Solvents and solvent selection for chromatography

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Solvent strength

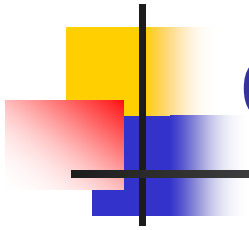
Single parameter estimate of a solvent's ability to cause migration in a chromatographic system

- Not a fundamental solvent property since it depends on the system
- Determined by experiment

Solvent selectivity

- The parameter that distinguished the ability of a solvent to provide separation as well as migration
  - Determined by the solvent's capability to enter into specific intermolecular interactions
    - Dispersion
    - Orientation
    - Induction
    - Hydrogen bonding

Methods for solvent selectivity characterization



- Solubility parameters
  - No general agreement on how to calculate partial polar solubility parameters
- Solvent triangle classification
  - Each intermolecular interaction associated with a single prototypical solute
- Solvatochromic parameters
  - Considers only the polar interactions of a solvent and not its cohesive energy

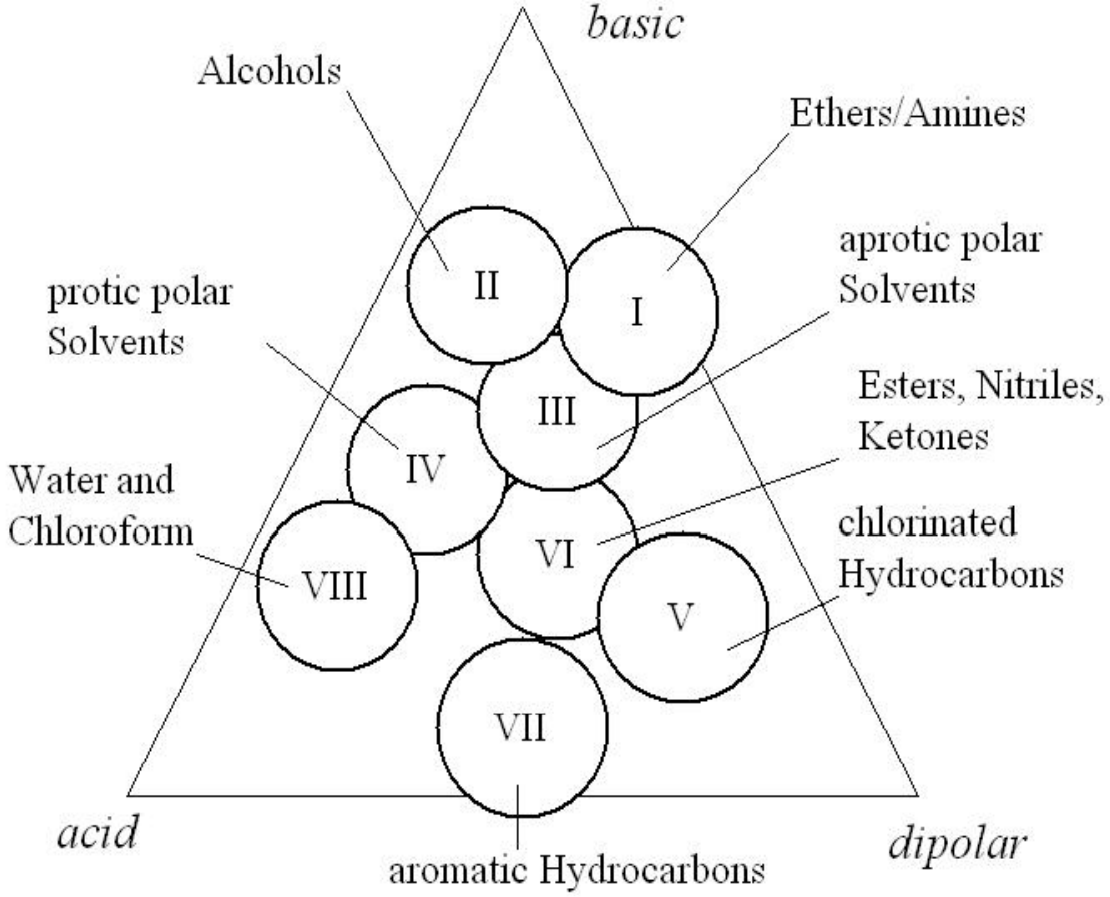
Prototypical solutes

Polar solutes with a single dominant intermolecular interaction are virtually unknown

All solutes that are hydrogen bonding are simultaneously dipolar

Ethanol	Nitromethane	Dioxane
S = 0.42	S = 0.95	S = 0.75
A = 0.37	A = 0.06	A = 0
B = 0.38	B = 0.31	B = 0.64

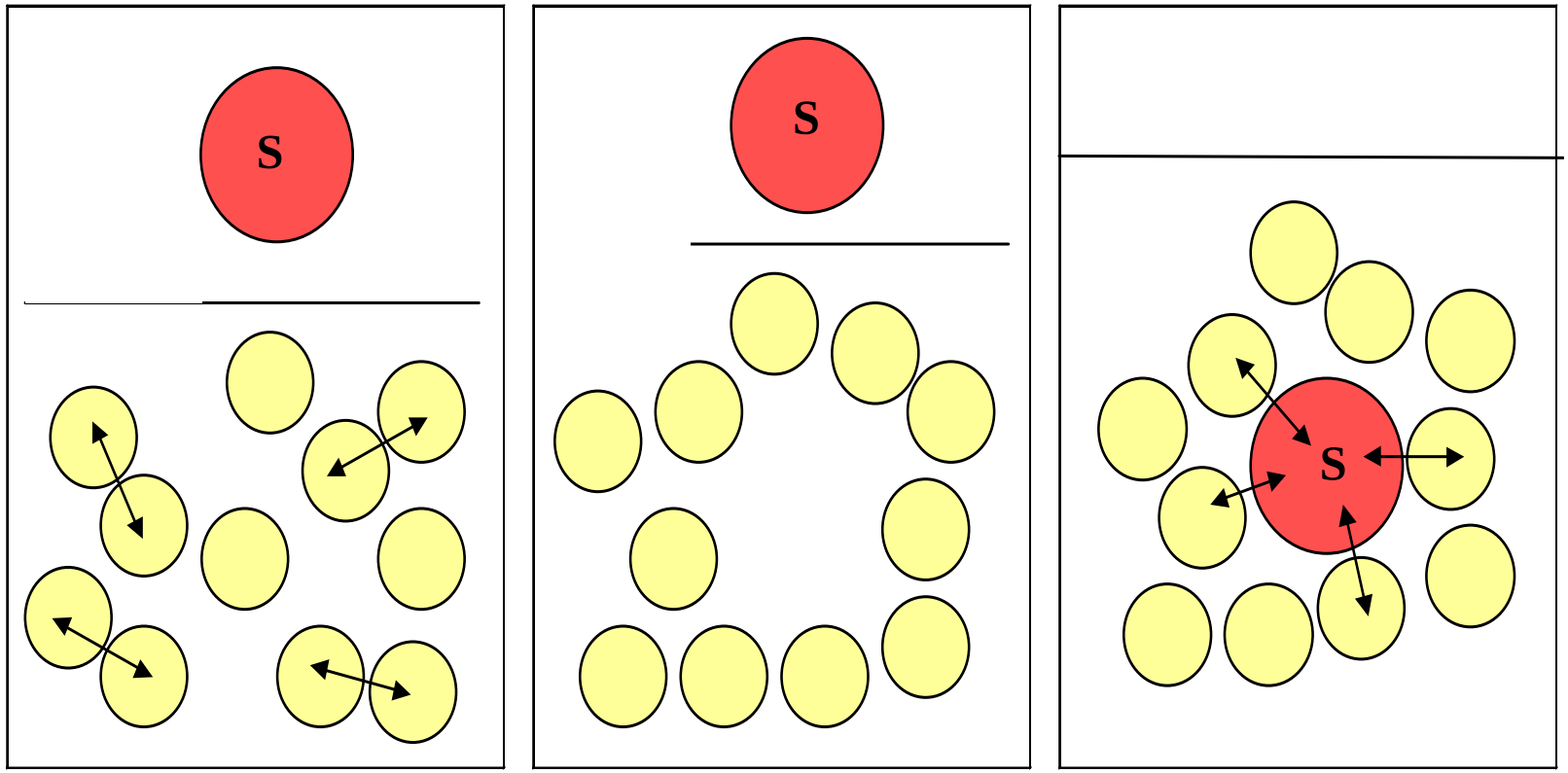
Solvent selectivity triangle



A.R. Johnson, M.F. Vitha, J. Chromatogr. A 1218 (2011) 556-586

Cohesive Energy

Cavity Formation → Reorganization → Solute-Solvent Interactions



Solvation parameter model

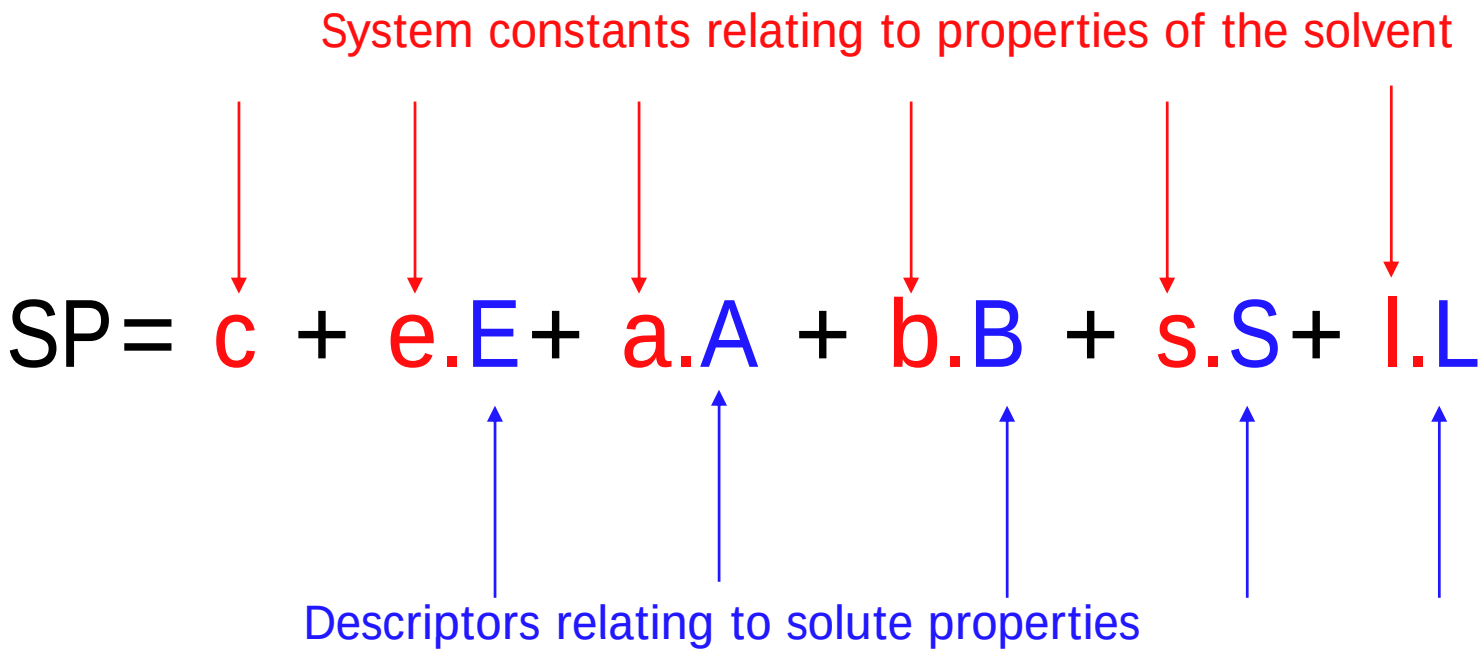
Contains a term to accommodate cavity formation

(differences in cohesive energy of solvents)

Assigns general properties to solutes based on their capability for simultaneous multiple interactions

- Dispersion
- Dipole-type (orientation and induction)
- Hydrogen bonding (donor and acceptor properties)

Solvation Parameter Model



SP = free energy related property

Solute descriptors

- V is McGowan's Characteristic Volume
- E is the excess molar refraction
- S is the solute dipolarity/polarizability
- A is the effective solute hydrogen-bond acidity
- B is the effective solute hydrogen-bond basicity
- L is the gas-liquid partition coefficient at 25°C with hexadecane as a solvent

C.F. Poole, S.N. Atapattu, S.K. Poole, A.K. Bell, Anal. Chim. Acta 652 (2009) 32-53.

Solvation parameter model

System Constant	Solute Descriptor	Free Energy Contribution
l	**L**	***Ease of cavity formation*** (solvent-solvent interactions) ***Dispersion interactions*** (solute-solvent interactions)
e	**E**	***Electron lone pair interactions***
s	**S**	***Dipole-type interactions***
a	**A**	***Solvent hydrogen-bond base-solute hydrogen-bond acid interactions***
b	**B**	***Solvent hydrogen-bond acid-solute hydrogen-bond base interactions***

Solvent properties

Transfer of solutes from the gas phase to a solvent is defined by 5 system constants

- The system constants are independent of solute identity
- System constants are calculated from the experimental properties of a number of varied compounds
- Data requirements established by statistical parameters

Solvent Properties

Solvent	System constants				
	e	*s*	*a*	*b*	*l*
N-Heptane	*-0.16*	*0*	*0*	*0*	*0.98*
Chloroform	*-0.59*	*1.26*	*0.28*	*1.37*	*0.98*
Acetone	*-0.39*	*1.73*	*3.06*	*0*	*0.87*
Methanol	*-0.22*	*1.17*	*3.70*	*1.43*	*0.77*
Trifluoroethanol	*-0.61*	*1.46*	*1.90*	*4.46*	*0.63*
Water	*0.82*	*2.74*	*3.90*	*4.81*	*-0.21*

Alkanes

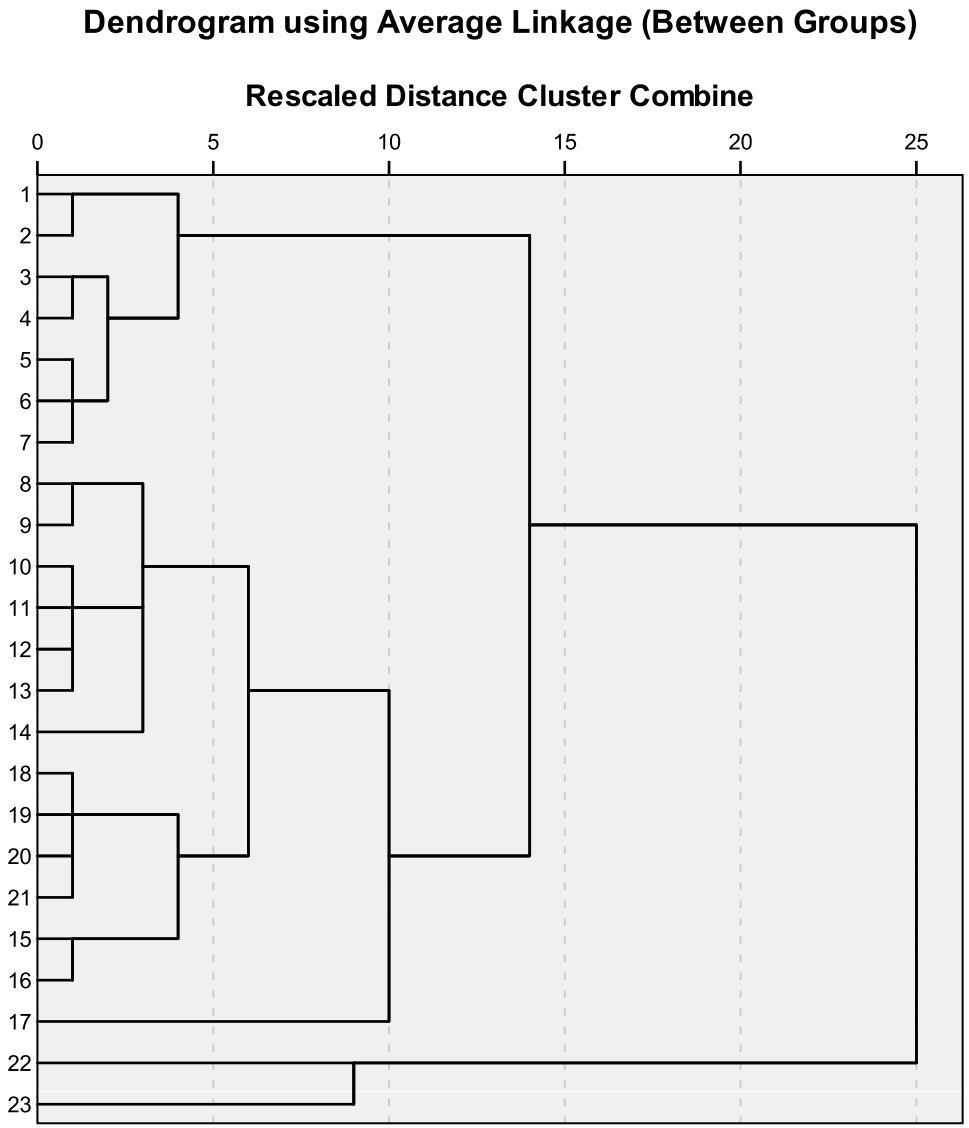
Aromatic Hydrocarbonds

Chloroalkanes

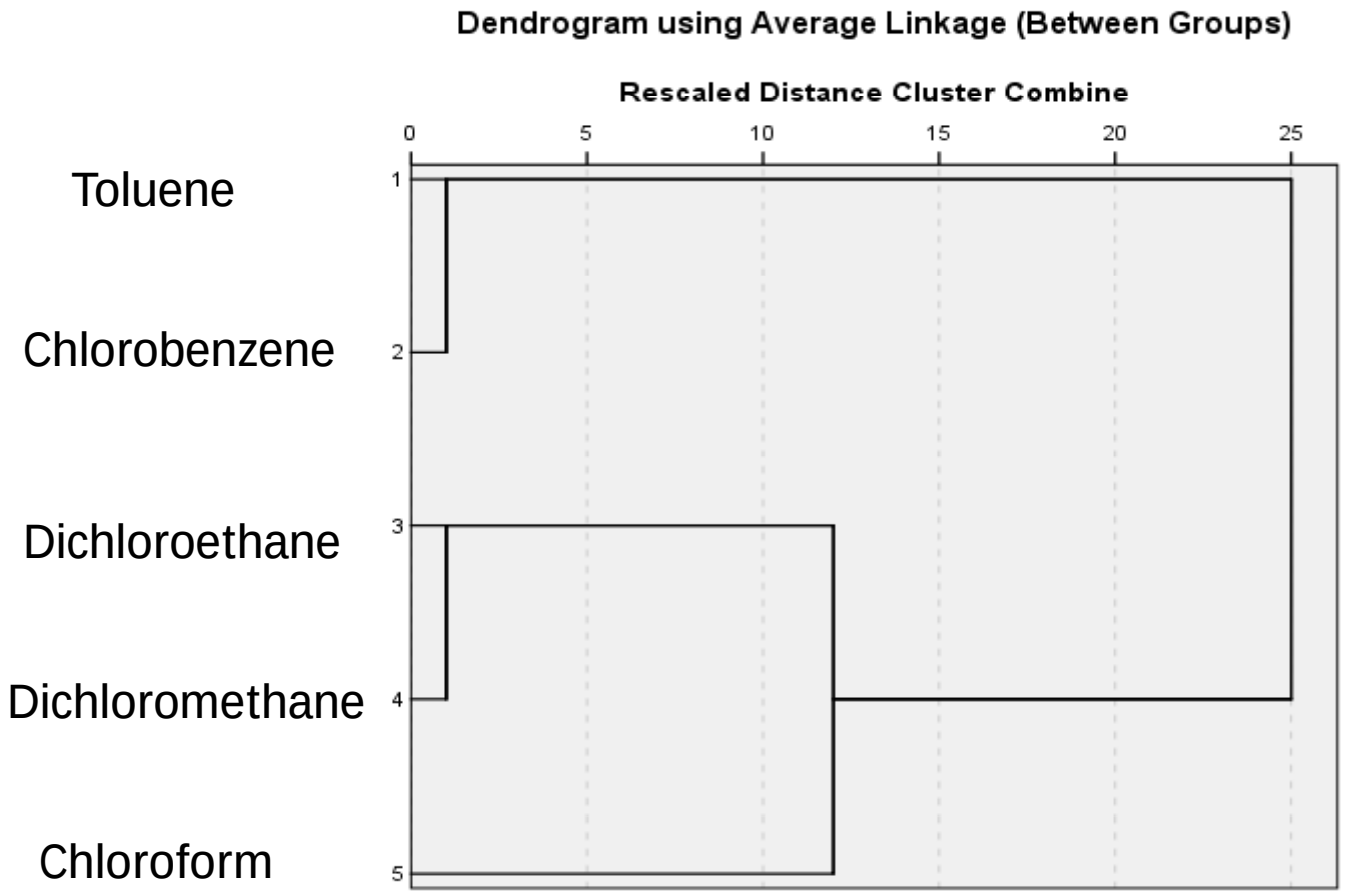
Ethers
Ketones
Esters

Alcohols

Water



Group 2


Dendrogram using Average Linkage (Between Groups)
Rescaled Distance Cluster Combine
0
5
10
15
20
25
1
2
3
4
5
Toluene
Chlorobenzene
Dichloroethane
Dichloromethane
Chloroform

Methyl *t*-Butyl Ether

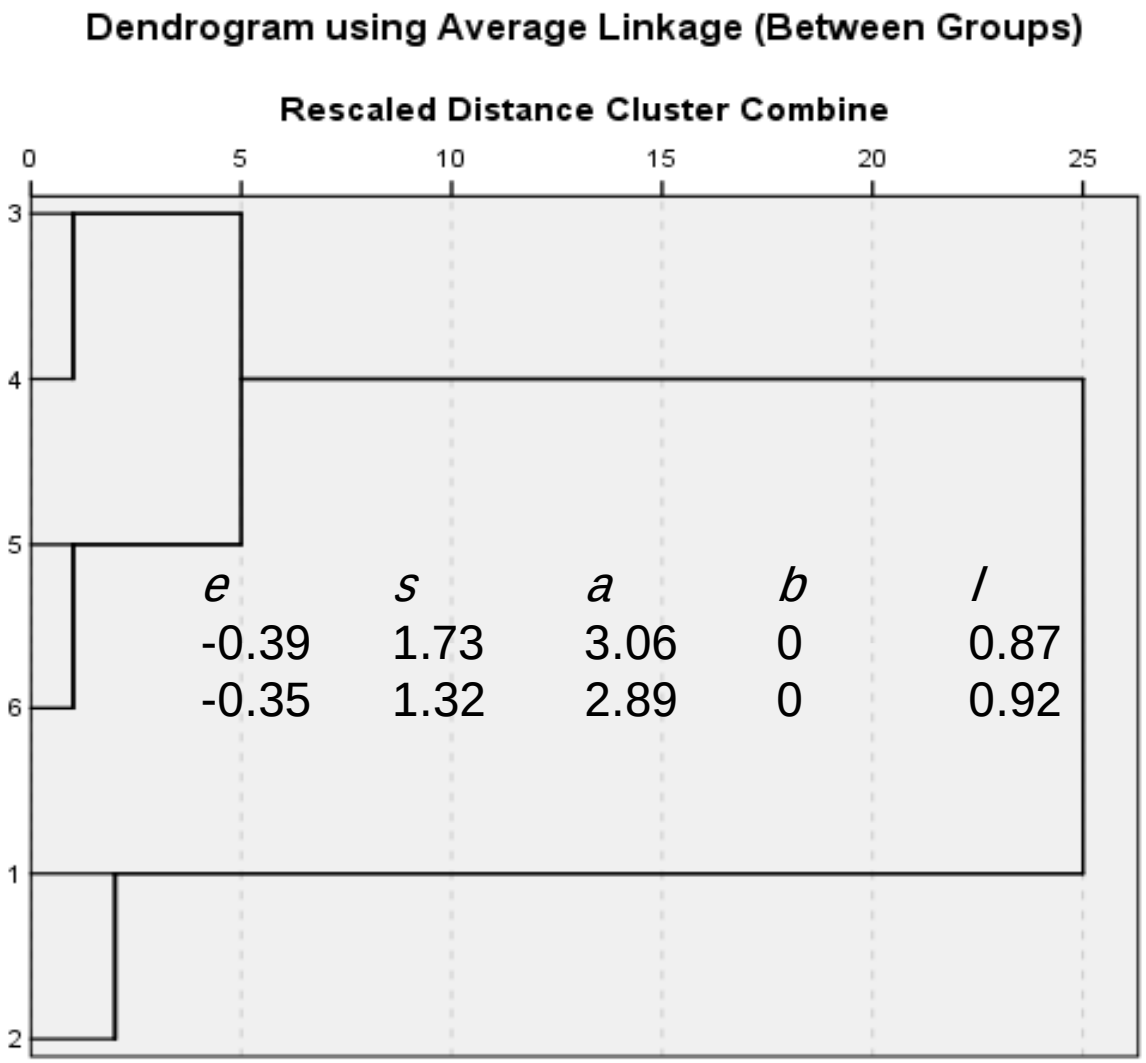
Diethyl Ether

Acetone

Ethyl Acetate

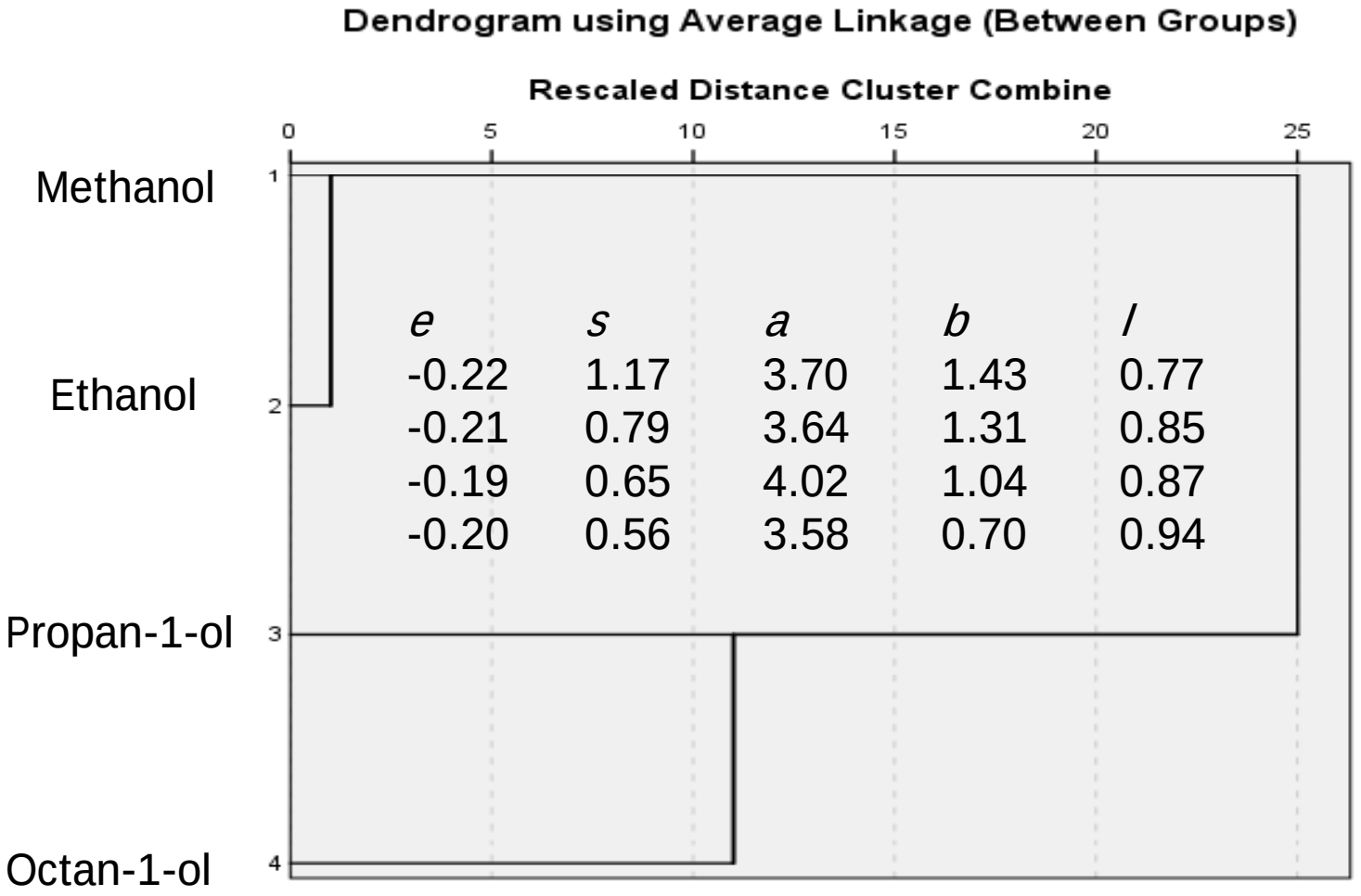
Acetonitrile

Propylene Carbonate

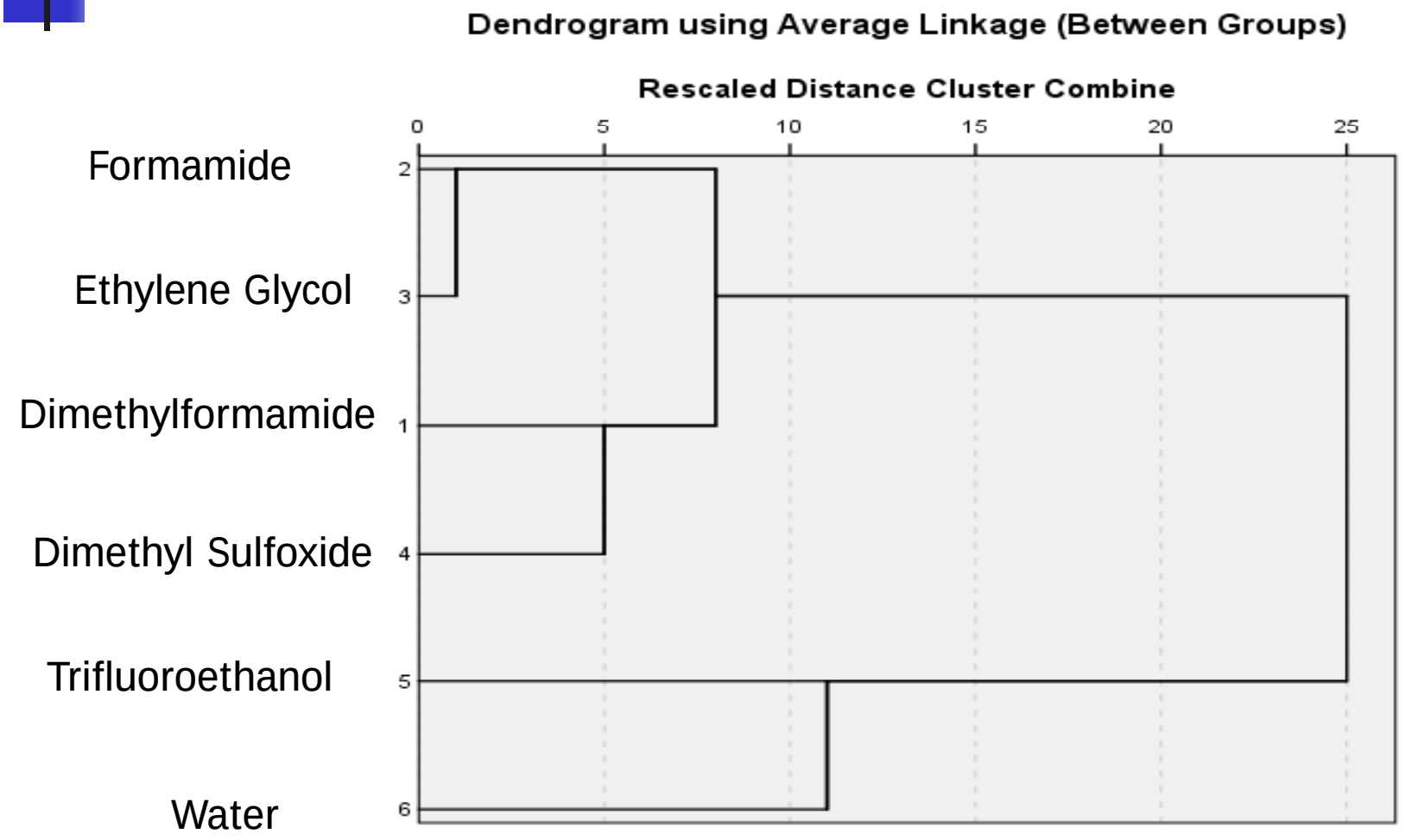


e	*s*	*a*	*b*	*l*
-0.39	1.73	3.06	0	0.87
-0.35	1.32	2.89	0	0.92

n-Alcohols


Dendrogram using Average Linkage (Between Groups)
Rescaled Distance Cluster Combine
0
5
10
15
20
25
Methanol
Ethanol
Propan-1-ol
Octan-1-ol
1
2
3
4
e s a b l
-0.22 1.17 3.70 1.43 0.77
-0.21 0.79 3.64 1.31 0.85
-0.19 0.65 4.02 1.04 0.87
-0.20 0.56 3.58 0.70 0.94

Solvents behaving independently



Solvents behaving independently

Solvent	**System constants**				
	e	*s*	*a*	*b*	*l*
Dimethylformamide	*-0.87*	*2.11*	*3.77*	*0*	*1.01*
Formamide	0.31	2.29	4.13	1.93	0.44
Ethylene Glycol	0.13	1.66	4.46	2.36	0.57
Dimethyl sulfoxide	*0.13*	*2.81*	*5.47*	*0*	*0.73*
Trifluoroethanol	-0.61	1.46	1.90	4.46	0.63
Water	0.82	2.74	3.90	4.81	-0.21

Solvent selection for method development in thin-layer chromatography

- n-Heptane
- Toluene
- Dichloromethane
- Chloroform
- Methyl *t*-Butyl Ether
- Acetone
- Acetonitrile
- Methanol
- Propan-1-ol
- Formamide
- Dimethylformamide
- Trifluoroethanol
- Water

Solvation parameter model

Gas → Condensed Phase

$$SP = c + eE + sS + aA + bB + lL$$

Condensed Phase → Condensed Phase

$$SP = c + eE + sS + aA + bB + vV$$

SP = free energy related property

Totally organic biphasic systems

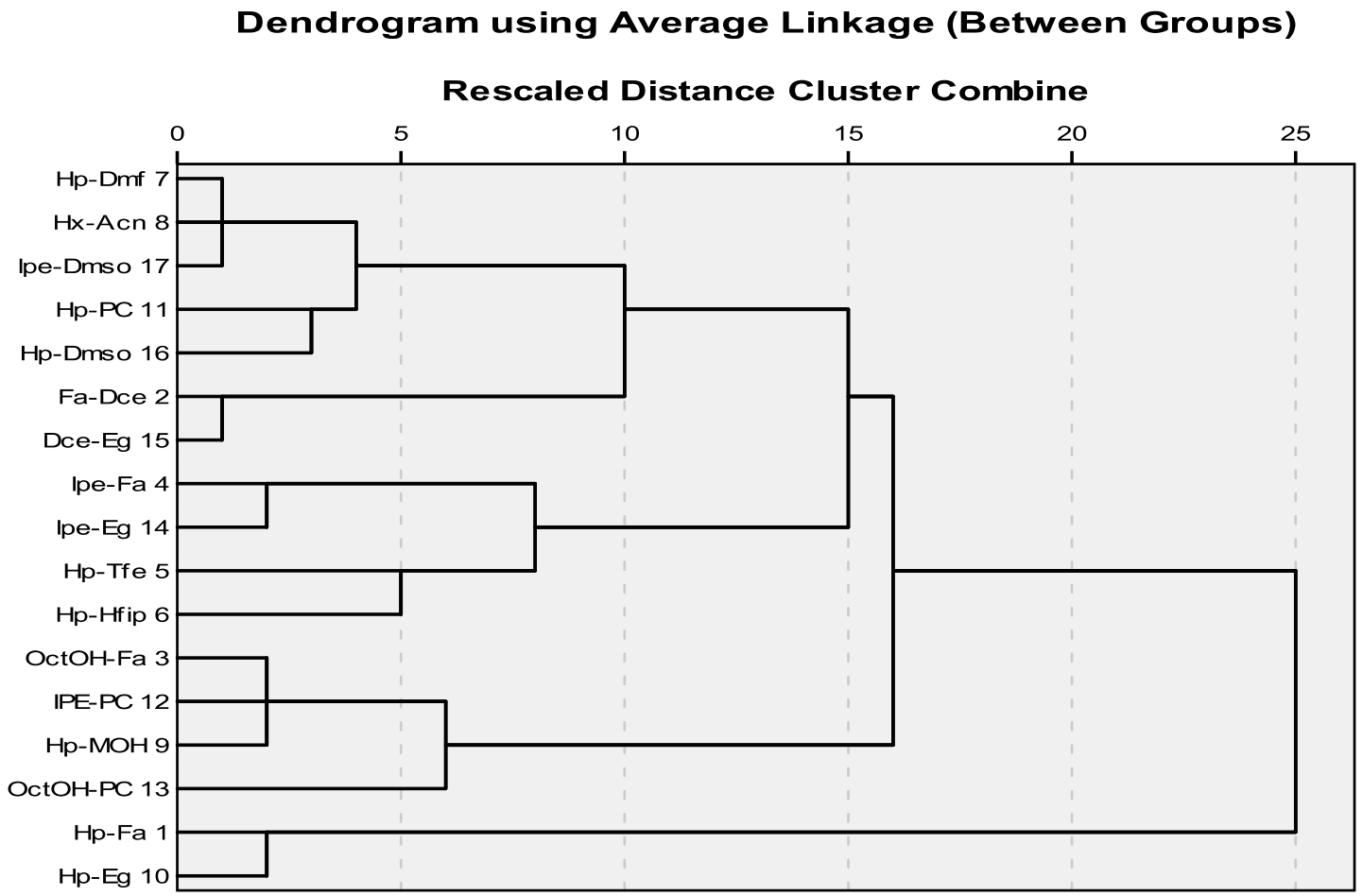
	Heptane	Isopentyl Ether	Dichloro-ethane	Octanol
Acetonitrile	IM	M	M	M
Propylene carbonate	IM	IM	M	IM
Formamide	IM	IM	IM	IM
Dimethylformamide	IM	IM	M	M
Dimethyl sulfoxide	IM	IM	M	M
Methanol	IM	M	M	M
Ethylene glycol	IM	IM	IM	M
Trifluoroethanol	IM	M	M	M

M = miscible and IM = low mutual solubility

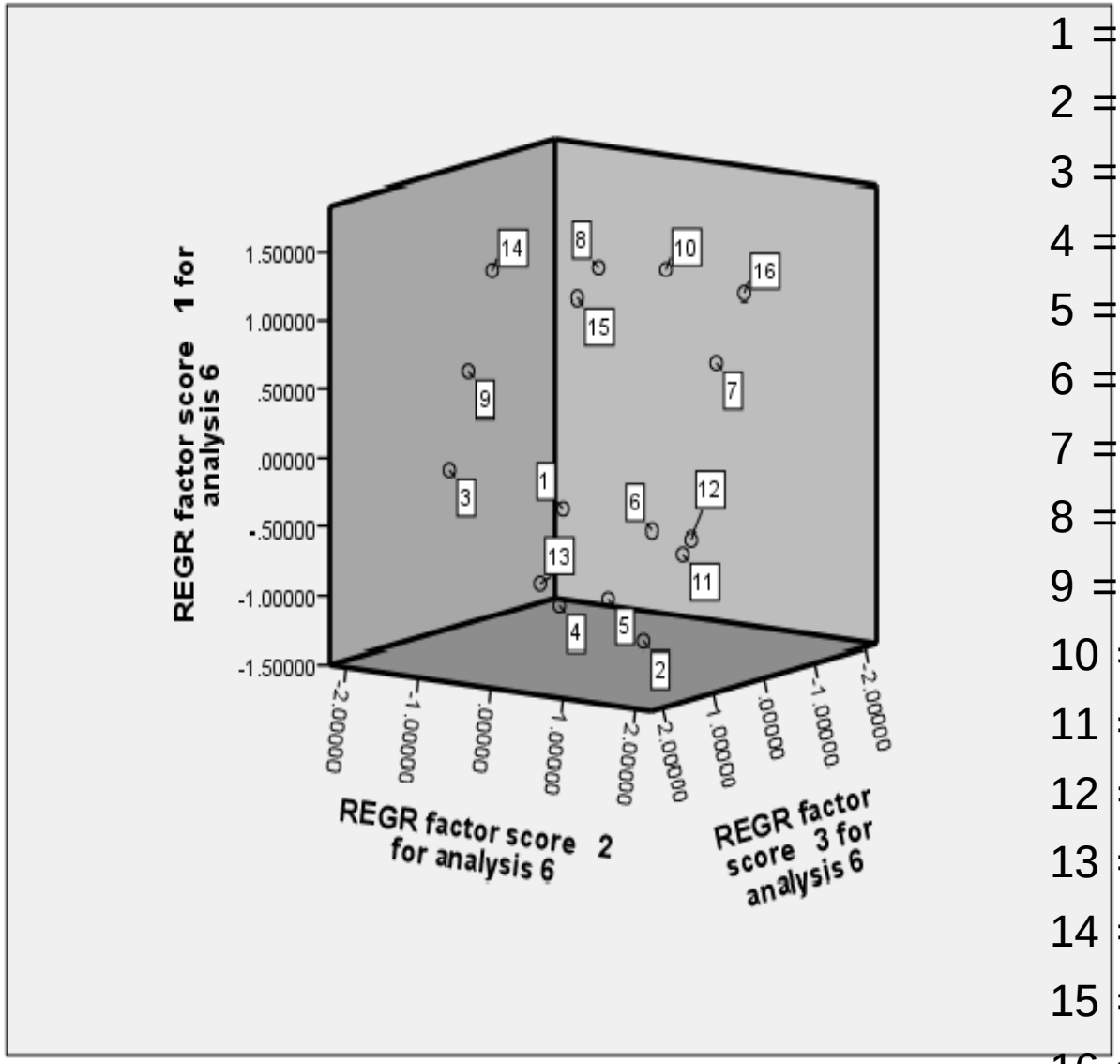
Biphasic systems formed with heptane

Counter Solvent	System constants *e*	*s*	*a*	*b*	*v*
Acetonitrile	0.35	-1.44	-1.61	-0.87	0.67
Methanol	0.19	-0.69	-1.10	-0.95	0.62
Ethylene glycol	0.09	-1.55	-3.78	-1.55	2.13
Formamide	0.56	-2.24	-3.25	-1.61	2.39
Dimethylformamide	0.04	-1.39	-2.16	-0.59	0.49
Dimethyl sulfoxide	0	-1.78	-3.09	-1.17	1.18
Propylene carbonate	0.45	-2.09	-2.65	-0.43	0.81
Trifluoroethanol	0.88	-1.56	-1.31	-2.93	1.30
Water	0.67	-2.06	-3.32	-4.73	4.54

Totally organic biphasic systems



Biphasic systems including water



1 = Heptane-Formamide
2 = Formamide-Dichloroethane
3 = Octanol-Formamide
4 = Isopentyl ether-Formamide
5 = Heptane-Trifluoroethanol
6 = Heptane-Dimethylformamide
7 = Heptane-Acetonitrile
8 = Heptane-Methanol
9 = Heptane-Ethylene glycol
10 = Chloroform-Water
11 = Cyclohexane-Water
12 = Octanol-Water
13 = Toluene-Water
14 = Di-n-Butyl ether-Water
15 = Heptane-Water
16 = Dichloroethane-water

Dimethyl sulfoxide-Heptane

Compound	Contribution to the partition coefficient (log K_p)				
	*s*S	*a*A	*b*B	*v*V	Estimated (K_p)
Anthracene	2.317	0	0.303	-1.716	4.12
Fluoranthene	2.639	0	0.323	-1.870	6.35
Pyrene	2.627	0	0.334	-1.870	6.33
Naphthalene	1.606	0	0.225	-1.280	1.83
1-Acetonaphthone	2.486	0	0.644	-1.632	16.2
1-Nitronaphthalene	2.629	0	0.338	-1.489	15.5
1-Naphthol	2.007	2.338	0.384	-1.350	1230
Bicyclohexyl	0.534	0	0	-1.867	0.024
Phenylcyclohexyl	1.058	0	0.082	-1.715	0.140

e = 0 for the heptane-dimethyl sulfoxide system

Inorganic Oxides

- Solvent strength parameter for silica gel

$\varepsilon^{\circ} = -0.264V + 0.199S + 0.384A + 0.355B + 0.272$

Can be used to estimate ε° values to about 0.04 units for solvents lacking experimental values