

Using Constrained Schrödinger Equations to Separate Resonant and Inductive Substituent Effects: A New Methodology for Parametrizing Simple Models in Chemistry

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Simple models of chemical phenomena can provide both useful insights and predictive power. These models are parametrized using data on model systems, which are chosen to allow the effects of interest to be isolated. Ab initio calculations can provide a useful source of such data. This article explores the use of constrained Schrödinger equations to generate rich sets of ab initio data that can support parametrization of a more diverse set of models than is possible with existing methods. The constraints are used to control the electronic configuration of the model compounds, such that data can be generated on electronic structure–property relationships. The current investigation uses constraints to modulate resonance in substituted benzene compounds. The resulting resonant and nonresonant benzenes are used to parametrize a simple model of inductive and resonant electronic substituent effects, which is similar to the Swain-Lupton substituent-effect model. This parametrization is benchmarked against the standard method of parametrizing such models: fitting inductive and resonant parameters to data from substituted bicyclo[2.2.2]octanes and benzenes. The comparison is made within a consistent model chemistry, as defined by the use of an STO-3G basis and inclusion of correlation via MP2 theory. The parameter sets obtained with the standard and constrained Schrödinger equation methods are very similar and perform equally well at predicting substituent effects in other molecules. The parameter set from the constrained method has a lower correlation between inductive and resonant parameters, suggesting that this method is better at separating these two effects. These results suggest that constrained Schrödinger equation methods can provide a useful means of generating ab initio data for models of electronic structure–property relationships.

1. Introduction

Chemists often explain chemical phenomena by invoking qualitative concepts such as electronegativity, or the partitioning of chemical perturbations into resonant, inductive, and steric effects. These concepts can be quantified through the construction of simple semiempirical models whose parameters capture the effect in question. Such models provide a qualitative framework for understanding chemical phenomena and are often useful in making predictions, especially for large chemical systems that are not amenable to more sophisticated computational approaches.

To generate meaningful predictions, simple models must be parametrized from high-quality sets of data on model systems. These model systems are generally designed to allow the isolation of the effects of interest. For instance, models that separate resonant from inductive substituent effects can be parametrized from data on saturated and unsaturated compounds.

Ab initio calculations can provide a useful complement to experimental data for parametrizing simple models. The primary advantage to a parametrization from ab initio data is that the inputs of a calculation on a model system can be independently varied in ways that are not feasible in experiments. For instance, one can calculate the energy change associated with well-defined changes to a single geometric parameter (bond length, torsional angle, etc.). This type of data has been useful in parametrizing force fields for molecular mechanics.^{1–3} One can also calculate responses to external fields or fixed-point charges, which perturb

the molecule's electronic structure. Such data has been widely used to parametrize such models as polarizable force fields⁶ and models of electronic substituent effects.^{4,5}

In this article, we consider a more flexible method of varying a system's calculated electronic configuration: constrained ab initio calculations. Solutions to the constrained Schrödinger equation were first used in quantum chemistry by Mukherji and Karplus to calculate a wave function that reproduced experimental values for observables.⁷ This general technique has been used, among other things, to calculate wave functions that reproduce X-ray diffraction data,⁸ to reproduce experimental fission barriers in nuclear physics,⁹ and to investigate impurities in continuous systems using density-functional calculations.¹⁰

Ichikawa and Kagawa (IK) used constrained Schrödinger equation techniques to suppress, or “turn off”, resonance in aromatic systems.^{11–14} This was done by applying a constraint that forced an aromatic system to adopt a nonresonant electronic configuration, corresponding to alternating double and single bonds (as shown for benzene in Figure 1). The change in energy associated with this constraint gives an ab initio estimate of the resonance energy, and the results agree well with those from thermochemical approaches.

Constrained Schrödinger equation methods have been used to obtain parameters for model tight-binding Hamiltonians, such as site energies and transfer integrals.¹⁵ We propose to generalize this approach, and use these methods to parametrize a wide variety of simple models of electronic structure–property relationships. In the current work, we test the utility of these methods by developing and benchmarking a constrained-

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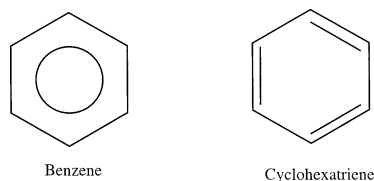


Figure 1. Electronic structures of benzene and nonresonant benzene (cyclohexatriene).

Schrödinger-equation-based parametrization for a simple model of electronic substituent effects.

Substituent effects are defined in molecules that contain a reaction center *RC* and one or more perturbing substituents *Sub*, separated by a bridge group *Bridge*,



A substituent effect is a change in some property of the reaction center (rate or equilibrium constant of a reaction, electronic structure, energy, etc.) that is induced by the substituent,¹⁶ defined relative to an unsubstituted bridge (*Sub* = *H*). The first quantitative treatment of substituent effects was by Hammett,¹⁷ who modeled the difference in a rate or equilibrium constant for a reaction involving substituted, *k*, and unsubstituted, *k*₀, molecules as

$$\log(k/k_0) = \rho\sigma \quad (1)$$

where σ is a substituent's ability to cause an effect and ρ is a reaction center's susceptibility to such effects.

Conceptually, substituent effects can be partitioned into effects such as electric field, polarization, resonance, and steric. This concept has been quantified by the construction of simple models that partition the Hammett σ and ρ parameters.¹⁶ These multiparameter models are currently widely used for making predictions about large systems such as biological macromolecules.¹⁸

The dual-parameter model of Swain and Lupton¹⁹ partitions the Hammett substituent effect parameters into global sets of inductive and resonant components

$$\sigma = fF + rR \quad (2)$$

The resonant effect *R* is the portion of a substituent's electronic effect that is transmitted through a conjugated π system linking substituent and reaction center. The inductive effect *F* is the electronic effect transmitted through space and/or through the polarization of a network of σ -bonds.^{22,23} Parameters *f* and *r* in eq 2 are substituent-independent constants that are functions of only the reaction being studied, i.e., the bridge and reaction center.

The Swain–Lupton model can be parametrized from data on model systems which are expected to have similar inductive substituent effects but very different resonant substituent effects. In the initial Swain–Lupton parametrization,¹⁹ the inductive substituent parameters *F* were fit to substituent effects in substituted bicyclo-[2.2.2]octanes. The resonant substituent parameters *R* were then fit to substituent effects in *para*-disubstituted benzenes using

$$\sigma_p = \alpha F + R \quad (3)$$

where the fitted parameter $\alpha = 0.921$ accounts for slight differences between the transmission of inductive substituent

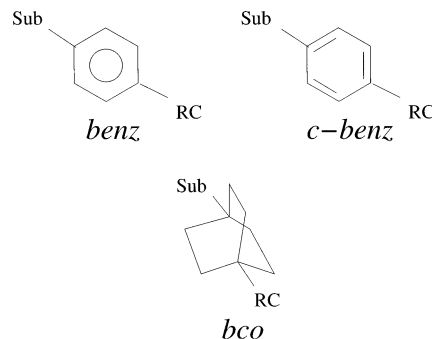


Figure 2. Structures of the $[\text{Sub}] - [\text{Bridge}] - [\text{RC}]$ molecules used in this investigation. *benz* and *c-benz* stand for *para*-substituted benzene bridges with unconstrained and constrained π -systems, respectively. *bco* stands for a bicyclo-[2.2.2]octane bridge group.

effects through the two bridges.¹⁶ Structures of bicyclo-[2.2.2]-octane (*bco*) and benzene (*benz*) bridged molecules are given in Figure 2.

The Swain–Lupton parametrization rests on the assumption that *bco* is a good model of *benz*'s ability to transmit inductive substituent effects. Although the overall distance between the substituents in *bco* is similar to that in *benz*, the two σ -bond networks do have some significant differences. Most notable is the presence of three bridges between the substituted carbon atoms of *bco*, as opposed to the two bridges in *benz*. The σ bonds in *bco* are also somewhat longer than those of *benz* (1.56 and 1.39 Å, respectively). Despite these differences, both *bco* and *para*-disubstituted cyclohexanes²⁰ have been used to generate inductive parameters for the Swain–Lupton model. These parametrizations are consistent with one of the fundamental assumptions of the Swain–Lupton model, namely, that the transmission of inductive substituent effects through different bridge groups is equivalent to within a constant factor.

In the current investigation, constrained Schrödinger equation methods similar to those of IK are used to develop an alternate method for partitioning inductive and resonant substituent effects. Constraining the π -system of a *benz*-bridged molecule can produce the cyclohexatriene-bridged *c-benz* molecules shown in Figure 2. Our hypothesis is that the *c-benz* bridge will be as good as, if not better than, the *bco* bridge at modeling the *benz* bridge's transmission of inductive substituent effects. The *c-benz* bridge, unlike the *bco* bridge, has the same geometry and connectivity as the reference *benz* system. Given this, we expect that *c-benz* will be a better model for *benz*'s inductive substituent-effect transmittance. Note that *c-benz*, and constrained systems in general, are theoretical constructs which do not necessarily correspond to any existing molecular systems. They are introduced solely as a convenient means of separating various chemical effects.

To test our hypothesis, we compare the substituent effects transmitted through the *bco* and *c-benz* bridges. The results presented here illustrate that (a) substituent effects through the two bridges are very similar, and (b) parametrization of a Swain–Lupton-type model from either of these two model systems gives similar sets of parameters. This suggests that constrained Schrödinger equation methods could provide a viable extension of ab initio methods for parametrizing simple models.

The techniques used to constrain the electron density are described in section 2. In section 3 various π -system constraints are investigated within Hückel theory, to determine which constraint best eliminates resonant substituent effects. In section 4, ab initio data are generated for a large set of *benz*, *c-benz*,

and *bco* – bridged molecules to determine whether *c-benz* and *bco* transmit substituent effects in a similar manner. In section 5, these ab initio data are used to parametrize a simple substituent-effect model similar to that of Swain and Lupton. The model is parametrized twice, using either *c-benz* or *bco* as a model for inductive effects through *benz*. Section 6 considers a variety of constrained and unconstrained bridge groups to test the transferability of the parameters to other bridges. Sec. 7 briefly summarizes the results and discusses possible extensions.

2. Constraints on Electronic Structure

The derivation of constrained Schrödinger equation techniques given below follows that of IK.¹¹ To summarize, constraints on a system's one-electron-density matrix are enforced by adding a matrix of Lagrange multipliers to the Hamiltonian. The values of the individual Lagrange multipliers are numerically fitted to give the desired density matrix elements. This procedure can be thought of as finding a one-electron perturbation operator whose application causes the electrons to adopt a desired configuration.

The stationary-state wave function $|\Psi\rangle$ of an N-electron system can be determined by solving the time-independent Schrödinger equation

$$H|\Psi\rangle = \mathcal{E}|\Psi\rangle \quad (4)$$

where H is the system's Hamiltonian operator and \mathcal{E} is the energy. The energy is minimized subject to a normalization constraint by determining the stationary points of the functional

$$\mathcal{L} = \langle\Psi|H|\Psi\rangle - E(\langle\Psi|\Psi\rangle - 1) \quad (5)$$

where E is a Lagrange multiplier. The stationary point $\delta\mathcal{L} = 0$ at which the functional's second derivative is positive is a minimum for the functional.²¹

A molecule's electron distribution and bond order can be conveniently described in terms of the one-electron density matrix

$$n(e_1, e_1') = \int \Psi(e_1, e_2, \dots, e_N) \Psi(e_1', e_2, \dots, e_N) d(e_2, \dots, e_N) \quad (6)$$

where e_i are the coordinates of electron i . Both the N-electron wave function $|\Psi\rangle$ and the one-electron density matrix n can be expressed in a basis of nonorthogonal one-electron functions, the atomic orbitals $|\phi_i\rangle$. Elements of the one-electron density matrix in the atomic orbital basis may be written as $n_{x,y}$, where the indices x and y label atomic orbitals.

We will be concerned with constraining some element of the density matrix $n_{x,y}$ to a target value $n_{x,y}^{\text{tar}}$. This constraint on n is enforced by an operator which is expressed as the product of a Lagrange multiplier $\lambda_{x,y}$ and a one-electron operator $\Gamma_{x,y}$ defined in the atomic orbital basis as

$$\langle\phi_i|\Gamma_{x,y}|\phi_j\rangle = \delta_{xi}\delta_{yj} \quad (7)$$

For example, a constraint on $n_{1,2}$, the off-diagonal density matrix element between orbitals $|\phi_1\rangle$ and $|\phi_2\rangle$, is enforced by an operator $\lambda_{1,2}\Gamma_{1,2}$ with the matrix representation

$$\lambda_{1,2} \begin{pmatrix} 0 & 1 & 0 & \dots \\ 0 & 0 & 0 & \dots \\ 0 & 0 & 0 & \dots \\ \vdots & \vdots & \vdots & \dots \end{pmatrix} \quad (8)$$

The one-electron density matrix is a Hermitian operator,²⁴ and so the same constraint must be applied to density matrix element $n_{2,1}$.

A set of constraints $\{n_{x,y}^{\text{tar}}\}$ may be summed into a single one-electron operator, V_c , whose matrix elements are Lagrange multipliers

$$(V_c)_{x,y} = \lambda_{x,y}\Gamma_{x,y} \quad (9)$$

The constraint operator V_c can be added to the functional of eq 5 to give a new functional

$$\mathcal{L}' = \langle\Psi|H|\Psi\rangle - E(\langle\Psi|\Psi\rangle - 1) - \sum_{xy}^{\text{constraints}} \lambda_{x,y}(\langle\Psi|\Gamma_{x,y}|\Psi\rangle - n_{x,y}^{\text{tar}}) \quad (10)$$

This functional is minimized in the usual way by setting its first variation equal to zero,²¹ such that

$$0 = \langle\delta\Psi|(H - E - \sum_{xy}^{\text{constraints}} \lambda_{x,y}\Gamma_{x,y})|\Psi\rangle \quad (11)$$

is true for all $\langle\delta\Psi|$. Substituting the definition of the constraint operator V_c into eq 11 gives

$$0 = [(H - V_c) - E]|\Psi\rangle \quad (12)$$

The Lagrange multipliers of the constraint operator V_c are generally obtained by numerical fitting.

The density matrix constraint method described above can be used in any calculation that produces a one-electron density matrix. In particular, the functional in eq 10 can be minimized in any basis set, and for either a single-determinant or multideterminant wave function.

3. Testing Constraint Operators within Hückel Theory

Our investigation requires a constraint operator that prevents a conjugated π -system from transmitting resonant substituent effects. We begin by developing such a constraint operator within the Hückel-theory model of Figure 3, which models the π -system of disubstituted benzene. In this model, each substituent and bridge atom contains one p orbital and contributes one electron. H_0 in Figure 3 is the system's unconstrained Hamiltonian. V_c is the matrix of Lagrange multipliers λ_i defined in eq 9, which is added to H_0 to enforce the density-matrix constraints as in eq 12. The substituent's diagonal energy ϵ_{sub} , defined relative to the diagonal energies of the bridge atoms (which are set to zero), is varied to model the effects of different substituent groups.

The resonant substituent effects are quantified by monitoring the diagonal density-matrix element (occupancy) of the reaction center RC as a function of the substituent's energy ϵ_{sub} . The bridge-mediated coupling between Sub and RC provides a measure of the bridge's ability to transmit substituent effects. These substituent effects are necessarily resonant effects, because the system has no Coulomb interactions or sigma bonds. The results are shown in Figure 4. Similar results are obtained if the reaction center's diagonal energy is shifted relative to the bridge, if the bridge-substituent or bridge-reaction center coupling is altered, or if the substituent and reaction center contain multiple π electrons and/or orbitals (data not shown).

In the unconstrained system ($\lambda_i = 0$), electron density is transferred smoothly from Sub to RC as ϵ_{sub} is increased from negative to positive values.

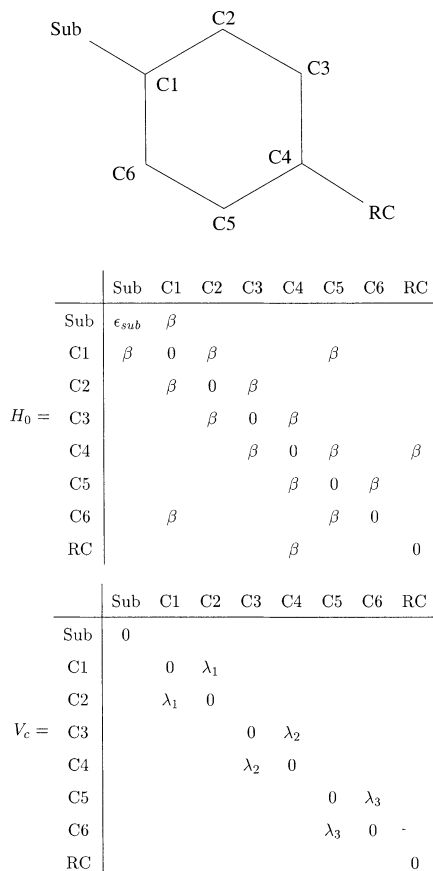


Figure 3. Model Hückel system for testing constraint operators. A schematic representation of the system is shown above its unperturbed Hamiltonian H_0 . The constraint operator V_c is added to H_0 to implement the constraints. Different constraints are modeled by varying the λ_i parameters.

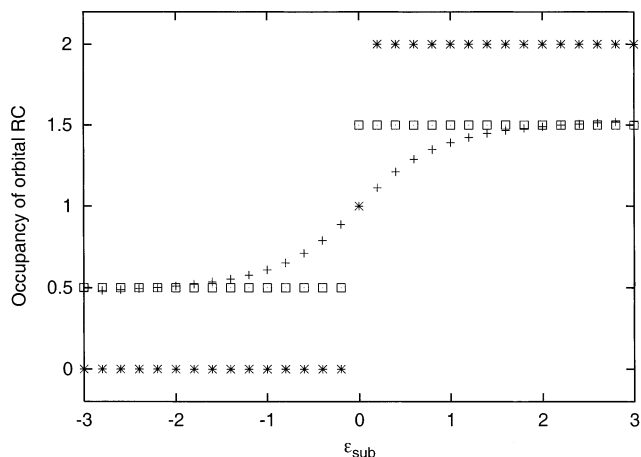


Figure 4. RC occupancy versus ϵ_{sub} for the system in Figure 3. Crosses correspond to an unconstrained system, stars to a zeroing constraint, and squares to a bond-order maximization constraint (see section 3 for details).

IK generated nonresonant benzene using a constraint that “zeroed” the π density matrix elements between the singly bound carbons of the cyclohexatriene structure of Figure 1.¹² We implement this constraint by setting $\{\lambda_i\} = -\beta$, which forces the π -bond orders of bonds C1–C2, C3–C4, and C5–C6 to zero. This constraint succeeds in turning off resonance in an unsubstituted benzene molecule. However, the results in Figure 4 indicate that this constraint does not turn off the transmission of resonant substituent effects. When this constraint is applied, the substituent groups *Sub* and *RC* each remain coupled to one

of the double bonds in the bridge. As ϵ_{sub} is increased from negative to positive values, an electron pair moves from $\{Sub, C1, C6\}$ to $\{C4, C5, RC\}$. This is seen in Figure 4 as a change in the occupancy of *RC* from 0.5 to 1.5 as ϵ_{sub} passes through 0.

Since zeroing the bridge π -bond orders does not turn off resonance with the substituents, we tested a complimentary method: constraining alternating bridge π -bond orders to one. This “bond-order maximization” constraint can be implemented by choosing very large negative values for $\{\lambda_i\}$, which forces the π -bond orders of bonds C1=C2, C3=C4, and C5=C6 to one.²⁵ The results in Figure 4 indicate that this constraint successfully turns off all bridge-mediated communication between the substituents *Sub* and *RC*. An electron pair jumps from *Sub* to *RC* as ϵ_{sub} passes through zero. This is the behavior expected when *Sub* and *RC* do not resonate with the bridge. This constraint is used to generate nonresonant benzene bridges (*c-benz*) in the subsequent ab initio calculations.

The bond-order maximization constraint is relatively simple to implement in a minimal basis. Any sufficiently large negative value of λ_i between two p orbitals will maximize their bond order. This is in contrast to the bond-order zeroing constraint which, in ab initio calculations, requires numerical determination of the precise value of λ_i at which the bond order becomes zero.

4. Constrained ab Initio Calculations

This section presents results from a numerical experiment that compares the transmission of substituent effects through bicyclo-[2.2.2]octane and constrained and unconstrained *para*-substituted benzene bridges (the *bco*, *c-benz*, and *benz* bridges shown in Figure 2). If our constraint-operator techniques are successful, the *c-benz* bridge will not transmit resonant substituent effects. This will cause it to transmit substituent effects in a manner similar to the *bco* bridge for a wide variety of substituent and reaction center groups.

All unique structures of the form [*Sub*] – [*Bridge*] – [*RC*], with *Sub* and *RC* selected from the list of 20 chemical groups in Table 1, were constructed for each of the three bridges. Ab initio calculations were performed on each structure. Each of the functional groups in Table 1 was used both as a reaction center, *RC*, and as a perturbing substituent, *Sub*.

Previous ab initio investigations of substituent effects define substituent effects using either energetic or electronic criteria.^{5,4,26} Here, we use the Mulliken population²⁷ of the reaction center *RC* to define the substituent effect *SE* of a substituent in a [*Sub*] – [*Bridge*] – [*RC*] molecule

$$SE = \sum_i [n_\alpha \cdot S]_{ii} - [n_0 \cdot S]_{ii} \quad (13)$$

where n_α is the molecule’s one-electron density matrix, n_0 is the density matrix of the unsubstituted (*Sub* = H) compound, S is the atomic-orbital overlap matrix, and the index i is summed over the atomic orbitals of the reaction center *RC*.

The ab initio calculations are gas-phase RHF+MP2 calculations in the STO-3G basis. All calculations were performed using the GAMESS electronic structure program.²⁸ We modified the code to allow the addition of arbitrary one-electron constraint operators to the Hamiltonian, and wrote a series of C++ wrapper classes to support batch calculations.

Geometries were constructed as follows. The geometries of the benzene and bicyclo-[2.2.2]octane bridge groups were optimized with –H as both substituent and reaction center. The geometries of the substituent groups in Table 1 were each optimized for the substituent bound to unconstrained benzene. These geometries were then used to construct molecules of the

TABLE 1: Substituent-Effect Parameters Obtained from the Fits Described in Section 5

| group | <i>c-benz</i> bridge | | | | <i>bco</i> bridge | | | |
|------------------------------|----------------------|----------|------------|----------|-------------------|----------|------------|----------|
| | σ_I | ρ_I | σ_R | ρ_R | σ_I | ρ_I | σ_R | ρ_R |
| H | 0.00 | -0.68 | 0.00 | -0.27 | 0.00 | -0.62 | 0.00 | -0.27 |
| F | 0.55 | -0.51 | -0.88 | -0.33 | 0.37 | -0.61 | -0.92 | -0.31 |
| Cl | 0.83 | -0.94 | -0.02 | -0.50 | 0.64 | -1.13 | -0.27 | -0.50 |
| Br | 0.62 | -1.06 | -0.19 | -0.57 | 0.50 | -1.29 | -0.47 | -0.58 |
| CN | 0.82 | -0.73 | 1.34 | -0.55 | 0.78 | -0.93 | 0.60 | -0.57 |
| CCH | 0.26 | -0.75 | 0.54 | -0.56 | 0.29 | -1.00 | 0.10 | -0.56 |
| CHO | 0.15 | -0.75 | 0.55 | -0.59 | 0.25 | -0.99 | 0.21 | -0.62 |
| NO ₂ | 0.92 | -0.86 | 0.51 | -0.57 | 0.83 | -1.06 | -0.16 | -0.57 |
| CH ₃ | -0.08 | -0.74 | -0.35 | -0.39 | -0.01 | -0.90 | -0.42 | -0.38 |
| CF ₃ | 0.46 | -0.81 | 0.65 | -0.46 | 0.42 | -0.99 | 0.32 | -0.47 |
| CFH ₂ | 0.09 | -0.77 | -0.14 | -0.40 | 0.13 | -0.93 | -0.35 | -0.39 |
| OMe | 0.39 | -0.69 | -1.78 | -0.52 | 0.22 | -0.90 | -1.66 | -0.51 |
| OH | 0.48 | -0.62 | -1.57 | -0.45 | 0.26 | -0.78 | -1.54 | -0.45 |
| SH | 0.70 | -1.05 | -0.35 | -0.56 | 0.48 | -1.28 | -0.47 | -0.55 |
| NH ₂ | 0.18 | -0.65 | -2.80 | -0.58 | -0.04 | -0.85 | -2.38 | -0.58 |
| O- | -5.97 | -0.61 | -14.73 | -0.76 | -5.50 | -0.89 | -10.11 | -0.68 |
| S- | -4.58 | -0.93 | -7.82 | -0.74 | -4.15 | -1.17 | -4.72 | -0.76 |
| CO ₂ | -4.64 | -0.90 | -4.77 | -0.44 | -3.96 | -1.15 | -2.27 | -0.31 |
| NH ₃ ⁺ | 5.29 | -0.73 | 4.67 | -0.43 | 4.65 | -0.91 | 1.06 | -0.52 |
| CH ₂ ⁺ | 5.14 | -0.57 | 19.27 | -4.13 | 5.41 | -1.59 | 13.69 | -4.83 |

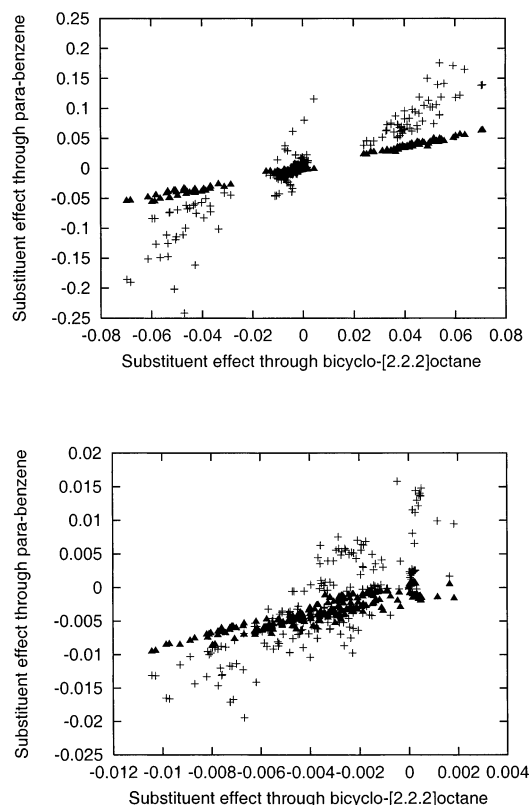


Figure 5. Correlation plots of the calculated substituent effects through [Sub] – [bridge] – [RC] molecules with benzene or bicyclo-[2.2.2]-octane bridges. Each point represents data for a single {Sub, RC} pair. A point's *x* coordinate is the calculated substituent effect through a bicyclo-[2.2.2]octane bridge, and its *y* coordinate is the calculated substituent effect through a constrained (triangles) or unconstrained (crosses) *para*-substituted benzene bridge (*c-benz* or *benz*, respectively). Data are plotted for all (upper panel) and all uncharged (lower panel) substituent and reaction-center groups in Table 1.

form [Sub] – [Bridge] – [RC], with no further geometry optimization.

Figure 5 is a correlation plot of the substituent effects transmitted through the *benz*, *c-benz*, and *bco* bridge groups of Figure 2.²⁹ Substituent effects calculated through the *benz* and *c-benz* bridges (crosses and triangles, respectively) are plotted against the substituent effects calculated through the *bco* bridge.

The results demonstrate that application of the bond-order maximization constraint causes a *para*-substituted benzene bridge to transmit substituent effects like a bicyclo-[2.2.2]octane bridge. The correlation coefficient between the substituent effects measured through the *benz* (unconstrained benzene) and *bco* bridges is 0.94 for all substituents and 0.80 for just the uncharged substituents. These correlations go to >0.99 and 0.92, respectively, when the constraints are applied to the benzene bridge. The increased correlation can be clearly seen in Figure 5. The correlation between *c-benz* and *bco* is not expected to be perfect because of the different geometries and connectivities of the bridges' σ -bond networks.

The slope of the correlation between substituent effects through *c-benz* and *bco* (the triangles in the upper panel of Figure 5) is 0.86, indicating that the *bco* bridge transmits substituent effects better than the *benz* bridge. This result is similar to that obtained by Swain and Lupton, who used a factor of 0.92 (the α parameter of eq 3) to account for the difference in inductive substituent effects transmitted through unconstrained benzene and *bco*.

5. Parametrizing Simple Substituent-effect Models

The results of the previous section indicate that constrained *para*-substituted benzene (*c-benz*) transmits substituent effects in a manner similar to that of substituted bicyclo-[2.2.2]octane (*bco*). Given this, the discussion in section 1 suggests that either bridge group can be treated as a "model nonresonant bridge", i.e., a bridge group that transmits inductive effects in a manner similar to an unconstrained *para*-substituted benzene (*benz*) bridge but that does not transmit resonant substituent effects. Hence, data from either bridge can be used, along with data from a *benz* bridge, to fit resonant and inductive substituent-effect parameters. In this section, we parametrize a dual-parameter model of substituent effects from the data presented in section 4, using methods similar to those of Swain and Lupton (see section 1). The parameters obtained when *bco* is used as the nonresonant bridge are compared with those obtained when *c-benz* is used as the nonresonant bridge.

Like the Swain–Lupton model, our model of substituent effects uses a global set of inductive and resonant parameters. The substituent effect *SE* for any [Sub] – [Bridge] – [RC] molecule, calculated as in eq 13, is modeled as

$$SE^{pred} = \frac{1}{100}[\sigma_I^{Sub} T_I^{Br} \rho_I^{RC} + \sigma_R^{Sub} T_R^{Br} \rho_R^{RC}] \quad (14)$$

where σ is the substituent's ability to induce an effect, ρ is the reaction center's susceptibility to substituent effects, and T is the bridge's ability to transmit such effects. Subscripts I and R distinguish inductive from resonant effects. The parameters σ_I and σ_R of eq 14 correspond to the Swain–Lupton F and R parameters, respectively. The 1/100 prefactor is used to scale the σ and ρ parameters to the order of 10^{-1} , to aid in comparisons with the Swain–Lupton parameters.

Model parameters are fit by minimizing the absolute deviation in the predicted substituent effects,

$$\text{Error}_{Bridge} = 100\% \frac{\sum_{Sub} \sum_{RC} |SE - SE^{pred}|}{\sum_{Sub} \sum_{RC} SE} \quad (15)$$

where Error_{Bridge} is the error in the model's description of the substituent effects through the data set of all $[Sub] - [Bridge] - [RC]$ molecules, SE is the calculated substituent effect of eq 13, the predicted substituent effect SE^{pred} is given by eq 14, and the sums are over all substituents and reaction centers in the data set.

As in the Swain–Lupton model, we fit our model parameters using data on two bridge groups, where both bridges transmit inductive substituent effects in a similar manner but only one bridge is expected to transmit resonant substituent effects. The model parameters are fit in two steps. First, the inductive substituent parameters, σ_I and ρ_I , are obtained from a fit to the calculated SE through all $[Sub] - [nonresonant\ bridge] - [RC]$ molecules, where the nonresonant bridge group is either *bco* or *c-benz*. This fit is performed with $T_I = 1$ and $T_R = 0$ in eq 14. Second, the resonant parameters, σ_R and ρ_R , are obtained from a fit to the calculated SE through all $[Sub] - [benz] - [RC]$ molecules, using without modification the inductive parameters from the first step. In this second fit, T_R is fixed at 1 and T_I is treated as a fitting parameter analogous to the α parameter of eq 3. The procedure corresponds to fitting 81 parameters to 780 pieces of data.²⁹

Table 1 shows the substituent parameters obtained from the fitting procedure above. In the first step, the model is able to reproduce the nonresonant bridge's substituent effects with errors of 2.5% for the *c-benz* bridge and 3.6% for the *bco* bridge. In the second step, the model is able to reproduce the substituent effects through benzene with errors of 15.4% for a fit from the *c-benz* inductive parameters and 16.5% for a fit from the *bco* inductive parameters. These errors are reasonable, as inductive substituent effects are generally described better by global parameter sets than are resonant substituent effects.¹⁶

The parameters obtained from using *c-benz* as a model nonresonant bridge are similar to those obtained using *bco*. When all substituents are included, the correlation coefficient between the $\{\sigma_I\}$ parameter set from *c-benz* and the $\{\sigma_I\}$ parameter set from *bco* is > 0.99 . The same value is obtained for the correlation between the $\{\sigma_R\}$ parameter sets. As in Figure 5, the correlation between the *c-benz* and *bco* results is somewhat less strong when only uncharged substituents are included, being 0.94 and 0.99 for $\{\sigma_I\}$ and $\{\sigma_R\}$, respectively. These results, like those of section 4, indicate that *c-benz* and *bco* transmit substituent effects in a similar manner.

The correlation between the inductive and resonant parameters of a given parametrization indicates how well these two effects

TABLE 2: Correlations between Inductive and Resonant Parameters for the Swain–Lupton Models^{31,32} and the *bco* and *c-benz* Parameters of Table 1

| parameter set | correlation |
|--------------------|-------------|
| <i>bco</i> | 0.56 |
| <i>c-benz</i> | 0.26 |
| Swain–Lupton model | 0.18 |

have been (or how well they can be) separated. Correlation between inductive and resonant parameters indicates that the model has not succeeded in separating the effects, or that there is some intrinsic relation between inductive and resonant effects. The correlations between the σ_I and σ_R parameters for all uncharged substituents in Table 1 are shown in Table 2.

The smaller correlation seen for the *c-benz* parameters³⁰ suggests that the inductive parameters obtained from *c-benz* provide a better measure of benzene's nonresonant transmittance than the inductive parameters obtained from *bco*. This implies that the combination of data from the *benz* and *c-benz* bridges provides a better set of pure inductive and pure resonant parameters than those obtained from data on the *benz* and *bco* bridges. This result does not imply that *bco* transmits "resonant substituent effects", but that *bco* is not the best model of *benz*'s transmission of inductive substituent effects. We speculate that this is due to the differences between the σ -bond networks of *benz* and *bco*, which were discussed in section 1.

The inductive and resonant parameters for the charged substituents are always fairly strongly correlated with each other. We speculate that this is due to the very large inductive effects calculated for charged substituents (compare the upper and lower panels of Figure 5), which can be attributed to the absence of charge-stabilizing solvent interactions in our calculations.³³

The comparisons between our results for *c-benz* and *bco* bridges are made within a specific model chemistry,³⁵ as defined by the level of ab initio theory, the definition of substituent effects in terms of the Mulliken charges, and the absence of solvent effects. A measure of the validity of this model chemistry can be obtained by comparing the derived parameters with literature values of the corresponding Swain–Lupton parameters.^{31,32} These literature values are obtained from experiment as discussed in Sec. 1. Correlation plots between our parameters $\{\sigma_I, \sigma_R\}$ and the corresponding Swain–Lupton parameters $\{F, R\}$, for all uncharged substituents in Table 1, are shown in Figure 6. Correlation coefficients between the inductive parameter sets are 0.90 for the *c-benz* parameters and 0.93 for the *bco* parameters. Correlation coefficients between the resonant parameter sets are 0.97 for the *c-benz* parameters and 0.96 for the *bco* parameters. These correlations are reasonable, given the fairly large difference in definition of substituent effects and our use of gas-phase calculations with a minimal basis. Our parameters for charged substituents are not well correlated with those of Swain and Lupton. Again, this result can be rationalized in terms of the importance of solvent effects on charged substituents and the absence of solvent in our calculations.

6. Calculations on Other Bridge Molecules

This section tests the extent to which the substituent-effect parameters obtained in the previous section can be transferred to other bridge groups. Using the procedure described in section 4, the substituent effect was calculated for all structures of the form $[Sub] - [Bridge] - [RC]$, with *Sub* and *RC* selected from the substituents listed in Table 1 and the bridges selected from those listed in the first column of Table 3.³⁴

The *cis*-butadiene bridges are constrained to the x - y plane. The substituents on their terminal carbon atoms lie on the axis

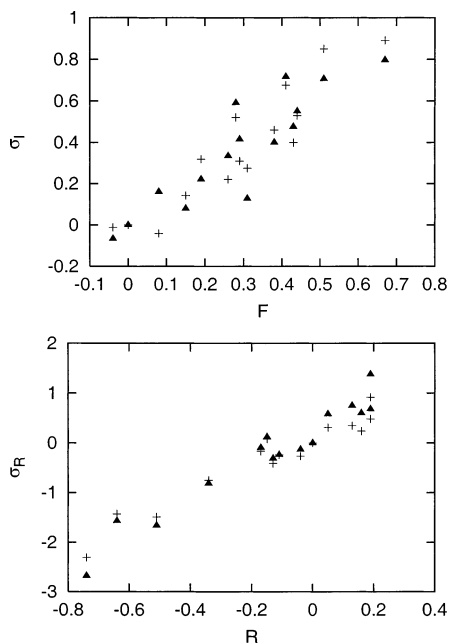


Figure 6. Correlation plots of substituent-effect parameters for uncharged substituents. The σ parameters of Table 1 are plotted against the corresponding Swain–Lupton parameters.^{31,32} The upper panel compares inductive-effect parameters, and the lower panel compares resonance-effect parameters. The *bco* and *c-benz* parameters of Table 1 are plotted with crosses and triangles, respectively.

connecting the centers of the terminal bridge carbon atoms, making them an interesting analogue of the benzene bridge. The (2-vinyl) substituted benzenes (phenylenevinylenes) are constrained to the x – y plane, with one substituent on atom 2 of the vinyl group and another substituent *meta* or *para* to the vinyl group. The bridges labeled “const” have a bond-order maximization constraint applied to their π -systems, similar to the constraint used to turn off resonance in constrained benzene. The results tabulated as “(1,4) *cis*-butadiene (zeroed)” are for a planar *cis*-butadiene bridge with the π -bond order between the two internal bridge carbons constrained to zero. The resulting bridge is analogous to a benzene bridge with the bond-order zeroing constraints used by IK and discussed previously in section 3.

The second and third columns of Table 3 give the correlation coefficient between the substituent effects calculated for each bridge and the substituent effects calculated for the *benz* and *c-benz* bridges, respectively. Results for the *benz*, *c-benz*, and *bco* bridges of section 4 are presented at the bottom of the table for comparison.

The remainder of Table 3 presents the results obtained when the calculated substituent effects through each bridge are modeled using the substituent-effect parameters of Table 1. The data for each bridge were fit to the model of eq 14, using without modification the σ and ρ parameters given in Table 1, and fitting only the two bridge transmittance parameters T_I and T_R . Errors in the fit were calculated from eq 15. Transmittance parameters for each bridge were fit twice, once using the substituent parameters obtained with *c-benz* as the nonresonant bridge and once using the parameters obtained with *bco* as the nonresonant bridge. The results of these two fits are presented in columns 4–6 and columns 7–9 of Table 3, respectively.

The results indicate that the constraint operator technique works on bridges other than benzene, since the substituent effects through all of the constrained bridges are strongly correlated with those through *c-benz*. Also, the parameters from

c-benz give lower errors than those from *bco* in modeling the constrained bridges, while the unconstrained bridges are described equally well by both sets of parameters.

The results also indicate that the substituent parameters are transferable to different bridge groups. The fitting procedure for modeling the new bridge groups used only two free parameters for 390 data points,²⁹ and was able to reproduce the calculated substituent effects to better than about 30%. The two parameter sets gives similar results, as expected since the correlation between the parameter sets is >0.99 . The methane and anti-ethane bridges were not well-described by the substituent parameters. This result can be rationalized in terms of the close spatial proximity between Sub and RC for these bridges, such that short-range effects dominate the Sub-RC interactions.¹⁸

The T_I and T_R parameters obtained for the bridges follow chemically reasonable trends. Inductive transmittances T_I decrease as the distance between substituent and reaction center increases. The inductive transmittance of the *meta*-substituted bridges [*meta*-benzene, (1,3)*cis*-butadiene, 1(2-vinyl)3-benzene] is always larger than the inductive transmittance of the corresponding *para*-substituted bridges. The resonant transmittance T_R of the *meta*-substituted bridges is always less than that of the corresponding *para*-substituted bridges, with the ratio between resonant transmittances in *meta*- and *para*-substituted benzenes being 0.41.

The “(1,4) *cis*-butadiene (zeroed)” bridge provides a test of the ability of a zero-bond-order constraint to turn off resonant transmission through a bridge. The Hückel calculations of section 3 suggest that this constraint would not be as effective at turning off the transmission of resonant substituent effects as the bond-order maximization constraint labeled as “const” in Table 3. This conclusion is supported by the results for the (1,4) *cis*-butadiene (zeroed) bridge, whose resonant-effect transmittance parameter T_R is significantly larger than that of the corresponding (1,4) *cis*-butadiene (const) bridge in both parametrizations.

7. Discussion

This article investigates the use of constrained Schrödinger equation methods to generate ab initio data with which to parametrize simple models. These methods provide a flexible means of controlling a molecule’s electronic distribution. This enables construction of model systems that isolate particular electronic effects of interest. We tested this approach by generating data for a model that separates resonant from inductive substituent effects. This test case was chosen because the results could be benchmarked against the standard approach for partitioning resonant and inductive effects, namely, the use of substituted bicyclo-[2.2.2]octane (*bco* of Figure 2) as a model for the inductive substituent effects transmitted through *para*-substituted benzene. Our approach replaces *bco* with substituted benzenes whose π -systems are constrained to prevent transmission of resonant substituent effects (*c-benz* of Figure 2).

The comparison between *bco* and *c-benz* as nonresonant model compounds is made within a well-defined model chemistry, as discussed in section 5. Certain inaccuracies relative to experiment are expected in this model chemistry, due to the relatively small basis set (STO-3G), the level of correlation (MP2) and the lack of solvent effects. These inaccuracies are reflected in the differences between the substituent parameters obtained here and the literature values (see Figure 6). However, these disagreements arise from the choice of model chemistry, not from the use of *c-benz* as opposed to *bco* as a nonresonant

TABLE 3: Results Obtained Using the Substituent Parameters of Table 1 to Model Substituent Effects of Other Bridges

| bridge | R(<i>benz</i>) ^a | R(<i>c-benz</i>) | <i>c-benz</i> bridge params | | | <i>bco</i> bridge params | | |
|--|-------------------------------|--------------------|-----------------------------|-----------------------------|----------------------|--------------------------|----------------|---------|
| | | | T _I | T _R ^b | % error ^c | T _I | T _R | % error |
| CH ₂ | 0.91 | 0.93 | 2.77 | 0.28 | 36.6 | 2.63 | 0.00 | 38.0 |
| CH ₂ CH ₂ anti | 0.92 | 0.93 | 2.41 | 0.56 | 37.5 | 2.26 | 0.47 | 37.7 |
| CH ₂ CH ₂ gauche | 0.91 | 0.99 | 2.04 | 0.01 | 15.0 | 2.05 | -0.26 | 16.5 |
| <i>meta</i> -benzene | 0.97 | 0.98 | 1.40 | 0.41 | 12.4 | 1.42 | 0.28 | 12.5 |
| (1,3) <i>cis</i> -butadiene | 0.97 | 0.97 | 1.38 | 0.32 | 29.9 | 1.39 | 0.20 | 30.1 |
| (1,4) <i>cis</i> -butadiene | 1.00 | 0.90 | 0.85 | 1.07 | 18.0 | 0.99 | 1.11 | 17.8 |
| 1(2-vinyl) 3-benzene | 0.96 | 0.94 | 0.71 | 0.43 | 33.9 | 0.76 | 0.42 | 33.9 |
| 1(2-vinyl) 4-benzene | 0.99 | 0.89 | 0.70 | 0.70 | 29.2 | 0.80 | 0.69 | 30.2 |
| <i>meta</i> -benzene (const) | 0.90 | 0.99 | 1.21 | -0.03 | 12.7 | 1.19 | -0.20 | 15.9 |
| (1,3) <i>cis</i> -butadiene (const) | 0.90 | 0.98 | 1.22 | -0.01 | 14.7 | 1.18 | -0.14 | 18.9 |
| (1,4) <i>cis</i> -butadiene (const) | 0.91 | 1.00 | 0.96 | 0.00 | 5.3 | 0.95 | -0.12 | 9.6 |
| 1(2-vinyl) 3-benzene (const) | 0.91 | 1.00 | 0.55 | 0.00 | 5.8 | 0.53 | -0.06 | 10.9 |
| 1(2-vinyl) 4-benzene (const) | 0.91 | 1.00 | 0.51 | 0.00 | 5.7 | 0.48 | -0.03 | 9.8 |
| (1,4) <i>cis</i> -butadiene (zeroed) | 0.96 | 0.96 | 0.98 | 0.49 | 24.4 | 1.00 | 0.49 | 24.7 |
| benz | 1.00 | 0.91 | 0.95 | 1.00 | 15.7 | 1.05 | 1.00 | 15.4 |
| cbenz | 0.91 | 1.00 | 1.00 | 0.00 | 2.5 | 0.98 | -0.12 | 7.5 |
| bco | 0.94 | 1.00 | 1.00 | 0.12 | 7.2 | 1.00 | 0.00 | 3.5 |

Results are shown for both sets of parameters in Table 1 (*c-benz* and *bco*). ^a R(*br*) entries are the correlation between substituent effects through the current bridge and substituent effects through bridge *br*. ^b Bridge's ability to transmit inductive (I) or resonant (R) substituent effects. ^c Defined in eq 15.

model compound. This is evidenced by the strong correlation between the *bco* and *c-benz* parameters, and the similar disagreements with experiment seen when either *bco* or *c-benz* are used as the nonresonant bridge. The agreement between *bco* and *c-benz* within the model chemistry suggests that the use of constraint-operator techniques is a valid approach to constructing model compounds, and does not introduce inaccuracies beyond those associated with the use of a particular level of ab initio theory.

The substituent parameters obtained from the use of constraint operators to turn off resonance (the *c-benz* parameter set) are at least as good as the parameters obtained using *bco* as a model nonresonant system (the *bco* parameter set). The two parameter sets are strongly correlated with each other, indicating that *c-benz* and *bco* transmit substituent effects in a similar manner. Both parameter sets are equally able to model substituent effects through other bridges. In addition, the *c-benz* parameter set has a lower correlation between the inductive and resonant parameters. This better separation of inductive and resonance effects suggests that *c-benz* provides a better model of benzene's inductive effects than *bco*.

The results presented here suggest that constrained Schrödinger equation methods may prove to be a powerful tool for generating ab initio data with which to parametrize simple models. The constraints on the system are expressed in terms of the one-electron density matrix, and so this approach is useful for models whose parameters relate to an aspect of electronic structure that can be expressed in terms of the density matrix. In future work, we plan to explore applications of this technique to other simple models. We will investigate the decomposition of inductive substituent effects into a sum of electric-field and bond-polarization effects.^{36–39} There is no way to synthesize a real bridge group that cannot transmit inductive substituent effects, as such a bridge would need to contain perfectly unpolarizable σ bonds. This dual-parameter model of inductive substituent effects has been investigated through an ab initio analysis of the response of a [Sub] – [Bridge] – [H] molecule to a perturbative point charge, in the presence or absence of system polarization.⁵ Constraint-operator methods, however, offer the prospect of simultaneous and independent control over the polarization of substituent, bridge, and reaction-center groups. For example, one can envision constraining the σ bonds

of a model bridge to have the same electron distribution, regardless of the nature of the substituent and reaction-center groups. Such a bridge may provide a good nonpolarizable model system for isolating the electric-field effects, in the same way that a *c-benz* or *bco* bridge provides a good model system for isolating the inductive effects. In addition to models of polarization, we are currently exploring the use of constrained Schrödinger equation methods to derive diabatic surfaces for use in Marcus-theory models of electron transfer,⁴⁰ the key being to define an electronic constraint that can keep the molecule on one or the other diabatic surface.

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