RESTRICTED INTRAMOLECULAR ENERGY FLOW IN LARGE MOLECULES. HETEROGENEOUS AND ENZYME CATALYSIS

Milan SOLC

Institute of Inorganic Chemistry, Academy of Sciences of the Czech Republic, 160 00 Prague 6, Czech Republic; e-mail: solc@iic.cas.cz

Received October 8, 1996
Accepted December 9, 1996

Dedicated to Professor Jaromir Plesek on the occasion of his 70th birthday in recognition of his outstanding contributions to organic, borane and carborane chemistry.

The free intramolecular energy flow can be restricted by the presence of a heavy atom in the molecule. As a result of this restriction, adsorbed molecules bonded on the metal surface and/or substrate molecules in the enzyme–substrate complex with a metal atom near the binding site can have a higher vibrational energy than the surroundings. The reaction rate is then enhanced by this energy localization.

Key words: Intramolecular energy flow; Enzyme catalysis; Heterogeneous catalysis; Heavy atoms.

The idea of intramolecular energy flow is the key concept in the theory of unimolecular decomposition – dissociation or isomerization – of polyatomic molecules after the collisional and chemical activation or photon absorption. Experiments and theoretical calculations suggest that a statistical redistribution (randomization) of the vibrational energy in molecules of medium size (represented by tens of oscillators) occurs on a picoseconds time scale and that it does not depend on the way of activation (see the review[1]). The energized molecule decomposes after a random fluctuation of vibrational energy in which an energy greater than a critical value ε_0 concentrates at a critical site (bond, oscillator) of the molecule. If, immediately after the activation, the excitation energy is concentrated at a certain site of the molecule, then the influence of this localization of energy on the kinetics of decomposition disappears on a picoseconds time scale and the molecule loses ("forgets") the information about the way of its energization[1].

Can the concept of a rapid statistical intramolecular redistribution of vibrational energy be used in the case of large molecules containing thousands or even more representative oscillators? We can put this question in the explanation of the fragmentation of large polyatomic ions in the mass spectrometer[2–4], the rate of one-substrate enzy-

matic reactions[5,6], or the mechanism of chemisorption and surface unimolecular reaction[7,8].

Now, explain what we mean by the term statistical redistribution (randomization) of vibrational energy. Let us consider an energized polyatomic molecule represented by n classical harmonic oscillators with the total vibrational energy $\varepsilon > \varepsilon_0$. Further, assume that a free and rapid exchange of energy among representative oscillators occurs. Then the probability, $P(\varepsilon_i > \varepsilon_0)$, $1 \le i \le n$, that the energy of a randomly selected oscillator in the molecule is greater than the threshold energy ε_0 is given by the classical Rice–Ramsperger–Kassel (RRK) expression[9]

$$P(\varepsilon_i > \varepsilon_0) = (1 - \varepsilon_0/\varepsilon)^{n-1} \quad . \tag{1}$$

A molecule satisfying this relation is referred to as a molecule with statistical (randomized) distribution of vibrational energy. Strictly speaking, for statistical (randomized) distribution the probability that the energy of representative oscilators of the molecule will lie within the limits ε_1 to $\varepsilon_1 + d\varepsilon_1$, ε_2 to $\varepsilon_2 + d\varepsilon_2$, … ε_n to $\varepsilon_n + d\varepsilon_n$ is equal to $d\varepsilon_1\, d\varepsilon_2 ... d\varepsilon_n / \int ... \int d\varepsilon_1 d\varepsilon_2 ... d\varepsilon_n$, where the integration is over the region $\varepsilon < \varepsilon_1 + \varepsilon_2 + ... + \varepsilon_n \le \varepsilon + d\varepsilon$. The process of vibrational energy redistribution from the original state with localized energy to the final state with statistically redistributed energy is called intramolecular vibrational energy redistribution (IVR). The statistical Rice–Ramsperger–Kassel (RRK) theory of unimolecular decomposition[9] is based on the assumption that the probability of accumulation of energy larger than the threshold energy in the critical oscillator is, owing to the rapid exchange of energy among oscillators, always equal to $(1 - \varepsilon_0/\varepsilon)^{n-1}$ regardless of the time lag between activation and decomposition. Our question now is: can the RRK theory be applied even in the case of decomposition of very large molecules? The consequences of the affirmative answer to this question were discussed by Bunker and Wang[5]. Let us assume that the answer to this question is yes. Then for large values of n, an arbitrarily selected oscillator is in permanent contact with the remaining $n - 1$ oscillators which constitute a heat bath[3]. For this heat bath we can introduce the temperature of oscillators[10] defined by the relationship $T_{osc} = \bar{\varepsilon}/n\boldsymbol{k}$, where $\bar{\varepsilon}$ is the mean energy of the system and $\boldsymbol{k}$ is the Boltzmann constant. Substituting the value of $\bar{\varepsilon}$ for ε in Eq. (*1*), we find that the stationary probability that the energy of a randomly chosen oscillator will be greater than ε_0 is given by the expression

$$P(\varepsilon_i > \varepsilon_0) = (1 - \varepsilon_0/\bar{\varepsilon})^{n-1} \approx (1 - \varepsilon_0/n\boldsymbol{k}T_{osc})^{n-1} \approx \exp(-\varepsilon_0/\boldsymbol{k}T_{osc}) \quad , \tag{2}$$

which is an expression derived for a canonical ensemble of harmonic oscillators. Using the RRK theory even in the case of large molecules, we find that the rate constant of decomposition of molecules with the mean vibrational energy $\bar{\varepsilon} = n\boldsymbol{k}T_{\mathrm{osc}}$ is

$$k(\bar{\varepsilon}) \approx \nu \exp(-\varepsilon_0/\boldsymbol{k}T_{\mathrm{osc}}) = \nu \exp(-n\varepsilon_0/\bar{\varepsilon}) \ , \qquad (3)$$

where ν is the preexponential factor of the order of 10^{13} s^{-1}, regardless of the way of activation.

Experimental[11,12] and theoretical[13] studies of the decomposition of the decyl radical produced in the reaction of the hydrogen atom with the 1-decene molecule suggest that the energy flow from the originally excited site to the rest of the molecule is a sequential process and the energy flows to the neighboring bonds in the first place. The time interval between transition of energy from the bond to the neighboring one is approximately fifty femtoseconds[13]. Extrapolation of the concept of sequential energy redistribution to the case of very large and generally nonlinear molecules would lead to times of statistical redistribution of the order of tens or hundreds of picoseconds or even larger values. This would mean that in very large molecules, the basic condition of RRK theory – rapid randomization of total vibrational energy – is not fulfilled[4] even after tens or hundreds of picoseconds after the activation and the ensemble of representative oscillators cannot be characterized by a single temperature of oscillators. Then there exist "hot" and "cold" oscillators in the molecule. When the critical oscillator is a "hot" oscillator, the probability of molecular decomposition is larger than that corresponding to the RRK theory[14], whereas if it is a "cold" oscillator, the probability of molecular decomposition is smaller than the RRK theory predicts. In both cases, the probability of molecular decay will approach (from above or from below) the stationary RRK value[15].

ROLE OF INTRAMOLECULAR ENERGY FLOW IN HETEROGENEOUS AND ENZYME CATALYSIS

The lifetime of the vibrationally "hot" site in the molecule depends on the rate of the energy flow from this site to the rest of the molecule. Can this energy flow be restricted? Some experiments with medium size molecules containing a covalently bonded metal suggest that a heavy atom can form a barrier to the rapid energy flow[16–19]. In such case, an alternative theory of unimolecular decomposition of adsorbed polyatomic molecules and/or of substrate–enzyme complexes can be suggested[6–8].

Heterogeneous Catalysis

Let us consider a catalytic decomposition – dissociation or isomerization – of a polyatomic molecule AB from the gas phase on surface centers formed by atoms of a metal M. The molecule AB adsorbs on the center M and the bond AB–M is formed. The adsorption energy, ε_{ads}, released in adsorption is originally localized in the newly formed bond AB–M and then flows to neighboring vibrational degrees of freedom; this situation is similar to that after the chemical photon activation. In the theory of heterogeneous catalytic reactions it is assumed that the adsorption energy flows from the AB–M bond into the catalyst bulk phase[20,21]. The polyatomic system AB–M–bulk phase represents a large molecule[22]. The bulk phase represents a large heat bath from which, at a random fluctuation, an energy greater than the threshold energy, ε_0, flows through the atom M into the adsorbed molecule AB and, if it concentrates at a critical oscillator, chemical change occurs[21]. The probability of this fluctuation is given by Eq. (*2*) where $\bar{\varepsilon} = (n_{bulk} + n_{AB})\boldsymbol{k}T + \varepsilon_{ads} \approx n_{bulk}\boldsymbol{k}T$, n_{bulk} and n_{AB} are the numbers of representative oscillators in the bulk phase and the adsorbed molecule, respectively, ($n_{bulk} >> n_{AB}$) and T is the temperature of bulk phase.

Another view arises if the atom M constitutes a serious obstacle to the energy flow. In such case the adsorption energy is redistributed among oscillators of the adsorbed molecule AB only. This redistribution should be sufficiently rapid for the molecules AB of medium size and the system AB–M can be thus considered a molecule satisfying the RRK theory of unimolecular decomposition[7,8]. Then the average vibrational energy, $\bar{\varepsilon}$, of the system AB–M is equal to $n_{AB}\boldsymbol{k}T + \varepsilon_{ads}$ where T is the temperature of the gas phase. Applying Eqs (*2*) and (*3*) and assuming sufficiently large values of n_{AB}, the rate constant of decomposition of the adsorbed molecules with the mean internal vibrational energy $\bar{\varepsilon}$ can be expressed by the relation

$$k(\bar{\varepsilon}) \approx \nu[1 - \varepsilon_0/(n_{AB}\boldsymbol{k}T + \varepsilon_{ads})]^{n_{AB}} \approx \nu \exp[-n_{AB}\varepsilon_0/(n_{AB}\boldsymbol{k}T + \varepsilon_{ads})] \quad . \qquad (4)$$

This expression can be interpreted as the rate constant of decomposition of molecules at the effective temperature $T_{eff} = T + \varepsilon_{ads}/n_{AB}\boldsymbol{k}$. The blocking of the intramolecular energy flow into the bulk phase of the catalyst increases the effective vibrational temperature of the adsorbed molecule AB and therefore increases the rate of its decomposition. This increase depends on the gas phase temperature and on the adsorption energy value. With increasing temperature T, increasing value of n_{AB} and decreasing value of ε_{ads}, the value of the ratio T_{eff}/T decreases to 1. Note that the process opposite to the energy flow from the bond AB–M into the adsorbed molecule AB, *i.e.* the process of energy accumulation from vibrationally "hot" oscillators of the adsorbed molecule AB in the AB–M bond leading to the subsequent break of this bond is known as the vibrationally induced desorption[23].

Enzyme Catalysis

Enzymes are highly effective, selective and specific catalysts, almost always of protein nature. The simplest mechanism of one-substrate enzyme catalyzed reaction can be described by the Michaelis–Menten scheme

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ES} \xrightarrow{k_2} \mathrm{E} + \mathrm{P} \ , \qquad (5)$$

where E denotes the enzyme, S the substrate, ES the complex enzyme–substrate and P the reaction product. According to this scheme, the stationary concentration of ES, c_{ES}, is

$$c_{ES} = k_1 c_E c_S/(k_{-1} + k_2) = c_E c_S/K_M \ . \qquad (6)$$

The reaction rate is then described by the well-known Michaelis–Menten equation

$$r = -\mathrm{d}c_S/\mathrm{d}t = k_2 c_{ES} = k_2 c_E^0 c_S/(K_M + c_S) \ , \qquad (7)$$

where c_E^0 is the total concentration of enzyme in the system, c_S the actual concentration of free substrate and $K_M = (k_{-1} + k_2)/k_1$ is the Michaelis constant[24,25].

In the theory of enzyme catalyzed reactions it is assumed that the chemical change in the complex ES is an activated process which requires activation energy ε_0. Furthermore it is assumed that only some part of the enzyme molecule is active, called the active centre or active site. The enzyme molecules are usually very large (10–100 nm). According to the present theory, the catalytic effect of the enzyme is influenced (besides other factors) by the amount of the energy released during the formation of the complex enzyme–substrate[25]. The situation is similar to that in the heterogeneously catalyzed reaction discussed above. If we admit a rapid intramolecular redistribution of the energy released in the ES complex formation among all vibrational modes of the enzyme molecule, then, due to the large magnitude of the enzyme, the probability of subsequent accumulation of energy in the critical bond is negligibly small. The concept of free intramolecular energy redistribution thus cannot explain the high catalytic activity of enzymes.

Now we can put forward a conjecture that the flow of released energy into the enzyme is restricted due to the presence of a metal atom near the active site. The effective vibrational temperature of the substrate bonded in the complex ES is then higher than the temperature of the heat bath – the enzyme molecule. The activity of many enzymes is greatly influenced by the presence of metal ions, certain ions are

absolutely necessary for the activity of some enzymes. In metalloenzymes the metal alone is a constituent of the enzyme itself, in other cases the enzyme is activated by the addition of particular metal ions[26]. The following effects have been considered in relation to the role of metal ions in the enzyme function: the metal ion (i) helps to ensure that the spatial structure of the enzyme (essential for its activity) is maintained, (ii) contributes to the binding of substrate, and/or (iii) assists in the catalytic process[27]. We suggest that in addition to these three factors, a fourth factor can operate, namely that the metal atom forms a barrier to the intramolecular energy flow into the enzyme molecule and provides for the concentration of energy in the substrate molecule.

According to Dixon and Webb[26], sixteen different metal ions have been found to activate enzymes, *viz*. Na, K, Rb, Cs, Mg, Ca, Zn, Cd, Cr, Cu, Mn, Fe, Co, Ni, Al and Mo ions. Their atomic numbers range between 11 and 42 and atomic weights between *ca* 23 and 96. It was also found that diphosphoglycerate phosphatase is strongly activated by Hg (atomic weight 201) and Ag (atomic weight 108)[26]. It is widely assumed that the metal forms an essential part of the enzyme active centre or that it even acts as a binding link between enzyme and substrate. The metals mentioned have no common redox properties. Most of them are heavy atoms. The idea that they form, in some cases at least, an obstacle to free energy flow seems plausible.

Assume that the energy, ε_1, released during the formation of the ES complex is concentrated in the bonded substrate molecule, the effective vibrational temperature of the bonded substrate is $T_{\text{eff}} = T + \varepsilon_1/n_s\boldsymbol{k}$ where n_s is the number of representative oscillators of the substrate, and the first approximation of the rate constant k_2 of molecules with the average energy $\bar{\varepsilon} = n_s\boldsymbol{k}T_{\text{eff}} = n_s\boldsymbol{k}T + \varepsilon_1$ is (see Eq. (*3*))

$$k_2(\bar{\varepsilon}) = \nu \exp\left[-n_s\varepsilon_0/(n_s\boldsymbol{k}T + \varepsilon_1)\right] \quad . \tag{8}$$

The lifetime of the ES complex is the key factor. In complexes with a short lifetime (of the order of picoseconds) the energy remains concentrated near the binding site. In complexes with long lifetime the energy flows into all oscillators of the substrate. In our hypotheses, the heavy atom restricts the energy flow into the enzyme and the probability of reaction is high due to a higher vibrational temperature of the bonded substrate. The lower limit of the complex lifetime is of the order of 10^{-9} s (ref.[6]). This is a rather high value. The blocking effect has been observed experimentally on the time scale of 10^{-10}–10^{-9} s (refs[16,17]). The model calculation, however, suggests that the blocking effect of the metal atom can continue for considerably longer times[28].

TWO-CHANNEL MODEL

Consider the one-substrate enzyme catalyzed reaction. Equation (*8*) can be easily interpreted but it represents an oversimplification for the following reasons: (i) a not very

large ensemble of representative oscillators is characterized by the effective vibrational temperature; (ii) the reaction rate is expressed as the rate of complexes with the mean vibrational energy; and (iii) it is assumed that the reaction ES → E + P is the rate determining step. Now, let us abandon the assumptions (i), (ii) and (iii) and assume the two-channel decomposition pathway for ES where both reactions ES → E + S and ES → E + P are the RRK decompositions. Two processes compete in the ES complex: the proper conversion of the substrate into the product, and the decomposition of ES into the enzyme and the unchanged substrate.

Therefore, we start from the stationary concentration of ES, c_{ES}, given by the condition $k_1 c_E c_S = k_2 c_{ES} + k_{-1} c_{ES}$ (*cf.* Eq. (*6*)). Assume again that all the evolved energy ε_1 is stored in the bonded substrate. Let $c_{ES}(\varepsilon)\,\mathrm{d}\varepsilon$ be the concentration of the ES complexes possessing the total internal vibrational energy in the bonded substrate from $\varepsilon + \varepsilon_1$ to $\varepsilon + \varepsilon_1 + \mathrm{d}\varepsilon$ and $c_S(\varepsilon)\,\mathrm{d}\varepsilon$ the concentration of free substrate with internal vibrational energy from ε to $\varepsilon + \mathrm{d}\varepsilon$. Then

$$zpc_E c_S(\varepsilon)\,\mathrm{d}\varepsilon = \left\{\nu_2\,[1 - \varepsilon_0/(\varepsilon + \varepsilon_1)]^{n_S - 1} + \nu_{-1}[1 - \varepsilon_1/(\varepsilon + \varepsilon_1)]^{n_S - 1}\right\} c_{ES}(\varepsilon)\,\mathrm{d}\varepsilon \ , \qquad (9)$$

$\varepsilon > \varepsilon_0 - \varepsilon_1$, where z is the collision (encounter) number[29] for E and S, p is the probability that in the collision of E and S the ES complex will be formed, $k_2(\varepsilon) = \nu_2[1 - \varepsilon_0/(\varepsilon + \varepsilon_1)]^{n_S - 1}$ is the RRK rate constant of conversion of the bonded substrate with the total vibrational energy from $\varepsilon + \varepsilon_1$ to $\varepsilon + \varepsilon_1 + \mathrm{d}\varepsilon$ into the product (the activation energy of this process is ε_0), $\nu_{-1}[1 - \varepsilon_1/(\varepsilon + \varepsilon_1)]^{n_S - 1} = \nu_{-1}[\varepsilon/(\varepsilon + \varepsilon_1)]^{n_S - 1}$ is the RRK rate constant of decomposition of the ES complex into free molecules E and S (the activation energy of this process is ε_1) and ν_2 and ν_{-1} are RRK preexponential factors (for the sake of simplicity we will assume that $\nu_2 = \nu_{-1} = \nu$).

The equilibrium fraction of free substrate molecules with the total vibrational energy in n_S degrees of freedom within the limits ε to $\varepsilon + \mathrm{d}\varepsilon$ is[9] $c_S(\varepsilon)\,\mathrm{d}\varepsilon = c_S f(\varepsilon)\,\mathrm{d}\varepsilon$, where $f(\varepsilon) = \varepsilon^{n_S - 1} \exp(-\varepsilon/\boldsymbol{k}T)/\Gamma(n_s)(\boldsymbol{k}T)^{n_S}$. The steady-state concentration $c_{ES}(\varepsilon)\,\mathrm{d}\varepsilon$ is

$$c_{ES}(\varepsilon)\,\mathrm{d}\varepsilon = zpf(\varepsilon)c_S c_E\,\mathrm{d}\varepsilon/\nu\left\{[1 - \varepsilon_0/(\varepsilon + \varepsilon_1)]^{n_S - 1} + [\varepsilon/(\varepsilon + \varepsilon_1)]^{n_S - 1}\right\} \qquad (10)$$

and the reaction rate is (we assume $\varepsilon_1 < \varepsilon_0$)

$$r = \int_{\varepsilon_0 - \varepsilon_1}^{\infty} k_2(\varepsilon) c_{ES}(\varepsilon)\,\mathrm{d}\varepsilon = zpc_S c_E \int_{\varepsilon_0 - \varepsilon_1}^{\infty} f(\varepsilon)\,\mathrm{d}\varepsilon/\left\{1 + [\varepsilon/(\varepsilon + \varepsilon_1 - \varepsilon_0)]^{n_S - 1}\right\} =$$

$$= \int_{\varepsilon_0 - \varepsilon_1}^{\infty} F(\varepsilon)\,\mathrm{d}\varepsilon \ . \qquad (11)$$

If the released energy is dissipated into the enzyme molecule, $k_2(\varepsilon) = \nu_2(1 - \varepsilon_0/\varepsilon)^{n_S-1}$ and the reaction rate is

$$r_0 = zpc_S c_E \int_{\varepsilon_0}^{\infty} f(\varepsilon)\, d\varepsilon / \{1 + [(\varepsilon - \varepsilon_1)/(\varepsilon - \varepsilon_0)]^{n_S-1}\} = \int_{\varepsilon_0}^{\infty} G(\varepsilon)\, d\varepsilon \ . \qquad (12)$$

Now we can easily prove that $r > r_0$:

$$r = \int_{\varepsilon_0-\varepsilon_1}^{\varepsilon_0} F(\varepsilon)\, d\varepsilon + \int_{\varepsilon_0}^{\infty} F(\varepsilon)\, d\varepsilon > \int_{\varepsilon_0}^{\infty} F(\varepsilon)\, d\varepsilon > \int_{\varepsilon_0}^{\infty} G(\varepsilon)\, d\varepsilon = r_0 \qquad (13)$$

as $F(\varepsilon) > G(\varepsilon)$ for $\varepsilon_1 < \varepsilon_0$.

We see that even in this amended model the blocking of the energy flow into the enzyme enlarges the rate of chemical change of the bonded substrate. A similar result can be obtained for unimolecular heterogeneously catalyzed reaction.

This work was supported by the Grant Agency of the Czech Republic (Grant No. 203/95/0003).

REFERENCES

1. Solc M., Herman Z.: Collect. Czech. Chem. Commun. *57*, 1157 (1992).
2. Schlag E. W., Levine R. D.: Chem. Phys. Lett. *163*, 523 (1989).
3. Bernshtein V., Oref I.: J. Phys. Chem. *98*, 136 (1994).
4. Weinkauf R., Aicher P., Wesley G., Grotemeyer J., Schlag E. W.: J. Phys. Chem. *98*, 8381 (1994).
5. Bunker D. L., Wang F.-M.: J. Am. Chem. Soc. *99*, 7457 (1977).
6. Solc M.: J. Theor. Biol. *175*, 57 (1995).
7. Solc M.: Catal. Lett. *18*, 177 (1993).
8. Solc M.: J. Mol. Catal. *101*, 163 (1995).
9. Laidler K. J.: *Theories of Chemical Reaction Rates*. McGraw–Hill, New York 1969.
10. Oref I., Gordon N.: J. Chem. Phys. *82*, 2035 (1978).
11. Trenwith A. B., Rabinovitch B. S.: J. Chem. Phys. *85*, 1694 (1986).
12. Trenwith A. B., Oswald D. A., Rabinovitch B. S., Flowers M. C.: J. Phys. Chem. *91*, 4398 (1987).
13. Lami A., Villani G.: J. Phys. Chem. *94*, 6959 (1990).
14. Reinhardt W. P., Duneczky C.: J. Chem. Soc., Faraday Trans. 2 *84*, 1511 (1988).
15. Solc M.: Z. Phys. Chem., Neue Folge *166*, 103 (1990).
16. Rogers P., Montague D. C., Frank J. P., Tyler S. C., Rowland F. S.: Chem. Phys. Lett. *89*, 9 (1982).
17. Rogers P. J., Selco J. I., Rowland F. S.: Chem. Phys. Lett. *97*, 313 (1983).
18. Sakai Y., Iyer R. S., Rowland F. S.: J. Phys. Chem. *94*, 3368 (1990).
19. Kerstel E. R. Th., Lehmann K. K., Mentel T. F., Pate B. H., Scoles G.: J. Phys. Chem. *95*, 8282 (1991).

20. Bond G. C.: *Catalysis by Metals*. Academic Press, New York 1962.
21. Bond G. C.: Catal. Today *17*, 399 (1993).
22. Wilson K. R., Levine R. D.: Chem. Phys. Lett. *152*, 435 (1988).
23. Ewing G. E.: Acc. Chem. Res. *25*, 292 (1992).
24. Laidler K. J., Bunting P. S.: *The Kinetics of Enzyme Action*. Clarendon Press, Oxford 1973.
25. Vodrazka Z.: *Biochemie*, Vol. 1. Academia, Praha 1992.
26. Dixon M., Webb E. C.: *Enzymes*. Longman, London 1967.
27. Gray C. J.: *Enzyme-Catalyzed Reactions*. Longmans, London 1971.
28. Lopez V., Marcus R. A.: Chem. Phys. Lett. *93*, 232 (1982).
29. Fowler R. H., Slater N. B.: Trans. Faraday Soc. *24*, 81 (1938).