SYSTEMATIC TABLES OF MONO- AND POLY-*N*-METHYLATED ADENINES: ACID DISSOCIATION CONSTANTS AND UV AND NMR SPECTRAL DATA

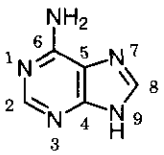
Tozo Fujii* and Taisuke Itaya

Faculty of Pharmaceutical Sciences, Kanazawa University, Takara-machi, Kanazawa 920-0934, Japan

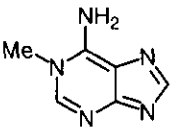
Abstract —— Available data regarding acid dissociation constants and UV, ^{1}H NMR, and ^{13}C NMR spectra of all the five positional isomers (**2–6**) of N^x-methyladenine, 10 known isomers (**7–16**) of N^x,N^y-dimethyladenine, nine known isomers (**17–25**) of N^x,N^y,N^z-trimethyladenine, and five known isomers (**26–30**) of tetra-*N*-methylated adenine are tabulated for convenience of ready comparison, with 117 reference citations.

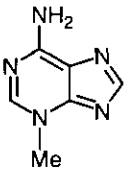
Because of its unique chemical structure of bearing one exocyclic and four endocyclic nitrogen atoms, adenine (**1**) permits a variety of *N*-substitution patterns in principle: five kinds of mono-*N*-substitution, 11 kinds of di-*N*-substitution, 15 kinds of tri-*N*-substitution, 15 kinds of tetra-*N*-substitution, 11 kinds of penta-*N*-substitution, five kinds of hexa-*N*-substitution, and one kind of hepta-*N*-substitution. Indeed, all kinds of mono- and di-*N*-substitution patterns (with the exception that genuine 1,3-disubstituted adenines still remain unknown), most of the tri-*N*-substitution patterns, and several of the tetra-*N*-substitution patterns have been shown to occur in nature as well as by chemical synthesis.[1–8]

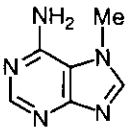
Our recent review articles have treated the chemistry, physicochemical properties, and biological activities of N^x-methyladenines,[6] N^x,N^y-dimethyladenines,[7] N^x,N^y,N^z-trimethyladenines,[8] more highly *N*-methylated adenines[8] (all of them are the prototypes of known *N*-substituted adenines), and N^x-oxygenated adenines.[9] Among physicochemical properties, the acid dissociation constants and UV absorption spectra are important criteria of identity and homogeneity, frequently the most useful, for purines, as Lister pointed out in his monograph[10a] and quoted earlier examples of use of these techniques for structural assignments.[10b,c] Later on, the rapid development of NMR spectroscopy has revolutionized the approach to structural and kinetic problems in this field.[10d] It is the intention of the present review to tabulate available data concerning acid dissociation constants and UV, ^{1}H NMR, and ^{13}C NMR spectra of all the five positional isomers (**2–6**) of N^x-methyladenine, 10 known isomers (**7–16**) of N^x,N^y-dimethyladenine, nine

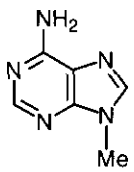

1


2

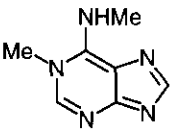

3

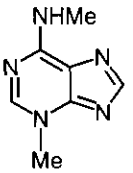

4

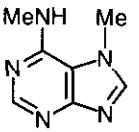

5

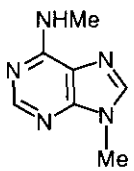

6

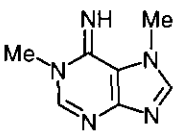

7

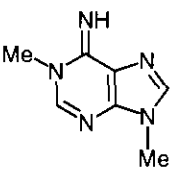

8

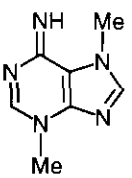

9

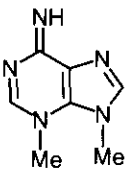

10

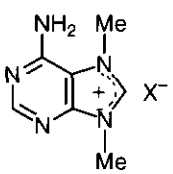

11

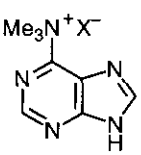

12

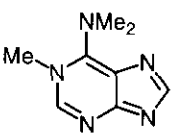

13

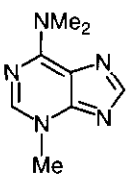

14

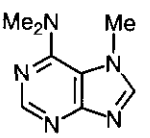

15

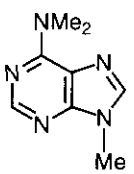

16

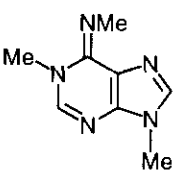

17

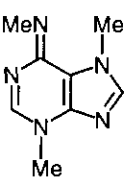

18

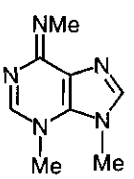

19

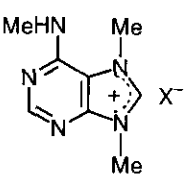

20

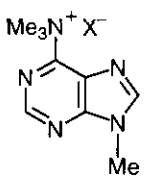

21

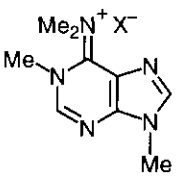

22

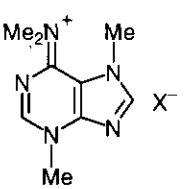

23

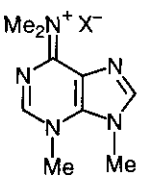

24

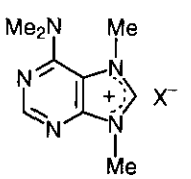

25


26


27


28


29


30

known isomers (**17–25**) of N^x,N^y,N^z-trimethyladenine, and five known isomers (**26–30**) of tetra-*N*-methylated adenine for convenience of ready comparison (Tables I–VIII). Such tabulation of physicochemical data stands as supplements to that appeared in earlier reviews[1–3,11] and to our recent reviews.[6–8]

TABLE I. pK_a Values of Mono- and Poly-*N*-methylated Adenines

Compound (No.)	Solvent[a]	Method[b]	pK_a		Literature (ref. No.)
			basic	acidic	
N^6-Methyladenine (**2**)	H_2O[c]	(T)	<1, 4.18 ± 0.02	9.99 ± 0.05	(12, 27)
	H_2O	(U)	4.1	10.0	(13)
	H_2O[d]	(U)	4.2	10.0	(14, 15)
	D_2O[e]	(N)	4.1	10	(13)
1-Methyladenine (**3**)	A	(T)	6.95	11.9	(16)
	H_2O[c]	(U)	7.11 ± 0.05		(17)
	H_2O[f]	(U)	7.35 ± 0.03		(17)
	H_2O	(U)	7.2	11.0	(14, 18)
3-Methyladenine (**4**)	A	(T)	5.3		(16)
	H_2O	(U)	5.7		(19)
	H_2O	(U)	6.1		(20, 21)
7-Methyladenine (**5**)	A	(T)	3.6		(16)
	A	(T)	3.5		(22)
	H_2O	(U)	3.6		(21)
	H_2O	(U)	4.2		(20)
	B	(U)		14.7	(23)
9-Methyladenine (**6**)	A	(T)	3.25		(16)
	H_2O[g]	(T)	3.88 ± 0.01		(24)
	H_2O	(U)	3.9		(20, 21)
	H_2O[c]	(U)	3.92		(15)
	C	(T)	4.45 ± 0.03		(25)
	DMSO[g]	(T)	3.69 ± 0.02		(24)
	B	(U)		16.7	(23)
	B[g]	(U)		17.0	(26)
N^6,N^6-Dimethyladenine (**7**)	H_2O	(T)	3.87	10.5	(12, 15, 27, 28)
	H_2O	(U)	3.9	10.0	(14)
	H_2O[e]	(N)	4.3	10	(13)

(*continues*)

TABLE I (*continued*)

Compound (No.)	Solvent[a)]	Method[b)]	pK_a basic	pK_a acidic	Literature (ref. No.)
	H_2O	(U)	4.4	10.1	(19)
	H_2O	(U)	4.45	9.95	(13)
	D_2O	(T)	4.10[h)]		(29)
	D	(T)		10.54	(30)
	DMSO	(T)		13.0	(31)
	E	(T)		14.7	(32)
N^6,9-Dimethyladenine (**11**)	H_2O[c)]	(U)	4.02 ± 0.03		(33)
	H_2O[i)]	(U)	4.12 ± 0.03		(34)
	F	(U)	3.8 ± 0.05		(35)
1,7-Dimethyladenine (**12**)	H_2O[c)]	(U)	6.50 ± 0.10		(17)
12·$HClO_4$	H_2O[j)]	(U)	7.86 ± 0.03		(36)
1,9-Dimethyladenine (**13**)	H_2O[c)]	(U)	9.03 ± 0.05		(17)
	F	(U)	9.1 ± 0.05		(35)
13·$HClO_4$	H_2O[c)]	(U)	9.08 ± 0.07		(33)
	H_2O[j)]	(U)	8.94 ± 0.05		(33)
	H_2O[k)]	(U)	8.96 ± 0.06		(37)
	H_2O[k)]	(U)	8.97 ± 0.03		(38)
N^6,N^6,N^6-Trimethyladenine [**17** (X = Cl)]	H_2O[c)]	(U)		6.46	(15)
	H_2O	(T)		6.8	(39)
	H_2O[c)]	(U)		6.85	(40)
N^6,N^6,3-Trimethyladenine (**19**)	H_2O	(U)	5.8		(19)
N^6,N^6,9-Trimethyladenine (**21**)	H_2O[c)]	(U)	4.04		(15)
	H_2O[g)]	(U)	–0.75 ± 0.20, 4.15 ± 0.05		(41)
N^6,1,9-Trimethyladenine hydriodide (**22**·HI)	H_2O	(T)	10.00 ± 0.01		(42)
N^6,3,7-Trimethyladenine hydriodide (**23**·HI)	H_2O	(T)	11.60		(42)

(*continues*)

TABLE I (*continued*)

Compound (No.)	Solvent[a]	Method[b]	pK_a		Literature (ref. No.)
			basic	acidic	
N^6,3,9-Trimethyladenine hydriodide (**24**·HI)	H_2O	(T)	11.00 ± 0.04		(42)

a) A = 50% aqueous DMF; B = aqueous DMSO containing tetramethylammonium hydroxide; C = 0.1 M aqueous $NaClO_4$ at 298.2 K; D = 59% (v/v) aqueous EtOH; E = $MeOCH_2CH_2OH$; F = 0.1 M aqueous NaCl. *b*) The letter in parentheses refers to the determination method with N, ^1H NMR spectroscopy; T, titrimetry; U, UV spectrophotometry. *c*) At 20°C. *d*) At 25°C and ionic strength 0.10. *e*) At *ca.* 40°C. *f*) At 12°C. *g*) At 25°C. *h*) For the N(1)-deuterated species. *i*) At 20°C and ionic strength 0.01. *j*) At 40°C and ionic strength 0.5. *k*) At 40°C and ionic strength 1.0.

TABLE II. UV Spectral Data of N^x-Methyladenines (**2**–**6**)[a]

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
N^6-Methyladenine (**2**)	95% E[b]		266	15.8	(43)
	95% E[b]		267	15.7	(44)
	MeOH		267	17.6	(45)
	H_2O		266	16.4	(46)
	H_2O	acidic	267	14.9	(16)
	H_2O	–8.4– –11.1	264	17.2	(13)
		–4.4	263, 270	13.6, 13.1	(13)
		–0.3–1.0	264, 269	14.6, 14.6	(13)
		1	266	15.8	(46)
		1	266	14.9	(43)
		1	267	14.9	(44, 47, 48)
		1	267	15.2	(14)
		1	267	16.3	(45)
		2.02	267	(log ε 4.18)	(27a)
		6.8	267	16.0	(13)
		7	266	15.8	(43)
		7	267	15.8	(44)
		7.12	266	(log ε 4.21)	(27a)
		basic	272	15.2	(16)
		11	272	15.3	(47, 48)
		11	272	17.2	(45)
		12.00	273	(log ε 4.20)	(27a)

(*continues*)

TABLE II (*continued*)

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
	H_2O	12.9	278	15.6	(13)
		13	272	16.3	(46)
		13	273	15.6	(43, 44)
		13	273	15.8	(14)
1-Methyladenine (**3**)	H_2O	acidic	259	11.7	(16)
		1	257.5	11.8	(49)
		1	259	11.6	(14)
		4	259	11.7	(18, 50)
		8	270	11.9	(51)
		basic	270	14.4	(16)
		11	268.5	12.1	(49)
		13	270	14.4	(14, 18, 50)
3-Methyladenine (**4**)	H_2O	acidic	274	17.0	(16)
		acidic	274[c]	15.9	(50)
		1	274	17.0	(48)
		1	274	17.9	(52)
		1	274[d]	15.9	(51, 53)
		2	274	15.9	(18)
		7	274	(log ε 4.01)	(54)
		basic	272[c]	13.6	(50)
		basic	273	13.3	(16)
		11	273	13.3	(48)
		11	273	13.1	(52)
		11	272[d]	13.6	(53)
		13	273	12.8	(18)
7-Methyladenine (**5**)	EtOH		269, 283[e]	11.6, 6.9	(55)
	EtOH		272	9.5	(56)
	A[f]		271	(log ε 4.01)	(23)
	H_2O		269, 280[e]	11.9, 7.3	(55)
	H_2O	acidic	272	15.05	(16)
		1	273	14.0	(48)
		1	272	15.05	(57)
		1	272	15.4	(55)
		1	272[g]	13.8	(53)
		1.20	273.5[h]	16.3	(50)

(*continues*)

TABLE II (*continued*)

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
	B[i]		269	14.6	(58)
	H_2O	basic	270	10.5	(16)
	C[j]		300	(log ε 4.06)	(23)
	D[k]		269	11.4	(58)
	H_2O	11	270	10.55	(57)
		11	268	10.6	(48)
		11.95	270.5[h]	12.5	(50)
		12	270[g]	10.5	(53)
		13	270	11.1	(55)
9-Methyladenine (**6**)	EtOH		262	12.5	(56)
	A[f]		262	(log ε 4.18)	(23)
	B[i]		260	15.5	(50)
			260	14.2	(58)
	H_2O	acidic	260	14.2	(16)
		1	261	14.6	(59)
		1	260	13.7	(48)
		6	261	13.1	(60)
		7	263.0	(log ε 4.09)	(54)
	C[j]		286	(log ε 3.99)	(23)
	H_2O	basic	260	14.7	(16)
	D[k]		260	14.7	(58)
			260	15.5	(50)
	H_2O	11	262	11.9	(59)
		11	261	14.0	(48)

a) Selected from the literature recording λ_{max} values together with molar absorptivities for N^x-methyladenines.
b) 95% aqueous EtOH.
c) All other spectra at different pH's cross at the isosbestic points at 240 and 281 nm.
d) All other spectra at different pH's go through the isosbestic points at 240 and 281 nm.
e) Shoulder.
f) 30–55 mol% aqueous DMSO.
g) All other spectra at different pH's cross at the isosbestic points at 221, 232, and 251 nm.
h) All other spectra at different pH's cross at the isosbestic points at 222, 236, and 250 nm.
i) 0.05 N aqueous HCl.
j) 86–96 mol% aqueous DMSO containing tetramethylammonium hydroxide.
k) 0.05 N aqueous NaOH.

TABLE III. UV Spectral Data of N^x,N^y-Dimethyladenines[a)]

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
N^6,N^6-Dimethyladenine (**7**)	H_2O	–11	269.5	18.3	(13)
		–3.4– –4.4	237	14.4	(13)
		1	277	15.6	(14, 17)
		1.0–2.0	276	16.0	(13)
		1.70	276	(log ε 4.19)	(27a)
		6.0	275	19.0	(13)
		6.98	275	(log ε 4.25)	(27a)
		neutral	275	17.3	(61)
		basic	281	17.6	(61)
		11	281	17.0	(47)
		12.8–13.7	281, 289	19.0, 15.4	(13)
		13	281	17.8	(14)
		13.0	221, 281	(log ε 4.21, 4.25)	(27a)
7·HCl	H_2O	1	277	15.6	(62)
N^6,1-Dimethyladenine (**8**)	MeOH		276	12.2	(45)
	H_2O	1	262.5	10.4	(63)
		1	261	12.9	(45)
		7	269	9.6	(63)
		11	274	12.7	(45)
		13	275	10.8	(63)
N^6,3-Dimethyladenine (**9**)	95% E[b)]		291	13.6	(43)
	H_2O	1	282	18.6	(43)
		1	281	19.62	(52)
		7	285	14.5	(43)
		11	287	14.50	(52)
		13	286	14.1	(43)
N^6,7-Dimethyladenine (**10**)	EtOH		276	18.6	(57)
			272, 278	(log ε 4.11, 4.12)	(65)
	95% E[b)]		273,[c)] 278	13.8, 14.1	(66)
	H_2O	1	280	16.0	(57)
		1	279	16.8	(66)
		1	278	(log ε 4.24)	(65)

(*continues*)

TABLE III (*continued*)

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
	H_2O	7	276	15.1	(66)
		11	275	14.3	(57)
		13	276	15.0	(66)
N^6,9-Dimethyladenine (**11**)	95% E[b]		268	14.7	(33)
	H_2O	1	265	16.0	(33)
		1	265	15.3	(59)
		1.9	209, 264[d]	(log ε 4.25, 4.23)	(34)
		6.5	209, 267	(log ε 4.27, 4.20)	(34)
		7	268	(log ε 4.10)	(54)
		7	268	15.1	(33)
		13	268	15.1	(33)
		13	268	14.0	(59)
N^6,9-Dimethyladenine-2-*d*	H_2O	1	263	16.7	(67)
		7	267	15.7	(67)
		13	267	15.9	(67)
1,7-Dimethyladenine (**12**)	EtOH		264.5	(log ε 3.93)	(65)
	H_2O	1	270	(log ε 3.86)	(65)
12·3/5H_2O	H_2O	1	269, 282[c]	9.50, 5.30	(68)
		7	269, 282[c]	9.50, 5.30	(68)
		13	264.5	11.1	(68)
12·$HClO_4$·1/5H_2O	H_2O	1	270, 282[c]	9.42, 5.40	(69)
		7	270, 283[c]	10.1, 5.80	(69)
		13	265	12.1	(69)
1,9-Dimethyladenine (**13**)	H_2O	acidic	259	13.0	(17)
13·TsOH	H_2O	1	259	10.6	(45)
		11	259	10.4	(45)
13·$HClO_4$	95% E[b]		261	13.5	(33)
	H_2O	1	261	13.6	(33)
		7	261	13.3	(33)
		13	261	14.1	(33)

(*continues*)

TABLE III (*continued*)

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
1,9-Dimethyladenine-2-*d* hydriodide (**13**-2-*d*·HI)	95% E[b]		259	11.6	(67)
	H_2O	1	260	12.3	(67)
		7	259	12.3	(67)
		13	260	13.2	(67)
3,7-Dimethyladenine (**14**)					
14·HI	95% E[b]		276	16.2	(70)
	MeOH		278	16.9	(45)
	H_2O	1	276	16.3	(45)
		1	225, 277	24.2, 16.3	(70)
		7	225, 277	24.4, 16.6	(70)
		13	225, 282	19.5, 14.7	(70)
		14	225, 281	17.8, 14.0	(45)
14·$HClO_4$	95% E[b]		225, 279	9.50, 14.7	(71)
	H_2O	1	223, 277	11.4, 16.7	(71)
		7	223, 277	11.4, 16.7	(71)
		13	282	14.8	(71)
3,9-Dimethyladenine (**15**)					
15·HCl·0.4H_2O	95% E[b]		272	15.5	(72)
	H_2O	1	270	15.7	(72)
		7	270	15.6	(72)
		13	unstable		(72)
15·$HClO_4$	95% E[b]		272	15.4	(72)
	H_2O	1	270	15.6	(72)
		7	270	15.4	(72)
		13	unstable		(72)
3,9-Dimethyladenine-2-*d* hydrochloride (**15**-2-*d*·HCl)	95% E[b]		272	15.5	(73)
	H_2O	1	271	15.5	(73)
		7	271	15.5	(73)
		13	unstable		(73)
15-2-*d*·$HClO_4$	95% E[b]		272	12.6	(73)
	H_2O	1	271	15.7	(73)
		7	271	15.7	(73)

(*continues*)

TABLE III (*continued*)

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
	H_2O	13	unstable		(73)
7,9-Dimethyladenine (**16**)					
16 (X = I)	95% E[b]		273.5	11.6	(74)
	MeOH		270	11.9	(75)
	H_2O	1	269	12.0	(74)
		7	270	12.0	(74)
		13	unstable		(74)
16 (X = ClO_4)	95% E[b]		273	11.5	(71)
	H_2O	1	268	11.9	(71)
		7	269	12.1	(71)
		13	unstable		(71)
7,9-Dimethyladenine-*2-d* (**16**-*2-d*)					
16-*2-d* (X = I)	95% E[b]		272	11.8	(66)
	H_2O	1	268	12.1	(66)
		7	269	12.3	(66)
		13	unstable		(66)

a) Selected from the literature recording λ_{max} values together with molar absorptivities for N^x,N^y-dimethyladenines. *b*) 95% aqueous EtOH. *c*) Shoulder. *d*) With a shoulder at 271 nm (log ε 4.17).

TABLE IV. UV Spectral Data of Tri- and Tetra-*N*-methyladenines[a]

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
N^6,N^6,N^6-Trimethyladenine (**17**)					
17 (X = Cl)	H_2O	1	265.7	8.27	(76)
		4.0	265	(log ε 3.95)	(40)
		5	267	10.0	(51)
		9.0	209, 272	(log ε 4.32, 3.89)	(40)
A 1:1 mixture of **17** (X = Cl) and **17** (X = MeO)	H_2O	1	266	7.90	(77)
		7	268	6.75	(77)
		13	273.5	6.71	(77)

(*continues*)

TABLE IV (*continued*)

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
zwitterionic form (6-trimethylammoniopurinide)	H_2O	1	265	(log ε 3.94)	(39)
		10	274	(log ε 3.86)	(39)
N^6,N^6,1-Trimethyladenine (**18**)	H_2O	1	221, 293	13.5, 12.2	(78)
		1	293	12.2	(64)
		7	215, 298	14.0, 12.6	(78)
		7	298	12.6	(64)
		12	232, 301	13.4, 13.6	(78)
		12	301	13.6	(64)
N^6,N^6,3-Trimethyladenine (**19**)	EtOH		277,[b] 297	9.8, 18.0	(79)
	95% E[c]		299	15.6	(80)
	H_2O	1	291	20.4	(80)
		1	290	20.4	(78)
		5	291	16.6	(51)
		7	294	16.8	(80)
		7	222, 292	11.3, 16.6	(78)
		12	293	16.4	(78)
		13	295	16.3	(80)
N^6,N^6,7-Trimethyladenine (**20**)	H_2O	1	223, 293	9.0, 18.1	(78)
		1	293	18.7	(64)
		7	222, 291	13.0, 14.4	(78)
		7	291	14.4	(64)
		12	291	14.4	(64, 78)
N^6,N^6,9-Trimethyladenine (**21**)	95% E[c]		277	17.6	(80)
	H_2O	1	270	19.5	(81)
		1	270	17.6	(80)
		1	269	15.6	(78)
		1	269	14.4	(59)
	A[d]	acidic	269.5	17.6	(82)
	H_2O	7	278	18.3	(80)
		7	276	18.1	(81)
		7	214, 276	15.5, 16.0	(78)
		11	277	16.8	(59)
		12	276	16.3	(78)

(*continues*)

TABLE IV (*continued*)

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
	H_2O	13	278	18.3	(80)
		14	277	18.1	(81)
	B[e]	basic	276	18.5	(82)
N^6,1,9-Trimethyladenine (**22**)					
22·HI	H_2O		262–264	(log ε 4.10)	(42)
22·$HClO_4$	95% E[c]		263	13.5	(43)
	H_2O	1	263	13.7	(43)
		7	263	13.7	(43)
		13	263[f]	14.9	(43)
N^6,3,7-Trimethyladenine (**23**)					
23·HI	H_2O		284–286	(log ε 4.25)	(42)
23·$HClO_4$	95% E[c]		286	18.5	(43)
	H_2O	1	284	18.5	(43)
		7	284	18.5	(43)
		13	285	10.9	(43)
N^6,3,9-Trimethyladenine (**24**)					
24·HI	H_2O		280–282	(log ε 4.16)	(42)
24·$HClO_4$	95% E[c]		282	15.3	(43)
	H_2O	1	221, 281	23.3, 15.9	(43)
		7	221, 280	23.1, 15.8	(43)
		13	unstable		(43)
N^6,7,9-Trimethyladenine (**25**)					
25 (X = I)	H_2O		278–280	(log ε 4.16)	(42)
N^6,N^6,N^6,9-Tetramethyladenine (**26**)					
26 (X = Cl)	H_2O	4.0	267	(log ε 3.89)	(40)
26·2.5H_2O (X = Cl)	H_2O	1	267.5	7.80	(83)
		7	268	7.80	(83)
N^6,N^6,1,9-Tetramethyladenine (**27**)					
27 (X = I)	H_2O		292	(log ε 4.12)	(84)

(*continues*)

TABLE IV (*continued*)

Compound (No.)	Solvent	pH	λ_{max} (nm)	$\varepsilon \times 10^{-3}$	Literature (ref. No.)
N^6,N^6,3,7-Tetramethyladenine (**28**)					
28 (X = I)	H_2O		298	(log ε 4.29)	(84)
28 (X = ClO_4)	H_2O		298	(log ε 4.29)	(84)
N^6,N^6,3,9-Tetramethyladenine (**29**)					
29 (X = I)	95% E[c]		290	18.1	(85)
	H_2O		286	(log ε 4.31)	(84)
	H_2O	1	223, 288	24.0, 18.1	(85)
		7	223, 288	24.2, 18.2	(85)
		13	unstable		(85)
N^6,N^6,7,9-Tetramethyladenine (**30**)					
30 (X = I)	H_2O		296	(log ε 4.18)	(84)

a) Selected from the literature recording λ_{max} values together with molar absorptivities for tri- and tetra-*N*-methyladenines. *b*) Shoulder. *c*) 95% aqueous EtOH. *d*) 0.1 N aqueous HCl + 10% EtOH. *e*) 0.1 N aqueous NaOH + 10% EtOH. *f*) With shoulders at 270 (ε 12800) and 295 nm (ε 3400).

TABLE V. ^{1}H NMR Spectral Data of N^x-Methyladenines (**2–6**)

Compound (No.)	Solvent[b]	Chemical shift (δ)[a]					Literature (ref. No.)
		Me	C(2)-H	C(8)-H	C(6)-NH or $-NH_2$	NH	
N^6-Methyladenine (**2**)	A	3.01	8.22	8.07	7.26–7.66[c]	12.30–13.40[c]	(46)
	A	2.97	8.10	8.22			(64)
	A	2.96	8.07[c]	8.19[c]	7.56	12.88	(44)
	B	3.28	8.39	8.49			(13)
	C	2.97	7.94	7.94			(13)
	D	3.12	7.95	8.19			(13)
1-Methyladenine (**3**)	A	3.76	8.16	8.40			(64)
	A	3.70	8.15	7.84			(21)
3-Methyladenine (**4**)	A	3.91	7.77	8.29	7.83		(86)
	A	3.89	8.29	7.76	7.76		(87)

(*continues*)

TABLE V (*continued*)

Compound (No.)	Solvent[b]	Chemical shift (δ)[a]					Literature (ref. No.)
		Me	C(2)-H	C(8)-H	C(6)-NH or $-NH_2$	NH	
	A				7.8		(88)
	A	3.90	8.30	7.77	7.83		(21)
	A	3.91	8.27	7.77			(89)
	E	3.97	8.65	8.72	9.17, 9.20		(90)
	F	3.99	7.79	8.22			(90)
4·HCl	A	4.00	8.73	8.61			(89)
7-Methyladenine (**5**)	A	3.99	8.12	8.12	6.78		(86)
	A				6.8		(88)
	A	3.91	8.16	8.16	6.90		(21)
5·$HClO_4$	G	4.21	8.67[c]	8.77[c]	8.91	9.78	(55)
9-Methyladenine (**6**)	A	3.71	8.08	8.14	7.17		(26)
	A	3.71	8.14	8.08	7.19		(91)
	A	3.73	8.07	8.01	7.10		(92)
	A	3.71	8.06[c]	8.13[c]	7.17		(93)
	A	3.70	8.07[c]	8.13[c]	7.18		(94)
	A	3.72	8.16	8.08	7.18		(95)
	A	3.69	8.13	8.06	7.13		(96)
	A	3.72	8.15	8.09	7.12		(21)
	H		8.22[d]	8.06[d]			(97)
	H	3.78	8.07	8.03			(98)
	I		8.31	8.17			(99)
	A	3.72	8.15	8.08	7.16		(100)
9-Methyladenine-2-*d*	A	3.72	——	8.08	7.16		(100)

a) In ppm, relative to Me_4Si.

b) The letter refers to the solvent with A, DMSO-d_6; B, D_2O at pH 1–2.8; C, D_2O at pH 5.5; D, D_2O at pH 12.3; E, DMSO-d_6 + 1% CF_3CO_2D; F, acetone-d_6; G, DMSO; H, D_2O; I, CD_3CO_2D.

c) Not particularly assigned in the literature quoted.

d) Relative to 4,4-dimethyl-4-silapentanesulfonic acid.

TABLE VI. ^{1}H NMR Spectral Data of N^x,N^y-Dimethyladenines

Compound (No.)	Solvent[b]	Chemical shift (δ)[a]						Literature (ref. No.)
		N-Me	*N*-Me	C(2)-H	C(8)-H	NH_2	NH	
N^6,N^6-Dimethyl-	A			8.19	8.07			(101)
adenine (**7**)	A			8.19[c]	8.07[c]			(102)
	B			8.20[d]	8.07[d]			(103)
	B	3.44[e]		8.18	8.09			(104)
	B	3.87[e]		8.32	8.20			(105)
	C	3.58[e]		8.39	7.96			(106)
	D	3.45[e]		8.21	8.11			(107)
	E	3.65[e]		8.35	8.43			(13)
	F	2.91[e]		7.63	7.53			(13)
	G	3.37[e]		7.92	8.08			(13)
N^6,1-Dimethyl-	D	2.93[d]	3.16[d]	7.64[d]	7.74[d]			(63)
adenine (**8**)								
N^6,7-Dimethyl-	C			8.55	7.81			(108)
adenine (**10**)								
N^6,9-Dimethyl-	C[f]	3.15[g]	3.76[h]	8.38	7.65		*ca.* 6.4[i]	(109)
adenine (**11**)	C	3.22[g]	3.83[h]	8.44	7.71		5.82[i]	(67)
	C	3.23[g]	3.82[h]	8.43	7.71		5.80[i]	(110)
	H	3.20[g]	3.79[h]	8.19	7.49			(111)
	B	2.98[g]	3.72[h]	8.22	8.07		7.61[i]	(67)
	I[f]	3.44, 3.51[g]	4.23[h]	8.73[d]	9.25[d]			(42)
	D[j]	3.13[g]	3.81[h]	8.29	8.00			(107)
N^6,9-Dimethylade-	C	3.22[g]	3.83[h]	——	7.71		5.84[i]	(67)
nine-2-*d* (**11**-2-*d*)	B	2.98[g]	3.72[h]	——	8.07		7.61[i]	(67)
1,7-Dimethyladenine (**12**)								
12·3/5H_2O	B	3.37[k]	4.00[l]	7.88[d]	7.90[d]		6.84	(68)
12·$HClO_4$·1/5H_2O	B	3.80[k]	4.12[l]	8.54[d]	8.61[d]		8.82	(69)
1,9-Dimethyladenine-2-*d* hydrio-								
dide (**13**-2-*d*·HI)	B	3.80[k]	3.83[h]	——	8.47		9.1, 9.7	(67)
3,7-Dimethyladenine (**14**)								

(*continues*)

TABLE VI (*continued*)

Compound (No.)	Solvent[b]	Chemical shift (δ)[a]						Literature (ref. No.)
		N-Me	*N*-Me	C(2)-H	C(8)-H	NH_2	NH	
14·HI	B	3.95[m]	4.11[l]	8.60[d]	8.73[d]		——[n]	(70)
3,9-Dimethyladenine (**15**)								
15·HCl·0.4H_2O	B	4.21[m]	4.11[h]	8.61	8.34		9.10, 9.16	(73)
15·$HClO_4$	B	4.19[m]	4.10[h]	8.58	8.32		9.10, 9.17	(72)
3,9-Dimethyladenine-*2-d* (**15**-*2-d*)								
15-*2-d*·HCl	B	4.21[m]	4.10[h]	——	8.34		9.10, 9.17	(73)
15-*2-d*·$HClO_4$	B	4.19[m]	4.10[h]	——	8.31		9.10, 9.17	(73)
7,9-Dimethyladenine (**16**)								
16 (X = I)	B	4.19[l]	3.89[h]	8.44	9.57	7.93		(74)
	B			8.44	9.65			(75)
16 (X = ClO_4)	B	4.14[l]	3.85[h]	8.40	9.50	7.89		(71)
16-*2-d* (X = I)	B	4.18[l]	3.88[h]	——	9.56	7.95		(66)

a) In ppm, relative to Me_4Si.

b) The letter refers to the solvent with A, DMSO; B, DMSO-d_6; C, $CDCl_3$; D, D_2O; E, H_2O at pH 2.6; F, H_2O at pH 5.5; G, H_2O at pH 12.3; H, CCl_4; I, CF_3CO_2H.

c) Relative to sodium 3-trimethylsilyl-1-propanesulfonate.

d) Not particularly assigned in the literature quoted.

e) N^6-Me_2 proton signal.

f) Hexamethyldisiloxane was used as an internal reference.

g) N^6-Me proton signal.

h) N(9)-Me proton signal.

i) C(6)-N*H*Me signal.

j) *t*-BuOH was used as an internal reference.

k) N(1)-Me proton signal.

l) N(7)-Me proton signal.

m) N(3)-Me proton signal.

n) Two broad one-proton signals at δ 8.25–8.65 and 9.0–9.35.

TABLE VII. ^{1}H NMR Spectral Data of Tri- and Tetra-*N*-methyladenines

Compound (No.)	Solvent[b]	Chemical shift (δ)[a]						Literature (ref. No.)
		N^6-Me	*N*-Me	*N*-Me	C(2)-H	C(8)-H	NH	
N^6,N^6,N^6-Trimethyladenine								
17 (X = Cl)	A[c]	3.95			8.95	8.70		(40)
	B[d]	3.83			8.93	8.67		(83)
	C[c]				9.28	9.03		(102)
zwitterionic form	B[d]	3.87			8.97	8.75		(83)
N^6,N^6,3-Trimethyladenine (**19**)	D[e]	3.64, 3.77	4.20[f]		8.62[g]	8.99[g]		(84)
	E	3.40, 3.88[g]	4.00[g]		7.92[g]	8.02[g]		(80)
	F	3.40	3.90[f]		8.25	8.35		(51)
N^6,N^6,9-Trimethyladenine (**21**)	D[e]	3.75	4.14[h]		8.70[g]	9.17[g]		(84)
	G	3.51[g]	3.76[g]		7.50[g]	8.12[g]		(80)
	E	3.54	3.81[h]		8.37	7.70		(67)
	E	3.53	3.78[h]		8.35	7.69		(92)
	F	3.44	3.72[h]		8.19	8.05		(112)
	F	3.45	3.72[h]		8.22	8.10		(67)
N^6,1,9-Trimethyladenine (**22**)								
22·HI	D[e]	3.72, 3.80	4.11[i]	4.18[h]	8.78[g]	9.46[g]	8.28–8.58	(42)
N^6,3,7-Trimethyladenine (**23**)								
23·HI	D[e]	3.30, 3.40	4.23[f]	4.38[j]	8.78[g]	9.08[g]	7.78	(42)
N^6,3,9-Trimethyladenine (**24**)								
24·HI	D[e]	3.37, 3.44	4.46[f]	4.51[h]	8.76[g]	9.51[g]	9.43	(42)
N^6,7,9-Trimethyladenine (**25**)								
25 (X = I)	D[e]	3.53	4.61[j]	4.23[h]	8.93[g]	9.63[g]	8.38–8.63	(42)
N^6,N^6,N^6,9-Tetramethyladeninium chloride								
[**26** (X = Cl)]	A[c]	3.95	4.08[h]		9.15	8.81		(40)
N^6,N^6,1,9-Tetramethyladeninium iodide								
[**27** (X = I)]	D[e]	3.76	4.16[i]	4.23[h]	8.83[g]	9.58[g]		(84)
N^6,N^6,3,7-Tetramethyladeninium iodide								
[**28** (X = I)]	D[e]	3.58	4.13[f]	4.31[j]	8.48[g]	9.08[g]		(84)

(*continues*)

TABLE VII (*continued*)

Compound (No.)	Solvent[b]	Chemical shift (δ)[a]						Literature (ref. No.)
		N^6-Me	*N*-Me	*N*-Me	C(2)-H	C(8)-H	NH	
N^6,N^6,3,9-Tetramethyladeninium iodide								
[**29** (X = I)]	D[e]	3.55, 3.75	4.35[g]	4.43[g]	8.41[g]	9.20[g]		(84)
	F	3.39, 3.86	4.11[g]	4.22[g]	8.32[g]	8.60[g]		(85)
N^6,N^6,7,9-Tetramethyladeninium iodide								
[**30** (X = I)]	D[e]	3.68	4.42[j]	4.14[h]	8.75[g]	9.54[g]		(84)

a) In ppm, relative to Me_4Si.
b) The letter refers to the solvent with A, 1.2 M DCl; B, D_2O; C, DMSO; D, CF_3CO_2H; E, $CDCl_3$; F, DMSO-d_6; G, CCl_4.
c) Sodium 3-trimethylsilyl-1-propanesulfonate was used as an internal reference.
d) Acetonitrile was used as an internal reference.
e) Hexamethyldisiloxane was used as an internal reference.
f) N(3)-Me proton signal.
g) Not particularly assigned in the literature quoted.
h) N(9)-Me proton signal.
i) N(1)-Me proton signal.
j) N(7)-Me proton signal.

TABLE VIII. ^{13}C NMR Spectral Data of Mono- and Poly-*N*-methylated Adenines

Compound (No.)	Solvent[b]	Chemical shift (δ)[a]						Literature (ref. No.)
		C(2)	C(4)	C(5)	C(6)	C(8)	*N*-Me	
N^6-Methyladenine (**2**)	A	152.42	150.0	118.2	154.72	138.76	27.22	(113)
1-Methyladenine (**3**)	B	146.7	157.4	121.3	151.7	155.2	39.7	(21)
3-Methyladenine (**4**)	A	143.6	150.2	120.2	154.8	152.3	35.7	(21)
	C	152.9	151.1	120.8	156.8	146.0	36.9	(90)
7-Methyladenine (**5**)	D	152.3	159.8	111.7	151.9	145.9	33.7	(114)
	A	152.1	159.5	111.6	151.7	145.8	33.6	(21)
9-Methyladenine (**6**)	D	152.5	149.9	118.7	155.9	141.4	29.3	(114)
	A	152.3	149.8	118.6	155.8	141.3	29.2	(92)
	A	152.23	149.77	118.57	155.74	141.22	29.17	(91)

(*continues*)

TABLE VIII (*continued*)

Compound (No.)	Solvent[b]	Chemical shift (δ)[a]						Literature (ref. No.)
		C(2)	C(4)	C(5)	C(6)	C(8)	*N*-Me	
	A	152.70	150.23	120.3	156.13	141.89	29.74	(93)
	A	152.4	149.8	118.3	155.8	141.3	29.3	(96)
	A	152.3	149.8	118.5	155.8	141.3	29.2	(21)
N^6,N^6-Dimethyl-	A	151.76	151.23	118.97	154.29	137.74	37.84	(113)
adenine (**7**)	A	151.76	151.23	118.95	154.29	137.74	37.84	(104)
	A	151.67	150.97	118.88	154.11	137.62	37.74	(105)
	——[c]	151.7	151.7	119.4	158.4	140.3	36.5, 39.1	(106)
N^6,N^6,N^6-Trimethyladeninium chloride [**17** (X = Cl)]	A	150.33[d]	151.62[d]	137.74	156.59[d]	147.32[d]	54.24	(113)
N^6,N^6,9-Trimethyl-								
adenine (**21**)	A	152.4	151.0	120.1	155.0	138.7	38.5,[e] 29.6[f]	(92)

a) In ppm, relative to Me_4Si.
b) The letter refers to the solvent with A, DMSO-d_6; B, D_2O; C, CD_3OD; D, DMSO.
c) Measured in a solid state using hexamethylbenzene as an external reference.
d) This assignment is uncertain.
e) N^6-Me_2 signal.
f) N(9)-Me signal.

REFERENCES AND NOTES

1. J. H. Lister, 'Fused Pyrimidines. Part II: Purines,' ed. by D. J. Brown, Wiley–Interscience, New York, 1971.
2. G. Shaw, 'Rodd's Chemistry of Carbon Compounds,' 2nd ed., Vol. IV, Part L, ed. by S. Coffey, Elsevier Scientific Publishing Co., Amsterdam, 1980, Chapter 57, pp. 1–115.
3. G. Shaw, 'Comprehensive Heterocyclic Chemistry,' Vol. 5, ed. by K. T. Potts, Pergamon Press, Oxford, 1984, Chapter 4.09, pp. 499–994.
4. R. H. Hall, 'The Modified Nucleosides in Nucleic Acids,' Columbia University Press, New York, 1971.
5. Atta-ur-Rahman and M. I. Choudhary, 'The Alkaloids,' Vol. 38, ed. by A. Brossi, Academic Press, New York, 1990, Chapter 3, pp. 225–323.
6. T. Fujii and T. Itaya, *Heterocycles*, 1998, **48**, 1673.
7. T. Fujii and T. Itaya, *Heterocycles*, 1999, **51**, 393.
8. T. Fujii and T. Itaya, *Heterocycles*, 1999, **51**, 1141.
9. T. Fujii and T. Itaya, *Heterocycles*, 1999, **51**, 1971.
10. (a) See ref. 1, pp. 439–528; (b) For a general method utilizing acid dissociation constant and UV

spectral data for distinguishing between 3-, 7-, and 9-substituted adenines, see ref. 16; (c) For UV spectral characteristics which makes it possible to distinguish among possible N^x,N^y-disubstituted adenines, see N. J. Leonard, K. L. Carraway, and J. P. Helgeson, *J. Heterocycl. Chem.*, 1965, **2**, 291; (d) For the utilization of the difference in chemical shift between the C(2)-H and C(8)-H protons for structural assignments of N^x-substituted adenine, see ref. 78.

11. A. Albert, 'Synthetic Procedures in Nucleic Acid Chemistry,' Vol. 2, ed. by W. W. Zorbach and R. S. Tipson, Wiley–Interscience, New York, 1973, pp. 1–46 and pp. 47–123.
12. A. Albert and D. J. Brown, *J. Chem. Soc.*, 1954, 2060.
13. G. Fraenkel and Y. Asahi, *Takeda Kenkyusho Nempo*, 1965, **24**, 209 (*Chem. Abstr.*, 1966, **64**, 4909*c*).
14. E. R. Garrett and P. J. Mehta, *J. Am. Chem. Soc.*, 1972, **94**, 8532.
15. A. J. S. C. Vieira and S. Steenken, *J. Phys. Chem.*, 1987, **91**, 4138.
16. N. J. Leonard and J. A. Deyrup, *J. Am. Chem. Soc.*, 1962, **84**, 2148.
17. M. Dreyfus, G. Dodin, O. Bensaude, and J. E. Dubois, *J. Am. Chem. Soc.*, 1977, **99**, 7027.
18. P. Brookes and P. D. Lawley, *J. Chem. Soc.*, 1960, 539.
19. B. C. Pal and C. A. Horton, *J. Chem. Soc.*, 1964, 400.
20. B. C. Pal, *Biochemistry*, 1962, **1**, 558.
21. T. Saga, T. Kaiya, S. Asano, and K. Kohda, *Nucleosides Nucleotides*, 1996, **15**, 219.
22. R. Denayer, A. Cavé, and R. Goutarel, *Compt. Rend.*, 1961, **253**, 2994.
23. R. Stewart and M. G. Harris, *Can. J. Chem.*, 1977, **55**, 3807.
24. R. L. Benoit, D. Boulet, L. Séguin, and M. Fréchette, *Can. J. Chem.*, 1985, **63**, 1228.
25. J. Arpalahti and E. Ottoila, *Inorg. Chim. Acta*, 1985, **107**, 105.
26. S. E. Taylor, E. Buncel, and A. R. Norris, *J. Inorg. Biochem.*, 1981, **15**, 131.
27. (a) S. F. Mason, *J. Chem. Soc.*, 1954, 2071; (b) *Idem*, 'The Chemistry and Biology of Purines,' ed. by G. E. W. Wolstenholme and C. M. O'Connor, Little, Brown and Co., Boston, 1957, pp. 60–71.
28. B. M. Lynch, R. K. Robins, and C. C. Cheng, *J. Chem. Soc.*, 1958, 2973.
29. T. P. Pitner and J. D. Glickson, *Biochemistry*, 1975, **14**, 3083.
30. J. A. Montgomery and K. Hewson, *J. Am. Chem. Soc.*, 1960, **82**, 463.
31. U. Mikstais, A. P. Kreshkov, N. T. Smolova, and A. Veveris, *Latv. PSR Zinat. Akad. Vestis, Kim. Ser.*, 1977, 435 (*Chem. Abstr.*, 1978, **88**, 44543).
32. A. Veveris, N. T. Smolova, B. Spince, and U. Mikstais, *Latv. PSR Zinat. Akad. Vestis, Kim. Ser.*, 1980, 335 (*Chem. Abstr.*, 1980, **93**, 142354).
33. T. Itaya, F. Tanaka, and T. Fujii, *Tetrahedron*, 1972, **28**, 535.
34. D. J. Brown and N. W. Jacobsen, *J. Chem. Soc.*, 1965, 3770.
35. B. Lippert, H. Schöllhorn, and U. Thewalt, *Inorg. Chim. Acta*, 1992, **198–200**, 723.
36. T. Itaya, N. Ito, T. Kanai, and T. Fujii, *Chem. Pharm. Bull.*, 1997, **45**, 832.
37. T. Fujii, T. Itaya, and T. Saito, *Chem. Pharm. Bull.*, 1975, **23**, 54.
38. T. Fujii, T. Saito, and S. Mori, *Chem. Pharm. Bull.*, 1990, **38**, 2591.
39. R. Klemm, H. Schulze, M. G. Ettlinger, and A. R. Bader, *J. Med. Chem.*, 1966, **9**, 981.
40. G. B. Barlin and A. C. Young, *J. Chem. Soc. (B)*, 1971, 821.
41. C. Meiser, B. Song, E. Freisinger, M. Peilert, H. Sigel, and B. Lippert, *Chem. Eur. J.*, 1997, **3**, 388.
42. A. V. El'tsov, Kh. L. Muravich-Aleksandr, and I. Él'-Sakka, *J. Org. Chem. USSR* (*Engl. Transl.*), 1973, **9**, 1308 [*Zh. Org. Khim.*, 1973, **9**, 1280 (*Chem. Abstr.*, 1973, **79**, 105193)].
43. T. Fujii, T. Saito, and T. Muramoto, *Chem. Pharm. Bull.*, 1983, **31**, 4270.
44. T. Itaya, K. Ogawa, Y. Takada, and T. Fujii, *Chem. Pharm. Bull.*, 1996, **44**, 967.
45. A. D. Broom, L. B. Townsend, J. W. Jones, and R. K. Robins, *Biochemistry*, 1964, **3**, 494.

46. M. Mano, T. Seo, and K. Imai, *Chem. Pharm. Bull.*, 1983, **31**, 3454.
47. G. B. Elion, E. Burgi, and G. H. Hitchings, *J. Am. Chem. Soc.*, 1952, **74**, 411.
48. G. B. Elion, *J. Org. Chem.*, 1962, **27**, 2478.
49. J. W. Jones and R. K. Robins, *J. Am. Chem. Soc.*, 1963, **85**, 193.
50. K. Morita, S. Kobayashi, H. Shimadzu, and M. Ochiai, *Tetrahedron Lett.*, 1970, 861.
51. T. Monsees, L. Meijer, and B. Jastorff, *Eur. J. Biochem.*, 1993, **213**, 155.
52. J. W. Jones and R. K. Robins, *J. Am. Chem. Soc.*, 1962, **84**, 1914.
53. R. Denayer, *Bull. Soc. Chim. Fr.*, 1962, 1358.
54. K. Yamauchi, T. Tanabe, and M. Kinoshita, *J. Org. Chem.*, 1976, **41**, 3691.
55. N. J. Leonard, T. Fujii, and T. Saito, *Chem. Pharm. Bull.*, 1986, **34**, 2037.
56. G. C. Magnin, J. Dauvergne, A. Burger, and J.-F. Biellmann, *Tetrahedron Lett.*, 1996, **37**, 7833.
57. R. N. Prasad and R. K. Robins, *J. Am. Chem. Soc.*, 1957, **79**, 6401.
58. J. M. Gulland and E. R. Holiday, *J. Chem. Soc.*, 1936, 765.
59. R. K. Robins and H. H. Lin, *J. Am. Chem. Soc.*, 1957, **79**, 490.
60. J. W. Daly and B. E. Christensen, *J. Org. Chem.*, 1956, **21**, 177.
61. J. A. Montgomery and H. J. Thomas, *J. Org. Chem.*, 1966, **31**, 1411.
62. S. R. Breshears, S. S. Wang, S. G. Bechtolt, and B. E. Christensen, *J. Am. Chem. Soc.*, 1959, **81**, 3789.
63. T. Toraya, T. Kida, S. Tanaka, M. Matsushita, T. Tsurukai, and H. Shinotsuka, *Biosci. Biotechnol. Biochem.*, 1998, **62**, 72.
64. V. S. Volkov, A. M. Poverennyi, and E. D. Sverdlov, *Bioorg. Khim.*, 1987, **13**, 1230 (*Chem. Abstr.*, 1988, **108**, 70770).
65. E. C. Taylor and P. K. Loeffler, *J. Am. Chem. Soc.*, 1960, **82**, 3147.
66. T. Saito, I. Inoue, and T. Fujii, *Chem. Pharm. Bull.*, 1990, **38**, 1536.
67. T. Fujii, T. Saito, T. Itaya, K. Kizu, Y. Kumazawa, and S. Nakajima, *Chem. Pharm. Bull.*, 1987, **35**, 4482.
68. T. Fujii, T. Saito, T. Suzuki, and M. Kunugi, *Chem. Pharm. Bull.*, 1994, **42**, 151.
69. T. Fujii, T. Saito, K. Yamamoto, and R. Ii, *Chem. Pharm. Bull.*, 1993, **41**, 2047.
70. T. Fujii, T. Saito, I. Inoue, Y. Kumazawa, and N. J. Leonard, *Chem. Pharm. Bull.*, 1986, **34**, 1821.
71. T. Fujii, T. Itaya, F. Tanaka, T. Saito, K. Mohri, and K. Yamamoto, *Chem. Pharm. Bull.*, 1983, **31**, 3149.
72. T. Fujii, T. Itaya, T. Saito, K. Mohri, M. Kawanishi, and T. Nakasaka, *Chem. Pharm. Bull.*, 1989, **37**, 1504.
73. T. Fujii, T. Saito, T. Nakasaka, and K. Kizu, *Chem. Pharm. Bull.*, 1990, **38**, 99.
74. T. Fujii, T. Saito, T. Sakuma, M. Minami, and I. Inoue, *Chem. Pharm. Bull.*, 1990, **38**, 652.
75. Y. Maki, K. Kameyama, M. Suzuki, M. Sako, and K. Hirota, *J. Chem. Res. (M)*, 1984, 3601.
76. J. P. Horwitz, 'Synthetic Procedures in Nucleic Acid Chemistry,' Vol. 1, ed. by W. W. Zorbach and R. S. Tipson, Interscience Publishers, New York, 1968, pp. 39–40.
77. E. J. Reist, A. Benitez, L. Goodman, B. R. Baker, and W. W. Lee, *J. Org. Chem.*, 1962, **27**, 3274.
78. L. B. Townsend, R. K. Robins, R. N. Loeppky, and N. J. Leonard, *J. Am. Chem. Soc.*, 1964, **86**, 5320.
79. E. D. Bergmann, H. Weiler-Feilchenfeld, and Z. Neiman, *J. Chem. Soc. (B)*, 1970, 1334.
80. T. Itaya, H. Matsumoto, and K. Ogawa, *Chem. Pharm. Bull.*, 1980, **28**, 1920.
81. B. R. Baker, R. E. Schaub, and J. P. Joseph, *J. Org. Chem.*, 1954, **19**, 638.
82. J. L. Kelley, M. P. Krochmal, J. A. Linn, E. W. McLean, and F. E. Soroko, *J. Med. Chem.*, 1988, **31**, 606.

83. J. Kiburis and J. H. Lister, *J. Chem. Soc.* (*C*), 1971, 3942.
84. Kh. L. Muravich-Aleksandr, A. V. El'tsov, and I. Él'-Sakka, *J. Org. Chem. USSR* (*Engl. Transl.*), 1973, **9**, 1316 [*Zh. Org. Khim.*, 1973, **9**, 1288 (*Chem. Abstr.*, 1973, **79**, 105194)].
85. T. Itaya, K. Ogawa, H. Matsumoto, and T. Watanabe, *Chem. Pharm. Bull.*, 1980, **28**, 2522.
86. T. Platzek, G. Bochert, U. Rahm, and D. Neubert, *Z. Naturforsch.*, 1987, **42c**, 613.
87. W. S. Sheldrick and P. Gross, *Inorg. Chim. Acta*, 1989, **156**, 139.
88. A. B. Reitz, D. W. Graden, A. D. Jordan, Jr., and B. E. Maryanoff, *J. Org. Chem.*, 1990, **55**, 5761.
89. M. Ishino, T. Sakaguchi, I. Morimoto, and T. Okitsu, *Chem. Pharm. Bull.*, 1981, **29**, 2403.
90. D. L. Boger, R. M. Garbaccio, and Q. Jin, *J. Org. Chem.*, 1997, **62**, 8875.
91. J.-P. Charland, M. T. Phan Viet, M. St-Jacques, and A. L. Beauchamp, *J. Am. Chem. Soc.*, 1985, **107**, 8202.
92. H. Lönnberg, J. Ylikoski, J. Arpalahti, E. Ottoila, and A. Vesala, *Acta Chem. Scand., Ser. A*, 1985, **A39**, 171.
93. A. Holý, I. Rosenberg, and H. Dvoráková, *Collect. Czech. Chem. Commun.*, 1989, **54**, 2190.
94. J. Bergman, P.-O. Norrby, and P. Sand, *Tetrahedron*, 1990, **46**, 6113.
95. A. H. M. Al-Shaar, R. K. Chambers, D. W. Gilmour, D. J. Lythgoe, I. McClenaghan, and C. A. Ramsden, *J. Chem. Soc., Perkin Trans. 1*, 1992, 2789.
96. L. Schenetti, A. Mucci, and B. Longato, *J. Chem. Soc., Dalton Trans.*, 1996, 299.
97. J. H. J. den Hartog, H. van den Elst, and J. Reedijk, *J. Inorg. Biochem.*, 1984, **21**, 83.
98. E. G. Talman, W. Brüning, J. Reedijk, A. L. Spek, and N. Veldman, *Inorg. Chem.*, 1997, **36**, 854.
99. (a) S. P. Lam, F. Devinsky, and J. W. Gorrod, *Eur. J. Drug Metab. Pharmacokinet.*, 1987, **12**, 239; (b) S. P. Lam, D. J. Barlow, and J. W. Gorrod, *J. Pharm. Pharmacol.*, 1989, **41**, 373.
100. (a) T. Fujii, T. Saito, K. Kizu, H. Hayashibara, Y. Kumazawa, and S. Nakajima, *Heterocycles*, 1986, **24**, 2449; (b) T. Fujii, T. Saito, K. Kizu, H. Hayashibara, Y. Kumazawa, S. Nakajima, and T. Fujisawa, *Chem. Pharm. Bull.*, 1991, **39**, 301.
101. W. C. Coburn, Jr., M. C. Thorpe, J. A. Montgomery, and K. Hewson, *J. Org. Chem.*, 1965, **30**, 1114.
102. J. H. Keck, Jr., R. A. Simpson, and J. L. Wong, *J. Org. Chem.*, 1978, **43**, 2587.
103. M. Miyaki and B. Shimizu, *Chem. Pharm. Bull.*, 1970, **18**, 1446.
104. L. Grenier, J.-P. Charland, and A. L. Beauchamp, *Can. J. Chem.*, 1988, **66**, 1663.
105. M. S. Motawia, M. Meldal, M. Sofan, P. Stein, E. B. Pedersen, and C. Nielsen, *Synthesis*, 1995, 265.
106. A.-M. Lebuis and A. L. Beauchamp, *Inorg. Chim. Acta*, 1994, **216**, 131.
107. W. Schimmack, H. Sapper, and W. Lohmann, *Biophys. Struct. Mech.*, 1975, **1**, 311.
108. K. Doyama, F. Hama, Y. Sakata, and S. Misumi, *Tetrahedron Lett.*, 1981, **22**, 4101.
109. J. D. Engel and P. H. von Hippel, *Biochemistry*, 1974, **13**, 4143.
110. F. Seyama, K. Akahori, Y. Sakata, S. Misumi, M. Aida, and C. Nagata, *J. Am. Chem. Soc.*, 1988, **110**, 2192.
111. W. Schimmack, H. Sapper, and W. Lohmann, *Biophys. Struct. Mech.*, 1975, **1**, 113.
112. T. Okano, A. Takadate, and T. Kano, *Gann*, 1969, **60**, 557.
113. M. C. Thorpe, W. C. Coburn, Jr., and J. A. Montgomery, *J. Magn. Reson.*, 1974, **15**, 98.
114. M.-T. Chenon, R. J. Pugmire, D. M. Grant, R. P. Panzica, and L. B. Townsend, *J. Am. Chem. Soc.*, 1975, **97**, 4627.

Received, 6th May, 1999