Relative Electron Donor Strengths of Tetrathiafulvene Derivatives: Effects of Chemical Substitutions and the Molecular Environment from a Combined Photoelectron and Electrochemical Study

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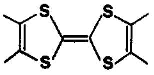
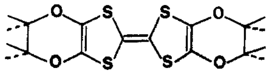
Abstract: Interest in organic metals and superconductors has prompted studies of the effects of chemical substituents on the organic electron donor tetrathiafulvalene (TTF). Electron-donating substituents on TTF should lead to reduced ionization potentials and generally greater electron transfer in organic donor/acceptor compounds. However, the relative electron donor abilities may also be influenced by their molecular environment and intermolecular interactions. In order to address these questions, the valence ionization potentials of TTF and two derivatives, bis(ethylenedioxo)tetrathiafulvalene (BEDO-TTF) and bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF), have been measured in the gas phase by photoelectron spectroscopy and compared with oxidation potentials from solution electrochemical measurements in a variety of solvents. The order of decreasing first ionization potentials is BEDT-TTF ≈ TTF (6.7 eV) > BEDO-TTF (6.46 eV). However, the order of solution oxidation potentials is BEDT-TTF > BEDO-TTF > TTF. The solvent dependence of these oxidation potentials scales linearly with the cation solvation power of the solvent, expressed as the difference between the first and second oxidation potentials of BEDO-TTF. Extrapolation to the zero-solvation limit (i.e., the gas phase) reproduces the order of ionization potentials determined by photoelectron spectroscopy. When predicting whether a derivative is a better electron donor than TTF, it is therefore necessary to consider the molecular environment of the donor molecule. The nature of solvation and/or interaction with the acceptor molecules may result in trends that are opposite to those based purely on ionization potentials or theoretical calculations on single isolated molecules.

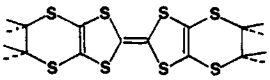
The past decade has witnessed the growth of the field of organic metals and, more recently, organic superconductors formed as solid compounds of electron donor and acceptor molecules.[1] Tetrathiafulvalene (TTF) (**1a**) and its derivatives have been the most widely investigated electron donors.[1] We have recently reported a derivative of TTF that has sp^3 hybridized oxygen atoms directly attached to TTF.[2] This compound, bis(ethylenedioxo)tetrathiafulvalene (BEDO-TTF, further abbreviated to BEDO) (**1b**), which is the oxygen analogue of the well-known bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF, or BEDT)[3] (**1c**), was synthesized in the belief that π donation from the oxygen substituents into the TTF π system will lower the first ionization energy, thereby making the substituted TTF a better electron donor than TTF itself. In this way it is hoped to make donor/acceptor solids with superior conducting and superconducting properties.[2]


TTF

1a


BEDO

1b


BEDT

1c

In order to evaluate the effect of derivatization on the ionization of TTF, we report here the gas-phase photoelectron (PE) spectrum of BEDO and BEDT, together with a remeasurement of the spectrum of TTF. Better electron-donating capabilities are favored if the first ionization potential (IP) is lowered. Qualitatively, the substitution of the hydrogen atoms on the external carbons of TTF by oxygen atoms can have two effects. First, π donation into the high-lying occupied π molecular orbitals (MOs) of TTF should raise them, thereby lowering the IPs. However, substituting hydrogen with the more electronegative oxygen can also result in a stabilization of the TTF MOs by withdrawing electron density through the σ framework. The relative strengths of these two effects will determine the direction of the shift of the IPs. In addition to qualitative MO arguments, the results of MO calculations of the extended Hückel and Fenske–Hall varieties are used to help understand differences in the PE spectra.

Another factor capable of influencing the relative ease of electron donation is likely to be the environment of the molecules in the donor/acceptor compound. This is essentially a solid-state solvation effect and depends on crystal packing and charge localization. An indication of the importance of solvation effects can be obtained by comparing solution-phase electrochemical oxidation potentials with the ionization potentials determined in the gas phase. It has been found, for example, that the electrochemical oxidation of BEDO to its radical cation in acetonitrile/0.1 M $(TBAP)F_6$ (tetrabutylammonium hexafluorophosphate) occurs at higher potentials than for TTF,[2] in contrast (vide infra) to the results of photoelectron spectroscopy and molecular orbital calculations that are presented in this paper. In order to test the assumption that this discrepancy is due to solvation effects, we investigate the oxidation processes for TTF, BEDO, and BEDT in a variety of solvent/electrolyte systems. The oxidation potentials are determined and related to various solvent parameters. The

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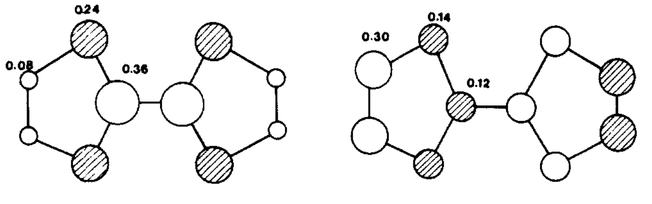
direction and magnitude of the solvent effect serves to clarify the differing results of the photoelectron spectroscopy and electrochemical measurements.

Experimental Section

Photoelectron Spectroscopy. Photoelectron data were recorded on an instrument with a 36-cm radius (10-cm gap) hemispherical analyzer, employing customized sample cell, HeI excitation source, detection and control electronics, and data collection methods that have been described previously.[4] The argon $^2P_{3/2}$ ionization at 15.759 eV was used as an internal calibration lock, with the methyl iodide $^2E_{1/2}$ ionization at 9.538 eV serving as an external calibration of the energy scale.

The spectrum of TTF was collected at a sample cell temperature of 80 °C. TTF sublimed cleanly without evidence of decomposition over a wide range of temperatures. The spectrum of BEDO was collected in the range of 140–145 °C. The signal-to-noise ratio in the BEDO spectrum is not as good as in the spectrum of TTF because the sample pressure and temperature had to be kept sufficiently low to avoid contributions to the photoelectron spectrum from decomposition products. As the sample temperature was raised to 143 °C the clean spectrum of BEDO began to appear. At 150 °C new ionizations associated with the decomposition product(s) began to dominate the spectrum. Careful optimization of the rate of heating and temperature allowed collection of data that are free of appreciable contributions from contaminating species. The valence ionizations shown in Figure 3 were the same in all data collections below the decomposition temperature. The spectrum of BEDT was obtained at approximately 196 °C. This spectrum also showed evidence of partial decomposition. Intense peaks (marked with asterisks on Figure 5) due to ionization of CS_2 ($^2\Sigma_u^+$ at 14.48 eV and $^2\Pi_g$ which is split by spin–orbit coupling into components $^2\Pi_{3/2}$ at 10.07 eV and $^2\Pi_{1/2}$ at 10.13 eV)[5] were observed at the sublimation temperature, with another intense peak attributable to H_2S ($^2B_1 \approx 10.5$ eV)[19] growing at $\sim$5° above the sublimation temperature. This is discussed more in the results section.

Electrochemistry. The oxidation potentials for the two successive oxidations of TTF, BEDO, and BEDT were determined from cyclic voltammograms. Since the electrode processes are Nernstian the oxidation potentials—in terms of reversible half-wave potentials—were taken as the average of the oxidation and reduction peak potentials for each oxidation step. The electrochemical instrumentation used consisted of a BAS 100A electrochemical analyzer and a Houston PL-10 digital plotter. A three-electrode configuration was employed throughout. The working electrodes were platinum or glassy carbon disks (diameters 1.6 and 3.5 mm, respectively), sealed in Kevlar. A Pt wire was used as the counterelectrode. The reference electrode was a Ag/AgCl electrode filled with a 3 M NaCl gel that was separated from the working electrode compartment by means of a porous frit. Positive feedback resistance compensation was employed. The measurements were carried out at +25 ± 1 °C under an argon atmosphere in 0.1 M solutions of tetrabutylammonium (TBA) hexafluorophosphate. The 1,2-dichloroethane solution was 0.2 M in (TBA)BF_4. The supporting electrolytes (Fluka, electrochemical grade) were used without further purification. The solvents were purified according to published procedures.[6]



HOMO (b_{1u}) SHOMO (b_{3g})

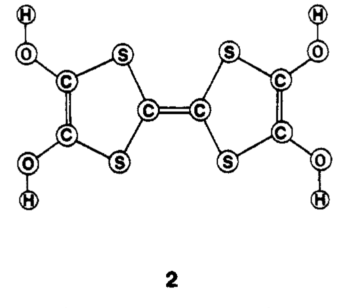
Figure 1. Orbital characters of the highest occupied molecular orbital (HOMO) and the second highest occupied molecular orbital (SHOMO) of tetrathiofulvalene. The coefficients of the atomic Pπ orbitals are from the charge density matrix of the extended Hückel calculation.

Table I. Measured Ionization Potentials (eV) of TTF

band	this work[a]	Gleiter[b]	Berlinsky[c]
1 (b_{1u})	6.70	6.83	6.92
2 (b_{3g})	8.58	8.69	8.67
3	9.71	9.76	9.73
4	10.09	10.18	10.16
5	10.50[d]	10.56	10.49

[a] Peak position (±0.02 eV) determined from close-up spectrum by using the program GFIT. [b] Reference 11. [c] Reference 14. [d] Position (±0.05 eV) of highest intensity measured from full spectrum.

Molecular Orbital Calculations. Orbital eigenvalues and characters were calculated by the extended Hückel method[7] in order to estimate the π-donating effects of oxygen substitution. Fenske–Hall self-consistent-field (SCF) MO calculations[8] were also used to determine whether the inclusion of charge potential effects was likely to significantly change the predicted orbital energy shifts. For the extended Hückel calculations, standard parameters were used for H, C, O,[7a] and S,[9] with the exception that the H_{ii}'s used for sulfur were those adopted by Gleiter et al. in a previous study of sulfur-containing organic molecules [$H_{ii}(3s) = -20.0$ eV; $H_{ii}(3p) = -13.3$ eV].[10,11] For the Fenske–Hall calculations, atomic basis functions supplied by M. B. Hall were utilized for all elements. These basis functions were generated, using ground-state atomic configurations, by the numerical Xα atomic orbital program of Herman and Skillman[12a] and converted to an orthogonal Slater basis with the program of Bursten and Fenske.[12b,c] The core functions are single-ζ fits and the valence s and p functions are double-ζ expansions. The basis set did not include d orbitals on the atoms. Bond lengths and angles were taken from the crystal structure of TTF[13] and the geometry was idealized to D_{2h}. The planar tetrahydroxy-TTF molecule **2** was used to model BEDO, and



2

the deviation of BEDO from planarity was modeled by allowing the OH bonds to rotate out of the plane of the TTF core. The C–O and O–H bond lengths were set to 1.36 and 1.00 Å, respectively.

Results and Discussion

Molecular Orbital Calculations. Though different MO calculations on TTF make the assignment of some of the lower (more

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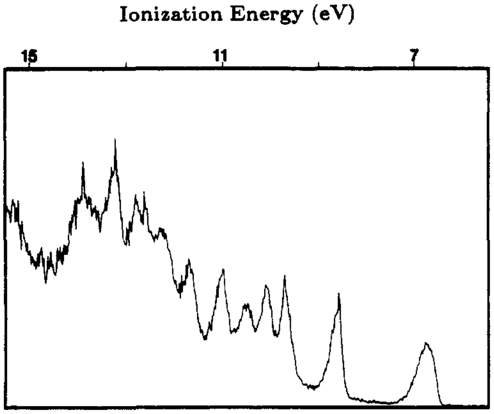

Figure 2. Valence region HeI photoelectron spectrum of TTF.

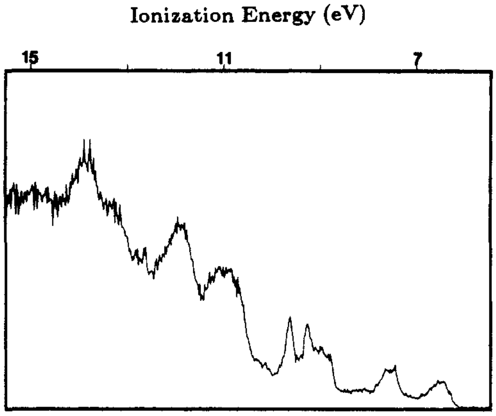

Figure 3. Valence region HeI photoelectron spectrum of BEDO.

tightly bound) MOs somewhat ambiguous, there is complete agreement as to the nature of the two highest lying occupied orbitals.[10,11,14,15] The calculated highest occupied MO (HOMO) and second highest occupied MO (SHOMO) of TTF are shown in Figure 1. The orbital characters shown for the two MOs are taken from the charge density matrix calculated by the extended Hückel method.

The effect of π donation, when the terminal hydrogens are replaced by oxygen atoms, should be to raise the energies of both the HOMO and the SHOMO and thus (by applying Koopmans' approximation[16]) to lower the first and second IPs, provided that the charge potential effect of substituting hydrogen by the more electronegative oxygen (which will tend to stabilize the orbitals of the ring) does not overcome π donation. Also, since the charge density at the outer carbons (i.e., those where the substitution takes place) is greater in the SHOMO, this orbital should be destabilized more by π donation than the HOMO.

Extended Hückel calculations (which only include the π-donation effects) on TTF and the model tetrahydroxy-TTF molecule **2** confirm the qualitative ideas presented above. For completely planar tetrahydroxy-TTF the HOMO is destabilized by 0.20 eV and the SHOMO by 0.69 eV, leading to a decrease of the calculated HOMO–SHOMO gap from 1.86 to 1.37 eV. The shifts and decrease in the HOMO–SHOMO gap are reduced when the hydrogens of the OH groups are rotated out of the plane, thereby reducing oxygen ring π conjugation.

More sophisticated Fenske–Hall SCF MO calculations, which include charge as well as overlap (π-donation) effects, indicate the same trends, though the HOMO is calculated to have a very low binding energy due to an overestimation of the S–C antibonding overlap.

Photoelectron Spectroscopy. The gas-phase HeI PE spectrum of TTF, in the ionization energy range 5.5–15.5 eV, is shown in Figure 2. The energies of the first five ionizations are given in Table I, together with the values reported in previous studies by Gleiter et al.[11] and Berlinsky et al.[14] Though the absolute values of the ionization energies differ slightly (due to differences in calibration), the relative spacings of the peaks are in reasonable agreement.

It is important to note that in the following discussion of the PES and electrochemical data, the terms "ionization energy" and "ionization potential" are interchangeable and refer to single ionizations of the neutral molecule, whereas "oxidation potential" (OP) refers to the electrochemical measurement. The two fields have developed different natural conventions for their terminology. Thus, the "first IP" and the "first OP" of TTF is the energy required to create TTF^+ in its ground electronic state from TTF^0 in the gas phase and in solution, respectively. There is no such correspondence between the terms "second IP" and "second OP". The second IP is the energy required to create TTF^+ in its first excited electronic state from TTF^0 in the gas phase, whereas the second OP is the energy to create TTF^{2+} (the second oxidation state) from TTF^+ in solution.

The spectrum of BEDO in the 5.5–15.5 eV range is shown in Figure 3. To facilitate comparison of the low-binding region of the valence spectra, the close-up (5.5–10.5 eV) spectra were recorded for both TTF and BEDO and these are presented together in Figure 4. The peaks in the TTF (Figure 4A) spectrum have been fit with asymmetric Gaussian functions (where the Gaussian function width on the high binding energy side of the peak is W_h and on the low binding energy side is W_l) by using the program GFIT[17] to enable the more accurate evaluation of peak positions and peak widths [full width at half-maximum [fwhm] = $(W_h + W_l)/2$]. The confidence limits of the peak positions and widths are generally ±0.02 eV. GFIT was also used to obtain the widths and peak positions of the first two peaks in the close-up BEDO spectrum, though the whole spectrum shown in Figure 4B has not been analyzed in similar detail.

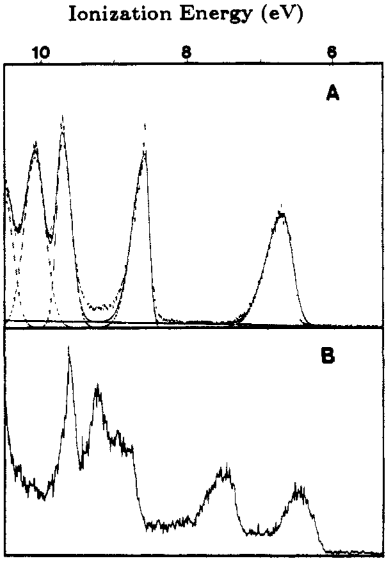

Figure 4. Comparison of the low binding energy regions of the HeI photoelectron spectra of (A) TTF and (B) BEDO.

Since we are concerned here with the relative abilities of TTF and BEDO to act as electron donors, we are primarily interested in the comparison of the first ionization energies. In addition, however, important electron information can be obtained by considering the shift in the second ionization band relative to the first. Thus, comparing the spectra shown in Figure 4 reveals that the energies of both the first and second ionizations are lowered on going from TTF to BEDO. The gap between the first and second ionizations is lowered (from 1.88 to 1.01 eV) because the decrease in ionization energy of the first peak (0.24 eV) is considerably smaller than that of the second (1.11 eV). These results, which agree well with the results of the extended Hückel calculations presented above, are summarized in Table II. We have used the vertical ionization energies for these comparisons because these energies are measured with more certainty than the adiabatic ionization energies. Also, these energies correspond more directly to the orbital energies from the calculations, which do not include geometry relaxation in modeling the ionization energies. For

Table II. Comparison of the First and Second Ionization Bands of TTF and BEDO[a]

molecule	IP	IP(2) - IP(1)	W_h	W_l
TTF	6.70		0.55	0.31
	8.58	1.88	0.41	0.12
BEDO	6.46		0.48	0.38
	7.47	1.01	0.55	0.26

[a] All data in electronvolts, ±0.02 eV.

comparison with the electrochemical oxidation potentials, the adiabatic ionization energies are more appropriate, because these include geometry relaxation. As shown in Table II, the half widths on the low-energy side of the ionizations of the BEDO complex are greater than those of the TTF complex. Thus, the shifts to lower ionization energies for BEDO compared to TTF as shown by the vertical ionizations are probably even greater for the adiabatic ionizations.

The shifts to lower binding energy observed for the first two PE peaks, on going from TTF to BEDO, indicate that the π donation from oxygen (overlap effect) overcomes any inductive withdrawal of electron density from the outer carbons through the σ framework (charge effect). Both the extended Hückel and Fenske–Hall calculations predict such shifts to occur, together with a narrowing of the HOMO–SHOMO gap. Experimentally, this narrowing, which was initially predicted from qualitative arguments based on the differing amounts of outer carbon character in the HOMO and SHOMO, is manifested in the smaller energy difference between the first two ionization features of BEDO compared with TTF.

Vibrational fine structure or vibrational broadening of ionization bands can give additional insight into the bonding characteristics of a given orbital.[18] Broad bands are generally associated with ionizations from orbitals with a significant amount of bonding or antibonding character, so that upon ionization there is a relatively large change in the equilibrium bond length and, thus, a considerable degree of vibrational excitation. For instance, the greater width of the first band of TTF compared with the second is probably due to the fact that the HOMO has more carbon–sulfur antibonding character (see Figure 1).

Comparison of the shape of the second ionization bands of TTF and BEDO (Figure 4 and Table II) reveals a significant broadening of the band for BEDO (fwhm = 0.41 eV; cf. TTF, fwhm = 0.27 eV), with a drop in relative intensity at the low-binding edge. The broadening of the second peak on going from TTF to BEDO is consistent with greater oxygen character in the SHOMO of the BEDO derivative, with extra vibrations (such as the symmetric[19] C–O and C–C stretches) contributing to the vibrational envelope of the band. This is consistent with the significant destabilization of the SHOMO that occurs upon annelation, due to π donation from oxygen (i.e., C–O π-antibonding character is mixed into the SHOMO). Table II shows that the first peak is less asymmetric in BEDO than TTF, though the fwhm's are essentially identical (~0.43 eV). The small change in the shape of the first ionization peak indicates that the HOMO of BEDO has less oxygen character than the SHOMO, consistent with it being less destabilized upon annelation.

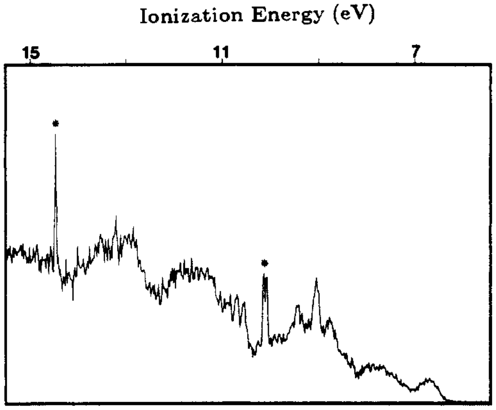

Figure 5. Valence region HeI photoelectron spectrum of BEDT. Starred peaks are due to CS_2, one of the decomposition products.

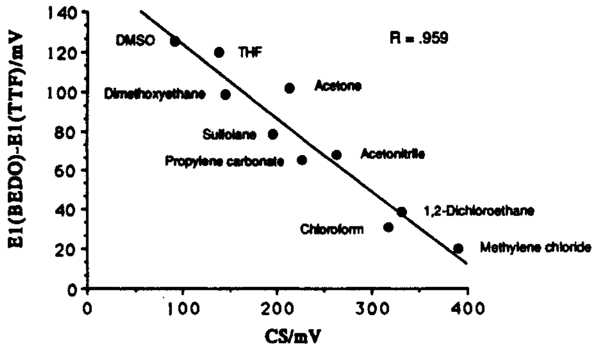

Figure 6. Plot of $E1$(BEDO) − $E1$(TTF) vs CS [ΔE(BEDO)] for a variety of solvents.

The PE spectrum obtained for BEDT at 196 °C (see Figure 5) includes ionizations from volatile decomposition products as discussed in the Experimental Section. The volatile decomposition products are small molecule species (CS_2 and H_2S) that are easily identified by their sharp ionizations and variable intensity with temperature relative to the broad ionizations of BEDT. Although the ionizations of these small molecule species are relatively intense, the integrated areas relative to the spectrum of BEDT are small and indicate that the decomposition is only a few percent at the temperature at which the spectrum was collected. The overall appearance of the spectrum of BEDT is quite similar to that of BEDO. The first ionization peak of BEDT occurs at around 6.7 eV, i.e., the same as for TTF and higher than that of BEDO, consistent with the poorer π-donor properties of sulfur compared with oxygen. Although very broad, the second ionization feature appears to be much closer in energy to the first for BEDT than for TTF, again consistent with greater π donation into the SHOMO than the HOMO. The exact position of the peak is uncertain due to the width of the peak and the low signal-to-noise ratio for collecting data without appreciable decomposition.

Electrochemistry. The electrochemical oxidation of TTF, BEDO, and BEDT gives rise to electrochemically and chemically

Table III. Electrochemical Oxidation Data (mV) for TTF, BEDO, and BEDT[a]

solvent	$E1$(TTF)	$E2$(TTF)	$E1$(BEDO)	$E2$(BEDO)	$E1$(BEDT)	$E2$(BEDT)
DMSO	418 ± 17	620 ± 37	543 ± 27	634 ± 37	603 ± 37	700 ± 40
THF	500 ± 27	757 ± 40	620 ± 37	758 ± 40	682 ± 40	832 ± 50
acetone	422 ± 17	755 ± 40	524 ± 30	737 ± 40	648 ± 37	848 ± 50
1,2-dimethoxyethane	522 ± 27	800 ± 50	621 ± 37	766 ± 40	730 ± 40	885 ± 53
sulfolane	397 ± 17	712 ± 40	476 ± 19	671 ± 40	546 ± 27	738 ± 40
propylene carbonate	359 ± 10	698 ± 40	424 ± 17	651 ± 37	546 ± 27	*b*
methanol	359 ± 10	720 ± 40	*c*	*c*	*c*	*c*
acetonitrile	367 ± 10	748 ± 40	435 ± 17	699 ± 40	567 ± 27	829 ± 50
$CHCl_3$	392 ± 15	*b*	423 ± 17	751 ± 40	536 ± 27	846 ± 50
1,2-dichloroethane[d]	494 ± 27	*b*	533 ± 30	865 ± 50	640 ± 37	974 ± 60
CH_2Cl_2	380 ± 10	*b*	400 ± 17	790 ± 50	485 ± 19	892 ± 53

[a] Experimental conditions: +25 ± 1° C; 0.1 M $(TBAP)F_6$ unless otherwise indicated; vs Ag/AgCl. [b] Second wave is irreversible in these solvents. [c] Insoluble in MeOH. [d] 0.2 M $(TBAB)F_4$.

Table IV. Comparison of Differences in Oxidation Potentials with Solvation Parameters[a]

solvent	$E1$(BEDO) − $E1$(TTF)	$E2$(BEDO) − $E2$(TTF)	ΔE(TTF)[b]	ΔE(BEDO)[b]	ΔE(BEDT)[b]	DN[c]	dielec const[d]
DMSO	125	14	202	91	97	29.8	48.9
THF	120	1	257	138	150	20.0	7.4
acetone	102	−18	333	213	200	17.0	20.7
1,2-dimethoxyethane	99	−34	278	145	155		7.0
sulfolane	79	−41	315	195	192	14.8	44.0
propylene carbonate	65	−47	339	227		15.1	65.1
acetonitrile	68	−49	381	264	262	14.1	37.5
$CHCl_3$	31			328	310		4.7
1,2-dichloroethane	39			332	334	~0	10.4
CH_2Cl_2	20			390	407		8.9

[a] Experimental condition as in Table III. [b] $\Delta E = E2 - E1$. [c] Donor number; ref 20d. [d] Reference 22.

reversible cyclic voltammograms in all solvent systems used. The first oxidation potentials, $E1$ (referring to the process $M^0_{(solv)} \rightarrow M^+_{(solv)}$), and the second oxidation potentials, $E2$ (referring to the process $M^+_{(solv)} \rightarrow M^{2+}_{(solv)}$), for TTF, BEDO, and BEDT in the various solvents are listed in Table III. In all solvent/electrolyte systems studied, BEDO is oxidized at higher oxidation potentials compared to TTF, and BEDT is oxidized at higher potentials than either TTF or BEDO, in agreement with the earlier study.[2]

These solvent effects correlate fairly well with Gutmann's scale of donor numbers (DN),[20] with DN being defined as the negative of the enthalpy of reaction between the solvent and antimony pentachloride. The order of decreasing DN values is DMSO > ether solvents (THF, dimethoxyethane) > chlorinated solvents (e.g., dichloroethane, DN ≈ 0) in agreement with our experimental findings. The DN values of the solvents used in this study are listed in Table IV along with the corresponding first OP differences, $E1$(BEDO) − $E1$(TTF). It should be noted that the solvent effects observed here do not correlate well with the solvent dielectric constant.[21] Similarly, it has been found that there is no correlation with the empirical parameter E_T.[22]

The clearest and most direct indication of the solvent effect on the oxidation potentials of TTF, BEDO, and BEDT is the measured difference in the first and second oxidation potentials, ΔE ($\Delta E = E2 - E1$) (see Table IV).[21] In general, the stronger the solvent effects, the less the electronic features of the individual TTF, BEDO, and BEDT molecules contribute to separating the first and second OPs. In the case of the ethers under study, 1,2-dimethoxyethane and THF, relatively large differences between $E1$(BEDO) and $E1$(TTF) are accompanied by relatively small values for the differences in the first and second OPs for all three compounds. In contrast, in the three halogenated solvents investigated, small differences in $E1$ correspond to large values of ΔE. The ΔE values have the advantage that they take into account all features of the solvent and the supporting electrolyte that influence the oxidation potentials of these molecules. Remarkably linear correlations exist between the ΔE values for all three compounds. Plots of ΔE for TTF and BEDT vs ΔE(BEDO) reveal nearly identical slopes.[21] Therefore, the oxidation processes (and hence the OPs) of all three compounds are affected in essentially the same way when the solvent is changed. Interestingly, for a given solvent the ΔE values for BEDO and BEDT were found to be virtually identical, their magnitude varying only from solvent to solvent.

The above mentioned correlations indicate that the ΔE value for any one of the compounds may be used as a measure of the solvation effect of a given solvent. A new specific solvent "cation stabilization" property, CS [CS = ΔE(BEDO)], has been defined previously.[21] Large values of CS correspond to effective removal of solvent leveling effects that reduce the separation of the first and second oxidation potentials. CS values in each of the solvents studied are included in Table IV. Figure 6 shows a plot of $E1$(BEDO) − $E1$(TTF) vs CS. Despite some scatter, there is a good correlation ($R = 0.959$). The negative slope unequivocally reveals that (although still larger) the first OP for BEDO approaches that of TTF as the solvating power of the solvent/electrolyte system (expressed as CS) decreases. This can be taken as strong evidence for the medium-induced facilitation of TTF oxidation relative to BEDO.

Comparison of Photoelectron and Electrochemical Data

Extension of the graph in Figure 6 to the gas-phase zero-solvation limit, where CS = $E2 - E1$ [or rather $I2 - I1$, with Ix being the ionization potential for the process $M^{(x-1)+}(g) \rightarrow M^{x+}(g)$] is very large, shows that the sign of $E1$(BEDO) − EI(TTF) does indeed become negative, in agreement with the PES data. Thus it is apparent that the reason for the different trends in ease of ionization observed in the gas phase and in solution are due to solvation effects. In particular, it appears that there is a significant extra stabilization in solution of the TTF^+ cation that is not present for either $BEDO^+$ or $BEDT^+$ [$E1$(TTF) < $E1$(BEDO)]. Possible explanations for this difference are discussed below.

First, for BEDO and BEDT the lone pairs on the oxygen or sulfur atoms of the outer rings may restrict access for the solvent molecules to approach to positively charged TTF center closely, thereby reducing the solvation energy of the cation. Also, the smaller size, and hence greater polarizing power, of TTF compared with the derivatives may lead to greater solvation.

Second, it is known that the central TTF cores of BEDO and BEDT are significantly nonplanar in the solid state,[2,3] which is partly due to crystal-packing forces.[3] If the solvent molecules induce such marked nonplanarity in solution, then the stabilization of the cation due to π delocalization will be lessened. In a previous study, Coffen et al. found that the $E1$ and $E2$ values for a number of TTF analogues decrease as the extent of π conjugation increases.[15] In the gas phase, where there are essentially no intermolecular interactions, the deviation from planarity is likely to be much smaller.

The dications of TTF, BEDO, and BEDT are stabilized by solvation to a greater extent than the monocations because of their greater charge. Previous studies on TTF and some related compounds have indicated that solvation energies of the dications can be as high as 6–8 eV.[23] The differences in solvation energies for the TTF, BEDO, and BEDT dications are apparently less than the differences for the monocations. For instance, the differences in second oxidation potentials between TTF and BEDO [$E2$(TTF) − $E2$(BEDO)] are shown in the second column of Table IV. These differences are shifted downward ~120 mV from the differences in the first oxidation potentials [$E1$(TTF)−$E1$(BEDO)]. Although the differences in second oxidation potentials are small in relation to the uncertainties in these comparisons, there is a clear tendency toward negative values. Thus, the second oxidation of BEDO is at lower energy than that of TTF when solvation energy differences

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(20) (a) Gutmann, V. *Coord. Chem. Rev.* **1967**, *2*, 239. (b) Gutmann, V. *Coordination Chemistry in Non-Aqueous Solutions*; Springer-Verlag: Vienna, 1968. (c) Popovych, O.; Tompkins, R. P. T. *Non-Aqueous Solution Chemistry*; John Wiley & Sons: New York, 1981. (d) Burger, K. *Solvation, Ionic and Complex Formation Reactions in Non-Aqueous Solvents*; Elsevier: New York, 1983.

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are minimized, in agreement with the theoretical calculations and the photoelectron measurements.

The observation that the first oxidation potential changes more with changing solvent than the second oxidation potential also explains the reduction of ΔE with increasing solvating power of solvent. The linear relationship observed for the ΔE values for the three compounds shows that differences between $E2$ and $E1$ have the same solvent dependence and are therefore likely to be mostly charge dependent. As mentioned above, the ΔE values for BEDO and BEDT are virtually identical for any given solvent.[24] By contrast, the values of ΔE(TTF) are consistently around 0.1 V higher than the corresponding BEDO and BEDT values. It follows that TTF^+ is stabilized to a greater extent by the solvent–electrolyte combination than are $BEDO^+$ or $BEDT^+$.

Conclusions

The PES results indicate that, in agreement with theoretical models, substituting the terminal hydrogen atoms of TTF by electron- (π-) donating oxygen atoms does lead to a reduction of the first IP, while substitution by sulfur makes almost no difference. The electrochemical studies, however, have revealed that solvent effects play a large part in determining the relative ease of oxidizing TTF and its derivatives in solution. It is likely that the ability of TTF derivatives to function as electron donors in the solid state will also depend critically on their environment in the solid and the extent to which they are "solvated" by themselves and by the acceptor molecules. Interestingly, as this work was being submitted, such factors were identified in a comprehensive study of a pthalocyanine molecular metal reported in this journal by Marks and co-workers.[25]

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(24) A reviewer suggested that in the dications "the two five-membered rings twist [by] ca. 90° [relative] to one another. This would have the effect of increasing the coefficients on the "outer" carbons in the HOMO, thereby allowing more resonance stabilization by the oxygens in BEDO".

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A Theoretical Approach to Drug Design. 1. Relative Solvation Thermodynamics for the Antibacterial Compound Trimethoprim and Ethyl Derivatives Substituted at the 3′, 4′, and 5′ Positions

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Abstract: Free energy simulation methods are used to compute the relative solvation thermodynamics of the antibacterial drug trimethoprim [2,4-diamino-5-(3′,4′,5′-trimethoxybenzyl)pyrimidine] and a family of congeners derived from methoxy → ethyl substitution on the benzyl ring. The aqueous solubility is found to decrease as more hydrophobic character is introduced into the parent molecule. Nearly additive effects on the solvation free energy are observed for the mono- and disubstituted derivatives, with exception of the 3′,5′-diethyl derivative. This compound shows an increased aqueous solubility (over that of the other diethyl compound), which is linked to anomalous entropic effects of the *p*-methoxy group. The triethyl-substituted molecule exhibits a similar solvation free energy to that of the 3′,4′-diethyl compound, which appears as additive contributions from the 3′,5′-diethyl and 4′-monoethyl derivatives.

I. Introduction

The thermodynamics of solvation play a critical role in understanding molecular association. For example, consider the "drug design" paradigm, which involves the *relative* thermodynamics for the inhibitor displacement reaction

$$I_b(aq) + E{:}I_a \rightleftharpoons I_a(aq) + E{:}I_b \qquad (1)$$

In this reaction, inhibitor a (I_a) is initially bound to the receptor (enzyme, E), and inhibitor b (I_b) is present in aqueous solution. Inhibitor b is then *desolvated* and a is *solvated*, with the overall change in binding affinity being attributed to the *relative solvation* thermodynamics of a versus b, as well as the *relative interaction* thermodynamics with the receptor E. The objective in studying this process, as viewed from the drug design paradigm, is to optimize (or to find some strategy to optimize) certain characteristics of the interaction of I_b with E compared to I_a with E. The overall success of this procedure requires knowledge of inhibitor–enzyme interactions and aqueous solubilities. Thus, understanding solvation thermodynamics is crucial to the development of detailed models for the rationalization and prediction of inhibitor binding.

Computer simulation methodologies developed over the past several years[1,2] now serve as an aid in the molecular interpretation

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