Parameter-Free Structure−Property Correlation via Progressive Reaction Posets for Substituted Benzenes

T. Ivanciuc and D. J. Klein*

Texas A&M University at Galveston, Galveston, Texas 77553

Progressive reaction networks as frequently arise in chemistry are naturally identifiable as "partially ordered sets" (or posets). Here the direction of the reaction identifies the partial ordering of the set of molecular species. The possibility that different properties are similarly ordered is a further natural consideration and is here investigated for a suite of over 30 properties for (methyl and chloro) substituted benzenes. Such a posetic correlation is favorably demonstrated for these substituted benzenes, and it is illustrated how suitable properties may be simply predicted in an interpolative parameter-free (albeit not model-free) fashion through the use of the reaction poset. Some numerical model-quality indicators are identified, and the simple approach is deemed quite reasonable.

INTRODUCTION

Progressive reaction networks are ubiquitous throughout chemistry. Indeed this has been[1] earlier emphasized, with a listing of several examples. A typical example considers a molecular skeleton upon which substituents are progressively introduced one after another, with earlier substituents not moving from their earlier positions. A classical example concerns the addition of substituents of a given type to benzene, whence the reaction diagram is as in Figure 1. If the substituents are chloro groups, one then starts with benzene at the top of this figure and ends with hexachlorobenzene at the bottom, while all the different patterns of substitution are found in between. In particular it is noted that from *p*-chlorobenzene only a single trichlorobenzene is obtained, while from *o*-chlorobenzene two trichlorobenzenes are obtained, and from *m*-chlorobenzene all three trichlorobenzenes may be obtained. Historically this diagram was of some importance, when described in 1870 by Körner,[2] in that this diagram provides further information about the structure of benzene beyond the number of substitutional isomers at each stage of substitution. Körner's work was also summarized quite early on,[3] and the reaction diagram has appeared more or less independently on other occasions as in ref 4. And of course there are many other progressive reaction networks, several of which have been noted in ref 1. One further nice example (with an indication of its mathematical character) is found in ref 5, and further examples also not noted in ref 1 are found in refs 6 and 7.

Now granted such a progressive reaction network a "partial ordering" is implied. Formally a general "partially ordered set" or a *poset* is a collection $\mathcal{C}$ of members along with a *partial ordering relation* $\to$ so that with α and β members of this collection it may be that $\alpha \to \beta$ and we say that β *follows* α or that α *precedes* β. If two elements each precede the other, then the two elements are the same (i.e., are =), and conversely, if α and β are the same, then $\alpha \to \beta$ and $\beta \to \alpha$. Finally the elements satisfy *transitivity*: if $\alpha \to \beta$ and $\beta \to \gamma$, then $\alpha \to \gamma$. A simple example of a poset is that of
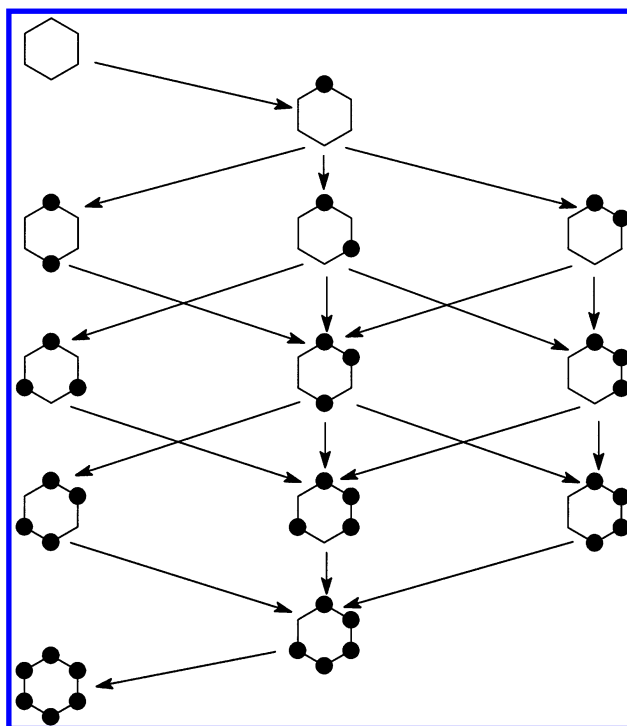

Figure 1. The benzene substitution reaction poset. The darkened disks indicate the sites on which an H atom of C_6H_6 has been replaced by the substituting ligand.

the ordinary numbers with the partial ordering relation being the ordinary ≤ relation. But more generally given two distinct elements α and β of $\mathcal{C}$ it is not required that either $\alpha \to \beta$ or $\beta \to \alpha$. That is, two elements α and β need not necessarily be comparable (via $\to$). In the present context the elements of $\mathcal{C}$ are the different substituted benzenes and structure α precedes structure β if β can be obtained from α via further substitution. Further (countable) posets may be generally represented in terms of what is called a *Hasse diagram*: each element of the poset $\mathcal{C}$ is positioned at a node or vertex and two such nodes α and β are connected by a directed line from α to β with $\alpha \to \beta$ such that α and β are as near as possible (i.e., there is no other element $\gamma \epsilon \mathcal{C}$ such that $\alpha \to$
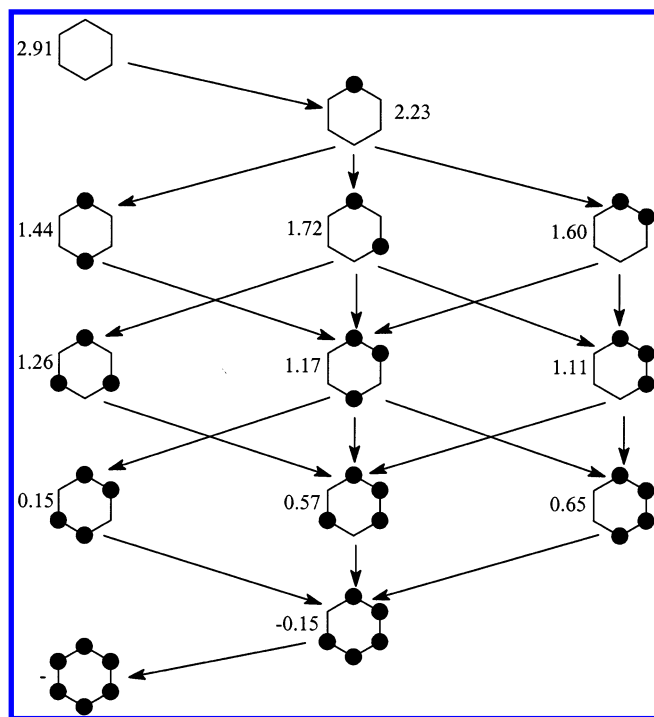
Figure 2. The posetic presentation of aqueous toxicities (as − log-(LC$_{50}$)) for the chlorobenzenes.

Figure 3. The posetic presentation of chromatographic retention coefficients of the methylbenzenes.

γ and $\gamma \rightarrow \beta$). Granted that $\mathscr{C}$ is a poset, the transitivity condition implies that the Hasse diagram may be arranged on a sheet of paper such that all the directed line segments are directed downward—and in fact this is usually demanded of a Hasse diagram. Evidently our reaction diagram is naught but a Hasse diagram for our progressive substitution partial ordering. Thence general ideas related to posets might be implemented for such reaction networks. Indeed applications of posetic ideas in chemistry have previously been indicated, particularly in refs 8−11 and also in a special issue[12] of MatCh dedicated to the topic.

It is rather natural to consider that different chemical properties might be ordered in concert with the partial ordering of a progressive reaction poset. Thence this idea is explored in the next section for a suite of over two dozen properties, including a bioactivity. The subsequent section addresses a simple scheme to make parameter-free predictions by interpolative averaging over posetic neighbor species. Comparisons are made between such predicted values and experimental values for over 30 properties of methylbenzenes and chlorobenzenes. A few property predictions are made for cases without experimental data yet available.

POSET ISOTONICITY FOR PROPERTY VALUES

There is the possibility that a particular property might be ordered similarly to the reaction poset. That is, for general structures A and B in the reaction poset such that B follows A, then property X might be ordered such that $X(A) < X(B)$. If this is true for every such pair, then the ordering for X is consonant with the partial ordering of the reaction network. Even if whenever B follows A, it turns out that $X(A) > X(B)$, the property ordering is still consonant with the partial ordering of the reaction network—the sense of the correspondence between the two orderings is just reversed. Such
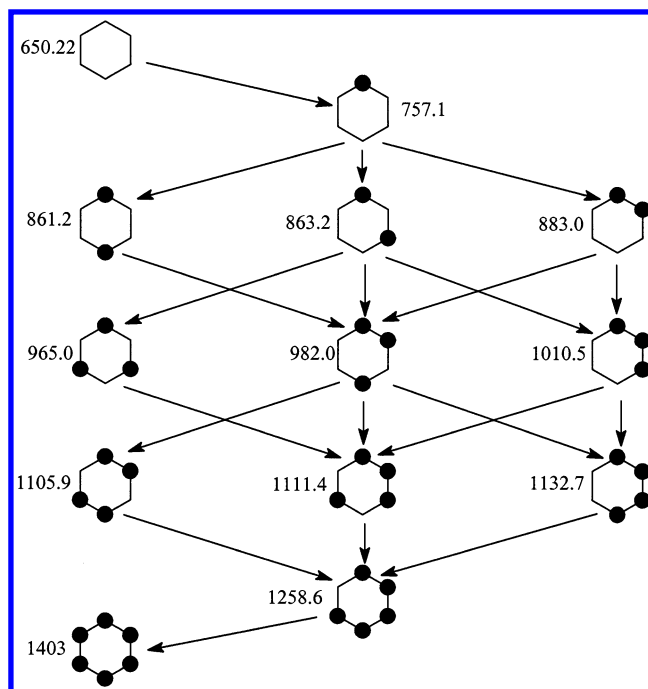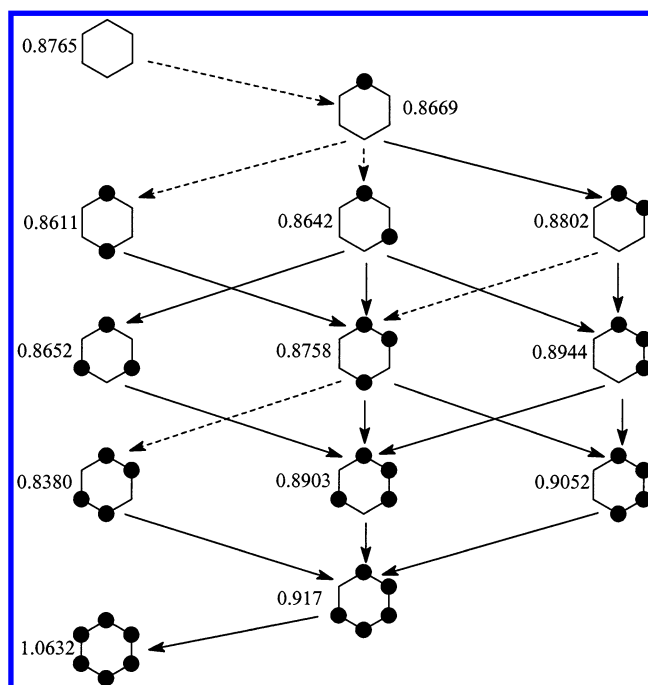

Figure 4. The posetic presentation of densities (in g/cm^3) of the methylbenzenes. The incorrectly ordered pairs of the reaction poset are indicated by dashed arrows.

consonance is more technically termed *isotonicity*. This indeed does happen, e.g., as illustrated in Figure 2, for toxicities of the chlorobenzenes, and in Figure 3 for chromatographic retention indices (on squalene at 96 °C) of methylbenzenes.

Beyond perfect isotonicity for a property X there is also the possibility of "imperfect isotonicity". Such sometimes occurs, e.g., as in Figure 4, for density (in g/cm^3) of methylbenzenes. Here there are several neighbor pairs (indicated in the figure with dashed arrows) in the diagram such as to be ordered differently than the other neighbor

pairs. Generally to each property one might associate an *isotonicity score*, defined as the ratio of the number of correctly ordered neighbor pairs to the total number of neighbor pairs. Thus for our benzene substitution poset, as of Figure 1, one sees 20 neighbor pairs, and in Figure 3 a perfect isotonicity score of 20/20 is attained, while for Figure 4 with a misordering the (rather poor) score is 15/20.

In some cases it might be that property values for all species in a reaction network are not available. Even in such cases one can make an isotonicity score, just by taking into account neighbor pairs of species such that property values for both are known. Thus for instance, if the property value for the hexa-substituted species (ϕCl_6) were not available, then the remaining available number of neighbor pairs would be 19, as in Figure 2. Thence the property score for this figure is seen to be 19/19.

An examination of the literature has been made, to find reasonably complete tabulations of over two dozen properties for chloro- and methylbenzenes. These properties and their isotonicity scores are reported in Table 1 for chlorobenzenes and Table 2 for methylbenzenes. There it is seen that most properties have fairly high isotonicity scores, with several being perfect. There are a few properties which exhibit lower isotonicity scores—these properties include, melting point, heat of fusion, and entropy of fusion. Also in these tables one finds a "degree of indifference" score, such as has to do with a comparison to another somewhat natural partial ordering, wherein every ϕCl_n is viewed to precede every ϕCl_{n+1}. That is, one might imagine that some properties are ordered such that the values of every *n*-substituted species are similarly ordered with respect to every *n*+1-substituted species—one especially simple such property being the molecular weight. This alternative more extensive partial ordering has an additional 6 pairs in the Hasse diagram, and the *degree of indifference* is defined as the fraction of these additional relations which would also be satisfied by a considered property. E.g., from Figure 2 one sees that the toxicity values simply increase with the number of substituted Cl-atoms, so that the degree of indifference is 6/6. It is seen that the degree of indifference is often high—but not always, more-so for the case of methylbenzenes.

Finally in these tables there are further found standard deviations $\sigma(X)$ associated to each property X. This is not a standard deviation for experimental errors but rather a standard deviation between the predictions of the model used and the (presumed correct) corresponding experimental values. Of course, then one needs a model, such as that suggested in the next section. Typically our current very simple model does not make predictions for every position in the poset, in which case the standard deviation is taken just for the set of properties for which it does make predictions. This number of positions where the prediction is applicable and where also the experimental value is available for comparison in Tables 1 and 2 is generally different in different cases. It is seen that in many cases quite reasonable standard deviations apply.

POSETIC PROPERTY PREDICTION

What is perhaps a simplest sort of model to predict property values is here considered. By this scheme a
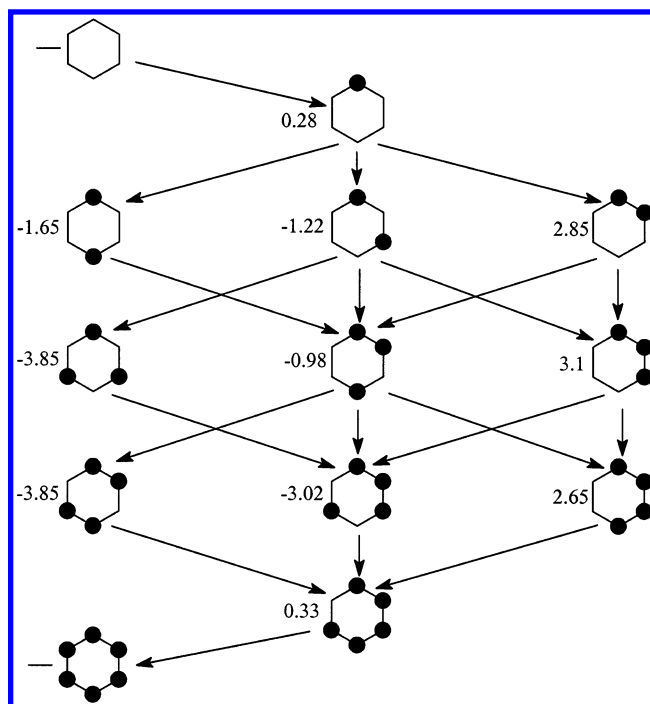

Figure 5. The posetic presentation of the errors for the boiling points (in °C) of the methylbenzenes.

prediction $\bar{X}(B)$ is made for a property X at a position B in the poset if the property values are available for all other positions immediately adjacent to A in the Hasse diagram. We take $\bar{X}(B)$ as the average of two values: first the average of all $X(A)$ with A just above B, and second the average of all $X(C)$ with C just below B. Thence for *o*-dichlorobenzene the predicted toxicity from the data for chlorobenzene and for 1,2,3- and 1,2,4-trichlorobenzenes is

$$\bar{X}(oCl_2\phi) = \frac{1}{2}\left\{X(Cl\phi) + \frac{1}{2}[X(123Cl_3\phi) + X(124Cl_3\phi)]\right\}$$

$$= \frac{1}{2}\left\{2.23 + \frac{1}{2}[1.17 + 1.11]\right\}$$

$$= 1.685$$

This scheme is notably rather like the neighbor-averaging scheme originally used by Mendeleev[13] to make predictions for selected properties of (then) missing elements (e.g. eka-silicon, later named germanium). Indeed this scheme in application to Mendeleev's periodic table is often described in texts for introductory chemistry courses. Notably Mendeleev's scheme evidently appears to have even more in common with our present work when Mendeleev's periodic table is viewed as a poset (such as indeed has been suggested[6]). Errors (as BP(A) $-$ $\overline{BP}$(A)) for the so predicted boiling points of the methylbenzenes are exhibited in Figure 5.

In the general posetic context the patterning of different associated properties has previously been noted in different cases,[1,9,14,15] though typically these authors restrict attention to ordering (or ranking) of the property values. Particularly in the work of Carleson[9] (and also in that of Brüggemann[8]) the considered poset is not determined a priori but rather is defined in terms of the considered property values, so that at least these property values are strictly isotonic. What is different in the current approach is that miss-orderings of

Table 1. Properties and Their Isotonicity Scores for Chlorobenzenes

no.	property		references	score ϕCl_n	degree indifference	$\sigma_{\phi Cl_n}$
1	logP	partition coefficients octanol/water		*Chemosphere* **2000**, *20*, 457−512	20/20	6/6	0.089
				J. Mol. Struct. **2003**, *622*, 127−145		6/6	0.065
						6/6	0.142
2	RI	retention indices		*J. Chromatogr. A* **2003**, *1002*, 155−168	20/20	6/6	23.299[a]
				J. Chromatogr. **1985**, *319*, 1−8	20/20	6/6	42.949[b]
						6/6	69.299[c]
						6/6	16.627[d]
3	k	capacity factor		*J. Chromatogr. A* **1996**, *734*, 277−287	20/20		2.182[d]
				J. Chromatogr. A **2003**, *1002*, 155−168			0.876[e]
4	t_R	retention time	min	*J. Chromatogr. A* **1999**, *835*, 19−27	20/20		1.064
				Electroanal. Chem. Interfacial Electrochem. **1975**, *61*, 303−313	19/19	6/6	0.713
5	$\Delta_f H^{\circ}_{gas}$	enthalpy of formation of gas	[kJ/mol]	www.nist.gov/chemistry NIST Chemistry Webbook	20/20	6/6	6.992
				J. Phys. Chem. A **2002**, *106*, 6618−6627			
6	log S	water solubility	[mol/l]	*J. Chem. Inf. Comput. Sci.* **1996**, *36*, 100−107	20/20	6/6	0.438
				J. Chem. Inf. Comput. Sci. **1998**, *38*, 283−292			
				Chemosphere **1997**, *34*, 275−298		6/6	0.380
7	$logV_p$	vapor pressure at 25 °C	[Pa]	*J. Chem. Inf. Comput. Sci.* **1999**, *39*, 1081−1089	20/20	6/6	0.156
				http://cas.org./SCIFINDER/SCHOLAR			
8	$\Delta_{vap}H^{\circ}$	enthalpy of vaporization	[kJ/mol]	*Thermochim. Acta* **1991**, *179*, 81−88	20/20	6/6	0.534
				http://cas.org./SCIFINDER/SCHOLAR		6/6	1.514
9	$ln(\gamma M_s)$	molecular activities on SE−30 stationary phase		*J. Chromatogr. A* **2003**, *1002*, 155−168	19/20	6/6	0.515
							0.289
10	ΔH_f	enthalpy of fusion	[kJ/mol]	*Thermochim. Acta* **1991**, *179*, 81−88	17/20	3/6	3.020
11	T_f	temperature of fusion	[K]	www.nist.gov/chemistry NIST Chemistry Webbook	16/20	4/6	47.770
				Thermochim. Acta **1991**, *179*, 81−88			
12	ΔS_f	entropy of fusion	[J/molK]	*Thermochim. Acta* **1991**, *179*, 81−88	15/20	4/6	3.120
13	log LC_{50}	aqueous toxicity for *Poecilia reticulata*		*J. Chem. Inf. Comput. Sci.* **2001**, *41*, 1162−1176	19/19	6/6	0.164
14	E_{2d}	reduction potential	[V]	*Electroanal. Chem. Interfacial Electrochem.* **1975**, *61*, 303−313	19/19	6/6	0.017
15	$ln\gamma^{\infty}$	infinite dilution activity coefficients in water at 298.15 K		*Fluid Phase Equilibra* **2003**, *205*, 303−316	15/19		2.031
				Fluid Phase Equilibra **1997**, *131*, 145−179			
16	p	solute polarity parameter		*J. Chem. Inf. Comput. Sci.* **2003**, *43*, 1240−1247	16/16		0.101
17	IP	ionization potential	[eV]	*J. Phys. Chem. A* **2003**, *34*, 6580−6586	12/16		0.087
18	ϱ	density	[g/cm³]	*CRC Handbook of Chemistry and Physics*, 8th ed.; 1997−1998; pp 5−43	12/12		0.102
19	n_D	refractive index at 20 °C		*Physical Properties of Chemical Compounds*; American Chemical Society: Washington, DC, 1995; pp 1−87	10/10		0.010
				J. Chem. Inf. Comput. Sci. **1998**, *38*, 840−844			
20	p_c	critical pressure	[bar]	http:/159.226.63.177/scripts/opes/properties Engineering Chemistry Database	9/9		0.357
				Comput. Chem. **2002**, *26*, 159−169			
21	T_c	critical temperature	[K]	http:/159.226.63.177/scripts/opes/properties Engineering Chemistry Database	8/9		11.079
22	V_c	critical volume	[ml/g]	*Physical Properties of Chemical Compounds*; American Chemical Society: Washington, DC, 1995; pp 1−87	8/9		36.530
				http:/159.226.63.177/scripts/opes/properties Engineering Chemistry Database			
23	ρ_c	critical density	[g/mL]	*Physical Properties of Chemical Compounds*; American Chemical Society: Washington, DC, 1995; pp 1−87	6/6		0.015
24	$\Delta_f H^{\circ}_{liquid}$	enthalpy of formation of liquid	[kJ/mol]	www.nist.gov/chemistry NIST Chemistry Webbook	5/5		2.443
				CRC Handbook of Chemistry and Physics, 8th ed.; 1997−1998; pp 5−43			

[a] Retention indices on SE-30 column, nonpolar stationary phase, at 120 °C. [b] Retention indices on CARBOWAX 20M column, polar stationary phase, at 140 °C. [c] Retention indices on SE-30 column, nonpolar stationary phase, at 160 °C. [d] Retention indices and capacity factor on HP-5 column at 120 °C. [e] Capacity factor on HP-5 column at 140 °C.

the experimental values are allowed, quantitative predictions are entertained, and consequent standard deviations are obtained. That is, with predicted values $\bar{X}(B)$ comparisons with measured values and consequent standard deviations are naturally made, as in the preceding section. Both the isotonicity score and the standard deviation provide measures of the degree of organization achieved by the posetic classification. The overall results as reported in Table 1 seem
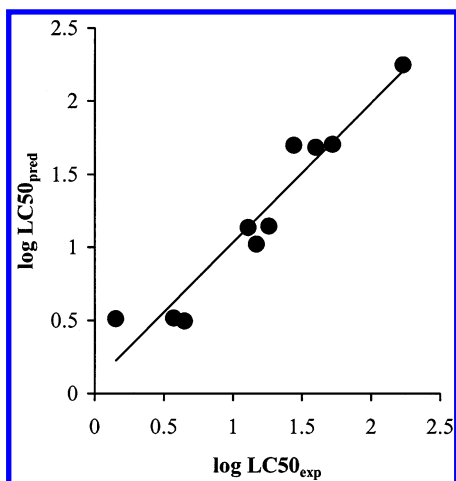
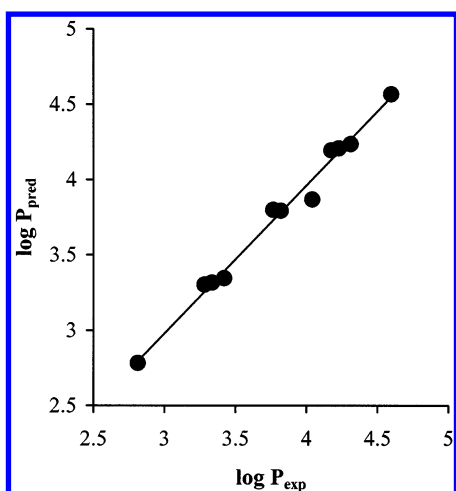**Figure 6.** Comparison of predicted and measured toxicities for chlorobenzenes.

Figure 7. Comparison of predicted and measured partition coefficients (as logP = −log K_{ow} for chlorobenzenes.
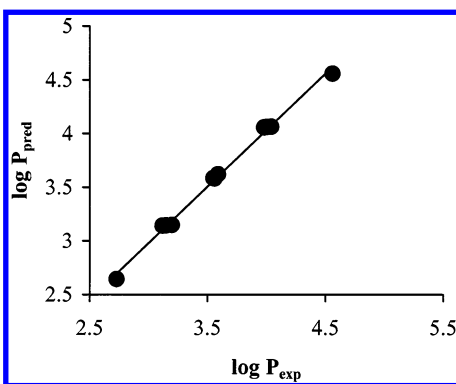

Figure 8. Comparison of predicted and measured partition coefficients for methylbenzenes.

encouraging. A further indication of the utility of the results is made upon making plots of predicted vs measured property values as indicated: in Figure 6 for aquatic toxicities of chlorobenzenes; in Figure 7 for octanol−water partition coefficients for chlorobenzenes; in Figure 8 for octanol−water partition coefficients for methylbenzenes; and in Figure 9 for aqueous solubility of methylbenzenes.

Significantly, beyond predicting already known property values so as to make comparisons, one may also make predictions for property values such as have not been
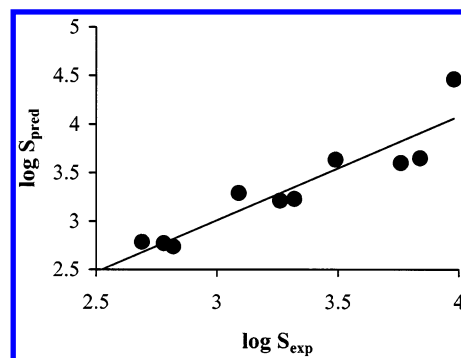

Figure 9. Comparison of predicted and measured aqueous solubilities (mole/L) for methylbenzenes.

experimentally reported (at least in the sources we used). Such predictions are reported in Table 3. There also are given the range of the property values which are known for the substituted species considered, along with the relevant standard deviation from Tables 1 and 2. Such ranges and standard deviations (σ) give an idea of the reliability of the predictions. Thence it is seen that for the polarity parameter for 1,2,3-Cl$_3\phi$ the relative accuracy of the prediction would seem to likely be quite high, whereas for the heat of fusion of 1,3,5-Me$_3\phi$ the relative accuracy indicated would not be very high. The case of the ionization potential for 1,3,5-Cl$_3\phi$ is a little better than the numbers would suggest since the range does not encompass what are likely the extreme values at ϕ and Cl$_6\phi$. Overall the predictions (as judged from the range and σ values) would seem to be likely quite reasonably useful.

GENERAL DISCUSSION

It may be worthwhile to emphasize a little further the generality and ubiquity of the general framework considered here. The idea of progressive reaction posets can be argued to underlie the general idea of periodic tables, with Mendeleev's periodic table of the elements providing naught but the most conspicuous example of such a periodic table. E.g., there also is Randić and Wilkins[12,13] "periodic table of alkanes" (such as appears[16] on a cover of *J. Chem. Ed.*), Dias'[17,18] "formula periodic table of benzenoids", and a[19,20] "periodic table of all acyclics". All these periodic tables fall into two-dimensional arrangements with one type of reaction down columns and another type along rows. Most of these periodic table examples end up with more than one chemical species at each position (or node) of what then is recognized as a reaction network. More details about such an interpretation (for all these periodic tables as well as several others) may be found elsewhere.[21] Especially in Randić and Wilkins[12,13] periodic-table poset for alkanes the type of techniques developed here should be rather directly applicable. In the progressive reaction poset for substituted benzenes it may even be mentioned that our diagram of Figure 1 may be viewed to anticipate a second type of reaction−namely a rearrangement reaction going across rows of the diagram. Here it is understood that we start with the most symmetric species (of a given overall composition) and then proceed to an increasingly asymmetric species with each horizontal (rearrangement) step to the right, so that, e.g., the molecular dipole moment should

Table 2. Properties and Their Isotonicity Scores for Methylbenzenes

no.		property		references	score ϕMe_n	degree indifference	$\sigma_{\phi Men}$
1	logP	partition coefficients octanol/water		*Chemosphere* **2000**, *20*, 457−512	20/20	6/6	0.046
				Chemosphere **1992**, *24*, 453−464		6/6	0.122
				J. Mol. Struct. **2003**, *622*, 127−145			
2	log S	water solubility	[mol/L]	*J. Chem. Inf. Comput. Sci.* **1996**, *36*, 100−107	20/20	6/6	0.187
				J. Chem. Inf. Comput. Sci. **1998**, *38*, 283−292			
				J. Chem. Inf. Comput. Sci. **2001**, *41*, 1177−1207			
				Chemosphere **1997**, *34*, 275−298			
3	RI	retention indices		*J. Chromatogr.* **1982**, *234*, 285−302	20/20	6/6	10.745[a]
				SAR QSAR Environ. Res. **2001**, *11*, 419−452	19/19	6/6	10.991[b]
						6/6	15.632[c]
4	k	capacity factor		*J. Chromatogr.* **1988**, *437*, 177−183	20/20	5/6	0.213[d]
					20/20	5/6	0.152[e]
5	t_R	retention time	[cm]	*J. Chromatogr.* **1988**, *437*, 177−183	20/20	5/6	0.416[d]
					20/20	5/6	0.299[e]
6	T_c	critical temperature	[K]	http:/159.226.63.177/scripts/opes/properties Engineering Chemistry Database	20/20	6/6	6.201
7	$\Delta_f H^\circ_{gas}$	enthalpy of formation of gas	[kJ/mol]	www.nist.gov/chemistry NIST Chemistry Webbook	20/20	6/6	3.165
				CRC Handbook of Chemistry and Physics, 8th ed.; 1997−1998; pp 5−43			
				J. Chromatogr. **1985**, *322*, 35−42			
8	$\Delta_{vap} H^\circ$	enthalpy of vaporization	[kJ/mol]	*Thermochim. Acta* **1991**, *179*, 81−88	20/20	6/6	0.792
9	$\Delta_c H^\circ_{liquid}$	enthalpy of combustion of liquid	[kJ/mol]	www.nist.gov/chemistry NIST Chemistry Webbook	20/20	6/6	6.989
10	$C_{p,gas}$	constant pressure heat capacity of gas	[kJ/molK]	www.nist.gov/chemistry NIST Chemistry Webbook	20/20	6/6	3.238
11	$logV_p$	vapor pressure at 25 °C	[Pa]	*J. Chem. Inf. Comput. Sci.* **1999**, *39*, 1081−1089 http://cas.org./SCIFINDER/SCHOLAR	20/20	6/6	0.081
12	T_f	temperature of fusion	[K]	www.nist.gov/chemistry NIST Chemistry Webbook	15/20	3/6	49.773
13	IPs	relative ionization potential to benzene	[kcal/mol]	*Chem. Phys. Lett.* **1999**, *311*, 215−220	17/19	-	2.868
14	n_D	refractive index at 20 °C		*CRC Handbook of Chemistry and Physics*, 8th ed.; 1997−1998; pp 5−43	15/19	4/6	0.004
				J. Chem. Inf. Comput. Sci. **1998**, *38*, 840−844			
15	ϵ	dielectrical constant at 25 °C		*Physical Properties of Chemical Compounds*; American Chemical Society: Washington, DC, 1995; pp 1−87	14/19	4/6	0.056
16	ϱ	density	[g/mL]	*Physical Properties of Chemical Compounds*; American Chemical Society: Washington, DC, 1995; pp 1−87	14/19	4/6	0.001
			[g/cm³]	*Geochim. Cosmochim. Acta* **1998**, *62*, 985−108			
					16/16		0.008
17	ρ_c	critical density	[g/mL]	*Physical Properties of Chemical Compounds*; American Chemical Society: Washington, DC, 1995; pp 1−87	12/19	3/6	0.020
18	V_c	critical volume	[ml/g]	*Physical Properties of Chemical Compound*; American Chemical Society: Washington, DC, 1995; pp 1−87	9/19	2/6	0.244
19	ΔH_f	enthalpy of fusion	[kJ/mol]	www.nist.gov/chemistry NIST Chemistry	9/18	-	5.319
				CRC of Chemistry and Physic, 8th ed.; 1997−1998; pp 6−125 Webbook			
20	p_c	critical pressure	[bar]	*Comput. Chem.* **2002**, *26*, 159−169 *Geochim. Cosmochim. Acta* **1998**, *62*, 985−108	16/16	6/6	1.299
21	S°_{liquid}	entropy of liquid	[J/molK]	www.nist.gov/chemistry NIST Chemistry Webbook	16/16	4/6	9.262
22	$C_{p,liquid}$	constant pressure heat capacity of liquid at 298.15 K	[J/molK]	www.nist.gov/chemistry NIST Chemistry Webbook	16/16	6/6	2.875
23	$\Delta_f H^\circ_{liquid}$	enthalpy of formation of liquid	[kJ/mol]	www.nist.gov/chemistry NIST Chemistry Webbook	16/16	6/6	1.275
				CRC Handbook of Chemistry and Physics, 8th ed.; 1997−1998; pp 5−43			
24	ΔS_f	entropy of fusion	[J/molK]	www.nist.gov/chemistry NIST Chemistry Webbook	9/15		12.051
25	T_{fr}	normal freezing temperature	[K]	http:/159.226.63.177/scripts/opes/properties Engineering Chemistry Database Handbook	10/11		41.733
26	IP	ionization potential	[eV]	*Spectrochim. Acta* **1959**, *14*, 45−55	10/10		0.066
27	$ln\gamma^\infty$	infinite dilution activity coefficients in water at 298.15 K		*Fluid Phase Equilibra* **2003**, *205*, 303−316	10/10		0.363
28	K_p	partition coefficients in hexane-acetonitrile		*J. Chromatogr. A* **2001**, *923*, 127−136	9/9		0.054

[a] Retention indices on squalane column at 96 °C. [b] Retention indices on squalane column at 71 °C. [c] Retention indices on CIT-A4 column at 70 °C. [d] Retention times and capacity factor on alumina column with 0.5% concentration of water in moisture control system. [e] Retention times and capacity factor on alumina column with 1% concentration of water in moisture control system.

Table 3. Table of Predictions for Chlorobenzenes and Methylbenzenes

compound		property		references	X′	σ	range
$1,2,3\text{-}Cl_3\phi$	p	solute polarity parameter		*J. Chem. Inf. Comput. Sci.* **2003**, *43*, 1240−1247	5.66	0.101	3.66
$1,3,5\text{-}Cl_3\phi$	IP	ionization potential	[eV]	*J. Phys. Chem. A* **2003**, *34*, 6580−6586	9.06	0.087	0.27
$1,3,5\text{-}Cl_3\phi$	$\ln\gamma^\infty$	infinite dilution activity coefficients in water at 298.15 K		*Fluid Phase Equilibra* **2003**, *205*, 303−316	13.07	2.031	14.05
				Fluid Phase Equilibra **1997**, *131*, 145−179			
$1,2,3,4\text{-}Cl_4\phi$	ϱ	density	[g/cm³]	*CRC Handbook of Chemistry and Physics*, 8th ed.; 1997−1998; pp 5−43	1.645	0.102	1.168
$1,3,5\text{-}Me_3\phi$	ΔH_f	enthalpy of fusion	[kJ/mol]	www.nist.gov/chemistry NIST Chemistry Webbook	12.249	5.319	10.714
				CRC Handbook of Chemistry and Physics, 8th ed.; 1997−1998; pp 6−125			
$1,2,3,4,5\text{-}Me_5\phi$	p_c	critical pressure	[bar]	*Comput. Chem.* **2002**, *26*, 159−169	25.77	1.299	26.6
				Geochim. Cosmochim. Acta **1998**, *62*, 985−108			
$1,2,3,4,5\text{-}Me_5\phi$	$\Delta_f H^\circ_{\text{liquid}}$	enthalpy of formation of liquid	[kJ/mol]	www.nist.gov/chemistry NIST Chemistry Webbook	−118.6	1.275	190.95
				CRC Handbook of Chemistry and Physics, 8th ed.; 1997−1998; pp 5−43			
$1,2,3,4,5\text{-}Me_5\phi$	$C_{p,\text{liquid}}$	constant pressure heat capacity of liquid at 298.15 K	[J/molK]	www.nist.gov/chemistry NIST Chemistry Webbook	240.25	2.875	109.95

increase from left to right. Thence the present poset of substituted benzenes might be viewed as a (simple) "periodic table". Overall it seems that the general ideas underlying our approach are widespread, and perhaps many applications of the general theory of posets may be made, maybe with some of the techniques specifically adapted to the evidently ubiquitous case of progressive reaction posets.

PROGNOSIS

Here in the development of general techniques for progressive reaction posets attention is directed to isotonic correspondences for property values. Notably misorderings of associated property values are tolerated, quantitative parameter-free predictions are entertained, and consequent standard deviations are obtained. Simple quality-of-fit indices (isotonicity score and standard deviation) for the organizational ability of the poset are described. Other schemes (i.e., "models") for the prediction of properties might be imagined and perhaps even useful. More generally parameter-dependent fittings as combinations of isotonic functions might be sought. Further it has not escaped our attention that the substitutional progressive reaction networks are very special posets: they are "graded" in the sense that every isotonic path from any one fixed member to a successive fixed member are of the same length, and in fact these posets are even more special. And for "periodic table" posets there are often two types of reactions (such that they might perhaps be viewed as "orthogonal") so that there are two particular spanning posets. Thence with such additional structure additional theory concerning associated isotonic functions may be relevant. All this presumably should be pursued, though we do not do so here. Even with the simple approach here, oft-times tolerable standard deviations are obtained, and some predictions beyond the reported experimentally reported values are made.

Overall some success is evidenced in the current initial investigation which indicates a potentially wide-range of possible chemical applications. Further posetic techniques should perhaps be developed.

REFERENCES AND NOTES

(1) Klein, D. J.; Bytautas, L. Directed Reaction Graphs as Posets. *MATCH Commun. Math., Comput. Chem.* **2000**, *42*, 261−289.

(2) Körner, W. *Gazz. Chim. Ital.* **1874**, *4*, 305.

(3) Körner, W. as summarized by Armstrong, H. E. *J. Chem. Soc.* **1876**, *29*, 204−241.

(4) Dolfing, J.; Harrison, B. K. Redox and reduction potentials as parameters to predict the degradation pathway of chlorinated benzenes in anaerobic environments. *REMS Microbiol. Ecol.* **1993**, *13*, 23−30.

(5) Shtarev, A. B.; Pinkhassik, E.; Levin, M. D.; Stibor, I.; Michl, J. Partially Bridge-Fluorinated Dimethyl Bicyclo[1.1.1]pentane-1,3-dicarboxylates: Preparation and NMR Spectra. *J. Am. Chem. Soc.* **2001**, *123*, 3484−3492.

(6) Hendrickson, J. B. A Logical Characterization of Organic Chemistry. *J. Chem. Educ.* **1978**, *55*, 216−220.

(7) Hass, E. C.; Plath, P. J. The principle of valency conservation. The skeleton influence on pericyclic reactions. *I. Discuss. Appl. Math.* **1998**, *19*, 215−237.

(8) Klein, D. J. Similarity & Dissimilarity in Posets. *J. Math. Chem.* **1995**, *18*, 321−348.

(9) Klein, D. J.; Babić, D. Partial Orderings in Chemistry. *J. Chem. Inf. Comput. Sci.* **1997**, *37*, 656−671.

(10) Brüggemann, R.; Mhnzer, B.; Halfon, E. An algebraic/Graphical Tool to compare Ecosystems with respect to their Pollution − the German River "Elbe" as an Example - Hasse Diagrams. I. *Chemosphere* **1994**, *28*, 863−872.

(11) Carlsen, L.; Sørensen, P. B.; Thomsen, M. Partial order ranking-based QSAR's: estimation of solubilities and octanol−water partitioning. *Chemosphere* **2001**, *43*, 295−302.

(12) Whole issue of *MATCH Commun. Math., Comput. Chem.* **2000**, *42*.

(13) Mendeleev, D. I. *Zh. Russ. Khim. Obshch.* **1869**, *1*, 60 [translated, to German] *Berichte* **1869**, *2*, 553.

(14) Wilkins, C. L.; Randić, M. Graph Theoretical Ordering of Structures as a Basis for Systematic Searches for Regularities in Molecular Data. *J. Phys. Chem.* **1979**, *83*, 1525−1540.

(15) Randić, M.; Wilkins, C. L. On a graph-theoretical basis for the ordering of structures. *Chem. Phys. Lett.* **1979**, *63*, 332−336.

(16) Randić, M. Chemical Structure − What is 'She'. *J. Chem. Educ.* **1992**, *69*, 713−718.

(17) Dias, J. R. A Periodic Table for Polycyclic Aromatic Hydrocarbons. *Acc. Chem. Res.* **1985**, *18*, 241−248.

(18) Dias, J. R. A formula periodic table for benzenoid hydrocarbons and the *aufbau* and excised internal structure concepts in benzenoid enumerations. *J. Math. Chem.* **1990**, *4*, 17−30.

PARAMETER-FREE STRUCTURE—PROPERTY CORRELATION

J. Chem. Inf. Comput. Sci., Vol. 44, No. 2, 2004 **617**

(19) Bytautas, L.; Klein, D. J. Formula Periodic Table for the Isomer Classes of Acyclic Hydrocarbons − Enumerative and Asymptotic Characteristics. *Croat. Chem. Acta* **2000**, *73*, 331−357.

(20) Bytautas, L.; Klein, D. J.; Schmalz, T. G. All acyclic hydrocarbons: formula periodic table and property overlap plots via chemical combinatorics. *New J. Chem.* **2000**, *24*, 329−336.

(21) Klein, D. J. Periodic Tables and the Formula Periodic Table for All Acyclic Hydrocarbons. Proceedings of Wiener Conference on Periodic Tables.