[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF WASHINGTON.]

COMPARATIVE SOLUBILITIES IN WATER, IN PYRIDINE AND IN AQUEOUS PYRIDINE.

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In determining by the colorimetric method the solubilities of helianthine in water, in pyridine and in aqueous mixtures of the two, the following values were obtained:

Solvent.	Solubility.	Ratio to 50% pyridine.
Water	0.02	3125
Pyridine	0.75	83.3
50% pyridine	62.50	1

That helianthine is so vastly more soluble in mixtures of the two than in either of the solvents, led to the present investigation to ascertain what compounds show similar solubilities and to learn, if possible, the cause of this remarkable property.

In examining the literature for analogous solubilities, the papers of Holleman and Antusch,[1] Herz and Knoch[2] revealed maxima of solubility in mixtures of two solvents. The former found such with benzamide, acetanilide,[3] acetnaphthalide, etc., in water and alcohol; the latter, with certain inorganic salts and with succinic acid in water and acetone.

The following table of solubilities is made up of both original determinations and such others as were given in the literature.[4] Solubilities of compounds in pyridine were found to have been studied only in rare cases.[5] This is surprising, in view of the fact, as shown below, that it possesses unique properties as an organic solvent.

The determinations of solubilities were all made at room temperatures of 20° to 25° and are expressed as grams of solute to 100 g. of solvent.

Excesses of the substances and 5 cc. of solvent were enclosed in small vials, which when stoppered were shaken or were let stand until equilibria were established. The solutions were filtered into weighed crucibles and reweighed. After drying in vaccum desiccators or on the water bath, the crucibles were again weighed and the loss of solvent calculated.

Since these experiments are merely intended for a preliminary survey of the field, no great accuracy is claimed for the following reasons:

(1) The compounds tested, though mostly from reliable firms, evidently were not always pure.

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[1] *Rec. trav. chim.*, 13, 277 (1894).

[2] *Z. anorg. Chem.*, 1, 315 (1904).

[3] THIS JOURNAL, 29, 1088 (1907). Seidell studied the solubilities of acetanilide in mixtures of water and alcohol at different temperatures and obtained similar curves.

[4] Seidell's "Solubilities of Inorganic and Organic Substances," 1907, was an invaluable aid in this connection.

[5] Holty, *J. Phys. Chem.*, 9, 764 (1905); Schmoltz, *Arch. Pharm.*, 250, 418 (1913).

(2) Some of the compounds, being somewhat volatile, were partially lost by evaporation with the solvent.

(3) Many of the compounds formed salts which variously gave up pyridine either easily, slowly or not at all.

(4) Some of the salts being insoluble, protected the original substance from dissolving in the solvent, hence true equilibria at room temperatures may not have been obtained in all cases.

(5) Errors of weighing, of supersaturation, etc., may also be involved.

(6) Most of the omissions of the table resulted from lack of material.

GRAMS OF SUBSTANCES SOLUBLE IN ONE HUNDRED GRAMS OF SOLVENTS AT 20–25°.

	Name.	Water.	$C_5H_5N.H_2O$.	C_5H_5N.
1.	Acetamide	97.50+	84.70	17.75
2.	Acetanilide	0.55+	55.55	48.61
3.	Alanine (alpha)	16.47+	0.16	0.16
4.	Albumin (egg)	100.00	6.29	0.10
5.	Alizarine	0.04	∞[6]	∞
6.	Antipyrine	100.00+	79.61	38.00
7.	Asparagine	2.40+	0.15	0.03
8.	Atropine	0.22+	....	73.00+
9.	Azobenzene	0.03	16.78	76.44
10.	Azolitmin	39.50	0.12	0.05
11.	Benzamide	1.35+	39.15	31.23
12.	Benzoin	0.03	6.63	20.20
13.	Brucine	0.05+	46.11	28.00+
14.	Caffein	2.19+	11.12	34.39
15.	Carmine	0.13	2.03	3.34
16.	Casein	2.01	0.56	0.09
17.	Chloral hydrate	383.00+	374.00	80.90
18.	Cholesterol	0.26	1.10	68.10
19.	Cinchonidine	0.025+	10.00	7.78
20.	Cinchonine	0.024+	....	1.40
21.	Cocaine[2]	0.04+	....	80.00+
22.	Congo red	11.60	7.32	0.29
23.	Cumarin	0.01	60.08	87.7
24.	Diazoaminobenzene	0.05	67.70	136.70
25.	Dimethylaminoazobenzene	0.016	4.51	27.90
26.	Dinitrobenzene (meta)	0.05+	45.50	106.30
27.	Diphenylamine	0.03	two layers[3]	302.00
28.	Diphenylurea	0.015	5.3	6.85
29.	Edestin[4]	0.0	9.05	0.07
30.	Erythritol	61.50	8.47	2.50+
31.	Fluorescene[5]	0.005	37.22	13.29
32.	Galactose	68.30	6.83	5.45+
33.	Gelatin	....	0.07	....
34.	Glucose	82.00+	49.17	7.62+
35.	Glycocoll	51.00	0.74	0.61
36.	Haemoglobin	15.16	0.77	0.15
37.	Hippuric acid	0.42	88.00	∞[6]
38.	Hydroquinol	7.18+	∞	∞

GRAMS OF SUBSTANCES SOLUBLE IN ONE HUNDRED GRAMS OF SOLVENTS AT 20–25° (*continued*).

	Name.	Water.	$C_5H_5N.H_2O$.	C_5H_5N.
39.	Iodoeosine	90.00	71.60	4.63
40.	Iodoform	0.01+	22.39	173.10
41.	Keratin	8.71	16.00	∞
42.	Lactose[1]	19.54+	1.98	2.18+
43.	Laevulose	....	85.42	18.48+
44.	Maltose	108	43.07	98.10
45.	Mannitol	18.98+	2.46	0.47+
46.	Mannose	....	78.70	29.90
47.	Methyl orange	0.02	51.50	1.80
48.	Methyl oxalate	6.18	93.10	4.80
49.	Methylene blue	4.36	0.74	0.26
50.	Michler's ketone	0.04	3.59	9.92
51.	Morphine	0.03+	....	19.00+
52.	Narcotine	....	....	2.30+
53.	Nitrobenzene (ortho)	0.21+	173.00	260
54.	Nitrobenzene (meta)	2.14+	Two layers	394
55.	Nitrobenzene (para)	1.32+	85.30	53.20
56.	Papaverine	....	....	8.00+
57.	Peptone	42.20	12.60	0.22
58.	Phenacetin	0.10+	28.94	17.39
59.	Phenolphthalein	0.04	300.00	769.00
60.	Phloroglucinol	1.13	134.00	296.00
61.	Phthalic anhydride	0.60+	∞[6]	83.50
62.	Phthalimide	0.06	7.74	14.15
63.	Picrotoxine	0.41+	81.00	102.00
64.	Piperine	0.01	11.39	22.46
65.	Pyrocatechol	45.10+	251.0	∞
66.	Quinine	0.057+	59.4	101.00+
67.	Raffinose	14.30+	8.76	75.00
68.	Resorcinol	103.00+	901.00	∞[6]
69.	Rosaniline	0.03	35.10	41.50
70.	Rosolic acid	0.12	80.00	160.00
71.	Salol	0.04	two layers[3]	381.00

[1] The solubilities of the sugars in pyridine are given by Holty, *Loc. cit.*

[2] The solubilities of the alkaloids in pyridine are given by Schmoltz, *Loc. cit.*

[3] Diphenylamine and salol formed too layers in $C_5H_5N.H_2O$. The formation of two layers by a solute in mixtures of two solvents has frequently been observed. Traube and Neuberg, *Z. physik. Chem.*, **1**, 509 (1897); Bodländer, *Ibid.*, **7**, 308 (1901); Hertz and Knoch, *Z. anorg. Chem.*, **41**, 315 (1904).

[4] Edestin is held by Osborne to be entirely insoluble in water. *The Vegetable Proteins*, **1909**, 22.

[5] A colorless addition product of fluorescence and pyridine is described by Oddo, *Gazz. chim. ital.*, **44**, I, 713 (1914).

[6] The sign ∞ is used to indicate that the pyridine and the substance completely solidified. that is, both liquid and solid phases did not exist in the presence of an excess of the solute. It will be observed that cases of this kind involve acids, pseudo-acids and phenols and thus salt formation is indicated. The case of phthalic anhydride was especially interesting as it solidified only in the presence of $C_5H_5N.H_2O$, thus indicating simultaneous hydration and salt formation.

GRAMS OF SUBSTANCES SOLUBLE IN ONE HUNDRED GRAMS OF SOLVENTS AT 20–25° (*continued*).

	Name.	Water.	$C_5H_5N.H_2O$.	C_5H_5N.
72.	Santonin	0.02+	12.35	12.72
73.	Strychnine	0.02+	2.43	1.23+
74.	Sucrose[1]	204.00+	38.50	6.45+
75.	Thebaine	....	....	9.00+
76.	Thiourea	9.10+	41.20	12.50
77.	Toluidine (para)	6.54+	96.10	126.00
78.	Tribromobenzene	0.004	2.01	24.30
79.	Urea	79.00+	21.53	0.96
80.	Urethane	153.33+	101.10	21.32
81.	Uric acid	0.006+	0.75	0.21
82.	Vanillin	1.00	....	316.00
83.	Veratrine	0.057+	....	175.00+
84.	Vesuvin	8.50	31.40	11.10
85.	Dextrine	....	102.00	65.44

General Observations.

(1) Many substances besides helianthine are more soluble in $C_5H_5N.H_2O$ than in pure water or in pure pyridine. See especially numbers 2, 11, 13, 19, 29, 31, 47, 48, 55, 58, 61, 73, 76, 81, 84. It will be observed that certain dyes, alkaloids, and other nitrogen-containing compounds are especially susceptible to this influence.

(2) Some sugars as lactose, maltose and raffinose are *less* soluble in $C_5H_5N.H_2O$ than in pure water or in pure pyridine.

(3) More than twenty of the compounds studied are most soluble in pure water.

(4) More than twenty of the compounds studied are most soluble in pure pyridine.

Using one solute and two solvents (A) and (B) and their mixtures (AB), as showed above, it is observed that a number of possibilities arise.[2] The respective solubilities are: (1) Greatest in some mixture of (AB); (2) least in some mixture of (AB); (3) greatest in (A), and (4) greatest in (B). All four of these cases are met with when pyridine and water are used.

Rules of Solubility.

The most general and useful rules of solubility are given by Bigelow[3] (1), Ostromysslensky[4] (2, 3, 4) and Carnelly[5] and Thomson (5, 6, 7, 8):

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[1] The solubilities of the sugars in pyridine are given by Holty, *Loc. cit.*

[2] As examples of curves of solubility in mixtures of alcohol and water, typifying these cases may be mentioned: (1) acetanilide, benzamide, etc., of Holleman and Antusch (*loc. cit.*); (2) no cases are known; (3) triphenylguanidine, trinitrobenzene of Holleman and Antusch and various simple esters of Bancroft (*Phys. Rev.*, **3**, 205 (1895–96)); (4) sucrose of Schrefeld, *Z. Ver. Zuckerind.*, **49**, 971 (1894).

[3] "Theoretical and Physical Chemistry," **1914**, 335.

[4] *J. prakt. Chem.*, **76**, 264 (1908).

[5] *J. Chem. Soc.*, **53**, 791 (1888). Bogojawlenski, Bogoljuboff and Winogradoff, *Chem. Zentr.*, **1907**, 1738, confirm all the rules of Carnelly and Thomson except the last.

(1) "Chemically similar substances are usually mutually soluble and chemically dissimilar substances are usually but very slightly soluble in each other."

(2) "Homologs are mutually soluble."

(3) "Stereoisomers are mutually soluble."

(4) "Poly-substituted products are mutually soluble."

(5) "The most fusible isomeric substances are the most soluble."

(6) "The most fusible isomeric acids are the most soluble; the solubilities of their salts are in the same order."

(7) "The order of solubility of isomeric compounds is the same in all solvents."

(8) "The ratio of solubility of two isomers in any given solvent is nearly constant and is independent of the nature of the solvent."

When pyridine is dissolved in water, heat is evolved and one or more hydrates[1] are formed. The most commonly recognized hydrate is $C_5H_5N.2H_2O$. It is thus very probable that a pyridonium form,[2] such as $C_5H_5N : H_2O$, or its further hydrated molecule, is the true solvent. Therefore, we are really dealing with three different physical solvents, *viz.*, H_2O, $C_5H_5N : H_2O$ and C_5H_5N. The situation is further complicated by the *chemical* properties of the pyridine—it easily forms additive salts and tends to form other additive compounds.[3]

Special Observations.

(1) Acids, pseudo acids and phenols apparently form salts with pyridine though few of these salts have been studied. These salts bear to pyridine the relation expressed by the first rule of solubility, hence the greater solubility of these substances in pure pyridine.

(2) Other substances not recognized as forming salts or additive com-

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[1] Goldsmith and Constam give the hydrate $C_5H_5N.3H_2O$ boiling at 92–3° (*Ber.*, **16**, 2977 (1883)). In a private communication to the Beilstein, Henry gives the hydrate $C_5H_5N.H_2O$. Band gives $C_5H_5N.2H_2O$ and $C_5H_5N.6H_2O$ (*Compt. rend.*, **148**, 96 (1909)). Later he finds the maximum density, refraction and heat evolution at 65–6% of pyridine, corresponding to the formula $C_5H_5N.2H_2O$, a solid whose aqueous solutions are considerably dissociated. *Bull. soc. chim.*, **5**, 1022 (1910). Timmumans also shows that the dihydrate is formed. *Bull. soc. chim. belg.*, **26**, 382 (1913). See also deConinck's hydrate, boiling at 91–2°. *Ibid.*, **24**, 55 (1910).

Other studies of aqueous pyridine indicate that hydrates are formed. "Density, viscosity, etc., experiments." Dunstan, Thole and Hunt, *J. Chem. Soc.*, **91**, 1732 (1907); **93**, 561 (1908); Hartley, Thomas and Applebey, *Ibid.*, **93**, 538 (1908); Holmes, *Ibid.*, **90**, 1784 (1906). "Electrical Conductivities," Hantzsch and Caldwell, *Z. physik. Chem.*, **61**, 227 (1908); Morgan and Kanoth, THIS JOURNAL, **28**, 5721 (1906); Baskov, *J. Russ. Phys. Chem. Soc.*, **46**, 1699 (1914). "Critical Solution Concentration," Flashner, *J. Chem. Soc.*, **95**, 675 (1909). "Vapor Pressures," Zawidzki, *Z. physik. Chem.*, **35**, 129 (1900). "Absorption of Electric Waves," Bredig, *Z. Electrochem.*, **7**, 767 (1901).

[2] Dunstan, Thole and Hunt, *J. Chem. Soc.*, **91**, 1732 (1907).

[3] For additive compounds of pyridine see Beilstein and THIS JOURNAL, **33**, 1594 (1911); **34**, 295, 1408, 1413 (1912); **36**, 2101 (1914); **37**, 2130 (1915).

pounds may yield these very additive compounds. For instance, iodoform is 17000 times more soluble in pyridine than in water; it is also known to form additive compounds with pyridine.[1] So also other substances possibly may form molecular compounds with pyridine and thus their solubilities in pyridine may be accounted for by Rules 1 and 2.

(3) Certain dyes (31, 47, 84), alkaloids (13, 19, 73), and allied substances (2, 11, 58, 76) are most soluble in $C_5H_5N.H_2O$. If these substances can be shown to form hydrates, such solutes and the solvent are observed to fall under Rules 1 and 2.

(4) Sugars are invariably most soluble in water, hence probably do not unite with the pyridine molecules. Maltose, lactose, and raffinose, however, are least soluble in $C_5H_5N.H_2O$. Being di- and tri-saccharides these three possibly absorb the molecule of water and the new solutes bear to the pyridine or to the $C_5H_5N.H_2O$ a relation of lowered solubility.

(5) Cholesterol is 262 times more soluble in pyridine than in water. As is well known, cholesterol is an antidote for saponins, toxalbumins, etc., substances of a basic nature. If it can be shown that cholesterol unites with pyridine and other bases, the detoxifying influence of it can be accounted for. This property of cholesterol, accurate studies of solubility in pyridine and its tendency to form additive compounds will be pursued.

The views expressed above are in accord with the views of many authors. For example, Hertz and Knoch[2] arrive at the conclusion that the solute combines with one of the mixed solvents. Holleman and Antsch[2] postulate that: (1) The two solutes form a molecular compound; (2) the solute combines with one of the solvents, or (3) the solute combines with molecular compound of the two solvents. The work of Hudson,[3] Abegg[4] and others assume attraction between the solute and the solvents to account for certain properties of solubility.

More extensive and accurate studies of pyridine, quinoline and other solubilities are to be made, also efforts will be made to prepare the molecular compounds indicated.

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STUDIES IN THE CYCLOPROPANE SERIES.

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Owing to the influence of Baeyer's "Strain Theory," most recent investigators of cyclopropane derivatives have been interested mainly

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[1] THIS JOURNAL, **34**, 1413 (1913).

[2] *Loc. cit.*

[3] *Z. physik. Chem.*, **17**, 114 (1904); *Phys. Rev.*, **23**, 370 (1906); THIS JOURNAL, **31**, 63 (1909).

[4] *Z. Electrochem.*, **7**, 677 (1901).