TITLE: ~~BUFFER COMPOUNDS~~
METHOD FOR BUFFERING A CHEMICAL OR BIOLOGICAL COMPOSITION

TECHNICAL FIELD

The present invention relates to buffer compounds, especially buffer compounds for use in biological systems, in which the buffer compound comprises amine-quaternary ammonium compounds. More particularly, the invention relates to buffer compounds in which the buffer molecule contains both an amine nitrogen atom and a quaternary ammonium nitrogen atom.

BACKGROUND

Classical buffer compounds are chemical compounds or agents that resist or minimize changes in hydrogen-ion concentrations when a system of interest is placed under chemical stress or physical stress. Chemical stress includes generation or consumption of hydrogen ions, change in ionic strength and change in solvent properties. Physical stress includes changes in temperature and/or pressure. In many circumstances it is useful or necessary to keep the pH constant or within a narrow range. Buffer compounds are often used in homogeneous aqueous solution, but they may also be used in solid or semisolid mixtures, in non-aqueous polar solvents or in creams, ointments or suspensions. Natural buffer compounds are used in biological systems or living cells to maintain or modulate the proper pH conditions. Natural and synthetic buffer compounds are used commercially in water treatment and sanitation, in agents to control corrosion, in fertilizer mixtures for agriculture, in medicinal formulations and personal care products, in foods and beverages, in fermentation and brewing, in paints and coatings, in human or animal drugs and in many other applications.

pH is a measurement of solvated hydrogen-ion activity, which is directly related to hydrogen ion concentration: $-\log[H^+]$. The strength of a monoprotic neutral acid (HA) or monoprotic conjugate acid of a neutral base (HB^+) are measured by the pK_a values for the respective reactions which are defined by:

$$HA + H_2O \rightleftharpoons OH_3^+ + A^- \qquad HB^+ + H_2O \rightleftharpoons OH_3^+ + B$$

$$pK_a = -\log K_a \text{ where } K_a = [OH_3^+][A^-] / [HA] \text{ or } K_a = [OH_3^+][B] / [HB^+]$$

Rearranged, these equations give:

Table 1 Reactions and Compounds

Cmpd	Method	Amine	Alkylating Agent	Est. pK_a	Chemical Formula	Molecular Weight
1	4	Morpholine [110-91-8]	gmac	---	$C_{10}H_{23}N_2O_2Cl$	238.76
1a		***1***·HCl		~5.6	$C_{10}H_{24}N_2O_2Cl_2$	275.22
2	4	Bis(2-methoxyethyl)amine [111-95-5]	gmac	---	$C_{12}H_{28}N_2O_3Cl$	283.83
2a		***2***·HCl		~5.9	$C_{12}H_{29}N_2O_3Cl_2$	320.29
3	4	Diethanolamine [111-42-2]	gmac	---	$C_{10}H_{25}N_2O_3Cl$	256.78
3a		***3***·HCl		~6.1	$C_{10}H_{26}N_2O_3Cl_2$	293.24
4	4	N-Methyl(2-methoxyethyl)amine [38256-93-8]	gmac	---	$C_{10}H_{25}N_2O_2Cl$	240.78
4a		***4***·HCl		~7.0	$C_{10}H_{26}N_2O_2Cl_2$	277.24
5	4	N-Methylethanolamine [109-83-1]	gmac	---	$C_9H_{23}N_2O_2Cl$	226.75
5a		***5***·HCl		~7.1	$C_9H_{24}N_2O_2Cl_2$	263.21
6	4	N-Ethyl-2-methoxyethylamine [34322-82-2]	gmac	---	$C_{11}H_{27}N_2O_2Cl$	254.81
6a		***6***·HCl		~7.3	$C_{11}H_{28}N_2O_2Cl_2$	291.27
7	4	N-Ethylethanolamine [110-73-6]	gmac	---	$C_{10}H_{25}N_2O_2Cl$	240.78
7a		***7***·HCl		~7.4	$C_{10}H_{26}N_2O_2Cl_2$	277.24
8	4	Dimethylamine [124-40-3]	gmac	---	$C_8H_{21}N_2OCl$	196.73
8a		***8***·HCl		~7.9	$C_8H_{22}N_2OCl_2$	233.19
8	5	N,N,N',N'-Tetramethyl-2-hydroxy-1,3-diaminopropane [5866-51-8]	CH_3Cl	---	$C_8H_{21}N_2OCl$	196.73
9	4	Piperidine [110-89-4]	gmac	---	$C_{11}H_{25}N_2OCl$	236.79
9a		***9***·HCl		~8.3	$C_{11}H_{26}N_2OCl_2$	273.25
10	4	Diethylamine [109-89-7]	gmac	---	$C_{10}H_{25}N_2OCl$	224.78
10a		***10***·HCl		~8.5	$C_{10}H_{26}N_2OCl_2$	261.24
11	4	Pyrrolidine [123-75-1]	gmac	---	$C_{10}H_{23}N_2OCl$	222.76
11a		***11***·HCl		~8.7	$C_{10}H_{24}N_2OCl_2$	259.22
12	10	Morpholine [110-91-8]	bptab	---	$C_{10}H_{23}N_2OBr$	267.22
12a		***12***·HBr		~5.8	$C_{10}H_{24}N_2OBr_2$	348.13
13	10	Diethanolamine [111-42-2]	bptab	---	$C_{10}H_{25}N_2O_2Br$	285.23
13a		***13***·HBr		~6.3	$C_{10}H_{26}N_2O_2Br_2$	366.14
14	10	N-Methylethanolamine [109-83-1]	bptab	---	$C_9H_{23}N_2OBr$	255.20

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14a		***14***·HBr		~7.3	$C_9H_{24}N_2OBr_2$	336.12
15	10	N-Ethylethanolamine [110-73-6]	bptab	---	$C_{10}H_{25}N_2OBr$	269.23
15a		***15***·HBr		~7.6	$C_{10}H_{26}N_2OBr_2$	350.14
16	10	Piperidine [110-89-4]	bptab	---	$C_{11}H_{25}N_2Br$	281.24
16a		***16***·HBr		~8.5	$C_{11}H_{26}N_2Br_2$	362.15
17	10	Diethylamine [109-89-7]	bptab	---	$C_{10}H_{25}N_2Br$	253.23
17a		***17***·HBr		~8.7	$C_{10}H_{26}N_2Br_2$	334.14
18	10	Pyrrolidine [123-75-1]	bptab	---	$C_{10}H_{23}N_2Br$	251.21
18a		***18***·HBr		~8.9	$C_{10}H_{24}N_2Br_2$	332.13
19	4	Tris(hydroxymethyl)aminomethane [77-86-1]	gmac	---	$C_{10}H_{25}N_2O_4Cl$	272.77
19a		***19***·HCl		~5.8	$C_{10}H_{26}N_2O_4Cl_2$	309.24
20	5	N,N'-Dimethyl-N,N'-bis(2-hydroxyethyl)ethylenediamine [14037-83-3]	CH_3Cl	---	$C_9H_{23}N_2O_2Cl$	271.20
20a		***20***·HCl		~5.2	$C_9H_{24}N_2O_2Cl_2$	352.12
21	5	1,4-Diazabicyclo[2.2.2]octane [280-57-9]	CH_3Cl	---	$C_6H_{15}N_2Cl$	150.66
21a		***21***·HCl		~3.1	$C_6H_{16}N_2Cl_2$	187.12
22	5	1,4-Dimethylpiperazine [106-58-1]	CH_3Cl	---	$C_7H_{17}N_2Cl$	164.68
22a		***22***·HCl		~4.3	$C_7H_{18}N_2Cl_2$	201.14
23	5	1,4-Diethylpiperazine [6483-50-7]	C_2H_5Br	---	$C_{10}H_{23}N_2Br$	164.68
23a		***23***·HBr		~4.6	$C_{10}H_{24}N_2Br_2$	201.14
24	5	1-Methyl-4-isopropylpiperazine [13480-33-6]	CH_3Cl	---	$C_9H_{21}N_2Cl$	164.68
24a		***24***·HCl		~5.0	$C_9H_{22}N_2Cl_2$	201.14
25	5	1-Methyl-4-cyclohexylpiperazine [7560-86-3]	CH_3Cl	---	$C_{12}H_{25}N_2Cl$	232.80
25a		***25***·HCl		~5.2	$C_{12}H_{26}N_2Cl_2$	269.26
26	5/8c[a]	4-(dimethylamino)-1-benzylpiperidine [64168-08-7]	CH_3Br (2 eq)	---	$C_9H_{21}N_2Br$	237.19
26a		***26***·HBr		~6.2	$C_9H_{22}N_2Br_2$	318.11
27	5	N,N,N',N'-Tetramethylethylenediamine [110-18-9]	CH_3Cl	---	$C_7H_{19}N_2Cl$	166.70
27a		***27***·HCl		~6.1	$C_7H_{20}N_2Cl_2$	203.16
27b	12	***27*** as the hydroxide salt		---	$C_7H_{20}N_2O$	148.25
27c	13	***27*** as the hemicarbonate salt		---	$C_{15}H_{38}N_4O_3$	322.50
28	5	N,N,N',N'-Tetraethylethylenediamine [150-77-6]	CH_3Cl	---	$C_{11}H_{27}N_2Cl$	222.81
28a		***28***·HCl		~6.7	$C_{11}H_{28}N_2Cl_2$	259.27
29	5	N,N,N',N'-Tetramethyl-1,3-diaminopropane [110-95-2]	CH_3Cl	---	$C_8H_{21}N_2Cl$	180.73

29a		***29***·HCl		~8.1	$C_8H_{22}N_2Cl_2$	217.19
29b	10	Dimethylamine [124-40-3]	bptab	---	$C_8H_{21}N_2Br$	225.18
29c		***29b***·HBr		~8.1	$C_8H_{22}N_2Br_2$	306.09
29a	9	N-(3-Aminopropyl)trimethylammonium chloride [19223-69-9]	fo+fa (xs)	~8.1	$C_8H_{22}N_2Cl_2$	217.19
29d	12	***29*** as hydroxide salt		---	$C_8H_{22}N_2O$	162.28
29e	13	***29*** as hemicarbonate salt		---	$C_{17}H_{42}N_4O_3$	350.56
30	5	N,N,N',N'-Tetraethyl-1,3-diaminopropane [60558-96-5]	CH_3Cl	---	$C_{12}H_{29}N_2Cl$	236.84
30a		***30***·HCl		~8.7	$C_{12}H_{30}N_2Cl_2$	273.30
31	5	N,N,N',N'-Tetramethyl-1,4-diamino-2,3-dihydroxybutane [84808-89-9]	CH_3Cl	---	$C_9H_{23}N_2O_2Cl$	271.20
31a		***31***·HCl		~8.7	$C_9H_{24}N_2O_2Cl_2$	352.12
32	5	N,N,N',N'-Tetramethyl-1,4-diaminobutane [111-51-3]	CH_3Cl	---	$C_9H_{23}N_2Cl$	239.20
32a		***32***·HCl		~8.9	$C_9H_{24}N_2Cl_2$	320.12
33	5	N,N,N',N'-Tetramethyl-1,6-diaminohexane [111-18-2]	CH_3Cl	---	$C_{11}H_{27}N_2Cl$	267.26
33a		***33***·HCl		~9.5	$C_{11}H_{28}N_2Cl_2$	348.17
34	5	N,N,N',N'-Tetraethyl-1,6-hexanediamine [7136-51-8]	CH_3Cl	---	$C_{15}H_{35}N_2Cl$	323.37
34a		***34***·HCl		~10.1	$C_{15}H_{36}N_2Cl_2$	404.28
35	5	trans-1,2-bis(dimethylamino)cyclohexane [53152-69-5]	CH_3Cl	---	$C_{11}H_{25}N_2Cl$	220.79
35a		***35***·HCl		~3.8	$C_{11}H_{26}N_2Cl_2$	257.25
36	5	1,4-Dimethylhomopiperazine [61134-91-6]	CH_3Cl	---	$C_8H_{19}N_2Cl$	178.71
36a		***36***·HCl		~6.2	$C_8H_{20}N_2Cl_2$	215.17
37	5	1,4-Dimethyl-6-hydroxyhomopiperazine [33468-98-3]	CH_3Cl	---	$C_8H_{19}N_2OCl$	194.71
37a		***37***·HCl		~5.8	$C_8H_{20}N_2OCl_2$	231.17
38	10	N-Methyl(2-methoxyethyl)amine [38256-93-8]	bptab	---	$C_{10}H_{25}N_2OBr$	269.23
38a		***38***·HBr		~7.2	$C_{10}H_{26}N_2OBr_2$	350.15
38b	12	***38*** as the hydroxide salt (31% aqueous)		---	$C_{10}H_{26}N_2O_2$	206.33
38c	13	***38*** as the hemicarbonate salt (34% aqueous)		---	$C_{21}H_{50}N_4O_5$	438.66
39	4	2-oxopiperazine [5625-67-2]	gmac	---	$C_{10}H_{22}N_3O_2Cl$	251.76
39a		***39*** HCl		~4.4	$C_{10}H_{23}N_3O_2Cl_2$	288.22
40	4	N-Acetylpiperazine [13889-98-0]	gmac	---	$C_{12}H_{26}N_3O_2Cl$	279.81
40a		***40***·HCl		~5.0	$C_{12}H_{27}N_3O_2Cl_2$	316.27

41	4	N, N'-Dimethylglycinamide [44565-47-1]	gmac	---	$C_{10}H_{24}N_3O_2Cl$	253.77
41a		***41***·HCl		~5.6	$C_{10}H_{25}N_3O_2Cl_2$	290.24
42	4	N-Acetyl-N,N'-dimethylethylenediamine [27725-41-3]	gmac	---	$C_{12}H_{28}N_3O_2Cl$	281.83
42a		***42***·HCl		~6.5	$C_{12}H_{29}N_3O_2Cl_2$	318.29
43	4	N,N'-Dimethyl-β-alanamide [50836-82-3]	gmac	---	$C_{11}H_{26}N_3O_2Cl$	267.80
43a		***43***·HCl		~6.7	$C_{11}H_{27}N_3O_2Cl_2$	304.26
44	4	4-Hydroxypiperidine [106-52-5]	gmac	---	$C_{11}H_{25}N_2O_2Cl$	252.79
44a		***44***·HCl		~7.1	$C_6H_{16}N_2Cl_2$	289.25
45	4	N-Ethylmethylamine [627-78-2]	gmac	---	$C_9H_{23}N_2OCl$	210.75
45a		***45***·HCl		~8.2	$C_7H_{18}N_2Cl_2$	247.21
46	7b	N-Methyltaurine [107-86-6]	gmac	~6.4	$C_9H_{22}N_2O_4S$	254.35
47	7b	N-Methyl-2-hydroxyhomotaurine [7013-34-5]	gmac	~7.1	$C_{10}H_{24}N_2O_5S$	284.38
48	7b	N-Methylhomotaurine [163221-06-5]	gmac	~7.3	$C_{10}H_{24}N_2O_4S$	268.38
49	7b	N-(2-Hydroxyethyl)taurine [29706-49-8]	gmac	~5.5	$C_{10}H_{24}N_2O_5S$	284.38
50	7b	N-(2-Hydroxyethyl)-2-hydroxyhomotaurine [725202-09-05]	gmac	~6.2	$C_{11}H_{26}N_2O_6S$	314.40
51	7b/7c	N-(2Hydroxyethyl)homotaurine [1119-23-9]	gmac	~6.4	$C_{11}H_{26}N_2O_5S$	298.40
52	7b	N-(4-sulfobutyl)methylamine [89282-74-6]	gmac	~8.0	$C_{11}H_{26}N_2O_4S$	282.40
53	7b/7c	N-(2-Hydroxyethyl)-N-(4-sulfobutyl)amine [54960-64-4]	gmac	~7.1	$C_{12}H_{28}N_2O_5S$	312.43
54	6	N,N,N',N'-Tetramethylethylenediamine [110-18-9]	ps	~6.1	$C_9H_{22}N_2O_3S$	238.35
55	6	N',N'-Diethyl-N,N-dimethylethylenediamine [123-10-4]	ps	~6.7	$C_{11}H_{26}N_2O_3S$	266.41
56	6	N,N'-Dimethyl-N,N'-bis(2-hydroxyethyl)-1,3-diaminopropane [10394-83-9]	ps	~7.3	$C_{12}H_{28}N_2O_5S$	312.43
57	6	N,N,N',N'-Tetramethyl-1,3-diaminopropane [110-95-2]	ps	~8.1	$C_{10}H_{24}N_2O_3S$	252.38
58	6	N',N'-Diethyl-N,N-dimethyl-1,3-diaminopropane [62478-82-4]	ps	~8.7	$C_{12}H_{28}N_2O_3S$	280.43
59	8b/8c	N,N'-Dimethyl-N,N'-bis(2-sulfoethyl)-1,3-diaminopropane [185305-85-5]	brc	~6.5, 8.0	$C_{14}H_{33}N_3O_7S_2$	419.56
60	11b	***79a***	HCl[b]	~6.8, 8.2	$C_{10}H_{25}N_2O_3P$	252.30
61	11b	***80a***	HCl[b]	~6.0, 7.4	$C_{10}H_{25}N_2O_3P$	252.30
62	3	1-Methylpiperazine [109-01-3]	ps (2 eq)	~3.7	$C_{11}H_{24}N_2O_6S_2$	344.45
63	3	1-Methylhomopiperazine [4318-37-0]	ps (2 eq)	~5.6	$C_{12}H_{26}N_2O_6S_2$	358.48

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64	3	N,N-Dimethyl-N'-benzylethylenediamine [103-55-9]	ps (2 eq)	~4.6	$C_{17}H_{30}N_2O_6S_2$	422.57
65	3	N,N-Dimethyl-N'-ethylethylenediamine [204-646-0]	ps (2 eq)	~5.8	$C_{12}H_{28}N_2O_6S_2$	360.49
66	3	N,N,N'-Trimethylethylenediamine [142-25-6]	ps (2 eq)	~5.5	$C_{11}H_{26}N_2O_6S_2$	346.47
67	3	N,N,N'-Trimethyl-1,3-diaminopropane [4543-96-8]	ps (2 eq)	~7.5	$C_{12}H_{28}N_2O_6S_2$	360.49
68	3	N,N,N'-Trimethylethylenediamine [142-25-6]	bes (2 eq)	~4.6	$C_9H_{22}N_2O_6S_2$	318.41
69	3	N,N,N'-Trimethyl-1,3-diaminopropane [4543-96-8]	bes (2 eq)	~6.6	$C_{10}H_{24}N_2O_6S_2$	322.44
70	3	N,N,N'-Trimethylethylenediamine [142-25-6]	bs (2 eq)	~6.2	$C_{13}H_{30}N_2O_6S_2$	374.52
71	3	N,N,N'-Trimethyl-1,3-diaminopropane [4543-96-8]	bs (2 eq)	~8.2	$C_{14}H_{32}N_2O_6S_2$	388.55
72	3	N,N,N'-Trimethylethylenediamine [142-25-6]	bp (2 eq)	~6.2	$C_{11}H_{22}N_2O_4$	246.31
73	3	N,N,N'-Trimethyl-1,3-diaminopropane [4543-96-8]	bp (2 eq)	~8.2	$C_{12}H_{24}N_2O_4$	260.34
74	5b	4-(isopropylamino)piperidine [534595-53-4]	C_2H_5Br (3 eq)	----	$C_{14}H_{31}N_2Br$	307.33
74a		***74***·HBr		~7.4	$C_{14}H_{32}N_2Br_2$	388.24
75	2	N-(2-Aminoethyl)trimethylammonium chloride [339-67-5]	tmcfc	~11.9	$C_{10}H_{26}N_4Cl_2$	267.21
76	1	1,1,3,3-Tetramethylguanidine [80-70-6]	bptab	~12.9	$C_{11}H_{28}N_4Br_2$	376.18
77	2	N-(2-Aminoethyl)trimethylammonium chloride [339-67-5]	cdmic	~11.1	$C_{10}H_{24}N_4Cl_2$	267.21
78	4	Ethanolamine [141-43-5]	gmac	----	$C_8H_{21}N_2O_2Cl$	212.72
78a		***78***·**HCl**		~7.8	$C_8H_{22}N_2O_2Cl_2$	249.18
79a	11a	N,N,N',N'-Tetramethyl-1,3-diaminopropane [110-95-2]	debpp	~8.1	$C_{20}H_{35}N_2O_3PBr_2$	542.31
80a	11a	N,N,N',N'-Tetraethylethylenediamine [150-77-6]	debbp	~6.1	$C_{20}H_{35}N_2O_3PBr_2$	542.31
81	8b	N,N'-dimethyl-N,N'-bis(2-sulfoethyl)trimethylenediame di-inner salt [185305-85-5]	brc	~6.1	$C_{21}H_{39}N_3O_7S_2$[c]	509.69
82	8c	***81***	H_2/Pd	~6.5, 8.0	$C_{14}H_{33}N_3O_7S_2$[c]	419.57

a) No acid added during hydrogenation reaction (debenzylation)
b) Acid hydrolysis of phosphonate ester
c) Mixture of diastereomers

gmac = N-(Glycidyl)trimethylammonium chloride [3033-77-0]
bptab = N-(3-Bromopropyl)trimethylammonium bromide [3779-42-8]
tmcfc = N,N,N',N'-tetramethylchloroformamidinium chloride [13829-06-6]

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cdmic = 2-Chloro-1,3-dimethylimidazolinium chloride [37091-73-9]
fo+fa = formaldehyde [50-00-0] and formic acid [64-18-6]
CH_3Cl = Methyl chloride [74-87-3]
CH_3Br = Methyl bromide [74-83-9]
C_2H_5Br = Ethyl bromide [74-96-4]
ps = 1,3-Propanesultone [1120-71-4]
bs = 1,4-Butanesultone [1633-83-6]
bes = 2-Bromoethanesulfonic acid, sodium salt [4263-52-9]
chps = 3-Chloro-2-hydroxypropanesulfonic acid, sodium salt [143218-48-8]
bp = 3-Bromopropanoic acid [590-92-1]
debpp = Diethyl 3-Bromopropanephosphonate [1186-10-3]
debbp = Diethyl 4-Bromobutanephosphonate [2004-10-25]
brc = N-(3-Chloro-2-hydroxypropyl)benzyldimethylammonium chloride ("benzyl reagens") [67304-25-0]
bpbdab = N-(3-Bromopropyl)benzyldimethylammonium bromide [113222-03-6]
HCl = Hydrochloric Acid [7647-01-0]