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Note

Grouping solvents by statistical analysis of solvent property parameters: implication to polymorph screening

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Abstract

The success rate of discovering new polymorphs by crystallization from solution may be increased if solvents with diverse properties are used during initial polymorph screening. In this study, eight solvent parameters, including hydrogen bond acceptor propensity, hydrogen bond donor propensity, polarity/dipolarity, dipole moment, dielectric constant, viscosity, surface tension and cohesive energy density (equal to square of solubility parameter), of 96 solvents were collected. Using the cluster statistical analysis of the parameters, these 96 solvents were separated into 15 solvent groups. Such solvent groups may provide guidelines for the judicious choice of solvents with diverse properties for polymorph screening.

Keywords: Cluster analysis; Polymorph screening; Solvent group; Solvent parameter

Polymorph screening is routinely conducted by crystallization from different solvents using either conventional (Guillory, 1999) or high throughput crystallization technology (Remenar et al., 2003; Carlson et al., 2003). It is often observed that a particular polymorph preferentially crystallizes from a specific solvent, especially when no seeds are present (Weissbuch et al., 1995; Blagden et al., 1998; Gidalevitz et al., 1997). This phenomenon has been attributed to the controlling effect of solvent–solute interactions on the nucleation, crystal growth and solvent-mediated polymorph transformation (Weissbuch et al., 2003; Gu et al., 2001), which consequently affect the appearance of polymorphs. In addition to the solvent–solute

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interaction at the molecular level, bulk properties of solvents, such as viscosity and surface tension, may also affect the crystallization kinetics and the appearance of polymorphs (Mullin, 1993). Therefore, using a group of solvents with diverse properties may increase the success rate of discovering new polymorphs during polymorph screening (Carlson et al., 2003).

The solvent properties may be described by solvent property parameters, including molecular descriptors, e.g. hydrogen bond donor or acceptor propensity descriptors, and bulk property parameters, e.g. viscosity. Since crystallization is influenced by both solvent–solute interactions and bulk solvent properties, it is almost impossible to know a priori which property parameters are important for polymorph screening. Therefore, all parameters should be included to classify the solvents into groups, based on statistical similarity of these parameters. Previous studies have classified the solvents based on the solubility of test solutes in a given solvent (Snyder, 1978) or by the factor analysis of the solvent descriptors (Carlson, 1992). However, these analyses fail to include some solvent parameters, such as hydrogen bonding propensity and viscosity, known to be important to crystallization. In the current study, eight solvent parameters, namely hydrogen bond acceptor propensity, hydrogen bond donor propensity, polarity/dipolarity, dipole moment, dielectric constant, viscosity, surface tension, and cohesive energy density, which is equal to square of Hildebrand–Scott solubility parameter, of 96 solvents, listed in Appendix A, were collected from the literature (Abraham, 1993a,b; Lide, 1995; Marcus, 1993; Winget et al., 1999). These solvent parameters were analyzed by the cluster method to classify the solvents into 15 discrete groups. These groups may provide guideline to the selection of solvents during initial polymorph screening.

Using PROC CLUSTER in SAS^{TM} version 8.02, cluster analysis was performed to place solvents into clusters based on solvent property parameters (Everitt, 1980; Massart and Kaufman, 1983). The STD option in the PROC CLUSTER was used to transform the solvent parameters to a common scale with mean 0 and variance 1 because variables with large variances will have more effects on the resulting clusters than those with smaller variances. Among 11 available cluster methods, the average linkage method, with proven performance (Milligan, 1981), was chosen to hierarchically cluster the solvents into a pre-selected number of groups (15 in this case). Each solvent began in a cluster by itself. The two closest clusters were merged to form a new cluster that replaced the two old clusters. Merging of the two closest clusters was repeated until only one cluster was left. The list of solvents in each cluster was then provided based on any pre-selected number of groups (SAS/STAT^{TM} user's guide, 1988).

The distance between two clusters is computed differently by different cluster method. In the average linkage method (Sokal and Michener, 1958), the distance between two clusters is defined as the average distance between pairs of observations, which is calculated as follows. Let x_i be the ith observation in cluster C_K, x_j the jth observation in cluster C_L. The average linkage distance D_{KL} between clusters C_K and C_L is:

$$D_{KL} = \sum_{i \in C_K} \sum_{j \in C_L} \frac{d(x_i, x_j)}{(N_K N_L)} \quad (1)$$

where $d(x_i, x_j)$ is the Euclidean distance between observations x_i and x_j, N_K and N_L are the number of observations in clusters C_K and C_L, respectively. The summation is taken across all the pair wise distances between two clusters and then divided by the total number of pairs, i.e. $N_K N_L$.

In analysis 1, all eight solvent parameters listed in Appendix A were used to classify the 96 solvents into 15 groups and the results are presented in Table 1. For solute molecules with strong propensity of molecular interactions, the strength of solute–solvent interaction may play a dominant role in determining polymorph formation. Therefore, parameters that are critical for direct solvent–solute interactions (solvation) were used for solvent classification in analysis 2. These parameters include dipole moment, dielectric constant, hydrogen bond acceptor propensity, hydrogen bond donor propensity, and polarity/dipolarity (Marcus, 1993). The cohesive energy density characterizes the strength of solvent–solvent interaction and is not included in analysis 2. The results of analysis 2 are presented in Table 2. Comparison of these two analyses revealed that the results are similar in general except that some solvents are grouped into different clusters using different pa-

Table 1
Solvent groups based on cluster analysis of following solvent parameters, hydrogen bond acceptor propensity, hydrogen bond donor propensity, polarity/dipolarity, dipole moment, dielectric constant, viscosity, surface tension, and cohesive energy density

Group 1	Cyclohexane (1.4), mesitylene (8.3), *cis*-decalin (10.5), *p*-xylene (14.7), *m*-xylene (15.9), carbon tetrachloride (28.0), toluene (34.1), *n*-pentane (54.7), *n*-hexane (55.5), *n*-heptane (55.7), *n*-octane (60.3), tetrachloroethene (60.7), benzene (61.7), *n*-decane (69.1), *n*-dodecane (70.5), carbon disulfide 147.0)
Group 2	Butylamine (27.8), diethyl ether (38.9), methyl tertiary-butyl ether (43.2), triethylamine (64.5), diisopropyl ether (81.1), dibutylether (96.1), 1,4-dioxane (103.8)
Group 3	Tetrahydrofuran (5.1), chloroform (5.8), anisole (7.7), *o*-dichlorobenzene (10.5), ethyl formate (11.6), trichloroethene (12.3), methyl benzoate (12.3), iodobenzene (12.6), chlorobenzene (13.2), methyl ethanoate (18.7), dimethyl disulfide 20.1), 1,1-dichloroethane (22.2), fluorobenzene (28.8), ethyl phenyl ether (32.3), ethyl acetate (34.7), 1,2-dichloroethane (34.8), 1,2-dibromoethane (43.2), 1-iodobutane (51.2), 1,1,1-trichloroethane (59.1), propyl ethanoate (61.5), diethyl sulfide (63.8), dichloromethane (66.4), butyl ethanoate (77.4), methyl methanoate (79.0), bromoform (95.4), dibromomethane (103.8)
Group 4	2-methyl-1-propanol (6.4), 2-butanol (11.4), *m*-cresol (17.0), 2-methoxyethanol (19.0), 1-butanol (19.8), propanoic acid (28.8), morpholine (34.0), 2-methyl-2-propanol (38.1), 1-pentanol (39.4), pentanoic acid (45.3), acetic acid (56.4), 2-propanol (63.2), 1- propanol (94.1), 1-octanol (144.9), ethanol (192.7)
Group 5	Butanone (9.0), 2,4-dimethylpyridine (10.0), acetophenone (17.3), 2,6-dimethylpyridine (20.4), 3-pentanone (27.6), 2-pentanone (31.4), 4-methylpyridine (39.4), acetone (42.9), cyclohexanone (45.4), 2-hexanone (46.1), cyclopentanone (62.2), 2-heptanone (66.3), 4-methyl-2-pentanone (68.1), pyridine (85.0)
Group 6	*N*-methyl-2-pyrrolidone (21.0), *N*,*N*-dimethylformamide (35.1), *N*,*N*-dimethylacetamide (59.1), dimethylsulfoxide (74.7)
Group 7	Benzonitrile (38.7), propanenitrile (46.3), acetonitrile (61.3), butanenitrile (103.8), nitromethane (125.6)
Group 8	Aniline (13.3), benzyl alcohol (13.3)
Group 9	Formic acid
Group 10	Ethylene glycol
Group 11	Methanol
Group 12	Diethylamine
Group 13	Diiodomethane
Group 14	Glycerol
Group 15	Water

The Euclidean distance of each solvent to the center of the corresponding group is provided in the parentheses.

rameter sets. The results of both analyses indicate that solvents with the same functional groups, e.g. alcohols and ketones, generally belong to the same cluster. Since the current understanding of the influence of solvent properties on the appearance of polymorphs is limited, it is difficult to choose which set represents the solvent group more appropriately. Therefore, it is recommended to combine the solvents routinely used for polymorph screening, such as methanol and water, with the solvents from clusters not represented by common solvents for the initial polymorph screening. For a particular compound, if certain solvent properties are known to be important for the formation of polymorphs, the specific solvent parameters may be selected for analysis to separate solvents using the cluster method presented.

To choose a typical solvent from each cluster, the Euclidean distance of each solvent to the cluster center, which is the arithmetic average of the solvent parameters within the cluster, was calculated (Tables 1 and 2). The solvent with the shortest Euclidean distance may be assumed to be the typical solvent of each group. An alternative approach is to choose commonly used solvents from each group for polymorph screening, which may be more practical. Once a polymorph is discovered from a particular solvent, the solvent clusters may assist the choice of solvents for process optimization by choosing the solvents from the same cluster. Due to solubility difference in different solvents, in practice, appropriate crystallization techniques, such as cooling a supersaturated solution, antisolvent, evaporation, solvent-mediated polymorph screening,

Table 2
Solvent groups based on cluster analysis of following solvent property parameters, hydrogen bond acceptor propensity, hydrogen bond donor propensity, polarity/dipolarity, dipole moment, and dielectric constant

Group 1	*n*-Dodecane (0.0), *n*-decane (0.1), Cyclohexane (0.1), *n*-octane (0.1), *n*-hexane (0.2), *n*-heptane (0.2), *cis*-decalin (0.2), *n*-pentane (0.2), carbon tetrachloride (0.3), tetrachloroethene (0.3)
Group 2	Ethyl acetate (0.2), diethyl sulfide (0.4), propyl ethanoate (0.6), methyl benzoate (0.8), methyl ethanoate (0.8), butyl ethanoate (1.1), tetrahydrofuran (1.4), methyl tertiary-butyl ether (1.6), diethyl ether (1.9), ethyl formate (2.3), diisopropyl ether (2.8), methyl methanoate (2.8), dibutylether (3.1), dimethyl disulfide (3.5)
Group 3	2-methyl-1-propanol (0.3), 2-butanol (0.5), 1-butanol (0.9), 2-methoxyethanol (1.1), 1-pentanol (1.3), 2-propanol (2.8), 2-methyl-2-propanol (4.0), 1-propanol (4.1), 1-octanol (6.6), ethanol (8.4), morpholine (9.0), butylamine (11.9), methanol (16.2)
Group 4	*m*-Xylene (0.1), *p*-xylene (0.1), benzene (0.1), mesitylene (0.2), carbon disulfide (0.3), toluene (0.3)
Group 5	2-hexanone (0.0), cyclopentanone (0.8), 2-pentanone (1.1), pyridine (1.2), 4-methyl-2-pentanone (1.2), cyclohexanone (1.5), 4-methylpyridine (2.2), 2-heptanone (2.5), 3-pentanone (2.7), acetophenone (3.4), butanone (4.1), 2,4-dimethylpyridine (4.7), acetone (6.4), 2,6-dimethylpyridine (7.0)
Group 6	*N*,*N*-dimethylacetamide (0.8), *N*,*N*-dimethylformamide (1.3), *N*-methyl-2-pyrrolidone (6.3), dimethylsulfoxide (8.3)
Group 7	1-iodobutane (0.4), chlorobenzene (0.6), fluorobenzene (0.8), 1,1,1-trichloroethane (0.9), dibromomethane (1.0), diiodomethane (1.0), 1,2-dibromoethane (1.4), chloroform (1.6), iodobenzene (1.7), anisole (2.0), bromoform (2.1), ethyl phenyl ether (2.1), dichloromethane (2.7), trichloroethene (2.9), 1,1-dichloroethane (3.8), *o*-dichlorobenzene (3.9), 1,2-dichloroethane (3.9)
Group 8	Acetic acid (0.1), propanoic acid (2.8), pentanoic acid (3.5), *m*-cresol (6.2)
Group 9	Propanenitrile (1.0), benzonitrile (4.7), acetonitrile (5.4), butanenitrile (6.0), nitromethane (6.3)
Group 10	Benzyl alcohol (2.8), aniline (2.8)
Group 11	Triethylamine (0.4), 1,4-dioxane (0.4)
Group 12	Formic acid (4.9), ethylene glycol (4.9)
Group 13	Diethylamine
Group 14	Glycerol
Group 15	Water

The Euclidean distance of each solvent to the center of the corresponding group is provided in the parentheses.

may be used with solvents from different groups to screen polymorphs.

In the present study, only pure solvents were analyzed since many property parameters are unavailable for solvent mixtures. For a given solute, one cluster of solvents may act as antisolvent in comparison to another cluster. Therefore, solvents from different clusters may be combined to screen polymorphs using crystallization by antisolvent methods.

The results currently presented are not a solution to solvent selection for polymorph screening but merely an approach to a solution. Crystallization is a complicated kinetic process, whose nature is not fully revealed (Weissbuch et al., 2003). Many kinetic factors, such as desupersaturation rate, significantly influence the appearance of polymorphs but cannot be included in the solvent property analysis. Moreover, in the current analysis, each parameter is treated with equal weight, which may not be true for a specific solute. It is also possible that additional parameters may need to be included in the analysis. Nevertheless, the present analysis provides a guideline for rational selection of solvents significantly different in properties. Crystallization in diversified solvent environments may then increase the success rate of discovering polymorphs. In addition, the solvent groups may also provide guidelines for the selection of "similar" solvents for process optimization. Experiment work is ongoing to establish a correlation between the proposed solvent grouping and isolation of polymorphs. As more and more compounds are studied by high throughput polymorph screening using solvents from different groups, the utility of selecting diverse solvents for polymorph screening will be verified from the throughput results (Desrosiers et al., 2003).

Appendix A. Solvent property parameters of 96 solvents

Solvent name	π[a]	$\Sigma\alpha$[b]	$\Sigma\beta$[c]	Dipole moment[d]	Dielectric constant[e]	Cohesive energy density[f]	Viscosity[g]	Surface tension[h]
1,1,1-trichloroethane	0.49	0.00	0.09	1.76	7.08	275.25	0.79	36.24
1,2-dibromoethane	0.75	0.10	0.17	1.20	4.93	374.93	1.60	56.93
1,1-dichloroethane	0.48	0.10	0.10	2.06	10.00	313.91	0.46	34.64
1,2-dichloroethane	0.81	0.10	0.11	1.80	10.13	368.46	0.78	45.86
1,4-dioxane	0.51	0.00	0.64	0.00	2.21	372.17	1.18	47.14
1-butanol	0.47	0.37	0.48	1.66	17.33	446.01	2.54	35.88
1-iodobutane	0.47	0.00	0.15	1.90	6.17	282.86	0.83	40.65
1-octanol	0.40	0.37	0.48	1.80	9.86	281.82	7.29	39.01
1-pentanol	0.40	0.37	0.48	1.70	15.13	387.31	3.62	36.50
1-propanol	0.52	0.37	0.48	1.55	20.52	520.37	1.95	33.57
2,4-dimethylpyridine	0.73	0.00	0.63	2.30	9.42	312.93	0.89	46.86
2,6-dimethylpyridine	0.80	0.00	0.63	1.70	7.17	301.53	0.87	44.64
2-butanol	0.40	0.33	0.56	1.80	15.94	416.88	3.10	32.44
2-heptanone	0.61	0.00	0.51	2.60	11.66	254.45	0.71	37.60
2-hexanone (MBK)	0.72	0.00	0.51	2.70	14.14	274.77	0.58	36.63
2-methoxyethanol	0.53	0.30	0.84	2.36	17.20	443.97	1.60	44.39
2-methyl-1-propanol	0.40	0.37	0.48	1.64	16.78	425.37	3.33	32.38
2-methyl-2-propanol	0.41	0.31	0.60	1.70	12.47	389.69	4.31	28.73
2-pentanone	0.65	0.00	0.51	2.70	15.20	290.45	0.47	33.46
2-propanol	0.48	0.33	0.56	1.56	19.26	489.11	2.04	30.13
3-pentanone	0.72	0.00	0.51	2.80	16.78	293.91	0.44	35.61
4-methyl-2-pentanone	0.65	0.00	0.51	2.81	12.89	253.06	4.07	33.83
4-methylpyridine	0.84	0.00	0.54	2.70	11.96	359.06	1.00	50.17
acetic acid	0.64	0.61	0.44	1.70	6.25	370.80	1.06	39.01
Acetone	0.71	0.04	0.49	2.88	20.49	362.07	0.31	33.77
Acetonitrile	0.75	0.07	0.32	3.92	35.69	522.95	0.37	41.25
Acetophenone	0.90	0.00	0.48	3.02	17.44	310.80	1.68	56.19
Aniline	0.73	0.26	0.41	1.13	6.89	437.98	3.85	60.62
Anisole	0.73	0.00	0.29	1.38	4.22	335.71	1.06	50.52
Benzene	0.59	0.00	0.14	0.00	2.27	316.69	0.60	40.62
Benzonitrile	0.90	0.00	0.33	4.18	25.59	425.00	1.27	55.83
Benzyl alcohol	0.98	0.33	0.56	1.71	12.46	462.68	5.47	52.96

Appendix A (*Continued*)

Solvent name	π[a]	$\Sigma\alpha$[b]	$\Sigma\beta$[c]	Dipole moment[d]	Dielectric constant[e]	Cohesive energy density[f]	Viscosity[g]	Surface tension[h]
Bromoform	0.62	0.15	0.06	0.99	4.25	426.97	1.86	64.58
Butanone	0.67	0.00	0.51	2.78	18.25	321.92	0.41	34.50
Butanenitrile	0.71	0.00	0.36	4.07	24.29	358.53	0.55	38.75
Butyl ethanoate	0.46	0.00	0.45	1.90	4.99	256.96	0.69	35.81
Butylamine	0.31	0.16	0.61	1.00	4.62	297.23	0.57	33.74
Carbon disulfide	0.61	0.00	0.07	0.00	2.61	401.86	0.35	45.45
Carbon tetrachloride	0.28	0.00	0.00	0.00	2.23	283.14	0.91	38.04
Chlorobenzene	0.71	0.00	0.07	1.69	5.70	321.47	0.75	47.48
Chloroform	0.58	0.15	0.02	1.04	4.71	332.00	0.54	38.39
m-cresol	0.68	0.57	0.34	1.50	12.44	429.58	12.90	51.37
Cyclohexane	0.00	0.00	0.00	0.00	2.02	254.59	0.89	35.48
Cyclohexanone	0.76	0.00	0.56	2.87	15.62	365.28	2.02	49.76
Cyclopentanone	0.76	0.00	0.52	3.30	13.58	382.57	2.25	47.21
cis-decalin	0.11	0.00	0.00	0.00	2.21	249.80	3.04	45.45
n-Decane	0.03	0.00	0.00	0.00	1.98	186.10	0.84	33.64
Dibromomethane	0.92	0.10	0.10	1.43	7.23	436.99	0.98	56.21
Dibutylether	0.27	0.00	0.45	1.17	3.05	365.54	0.64	35.98
o-Dichlorobenzene	0.80	0.00	0.04	2.50	9.99	330.67	1.32	52.72
Dichloromethane	0.82	0.10	0.05	1.60	8.93	400.22	0.41	39.15
Diethyl ether	0.27	0.00	0.41	1.15	4.24	231.34	0.22	23.96
Diethyl sulfide	0.46	0.00	0.32	1.54	5.72	270.69	0.42	35.36
Diethylamine	0.24	0.80	0.69	0.92	3.58	256.83	0.32	28.57
Diiodomethane	0.65	0.05	0.23	1.10	5.32	496.28	3.04	95.25
Diisopropyl ether	0.27	0.00	0.41	1.13	3.38	188.66	0.38	24.86
Dimethyl disulfide	0.57	0.00	0.28	1.80	9.60	353.29	0.59	48.06
N,*N*-dimethylacetamide	0.88	0.00	0.78	3.70	37.78	439.94	1.96	47.62
N,*N*-dimethylformamide	0.88	0.00	0.74	3.82	37.22	463.96	0.79	49.56
dimethylsulfoxide	1.00	0.00	0.88	3.96	46.83	572.58	1.99	61.78
n-Dodecane	0.05	0.00	0.00	0.00	2.01	184.70	1.38	35.85
Ethanol	0.54	0.37	0.48	1.69	24.85	618.87	1.07	31.62
Ethyl acetate	0.55	0.00	0.45	1.78	5.99	300.64	0.42	33.67
Ethylene glycol	0.92	0.90	0.52	2.28	41.40	857.86	16.10	69.07

Appendix A (*Continued*)

Solvent name	π[a]	$\Sigma\alpha$[b]	$\Sigma\beta$[c]	Dipole moment[d]	Dielectric constant[e]	Cohesive energy density[f]	Viscosity[g]	Surface tension[h]
Ethyl formate	0.61	0.00	0.38	1.90	8.33	339.37	0.38	33.36
Ethyl phenyl ether	0.69	0.00	0.32	1.45	4.18	301.94	0.82	46.65
Fluorobenzene	0.62	0.00	0.10	1.60	5.42	305.61	0.55	38.37
Formic acid	0.65	0.75	0.38	1.41	51.10	535.98	1.61	53.44
Glycerol	0.62	1.21	0.51	2.60	46.53	801.55	934.00	91.10
n-Heptane	−0.08	0.00	0.00	0.00	1.91	200.08	0.39	28.28
n-Hexane	−0.04	0.00	0.00	0.00	1.88	200.76	0.30	25.75
Iodobenzene	0.81	0.00	0.12	1.70	4.55	332.24	1.55	55.72
Mesitylene	0.41	0.00	0.19	0.00	2.27	262.91	1.15	39.65
Methanol	0.60	0.43	0.47	1.70	32.61	808.26	0.54	31.77
Methyl benzoate	0.71	0.00	0.46	1.90	6.74	327.01	1.86	53.50
Methyl ethanoate	0.60	0.00	0.45	1.72	6.86	350.86	0.36	35.59
Methyl methanoate	0.62	0.00	0.38	1.77	8.84	412.43	0.33	35.06
N-methyl-2-pyrrolidone	0.92	0.00	0.77	4.10	32.20	518.28	1.67	58.58
Methyl tertiary-butyl ether	0.27	0.00	0.40	1.20	4.50	226.70	0.35	26.34
Morpholine	0.39	0.29	0.70	1.55	7.42	397.61	2.02	54.16
Nitromethane	0.85	0.06	0.31	3.46	36.56	587.22	0.63	52.58
n-Octane	0.01	0.00	0.00	0.00	1.94	195.23	0.51	30.43
n-Pentane	−0.08	0.00	0.00	0.00	1.84	202.42	0.22	22.30
Pentanoic acid	0.54	0.60	0.45	1.60	2.69	382.72	1.97	38.40
Propanoic acid	0.58	0.60	0.45	1.75	3.44	399.75	1.03	37.71
Propanenitrile	0.71	0.02	0.36	4.05	29.32	416.20	0.29	38.50
Propyl ethanoate	0.50	0.00	0.45	1.80	5.52	273.15	0.54	34.26
Pyridine	0.87	0.00	0.52	2.22	12.98	404.96	0.88	52.62
Tetrachloroethene	0.28	0.00	0.00	0.00	2.27	315.31	0.84	45.19
Tetrahydrofuran	0.58	0.00	0.48	1.75	7.43	336.92	0.46	39.44
Toluene	0.54	0.00	0.14	0.38	2.37	289.05	0.56	40.20
Trichloroethene	0.53	0.08	0.03	0.80	3.42	322.31	0.55	41.45
Triethylamine	0.14	0.00	0.79	0.66	2.38	205.06	0.35	29.10

Appendix A (*Continued*)

Solvent name	π[a]	$\Sigma\alpha$[b]	$\Sigma\beta$[c]	Dipole moment[d]	Dielectric constant[e]	Cohesive energy density[f]	Viscosity[g]	Surface tension[h]
Water	1.09	1.17	0.47	1.87	78.36	2095.93	0.89	104.70
m-Xylene	0.47	0.00	0.16	0.00	2.35	270.42	0.58	40.98
p-Xylene	0.43	0.00	0.16	0.00	2.27	269.45	0.60	40.32

[a] Polarity/dipolarity of the solvent (Marcus, 1993).
[b] Summation of the hydrogen bond donor propensities of the solvent (Abraham, 1993a,b; Winget et al. 1999).
[c] Summation of the hydrogen bond acceptor propensities of the solvent (Abraham, 1993a,b; Winget et al. 1999).
[d] Dipole moment in the unit of debye (Lide, 1995).
[e] Dielectric constant (Lide, 1995).
[f] Cohesive energy density in the unit of J mol/ml was calculated from the equation, $(\Delta H_{vap} - RT)/V$, where ΔH_{vap} is the enthalpy of vaporization, R is the gas constant, T is temperature of interest and 298.15 K was used in the calculation, and V is the molar volume at 298.15 K. The value of ΔH_{vap} and V was collected from the reference (Lide, 1995).
[g] Viscosity of the solvent at 25 °C in the unit of mPa s (Lide, 1995).
[h] Surface tension of the solvent at 25 °C in the unit of cal/(mol Å^2) (Lide, 1995, Winget et al. 1999).

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