nitrogen. For precise determination of peak potentials, compensation of iR drop in the cell was made using feedback circuitry available with the instrument.

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Registry No.—I, 15008-36-3; II, 68582-39-8; III, 68582-40-1; IV, 68582-41-2; V, 68582-42-3; VI, 23308-55-6; VII, 40660-35-3; VIII, 68582-43-4; IX, 68582-44-5; X, 68582-45-6; XI, 68582-46-7; XII, 33978-57-3; XIII, 68582-47-8; XIV, 68582-48-9; XV, 68582-49-0; fluorenone, 486-25-9; *N,N*-diethylaniline, 91-66-7; dimethylaniline, 121-69-7; acetophenone, 98-86-2.

Supplementary Material Available: Peak potentials of oxidation steps O_I, O_{II}, and O_{III} for I–III vs. $\Sigma\sigma^*$ for substituents on nitrogen (Figure 5), peak potentials of oxidation steps O_I, O_{II}, and O_{III} for I and VII–X vs. σ for phenyl ring substituents (Figure 6), cyclic voltammograms of X, VI, XII, and XI (Figures 7–10), and absorption spectra of I as a function of length of irradiation (Figure 11) (8 pages). Ordering information is given on any current masthead page.

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Transfer Hydrogenation and Transfer Hydrogenolysis. 20. Dehydrogenation by 7,7,8,8-Tetracyanoquinodimethane

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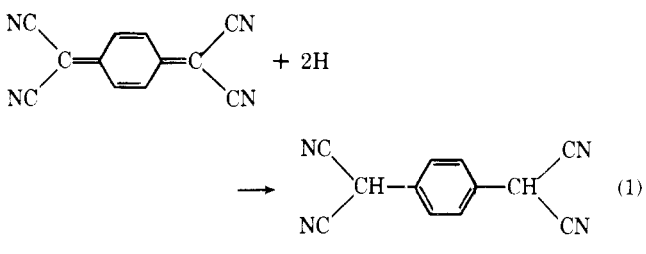
Benzyl-type alcohols and hydroaromatic compounds were dehydrogenated by 7,7,8,8-tetracyanoquinodimethane (TCNQ). The fact that the reactivity of 1,2-dihydronaphthalene was comparable to that of 1,2-dihydro-1,1-dimethylnaphthalene, which gave 1,2-dimethylnaphthalene, suggests that the dehydrogenation of 1,2-dihydrobenzenes proceeds via the formation of a carbonium ion by a rate-determining hydride abstraction (two-step ionic mechanism). The hydrogen transfer from 1-phenylpropanol was studied in detail. The yield of propiophenone increased when solvents which would be expected to increase the concentration of the complex between TCNQ and the alcohol were used. Initial rates of the reaction were proportional to the concentration of the hydrogen donor and the hydrogen acceptor. In the reaction of several para- or meta-substituted 1-phenylpropanols in dioxane at 140 °C, −3.76 was obtained as a value of the reaction constant. Relative rates of the reaction of PhCH(OH)Et, PhCH(OD)Et, PhCD(OH)Et, and PhCD(OD)Et were 4.0, 4.0, 1.0, and 1, respectively. This means that the transfer of the hydrogen attached to the α position of the alcohol is the rate-determining step. This and some other results support a two-step ionic mechanism for the dehydrogenation of alcohols.

The thermal hydrogen transfer from some types of organic compounds to high potential quinones is well known.[1] In the previous paper,[2] we reported the dehydrogenation by tetracyanoethylene (TCNE) and discussed the mechanism of the hydrogen transfer from benzyl-type alcohols to TCNE. 7,7,8,8-Tetracyanoquinodimethane (TCNQ) would also be expected to dehydrogenate organic compounds because it has structural similarity to both quinones and TCNE. Although dehydrogenations by TCNQ have not been reported, we find them to occur readily and have studied them in detail.

Results and Discussion

Hydrogen-Donating Ability. At first the susceptibility of organic compounds to dehydrogenation by TCNQ was investigated under the following reaction conditions. A hydrogen donor (0.1 M) and TCNQ (0.1 M) were heated at 140 °C for 6 h in dioxane. This was used as a solvent for dehydrogenation by dichlorodicyanobenzoquinone (DDQ). In these dehydrogenations TCNQ was reduced to *p*-benzenedimalononitrile, which was isolated as a white crystalline compound and identified by its melting point and IR spectrum.[3] This fact shows that the reaction in eq 1 proceeded.



(1)

TCNQ, like other hydrogen acceptors of thermal hydrogen transfer,[1,2] has been reported to react with compounds having active hydrogens.[4] In some cases extensive side reactions occur. We have determined not only the yield of dehydrogenation product but also the amount of starting material that

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Table I. Dehydrogenation by TCNQ[a]

hydrogen donor	registry no.	yield of dehydrogenation product, %	recovery of hydrogen donor, %
9,10-dihydroanthracene	613-31-0	91	5
1,4-dihydronaphthalene	612-17-9	86	5
cinnamic alcohol	104-54-1	65	11
2,5-dihydrofuran	1708-29-8	60	0
1,2,3,4-tetrahydroquinoline	635-46-1	29	29
1,2-dihydronaphthalene	447-53-0	26	43
indoline	496-15-1	26	0
1-phenylpropanol	1335-12-2	14	85
1-phenylpropanol[b]		75	18
benzhydrol	91-01-0	13	58
benzyl alcohol	100-51-6	8	95
1,2-dihydronaphthalene[c]		13	50
1,2-dihydro-1,1-dimethylnaphthalene[c]	2733-79-1	12	74

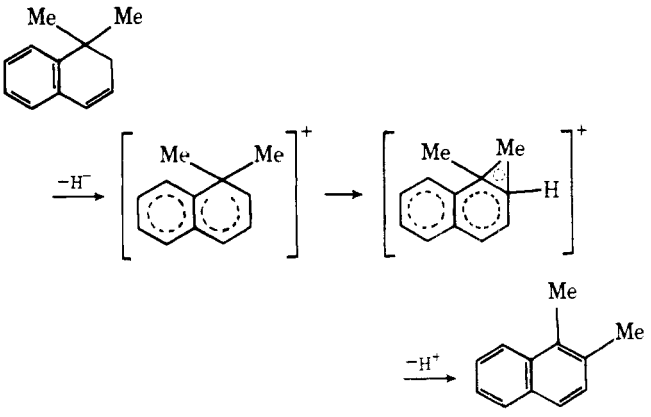
[a] TCNQ (0.1 M) (registry no., 1518-16-17) and a hydrogen donor (0.1 M) were heated at 140 °C for 6 h in dioxane. [b] Reaction time was 44 h. [c] TCNQ (0.2 M) and a hydrogen donor (0.2 M) were heated at 140 °C for 3 h in dioxane.

remains. Several hydroaromatic compounds and alcohols were examined as hydrogen donors. They all gave the dehydrogenated products, aromatic or carbonyl compounds, respectively.

As shown in Table I, the yield of dehydrogenation products decreased in the following order: 9,10-dihydroanthracene > 1,4-dihydronaphthalene > cinnamic alcohol > 2,5-dihydrofuran > 1,2,3,4-tetrahydroquinoline > 1,2-dihydronaphthalene > indoline > 1-phenylpropanol > benzhydrol > benzyl alcohol. Side reactions were extensive in the case of indoline and considerable in 1,2-dihydronaphthalene, 1,2,3,4-tetrahydroquinoline, 2,5-dihydrofuran, benzhydrol, and cinnamic alcohol. This order indicates that the relative reactivity of alcohols in the reaction with TCNQ was lower than that in the reaction with TCNE.[2]

When 1,2-dihydro-1,1-dimethylnaphthalene was used as a hydrogen donor, migration of a methyl group occurred and 1,2-dimethylnaphthalene was formed. This fact suggests that an electron deficient species is formed by the hydride abstraction at the 2 position of the hydrogen donor. Moreover, the reactivity of 1,2-dihydro-1,1-dimethylnaphthalene was equal to that of 1,2-dihydronaphthalene. This result suggests that these two compounds are dehydrogenated by the same mechanism and that the hydride transfer process is the rate-determining step.

As a hydrogen donor, 1-phenylpropanol and its derivatives were used in the experiments described hereafter because (1) mechanistic studies of thermal hydrogen transfer from alcohols seem to be relatively scarce, (2) the alcohol undergoes few side reactions, and (3) ring-substituted 1-phenylpropanols are easy to obtain. 1-Phenylpropanol gave propiophenone in 75% yield in the reaction after 44 h.



Reaction Solvent. Solvent effects were investigated to clarify the mechanism of the dehydrogenation. Solvents that dissolved TCNQ well and did not cause observable side reactions were chosen, and the results are summarized in Table II.

Based on analogy to similar reactions[1,2] and on the fact that TCNQ forms charge-transfer (CT) complexes with several compounds,[5] it is inferred that the dehydrogenation by TCNQ also occurs via the formation of CT complexes. Therefore, the influence of solvents may be interpreted by the stabilization of the CT complexes and/or other active species including the transition state of the reaction by solvation. At first, we tried to identify the absorption band belonging to the TCNQ/1-phenylpropanol complex in various solvents; however, the band could not be identified clearly, partly because of the lower complexing ability of TCNQ and partly because of the presence of the strong bands attributable to the CT complexes between TCNQ and the solvents. Eventually, the relative amount of the TCNQ/hexamethylbenzene complex was measured to estimate roughly the relative amount of the TCNQ/1-phenylpropanol complex in the designated solvent.

The wavelength at the maximum absorption (λ_{CT}) and the absorbance [log (I_0/I)] are shown in Table II, along with the transition energy for the CT bands of pyridinium *N*-phenolbetaine (E_T) in a given solvent.[6] The latter parameter is regarded as a quantitative measure of ionizing power.[6] The yield of propiophenone had close relationship with the value of absorbance, and this result suggests that the dehydrogenation proceeds via the formation of CT complexes lying before the rate-determining step of the reaction. The yield of the ketone and the absorbance may also be correlated with E_T in a rough sense when structurally similar solvents are used. Perhaps, this will suggest that the CT complex and/or the transition

Table II. Effect of Solvents[a]

solvent	yield of ketone, %	recovery of alcohol, %	λ_{CT},[b] nm	log (I_0/I)[c]	E_T,[d] kcal mol^{-1}
ethyl acetate	38	56	550	0.69	38.1
tetrahydrofuran	33	58	547	0.54	37.4
dioxane	31	60	563	0.47	36.0
chloroform	14	79	590	0.36	39.1
anisole	13	78	*e*	*e*	37.2
chlorobenzene	11	83	590	0.26	37.5
benzene	10	87	575	0.08	34.5

[a] 1-Phenylpropanol (0.05 M) and TCNQ (0.05 M) were heated at 140 °C for 35 h. [b] Wavelength of the absorption maxima of the band owing to the CT complex between TCNQ (2.5 mM) and hexamethylbenzene (0.05 M). [c] Absorbance of the band described above. [d] Molar transition energy of pyridinium *N*-phenolbetaine in the designated solvents. [e] The absorption of the CT complex was covered by that of the solvent.

Table III. Effect of Additives[a]

additive	registry no.	additive, M	yield of ketone, %	recovery of alcohol, %
none			14	85
AIBN	78-67-1	0.01	21	76
AIBN[b]		0.01	3	91
AIBN + hydroquinone	123-31-9	0.01 0.1	16	85
di-*tert*-butyl peroxide	110-05-4	0.01	21	80
di-*tert*-butyl peroxide[b]		0.01	3	92
tert-butyl hydroperoxide	75-91-2	0.01	20	81
benzoyl peroxide	94-36-0	0.01	18	75
benzoyl peroxide[b]		0.01	2	98
dichloroacetic acid	79-43-6	0.1	26	73
dichloroacetic acid[b]		0.1	0	95
N,N-dimethylacetamide	127-19-5	0.1	17	82
acetonitrile	75-05-8	0.1	16	84
acetic acid	64-19-7	0.1	16	84
hydroquinone		0.1	15	83
oxygen	7782-44-7	*c*	15	75
pyridine	110-86-1	0.1	14	80
sodium acetate	127-09-3	0.1	11	83
triethylamine	121-44-8	0.1	11	81

[a] 1-Phenylpropanol (0.1 M), TCNQ (0.1 M), and an additive were heated at 140 °C for 6 h in dioxane. [b] TCNQ was not added. [c] Oxygen, the volume of which was three times as large as the solution, was sealed in the reaction vessel.

state of the rate-limiting step are solvated and considerably charge-separated.

Effect of Additives. In the dehydrogenation by quinones, a mechanism involving a radical process has been proposed.[7] Therefore, the validity of the radical mechanism was examined in our case. Several compounds known as inhibitors or initiators in the radical reaction were added to the reaction mixture, and the results are summarized in Table III. It is seen from Table III that hydroquinone does not retard the dehydrogenation and α,α'-azobis(isobutyronitrile) (AIBN), di-*tert*-butyl peroxide, *tert*-butyl hydroperoxide, and benzoyl peroxide have promoted the formation of the ketone. These radical sources were found to convert 1-phenylpropanol to propiophenone in the absence of TCNQ. Further, neither AIBN in the presence of hydroquinone nor oxygen alone affected the dehydrogenation. These results suggest that the radical sources did not promote the dehydrogenation by TCNQ, but directly dehydrogenated the alcohol. A large negative value for the activation entropy (as seen later) also suggests that a radical process is not likely, although the existence of some radical intermediates is not completely ruled out.

It has been reported that the dehydrogenation of 1,4-dihydronaphthalene by quinones is catalyzed by acids.[8] In the dehydrogenation of 1-phenylpropanol by TCNE, however, no catalysis by acids was found.[2] In our present system, dichloroacetic acid promoted the reaction, while acetic acid had little effect. This fact may be explained by the assumption that the protonation on the hydrogen acceptors increases the hydride-accepting ability and the protonation on TCNQ takes place more easily than that on TCNE because of the higher basicity of the cyano groups of TCNQ than those of TCNE. This assumption is supported by the fact that dichloroacetic acid and 1-phenylpropanol did not give propiophenone in the absence of TCNQ, although acid-catalyzed disproportionation reactions have been reported.[9]

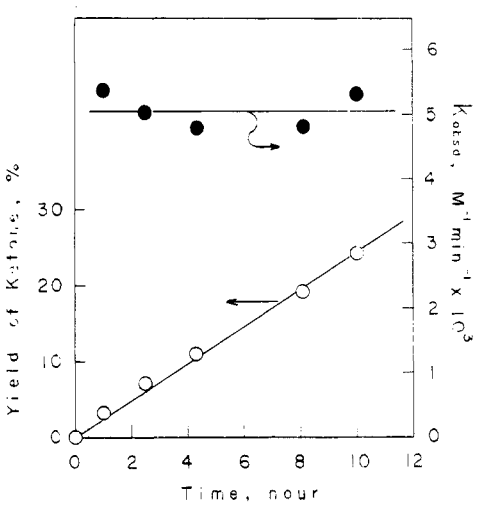


Figure 1. Plots of the yield of the ketone (○) and rate constant (●) vs. reaction time. TCNQ (0.1 M) and 1-phenylpropanol (0.1 M) were heated at 140 °C in dioxane.

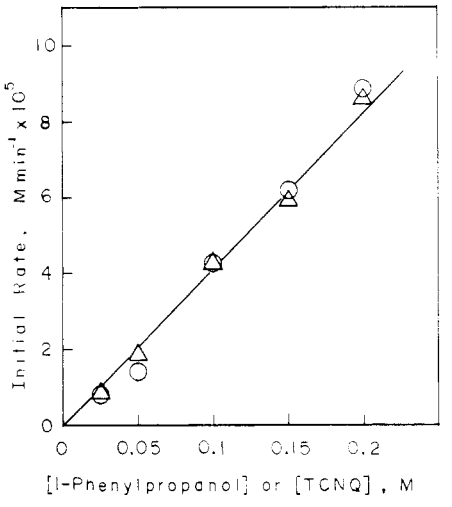


Figure 2. Plots of initial rate vs. the concentration of 1-phenylpropanol (○) and tetracyanoquinodimethane (△); the concentration of the other reactant was 0.1 M, the temperature was 140 °C, and the solvent was dioxane.

Strongly polar compounds such as *N,N*-dimethylacetamide and acetonitrile raised the yield of the ketone to some extent, while methanol did not have such an effect.

Addition of strong bases, such as pyridine, sodium acetate, and triethylamine, lowered the yield of the ketone a little.

Measurement of Reaction Rates. In Figure 1, a plot of the yield of propiophenone against the reaction time is shown. At the initial stage of the reaction the yield of the ketone was proportional to the time. The initial rate of the reaction was derived from the linear part of the plot.

In most of the dehydrogenations by quinones[1] and the hydrogen transfer from 1-phenylpropanol to TCNE,[2] second-order kinetics have been reported. Also, in the dehydrogenation by TCNQ, the initial rate was found to be proportional to the concentration of 1-phenylpropanol and TCNQ as shown in Figure 2. The proportionality is observed over a wide range of the concentration of the reactants (Figure 2). Therefore, if this reaction proceeds via the formation of a complex between TCNQ and the alcohol, the concentration of the complex would not be very high because formation of the complex in high concentration would lead to deviation from linearity.

As already mentioned, the rate is inferred to be proportional

to the concentration of the CT complex. Therefore, the reaction scheme and rate may be expressed as in eq 2 and 3, where HD, K, k, and k_{obsd} represent 1-phenylpropanol, the equilibrium constant between the reactants and the CT complex, the rate constant of the rate-determining step, and the observed second-order rate constant, respectively.

$$\text{TCNQ} + \text{HD} \overset{K}{\rightleftarrows} [\text{complex}] \overset{k}{\rightarrow} \text{products} \quad (2)$$

$$\text{rate} = k_{obsd}[\text{TCNQ}][\text{HD}] = k[\text{complex}] = kK[\text{TCNQ}][\text{HD}] \quad (3)$$

The values of the observed second-order rate constants were found to be almost unchanged up to 25% conversion as shown in Figure 1. This result indicates that side reactions and autocatalysis by the products are not important in the initial stage of the reaction.

The observed second-order rate constants were measured in dioxane at temperatures ranging from 100 to 140 °C. A plot of the logarithm of the rate constants against the reciprocal of the reaction temperatures (K) showed a good linear relationship, indicating that the kinetics of this system are not complicated. From the plot, 20.4 kcal mol^{-1}, 19.6 kcal mol^{-1}, and −30.7 eu were obtained for the Arrhenius energy of activation, the activation enthalpy, and the activation entropy at 100 °C, respectively. These values are comparable to those of the corresponding kinetic parameters reported in the hydrogen transfer from 1,4-dihydronaphthalene to benzoquinone in phenetole at 100 °C[8] and in the hydrogen transfer from 1-phenylpropanol to TCNE in dioxane.[2] Such a similarity of the kinetic parameters would suggest a similarity in the reaction mechanism.

Effect of Substituents. In a review Jackman has reported that in the dehydrogenation of a series of 6- and 7-substituted 1,2-dihydronaphthalenes by a quinone, the rates are correlated with the Hammett σ, or still better with the σ^+, values of the substituents, and a large negative ρ value obtained (−2.7) is indicative of a fairly high sensitivity of the reaction toward the changes in substituents.[1a] In the hydrogen transfer from p-methyl, p-chloro, p-bromo, m-chloro, and m-bromo derivatives of 1-phenylpropanol to TCNE,[2] −3.13 was obtained for the ρ value using σ, and −2.63 using σ^+. To discuss the electronic effect of the substituents on 1-arylpropanols in the dehydrogenation by TCNQ, the second-order rate constants were measured at 140 °C in dioxane. Using least squares, the logarithms of the rate constants were correlated to σ to give a ρ value of −3.76 and a correlation coefficient r of −0.849, while correlating to σ^+ gave ρ = −3.19 and r = −0.852 (Figure 3). The fairly large negative values of ρ suggest that the transition state of the rate-determining step is much more charge-separated than the species which lie before the rate-limiting step. These values are comparable to those reported.[1a,2] The similarity of the ρ values suggests that the reaction mechanisms of the dehydrogenation of alcohols by TCNQ or TCNE and of 1,2-dihydronaphthalenes by quinones are much the same.

Kinetic Isotope Effect. Müller has reported that the rate of dehydrogenation of 1,4-cyclohexadiene by DDQ is ten times faster than that of 1,4-cyclohexadiene-d_8 and, based on such an enormously large isotope effect, assumed that the cleavages of C_1–H and C_4–H bonds occur simultaneously at the rate-determining step.[10] Burstein and Ringold have found that the dehydrogenation of 3α-deuterio-Δ^4-3-hydroxy steroids by DDQ shows a primary isotope effect (ca. fivefold).[11] However, Hashish and Hoodless observed no primary isotope effect in the hydrogen transfer from 1,4-dihydronaphthalene to tetrachloro-p-benzoquinone in phenetole and concluded that the rate-determining step was not at the hydrogen transfer but at the electron transfer processes between CT complexes.[12]

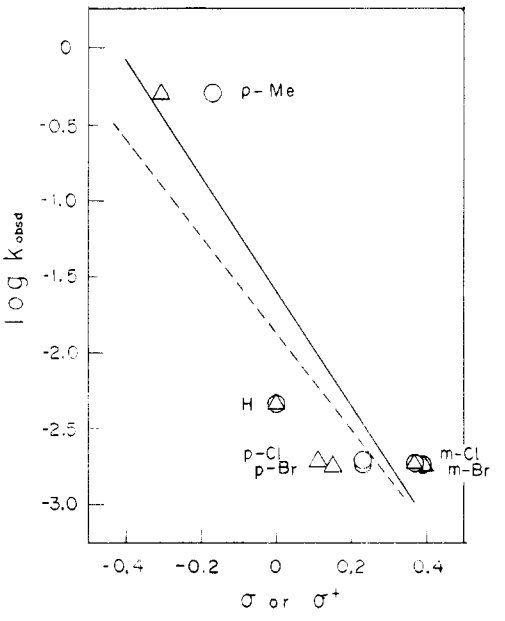


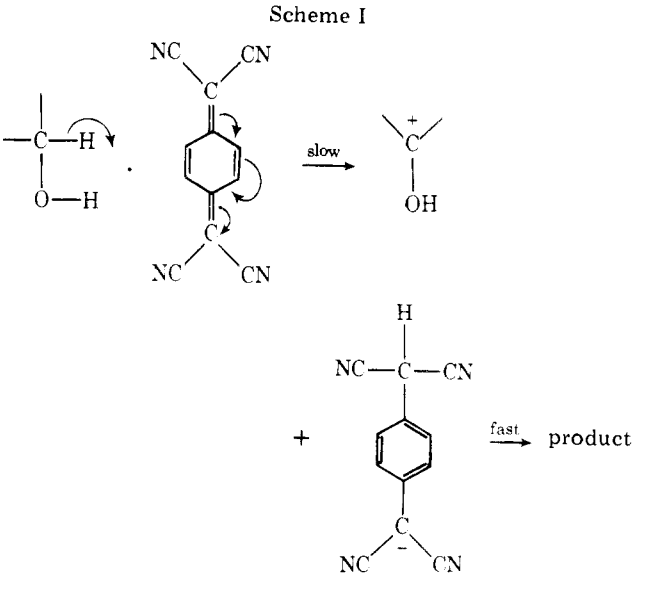
Figure 3. Plots of log k_{obsd} vs. σ (—O—) and σ^+ (—Δ—). TCNQ (0.1 M) and a para- or meta-substituted 1-phenylpropanol (0.1 M) were heated in dioxane.

In the dehydrogenation by TCNE, the deuteration of the hydrogen atom attached at the α carbon of 1-phenylpropanol showed a primary kinetic isotope effect.[2] In the dehydrogenation by TCNQ at 140 °C in dioxane, the relative rates of the reaction of PhCH(OH)Et, PhCH(OD)Et, PhCD(OH)Et, and PhCD(OD)Et were 4.0, 4.0, 1.0, and 1, respectively. The fact that a primary isotope effect was observed only when the hydrogen attached at the α carbon of the alcohol was deuterated would indicate that the cleavage of the C_α–H bond is of primary importance in the rate-determining step and that the cleavage of the O–H bond is only of secondary importance or not involved in the step.

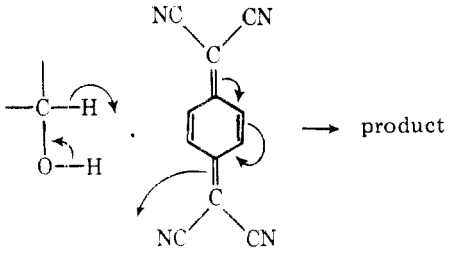
Mechanistic Discussion. As for the dehydrogenation of 1,4-cyclohexadienes by quinones, four reaction mechanisms have been proposed.[1a,10,13] By analogy, the five reaction schemes shown in Schemes I–V may be considered for the hydrogen transfer from alcohols to TCNQ.

Scheme I involves a rate-limiting hydride transfer to give a carbonium ion in the alcohol which loses a proton in the subsequent rapid step. Schemes II–IV represent concerted cyclic mechanisms in which two hydrogen atoms in the alco-

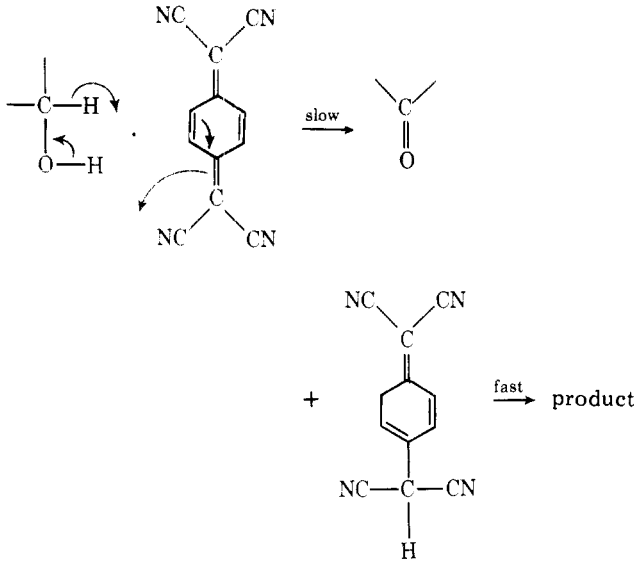
Scheme I



Scheme II



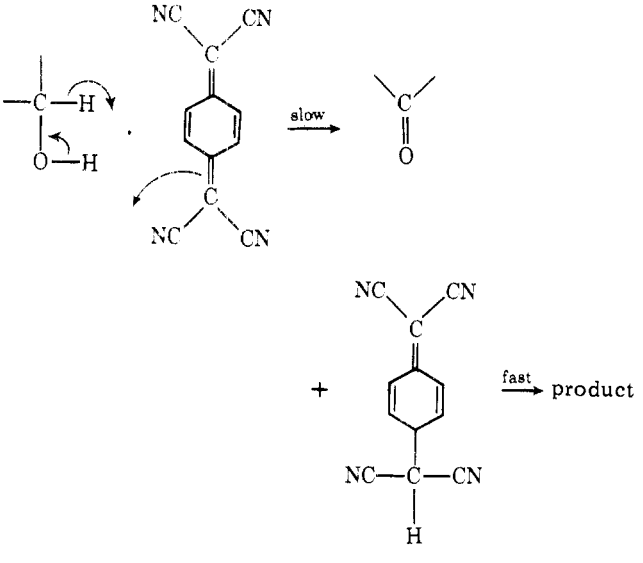
Scheme III



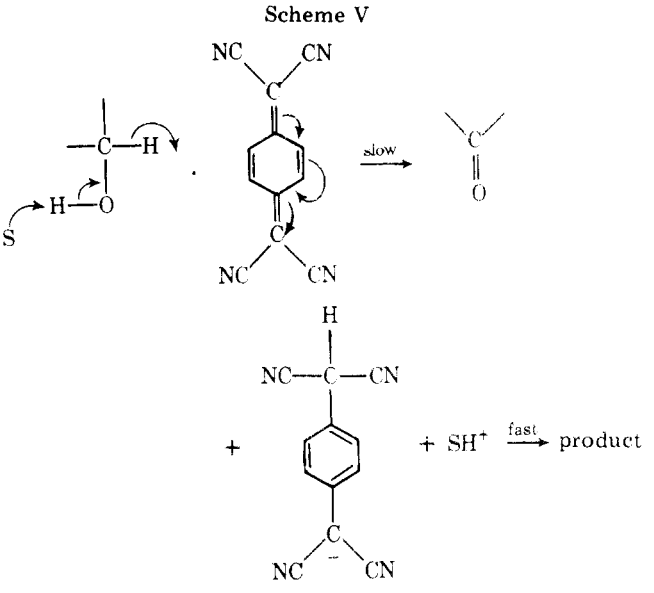
hols are transfered in a single step to the 7 and 8 (1,6-addition, Scheme II), 2 and 8 (1,4-addition, Scheme III), or 1 and 7 positions (1,2-addition, Scheme IV) of TCNQ. In Schemes III and IV, isomerization to *p*-benzenedimalononitrile follows the initial steps. The 1,6- and 1,2-additions are symmetry allowed, while the 1,4-addition is not. Further, the mechanism involving solvents (S) as the proton acceptors is also imaginable (Scheme V).

Among these, Scheme I, which involves a two-step ionic process, is most likely because (1) a highly charge-separated transition state should be considered from the fairly large negative value of ρ, (2) a primary isotope effect was observed

Scheme IV



Scheme V



in the C_α–H bond cleavage of 1-phenylpropanol and was not observed in the O–H bond cleavage, (3) almost all of the observations, including kinetic parameters, are similar to those in the hydrogen transfer from 1-phenylpropanol to TCNE, which has been inferred to occur via a process analogous to Scheme I, (4) in the dehydrogenation of 1,2-dihydro-1,1-dimethylnaphthalene and 1,2-dihydronaphthalene by TCNQ, intermediates having carbonium ion character are considered to form, as described before, and (5) no phenomenon which conflicts with this scheme has been observed thus far. In this scheme, the possibility of solvent participation in a non-rate-determining step is not ruled out. Schemes II–IV are not likely because no primary kinetic isotope effect has been observed in the transfer of the hydroxyl hydrogen of 1-phenylpropanol and the transition state is considered to be much more polarized than those for these concerted cyclic processes. Scheme V is a two-step mechanism in which the rate-limiting step is at a concerted process involving a solvent as a proton acceptor. This scheme too is presumed not to be reasonable because no primary isotope effect was observed in the O–H bond cleavage. Further, Scheme V would be less consistent with the highly charge-separated transition state required than Scheme I.

Experimental Section

Materials. *p*-Benzenedimalononitrile,[3] 1,2-dihydro-1,1-dimethylnaphthalene,[14] and *p*-methyl,[15] *p*-chloro,[15] *m*-chloro,[15] *p*-bromo,[16] and *m*-bromo derivatives[17] of 1-phenylpropanol were prepared by the methods reported in the literature. The preparation and purity of the deuterated 1-phenylpropanols were reported in the previous paper.[2] All of the reagents purchased were purified by distillation or recrystallization.

Example of Transfer Hydrogenation. 1-Phenylpropanol (6.9 μL, 0.05 mmol) and TCNQ (10.2 mg, 0.05 mmol) were put into a Pyrex glass tube which had been sealed at one end. Dioxane was added, and the total volume of the solution was made to 0.5 mL. The tube was sealed under vacuum after a freeze–pump–thaw cycle at 10^{-3} torr on a vacuum line in a liquid nitrogen bath. The sealed tube was heated in a polyethylene glycol bath kept at 140 ± 1 °C. To analyze the reaction mixture, GC was performed at 150 °C on a Hitachi 163 instrument equipped with a flame ionization detector using 5 μL of phenylcyclohexane as an internal standard. A 1 m × 6 mm stainless steel column packed with 12% diethylene glycol succinate on Diasolid L was used. The other transfer hydrogenations were carried out in a similar way.

Example of Kinetic Measurements. Sealed tubes (five) that were prepared by the method described above were heated on a polyethylene glycol bath kept at 140 ± 1 °C for 1, 2.5, 4.3, 8, and 10 h, respectively. Each reaction mixture was submitted to GC analysis. The reaction rates were obtained by the gradation of time against the yield of ketone plot.

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Fluorodehydroxylation, a Novel Method for Synthesis of Fluoroamines and Fluoroamino Acids

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The alcoholic hydroxyl groups in hydroxyamines and hydroxyamino acids are selectively replaced by fluorine by reaction with sulfur tetrafluoride (SF_4) in liquid hydrogen fluoride solution. In contrast to the traditional methodology of fluorination with SF_4 (50–250 °C, in a high pressure reactor) this method, called fluorodehydroxylation, can usually be run at −78 °C and atmospheric pressure. This indicates a large increase in the reactivity of SF_4. The mechanism of fluorodehydroxylation involves carbocation intermediates in some instances and S_N2 mechanism in others, probably always proceeding via a $ROSF_3$ intermediate.

This paper amplifies and extends our earlier communication[1] on a novel method of organofluorine synthesis which we call *fluorodehydroxylation*. The term denotes a general method for the transformation of hydroxyamines and hydroxyamino acids into fluoroamines and fluoroamino acids, respectively. The method involves reacting sulfur tetrafluoride, SF_4, with the above substrates in liquid hydrogen fluoride solvent at low temperatures, usually at −78 °C, and at atmospheric pressure. A wide variety of alcohols containing basic nitrogen can serve as substrates. An important area of application is the synthesis of antimetabolites by employment of a particular principle in design of antimetabolites and drugs, namely, the principle of isogeometric modification of metabolites with maximal shift of electron distribution.[2]

The development of fluorodehydroxylation was motivated mainly by the lack of methods for the synthesis of fluoroamines and fluoroamino acids via fluorination of the corresponding hydroxy precursors. A large number of such hydroxy compounds are easily accessible, many of them in optically active form and with established stereochemistry. Whereas there are excellent methods available for the ROH–RF transformation for a large variety of alcohols, these methods invariably fail with substrates containing unprotected primary and secondary amines.[3] Moreover, even in cases where protection of the amine function (e.g., by phthaloylation) allows fluorination of the hydroxyl group, deprotection is rarely feasible.[4] In our search for alternative methods, sulfur tetrafluoride, SF_4, was considered, although its known limitations in transforming alcohols into RF compounds[5] suggested that a new approach would be required. The first problem was to find an appropriate solvent which satisfied several requirements: namely, it had to be (a) a solvent for SF_4; (b) nonreactive with SF_4; (c) protective against the reaction[6] between SF_4 and $-NH_2$; and (d) readily removable. Since the failure of fluorination of serine with SF_4 in liquid HF at 150 °C was already reported,[7] our first attempt in the fluorination of this compound utilized −78 °C as the reaction temperature. It is to be noted that fluorinations of organic compounds with SF_4 are usually done between 50 and 150 °C in a sealed reactor, under pressure. We obtained rapid and clean fluorination of serine in the first experiment which furnished 3-fluoroalanine (**1**). This result suggested not only that the reactivity of SF_4 is substantially increased in liquid HF solvent, but also that there was an increase in the desired selectivity favoring the fluorination of the alcoholic hydroxyl group. DL-β-Fluorophenylalanine (**2**) was also readily prepared in this way.

Results and Discussion

Encouraged by the clean fluorination of serine, we decided to study the reactivity of this system on a variety of structural types. As results in Table I illustrate, liquid HF at −78 °C not only fulfills all of the requirements stated above, but also renders the carboxyl and carbonyl functions impervious to the transformations usually observed in "traditional" SF_4 chemistry. The inertness of these functionalities provides essential selectivity.

In Table II we illustrate the variety of hydroxyamino compounds which were successfully fluorodehydroxylated.

The thiamine analogue, deoxyfluorothiamine chloride (**4**), was readily prepared as was the deoxyfluoro derivative of quinine (**5**). It appears that the latter is a single diastereoisomer from an analysis of its ^1H NMR spectrum.

Although a 6-fluoro derivative of pyridoxol has been reported,[8] no fluorodeoxy derivatives have been mentioned. We have synthesized a number of these as outlined in Scheme I. It was not possible to fluorodehydroxylate pyridoxal itself directly to the 5-deoxy-5-fluoro derivative **6**, presumably because it exists as a hemiacetal involving the 5-hydroxymethyl group. **6** was readily obtained by MnO_2 oxidation of the 5-deoxy-5-fluoropyridoxol (**7**), which in turn was syn-

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