The Positional Dependence of Anodic Peak Potentials in *N*-Substituted Adenines[1)]

Takeo SATO,* Kentaro FUKUZAKI, and Tozo FUJII†
Department of Chemistry, Tokyo Metropolitan University, Setagaya-ku, Tokyo 158
†Faculty of Pharmaceutical Sciences, Kanazawa University, Takara-machi, Kanazawa 920
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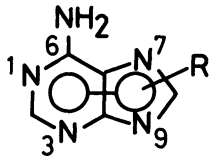
Synopsis. In order to determine the structural dependence on the anodic potential, cyclic voltammetric measurements were carried out for 1-, 3-, 7-, 9-, and N^6-alkyladenines in *N*,*N*-dimethylformamide (DMF) or in acetonitrile (AN). The anodic peak potential, E_{pa}, in DMF was found to be sensitive to the substitution and shifted anodic in the order, 7-<1-<3-, N^6-<9-substituted derivatives. These data, with the aid of solvent effects, are useful for determining the substitution pattern in *N*-alkyladenines.

Only 9-substituted adenines were previously found in biologically important nucleosides and nucleotides,[2)] although five *N*-substituted derivatives are possible, namely, 1-, 3-, 7-, 9-, and N^6-substituted derivatives (**1**). Until now, however, all five de-



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rivatives have been isolated from natural sources and have been synthesized.[2)] This has led to investigation of methods for the selective formation and structural determination of *N*-alkyladenines.[2,3)]

Besides chemical methods, three approaches have been reported[3)] to distinguish substitution in *N*-alkyladenines. UV spectral maxima in acidic or basic media were used to differentiate each of the 1-, 9-, and N^6-substitutions from a group of 3- and 7-substitutions. The pK_a' values were shown to differentiate 3- and 7- or 9-substitutions, and the value of λ_{min} (pH 1)$-\lambda_{min}$ (pH 7) was used to distinguish 3- from 7- or 9-substituted adenines. Sometimes, the first approach may not clearly differentiate substitution among imidazole rings, e.g. 7- from 9-substitution.[3)] In this note, we survey the anodic peak potentials of alkyladenines and related compounds in order to obtain a complementary method for structural determinations.

Dryhurst and Elving[4)] have carried out the anodic oxidation of adenine in aq acetic acid on a porous graphite electrode and observed an initial oxidation similar to an enzymatic type, followed by deep-seated fragmentation. We carried out cyclic voltammetric measurements for all the *N*-positional isomers of methyl-, ethyl-, and benzyladenines together with 9-phenethyladenine in acetonitrile (AN) or in *N*,*N*-dimethylformamide (DMF) using a platinum anode. All compounds except for 1-methyladenine showed an E_{pa} between +1.1 and +1.8 V vs. SCE at a scan rate of 50—500 mV s^{-1} but failed to show a reduction wave upon potential reversal. The data measured in DMF showed a significant positional dependence, the results determined at a scan rate of 250 mV s^{-1} are summarized in Table 1.

Adenine showed an E_{pa} at +1.75 V in DMF and +1.45 V in AN. In either solvent, the anodic peak potentials were found to depend on the substitution pattern and were essentially similar among the methyl, ethyl, and benzyl derivatives. In DMF, the 9-alkyl derivatives showed E_{pa}s at the highest anodic potential, observable only as a shoulder at ca. +1.7 V. Those having an N^6-substituent showed a slight cathodic shift with E_{pa}s at ca. +1.6 V. The 1- and 3-substituted adenines showed E_{pa}s at ca. +1.4 and 1.5 V, respectively. A significant cathodic shift was observed for the 7-alkyl derivatives which showed E_{pa}s at ca. +1.2 V. The E_{pa}s for alkyladenines in DMF increase in the order:

7-<1-<3-, N^6-<9-substituted derivatives

1-Methyladenine was practically insoluble in DMF and no voltammogram was recorded. Kinetin showed an E_{pa} at +1.63 V (+1.45 V in AN) as expected from N^6-substitution. Adenosine showed an E_{pa} at +1.23 V, a considerable cathodic potential. This was not expected from a 9-substituted derivative, and indicated that a one-electron transfer occurred on the sugar moiety. The above data showed that E_{pa} is sensitive to substitution and enables one to differentiate between 7- and 9-substitution quite easily.

The solvent effect on the CV measurements was then investigated. In *N*,*N*-dimethylacetamide, the 7-substituted derivatives showed E_{pa}s between +1.1 and 1.3 V, similar to those observed in DMF. In AN, however, a significant solvent-induced shift was noticed as compared with the amide solvents. Table 2 summarizes peak potentials for *N*-benzyladenines as well as the solvent shift in E_{pa}, ΔE_{pa} (AN–DMF).

Table 1. Anodic Peak Potential Data for *N*-Alkyladenines[a)]

Position of R	R			
	Me	Et	$PhCH_2$	$PhCH_2CH_2$
1	—[b)]	1.41	1.40	
3	1.54	1.54	1.52	
7	1.17	1.17[c)]	1.19	
9	1.68[c)]	1.68[c)]	1.70[c)]	1.76
N^6	1.58	1.54[c)]	1.56[c)]	

a) The cyclic voltammetry was carried out in DMF–TBAP (0.1 mol dm^{-3}) using a platinum inlay electrode as an anode and SCE as the reference at 250 mV s^{-1}. b) The compound is insoluble in DMF. c) Shoulder.

Table 2. The Anodic Peak Potential Data for *N*-Benzyladenines in Various Solvents[a]

Position of R		E_{pa} DMF	E_{pa} DMAc[b]	E_{pa} AN	ΔE_{pa} (AN-DMF)
Pyrimidine moiety	1	1.40		1.10	−0.30
	3	1.52		1.50	−0.02
	N^6	1.56[c]		1.48	−0.08
Imidazole moiety	7	1.19	1.10[c]	1.67	+0.48
	9	1.70[c]		1.62	−0.08

a) The measurements were carried out in the same way as described in Table 1. b) *N*,*N*-dimethylacetamide. c) Shoulder.

In AN, the 1- and N^6-substituted derivatives having a substituent in the pyrimidine moiety showed cathodic shifts of 0.3 and 0.1 V, respectively, whereas the 7-substituted derivatives showed an anodic shift of 0.5 V. The anodic shift for both 7-methyl- and 7-ethyladenines in AN was 0.4 V. Those substituted at the 3- and 9-positions showed no solvent-induced shift. This phenomena might be ascribable to the selective association between the 1- and N^6-positions of adenine with the amide solvent as in the adenine–thymine pair.

Whereas the UV, pK_a', and λ_{min} methods have been used to differentiate substitution between pyrimidine and imidazole rings of alkyladenines, the present CV method independently could differentiate not only substitution between 7- and 9- positions but also among pyrimidine rings, namely, 1-, 3-, and N^6-substitution, with the aid of solvent effects.

Experimental

Materials. The substrates used for the CV measurements were obtained commercially or were taken from stocks which had been prepared according to published procedures: 1-,[5] 3-,[6] 7-,[7] 9-,[8] and N^6-methyladenines;[9] 1-,[10] 3-,[11] 7-,[7] 9-,[8] and N^6-ethyladenines;[10] 1-,[12] 3-,[13] 7-,[13] 9-,[8] and N^6-benzyladenines;[12] 9-phenethyladenine.[8]

Cyclic Voltammetry. The measurements were carried out using a generator, Hokuto HB-107A, and a potentiostat, Hokuto HA-101. As an anode, a platinum inlay electrode, Beckman No. 39273, was used. To avoid contamination from moisture, the reference SCE was connected to a modified H-cell through two junction bridges each filled with a sat KCl solution and DMF or AN–tetrabutylammonium perchlorate (TBAP). Molecular sieve 1A (Wako chemicals) was added to the bridge directly immersed in the cell.

Sample concentrations were between 10^{-4} and 10^{-5} mol dm^{-3}. 1-Methyladenine was insoluble in DMF and no voltammogram was recorded. As an anolyte, TBAP was added to the solution to make 0.1 mol dm^{-3} solutions. The results recorded at 250 mV s^{-1} are shown in Tables 1 and 2. The data are expressed in +V vs. SCE. Highly anodic peaks, especially determined in DMF, appeared as a shoulder.

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