] The reaction path for isomerization was determined in the following way. The C2–C7 bond in the bicyclic species (benzene oxide, norcaradiene, or benzenimine) was increased in five increments beginning at the optimum bicyclic geometry (as determined by MINDO/3) and ending at the corresponding monocyclic isomer. For each C2–C7 separation along the way, the remaining geometrical degrees of freedom were optimized consistent with molecular C_s symmetry and fixed C–H bond lengths. For each of the three bicyclic molecules, the energy increased monotonically to the transition state, then decreased to the product isomer. There were no valleys along the pathway which would indicate the existence of metastable intermediates. [b] Only the C–CH_3 bond lengths and C–C–CH_3 torsion angles were optimized. Otherwise the optimum geometries for the *unsubstituted* benzene oxide, oxepin, or transition state species were used. [c] Only the C–CH_3 bond length was optimized. Otherwise, the optimum geometries for the *unsubstituted* norcaradiene, cycloheptatriene, or transition state species were used.

Scheme II. Low-Energy Resonance Structures for π-Electron Acceptors

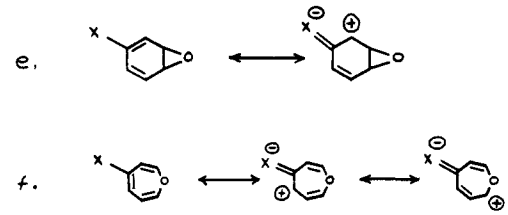
Substitution in the 2 Position:



Substitution at the 3 Position:



Substitution at the 4 Position:



in Table III are consistent with this valence-bond description.

We have already noted that 2-methyl substitution enhances oxepin at the expense of oxide. MINDO/3 also shows that symmetric dimethyl substitution (2,7-dimethyl) shows an even greater preference for oxepin and this is confirmed by experiment. Based on our calculations, we would like to suggest another set of substituents which should "lock" the system in the oxepin form. Thus, 2-amino favors oxepin even more than 2-methyl and we would predict that 2,7-diamino would produce an even more marked shift in the equilibrium than 2,7-dimethyl. Conversely, we would expect from the results in Table III that 3-amino would favor the oxide isomer more strongly than 3-methyl. Constructing the appropriate resonance structures shows that 3,6-diamino substitution should still further increase the amount of oxide. It must be pointed out that the experimental demonstration of these predictions will depend on the stability of these substituted oxides and oxepins with respect to rearrangement to entirely different species such as substituted phenols.

Barriers to Isomerization in the Benzene Oxide–Oxepin System. Although many substituted oxepins are thermodynamically more stable than the corresponding oxides, it is not necessarily the case that an initially formed oxide will *rapidly* convert to the oxepin. Thus, if the activation enthalpy for isomerization is large, it is conceivable that an oxide which is thermodynamically unstable may be quite stable kinetically. We have calculated activation enthalpies for isomerization for the parent benzene oxide–oxepin system and for a substituted system (2,7-dimethyl) in which the oxepin form is much more stable than the oxide. We present these results in Table IV. The reaction path for isomerization of benzene oxide was determined in the following way. The C2–C7 bond in the bicyclic species was increased in five increments beginning at the optimum bicyclic geometry (as determined by MINDO/3) and ending at the corresponding oxepin isomer. For each C2–C7 separation, the remaining geometrical degrees of freedom were optimized consistent with molecular C_s symmetry. The energy increased monotonically to the transition state, then decreased to the product isomer. There were no valleys along the pathway which would indicate the existence of metastable intermediates.

MINDO/3 predicts gas-phase activation enthalpies for **1** → **2** and **2** → **1** of 12.4 and 14.1 kcal/mol, respectively. The difference between these two numbers is, of course, just the calculated ΔH of reaction (−1.7 kcal/mol). Vogel[2] has determined solution-phase activation enthalpies for these reactions and finds them to be 9.1 kcal/mol for the forward reaction and 7.2 kcal/mol for the reverse. As mentioned earlier, the solvent can be expected to stabilize benzene oxide more than oxepin and reverse the relative magnitudes of the activation enthalpies for the forward and reverse reactions. These activation energies are low enough to suggest rapid interconversion of the isomers in the gas phase. Methyl substitution in both the 2 and 7 positions stabilizes oxepin much more than benzene oxide. There is also a significant (10 kcal/mol) stabilization of the transition state. The result of this is to lower the activation energy for the forward process from 12.4 to 5.6 kcal/mol. The reverse reaction is made much slower by this substitution owing to an increase in the activation enthalpy from 14.1 to 23.2 kcal/mol. Thus, the conversion of an initially formed 2,7-dimethylbenzene oxide to the thermodynamically favored oxepin is expected to be facile and the reverse process slow.

It is of interest to compare the structure of the transition-state complex to that of benzene oxide and oxepin. Most bond lengths and angles only change by small amounts in going from **1** to **2** and in almost all cases the corresponding variables for the transition-state complex lie somewhere between the two extremes. In the case of some geometrical variables, the transition state is more similar to **1** than **2** but with others the

Table V. Net Atomic Charges and Dipole Moments for Benzene Oxide, Oxepin, and the Transition State Complex

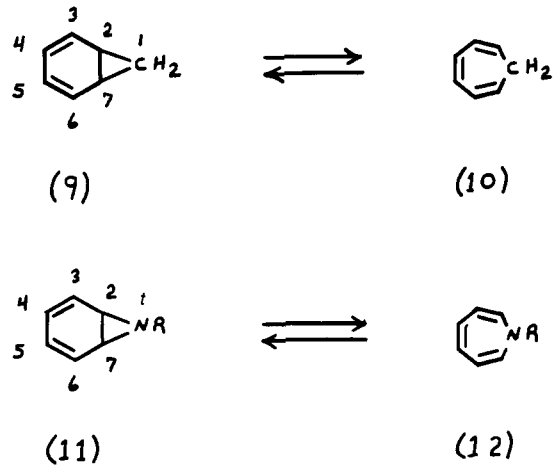
atom	charges, au		
	benzene oxide	transition state	oxepin
O	−0.381	−0.344	−0.403
C2, C7	0.257	0.309	0.355
C3, C6	−0.055	−0.122	−0.171
C4, C5	0.020	0.013	0.025
H2, H7	−0.040	−0.044	−0.018
H3, H6	0.011	0.019	0.022
H4, H5	−0.001	−0.004	−0.012
dipole moment, D	2.03	1.84	0.38

similarity is reversed. There are, however, two variables which change dramatically during the course of the isomerization. These are the C2-C7 bond length and the angle α (the angle the epoxide ring makes with the benzenoid ring). The C2-C7 bond lengths are 0.76 Å in benzene oxide, 1.21 Å in oxepin, and approximately 0.95 Å in the transition-state complex. The angles α are 73.4° in **1**, 2.3° in **2**, and 63.6° in the transition-state complex. Based on these two important geometrical variables, one would conclude that the transition state is structurally more similar to benzene oxide than to oxepin.

We have also examined the redistribution of charge as the molecule isomerizes and the results are presented in Table V. The calculated dipole moments for **1**, **2**, and the transition state are also included. The transition-state dipole moment is clearly quite large and is much closer to that of benzene oxide than to oxepin. We would expect the stabilizing effect of polar solvents to be similar for benzene oxide and the transition state and greater than for oxepin. Therefore, increasing the polarity of a solvent would be expected to have little effect upon the activation energy for **1** → **2** but should lower it for the reverse process **2** → **1**.

Isoelectronic Analogues of C_6H_6O: C_6H_6NH and $C_6H_6CH_2$. Valence isomerizations analogous to **1** → **2** have been reported for the isoelectronic system norcaradiene-cycloheptatriene (**9–10**)[18] and for substituted benzene imines-azepins (**11–12**).[19,20] The unsubstituted C_6H_6NH parent system is unknown. The similarity of these reactions to the benzene oxide-oxepin equilibrium is intriguing and suggests a study similar to that reported previously for **1** ⇄ **2**. In particular, we wish to know (1) of any structural changes which occur when O is replaced by CH_2 and NH, (2) of changes in the enthalpies of isomerization, and (3) of changes in the activation energies of isomerization.

It is known that substitution in the 1 position will shift the **9** ⇄ **10** equilibrium to either side depending on the particular substituent.[3,21] For the unsubstituted system, only the cycloheptatriene exists in measurable concentrations. Conversely, if the substitution is 1,1-dicyano, only norcaradiene can be detected. In the C_6H_6NX system, only the monocyclic species



is observed unless there are special geometrical constraints which force the system into the imine isomer.

All of our calculations on **9–12** were done with MINDO/3. Complete geometry optimizations (except R(C-H) = 1.09 Å = constant) consistent with C_s symmetry were performed on each of the molecules. The major structural features of these systems can be summarized briefly. All three bicyclic species are highly nonplanar with the three-membered ring making an angle of 60-70° with the plane defined by C2-C3-C6-C7 (benzene oxide, 73.4°; norcaradiene, 62.2°; benzenimine, 72.6°). In each of the molecules, the degree of nonplanarity of the six-membered ring is small. Thus, the angle between the two planes defined by C3-C4-C5-C6 and C2-C3-C6-C7 is calculated to be approximately 1-2°. The monocyclic species also have similar structures. Each is predicted to have an extremely shallow boat conformation. If we define two angles α and β with α being the angle between the 1-2-7 and 2-3-6-7 planes and β the angle between the 3-4-5-6 and 2-3-6-7 planes, then α is calculated to be 2-5° and β 1-3° in all three molecules.

It is of interest to compare the relative thermodynamic stabilities of **1** and **2** with **9** and **10**, and **11** and **12**. The MINDO/3 calculated enthalpies of formation for each of these species are included in Table VI and show the monocyclic cycloheptatriene and azepin to be preferred to the bicyclic isomers. Although this ordering of stabilities is the same as in the benzene oxide-oxepin system, the magnitude of the enthalpy difference between isomers is much greater in **9–12**. Hoffmann has noted that substituents at the 1 position which can interact favorably with the asymmetric component of the Walsh orbital in norcaradiene (such as cyanide) will stabilize the norcaradiene structure relative to cycloheptatriene. MINDO/3 is in agreement with this prediction, although 1-cyanocycloheptatriene is still predicted to be more stable than 1-cyanonorcaradiene by 5 kcal/mol (vs. 12 kcal/mol for the unsubstituted species). Furthermore, MINDO/3 predicts that 1-methyl and

Table VI.[a] MINDO/3 Calculated Heats of Formation of Benzene Oxide, Norcaradiene, and Benzenimine and Their Isomerization Products

bicyclic species	$\Delta H_f°$, kcal/mol	monocyclic species	$\Delta H_f°$, kcal/mol	$\Delta(\Delta H_f°)$, kcal/mol
benzene oxide	−0.2	oxepin	−1.9	−1.7
norcaradiene	48.0	cycloheptatriene	35.8	−12.2
1-cyanonorcaradiene	69.0	1-cyanocycloheptatriene	64.4	−4.6
1-methylnorcaradiene	43.2	1-methylcycloheptatriene	39.2	−4.0
1-difluoromethylnorcaradiene	−61.7	1-difluoromethylcycloheptatriene	−66.3	−4.6
2-methylnorcaradiene	52.8	2-methylcycloheptatriene	36.4	−16.4
benzenimine	50.6	azepin	42.1	−8.5

[a] The calculations on the unsubstituted C_6H_6O, $C_6H_6CH_2$, and C_6H_6NH involved complete geometry optimizations consistent with C_s symmetry and fixed C-H bond lengths (1.09 Å). With the substituted species MINDO/3 was used to optimize *only* the geometry of the substituent. The coordinates for the optimized unsubstituted parent species were used for the remainder of the molecule.

1-difluoromethyl (1-CHF_2) substitution also shifts the equilibrium toward norcaradiene while 2-methyl substitution favors cycloheptatriene in analogy with oxepin.

We have looked at the kinetic stability of norcaradiene and 2-methylnorcaradiene. As reported above, both species are thermodynamically unstable with respect to conversion to cycloheptatrienes. Table IV presents the results of our studies on the energetics of these isomerizations and shows that neither norcaradiene nor its 2-methyl derivative is locked into the unstable bicyclic form. Thus, the activation enthalpy for **9** → **10** is calculated to be 10.9 kcal/mol and for 2-methylnorcaradiene → 2-methylcycloheptatriene 8.8 kcal/mol. As we found in the case of benzene oxide → oxepin, methyl substitution in the 2 position lowers the barrier to isomerization significantly. Table IV also contains the results for the benzenimine → azepin conversion and shows once again that the barrier separating **11** from **12** is low and would not be expected to prevent rapid conversion of the less stable benzenimine to azepin.

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References and Notes

(1) (a) Union College; (b) University of Washington; (c) University of California.
(2) For a review see E. Vogel and H. Günther, *Angew. Chem., Int. Ed. Engl.*, **6**, 385 (1967).
(3) D. M. Jerina, H. Yagi, and J. W. Daly, *Heterocycles*, **1**, 267 (1973).
(4) W. J. Hehre, R. F. Stewart, and J. A. Pople, *J. Chem. Phys.*, **51**, 2657 (1969).
(5) R. Ditchfield, M. D. Newton, W. J. Hehre, and J. A. Pople, *J. Chem. Phys.*, **54**, 724 (1971).
(6) W. J. Hehre, W. A. Lathan, R. Ditchfield, M. D. Newton, and J. A. Pople, *QCPE*, **10**, 236 (1973).
(7) R. J. S. Bingham, M. J. S. Dewar, and D. H. Lo, *J. Am. Chem. Soc.*, **97**, 1285 (1975).
(8) M. J. S. Dewar, H. Metiu, P. J. Student, A. Brown, R. C. Bingham, D. H. Lo, C. A. Ramsdem, H. Killmar, P. Weiner, and P. K. Bischof, *QCPE*, **10**, 279 (1975).
(9) G. L. Cunningham, A. W. Boyd, R. J. Myers, W. D. Gwinn, and W. I. LeVan, *J. Chem. Phys.*, **19**, 676 (1951).
(10) W. A. Lathan, L. Radom, P. C. Hariharan, W. J. Hehre, and J. A. Pople, *Fortschr. Chem. Forsch.*, **40**, 1 (1973).
(11) P. Felker, D. M. Hayes, and L. A. Hull, *Theor. Chim. Acta*, in press.
(12) R. C. Bingham, M. J. S. Dewar, and D. H. Lo, *J. Am. Chem. Soc.*, **97**, 1294 (1975).
(13) P. Politzer and K. C. Daiker, "Excited States in Organic Chemistry and Biochemistry", B. Pullman and N. Goldblum, Eds., D. Reidel Publishing Co., Dordrecht, Holland, 1977, pp 331–344.
(14) W. J. Hehre and J. A. Pople, *J. Am. Chem. Soc.*, **92**, 2191 (1970).
(15) R. Ditchfield, W. J. Hehre, and J. A. Pople, *J. Chem. Phys.*, **54**, 724 (1971).
(16) In an isodesmic reaction, the number of each formal bond type is conserved. That is, reactants and products each have the same *total* number of C—C, C=C, C—O, C—H, etc., formal bonds.
(17) W. J. Hehre, *Acc. Chem. Res.*, **9**, 399 (1976).
(18) For a recent review see G. Maier, *Angew. Chem., Int. Ed. Engl.*, **6**, 402 (1967).
(19) For a recent review see L. A. Paquette, *Angew. Chem., Int. Ed. Engl.*, **10**, 11 (1971).
(20) For a recent review see O. C. Dermer and G. E. Ham, "Ethyleneimine and Other Aziridines", Academic Press, New York, 1969.
(21) R. Hoffmann, *Tetrahedron Lett.*, 2901 (1970).

On MO Calculations of Dimeric Interactions and Their Applicability to Crystal Structures. $(TCNQ)_2$ and $(TTF)_2$

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Abstract: Ramifications of simple MO considerations on charge-transfer dimer structures are considered. The missing extended Hückel energy minimum for slipped neutral $(TTF)_2$ is found and attributed to steric repulsion between sulfurs. The dimer energy vs. slip in $(TTF)_2$ is found to be sensitive to the presence of sulfur d AOs in the basis set. Discrepancies between earlier calculations are attributed to this basis-set dependence. The relevance of dimer structure calculations to crystal structures is discussed. Symmetry restrictions in the crystal are more severe than in the dimer, so some energy-lowering effects present for the dimer are forbidden in a uniform stack in the crystal. Such effects should favor phase transitions to nonuniform stacks. It is pointed out that the four distances in TTF-TCNQ crystals (two interplanar and two slip distances) are not independent. Our data suggest that the slip value of TTF in TTF-TCNQ is a passive parameter determined by the other three (active) parameters. Our data furthermore suggest that, in pure TTF crystals, the slip value is an active parameter.

I. Introduction

The crystalline organic charge-transfer complex tetrathiafulvene-tetracyanoquinodimethane (TTF-TCNQ) possesses an electrical conductivity (in one dimension) on the order of those of some of the less conductive metals (e.g., manganese).[1] This is many orders of magnitude more conductive than normal organic materials and has led to great interest in obtaining a detailed understanding of how the electrical properties of organic crystals are influenced by the properties of the individual molecules and also by the interactions between molecules in a crystal.[2] A facet of this problem has been to try to relate observed crystal structure to molecular structure. One approach to this restricted goal has been to perform molecular orbital (MO) calculations on "supermolecules", usually dimers, such as $(TCNQ)_2$ and $(TTF)_2$, to see whether energy minima can be found in the regions of observed stable crystal configurations. In this paper, we make some general observations concerning such calculations, and illustrate these observations by examining the results of MO calculations by us and others on the two dimer systems $(TCNQ)_2$ and $(TTF)_2$. Implications of our results for understanding TTF-TCNQ crystal structure are also discussed.

II. Crystal Structure of TTF-TCNQ

TTF-TCNQ in the room temperature conducting phase consists of parallel stacks of like molecules, the molecules in

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