JOURNAL OF PHYSICAL ORGANIC CHEMISTRY, VOL. 11, 261–272 (1998)

Solvent effects on C=O stretching frequencies of some 1-substituted 2-pyrrolidinones

J. B. F. N. Engberts,[1] G. R. Famini,[2] A. Perjéssy[3] and L. Y. Wilson[4]*

[1]Department of Organic and Molecular Inorganic Chemistry, University of Groningen, Groningen, The Netherlands
[2]US Army Edgewood Research, Engineering and Development Center, Aberdeen Proving Grounds, Maryland 21010, USA
[3]Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University, Bratislava, Slovak Republic
[4]Department of Chemistry, La Sierra University, Riverside, California 92515, USA

Received 3 June 1997; revised 25 August 1997; accepted 15 September 1997

ABSTRACT: In an effort to model solute–solvent interactions, the C=O stretching frequencies of five 1-substituted 2-pyrrolidinones and four other carbonyl-containing compounds were measured for 30 common solvents. These were then correlated with four empirical parameter sets and one theoretical (computational) parameter set. While an empirical parameter set gave the best correlation equations, the theoretical parameter equations are physically and statistically significant. Solvent volume, polarizability and hydrogen bond donor acidity (capacity) terms are significant in the correlation equations. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: 1-substituted 2-pyrrolidinones; C=O stretching frequencies; solvent effects

INTRODUCTION

Substituted 2-pyrrolidinones have seen wide use in medicinal chemistry, both as model compounds to study interactions of larger compounds and as pharmaceuticals. Cyclohexyl-2-pyrrolidinones have been used to study hydrophobic interactions[1] and as model compounds to mimic protein interactions.[2] Also, because their structure is similar to that of naturally occurring skin humidifiers, several derivatives have been used as auxiliary agents. In addition, oxotremorine, a derivative of 2-pyrrolidinone, has been successful in treating postencephalic Parkinsonism.[3]

Recent empirical studies have shown the effect of solvents on the C=O stretching frequency of 2-pyrrolidinones and how substituents in the solute affect the solute–solvent interaction.[4] These results provided a stimulus for infrared spectral studies of 1-substituted 2-pyrrolidinones as cyclopeptide model compounds.[5] Solvent effects play an important role in a wide variety of biological, chemical and physical properties. Many relationships in physical organic and medicinal chemistry can be interpreted in terms of solute–solvent interactions. Examples include partition coefficients, adsorption, solvent-influenced spectral shifts, reaction kinetics and toxicity. Several approaches have been used in attempting to characterize, correlate and predict how a solvent influences a solute.

**Correspondence to:* L. Y. Wilson, Department of Chemistry, La Sierra University, 4700 Pierce Street, Riverside, California 92515, USA.
E-mail: lwilson@lasierra.edu

One empirical approach uses correlative methods in what are called quantitative structure–activity (property) relationships (QSAR, QSPR). An example is the linear solvation energy relationship (LSER) concept developed by Kamlet *et al.*,[6] which, in turn, is based on linear free energy relationships (LFER). In a significant achievement for physical organic chemistry, Hammett[7] helped quantify LFER. A relatively recent (1988) and very readable presentation of correlation methods was given by Exner.[8] The LSER approach finds an equation, $P = \Sigma\, c_i\, p_i$, relating some empirical property, P, to a set of parameters, $\{p_i\}$, which have molecular structural interpretations; statistics (often multilinear regression) are used to find the coefficients, $\{c_i\}$. In general terms, the LSER model can be written as

$$\text{Property=bulk/cavity + dipolarity/polarizability} + \text{hydrogen bonding} \quad (1)$$

Kamlet and co-workers developed an empirical molecular parameter set known as solvatochromic parameters; this set is described below. Recently, these have been modified to give a solvation parameter set for solutes.[9]

In addition to the previously mentioned empirical approach, several theoretical treatments of solute–solvent interactions have been employed. Among the advantages provided by theoretical methods are conservation of laboratory space and chemicals, fewer safety and environmental problems and simplicity in interpretation. Three basic theoretical methods have been used to study solute–solvent interactions.

 CCC 0894–3230/98/040261–12 $17.50

Table 1. TLSER Descriptors[a]

Symbol	Name	Definition	Units	Range
V_{mc}	Molecular volume	Molecular volume	100 Å^3	0.3–3
π_I	Polarizability index	Polarizability/V_{mc}	None	0.07–0.16
ε_B	'Covalent' HB basicity	$0.30 - 0.01(E_{lw} - E_h)$	heV	0.1–0.17
q^-	'Electrostatic' HB basicity	Maximum |(−) charge| on an atom	acu	0–0.8
ε_A	'covalent' HB acidity	$0.30 - 0.01\ (E_l - E_{hw})$	heV	0.14–0.2
q^+	'Electrostatic' HB acidity	Maximum (+) charge on an H atom	acu	0–0.8

[a] heV = hectoelectronvolt; acu = atomic charge unit ; HB = hydrogen bond; E_1 = LUMO energy; E_h = HOMO energy; E_{hw} and E_{hw} refer to E_l = 5.4428 eV and E_h = −12.1911 eV for water, respectively; | | = Absolute magnitude.

The first and most rigorous method involves an explicit model such as free energy perturbation,[10] where the solute and solvent molecules are treated individually. This is very time consuming and, although employed in a few quantum mechanical studies, it has been used most frequently in molecular dynamics. This gives the most information including structure deformities as well as solute–solvent and solvent–solvent molecular interactions. The second method involves an implicit model in which the solute is treated explicitly but the solvent is represented by a continuum model such as in self-consistent reaction field theory[11,12]. This does not give information about specific solute–solute and solvent–solvent interactions, but does provide solvation free energies. It is rapid enough to permit the use of *ab initio* and semi-empirical quantum mechanical methods.

The third and most empirical method uses the LSER solvation concept with a set of molecular theoretical parameters. A relatively large set of property data (empirical) is required to generate meaningful correlation equations. This method offers the advantages of not requiring detailed solvent system information or a mathematical (potential energy) model. A major drawback is that the information derived is specific to the data set and only gives inferences to solvent behavior. Still, with complex systems such as receptor sites (which can be modeled as a solvent system), where it is unlikely that first two theoretical methods can be readily used, the QSAR (LFER, LSER) methods combined with theoretical descriptors can give useful insights into important binding features.[12] Politzer and Murray[13] have used LFER type regressions to correlate bulk properties with theoretically derived descriptors.

Based on the previous discussion, this paper uses correlation analysis with five parameter sets, one theoretical and four empirical, to examine the effect of 30 common solvents (Table 4) on the C=O stretching frequency for nine solutes. These solutes include five pyrrolidinones; four carbonyl-containing compounds (Table 3) are included for comparison purposes. The theoretical parameter set, denoted the theoretical linear solvation energy relationship (TLSER) parameter set, is complementary to and patterned after the LSER (solvatochromic) set. Its parameters are easily calculated, easy to interpret and have given good correlations for a wide number of properties.[14] These parameters, {V_{mc}, π_I, ε_B, q_-, ε_A, q_+}, are summarized in Table 1. A single solute–multiple solvent model for the (infrared) carbonyl stretching frequency, $\nu_{(C=O)}$, is shown in Eqn (2). The parameters refer to the solvent; $\nu_{(C=O)0}$, is the intercept and can be interpreted as the infrared stretching frequency of the carbonyl moiety.

$$\nu_{(C=O)} = aV_{mc} + b\ \pi_I + c\varepsilon_B + d\mathrm{q}_- + e\varepsilon_A fq_+ + \nu_{(C=O)0} \quad (2)$$

The coefficients {*a,b,c,d,e,f*} can be interpreted in terms of the properties of the solute. The coefficient *a* can be related to the energy required to form a solute molecule sized cavity in the solvent. In that case, it is proportional to the solute molecular volume and the solvent molecular volume can be replaced by the Hildebrand solubility parameter, δ_H^2. The coefficient *b* can be related to the solute polarizability. Coefficients *c* and *d* can be related to the solute acidity; similarly, *e* and *f* can he related to the solute basicity. The definitions of the TLSER parameters are based on chemical intuition. For the covalent basicity and acidity contributions, one might expect the highest occupied molecular orbital and the lowest unoccupied molecular orbital respectively, to be involved. The linear transformations were made to scale the size and give numerical values that increase with basicity and/or acidity. The electrostatic contributions for basicity and acidity could be related to the most negative atomic charge and most positive hydrogen charge, respectively.

The computational nature of the TLSER parameters permits the use of a multiple solute–single solvent equation similar to Eqn. (1). However, this type of study is not reported here since there were only nine solutes. An adequate sample size, *N*, should be at least 18 (three times the number of parameters) for the TLSER set. Furthermore, solute parameters were not readily available for all of the empirical parameter sets.

On a philosophical note, the TLSER parameters should model solutes better than solvents. The molecular calculations pertain to the gaseous state (isolated molecules). An analogy exists between the molecule

Table 2. Solvent parameters used in correlation equations

Parameter	Name	
AN	Acceptor number	(Gutmann)[19]
DN	Donor number (donicity)	(Gutmann)
E_{Tn}	Solvatochromic polarity (normalized)	(Reichardt)[18]
Y	Polarity function	(Koppel–Palm)[16]
P	Polarizability	(Koppel–palm)
MR	Molar refraction	(Koppel–palm)
δ_H^2	Hildebrand's solubility parameter[15]	
B	Basicity	(Swain)[17]
E	Acidity	(Swain)
π^*	Dipolarity–polarizability	(Kamlet–Taft–Abraham, LSER)[15]
β	HBAB[a]	(Kamlet–Taft–Abraham, LSER)
α	HBDA[b]	(Kamlet–Taft–Abraham, LSER)
V_{mc}	Molecular volume	(TLSER)[c]
π_I	Polarizability index	(TLSER)
ε_B	Covalent HBAB	(TLSER)
q^-	Electrostatic HBAB	(TLSER)
ε_A	Covalent HBDA	(TLSER)
q^+	Electrostatic HBDA	(TLSER)

[a] Hydrogen bond acceptor basicity.
[b] Hydrogen bond donor acidity.
[c] Table 1.

surrounded by a vacuum (isolated) and the molecule surrounded by solvent molecules. The latter case can be modeled by using the electrical permittivity for the solvent (continuum model) as compared with the vacuum permittivity used in the isolated case. In fact, the LSER parameters, models for developing the TLSER descriptors, may differ considerably for solutes and solvents.

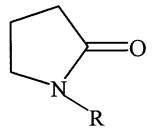
The idea behind the TLSER parameters is to use chemically meaningful, computational molecular parameters in place of empirical parameters. Consequently, adopting a pragmatic viewpoint, the TLSER solvent descriptors are calculated in the same way as for solutes. Solvent molecules are surrounded by other solvent molecules and, hence, are not 'isolated' in the sense that solute molecules are. However, there might be some relationship (albeit a crude approximation) between the properties of solvent molecules surrounded by other solvent molecules and the properties of isolated (vacuum) solvent molecules. A possible improvement would be to use the solvent permittivity (an empirical quantity) in the calculations (continuum) for solvent molecules.

In this context, it is important to note that the process of correlating the empirical quantities (which are solute–solvent interaction dependent) with theoretical parameters tends to incorporate the solute–solvent interactions in the term coefficients. In a sense it provides some 'corrections'. The adequacy of the model will show up in the quality (statistical and physical significance) of the correlation equations. It is important to recognize the theoretical limitations while noting that the final justification for any (albeit naive) model is found in whether or not the model works. To quote Exner,[8] 'any kind of regularity found in nature raises some kind of satisfaction'.

The empirical parameters used in the correlations are described in Table 2 and Table 5 lists their values along with their references. These were grouped into four sets. The Kamlet–Taft–Abraham[15] (solvatochromic) set consists of the Hildebrand solubility parameter, δ_H^2, the dipolarity–polarizability, π^*, the hydrogen bonding

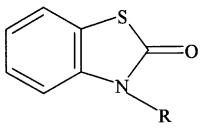
Table 3. List of solutes

Compound	Name
PY	2-Pyrrolidinone
MP	1-Methyl-2-pyrrolidinone
IPP	1-Isopropyl-2-pyrrolidinone
CHP	1-Cyclohexyl-2-pyrrolidinone
HEP	1-(2-Hydroxyethyl)-2-pyrrolidinone
OBT	2-Oxobenzothiazole
OOBT	3-Octyl-2-oxobenzothiazole
DMA	Dimethylacetamide
CH	Cyclohexanone



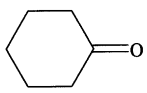
2-pyrrolidinones

R = H (PY)
R = CH_3 (MP)
R = $CH(CH_3)_2$ (IPP)
R = cyclo-C_6H_{13} (CHP)
R = CH_2CH_2OH (HEP)

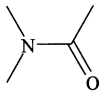


2-oxobenzothiazoles

R = H (OBT)
R = C_8H_{17} (OOBT)



cyclohexanone



N,N-dimethylacetamide

Table 4. C=O stretching frequencies (cm^{-1}) of solutes in solvents

No.	Solvent	Solute								
		PY	MP	IPP	CHP	HEP	OBT	OOBT	DMA	CH
1	Cyclohexane	1731.2 1711.2[a]	1712.4	1704.8	1703.2	1706.0 1688.0[c]	1724.8 1680.0[a]	1699.2	1673.2	1724.0
2	Hexane	1734.0 1712.4[a]	1712.2	1704.0	1704.0	1705.6 1691.2[c]	1728.0 1681.2[a]	1699.6	1672.7	1723.6
3	Heptane	1732.0 1712.0[a]	1712.8	1705.2	1704.1	—[e]	1727.6 1680.0[a]	1700.0	1673.6	1724.4
4	Triethylamine	1712.0	1707.6	1700.8	1699.2	1700.8 (1684.0)[c]	1712.0 (1680.0)[a]	1698.0	1669.6	1721.6
5	Tetrachloromethane	1699.6	1695.8	1691.2	1683.4	1690.4	1713.6 1675.2[a]	1690.0	1659.6	1715.0
6	1-Butoxybutane	1709.2	1707.2	1700.0	1698.8	1701.2 1685.0[c]	1716.0 1679.2[a]	1696.8	1668.4	1720.8
7	Toluene	1712.5 1700.4[a]	1699.2	1691.6	1688.4	1692.1 1676.0[c]	1714.4 1676.0[a]	1689.6	1661.2	1715.6
8	Benzene	1693.8	1692.8	1688.4	1687.6	1688.0	1713.2 1675.2[a]	1686.0	1658.6	1712.8
9	Ethoxyethane	1708.0	1703.6	1695.2	1695.6	1694.6	1715.6 1679.0[a]	1691.8	1662.8	1716.0
10	Chlorobenzene	1709.8 1699.2[a]	1692.4	1686.0	1681.6	1690.0 1672.0[c]	1711.2 1674.4[a]	1684.4	1654.0	1713.6
11	Tetrahydrofuran	1712.8	1699.2	1692.0	1688.4	1692.8 1677.0[c]	1711.2 (1680.0)[a]	1689.2	1660.8	1715.2
12	Bis(2-Methoxyethyl) ether	1711.6	1695.6	1690.4	1686.4	1692.8 (1677.0)[c]	1710.8 (1680.0)[a]	1688.0	1659.2	1715.2
13	*d*-Trichloromethane	1689.4	1674.5	1666.0	1664.0	1669.0	1708.8 1685.0[a]	1665.6	1635.5	1703.6
14	Dichloromethane	1690.0	1680.4	1671.0	1670.7	1670.4	1709.2 1673.6[a]	1674.0	1640.8	1704.2
15	Pyridine	1699.8	1687.2	1679.2	1677.0	1684.0	1703.2 1683.0[a]	1677.2	1646.2	1710.0
16	Nitrobenzene	1697.6	1683.4	1678.4	1677.7	1679.4	1708.0 (1676.0)[a]	1679.8	1643.2	1706.8
17	1,2-Dichloroethane	1699.2	1686.0	1677.2	1675.2	1677.1 1667.6[c]	1709.2 1674.4[a]	1680.0	1644.4	1707.6
18	Cyanobenzene	1695.2	1682.0	1676.4	1676.5	1680.8	1706.4 (1687.2)[a]	1679.2	1645.2	1705.6
19	Propanone	1693.8	1680.2	1676.8	1677.2	—[d]	—[d]	—[d]	—[d]	—[d]
20	1,4-Dioxane	1708.0	1691.0	1685.0	1682.0	1688.4	1708.4 (1678.0)[a]	1685.2	1653.2	1711.6
21	2-Methylpropan-2-ol	1676.0[b] (1688.0)	(1663.5)[b] 1682.0	(1654.3)[b] 1673.6	(1652.5)[b] 1670.8	(1657.5)[b] 1674.8	1702.0[b] (1724.0)	1667.2	1640.4	1706.8
22	Dimethyl sulfoxide	1687.0	1678.0	1672.4	1668.6	1674.8	1702.4 1688.8[a]	1673.2	1639.2	1702.6
23	Cyanomethane	1693.2	1684.6	1675.8	1674.6	1679.0	1706.0 1692.0[a]	1677.4	1635.8	1706.6
24	Nitromethane	1693.0	1680.2	1670.6	1673.4	1676.6	1702.4 (1688.0)[a]	1675.8	1639.0	1703.2
25	Propan-2-ol	1673.6[b] (1687.6)	(1660.0)[b] 1678.0	(1648.0)[b] 1671.2	(1647.0)[b] 1668.0	(1656.0)[b] 1673.6	1679.6[b] (1707.0)	1664.8	1638.4	1705.2
26	Butan-1-ol	1672.8[b] (1687.0)	(1660.0)[b] 1676.8	(1649.2)[b] 1668.0	(1644.5)[b] 1667.2	(1652.0)[b] 1673.2	1713.0 1678.4[b]	1662.8	1637.2	1704.8
27	Ethanoic acid	1659.2[b]	1653.9[b]	1638.5[b]	1636.1[b]	1645.0[b]	1705.3 1676.5[a]	1641.5	1621.0	1695.1
28	Ethanol	1673.6[b] (1687.0)	1659.2[b] (1675.0)	1647.3[b] 1666.0	1646.0[b] 1664.4	(1659.0)[b] 1672.5	1676.4[b] (1708.0)	1662.4	1633.0	1703.6
29	Methanol	1672.0[b] (1687.5)	(1657.0)[b] 1673.6	1646.0[b] 1665.2	1640.8[b] 1662.4	(1654.0)[b] 1671.2	1676.8[b] (1711.6)	1660.0	1635.0	1703.2
30	Deuterium oxide	1645.0[b]	1641.8[b]	1629.2[b]	1621.8[b]	1641.0[b]	—[e]	1644.2	1606.0	1691.0

[a] Cyclic dimers:' H-bonding between two solute molecules.
[b] H-bonding between solute C=O group and solvent OH group; data in parentheses corresponds to the less intense bands.
[c] Intramolecular hydrogen bonding in solute.
[d] Not measured because of strong solvent absorption.
[e] Insoluble.

Table 5. Non-TLSER solvent correlation parameters

No.	Solvent	*AN*	*DN*	E_{Tn}	*Y*	*P*	*MR*[d]	δ_H^2	*B*	*E*	π^*	β	α
1	Cyclohexane	—	0.0	0.006	0.254	0.256	27.2	0.67	0	0.000	0.00	0.00	0.00
2	Hexane[a]	0.0	0.0	0.009	0.235	0.236	34.5	0.55	0	0.06	−0.08	0.00	0.00
3	Heptane	0.0	0.0	0.012	0.235	0.236	34.5	0.55	0	0.00	−0.08	0.00	0.00
4	Triethylamine	1.4	61.0	0.043	0.321	0.243	33.8	0.78	650	0.00	0.14	0.71	0.00
5	Tetrachloromethane	8.6	0.0	0.052	0.292	0.274	26.4	0.74	00	0.00	0.28	0.00	0.00
6	Butoxybutane	—	19.0	0.071	0.407	0.242	41.0	0.97	285	0.000	0.24	0.46	0.00
7	Toluene	—	0.1	0.099	0.315	0.293	31.1	0.79	58	1.30	0.54	0.11	0.00
8	Benzene	8.2	0.1	0.111	0.300	0.295	26.3	0.85	48	2.10	0.59	0.10	0.00
9	Ethoxyethane	3.9	19.2	0.117	0.526	0.217	22.4	0.55	280	0.00	0.27	0.47	0.00
10	Chlorobenzene	—	3.3	0.188	0.606	0.306	31.0	0.90	38	0.00	0.71	0.07	0.00
11	Tetrahydrofuran	8.0	20.0	0.207	0.681	0.247	20.0	0.83	287	0.00	0.58	0.55	0.00
12	Bis(2-ethoxyethyl) ether	10.2	20.0	0.231	0.667	0.231	24.0	1.82	238	0.00	0.53	0.41	0.00
13	*d*-Trichloromethane[b]	23.1	4.0	0.256	0.559	0.252	21.3	0.87	14	3.28	0.58	0.00	0.44
14	Dichloromethane	20.4	1.0	0.269	0.729	0.256	16.4	0.98	23	2.70	0.82	0.00	0.185
15	Pyridine	14.2	33.1	0.302	0.790	0.299	24.2	1.15	472	0.00	0.87	0.64	0.00
16	Nitrobenzene	14.8	4.4	0.324	0.918	0.322	32.8	1.00	67	0.00	1.01	0.39	0.00
17	1,2-Dichloroethane	16.7	0.0	0.327	0.757	0.266	21.0	0.96	40	3.00	0.81	0.00	0.00
18	Cyanobenzene	15.5	11.9	0.333	0.890	0.308	31.4	0.71	155	0.00	0.90	0.41	0.00
19	Propanone	12.5	17.0	0.355	0.868	0.220	16.2	0.98	224	2.10	0.71	0.48	0.80
20	1,4-Dioxane	10.8	14.8	0.383	0.287	0.254	21.6	1.00	237	4.20	0.55	0.37	0.00
21	2-Methylpropan-2-ol	27.1	38.0	0.389	0.767	0.234	22.0	1.10	247	5.20	0.41	1.01	0.68
22	Dimethyl sulfoxide	19.3	29.8	0.444	0.941	0.283	20.1	1.44	362	3.20	1.00	0.76	0.00
23	Cyanomethane	19.3	14.1	0.460	0.924	0.211	11.1	1.42	160	5.20	0.75	0.31	0.19
24	Nitromethane	20.5	2.7	0.481	0.926	0.233	12.5	1.61	65	5.10	0.85	0.134	0.22
25	Propan-2-ol	33.5	36.0	0.546	0.852	0.230	17.7	1.32	236	8.70	0.48	0.95	0.76
26	Butan-1-ol	36.8	29.0	0.586	0.842	0.242	22.1	1.30	231	10.30	0.47	0.88	0.79
27	Ethanoic acid	52.9	20.0	0.648	0.631	0.227	13.0	1.02	139	14.60	0.64	0.495	1.12
28	Ethanol	37.1	32.0	0.654	0.886	0.221	12.9	1.69	235	11.60	0.54	0.77	0.83
29	Methanol	41.3	30.0	0.762	0.913	0.203	8.2	2.10	218	14.90	0.60	0.62	0.93
30	Deuterium oxide[c]	54.8	33.0	0.991	0.963	0.206	3.7	5.48	156	21.80	1.09	0.18	1.17

[a] Except for AN and DN, parameters are for heptane.
[b] Parameters for trichloromethane.
[c] Parameters for water.
[d] Scaled by a factor of 0.01.

acceptor basicity, β, and the hydrogen bond donor acidity, α. Based on the Kamlet–Taft–Abraham set, another empirical set was chosen to consist of the polarity function, *Y*, the polarizability function, *P*, and molar refraction, *MR*, along with the Hildebrand solubility parameter employed by Koppel and Palm[16] and the acidity, *E*, and basicity, *B*, parameters of Swain (Marcus).[17] The normalized solvatochromic polarity, E_{Tn}, of Reichardt[18] was used by itself while the acceptor number, *AN*, and donor number, *DN*, of Gutmann[19] were used as a fourth set. Strictly, *DN* should apply to the compound as a solute; it is measured under dilute conditions. However, it has been applied (again, in a pragmatic manner) under solvent conditions. Table 6 contains the TLSER values (calculated in this study) for the solvents and solutes.

The primary purpose of this study was to examine the use of these parameters sets in modeling the solvent mediated C=O stretching frequency shift for the five 1-substituted 2-pyrrolidinones in Table 3. Four other compounds were included for comparison purposes: two oxobenzothiazoles, dimethylacetamide and cyclohexanone. A secondary goal was to compare the TLSER correlations with those from the better established empirical parameter sets.

PROCEDURE

Experiment

Specifically for this study, frequencies were determined in the 1750–1600 cm^{-1} spectral region (infrared) at room temperature using Perkin-Elmer 841 and Zeiss Specord M 80 spectrophotometers. Concentrations were in the range 10^{-1}–10^{-4} mol dm^{-3} and NaCl cells of 0.1, 0.5, 1.0 and 2.6 mm were used. Alcoholic acetic acid and aqueous solutions were placed in 0.02 mm pathlength CaF_2 cells. The maxima corresponding to $\nu_{(C=O)}$ were measured within ± 0.5 cm^{-1} and are recorded in Table 4, where the solvent compounds are arranged in order of increasing value of Reichardt's E_T parameter. For all correlations, the following set of wavenumbers of the C=O stretching vibration were selected: for alcohols (solvents 21, 25, 26, 28, 29) the lower wavenumber bands (indicated in Table 4 by index b) were chosen; otherwise

Table 6. TLSER solvent and solute parameters

No.	Compound	V_{mc}	π_I	ε_B	q^-	ε_A	q^+	δ_H^2
1	Cyclohexane	1.0643	0.1055	0.1278	0.0101	0.1461	0.0051	0.67
2	Hexane	1.1988	0.0993	0.1248	0.0218	0.1450	0.0045	0.55
3	Heptane	1.3652	0.1010	0.1254	0.0217	0.1455	0.0045	0.55
4	Tetrachloromethane	0.9058	0.1172	0.1128	0.0703	0.1911	0.0000	0.74
5	Triethylamine	1.3301	0.1009	0.1507	0.4324	0.1520	0.0055	0.78
6	Butoxybutane	1.6382	0.1014	0.1361	0.3452	0.1478	0.0177	0.97
7	Toluene	1.0192	0.1207	0.1524	0.1007	0.1756	0.0598	0.79
8	Benzene	0.8457	0.1205	0.1513	0.0593	0.1744	0.0593	0.85
9	Ethoxyethane	0.9046	0.0995	0.1361	0.3423	0.1455	0.0071	0.55
10	Chlorobenzene	0.9951	0.1241	0.1490	0.1118	0.1794	0.0777	0.90
11	Tetrahydrofuran	0.7895	0.1020	0.1374	0.3277	0.1471	0.0209	0.83
12	Bis(2-Methoxyethyl) ether	1.4066	0.1034	0.1355	0.3579	0.1502	0.1280	1.82
13	*d*-Trichloromethane	0.7540	0.1114	0.1160	0.1122	0.1849	0.0876	0.87
14	Dichloromethane	0.6046	0.1036	0.1203	0.1602	0.1773	0.0555	0.98
15	Pyridine	0.7936	0.1200	0.1483	0.2299	0.1780	0.0835	1.15
16	Nitrobenzene	1.0079	0.1316	0.1421	0.3288	0.1860	0.0851	1.00
17	1,2-Dichlorobenzene	0.7858	0.1046	0.1210	0.1967	0.1789	0.0489	0.96
18	Cyanobenzene	0.9969	0.1276	0.1471	0.0867	0.1833	0.0696	0.71
19	Propanone	0.6401	0.0980	0.1376	0.2847	0.1715	0.0234	0.98
20	1,4-Dioxane	0.8547	0.1050	0.1387	0.3230	0.1478	0.0327	1.00
21	2-Methylpropan-2-ol	0.8943	0.0975	0.1338	0.3180	0.1442	0.1764	1.10
22	Dimethyl sulfoxide	0.7219	0.1045	0.1471	0.7204	0.1734	0.0500	1.44
23	Cyanomethane	0.4529	0.0937	0.1173	0.1146	0.1622	0.0209	1.42
24	Nitromethane	0.4740	0.1092	0.1298	0.3348	0.1818	0.0498	1.61
25	Propan-2-ol	0.7144	0.0962	0.1331	0.3200	0.1450	0.1781	1.32
26	Butan-1-ol	0.9082	0.0969	0.1322	0.3249	0.1449	0.1804	1.30
27	Ethanoic acid	0.5249	0.0956	0.1294	0.3651	0.1696	0.2161	1.02
28	Ethanol	0.5435	0.0924	0.1322	0.3234	0.1429	0.1799	1.69
29	Methanol	0.3647	0.0860	0.1310	0.3291	0.1402	0.1803	2.10
30	Deuterium oxide	0.1782	0.0630	0.1233	0.3256	0.1237	0.1628	5.48
	PY	0.8284	0.1092	0.1427	0.4451	0.1649	0.0398	n/a[a]
	MP	1.0081	0.1098	0.1455	0.4676	0.1653	0.0402	n/a
	IPP	1.3766	0.1074	0.1460	0.4542	0.1650	0.0399	n/a
	CHP	1.7930	0.1105	0.1464	0.4511	0.1652	0.0402	n/a
	HEP	1.2546	0.1085	0.1455	0.4624	0.1662	0.0411	n/a
	OBT	1.2030	0.1307	0.1552	0.3608	0.1815	0.2168	n/a
	OOBT	2.6333	0.1183	0.1560	0.3792	0.1809	0.0718	n/a
	DMA	0.9631	0.1027	0.1452	0.4670	0.1662	0.0281	n/a
	CH	1.0632	0.1065	0.1398	0.2831	0.1710	0.0335	n/a

[a] n/a, Not applicable.

the first wavenumber values were chosen. Any other combination of data appeared to be less significant in the correlation analysis.

The origins of the 1-substituted pyrrolidinones (PY, MP, IPP, CHP and HEP, Table 3) and related compounds (OBT, OOBT, DMA and CH, Table 3) have been described previously.[20] The solvents used were spectroscopically or analytically pure (purchased from Uvasol-Merck, Janssen Chimica or Aldrich). Some of them were dried and freshly distilled prior to use.

Computation

TLSER parameters were obtained as follows. *Z*-matrices (molecular models) were constructed with the aid of PCMODEL (Serena Software, Bloomington, IN, USA) and MMADS.[21] Molecular geometries were optimized with the MNDO algorithm in MOPAC.[22] The volume was calculated with an algorithm proposed by Hopfinger.[23]

Equation coefficients and statistical parameters were obtained by multilinear correlation analysis using MYSTAT (SYSTAT, Evanston, IL, USA). Only terms at the 0.95 significance level or higher were retained. The sample size, *N*, was chosen to be as large as possible with the restraint that *N* be at least three times the number of TLSER parameters (18 here). The quality of the linear equations is indicated by the standard error of the estimate (SD, the smaller the better), Fisher index of reliability (*F*, the larger the better) and correlation coefficient (*R*, variance = R^2, the closer to 1 the better). Outliers, compounds with Student(ized) residuals greater than 3.0, were retained. The VIF parameter, a measure of parameter orthogonality, is defined by $VIF = 1/(1\text{-}R^2)$, where *R* is the correlation coefficient for that particular

Table 7. Guttman parameter (*AN, DN*) correlation equations

$$\nu_{(C=O)} = \nu_{(C=O)0} + a\ AN + b\ DN$$

Parameter	PY	MP	IPP	CHP	HEP	OBT	OOBT	DMA	CH
N	26	26	26	26	24	24	25	25	25
SD	6.9	5.0	4.1	3.9	4.3	9.4	3.1	6.3	3.7
F	191	329	625	733	384	20.8	583	133	89.4
R	0.942	0.965	0.981	0.984	0.973	0.697	0.981	0.923	0.892
$\nu_{(C=O)0}$	1718.0	1705.2	1700.0	1699.0	1699.3	1718.2	1696.2	1665.2	1717.9
	761	1000	1300	1300	1100	528	1700	800	1400
a	−1.266	−1.201	−1.352	−1.409	−1.153	−0.649	−0.988	−0.961	−0.468
VIF	1.00	1.00	1.00	1.00	1.0	1.00	1.00	1.00	1.00
t-stat	13.8	18.1	25.0	27.1	19.6	4.56	24.1	11.5	9.46
b	n/s[a]	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
Outliers:[b] Table 4 No.	None	27	27	27	None	27	13	None	None

[a] n/s, Not significant at the 0.95 level.
[b] Retained.

parameter in terms of the others.[24] The closer the parameter *VIF* is to 1, the less cross correlation there is with the other parameters. Values in the range $1 < VIF < 10$ are considered acceptable; parameters with *VIF* values around 5 or less were retained in this study. When the *VIF* was too large, variables were eliminated to improve the cross correlation problem. In keeping with physical science practice, a correlation equation was considered to be acceptable if the product correlation coefficient, *R*, indicated that the equation accounted for more than 80% of the variance ($R^2 \geq 0.80$).

RESULTS

Table 4 lists the solvents along with the measured carbonyl stretching frequencies for the solutes. The correlation equations are given in Tables 7–14 while the TLSER solvent and solute parameters are given in Table 6. As mentioned in the Procedure section, these tables include statistical parameters (*N*, SD, *F*, *R*) for the equations as a whole and for the individual terms (*VIF*, *t*-stat). Tables 12–14 show the effect of eliminating TLSER variables with larger *VIF* parameters.

DISCUSSION

Examination of Tables 7–14 reveals some general features. There is considerable similarity among the five parameter sets. For example, each parameter set gives statistically significant equations ($R^2 \geq 0.80$) for eight of the nine solutes, OBT being the exception in each case. Furthermore, CH provided the lowest quality (other than OBT) correlation equations for four of the parameter sets; the LSER set is the exception. Another similarity is that not all parameters in multiple descriptor sets are statistically significant.

From a physical standpoint, the correlation equations suggest that the primary solute–solvent interactions involve capacities for solvent hydrogen bond donor

Table 8. Reichardt parameter (E_{Tn}) correlation equations

$$\nu_{(C=O)} = \nu_{(C=O)0} + a\ E_{Tn}$$

Parameter	PY	MP	IPP	CHP	HEP	OBT	OOBT	DMA	CH
N	30	30	30	30	28	28	29	29	29
SD	9.5	6.9	7.5	7.9	8.0	7.4	6.5	6.4	3.8
F	110	193	198	193	117	51.3	133	155	106
R	0.893	0.934	0.936	0.934	0.905	0.815	0.912	0.923	0.893
$\nu_{(C=O)0}$	1720.4	1708.0	1702.2	1700.8	1701.0	1721.7	1697.0	1668.0	1719.6
	597	808	744	710	662	715	852	850	1500
a	−75.42	−73.09	−80.24	−82.76	−67.77	−47.24	−56.89	−60.60	−30.01
VIF	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
t-stat	10.5	13.9	14.1	13.9	10.8	7.17	11.5	12.5	10.3
Outliers:[a] Table 4 No.	None	None	None	None	None	None	27	13	None

[a] Retained.

Table 9. Fundamental (*Y, P, B, E,* δ_H^2, *MR*) correlation equations

$$\nu_{(C=O)} = \nu_{(C=O)0} + a\ Y + b\ P + c\ B + d\ E + e\ \delta_H^2 + f\ MR$$

Parameter	PY	MP	IPP	CHP	HEP	OBT	OOBT	DMA	CH
N	30	30	30	30	28	28	29	29	29
SD	8.9	5.8	5.7	6.2	6.5	7.7	5.3	5.3	3.6
F	64.0	72.6	90.7	81.8	64.3	23.8	53.5	59.8	41.7
R	0.909	0.960	0.967	0.964	0.943	0.810	0.948	0.953	0.913
$\nu_{(C=O)0}$	1724.4	1738.2	1727.37	1731.1	1701.7	1726.1	1722.9	1694.1	1732.6
	382	165	166	153	470	442	172	159	244
a	−28.35	−30.73	−30.77	−27.42	−28.61	−22.09	−19.74	−21.81	n/s
VIF	1.30	1.39	1.39	1.39	1.37	1.26	1.47	1.90	
t-stat	3.89	6.27	6.35	5.22	4.95	3.43	4.21	4.10	
b	n/s[a]	−106.8	−93.88	−117.3	n/s	n/s	−101.2	−144.5	−127.8
		1.45	1.45	1.45			1.55	1.53	1.54
		2.68	2.38	2.75			2.63	3.52	4.92
c	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
d	−2.534	−3.190	−3.681	−3.823	−2.967	−1.362	−2.797	−1.714	−0.851
	1.30	3.05	3.05	3.05	2.44	1.20	3.19	2.81	2.77
	7.45	9.42	11.0	10.5	8.65	3.76	8.78	5.73	4.23
e	n/s	4.572	5.816	4.528	6.287	n/s	4.286	n/s	n/s
		2.49	2.49	2.49	2.44		2.49		
		2.40	3.10	2.22	2.95		2.45		
f	n/s	n/s	n/s	n/s	n/s	n/s	n/s	0.510	0.527
								3.65	2.71
								2.34	4.50
Outliers:[b] Table 4 No.	None	None	21	None	None	26	13	13	None

[a] n/s, Not significant at the 0.95 level.
[b] Retained.

acidity and, hence, solute hydrogen bond acceptor basicity. This is suggested by the acidity parameters (*E*, α, ε_A and $q+$) being the most significant (having the greatest *t*-stat values) in their corresponding equations; it also provides another example of the similarity among the parameter sets. Increasing acidity is associated with decreasing frequency; this is consistent with decreasing the C to O bond strength as modeled by the force

Table 10. LSER parameter (π^*, β, α, δ_H^2) correlation equations

$$\nu_{(C=O)} = \nu_{(C=O)0} + a\ \pi^* + b\ \beta + c\ \alpha + d\ \delta_H^2$$

Parameter	PY	MP	IPP	CHP	HEP	OBT	OOBT	DMA	CH
N	30	30	30	30	28	28	29	29	29
SD	7.7	5.6	6.5	7.2	3.8	7.6	2.5	3.6	2.0
F	90.9	155	137	117	205	24.3	343	271	230
R	0.933	0.959	0.954	0.947	0.981	0.812	0.988	0.977	0.973
$\nu_{(C=0)}0$	1722.5	1708.9	1701.6	1700.0	1700.7	1729.4	1697.5	1672.8	1723.0
	581	791	679	611	1000	397	1700	1200	2200
a	−28.46	−25.50	−24.59	−24.96	−26.59	n/s	−23.88	−31.19	−17.69
VIF	1.05	1.05	1.05	1.05	1.29		1.30	1.04	1.04
t-stat	6.05	7.44	6.18	5.65	9.50		13.8	14.1	14.4
b	n/s[a]	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
c	−38.50	−37.52	−42.50	−43.70	−43.99	−12.94	−35.14	−27.46	−12.56
	1.05	1.05	1.05	1.05	1.58	1.35	1.59	1.04	1.04
	10.5	14.0	13.7	12.7	19.0	2.71	22.8	15.4	12.7
d	n/s	n/s	n/s	n/s	3.741	−17.76	2.715	n/s	n/s
					1.94	1.35	1.96		
					3.37	4.14	3.68		
Outliers:[b] Table 4 No.	19	19	19	19	None	None	None	None	None

[a] n/s Not significant at the 0.95 level.
[b] Retained.

Table 11. TLSER parameter (V_{mc}, π_I, ε_B, q_- ε_A, $q+$) correlation equations

$$\nu_{(C=O)} = \nu_{(C=O)0} + a\ V_{mc} + b\ \pi_I + c\ \varepsilon_B + d_{q-} + e\ \varepsilon_A + f_{q+}$$

Parameter	PY	MP	IPP	CHP	HEP	OBT	OOBT	DMA	CH
N	30	30	30	30	28	29	29	29	29
SD	8.2	5.2	4.8	5.2	5.1	8.1	3.8	5.9	2.8
F	39.6	91.2	132	119	83.2	20.3	114	48.7	45.4
R	0.929	0.967	0.977	0.975	0.967	0.787	0.975	0.944	0.953
$\nu_{(C=O)0}$	1698.8	1684.6	1669.4	1665.4	1681.5	1699.2	1685.3	1653.5	1722.7
	102	159	171	157	161	276	221	139	293
a	16.82	19.65	20.45	20.01	15.92	17.57	13.71	20.16	11.57
VIF	2.26	2.26	2.26	2.26	2.14	1.20	2.23	2.23	2.25
t-stat	2.37	4.36	4.94	4.45	3.54	3.15	4.24	4.00	4.77
b	682.1	392.0	480.5	522.6	500.5	n/s	466.1	532.2	187.0
	4.83	4.83	4.83	4.83	5.16		5.12	5.12	5.30
	2.76	2.50	3.33	3.34	3.16		4.00	2.93	2.11
c	n/s[a]	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
d	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	−9.37
									1.19
									2.56
e	−456.6	−267.3	−275.6	−285.6	−332.1	n/s	−343.4	−427.5	−221.1
	4.23	4.23	4.23	4.23	4.32		4.43	4.43	4.46
	2.65	2.44	2.74	2.62	3.03		4.24	3.39	3.66
f	−193.2	−195.1	−215.2	−223.2	−190.4	−96.00	−153.6	−120.8	−55.40
	1.36	1.36	1.36	1.36	1.35	1.20	1.38	1.38	1.47
	7.30	11.6	13.9	13.3	11.3	3.78	12.5	6.30	5.83
Outliers:[b] Table 4 No.	None	None	12	None	12	None	None	30	18, 30

[a] n/s, Not significant at the 0.95 level.
[b] Retained.

Table 12. Extended TLSER parameter ($\delta_H{}^2$, π_I, ε_B, q_-, ε_A, q_+) correlation equations

$$\nu_{(C=O)} = \nu_{(C=O)0} + a\ \delta_H{}^2 + b\ \pi_I + c\ \varepsilon_B + dq_- + e\ \varepsilon_A + fq_+$$

Parameter	PY	MP	IPP	CHP	HEP	OBT	OOBT	DMA	CH
N	30	30	30	30	28	29	29	29	29
SD	8.4	6.8	6.6	6.4	6.2	7.8	4.9	6.2	3.5
F	37.4	68.0	88.4	77.6	72.1	22.8	87.0	42.0	42.0
R	0.926	0.942	0.954	0.962	0.949	0.804	0.955	0.935	0.921
$\nu_{(C=O)0}$	1737.9	1705.0	1690.2	1704.1	1696.1	1730.5	1699.5	1701.5	1743.2
	93.0	138	140	121	146	398	174	122	222
a	−5.117	n/s	n/s	−4.237	n/s	−16.72	n/s	−6.268	−2.995
VIF	2.06			2.06		1.57		2.10	2.18
t-stat	2.04			2.23		3.55		3.33	2.82
b	825.2	847.0	954.0	782.0	865.6	n/s	785.0	676.2	330.0
	3.80	2.70	2.70	3.80	2.98		2.98	4.28	3.93
	3.68	5.56	6.42	4.61	5.90		6.02	3.82	3.31
c	n/s[a]	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
d	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
e	−661.0	−570.4	−591.0	−548.7	−566.0	n/s	−555.8	−657.2	−336.1
	2.63	2.53	2.53	2.63	2.75		2.73	2.88	2.64
	4.75	5.18	5.51	5.21	5.31		5.97	6.04	5.98
f	−200.1	−224.5	−246.0	−238.0	−211.2	−68.84	−174.0	−130.4	−68.15
	1.29	1.14	1.14	1.29	1.18	1.57	1.17	1.29	1.29
	7.57	11.2	12.6	11.9	11.0	2.46	11.1	6.58	6.11
Outliers:[b] Table 4 No.	12	12	12	12	12	12	12	None	None

[a] n/s, Not significant at the 0.95 level.
[b] Retained.

Table 13. TLSER parameter (V_{mc}, π_I, ε_B, $q-$, ε_A, $q+$) correlation equations (reduced *VIF*)

$$\nu_{(C=O)} = \nu_{(C=O)0} + a\ V_{mc} + b\ \pi_I + c\ \varepsilon_B + d\ q_- + e\ \varepsilon_A + f_{q+}$$

Parameter	PY	MP	IPP	CHP	HEP	OBT	OOBT	DMA	CH
N	30	30	30	30	28	29	29	29	29
SD	8.9	6.8	6.6	6.8	6.2	8.1	4.9	7.4	4.0
F	43.2	68.0	88.4	88.3	72.1	20.3	87.0	37.3	33.1
R	0.913	0.942	0.954	0.963	0.949	0.787	0.955	0.904	0.894
$\nu_{(C=O)0}$	1716.2	1705.0	1690.6	1686.2	1696.1	1699.2	1699.5	1674.4	1730.5
	105	138	140	175	146	276	192	124	239
a	n/s[a]	n/s	n/s	n/s	n/s	17.57	n/s	n/s	n/s
VIF						1.20			
t-stat						3.15			
b	1071.4	847.0	954.0	985.8	865.6	n/s	785.0	1001.4	485.4
	2.70	2.70	2.70	2.70	2.98		2.98	2.98	2.98
	5.36	5.56	6.42	6.42	5.90		6.82	5.72	5.16
c	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
d	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
e	−715.9	−570.4	−591.0	−594.2	−566.0	n/s	−555.8	−740.0	−405.6
	2.53	2.53	2.53	2.53	2.75		2.73	2.73	2.73
	4.95	5.18	5.51	5.39	5.31		6.75	5.90	6.02
f	−218.4	−224.5	−245.9	−253.2	−211.2	−96.00	−146.1	−150.9	−77.92
	1.14	1.14	1.14	1.14	1.18	1.20	1.17	1.17	1.17
	8.30	11.2	12.6	12.5	11.0	3.78	11.9	6.76	6.50
Outliers:[b] Table 1. No.	None	12	12	12	12	None	12	30	None

[a] n/s, Not significant at the 0.95 level.
[b] Retained.

constant, *k*, in the model for harmonic oscillator frequency, $\nu = (2\pi c)^{-1}\ \sqrt{k/\mu}$ (wavenumbers). This suggests the physically reasonable nature of these equations. The polarizabilities also play a role in the interactions as indicated by the statistical significance of polarizability parameters in those sets which feature polarizability related parameters (E_{Tn}, *P*, *MR*, π^*, V_{mc} and π_I). However, the frequency decreases with E_{Tn}, *P* and π^* whereas it increases with *MR*, V_{mc} and π_I.

There are several measures by which the parameter sets may be compared. Based on the average *R* value for the nine solutes, the sequence is LSER > TLSER >

Table 14. TLSER parameter (V_{mc}, π_I, ε_B, q^-, ε_A, q^+) correlation equations (best *VIF*)

$$\nu_{(C=O)} = \nu_{(C=O)0} + a\ V_{mc} + b\ \pi_I + c\ \varepsilon_B + d\ q_- + e\ \varepsilon_A + f_{q+}$$

Parameter	PY	MP	IPP	CHP	HEP	OBT	OOBT	DMA	CH
N	30	30	30	30	28	29	29	29	29
SD	9.1	5.6	5.6	6.1	5.9	8.1	4.8	6.8	3.8
F	61.7	153	193	172	121	20.3	134	67.2	56.3
R	0.906	0.959	0.967	0.963	0.952	0.787	0.955	0.915	0.901
$\nu_{(C=O)0}$	1684.0	1675.2	1667.1	1665.5	1672.0	1699.2	1670.5	1630.5	1700.2
	265	423	428	393	388	276	477	327	618
a	30.30	27.45	29.50	29.71	25.35	17.57	22.66	30.72	16.03
VIF	1.23	1.23	1.23	1.23	1.22	1.20	1.27	1.27	1.27
t-stat	5.26	7.65	8.35	7.73	6.47	3.15	7.27	6.92	6.55
b	n/s[a]	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
c	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
d	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s	n/s
e	n/s	n/s	n/s	n/s		n/s	n/s	n/s	n/s
f	−182.2	−188.3	−211.6	−220.5	−185.9	−96.00	−146.1	−109.3	−52.12
	1.23	1.23	1.23	1.23	1.22	1.20	1.27	1.27	1.27
	6.56	10.9	12.4	11.9	10.1	3.78	9.71	5.09	4.41
Outliers:[b] Table 4 No.	6	None	None	None	None	None	None	None	None

[a] n/s, Not significant at the 0.95 level.
[b] retained.

Fundamental > Extended TLSER > Gutmann > Reichardt. Based on the average SD value, the order is LSER, Gutmann > TLSER > Fundamental > Extended TLSER > Reichardt. Using the average value of the *t*-stat for the parameter with the highest *t*-stat (most statistically significant), the order becomes Gutmann > LSER > Reichardt > TLSER > Extended TLSER > Fundamental. Based on the number of outliers, the order is Reichardt(2) > Fundamental, LSER(4) > Gutmann, TLSER(5) > Extended TLSER(7). Finally, using the average of the highest and lowest *VIF* values results in Gutmann, Reichardt > LSER > Fundamental > Extended TLSER > TLSER. Assigning numbers based on rank order and giving equal importance to each statistical parameter, the sequence becomes LSER > Gutmann > Reichardt > TLSER > Fundamental > Extended TLSER.

The previous paragraph indicates that the LSER parameter set provides the best overall correlation equations. The Gutmann equations are close in quality to those for LSER; however, there were parameters for only 26 compounds. The Gutmann and Reichardt equations had the advantage of no cross correlation (small *VIF*) because they have only one statistically significant parameter. The disadvantage of the Fundamental, TLSER and Extended TLSER equations is the larger parameter cross correlation. This is often the case with a multi-parameter set; the well designed LSER set is an exception. For the TLSER set, π_1 has *VIF* values around 5 and ε_A has values near 4; these are larger than those for any empirical parameter. Reduction of the number of parameters gives equations with lower *VIF* values; Tables 13 and 14 show the resulting TLSER correlation equations. Table 14 equations rank third, along with the Reichardt equations, in overall quality order. They do rank ahead of the Reichardt equations with regard to average *R*, SD and number of outliers, but rank behind in *VIF* and maximum parameter *t*-stat values.

As noted, previously OBT has the least significant correlation equations for all descriptors. This suggests that OBT is not typical of the other eight solutes, despite its structural similarity to PY and OOBT. OBT is more similar to PY (Table 3) than the other solutes; each has an unsubstituted amide moiety. Moreover, the aromatic structure and sulfur atom in OBT could provide extensive conjugation which could enhance the hydrogen acidity. The TLSER parameters (Table 6) support this idea; OBT has the largest values for the polarizability index, π_I, covalent acidity, ε_A, and (by far) the electrostatic acidity, q^+. Empirical data (Table 4) shows that OBT has higher C=O frequencies than does PY, thus, suggesting a stronger C=O bond. Strong hydrogen bonding could account for this; furthermore, OBT dimer complexes are possible.

In a related note, except for the LSER case, CH has the next least significant correlation equations. However, the CH correlation equations make good physical sense. The coefficients in its equations have the smallest magnitude; this is especially true for the polarizability related parameters, E_{Tn}, π^*, V_{mc} and π_I, in their respective parameter sets. Comparison of the molecular structures indicates that CH is expected to have the least polarizable molecule in this solute set. This suggests that the coefficients of the solvent polarizability terms, expected to be related to the polarizability of the solutes, should be smaller than those for the other solutes. In short, dispersion interactions would be smaller for the CH/solvent case. In this connection, the Reichardt parameter equation coefficients, *a*, correlate somewhat with solute polarizability. The cyclic amides (PY, MP, IPP, CHP, HEP, OBT, and OOBT) and non-cyclic amide have larger coefficients, *a*, than does the less polarizable non-amide CH.

Similarly, since the TLSER solvent acidity terms, those with ε_A and q^+, are significant, one might expect their coefficients, *e* and *f*, to be related to complementary solute basicity parameters, ε_B and q^-. The correlation equations between solute *e* and ε_B values and also *f* and ε_A values were not significant.

As noted earlier, the main disadvantage for the TLSER relationships is the larger *VIF* values (less orthogonality). Only four equations have outliers; bis(2-methoxyethyl) ether is an outlier in two equations and deuterium oxide occurs alone in another and with cyanobenzene for CH. The increase in frequency with increasing solvent acidity suggests the physical reasonableness of the TLSER correlations through decreased C=O bond strength through hydrogen bonding. Similarly increased solvent polarizability can suggest an increase in C=O bond strength through π interactions. This may account for the effect of V_{mc} since greater molecular mass (volume) accompanies increased polarizability. A convenience of the TLSER parameters is their ease of calculation and chemical interpretation.

The lower quality of the Extended TLSER parameter equation shows that there is no advantage in replacing the volume by the Hildebrand solubility parameter. Although there is more orthogonality than in the TLSER equations, there are more equations with outliers than in any of the other sets. Bis(2-methoxyethyl) ether is an outlier in seven of the nine equations. The reason for it being an outlier is not readily apparent. None of its parameters seem to be unusual when compared with those for other solvents. Data for similar solvents would help in understanding why this ether is an outlier.

The number of outlier compounds is reasonable; it averages less than one compound out of 30 for any equation. Outliers commonly occur in correlation analyses and their presence often can be accounted for in several ways. The compound might be different in structure from other compounds in the set, leading to different parameter values and/or a different interaction mechanism. Also, the model equation being 'fit' might be inadequate or, lastly, the experimental value might be in

error. For the LSER parameter set, best in overall quality, propanone is an outlier in four cases. Other than ethanoic acid, it is the only carbonyl-containing solvent.

At this point, it is natural to ask about multiple solute–single solvent correlation equations and correlations among the five parameter sets. This data set has only nine solutes for each solvent while 18 are needed to ensure statistical significance. Nevertheless, some multiple solute–single solvent correlations were performed; some solvent equations had acceptable *R* and SD values but showed too much cross correlation. Studies on more solutes are needed in order to examine multiple solute equations adequately. Correlations between sets of parameters are not included here since they would constitute another study.

CONCLUSION

The five parameter sets provide physically and statistically reasonable correlation equations for the carbonyl stretching frequencies in terms of solvent molecular structural features for this particular system, which consists of five 1-substituted 2-pyrrolidinones, two oxobenzothiazoles, dimethylacetamide and cyclohexanone in 30 common solvents. Increasing solvent hydrogen bond donor (capacity) acidity is associated with decreasing frequency while increasing solvent polarizability is associated with increasing frequency. The TLSER parameter set provides statistically and physically significant correlation equations. The ease in obtaining these TLSER parameter values and the ease in chemically interpreting their correlation equations along with their success in correlating many properties suggest their continued use.

REFERENCES

1. F. R. Mooijman and J. B. F. N. Engberts. *J. Org. Chem.* **54,** 3993 (1989).
2. E. Q. Lawson, A. J. Sadler, D. Harmatz, D. T. Brandau, R. Micanov, R. D. MacElroy and C. R. Middaugh. *J. Biol. Chem.* **259,** 2910 (1984).
3. J. A. Ferrendaelli, A. L. Steiner, D. B. McDougal Jr and D. M. Kipnis. *Biochem. Biophys. Res. Commun.* **41,** 1061 (1970).
4. J. B. F. N. Engberts, A. Perjéssy, M. J. Blandamer and G. Eaton. *J. Chem. Soc., Faraday Trans.* **88,** 2493 (1992); J. B. F. N. Engberts, A. Perjéssy, M. J. Blandamer, G. Eaton. *J. Chem. Soc., Faraday Trans.* **89,** 4199 (1994); D. Loos, A. Perjéssy, J. B. F. N. Engberts. *Monatsh. Chem.* **125,** 293 (1994); A. Perjéssy, J. B. F. N. Engberts, M. J. Blandamer. *Org. React.* **19,** 89 (1994).
5. A. Perjéssy and J. B. F. N. Engberts. *Monatsh. Chem.* **126,** 871 (1996).
6. M. J. Kamlet, R. M. Doherty, M. H. Abraham and R. A. Taft. *Quant. Struct.–Act. Relat.* **7,** 71 (1988).
7. L. P. Hammett. *J. Am. Chem. Soc.* **59,** 96 (1937).
8. O. Exner. *Correlation of Chemical Data.* Plenum Press, New York (1988).
9. M. H. Abraham, J. Andonian-Haftvan, C. M. Du, V. Diart, G. S. Whiting, J. W. Grate and R. A. McGill. *J. Chem. Soc., Perkin Trans. 2* 369 (1995).
10. W. L. Jorgenson and C. J. Ravimohan. *J. Chem. Phys.* **83,** 3050 (1985).
11. O. Tapia and O. Goscinski. *Mol. Phys.* **29,** 1653 (1975).
12. C. J. Cramer and D. G. Truhlar. *Science* **256,** 213 (1992).
13. P. Politzer and J. Murray. *Quantitative Treatment of Solute/Solvent Interactions*, p. 243. Elsevier, Amsterdam (1994).
14. A. H. Lowrey and G. R. Famini. *Struct. Chem.* **6,** 357 (1995); G. R. Famini, L. Y. Wilson. *Org. React.* **29,** 117 (1995); A. H. Headley, S. D. Starnes, L. Y. Wilson and G. R. Famini. *J. Org. Chem.* **59,** 8040 (1994); G. R. Famini and L. Y. Wilson. in *Quantitative Treatments of Solute/Solvent Interactions*, edited by P. Politzer and J. S. Murray, p.213. Elsevier, Amsterdam (1994); G. R. Famini, L. Y. Wilson. *J. Chem. Soc. Perkin Trans. 2* 1641 (1994).
15. M. J. Kamlet, J. L. -M. Abboud, M. H. Abraham and R. W. Taft. *J. Org Chem.* **48,** 2877 (1983); M. H. Abraham. *Chem. Soc. Rev.* **22,** 73 (1992).
16. V. Palm and N. Palm. *Org. React.* **28,** 125 (1993).
17. Y. Marcus. *J. Solution Chem.* **13,** 599 (1984); *Chem. Soc. Rev.* **23,** 409 (1993).
18. C. Reichardt. *Chem. Rev.* **94,** 2319 (1994).
19. V. Gutmann. *Electrochim. Acta.* **21,** 661(1976).
20. J. B. F. N. Engberts, A. Perjéssy and M. J. Blandamer. *J. Chem. Soc., Faraday Trans.* **89,** 4199 (1993).
21. J. M. Leonard and G. R. Famini. *A User's Guide to Molecular Modeling, Analysis and Display System*, CRDEC-R030. U S Army Chemical, Research, Development and Engineering Center, Aberdeen Proving Ground, MD (1989).
22. J. J. P. Stewart. *MOPAC Manual*, FJSRL-TR-88-007. Frank J. Seiler Research Laboratory, U S Air Force Academy, Colorado Springs, CO (1988); available through QCPE.
23. A. J. Hopfinger. *J. Am. Chem. Soc.* **102,** 7126 (1980).
24. D. A. Beisley, E. Kuh and R. E. Welsh. *Regression Diagnosis.* Wiley, New York (1980).

