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Determination of the Ionization Potential and the Electron Affinity of Various Biologically Active Substances by Polarography*

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Abstract

The electron affinity and ionization potential of various biological substances were measured by polarography and compared with their effect on growth of *E. coli*.

Introduction

Formation of charge transfer complexes may play an important role in the biology.[1] The ionization potential (I) and the electron affinity (EA) of the reactants are significant. The ionization potentials of biologically active substances have hitherto not been determined experimentally. These substances are mostly organic compounds with complicated structures. The possibility of charge transfer can be predicted from I and EA. The corresponding values in the gaseous state will be denoted by I_p and E_A. Matsen[2] has shown that for aromatic hydrocarbons (D) the gaseous electron affinity (E_A) can be related to the reductive half-wave potential $E_{1/2}^{red}$ versus the S.C.E., if the potential-determining step for reduction is reversible and can be represented as $D + e \rightleftharpoons D^-$, by

$$E_A \text{ (eV)} = E_{1/2}^{red} (V \text{ versus S.C.E.}) - \Delta E_{sol} + 5{\cdot}07 \quad (1)$$

ΔE_{sol}, the difference of solvation energy between D^- and D, cannot be exactly calculated. In this paper, the values for ΔE_{sol} were obtained by using equation (2) (see ref. 3), while the electron affinity of various biologically active molecules was determined by equation (1).

$$\Delta E_{sol} = \left(1 - \frac{1}{\epsilon}\right)\frac{e^2}{2r} \quad (2)$$

where ϵ is the optical dielectric constant of medium, r the radius of the molecule, and e the charge of electron. The ionization potential of gaseous aromatic hydrocarbon is related to equation (3) (see ref. 4) if the potential-determining step for oxidation of aromatic hydrocarbon is a reversible reaction and can be represented as $D - e \rightleftharpoons D^+$.

$$I_p \text{ (eV)} = E_{1/2}^{oxi} (V \text{ versus S.C.E.}) + \Delta E'_{sol} + 5{\cdot}07 \quad (3)$$

where $\Delta E'_{sol}$ is the difference of solvation energy between D^+ and D. This equation was also used in determining the I_p of organic molecules other than aromatic hydrocarbons.

The values of r were calculated from the molar refraction. The ϵ was given by the arithmetical means of the optical dielectric constants of mercury and the solvent, because the electrode reaction occurs at the intersurface between mercury drops and the solvents. Since the dielectric constant of mercury is taken as infinite, the dielectric constant of medium around the molecule was also taken as infinite.

Experimental

Materials

Lithium chloride, boric acid, citric acid, sodium hydrophosphate and DMSO were obtained from the Fisher Scientific Company, tetramethyl ammonium hydroxide from

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Eastman Organic Chemicals, lithium hydroxide from Merck Company; ethanol was U.S.P. All other chemicals used in this experiment are described in the tables.

Polarograms

A Sargent Polarograph Model XVI with an a.c. unit was used to obtain polarograms. All d.c. potentials were measured directly against the saturated calomel electrode and corrected for ohmic potential drop. The a.c. potentials were also measured to investigate the reversibility of electrode reaction, and good results were obtained in most cases. The samples were measured in alkaline or acidic solution at 23° c to exclude the effect of H^+ or OH^-. The supporting electrolytes and solvents used for the measurements are indicated in the tables. The concentrations of the various samples were in most cases between 10^{-3} and 10^{-1} mole.

Results and Discussion

The electron affinities of a number of organic compounds, determined by the polarographic method, are shown in Table I, and are compared with the values obtained by

TABLE I. Comparison of electron affinity determined by polarography with those obtained by direct method*

	r (Å)	ΔE_{sol} (eV)	$E_{1/2}^{red}$ (V versus S.C.E.)	E_A (eV) From $E_{1/2}$	E_A (eV) Directly
Acetophenone[a]	2·3	3·14	− 1·60[d]	0·33	0·33[5]
Benzaldehyde[b]	2·3	3·14	− 1·51[d]	0·42	0·45[5]
p-Benzoquinone[c]	2·3	3·14	− 0·54[e]	1·39	1·38[6]
1-Naphthaldehyde[a]	2·6	2·74	− 1·82[d]	0·51	0·67[5]
Chloranil	2·7	2·65	+ 0·01[10]	2·43	2·46[6]
Anthracene	2·8	2·57	− 1·94[9]	0·56	0·55[7]

* The figures in parentheses denote the cited literature.
[a] Eastman Organic Chemicals; [b] Merck & Company, Inc.; [c] Fisher Scientific Company; [d] Sörensen buffer pH 11/50% EtOH; [e] 0·1 M LiCl/EtOH.

TABLE II. Comparison of ionization potential determined by polarography with those obtained by another method*

	r (Å)	$\Delta E'_{sol}$ (eV)	$E_{1/2}^{oxi}$ (V versus S.C.E.)	I_p (eV) From $E_{1/2}^{oxi}$	I_p (eV) Another method
Ascorbic acid[a]	2·5	2·91	0·22[c]	8·20	8·32[e]
Eosin[b]	3·0	2·40	− 0·10[d]	7·37	7·47[12]
Phenol	2·2	3·14	0·71[11]	8·92	9·03[13]
p-Nitrophenol	2·3	3·14	0·96[11]	9·17	9·06[e]

* The figures in parentheses denote the cited literature.
[a] Fisher Scientific Company; [b] National Aniline Division; [c] McIlvaine buffer pH 2·2; [d] McIlvaine buffer pH 3·0; [e] calculated from the equation $E_{h.o.} = \alpha + \lambda_{h.o.}\ \beta$, as $\alpha = -7{\cdot}0$ eV, $\beta = -2{\cdot}5$ eV, respectively. Value of each $\lambda_{h.o.}$ are cited from the ref. 14.

TABLE III. Electron affinities of various biologically active substances, calculated from the half-wave potentials*

Substances	$E_{1/2}^{red}$ (V versus S.C.E.)	E_A (eV)
Glyceraldehyde	−1·63[15]	−0·18
Riboflavin	0·64[15]	2·33
Chloramphenicol	−0·75[15]	1·90
VK_3	−0·47[15]	1·77
Cortisone	−2·18[16]	0·74
Androstanectione	−2·25[16]	0·52
Testosterone	−2·26[16]	0·56
11-Ketoprogesterone	−2·22[16]	0.60
11-Dehydroprogesterone	−2·24[16]	0·58
Progesterone	−2·27[16]	0·55
Nicotinamide	−1·67[17]	0.40
Pyridoxine	−1·85[15]	0·52
α,β,γ,δ-Tetraphenylporphine	−1·05[18]	2·34
Cu α,β,γ,δ-Tetraphenylporphine	−1·20[18]	2·19
Mg α,β,γ,δ-Tetraphenylporphine	−1·35[18]	2·04
Ethioporphyrin I	−1·34[18]	1·90
Cu Ethioporphyrin IV	−1·48[18]	1·76
Chlorophyll a	−1·12[19]	2·15
Chlorophyll b	−1·02[19]	2·25
Stilboestrol	−2·80[16]	0·21
Equilenin	−2·17[16]	0·55
Estrone	−1·98[16]	0·75
Dihydrocortisone	−2·43[16]	0·49
$\Delta E'$ Prednisone	−1·88[16]	1·04

* The figures in parentheses denote the cited literature.

TABLE IV. Ionization potentials of biologically active substances, calculated from the half-wave potentials*

Substances	$E_{1/2}^{oxi}$ (V versus S.C.E.)	I_p (eV)
Adrenaline	0·19[15]	7·96
Stilboestrol	0·90[16]	8·03
Equilenin	1·10[16]	8·52
Estrone	1·19[16]	8·61
Estradiol	1·24[16]	8·66
Dihydrocortisone	2·04[16]	9·26
$\Delta E'$ Prednisone	2·24[16]	9·46

* The figures in parentheses denote the cited literature.

other methods.[5–7] In general there is good agreement. Since the electron affinities in the literature were measured directly by magnetron technique or electron-capture detector, they are assumed to be reliable, and hence the electron affinities determined by the polarographic method seem to be correct. It also appears reasonable to suppose that

TABLE V. Electron affinities of various aldehydes and ketones, calculated from the half-wave potentials

Substances	ΔE_{sol} (eV)	$E_{1/2}$ (V versus S.C.E.)	E_A (eV)
Formaldehyde[o]	5·21	− 1·71[a]	− 1·85
Acetaldehyde[o]	4·35	− 1·89[b]	− 1·17
Propionaldehyde[p]	3·90	− 1·92[b]	− 0·75
n-Butylaldehyde[p]	3·57	− 1·95[c]	− 0·45
Valeraldehyde[q]	3·33	− 2·09[d]	− 0·35
Heptaldehyde[q]	3·00	− 2·22[e]	− 0·15
Crotonaldehyde[q]	3·60	− 1·49[f]	− 0·02
Methylvinylketone[p]	3·60	− 1·49[g]	− 0·02
Mesityloxide[q]	3·17	− 1·64[h]	0·26
Glyoxal[o]	4·35	− 1·57[i]	− 0·85
Methylglyoxal[r]	3·90	− 0·80[i]	0·37
Ethylglyoxal[r]	3·55	− 1·04[j]	0·48
Propylglyoxal[r]	3·33	− 0·98[j]	0·76
2-Methoxybenzoquinone[s]	3·07	− 0·64[k]	1·36
2,6-Dimethoxybenzoquinone[s]	3·00	− 0·73[k]	1·34
2,3-Diketogulonic acid[s]	3·00	− 1·05[b]	1·02
Alloxan[q]	3.77	− 0·25[b]	1·05
D-Glucose[t]	2·87	− 2·16[b]	0·02
D-Mannose[u]	2·87	− 2·03[e]	0·17
D-Galactose[o]	2·87	− 2·07[e]	0·13
D-Xylose[o]	2·95	− 2·06[e]	0·06
D-Arabinose[q]	2·95	− 2·00[e]	0·12
glucuronolactone[v]	2·98	− 1·61[n]	0·48
D-Ribose[u]	2·95	− 2·10[e]	0·02
2-Butanone[o]	3·57	− 2·20[m]	− 0·70

[a] Sörensen buffer pH 12; [b] 0·1 M LiOH; [c] 0·1 M LiOH/30% EtOH; [d] 0·1 M Me_4N·OH/50% EtOH; [e] 0·1 M Me_4N·OH/75% EtOH; [f] Sörensen buffer pH 11; [g] Sörensen buffer pH 10/90% EtOH; [h] Sörensen buffer pH 11/50% EtOH; [i] Sörensen buffer pH 11, 0·1 M LiCl/DMSO; [j] Sörensen buffer pH 11; [k] 0·1 M LiCl/EtOH; [l] 0·1 M Me_4N·OH; [m] 0·1 M Me_4N·OH/90% EtOH; [n] N/15 Na_2HPO_4 + N/10 NaOH, pH 10; [o] Fisher Scientific Company; [p] Aldrich Chemical Company, Inc.; [q] Eastman Organic Chemicals; [r] Obtained from Dr. L. G. Együd; [s] Obtained from Dr. A. Szent-Györgyi; [t] Merck & Company, Inc.; [u] Nutritional Biochemicals Corp.; [v] Chugai Pharmaceutical Company.

only one electron is added to the reducing materials at the first step of electrode reaction, as long as the reaction occurs in a sufficiently alkaline medium or in an organic solvent. The ionization potentials of a number of organic molecules determined by polarographic method are compared with the values obtained by other methods in Table II, and are consistent.

The results indicate that the polarographic method can be used for the determination of the E_A and I_p of various kinds of organic molecules.

The E_A and I_p of miscellaneous biologically active substances were calculated from the half-wave potential values cited in the literature, and are summarized in Tables III and IV. The E_A of porphine derivatives, riboflavin, chloramphenicol, and menadione is high, that of various steroid hormones moderate. Steroid hormones give moderate I_p.

One must bear in mind that the I and the EA of molecules are dependent on the dielectric constant of the medium.[20–21] The ionization potential is lower and the electron affinity higher in an aqueous medium[22] than in organic solvents. Thus charge transfer is favoured by aqueous medium.

The electron affinities of various kinds of aldehydes and ketones were also determined polarographically as shown in Table V. The relationship between the electron affinity of the aldehydes or ketones and their inhibitory effect on the proliferation of *E. coli*[8] was compared. Figure 1 shows that the inhibitory effect on proliferation tends to increase with E_A. This makes it clear that a charge transfer between these compounds and electron donors in the cell is important for their inhibitory effect. It should also be noted that ketones with a high E_A (such as *p*-benzoquinone) are highly toxic, and ketones and aldehydes with a moderate electron affinity are reversible inhibitors.[8] Methylglyoxal shows a moderate E_A and was also found to be a reversible inhibitor on cell division.[8] The correlation, however, is rather rough, which indicates that other factors may be involved. Figure 1 indicates that the substances studied fall into two groups corresponding to the two different curves obtained.

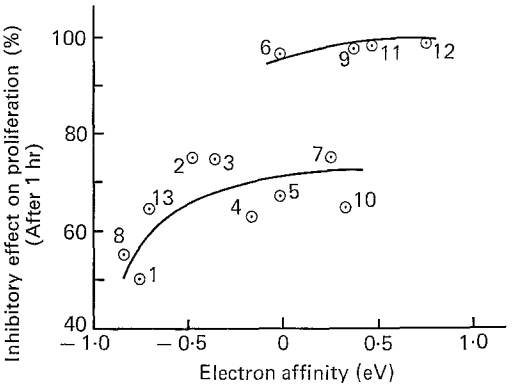

Figure 1. Relationship between the inhibitory effect of proliferation and electron affinity. 1, propionaldehyde; 2, *n*-butylaldehyde; 3, valeraldehyde; 4, heptaldehyde; 5, crotonaldehyde; 6, methylvinylketone; 7, mesityloxide; 8, glyoxal; 9, methylglyoxal; 10, Acetophenone; 11, ethylglyoxal; 12, propylglyoxal; 13, 2-butanone.

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